UBC Department of Psychiatry

Research Day

Creating knowledge, caring for minds

ORAL PRESENTATIONS

Presentation #1: **"Methodological approaches to situational analysis and formative research in global mental health: a scoping review."**
Dr. Jill Murphy, Postdoctoral Research Fellow (Faculty Supervisor: Dr. Raymond Lam)

Presentation #2: **"Validation of serotonin transporter as a suitable biomarker for depression: from animal model to patient."**
Dr. Raquel Romay-Tallon, Postdoctoral Fellow (Faculty Sponsor: Dr. Hector Caruncho)

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Presentation #7: **"Piezo1 is a novel calcium entry pathway in astrocytes."**
Dr. Leigh Wicki-Stordeur, Postdoctoral Research Fellow (Faculty Sponsor: Dr. Brian MacVicar)

Presentation #8: **"Relationship between mood disorders and regional brain activity as measured by SPECT."**
Dr. Joel Fox, PGY3 psychiatry research track (Faculty Sponsor: Dr. Robert Tarzwell)

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Dr. Nicholas Weilinger, Postdoctoral Fellow (Faculty Sponsor: Dr. Brian MacVicar)

Presentation #1: **Methodological approaches to situational analysis and formative research in global mental health: a scoping review**

Presenter: Dr. Jill Murphy, Postdoctoral Research Fellow

Authors: Dr. Jill Murphy

Faculty Sponsor: Dr. Raymond Lam

Introduction: Implementation Science (IS) is recognized as essential in in global mental health (GMH) to improve availability of evidence-based practice low resource settings. Situational analyses (SA) are an essential first step to understanding the implementation context. Despite their importance, literature on methodological approaches to SAs in GMH is limited. In the first phase of the *Enhanced Measurement Based care Effectiveness of Depression (EMBED)* study we will conduct an SA to identify barriers and drivers to the implementation of enhanced measurement-based care in Shanghai, China. In this scoping review, we identify methodological approaches and best practice for SA in GMH.

Methods: We conducted a scoping review of studies detailing methodological approaches to SAs in GMH, with 22 papers included in the review. We charted the results, capturing: study context, scope, methodology, equity focus, and limitations. We then collated results based on this framework.

Results: The context and scope of studies vary from intervention to system level. Methods include pre-existing or specifically-designed SA tools, priority setting activities and qualitative methods. Though equity is a key concern in GMH it is not extensively addressed in SAs.

Conclusion: Existing studies provide a methodological road map for GMH SAs, with mixed methods providing the most thorough contextual assessment. Additional design and testing of methodologies that address equity are needed to ensure interventions and policies benefit the most vulnerable and underserved populations.

Relevance/ implications: GMH is an emerging field that seeks to fill a critical gap in mental health services in low resource settings. This study will provide guidance to GMH researchers about methodological approaches and best practices for SAs in GMH. It also identifies equity as an important gap in GMH implementation research.

Presentation #2:	**Validation of serotonin transporter as a suitable biomarker for depression: from animal model to patient**
Presenter:	Dr. Raquel Romay-Tallon, Postdoctoral Fellow
Faculty Sponsor:	Dr. Hector Caruncho

Introduction: Depression is a psychiatric disorder which affects 16% of the population. It courses with a complex variety of symptoms, and 1/3 of patients do not respond to treatments. Biomarkers are objectively measured characteristics which facilitate an accurate diagnosis.

Methods: We evaluated size and number of membrane protein clusters (MPC) in peripheral lymphocytes in patients with depression, and in a preclinical model (rodents administered with 40mg/kg of corticosterone (CORT)). Lymphocytes were isolated using Ficoll-Paque gradient, and MPC were stained using immunofluorescence.

Results: An increase in the size of MPC is seen in both the preclinical model (SERT: 13%; 5HT2A: 7%,) and human depression patients (SERT: 25%; 5HT2A: 40%). In patients, these alterations correlate with higher score in Hamilton Depression Rating Scale, and their responsiveness to treatments. In the preclinical animal model, larger MPC correlate with increased immobility in the forced swim test, indicative of depression-like behavior. No changes have been detected in number of MPC.

Conclusions: Alterations in MPC in patients and the animal model suggests that MPC could be potential biomarkers for depression.

Relevance/implications: The parallelism between the animal model and human patients may open the possibility to identify more potential biomarkers and assess more effective therapies.

Potential current or future clinical relevance of this work

Validation of SERT as a potential biomarker for depression will facilitate an accurate diagnosis. In addition, these findings will allow us to distinguish between responders and non-responders to antidepressant treatments which will help to administrate personalized and more efficient therapies.

Presentation # 3: **Metabolic and Genetic Explorations in Refractory Schizophrenia Project – chromosomal variants in 1st 25 cases**

Presenter: Dr. Robert Stowe, Clinical Professor

Authors: Robert Stowe MD, FRCPC, UCNS;[1,2]; Monica Hrynchak, MD, FRCPC, FCCMG;[3] Agata Minor, PhD, DABMGG;[3] Christine Tyson, PhD, FCCMG;[4] Prescilla Carrion, MSc, CGC, CCGC;[1] Ashley DeGraaf MSc, CGC;[1] Pedram Laghaei, BSc; [1] Olga Leonova, MD, PhD;[1] Mahesh Menon, PhD;[1] Ivan Torres, PhD;[1] Jennifer Li, MD, PhD;[1] Harish Neelakant, MB, FRCPC;[1] Veerle Willaeys, MD; Randall White MD, FRCPC;[1] Clara Westwell-Roper, MD, PhD;[1] Clare Beasley, PhD; [1] William Honer, MD, FRCPC.[1]

Introduction: Chromosomal copy number variants (CNVs) are the most significant genetic contributors to schizophrenia risk. CNV data on the first 25 MAGERs research project patients with treatment-resistant psychosis (TRP) are presented.

Methods: Affymetrix Cytoscan HD, a high resolution SNP chromosomal microarray (CMA), identified CNVs containing ≥ 25 probes which were curated for reliability and annotated based on the frequency in the Database of Genomic Variants (DGV), ClinGen and DECIPHER overlap, gene content, and database/literature review.

Results: Using ACMG clinical guidelines, CNVs were clinically reported in 7 patients. Two likely pathogenic duplications and associated candidate genes were identified at 3p26.3 (CHL1) and 22q11.23 (SMARCB1, BCR, and SNRPD3). Nine variants of uncertain significance were reported: two deletions, at 1p11.2-p12.2 (NOTCH2) and at 22q11.21 (PRODH and DGCR2); a triplication at 6p21.2 (MDGA1); and six duplications, one each at 6q22.2-q22.31 (SLC35F1), 15q13.3 (CHRNA7), 15q21.3 (CGNL1), 22q11.2 (TOP3B), and two at Xp22.33 (SHOX, CSF2RA). With size filters removed, additional rare CNVs were identified, implicating novel as well as established schizophrenia risk genes involved in synaptic and immune function.

Conclusion: The diagnostic yield of CMA in TRP is significant, particularly when smaller variants are considered

Relevance/implications: CMA should be considered as a diagnostic modality in TRP cases.

Presentation #7: **Piezo1 is a novel calcium entry pathway in astrocytes**

Presenter: Dr. Leigh Wicki-Stordeur, Postdoctoral Research Fellow

Authors: Wicki-Stordeur LE, Ko RW, Weilinger NL, MacVicar BA

Faculty Sponsor: Dr. Brian MacVicar

Astrocytes are critical players in the regulation and support of various brain functions, including neuronal activity, synaptic plasticity and blood flow. While electrically unexcitable, the intracellular calcium levels within astrocytes show dramatic fluctuations in 'wave' and 'spark'-like patterns, which are believed to modify astrocyte function. Our lab previously demonstrated that calcium sparks within the fine processes of astrocytes were largely dependent on calcium influx from the extracellular space, rather than release from internal stores; however, the route of this calcium entry was not identified. Here we uncover a novel calcium entry mechanism in astrocytes. We show that Piezo1, a mechanosensitive cation channel, is expressed in astrocytes, both in primary culture and within the brain. Piezo1 expression decreases with age, and rebounds in astrocytes following tissue damage. Using pharmacological and genetic manipulations of Piezo1 function, we demonstrate that this channel contributes to astrocyte calcium sparks. Piezo1 activation also increases release of the gliotransmitter ATP, and modulates downstream signaling networks. Our work identifies a novel player in astrocyte calcium signaling and contributes to understanding the importance of this phenomenon within the brain.

Presentation #8:	**Relationship between mood disorders and regional brain activity as measured by SPECT**
Presenter:	Dr. Joel Fox, PGY3 psychiatry research track
Faculty Sponsor:	Dr. Robert Tarzwell

Introduction: Brain activity in elevated and depressed mood has been studied with fMRI and SPECT in small samples, yielding conflicting results. We studied this relationship using a large SPECT dataset.

Methods: 4641 Patients (Amen Clinics) had a full psychiatric assessment and brain SPECT. 4063 Had unipolar and 582 had bipolar mood disorders. Region of Interest (ROI) scores were compared with depression and mania rating scales. Classification algorithms were trained to differentiate unipolar from bipolar disorder.

Results: Five machine-learning algorithms were trained to classify bipolar disorder or unipolar depression, and then compared to their ability to classify PTSD or TBI (second value in parentheses): logistic regression (AUC=0.50 versus 0.60), SVM (AUC=0.50 versus 0.54), KNN (AUC=0.50 versus 0.52), decision tree (AUC=0.50 versus 0.56), and random forest (AUC=0.50 versus 0.60). Mania scores did not correlate with any brain region. Depression scores correlated weakly with four regions ($p < 0.00039$ after Bonferroni correction).

Conclusion: Regional brain activity as measured by SPECT does not correlate with mood disorder states or traits.

Relevance and Implications: This research might resolve long-standing questions about brain activity in mood disorders. The magnitude of regional brain activity does not appear responsible for elevations or depressions of mood. If specific regions of the brain are not correlated with mood disorder states or traits, this may affect future research in neurostimulation and diagnostics, turning the focus away from identifying depressogenic or mania-inducing brain regions.

Presentation #9:	Characterising dendritic chloride entry in cytotoxic edema using fluorescence lifetime imaging
Presenter:	Dr. Nicholas Weilinger, Postdoctoral Research Fellow
Faculty Sponsor:	Dr. Brain MacVicar

Introduction: Chloride (Cl-) flux controls cell volume by altering cytosolic tonicity. As such, intracellular [Cl-]i is tightly constrained within the neuronal plasmalemma to defend cell volume, as increases in [Cl-]i has been reported as the principal driver of osmotic water entry in cellular swelling (cytotoxic edema). We are using fluorescent lifetime imaging (FLIM) to ask how subcellular [Cl-]i is influenced by excitotoxic activity to glean insights into the mechanisms of Cl- influx and edema.

Methods: Layer 4 pyramidal neurons were whole-cell patch-filled with the Cl- sensitive dye MQAE and imaged using FLIM, enabling us to map shifts in [Cl-]i and commensurate changes in dendritic volume with NMDA application (to trigger edema).

Results: Patched neurons maintained dendritic (but not somatic) [Cl-]i at baseline levels by homeostatic function of the K+/Cl- cotransporter (KCC2). Depolarisation increased [Cl-]i and was exacerbated by blocking KCC2 with furosemide. In contrast to depolarisation alone, NMDA-triggered excitotoxicity elicited massive Cl- entry upwards of 80mM from rest (~10mM) and dendritic swelling/beading. Under these conditions, localised [Cl-]i heterogeneities were observed along dendritic shafts/spines, with severe beading occurring in regions where [Cl-]i was highest.

Conclusion: We conclude that dendritic [Cl-]i is stabilised at rest in patched neurons and is overwhelmed by NMDA activation, revealing distinct Cl- microdomains that couple directly to membrane beading in edema.

Clinical Relevance: Edema is the leading cause of death in stroke victims with severe infarctions, with over 14,000 reported deaths in 2009 (in Canada, www.statcan.gc.ca). Uncovering the membrane conduit(s) of Cl- entry at the cellular level holds considerable promise to inform novel treatments of brain swelling.

POSTERS: BASIC NEUROSCINCE AND TRANSLATION RESEARCH ABSTRACTS

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Poster #1: Effect of calpain on synaptosome-associated protein of 25 kDa in human postmortem Alzheimer's disease

Presenter: Jehan Alamri

Authors: Jehan S. Alamri[1], Alfredo Ramos-Miguel[2], Alasdair M. Barr[1], William G. Honer[2]

Faculty Sponsor: Dr. William Honer

Purpose: Disruption of SNARE protein-protein interactions contributes to faster rates of cognitive decline in Alzheimer's disease (AD). One of the mechanisms possibly linking AD pathology and SNARE complex dysfunction may be calpain dysregulation. Preclinical evidence suggests that calpain can cleave synaptosome- associated protein of 25 kDa (SNAP-25), and hence interfere with SNARE complex formation. While previous studies reported overall enhanced calpain activity in AD brains, particular alterations of this enzyme at the synaptic terminals, where SNARE assembly occurs, were not addressed.

Methods: For the present pilot study, hippocampal and cortical postmortem brain samples from AD cases and sex- and age-matched controls were collected from the Rush Memory and Aging Project. We first modified a classic technique to isolate synaptosomes from archival human tissues using multiple sucrose gradients. Homogenized brain tissues were sequentially centrifuged to separate nuclei, cytosol, myelinated axons, synaptosomes and mitochondria. The purity of the extracted tissue fractions was assessed by western blotting (WB) and immunofluorescence (IF). Calpain proteolytic activity was quantified using the selective fluorogenic substrate N-Succinyl-Leu-Tyr-7-amino-4-methylcoumarin

Results: Preliminary WB and IF studies showed that the modified methodology succeeded in extracting relatively pure fractions, especially for those enriched in both synaptic terminals and soluble cytosolic proteins. Compared to controls, synaptosomal calpain activity was modestly increased in severe AD cases (27% in cortex and 26% in hippocampus, $p>0.05$), although this difference did not reach statistical significance due to the relatively small samples size required for this type of studies. In contrast, these differences were not observed in the cortical or hippocampal cytosolic extractions or the crude tissue homogenates from the same AD and control brains.

Conclusion: The results may suggest the contribution of enhanced calpain activity to presynaptic protein alterations and synaptic dysfunction in AD. Future studies will determine the specific mechanisms linking calpain activity and SNAP-25 fragmentation in AD.

Poster #2:	**Brain pericytes are mesenchymal progenitors that support cerebrovascular regeneration after stroke**
Presenters:	Louis-Philippe Bernier
Authors:	Bernier LP, Hefendehl JK, Lewis CA, Scott RW, Dissing-Olesen L, Rossi FM, Underhill TM, MacVicar BA.

Abstract: Brain pericytes of the neurovascular unit are critical for the developmental maturation of cerebral blood vessels and for the integrity of the blood-brain barrier (BBB). Pericytes are perivascular mural cells that share similarities with mesenchymal progenitors (MP), a cellular pool critical in supporting tissue regeneration. Therefore we examined what role brain pericytes play in repairing and restoring the cerebral microvasculature following stroke using a new transgenic MP reporter mouse. We show that after stroke, pericytes enter the cell cycle to support cerebrovascular regeneration in a manner similar to their role during development. Following stroke, pericytes proliferate and migrate into the infarct region where they accumulate inside a border of reactive astrocytes. The pericyte-astrocyte interface forms an angiogenic zone that progressively migrates into the ischemic core, thereby supporting a wave of tissue revascularization. Within a few weeks normal vessels with an intact BBB are found perfusing the previously ischemic cortical area. Using single-cell and population RNA sequencing, we identify transcriptional signatures of naïve pericyte subpopulations as well as a functional and transcriptional profile of activated pericytes following trauma. Brain pericytes in the adult brain represent a major progenitor population that can modify their phenotype to contribute to the regeneration of cerebral blood vessels following injury in a process that recapitulates their role in developmental vasculogenesis.

Clinical relevance: Our understanding of the recovery potential of the brain after stroke is limited. We describe here a critical role played by pericytes in post-stroke revascularization that may lead to novel therapeutic options to promote tissue recovery after stroke.

Poster #3: **A presenilin-1 mutation causes Alzheimer disease without affecting Notch signaling**

Presenter: Fang Cai

Authors: Fang Cai[1], Shuting Zhang[1], Yili Wu[1], Tahereh Bozorgmehr[2], Zhe Wang[1], Catharine Rankin[2], Beisha Tang[3] and Weihong Song[11]Townsend Family Laboratories, Department of Psychiatry, [2] Department of Psychology, The University of British Columbia, Vancouver, Canada. [3]Department of Neurology, Xiangya Hospital, Central South University, Changsha, Chi

Faculty Sponsor: Dr. Weihong Song

Alzheimer's disease (AD) is the most common neurodegenerative disorder leading to dementia. Missense mutations in Presenilin 1 (PS1), Presenilin 2 (PS2) and Amyloid β Precursor Protein (APP) cause early onset familial AD (FAD). PS1 is the catalytic core of γ-secretase complex to process APP to generate amyloid β protein (Aβ), the central component of neuritic plaques in AD brain. Pathogenic mutations in PS1 gene has been shown to contribute to AD pathogenesis via impaired processing of APP. A novel PS1 mutation has been identified in the AD patients with early onset in a Chinese family. We extensively characterized the function of the PS1mutation in mammalian cells and established a transgenic mouse strain carrying the mutation. We found that this PS1 mutation altered γ-cleavage of APP to produce Aβ and promoted AD pathogenesis in PS1/APP double transgenic mouse model. However, this mutant PSEN1 displays normal functions on Notch cleavage and Notch signaling *in vitro* and *in vivo*, sparing the impairment of Notch signaling. Serine169 in PS1 could be a critical site as a potential target for the development of novel γ-secretase modulators without affecting Notch cleavage to treat AD.

Supported by Canadian Institute of Health Research

Poster #4: **Machine learning approach for predicting specific movement of mice from cortical mesoscale activity**

Presenter: Dongsheng Xiao

Authors: Dongsheng Xiao, Brandon Forys, Rene Tandun, Anna Luo Xiao, Timothy H Murphy

Faculty Sponsor: Dr. Timothy Murphy

Understanding how neuronal activity represents behavioral parameters, sensory inputs, and cognitive functions remain a big challenge. Cortical activity contains rich information about a subject's motor intentions, sensory experiences, allocation of attention, action planning, and decision making. Our goal is to examine whether machine learning can help in understanding the linkage between cortical mesoscale activity and specific movements. We do this by using wide-field calcium imaging techniques, which offer sufficient temporal and spatial resolution, and which have enabled functional maps to be discerned in mice brains. We use Raspberry Picam's RGB sensor to capture body movements under infrared illumination. We train a deep learning model to accurately tracking and quantify body movement. Periods of movement are identified as having a position variance of body part higher than [mean+SD]. We encode the definition of movement by labeling frames, movement is encoded as 1 and non-movement is encoded as 0. To investigate specific actions, in some cases associated movement was excluded from this binary classification. Movement categorization data and calcium images are input into a fully-connected neural networks to predict movement from calcium imaging sequences prior to or during the movement code. Deep classification algorithms were able to predict specific movement from cortical mesoscale activity with about 70~90% classification accuracy, across different mice and body parts. Classifier-based feature selection revealed specific movement are associated with distinct spatiotemporal patterns of cortical calcium dynamics. These results would contribute greatly to our understanding of how motor function is encoded in the brain; it would also allow us to computationally understand patterns of activity in the neural circuitry related to observable movement. The ability to predict movement from mesoscopic cortical activity allow brain-machine interface that modulates motor output.

Poster #5: **Frequency-dependent coupling between neuronal activity and mitochondrial Ca^{2+} dynamics *in situ*.**

Presenter: Chris Groten

Faculty Sponsor: Dr. Brian MacVicar

Introduction: The interaction between brain energy metabolism and neuronal activity is essential for normal brain function. Despite this, the mechanisms by which mitochondria-the principle site of cellular energy metabolism- influence/respond to neuronal function have not been fully examined in native brain tissue. As a first step towards understanding potentially unique aspects of this relationship, we examined a role for mitochondrial Ca^{2+} dynamics in the CNS. While this property has long been associated with pathological changes in ATP/ROS production and apoptotic signalling, its significance for brain function is unclear.

Methods: To address this, I utilized two-photon microscopy and examined the relationship between action potential frequency and cytosolic Ca^{2+}/mitochondrial Ca^{2+} in neurons from cortical brain slices.

Results: Current-clamp recordings from pyramidal neurons expressing the mitochondrial Ca^{2+} reporter mitoRGECO1.0 revealed a firing frequency threshold (5 Hz) above which a long-lasting change in the Ca^{2+} content of somato-dendritic mitochondria was observed. These responses were reduced by blocking voltage-gated Ca^{2+} channels or the mitochondrial Ca^{2+} uniporter (using Ru360). Consistent with these findings, Ru360 substantially enhanced the magnitude/duration of cytosolic Ca^{2+} signals only at firing frequencies above 5 Hz.

Conclusion/Relevance: Our findings demonstrate a state-dependent interaction between neuronal activity and the primary centre of cellular energy metabolism. This activity-dependent coupling could serve to facilitate energy production during periods of the heightened brain activity.

Clinical relevance of research: My research project reveals a potentially novel mechanism by which the cellular metabolic centres in the brain- the mitochondria- respond to/sustain elevated neuronal excitability states. This property could have implications for various psychiatric or neurodegenerative disorders, in which energy demanding brain excitability states, such as gamma oscillations, are often disrupted

Poster #6: Real-time evaluation of BACE1 activity on APP β-site through a novel cell-based protein reporter

Presenter: Bruno Herculano

Faculty Sponsor: Dr Weihong Song

Introduction: Current research on Alzheimer's Disease has at its core the generation of the Amyloid-beta peptide (Aβ) through the cleavage of the Aβ Precursor Protein (APP) by β-secretase (BACE1), though the dynamics of this cleavage are not yet completely understood. We developed a novel cell-based approach that mimics cleavage of APP by BACE1 that could be utilized for real-time assessment of BACE1 activity.

Methods:

We have generated a construct (ASGβ) containing the β-site of APP and reporters. The coding sequences for ASGβ and BACE1 were transfected into HEK cells, and selection was carried out in order to generate a stable cell line.

Results:

ASGβ is stably expressed at a high level upon transfection. Its cleavage by BACE1 causes the release of reporters into the medium and generates an intracellular fragment which can be used to confirm results obtained. Specificity of cleavage was confirmed through the use of BACE1 inhibitors.

Conclusions:

ASGβ can be specifically cleaved by BACE1, and its cleavage products can be used to estimate intracellular BACE1 activity.

Relevance:

Currently available methods for assaying BACE1 activity rely on in vitro assays, limiting their usefulness. ASGβ provides a more easily observable method to evaluate BACE1 activity in living cells.

Future relevance:

Use of ASGβ allows for specific real-time evaluation of BACE1 activity, which potentially makes it a useful

Poster #7: Alterations in fractalkine signaling and microglia in bipolar disorder.

Presenter: Sarah Hill

Faculty Sponsor: Dr. Clare Beasley

Introduction: While the pathophysiology underlying bipolar disorder (BD) has not yet been clearly established, evidence suggests that alterations in immune function may contribute. However, the degree to which immune activation impacts brain function remains to be determined. Microglia, the brain's resident immune cells, mount the neuro-immune response and are also critical in shaping synaptic connectivity. We previously identified decreased density of activated microglia in BD and hypothesize that reduced microglial activation may be mediated by alterations in fractalkine signaling.

Methods: Levels of the fractalkine receptor CX3CR1 and the fractalkine modulator ADAM10 were quantified in postmortem brain in BD, schizophrenia, and controls by immunoblotting. Correlations between CX3CR1, ADAM10, microglial measures, and additional immune and synaptic proteins were examined.

Results: CX3CR1 protein expression was lower in BD relative to controls, although only at the trend level. CX3CR1 correlated with density of activated microglia and levels of the synaptic protein SNAP25.

Conclusion: Our results suggest that fractalkine signaling contributes to microglial activation and modification of synaptic connectivity in BD, and add to evidence for immune dysfunction in this disorder.

Impact: Further investigation of mechanisms underlying immune dysregulation in BD is critical for informing future therapeutic interventions targeting the immune system in this disorder.

Poster #8: **Measuring glutamate transmission in Huntington disease using iGluSnFr, an optogenetic probe**

Presenter: Ellen Koch

Faculty Sponsor: Dr. Lynn Raymond

Introduction: Aberrant glutamate transmission is associated with many neurological disorders, including Huntington's Disease (HD), an inherited disorder that causes substantial degeneration of striatum, cortex, and other regions. In a transgenic mouse model of HD, cortico-striatal glutamate release was shown to be increased at 1 month of age and decreased at 12 months, and NMDA receptor signalling is altered in HD. However, little is known about alterations in modulation of cortical glutamate release onto striatal neurons in HD.

Methods: The iGluSnFR is an optogenetic probe that can be used to image glutamate dynamics in real-time. To study modulation of glutamate release, we exposed acute cortical-striatal brain slices to pharmacological and physiological manipulations expected to decrease cortical glutamate release onto striatal neurons.

Results/Conclusions: Activation of presynaptic Group II mGluRs, $GABA_B$, and CB1 receptors, as well as low calcium conditions all resulted in a decrease in evoked iGluSnFR responses, reflecting inhibition of glutamate release. Additionally, we demonstrated long term depression of glutamate release using a high frequency stimulation protocol.

Relevance/Implications: Our experiments validate iGluSnFR as an accurate tool to study modulation of glutamate release in brain slice, and will allow us to directly study mechanisms of glutamate transmission in HD.

This work contributes to our understanding of presynaptic contributors to early changes in glutamate transmission that ultimately lead to HD pathology. This will give us a better understanding of the disease pathogenesis and may lead us to potential therapeutic targets.

Poster #9: **The effects of SDC3 and FGFRL1 on neurodegeneration in Alzheimer's disease (AD) and Parkinson's disease (PD)**

Presenter: Juelu Wang

Faculty Sponsor: Dr. Weihong Song

Introduction: Neuritic plaques, the pathological hallmark of AD, are formed by extracellularly aggregated amyloid β protein, cleaved from amyloid β precursor protein (APP). PD is featured by intracellular Lewy bodies, primarily consisted of aggregated alpha-synuclein protein, encoded by SNCA gene. Extensive neuronal loss in AD and PD are characterized by basal forebrain cholinergic dystrophy and nigrostrital dopaminergic deficiency, respectively.

Methods: Cholinergic SN56 cells and dopaminergic MN9D cells were stably overexpressed with human wildtype/ mutant APP and SNCA. After performing whole genome expression profiling, differential gene expression was analysed in APP- and SNCA- related stable cells, separately.

Results: SDC3 and FGFRL1 were identified as differentially expressed genes in APP- and SNCA-related stable cells, respectively. In APP_{SWE} knock-in mice, SDC3 protein was more abundantly expressed in medium septal than substantial nigra. The expression of FGFRL1 protein was upregulated in dopaminergic but not cholinergic neurons in Prnp-$SNCA_{A53T}$ transgenic mice. In H_2O_2 treatment, knockdown of SDC3 showed protective effects in SN56-APP_{SWE} cells, while knockdown of FGFRL1 in SNCA-related stable cells only rescued cell death of MN9D-$SNCA_{A53T}$ cells.

Conclusion and Relevance: Differential expression of SDC3 and FGFRL1 in cholinergic and dopaminergic neurons may mediate the selective neurodegeneration in APP_{SWE}-associated AD and $SNCA_{A53T}$-associated PD. The data may help to find novel targets for alleviating neurodegeneration in these two disorders.

Poster #10: Assessing motor learning within the mouse home-cage: an open-source system for the study of rodent models of disease

Presenter: Cameron L. Woodward

Faculty Sponsor: Dr. Lynn Raymond

Introduction: Behavioural testing of genetically modified mice is an important step in determining the validity of these animals as models of disease and assessing the effects of potential therapeutics. To improve both the throughput and reproducibility of this testing, there has been an increase in the use of automated systems that assess behavioural phenotypes of mice within their own home-cage. These allow for the 24-hour testing and monitoring of group-housed mice. However, current commercially available systems are expensive and limited in their ability to test certain behaviours relevant to the study of neurological disorders, such as motor skill learning and fine motor control.

Methods: We have developed an open-source system to assess forelimb motor learning, reversal learning and kinematic measures of motor control within the mouse home-cage. Animals learn to pull a metal lever to a defined range over several weeks of continuous, self-directed testing, and high-resolution lever position analysis as well as video recording allows for automated assessment of learning and behaviour.

Results: We previously found several motor learning and control deficits in the YAC128 model of Huntington disease (HD) at an early stage of disease progression using this system. Current work has focused on refining the testing methodology and hardware of the system, and the development of new software applications.

Relevance: This platform should prove useful for preclinical drug trials toward improved treatments in HD and other neurodegenerative disorders.

Poster #11: Cleavage of potassium channel Kv2.1 by BACE2 reduces neuronal apoptosis

Presenter: Yun Zhang

Faculty Sponsor: Dr. Weihong Song

Abstract: Potassium channel Kv2.1 regulates potassium current in cortical neurons and potassium efflux is necessary for cell apoptosis. As a major component of delayed rectifier current potassium channels, Kv2.1 forms clusters in the membrane of hippocampal neurons. BACE2 is an aspartyl protease to cleave APP to prevent the generation of Aβ, a central component of neuritic plaques in Alzheimer's brain. We now identified Kv2.1 as a novel substrate of BACE2. We found that BACE2 cleaved Kv2.1 at Thr376, Ala717, and Ser769 sites and disrupted Kv2.1 clustering on cell membrane, resulting in decreased I_k of Kv2.1 and a hyperpolarizing shift in primary neurons. Furthermore, we discovered that the BACE2-cleaved Kv2.1forms, Kv2.1-1-375, Kv2.1-1-716, and Kv2.1-1-768, depressed the delayed rectifier I_k surge and reduced neuronal apoptosis. Our study suggests that BACE2 plays a neuroprotective role by cleavage of Kv2.1 to prevent the outward potassium currents, a potential new target for Alzheimer's treatment.

Potential clinical relevance:

This study provides novel insights into BACE2's role in neurodegeneration and its pharmaceutical potential for development of new drugs for Alzheimer's disease.

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Poster #12. Formaldehyde Induces Diabetes-related Cognitive Dysfunction

Presenter: Yun Zhang

Faculty Sponsor: Dr. Weihong Song

Abstract: Patients suffering from type 2 diabetes mellitus (T2DM) often experience a significant decline in cognitive function. Hyperglycemia is one of the most prominent characteristics of diabetes, but how glycemic state contributes to cognitive dysfunction in T2DM remains elusive. Mitochondrial aldehyde dehydrogenase (ALDH2) is the major enzyme responsible for oxidizing FA and is ubiquitously expressed to promptly metabolize excess FA. Here, we report that T2MD patients with mutations in *ALDH2* gene had higher levels of FA associated with more severe dementia. Ablation of *ALDH2* gene expression induced abnormally high levels of FA, leading to hyperglycemia and cognitive impairments in mice. In addition, we found that excess FA interacts with insulin and impairs insulin signaling pathway, which contributes to memory decline in diabetic rodents. Reduction of FA by transgenic overexpression of hALDH2 attenuates hyperglycemia and alleviates cognitive deficits in different diabetic mouse models. These findings indicate the deleterious role of excess FA in mediating diabetic-related dementia. Targeting FA and its metabolizing enzyme ALDH2 may be a promising approach for preventing and treating dementia in diabetics.

Potential clinical relevance:

In this study, we found that FA accumulation facilitates cognitive deficits during diabetes, suggesting that reduction of FA expression may be a promising drug target for preventing and/or reversing diabetic-related dementia.

POSTER PRESENTATIONS TRANSLATIONAL AND CLINICAL RESEARCH

Poster #1: **Self-Reported Cognitive Dysfunction in Patients with Major Depressive Disorder Treated with Desvenlafaxine: Relationship to Work Functioning**

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POSTER PRESENTATIONS ABSTRACTS CLINICAL SCIENCE

Poster #1: **Self-Reported Cognitive Dysfunction in Patients with Major Depressive Disorder Treated with Desvenlafaxine: Relationship to Work Functioning**

Presenter: Esther Alonso-Prieto, PhD, Research Coordinator

Faculty Sponsor: Dr. Raymond Lam

Background: MDD patients often report that cognitive difficulties such as memory problems or lack of concentration interfere with their work functioning. These difficulties could be interpreted as reflecting underlying neuropsychological problems. However, it is well established that patients' cognitive complaints are associated with the magnitude of their depressive symptomatology rather than their performance in neuropsychological batteries. Our lack of understanding of the relation between subjective and objective measures of cognition questions whether self-reported cognitive complaints provide information useful to assess MDD impact on work ability. We performed a secondary analysis to examine the association between self-reported cognitive complaints and work functioning as well as between objective and subjective cognitive impairments in employed patients with MDD treated with desvenlafaxine.

Methods: 36 adult outpatients with MDD (≥ 23 on the Montgomery Asberg Depression Rating Scale, MADRS) completed subjective (British Columbia – Cognitive Complaints Inventory, BC-CCI) and objective (Central Nervous System – Vital Signs, CNS-VS) cognitive assessments as well as work functioning scales (Lam Employment Absence and Productivity Scale, LEAPS and Health and Work Performance Questionnaire, HPQ) before and after 8 weeks of open-label treatment with flexibly-dosed desvenlafaxine (50-100 mg/day). Multiple regression analyses was used to assess the relationship between subjective cognitive measures and work functioning scales. Pearson's correlation analysis was used to determine associations between subjective and objective cognitive impairments.

Results: Patients showed significant improvements in clinical, neurocognitive and work functioning measures following treatment with desvenlafaxine. A predictive association was found between the subjective cognitive measure and the work functioning scale. Moreover, pre-treatment to post-treatment changes in objective and subjective cognitive assessments were correlated with each other.

Conclusions: These results indicate that self-reported questionnaires can provide an accurate method to evaluate the impact of MDD on occupational capabilities and monitor changes in cognitive functioning during antidepressant treatment.

Clinical Relevance: Based on these findings, physicians may use self-reported questionnaires to assess the possible contribution of cognitive difficulties to functional disability, to monitor changes in cognitive symptoms and adjust treatment reliably.

Poster #2: **Pain, substance use disorder and daily functioning among individuals with concurrent disorders**

Presenter: Cindy Chang, Research Assistant

Faculty Sponsor: Dr. Christian Schütz

Introduction: Data on the association between continued pain and substance use have been inconsistent. Before further studying pain as a potential factor in motivating drug use, we decided to describe the frequency, characteristics, impact, and treatment of pain in a population with complex concurrent disorder.

Methods: Inpatients (n = 58, 20 F) at a tertiary treatment centre for concurrent disorder completed self-report questionnaires regarding past substance use and any acute or chronic pain they may have experienced. Clinical charts were reviewed to record their medical diagnoses.

Results: 46% of all clients reported experiencing pain for most days during the last six months or longer. Most clients (86%) reported that the pain was severe enough to interfere with daily activities, and 71% indicated that they had taken non-prescribed drugs for the pain. Based on chart reviews, only 26% of all recruited clients has been diagnosed with clinical pain.

Conclusion: Despite the prevalence of pain amongst clients at the BCMHA and its association with functional impairment, it may not be adequately covered by health practitioners when assessing and diagnosing patients.

Implications: Pain is a contributor to drug abuse, making it important to further study the its relationship with drug use. Clinicians need to consider pain when treating patients with concurrent disorders.

Potential Current or Future Clinical Relevance: Timely and appropriate pain treatment may be crucial in order to prevent the development of substance-use disorders. Further, addiction treatment programs need to develop comprehensive and structured pain management programs. A drug abuse history should not promote the clinical misattribution of pain complaints to the addictive disorder.

Poster #3: **Risk factors for Hippocampal Perivascular Space Dilation in Marginally-**

Presenter: Alex Cheng, Graduate Student

Faculty Sponsor: Dr. William Panenka

Residents of single-room occupancy hotels in Vancouver's Downtown East-side represent a marginalized population with a high rate of viral infection, drug addiction, and mental illness. Striking morphological changes in the hippocampus, in the form of large hippocampal cavities, were found on MRI scans. Etiology of such morphological abnormalities are unclear from the literature. We aim to describe the risk factors for the extent of burden of hippocampal cavities in this population, to ascertain if these cavities change in size over time, and the ability of these risk factors to predispose cavity volume changes. Imaging with T1 and FLAIR MRI sequences were performed with a 3T Philips scanner and all scans reviewed by a board-certified neuroradiologist. An algorithm was created by a biomedical engineer (W.S.) in conjunction with a board-certified neurologist (W.P.) for hippocampal cavity segmentation and quantification.

Inter-rater reliability was >0.95 for hippocampal cavity segmentation. Risk factors were evaluated using negative binomial regression. Prevalence of cavities at baseline was 71.6%, with a mean cavity size of 13.89 voxels ($1mm^3$). Cavities were 4.9% larger at second timepoint than baseline ($p = 0.016$) over an average of 3.8 years. On average, a one-point increase in systolic bp and FTND score (measure of smoking addiction burden) increases expected cavity volumes by 2.4% ($p = 0.002$) and 12.5% ($p = 0.009$) respectively.

Clinical Relevance:

The clinical significance of perivascular space dilation is debated in the literature. Once considered benign, they are increasingly being recognized as associated with vascular disease and cognitive decline. We report that in addition to age and hypertension, smoking may be a risk factor for their development and evolution. Whether or not dilated hippocampal spaces are independently associated with cognitive changes is unknown, and will be the focus of future studies

Poster #4: **Understanding access and use of mobile technology among patients with severe and complex concurrent disorders**

Presenter: Fiona Choi, MA, PhD, Postdoctoral Research Fellow

Faculty Sponsor: Dr. Michael Krausz

Introduction: The use of mobile devices and access to web technology are on the rise. There is also a growing availability of effective web-based mental health interventions [1] where systematic reviews of both therapist-assisted and self-directed programs have demonstrated to be more effective than no treatment at all, and equally as effective as face-to-face treatment [2]. Web-based treatments have the added value of being cost-effective as it decreases the demand on clinicians' time; allows for wider dissemination; provides flexibility for participants to work through the material at their own pace and in private; and allows for easy monitoring of progress and outcome measurements [3-4]. However, there have been few studies on the use of web-based treatments for more severe illnesses complicated by comorbidity, which would typically present to inpatient psychiatric services. Several studies have also documented low access to the internet among those with more serious mental illness [5].

Methods: We conducted brief interviews with patients at the Burnaby Centre for Mental Health & Addiction and at St. Paul's Hospital in downtown Vancouver. The survey included questions about patients' access to mobile technology, their current use of mobile health and web-based services, and their interest in integrating web-based mental health tools into their treatment plan – both inpatient and following discharge.

Results: 98 participants completed the survey (age range: 21 – 66 years, mean age: 40.6; SD=10.8, 56.5% men; 41.3% women; and 2.2% transgender). 90% indicated they had access to a computer with internet access, while 68% had access to the internet at home or through a smartphone. 85% were interested in using a computer or smartphone for health management and 18% currently used a mobile health application on a regular basis.

Conclusion: Among the patients surveyed, access to the internet was substantially higher than previously reported. A large majority also had internet-access at home or through a personal smartphone and expressed interest in integrating web-based mental health tools into their treatment plan.

Relevance/implications: Given the level of access, it is possible to integrate mobile health technologies into inpatient care, which has the potential to positively affect outcome measures, reduce rates of relapse and re-admittance, and decrease the overall costs of the treatment system.

Poster #5:	**Using calibration to assess the confidence-accuracy relationship in violence risk assessment with the START**
Presenter:	Christian Farrell, Medical Student, UBC
Authors:	Christian Farrell, Medical Student, UBC, Karen Petersen, Postdoctoral Fellow, UBC Tonia L. Nicholls, Professor, Department of Psychiatry, UBC
Faculty Sponsor:	Dr. Tonia L. Nicholls

Introduction: Formulating accurate risk assessments is essential because these decisions carry hefty economic, social, legal, and human rights consequences. Rater confidence has been identified as potentially impacting risk assessment accuracy and may also have important implications for triers of fact. The present study employed an emerging statistical technique, calibration, to assess the confidence-accuracy relationship in the risk assessment field.

Methods: Using a structured risk assessment measure, research assistants rated 106 civil psychiatric patients' levels of risk and provided confidence ratings on seven patient safety outcomes at baseline (e.g., suicide, violence). Outcomes were recorded during a six month follow up period by RAs blind to the risk assessments.

Results: Small positive correlations between the risk estimate and outcome were found for most events. Comparing correlations between low and high confidence groups, there was rarely significant differences between groups. Calibration analyses identified raters were often overconfident at higher levels of confidence, and frequently underconfident at lower levels of confidence.

Conclusion: Calibration analyses were able to provide extensive detail regarding the confidence-accuracy relationship. Findings suggest raters are frequently overconfident in their ability to make accurate assessments of patient safety.

Implications: Understanding the confidence-accuracy relationship is important as risk assessments carry significant implications for the individual and the public.

Clinical Relevance: This research highlights how calibration can be used to elucidate the confidence-accuracy relationship in clinical decision making. Calibration results could be a novel addition to risk assessment, changing the way an expert witness communicates their assessment and how judicial decision-makers evaluate and integrate risk assessments

Poster #6: **An exploration of factors influencing patient outcomes of psychiatric genetic counseling**

Presenter: Sarah Gerrard, Intern

Authors: Sarah Gerrard[1], Angela Inglis[2,3], Emily Morris[2,3], Jehannine Austin[2,3]

Faculty Sponsor: Dr. Jehannine Austin

Introduction: Understanding the factors that influence patient outcomes of psychiatric genetic counseling (GC) is important, but little data on this topic currently exists.

Methods: We conducted a retrospective review of charts from patients who attended a specialist psychiatric GC clinic between February 1, 2012 and January 31, 2017. We extracted data to explore the effects of patient and session-related variables on Genetic Counseling Outcome Scale scores (GCOS, validated instrument that measures empowerment). We used ANOVA to analyze the pre-, to one-month post-GC change in GCOS scores in relation to eleven variables.

Results: 307 charts were included in analysis. Overall, GCOS scores significantly increased after GC ($p<0.0005$). No significant differences in GCOS change scores were identified with respect to: sex, ethnicity, diagnosis, self or provider referral, type of appointment, involvement of students/observers, or personal/family history of mental illness. Significant relationships were found between GCOS change scores and mode of delivery of GC ($p=0.048$, $\square^2 = 0.02$) and primary indication for referral (understanding recurrence risk versus other, $p=0.001$, $\square 2 = 0.04$).

Conclusion: This exploratory study provides the first data on how a number of characteristics of the patient and session influence outcomes of psychiatric genetic counseling.

Clinical Implications: Our data demonstrates that patients with different sexes, ethnicities and diagnoses benefit from psychiatric genetic counseling. Understanding the patient and session-related factors that do seem to influence outcomes may allow for adjustment of service delivery strategies to promote the best possible outcomes.

Poster #7: **Investigating the effect of a psychoeducational intervention on elite athletes' preparation for sport retirement**

Presenter: Zarina Giannone, MA, PhD. Student

Faculty Sponsor: Dr. David Kealy and Dr. John Ogrodniczuk

Background: Thousands of elite athletes retire each year, yet many Canadian sport organizations are currently ill-equipped to support their athletes' transition to retirement. Indeed, some retiring athletes are at risk for developing mental health challenges, including self-concept issues, anxiety, and depression. A formal partnership with AthletesCAN, the Association of Canada's National Team Athletes, was established to promote adaptive transitions from sport.

Methods: This study investigated a psychoeducational workshop intervention on transition from elite sport. A repeated measures design was employed among athlete participants to evaluate the effect of the intervention on personal growth initiative, mental health literacy, and attitudes toward help seeking. Surveys were administered at baseline and post-intervention ($N = 75$).

Results: Preliminary analyses have revealed significant improvements in mental health literacy, help seeking behaviours and the extent to which participants believe they can access and utilize resources to assist them with sport transition. Data collection is ongoing.

Conclusion: These findings suggest that participation in a brief psychoeducational workshop intervention may improve positive health behaviours among elite athletes. Psychoeducation may serve as a preparatory support for athletes, helping them cope with the challenges associated with sport retirement by enhancing their help-seeking, knowledge of mental health, and personal agency.

Implications: Given the limited help available to elite athletes regarding sport transition, our findings provide support for an innovative, economical, and practical solution for retiring athletes and Canadian sport organizations, contributing to enhanced psychological health and adjustment post-retirement.

Poster #8: **Psychological symptoms and concurrent disorders: A comparison between individuals with and without traumatic brain injury**

Presenter: Karla Glazewski Graduate Student

Faculty Sponsor: Dr. Christian Schütz

Introduction: Individuals who have sustained a traumatic brain injury (TBI) have reported a wide range of post-injury mental health issues including substance abuse, depression, violence, and difficulties with activities of daily life (e.g., work and school). It is therefore important to investigate the differences in mental health symptoms between individuals with and without reported TBIs who have concurrent substance use and mental health disorders.

Methods: 100 patients from the Burnaby Centre for Mental Health and Addiction will be asked questions relating to their mental and physical health history (Chart Review), current mental health symptoms (SCL-90-R), and difficulties experienced from health conditions (WHODAS 2.0).

Results: Descriptive statistics and multiple ANOVAs will be conducted to compare rates of depression, violence, and difficulties with life activities for individuals with and without TBIs who have concurrent substance use and mental health disorders.

Conclusions: It is expected that rates of depression, violence, and difficulties engaging in various life activities will be significantly higher for individuals who have sustained a TBI.

Implications: By comparing specific mental health concerns affecting individuals who have sustained a TBI and have concurrent disorders, mental health care programs can improve the efficacy of treatment plans for this specific subgroup of patients.

Potential Current or Future Clinical Relevance of This Work: Program developers and mental health professionals of treatment programs can use the knowledge gained from this study in order to design and implement treatment protocols that are tailored to the unique needs of individuals who have sustained a TBI and also have concurrent substance use and mental health disorders.

Poster #9: **The Impact of the Counseling Environment on Patient outcomes of Psychiatric Genetic Counseling**

Presenter: Jacob Best, Graduate Student

Authors: Jacob Best, Angela Inglis, Emily Morris, Jehannine Austin

Faculty Sponsor: Dr. Jehannine Austin

Introduction: Understanding how different facets of the genetic counselling (GC) encounter – like physical environment - impact outcomes of GC is important yet, at present, little data exists.
Methods: We conducted a matched cohort study using naturalistic data from a specialist psychiatric GC clinic where counselling sessions are typically held a medically oriented (M-type) room, with comfortably furnished (C-type) rooms used as available. Patient outcomes (empowerment, measured with the Genetic Counseling Outcome Scale (GCOS), and self-efficacy, measured by the Illness Management Self Efficacy scale (IMSES)) are routinely tracked: pre-, and 1 month post GC. Using charts of patients seen between Feb 2012 – Dec 2017, we matched each C-type patient to two M-type controls and used T- Tests to compare changes in GCOS and IMSES scores from pre- to post-GC between the groups.

Results: 54 patients (36 M-type and 18 C-type) were included in the analysis. C-type patients had greater increases in GCOS ($t = 2.20$, $P = 0.032$, $d = 0.613$) and IMSES ($t = 2.55$, $P = 0.014$, $d = 0.717$) scores from pre-GC to post-GC, effect sizes were moderate (suggesting clinical significance).

Conclusions/ Relevance/Implications: This study suggests counselling sessions in more comfortable spaces positively impacts patient outcomes of psychiatric GC.

Current or future clinical relevance of this work: These data suggest that modifications should be considered for the M-type rooms at the psychiatric GC clinic, specifically furnishing the rooms more comfortably to ensure all patients are getting the best possible outcomes.

Poster #10: **Postpartum depression and spinal cord injury: Results from a multi-centre retrospective study**

Presenter: Amanda Lee, Graduate Student

Authors: Betty Wen, Amanda H. X Lee, Theodor Holmgren, Stacy Elliott, Shea Hocaloski, Karen Hodge, Matthias Walter, Claes Hultling, Andrei V. Krassioukov

Faculty Sponsor: Dr. Andrei Krassioukov

Introduction: Postpartum depression (PPD) affects 7.5% of Canadian mothers and is associated with negative outcomes including impaired mother-infant bonding and maternal suicide. As motherhood after spinal cord injury (SCI) may be particularly challenging, our objective was to identify the prevalence of PPD among mothers with SCI.

Methods: An international sample of mothers with SCI who had attempted breastfeeding (n=102) completed two online surveys on their breastfeeding experiences and psychological wellbeing. Clinical diagnoses of major depressive disorder (MDD) and PPD were queried as well as self-reported PPD using the Pregnancy Risk Assessment Monitoring System-3D tool.

Results: In the cervical (C1-C8), upper thoracic (T1-T6), and lower SCI (T7 and below) injury groups, the prevalence of self-reported PPD was 37% (n=11), 33% (n=4), and 25% (n=15), respectively. These values were up to 4 times greater than the prevalence of clinically diagnosed PPD. In the cervical and lower SCI groups, 75% (n=3) and 70% (n=7) of women who had MDD prior to pregnancy developed PPD.

Conclusions: Self-reported PPD is more prevalent in mothers with SCI than in the general population. There are major discrepancies in the prevalence of clinically diagnosed PPD versus self-reported PPD. A large proportion of mothers with previous MDD experience PPD.

Relevance: PPD is prevalent in women with SCI and appears to be under-diagnosed. This indicates a need for early screening and management of post-partum depressive symptoms in women with SCI.

Poster #11: **Measuring cognitive dysfunction in depression: Incorporating patient feedback to create THINC-it tutorial videos**

Presenter: Allison Lui, Work Learn Student

Faculty Sponsor: Dr. Raymond Lam

Introduction: Impairments in cognition are common in depression (Conrad et al., 2011) but current cognitive tests can be cumbersome and time-consuming (McIntyre et al., 2017). THINC-integrated tool (THINC-it) (McIntyre et al., 2017) is delivered via an electronic device, to routinely assess various cognitive functions in a quick and effective way. However, some UBC Mood Disorders Clinic patients found the provided tutorials confusing, possibly skewing their results. Moreover, the tutorials did not educate patients on what cognitive domains were being tested. Patient feedback was collected to develop educational video tutorials.

Methods: 11 patients from the UBC Mood Disorders Clinic were recruited to collect their feedback on the current tutorials provided by THINC-it. After compiling patient feedback, educational video tutorials were produced which provided audio visual instructions and educated patients on the cognitive domains tested.

Results: Currently, the video tutorials are being piloted and patient feedback will be collected. Conclusion: Patient feedback will be summarized to further refine the video tutorials.

Relevance/Implications: Patients must fully understand how to complete the cognitive tests to ensure that their results are an accurate reflection of their current cognitive state. Moreover, informational videos educate patients on why they are completing certain cognitive tests.

Potential or future clinical relevance: UBC Mood Disorders Clinic plans to use THINC-it to routinely assess cognitive changes in depression. In psychiatry, there is a push to implement measurement-based care and THINC-it can support this. Patients must know how to correctly complete the tests to provide accurate results that better informs their care plan.

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Poster #12. **Relationship between Response Network and Default Mode Network Predicts Reaction Time in Stroop Task**

Presenter: Jessica Luk, Graduate Student

Faculty Sponsor: Dr. Todd Woodward

Schizophrenia has been consistently shown to be related to disrupted functional neural networks, yet few studies to date have investigated the relationships between networks. In the current study, 13 participants with schizophrenia and 13 healthy controls completed a task-switching version of the Stroop paradigm in an fMRI scanner. Imaging data was analyzed using fMRI-constrained principal component analysis, which allows extraction of independent sources of coordinated brain activity during a task period. This revealed two networks: a primary response network (RN) and the default mode network (DMN). A hemodynamic response (HDR) curve was extracted, and was then further submitted to a principal component analysis to investigate interrelationships existing between networks. The first of two components showed the end of the RN as being negatively correlated with the peak activity of the DMN, and correlated with the beginning and end of the DMN HDR. Importantly, the first component showed a significant negative correlation with reaction time in the colour incongruent condition ($r = -0.66$, $p < 0.02$). Moreover, this correlation was seen in the healthy group only, with a significant difference in correlations between groups ($p < 0.01$). These findings underline the importance of investigating both within and between neural networks.

Identifying the connection between neural network activity and behaviour, and how this activity may be disrupted in schizophrenia, will be fundamental in future clinical treatment of the disorder. Future work will utilize these techniques to identify the nature of the disruption between networks to specify target networks for intervention.

Poster #13: **Experiences of Overdose in Patients with Severe Concurrent Disorders**

Presenter: Michelle Zhang, Work Learn Student

Faculty Sponsor: Dr. Christian Schütz

Introduction: Canada continues to face an overdose crisis, with a record 1,448 overdose deaths in British Columbia in 2017. Fentanyl use, both intentional and through the contamination of illicit drugs is a leading contributor to this public health emergency. An understanding of substance use in this vulnerable population—particularly intentional and unintentional fentanyl use—is essential to reducing rates of overdose and death from overdose.

Methods: Inpatients (n=88) at the Burnaby Centre for Mental Health and Addiction, a tertiary care centre for people with severe concurrent mental illness and substance use disorder, completed a battery of cross-sectional questionnaires related to substance use, medical history, and experience with overdose. In addition, participants' medical charts were reviewed for patient history and diagnoses.

Results: 70.5% of participants reported overdosing at least once in their lifetime, and 73.3% reported witnessing an overdose. Additional analyses will be conducted related to demographics, lifetime number of overdoses, medical intervention in overdose, substance use history, and intentional and unintentional fentanyl use.

Conclusion: Overdose is common among people with severe concurrent disorders, as is witnessing overdose. Among participants who have a history of it, many report overdosing more than once in their lifetime. Harm reduction efforts should be inclusive of people with comorbidities such as concurrent disorder, as well as with the understanding that many people who use drugs (PWUD) have existing personal experience with overdose that informs their decision-making around substance use.

Potential Current or Future Clinical Relevance: People with severe concurrent disorders are among the most vulnerable PWUD, so developing a better understanding of their experience with substance use and overdose is essential. It can inform treatment approaches and harm reduction campaigns.

Poster #14: Academic Skills in Pediatric Obsessive-Compulsive Disorder: A Preliminary Study

Presenter: Juliana Negreiros, PhD

Authors: Juliana Negreiros, PhD, RPsych, Postdoctoral Fellow, Laura Belschner, MSc, Research Coordinator, Robert R. Selles, PhD, RPsych, Postdoctoral Research Fellow, Sarah Lin, MS, Research Coordinator, S. Evelyn Stewart, MD.

Faculty Sponsor: Dr. Evelyn Stewart

Background: Obsessive-compulsive disorder (OCD) is a common yet under-recognized illness that often begins in childhood and has a significant impact on the functioning of youth and their families. Given that schooling represents a considerable portion of youth's lives and is a key contributor to their development, identifying impacts of OCD on school performance is important.

Methods: This study investigated for academic skill differences in 7-18 years old OCD-affected youth (n=25) compared to matched healthy controls (HCs; n=25), as captured via standardized testing. Analysis of variance was used to examine group effects on the outcome variables.

Results: In comparison to HCs, OCD-affected youth presented with significantly poorer performance in math calculation (p=0.029), although mean scores fell in the normative range. Thirty-six percent of the OCD group were in the *Below Average* range compared to 12% of the HCs (p=0.047). There were no significant between-group differences in word reading or spelling. Academic skills were not associated with symptom severity.

Conclusions: Findings suggest that underperformance in math may be present in a higher than expected proportion of OCD-affected youth.

Relevance: Further studies are warranted to enhance the understanding of OCD-related difficulties in school and to develop interventions to optimize OCD-affected youth's school functioning.

Poster #15: **Comparing Opium Tincture (OT) and Methadone for Medication-assisted Treatment of Opioid Use Disorder: Preliminary Results from a Randomized Double – blind Controlled Clinical Trial**

Presenter: Mohammadali Nikoo, PhD Candidate

Faculty Sponsor: Dr. Michael Krausz

Introduction: Methadone is the most commonly used medication for Medication-assisted treatment (MAT) of opioid use disorder (OUD). However, there has been a growing interest in using opium tincture (OT) for this purpose in certain parts of the world, especially Iran due to its availability, cultural acceptability and its low cost (Nikoo et al., 2016). Opium tincture (OT) is a clear, reddish-brown hydroalcoholic preparation of opium. Morphine is its active ingredient of OT. Although a few studies exist assessing the safety and efficacy of OT for treating OUD with promising results, conclusive recommendations are not possible at this point (Nikoo et al., 2016). Thus, we aimed to compare the efficacy and safety of opium tincture (OT) with methadone for MAT of OUD.

Methods: In this multi-center, double-blind, non-inferiority controlled trial, a stratified sample of 200 participants with opioid use disorder were recruited from community outreach, drop-in centers, and triangular clinics. They were randomized to receive either OT or methadone with an allocation ratio of 1:1 using a patient-centered flexible dosing strategy. Participants were followed for 12-weeks. Primary outcome was retention in treatment, which was defined as attending more than 70% of the treatment visits (21 visits or more out of 30 visits for this report) for this report. The Ethics Board of University of British Columbia and Tehran University of Medical Sciences approved the study. (clinicaltrials.gov; NCT02502175) Preliminary

Results: Preliminary results are available for 67 participants from which 44 (65.7%) remained in the treatment. Retention in treatment were 88.2% for 34 participants in the methadone arm compared to 42.4% among 33 participants in OT arm. No serious adverse event was reported in either of two arms.

Conclusion: Definite conclusion must await the availability of the results for all participants. Preliminary results failed to show that OT is as equally effective as methadone in retaining participants in MAT.

Implications: If final results yield to same conclusion, OT must not be offered to all participants and its use must become limited to certain subgroups of patients.

Clinical relevance: If shown to be effective, OT will diversify the treatment options for MAT of OUD.

Poster #16: **CanTBI: The creation of a national database and biobank for patients with traumatic brain injuries**

Presenter: Victoria Purcell, Undergraduate Student

Faculty Sponsor: Dr. William Panenka

The effects of a traumatic brain injury (TBI) often manifest in a multitude of somatic, cognitive and psychological symptoms. Current diagnostic and prognostic procedures rely on crude classification instruments and algorithms that have limited classification and predictive ability. This multi-centre longitudinal study is recruiting 450 pediatric and adult patients from seven hospitals across Canada to create a national database and biobank for traumatic brain injuries. This is the largest TBI trial in Canada. The aims are to integrate large scale clinical, imaging, and biospecimens data to refine or diagnostic and prognostic ability in TBI, examine the socioeconomic impact of TBI in Canada and to inform future interventional trials in TBI. We are currently recruiting participants who experience a TBI in the previous 24 hours from the Vancouver General Hospital Emergency department, trauma wards and ICU, along with the BC Children's hospital Emergency department and ICU. Children and adults are followed up within 2 weeks, and at 3, 6, and 12 months after injury.

Statement:

Furthering our knowledge of the predictors of recovery will allow physicians to refine their management of these patients in order to minimize costs and maximize treatment effectiveness.

Poster #17: **Motivation in Choice of Medical Specialty: Role of Geography, Age, Sex, and Other Demographic Factors**

Presenter: Habibur Rahman, Undergraduate Student

Introduction: The choice of medical specialty in is influenced by different motivational factors in medical school students, such as special interests and income opportunities. The aim of this research is to investigate how demographic factors such as age, geography, and sex contribute to motivation for specialty choice in an international cohort of medical students.

Methods: A cross-sectional online survey was administered to 1150 medical students distributed across 6 universities in 4 countries. In total, 745 students (45.9% female) completed the 37-item questionnaire. The mean age of the study participants was 23.9 years (17-45 years).

Results: Most medical students decided to pursue Internal Medicine (14.9%) and General Medicine (9.9%) as their future specializations. Surgery was a more favoured specialization in Italy. 'Special interest' and 'matching of talents' were the most important motivational factors in students choosing their medical specialty, regardless of sex, and geography.

Conclusion: The motivation in choice of medical specialties is influenced by the interplay between different demographic variables.

Relevance: It is important to understand why medical students prefer certain specialties, especially across different medical systems, so that medical education can be improved and tailored to those motivations. Taking initiative in this area could translate to improved patient care.

Clinical Relevance: Provides insight into what motivates medical students to choose their specializations and how these motivations might vary across different demographic variables. Improves understanding of how the motivations in choice of medical specialty can improve educational quality and patient care.

Poster #18: **An Exploration of Mental Health Apps for Medication Management**

Presenter: Abnashi Singh Randhawa, Undergraduate Student

Faculty Sponsor: Dr. Michael Krausz

Introduction: Medication management can be challenging for all ages especially when taking multiple medications simultaneously. Mobile apps can offer personalized support "on the go." The aim of our review is to further examine the quality of mental health apps (based on users' comments) from a previously conducted systematic review.

Methods: Two reviewers performed identical searches independently (using the search terms: medication management; medication health monitor; pill reminder; medication helper); the final list of eligible solutions was categorized. Subsequently, users' reviews of mental health-related apps were selected, reviewed and categorized into one of five categories: laudatory talk, unfavorable feedback, community, wish-list comments, clinical/therapy.

Results: Only 7 apps focused on mental health out of the 330 categorized. For these 7 apps most comments were either laudatory talk or unfavorable feedback, with wish-list comments being the next most prevalent. The most prevalent features for the mental health apps were: reminders and symptom tracking. All of these apps were free-of-charge and the average user rating was 3.6/5.

Conclusions: Mental health apps are viewed positively, but improvements are often requested. Most of these apps focused on self-treatment ranging from mental health in general to specific conditions (ADHD, Schizophrenia, Bipolar Disorder).

Relevance/Implications: This review helps define features currently lacking in mobile mental health medication management apps based on users' reviews of the apps. This can help inform future development to provide users with more effective online tools for mental health.

Poster #19: **Does Worse Insight Predict Poorer Response to CBT? Results from an International Mega-Analysis**

Presenter: Robert Selles, PhD, Postdoctoral Research Fellow

Faculty Sponsor: Dr. Evelyn Stewart

Introduction: For youth with obsessive compulsive disorder (OCD), insight is believed to be a trait associated with poor response to cognitive behavioral therapy (CBT). However, this assumption is based on limited evidence from primarily adult samples.

Methods: Data for 507 OCD-affected youth was combined from 7 international CBT studies. Primary outcomes were The Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS) including Question 11 which evaluates insight.

Results: Poor insight youth substantially improved their insight during CBT (d = 2.97; p < .001). Baseline insight did not predict treatment improvement (t = 1.10; p = .27), although poorer post-treatment insight did (t = -7.56, p < .001), suggesting youth who do not improve their insight do not respond well.

Conclusion: Contrary to prevailing consensus, insight is malleable to treatment for the majority of youth and youth with poor baseline insight are equally likely to benefit from CBT; however, youth who are not able to gain insight, or develop worse insight, over treatment will likely experience limited benefit from continuing CBT without targeted modification.

Relevance/Implications: Poor insight should not be considered a barrier to initiation of CBT; however, for youth who retain poor insight following a CBT trial, alternative approaches may be warranted.

Current/Future Clinical Relevance: The results will improve clinical decision making for youth with poor/absent insight. They also illuminate new opportunities to identify why insight may remain resistant to CBT for only some youth and what approaches may best address this issue.

Poster #20: **Increases in hippocampal metabolite concentrations with aging in treatment resistant depression and healthy controls**

Presenter: Leo Sporn

Faculty Sponsor: Dr. Fidel Vila-Rodriguez

Introduction: Magnetic resonance spectroscopy (MRS) allows for the quantification of brain metabolites in vivo, including total N-Acetyl-Aspartate (tNAA), total creatine (tCr), total choline (tCho), glutamate & glutamine (Glu+Gln=Glx), and myo-inositol (mI). Previous hippocampal MRS studies have concluded that (1) metabolite levels remain stable during healthy aging, and (2) tNAA levels are reduced in people with treatment-resistant depression (TRD). However, these studies employed relatively short repetition times (TR=1.5-2.0s), which leads to substantial T_1-weighting and inaccurate concentration measurements.

Methods: 33 people with TRD and 38 sex and age-matched controls were scanned. MRS spectra were collected from the left hippocampus (6.75mL voxel). A long TR of 4s was used to minimize T_1-weighting effects. Spectra were fit using LCModel and quantified using intra-voxel water content measurements calculated from $3DT_1$ images.

Results: No difference in any metabolite concentrations were observed between people with TRD and controls. However, in both cohorts, [tNAA], [tCr], [tCho], and [mI] were observed to increase with age ($p<0.001$).

Conclusion: Our findings, collected using TR=4s, are in contrast to a majority of previous hippocampal MRS studies.

Implications: These results may illustrate the importance of otimizing MRS acquisition parameters, to improve the sensitivity of future studies by more accurately quantifying metabolite concentrations.

Brief statement regarding relevance of this work: To our knowledge, our study is the first to quantify hippocampal metabolites in-vivo using MRS with a TR significantly longer than metabolite T_1 values. Our results do not agree with previous literature using shorter TR's, which may suggest that future in-vivo MRS studies in the brain should use longer TR's.

Poster #21: **Chromosomal microarrays implicate genes regulating dendritogenesis – potential implications for precision medicine in bipolar disorder and schizophrenia**

Presenter: Dr. Robert Stowe, Clinical Professor

Introduction: Overabundant dendritic growth and branching is a developing treatment target in eurodevelopmental (NDDs) and major psychiatric disorders (MPDs).

Methods: Microarray screening was used to detect rare and novel chromosomal copy number variants (CNVs) in patients with NDDs and MPDs. Case-based genotype-phenotype correlation was performed.

Results: Chromosomal duplications impacting genes implicated in positively regulating dendritic growth were identified. Two patients with manic psychotic episodes associated with olfactory hallucinations had CNVs predicted to upregulate thrombospondin-1 (TSP-1) signaling. Gabapentin, which has mood-stabilizing effects, is a powerful TSP-1 receptor (α2dδ-1) antagonist.

A patient with intellectual disability and refractory psychosis was found to harbor the recurrent 16p11.2 proximal chromosomal microduplication known to confer an 11-fold increase in schizophrenia risk, and associated with increased dendritic arborization attributed to duplication of the MAPK3 gene, which encodes ERK1 kinase (a positive regulator of dendritogenesis). The patient was being treated unsuccessfully with divalproex and clozapine, which significantly *upregulate* ERK1/2 kinases.

Conclusions: Upregulated thrombospondin signaling may be a mechanism of interest in mania. In patients with pathological upregulation of ERK signaling, therapy for refractory psychosis may actually worsen the underlying pathophysiology.

Relevance: Genes that regulate dendritogenesis may be therapeutic targets in some patients with NDDs and major psychiatric disorders.

Poster #22: **Internal states of low self-efficacy can induce learned nocebo effects on thermal sensation in youth**

Presenter: Ella Weik, PhD student, UBC NRSC

Faculty Sponsor: Dr. Christine Tipper and Dr. Tim Oberlander

This study investigates if internal states can influence thermal sensation after an evaluative conditioning paradigm in youth. We hypothesize that statements engaging an internal sense of high and low self-efficacy (SE) can induce learned placebo- and nocebo -like effects to thermal stimulation. Twenty-six youth described an autobiographical memory related to high, low and neutral SE statements, completed a thermal perception paradigm, the Adult Hope Scale and the State-Trait-Anxiety-Inventory. During a thermal perception paradigm participants were asked to recall the memory associated with the presented SE statement. In a conditioning phase the high/low SE statement was paired with and low/high thermal intensity. During the testing phase, the low, high and neutral SE statements were presented with moderate thermal stimuli. Participants rated their discomfort from 0-100. Moderate thermal stimuli were rated as more uncomfortable when paired with a conditioned low SE compared to the conditioned high and neutral SE state (nocebo-like effect). There was no difference between high and neutral SE state (placebo-like effect). Higher anxiety and lower hope was associated with higher nocebo-like effects. Conditioning of thermal sensations with internal self-efficacy states result in significant nocebo effects. Personality factors such as hope and anxiety influence the magnitude of the nocebo-like effect.

Clinical Relevance: Given the frequent ineffectiveness of drug treatment in managing chronic pain in children, there is a pressing need for non-pharmacological approaches. Little is known about the underlying mechanisms of placebo effects in children and youth, or how these mechanisms may be harnessed for therapeutic benefit. This study shows how conditioning and personality traits can influence placebo- and nocebo-like effects in youths.

Poster #23: **Immune-mediated comorbidities in childhood-onset OCD: A multi-site study of lifetime prevalence**

Presenter: Clara Westwell-Roper, MD PhD

Authors: Clara Westwell-Roper, MD PhD and S. Evelyn Stewart, MD, FRCPC

Faculty Sponsor: Dr. Evelyn Stewart

Objective: Despite speculation about common genetic and environmental risks, little is known about autoimmune, inflammatory, and infectious comorbidities in childhood-onset obsessive compulsive disorder (CO-OCD). This study evaluated the lifetime prevalence of immune-mediated diseases in two cohorts of patients with CO-OCD.

Methods: Medical questionnaires were completed by 1401 probands in the multi-site OCD Collaborative Genetics Association Study (OCGAS) and 214 patients attending the BC Children's Hospital Provincial OCD Program (BCCH-POP). Lifetime prevalence was compared to highest available population range and reported as a point estimate with 95% adjusted Wald interval. Worst-episode severity was assessed with the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS).

Results: OCGAS probands reported higher than expected prevalence of encephalitis or meningitis (1.4 [0.9-2.1]% vs. 0.1-0.4%, $p<0.000$, $n=1393$), scarlet fever (4.0 [3.1-5.2]% vs. 1.0-2.0%, $p<0.0001$, $n=1389$), and rheumatic fever (0.6 [0.3-1.2]% vs. 0.1-0.2, $p<0.0001$, $n=1390$). A history of frequent ear/throat infections was associated with contamination/cleaning symptom severity. BCCH-POP participants reported high prevalence of Crohn's disease (1.9 [0.4-5.8]% vs. 0.5-0.1%, $p=0.008$, $n=155$), eczema (36.5 [29.4-44.3]% vs. 10-20%, $p<0.001$, $n=156$), and chronic urticaria (9.9 [5.9-16.0]% vs. 0.5-1%, $p<0.001$, $n=142$). There was no association between comorbidity and worst-episode severity.

Conclusion: These data suggest high rates of specific infectious/inflammatory comorbidities in CO-OCD.

Implications: While further multi-site studies are needed to characterize disease clusters, this work suggests directions for additional mechanistic studies and may ultimately facilitate the development of adjunctive immune-modulating therapies.

Relevance: This is the largest existing study of medical comorbidities in CO-OCD. It suggests that immune-related comorbidities previously thought to be associated only with acute-onset pediatric OCD may also be found in a "classic" OCD population, with implications for understanding the etiology of the disorder and for optimizing clinical assessment.