Journée du RQSHA, 22 novembre 2016 | *RQSHA Day, November 22, 2016*

Présentations orales – Oral Presentations

Présentation **Regroupement neurobiology des troubles de l'humeur, du suicide et comorbidités**

Presenter Nicolas Nunez

Supervisor Gabriella Gobbi

Title Therapeutic and clinical outcomes in bipolar depression and in treatment resistant depression.

Abstract Introduction:
According to the STAR*D study, more than 50% of patients suffer from treatment-resistant depression (TRD), since they do not respond to the first antidepressant trial (1). Authors suggest that 60% of TRD patients could be considered undiagnosed bipolar depression (BD) (2). However, very few studies have explored in details the psychopathological and therapeutic outcomes of TRD and BD patients (3).
Methods: Psychopathological features and clinical response was investigated prior to treatment (T0) and after treatment (T3) using MADRS, HAM-D17, QIDS-C16 and CGI-S in 100 TRD patients and 70 BD patients (Register of the Mood Disorder Clinic at the MUHC).
Results: TRD patients were older than BD patients (46.5±13.3 vs 39.9±14.5 p=0.003). First episode of depression in TRD appears later in life (37.6±15.3 vs 27±11.02 P<0.001) as well as their first hospitalization (40±15.0 vs 25.6±14.54 P<0.001). In addition, they show more suicidal ideations (81% vs 66% P=0.019) although less suicidal attempts compared to BD patients (23% vs 40% P=0.014). Compared to the BD group, TRD failed at least 3.6±2.6 vs 4.9± 2.4 antidepressant trials. Their Global functioning (GAF) was significantly lower compared to BD patients (55.5±8.6 vs 61.3±4.513; P<0.001). At baseline, compared to BD, TRD group evidenced higher MADRS and HAMD scores (30.8±0.7 vs 22.6±0.9 p<0.001; 18.6±0.7 vs 14.6±0.9 p<0.001 respectively). At T3, TRD group reflected a superior delta change in comparison with the BD group (p<0.001). Similar results were found when we analysed a subgroup of TRD (n=48) and BD (n=29) patients treated both with antidepressant and mood-stabilizers and/or antipsychotics. At T0, TRD group showed significantly higher baseline values on all scales (p<0.001). At T3, there was a significant decrease of depressive symptomatology of all scales (p<0.001). However, the TRD group showed a superior delta change compared to the BD group (MADRS: 14.1 vs 9.2 p=0.036; HAMD: 10.1 vs 5.0 p=0.022).
Conclusion: TRD patients exhibited distinct clinical features compared to BD and a significant greater pharmacological response compared to BD patients, when treated with combination therapies. These results suggest the importance of antipsychotic/mood stabilizer as a first-line treatment in patients with severe TRD as well as contributing evidence that TRD have distinct psychopathological features from BD even if they share some features with the bipolar spectrum.

REFERENCES
1. Kessler, R. et al .Jama, (2003). 289(23), 3095-3105. 2. Akiskal, H.S., et al. Journal of affective disorders, 2000. 59: p. S5-S30. 3. Cassano, G.B., et al. American Journal of Psychiatry, 2004. 161(7): p. 1264-1269.

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RÉSEAU QUÉBÉCOIS SUR LE SUICIDE,
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Présentation **Regroupement neurobiology des troubles de l'humeur, du suicide et comorbidités**
Presenter Jessica Di Sante
Supervisor Linda Booij
Title Méthylation de gènes liés au stress chez l'humain: étude de validation sur l'utilisation d'échantillons périphériques, et la pertinence pour la fonction cérébrale

Abstract L'environnement précoce influence l'expression génétique via la méthylation de l'ADN, un mécanisme épigénétique. L'utilisation d'échantillons périphériques est nécessaire en épigénétique puisque la méthylation de l'ADN ne peut être mesurée dans le cerveau. Cependant, la validité de l'utilisation d'échantillons biologiques pour la compréhension du fonctionnement du cerveau humain n'a pas été établie à ce jour. Notre but est de vérifier la stabilité et la validité de la méthylation de l'ADN de 2 gènes liés au stress (FKBP5 et NR3C1) au niveau de différents tissus périphériques, et la pertinence de cet indice pour le fonctionnement du cerveau. Nous comparons les niveaux de méthylation de 3 prélèvements d'un même individu, vérifions leur stabilité dans le temps, et évaluons lequel montre la plus forte association entre la méthylation et le fonctionnement fronto-limbique. 51 adultes de deux cohortes longitudinales ont été soumis à une IRM(f) combinée à une tâche de traitement d'émotions. Des échantillons biologiques périphériques ont été prélevés à 2 reprises (salive, cellules buccales, sang). Les résultats démontrent une corrélation entre la méthylation de FKBP5 au niveau de la salive et des cellules buccales, une stabilité de la méthylation de FKBP5 après 2 ans, ainsi qu'une association positive entre la méthylation de FKBP5 au niveau de la salive et des cellules buccales et la réactivité parahippocampique à des stimuli de tristesse, les cellules buccales montrant la plus forte association. Aucun de ces résultats n'a été trouvé pour le gène NR3C1. La stabilité inter-tissu et temporelle de la méthylation pourrait dépendre du gène étudié.

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Présentation **Regroupement Adversité précoce, régulation émotionnelle-comportementale et psychopathologie**
Presenters Jeffrey Henry
Supervisor Michel Boivin
Title Le développement des comportements d'insensibilité: étiologie génétique et environnementale au cours de l'enfance

Abstract Les comportements d'insensibilité (CI) chez l'enfant et l'adolescent – incluant l'absence d'empathie et de culpabilité, ainsi que l'expression superficielle des émotions – sont étroitement associés à l'abus de substances et à l'impulsivité. L'état actuel des connaissances indique que des facteurs génétiques sont largement responsables de la stabilité des CI au cours de l'adolescence. Néanmoins, l'étiologie génétique-environnementale de la stabilité des CI n'a jamais été étudiée au cours de l'enfance. L'objectif de la présente étude était d'étudier l'étiologie génétique et environnementale des CI entre les âges de 7, 9-10 et 12 ans. L'étude s'appuyait sur des données prospectives recueillies auprès d'un échantillon populationnel de 662 paires de jumeaux (Étude des Jumeaux Nouveau-nés du Québec; ÉJNQ). Les CI ont été évalués par des professeurs. Deux approches statistiques ont été adoptées – une première s'appuyant sur la décomposition de Cholesky des évaluations répétées d'insensibilité, et une deuxième reposant sur un modèle de courbe de croissance latente dérivé desdites évaluations répétées. Les résultats de la décomposition de Cholesky ont révélé que des contributions génétiques sont apparentes dès l'âge de 7 ans, et qu'elles persistent jusqu'à l'âge de 12 ans. Néanmoins, des contributions génétiques spécifiques ont également été observées à 9-10 et à 12 ans. Les contributions propres à

l'environnement étaient spécifiques à chaque âge. Les résultats du modèle de courbe de croissance latente suggèrent que des facteurs génétiques expliquent la plus grande partie des variations individuelles quant à l'intercept (niveau initial) dérivé des évaluations répétées d'insensibilité. La pente (tau de changement) d'insensibilité s'expliquait en grande partie par des facteurs propres à l'environnement. Dans leur ensemble, ces résultats suggèrent que des facteurs génétiques sont largement responsables de la stabilité des CI entre 7 et 12 ans. Bien que des facteurs génétiques initiaux à 7 ans tendent à jouer un rôle tout au long de cette période, de « nouvelles » contributions génétiques tendent à émerger à 9-10 et à 12 ans. Des contributions environnementales sont également avérées, mais la nature de ces contributions devra être clarifiée dans le cadre de futures études.

Présentation **Initiatives en sciences infirmières**

Presenters Lydia Ould-Brahim et Cezara Hanganu

Supervisor Catherine Gros

Title Helpful care for adults with suicide risk factors: The perceptions of hospitalized patients with concurrent disorders

Abstract Background: 30 - 50% of persons diagnosed with a mental illness also have a substance use problem or concurrent disorder (CD). This diagnosis is associated with increased suicide risk and presents specific challenges for frontline care providers. During psychiatric hospitalization, clients with CD have extensive contact with nursing personnel who play a significant role in their healing and recovery. However, the impact that helpful nursing care has on the health of clients with CD is unknown. Research Question: What actual and/or potential nursing interventions, attitudes, actions, and behaviours are perceived as helpful by clients with CD during psychiatric hospitalization? Methods: Qualitative-descriptive design; individual, semi-structured audio-recorded interviews with 12 inpatient adults diagnosed with CD.

Results: Responses to questions about helpful care yielded examples of both beneficial and harmful practices. Data represent 3 distinct areas of intervention: 1) promoting health and daily living within the hospital environment; 2) managing substance use in tandem with mental illness; 3) building a therapeutic relationship. Clinical implications: Data on helpful nursing emphasize the importance of relational interventions such as demonstrating respect. Helpful activities included responding promptly to requests and addressing client needs for learning and support; for example, by providing information about drug use and offering evidence-based responses to patients with addiction. The findings warrant further investigation and call for close assessment of current inpatient care practices. Conclusion: Study findings contribute to the development of knowledge regarding the care of clients with suicide risk factors, serve to inform clinical practice, and guide staff education.

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Présentations par affiche – Poster Presentations

Poster # **1**

Presenter Lise Thibodeau

Supervisor Elham Rahme

Title Development of individual, programmatic and systemic indicators of the quality of mental health care using a large health administrative database: an avenue to prevent suicide mortality

Abstract Suicide is a major public health issue in Canada. The quality of health care services, in addition to other individual and population factors, has been shown to affect suicide rates. In public managed care systems, such as those in Canada and the United Kingdom, the quality of health care is manifested at the system, program and individual levels. Suicide audits are used to assess health care services in relation to suicide mortality. Large health administrative databases are another data source used to inform population-based decisions at the system, program and individual clinical levels regarding mental health services that may affect the risk of suicide. This paper describes a project that we are conducting at the Institut national de santé publique du Québec (INSPQ) with the Quebec Integrated Chronic Disease Surveillance System (QICDSS) in collaboration with colleagues from the United Kingdom and Wales and the Norwegian Institute of Public Health. The study design describes the development of quality of care indicators at three levels and the corresponding statistical analysis strategies that we have planned. In total, we defined 15 quality of care indicators and systems and several population-level determinants, including primary care treatment and specialist care and the balance of these sectors, emergency room utilization, mental health and addiction budgets, unemployment rates and socioeconomic deprivation, among others.

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Poster # **2**
Presenter Robert Louis
Supervisor Docteur Yves Couturier, de l'Université de Sherbrooke et aussi rattaché au programme de doctorat en sciences humaines appliquées
Title Quelques pistes de réflexion pour une approche globale de prévention du suicide chez les jeunes
Abstract En mettant en commun des savoirs issus de plusieurs disciplines (Neurosciences, psychologie, psychiatrie, service social), certaines pistes apparaîssent comme dénominateur commun, en dépit des différences de genre quant aux motifs poussant les jeunes à commettre l'irréparable. Pourquoi le cerveau produit des pensées qu'on ne peut prévenir ? La dépression, jouerait-elle un rôle parfois paradoxal dans les comportements suicidaires ? Autant de questions qui feront l'objet de notre conférence dont le but est de proposer quelques pistes de réflexion pour une approche globale de prévention du suicide chez les jeunes
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Poster # **3**
Presenter Jeffrey Gross
Supervisor Gustavo Turecki
Title Variations in 5-methylcytosine and 5-hydroxymethylcytosine between human brain, blood, and saliva using oxBS and the Infinium methylationEPIC Array
Abstract Investigating 5-methylcytosine (5mC) has led to many hypotheses regarding molecular mechanism underlying human diseases and disorders. Many of these studies, however, utilize bisulfite conversion alone, which cannot distinguish 5mC from its recently-discovered oxidative product, 5-hydroxymthylcytosine (5hmC). Furthermore, previous array-based technologies do not have the necessary probes to adequately investigate both modifications simultaneously. In this manuscript, we use technical replicates of DNA from post-mortem human brain, human blood, and human saliva, in combination with oxidative bisulfite conversion and Illumina's Infinium MethylationEPIC array, to analyze 5mC and 5hmC at greater than 650,000 and 450,000 relevant loci, respectively, in the human genome. We show the presence of 5mC and 5hmC to be equally distributed across chromosomes and genomic features, while also being present in genomic regions with transcriptional regulatory properties. Our results confirm not only the efficacy of the oxidative bisulfite conversion, but also the sensitivity of the EPIC array to detect 5mC and 5hmC in all three tissue-types. Together, we present an important and cost-effective resource for future studies on these cytosine modifications.
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Poster # **4**
Presenter Corina Nagy
Supervisor Gustavo Turecki
Title Alterations to BEGAIN in Depression and Suicide
Abstract At present, little is known about Brain-enriched guanylate kinase-associated protein (BEGAIN). Previous studies in rodents have demonstrated that BEGAIN co-localizes with the post-synaptic density and based on its structure identifying it as part of the MAGUK superfamily of proteins, it is believed to be part of the PSD-95 scaffolding. Few studies have looked at its role beyond this, and no study to our knowledge, has explored a role for BEGAIN outside the central nervous system. Here we extend our previous finding on BEGAIN in the context suicide and depression, looking both centrally and peripherally, at alterations in expression associate with these pathological states. In our earlier work, we found a significant down regulation of BEGAIN in people who died by suicide showing astrocytic abnormalities. Interestingly, BEGAIN showed similar levels of expression in the same subgroup of suicide completers. Using chromatin immunoprecipitation and qRT-PCR, we examined levels DNA protein binding in the brain and gene expression levels of BEGAIN in other brain regions as well as in the periphery, of cases and controls. We found that binding of RNA polymerase II is decreases in cases, which is likely be attributable to the high levels of regional DNA methylation found in cases. Furthermore, we found variant specific expression in central and peripheral tissues, which appear to be influenced by disease state. Extending our exploration to the periphery has implicated BEGAIN in depression, particularly in males showing variant specific alterations in different tissues. These findings present a potential blood biomarker for males with depression.
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Poster # **5**
Presenter Daniel Almeida
Supervisor Gustavo Turecki
Title A novel PCR-amplicon based RRBS method
Abstract Reduced representation bisulfite sequencing (RRBS) is a widely used technique for the analysis of genome-wide methylation patterns at the level of a single nucleotide. Traditional RRBS employs restriction enzymes, such as MspI, to digest genomic DNA, followed by library construction via methyl adaptor ligation, bisulfite conversion and next generation sequencing. RRBS is ideal for the study of DNA methylation in 5'UTR's, promoter regions, and other regulatory regions with a high CpG content. There are many disadvantages associated with traditional RRBS; including, it's reliance on costly methylated adaptors, fragmentation of libraries during bisulfite conversion, labour intensity and length of the protocol, as well as a high number of duplicated reads. Here we describe a simple, PCR-amplification directed RRBS pipeline that ameliorates the need for adaptor based library construction. Briefly, our PCR-amplicon RRBS protocol involves three steps, MspI digestion, bilsulfite conversion and PCR amplification with uniquely designed primers integrating locked nucleic acid technology. Preliminary sequencing data following this method is of similar quality as that of RRBS using traditional library construction. In extension to this, our pipeline is capable of amplifying bisulfite converted gDNA from ~350 pyramidal cells captured from post-mortem samples using the Acrturus Laser Capture Microdissection System. In summary, we have developed a simple, fast and cost effective PCR-amplification directed RRBS method that has the potential to greatly accelerate high-throughput sequencing of many RRBS libraries

simultaneously. In extension to this, this method is compatible with DNA inputs extracted from as low as a few hundred cells.

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Poster # **6**
Presenter Arnaud Tanti
Supervisor Naguib Mechawar
Title Convergent epigenetic, transcriptional and morphological evidence associate child abuse with impaired myelination of the anterior cingulate cortex

Abstract Childhood abuse (CA) has devastating and long-lasting consequences on development, considerably increasing lifetime risk of negative mental health outcomes, including suicide. Yet, the neurobiological processes underlying this increase in vulnerability to psychopathology remain poorly understood.
To bridge this gap, we took advantage of a well-characterized post-mortem cohort of depressed suicides with a history of severe CA, as assessed though psychological autopsies. Using hypothesis-free approaches, we first conducted genome-wide screenings of DNA methylation and gene expression, using Reduced Representation Bisulfite Sequencing (RRBS) and RNA-Sequencing, respectively. Importantly, both data sets indicated that CA severely disrupts oligodendrocytes and myelin. Using Fluorescence-Activated Cell Sorting (FACS), we further demonstrated that part of the epigenetic reprogramming of myelin by CA selectively occurred in oligodendrocyte-lineage cells, but not neurons. Finally, the extent to which these molecular adaptations lead to structural changes was assessed using stereology and Coherent anti-Stokes Raman Scattering (CARS) microscopy, representing the first human high-throughput analysis of myelin at the level of individual axonal fibers. Our results demonstrate that CA selectively affects small diameter axons and their myelin sheaths. Altogether, our studies reveal with unprecedented resolution the impact of CA on ACC epigenomic and histopathological architectures, and unveil oligodendrocytes as a potential major substrate mediating long-term consequences of CA.

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Poster # **7**
Presenter Rixing LIN
Supervisor Gustavo Turecki
Title Small Nucleolar RNAs and Antidepressant Response
Abstract

Statement of Purpose: Major depressive disorder (MDD) is a prevalent disorder treated primarily by antidepressants. Although effective, on average 30%-40% of patients experience an inadequate response to treatment after several attempts. Thus, there is a great need to identify biomarkers associated with MDD that predict and/or mediate response to antidepressant treatment. Recent discoveries have pointed towards small non-coding RNAs (sncRNAs) as feasible biomarkers. While the majority of studies have focused on microRNAs, evidence suggests that small nucleolar RNAs (snoRNAs), which are involved in alternative splicing and chemical modifications of RNAs, may also act as novel biomarkers for antidepressant response.
Methods: A sample of 258 depressed patients were treated either with the antidepressant duloxetine (N=124) or placebo (N=134) for a period of 8 weeks. Blood samples were collected at baseline (T0) and 8 weeks into treatment (T8), and RNA sequencing was performed to detect expression changes of sncRNAs. At T8, patients were grouped into responders or non-responders to duloxetine, where responders were characterized as having a 50% reduction in the MADRS score from T0 to T8. The expression of the top snoRNAs, from responders of duloxetine, showing significant differences in their expression profiles from T0 to T8 were validated in a sub-group of patients taken from the same cohort as the small RNA sequencing. Furthermore, candidate snoRNAs were assessed in neural progenitor cells (NPCs) treated with duloxetine using qRT-PCR.
Results: Small RNA sequencing revealed SNORD43, SNORD11B, SNORD17, and SNORD99 to be significantly up-regulated in responders 8 weeks after duloxetine treatment. Further validation using a sub-group taken from the same cohort showed similar results as the small RNA sequencing. NPCs treated with duloxetine for 2 weeks also showed a significant up-regulation of all 4 candidate snoRNAs when compared to untreated controls. This is the first study profiling snoRNAs in MDD and antidepressant response, and these preliminary results suggest that the candidate snoRNAs may be good mediator biomarkers of antidepressant response.

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Poster # **8**
Presenter Yi Zhou
Supervisor Gustavo Turecki
Title Long non-coding RNAs in Depression and Suicide
Abstract

Background, Objectives, and Methods:
Early life stress can impact suicide completion in later life. To address the molecular mechanisms of this, we performed RNA-sequencing in the rostral anterior cingulate cortex (rACC) of 26 depressed suicide completers and 24 matched controls, all with detailed psychological autopsy information including for early life stress. Following this, we will use RT-qPCR to validate differentially expressed long non-coding

RNAs, a species of regulatory RNA.
Results:
A genome-wide long non-coding (lnc) RNA differential expression analysis revealed 19 lncRNAs that were differentially expressed between depressed suicide completers and controls. We are working to identify the function of select lncRNA and to determine the mechanisms underlying their regulation and how they may affect the expression other genes implicated in depression. This work highlights the importance of epigenetic factors that associate with depression and suicide, in relation to early life stress.

Authors Yi Zhou[1], Pierre-Eric Lutz[1], Raphael Poujol, and Gustavo Turecki[1]

Poster # **9**
Presenter Nuwan Hettige
Supervisor Vincenzo De Luca
Title Classification of suicide attempters in schizophrenia using sociocultural and clinical features: A machine learning approach

Abstract Background: Identifying patients at the highest risk for future suicide attempts remains a complex problem for psychiatric intervention. An increasing number of studies have suggested risk factors associated with suicide attempts among schizophrenia patients. Currently, it is unclear how to incorporate these risk variables to make clinically meaningful decisions regarding the individual risk for suicide. Classification models using machine learning offer the promise of integrating many risk variables to make predictions as to the probability of an individual patient attempting suicide.
Methods: We conducted a cross-sectional assessment on a sample of 345 participants diagnosed with schizophrenia spectrum disorders. Suicide attempters and non-attempters were identified using the Columbia Suicide Severity Rating Scale (C-SSRS) and the Beck Suicide Ideation Scale (BSS). Using two classification algorithms, lasso (least absolute shrinkage and selection operator) regression and random forest, we incorporated clinical and sociocultural risk variables to train our models.
Results: Both classification models performed similarly in correctly identifying suicide attempters and non-attempters. Our lasso regression demonstrated a mean accuracy of 66%, with a mean sensitivity of 76% and an area under the curve (AUC) of 0.71. On the other hand, our random forest model demonstrated a 65% mean accuracy, a mean sensitivity of 69% and an AUC of 0.67.
Conclusion: Machine learning algorithms offer a relatively successful method for incorporating many clinical features to predict individual risk for suicide attempts. Increased performance of these models using clinically relevant variables offers the potential to facilitate early treatment and intervention to prevent future suicide attempts.

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RÉSEAU QUÉBÉCOIS SUR LE SUICIDE, LES TROUBLES DE L'HUMEUR ET LES TROUBLES ASSOCIÉS

Poster # **10**
Presenter Angelica Torres-Berrio
Supervisor Cecilia Flores
Title Potential role of miR-218 in predicting vulnerability to depression-like behaviors across development
Abstract We recently identified the microRNA, miR-218, as repressor of the guidance cue receptor gene DCC (Deleted in colorectal cancer) and demonstrated that low miR-218, but exaggerated DCC, expression in the prefrontal cortex (PFC) are consistent traits of depression-like behaviors in humans and mice. Here, we assessed whether (1) the PFC expression pattern of miR-218 and Dcc varies across postnatal neurodevelopment, (2) miR-218 expression in blood predicts susceptibility to chronic social defeat stress (CSDS), and (3) overexpression of miR-218 in PFC prevent vulnerability to depression-like behaviors. We report first, that while miR-218 expression in PFC increases from adolescence to adulthood, Dcc expression decreases. Interestingly, mid-adolescence defines this pattern of transition. Second, miR-218 expression in blood reflects levels- of miR-218 in PFC and predicts vulnerability to stress-induced depression-like behaviors: Before CSDS exposure, susceptible mice have reduced miR-218 blood expression in comparison to controls. In contrast, resilient mice have greater miR-218 expression. After CSDS, susceptible mice continue exhibiting reduced miR-218 in blood and resilient mice reach levels observed in controls. Finally, we demonstrate that miR-218 is preferentially expressed by PFC pyramidal neurons and that miR-218 overexpression in the PFC prevents CSDS-induced social avoidance and anhedonia. PFC levels of miR-218 appear to maintain the dynamic pattern of Dcc expression throughout life. Furthermore, high baseline miR-218 expression seems to buffer deleterious effects of adverse experiences, most likely by preventing increases in Dcc expression. We propose that miR-218 expression in blood is a novel marker of vulnerability to stress and a promising target for early interventions.

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Poster # **11**
Presenter Gary G Chen
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Title Potential SAT1 lncRNA Functions in MDD and Stress
Abstract Long non-coding RNAs (lncRNAs) are well known modulators of genes expression whose levels are dynamically regulated under various conditions. The human brain is enriched with lncRNAs that show different expression profiles across cell types, such as in neurons and astrocytes. Our group has previously demonstrated that SAT1, a key regulatory enzyme in the polyamine catabolic pathway, has altered expression in subjects who were depressed and died by suicide. Although stress induced mRNA expression and enzyme activation of SAT1 can be partially explained by our previous findings implicating SNP, microRNAs and polyamine levels there are likely other mechanisms regulating SAT1 expression and

activity. Here we reveal preliminary findings of a lncRNA that may potentially target SAT1, and regulate it`s expression.. Our current data show that this lncRNA is expressed in human post-mortem brain, neural progenitor cells and HEK293 cells. The role of this lncRNA in regulating SAT1 mRNA and its splice variants expression is currently under investigation.

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Poster # **12**
Presenter Robbie Woods
Supervisor Jean-Philippe Gouin
Title A Silver Lining: The Moderating Role of Resilience Resources in Relation to Multiple ACE Exposures & Inflammation

Abstract Exposure to adverse childhood experiences (ACE) has been associated with elevated circulating inflammatory markers in adulthood. Despite the robust effect of ACE on later health outcomes, not all individuals exposed to ACE suffer from poor health. The goal of this study was to evaluate whether current resilience resources may attenuate the impact of ACE on inflammatory markers among individuals with elevated C-reactive protein (CRP) levels. Participants (N=174) completed self-report questionnaires assessing ACE exposure as well as current resilience resources, and provided blood samples for interleukin-6 (IL-6) and CRP analysis. Individuals who were exposed to multiple ACE had greater IL-6 than participants with lesser ACE exposure. However, current resilience resources significantly moderated this effect. Among individuals who reported multiple ACE, higher resilience resources was associated with lower IL-6 levels. These data suggest that resilience resources can mitigate the effects of ACE on later health outcomes.

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Poster # **14**
Presenter Sasha MacNeil
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Title Heart Rate Variability and Interpersonal Problems Predict Capitalization of Positive Affect

Abstract Capitalization of positive affect is an interpersonal process associated with greater positive emotions and less daily negative affect. According to the Circumplex model of interpersonal behaviours, interaction styles lie in a circular arrangement around two orthogonal dimensions of dominance and warmth. Using this model, individuals low on both dimensions tend to capitalize less on positive affect. Furthermore, heart rate variability (HRV), a measure of autonomic functioning, indexes a neurophysiological system supporting social engagement. The goal of this study is to examine the moderating effect of HRV on the association between interpersonal styles and daily capitalization of positive affect.
Method : 128 female undergraduates completed the Inventory of Interpersonal Problems – Circumplex Short Form at baseline. HRV was measured at rest during a laboratory session. Participants tracked their daily capitalization experiences for 14 days. Multilevel analysis examined interpersonal style and baseline HRV to predict daily capitalization of positive affect across the daily diary period.
Results : Individuals with a low nurturance and low dominance interpersonal style reported fewer capitalization experiences. There was a significant interaction between HRV and this interpersonal style,

such that the association between these interpersonal styles and lower capitalization of positive affect was attenuated among individuals with higher HRV.
Discussion: These results provide evidence for the moderating influence of HRV on the effect of interpersonal problems on daily capitalization of positive affect. Higher HRV may therefore be a protective mechanism promoting social engagement despite interpersonal impairments.

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Poster # **15**
Presenter William Affleck
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Title Cultural Conflict: Inuit Youth Suicide as a Challenge for Psychiatric Ethics
Abstract Suicide rates amongst the Canadian Inuit are at epidemic levels, ranging from 13-40 times the national average. A coroner's inquiry into this crisis recently recommend that the Mental Health Act be modified to allow healthcare workers to inform Inuit family members when a person is suicidal so that social support can be increased and traditional healing practices can be provided. While seemingly straightforward, this recommendation conflicts with standard approaches to patient confidentiality. While confidentiality is a central ethical standard in Canadian mental healthcare, it is tied into a cultural worldview and ethics that the Inuit do not share, and may impede Inuit families and communities from providing culturally appropriate and effective mental healthcare. Using a Participatory Action Research (PAR) design, this research study outlined in this presentation aims to critically re-consider the theoretical and practical implications of applying the standard approach to confidentiality in the case of Inuit suicide. The goal is to develop policy recommendations and practice changes where relevant and applicable. The knowledge produced by this study will help to improve Inuit mental healthcare, and through the PAR approach this project will help to build bridges between Canadian ethicists and researchers and the Inuit community, and help to build local research capacity within the Canadian Arctic.

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Poster # **16**
Presenter Chelsey Ju
Supervisor Gustavo Turecki
Title Differentially methylated regions may reveal biomarkers of antidepressant therapy response
Abstract Major depressive disorder (MDD) is a prevalent and severe diagnosis that affects millions of people worldwide, and deemed by the WHO to be a leading cause of disability. Antidepressant therapy (ADT) is the first-line treatment for MDD, but up to 60% of depressed patients do not respond to their first ADT exposure, and 20-30% don't respond to subsequent trials. No guidelines are available to consistently predict whether an ADT will be effective for a patient. Thus, the search for quantifiable, biological characteristics that can predict ADT response rates is an important topic of depression research. Currently, MDD has an unclear pathophysiological basis, but work by our lab, and others, has highlighted the importance of epigenetic mechanisms in the context of MDD etiology and ADT biomarkers. My project will examine differentially methylated regions as candidates for ADT response biomarkers. I will aim to identify (1) differentially methylated regions between non-responders and responders of ADT, (2) differentially expressed gene regions between non-responders and responders of ADT in relation to acquired methylation data, and (3) validate these findings in a similarly characterized cohort. Research objectives will be conducted on a large, well-established, national cohort consisting of 211 depressed patients who underwent ADT with open label escitalopram (a selective serotonin reuptake inhibitor) for 8 weeks, and

102 healthy controls. Findings from this project will contribute to a greater understanding of MDD pathophysiology, and the current therapies. If identified, epigenetic biomarkers will have large benefits for clinical application.

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Poster # **17**
Presenter Danilo De Gregorio
Supervisor Gabriella Gobbi
Title D-lisergic diethylamide (LSD) modulates dopaminergic neurons of Ventral Tegmental Area (VTA) via 5-HT1A, D2 and TAAR1 receptors

Abstract D-lysergic diethylamide (LSD) is a hallucinogen with potent psychotropic effects. The psychotropic properties of LSD have been attributed to its effects at the level of the serotonin (5-HT) system, but given the role of dopamine (DA) in psychosis, an interaction of LSD with the DA system cannot be excluded. Previous studies have demonstrated that LSD has affinity for D2 receptors, and for trace-amine associated receptor 1 (TAAR1). Thus, we examined the in-vivo effects of cumulative doses of LSD on Ventral Tegmental Area (VTA) DA neurons. Using in-vivo electrophysiology, we first studied the effects of cumulative doses of LSD (5-120 ug/kg, i.v.) on VTA DA neurons and on dorsal raphe nucleus (DRN) 5-HT neurons in male rats. Secondly, we tested the contribution of 5-HT1A, D2, and TAAR1 receptors in the mechanism of action of LSD upon VTA DA neurons by using the D2 antagonist haloperidol (50 µg/kg, i.v.), the 5-HT1A antagonist WAY-100,635 (500 µg/kg, i.v.), or the TAAR1 antagonist EPPTB (5 mg/kg, i.v.). LSD dose-dependently decreased VTA DA firing activity at doses higher (30-120 µg/kg, i.v.) than those (5-20 µg/kg, i.v.) inhibiting 5-HT neurons ($P<0.0001$). The effects of LSD on DA neurons were prevented by HALO, WAY and EPPTB, suggesting the involvement of D2, 5-HT1A and TAAR1 receptors in its mechanism of action. These results demonstrate that LSD at low doses affects the 5-HT system while at high doses modulates DA mesolimbic neuronal activity with a pleiotropic mechanism involving 5-HT1A, D2 and TAAR1 receptors.

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Poster # **18**
Presenter Warren Caldwell
Supervisor Jean-Philippe Gouin
Title The moderating role of respiratory sinus arrhythmia in the relationship between daily worry and perceived negative partner interactions

Abstract Worry and rumination are repetitive, negative cognitive processes associated with depression risk (Ehring & Watkins, 2008). Poor quality social relationships also increase depression risk (Teo, Choi, & Valenstein, 2013). While rumination is associated with negative interpersonal consequences (Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008), little is known about worry. Polyvagal theory proposes that respiratory sinus arrhythmia (RSA), the fluctuations in heart rate modulated by the vagus nerve, indexes a neurophysiological system that supports social engagement (Porges, 2003). Empirical evidence shows lower RSA moderates the association between negative affective states and spousal ratings of argumentativeness (Diamond, Hicks, & Otter-Henderson, 2011). We examined the association between daily worrying and perceptions of spousal negative social behaviours and the buffering effect of RSA. 82 heterosexual couples completed 4 diary entries/day over 6 consecutive days. Individuals recorded how much they worried and their partner's negative social beahviours (i.e. how much their partner argued with them and avoided them) in each entry and visited the lab for a 5 minute resting RSA assessment. Using hierarchical linear modeling, we found that greater daily worry is associated with partner perceptions of negative social behaviours ($b = 0.31$, $p = 0.0001$). The association is stronger when resting

RSA is low (b = -0.06, p = 0.03). Additionally, worrying more than one's average, but not greater worry overall, is associated with more negative ratings of partner's social behaviours. Likewise, RSA moderates this association.
The findings highlight the negative interpersonal consequences of worry and low RSA, which increases depression risk.

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Poster # **19**
Presenter Meghan Shaw
Supervisor Gustavo Turecki
Title The expression of myelin-related genes and proteins in the uncinate fasciculus of suicide completors with a history of child abuse

Abstract Postmortem studies involving psychiatric illnesses have recently highlighted the pathology of white matter in prefrontal brain regions. The uncinate fasciculus (UF) is a prominent frontotemporal white matter tract, consisting mostly of glial cells and myelinated axons, with putative functions relating to the intersection of memory and social-emotional processing. Atypical UF integrity has been associated with symptoms of major depressive disorder (MDD) and impulsivity, and impulsivity is a long-known factor for risk of suicide. Of interest, early life adversity (ELA) is a strong predictor of psychiatric pathology and suicide, but the effects of ELA on UF integrity, and their contribution to suicide, are unknown. We will first examine oligodendrocyte (OL) morphometry and myelin-related mRNA and protein expression using rapid-immunolabeling CNPase LCM, and correlate morphological changes in OL immunohistochemistry (IHC) with altered expression of structural components of myelin or constituents important for myelin compaction, maintenance, or differentiation. The expression of major myelin protein constituents will be measured by immunoblotting and qPCR, and will be assessed in a cohort of postmortem tissue of suicide non-abused (SNA), suicide-abused (SA), and matched sudden-death control subjects. Preliminary results suggest that the the expression of myelin-related proteins is altered in the UF of depressed suicides having suffered from ELA. In particular, myelin-related proteins MOG (myelin oligodendrocyte glycoprotein) and MBP (myelin basic protein) show significantly elevated expression in depressed suicides having suffered from ELA as compared to depressed suicides who have not experienced ELA. The proposed research will constitute the first comprehensive postmortem study of myelin and myelinating cells in depression and suicide with an emphasis on ELA.

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Poster # **20**
Presenter Gilles Maussion
Supervisor Gustavo Turecki
Title A truncated form of tropomyosin-related kinase B (TrkB) is deregulated in frontal cortex of suicide completers through molecular mechanisms involving its 3'UTR DNA sequence

Abstract TrkB-T1 is a BDNF receptor highly expressed in astrocytes. Previous studies indicate that downregulation of TrkB-T1 in frontal cortex may be involved in neurobiological processes underlying suicide.
Here we review different mechanisms involved in the expression changes of neurotrophins in a context of suicide, particularly those involving the TrkB-T1 3'UTR sequence. Using microarray approaches assessing the genome wide microRNA profile and the whole TrkB gene methylation pattern in the frontal cortex of suicide completers with low TrkB-T1 expression, significant differences were characterized. MicroRNAs Hsa-miR-185* and Hsa-miR-491-3p were upregulated in suicide completers with low expression of TrkB.T1 after correction for multiple testing. Bioinformatic analyses revealed five putative binding sites for the DiGeorge syndrome linked microRNA Hsa-miR-185*in the 3'UTR of TrkB-T1. The increase of Hsa-miR-185* in frontal cortex of suicide completers was validated and an inverse correlation between Hsa-miR-185* and TrkB-T1 expression was observed. The methylation array on the full TrkB gene has revealed five probes located in the TrkB-T1 3'UTR region and found hypermethylated in the frontal cortex of suicide completers. These results were validated for four CpGs sites spanning a 150 bp sequence by cloning and Sanger sequencing bisulfite treated DNA. Furthermore an inverse correlation between TrkB-T1 expression and methylation level at those sites was found. In vitro functional analyses confirm the role of microRNA binding and of methylation in the modulation of TrkB-T1 expression. These data suggest that TrkB-T1 3'UTR sequence may play a significant role in the important decrease of cortical TrkB-T1 expression observed among suicide completers

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Poster # **22**
Presenter Asli Buyukkurt
Supervisor Outi Mantere
Title Activity rhythms and eating behaviour in bipolar disorder

Abstract The mood disturbance in bipolar disorder (BD) is characterized by alternating symptoms of elevated or irritable mood and depressed mood. However, BD is also associated with dysregulated eating and sleep. For instance, cyclic changes in weight have been observed in bipolar patients, and are associated with metabolic disorders like obesity and diabetes. Furthermore, individuals under chronic stress or depression can experience food craving in a manner neurochemically similar to addiction. Individuals with active and remitted BD also display sleep irregularities including long sleep latency and fragmented sleep. The aim of

this short-term follow-up study was to explore the relationship between mood, eating, and sleep in BD. Based on patient interview and self-questionnaires during two in-person visits two weeks apart, information regarding eating, sleep, and mood over different time periods was obtained. Patients were outfitted with a GENEActiv Original wrist actigraphy device for continuous recording and supplied with a daily journal to record eating times for two weeks. Sleep rhythm was evaluated based on actogram observation, and eating pattern was evaluated based on journal completion. Statistical analysis revealed that current food craving but not body mass index was related to severity of depressed mood. Furthermore, participants that were categorized into an irregular eating pattern were more likely to also have an irregular sleep pattern. Thus, in these bipolar patients, current mood associated with motivation for eating, and an irregular sleep pattern associated with an irregular eating pattern.

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Poster # **23**
Presenter Elmira Ismaylova
Supervisor Linda Booij
Title Corrélats neurales du stress quotidien : étude chez les adultes en santé suivis depuis 30 ans

Abstract Niveaux élevés de stress quotidien peuvent influencer la santé mentale. Cette étude a pour but d'examiner les corrélations neurales fonctionnelles et anatomiques chez des adultes en santé. Ces associations ont été examinées chez 42 adultes en santé recrutés d'une cohorte longitudinale suivie depuis 30 ans. Ils ont passé une séance d'imagerie par résonance magnétique structurelle et fonctionnelle combinée avec une tâche de traitement des émotions, et ont rempli un questionnaire en ligne sur le stress quotidien pendant 5 jours consécutifs. Les scores moyens de 5 jours ont été utilisés pour les analyses. Les contrastes émotionnels et les images de matière grise ont été obtenus à l'aide de Statistical Parametric Mapping version 12 (pFWE≤0.05). Grâce à la boîte à outils VBM12, une association négative a été trouvée entre la rumination et le volume de l'hippocampe gauche. Aussi, une tendance positive a été observée entre la rumination et la réponse frontale inférieure gauche aux stimuli émotionnels positifs. L'affect positif a été associé à une plus grande réponse frontale médiale gauche aux stimuli émotionnels négatifs et à un plus grand volume frontal médian bilatéral. Ces résultats démontrent que la sensibilité au stress quotidien chez les individus en bonne santé est associée à la structure et fonction fronto-limbiques, particulièrement dans l'hippocampe et les régions préfrontales. Compte tenu de l'implication de ces régions dans le contrôle cognitif des pensées et des émotions, nos résultats pourraient suggérer que ces structures et activations neuronales constituent des marqueurs cérébraux protecteurs contre le développement de troubles liés au

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Poster # **24**
Presenter Madelyn Barton
Supervisor Naguib Mechawar
Title The link between child maltreatment and suicide: a morphometric characterization of pyramidal cells in prefrontal cortex

Abstract It is estimated that over 30% of adult psychopathology and disrupted patterns of behaviour, especially those related to suicide, are robustly linked to childhood maltreatment (CM). A major challenge faced by CM research is to understand how long-lasting effects of early-life experiences may be biologically embedded. Animal models, such as maternal deprivation, have been crucial in our understanding of morphometric, epigenomic, and transcriptomic alterations that result from early life stress. However, few studies have investigated this question in post-mortem human brain. Here we describe a prospective study that investigates morphometric alterations in layer 5/6 pyramidal cells of the prefrontal cortex from depressed suicides that experienced CM compared to those without a history of CM and non-psychiatric controls. Globally we aim to evaluate hypothesized morphometric consequences of CM in light of detailed epigenomic and transcriptomic investigations of pyramidal cells conducted in parallel.

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Poster # **26**
Presenter Scott Bell
Supervisor Carl Ernst
Title Combining CRISPR/CAS9 and iPSCs to model Rare Neurodevelopmental Disease

Abstract The development of accurate and informative models is essential to the investigation of any disease. Rare neurodevelopmental diseases face immense challenges developing credible models, as the scarcity of subjects and the difficulty of obtaining human neural cells have limited the resources available to researchers. However, many of the challenges that have handicapped models of rare neurodevelopmental disorders have been significantly reduced due to recent advances in cell culture and genome editing. Here we present novel, optimized methodologies for modelling rare developmental diseases of the nervous system in vitro. We have developed a more rapid protocol through which primary fibroblasts can be converted to induced pluripotent stem cells (IPSCs) using a episomal vector and differentiated into neurons. The insertion of the episomal vector may be combined with the addition of a CRIPSR-Cas9 plasmid to enable simultaneous genome editing and IPSCs induction. Through optimization of the purification of IPSCs and the growth factors used to induce IPSC differentiation, fibroblasts were able to be successfully converted into either electrically active cortical neurons within two months.
This methodology represents a significant decrease in the time, effort, and cost required to model rare neurodevelopmental diseases in vitro. This research represents a significant decrease in the cost, expertise

and time required to produce iPSC based models of neurodevelopmental diseases.

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Poster # **28**
Presenter Sarah Barnett-Burns
Supervisor Gustavo Turecki
Title Depression as a Gut Feeling: The role of the gut microbiome in the link between early life stress, neuro immune dysregulation and adult depression

Abstract Mammals have evolved in the midst of a biochemical dialogue with a complex gut microbial eco-system that contains a hundred trillion bacteria and has a collective genome that is 150 times larger than our own. Yet, despite this ubiquity, we have only begun to understand how this 'gut microbiome' impacts our health and even our behaviour. Recent preclinical research has expanded the conventional view of these bacteria from a requisite digestive aid to an important bidirectional modulator of almost every major system in the body, including the central nervous system. This paradigm shift has led to increased interest in the gut microbiome as a factor in the etiology of major psychopathologies, such as depression.
With high rates of treatment resistance and disease recurrence, depression remains one of the leading causes of disability in Canada. It is well established that early stress and neural inflammation are risk factors in the onset of depression, and growing evidence that the gut microbiome modulates these systems. However, a direct link between the gut microbiome and depression has not been established. I will investigate if the gut microbiome is a mediating factor in the established relationship between early stress and neural inflammation in a mouse model. I will then test this association in humans using postmortem brain and intestinal tissues from depressed suicides with, or without, a history of early life stress, in order to help advance the field of gut-microbiome-brain research into the clinical arena.

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Poster # **29**
Presenter Viktoria Stoudenikina
Supervisor Johanne Renaud
Title Body image and suicidal risk: a review across the spectrum of eating disorder symptoms

Abstract Context:
Suicide, the second most common cause of mortality in youth (ages 14-25), is more prevalent in individuals with Eating Disorders (ED). EDs are often characterized by altered body image. Negative body image has been associated with suicidal acts and self-harm behavior in clinical and non-clinical ED populations. To our knowledge, no review has focused on establishing a link between suicidal risk and body image disturbance.
Objective:
We aim to examine the association between body image disturbance and risk factors for suicidal behavior in the adolescent and young adult population (13 to 25 years old), with or without eating disorders.
Methods:
We will systematically conduct a search in Medline, EMBASE and PsychINFO databases, including studies examining young individuals (ages 13-25) concerned with both body image issues and factors related to suicide. We will evaluate studies including participants with an ED, participants with disordered eating, and participants from the general population, The review will include studies conducted in male and female subjects. Factors related to suicide include history of a suicidal attempt, suicidal ideations or suicidal thought processes. The definition of body image disturbance is most broad for the purpose of this review: it includes altered weight perception and body dissatisfaction.
Results:

Our search yielded 110 manuscripts for initial screening. 59 papers screened with full text. A total of 40 articles have been retained in the review. Synthesis of quantitative evidence and qualitative analysis will be presented.
Conclusions:
Our results will help shed light on whether or not body image constitutes an important risk factor for suicide in adolescents and young adults. Furthermore, our review will determine whether body image correlates with suicidal risk equally in youth with ED compared to youth without ED. We will present potential moderating factors, such as depression, hopelessness, and impulsivity, emphasize methodological limitations and suggest new research avenues.

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