Centre intégré universitaire de santé et de services sociaux de l'Ouest-de-l'Île-de-Montréal
Québec

Douglas Institut universitaire en santé mentale / Mental Health University Institute

McGill

2017 Research Day / Journée de la recherche 2017

Douglas Institute Research Centre and McGill Department of Psychiatry

Friday, June 2nd 2017, 8:45 AM - 7:00 PM
Mardi 2 juin 2017, 8h45 - 19h00

Douglas Hall, Douglas Mental Health University Institute
Pavillon Douglas, Institut universitaire en santé mentale Douglas

8:45 Welcome, opening remarks / Accueil et mots d'ouverture

Session 1 (Chairperson / Présidente de session: Kathryn Vaillancourt)

9:00 **O1**
Large-scale analysis of sex-dependent atypical cortical thickness in autism spectrum disorder
Saashi Bedford, Min Tae M. Park, Gabriel A. Devenyi, Stephanie Tullo, Evdokia Anagnostou, Simon Baron-Cohen, Michael C. Craig, Christine Ecker, Rhoshel Lenroot, Jason P. Lerch, Michael V. Lombardo, Declan G. M. Murphy, Armin Raznahan, Amber N. V. Ruigrok, Elizabeth Smith, Susan Swedo, Margot J. Taylor, Audrey Thurm, MRC AIMS Consortium, Meng-Chuan Lai, M. Mallar Chakravarty

9:15 **O2**
Role of dorsostriatal cholinergic interneurons in habit formation and cognitive flexibility: a transdiagnostic model of eating disorders in mice
Mathieu Favier, Helena Janickova, Luc Moquin, Erika Vigneault, Alain Gratton, Marco A.M. Prado, Vania F. Prado, Salah El Mestikawy

9:30 **O3**
The role of hippocampal memory engram in mediating stress susceptibility in an animal model of depression
Brittany Zhang, A.S. Wong, V. Wong, T.P. Wong

9:45 **Datablitz**
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10:30-11:15 Coffee break and poster session / Pause-café et session d'affiches

Session 2 (Chairperson / Président de session: Justin Miron)

11:15 **O4**
Impact of night shift work on circadian clocks in police officers
Anna Koshy, Marc Cuesta, Nicolas Cermakian, Diane B. Boivin

11:30 **O5**
Convergent epigenetic, transcriptional and morphological evidence associate a history of child abuse with impaired myelination in the anterior cingulate cortex
Arnaud Tanti, Pierre-Eric Lutz, Alicja Gasecka, Sarah Barnett-Burns, John J. Kim, Yi Zhou, Gang G. Chen, Marina Wakid, Meghan Shaw, Daniel Almeida, Marc-Aurele Chay, Jennie Yang, Vanessa Larivière, Marie-Noël M'Boutchou, Léon C. van Kempen, Volodymyr Yerko, Josée Prud'homme, Maria Antonietta Davoli, Kathryn Vaillancourt, Jean-François Théroux, Alexandre Bramoullé, Tie-Yuan Zhang, Michael J. Meaney, Carl Ernst, Daniel Côté, Gustavo Turecki, Naguib Mechawar

11:45 **O6**
Psychological and psychosocial interventions for negative symptoms in psychosis: a systematic review
Danyael Lutgens, Genevieve Gariepy, Ashok Malla

12:00 **O7**
Alcohol use, depressive symptoms and the incidence of diabetes-related complications
Randa Elgendy, Sonya S. Deschênes, Rachel J. Burns, Norbert Schmitz

12:15 **O8**
Medial septum optogenetic stimulations of parvalbumin interneurons to restore spatial reference memory impairments in freely behaving J20 APP mice
Guillaume Etter, Sylvain Williams

12:30-1:30 Lunch/ Dîner

Session 3 (Chairperson / Présidente de session: Laura Kervezee)

1:30 **O9**
DRD4 Exon 3 Genotype as Predictor of Symptom Severity and Treatment Outcome in Children with ADHD: Gene-Treatment and Gene-Environment Interaction Study
Darya Naumova, Natalie Grizenko, Sarojini M. Sengupta, Ridha Joober

1:45 **O10**
The antigen-specific CD8 T-cell response is controlled by their endogenous circadian clock: implications for antibacterial and antitumoral responses
Chloe Nobis, Silke Kiessling, Geneviève Dubeau-Laramée, Nathalie Labrecque, Nicolas Cermakian

2:00 **O11**
Sociodemographic and clinical predictors between unipolar-treatment resistant depression and bipolar depression: a retrospective analysis
Nicolas Nuñez, Stefano Comai, Maykel F. Ghabrash, John Tabaka, Marie Saint-Laurent, Stephen Vida, Theodore Kolivakis, Nancy Low, Pablo Cervantes, Linda Booij, Gabriella Gobbi

2:15 **O12**
Role of neonatal ventral hippocampus neuronal activity in regulating adult behaviours in mice
Antoneta Teresa Joseph, S. K. Bhardwaj and L. K. Srivastava

2:30 **O13**
Mutations in ACTL6B cause a novel developmental disease: Molecular insights into human neurodevelopment using brain cells derived from skin
Scott Bell, Huashan Peng, Ilaria Kolobova, Walla Al-Hertani, Phillipe Campeau, Carl Ernst

2:45-3:30 Coffee break and poster session / Pause-café et session d'affiches

Session 4 (Chairperson / Présidente de session: Sherri Lee Jones)

3:30 **O14**
miR-218: a key target for the alterations in dopamine development induced by abused doses of amphetamine in adolescence
Santiago Cuesta, José Maria Restrepo-Lozano, Steven Silvestrin, Cecilia Flores

3:45 **O15**
"I needed it to get better": a qualitative investigation into the positive, transformational role of first episode psychosis
Gerald Jordan, Tovah Cowan, Ashok Malla, Srividya N. Iyer

4:00 **O16**
The Genetic Architecture of Differential Susceptibility to Adversity; a Genome-wide Approach
Shantala A Hari Dass, Lawrence M Chen, Marie Forest, Kieran J O'Donnell, Celia MT Greenwood, Michael J Meaney

4:15 **O17**
Spontaneous use of spatial memory strategies is associated with greater cortical plasticity following a virtual spatial memory intervention program in healthy older adults
Daniel Ducharme, K. Konishi, D. Sodums, L. Dahmani, L. Bherer, V. D. Bohbot

Keynote lecture / Conférence de prestige (Chairperson / Présidente de session: Sherri Lee Jones)

4:30 *Of Blue Twos and Lucky Sevens: Explorations of Synaesthesia and Insights into Slot Machine Addictions*
Mike Dixon, Professor, Psychology, Waterloo University

5:15-5:30 Award ceremony / Cérémonie de remise de prix

5:30-7:00 Wine and cheese reception / Réception vins et fromages

We wish to thank our generous sponsors / Nous remercions nos généreux commanditaires:

Poster and datablitz presentations / Présentations par affiche et en datablitz

P1 *LCM-Seq: single cell-type whole genome bisulfite sequencing and transcriptomic profiling in post-mortem brain*
Daniel Almeida, Gang Chen, Maria-Antonietta Davoli, Naguib Mechawar, Gustavo Turecki

P2 *Investigating projections from the ventral hippocampus (vHC) to the prelimbic (PL) and infralimbic (IL) cortices in the mouse*
Polina Ash, Lalit Srivastava, Sylvain Williams

P3 *Generation of a mu opioid receptor-Cre driver line*
Julie Bailly, Marie-Christine Birling, Emmanuel Darcq, Brigitte Kieffer

P4 *The impact of video game experience on hippocampal grey matter integrity*
Jessica Benady-Chorney, G. West, K. Konishi, M. Diarra, , B. Drisdelle, L. Dahmani, D. Sodums, F. Lepore, P. Jolicoeur, V. Bohbot

P5 *Mu opioid receptors in the habenula: dissecting reward and aversion in addiction*
Laura-Joy Boulos, S. Ben Hamida, E. Darcq, B.L. Kieffer

P6 *Attachment styles and their relationship to the risk of psychopathology and the use of mental health care services*
Elias Chalet, Xiangfei Meng, Alain Brunet

P7 *Maternal symptoms of depression interact with child genetic risk for ADHD in prediction of socio-emotional problems*
Lawrence M. Chen, Shantala Hari Dass, Andrée-Anne Bouvette-Turcot, Elika Garg, Thao T. T. Nguyen, Patricia P. Silveira, Josie Dioro, Michael S. Kobor, Kieran J. O'Donnell, Michael J. Meaney, MAVAN Research Team

P8 *The neural correlates of functional compensation in high performing older adults.*
Abdelhalim Elshiekh, Sricharna Rajagopal, Stamatoula Pasvanis, Elizabeth Ankudowich, Natasha Rajah

P9 *mGluR5 in amphetamine response and sensitization*
Kelly Smart, Atsuko Nagano-Saito, Michele Milella, Diana Yae Sakae, Gassan Massarweh, Pedro Rosa-Neto, Salah El Mestikawy, Marco Leyton, Chawki Benkelfat

P10 *Neuroimaging study of genetic and environmental factors in children with ADHD*
Nellie Fotopoulos, Gabriel A. Devenyi, Mallar M. Chakravarty, Sherif Karama, Natalie Grizenko, Ridha Joober.

P11 *Police officers' psychomotor performance is affected by their circadian phase*
Fernando Gonzales, Philippe Boudreau, Diane B. Boivin

P12 *Noradrenergic neurons of the locus coeruleus play a role in susceptibility to acute environmental stress.*
Chloé Guinaudie, Elsa Isingrini, Erika Vigneault, Bruno Giros

P13 *Does the timing of maternal immune activation affect neuroanatomical and behavioural outcomes in the offspring?*
Elisa Guma, Jurgen Germann, Daniel R Gallino, Mallar Chakravarty

P14 *A manual structural magnetic resonance imaging segmentation protocol of the hypothalamic-pituitary-gonadal axis*
Sherri L. Jones, Chloe Anastassiadis, Jamie Near, David P. Laplante, Suzanne King, Jens Pruessner

P15 *The effect of night shift work on the human circadian transcriptome*
Laura Kervezee, Marc Cuesta, Nicolas Cermakian, Diane B. Boivin

P16 *Physiological Characterization of a Novel Selective Melatonin MT1 Receptor Partial Agonist*
Martha G. López-Canul, Seung Hyun Min, Luca Posa, Tania Sasson, Danilo De Gregorio, Rafael Ochoa-Sanchez, Stefano Comai, Gabriella Gobbi

P17 *Treatment delays and pathways to mental health care in Youth Protection Services in Montreal*
Kathleen MacDonald, Lise Laporte, Lyne Desrosiers, Srividya Iyer

P18 *Cerebellar volume mediates the association between prenatal maternal stress and motor performance in adolescent boys: Project Ice Storm*
Kyle McKee, Xavier Navarri, Guillaume Elgbeili, David P. Laplante, Sherri L. Jones, Gabriel A. Devenyi, Mallar Chakravarty, Suzanne King

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P20 *In Vivo, MRI based microstructural parcellation of the human hippocampus*
Raihaan Patel, Christopher Steele, Sejal Patel, Jurgen Germann, Christine Tardif, M. Mallar Chakravarty

P21 *Perfectionism and daily emotion regulation and well-being: An experience sampling study*
Julie Prud'homme, David Dunkley

P22 *Amphetamine disrupts prefrontal cortex development only during a defined critical period in adolescence*
Lauren M. Reynolds, Leora Yetnikoff, Michael Wodzinski, Julia G. Epelbaum, Laura C. Lambert, Mu Yun He, Matthew Pokinko, Marie-Pierre Cossette, Andreas Arvanitogiannis, Cecilia Flores

P23 *Imbalances in human resources for health: a cross-national, multilevel study of adolescent health outcomes and disparities*
Kira E Riehm, Frank J Elgar

P24 *Symptomatic and Functional Recovery in First Episode Psychosis: Predictive Value of Early Sub-threshold Psychotic Symptoms*
Rachel Rosengard, J. Shah, A.K. Malla, R. Joober, M. Bodnar, M. Lepage

P25 *Emotional rating of pseudo-speech is influenced by the spatial location of the acoustic source*
Ignacio Spiousas, Jorge L. Armony

P26 *Cognitive load impairs conscious access to sensory inputs while sparing gist effect*
Moriah Stendel, Mathieu Landry, David Milton, Amir Raz

P27 *Exploring Cognitive Dimensions of Body Ownership*
Rémi Thériault, Mathieu Landry, Shira Mattuck, Amir Raz

P28 *miR-218 Determines Vulnerability to Depression in a DCC-dependent Manner*
Angélica Torres-Berrío, Dominique Nouel, Santiago Cuesta, Gustavo Turecki, Eric J. Nestler, Cecilia Flores

P29 *MR-based age- and sex-related effects on the striatum, globus pallidus and thalamus in healthy individuals across the adult lifespan*
Stephanie Tullo, Alyssa Salaciak, Saashi Bedford, M. Mallar Chakravarty

P30 *Cardiometabolic risk markers in first-episode psychosis and socioeconomic disadvantage*
Franz Veru, Aldanie Rho, Ridha Joober, Srividya Iyer, Ashok Malla

P31 *Waiting for Cognitive Behavioural Therapy (CBT): A Randomized Controlled Trial Evaluating the use of a Computerized CBT Program for Outpatients on a Waitlist in a University CBT Unit*
Rosanne Villemaire-Krajden, Gail Myhr

P32 *Specificity of Neural Responses to Processing Emotional Acoustic Information: An fMRI-Adaptation Study*
Jocelyne C. Whitehead, Jorge L. Armony

P33 *Assessing predictors of perceived utility of biological testing among parents of a child with autism*
Afiqah Yusuf, Iskra Peltekova, Ruth Bruno, Jennifer Frei, Mayada Elsabbagh

P34 *Long Non-Coding RNAs in Depression and Suicide*
Yi (Daniel) Zhou, Pierre-Eric Lutz, Gustavo Turecki

Organizing committee / Comité organisateur:

The Douglas Student Committee for Academic Life / Le Comité étudiant pour la vie académique au Douglas: Richard Boyce, Weam Fageera, Lourdes Fernandez de Cossio Gomez, Elisa Guma, Daniel Hoops, Sherri Lee Jones, Kathleen MacDonald, Carolina Makowski, Justin Miron, Kathryn Vaillancourt, Yi (Daniel) Zhou and/et Nicolas Cermakian (Directeur des affaires académiques, Centre de recherche de l'institut Douglas)

O1

Abstract title: Large-scale analysis of sex-dependent atypical cortical thickness in autism spectrum disorder

Authors: Saashi Bedford[1,2], Min Tae M. Park[2,3], Gabriel A. Devenyi[2,15], Stephanie Tullo[1,2], Evdokia Anagnostou[4], Simon Baron-Cohen[5], Michael C. Craig[6], Christine Ecker[6,7], Rhoshel Lenroot[8], Jason P. Lerch[9], Michael V. Lombardo[5,10], Declan G. M. Murphy[6], Armin Raznahan[11], Amber N. V. Ruigrok[5], Elizabeth Smith[11], Susan Swedo[12], Margot J. Taylor[9], Audrey Thurm[12], MRC AIMS Consortium, Meng-Chuan Lai[5,9,13,14], M. Mallar Chakravarty[1,2,15,16]

Affiliation(s): 1. Integrated Program in Neuroscience, McGill University 2. Cerebral Imaging Centre, Douglas Mental Health University Institute 3.Schulich School of Medicine and Dentistry, Western University 4. Holland Bloorview Research Institute 5. Autism Research Centre, Department of Psychiatry, University of Cambridge 6. Institute of Psychiatry, Psychology and Neuroscience, King's College London 7. Department of Child and Adolescent Psychiatry, Psychosomatics, and Psychotherapy, Goethe University 8. Department of Psychiatry, University of New South Wales 9. The Hospital for Sick Children 10.Department of Psychology and Center for Applied Neuroscience, University of Cyprus 11.Child Psychiatry Branch, National Institute of Mental Health 12. Section on Behavioral Pediatrics, National Institute of Mental Health 13. Centre for Addiction and Mental Health 14. Department of Psychiatry, University of Toronto 15. Department of Psychiatry, McGill University 16. Department of Biological and Biomedical Engineering, McGill University

Background: Sex differences in autism spectrum disorder (ASD) prevalence and symptomatology are well-documented. Here, by performing a large-scale study, we address heterogeneity in the existing findings regarding sex-differences in neuroanatomy in ASD.

Methods: Structural MRI scans of 3100 subjects were obtained from the ABIDE (I & II), NIMH, Hospital for Sick Children, and UK MRC AIMS consortium. After quality control and site exclusion (<3 ASD females), 1834 subjects from 18 sites were analyzed (158 Female-ASD, 429 Female-Controls, 561 Male-ASD, 701 Male-Controls, age: 2-65). Cortical thickness (CT) processing, quality control, and analysis was conducted by one author (SB) using CIVET 1.1.12. Statistical analysis was performed using random-effects vertex-wise meta-analysis technique to account for site, and corrected for 5% FDR.

Results: Sex-specific brain-wide patterns of increases in CT in ASD males (superior temporal and postcentral gyri, peak Cohen's d = 0.33) and females (prefrontal and occipital cortices, peak Cohen's d = 0.49) relative to same-sex controls were observed (separate models per sex). Patterning of CT increases are only moderately correlated between sexes (left: r = 0.25, right: r=0.45). Sex-by-diagnosis interactions did not survive FDR. When stratified by age, a widespread sex-specific main effect of ASD diagnosis (ASD>Control in both sexes) was observed in subjects <16 years of age (438 ASD/701 Control), with minimal effect of ASD diagnosis in subjects >=17 years (217 ASD/323 Control), suggesting a normalization of CT toward late-adolescence.

Conclusions: Our findings suggest that atypical patterning of cortical thickness, substantially modulated by sex, is evident in children and adolescents with autism, but much less so in adults.

O2

Abstract title: Role of dorsostriatal cholinergic interneurons in habit formation and cognitive flexibility: a transdiagnostic model of eating disorders in mice services

Authors: Mathieu Favier, Helena Janickova, Luc Moquin, Erika Vigneault, Alain Gratton, Marco A.M. Prado, Vania F. Prado, Salah El Mestikawy

Affiliation(s): Douglas Mental Health University Institute, McGill University; Robarts Research Institute, Western University

Background: Eating disorders (EDs), an important cause of physical and psychosocial morbidity, are complex and poorly understood. Maladaptive habits and deficits in cognitive flexibility may be central gateways for the development and persistence of EDs. The striatum is pivotal for the regulation of these cognitive functions. Cholinergic interneurons (TANs) are well-identified regulators of striatal functions. TANs express the vesicular acetylcholine transporter (VAChT) and the vesicular glutamate transporter 3 (VGLUT3), and consequently signal with both ACh and glutamate. Our objective was to identify how ACh/glutamate co-transmission regulates the dorsal striatum.

Methods: We used loxed mutant to specifically delete VAChT or VGLUT3 in the striatum. In addition, AAV-Cre viruses were injected in specific striatal sub-compartments. Devaluation tests after sucrose self-administration training were used to assess the balance between goal-directed behaviors (GDB) and habits. Reversal learning procedure in touchscreens allowed us to investigate cognitive flexibility. Mutants mice were tested in two rodent models of EDs. Finally, dopamine (DA) release in sub-areas of dorsal striatum was detected by in vivo voltammetry.

Results: We found that TANs-dependent Glu release favored habits, whereas ACh promoted GDB. Silencing ACh signaling in the dorsostriatal induced a marked deficit in cognitive flexibility. These mice developed maladaptive/compulsive eating behaviors. Finally, silencing ACh or Glu released from TANs differentially impact DA neurotransmission in the sub-compartments of dorsal striatum.

Conclusion: Our study reveals the critical involvement of TANs and the dorsal striatum in the regulation of habit formation, cognitive flexibility and EDs.

Supported by (fellowship and/or granting agency)	Brain Canada, CIHR, NSERC

O3

Abstract title: The role of hippocampal memory engram in mediating stress susceptibility in an animal model of depression

Authors: Brittany Zhang, A.S. Wong, V. Wong, T.P. Wong.

Affiliation(s): Douglas Mental Health University Institute, Department of Psychiatry

Apart from mood changes, anhedonia and sleep disturbance, depression has been associated with a biased memory for negative stimuli. Imaging studies suggest this cognitive bias is related to enhanced functioning of the hippocampus. We hypothesize that the facilitated formation of hippocampal engram cells, cellular substrates for memory, is related to the cognitive bias for negative stimuli in depression.

We employ a chronic social defeat model to examine the relationship between hippocampal engram cell activation and depression-related behaviours. The TetTag mouse model allows the tagging of activated neurons by a reporter gene LacZ. TetTag mice were stressed by social defeat, consisting of attacks by and co-housing with an aggressive mouse. After 8 days of social defeat, mice were separated into susceptible (exhibiting social avoidance) and resilient groups according to their social behaviour. Engram cells are reactivated by an extra episode of social defeat to induce immediate early gene cFos expression. Neurons with both LacZ and cFos labeling represent engram cells.

We found more LacZ labeled hippocampal CA1 neurons in susceptible mice compared with resilient and nonstressed control mice. Such group difference was gone when we separately compared data from the dorsal and ventral hippocampus. Intriguingly, we found significantly more engram cells in susceptible mice than other mouse groups in both the dorsal and ventral hippocampus. No difference in LacZ labeled and engram cells was found in the dentate gyrus. Our findings suggest that enhanced hippocampal memory engram may underlie the lasting effect of social stress in susceptible mice.

Supported by (fellowship and/or granting agency)	CIHR

O4

Abstract title: Impact of night shift work on circadian clocks in police officers

Authors: Anna Koshy[1,2], Marc Cuesta[1,2], Nicolas Cermakian[2], Diane B. Boivin[1]

Affiliation(s): 1. Centre for Study and Treatment of Circadian Rhythms, Douglas Mental Health University Institute, Department of Psychiatry, McGill University 2. Laboratory of Molecular Chronobiology, Douglas Mental Health University Institute, Department of Psychiatry, McGill University

Background: A central clock and many peripheral clocks, located throughout the body, generate 24-hour rhythms in various physiological systems. During shift work, a temporal misalignment occurs between these circadian clocks and the environment, leading to the possible development of health issues.

Methods: We assessed 2 central clock markers and 2 separate peripheral clocks of 11 police officers, before and after 7 consecutive night shifts. Quantitative PCR was used to assess the circadian gene expression in peripheral blood mononuclear cells (PBMCs) and oral mucosa cells. ELISA was used to analyze the central clock markers, salivary cortisol and urinary 6-sulfatoxymelatonin.

Results: Before the week of night shifts, the rhythmic expression of certain clock genes in oral mucosa cells had a significant peak in the morning, while in PBMCs, a significant difference was observed for certain clock genes between 10h00 and 19h30. After 7 consecutive night shifts, the rhythmic clock gene expression in oral mucosa cells showed either a loss of rhythmicity or a loss of its temporal relation with the sleep-wake cycle, while in PBMCs, the significant difference that was observed at baseline was lost in all clock genes. Salivary cortisol and rhythmic urinary 6-sulfatoxymelatonin excretion were observed to show different levels of adaptation between individuals after 7 consecutive night shifts.

Conclusions: These results demonstrate, for the first time, that significant alterations occur in 2 central clock markers and 2 peripheral clocks, after working 7 consecutive night shifts. This study has important implications for understanding the health issues encountered by shift workers.

Supported by (fellowship and/or granting agency)	Canadian Institutes of Health Research (CIHR), Institut de recherche Robert-Sauvé en santé et en Sécurité du travail (IRSST)

O5

Abstract title: Convergent epigenetic, transcriptional and morphological evidence associate a history of child abuse with impaired myelination in the anterior cingulate cortex

Authors: Arnaud Tanti[1], Pierre-Eric Lutz[1], Alicja Gasecka[2,3], Sarah Barnett-Burns[1], John J. Kim[1], Yi Zhou[1], Gang G. Chen[1], Marina Wakid[1], Meghan Shaw[1], Daniel Almeida[1], Marc-Aurele Chay[1], Jennie Yang[1], Vanessa Larivière[1], Marie-Noël M'Boutchou[4], Léon C. van Kempen[4], Volodymyr Yerko[1], Josée Prud'homme[1], Maria Antonietta Davoli[1], Kathryn Vaillancourt[1], Jean-François Théroux[1], Alexandre Bramoullé[1], Tie-Yuan Zhang[6], Michael J. Meaney[6], Carl Ernst[1,5], Daniel Côté[2,3], Gustavo Turecki[1,5] *, and Naguib Mechawar[1,5] * (*: equivalent contribution)

Affiliation(s): 1. McGill Group for Suicide Studies, Douglas Mental Health University Institute, McGill University 2. Institut universitaire en santé mentale de Québec 3. Centre d'optique, photonique et laser, Université Laval 4. Segal Cancer Centre, Lady Davis Institute, Jewish General Hospital, McGill University 5. Department of Psychiatry, McGill University 6. Sackler Program for Epigenetics and Psychobiology at McGill University and The Ludmer Centre for Neuroinformatics and Mental Health, Douglas Mental Health University Institute, McGill University

Background: Child abuse has devastating and long-lasting consequences on individuals, considerably increasing the lifetime risk of negative mental health outcomes such as depression and suicide. Yet, the neurobiological processes underlying this increase in vulnerability remain poorly understood. Here, we investigated the hypothesis that child abuse is associated with epigenetic, transcriptomic and cellular adaptations in the anterior cingulate cortex.

Method: Post-mortem brain samples from depressed individuals who died by suicide, with (N=27) or without (N=25) a history of severe child abuse, as well as psychiatrically healthy controls (N=26) were used in this study. Genome-wide DNA methylation and gene expression were investigated using Reduced Representation Bisulfite Sequencing and RNA-Sequencing, respectively. Cell-type specific validation of differentially methylated loci was performed following fluorescence-activated cell sorting of oligodendrocyte and neuronal nuclei. Differential gene expression was validated using Nanostring technology. Finally, oligodendrocytes and myelinated axons were analysed using stereology and Coherent Anti-stokes Raman Scattering microscopy.

Results: A history of child abuse associated with cell-type specific changes in DNA methylation of oligodendrocyte genes and a global impairment of the myelin-related transcriptional program. These effects specifically occurred as a function of child abuse, as they were absent in depressed suicides with no history of early life adversity. Furthermore, a selective and significant reduction in the thickness of myelin sheaths around small-diameter axons was observed in individuals with history of child abuse.

Conclusion: This study indicates that child abuse, in part through epigenetic reprogramming of oligodendrocytes, may lastingly disrupt cortical myelination, a fundamental feature of cerebral connectivity.

Supported by (fellowship and/or granting agency)	CIHR, FRQS

O6

Abstract title: Psychological and psychosocial interventions for negative symptoms in psychosis: a systematic review

Authors: Danyael Lutgens, Genevieve Gariépy, Ashok Malla

Affiliation(s): Douglas Mental Health University Institute

Background: Negative symptoms such as, reduced expression, pleasure and motivation for life's goals and activities are present in one third of psychosis patients and remain critical predictors of quality of life and functioning. Antipsychotic medications, while highly effective for the treatment of positive symptoms, only minimally impact negative symptoms. Given the paucity of treatment options, current best practice suggests the use of psychological and psychosocial interventions in addition to medication for negative symptoms. However, evidence to support such interventions warrants further exploration.

Objective: Our objective was to systematically review the literature on the effectiveness of psychological and psychosocial interventions for the treatment of negative symptoms in psychotic disorders.

Methods: We searched all major English language databases from inception to October 19th, 2015 for randomized controlled studies of psychological and psychosocial interventions in psychotic disorders that reported outcome on negative symptom.

Results: Ninety-three studies were identified that met our criteria. Interventions fell under the following domains: cognitive behavioural therapy (CBT), neurocognitive therapy, skills based training, exercise training, family education, arts training, and miscellaneous treatments. Compared to treatment as usual CBT, skills based training, exercise, and music treatments provide significant benefit. Skills based treatments may have greater efficacy at end of treatment, while the effectiveness of CBT may be most likely to be maintained over time. Skills based, and to a lesser extent neurocognitive treatments have a greater impact on negative symptoms when compared to other active interventions. The quality of the evidence was overall moderate.

Conclusions: Psychological and psychosocial interventions may have some utility in the amelioration of negative symptoms in psychosis and should be incorporated within patient treatment plans. Despite this, more effective treatments for negative symptoms are needed.

Supported by (fellowship and/or granting agency)	CIHR, FRQS

O7

Abstract title: Alcohol use, depressive symptoms and the incidence of diabetes-related complications

Authors: Randa Elgendy, Sonya S. Deschênes, Rachel J. Burns, Norbert Schmitz

Affiliation(s): Douglas Mental Health University Institute, McGill University

Background: Heavy alcohol consumption in individuals with type 2 diabetes (T2D) is related to an increased risk of developing diabetes-related complications, including retinopathy, neuropathy, nephropathy, and coronary artery disease (CAD). Depression, often comorbid with diabetes, may be relevant to consider in this relation, as depression is also related to an increased risk of diabetes-related complications. Therefore, individuals with T2D and depression who drink heavily may be at a particularly high risk for developing complications.

Objectives: We expected that among individuals with T2D, those with high depressive symptoms and heavy alcohol use would be at an increased risk for CAD, retinopathy, neuropathy, and nephropathy, compared to individuals with either heavy alcohol use or high depressive symptoms alone.

Methods: Data were from the five waves of the Evaluation of Diabetes Treatment study, an annual telephone survey of 2028 adults with T2D at baseline. Data on alcohol quantity and frequency, depressive symptoms, and diabetes-related complications were collected yearly. Multilevel logistic regression analyses with generalized estimating equations were used to investigate the development of each complication over time.

Results: Results indicated no significant interaction between depressive symptoms and alcohol use on any complication. However, elevated depressive symptoms were associated with increased odds of developing each complication. Alcohol frequency was related to decreased odds of developing neuropathy, nephropathy, and marginally significantly related to decreased odds of CAD. Alcohol quantity was marginally significantly related to increased odds of retinopathy.

Conclusion: This study suggests that alcohol use and depressive symptoms are both independently associated with diabetes-related complications.

Supported by (fellowship and/or granting agency)	CIHR

O8

Abstract title: Medial septum optogenetic stimulations of parvalbumin interneurons to restore spatial reference memory impairments in freely behaving J20 APP mice

Authors: Guillaume Etter, Sylvain Williams

Affiliation(s): Douglas Mental Health Institute, McGill University

Alzheimer's disease (AD) has been associated with amyloid beta (Ab) aggregation, subsequent hippocampal neurodegeneration and memory defects. Theta-gamma cross-frequency coupling (CFC), a physiological phenomenon that has been associated with memory encoding and retrieval, has been previously shown to be decreased in complete hippocampus preparations from 3 weeks old transgenic AD mice model.

In the present study, we have monitored CA1 local field potentials in the freely behaving J20 AD mice model (PDGF-APPSw, Ind) trained to seek a reward on a modified appetitive version of the Barnes maze as well as during REM sleep. At 6 months, J20 mice display more spatial errors as well as non-targeted exploration during the probe trial compared to non-transgenic (NTg) counterparts. Using a standardized measure of CFC, we show that theta-gamma CFC is reduced in J20 mice during both wakefulness and REM sleep. Parvalbumin (PV) interneurons of the medial septum send long-range projections to the hippocampus and have been recently shown to robustly drive hippocampal oscillations. Using J20 AD x PV-Cre crossed mice, we stimulated with light PV interneurons of the medial septum in the gamma range and were able to restore normal electrophysiological activity.

This study suggests that circuits underlying cross-frequency coupling are affected very early in AD mice models and might underlie the spatial memory defects and suggests that the CFC may be an early biomarker of AD. We propose that selective stimulations of medial septum PV interneurons could be of therapeutic relevance to restore memory defects in AD conditions.

Supported by (fellowship and/or granting agency)	Brain Canada

O9

Abstract title: DRD4 Exon 3 Genotype as Predictor of Symptom Severity and Treatment Outcome in Children with ADHD: Gene-Treatment and Gene-Environment Interaction Study

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Background: This study explores the role of dopamine receptor 4 (DRD4) gene polymorphism in childhood ADHD. First, we examine the effect of DRD4 exon 3 genotype on response to methylphenidate (MPH) with a pharmacodynamic design. Second, we explore an interaction between the genotype and exposure to maternal stress during pregnancy and their effect on symptom severity in children with ADHD.

Methods: Children with ADHD (ages 6-13) were recruited from an ongoing clinical trial at the Douglas Institute. Response to MPH was evaluated by parents and teachers; child symptom severity was reported by the parents; stress during pregnancy was classified into low and high. A total of 404 subject were included and classified into three genotype groups: homozygotes for short alleles, SS (n=270); homozygotes for long alleles, LL (n=21); and heterozygotes, SL (n=92).

Results: There was a significant interaction between DRD4 genotype and treatment course (p=.037). Children with LL genotype had a better response to placebo, and lower symptomatology at both placebo and active medication weeks, as evaluated by the parents. Gene-by-environment analysis revealed a significant interaction (p=.003) on overall CBCL score, and externalizing sub-scores, but not internalizing and attentional problems. Exposure to high stress pregnancy resulted in more attentional problems only in children with LL genotype.

Conclusions: Children with LL genotype showed a better response to MPH treatment and more attention problems when exposed to high stress during pregnancy. This suggests that DRD4 genotype could be used to predict response to MPH treatment and clinical outcomes in children with ADHD.

Supported by (fellowship and/or granting agency)	CIHR, FRQS, F.S.B. Miller Fellowship from the Faculty of Medicine, McGill University

O10

Abstract title: The antigen-specific CD8 T-cell response is controlled by their endogenous circadian clock: implications for antibacterial and antitumoral responses

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Background: Circadian clocks cause 24 h rhythms of various aspects of the immune system. However, the circadian control of the adaptive (antigen-specific) immune response remains poorly understood. Recent work in the laboratory showed that the CD8 T cell response to the OVA antigen presented by dendritic cells (DCs) exhibits a circadian rhythm.

Methods and Results: To identify which circadian clock causes the rhythm of the CD8 T cell response, we generated mice with the essential clock gene Bmal1 deleted specifically in mature CD8 T cells. Interestingly, the rhythm of CD8 T cell expansion and cytokine production observed in WT mice was abolished in these CD8 T cell-specific clock-deficient mice. This demonstrates that the clock in CD8 T cells controls the rhythm of their response. To further define at which step of the CD8 T cell response the circadian clock acts, we have followed the early response of adoptively transferred OVA-specific CD8 T cells to vaccination with OVA-loaded DCs. At day 3 post-vaccination, we observed a day/night difference in the rate of CD8 T cell proliferation. We have also shown that following DC-OVA immunizations there is a rhythm of the bacteria clearance by CD8 T cells in the spleen and a rhythm of the immune response against tumor cell development.

Conclusion: In conclusion, the CD8 T cell-intrinsic clock controls the response to antigen presentation and the initial CD8 T cell activation events, and this has implications for antibacterial and antitumoral responses.

Supported by (fellowship and/or granting agency)	CIHR, Université de Montréal

O11

Abstract title: Sociodemographic and clinical predictors between unipolar-treatment resistant depression and bipolar depression: a retrospective analysis

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Background: According to multiple studies up to 30% of depressive patients will not respond effectively to subsequent pharmacotherapies constituting unipolar treatment-resistant depression (UP-TRD)(1). Different authors have suggested a high rate of conversion to bipolar disorders (BP) of these patients suggesting that undiagnosed bipolar disorder might account for the apparent cases of UP-TRD(2, 3). However no clinical studies have yet compared psychopathological aspects of depression between UP-TRD from BP patients raising the question as where does UP-TRD lies in the spectrum model for affective disorders.

Methods: Sociodemographic and Psychopathological features were analyzed by a retrospective chart analysis in 194 patients with moderate to severe depression either with a diagnoses of UP-TRD, BPI or BPII. Symptom severity was assessed by the following behavioral scales: (MADRS); (CGI-S); (QIDS-C16) and (HAM-D17). A Multinomial logistic regression was used as to analyze different psychopathological variables associated with diagnosis.

Results: UP-TRD patients showed a lower global assessment of functioning (GAF) with a greater severity with melancholic features compared to BPII patients. Our multinomial logistic regression showed that a greater number of failed pharmacotherapies (p=0.009; OR=1.388), anxiety disorders (p=0.005; OR=7.954), higher level of GAF (p= 0.006;OR=1.156) and suicidal ideations (p= 0.047;OR=4.889) were highly associated with BP2 compared to UP-TRD. BPI patients had 19 times the likelihood of anxiety disorders, 6 times more unemployment and 5 times more suicidal ideations than UP-TRD. Additionally they were 4 times more likely to have first degree relatives with affective disorders, 10 times more likely to suicidal attempts and 13 times the likelihood of unemployment when compared to BPII.

Conclusions: Predictive variables were described suggesting that UP-TRD exhibited distinct psycho pathological features underscoring its separation from BPI and BPII. Further analysis considering pharmacological outcomes should strengthen this proposal towards improving management of patients with depressive disorders.

Supported by (fellowship and/or granting agency)	FRQS, RQRS

O12

Abstract title: Role of neonatal ventral hippocampus neuronal activity in regulating adult behaviours in mice

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Ventral hippocampus (VH) modulates behaviours such as executive control, emotions and goal directed behaviours by connectivity to various cortical and limbic regions. VH sends excitatory glutamatergic monosynaptic projections from VH to prefrontal cortex (PFC), nucleus accumbens and amygdala. Neuronal activity in the VH modulates oscillatory neuronal activity in the PFC to control cognitive functions. Developmental behavioural disorders such as schizophrenia are hypothesized to arise from a disruption in VH-PFC/limbic connectivity. A model to test this hypothesis, the neonatal ventral hippocampus lesion (NVHL) model in rats, has revealed that lesion of the VH in pups leads to adult schizophrenia-like behavioural deficit including hyperlocomotion, prepulse inhibition (PPI) deficit and cognitive deficits. Since NVHL model uses the robust excitotoxicity of the ibotenic acid to lesion (loss of cells) the VH, the specific role of the neonatal VH neuronal populations on adult behaviour cannot be inferred from this model. Thus, we hypothesised that neonatal inhibition of the VH neuronal activity would lead to adult behavioural deficits. In order to test this hypothesis a modified DREADD (designer receptors activated by designer drugs) short-term Herpes simplex virus (STHSV1) vector was used. ST HSV-hM4Di-mCherry (0.1µl, 5x104 transducing units) or saline was microinfused in the VH of C57Bl6/J mice (P10). The animals received intraperitoneally (IP) injection with saline or clozapine-N-oxide (CNO) daily for 7 days (P11-P17) making 4 groups- Control-Saline, Control-CNO, STHSV-hM4Di-Saline and STHSV-hM4Di-CNO. Adult male and female pups were used to assess behaviors relevant to schizophrenia. Our data showed an increase in locomotor activity and a deficit in PPI in the STHSV-hM4Di-CNO group as compared to the control groups. This shows that specific neonatal inhibition of the VH neuronal activity can lead to adult behavioural deficits. The data also suggests that neonatal neuronal inactivity of the VH could be a key molecular mechanism in the NVHL model. Ongoing work examining cognitive behaviours should reveal the extent of adult behavioural repertoires that are dependent on neonatal VH neuronal activity.

Supported by (fellowship and/or granting agency)	CIHR

O13

Abstract title: Mutations in ACTL6B cause a novel developmental disease: Molecular insights into human neurodevelopment using brain cells derived from skin

Authors: Scott Bell, Huashan Peng, Ilaria Kolobova, Walla Al-Hertani, Phillipe Campeau, Carl Ernst

Affiliation(s): McGill University, Douglas Hospital, Université de Montréal

We performed whole genome sequencing on a family with two brothers who presented seizures and intellectual disability due to an unknown severe neurodevelopmental disorder. A mutation in ACTL6B, a gene that makes a protein that is a subunit of the BAF complex, was identified as a likely cause of the disease. In all mammals, BAF is essential for brain development and functions to unpack DNA to turn genes on and off. We have identified four other unrelated cases with mutations in this gene and with a similar clinical profile. All mutations are absent from 65 000 healthy individuals, strongly suggesting that mutations in ACTL6B cause disease. Using the index case and healthy controls, we have made neurons from skin and performed whole genome gene expression (RNAseq) analysis and mapped the binding sites of the BAF complex (ChIPSeq). We have also made isogenic control cells with CRISPR/Cas9 technology where we have repaired the patient mutation and deleted the gene itself, two ways to generate excellent comparison data for rare diseases. Mouse Actl6b Knock-out models have shown that mice develop aberrant dendrites, and we show that human mutant ACTL6B causes increased binding of BAF to SEMA4D, a gene important for dendrite development, providing a molecular consequence of mutant ACTL6B leading to a measurable neuronal phenotype. These data identify a new neurodevelopmental disorder, reveal new genetics about how the human brain grows, and provide a molecular mechanism for how mutations in a BAF

Supported by (fellowship and/or granting agency)	Canadian Institutes of Health Research, GeneSpark Foundation

O14

Abstract title: miR-218: a key target for the alterations in dopamine development induced by abused doses of amphetamine in adolescence

Authors: Santiago Cuesta, José Maria Restrepo-Lozano, Steven Silvestrin, Cecilia Flores

Affiliation(s): Department of Psychiatry, McGill University

Background: Drug use in adolescence is a predictor of lifetime abuse. We showed that abused doses of amphetamine in adolescence disrupt prefrontal cortex dopamine development, altering cognitive functions in adulthood. This is mediated by drug-induced alterations in the expression of the guidance cue receptor gene Dcc in ventral tegmental area (VTA) dopamine neurons. While amphetamine in adolescence downregulates Dcc, it upregulates the microRNA repressor of Dcc, miR-218. We used the antagomiR technology to examine whether miR-218 in dopamine neurons mediates adolescent amphetamine-induced effects on Dcc expression, mesocortical development, and behavior in adulthood. We also examined possible mechanisms mediating drug-induced changes in miR-218.

Methods: We infused a miR-218 antagomiR in the VTA of early adolescent mice, 1 day before repeated amphetamine exposure. Then, we determined drug effects on Dcc expression, dopamine innervation, and behavior. To examine the mechanisms mediating amphetamine-induced increases in miR-218, we administered the D2R antagonist Raclopride, 30min prior to drug/saline injections. One week after, we quantified miR-218, Dcc and another miR-218-validated target, Robo1, to verify specificity.

Results: Increased miR-218 levels in dopamine neurons are required for amphetamine in adolescence to downregulate Dcc and to induce lasting developmental effects. Furthermore, the effects of amphetamine on miR-218 and Dcc, are mediated by dopamine D2R activation. Robo1 mRNA was unchanged in all the experiments.

Conclusions: miR-218 regulation of Dcc in dopamine neurons is a mechanism by which environmental events, like drugs of abuse, produce enduring molecular, developmental, and behavioral effects. Our results suggest that miR-218-mediated repression of Dcc by amphetamine is target-specific.

Supported by (fellowship and/or granting agency)	NIH

O15

Abstract title: "I needed it to get better": a qualitative investigation into the positive, transformational role of first episode psychosis

Authors: Gerald Jordan, Tovah Cowan, Ashok Malla, Srividya N. Iyer

Affiliation(s): McGill University

Background: A first episode of psychosis (FEP) is arguably the most severe mental disorder emerging during youth. However, FEP may also represent an opportunity for positive, transformational change, an area which has received very little attention. This presentation will answer two questions: 1) What positive, transformational changes do youth experience following FEP, and 2) What factors or processes do youth feel facilitate such changes?

Methods: A qualitative descriptive design guided the project. Data were gathered through semi-structured interviews conducted with eleven purposefully sampled youth receiving early intervention services for FEP at two time points. Interviews were transcribed verbatim and subject to thematic analysis using inductive and deductive methods by two researchers.

Results: Youth described how FEP led them to feel stronger, more grounded, and more authentic in their interactions and lifestyle choices; gain self-awareness, maturity, and purpose in life; develop stronger, wiser connections with others; and give back in the form of community engagement. Experiencing positive change was achieved through a process of negotiating adversity that was present prior to one`s FEP; experiencing a sense of healing; capitalizing on one's strengths, passions and interests; being supported by others; and receiving services from empathetic clinicians—especially psychotherapists.

Conclusions: The findings validate the experiences of youth who have experienced positive change as a result of their experience of FEP. The findings also provide an evidence base that clinicians can draw from in order to better provide hopeful, recovery-oriented, strengths-based services to youth experiencing FEP.

Supported by (fellowship and/or granting agency)	Canadian Institutes of Health Research--Banting

O16

Abstract title: The Genetic Architecture of Differential Susceptibility to Adversity; a Genome-wide Approach

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Affiliation(s): 1. Douglas Mental Health University Institute 2. Jewish General Hospital

Exposure to stressful events can cause differing sequelae depending on the level of stress susceptibility of each person. Here we studied susceptibility in the context of the development of substance dependency upon exposure to adversity. Susceptible individuals were defined as those subject with a substance dependence and a history of adversity. Resilient individuals were defined as subjects with no evidence for substance dependence, but positive for a history of adversity. We performed a genome-wide association study (GWAS) of susceptibility. 59 SNPs passed a suggestive threshold ($p<1x10-5$). The smallest P-value for our study was observed with a marker on chromosome 3, rs709465 ($p=8.1x10-7$,beta= -0.3). We devised a polygenic risk score (PRSsus) to facilitate the comprehensive quantification of the genetic risk for susceptibility. In an independent subset of data, our PRSsus could differentiate between susceptible and resilient individuals. Our PRSsus was highly specify and sensitive in predicting the substance addiction only among individuals with a history of adversity (ROC;AUC =0.85,accuracy = 0.89) and not in subjects with no history of adversity (AUC=0.54 and accuracy=0.55).We, further, examined the predictive validity of our PRSsus in second independent cohort. We found a positive and significant association between PRSsus and mental health diagnoses only among participants with a history of child maltreatment. We propose that our PRSsus reflects the underlying genetic architecture of differential susceptibility to adversity, including childhood adversity, and not directly to the specific mental health outcome. This is one of the first genome wide studies of the genetic architecture of differential susceptibility.

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O17

Abstract title: Spontaneous use of spatial memory strategies is associated with greater cortical plasticity following a virtual spatial memory intervention program in healthy older adults

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The hippocampus (HPC) shows accelerated atrophy during normal aging. To stimulate the HPC, we developed a computerized spatial memory intervention program (SMIP) that promotes spatial memory, a function that depends on the HPC. We investigated whether spontaneous navigation strategy affects how people respond to SMIP. Spatial learners use a strategy that depends on the HPC, while response learners use a strategy that is HPC-independent. 54 healthy older adults underwent the SMIP or control condition. They were also tested on a battery of neuropsychological and navigational tasks before and performed a structural MRI scan. We found increased grey matter in the HPC. As anticipated, spontaneous strategy use predicted plasticity: 88% of spatial learners showed HPC plasticity as a result of the SMIP, as opposed to only 25% of response learners. These results indicate that SMIP induces HPC growth and that navigation strategy is a modulating factor of HPC plasticity during SMIP. These results indicate the potential efficacy of a spatial memory training program at increasing HPC grey matter, and sheds further light on the relationship between navigational strategy, the HPC and its associated cortical circuits. Specifically, we showed that spontaneous spatial navigational strategies are associated with greater grey matter plasticity as opposed to the response strategy which is associated with cortical rigidity. Such evidence has substantial implications in regards to the potential of spatial memory training programs at reducing the chances of developing memory deficits through the beneficial effect on HPC grey matter.

Supported by (fellowship and/or granting agency)	CIHR

P1

Abstract title: LCM-Seq: single cell-type whole genome bisulfite sequencing and transcriptomic profiling in post-mortem brain

Authors: Daniel Almeida[1,2], Gang Chen[1], Maria-Antonietta Davoli[1], Naguib Mechawar[1,3], Gustavo Turecki[1,3]

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The epigenome and transcriptome of a cell constitutes an essential piece of cellular identity and accounts for the multifaceted complexity and heterogeneity of cell types within the mammalian brain. During neurodevelopment, spatiotemporal control over gene expression through epigenetic regulation of promoters and enhancers leads to precisely defined cellular fates. Each discrete cellular population is also differentially influenced by extrinsic signals from their local environments and neighbouring cells. Thus, while a wealth of studies have investigated epigenomic and transcriptomic alterations underlying the neurobiology of psychiatric or neurological illnesses, the use of bulk-tissue homogenates have masked their ability to determine cell-type specific molecular dysfunctions. Here we describe our progress on a pipeline that employs laser capture microdissection (LCM) of prefrontal layer V pyramidal cells followed by downstream whole-genome bisulfite sequencing (WGBS) and transcriptomic profiling. Using this method, we achieve a 59% mapping rate efficiency, bisulfite conversion rates within the expected rage and optimal coverage of CpG sites for WGBS. RNA sequencing resulted in a mapping efficiency rate of 98% and captured a wide distribution of transcripts that map back to 13,141 genes. The major utility of this pipeline is its capacity to allow for the investigation of DNA methylation and expression patterns from the exact same dissected population of cells derived from post-mortem human brain tissue. Our goal is to use this pipeline to investigate molecular dysfunction underlying the relationship between childhood abuse, depression and suicide.

Supported by (fellowship and/or granting agency)	CIHR

P2

Abstract title: Investigating projections from the ventral hippocampus (vHC) to the prelimbic (PL) and infralimbic (IL) cortices in the mouse

Authors: Polina Ash[1], Lalit Srivastava[2], Sylvain Williams[2]

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The vHC to prefrontal cortex (PFC) circuit is composed of monosynaptic long range projections originating in the vHC and terminating in the mPFC. This pathway plays a vital role in functions such contextual memory and emotional processing and dysfunction in it has been associated with a large variety of neuropsychiatric disorders such as anxiety and schizophrenia. The identity and extent of long range projections from different components of the vHC (CA1 and Sub) to the mPFC (IL and PL) and their functional role in a richer repertoire of behaviors has not been investigated in the mouse. Mice were ipsilaterally injected with the retrograde tracer CTB into the PL and IL or anterograde AAV into the vHC. Our results indicate greater vHC innervation of the IL rather than PL, with a small population of neurons projecting to both. In addition, we found a lack of GABAergic vHC projections to the mPFC. Lastly, we were able to use the molecular marker Neurotensin to target a subpopulation of cells topographically restricted to distal CA1 and proximal Sub with a unique pattern of PFC innervation. Future experiments will investigate the functional role of this newly identified pathway in anxiety and social memory. Greater understanding of this circuit in rodent models could shed light on the ways information integration between these brain regions supports their functional roles, and how their functions are disrupted by disease.

Supported by (fellowship and/or granting agency)	CIHR

P3

Abstract title: Generation of a mu opioid receptor-Cre driver line

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Les opiacés sont des composés largement utilisés dans la médecine actuelle et notamment connu pour leur risque de dépendance et leur effets secondaires. Leur principale cible est le récepteur opioïde μ (MOR), un récepteur à sept domaines transmembranaires activé par de nombreux peptides endogènes mais également par la morphine et autres opiacés. Le récepteur μ est ainsi essentiellement impliqué dans les effets analgésiques et récompensant des opiacés via des circuits comprenant des structures tel que l'aire tegmentale ventrale, le noyau accumbens, le cortex préfrontal ou l'habenula, soulevant un intérêt considérable dans le cadre de la recherche sur l'addiction. Depuis quelques années, de nouvelles techniques comme l'opto- ou chemogénétique permettant de manipuler les neurones de notre choix ont vu le jour. Ainsi, afin de moduler les circuits neuronaux exprimant MOR, nous avons généré une nouvelle lignée MOR-Cre utilisant une stratégie knock-in permettant l'expression d'une eGFP-Cre recombinase détectable et fonctionnelle sous le contrôle du promoteur MOR. Ici, nous caractérisons le pattern d'expression du récepteur μ et de l'eGFP-Cre via, tout d'abord, la visualisation directe de la fluorescence intrinsèque et amplifiée dans le tissu. Ensuite, l'expression d'ARN du récepteur μ et de l'eGFP-Cre est également évaluée par qPCR à travers le cerveau. La fonction du MOR est vérifiée en utilisant des techniques comportementales permettant de vérifier la propriété analgésique et hyperlocomotrice induite par l'activation de MOR. Ensuite, le signal intracellulaire du récepteur est évalué par GTPγs. Finalement, la recombinaison dans les neurones MOR-positifs est détectée en utilisant une souris rapportrice dt-Tomato. Les résultats préliminaires indiquent un avenir extrêmement prometteur pour la nouvelle lignée.

Supported by (fellowship and/or granting agency)	Center for Study of Opioid Receptors and Drugs of Abuse (CSORDA)

P4

Abstract title: The impact of video game experience on hippocampal grey matter integrity

Authors: J. Benady-Chorney[1], G. West[2], K. Konishi[1], M. Diarra[2], B. Drisdelle[2], L. Dahmani[1], D. Sodums[1], F. Lepore[2], P. Jolicoeur[2], V. Bohbot[1]

Affiliation(s): 1. Douglas Mental Health University Institute Research Centre, Department of Psychiatry, McGill University 2. Centre de Recherche en Neuropsychologie et Cognition, Université de Montréal

Background: Action video games have previously been hypothesized to have an impact on grey matter in the hippocampus, and low grey matter in the hippocampus has been identified to increase the risk of numerous neurological and psychiatric disorders across people's lifespan. Previous research has shown that habitual action video game players favour non-hippocampal dependent navigation strategies. People who use non-hippocampal dependent navigation strategies typically display lower grey matter in the hippocampus.

Methods: We first compared grey matter in the hippocampus between a group of action video game players (AVGs) and non-action video game players (NVGs) using voxel based morphometry. We next investigated the causal relationship between changes in grey matter in the hippocampus and experience with action video games by having people train on either action or 3-D platform video games for a total of 90 hours. Subjects were randomized into either group, balanced for spontaneous spatial and response learning strategies in the 4/8VM at pre-training.

Results: AVGs have reduced grey matter within the left hippocampus compared to NVGs. First-person shooting games reduce grey matter within the hippocampus and increase grey matter within the amygdala in participants using non-spatial memory strategies. Participants who use hippocampus-dependent spatial strategies showed increased grey matter in the hippocampus after training on first-person shooting games. The group that trained on 3D-platform games displayed growth in either the hippocampus or the functionally connected entorhinal cortex.

Conclusion: Video games can be beneficial or detrimental to the hippocampal system depending on the individual who is playing and the genre of the game.

Supported by (fellowship and/or granting agency)	CIHR, FRQNT, NSERC

P5

Abstract title: Mu opioid receptors in the habenula: dissecting reward and aversion in addiction

Authors: L-J. Boulos, S. Ben Hamida, E. Darcq, B.L. Kieffer

Affiliation(s): Douglas Mental Health University Institute Research Center, Department of Psychiatry, Faculty of Medicine, McGill University; Institut de Génétique et de Biologie Moléculaire et Cellulaire (LJB)

Reward highly impacts our daily decision-making processes and its dysfunction can lead to aversive states and severe psychiatric disorders such as addiction. Reward and aversion research have traditionally focused on dopamine and associated circuitry. Recent studies however show the implication of other brain regions, mainly the habenula (Hb). This structure contains the highest density of mu opioid receptors (MORs), a key protein in reward and aversion. Nonetheless, the role of Hb MORs remains to be investigated. Our project addresses this gap in the existing literature with the overarching hypothesis that Hb MORs constitute the pillar of reward and aversion circuitries. We used a conditional knockout mouse model that lacks mu opioid receptors specifically in the habenula and combined biomolecular and morphine-driven behavioral tests with a stress on translational techniques, mainly TouchScreen paradigms. Our findings suggest that the absence of Hb MORs induces dysfunction of aversive but not reward-related systems. Our work will impact the medical understanding of the panoply of brain illnesses that have been strongly associated with reward and aversion.

Supported by (fellowship and/or granting agency)	Canada Research Chairs, Monique H. Bourgeois Chair in Pervasive Developmental Disorders, NIH

P6

Abstract title: Attachment styles and their relationship to the risk of psychopathology and the use of mental health care services

Authors: Elias Chalet, Xiangfei Meng, Alain Brunet

Affiliation(s): Douglas Mental Health University Institute, McGill University

Background: Previous studies have explored the association between specific attachment styles and psychopathology, however there has not been a study exploring this relationship in a nationally representative sample of the general population. This study aimed to explore the relationship between adult attachment style and 1) psychopathology and 2) utilization of mental health care services.

Methods: Data used in this study was from the National Comorbidity Survey Replication Study. We selected all participants (N = 5,647) with complete information on both attachment style and mental disorders. Descriptive analyses and multivariate logistic regressions were used to explore the relationship after adjusting for socio-demographic characteristics, other mental disorders and somatic illness.

Results: Individuals with insecure-avoidant attachment were more likely to develop post-traumatic stress disorder (adjusted odds ratio [AOR] = 1.89, 95% confidence interval [CI] 1.5-2.3), attention deficit disorder (AOR = 1.41, 95% CI 1.1-1.8), generalized anxiety disorder (AOR = 1.48, 95% CI 1.2-1.8), major depressive disorder (AOR = 1.18, 95% CI 1.0-1.4) and alcohol dependence (AOR = 1.55, 95% CI 1.2-2.0). Individuals with insecure-anxious attachment were more likely to have a lifetime diagnosis of attention deficit disorder (AOR = 2.01, 95% CI 1.3-3.0) and generalized anxiety disorder (AOR = 1.67, 95% CI 1.2-2.3). Moreover, univariate analysis indicated that insecure attachment was associated with greater service use.

Conclusions: This study highlights insecure attachment as a potential risk factor for psychopathology. Further studies could use a longitudinal design in order to further characterize the role of attachment as a risk factor for psychopathology.

P7

Abstract title: Maternal symptoms of depression interact with child genetic risk for ADHD in prediction of socio-emotional problems

Authors: Lawrence M. Chen, Shantala Hari Dass, Andrée-Anne Bouvette-Turcot, Elika Garg, Thao T. T. Nguyen, Patricia P. Silveira, Josie Dioro, Michael S. Kobor, Kieran J. O'Donnell, Michael J. Meaney, MAVAN Research Team

Affiliation(s): McGill University

Background: Antenatal depression is associated with the offspring's emotional behavioural problems. However, the impact varies across the population, as some children seem resilient. Genetic factors may define vulnerability/resilience to the environment, effects that likely span many molecular pathways. We sought to identify genes and biological pathways that moderate the relationship between prenatal maternal depressive symptoms and emotional behaviours in 60-month-old children.

Methods: This study included 190 mother-child dyads from a cohort with data on maternal depressive symptoms, genome-wide genotyping, and child emotional behaviour. We constructed genetic scores that account for polygenic risk for psychiatric disorders and applied them in our gene-environment interaction model, selecting a subset of genetic variants that constituted the best-fit genetic score in the interaction model with significance levels less than 0.01 and used MetaCore to examine the enriched gene ontology.

Results: Polygenic risk for ADHD moderated the influence of maternal depressive symptoms on child internalizing problems ($t(186)=3.22$, $p<0.05$). Children with high genetic risk are sensitive to prenatal stress whereas children with low risk are resilient. The most significant genes underlying this moderating effect of the genetic risk score were enriched in pathways and functions related axonal development and synaptic function.

Conclusions: This study suggests that specific genes involved in the biological framework for prenatal neurodevelopment can confer sensitivity or resilience to the influences of maternal antenatal depression.

Supported by (fellowship and/or granting agency)	Brain Canada Foundation, Kids Brain Health Network

P8

Abstract title: The neural correlates of functional compensation in high performing older adults

Authors: Abdelhalim Elshiekh, Sricharna Rajagopal, Stamatoula Pasvanis, Elizabeth Ankudowich, Natasha Rajah

Affiliation(s): Integrated Program in Neuroscience, McGill University

Despite the common belief that cognitive decline is inevitable in older adulthood, recent evidence suggest that some older adults perform similarly to younger adults (YA) in a variety of cognitive tasks, including episodic memory tasks. Prior fMRI studies revealed that these "high"-performing older adults (HOA) exhibit increased PFC activity compared to lower-performing older adults (LOA), which may reflect functional compensation in the aging brain. However, this assumes that these groups only differ in brain activation patterns and performance, when in fact they may represent distinct subsamples in the population. In this fMRI study, we compared performance-related brain activity in YA, LOA and HOA during successful encoding and retrieval of spatial context memory tasks. The goal was to determine the patterns of functional compensation in HOA vs LOA compared to YA. We tested 24 LOA, and 20 HOA who were split based on performance on a separate temporal context memory task, and 45YA. Multivariate behaviour partial least square analysis (B-PLS) was used to identify patterns of whole-brain activity that correlate with performance across groups. Behaviourally, independent samples t-tests show that YA performed better than LOA but not HOA, while HOA scored higher than LOA. The B-PLS analysis indicated that compared to LOA, activity in medial PFC and ventral visual areas in HOA was predictive of successful encoding and retrieval. Interestingly, activity in those same areas was predictive of successful encoding and retrieval in HOA vs YA despite the comparable performance in both groups. Theoretical implications of these findings will be discussed.

Supported by (fellowship and/or granting agency)	CIHR

P9

Abstract title: mGluR5 in amphetamine response and sensitizationmGluR5 in amphetamine response and sensitization

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Background: Repeated psychostimulant drug exposure induces behavioural sensitization, which may index neuroplastic events implicated in the development of addiction. In rodents, repeated stimulant drug exposure changes expression of the metabotropic glutamate receptor subtype 5 (mGluR5). mGluR5 regulates some forms of synaptic plasticity, and its availability is reduced in people with cocaine dependence. The goal of this study is to understand how an amphetamine sensitization regimen affects mGluR5 levels.

Methods: Sixteen healthy volunteers received 3 doses of d-amphetamine (0.3 mg/kg, po) or placebo followed by a 16-day washout and final amphetamine challenge. Receptor availability was measured using PET and the mGluR5-specific radioligand [11C]ABP688 before drug on day 1 and before the final dose on day 21. Mice (n=30) underwent a similar sensitization regimen using 3 doses of 2mg/kg amphetamine (i.p.) or saline followed by amphetamine challenge. Receptor availability was measured post-mortem using 3H-ABP688 autoradiography.
compared to baseline (p=0.01), an effect not seen in placebo treated participants. No change in receptor availability was observed in mice. In both humans and mice, lower mGluR5 availability was associated with a stronger locomotor response to amphetamine (humans: r=-0.8, p=0.03; mice: r=-0.8, p=0.003).

Conclusions: These preliminary results confirm that mGluR5 is linked to stimulant response. Altered mGluR5 expression may contribute to the development of sensitization. mGluR5 should be considered a potential target to treat addiction.

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P10

Abstract title: Neuroimaging study of genetic and environmental factors in children with ADHD

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Despite the high heritability of ADHD (76%), causal genes have yet to be determined. A linkage study detected a marginal overtransmittance of a NET polymorphism (rs36021) in ADHD children. However, upon stratification according to exposure to maternal smoking during pregnancy (MSDP), this result became highly significant in exposed children. These findings suggest that MSDP plays a role in the etiology of ADHD, and should be considered in future genetic investigations.

Our objectives are to explore the (1) independent and (2) interactive effects of MSDP and NET polymorphism on brain structure in children with ADHD. We expect to find the largest variations in cortical measurements in carriers of the risk allele exposed to MSDP.

Participants (6-12 years) are recruited from an ongoing trial at the Douglas Institute and scanned using 3T Siemens MRI. Genetic, environmental, cognitive, clinical and structural data are collected. Cortical measurement acquisition and linear modeling are performed using CIVET-1.1.12/RMINC. Our model uses age, sex, diagnosis, medication and MSDP as predictors, and cortical thickness and surface area measurements as main outcome measures.

Consistent with recent reports, we found no significant difference in brain structure measurements between cases and controls. In a preliminary analysis, we found increased surface area measurements in children exposed to MSDP (t-value = 3.61; FDR = 5%) in the left lateral parieto-occipital sulcus. If reproduced in a larger sample, these findings can provide insight into the pathophysiology of ADHD. We plan to further explore the effects of genetic risk factors on brain structure in our sample.

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P11
Abstract title: Police officers' psychomotor performance is affected by their circadian phase

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Shift work is associated with circadian and sleep-wake disturbances. Shift workers, such as police officers, are exposed to increased fatigue and impaired performance at work due to circadian misalignment. The aim of this study was to document psychomotor performances throughout a complete work roster in police officers working rotating shifts.

A total of 25 municipal police officers from Quebec (17 men, 8 women) aged 31.3±4.5 years (mean ± SD) were enrolled in a 35-day field study. Their rotating schedule comprised 9- or 12-hour day (0700-1600 or 0700-1900), evening (1500-2400), and night (2230-0730 or 1900-0700) shifts, alternating with rest days. During this period, they filled out a 5-minute Psychomotor Vigilance Task (PVT) at the beginning and end of their shifts. The diurnal variation of median reaction time (RT), mean reaction speed (RS), and minor lapses (RT $\geq$ 500 ms) was analyzed using a nonlinear mixed model.

Significant 24-h variation was present for median RT and mean RS ($p \leq 0.001$) with the fitted lowest performance at 07:43±00:30h (mean ± SD) and the highest at 19:43±00:30h. A trend was also observed for minor lapses ($p=0.083$).

This study has demonstrated that the circadian phase affects performance in rotating shift workers. The circadian nadir in the early morning suggests that their circadian system is adjusted to a day-oriented schedule independent of the shift worked. The results of this work have practical implications in terms of safety and productivity at work, as it identified critical times of reduced performances, namely at the start of day shifts and end of night shifts.

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P12

Abstract title: Noradrenergic neurons of the locus coeruleus play a role in susceptibility to acute environmental stress

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Background: Anxiety and mood disorders are the most common mental disorders, causing important socioeconomic consequences. Stress exposure has been shown to be an important risk factor for the onset of these pathologies. Interestingly, not all individuals exposed to stress develop a disorder and are considered resilient. Researchers have placed intense interest in understanding the neural basis of susceptibility and resilience to stress. The noradrenergic system is thought to play a key role in the regulation of stress responses and it has been proposed that the locus coeruleus (LC) may play a modulatory role in stress related behaviour.

Methods: In the present study, we investigated the role of the LC in susceptibility and resilience to environmental acute stress using the learned helplessness mouse model which produces two behavioural phenotypes: helpless mice that are susceptible to stress and non-helpless mice that are resilient to stress. We compared VMAT2DBHcre KO mice which are depleted in noradrenaline transmission to wild-type mice (WT). We also measured LC activity using electrophysiological recording in WT controls, helpless and non-helpless mice.

Results: We found that depletion of noradrenaline transmission alleviated helpless behaviour in males but not in female mice. Furthermore, in-vivo electrophysiological recordings of LC noradrenergic neurons showed an increase of LC neuronal firing in helpless mice compared to non-helpless and control mice.

Conclusion: Taken together, these findings suggest that the LC plays a modulatory role in response to acute environmental stress and that increased LC activity results in helpless behaviour.

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P13

Abstract title: Does the timing of maternal immune activation affect neuroanatomical and behavioural outcomes in the offspring?

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Background: Maternal immune activation (MIA) during gestation, a known risk factor for mental illness in humans, has been shown to induce schizophrenia- and autism-related deficits in rodent offspring. We examine how MIA timing affects neuroanatomical and behavioural development.

Methods: Offspring (C57bl/6) exposed to prenatal MIA by Poly I:C (5mg/kg, intraperitonially) in early (day 9; n=8) or late (day 17; n=5) gestation were examined. Structural MRIs (100um isotropic) were collected in vivo at postnatal day 21, 38-39, and 89-95. Deformation based morphometry was performed to investigate voxel-level volume differences in the maturing brain. MIA timing-by-age interactions were examined using linear mixed effects models (False Discovery Rate [FDR] corrected). Assessment of locomotion, social preference, marble burying, and prepulse inhibition (PPI) were performed at second (adolescent) and third (adult) timepoints. MIA timing-by-age effects were tested using linear models.

Results: Trajectories in the hippocampus, thalamus, amygdala, anterior cingulate cortex, and medial septum differed significantly. Local volumes in early MIA start smaller than those of late MIA at but show accelerated growth. Late MIA exhibit stunted growth in these regions (<1%FDR). Early MIA offspring exhibit greater PPI deficits at adolescence ($p=0.006$), bury more marbles ($p=0.08$), show decreased locomotor activity ($p=0.02$), and have impaired social behaviour ($p=0.06$) at adolescence and adulthood.

Conclusion: Mice exposed to early MIA show greater alteration to brain development and more behavioural deficits. A better understanding of the timing of MIA could help elucidate mechanisms underlying neurodevelopmental disorders.

P14

Abstract title: A manual structural magnetic resonance imaging segmentation protocol of the hypothalamic-pituitary-gonadal axis

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Background: The hypothalamus is a sexually dimorphic brain structure that signals to the pituitary, in turn regulating endocrine glands, such as the gonads in what is known as the hypothalamic-pituitary-gonadal (HPG) axis. This axis controls reproductive behavior and physiology, and may be involved in sexually differentiated psychopathologies. However, there is no protocol for the in vivo assessment of the entire HPG axis.

Objective: To develop a structural magnetic resonance imaging (MRI) segmentation protocol to study the HPG axis in vivo.

Methods: T1 and T2 weighted images were acquired on a 3T Siemens scanner, and segmented using Display 2.0 (Montreal Neurological Institute). Hypothalamic segmentation includes subregions, such as the preoptic area, lateral hypothalamus, and the ventromedial and dorsomedial nuclei, the pituitary stalk, anterior and posterior pituitary glands, and the gonads.

Results: Preliminary data on 18.5 year olds (8 men, 8 women) are consistent with expected sex differences in total hypothalamic volume (men > women, Cohen's d=0.58), and whole pituitary volumes (women > men, Cohen's d=0.623). Intra-rater Dice kappa similarity coefficients (DSC) are high (.80, .80, .91, and .89 for the hypothalamus, pituitary stalk, anterior and posterior pituitary glands, respectively, n=2), as are inter-rater DSC (n=5) for the anterior (.83), posterior (.81) pituitary, and the posterior bright spot (.73) thought to represent vasopressin vesicles. Gonadal measures include total volume, and antral follicle counts.

Conclusion: This appears to be a valid tool for the structural assessment of the HPG axis. Next, we will test whether prenatal maternal stress alters HPG axis integrity.

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P15

Abstract title: The effect of night shift work on the human circadian transcriptome

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Background: Night shift work is associated with various health problems, including diabetes, obesity, cardiovascular disorders and cancer. Disruption of the internal biological clock by night shift work is thought to be a main contributor to these adverse health effects. Various studies have shown that a substantial fraction of the human transcriptome displays a circadian rhythm. In this study, the objective is to determine the effect of night shift work on genome-wide gene expression levels.

Methods: We performed transcriptomic analysis on blood samples collected from healthy human subjects (n=8) over a period of 24 hours in a constant posture procedure at baseline and after a three-day simulated night shift work protocol. The proportion of genes that show a circadian rhythm at baseline and after the night shift work protocol was calculated using cosinor analysis and the phases and amplitudes were determined.

Results: On the individual level, ~13.8±3.9% of the genes show a significant rhythm, which is reduced to 10.4±2.6% after night shift work. Moreover, 6.7% of all transcripts show a significant rhythm at baseline in at least half of the subjects, compared to 2.8% after night shift work. Interestingly, the phases of the circadian transcripts show a bimodal distribution over the 24-hour period at baseline, while this pattern is attenuated after night shift work.

Conclusions: These findings suggest that rhythms in gene expression are disrupted following night shift work and thereby are a first step towards elucidating the molecular underpinnings of the negative health effects associated with irregular working hours.

Supported by (fellowship and/or granting agency)	CIHR

P16

Abstract title: Physiological Characterization of a Novel Selective Melatonin MT1 Receptor Partial Agonist

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Melatonin (MLT) is a neuro-hormone involved in mood, sleep, pain and temperature regulation, via binding to G-protein coupled receptors MT1 and MT2. However, the differential roles of MT1 and MT2 are poorly understood due to the lack of selective compounds. Here, we investigated the novel selective MT1 receptor partial agonist N-(2-{Methyl-[3-(4-phenylbutoxy)phenyl]amino}ethyl)acetamide (UCM871) on temperature modulation, sleep-awake cicle and activity on Locus Ceruleus (LC) across 24 hours. LC neurons may represent the critical waking-promoting neurons that control the sleep-waking switch by discharging at highest rates during wakefulness (W), at lower rates during not rapid eye movement (NREM), and exhibiting complete cessation of discharge during rapid eye movement (REM) sleep. Indeed, NREM sleep is associated with a decrease in temperature whereas REM sleep and W is associated whit increase in temperature. Subcutaneous administration of UCM871 (14 mg/kg) shown a effect mostly during the dark phase in which is able to increase the temperature, increase the NREM sleep and decrease sharply the neuronal firing rate in the LC. In contrast, during light phase UCM871 does not change the body temperature, decrease NREM sleep and have minor effect in the LC noradrenergic cells compared with vehicle treated rats. These results show that MT1 receptors play an important role in temperature regulation, sleep-awake cycle and adrenergic function, but in a distinct manner. MT1 activation by UCM871 is more pronounced in the dark than in the light phase, this could be associated by different expression of this receptor through the 24 hours.

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P17

Abstract title: Treatment delays and pathways to mental health care in Youth Protection Services in Montreal

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Background: Mental illness is the leading contributor to burden of disease among adolescents. Young people in Youth Protection Services are particularly affected, as an estimated 50-60% of adolescents in this group suffer from mental health problems.

Objectives : The aim of this study was to establish and describe how individuals in Youth Protection Services access mental health services in Montreal , with a focus on the types of treatment and evaluation offered, and the pathways and delays experienced before reaching appropriate services.

Methods: We reviewed 200 clinical files of young people aged 12-18 years old who were under care of Youth Protection Services in Montreal for at least one year. Data pertaining to symptom onset, diagnosis, pathways to care, mental health service utilization, hospitalization and treatment delays were collected.

Results: Almost all clinical files (198/200) described mental health concerns or need for mental health services. Overall, young people in youth protection were more likely to obtain evaluation or crisis management interventions than treatment. Results also show that delays between onset of mental health problems and care are very common among this population. Maps of referral pathways and trajectories to care will be presented.

Conclusions: Young people with mental health problems under Youth Protection services are a particularly vulnerable and underserved population. Their access to mental health services is often tainted by complex and circuitous attempts to get appropriate treatment. These results will help inform interventions to simplify pathways into care for this group.

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P18

Abstract title: Cerebellar Volume Mediates the Association Between Prenatal Maternal Stress and Motor Performance in Adolescent Boys: Project Ice Storm

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Introduction: While prenatal maternal stress (PNMS) reduces cerebellar volume in laboratory animals, ethical constraints limit human research. However, natural disasters expose pregnant women to varying levels of stress in a quasi-random fashion.

Objectives: First, to determine whether PNMS is associated with differences in cerebellar gray matter volume (CGV), and whether this relationship is moderated by fetal sex and/or by the timing of the PNMS exposure in gestation. Second, to investigate whether CGV mediated the association between PNMS and motor performance in adolescents.

Methods: Measures of PNMS were obtained from mothers shortly after the 1998 Quebec Ice Storm. At age 11½, structural MRIs were collected. GGVs were obtained using the MAGeTbrain pipeline. Motor performance (balance) was evaluated at age 13½.

Results: In boys only, higher objective PNMS predicted smaller CGV if they were exposed during preconception, but predicted larger CGV if exposed at the 9th week of gestation or later. Moreover, CGV mediated the association between objective PNMS and motor functioning at 13½ years in late-exposed boys: higher objective stress was associated with larger CGVs, which were associated with poorer balance.

Conclusion: The results demonstrate that CGV mediates the relationship between objective PNMS and motor functioning in adolescence, that boys appear to be more vulnerable than girls, and that these associations depend on the timing of the stressor in gestation. This is the first demonstration in humans that prenatal exposure to a sudden-onset, independent stressor influences development of the cerebellum, which then predicts motor functioning.

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P19

Abstract title: Identification of structural neuroadaptation dependent of MOR by in-vivo and ex-vivo MRI

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Background: In humans, resting state magnetic resonance neuroimaging (MRI) has opened the era of connectome/imaging genetics, in order to elucidate how genetic factors affect brain organization in healthy individuals and disease. Yet the causal impact of a single gene on anatomical structure remains largely unknown, and animal research is best suited to this goal. Here, we tested whether structural MRI in living as well as perfused animals would reveal structural changes upon total targeted inactivation of a single gene, the mu opioid receptor (MOR) gene. MOR is broadly distributed throughout the nervous system and mediates the remarkably potent analgesic and addictive properties of opiates like morphine. This receptor facilitates rewarding effects of both drugs of abuse and social interactions with potential implications for autism.

Methods: All resting-state structural MRI in-vivo and ex-vivo image acquisitions were performed using 7 tesla MRI scanners. To visualize and compare the mouse brains, the images from the anatomical MRI scans were registered for each of the mice using MBM and MAGeT. The volume changes of each 159 regions were measured for each subject on both live and perfused group. The brain data are also available on a voxelwise basis to examine the localized changes between the groups throughout the brain.

Results: Our analysis of mutant mice lacking the mu opioid receptor gene in the whole organism using MRI shows specific and pronounced differences compared to WT in both groups. Importantly, our results document robust neuroanatomical changes between WT & KO predominantly in 'habenular commissure', 'nucleus accumbens', 'medial septum'.In addition, the volumes of 115 regions (70%) are identical between in-vivo and ex-vivo groups.

Conclusion: Our work demonstrates that mouse brain structure is influenced by MOR. More studies will be necessary to determine MOR function in brain structure. Importantly, both in- and ex-vivo produce equivalent results, opening new perspectives for longitudinal studies.

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P20

Abstract title: In Vivo, MRI based microstructural parcellation of the human hippocampus

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Background: The hippocampus, a region of the brain intimately linked with learning and memory, is thought to be composed of five major subfields. However, this perspective parses the hippocampus along only a single neuroanatomical dimension. In contrast, a recent high-profile paper demonstrated that brain structure can be parcellated using several dimensions of architecture, including assays that quantify potential cytoarchitectonic boundaries, grey matter myelination profiles, and brain function using semi-automated methods. Here, we apply this concept to derive a de novo parcellation of the hippocampus using MRI-based microstructural measures.

Methods: We used structural (0.7mm3) and diffusion (1.25mm3) data from the Human Connectome Project. MRI-based microstructural parcellations of the hippocampus were developed using non negative matrix factorization (NMF), a method previously used to cluster the mouse hippocampus based on gene-expression. Microstructure was defined by voxel-wise measures of T1w/T2w ratio (proposed measure of myelination), three principal eigenvalues of the diffusion tensor, and mean diffusivity.

Results: NMF decomposition of the hippocampus produced spatially contiguous components for values of k from 2 to 7, showing spatial differentiation along the anterior-posterior (longitudinal) and dorsal-ventral axes of the hippocampus.

Conclusions: NMF produced spatially contiguous (without spatial constraints), reproducible microstructural parcellations showing differentiation along the longitudinal hippocampal axis in agreement with previous research.

Supported by (fellowship and/or granting agency)	NSERC, CIHR, FRQS, BBME McGill

P21

Abstract title: Perfectionism and daily emotion regulation and well-being: An experience sampling study

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Background: Over the past three decades, perfectionism has emerged as a cognitive-personality vulnerability factor associated with various psychological problems, such as depression and anxiety. Given that perfectionistic individuals exhibit an elevated vulnerability to stress and enduring distress, it is important to determine whether certain emotion regulation strategies make emotional reactions worse or serve a protective role for these individuals. This study of 131 community adults examined the role of perfectionism in daily stress, emotion regulation, and negative affect.

Methods: Participants completed measures of two higher-order dimensions of perfectionism, self-critical perfectionism (SCP) and personal standards perfectionism (PSP). Then, over eight consecutive days, they completed an experience sampling methodology (ESM) consisting of five repeated within-day reports and one retrospective daily report of stress, emotion regulation (i.e., rumination, expressive suppression, reappraisal), and affect (i.e., negative affect, sadness).

Results: In contrast to PSP, SCP was moderately to strongly associated with the maintenance of stress, rumination, expressive suppression, negative affect, and sadness. Multilevel modeling indicated that individuals with higher SCP/PSP, relative to those with lower scores, exhibited heightened emotional reactivity in response to daily stressors. Moreover, engaging in more rumination and expressive suppression than usual was coupled with greater increases in negative affect and sadness in high-SCP/PSP individuals. On the other hand, using more reappraisal than usual was associated with greater decreases in negative affect and sadness for high-SCP/PSP individuals.

Conclusions: These findings underline the importance of targeting emotion regulation tendencies in daily life to reduce distress for perfectionistic individuals.

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P22

Abstract title: Amphetamine disrupts prefrontal cortex development only during a defined critical period in adolescence

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Introduction: Adolescent onset of drug use increases the risk of addiction throughout the lifetime, with greater vulnerability conferred to younger initiates. Here we report that drugs of abuse interfere with prefrontal cortex development and cause distinct deficits in cognitive control that persist throughout adulthood only when drug exposure occurs during the earliest stage of adolescence.

Methods: Mice were treated with amphetamine (4 mg/kg) or saline during early adolescence (PND 22±1 - 31±1), mid-adolescence (PND 35±1 - 44±1), or adulthood (PND 75±15 – 84±15). Six weeks later, when all mice were adults, we measured behavioral inhibition with a Go/No-Go task as well as risk-taking behavior and locomotor activity in the open field. We then assessed the organization of dopaminergic synapses and baseline content of dopamine in the medial prefrontal cortex (mPFC).

Results: Amphetamine exposure specifically during early adolescence impaired behavioral inhibition and increased risk taking in adulthood. These impairments were not observed when amphetamine exposure occurred during mid-adolescence or adulthood. Concomitantly, only amphetamine exposure during early adolescence reduced the synapse density of mPFC dopamine axons and levels of the extracellular dopamine metabolite HVA, indicating a decrease in mPFC dopamine turnover.

Conclusions: Our findings establish early adolescence as a critical period of vulnerability to the enduring effects of amphetamine, and demonstrate that such vulnerability is due to the unique action of the drug on early adolescent mPFC development. Alterations in adult prefrontal cortex dopamine function and cognitive behaviors following early adolescent drug use may contribute to addiction vulnerability in early user populations.

Supported by (fellowship and/or granting agency)	CIHR, NSERC, NIH-NIDA

P23

Abstract title: Imbalances in human resources for health: a cross-national, multilevel study of adolescent health outcomes and disparities

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Background: Health care systems are a robust determinant of health, and the availability of human resources for health is of particular importance. However, the distribution of the health workforce is highly imbalanced in terms of geographical location, resulting in inequitable access to health care between socioeconomic groups. Disparities in access to health services may, in turn, contribute to health inequalities by socioeconomic status (SES), but this hypothesis has not been tested in adolescents.

Methods: This thesis is a cross-sectional, multilevel analysis of individual and country data from 38 countries. Data from 218,790 adolescents were drawn from the 2014 Health Behavior in School-aged Children (HBSC) international survey. We tested the fit of multilevel regression models of health to examine the association between human resources and health inequalities between socioeconomic groups.

Results: Multilevel analyses showed that a higher density of psychologists at the country-level was associated with greater self-reported mental health in adolescents ($p < 0.05$), whereas the densities of doctors and psychiatrists were not predictive of better adolescent health ($p > 0.05$). Cross-level interaction terms between human resources for health and SES were not significant, indicating that countries with a higher density of human resources for health did not have greater SES inequalities in adolescent health.

Conclusions: This thesis found that adolescents in countries with a higher density of psychologists report better mental health. Given the importance of adolescent health in ensuring a healthy adulthood, public health practitioners should consider issues regarding human resources for health in future adolescent health policies.

Supported by (fellowship and/or granting agency)	Frederick Banting and Charles Best Canada Graduate Scholarship (CIHR)

P24

Abstract title: Symptomatic and Functional Recovery in First Episode Psychosis: Predictive Value of Early Sub-threshold Psychotic Symptoms

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Individuals with attenuated positive and sub-threshold psychotic symptoms (APSPS) are considered at-risk for psychosis. However, few studies of first episode psychosis (FEP) differentiate between FEP patients with and without a reported history of APSPS (APSPS+ and APSPS-, respectively). Our longitudinal investigation compares outcome between these groups. Patients (N=263) were recruited from PEPP-Montreal, a FEP clinic, and followed for two years of treatment. The Circumstances of Onset and Relapse Schedule was used to identify youth who recalled at least one of nine consensus-selected APSPS prior to their FEP. Symptom severity was measured using the Scale for the Assessment of Negative Symptoms (SANS) and Scale for the Assessment of Positive Symptoms (SAPS). Functioning was measured using the Global Assessment of Functioning (GAF), which captured both severity and functioning, and the Social and Occupational Functioning Assessment Scale (SOFAS), which solely captured functioning. Mixed ANOVA were applied to analyze group differences across three time-points: Baseline (T0), after 1 year (T1), and after 2 years of treatment (T2). Despite no differences at T0, a significant group by time interaction was observed among GAF scores, revealing lower functioning and worse symptoms among APSPS+ in T1 only. A significant main group effect for SOFAS scores (ps<0.05) revealed persistent lower functioning among APSPS+ patients. These results suggest that: (1) APSPS+ patients exhibit worse symptoms and functioning in the first year of treatment while, (2) after two years of treatment, group differences persist only in functioning. Our findings provide evidence that APSPS+ patients are specifically resistant to functional recovery.

Supported by (fellowship and/or granting agency)	CIHR

P25

Abstract title: Emotional rating of pseudo-speech is influenced by the spatial location of the acoustic source

Authors: Ignacio Spiousas, Jorge L. Armony

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Background: The rapid and accurate decoding of emotional expressions is crucial for social interactions and, in some cases, even for survival. Emotional information is often multimodal, typically relying on the visual and auditory systems. However, when such stimuli originate outside the individual's visual field, only the acoustic information is present. It has therefore been hypothesized that in such cases the perceived emotional value of these stimuli should be enhanced.

Methods: We investigate how the relative spatial location of a vocal expression (pseudo-speech prosody) affects its perceived emotional value. To this end, we employed a spherical array of loudspeakers (diameter 1.8m), housed in a semi-anechoic chamber, which allowed us to explore different source locations, including some above the horizontal plane (e.g. at the top of the head) and outside the visual field (e.g., behind the listener). Thirty-five healthy participants were asked to rate, using a continuous visual-analog scale, the perceived valence of a set of 30 pseudo-sentences, from five emotional categories (angry, fearful, happy, sad and neutral), arriving from nine different spatial locations.

Results: Fearful expressions originating directly at the back were perceived as more negative, and angry expressions presented in the front were rated as less negative, compared to the same stimuli presented in the other locations. No other significant effects were observed.

Conclusions: While our results confirm the influence of spatial location on emotional perception, they show that these effects occur only for threat-related emotions and that they are specific to "biologically-relevant" positions along horizontal plane of the perceiver.

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P26
Abstract title: Cognitive load impairs conscious access to sensory inputs while sparing gist effect

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A central debate in the consciousness literature revolves around the question – is our conscious experience rich or sparse? Proponents of the 'sparse' theory assert that conscious perception is limited by access mechanisms (e.g. attention) to sensory inputs. Conversely, advocates of the 'rich' theory contend that our conscious experience overflows access mechanisms. To further understand the role of attention in the richness of conscious experience, the present study employs a between-groups modified Sperling paradigm where one group is subject to a cognitive load. Each participant completed three tasks: a colour detection task where they reported whether a colour was present from the entire display, a colour detection task where they reported whether a colour was present at a post-cued location, and a colour identification task where they used a colour-wheel to report the exact colour at a post-cued location. Our findings show that participants adopted a more conservative decision criterion when attention was oriented to a post-cued location. Additionally, we found an interaction between post-cueing and the load manipulation for both sensory (d') and metacognitive sensitivity (meta-d'), intimating that the load manipulation impacted one's ability to access sensory inputs and higher-order representations during introspection. Beyond replicating previous findings, our results suggest that the load manipulation hardly affects the subjective experience of gist and solely impairs access mechanisms.

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P27
Abstract title: Exploring Cognitive Dimensions of Body Ownership

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Background: In the Rubber Hand Illusion (RHI), synchronized tactile and visual sensory events yield distorted subjective feelings of ownership over a fake rubber hand. While this illusion largely rests on feedforward multimodal integration of sensory information, recent studies suggest that higher-order cognitive processes modulate these phenomenological distortions.

Methods: The present study aimed to 1) replicate the neural correlates of the RHI through electroencephalography (EEG) as well as to 2) explore the effects of cognitive load on both subjective (self-report) and objective (EEG and electrodermal activity, EDA) indicators of the RHI.

Results: Our results replicate previous findings by showing that the RHI corresponds to subjective changes in feelings of Embodiment, Loss of own hand, and Deafference, while EDA pertains to feelings of embodiment. Evidence from neural activity suggests that individuals susceptible to the RHI show increased activity in the visual and frontal regions in response to a threatening event during the synchronous condition. Moreover, we show that the load manipulation affected the strength of the illusion whereby high load related to stronger illusion strengths.

Conclusions: Our results imply that cognitive resources modulate the RHI. However, these effects only emerge at the level of subjective appraisals of the RHI.

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Abstract title: miR-218 Determines Vulnerability to Depression in a DCC-dependent Manner

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Introduction: We recently identified miR-218 as repressor of the guidance cue receptor gene DCC (Deleted in colorectal cancer). Indeed, low miR-218, but exaggerated DCC, expression in the prefrontal cortex (PFC) are consistent traits of human depression, and stress-induced depression-like behaviors in mice. Remarkably, miR-218 can be measured in blood, suggesting its potential role as biomarker of depression.

Methods: We used C57BL/6 mice, viral-mediated gene transfer, and quantitative-PCR to assess whether (1) direct manipulation of miR-218 in the PFC determines resilience or susceptibility to chronic social defeat stress (CSDS), (2) miR-218 expression in blood correlates with depression-like behaviors, and (3) variations in blood expression of miR-218 depends on changes in miR-218 levels in PFC.

Results: We report that overexpression of miR-218 selectively in PFC pyramidal neurons promotes resilience to CSDS. Conversely, inhibition of miR-218 induces susceptibility to stress. Furthermore, blood expression of miR-218 correlates with depression-like behaviors and susceptible, but not control or resilient, mice exhibit low levels of miR-218 in blood. Most importantly, we demonstrate that changes in blood expression of miR-218 resemble the ones observed in the PFC.

Conclusion: MiR-218 in the PFC functions as a molecular switch that determines resilience or susceptibility to CSDS. Remarkably, stress-induced variations in PFC levels of miR-218 can be readily detected in blood. We are currently assessing whether miR-218 levels in PFC and blood change in response to antidepressants. We propose that blood expression of miR-218 might function as potential biomarker of vulnerability to stress and predict the outcome of therapeutic interventions.

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P29

Abstract title: MR-based age- and sex-related effects on the striatum, globus pallidus and thalamus in healthy individuals across the adult lifespan

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Introduction: While age-related changes are major risk factors in neurodegenerative diseases, there are limited studies investigating changes in subcortical morphology associated with healthy aging. Furthermore, since prevalence, onset age and symptomatology of many neuropsychiatric disorders differ between males and females, we examined the effect of age and sex, as well as motor performance on the volume of the striatum, globus pallidus and thalamus in healthy individuals.

Methods: Ninety-one healthy subjects underwent T1-weighted MR imaging (18-80 years old; Siemens 3T Trio; 1mm3). Images were segmented using MAGeTbrain to estimate the volume of the striatum, globus pallidus and thalamus. A general linear model was performed to examine the association between age, sex and their interaction, and subcortical volume. Total brain volume was used as a nuisance variable. A secondary analysis included performance on the grooved pegboard task in the model.

Results: Bilateral age-related volumetric decreases were observed in all three structures of interest ($p<0.01$). Sex-specific rates of bilateral striatal volumetric decline were observed; steeper rate of decline in females (left $p=0.03$; right $p=0.05$). Moreover, larger contralateral thalamic volume predicted higher grooved pegboard scores (left $p=0.05$; right $p=0.04$).

Conclusion: These results expand knowledge of age-related changes in the healthy aging brain, suggesting a substantial modulation of sex on the rate of volumetric decline. Improved understanding of sex-specific trajectories across the lifespan can improve our understanding of sex-specific prevalence and symptomatology in neuropsychiatric disorders (e.g: Parkinson's disease, schizophrenia, and geriatric depression).

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P30

Abstract title: Cardiometabolic risk markers in first-episode psychosis and socioeconomic disadvantage

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The three-fold increase in mortality rates and 14-year reduction in life expectancy observed in schizophrenia can be considerably attributed to high rates of cardiometabolic disease. This association has been traditionally explained by the side effects of antipsychotics and sedentary lifestyles often seen in these patients. However, metabolic anomalies are already present in first-episode psychosis patients, and the high comorbidity between schizophrenia and diabetes was documented long before the introduction of antipsychotics. Thus, other risk factors might contribute to this epidemiological association. Socioeconomic deprivation increases incidence rates for obesity, diabetes and psychosis, placing itself as a possible link. The objective of the present study is to determine the influence of socioeconomic deprivation on cardiometabolic risk markers in first-episode psychosis patients. Patients accepted to PEPP-Montréal, aged 14-35 years, participated in the study (n=377). Census-derived indices of social and material deprivation (determined by postal code) were used to predict the following indicators of cardiovascular risk: levels at admission of total cholesterol, HDL, LDL, and triglycerides. After controlling for levels of inactivity (sedentary behavior), indices of social deprivation significantly predicted levels of total cholesterol ($p=0.04$) and HDL ($p=0.01$) only in women. Material deprivation had no significant influence on any marker in both sexes. The present results indicate that women with psychotic disorders bear an increased vulnerability for the development of cardiometabolic disease which is associated with social disadvantage. Such vulnerability could explain (in part) why women with psychosis have higher rates of cardiovascular mortality than men, opposite to what happens in the general population.

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Abstract title: Waiting for Cognitive Behavioural Therapy (CBT): A Randomized Controlled Trial Evaluating the use of a Computerized CBT Program for Outpatients on a Waitlist in a University CBT Unit

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Background: Computerized Cognitive-Behavioural Therapy (cCBT) is increasingly being considered as an alternative or adjunct to face-to-face CBT, which remains relatively inaccessible despite rising demand.

Objective: To determine if a cCBT program, designed for depression and anxiety, can reduce symptom severity in outpatients on a waitlist, referred for CBT for a wide variety of problems.

Methods: Sixty-four outpatients were randomized to one of two conditions: cCBT using the Good Days Ahead program, or a control condition referred to an online self-help workbook. Outcome measures (CORE OM, BDI, BAI, and Autonomous and Controlled Motivation for CBT) were evaluated at start of study (T1) and at assessment (T2; n = 28).

Results: No significant differences were found in outcome measures over time, with the exception of Autonomous Motivation, which decreased. The cCBT group did not do better than the control group. Interestingly, the majority (60%; n = 15) of cCBT participants reported that the program was "very" or "extremely useful", while only 14% (n = 14) of the control group felt the same about the workbook.

Conclusions: Offering a general cCBT program to waitlist patients may not confer an advantage over simply referring them to online reading material. It is to be noted, however, that the sample size at T2 is insufficient for reaching 80% statistical power. The decline in motivation for CBT could in part be due to difficulties in translating knowledge into practice, especially if participants' main problem was not directly addressed by the program or workbook.

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P32

Abstract title: Specificity of Neural Responses to Processing Emotional Acoustic Information: An fMRI-Adaptation Study

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Background: Emotions portrayed through the auditory domain can convey critical information that enables the listener to interpret the intent and affective state of the emitter. Evident parallels between music and voice and their effects on the brain, have generated discussion amid researchers in the field. In the current literature, it is largely unknown whether these unique classes of acoustic stimuli are processed by the same neural populations, or rather independent, yet overlapping category-specific neurons.

Methods: To directly address this question, we employed a functional magnetic resonance imaging (fMRI) adaptation paradigm in two experiments that is designed to measure the neural response to social communicative signals as a function of their category (music vs. voice) and affective value (neutral vs. fear). We used a fast (TR=529ms), high-resolution (8 mm3 isotropic) multiband sequence to maximize temporal and spatial specificity of the observed responses, as well as statistical power.

Results: Our results confirmed voice-specific adaptation effects in the superior temporal gyrus that could not be explained solely by differences in the basic physical properties of each category. Moreover, emotion-specific adaptation effects were identified in response to musical stimuli.

Conclusions: Overall, our results support the argument for the existence of independent neuronal subpopulations that are functionally separable in response to specific categories and emotions. Our findings for music, a powerful, emotionally arousing stimulus with no obvious survival or evolutionary relevance, are of particular interest as they create a distinction between the neural responses to music and voice, in the ongoing debate over neural overlap.

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Abstract title: Assessing predictors of perceived utility of biological testing among parents of a child with autism

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Background: Establishing clinical utility for biological testing in complex and heterogeneous conditions like autism requires assessing the perspectives of those receiving the test i.e. perceived utility of a biological test. Recent research has found mixed results for perceived utility of biological testing. Understanding the role of predictors in perceived utility could clarify the inconsistent results among the diverse families with autism. Our aim is to examine the extent to which perceived utility of biological testing among parents of a child with autism is associated with child and family functioning, parental autism knowledge, and family-centred care, after controlling for sociodemographic factors.

Methods: Data were drawn from an ongoing prospective study, ASD Genome to Outcome. Children were enrolled when being referred for an autism evaluation for which genetic testing is recommended. Respondents (n=47) had a mean age of 39 years old and 5 months (SD=8 years and 2 months) and were mostly mothers (94%). Their child with autism (n=33 males) had a mean age of 6 years and 6 months old (SD=3 years and 6 months).

Results: A backward multiple regression analysis found that after controlling for parent age and income, parents of a child with greater severity reported higher utility for testing. Higher perceived utility is also associated with lower levels of parental knowledge, family functioning, and family-centred care.

Conclusions: Families who are underserved may expect greater utility for biological testing. Genetic counseling tailored to families could mediate anticipated perceived utility of genetic testing especially for negative results.

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P34
Abstract title: Long Non-Coding RNAs in Depression and Suicide

Authors: Yi (Daniel) Zhou, Pierre-Eric Lutz, and Gustavo Turecki

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While various biological systems have been identified to be involved in depression, the mechanisms underlying their dysregulation remain unclear. Recently, a regulatory class of non-coding RNAs called long non-coding RNAs (lncRNAs) have been implicated in depression and their regulatory targets and mechanisms of action are now being uncovered. Here, we performed RNA-sequencing in the rostral anterior cingulate cortex of 26 depressed suicide completers and 24 matched controls. We identified 21 lncRNAs that were differentially expressed between depressed suicide completers and controls as well as putative protein-coding cis gene targets which also showed differential expression. Furthermore, using weighted gene co-expression network analysis, we have identified putative trans targets of these lncRNAs as well. We focused on lncRNA RP11-326I11.3 and knocked its lncRNA transcript down in HEK293 cells. We did not see an effect on IRF2 or REST expression, the RP11-326I11.3's putative cis and trans gene targets, suggesting that other mechanisms, besides the lncRNA transcript itself, may be important for gene regulation. This work highlights the importance of lncRNAs in the brains of depressed subjects who committed suicide as well as their potential regulatory role in cells.