Southern Ontario Neuroscience Association
37\textsuperscript{th} Annual Meeting, May 5\textsuperscript{th}, 2017
Brock University
SONA 2017

General information
The Southern Ontario Neuroscience Association (SONA) is a chapter of the international Society for Neuroscience (SfN). The chapter aims to promote research, education, and outreach in neuroscience through its annual meeting, sponsored events throughout the year, and travel awards for trainees.

Our annual meeting is made possible through the support of the host institution, external sponsors, and organizers. Special thanks to Prof. Paul Mallet (Department of Psychology, Wilfrid Laurier University) for his help organizing the meeting.

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Institutional sponsors
Faculty of Mathematics and Science
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8:00h – Registration and Breakfast

9:00h – Opening Remarks: room AS204

9:15h – 10:30h – Morning Keynote Speaker: room AS204
Dr Robert Gerlai (University of Toronto)
Embryonic alcohol exposure in zebrafish: Modeling the milder and more prevalent form of Fetal Alcohol Spectrum Disorders

10:30h – 12:30h – Poster Session I

Lunch available from 11:30h until 13:00h

SONA Counselors Meeting in room AS202 from 11:45h to 12:45h

12:50h – 14:00h – “Trainee Talk” Session: room AS204
Sarah Donato (University of Guelph): Identification of stem cells in the body spinal cord of the leopard gecko
Kevin MacDonald (Brock University): Naps containing REM sleep increase stimulus-preceding negativity in anticipation of threat judgements
Gilda Stefanelli (University of Toronto): The histone chaperone Anp32E removes H2A.Z from specific targets and regulates memory formation in the hippocampus

14:00h – 16:00h – Poster Session II

16:00h – 17:00h – Afternoon Keynote Speaker: room AS204
Dr Steven Laviolette (Western University)
Understanding the Positive and Negative Effects of Marijuana on Mental Health

17:00h – Social with appetizers at Alphie’s Trough
A1) THE EFFECTS OF PERINATAL EXPOSURE TO THC AND ACUTE COCAINE ADMINISTRATION ON ATTENTION AND INHIBITORY CONTROL
Aamna Qureshi, Alysha Sultan and Dr. Paul Mallet; Department of Psychology, Wilfrid Laurier University, Waterloo, ON

Cannabis and cocaine are two of the most commonly abused substances in Western populations. Recently, perinatal exposure to the main psychoactive ingredient in cannabis, Δ9-tetrahydrocannabinol (THC), has become increasingly prevalent. Moreover, cocaine use is often reported after early exposure to THC. This study aimed to investigate the relationship between perinatal exposure to THC and the effects of acute cocaine administration on attention and inhibitory control. 24 male CD(SD)I GS rats were used, 12 of which were exposed to 5 mg/kg of THC from postnatal day 4 to 14. Behavioural testing began in adulthood using the 5 Choice Serial Reaction Time Task as a measure of attention and inhibitory control. Each rat’s performance was measured after the administration of 2 mg/kg, 5 mg/kg, 15 mg/kg of cocaine, and a vehicle injection. A significant interaction was reported when examining the latency to make an incorrect response which suggested that higher doses of cocaine increased the latency to make an incorrect response when perinatally exposed to THC and the opposite was observed for lower doses. This finding suggests a potential influence of perinatal exposure to THC on the behavioural outcomes of cocaine administration, specific to inhibitory control.

A2) OPTOGENETIC STIMULATION OF THE MEDIAN RAPHE NUCLEUS PRODUCES ANXIETY-LIKE BEHAVIOR
A.R. Abela1,2, C. J. Browne1,2, A.D. Lé1 and P.J. Fletcher1,2,3 1Biopsychology section, Centre for Addiction and Mental Health, Toronto, ON, 2Department of Psychiatry and 3Department of Psychology, University of Toronto, Toronto, ON

There is a large body of evidence indicating that serotonin (5-hydroxytryptamine; 5-HT) neurons originating in the midbrain raphe nuclei contribute to the regulation of stress and anxiety. In laboratory animals, anxiety-like behavior is assessed using tests of approach-avoidance conflict in an innately fear-provoking context (e.g., open spaces). In such tests, pharmacological and genetic manipulations that enhance 5-HT activity induce avoidance of open spaces (Olivier et al., Neuroscience, 2008; Draper et al., Behav Brain Res, 2007). However, pharmacological manipulations often produce non-selective receptor activity at other targets, and genetic knock-out animals may be prone to compensatory mechanisms occurring during development. We examined whether optogenetic stimulation of 5-HT neurons originating in the median raphe nucleus (MRN) modulated the expression of anxiety-like behavior in three approach-avoidance contexts: 1) the elevated-plus maze, 2) novelty-suppressed feeding, and 3) marble burying. The optogenetic construct was created through expression of channel rhodopsin (ChR2) under the control of a serotonergic cre-driver, using a cross-breeding procedure of two mouse lines (Ai32 mice and ePet-cre mice). A chronically implanted optical fiber enabled delivery of 10 ms pulses of 10 mW blue light to the MRN. Optogenetic stimulation of the MRN at 4 Hz produced a set of behaviours consistent with an anxiety-like phenotype. These results demonstrate that 5-HT output from the MRN rapidly regulates the expression of anxiety-like behaviors, in contexts that innately illicit fear and approach-avoidance conflict. (Acknowledgements: Supported by NSERC and CIHR)

A3) DISRUPTING THE CRITICAL CIRCADIAN REGULATOR CLOCK ALTERS PREFRONTAL NEURON MORPHOLOGY, LEARNING AND MEMORY, AND RESPONSE TO MYOCARDIAL INFARCTION
Austin T.H. Duong1,2, Cristine J. Reitz1,2, Emma L. Louth3, Samantha D. Creighton3, Boyer D. Winters3, Tami A. Martin2,1, Craig D.C. Bailey1,2 1Centre for Cardiovascular Investigations, 2Department of Biomedical Sciences and 3Department of Psychology, University of Guelph, Guelph, ON

Circadian rhythms regulate many physiological processes and disrupted rhythms have adverse consequences on cardiovascular and neurological systems. However, the influence of circadian disruption on neurological responses to heart disease is unknown. We sought to determine whether the circadian factor CLOCK regulates responses to the cardiovascular system and to prefrontal neuron morphology and behaviour following myocardial infarction (MI; heart attack). Wild-type and functionally-deficient Clock1/Δ19 mice underwent either an MI or sham procedure. Post-MI, Clock1/Δ19 mice show reduced infarct expansion in the heart and preserved cardiac output compared with wild-type mice (12.18 ± 0.40 mL/min, 9.99 ± 0.58 mL/min respectively; p<0.05), indicating retention of cardiac structure and function. Prefrontal neuron morphology was assessed using the Golgi-Cox staining method. Apical dendrite length was lower in Clock1/Δ19 mice than in wild-type mice (339.1 ± 22.0 μm, 534.5 ± 26.5 μm respectively; p<0.05). However, MI increased apical dendrite length in Clock1/Δ19 mice, eliminating this genotype effect. To examine functional consequences of altered neuron morphology, a prefrontal-dependent object-in-place (OIP) recognition test was performed. Here, Clock1/Δ19 mice show OIP memory retention following an immediate time delay but impaired memory compared with wild type at a 5-minute time delay. These findings demonstrate that CLOCK plays an important role in normal prefrontal neuron morphology and can play a direct role in neurobehavioural responses post-MI.

A4) FOREST FOR THE TREES AFTER INHIBITING PREPOTENT RESPONSES: THE ASSOCIATION BETWEEN REWARD RESPONSIVENESS AND LOCAL FOCUS
Overriding one’s dominant response tendencies has been suggested to affect whether people see the “forest or the trees” (i.e., global/local bias), which is corroborated by evidence from both behavioural and electrophysiological measures. Since there are reliable individual differences in global/local processing, the extent to which inhibiting dominant tendencies is producing this change - above and beyond the effect of people’s individual differences in trait-like bias - is still unclear. Here undergraduate participants viewed hierarchical letters (e.g., the letter F made of T’s), both before and after completing incongruent (i.e., colour and meaning mismatch) or congruent (control) colour Stroop tasks, and they were asked to report the target letters within the global and local levels of the images as quickly as possible. Also, participants completed self-report questionnaires to measure their general trait-like tendencies (i.e., BIS BAS). Higher reward-focused participants tended to show a greater local bias after inhibiting during the incongruent Stroop task compared to the pre-Stroop baseline, relative to people with lower BAS. Importantly, no effects were found in the congruent Stroop. The findings from this study provide further support that approach-motivated tendencies are integral to better understanding the effect that executive functioning has on global/local bias. (Acknowledgements: Supported by NSERC)

A7) HYPERGLYCEMIA LINKED CHANGES IN HIPPOCAMPAL PHYSIOLOGY AND MEMORY PERFORMANCE OF GOTO-KAKIZAKI RATS

Chelsey Damphousse, Briana Renda, Diano Marrone; Wilfrid Laurier University, Waterloo, ON

Within the past five decades, prevalence of the common metabolic disorder, diabetes mellitus, has been increasing rapidly. Although the pathology of type I and type II diabetes differs, both are characterized by hyperglycemia, and both have been associated with cognitive decline and an increased risk of dementia. Using Goto-Kakizaki (GK) rats

A6) EFFECTS OF PHARMACOLOGICAL, GENETIC, AND OPTOGENETIC ENHANCEMENT OF 5-HT ACTIVITY ON RESPONDING FOR A PRIMARY REINFORCER

Caleb J. Browne1,2, Xiaodong Ji, Paul J. Fletcher1,2, 1Department of Psychology and 2Department of Psychiatry, University of Toronto, Toronto, ON, 3Section of Biopsychology, Centre for Addiction and Mental Health, Toronto, ON

Many lines of evidence suggest that serotonin (5-hydroxytryptamine; 5-HT) exerts an inhibitory influence over motivated behaviour. This effect has been hypothesized to be mediated by 5-HT neurons originating in the dorsal raphe nucleus (DRN), which densely innervate brain regions involved in reward processing. In the present experiments, we first examined the effects of acute or chronically elevated whole-brain 5-HT on lever pressing for the primary reinforcer saccharin (0.2%, 0.1 ml) in mice. Acute blockade of the serotonin transporter (SERT) with 10 mg/kg of the selective 5-HT reuptake inhibitor citalopram significantly reduced responding for saccharin. Similarly, constitive genetic deletion of the SERT (SERT-KO), which chronically elevates extracellular 5-HT, reduced responding for saccharin. Next, we examined whether these inhibitory effects of elevated 5-HT on responding for saccharin could be recapitulated by optogenetic activation of DRN 5-HT neurons. To generate this optogenetic construct, Ai32 mice, which can express ChR2 via cre-mediated excision of an upstream floxed-STOP cassette were crossed with the serotonegic cre-driver line ePet-cre. Photostimulation of DRN 5-HT neurons had no effect on responding for saccharin at a range of frequencies (1, 5, 10, 20 Hz). However, combining DRN photostimulation with citalopram produced a synergistic decrease in responding for saccharin. Together, these results suggest that increasing 5-HT DRN output has an inhibitory influence on incentive motivation, but this effect depends heavily on the function of the SERT. (Acknowledgements: NSERC Doctoral Scholarship to CJB; CIHR operating grant to PJF)

A5) INVESTIGATING THE ROLE OF THE VENTROMEDIAL PREFRONTAL CORTEX IN AFFECTIVE THEORY OF MIND AFTER MILD HEAD INJURY

Caitlyn Gallant* and Dr. Dawn Good1,2; 1Department of Psychology and 2Centre for Neuroscience, Brock University, St. Catharines, ON

The ability to infer the mental states of others – known as theory of mind (ToM; Baron-Cohen et al., 1985) – is an essential component of social cognition. ToM allows us to understand and anticipate others’ thoughts and feelings, facilitating interpersonal relationships. Following mild head injury (MHI), this ability is largely compromised, particularly with respect to affective ToM or emotional inferences (e.g., Bellerose et al., 2015). Affective ToM is thought to depend on the internal simulation of others’ affective states (Kalbe et al., 2007) and is subserved by the ventromedial prefrontal cortex (vmPFC; Leopold et al., 2012) – a region that is highly susceptible to disruption in closed-head injury (Morales et al., 2007). Indeed, vmPFC damage after MHI has been associated with attenuated physiological arousal (van Noordt & Good, 2011) and decreased vigilance to emotional cues (Gallant & Good, 2016). The current study investigated physiological arousal as a mechanism of affective ToM impairment after MHI. 70 students (N=30, N=40) read and responded to affective and cognitive ToM scenarios while electrodermal activation (EDA) was recorded. In the MHI group, EDA during the reading of affective scenarios significantly predicted affective ToM performance, b = 2.89, 95% CI [1.007, 4.776], while no relationship was observed for cognitive scenarios. In contrast, arousal during affective scenarios was unrelated to ToM performance, b = .092, 95% CI [-.306, .490] in the no-MHI group. These results may reflect the role of arousal cues regarding others’ emotional states, and support the vmPFC’s role in affective ToM. (Acknowledgments: Supported by the Canadian Institutes of Health Research (CIHR) – Frederick Banting and Charles Best Canada Graduate Scholarship)

A4) GENETIC, AND OPTOGENETIC ENHANCEMENT OF 5-HT ACTIVITY ON RESPONDING FOR A PRIMARY REINFORCER

Chelsey Damphousse, Briana Renda, Diano Marrone; Wilfrid Laurier University, Waterloo, ON

Within the past five decades, prevalence of the common metabolic disorder, diabetes mellitus, has been increasing rapidly. Although the pathology of type I and type II diabetes differs, both are characterized by hyperglycemia, and both have been associated with cognitive decline and an increased risk of dementia. Using Goto-Kakizaki (GK) rats
bred for persistent hyperglycemia in the absence of obesity, our research investigates the link between chronic hyperglycemia and diminished cognitive abilities. Through examination of memory performance and function within the hippocampus, preliminary data indicates deficits in performance on a what-where-when test of episodic-like memory in GK’s in comparison to Wistar rats of the same age. In addition, we are examining pattern expression of immediate early gene Arc, within the hippocampus of GK’s during completion of this task, or following spatial navigation. More specifically, pattern expression within the dentate gyrus will be analyzed, as this is the most likely brain region to mediate performance in a task involving high-interference stimuli. Our results will help to identify a functional link between hyperglycemia and hippocampal physiological changes.

A8) ELECTROPHYSIOLOGICAL EVIDENCE FOR TEMPORALLY DISTINCT EFFECTS OF ENCODING, MAINTENANCE, AND PERCEPTUAL FIDELITY IN OBJECT-SUBSTITUTION MASKING
Christine M. Salahub, Stephen M. Emrich; Department of Psychology, Brock University, St. Catharines, ON
Previous studies examining visual working memory (VWM) as well as those investigating visual awareness have studied an electrophysiological component called the sustained posterior contralateral negativity (SPCN). In VWM tasks this component is modulated by changes in working memory load, whereas in awareness-related tasks it is attenuated by conditions of unawareness. Therefore, the goal of the current study was to examine the concurrent effects of set size and visual awareness on the SPCN component. To study changes in awareness we used an object-substitution masking (OSM) paradigm wherein a target item is rendered invisible by a sparse four-dot mask. Participants were shown either two or four Landolt-Cs from which they had to find the target (masked or unmasked). It was found that the two manipulations (set size and mask) had temporally distinct effects on the SPCN. Mask condition had an effect in the early delay period (eSPCN) and set size in the late period (lSPCN). The eSPCN had greater amplitude during masked trials, whereas the lSPCN increased in amplitude for larger set sizes. Additionally, both early and late SPCN amplitudes were related to response precision, such that more precise responses resulted in greater amplitude than less precise responses. Overall, results from this study demonstrate that the SPCN reflects multiple processes occurring over time, including working memory encoding and maintenance as well as the fidelity of information maintained in memory.

A9) MEDIAL FRONTAL ALPHA ATTENUATION AND TRAIT ANXIETY IN AN ANTISACCADE TASK
Cody Gogo1,2, Melissa Nichol2, Jan Frijters2, and Ayda Tekok Kilic1,2; 1Department of Psychology and 2Department of Child and Youth Studies, Brock University, St. Catharines, ON
Medial frontal alpha modulation has been implicated as an important factor in successful completion of tasks that require effortful control. This effect has further been shown to interact with anxiety levels. In this study, we were interested in exploring the relationship between medial frontal alpha and trait anxiety. We employed a saccade/antisaccade paradigm in tandem with EEG to assess medial frontal alpha modulations in people with high and low trait anxiety during a difficult preparatory task. 23 participants responded to cues which signaled either pro-saccades or anti-saccades to response probes. A cluster of medial frontal EEG sites was then submitted to resampling, and spectral power for pro- and anti-saccade trials was extracted and compared for high and low anxiety groups. The results show an interaction such that low anxiety individuals exhibit reduced alpha power during the preparatory period for correct anti-saccade responses when compared to the high anxiety group, while no difference occurs for correct pro-saccade responses. Moreover, this observed alpha attenuation was not present for error trials in both high and low anxiety groups. These findings may highlight possible neurophysiological differences underlying cognitive control in people with high and low trait anxiety.

A10) DELTA-9-TETRAHYDROCANNABINOL (THC) IN THE HIPPOCAMPUS STRONGLY MODULATES PREFRONTAL CORTICAL NEURONAL ACTIVITY STATES AND THETA-WAVE OSCILLATORY PATTERNS: IMPLICATIONS FOR MARIJUANA-RELATED COGNITIVE DEFICITS
Dinat Khan1 and Dr. Steven Laviolette1,2; 1Department of Neuroscience and 2Department of Anatomy and Cell Biology, Western University, London, ON
Exposure to marijuana has been shown to be correlated with cognitive deficits in working and episodic memory. Delta-9-tetrahydrocannabinol (THC) is the primary psychoactive compound in marijuana and it activates the cannabinoid CB1 receptors distributed in the limbic cortex. THC infusions into the ventral hippocampus (vHIPP) activates vHIPP neurons as well as inducing hyperactivity in the nucleus accumbens and ventral tegmental area, two neural regions that are functionally connected to the hippocampus (Loureiro et al., 2015, 2016). However, the effects of hippocampal THC on prefrontal cortical (PFC) neurons has yet to be explored. The objective of this study is to determine how infusing THC into the hippocampus will affect neuronal activity in the mPFC. Male Sprague Dawley rats were used for in vivo electrophysiology, and were infused with THC or vehicle control in the dorsal or ventral hippocampal regions. An electrode was inserted into the mPFC to measure cell activity. Preliminary results show an increase in mPFC cell bursting activity when THC is infused into the vHIPP. This is of particular interest as neuron burst activity in the PFC is correlated with the consolidation and formation of associative emotional memories. Additionally, a significant decrease in theta oscillations was observed in the PFC. These cortical oscillatory patterns are associated with working memory functioning. Thus, our preliminary results identify the ventral hippocampal-PFC pathway as an important neural circuit mediating central effects of THC on cognition-related neuronal activity patterns.
A11) ANDROGEN RECEPTOR OVEREXPRESSION LEADS TO A REVERSIBLE DEFICIT IN FEAR-CONDITIONING IN MALE MICE

Firyal Ramzan1,2, Amber Azam1, Ashlyn Swift-Gallant4, Ashley Monks1,2,3, Iva Zovkic1,3; 1Department of Psychology, 2Neuroscience and 3Cell and Systems Biology, University of Toronto, Toronto, ON, 4Dept. of Neuroscience, Michigan State University, East Lansing, MI, USA.

Hormones have a significant effect on fear memory. Ovarian steroid hormones (e.g. estrogen) facilitate contextual and cued fear conditioning in female mice. In fact, the ERβ plays an important role in regulating contextual fear conditioning in both male and female mice. While estrogen and its receptors have been relatively well-studied in the context of fear conditioning, much less is known about the role of androgens (e.g. testosterone) and the androgen receptor (AR) in memory formation. We attempt to fill the gap in the literature pertaining to modulation of fear memory through AR. Previous literature shows mixed results, showing that testosterone either leads to either a reduced or an enhanced contextual fear response. We generated transgenic mice that overexpress ARs and compared transgenic males with their wild-type (WT) conspecifics. Behaviourally, we see that AR overexpression leads to deficits in fear memory. Gonadectomy eliminated group differences between AR-overexpressing and WT males, implicating testosterone as a negative regulator of fear memory. Further, upon treatment with the AR-blocker flutamide, the original deficit in freezing is rescued and is comparable to WT controls, suggesting AR as a protective factor against fear conditioning. We additionally found that gene expression of h2afz (as well as other genes implicated in memory and/or epigenetics) was altered in transgenic males after gonadectomy and flutamide treatment. These results suggest a role of AR in modulating fear memory and genetic expression in the CA1 region of the hippocampus. (Acknowledgment: Natural Sciences and Engineering Research Council of Canada (NSERC) Discovery Grant awarded to Dr. Ashley Monks; NSERC Grant and Connaught Fund awarded to Dr. Iva Zovkic)

A12) AGE OF ONSET OF OBSESSIVE-COMPULSIVE DISORDER PREDICTS BEHAVIOURAL SYMPTOM SEVERITY IN WOMEN DURING THE PERINATAL PERIOD

Gabriella F. Mattina1,2, Lauren Mak2, Geoffrey Hall2, Meir Stein2,4; 1McMaster Integrative Neuroscience and Discovery & Study (MINDS), McMaster University, Hamilton, ON, 2Women’s Health Concerns Clinic, St. Joseph’s Healthcare, Hamilton, ON, 3Centre for Neuroscience Study, Queen’s University, Kingston, ON, 4Department of Psychiatry and Behavioural Neurosciences, McMaster University, Hamilton, ON.

Obsessive-compulsive disorder (OCD) is a debilitating psychiatric disorder, with sex and age of onset (AO) differences. Women are at higher risk for exacerbation of obsessive-compulsive (OC) symptoms during the perinatal period, where new symptoms focused on the fetus/newborn may emerge. We explored whether AO was a predictor of OC symptom severity and mood during the perinatal period. Eighteen women with pre-existing OCD, including comorbid depression, were seen during 2nd-3rd trimester of pregnancy and 3-6 months postpartum. Behavioural measures collected at each time point included the Perinatal Obsessive-Compulsive Scale (POCS), Y-BOCS, EPDS and STAI. AO was defined as age at symptom presentation. Linear regression models examined whether AO predicted behavioural symptoms, with age and depression comorbidity as covariates. AO was a significant predictor of perinatal OC symptom severity in postpartum only, p=0.01, R²=0.44. During pregnancy, AO predicted depression scores, p=0.01, R²=0.42, and state anxiety scores, p=0.003, R²=0.53, but not trait anxiety. It failed to predict non-perinatal OC severity, as well as anxiety or depressive scores postpartum. In summary, earlier AO was associated with increased state anxiety and depression scores in pregnancy and more severe perinatal OC symptoms postpartum. Women with an earlier OCD AO may be more vulnerable to worsened behavioural symptoms in the perinatal period. (Acknowledgements: Supported by The Effort Trust Company)

A13) NEUROPHYSIOLOGICAL CORRELATES OF STEREOTYPIC BEHAVIOUR IN AMERICAN MINK (NEOVISON VISON)

Maria Diez-León1, Lindsey Kitchenham2, Rob Duprey2, Craig Bailey3, Elena Choleris1, Mark Lewis3, Georgia Mason1; 1Department of Animal Biosciences, 2Department of Psychology and 3Department of Biomedical Sciences, University of Guelph, Guelph, ON, 4Department of Psychology, University of Florida, USA.

Stereotypic behaviour (SB) is symptomatic of disorders such as autism. In addition, millions of caged animals (e.g. on farms and in zoos) perform SB. To date, data on the neural bases of cage-induced SB come from only three species. In barren-housed deer mice, SB results from disinhibition of the basal ganglia (BG)’s ‘motor loop’. SB in horses and C57Bl/6 mice instead results from overactivation of the ‘limbic loop’. We investigated whether similar housing-induced changes in motor or limbic loops are responsible for SB in a model carnivore, the American mink. We raised 32 males in non-enriched (NE) vs enriched (E) cages and assessed SB after 2 years. Post-mortem, neuronal activity was analysed via cytochrome oxidase (CO) staining of dorsal striatum (caudate; putamen, PT), globus pallidus (externus, GPe; internus, GPi), subthalamic nucleus (STN) and nucleus accumbens (NAC). The GPe:GPi ratio was also calculated to assess relative activation of inhibitory/excitatory pathways in the motor loop. NE mink stereotyped more, and had lower GPe:GPi ratios (but with no one single BG area being affected by housing). Stepwise regressions revealed that mink SB is best explained by a combination of activity in the PT, NAC, relative activities of inhibitory/excitatory pathways, and housing conditions per se. These results thus implicate both motor and limbic loops, but also highlight that BG function alone does not fully explain housing effects on SB, with areas outside of the
A14) SEX-SPECIFIC EFFECTS OF REPEATED CB1 RECEPTOR ANTAGONISM AND CONFINEMENT STRESS ON ANXIETY AND STRESS RESPONSES, AND ON CORTICOLIMBIC PROTEIN EXPRESSION, IN ADOLESCENT LONG-EVANS RATS
Jonathan J. Simone1, Jennet L. Baumbach2, and Cheryl M. McCormick1,2,3, 1Department of Biological Sciences, 2Department of Psychology and 3Centre for Neuroscience, Brock University, St. Catharines, ON
The endocannabinoid system continues to mature in adolescence, however, little is known about the consequences of altered endocannabinoid signalling during this period. We hypothesized that repeated CB1 receptor antagonism during adolescence would increase neuroendocrine stress responses and anxiety, and alter the expression of plasticity-related proteins in the hippocampus and prefrontal cortex, and that these effects would be potentiated when paired with repeated isolation stress in male (experiment 1) and female (experiment 2) rats. For each experiment, rats were treated daily on postnatal days (P)30-44 with either no injection, vehicle, or AM251 (1 mg / kg), and half of each group was either returned to the homecage (No Stress) or underwent 1h confinement (Stress). On P45, measures were obtained in subgroups on anxiety in the elevated plus maze (EPM), plasma corticosterone (CORT) release to confinement stress, and baseline protein expression in the hippocampus and prefrontal cortex. Another subgroup was tested on P46 for activity in a novel environment and interactions with a novel conspecific. Our results demonstrate independent effects of repeated CB1 receptor antagonism and repeated confinement stress during adolescence on anxiety behaviours, neuroendocrine stress responses, and corticolimbic protein expression in both males and females. Further, we observed a different pattern of effects in male and female rats. Together our results demonstrate a sex-specific role of adolescent endocannabinoid signalling in the regulation of stress and anxiety responses. (Acknowledgements: Supported by a NSERC Discovery Grant)

A15) THE EFFECTS OF RESISTANCE TRAINING ON COGNITIVE FUNCTION IN OLDER ADULTS WITH PRE-DIABETES
Joyla Furlano, Phil Parrot-Migas, Michelle Wong, Dr. Lindsay Nagamatsu; Neuroscience, Schulich School of Medicine and Dentistry, Western University, London, ON
Evidence suggests that brain and cognitive health worsen as pre-diabetes progresses to type II diabetes. Older adults are especially at high-risk of developing type II diabetes due to increased sedentary lifestyles and naturally declining health. Baker and colleagues (2010) showed that increased levels of aerobic training improve cognitive function (executive function, memory) in pre-diabetic older adults; but research has not yet looked at whether resistance training (RT) produces similar results in this population. To address this question, we will conduct a 6-month randomized control trial exercise intervention on older adults with pre-diabetes. Specifically, we will examine whether RT can improve associative memory and whether this will correlate with increased functional activation in the hippocampus and increased hippocampal volume, as shown in other populations of older adults. Our findings have the potential to unveil a cost-friendly intervention strategy to preserve and improve cognitive function in pre-diabetics, reduce the prevalence of diabetes and associated diseases such as dementia, and improve the overall quality of life for older adults.

A16) PRESERVED FACE SENSITIVITY OF THE N170 ERP COMPONENT ACROSS FACE SIZE
Karisa B. Parkington, R. Elif Ermis, & Roxane J. Itier; Department of Psychology, University of Waterloo, Waterloo, ON
The N170 is an early face- and eye-sensitive ERP component. Recent evidence has demonstrated an N170 sensitivity to eyes even within the context of a whole face, questioning the generally accepted view that this ERP component reflects holistic processing. The present study tested whether this eye sensitivity varied with face size. We compared N170 modulations when facial features (left eye, right eye, nose, and mouth) were fixated within faces of varying sizes. One group of participants viewed small faces (2°, 4°, 6°, and 8°), and a second group of participants viewed larger faces (8°, 10°, 12°, and 14°). Featural fixation was enforced using a gaze-contingent eye-tracking procedure. The N170 did not vary with larger face sizes; however, the smallest face size (2°) elicited attenuated amplitudes compared to mid-range sizes (6° and 8°) for left eye fixation only. Critically, an eye sensitivity was observed for all face sizes, with larger and later N170 responses to faces fixated on an eye, compared to nose or mouth fixations, which did not differ. These results highlight the particular sensitivity of the N170 to eye information, and demonstrate that this sensitivity starts at 2° size and is fully established at 4° and beyond. In line with recent gaze-contingent ERP studies, these findings support the view that the N170 does not reflect a purely holistic process. Early face perception may instead rely on a complex integration of featural and holistic processing mechanisms where eyes play a central role. Implications for theories of face perception will be discussed. (Acknowledgements: This project was funded in part by the Ontario Provincial Government Early Researcher Award (ER11-08-172), Natural Sciences and Engineering Research Council of Canada (NSERC) Discovery Grant (418431), Canada Foundation for Innovation (CFI; 213322), and the Canada Research Chair program (213322, 230407). The presenting author is also supported by a Canadian Institutes of Health Research (CIHR) Frederick Banting and Charles Best Doctoral Research Award.)
A17] PRIOR EXPOSURE TO STRESS IN ADOLESCENCE ALTERS ADULT FEMALE RATS’ TRYPHTOPHAN HYDROXYLASE PROFILES IN THE DORSAL RAPHE

Katheron A. Intson1, Cindy Tao1, and Janet L. Menard2,1; 1Department of Psychology and 2Centre for Neuroscience Studies, Queen’s University Kingston, ON

Prior studies link anxiety to alterations in serotonergic neurotransmission. We previously found that female rats exposed to intermittent physical stress (IPS) during early adolescence display increases in anxiety-behaviour associated with alterations in serotonin (5-HT) fiber density in the medial prefrontal cortex (Tao, Dhamija, Booji, & Menard, submitted). It is not known whether IPS in early adolescence also alters 5-HT-producing cells in the dorsal raphe. This question was addressed using archival brains from the original IPS study. Half the female rats in that study had been exposed to IPS, and the remaining animals served as a handled control group. At the end of the stress regimen, the rats were left undisturbed until their brains were harvested in adulthood. After slicing the archival brain tissue, I used tryptophan hydroxylase (TPH) immunoreactivity (-IR) to label 5-HT cells in the dorsal raphe. An independent-samples t-test indicated that the IPS animals had higher levels of TPH-IR in the ventrolateral region of the dorsal raphe, t(6.88) = 2.39, p = 0.049, but not the dorsal portion of the dorsal raphe, as compared to controls. This suggests that adversity in early adolescence has a lasting impact on serotonergic cell function in adulthood. Future studies should replicate these findings in animals exposed to behavioural testing, and investigate whether TPH-IR correlates to levels of anxiety-like behaviour. (Acknowledgements: Supported by NSERC)

A18] MODULATION OF THE ENDOCANNABINOID SYSTEM ATTENUATES NALOXONE-PRECIPITATED MORPHINE WITHDRAWAL-INDUCED PLACE AVERSIONS IN ACUTELY DEPENDENT RATS

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Modulation of the endocannabinoid system is effective in reducing somatic symptoms of opioid withdrawal, however, much less is known regarding its ability to reduce affective opioid withdrawal. Affective opioid withdrawal can be quantified using a naloxone-precipitated morphine withdrawal (MWD) induced conditioned place aversion (CPA). Rats are made acutely dependent with a single high dose of morphine and withdrawal is precipitated 24 hours later with naloxone. Using this paradigm, the ability of systemically administered CB1 receptor antagonists/neutral antagonists (AM251, AM4113, AM6527) and inhibitors of endocannabinoid hydrolysis (fatty acid amide hydrolase, FAAH; monoacylglycerol lipase, MAGL) were evaluated to prevent the establishment of the MWD CPA. All CB1 receptor antagonists tested and the MAGL inhibitor (elevates 2-arachidonoyl glycerol), MJN110, interfered with the MWD CPA. The two FAAH inhibitors tested (elevates anandamide), PF3845 and URB597, were without significant effect. An evaluation of the brain regions mediating the systemic effects of these compounds revealed a double dissociation of CB1 receptor antagonism and agonism to reduce establishment of the MWD CPA in the extended amygdala and associated regions. Specifically, the CB1 receptor antagonist, AM251, interfered with the CPA when microinfused into the central nucleus of the amygdala and the bed nucleus of the stria terminalis, whereas the MAGL inhibitor, MJN110, interfered with the CPA when microinfused into the basolateral amygdala and the interceopective insular cortex. The findings presented suggest that modulation of the endocannabinoid system may have therapeutic potential in the treatment of affective opioid withdrawal. (Acknowledgements: Funded by grants from the Natural Sciences and Engineering Council of Canada, Canadian Institutes of Health Research, and the National Institutes of Health)

A19] INVESTIGATING POST-CONCUSSIVE IRRITABILITY, FATIGUE, ANXIETY, AND AUTONOMIC AROUSAL FOLLOWING MILD HEAD INJURY

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Irritability, fatigue and anxiety symptoms are common complaints in the general population. However, following mild head injury (MHI), the frequency, intensity, and duration of these types of symptoms may be more evident and/or exacerbated, and possibly reflect a contributing underlying neural mechanism. This study investigated differences in self-reported anxiety-related post concussive symptoms, in university students with and without a reported history of MHI. Differences in symptomology as a function of area of injury were also examined, as was overall physiological arousal (as indicated by electrodermal activation [EDA]). Students who reported a history of MHI endorsed more frequent, intense, and prolonged symptoms of irritability, fatigue, and anxiety; this was particularly evident for individuals who reported injury towards the front of the head. Lastly, despite increased anxiety-related behavioural descriptions, EDA levels were lower in students who reported a MHI. These outcomes may be due to disruption between the ventromedial prefrontal cortex (VMPFFC) and subcortical structures involved in regulating autonomic arousal levels. Dysregulation may result in irritability and anxiety-like symptoms due to overreaction of an otherwise dampened autonomic arousal system in persons with MHI; lessened physiological arousal lowers one's cognitive monitoring and preparedness of the environment resulting in frequent unexpected outcomes. Further the higher
incidence of fatigue and anxiety in individuals with frontal injury may provide support for VMPFC-subcortical disruption.

A20)  Dopamine Antagonism Blocks Morphine Reward in Neuropathic and Pain-naïve States

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The rewarding properties of opiates are mediated through the mesolimbic dopamine (DA) pathway, although this may be limited to drug naïve states. Morphine reward is mediated through non-DA systems when animals are drug dependent. This study examined whether the same phenomenon extends to pain conditions by testing whether DA mediates morphine reward in both chronic neuropathic pain and pain-naïve states. Using the conditioned place preference (CPP) paradigm as a measure of drug reward, rats (n = 7-8 per group) were injected with 4mg/kg morphine or saline over four sessions. In a separate experiment, rats underwent a chronic constriction injury (or sham) surgery to induce neuropathic pain. In the CPP, all animals received injections of the DA antagonist 0.8mg/kg flupenthixol with 4mg/kg morphine or saline alone. Rats treated with morphine spent more time (s) in the drug-paired compartment, indicating that the drug was rewarding. DA antagonism blocked morphine reward in both chronic neuropathic pain and pain naïve states, suggesting no dissociation between the two. The mesolimbic DA pathway appears to mediate morphine reward in both chronic neuropathic pain and pain-naïve conditions, although the CPP blockade by DA antagonism may also reflect learning deficits. (Acknowledgements: Supported by NSERC and CIHR)

A21)  Ethanol Exposure Reduces Vibration Induced Anxiety-like Behavior in Zebrafish

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Current behavioral tests for anxiety in zebrafish include the open-field, light-dark preference, and novel tank test. The purpose of the current study was to develop a high-throughput anxiety test for zebrafish. To achieve this, we designed a manual release bridge containing a weight that could be released from the right or left side of the tank, creating a physical barrier that zebrafish have to overcome to reach food. By placing 4mg/kg morphine on the right side, we expected to be aversive for the zebrafish. To pharmacologically validate our behavioral paradigm, 100 zebrafish were individually exposed to a solution containing 0, 0.25, 0.5 or 1 vol/vol % ethanol, an anxiolytic substance at the doses employed, for 60 minutes in a 37L tank. The weight was released to hit the side of the tank after 50 minutes. We measured numerous behavioral responses of zebrafish including total distance traveled, distance to tap side, absolute turn angle, distance to bottom, and variance of distance from the bottom. The machine successfully induced anxiety-like behaviors in zebrafish and ethanol exposure was observed to reduce these behaviors. For example, ethanol decreased the total distance travelled post-tap, increased vertical exploration, decreased distance away from tap side and also decreased absolute turn angle (likely because of reduced erratic movement). We conclude that the tapping assay as designed will be appropriate for high throughput screens of anxiolytic compounds.

A22)  The Relationship between Trait Mindfulness and Post-concussive Symptoms

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A variety of affective, cognitive and somatic symptoms occur following a head injury, such as anxiety, attention deficits, and headaches. These symptoms may continue to persist even after 1 year post-injury. Previous studies have found that there is a relationship between anxiety and cognitive impairment following moderate to severe head injury (Spitz et al., 2013; Gould et al., 2014; Linn, Allen & Willer, 1994). The current study extends this research by examining the relationship between anxiety and cognitive impairment in a mild head injury student population (MHI). Results indicate that individuals with high cognitive impairment following MHI also had high anxiety. Mindfulness may be useful in reducing post-concussive symptoms because it involves a non-judgmental contact with the environment where one is constantly aware of the present moment. The current study investigates the relationship between mindfulness, anxiety and cognitive impairments following mild head injury using self-report questionnaires in an undergraduate student population. Results indicate that individuals high in mindfulness had low anxiety and low cognitive impairments in working memory, cognitive flexibility and inhibition. These findings suggest that mindfulness can mitigate anxiety and cognitive impairments following MHI and a mindfulness based intervention could be useful following MHI.

A23)  Rapid Facilitation of Social Recognition by Estrogen Receptor Alpha or G-Protein Coupled Estrogen Receptor Activation in the Dorsal Hippocampus Is MEK/ERK Pathway Dependent

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Estrogens affect learning and memory through classical/genomic/delayed (hours-days) and non-classical/rapid (within minutes) mechanisms. Social recognition (SR) is rapidly facilitated by systemic administration of 17β-estradiol (E2), estrogen receptor (ER) agonist PPT, ERα agonist DPN, and the G-protein coupled estrogen receptor (GPER1) agonist G-1 (Phan et al., 2011, 2012; Gabor et al., 2015). Dorsal hippocampal infusion of E2, PPT, or G-1, but not DPN, also facilitated SR (Phan et al., 2015; Lymer et al., 2017). Through activation of the MEK/ERK pathway, estrogens rapidly affect object and spatial memory consolidation (Fernandez et al., 2008; Fan et al., 2010; Fortress et al., 2013), dendritic spine density (Sellers et al., 2015; Tuscher et al., 2016), and SR (Sheppard et al., 2016). These results suggest the MEK/ERK pathway may also mediate rapid action of ERα and GPER1 on SR. In this study, young adult, ovariecotomized mice received bilateral intrahippocampal infusions of MEK/ERK inhibitor U0126 (0.5μg/side) 5min prior to PPT (19.32pg/side) or G-1 (41.22pg/side). Subjects performed a SR task in which two conspecifics were presented for two 5min sample phases and one 5min test with a choice between a previously encountered conspecific and a novel conspecific. This paradigm took only 40min from ER agonist/control treatment to completion; likely too little time for genomic actions. U0126 was capable of blocking facilitation of SR by PPT or G-1, suggesting that downstream signaling through MEK/ERK by ERα or GPER1 activation is necessary for their facilitating effects. (Acknowledgements: Supported by NSERC)

A24) ANTAGONIZING NUCLEUS ACCUMBENS DOPAMINE D1-TYPE RECEPTORS AFFECTS SOCIAL LEARNING BUT NOT FOOD INTAKE IN MALE AND FEMALE MICE

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Through social learning animals acquire novel information from conspecifics. The neurobiological mechanisms underlying social learning are little understood. With systemic treatments, we showed a role for dopamine (DA) D1-type receptors in social learning, and D2-type receptors in feeding behavior in the social transmission of food preferences (STFP) in mice. The brain regions of action are being investigated. DA projections from the ventral tegmental area ascend to various limbic structures including the hippocampus and nucleus accumbens (NAc). We showed that hippocampal D1-type and D2-type receptors mediate female social learning, whereas only hippocampal D1-type receptors mediate male social learning. NAc D1-type receptors are implicated in social behavior and individually acquired food preferences in rodents. Hence, in this study we investigated the role of NAc D1-type receptors in the STFP. We infused the D1-type receptor antagonist SCH23390 (at 1, 2, & 4 μg/μL) bilaterally into the NAc shell of adult male and female CD-1 mice 15 min before a 30-min social interaction (where social learning occurs) with a recently fed same-sex conspecific. We found that SCH23390 at 1 μg/μL blocked social learning in males, and SCH23390 at 4 μg/μL blocked social learning in females. This social learning blockade could not be explained by generalized changes in feeding behavior, since SCH23390 did not significantly affect total food intake in either sex. Hence, these results add the NAc shell as one site of DA/D1-type receptors mediation of social learning. (Acknowledgements: Supported by NSERC)

A25) KEEPING IT TOGETHER: INTER-TRIAL COHERENCE OF EVENT-RELATED POTENTIALS AFTER SLEEP DEPRIVATION

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Sleep deprivation is known to impair brain function and leads to increased variability in tasks requiring a timed response. Jackson et al. (2008) showed that 27 hours of sleep deprivation has no effect on the P100 amplitude, but diminishes the P300 amplitude, concluding that the effects of sleep deprivation occurs during cognitive processing. Instead of examining only averaged ERP amplitudes after sleep deprivation, we also examined the inter-trial coherence (ITC), a measure of phase angle alignment across trials in the following ERP components: P100, CRN and P300. The P100 is stimulus locked and elicited during early stages of visual processing. The CRN is response locked and produced after correct responses, and the P300 is stimulus locked and is thought to represent attention or resource allocation. Participants (N=11, mean age=20 y, SD = 1.9) were tested after 2 hours and after 20 hours of wakefulness (counterbalanced). A flanker task was presented during each session and 128-channel EEG was recorded. Trials were bootstrapped 1000 times with 20% trimmed means to produce the ITC results. After sleep deprivation, the amplitude of the P100 was reduced and there was increased ITC at 150 ms. The amplitude of the CRN and the ITCs for both the CRN and P300 were higher in the alert condition. These results provide evidence that the effects of sleep deprivation occur during cognitive decision making and some stages of early visual information processing. (Acknowledgements: Supported by NSERC to SJ)

A26) THE ROLE OF MEMBRANE-BOUND ESTROGEN RECEPTORS IN RAPID ENHANCEMENTS OF LEARNING AND MEMORY WITHIN THE HIPPOCAMPUS OF FEMALE MICE

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In addition to producing genomic effects, estrogens are known to enhance various types of learning and memory within a rapid timescale. Intra hippocampal infusions of 17β-estradiol, a potent and naturally produced estrogen, produce enhancements of recognition learning in ovariecotomized female mice within 40-minutes of drug
administration. The 40-minute timescale suggests that these enhancements are likely produced by non-genomic mechanisms as opposed to the better-documented genomic mechanisms of estrogenic enhancements of learning and memory. In order to begin to uncover the specific mechanisms underlying these rapid enhancements within the hippocampus, the role of membrane-bound receptors, specifically, was investigated. Using 40-minute rapid learning paradigms, performance on social recognition, object recognition and object placement, or the abilities to discriminate between conspecifics, objects or object spatial positions, were assessed following intrahippocampal infusions of bovine serum albumin conjugated estradiol (BSA-E2). By conjugating the estradiol with a large protein molecule (BSA), the estradiol is no longer able to pass through the cell membrane as it normally would, and thus, from binding to intracellular receptors. Significant enhancements of learning and memory were seen following the BSA-E2 infusions at similar doses to the unconjugated estradiol, suggesting that membrane-bound estrogen receptors within the hippocampus play an important role in the previously reported rapid estrogenic enhancements of learning and memory within the hippocampus. (Acknowledgments: Supported by NSERC)

A27) RAPID EFFECTS OF HIPPOCAMPALLY SYNTHESIZED ESTROGENS ON RECOGNITION LEARNING IN FEMALE MICE
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Estrogens are involved in learning and memory, and enhance stimulus recognition when administered exogenously either systemically or in the dorsal hippocampus (HPC). These effects are mediated by rapid, non-genomic, mechanisms of action. Furthermore, the hippocampus and other brain regions synthesize estrogens and the role of these physiological estrogens remains unclear. In the current study, we investigated the role of endogenous estrogens within the HPC and their rapid effects on recognition learning. We administered the potent aromatase inhibitor Letrozole (0.005, 0.025, and 0.05 μg/hemisphere) or 2% dimethyl sulfoxide (DMSO) vehicle bilaterally into the HPC of 2-month old ovariectomized mice 15 minutes before testing in either Social or Object Recognition. In order to explore the rapid effects of estrogens, these paradigms were run within 40-minutes of treatment. Mice underwent three 4-minute habituations (where either two objects or two same-sex gonadectomized conspecífics were repeatedly presented), followed by a 4-minute test (where one repeated stimulus was exchanged for a novel one), all separated by 3-minute rest periods. The data are currently being collected. These findings could potentially contribute to the understanding of the rapid mechanisms through which estrogens act within the HPC and their physiological role in recognition learning. These results may also provide insights into how to develop more specific treatments for post-menopausal women experiencing cognitive deficits, as current pharmacological treatments produce unwanted side effects, which has led to fewer women seeking treatment. (Acknowledgments: Supported by NSERC)

A28) DISPOSITIONAL AFFECT AND SENTENCE PROCESSING
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Affective state is known to influence cognitive processing (Loftus et al., 1987). Here we investigate whether this relation extended to linguistic processing. In a self-paced reading study, we examined whether individual differences in dispositional affect interact with sentence processing strategies. We focused on quantifier scope sentences such as (i) Every kid climbed a tree. These sentences lack any syntactic or lexical ambiguity, however, two possible meanings are available, where either many trees, or just one tree, was climbed. In Dwivedi (2013), it was proposed that these sentences are processed using “Heuristic first, algorithmic second” mechanisms. Presently, we hypothesized that individuals who report high positive affect would display a more global processing style and rely on heuristics when processing sentences (Clore & Huntsinger, 2007; see Chwilla et al., 2011) vs. those reporting negative affect, whom we expect would display a more local, algorithmically based (i.e. grammatical) processing mechanism. 27 participants read sentences such as (i), followed by either plural or singular continuation sentences, and then the question How many trees were climbed. Given the hypotheses above, we predicted that on-line reading times would correlate with positive affect scores, and question-response accuracy would correlate with negative scores, since the model posits Heuristic first (i.e., during on-line processing); algorithmic second (i.e., only if required by task demands). Results revealed a partial replication of Dwivedi (2013) reading time results, as well as significant correlations in the pattern expected. (Acknowledgements: Supported by SSHRC and CFI)

A29) COGNITIVE AND NON-COGNITIVE PHENOTYPES IN THE 5XFAD MODEL OF ALZHEIMER’S DISEASE
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Alzheimer’s Disease (AD) is a disabling chronic disorder characterized by progressive cognitive impairment, often beginning with memory loss and executive abnormalities. Patients may also experience gait disturbances. Given the high prevalence and poor prognosis of AD, the characterization of animal models with face validity reproducing cognitive and non-cognitive disturbances is extremely important. In this study, we performed a longitudinal evaluation of visual discrimination and cognitive flexibility in the 5xFAD mouse model of AD using the Bussey-Saksida pairwise visual discrimination (PVD) touchscreen task at 4, 7 and 10 months of age. Following the completion of the last time-
point, the mice were tested for various non-cognitive measures, including locomotor activity, gait and grip strength. Lastly, amyloid pathology was confirmed in these mice and because they were food restricted to perform touchscreen tests, the effect of mild food restriction on this pathology was also investigated. Food restriction did not affect amyloid pathology and at all time-points 5xFAD mice had no deficits in the PVD task. However, at 10 months of age these mice take longer than controls to respond to the task and collect their reward. 5xFAD mice also demonstrate gait disturbances, which could explain the delays that we observed in PVD. These gait impairments could not be attributed to neuromuscular function as grip strength was not affected. In summary, we provide a comprehensive evaluation of phenotypes in the 5xFAD mouse line that could be used for testing potential AD treatments. (Acknowledgements: Supported by CIHR and Weston Brain Institute)

A30) FROM AN ADOLESCENT STRESSED TO A SICK ADULT: THE LONG-TERM EFFECTS OF A MILD UNPREDICTABLE STRESS ON IMMUNITY

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Adolescence is one of the critical periods of development and have a great importance to health for an individual as an adult. Stressors have been shown to suppress immune function and increase susceptibility to inflammatory diseases. Thus, this study aimed to investigate the changes in sickness behavior, splenic T-lymphocytes subsets and macrophages induced by LPS treatment employing a mouse stress model during adolescence. 30 days old Balb/c male mice were subjected to a random pattern of stressful situations twice daily for ten days. Twenty days after the end of the stress protocol, the animals were challenged by LPS. The sickness behavior was assessed by observed symptoms and 48 hours later, mice were euthanized and splenic cells and blood were collected for phenotypic analysis. The experiments were performed in accordance with the guidelines of the Bioethical Committee of FMVZ, USP, Brazil (n◦ 4485180614). The sickness behavior assessment showed that stressed and challenged by LPS animals recovered more slowly than non-stressed and challenged by LPS group. Animals only stressed showed decreased in lymphocytes TCD8 and TCD4 subsets and animals stressed and challenged by LPS showed increased in macrophages and a decreased in macrophages MHC+ subset. In addition, there was a decrease of CD49b in all groups compared to the control group. Therefore, this unpredictable stress model causes long-term effects on immunity and appears to be a useful model in neuroimmunomodulation studies. (Acknowledgements: Supported by CAPES and CNPq)

A31) INVOLVEMENT OF PREFRONTAL GABAERGIC TRANSMISSION IN SCHIZOPHRENIA-LIKE BEHAVIOUR INDUCED BY CHRONIC ADOLESCENT THC EXPOSURE

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Chronic adolescent marijuana (MJ) use has been linked to the later development of schizophrenia (SCZ). GABAergic hypofunction in the prefrontal cortex (PFC) is a cardinal pathological feature of SCZ and may be a mechanism by which the PFC loses its ability to regulate sub-cortical dopamine (DA) resulting in SCZ-like neuropsychopathology. In the present study, we hypothesized that adolescent exposure to THC, the psychoactive component of MJ, can induce a SCZ-like phenotype in later adulthood by altering PFC GABAergic function resulting in dysregulation of sub-cortical DA transmission. We exposed adolescent rats (postnatal day (PND) 35 to 45) to THC. At adulthood (PND75), we studied the functionality of PFC GABAergic neurotransmission using molecular analyses, behavioural tasks and in vivo electrophysiological recordings of neurons in the PFC and the mesolimbic pathway. Our results show persistent (1) reduction of the GABAergic marker GAD 67 in the adult PFC and (2) hyperactive neuronal state in PFC neurons and associated disruptions in cortical gamma oscillatory activity. Finally, adolescent THC exposure-induced SCZ-like behaviours are reversed by infusions of a GABA-A receptor selective agonist muscimol in the adult PFC. Furthermore, activation of adult PFC GABA-A receptors normalizes the spontaneous firing of VTA DAergic neurons. Together, these results identify a mechanistic link between dysregulated frontal cortical GABAergic inhibition and sub-cortical DAergic dysregulation, characteristic of well-established SCZ endophenotypes. (Acknowledgments: This work was supported by the Canadian Institutes of Health Research (CIHR; MOP 246144) and the National Science and Engineering Research Council of Canada (NSERC))

A32) DEPRESSION DURING PREGNANCY AND SCHOOL READINESS IN SIBLINGS: A WORK-IN-PROGRESS

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Prenatal mental illness increases the likelihood of cognitive delays in offspring. This study used a within-family design to examine if differential maternal mental health status during 2 consecutive pregnancies predicts differences in school readiness between siblings. Data from 34 mother-sibling trios enrolled in the Hamilton cohort of the
Developmental ethanol exposure can lead to teratogenic outcomes in humans that are known as Fetal Alcohol Spectrum Disorders (FASD). One of the most prevalent neurocognitive impairments associated with FASD is attention deficits. We have shown previously that mice exposed to ethanol during development exhibit impaired attention in adulthood, and also exhibit altered physiology and morphology of pyramidal neurons located within layer VI of the medial prefrontal cortex (mPFC) that support this cognitive function. Here, we sought to determine whether these developmental ethanol-induced alterations to mPFC layer VI neurons are also present early in postnatal life.

A33) REDUCED FOS EXPRESSION TO SOCIAL INTERACTION AND ALTERED SYNAPTIC PLASTICITY IN SOCIAL BRAIN AREAS AFTER SOCIAL INSTABILITY STRESS IN ADOLESCENT MALE RATS

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In 3 experiments, we investigated how adolescent male rats exposed to social instability stress (SS; 1h isolation + return to unfamiliar cage daily from postnatal day (P) 30-45) differed from non-stressed controls (CTL) in social interactions with unfamiliar peers and on neural measures. In Expt. 1, SS and CTL rats were tested on an elevated plus maze (EPM) on P46, and on P47 they underwent a 15-min social interaction task. After controlling for locomotor activity on the EPM, a binary logistic regression found that SS rats spent less time in social interaction than did CTL rats (p=0.03). In Expt. 2, we measured Fos expression in several social brain areas of CTL and SS rats 1h after social interaction on P46. SS rats had lower Fos expression than did CTL rats in all brain regions (p=0.008). Further, CTL rats had a significant positive correlation between Fos expression in the medial amygdala (MeA) and time spent in social interaction (r=0.72), not found in SS rats. In Expt. 3, western blotting was used to investigate whether SS affected synaptic plasticity in the MeA and lateral septum (LS) at P46. Lower synaptophysin in the MeA and greater CaMKII in the LS were found in SS rats compared with CTL rats (p's=0.03). In conclusion, neural changes in the MeA and LS could underlie the reduced social interaction found in adolescent male SS rats. (Acknowledgements: Supported by NSERC)

A34) REDUCED EXPRESSION OF SYNAPSIN II IN THE MPFC MANIFESTS BEHAVIOURAL AND BRAIN METABOLIC CHANGES: IMPLICATIONS IN THE PATHOPHYSIOLOGY OF SCHIZOPHRENIA

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Schizophrenia (SZ) is a psychiatric disorder with few antipsychotic drugs (APDs) alleviating the associated spectrum of symptoms. Negative and cognitive symptoms, manifesting as social withdrawal and memory impairment respectively, evade current APDs. SZ treatment relies on targeting APDs to the underlying pathophysiology thus, elucidation is crucial for SZ APD design. Synapsin II (SynII) is a phosphoprotein responsible for vesicle trafficking of neurotransmitters involved in SZ. SynII has been implicated in SZ by genome wide association studies and reduced SynII mRNA levels in SZ post-mortem studies. To consolidate SynII's role in SZ, our study explored SZ-like behavioural phenotypes and brain metabolic changes after SynII knockdown (KD). A scrambled control or SynII lentiviral-mediated shRNA was infused in vivo. Rats were then tested for negative symptoms using a social interaction paradigm, and cognitive symptoms, specifically working memory, using the 8-arm radial maze. Post cognitive stimulation, computerized tomography and positron emission test images were fused for accurate region-specific glucose metabolism profiles. Behavioural results showed SynII KD animals spent significantly less time interacting and cognitive deficits when compared to controls. Functional brain imaging revealed global neural hyperactivation in SynII KD animals. These behavioural changes and altered glucose metabolism are consistent with SZ. These findings corroborate reduced SynII in the pathophysiology of SZ, suggesting SynII as a potential therapeutic target. (Acknowledgments: Funded by CIHR)

A35) PHYSIOLOGICAL AND MORPHOLOGICAL CONSEQUENCES OF DEVELOPMENTAL ETHANOL EXPOSURE ON PREFRONTAL LAYER VI NEURONS OF YOUNG POSTNATAL MICE

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Developmental ethanol exposure can lead to teratogenic outcomes in humans that are known as Fetal Alcohol Spectrum Disorders (FASD). One of the most prevalent neurocognitive impairments associated with FASD is attention deficits. We have shown previously that mice exposed to ethanol during development exhibit impaired attention in adulthood, and also exhibit altered physiology and morphology of pyramidal neurons located within layer VI of the medial prefrontal cortex (mPFC) that support this cognitive function. Here, we sought to determine whether these developmental ethanol-induced alterations to mPFC layer VI neurons are also present early in postnatal life.
Developing mice were exposed to ethanol or air (control) using vapour chambers from gestational days 10 to 18 (term, 19 days) and from postnatal days (P) 4 to 14. Electrophysiological analysis of mPFC layer VI pyramidal neurons at P15 and P25 reproduced known effects of age and sex on neuron physiology in control mice. However, these experiments found developmental ethanol exposure to increase nicotinic acetylcholine responses for female mice only. Since this outcome has been found previously in adult male mice, these results suggest that altered nicotinic signaling following developmental ethanol exposure varies by sex and occurs earlier in females. Morphological analysis of these neurons found developmental ethanol exposure to decrease dendrite branching in male mice only. Together, these analyses demonstrate sex-specific alterations to mPFC neuron physiology and morphology following developmental ethanol exposure. (Acknowledgements: Supported by the Banting Research Foundation, NSERC, the Canada Foundation for Innovation, the Ontario Graduate Scholarship Program and the Ontario Veterinary College)

A36) BCL-2 ASSOCIATED ATHANOGENE 5 MODulates APOPTOSIS FOLLOWING MITOCHONDRIAL AND PROTEASOMAL STRESS

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Parkinson’s disease (PD) is characterized by dopaminergic neurodegeneration in the substantia nigra. Mitochondrial and proteasome dysfunction have been implicated in the pathogenesis of PD. Bcl-2 Associated Athanogene 5 (BAG5) is a co-chaperone protein that promotes proteasome dysfunction and enhances dopaminergic neurodegeneration in vivo. Recent studies suggest that BAG5 may promote cell survival in certain contexts. We hypothesized that BAG5 plays a modulatory role in cell death, promoting survival in some contexts and death in others. Cell viability assays were performed with four toxins (CCCP, MG132, Tunicamycin and MPP+) using H4 and SH-SY5Y dopaminergic cell lines. GFP-tagged BAG5 was stably inserted into H4 cells, and specifically inserted into the AAVS1 safe-harbour of SH-SY5Y cells. Viability was assessed using the PrestoBlue reagent, death was assessed using propidium iodide, and intracellular apoptosis pathways were assessed via western blot. In H4 cells, BAG5 decreased viability following high-dose exposure to Tunicamycin, CCCP and MG132, but increased viability with MPP+ exposure. In SH-SY5Y cells, BAG5 decreased viability with high-dose MG132 and CCCP, but increased viability with low-dose MG132. The increase in cell death caused by BAG5 following CCCP exposure was recapitulated in the propidium iodide assay, and corresponded with increased caspase-3 and PARP cleavage. In conclusion, BAG5 plays a modulatory role in mitochondrial/proteasomal stress-induced apoptosis, having context-dependent effects that vary based on toxin, toxin concentration and cell type. (Acknowledgements: Supported by CIHR and Michael J Fox Foundation)

A37) MECHANISMS OF TAU-INDUCED BRAIN-DERIVED NEUROTROPHIC FACTOR DOWNREGULATION IN A CELLULAR MODEL OF ALZHEIMER’S DISEASE AND RELATED TAUOPATHIES

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Alzheimer’s disease (AD) and related tauopathies are characterized by abnormal modifications of the microtubule-associated protein tau, including hyperphosphorylation, misfolding, and aggregation. In the cortex of subjects with AD or non-AD tauopathies, mRNA and protein levels of brain-derived neurotrophic factor (BDNF) are significantly reduced. BDNF downregulation is implicated in synaptic loss and cellular dysfunction that correlate with deficits in learning and memory. Alternative splicing results in at least 17 BDNF transcripts, of which transcript IV accounts for approximately half of the total BDNF mRNA in the cortex. Recent research demonstrates that overexpression of wild-type human tau (hTau40) in animal and cellular models downregulates total BDNF and BDNF transcript IV, although the precise mechanism of tau-induced BDNF downregulation remains poorly understood. This study aimed at investigating whether hTau40 overexpression in human neuroblastoma SH-SY5Y cells affects transcription factors that regulate BDNF transcript IV, specifically cAMP response element binding protein (CREB) and upstream stimulatory factor 1 (USF1). Using Western blotting, no significant differences were observed in CREB expression, nuclear localization, or activation between hTau40-overexpressing and control SH-SY5Y cells. Rather, overexpression of hTau40 significantly increased USF1 protein expression and nuclear localization. These findings suggest that tau-induced BDNF downregulation in SH-SY5Y cells may be mediated by USF1, but not by CREB. (Acknowledgements: Supported by a grant from the Alzheimer’s Society of Canada to MF)

A38) TEMPORAL ANALYSIS OF INTRA-BLA MOLECULAR CHANGES FOLLOWING CHRONIC OPIATE EXPOSURE

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The rewarding effects of opiate drugs facilitate the formation of associative memories linked to the drug-taking experience. Processing of these memories occurs within the basolateral amygdala (BLA), and is mediated by different dopamine receptors as a function of opiate exposure state. Dopamine D1 receptors (D1Rs) are required for acute opiate memory formation in the previously drug-naive state, but D2R and D3R signaling is necessary for memory
formation during opiate dependence and withdrawal. Downstream signaling targets of D1 (ERK1/2) and D2/3 (CaMKIIa, calcineurin, cdk5) are similarly altered in an opiate exposure state-dependent manner. The time course and permanence of these changes, however, is poorly understood. Furthermore, it is unknown which alterations are a result of opiate dependence, and which are a consequence of opiate withdrawal specifically. Here, we performed a temporal analysis of changes to dopamine receptor signaling targets, looking from acute to protracted states of opiate dependence to better understand the mechanisms underlying the disordered reward memory processing that is becoming increasingly evident as a hallmark of opiate addiction. BLA tissue was isolated from rats that were chronically exposed to heroin at 3h, 7d, 14 and 30d following their last dose. Western blot analysis revealed that calcineurin and CaMKIIa appear to be involved more in the early memory processing and withdrawal, whereas cdk5 may be further involved in the long-term maintenance of opiate reward-related memories. These results will help us to better understand the temporal dynamics of the molecular changes that occur as a consequence of opiate addiction. Ultimately, this may help guide treatment from the recovery of opiate addiction appropriately for the different phases of this chronic disorder. (Acknowledgements: Supported by the Alzheimer’s Society of Canada and the Canadian Institutes of Health Research)

A39)  UNDERSTANDING THE ROLE OF THE CO-CHAPERONE BAG5 IN PINK1/PARKIN DEPENDENT MITOCHONDRIAL QUALITY CONTROL
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The clearance of dysfunctional mitochondria by selective autophagy has been implicated in the etiology of Parkinson’s disease (PD). Mutations in the genes encoding the kinase, PINK1, and the E3 ubiquitin ligase, parkin, are known to cause familial PD. PINK1 and parkin act in the same pathway where PINK1 identifies damaged mitochondria and recruits parkin from the cytosol where parkin then ubiquitinates the mitochondria for proteasomal degradation and lysosomal clearance. Bcl-2 associated athanogene 5 (BAG5) is an Hsp70 interacting co-chaperone that has been shown to also interact with parkin, inhibiting its ubiquitin ligase activity. Further, BAG5 is shown to exacerbate neurodegeneration in rodent models of PD. We hypothesize that BAG5 is a negative regulator of PINK1 and parkin dependent mitochondrial quality control. The effect of BAG5 was evaluated in cell culture models where the protonophore, CCCP, was used to dissipate mitochondrial membrane potential. Western blotting of mitochondrial fractions showed that BAG5, as well as BAG5-DARA, a mutant incapable of Hsp70 interaction, both increased PINK1 proteins levels in response to CCCP treatment while knockdown had the opposite effect. In U2OS cells stably expressing GFP-Parkin cells, overexpression of BAG5 was both found to modulate parkin recruitment following mitochondrial depolarization. Finally, BAG5 was also found to impair mitophagy as measured by a mitochondrially targeted variant of the fluorescent reporter protein, keima, that exhibits a spectral shift upon entering the acidic environment of the lysosome. (Acknowledgements: Supported by the Michael J Fox Foundation and NSERC)

A40) TAU PHOSPHORYLATION AT THE AT8/AT100 SITE HAS NO EFFECT ON TAU-INDUCED BDNF DOWN-REGULATION IN AN IN VITRO MODEL OF ALZHEIMER’S DISEASE
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In Alzheimer’s disease (AD), tau protein becomes hyperphosphorylated and forms toxic soluble aggregates. However, it is unclear how site-specific phosphorylation of tau may contribute to its toxicity. Our focus is on the ability of pathological tau to alter the expression of brain-derived neurotrophic factor (BDNF), a critical protein for neuronal survival, plasticity, and memory. We have shown that there is significant down-regulation of BDNF in the human cortex of tauopathy subjects, and that tau over-expression in vitro and in vivo also reduces BDNF expression. We are investigating whether phosphorylation of tau at specific sites is responsible for its neurotoxicity, as measured by BDNF down-regulation. In this study, we examined two sites of tau that are commonly hyperphosphorylated in AD: AT8 and AT100. Human neuroblastoma SH-SY5Y cells were stably transfected with a plasmid containing the human tau gene mutated at both AT8 (S202&T205) and AT100 (T212&S214) epitopes to prevent phosphorylation. Cells were then differentiated for 10 days, RNA was extracted using TRIzol and BDNF mRNA was measured using qRT-PCR, β-actin mRNA was measured as a housekeeping gene. We found that both AT8 and AT8/AT100-transfectants significantly down-regulated BDNF mRNA compared to non-transfected controls (p<0.05). This result, combined with our previous findings, suggests that over-expression of tau, whether mutated at AT8/AT100 sites or not, reduces BDNF expression. (Acknowledgements: Supported by the Alzheimer’s Society of Canada and the Canadian Institutes of Health Research)

A41) ESTABLISHING THE UNDERLYING NEUROPROTECTIVE EFFECTS OF MOOD STABILIZERS USED IN BIPOLAR DISORDER
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Bipolar Disorder (BD) is a mood disorder characterized by episodes of mania and depression. A biological target of interest contributing to the pathophysiology of BD is the altered expression of neurotrophic factors (NTFs), namely cerebral dopamine NTF (CDNF) and mesencephalic astrocyte-derived NTF (MANF). These naturally occurring proteins promote survival, differentiation and maintenance of neurons. Both MANF and CDNF have been implicated in the endoplasmic reticulum (ER) stress response, which is impaired in BD pathophysiology. This suggests a potential role for NTFs to act as therapeutic targets, and help alleviate BD symptoms by regulating the ER stress response. In our study, we established an in vitro model using a differentiated human neuroblastoma cell line – SH-SY5Y cells, to determine whether common drugs prescribed to BD patients affect expression of NTFs. These cells were treated with two mood stabilizers – 3 mM lithium (LiCl) or 1 mM valproic acid (VPA). The resultant mRNA expressions of CDNF and MANF were measured using quantitative reverse transcription PCR. Both LiCl and VPA administration significantly increased mRNA expression of MANF and CDNF. These results suggest that mood stabilizers may ameliorate BD symptoms by upregulating certain NTFs, and acting via the ER-stress response. This novel finding allows us to elucidate the neuroprotective role of CDNF and MANF and their potential involvement as therapeutic targets for BD. Future directions involve determining the underlying mechanisms, and using an animal model to replicate these findings. (Acknowledgements: Supported by CIHR)

**A42) DIFFERENTIAL GENE EXPRESSION IN BRAIN SAMPLES FROM LIVING PARKINSON’S DISEASE PATIENTS**

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**Introduction:** Differential gene expression in the central nervous system (CNS) of living Parkinson’s disease (PD) patients has not been previously reported and may offer critical biomarkers that define pathogenic mechanisms, new therapeutic targets, early diagnosis and disease progression. The current objective was to examine the transcriptome for gene alterations using RNA isolated from fresh brain specimens in living PD and control patients. Methods: RNA-sequencing was performed using cortical biopsies in 6 patients with PD and 6 healthy controls. Sequences, averaging approximately 90 million reads per sample, were trimmed to remove adapters and low quality bases, aligned to the human genome (Hg19), counted using HTSeq (v.0.6.1p2) and analyzed for differential expression using edgeR (v.3.8.6). Results: At a corrected p-value threshold of <0.05, 764 differentially expressed genes were identified, 25 of which had >4-fold change in expression. The expression of GDNF, a potent neuroprotective and putative therapeutic agent, was significantly reduced in PD specimens and one of several dysregulated genes with experimental linkages to neurodegeneration. Further, pathway analysis of differential gene expression corroborates findings in other research of dysregulation of inflammatory processes. Conclusions: To our knowledge this is the first demonstration of differential CNS gene expression in living PD patients. This methodology offers new potential to identify genetic biomarkers that may facilitate diagnosis and treatment for PD and other neurodegenerative diseases. (Acknowledgements: Supported by OGS, the Lawson Health Research Institute and the Michael J. Fox Foundation)

**A43) A NOVEL METHOD TO STUDY CONDITIONED AND UNCONDITIONED SOCIAL PREFERENCE IN LABORATORY RATS**

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Anhedonia is a cardinal feature of depression that is characterized by deficits in processing of both primary (unconditioned) and secondary (conditioned) reinforcing stimuli. One of the most prominent features of depression is social anhedonia, characterized by decreased motivation for, and pleasure derived from social interactions. In order to study deficits in conditioned and unconditioned social stimuli processing, a novel social preference procedure was developed. Male Sprague-Dawley rats were first habituated to a Y-maze apparatus, followed by four conditioning sessions where rats were presented with a social (i.e. conspecific) or object stimulus in adjacent arms of the maze. Finally, rats were tested for a conditioned place preference (CPP) by measuring time spent in each arm of the Y-maze with the stimuli removed. During the conditioning sessions, rats spent significantly more time investigating the social compared to the object stimulus, and during the CPP test, rats spent significantly more time in the arm previously paired with the social compared to the object stimulus. Thus, rats showed a preference for both unconditioned and conditioned social stimuli. Future research in our laboratory will use pharmacological and physical stressors to attenuate primary and secondary social reinforcement, creating a novel method for assessing social anhedonia in rodents. The ultimate goal of this research is to block these deficits by administering an antidepressant, the selective serotonin reuptake inhibitor (SSRI) escitalopram, and identifying biological markers unique to animals that are effectively treated by the drug. (Acknowledgments: Supported by CAN-BIND)

**A44) SEX DIFFERENCES IN STRESS ADAPTATION: NEUROPLASTICITY WITHIN THE PARAVENTRICULAR NUCLEUS OF THE HYPOTHALAMUS**

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The hypothalamic-pituitary-adrenal (HPA) axis is sexually dimorphic. However, little is known about sex differences in the HPA axis adaptation to chronic stress. Here, we studied sex-dependent neural plasticity mechanisms relevant to
habituation of the HPA axis to repeated stress that manifests as a decrease in the excitability of HPA axis output neurons [neuroendocrine neurons that express corticotropin releasing hormone (CRH) in the paraventricular nucleus of the hypothalamus (PVN)]. To study habituation to repeated restraint stress and subsequent recovery, mice were first subjected to daily 1 hour restraint stress for 3 weeks, and then challenged with the same stressor one additional time either on the following day of the last stressor, or after 1 week or 4 weeks of no-stress recovery periods. As controls, one group of mice received 1 hour restraint without prior repeated stress, and another group received no stress. Using immunohistochemistry, we quantified the induction of immediate early gene (IEG) c-Fos in PVN-CRH neurons. We found that, in both sexes, 3 weeks of repeated stress caused an expected decrease in the restraint-induced c-Fos expression in the PVN-CRH neurons (habituation), and the no-stress recovery period fully reversed this habituation. However, females showed greater habituation and its recovery was slower. In summary, we found sex differences in the neural plasticity associated with the HPA axis habituation to and recovery from repeated stress. (Acknowledgements: Supported by CIHR, NSERC and OMHF)

A45) α4β2+ NICOTINIC ACETYLCHOLINE RECEPTOR AND CALCIUM-ACTIVATED POTASSIUM CHANNEL SIGNALING IN THE DEVELOPMENT OF THE HIPPOCAMPAL FORMATION NEURONAL NETWORK
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The classical view of information flow in the hippocampal formation (HF) includes a series of excitatory glutamatergic synapses involving the principal neurons of the dentate gyrus (DG), cornu ammonis area 3 (CA3), CA1, subiculum (SUB), and entorhinal cortex (EC) layer VI. The normal development and function of this neuronal network depends on the ability of nicotinic acetylcholine receptors (nAChRs) to mediate cholinergic signaling. While the α4β2+ nAChR subtype constitutes a major class of nAChR in the HF, the function of this nAChR in principal neurons of the HF during early postnatal development has not been investigated. We first sought to determine whether functional α4β2+ nAChRs are present on principal neurons of the CA1, CA3, DG, SUB and EC layer VI of male CD1 strain mice by measuring their whole-cell electrophysiological responses to acetylcholine (ACh) within acute brain slices. We found that α4β2+ nAChRs elicit postsynaptic inward currents and facilitate neuronal excitation in principal neurons of all regions investigated, with the greatest responses in the SUB and EC layer IV. Interestingly, responses to ACh in active neurons that were induced to fire action potentials were of similar magnitude across all regions. Our findings suggest that these similar ACh responses in firing neurons are regulated by the calcium-activated potassium channels of the small conductance type. The presence of α4β2+ nAChRs on HF principal neurons during this period of development suggests a role for these receptors in the development and synchrony of HF learning and memory networks. (Acknowledgements: Supported by NSERC, Canada Foundation for Innovation, Ontario Graduate Scholarship, and the Ontario Veterinary College)

A46) CHARACTERIZATION OF A NOVEL APPROACH TO ENRICH PROTEINS PRESENT AT THE SURFACE OF SYNAPTIC TERMINALS
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Although receptor trafficking is regarded as a key process in neuronal plasticity, studying the phenomenon is challenging due to the lack of techniques that efficiently isolate the cell surface fraction of synapses. At present, the most common procedure for studying cell surface proteins is biotinylation (Bio), wherein biotin is conjugated with cell surface proteins and the complexes are isolated with the use of avidin. Although highly sensitive, the Bio technique is not specific, and captures proteins from various cell types and neuronal sub-regions (e.g., somatic, synaptic). One method for the isolation of synaptic terminals is a procedure that utilizes differential filtration to achieve intact synaptic terminals (i.e., a synaptoneurosome preparation; Syn). To more efficiently investigate receptor trafficking, we combined the Bio and Syn techniques (BioSyn) to enrich synaptic surface proteins. Tissue slices (350 µm) were prepared from Sprague-Dawley rats and incubated with 1 mg/mL of biotin for 40 minutes at 4°C. Following homogenization, synaptoneurosomes were isolated and then incubated with NeutrAvidin beads for 4 h at 4°C. The presumptive synaptic surface fractions were assessed via Western blotting. The data reveal that the BioSyn samples displayed enriched synaptic surface proteins (NR1, Neuriligin, NCAM), and the absence of internal neuronal proteins (actin, GAPDH) and glial specific proteins (GFAP). Subsequent work will further characterize the technique by examining various stimuli thought to change the density of receptors at the synaptic surface. (Acknowledgments: Supported by NSERC)

A47) STABLE CHANGES IN H2A.Z BINDING AND ACETYLATION DURING MEMORY FORMATION AND MAINTENANCE
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Memory formation is a protracted process that initially involves the hippocampus and becomes increasingly dependent on the cortex as the memory ages. Existing research has implicated stable changes in DNA methylation as a contributor to this process, whereas changes in histone modifications are typically found to be transient. Here, we investigated whether histone H2A.Z, a newly identified epigenetic regulator of learning and memory, is stably modified
in the hippocampus and the cortex at delayed time points after learning. Mice were exposed to contextual fear conditioning and brains were collected either 24 hours or 30 days after learning. Using chromatin immunoprecipitation, we quantified H2A.Z and acetylated H2A.Z (AcH2A.Z, a positive marker of transcription) binding on memory-related genes. After 24h, we observed increased levels of H2A.Z acetylation on immediate early genes in fear conditioned mice in the hippocampus, demonstrating the persistence of this epigenetic modification beyond the initial consolidation window (up to 6h). 30 days after training, we detected lasting changes in both H2A.Z binding and H2A.Z acetylation in the medial prefrontal cortex (mPFC), particularly on synapse-related genes. Previously, we showed that H2A.Z in both the hippocampus and the cortex is transiently modified after learning. Here, we show that H2A.Z is stably regulated, but that this regulation is gene-specific, such that changes associated with immediate-early genes are no longer evident at 30 days, whereas, changes associated with synaptic genes persist to support memory maintenance. (Acknowledgements: Supported by NSERC)

**A48) GCAMP IMAGING REVEALS THAT COMBINED CHANGES IN AXONAL EXCITABILITY AND INTRACELLULAR CHLORIDE ARE NECESSARY TO PERMIT GABA-EVOKED SPIKING IN THE CENTRAL AXON TERMINALS OF PRIMARY AFFERENT NEURONS**

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Under normal conditions, spikes in primary afferent neurons originate in peripheral axon terminals and propagate to the CNS. However, GABA acting on central axon terminals causes primary afferent depolarization (PAD), which, while normally inhibitory, can lead to spikes that propagate antidromically. From somatic recordings, PAD-evoked spiking has been shown to require both a depolarizing shift in $E_{\text{GABA}}$ and reduced $K^+$ conductance. This combination of effects can arise in damaged peripheral nerves via enhanced function of the Na-K-Cl cotransporter, NKCC1, and by downregulation of $K_v1$-type potassium channels, respectively. However, it remains unclear if these requirements are met at central axon terminals. Using GCaMP6f transgenic mice, action potential evoked calcium transients were measured in somata in the dorsal root ganglion with high spatial and temporal resolution, allowing us to view antidromically propagating spikes evoked by application of GABA to axon terminals in the spinal cord. Aldosterone, an NKCC1 enhancer, was found to depolarize $E_{\text{GABA}}$, and only when aldosterone was simultaneously applied with a $K_v1$-type channel blocker, 4-AP, could GABA initiate antidromically propagating spikes from central axon terminals. These data confirm that enhanced chloride loading via NKCC1 and enhanced excitability caused by reduced $K_v1$-type conductance are necessary for PAD-evoked spike initiation at central axon terminals. Consequently, these GABA-evoked spikes can propagate antidromically to cause neurogenic inflammation via the peripheral release of inflammatory mediators. (Acknowledgements: Supported by NSERC, OGS, and a Hospital for Sick Children Research Training Centre Graduate Student Fellowship)

**A49) THE ROLE OF SYNAPSIN II IN THE PHENCYCLIDINE PRE-CLINICAL RAT MODEL OF SCHIZOPHRENIA**

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Schizophrenia (SZ) is a mental disorder characterized by positive symptoms, negative symptoms, and cognitive dysfunction. Phencyclidine (PCP)—a N-methyl-D-aspartate (NMDA) receptor antagonist—induces symptoms indistinguishable from those of SZ. The study assessed short-term and longer-term biochemical effects of NMDA receptor antagonism, which have implications for the pathophysiology of SZ. Sprague Dawley rats were implanted subcutaneously with osmotic mini-pumps containing saline or PCP (15mg/kg/day) for 14 days. The rats were then tested on behavioral paradigms, including locomotion (positive symptoms), social interaction (negative symptoms), and pre-pulse inhibition (PPI). A second cohort was treated with PCP twice a day for 7 days followed by 7 days of drug withdrawal. Brain regions of the saline-treated rats were isolated for protein analysis post-treatment. Compared to saline-treated rats of the first cohort, PCP-induced rats demonstrated a hyper-locomotive state ($p<0.05$), reduced social interaction ($p<0.01$), and reduced PPI ($p<0.001$). While mPFC synapsin II levels of the first cohort were reduced in PCP-treated rats compared to the saline group ($p<0.001$), PFC synapsin II levels in the second cohort were increased ($p<0.05$). The behavioral outcomes produced validate the PCP model of SZ. The differences in synapsin II levels in the acute and non-acute testing regimens suggest underlying mechanistic differences between the immediate and longer-term consequences of NMDA receptor antagonism, offering novel insights into the pathophysiology of SZ. (Acknowledgements: Supported by CIHR)

**A50) DYNAMICS OF EXCITABILITY OF MOTOR SYSTEM EXCITABILITY DURING AUDITORY ANTICIPATION**

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The ability to anticipate complex sounds, like words in speech or the beat in music, is an important aspect of human perception. However, the changes of excitability in the motor system during auditory anticipation have not been characterized. Here, we applied single-pulse Transcranial Magnetic Stimulation (TMS) to the primary motor cortex to
elicit motor evoked potentials (MEPs) from the first dorsal intersosseus muscle, the amplitude of which indexes motor system excitability. Healthy right-handed participants (N = 20) underwent TMS stimulation during listening to regular (periodic) tone sequences at three rates (200ms, 550ms, and 900ms) and irregular tone sequences. We assessed MEP amplitudes over time, to test fluctuations in excitability during auditory anticipation (listening to regular sequences), and in the absence of auditory anticipation (listening to irregular sequences). We hypothesize that motor system excitability fluctuates at the rate of auditory stimulation, and peaks in anticipation of regular sounds. Results do not show evidence that motor system excitability fluctuates at the rate of regular or irregular auditory tones. Also, the results do not show evidence of an increase in excitability in anticipation of regular or irregular sounds. These results do not suggest synchronization of motor system excitability to regular sounds, informing our understanding of auditory-motor integration. (Acknowledgements: We are grateful to our funding sources: NSERC, McDonnell Foundation, and the Canadian Foundation for Innovation)

A51) EARLY AUDITORY SYSTEM PROCESSING AS ASSESSED BY SENSORY SENSITIVITY, SENSORY FILTERING, AND SENSORY-MOTOR GATING

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Individuals with autism spectrum disorder (ASD) have an altered reactivity to sensory input and communication deficits. Though differences in auditory processing measures have been shown, the consistency of behavioural results assessing the maturation of the early auditory system in humans remains variable. To address this knowledge gap, I used a genetic rat model of autism (CNTNAP2 knockout) as a tool to investigate the maturation of auditory processing by examining measures of auditory sensitivity (IO function), sensory filtering (habituation), and sensory motor gating (prepulse inhibition) using the acoustic startle response (ASR). Since this response relies on brainstem auditory structures, and structures up to and including the inferior colliculus when measuring sensory-motor gating, it acts as a motor readout of the early auditory pathway. It can therefore be used to assess if differences in these measures exist and/or improve with age in my animal model, as is the trend with behaviours in some populations of individuals with ASD. To that end, male and female Sprague Dawley rats (wildtype, heterozygous knockout, or homozygous knockout) underwent the startle testing paradigm on post-natal day 44 and 72. Magnitude and latency to the peak of the startle response were measured. Differences in sensory sensitivity and sensory filtering were observed, as well as a significant sensory motor gating deficit that does not improve with age. Overall, these results provide insight into the differences in non-attentive auditory behaviours in individuals with ASD.

A52) THE EFFECTS OF METHYLPHENIDATE ON SOSENSORY FILTERING AND SOCIAL BEHAVIOR IN PRENATALLY VALPROIC ACID EXPOSED RAT MODEL

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Valproic acid (VPA) is an anti-epileptic drug with teratogenicity which shown to produce structural and behavioral deficits in prenatally exposed rodents. Methylphenidate(MPH) is a psychostimulant which acts as a dopamine and norepinephrine reuptake inhibitor. Previous studies suggest that MPH could have a beneficial dose-dependent impact on rodents with behavioral deficits. In this study, we investigated the effects of low dose(2.5mg/kg) or high dose (10mg/kg) MPH on two domains, sensory filtering and social behavior on the rat model produced by prenatal intravenous injection of VPA(600mg/kg) at gestation day 12.5. Offspring was tested at 5 months of age. Habituation and prepulse inhibition of acoustic startle response were used for the measurement of sensory filtering. For results, all prenatally exposed VPA rats were born with a prominent tail structural malformation. High dose MPH treatment impaired social novelty but improved habituation in VPA males. PPI was not significantly affected by neither concentration of MPH. No significant difference was detected between low dose MPH treatment and saline for all behaviors tested. The permanent tail malformation found in all rats differed from the previously reported 30% incidence rate. For VPA rat model, the more effective dose shown to be 10mg/kg. The impairment on social novelty in high dose could be due to the disrupted dopamine function. PPI values stayed relatively normal throughout the test, a standardized control group is needed to confirm the impairment in adult VPA model.

A53) EFFECT OF DREADD-INDUCED INHIBITION OF LDT ACETYLCHOLINE ON SENSORIMOTOR GATING

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Sensorimotor gating is a state-dependent pre-attentive response that filters out seemingly unnecessary stimuli our brains would otherwise be overwhelmed with. Prepulse inhibition (PPI) of the acoustic startle response (ASR) is an operational measure for sensorimotor gating. Impairment of PPI is seen in patients with an array of neurological deficits, such as Autism Spectrum Disorder, and is a biomarker for schizophrenia. Underlying mechanisms of sensorimotor gating are unknown, yet some literature suggests that lesioning the laterodorsal tegmental nucleus (LDT) severely attenuates PPI in rats. The aim of our study was to inhibit the cholinergic neurons of the rat LDT, and determine the effect on PPI of the ASR. We used a chemogenetic technique, DREADDs (Designer Receptor Exclusively Activated by Designer Drugs), to intracranially deliver and inhibit ACh in adult Long-Evans rats. This DREADD is a Cre-dependant virus so subjects are from a bacterial artificial chromosome transgenic ratline
expressing Cre recombinase in cholinergic neurons (ChAT-Cre). Three weeks post-surgery recovery, subjects received the designer ligand CNO to temporally inhibit ACh, and were tested for PPI of the ASR. Preliminary results suggest PPI is disrupted in subject with the DREADD-induced ACh inhibition in the LDT. Our data provides a deeper mechanistic understanding of sensorimotor gating, and the crucial brain regions and neurons involved in PPI of the ASR. (Acknowledgements: Supported by NSERC and CIHR)

A54) FEMALE MICE DO NOT REQUIRE DISTRIBUTED BOUTS OF CLITORAL STIMULATION FOR SEXUAL REWARD
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While the clitoris has been established to be an important organ for genitosensory stimulation, there are few animal models for studying clitoral function in sexual reward. Clitoral stimulation of sexually naïve female rats with a paintbrush is sufficient to produce conditioned place preference (CPP). However, only stimulation that reproduces the temporal patterning of rat copulatory bouts is effective in producing CPP. In light of the increasing importance of genetic mouse models for behavioral neuroscience, and of differences in the temporal patterns of copulatory behavior between rats and mice, the present study employed an adapted version of the rat protocol to mice. Thirteen adult female C57BL/6 mice were randomly assigned to undergo either distributed clitoral stimulation or continuous clitoral stimulation. Stimulation occurred for 1 minute and distributed consisted of 1 stimulation every 5 seconds and continuous consisted of 1 stimulation every second. A session of conditioning consisted of 5 rounds of stimulation and place exposure per day. Conditioning sessions alternated with sham sessions in which mice were similarly handled but no clitoral stimulation occurred. Place exposure was for non-preferred side (conditioning) and preferred side (sham). CPP was assessed once all animals had completed 5 conditioning and sham sessions. In contrast to rats, all females developed a significant CPP regardless of the type of stimulation they received, suggesting important differences in the response of female mice to this test. (Acknowledgements: Funded by NSERC discovery grant RGPIN-2016-06302 (AM))
Poster Abstracts (Afternoon Session)

B1) THE ROLE OF VISUAL WORKING MEMORY IN FACILITATION VERSUS INHIBITION OF FEATURES WITHIN A GUIDED VISUAL SEARCH TASK
Alexandria N. DiCosimo and Stephen M. Emrich; Department of Psychology, Brock University, St. Catharines, ON
Visual working memory (VWM) is known to play a role in visual search tasks, however its exact role has long been debated. Using a guided memory search task, VWM was compared across conditions in which participants received target information (facilitation) versus distractor information (inhibition) to hold in memory. Each search array contained a target and a distractor, with one item placed left or right of fixation (horizontal) and the other placed above or below fixation (vertical). Using this arrangement lateralized event related potential (ERP) components were analyzed to reveal differences in how participants treated targets and distractors held in VWM. Analysis of the contralateral delay activity (CDA) during the memory delay revealed now difference between the two experimental conditions. The N2pc component was analyzed during the search display to examine the target negativity (N1) and distractor positivity (P3) components. During facilitation trials, the N1 was stronger when the target was placed in the horizontal position, but for inhibition trials, the N1 was stronger when the target was placed in the vertical position. Comparatively, during inhibition trials, the P3 was stronger when the distractor was placed in the horizontal position, but for inhibition trials, the P3 was stronger when the distractor was placed in the vertical position. Overall, the results uncover differences that are present when information in working memory is prioritized as target or distractor features.

B2) EFFECTS OF PERINATAL EXPOSURE TO DELTA-9-TETRAHYDOCANNABINOL ON ANXIETY, LEARNING, VISUOSPATIAL ATTENTION, AND IMPULSIVITY
Alysha Sultan, Aamna Qureshi and Paul E. Mallet; Department of Psychology, Wilfrid Laurier University, Waterloo ON
The present study examined the long-term impact of moderate dose perinatal THC exposure on learning, anxiety, visuospatial attention and impulsivity. Forty-eight 4-day old male and female Crl:CD(SD) rats were injected with vehicle or delta-9 tetrahydrocannabinol (THC, 5 mg/kg) once daily for 10 consecutive days. Following a 56-day drug-free period, locomotion and anxiety-related behaviours were examined using the elevated plus-maze and emergence tasks. Subsequently, visuospatial attention and impulsivity in the male animals were examined using the 5-choice serial reaction time task (5-CSRTT). Preliminary data analysis revealed that perinatal THC had no effect on any measures of anxiety; however, THC-treated female rats displayed greater locomotor activity (distance travelled) compared to vehicle-treated rats. Acquisition of the 5-CSRTT was similar in both THC- and vehicle-treated animals; perinatal drug treatment had no significant effect on the number of correct or incorrect responses. However, perinatal THC significantly increased the number of omission trials, and significantly decreased the number of premature responses. The finding that THC administration increased the number of omission trials suggests that early life exposure to THC may impair visuospatial attention in adulthood. Additional data analyses are in progress.

B3) DISPOSITIONAL AFFECT PREDICTS COGNITIVE BREADTH
Karen M. Arnell1, Andrew Chung1, Gillian Dale1, Mary H. MacLean2; 1Brock University, 2University of Wisconsin-Madison, 3University of California-Santa Barbara
The influence of mood states on attentional breadth (e.g. seeing the entire forest or the individual trees) and conceptual breadth (e.g. the flexibility and inclusiveness of one’s thinking), have been widely investigated. Earlier studies have shown that participants in an induced positive mood demonstrated increased cognitive breadth, while a reduced cognitive breadth was observed for those in an induced negative mood. However, more recent research has shown that previous studies have confounded the affective dimensions of motivational intensity (the degree to which one wants to approach or avoid a stimulus) and valence. When unconfounded, high motivational intensity states have been shown to promote a reduced cognitive breadth, while low motivational intensity states have been shown to promote increased cognitive breadth. Here we investigated if dispositional affect can predict both attentional breadth (measured using both the global-local Navon letter task and the hierarchical shape task), and conceptual breadth (measured using both the Remote Associates Task and the Object Categorization Task). A consistent valence-activation interaction was shown for all cognitive breadth measures. For participants who were high in positive affect, low in activation showed the most cognitive breadth, and the least breadth with higher activation. The influence of activation was not shown for those low in positive affect such that intermediate breadth was observed. In predicting cognitive breadth, the present findings suggest the importance of valence-activation interactions.

B4) SIMULTANEITY AND TEMPORAL ORDER PERCEPTION ASSESSED IN YOUNGER AND OLDER ADULTS USING EEG
Aysha Basharat, Meaghan Adams, Jesse P Varaghese, Gillian Bedard, Richard W Staines, Michael Barnett-Cowan; Department of Kinesiology, University of Waterloo, Waterloo, ON
Multisensory integration is required for a number of daily living tasks where the inability to accurately identify simultaneity and temporal order of multisensory events results in errors in judgment and can lead to dangerous behaviour. Research indicates that the ability to discriminate simultaneity and temporal order of events changes with age. Simultaneity Judgment (SJ) and Temporal Order Judgment (TOJ) tasks can be utilized to investigate age-related changes in multisensory integration. Here, participants are asked to assess whether an audiovisual pair of stimuli
presented appeared simultaneously or successively (SJ task) and which stimuli came first (TOJ task). Previous research has suggested that different perceptual mechanisms subserve SJs and TOJs and should not be used interchangeably. It has also been shown that simultaneity perception may be preserved over the lifespan, whereas temporal order perception may not be. We tested 28 healthy young and 28 healthy older adults who were asked to complete the audiovisual SJ and the TOJ tasks in random order while electroencephalography was collected. Results show differences in visual evoked P1 and auditory evoked N1 event related potentials across these tasks and between younger and older adults. Behavioural results also show significant differences across the tasks and between the two groups. We conclude that impaired audiovisual integration in older adults may be attributable to changes in the cortical excitability of the older adult brain. (Acknowledgements: This work was generously supported by a Natural Sciences and Engineering Research Council of Canada (NSERC) Discovery Grant (#RGPIN-05435-2014) and a Network in Aging Research Emerging Scholar Grant to MB-C)

B5) INVESTIGATING THE RELATIONSHIPS BETWEEN MILD HEAD INJURY, SUBSTANCE USE, & ATHLETIC STATUS AMONG UNIVERSITY STUDENTS
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Self-reported history of head injury is associated with increased substance use during adolescence (Ilie et al., 2015), and mild head injuries (MHI) sustained during childhood have been linked to problematic alcohol use in adolescence and early adulthood (Kennedy et al., 2017). However, given the high prevalence of sports-related MHI in high school and university student populations (Halstead et al., 2010; Baker & Good, 2014), these effects may be confounded with premorbid personality characteristics, since athletes typically have ‘riskier’ personalities and engage in greater alcohol use compared to non-athletes (Sonderlund et al., 2014). It is unclear whether this elevated alcohol consumption is due to the head injury itself or whether pre-injury personality characteristics account for these apparent changes post-injury. To further examine these relationships, a cross-sectional design was employed, whereby university students completed a series of self-report and performance-based measures at Brock University. As expected, those with a history of MHI reported significantly greater alcohol use than their non-injured cohort, t(38) = -2.20, p < .05. Moreover, MHI was found to be a significant predictor of alcohol consumption, F(1, 38) = 4.82, p < .05, r = .34, over and above the effects of athletic status. These findings suggest that post-injury risk-taking behaviours are likely a consequence of the MHI itself, perhaps reflecting disruption to the orbitofrontal cortex, an area implicated in emotional regulation/inhibitory control (Dias et al., 1997). (Acknowledgements: Supported by CIHR)

B6) THE BIRDS AND THE BEATS: CAN SONGBIRDS PERCEIVE REGULARITY IN RHYTHMIC AUDITORY SEQUENCES?
Brendon Samuels1,2, Scott MacDougall-Shackleton3, Jessica Grahn3, Molly Henry1,3; 1Brain and Mind Institute, 2Schulich School of Medicine & Dentistry and 3Department of Psychology, Western University, London, ON
Beat perception is a complex cognitive skill that enables humans to “feel” a regular pulse in music, and is an essential component of synchronization of behavior and dance. The mechanisms in the human brain that facilitate beat perception are not entirely understood, and have only been studied thus far using non-invasive measures in awake subjects. An animal model could enable use of techniques that are prohibitive in testing beat perception in human subjects, such as lesions or developmental manipulations. Some animals, such as bird species, also seem to be able to detect the beat in rhythms, though this has never been formally tested independent of motor synchronization. In this research, an operant experiment is used to assess if European starlings, a type of songbird, are capable of categorizing acoustic rhythms on the basis of whether or not a beat is perceived. An analogous human experiment is conducted with human participants using the same paradigm and experimental stimuli, to allow for direct comparisons between human and avian subjects’ performance on the task. The paradigm used here could be adapted to test for beat perception in other species, providing further insight on the evolution of this cognitive ability. Future research is warranted into structures in the brain implicated in beat perception, as well as variation between songbird species and animals in general. (Acknowledgements: Supported by NSERC)

B7) INVOLVEMENT OF CHOLINERGIC MUSCARINIC RECEPTORS IN RATS’ PERFORMANCE OF A NOVEL TEST OF VIEW-INVARIANT OBJECT RECOGNITION
Cassidy E. Wideman1, Ethan Huff2, Krista A. Mitchnick1, Daniel Palmer1, Bruce L. McNaughton2, and Boyer D. Winters3; 1Department of Psychology and Collaborative Neuroscience Program, University of Guelph, Guelph, ON, 2Lethbridge Brain Dynamics, University of Lethbridge, Lethbridge, AB
View invariant recognition marks the ability to recognize objects, despite identity preserving changes, such as in rotation, size or occlusion. The mechanisms by which the brain performs this cognitive ability are not well understood. The current study focused on the development and validation of a behavioural task to assess view-invariant object recognition (VIOR) abilities of rats. This task involved a series of object pre-exposure sessions followed by a variation of the spontaneous object recognition test. In this VIOR task, rats were tested on their ability to recognize objects that had been rotated. Only when rats had been pre-exposed to the test objects were they capable of recognizing objects despite rotation. This VIOR task was then used to investigate the neurobiological basis of view-invariant object recognition; specifically, we assessed the potential involvement of cholinergic muscarinic receptors (mAChR).
Systemic injections of the mAChR antagonist scopolamine significantly impaired performance in the VIOR task. This is the first study to implicate cholinergic muscarinic receptors in VIOR, and these findings, along with the demonstration of rats' ability to perform VIOR, have important implications for understanding how the mammalian brain is able to form comprehensive, view-invariant object representations that can be used flexibly to guide behaviour. (Acknowledgments: Supported by NSERC)

B8) COGNITIVE FUNCTION IN VARSITY FOOTBALL ATHLETES IS MAINTAINED IN THE ABSENCE OF REPORTED CONCUSSION

Danielle Brewer-Deluce, Timothy D. Wilson, and Adrian M. Owen; 1Department of Anatomy and Cell Biology and 2Brain and Mind Institute, Western University, London ON

Repeticive sub-clinical head impacts (SHI) are linked to progressive cognitive decline and post mortem CTE diagnoses in pro contact-sport athletes, though there remains little knowledge on the onset of trauma-related cognitive decline in younger athletes. We tested the hypothesis that cognitive function would be impaired as a function of career- and season-long exposure to SHI in collegiate level football athletes. Methods: male football athletes (n=31 age 22.3 ±1.6) completed the Cambridge Brain Sciences (CBS) cognitive battery in the pre- and post-season. Scores were compared in a repeated measures design against an age (20.6 ±1.2) and sex matched control group (n=35). Those with a concussion in the last year were excluded. Pre-season scores were also compared to age- and sex-matched normative values (n>18 000), and transformed into linear composites representing cognitive network function (short-term memory, reasoning, verbal ability). Post-season control tests are ongoing. Results: In the pre-season, there were no significant differences between footballers and controls on any tests, or based on the network composite analysis. Preliminary results suggest that pre-to-post season scores do not differ either between or within groups. Footballers and controls differed from normative values on 6 and 4 tests of cognitive function respectively. Conclusions: Results suggest the maintenance of normal cognitive function, as assessed behaviourally, in the absence of concussion in an elite sport population. Differences between normative and sample means warrant further exploration. (Acknowledgements: Supported by CERC to AMO)

B9) THE EFFECTS OF A HYPERANDROGENIC PRENATAL ENVIRONMENT ON SOCIAL RECOGNITION AND THE EXPRESSION OF ESTROGEN RECEPTOR ALPHA IN THE MEDIAL AMYGDALA OF FEMALE MICE

Emily R. Martin, Michael Marcotte, Cameron S. Wasson, Colin Howes, Hailey Katzman, Anthony J. Giuga, Neil J. MacLusky, & Elena Cholenski; 1Department of Molecular and Cellular Biology, 2Department of Psychology and Neuroscience Program and 3Department of Biomedical Sciences, University of Guelph, Guelph, ON

Gonadal hormones play an instrumental role in sexual differentiation during development and are involved in organizing sexual dimorphisms in the brain and sex differences in behaviour. Females tend to score higher on socially sensitive tasks than males, which may partly be explained by sex differences in brain regions such as the medial amygdala (MeA). Previous studies in female mice have demonstrated that estrogens affect social recognition (SR) via a mechanism involving estrogen receptor alpha (ERα) in the MeA. The current study assessed the effects of a hyperandrogenic prenatal environment on the expression of ERα in the MeA and on the ability to perform SR in adolescence and adulthood. Pregnant female mice were treated with 10 µg of testosterone propionate (TP) on embryonic days 12, 14 and 16. SR was tested using a social discrimination paradigm at puberty and in adulthood, while the expression of ERα in adult brains was assessed using immunohistochemistry. TP treatment enhanced the ability to perform SR in adolescence but had no effect in adulthood, suggesting that increased prenatal androgens may cause mice to develop earlier, allowing them to successfully perform SR at a younger age. Prenatal TP caused a decrease in ERα expression in the posterodorsal MeA but not in other subregions of the amygdala, which may be due to masculinizing effects by testosterone during development. These findings suggest that excess prenatal androgens may alter the development of SR behaviour, at least in part via effects on MeA ERα expression. (Acknowledgements: Supported by OMHF)

B10) IMPULSIVITY AND RISK TAKING IN INDIVIDUALS WITH MILD HEAD INJURY

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Although traumatic brain injury is the leading cause of disability for individuals under the age of 45 (Canadian Institutes of Health Research, 2012), milder head injuries are still underestimated as a serious health concern and their long-term neuropsychological consequences are often overlooked. Mild head injuries (MHI) affect 100-300/100 000 individuals per year in Canada (Carroll et al, 2004) and previous research has shown that the symptoms of MHI, including cognitive, social, and behavioural deficits, persist in a subset of individuals (Vanderploeg et al, 2007). Research demonstrates that individuals with a prior MHI present with decreased physiological arousal compared to their non-injured peers (Baker & Good, 2014). Attenuated physiological arousal is thought to mediate the relationship between MHI and poor social and behavioural outcomes due to a decreased responsivity to sympathetic cues about environmental factors and interpersonal situations (van Noordt & Good, 2011). By measuring electrodermal activation (EDA) as a proxy of physiological arousal, the current study examined the relationship between baseline arousal and a number of variables related to impulsivity and risk-taking. In particular, sensation-seeking and perseverance were examined. Consistent with previous literature (Baker & Good, 2014; Barry & Good, 2016), individuals with a history of
MHI presented with decreased physiological arousal, as well as significantly greater sensation-seeking behaviour $t(289) = -2.14, p = .032$. Moreover, injury severity was found to account for 32.5% of the variance in sensation-seeking scores, such that more severe injuries were associated with greater sensation-seeking. Lastly, a trend was observed for perseveration, whereby individuals with a history of MHI showed a significant lack of perseveration, $t(281) = 1.652, p = .100$. Taken together, the current findings imply that reduced physiological arousal and preparedness leads individuals with MHI to engage in more impulsive behaviours.

B11) ABSENCE OF WHITE/BLACK PREFERENCE IN ZEBRAFISH LARVAE: A PSYCHOPHARMACOLOGY ANALYSIS
Hifsa Zahid1 and Benjamin Tsang1, Hira Ahmed1, Richard Lee1, Steven Tran2 and Robert Gerlai1,3; 1Department of Psychology, University of Toronto, Mississauga, ON, 2Division of Biology and Biological Engineering, California Institute of Technology, CA, 3Department of Cell and Systems Biology, University of Toronto, Mississauga, ON
The objective of this study was to establish a new black/white anxiety test for larval zebrafish and to investigate the effects of diazepam. Previously, zebrafish larvae were shown to exhibit a preference for light areas over dark. Recently, we found adult zebrafish to show preference for black to white areas. We hypothesized that diazepam will induce a concentration dependent increase of white preference in a black/white preference task using zebrafish larvae. 5-6 (dpf) zebrafish larvae were placed in a single well plate containing their original tank water with varying concentrations of diazepam, and their movements recorded for 45-minute testing periods. A white and black background was placed under the well plate to create a black zone on one side and a white zone on the other side of the well. 120 zebrafish larvae divided into three groups consisting of 0 μM (control), 0.25 μM (low), and 2.5 μM (high) concentration of diazepam was tested. Unexpectedly, however, we found zebrafish larvae not to exhibit a preference for either the black or white background regardless of diazepam exposure. Although zebrafish larvae have been previously reported to exhibit a preference for black in the black-white preference task, our results contradict this finding. We are currently exploring whether this contradiction is the result of failure to distinguish the effect of black/white background vs high/low illumination level. (Acknowledgements: UTM Undergraduate Research Grant)

B12) EVIDENCE FROM ERPS THAT POSITIVE INDIVIDUALS ARE SENSITIVE TO REFERENTIAL CUES
Veena Dwivedi, Victoria Witte, Janahan Selvanayagam; Brock University, St. Catharines, ON
Affective state is known to influence cognitive processing (Loftus et al., 1987). Here we investigate whether this relation extended to linguistic processing. In an event-related potential (ERP) study, we examined whether individual differences in dispositional affect interact with sentence processing strategies. We focused on quantifier scope sentences such as (i) Every kid climbed a tree. These sentences lack any syntactic or lexical ambiguity, however, two possible meanings are available, where either many trees, or just one tree, was climbed. In Dwivedi (2013), it was proposed that these sentences are processed using “Heuristic first, algorithmic second” mechanisms. Presently, we hypothesized that individuals who report high positive affect would display a more global processing style and rely on heuristics when processing sentences (Clore & Huntsinger, 2007; see Chwilla et al., 2011) vs. those reporting negative affect, whom we expect would display a more local, algorithmically based (i.e. grammatical) processing mechanism. 12 participants read sentences such as (i) presented in 1- and 2-word chunks and judged, at the target word tree, whether 1 or 2 words appeared on the computer screen (Berent et al., 2005). Preliminary results revealed a partial replication of the ERP results of Dwivedi & Gibson (2017). Interestingly, no correlations were found for ERP responses for individuals reporting negative affect, whereas trends were revealed for those reporting positive affect in control conditions. We interpret the positive affect findings in terms of global/discourse processing and sensitivity to referential cues. (Acknowledgements: Supported by SSHRC and CFI)

B13) THE RECONSTRUCTION OF WORKING MEMORY REPRESENTATION FROM INDUCED ALPHA EEG ACTIVITY SHOWS EVIDENCE FOR A DE-SELECTION OF CTFs AFTER A MENTAL TRANSFORMATION
Joel Robitaille and Stephen M. Emrich; Department of Psychology, Brock University, St. Catharines, ON
Previous fMRI studies have been able to decode features of an item held in working memory (Harrison & Tong, 2009) and track the changes applied to these features (Albers et al., 2012) from the activity detected within the visual cortex. More recently, Foster et al. (2016) were able to reconstruct orientation selectivity profiles from induced alpha-band (8 – 12 Hz) oscillations of electroencephalographic (EEG) data, enabling the identification of the contents held in visual memory. In an attempt to extend these findings this study examined whether the induced alpha activity, which has been shown to mediate the representation of orientations held in visual working memory, can be used to track an imagery manipulation of these representation via a mental rotation. A forward encoding model was applied to EEG activity recorded while participants were holding the orientation of a line in working memory and then applied a 60° mental rotation to the presented stimulus. The results replicate previous findings, revealing that induced posterior alpha-band activity contains sufficient information that allows for the identification of the representation maintained in working memory. Furthermore, the reconstruction of orientation selectivity profiles revealed reliable changes in the mental representation during the imagery manipulation suggesting a de-selection of the orientation presented at the beginning of the experiment. (Acknowledgment: Supported by NSERC Discovery Grant [#435945] and NSERC Research Tools and Instruments Grant [#458707])
B14)  FEMALE SEX HORMONES PLAY A ROLE IN VULNERABILITY TO SLEEP LOSS ON EMOTION PROCESSING TASKS
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This study investigated the relationship between sex hormones and emotion processing following sleep restriction. Sleep restriction groups slept 3am-7am (13 men, 13 women in follicular phase, 10 women in luteal phase of menstrual cycle), and control groups slept 11pm-7am (12 men, 12 follicular women, 12 luteal women). Saliva samples were collected during an evening baseline, and in the morning and afternoon after sleep restriction to measure estradiol and progesterone. Event-related potentials were recorded during presentation of images and faces to index neural processing of emotional stimuli. Luteal women showed lower overall accuracy categorizing emotional images after sleep restriction ($F(1,42) = 4.134, p = .048$), and there was a correlation with progesterone and negative accuracy in SR luteal women ($r = .826, p = .022$); progesterone was also correlated with the LPP amplitude difference between negative and neutral images ($r = .778, p = .039$). In sleep-restricted women, higher progesterone was associated with worse accuracy on sad faces ($r = .842, p = .009$) and a larger N170 to sad faces ($r = -.754, p = .031$), reflecting greater reactivity. Women higher in progesterone were more vulnerable to the effects of sleep restriction. This study highlights a role for sex and sex hormones in understanding individual differences in sleep loss outcomes.

B15)  EFFECTS OF MUSCARINIC ACETYLCHOLINE RECEPTOR BLOCKADE ON SOCIAL LEARNING IN INTACT AND OVARIECTOMIZED FEMALE MICE
Kelsy Ervin, Cecil Dana Main, Elena Choleris; Department of Psychology and Neuroscience Collaborative Program, University of Guelph, Guelph, ON
Through social learning animals acquire information from others. One type of social learning in rodents is the social transmission of food preferences (STFP), in which an “observer” preferentially eats a novel food it smelled on the breath of a conspecific “demonstrator” during a previous social interaction. The STFP is enhanced by estrogens in female mice and is impaired by muscarinic acetylcholine (ACh) receptor blockade with scopolamine (SCOP) in male rats. Whether muscarinic ACh signaling plays a similar role in female mice, or how it is influenced by gonadal hormones is unknown. In a pilot experiment, we found that, when tested immediately after acquisition, SCOP blocked social learning in gonadally intact female mice at lower doses (2mg/kg) than ovariectomized (OVX) mice (3mg/kg), suggesting that OVX mice were less sensitive to disruption by SCOP. However, SCOP also inhibited feeding behavior, confounding effects on STFP. Thus, we tested the effects of SCOP in 48h after social learning to rule out effects on feeding. Female observer mice received either sham or OVX surgery 15d prior to testing. Observers were treated with 0.1, 1, or 2mg/kg SCOP or saline 30min prior to interaction with the demonstrator (acquisition phase). Observers were then separated from the demonstrator and tested for a food preference 48h later. Preliminary results show that social learning was blocked in intact mice by 1 and 2mg/kg SCOP. Testing of OVX mice is ongoing. This will give us an understanding of the role of ACh in female social learning, and its interactions with gonadal hormones. (Acknowledgements: Funded by NSERC)

B16)  THE HISTONE ACETYLTRANSFERASE PCAF INTERACTS WITH ESTROGEN RECEPTOR ALPHA TO REGULATE SHORT-TERM MEMORY THROUGH A NON-EPIGENETIC MECHANISM
Krista A. Mitchnick1,2, Cassidy E. Wideman1,2, Rhiannon Jameison-Williams3, Allison LaCoursiere1, Sabrina Castellano4, Citro Milite4, Gianluca Sbardella5, Elena Choleris1,2, and Boyer D. Winters1,3; 1Department of Psychology, 2Collaborative Neuroscience Program and 3Department of Molecular and Cellular Biology, University of Guelph, Guelph, ON, 4Department of Medical Chemistry, University of Salerno, Salerno, Italy
The involvement of histone acetylation and histone acetyltransferases (HATs) in long-term memory (LTM) is well established, and we have recently demonstrated that inhibition of the HAT PCAF in perihinal cortex or hippocampus (HPC) impairs long-term object-in-place (OIP) memory in rats. Interestingly, HPC PCAF inhibition also impaired short-term memory (STM), suggesting a non-genomic effect. Indeed, HATs can acetylate lysine residues on histone and non-histone proteins, and are broadly referred to as lysine acetyltransferases. As PCAF has been shown to activate nuclear hormone receptors, and nuclear estrogen receptors (ERs) are known to be involved in STM, we investigated the potential interaction of PCAF and ERs in the rapid regulation of OIP memory in the HPC of male rats. Behavioural experiments utilizing intra-HPC administration of pharmacological agents that enhance or inhibit the function of PCAF, ERα, and ERβ, demonstrate that PCAF’s ability to modulate STM in the HPC is mediated through functional interactions with ERα. Specifically, an ERαβ antagonist blocked the enhancing effects of PCAF activation on STM, but not LTM, and a PCAF inhibitor blocked the enhancing effects of ERα agonism on STM. Furthermore, aromatase inhibition demonstrated HPC estrogen biosynthesis to be necessary for STM, but not for the STM-enhancing effects of PCAF activation. Thus, PCAF appears to regulate STM and LTM via dissociable mechanisms, and indicates that PCAF can have activational effects on ERα in the male rat HPC, in a ligand-independent manner, to support short-term OIP memory. (Acknowledgements: NSERC)

B17)  THE MODERATING EFFECTS OF COGNITIVE FUNCTIONING ON TRAIT MINDFULNESS IN A SUBSYNDROMAL BIPOLAR POPULATION WITH HYPOMANIC SYMPTOMS
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Objective: Research indicates that patients with bipolar disorder (BD) demonstrate impairments in working memory and attention. Recently, mindfulness-based practices have been examined in BD as a therapeutic approach for reducing mood symptoms. Retentive working memory and sustained attention are key for effective results in mindfulness-based interventions. Research suggests mindfulness practices reduce anxiety and depressive symptoms in BD. However, manic symptoms remain unaffected. Research indicates elevated levels in mania, and impairments in working memory and attention decrease the effectiveness of mindfulness-based interventions. Accordingly, we examined the relationship between manic symptoms and trait mindfulness. Furthermore, we examined whether cognitive functioning moderates this relationship. We hypothesized that impaired cognitive functioning would predict elevations in manic symptoms, which would lead to reductions in trait mindfulness. Method: 125 participants completed BRAIN screen, the Five-Facet Mindfulness Questionnaire (FFMQ), and the Halberstadt Mania Inventory (HMI). Results: We examined a positive association between manic symptoms and trait mindfulness. Cognitive functioning significantly moderated the association between manic symptoms and trait mindfulness. Working memory had the largest effect on this association, when compared with overall cognitive functioning or sustained attention. Conclusions: The relationship between manic symptoms and trait mindfulness may be explained by heightened sensory processing that is often present in acute mania. Moderation analyses on cognitive functioning confirm previous findings that working memory is associated with trait mindfulness. Nonetheless, future research including possible interacting factors, such as state mindfulness and heightened sensory processing, is encouraged to conclusively interpret the impact of mindfulness on reducing manic symptoms.

B18) **EFFECTS OF STRESS ON PLACE CONDITIONING PRODUCED BY Δ9-TETRAHYDROCANNABINOL AND FAAH INHIBITION IN SPRAGUE DAWLEY RATS**

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The compound Δ⁹-tetrahydrocannabinol(THC) is a partial agonist of the cannabinoid 1(CB1) receptor of the endocannabinoid(eCB) system. Research on the rewarding/aversive effects of THC produce inconsistent results with most studies finding it aversive to rodents. It remains unclear what factors modulate rewarding/aversive effects of THC. Research indicates that prior stress results in decreased eCB function and enhances anxiety-like behaviours in rodents. Blocking the catabolic enzyme of the eCB anandamide(AEA), fatty acid amide hydrolase(FAAH) prevents enhancement of anxiety-like behaviours in previously stressed animals via CB1 mechanisms. Since THC and inhibiting FAAH increase CB1 signalling, prior stress may alter the rewarding effects of THC or a FAAH inhibitor(URB597). The effect of prior stress on the rewarding/aversive effects of THC (1, 0.1, 0.5mg/kg) and URB597(0.3mg/kg) were determined using an unbiased place conditioning procedure. Sprague Dawley rats were exposed to footshock stress or no stress 24h prior to conditioning. To take advantage of prior fear conditioning, the potential of THC and URB597 to alter the expression of conditioned fear was also examined. 1 mg/kg THC produced a conditioned place aversion that was not modified by stress. There were no effects on place conditioning by 0.5, 0.1 mg/kg THC, or by URB597. Expression of conditioned fear was reduced by 1mg/kg THC, and prolonged by 0.1mg.kg THC. URB597 and 0.5mg.kg THC had no effect on conditioned fear. In conclusion, footshock stress did not alter a place conditioning produced by THC or URB597. (Acknowledgments: This research was supported by grants from NSERC (92057) and CIHR (137122) to L. Parker)

B19) **EFFECT OF SOCIAL INSTABILITY STRESS AND SOCIAL CONTEXT ON THE INTAKE ETHANOL AND SUCROSE IN ADOLESCENT MALE RATS**

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**Introduction:** Social instability stress in adolescent rats (SS; postnatal day 30-45, daily 1 hour isolation + new cage partner) alters behavioural responses to psychostimulants and increases anxiety-like behaviour, but differences in voluntary consumption of natural and drug rewards are unknown. Here, we investigated whether SS rats would show increased consumption of rewards relative to CTL, particularly in the presence of an unfamiliar peer. **Methods:** Male no-stress (CTL) and SS rats were placed in an apparatus divided in half by a mesh, either alone or with an unfamiliar partner (social) on the other side of the mesh, and were randomly assigned to have access to 10% ethanol (EtOH) or 1% sucrose. **Results:** For EtOH groups, CTL rats had a longer latency to drink than SS rats (p=0.015) and alone rats had a longer latency than social rats (p=0.023). SS rats spent more time drinking EtOH than did CTL rats (p=0.030), and no effect of social condition was found. For Sucrose groups, there were no effects on latency to drink. Alone rats spent more time drinking (p=0.020) than social rats, and no effect of stress was found. **Conclusions:** The increased EtOH consumption of SS rats compared with CTL may be associated with evidence of increased anxiety in SS rats and the anxiolytic properties of EtOH. SS and CTL rats do not differ in sucrose intake, which suggests no differences in sensitivity to the “hedonic” properties of sucrose. The effect of peer presence on intake in both conditions is in the opposite direction to previous reports with sweetened EtOH, which suggests that the effect of peers may depend on the degree of reward value of the substance. (Acknowledgments: Support by NSERC and OTS)

B20) **THE EFFECTS OF ESCITALOPRAM AND ARIPIPRAZOLE ON HEDONIC RESPONSES TO A NATURAL INCENTIVE IN RATS**
Augmentation and combination strategies have been employed in an effort to make current SSRI treatments more effective for the treatment of depression. One of these strategies includes combining Escitalopram (ESC; selective-serotonin reuptake inhibitor) with the atypical antipsychotic Aripiprazole (ARI; partial agonist for the DA D2 receptor). It was hypothesized that ARI enhances the effect of SSRIs by enhancing their effect on reward reactivity. Male Sprague-Dawley rats were treated chronically with 0 mg/kg/day ESC, 10 mg/kg/day ESC, and 10 mg/kg/day ESC+2 mg/kg/day ARI combinations and tested on operant intraoral self-administration of high fructose corn syrup on a continuous (FR1) and progressive ratio (PR) schedule of reinforcement, as well tested on taste reactivity before, during, and after treatment. At the conclusion of experiments, mRNA expression was quantified for genes involved in appetite, reward, and depression: MOR in the nucleus accumbens (core and shell), D2 dopamine receptor (DR2) in the caudate-putamen (CPu), pro-opiomelanocortin in the hypothalamus and brain derived neurotrophic factor in the hippocampus. It was found that chronic ESC + ARI decreased responding on the PR schedule, but did not alter the number of infusions obtained on FR, nor affected the number of tongue protrusions on tests of taste reactivity. Gene expression analysis revealed that ESC + ARI differed from ESC alone only on the expression of D2R mRNA in the CPu. These findings indicate that ARI augmentation does not alter hedonic responses to natural incentives. (Acknowledgements: Supported by the Canadian Biomarker Integration Network in Depression (CAN-BIND))

**B21) PHYSIOLOGICAL ROLES OF GLUTAMATE SECRETED FROM VGLUT3-EXPRESSING NEURONS**

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Vesicular glutamate transporter 3 (VG3) stores glutamate (Glu) in vesicles of neurons that commonly secrete other neurotransmitters, such as striatal cholinergic interneurons (CINs). In CINs, VG3 expression allows for Glu release and can facilitate acetylcholine (ACh) storage. Whether Glu released by VG3-expressing neurons has significant physiological functions beyond supporting ACh neurotransmission is still poorly understood. We generated two mouse lines, one in which an excitatory DREADD (Drd) is expressed in VG3-positive cells (VG3creDrd) and a second line in which we knocked out release of ACh (VG3CreFxDrd) in addition to expressing Drd. This allowed us to activate neurotransmitter secretion and start to isolate Glu released from VG3-positive cells. Upon CNO injection, we found that activation of VG3CreDrd cells caused decreased exploratory activity. However, the hypoaactivity was not related to motor deficits or alterations in mood and anxiety. Moreover, elimination of ACh release in VG3CreFxDrd mice produced the same behavioural phenotypes, indicating ACh release may not impact the hypoaactive phenotype. Thus, these results suggest activation of VG3-positive neurons produces the overall suppression of movement. Future experiments will investigate the brain regions involved in this phenotype and the contributions of other neurotransmitters. Ultimately, these experiments will broaden our understanding of glutamatergic transmission, specifically clarifying if Glu secretion from VG3 neurons has specific physiological functions independent of their co-transmitter. (Acknowledgements: Supported by CIHR, Brain Canada Project)

**B22) REDUCTION OF PALATABLE FOOD INTAKE BY A CANNABINOID RECEPTOR NEUTRAL ANTAGONIST**

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The present study compared the effects of the cannabinoid receptor neutral antagonist O-2050 and the cannabinoid receptor antagonist/inverse agonist rimonabant on food consumption when animals were given either limited or unlimited access to a high-carbohydrate diet. Non-deprived male CD(SD)IGS rats were divided in two conditions: limited access (LA) to palatable food and unlimited access (UA) to palatable food. Rats were habituated to the testing apparatus, then injected intraperitoneally with vehicle, O-2050 (0.03-3.0 mg/kg) or rimonabant (3.0 mg/kg) prior to 4 h test sessions. LA animals consumed more food than UA animals. Food consumption was significantly reduced by both drugs in the LA condition only at hour 1. Rimonabant, but not O-2050, significantly reduced food intake in UA animals. O-2050 (3.0 mg/kg) reduced locomotion at hours 2, 3 and 4. Our results suggest that O-2050 suppresses consumption of a high-carbohydrate diet similar to rimonabant. Further studies are needed to examine the utility of O-2050 in the treatment of obesity and binge-eating disorders.

**B23) SOCIAL RECOGNITION IS FACILITATED BY 17ß-ESTRADIOL IN THE PARAVENTRICULAR NUCLEUS OF FEMALE MICE**

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Social recognition (SR) is the ability to identify familiar individuals based on information acquired from previous interactions. It is an important ability for the development of social bonds with others. Past studies have implicated both estrogens and oxytocin (OT) in having facilitative effects on SR. We hypothesize this will occur in the paraventricular nucleus (PVN) of the hypothalamus. Circulating estrogens will enter the PVN and bind with estrogen receptor beta (ERβ) and/or the G-protein coupled estrogen receptor (GPER) and will facilitate the production and
release of OT. In the medial amygdala estrogens binding to ER regulate OTR production. The OT that was produced in the PVN will bind to OTR in the medial amygdala and facilitate SR. To test this, we will infuse 17 -estradiol (E2) into the PVN of ovariectomized mice and using a SR paradigm determine if estrogens can facilitate SR. Doses of 25, 50, or 100nM of E2 will be infused into the PVN and after 15 minutes, they will be exposed two stimulus mice for two five-minute habituation phases. Then in the test phase they will be exposed two stimulus mice, one from the habituation phase and a novel stimulus mouse. If it is found that the novel stimulus mouse is investigated more than the familiar, it would suggest that the familiar mouse is recognized and that SR occurred. It also takes place within 40 minutes to test the rapid effects of estrogens. The infusions of the 25 and 50nM doses were able to rapidly facilitate SR, showing support for the idea that estrogens in the PVN can influence SR. (Acknowledgements: Funded by NSERC).

B24) DELTA-9-TETRAHYDROCANNABINOL AND CANNABIDIOL PRODUCE DIFFERENTIAL EFFECTS ON AVERSED AND REWARDING EMOTIONAL MEMORY FORMATION AND SALIENCE ATTRIBUTION THROUGH ACTIONS IN THE VENTRAL HIPPOCAMPUS

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Disturbances in emotional processing and salience attribution are core features of schizophrenia and other neuropsychiatric disorders. The ventral hippocampus (VHipp) contains large distributions of cannabinoid receptors that regulate emotional memory formation by modulating dopamine (DA) signaling in mesolimbic structures such as the ventral tegmental area (VTA). Delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) are phytocannabinoids that differentially impact DA activity and emotional processing. Nevertheless, the mechanisms through which intra-VHipp THC and CBD may modulate emotional memory remain unknown. We examined whether intra-VHipp THC and CBD differentially control the salience of reward and aversion-related associative memory using assays of social reward, morphine place preference and fear conditioning. In addition, we measured VTA DAergic neuronal responses to intra-VHipp THC using extracellular single unit recordings. Intra-VHipp THC induced deficits in social memory formation but enhanced memory for rewarding and aversive associative cues. CBD alone had no effect, but when combined with THC increased social memory and disrupted THC-induced changes in emotional memory formation. In addition, intra-VHipp THC altered VTA DA firing patterns by increasing population activity and reducing phasic bursting levels. Our findings implicate the VHipp as a critical site for modulation of both reward and aversion-related emotional memory formation and have implications for understanding the efficacy of cannabis-derived phytochemicals in neuropsychiatric symptomology.

B25) TIME COURSE OF FACE PROCESSING MODULATIONS BY CONTEXTUAL SELF-RELEVANCE AND SUBCLINICAL SOCIAL ANXIETY

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Individuals with high social anxiety (HSA) are more likely than those with low social anxiety (LSA) to interpret negatively-valenced stimuli as self-relevant. As fear of negative evaluation is thought to be one of the key components of HSA, this altered self-referential processing is thought to contribute to its development and maintenance. Contextual self-relevance and valence have been shown to influence early face perception, so we hypothesised that these effects on face processing vary as function of subclinical social anxiety. The present study used electroencephalography (EEG) to examine these context effects in groups with self-reported HSA (n=26) and LSA (n=30). We also investigated if context would interact with another self-referential cue – whether the faces were looking at or away from the participants. Positive and negative sentences (valence manipulation) referring to the participant or to someone else (self-relevance manipulation) were used as primes for neutral faces with direct or averted gaze (gaze manipulation). Eye-tracking ensured that participants read the sentences and fixated on faces. Mean amplitude analyses of 100ms time-windows post-face presentation (150-750ms) tracked the time-course of effects. While valence, gaze and self-relevance interacted to modulate face processing in both groups, self and other relevant contexts were distinguished at the neural level 100ms earlier in the HSA group than in the LSA group. These results provide support for altered self-referential processing in HSA, and characterize these differences at the neural level. (Acknowledgements: Supported by grants from the Natural Sciences and Engineering Research Council of Canada (NSERC Discovery Grant #418431), the Ontario government (Early Researcher Award, ER11-08-172), the Canada Foundation for Innovation (CFI, #213322), and the Canada Research Chair (CRC, #213322 and #230407) program to RJI. SDM was supported by a Queen Elizabeth II Graduate Scholarship for Science and Technology (QEII-GSST))

B26) COMPARISON OF SALIVARY AND AXILLARY PERSPIRATORY TESTOSTERONE, CORTISOL, AND ESTRADIOL LEVELS ACROSS THE FEMALE MENSTRUAL CYCLE

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Steroid hormones, such as androstadienone, have been investigated for pheromonal properties in humans but other steroids are secreted from the axilla in high concentrations. In men, it has been found that testosterone, estradiol and cortisol in human axillary perspiration are highly variable and in quantities up to1000 times higher than blood or saliva,
and both testosterone and estradiol are secreted proportionally to sexual arousal in males. Little is known about these steroids in axillary perspiration in women and their pheromonal capability. In this study, we investigated how cortisol, estradiol and testosterone (in saliva and axillary perspiration) varied across the menstrual cycle and how they related to personal or behavioural variables. Participants (females ages 17-32) filled out questionnaires inquiring about their menstrual cycle, current relationship status, exercise habits, sport involvement, and sexuality. They also provided perspiration samples after exercising and saliva samples before and after exercising for hormone analysis. We hypothesized that there would be a change in steroid levels across the menstrual cycle. Preliminary data have shown that there was no significant change in cortisol, estradiol, and testosterone (salivary or axillary) levels across the cycle. However, axillary testosterone levels were up to 3000 times higher than salivary testosterone levels on average and all axillary steroids were highly correlated with each other.

B27) THE ROLE OF THE PERIPHERAL IMMUNOPHENOTYPE IN BEHAVIOUR

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Recent studies in our lab revealed decreased anxiety-like behaviour in T cell deficient mice. Specifically, mice lacking the β and δ chains of the T cell receptor (TCRβ/-δ/-) showed reduced anxiety-like behaviour in several approach/avoidance behavioural tests including the elevated plus maze (EPM), open field test, and light/dark box test in adulthood. This study examines peripheral immune cells and behaviour in adolescence and adulthood in wild type and TCRβ/-δ/- mice. Behaviour was assessed using the EPM at postnatal day 28 (P28, pre-puberty in mice), open field at P56, and fear conditioning at week 16. Both male and female TCRβ/-δ/- mice showed increased exploratory behaviour measured by time spent in the intersection zone of the EPM and reduced anxiety-like behaviour measured by increased number of open arm entries. Increased locomotor activity was observed in the open field. Genotype and sex-by-genotype effects were observed in both cued and contextual fear conditioning in TCRβ/-δ/- mice. Results of FACS analysis shows decreased neutrophil numbers in both male and female TCRβ/-δ/- mice, and increased monocyte numbers. The behavioural differences observed in T cell deficient mice pre-puberty mirror previous findings in adult mice, suggesting that T cells influence the central nervous system early in development. While additional analysis is ongoing, these initial findings suggest that changes in the profile of peripheral immune cells influences behaviour. (Acknowledgements: Funding support by the Ontario Brain Institute)

B28) ADOLESCENT NICOTINE EXPOSURE INDUCES LONG-TERM ANXIETY AND DEPRESSION-LIKE SYMPTOMS THROUGH MOLECULAR AND NEURONAL DYSREGULATION OF MESOCORTICOLIMBIC DOPAMINE D1 AND ERK1-2 SIGNALING PATHWAYS

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Cigarette smoking is strongly correlated with mood disorders. Most smokers begin smoking in adolescence, a critical period of neurodevelopment, and the possible effects of nicotine (NIC) exposure on adolescent brain development are not well understood. Using a preclinical rodent model of adolescent NIC exposure, we examined if chronic adolescent NIC exposure might lead to deficits associated with mood disorders in adulthood and whether these effects may be related to molecular and neuronal activity alteration in the mesocorticolimbic dopamine (DA) system. We report that adolescent NIC exposure causes persistent increases in anxiety and depressive-like behaviours and higher-order cognitive deficits. These behavioural deficits were associated with alterations in selective molecular markers in the DA prefrontal cortex characterized by changes in DA D1 receptor and phosphorylated extracellular-signal-related kinase (ERK 1-2) expression levels. In addition, using in vivo neuronal electrophysiological recordings, we report that adolescent NIC exposure causes increased firing and bursting rates in ventral tegmental area DAergic neurons. Together, our findings demonstrate that adolescent NIC exposure causes long-term dysregulation in affective processing and cognition, consistent with mood disorder-like disturbances. These findings provide a better understanding of the long-term effects of adolescent NIC abuse and are the first identification of a specific neuronal and molecular mechanism linking adolescent NIC exposure with the development of later adulthood psychopathology.

B29) HOMEOSTATIC NEUROGENESIS IN THE LIZARD BRAIN

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Neurogenesis has been documented within various regions of the adult brain. Across vertebrates, the distribution of neural stem/progenitor cells (NSPCs) and the capacity for homeostatic neurogenesis vary greatly. Species in which NSPCs contribute to high levels of constitutive neurogenesis appear to be better able to replace neurons following brain injury. Here we investigate neurogenesis in an emerging model of brain regeneration, the leopard gecko. Cells lining the lateral ventricles (ventricular zone [VZ] cells) express stem cell markers SOX2 and Musashi-1. In addition, they share features with radial glia: a lengthy radial process and expression of glial markers Vimentin and glial fibrillary acidic protein (GFAP). As evidenced by proliferating cell nuclear antigen and phosphorylated histone H3, VZ cells are mitotically active. To track the fate of newly generated cells we conducted a bromodeoxyuridine (BrdU)
pulse-chase experiment. Following the pulse, BrdU+ cells are confined to SOX2+ NSPCs within the VZ. Following a 10-day chase, BrdU+ cells are displaced from the ventricular surface and are closely associated with GFAP+ apical processes. Notably, following a 30-day chase, BrdU+ cells are observed within the cerebral cortex and express mature neuronal marker NeuN. Thus, we have identified the VZ of the lateral ventricles as a constitutively active NSPC population. The generation of newborn neurons within a limited timeframe make the leopard gecko an excellent model for the study of postnatal neurogenesis and speaks to the regenerative potential of the gecko brain. (Acknowledgements: Supported by NSERC Discovery Grant 400358)

**B30) MICRONRNAS AND THEIR REGULATION OF RETINOIC ACID INDUCED GROWTH CONE TURNING IN NEURONS**

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During development and regeneration, neurons navigate through a changing and highly complex environment to establish remarkably accurate connections with their target cells. The tips of these growing axons, growth cones, rapidly respond to various environmental cues, including the Vitamin A metabolite, retinoic acid. Retinoic acid is a vital signaling molecule during the regeneration of the central nervous system (CNS), and has been shown to act as a chemotactrant for neurons in vitro. Little is known, however, about the underlying regulatory molecules involved in regulating the growth cone turning response to a gradient of retinoic acid. MicroRNAs (miRNAs), a class of conserved non-coding RNA transcripts, have recently been proposed to regulate gene expression and local protein synthesis during growth cone turning. Our goal is to determine the role that miRNAs play as mediators of axonal guidance in response to a non-traditional guidance cue, retinoic acid. We have evidence for the compartmentalization of miR-124 in these growth cones and axons, as well as its changing distribution within the growth cone during a turning response towards retinoic acid. Together, these studies will advance our knowledge of growth cone dynamics, especially the underlying mechanisms of retinoic acid-induced chemoattraction during CNS regeneration. (Acknowledgements: Funding was provided by Discovery Grants to RLC and GS from NSERC and Brock University)

**B31) DISTRIBUTION OF NEURAL/STEM PROGENITOR CELLS IN THE BRAIN OF THE LEOPARD GECKO (Eublepharis macularius)**

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Endogenous neural stem/progenitor cells (NSPCs) have been identified across vertebrate species. Among adult mammals, NSPCs are spatially restricted to just two neurogenic regions: the subventricular zone of the lateral ventricle, and the subgranular zone of the hippocampal dentate gyrus. In other species – including teleost fish and urodeles – NSPCs are known to have a much broader distribution. For reptiles, less is known. Here we identify NSPCs along the rostral caudal axis of the brain of the leopard gecko (Eublepharis macularius). The ventricular system of the gecko brain is bordered by a distinct neurogenic niche, the ventricular zone (VZ). All VZ cells (including those of the lateral, third and fourth ventricles) constitutively express the hallmark transcription factor of stemness, SOX2. Additionally, VZ cells have a radial-like morphology and pattern of protein expression (shown by immunostaining for intermediate filaments Vimentin and glial fibrillary acid protein [GFAP]), closely comparable to mammalian embryonic radial glial cells. At the level of the cerebellum, putative NSPCs (SOX2+) were also identified independent of the ventricular system. Across the brain, proliferating cells (identified by phosphorylated histone H3 expression) are most abundant in the VZ of the lateral ventricle and within cerebellar granular layer. The presence of NSPCs, both dormant and constitutively active, across the lizard brain offers compelling evidence for its neurogenic and possibly regenerative capacity. (Acknowledgements: Supported by NSERC Discovery Grant)

**B32) PATIENT-DERIVED GlioBLASTOMA CELLS ARE SUSCEPTIBLE TO INTRATUMORAL MODULATION THERAPY IN BOTH 2D AND 3D CULTURE**

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**Introduction:** Intratumoral modulation therapy (IMT) is a putative new treatment modality for the aggressive brain cancer glioblastoma (GBM). IMT delivers electrical stimulation directly into tumor-affected brain regions to induce tumor cell death. Our group has shown that IMT significantly reduces tumor burden in a syngeneic rat GBM model, however there is no direct evidence that human tumor cells would respond similarly to IMT. This study is designed to quantify IMT efficacy in patient-derived tumor cells. **Methods:** Patient-derived glioblastoma (GBM) cells were obtained during surgical resection and cultured in both 2D and 3D culture conditions. GBM tumor cells, neurospheres and rat embryonic neurons received 72 hours of IMT using a continuous sinusoidal waveform (200 kHz, 4V peak-to-peak). Treatment effect was assessed using MTT, flow cytometry for apoptotic markers and immunolabeling of cleaved-caspase3. **Results:** IMT produced caspase-dependent apoptosis, with a significant (>30% vs. sham; p<0.01) reduction in GBM cell viability for each patient tested. However, IMT did not affect the viability of neuronal cultures. **Conclusions:** All three patient-derived GBM cell lines examined are sensitive to IMT above field
intensity of 1 V/cm. These results will guide development of customized bioelectrodes for optimal IMT tumor coverage to maximize efficacy as a novel therapeutic approach to treating GBM.

B33) SUBREGIONAL AMYGDALA-HIPPOCAMPAL FUNCTIONAL CONNECTIVITY IS ASSOCIATED WITH PTSD AND DEPRESSIVE SYMPTOMS
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Alteration of amygdala-hippocampal functional connectivity following trauma is hypothesized to underlie symptoms associated with posttraumatic stress disorder (PTSD). The present study investigated subregional hippocampal-amygdala resting state functional connectivity (rsFC) and its relationship to PTSD and depressive symptoms in a sample of trauma-exposed individuals (n = 24). Eleven participants met criteria for PTSD while 13 were trauma-exposed controls. Cytoarchitecturally defined hippocampal and amygdalar subregions were created using Anatomy Toolbox. PTSD symptoms, as measured with the Clinician-Administered PTSD Scale, were positively associated with FC between the left basolateral amygdala (BLA) and the left entorhinal cortex within the control group. Depression scores on the Beck Depression Inventory were positively correlated with FC between the left BLA and the subiculum bilaterally, across the entire sample. These associations hold when partialing out shared variance between PTSD and depression symptom scores. These results highlight relations between FC and PTSD and depressive symptoms, particularly with the left BLA, which is involved in emotional and mnemonic processes. These findings point to the importance of investigating medial-temporal FC at the subregional level and provide support for future investigations of imaging biomarkers predictive of disease progression.

B34) INFLUENCE OF PARENTAL STATUS ON METHADONE MAINTENANCE TREATMENT OUTCOMES IN PATIENTS WITH OPIOID USE DISORDER: A CROSS-SECTIONAL STUDY
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Introduction: Currently, Canada has the second highest prevalence of opioid use disorder (OUD) in the world. The most common treatment for OUD is methadone maintenance treatment (MMT). Methadone is a synthetic opioid that prevents opioid withdrawal symptoms, and minimizes craving for opioids. Although MMT has been shown to be effective in combating OUD, the role of parental status in MMT outcomes remains unclear. The aim of this study is to investigate the influence of parental status on MMT treatment outcomes. Methods: Data is retrieved from the larger Genetics of Opioid Addiction program, a prospective cohort study investigating the genetic determinants of MMT response. All participants are 18+ years old, provided informed consent, and are currently receiving MMT. We performed a multivariate logistic regression to determine the association between treatment outcomes and parental status, controlling for potential confounders and effect modifiers. We performed subgroup analyses in males, females, and individuals who had children younger than 18. Results: Out of 1099 participants, 707 have children. Having children was not significantly associated with positive urine screens for illicit opioids (OR 1.019, p>0.05), and there were no significant interactions between having children and sex of the participant. In the subgroup analyses, there were no significant associations. Conclusion: Our results deviated from our expected results. We predicted parents to have differing outcomes than non-parents perhaps from stress of child-care responsibilities, or children as an agent of motivation to adhere to treatment. Our results suggest that future research should focus on investigating the association between child-care responsibilities and MMT outcomes.

B35) SELECTIVE KNOCKDOWN OF HSP70 HEAT SHOCK PROTEIN HSPA6 VS HSPA1A SUGGESTS THEY EXHIBIT DIFFERING CONTRIBUTIONS TO THE ABILITY OF DIFFERENTIATED HUMAN NEURONAL CELLS TO SURVIVE THERMAL STRESS
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Heat shock proteins (Hsps) are highly conserved proteins that play important roles in cellular repair and protective mechanisms to counteract protein misfolding and aggregation that are features of neurodegenerative diseases. HSPA6 (Hsp70B') is an inducible member of the HSPA (Hsp70) multigene family that has received little attention compared to the more widely studied HSPA1A (Hsp70-1). Interestingly, the HSPA6 gene is found in the human genome but is not present in mouse and rat. Hence it is absent in current animal models of neurodegenerative diseases which have been characterized as protein misfolding disorders. To advance knowledge of this little studied HSPA member, the effect of selective knockdown of expression of HSPA6 vs HSPA1A was examined in relation to the ability of differentiated human neuronal cells to survive thermal stress. Induction of Hsps by low dosage co-application of celastrol and arimoclomol was observed to enhance the ability of differentiated neuronal cells to survive heat shock. Selective siRNA knockdown of HSPA6 alone, or HSPA1A alone, resulted in loss of the protective effects of co-application of celastrol/arimoclomol with more pronounced effects observed at 44°C heat shock compared to 43°C. These results suggest that HSPA6 and HSPA1A exhibit differing functions and that induction of both is required for the protection of differentiated human neuronal cells against cellular stress. (Acknowledgements: Supported by grants from NSERC to I.R.B)
B36) BLOCKING A SPECIFIC PHOSPHORYLATION SITE LINKED TO TAU AGGREGATION, A PATHOLOGICAL HALLMARK IN ALZHEIMER’S DISEASE, DOES NOT AFFECT BRAIN DERIVED NEUROTROPHIC FACTOR (BDNF) LEVELS IN VITRO

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Tau is abnormally hyperphosphorylated in the Alzheimer’s disease (AD) brain at specific sites and detach from microtubules, forming toxic, soluble, tau aggregates. How tau aggregation leads to synaptic and neuronal loss is unclear. One potential mechanism is by reducing brain-derived neurotrophic factor (BDNF), a protein critical for neuronal survival, function and for learning and memory. BDNF expression is down-regulated in the brains of patients with tauopathies, diseases in which tau is hyperphosphorylated and aggregated, and in tau-expressing cells and transgenic mice. Our hypothesis is that the recruitment of tau into aggregates down-regulates BDNF transcription. In this study, we investigated tau phosphorylation at Serine 422, which results in tau aggregation in the AD brain. We hypothesized that BDNF down-regulation would be rescued by preventing phosphorylation leading to tau aggregation. Human neuroblastoma SH-SY5Y cells were stably transfected with a plasmid coding for human wild-type tau (htau40) containing a mutation at phosphosite S422, implicated in AD and tau aggregation. Cells were differentiated and BDNF levels were measured using qRT-PCR and Western blotting. BDNF levels were down-regulated in SH-SY5Y cells stably transfected with tau mutated at phosphosite S422 compared to controls, suggesting that BDNF down-regulation may not require tau aggregation. Alternatively, it is possible that BDNF down-regulation may depend on phosphorylation of multiple sites in a sequential order. Further experiments will be carried out to investigate these possibilities. (Acknowledgments: Supported by the Alzheimer’s Society of Canada)

B37) INVESTIGATING THE POTENTIAL OF N-3 FATTY ACIDS AS ACTIVATORS OF THE ANTIOXIDANT RESPONSE PATHWAY

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The unregulated production of reactive oxygen species (ROS) by dysfunctional mitochondria and the impairment of proteostatic function are key factors that contribute to the death of neurons in Parkinson’s Disease (PD). One mechanism that neurons can utilize to counter the stress caused by ROS accumulation is activation of the transcriptionally encoded antioxidant response, initiated by Nuclear factor E2-related factor 2 (Nrf2). We postulate that n-3 fatty acids can act as exogenous activators of the Nrf2/antioxidant pathway and may therefore protect neurons from PD pathogenesis. Under basal conditions, Nrf2 is sequestered in the cytoplasm by an actin-associated protein, Keap1. ROS accumulation leads to oxidative modification of Keap1, changing its conformation and thereby allowing Nrf2 to enter the nucleus and transcribe antioxidant response element (ARE) driven genes. Using SH-SY5Y cells and primary rat neurons exposed to n-3 fatty acids in combination with Nrf2 gain of function/loss of function analysis we will determine whether fatty acid supplementation promotes Nrf2-mediated ARE activation. In addition, we will determine whether elevated n-3 fatty acids induce nuclear translocation of Nrf2 in vivo utilizing the fat-1 transgenic mouse. This mouse expresses a C. elegans n-3 desaturase that allows for the endogenous conversion of omega-6 fatty acids to n-3 fatty acids throughout the brain. Our preliminary evidence suggests that n-3 fatty acids do indeed promote ARE activation. This work may lead to new therapeutic targets against PD. (Acknowledgements: Supported by NSERC, OMAFRA and Soy20/20)

B38) MINIMALLY INVASIVE STEM-CELL THERAPY AS A POTENTIAL TREATMENT FOR ALS

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Amyotrophic Lateral Sclerosis (ALS) is a fatal neurodegenerative disorder; motor neuron loss is one of the major aspects of this disease. We investigated a minimally-invasive, stem cell replacement therapy as a disease modifying treatment in a mouse model of fALS (SOD1G93A) mutant. MRI guided focused ultrasound (MRigFUS) technique was used to temporarily increase blood-splinal cord barrier permeability in a targeted region of the murine spinal cord (SC) while intravenously injecting GFP⁺, neural-differentiated cartilage-derived stem cells (NCSCs). Muscle strength was measured by rotarod and hanging-wire tests and organs were harvested for immunohistochemical analysis at end points. We found few GFP⁺ cells in the SC of treated mice; moreover, brain, heart, kidneys and liver were mainly clear. Largest deposition of GFP⁺ cells was found in the spleen; lungs also retained a high number of injected cells. Rotarod (F(2)=0.02,p>0.05), hanging-wire test (F(2)=3.34,p=0.06), disease onset (χ²(1)=0.50,p>0.05) or survival (χ²(2)=0.43,p>0.05) in Tg mice were not statistically significantly affected by treatment, but a trend towards improved behaviour was detected. Our results suggest that few cells reached the SC, perhaps due to multiple organ cell filtrations. An improved outcome may occur following intravascular cellular delivery. This research has shed light on the issue of the route of cellular delivery to the SC in the presence of MRigFUS. Nonetheless, the potential of
B39)  SYSTEMIC AUTOIMMUNITY: A SEX-SPECIFIC FACTOR IN ALZHEIMER'S-LIKE DISEASE

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The 3xTg-AD mouse is an established model of Alzheimer’s disease (AD). Our lab recently reported that 3xTg-AD males no longer exhibit AD-like plaque/tangle pathology at 1 year of age, but display anxiety-like behavior, learning/memory deficits, and signs of systemic autoimmunity within the first 6 months. This study was designed to compare immune status in both sexes and to determine whether autoimmunity is damaging or protective. 3xTg-AD and non-transgenic mice were administered the immunosuppressant cyclophosphamide from 4 weeks to 6 months of age. Mice underwent behavioral testing and were euthanized for assessment of immune status and molecular markers of AD. Immunosuppression abolished autoimmunity and reduced soluble Aβ, but failed to normalize brain mass, brain-derived neurotrophic factor expression and spatial learning in 3xTg-AD mice. Interestingly, it worsened their performance in anxiety-related tasks and produced distinct patterns of fur graying between sexes. Signs of autoimmunity were exacerbated in untreated 3xTg-AD males than females, suggesting sex is a factor in determining immune changes. This study points to early, sex-dependent autoimmunity that is associated with increased Aβ load and reduced anxiety-like behavior in 3xTg-AD mice. Consistent with evidence implicating the immune system in AD, our results suggest a complex role for autoimmunity in modulating brain and body physiology in an endpoint-dependent manner. These findings may shed light on the increased prevalence of AD in women and provide a novel framework to understand, diagnose and treat AD. (Acknowledgements: Supported by CIHR)

B40)  UNDERSTANDING AND IMPROVING CELL REPLACEMENT THERAPY FOR PARKINSON'S DISEASE

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Parkinson’s Disease (PD) is the world’s most common movement disorder, affecting approximately 1% of the population over the age of 65. Typically, intracellular aggregation of the protein alpha-synuclein (α-syn) precedes the progressive decline of A9-type dopaminergic neurons of the substantia nigra. To date, there is no known treatment capable of halting or reversing disease pathology. Nevertheless, stem cell therapy might be capable of repopulating this brain region, restoring function and in turn improving patient quality of life. However, recent post-mortem brain analysis from patients who received fetal grafts revealed α-syn aggregates in grafted tissue. This finding raises concerns regarding the effect of the host environment on grafted cells, and suggests that host pathology might transmit to grafted cells over time. Indeed, our lab was the first to demonstrate that endogenous mutant α-syn from patient-derived cells is capable of transmitting pathology to previously healthy cells in vitro. To investigate further, we aim to demonstrate that α-syn can propagate from PD-induced mouse tissue to grafted human A9-type dopaminergic neurons. We will further explore whether aggregation requires endogenous α-syn by using the CRISPR/Cas9 genome editing technology to knockout α-syn in healthy cells. Overall, this study will elucidate whether a combinatorial therapeutic approach might improve cell grafts for the treatment of PD. (Acknowledgements: Supported by PSC, NSERC & OGS. Further acknowledgments to OIRM’s genome editing workshop)

B41)  INVESTIGATING THE ROLE OF MANF IN THE PATHOPHYSIOLOGY OF PARKINSON’S DISEASE

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Mesencephalic astrocyte-derived neurotrophic factor (MANF) is a member of a recently discovered neurotrophic factor family implicated in supporting survival and protection of midbrain dopaminergic neurons in the nigrostriatal pathway, which degenerate in Parkinson’s Disease (PD). Increasing evidence demonstrated that MANF overexpression using viral vectors resulted in significant protection and repair of TH+ cells and DA neurons in the substantia nigra (SN). Thus, this study aims to investigate whether selective knockdown (K/D) of MANF leads to behavioural manifestation of PD in preclinical models. 2 μL at 0.5 μL/minute of MANF (N=8) and a scrambled control (N=8) of rat shRNA lentiviral formulations were infused unilaterally into the SN of male Sprague-Dawley rats in reference to bregma A/P=−5.3 mm, M/L=±2.3 mm, D/V=−7.8 mm. From months 2-4 post-surgery, increased latency and traversal durations, as well as increased contralateral and total errors were observed in MANF K/D rats in the beam traversal test (P<0.05). Moreover, fixed speed rotarod testing at 10, 20 and 35 rotations per minute revealed an increased latency to fall in MANF K/D rats at 4 and 5 months (P<0.05). The cylinder test revealed an ipsilateral paw preference during months 4 and 5 (P<0.05). The effects of the MANF shRNA vector on MANF mRNA and DA levels in the SN and striatum remains to be determined. While the etiology of PD remains unknown, this is the first study to demonstrate that MANF K/D recapitulates key features of parkinsonism, such as impairments in balance, motor coordination and forelimb use. (Acknowledgements: Supported by CIHR and NSERC)

B42) DOES ACUTE AEROBIC EXERCISE PROMOTE THE FORMATION OF SYNAPTIC ANCHORING ASSEMBLIES?
The long-term potentiation (LTP) of synaptic strength is thought to be achieved, in part, by the migration and capture of ionotropic glutamate receptors (particularly, AMPA receptors; AMPAR) at synaptic terminals. Notably, the process is believed to be chaperoned by AMPAR channel anchoring assemblies (ACAA). Thus, stimuli that increase the formation of ACAAs prior to LTP may promote enhanced receptivity of a synapse to LTP. Although aerobic exercise has been identified as a stimulus that promotes LTP, the mechanisms by which this occurs remain unclear. We hypothesize that the ability of aerobic exercise to prime LTP may be related to increased ACAA formation. As a result, male Sprague-Dawley rats were exposed to a single session of either rest, moderate, or exhaustive exercise on a metabolic treadmill. Following exercise, rats were sacrificed, and whole cell lysates prepared from sensorimotor cortices and hippocampi. Since ACAAs are transient structures dependent on the interaction of NMDA receptors with activated CaMKII, we co-immunoprecipitated NMDA-CaMKII complexes as a surrogate of ACAA formation. We hypothesized a relative enhancement in NMDA-CaMKII complex formation following exercise conditions compared to rest. Our preliminary data suggest that, under basal conditions, NMDA-CaMKII complexes can be co-immunoprecipitated, and our subsequent work will aim to repeat these experiments using tissue from animals that received exercise. (Acknowledgments: Supported by NSERC)

B43) RETINOIC ACID STABILIZES THE CLOSED AND INACTIVATED STATES OF VOLTAGE-GATED Ca2+ CHANNELS
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Retinoic Acid, the active metabolite of Vitamin A, regulates cellular function by binding to receptors (RARs and RXRs), and can exert both genomic and nongenomic effects within the cell. In vertebrates, retinoic acid plays a role in long-term memory as well as the synaptic plasticity thought to be associated with learning. In particular, retinoic acid and Ca2+ signaling interact postsynaptically, to mediate homeostatic synaptic plasticity (a type of synaptic plasticity thought to stabilize memories) by producing an increase in glutamate receptor expression in hippocampal neurons. Ca2+ signaling can also mediate homeostatic synaptic plasticity presynaptically, by altering voltage-gated Ca2+ channel function. Voltage-gated Ca2+ channels are ubiquitous within the CNS and mediate the release neurotransmitters at chemical synapses. In this study, we used voltage clamp electrophysiology recordings to investigate the effect of retinoic acid on voltage-gated Ca2+ channels of central neurons. We found that retinoic reduces the current through voltage-gated Ca2+ channels as well as shifts the voltage-dependence of channel activation. In addition, we found that retinoic acid increases the rate at which voltage-gated Ca2+ channels transition from the open state to both the closed and inactivated states. These data suggest that retinoic acid may reduce Ca2+ influx through voltage-gated Ca2+ channels by producing a preference for the closed and inactivated states of voltage-gated Ca2+ channels. These studies provide further insight into the cellular mechanisms of how retinoic acid alters synaptic communication and/or network activity during learning and memory.

B44) CHARACTERISTICS OF ICTL EEG IN MAGNETIC SEIZURE THERAPY AT VARIOUS STIMULATION FREQUENCIES
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Background: Magnetic Seizure Therapy (MST), an alternative to electroconvulsive therapy (ECT), is under investigation for the treatment of depression. Electrophysiological (EEG) recordings during therapeutically-induced seizures can predict response to ECT. The relationship between seizure characteristics and MST treatment outcome is unclear, as is the effect of treatment frequency on seizure characteristics. Hypothesis: 25 Hz MST has better seizure characteristics than 50 or 100 Hz, and seizure characteristics can predict clinical outcome. Methods: We analyzed seizure characteristics of depressed patients receiving MST at three separate stimulation frequencies: 25(n=34), 50(n=16) and 100 Hz(n=11). Mixed effect models were used to evaluate the effect of frequency on seizure characteristics and the relationships between seizure characteristics and clinical outcome. Results: 100 Hz had lower seizure adequacy ratings than 50 and 25 Hz groups, F(2,153)=10.585, p<.001. 50 Hz had longer slow-wave phase F(2,212)=6.254, p=.002 and total EEG durations F(2,171)=6.190, p=.003 than the 100 and 25 Hz groups. Motor seizure duration was longer in 50 Hz than the 100 and 25 Hz groups F(2,171)=8.613, p<.001. Global Seizure Strength was less robust in the 100 Hz group than the 25 and 50 Hz groups F(2,155)=5.735, p=.004. Polyspike duration F(1,146)=5.812, p=.017 and slow-wave amplitude F(1,150)=3.986, p=.046 negatively predicted reductions in depressive symptoms. Conclusion: Stimulation frequency affects seizure adequacy and some seizure characteristics may predict clinical response. (Funding Support: Funding for this project was supported by the Canadian Institutes of Health Research (CIHR), the Government of Ontario, the University of Toronto, the CAMH Foundation, and the Temerty Family Foundation)
B45) MOTOR SYSTEM EXCITABILITY FLUCTUATIONS DURING AUDITORY ANTICIPATION AND BEAT PERCEPTION
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Humans tend to spontaneously move to the regular beat of musical rhythm. Beat perception is the tendency to sense and anticipate the regular time positions (beats) that movements synchronize with. The neural motor system plays an important role in beat perception, but the dynamics of excitability in the motor system associated with beat perception have not been characterized. This project investigated motor system excitability fluctuations using transcranial magnetic stimulation and electromyography during perception of beat-based and non-beat-based rhythms. We applied single-pulse TMS over the left primary motor cortex of healthy participants as they listened to three types of rhythms that varied in the degree to which they induced beat perception. TMS elicited motor evoked potentials (MEPs) from the first dorsal interosseous muscle. MEP amplitude serves as a proxy for real-time motor system excitability. Furthermore, a beat tapping and rhythm reproduction behavioral task was also given following TMS where participants tapped back or reproduced rhythms of varying beat strength they heard during the TMS experiment. We hypothesized that during beat perception, motor system excitability may fluctuate at the rate of the perceived beat. Furthermore, we predicted that the beat tapping and rhythm reproduction task would be more consistent and more accurately reproduced for rhythms with a strong beat. We found that beat perception was not associated with anticipatory increases in motor system excitability, or with ongoing fluctuations in excitability at multiple rates associated with the beat. However, we found that the beat tapping and rhythm reproduction task were more consistent and more accurately reproduced for rhythms with a strong sense of beat. These results inform our understanding of the neural mechanisms of beat perception, and the involvement of an auditory-motor coupling system during behavioral tasks. (Acknowledgements: Supported by NSERC, McDonnell Foundation, and the Canadian Foundation for Innovation)

B46) NON-CANONICAL cAMP-DEPENDENT MECHANISM FOR STRESS HABITUATION
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To protect against the effects of chronic stress, there are mechanisms in place that allow the stress response systems to habituate. The hypothalamic-pituitary-adrenal (HPA) axis—the body’s main stress response system—is known to undergo habituation in response to chronic stress, but the underlying mechanism for this habituation is not known. Activation of the HPA axis relies on the release of corticotropin releasing hormone (CRH) from neurons in the paraventricular nucleus of the hypothalamus (PVN). These PVN-CRH neurons are positioned to fine-tune the HPA axis stress response, and therefore, changes in their synaptic transmission can inform changes in the stress response. As many neuromodulators activate CRH neurons through the cAMP pathway, here, we use the drug forskolin (an activator of cAMP) to study CRH neuron synaptic transmission. By using patch clamp electrophysiology in ex vivo mice brain slices, we report that forskolin potently stimulates transmission onto PVN-CRH neurons, and that this cAMP-mediated synaptic stimulation is attenuated following habituation to a repeated mild stressor ( restraint stress). When this synaptic potentiation was further investigated in naïve mice, we found that inhibiting the cAMP targets, PKA, EPAC, or ERK did not prevent the forskolin-induced potentiation, however, it was abolished following inhibition of HCN channels (a target for cAMP). This result highlights a possible mechanism for stress habituation (the attenuation of cAMP-mediated synaptic transmission) and suggests a role for HCN channels in PVN-CRH synaptic transmission.

B47) INVESTIGATION OF NITRIC OXIDE-DEPENDENT MECHANISMS OF COCAINE-INDUCED PLACE PREFERENCE AND MU OPIOID RECEPTOR EXPRESSION
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Cocaine administration increases both mu opioid receptor (MOR) expression and nitric oxide (NO) production in brain areas associated with reward. The present study investigated whether the in vivo cocaine-mediated increase in MOR expression is NO-dependent and whether inhibition of this mechanism blocks cocaine reward, as assessed by conditioned place preference (CPP). Male Sprague-Dawley rats were treated with 7-nitroindazole (7-NI) (25mg/kg or 50mg/kg, i.p.), a selective neuronal nitric oxide synthase (nNOS) inhibitor, prior to cocaine administration (20mg/kg, i.p.) during place conditioning (biased design, 4 drug and 4 vehicle pairings). Seventy-two hours following CPP testing, mRNA and protein levels of MOR and nNOS were measured using qPCR and western blotting, respectively. Pre-treatment with either dose of 7-NI attenuated cocaine CPP, as well as the increase in MOR mRNA in the nucleus accumbens (NAc). However, no changes in MOR protein levels were observed. In rats pre-treated with 7-NI, nNOS mRNA was significantly elevated in the NAc, whereas nNOS protein levels were significantly reduced. These results suggest that NO plays a role in the motivational effects of cocaine and in the modulation of cocaine-induced MOR expression. Furthermore, the increase in nNOS mRNA in rats pretreated with 7-NI suggests there may be a compensatory response to the decreased nNOS protein levels that resulted from the inhibition of nNOS activity and NO production. (Acknowledgments: Support by NSERC, CIHR, and the Ontario Veterinary College.)
**B48) ASSESSING SOLUBILIZATION OF LURASIDONE AND HALOPERIDOL WITH MICROGEL POLYMERS**

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Brain neurotherapeutic delivery is difficult as the blood brain barrier prevents admission of many small hydrophilic and nearly all large molecules from blood circulation. The olfactory route offers a possibility for brain targeting of drug. Due to inadequate aqueous solubility, most neurotherapeutics will require a vehicle to accommodate this limitation. This study investigated hydrophobic microgel polymer-based formulations to entrap haloperidol (HP), a typical antipsychotic drug, and lurasidone (LRD), an atypical antipsychotic, both used in schizophrenia. We assessed potential of 2 structurally different microgel polymers (MMA and BMA) to solubilize HP and LRD formulation. We continued with in vivo testing of the most optimal HP formulation to assess how efficacious the solution was in delivering HP to Sprague-Dawley brain by evaluating behavioural responses. Formulations were prepared with solvation of HP/LRD in ETOH, then subsequently equilibrated with microgel. Dispersed formulations were centrifuged for removal of microgel buffer and excess ETOH. Intranasal (IN) and intraperitoneal (IP) routes were utilized for behavioral assessment of catalepsy (30, 60, 90 minutes post-administration) and locomotor suppression in Sprague-Dawley rats in vivo of HP-loaded microgel. HP drug loading was found to be higher in MMA formulation than BMA. LRD drug loading was found to be inconclusive dependent on preparation. IN administration showed early catalepsy induction and longer lasting cataleptic effects than IP route with HP-microgel. IN and IP routes showed locomotion suppression with HP-microgel administration. Efficacy of HP-loaded microgel polymer via nasal route and its potential for drug to brain targeting with non-invasive administration were demonstrated.

**B49) ASCENDING THE REINFORCEMENT GRADIENT DURING SENSORIMOTOR LEARNING**

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For the past 25 years, the field of sensorimotor learning has been dominated by the notion that error feedback alone drives motor learning. Recently, it has been shown that sensorimotor learning is accelerated and better retained when reinforcement feedback is combined with error feedback. Here we designed a novel hand-aiming task to isolate the role of reinforcement feedback during sensorimotor learning. Participants grasped the handle of a robotic manipulandum and reached forward to a virtual target. We informed participants that they would receive reward (visual, auditory, monetary components) for successfully hitting the virtual target. We made reinforcement gradients by providing reward probabilistically as a function of reach angle. Unbeknownst to them and depending on the reinforcement gradient, they had a higher probability of receiving reward if they reached to the right and or left of their baseline reaching behaviour. In Experiment 1, we predicted that increasing gradient steepness—the rate at which the probability of reinforcement increased—would accelerate learning. In Experiment 2, the probability of reinforcement increased in two directions but at different rates. We predicted that participants would reach in the direction of the steeper gradient. In Experiment 1, we found that a steeper gradient accelerated learning. In Experiment 2, a higher proportion of participants reached in the direction of the steeper gradient. Taken together, we found that reinforcement landscapes contain salient information that can shape our behaviour during reaching. (Acknowledgements: Supported by CIHR)

**B50) AGE RELATED ALTERATIONS IN NEURAL CONTROL FOLLOWING A PERTURBED GAIT INITIATION TASK**

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**Introduction:** Transient tasks such as gait initiation (GI) are completed with increased difficulty in older adults (OA). GI presents a complex challenge to the central nervous system as upright posture must be preserved when transitioning from quiet stance to steady state gait. Proactive strategies must be generated to counteract this tonic perturbation and ensure stability; unfortunately, a large proportion of falls occur during this dynamic phase of the gait cycle. In the event of an unexpected perturbation, even quicker reactions must be generated. Our goal was to explore age related differences in reactive strategies generated following an unexpected perturbation of the support surface.

**Methods:** Nine healthy University aged young adults (YA) and 8 older, community-dwelling adults were recruited for this study. Gait was initiated from quiet stance on one of two force plates mounted on a robotic platform. A total of 35 GI trials were collected: 4 anterior, 6 posterior, 6 left, 4 right and 15 no perturbation. Step width and length, in addition to forward velocity of the pelvis center of mass at heel contact was calculated for the first recovery step. **Results:** OA reduced pelvis velocity (F1, 14)=8.86, p=0.007; OA 0.52±0.27, YA 0.73±0.16 m/sec), perhaps to reduce forward momentum following the perturbation. Of concern, these older adults also decreased their base of support (step length; F1, 14)=22.12, p=0.0001, OA 0.35±0.12, YA 0.49±0.9 meters) in the step immediately following the perturbation which may present an increased risk for falls. (Acknowledgments: Supported by NSERC)

**B51) SENSORY FILTERING AND SOCIAL BEHAVIOUR DEFICITS IN A PRENATAL IMMUNE ACTIVATION MODEL OF ALTERED NEURODEVELOPMENT**
Delayed Sox9 Ablation in a Mouse Model of Chronic Spinal Cord Injury

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The majority of individuals who have suffered from traumatic spinal cord injury (SCI) have longstanding damage leading to debilitating sensory and motor impairments. These impairments are due to the loss of functional neuronal connections that occurs in the spinal cord following trauma. The molecular environment of the spinal cord is not permissive to axonal growth and thus neuroplasticity after injury is limited. Perineuronal nets containing chondroitin sulfate proteoglycans (CSPGs) are extracellular matrix structures surrounding neurons and are known to be major inhibitors of axonal sprouting. Our laboratory has identified that the transcription factor SOX9 regulates a battery of genes involved in CSPG biosynthesis. Using Sox9 conditional knock-out mice, we have shown that ablating Sox9 just before injury decreases CSPG levels in the injured spinal cord, leads to improved locomotor recovery and increases neuroplasticity. However, it is not known whether delayed ablation of Sox9 following spinal cord injury leads to similar recovery. To investigate this question, Sox9 was ablated in mice 3 weeks post-spinal cord injury. Levels of perineuronal net matrix, neuroplasticity, and locomotor recovery will be presented. (Acknowledgements: Supported by NSERC and CIHR)

Balance Control and Motion Sickness in Real and Virtual Environments

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Virtual reality (VR) is an interactive computer interface that immerses the user in a three-dimensional environment giving the illusion of being in that setting. While VR technology has the potential for innovation beyond entertainment, its adoption is restricted by reports of cyber sickness. The reason why some people are more prone to feeling unwell in VR has not been established. However, previous research suggests that individual differences in balance control may be related to an increased likelihood for people to self-report motion/cyber sickness during activities where this happens most (e.g., riding in a car, watching large field of view movies, playing VR games). Amongst theories of motion sickness (MS) and cybersickness in VR, is the sensory conflict theory stating that a conflict between the vestibular and vision system causes these symptoms. At the Ontario Science Centre our lab was able to collect data from 120 participants (ages 5-56) for measures of 1) past susceptibility to MS, 2) balance control, 3) ratings of cybersickness for two Oculus VR experiences rated by users as “comfortable” or “intense”, as well as 4) saliva samples to assess whether susceptibility to MS can be explained by genetics. Candidate genes include BDNF, APOE, COMT and KIBRA, which are polymorphic in the general population and are related to performance on neurological tasks. The results of this experiment will be discussed to provide further insight into the nature of individual differences and susceptibility to sickness in VR. (Acknowledgements: This work was generously supported by an Natural Sciences and Engineering Research Council of Canada (NSERC) Discovery Grant (#RGPIN-05435-2014) to MB-C)

Theta Burst Stimulation over the Hand and Leg Regions of the Motor Cortex

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Continuous theta burst stimulation (cTBS) is a repetitive form of transcranial magnetic stimulation (TMS) that can transiently reduce corticospinal excitability. Many studies have observed a reduction in motor-evoked potential (MEP) amplitude following cTBS over the primary motor cortex (M1) area representing the first dorsal interosseous (FDI; finger muscle). However, it has yet to be determined if cTBS can reduce MEP amplitude in lower limb muscles. Therefore, the purpose of this study is to compare the effects of cTBS over the soleus (SOL) and FDI regions of M1.
Participants will complete two experimental sessions; TMS will target the FDI and SOL for the first and second sessions, respectively. For each session, 15 MEPs, elicited at 120% of resting motor threshold (RMT), will be collected to serve as a baseline measure. This will be followed by the application of cTBS (bursts of three pulses at 30 Hz, repeated at 6 Hz for a total of 300-600 pulses) at an intensity of 60% RMT. Following cTBS, 15 MEPs will be collected at 5, 10, and 20 min post-cTBS. Preliminary data (n=4) indicate a 50-75% reduction in MEP amplitude of the FDI. In contrast, when cTBS was applied to the SOL, a 30% MEP reduction was observed in one participant and no change in MEP amplitude in two participants. Although more data are required, this initial data suggest the possibility of applying cTBS to reduce SOL corticospinal excitability. This may prove to be a valuable technique for future studies examining the cortical mechanisms involved in balance control. (Acknowledgements: Supported by NSERC)

B55) OPTOGENETIC APPROACHES TO THE INVESTIGATION OF NEURODEGENERATIVE DISEASE

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Neurodegenerative diseases such as Huntington’s disease (HD) and Alzheimer’s disease (AD) impose significant burdens on healthcare systems worldwide. Thus, understanding the mechanistic basis of these diseases at the molecular, genetic, and cellular levels is of critical importance for the development of novel therapeutic strategies. Although our understanding of the mechanisms that drive disease pathology in HD and AD has advanced significantly in recent years, there exist fundamental limitations to our knowledge of how molecularly defined mutations contribute to disease progression. These limitations exist primarily as a consequence of the inability to monitor disease progression in real time and in the context of a developing organism. In order to directly identify the mechanisms driving both HD and AD disease pathology we have taken an approach involving the generation of novel optogenetic tools which allow us to simultaneously control the function of the key drivers of HD and AD with light, and directly visualize the cell-biological consequences of gene product inactivation in real time, and in the context of Drosophila neurogenesis. Our approach relies upon endogenous gene tagging, which allows us to ‘knock-in’ optogenetic tags into the Huntingtin gene (HD), and the nicastrin gene; an integral component of the gamma secretase complex responsible for AD pathogenesis. We are currently developing novel techniques for studying the role of Huntingtin in intracellular trafficking, with a particular emphasis on its role in autophagosome biogenesis. In addition, we are developing strategies to identify and exploit biases in substrate cleavage to identify novel compounds capable of blocking the production of toxic gamma secretase cleavage products while maintaining normal functionality with respect to the processing of essential signaling components including the Notch receptor.
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