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Game of Hormones: Why Sex Matters for Brain Health

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Effect of prior treatment history and sex on antidepressant response to subanesthetic ketamine infusions. *Adel Farah, Sandhaya Norris, Jeanne Talbot, Pierre Blier, Jennifer L. Phillips.* From the Mood Disorders Research Unit, The Royal Ottawa Mental Health Centre and The Royal's Institute of Mental Health Research, affiliated with the University of Ottawa, Ottawa, Ont., Canada.

Background: Only 35% of patients with major depressive disorder remit after first-line treatment on medications with antidepressant properties. Furthermore, sex differences in antidepressant response have been documented. In treatment-resistant depression (TRD), ketamine has emerged as a medication that provides rapid onset decrease in symptoms, despite responses being transient in nature. **Methods:** Forty-one individuals with TRD underwent a randomized double-blind, crossover trial during which they each received a single infusion of intravenous ketamine. Following relapse of depressive symptoms, participants received a course of 6 repeated infusions of ketamine, administered 3 times weekly ($n = 39$). Response to ketamine was assessed by change in Montgomery-Åsberg Depression Severity Rating Scale (MADRS) scores. Linear regression models tested whether the number of past treatment trials or sex predicted antidepressant response to the single ketamine infusion or the course of repeated infusions. **Results:** With the course of repeated ketamine infusions, patients exhibited cumulative antidepressant effects and doubling of response rate in comparison to the single dose of ketamine, regardless of sex. Fewer previous treatment trials predicted a larger decrease in MADRS scores (improvement in depression severity) only after the course of 6 repeated ketamine infusions ($p = 0.025$). This trend remained when sex was added into the model ($p = 0.044$). Sex was not a significant predictor of change in MADRS scores after single or repeated ketamine infusions ($p = 0.34$). **Conclusion:** Earlier utilization of ketamine may result in improved antidepressant effects in patients with TRD, regardless of sex. This may minimize unnecessary delays in relieving depressive symptoms.

Chronic social defeat in male mice elicits long-lasting changes to intestinal barrier integrity and proinflammatory cytokine expression. *Ana Santos, Natasha Osborne, Hymie Anisman, Marie-Claude Audet.* From the Department of Neuroscience, Carleton University (Santos, Anisman, Audet); the Department of Nutrition Sciences, University of Ottawa (Audet); The Royal's Institute of Mental Health Research, affiliated with the University of Ottawa (Santos, Osborne, Anisman, Audet); and the Department of Cellular and Molecular Medicine, University of Ottawa (Osborne, Audet), Ottawa, Ont., Canada.

Background: Social stressors that elicit depressive- and anxiety-like behaviours in mice also disturb the composition of the gut microbiota and increase circulating and brain expression of proinflammatory cytokines. It has been suggested that stress-induced inflammatory activation may stem from proinflammatory shifts within the gut environment and be facilitated by damages to the integrity of intestinal membranes. We hypothesized that a chronic social stressor in male mice

would elicit long-lasting alterations in intestinal barrier permeability and elevations in cytokine expression along the gut-brain axis. **Methods:** For 10 consecutive days, male C57BL/6 mice experienced social defeat (10-min exposure to an aggressive resident mouse, followed by 24 h of sensory contact; $n = 14$) or a control condition (24 h of sensory contact with a nonaggressive resident; $n = 8$). Five weeks later, tissues from the jejunum and the hippocampus were collected for the determination of mRNA expression of the proinflammatory cytokines interleukin (IL)-6, IL-1 β , and tumour necrosis factor (TNF)- α ; the neurotrophin brain-derived neurotrophic factor (BDNF); and the tight junction proteins occludin-1, zonula occluden-1, claudin-2, and claudin-3. **Results:** Compared with nonstressed mice, chronically defeated mice had increased IL-1 β and TNF- α ($p < 0.05$ and $p < 0.0001$, respectively) and reduced occludin-1 ($p < 0.001$) expression within the jejunum. In the hippocampus, only BDNF was reduced by the chronic social stressor ($p < 0.05$). **Conclusion:** These findings suggest that chronic social defeat elicits long-lasting inflammatory activation and changes to barrier integrity within the jejunum. Stress-induced perturbations of the intestinal barrier may promote microbial-driven changes along the gut-brain axis relevant to stress-related disorders.

The epigenetics of alcohol use disorder: results from analysis of peripheral blood and neural tissue methylation. *Arunima Roy, Falk W. Lohoff, Zachary A. Kaminsky.* From the Department of Cellular and Molecular Medicine, University of Ottawa, Ottawa, Ont., Canada (Roy, Kaminsky); The Royal Ottawa's Institute of Mental Health Research, affiliated with the University of Ottawa, Ottawa, Ont., Canada (Kaminsky); and the National Institute of Drug Abuse, Rockville, MD, USA (Kaminsky).

Background: Alcohol use disorder (AUD) is associated with long-term changes in behaviour and cognition. Our understanding of the neurobiological pathways to such cognitive changes may be improved by examining DNA methylation, an important regulator of gene expression, in individuals with AUD. Previous studies on AUD and methylation, however, have been limited by either small sample sizes or reliance solely on non-neural tissues. **Methods:** We examined associations between AUD status and DNA methylation in blood in a discovery (AUD: $n = 336$; control: $n = 203$) and a replication cohort (AUD: $n = 43$; control: $n = 43$). The replication cohort also included functional magnetic resonance imaging (fMRI) to assess brain activity as blood-oxygen level-dependent (BOLD) signal. Genome-wide DNA methylation generated on Illumina Methyl-EPIC microarrays was regressed separately on AUD status and BOLD signal, controlling for age, sex, ethnicity and cell type. Probes showing significant associations in both blood-based cohorts were further examined in 2 post-mortem cohorts with information on brain-tissue methylation. **Results:** We identified 20 differentially methylated probes associated with BOLD estimates in the amygdala, prefrontal cortex, anterior cingulate cortex, and insula. These probes were located in genes associated with neurogenesis (*AMBRA1*, *PRKCZ*, *MYH10*), neurodegeneration (*ZGPAT*,

USP6NL, UBE2E1), cognition (*RASGRP1*) and neurodevelopmental disorders (*TSC2, KAT6A, ATP6V1B2*). Methylation levels of select probes (*PRKCZ, ATP6V1B2, TSC2, MYH10, RASGRP1, CSF2*) mediated pathways from AUD to BOLD correlates of prefrontal cortex and insula. **Conclusion:** AUD affects DNA methylation levels, in turn altering neural connectivity. Thus, effects of alcohol on DNA methylation may explain the poor cognitive and behavioural outcomes associated with prolonged alcohol use.

Chronic fluoxetine induces serotonin axonal plasticity in a poststroke depression model in mice. *Amin Zahrai, Farnak Vahid-Ansari, Paul R. Albert.* From the **uOttawa Brain and Mind Research Institute, University of Ottawa (Zahrai, Vahid-Ansari, Albert); and the Department of Neuroscience, Ottawa Hospital Research Institute (Albert), Ottawa, Ont., Canada.**

Background: Fluoxetine increases synaptic serotonin (5-HT) levels by blocking 5-HT transporters (SERT). It can improve recovery from stroke, including from poststroke depression (PSD). But as fluoxetine is not always effective, we developed a PSD model to address and enhance its mechanism of action. Microinjection of endothelin-1 into the left medial prefrontal cortex (mPFC) of male C57BL6 mice induced a focal stroke that resulted in chronic anxiety/depression. Chronic fluoxetine treatment induced recovery from PSD and rebalanced the activity of ipsi/contralateral sides. Since 5-HT axons can regrow months after injury, we hypothesized that fluoxetine may restore 5-HT innervation to mediate PSD recovery. **Methods:** Mouse brains ($n = 3$) of sham control, PSD, and PSD with chronic exercise or fluoxetine treatment for 5 weeks were stained for SERT and imaged at 63X using ZEN software. Densities of 5-HT axons and varicosities were quantified in the left versus the right mPFC (cingulate gyrus and pre/infralimbic regions), nucleus accumbens, lateral septum, hippocampus (CA1, CA2/CA3, dentate gyrus), basolateral amygdala (BLA) and dorsal raphe. **Results:** Densities of 5-HT axons and varicosities were reduced in the ipsilesional sides of mPFC and BLA in untreated or exercise-treated PSD versus sham mice, with no changes in other areas. Chronic fluoxetine treatment restored these densities to levels in sham or the contralesional sides in the mPFC and BLA of PSD mice ($p < 0.05$). **Conclusion:** Using our PSD mouse model, chronic fluoxetine but not exercise reversed the behavioural phenotypes and induced a novel recovery of 5-HT innervation in the mPFC and BLA.

Distribution of the β -klotho coreceptor within the hypothalamus and hippocampus. *Bianca S. Bono, Melissa J. Chee.* From the **Department of Neuroscience, Carleton University, Ottawa, Ont., Canada.**

Background: Fibroblast growth factor 21 (FGF21) is a novel endocrine hormone that regulates energy homeostasis and is being considered a therapeutic agent for diabetes and obesity. It is synthesized primarily by the liver and acts on various tissues to increase energy expenditure. The brain is one of the most robust effectors for FGF21 action, but the brain regions

that mediate the central actions of FGF21 are not well-defined. FGF21 has a low affinity to FGF receptors and thus forms a complex with the obligate coreceptor, β -klotho (KLB), to facilitate its signalling. To determine the site(s) of FGF21 action in the brain, we determined the neuroanatomical distribution of Klb mRNA. **Methods:** We performed in situ hybridization for Klb mRNA using RNAscope technology throughout the rostro-caudal extent of 2 wild-type mouse brains. We then used tyramide signal amplification of Cyanine 3 to label Klb hybridization, which thus appeared as punctate red fluorescent "dots." Confocal photomicrographs were analyzed to assess the expression and colocalization of Klb within 4',6-diamidino-2-phenylindole (DAPI)-labelled soma. **Results:** We found widespread, differential expression of Klb throughout the brain, most notably in the hypothalamus and hippocampus. The suprachiasmatic nucleus in the rostral hypothalamus contained the densest expression of Klb (> 4 dots per cell). Toward the caudal hypothalamic regions, such as within the periventricular nucleus, paraventricular nucleus, ventromedial nucleus, and dorsomedial nucleus, we found low (1–2 dots) but notable levels of Klb expression per cell. Interestingly, we also found Klb expression throughout the hippocampal formation, where Klb was largely restricted to the pyramidal cell layers. There were moderate levels of Klb expression (3–4 dots) in hippocampal subfields CA2 and CA3, but low levels of Klb expression (1–2 dots) in the dentate gyrus and CA1. **Conclusion:** The broad expression of Klb in several hypothalamic regions is consistent with the known roles of FGF21 in energy expenditure. Additionally, Klb expression in higher-order brain regions signals a potential role of FGF21 that integrates homeostatic and cognitive processes in the central regulation of energy balance.

Altered cellular integrity in porcine brains following an ex-vivo traumatic brain injury model. *Brendan Hoffe, Ashley Mazurkiewicz, Thuwan Piehler, Rohan Banton, Oren Petel, Matthew R. Holahan.* From the **Departement of Neuroscience, Carleton University, Ottawa, Ont., Canada (Hoffe, Holahan); the Department of Mechanical and Aerospace Engineering, Carleton University, Ottawa, Ont., Canada (Mazurkiewicz); and the US Army Research Laboratory, Aberdeen Proving Ground, MD, USA (Piehler, Banton).**

Background: Traumatic brain injury (TBI) is one of the more common forms of injury, affecting millions of individuals around the world each year. The movement of the brain and the resulting forces have been shown to create high amounts of strain within the brain, particularly in the apex of the sulcus. Given the vulnerability of the sulcus, the traditional rodent model is not a suitable model for translating TBI-associated pathology to humans. We explored the utility of a larger, more gyrified pig brain to better represent the dynamic forces the brain experiences during an impact. **Methods:** Using an ex-vivo model of TBI, 5 mm pig brain slabs were placed in a silicone encasement and dropped from a height of 0.9 m at 4 m/s. Following impact, the brain slabs were incubated in bubbling artificial cerebral spinal fluid to allow for acute cellular processes to occur. The brain slabs were sectioned and assessed for cellular morphological, density and

microtubule changes using MAP-2, NeuN and Cresyl-Violet. **Results:** Initial staining revealed less MAP-2 and NeuN staining in the impacted sections than the control sections. This was particularly evident in the deep valley (apex) of the sulcus. Cell staining patterns along the sulcus wall were similar between the impacted and control brains. **Conclusion:** These findings using a pig model of TBI shed light on what may occur within the sulcus during a head impact and possibly reflect what is seen in humans after a head impact.

Comparing mismatch negativity responses in children and adults using multi-deviant optimized and single-deviant odd-ball gap in noise paradigms. *Brittany Dugan, Victoria Duda, Kenneth Campbell, Amineh Koravand.* From the Department of Neuroscience, Carleton University, Ottawa, Ont., Canada (Dugan); the École d'orthophonie et d'audiologie, Université de Montréal, Montréal, Qué., Canada (Duda); the School of Psychology, University of Ottawa, Ottawa, Ont., Canada (Campbell); and the School of Rehabilitation Sciences, University of Ottawa, Ottawa, Ont., Canada (Duda, Koravand).

Background: Temporal resolution is a critical component of sound processing, measuring the time taken to distinguish between distinct auditory events. To measure temporal distinction thresholds, deviant stimuli containing a silent gap period are played among standard stimuli. Detection of these gaps can be measured using electroencephalogram (EEG) recordings, as these deviants could elicit an event-related potential known as the mismatch negativity (MMN). We compared gap thresholds of frontal and central scalp distributions in children and adults and investigated whether an optimized paradigm with multiple gap deviants could be used to reduce testing duration. **Methods:** Fifteen adults (mean age 30 yr) and 14 children (mean age 9 yr) passively listened to 3 trials of 4 different paradigms: 3 single-deviant and 1 multi-deviant. The single-deviant paradigm contained 1 gap duration (5, 20, or 40 ms), whereas the multi-deviant paradigm contained 6 durations (2, 5, 10, 20, 30 and 40 ms). Deviant presentation was pseudorandomized. Fz, F3 and F4 electrodes represented frontal distribution, whereas Cz, C3 and C4 represented central distribution. **Results:** The single-deviant paradigm elicited significantly different MMN wave latencies and amplitudes between adults and children for 20-ms gaps in both scalp distributions, whereas the 40-ms gap differed only in frontal distribution. The multi-deviant paradigm successfully elicited MMNs in adults for both scalp distributions, but was unsuccessful in children. **Conclusion:** An optimized paradigm containing multiple deviants may not be suitable in school-aged children, but elicits MMN in adults. Additionally, MMN does mature and is frontally distributed in adults.

Alpha power and coherence in major depressive disorder: association with symptom severity and adverse childhood experiences. *Bronwen Schryver, Natalia Jaworska, Sara de la Salle, Meagan Birmingham, Jennifer Phillips, Verner Knott, Pierre Blier.* From the Department of Psychology, University of Ottawa (Schryver, Jaworska, de la Salle, Knott); The Royal's Institute of Mental Health Research,

affiliated with the University of Ottawa (Schryver, Jaworska, de la Salle, Birmingham, Phillips, Knott, Blier); and the Mood Disorders Research Unit, The Royal Ottawa Mental Health Centre (Blier), Ottawa, Ont., Canada.

Background: Electroencephalogram (EEG)-derived α activity has been found to be modulated in patients with major depressive disorder (MDD) and may be related to treatment outcome. Furthermore, α coherence, a measure of α connectivity, has been found to be altered in MDD patients. There is some evidence indicating that adverse childhood experiences (ACEs), a risk factor for MDD, are associated with distinct α power profiles. However, to the best of our knowledge, α coherence has not been assessed in association with ACE history in the context of MDD. We examined relations between α power and coherence in MDD patients with depression severity indices and ACE history. **Methods:** Resting-state EEG activity was acquired from 28 MDD patients from which α power and coherence were assessed. Montgomery-Asberg Depression Rating Scale (MADRS) and ACE Questionnaire scores were used to subdivide the sample into moderate ($n = 16$) versus severe ($n = 11$) depression severity and low ($n = 13$) versus high ($n = 10$) ACE history groups. Relations between these measures and α profiles were examined. **Results:** No significant effects of symptom severity or ACE history on α power emerged. However, those with high versus low ACEs had greater interhemispheric parietal (P7–P8) α coherence ($p = 0.025$). Furthermore, higher interhemispheric parietal (P7–P8) α coherence was positively correlated with total ACE scores across the sample ($r = 0.64$, $p = 0.002$, $n = 18$). **Conclusion:** Results highlight the influence of childhood adversity on α coherence and show the utility of α coherence measures in potentially identifying unique brain profiles in MDD patients with varying histories of childhood adversity.

The utility of electroencephalography in improving prescription accuracy of psychoactive drugs in mentally disordered offenders in a secure treatment unit with depression-related conditions: a study proposal. *Brooke Carroll, Amelie Vezina, Colin Cameron, Verner Knott.* From the Integrated Forensic Program, Secure Treatment Unit, Brockville Mental Health Centre, Brockville, Ont., Canada (Carroll, Cameron); the Department of Clinical Neuroelectrophysiology, The Royal's Institute of Mental Health Research, affiliated with the University of Ottawa, Ottawa, Ont., Canada (Carroll, Vezina, Knott); and the Department of Psychiatry, University of Ottawa, Ottawa, Ont., Canada (Knott).

Background: Serious mental illness (e.g., major depression) is 3 times more prevalent within the prison population than the general population. Quantitative electroencephalography (qEEG) is a promising, objective tool in guiding psychotropic medication response, significantly reducing trial and error pharmacotherapy. We will evaluate the efficacy of the Psychiatric EEG Evaluation Registry (PEER) Interactive, a technology using qEEG and machine-learning, versus treatment as usual in guiding medication response. **Methods:** This will be a prospective, single-blind, randomized control trial (RCT)

including mentally disordered offenders ($n = 150$) within the Secure Treatment Unit, Brockville Mental Health Centre. Participants will undergo a qEEG and clinical interview (Hamilton Rating Scale for Depression [HAM-D]) and complete self-report questionnaires (Concise Health Risk Tracking Scale-7SR, Quick Inventory of Depressive Symptomatology [QIDS]-SR16, PTSD Checklist for DSM-5, and Clinical Global Impression Scale-Improvement [CGI-I]), and psychiatrists will complete a clinical evaluation at various time points over 3 months (CGI-I and CGI-Severity). Primary efficacy end point is the QIDS-SR16 and secondary end points are the CGI-I, CGI-S, and HAM-D. **Results:** Expected findings are discussed in the context of previous RCT publications with PEER in depressed populations. Suffin and colleagues (2007) and Losifescu and colleagues (2016) found significant decline in clinician-rated ($p < 0.009$) and self-report measures ($p = 0.029$), respectively, when following PEER Interactive guidance. Debattista and colleagues (2009, 2011) found greater mean change improvements in depressive symptoms when comparing PEER to similar technologies, the Texas Medication Algorithm Project and Sequenced Treatment Alternatives to Relieve Depression, respectively. **Conclusion:** PEER technology appears to be promising; however, more RCTs, such as the proposed study, are needed to support clinical use.

Effects of early-life stress on AMPA receptors in the auditory cortex. *Carinna Moyes, Aycheh Al-Chami, Hongyu Sun.* From the Department of Neuroscience, Carleton University, Ottawa, Ont., Canada.

Background: Critical period (CP) plasticity in the auditory cortex (A1) is known to be crucial for both functional brain development and cognitive function. Impaired A1 development during a CP for tonotopic mapping has been implicated in many neurologic disorders of learning and memory, including autism. Our recent results have shown a critical role for α -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptors (AMPA) in the auditory CP for tonotopic mapping. Here, we aim to determine if early-life stress (ELS) during rapid synaptic development affects the function of AMPARs required for normal CP plasticity. **Methods:** ELS was induced at P3–11 in a *c-Fos*-based transgenic mouse model. Using whole-cell patch-clamp recordings, we recorded pyramidal cells in layer IV of A1 to measure AMPAR function and the maturation of glutamatergic synapses in P12–15 mice. **Results:** We found that AMPAR functional maturation is highly correlated to the opening of A1 tonotopic CP plasticity during normal development. We further identified that ELS selectively activated a subpopulation of A1 pyramidal neurons, as evidenced by selective activity-dependent green fluorescent protein (GFP) tagging. Interestingly, although ELS did not cause significant changes in AMPAR function in overall randomly sampled neurons, ELS-activated neurons showed enhancement of AMPAR function compared with nonactivated neurons. **Conclusion:** These results provide a potential synaptic mechanism following exposure to a stressor during a CP of brain development and might identify novel strategies to modulate ELS-induced neurodevelopmental effects.

Impacts of early-life adversity on microbiota and inflammatory profiles in individuals with major depressive disorder. *Carley Richards, Kelsey Collimore, Sabrina Paterniti, Marie-Claude Audet.* From the Department of Neuroscience, Carleton University (Richards, Audet); The Royal's Institute of Mental Health Research, affiliated with the University of Ottawa (Richards, Collimore, Audet); the Mood and Anxiety Disorders Program, Royal Ottawa Mental Health Centre (Collimore, Paterniti); the School of Nutrition Sciences, University of Ottawa (Audet); and the Department of Cellular and Molecular Medicine, University of Ottawa (Audet), Ottawa, Ont., Canada.

Background: Proinflammatory cytokine elevations and differences in gut microbiota composition have been reported in individuals with major depression. Early-life adversity may contribute to depression vulnerability, possibly by impacting gut microbial colonization patterns and immune system development. We hypothesized that increases in circulating levels of proinflammatory cytokines and changes in gut bacterial populations in individuals with depression would be more pronounced in those with a history of childhood adversity. It was also expected that childhood adversity would moderate the associations between inflammatory/bacterial changes and depression severity. **Methods:** Thirty-nine individuals with a current episode of major depressive disorder and 43 healthy volunteers, recruited from the general population, completed questionnaires to determine severity of depressive (Beck Depression Inventory-II) and anxiety (Beck Anxiety Inventory) symptoms and history of childhood adversities (Childhood Trauma Questionnaire-Short Form). Blood and stool samples were collected to determine plasma levels of proinflammatory cytokines and fecal abundance of specific bacterial taxa, respectively. **Results:** Plasma interleukin (IL)-6:IL-10 ratios were positively correlated with depression severity, and childhood trauma explained variance in severity of depressive symptoms above and beyond that accounted for by the IL-6:IL-10 ratios. Decreased abundance of *Faecalibacterium prausnitzii* was apparent in depressed participants compared with healthy controls and was correlated with severity of symptoms only in participants who had experienced moderate to severe physical neglect during childhood. **Conclusion:** These findings suggest that associations between particular gut bacteria and depression severity may depend on specific types of trauma experienced in early life.

Using a smartphone application to assess cognition in individuals with schizophrenia. *Cecelia Shvetz, Feng Gu, John Torous, Synthia Guimond.* From the School of Psychology, University of Ottawa, Ottawa, Ont., Canada (Shvetz, Guimond); The Royal's Institute of Mental Health Research, affiliated with the University of Ottawa, Ottawa, Ont., Canada (Shvetz, Gu, Guimond); the Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA (Torous, Guimond); and the Department of Psychiatry, University of Ottawa, Ottawa, Ont., Canada (Guimond).

Background: Schizophrenia is a severe mental illness marked by disabling cognitive impairments that persist despite treatment with antipsychotics and dissipation of other clinical symptoms. The present study investigates the validity of a smartphone application to assess cognition in individuals with schizophrenia. **Methods:** A total of 29 participants were recruited from the community and the outpatient programs at the Royal Mental Health Centre. Participants included 14 with a diagnosis of schizophrenia or schizoaffective disorder and 15 healthy controls. Processing speed and cognitive flexibility were assessed using both the pen-and-paper Trail Making Test (Parts A and B) and the smartphone-adapted Jewel Trail (Parts A and B). We predicted that scores from the pen-and-paper and smartphone cognitive tests would positively correlate. Additionally, we hypothesized that individuals with schizophrenia would have lower cognitive performance on all tests than controls. **Results:** Preliminary results indicated significant positive correlations between both the Parts A ($r = 0.65, p < 0.001$) and B ($r = 0.44, p = 0.029$) of the pen-and-paper and smartphone tests. Significant differences were also observed between patients and controls on Parts A of the pen-and-paper ($p < 0.001, t = -3.89$) and smartphone tests ($t = -4.52, p < 0.001$) and Part B of the smartphone test ($t = -2.99, p = 0.008$). We observed a trend-level difference on Part B of the pen-and-paper test ($t = -1.80, p = 0.086$). **Conclusion:** Although preliminary, our findings suggest that a smartphone application can be used to assess processing speed and cognitive flexibility impairments in individuals with schizophrenia. This novel tool has the potential to enable dynamic, scalable and longitudinal assessments of cognition in research and clinical settings.

What is the optimal duration of theta burst stimulation of the prefrontal cortex? *Manon Desforges, Itay Hadas, Brian Mihov, Mathilde Rochette-Braün, Yan Morin, Martin Lepage, Zafiris J. Daskalakis, Sara Tremblay.* From the **Université de Montréal, Montreal, Que., Canada (Desforges, Rochette-Braün, Morin); the Centre for Addiction and Mental Health, Toronto, Ont., Canada (Hadas, Daskalakis); the Department of Psychology, McGill University, Montreal, Que., Canada (Mihov); the Douglas Mental Health University Institute, Montreal, Que., Canada (Lepage); and The Royal's Institute of Mental Health Research, affiliated with the University of Ottawa, Ottawa, Ont., Canada (Desforges, Tremblay).**

Background: Repetitive transcranial magnetic stimulation (rTMS) is used as a functional treatment of mental disorders such as depression. A new form of rTMS, theta-burst stimulation (TBS), has recently emerged as a promising tool offering reduced stimulation time. Applied intermittently (iTBS) to the left dorsolateral prefrontal cortex (DLPFC), it is thought to increase cortical excitability leading to antidepressant effects. However, although it is applied in clinic, we do not know the optimal duration of stimulation. Thus, this study aims to determine the optimal iTBS duration to activate the left DLPFC among the 3 most frequently used durations: 600, 1200 and

1800 pulses. **Methods:** Fourteen healthy participants took part in the following 3 experimental conditions: 600, 1200 and 1800 pulses (counterbalanced order, 7 days between each session). By the combined use of TMS and electroencephalography (TMS-EEG), measures of brain excitability were taken before and after each iTBS. The study focuses more specifically on TMS-EEG components representing inhibition and excitation: P30, N45, P60, N100 and P200. **Results:** All 3 iTBS conditions induced a significant reduction of the amplitude of TMS-EEG indexes of cortical excitability (P30, P60 and P200) and increase of measures of cortical inhibition (N45). **Conclusion:** Our results suggest no difference among the 3 durations on the modulation of cortical excitability. This has important clinical implications, as it suggests the absence of a linear effect of stimulation duration on brain excitability in the left DLPFC. Further analyses, including TMS-induced cortical oscillations, will help determine the optimal duration of iTBS.

Mental health services: How does your university's website stack up? *Dana Tabet, Anne T.M. Konkle.* From the **Interdisciplinary School of Health Sciences, University of Ottawa (Tabet, Konkle); the School of Psychology, University of Ottawa (Konkle); and the University of Ottawa Brain and Mind Research Institute (Konkle), Ottawa, Ont., Canada.**

Background: One in 5 Canadians will experience a mental health issue, with 15- to 24-year-olds being the age group with greater potential to develop an illness. An emphasis has been placed on the allocation of mental health resources but, to our knowledge, no research has yet considered evaluating the accessibility of these resources. Thus, the objective of this study was to evaluate the ease of locating and accessing information regarding mental health resources on Canadian university websites. **Methods:** Ten Canadian universities were randomly selected, from the existing 96 Canadian universities. The websites were evaluated using a tool adapted from others, designed to assess online mental health resources and university websites. We qualitatively and quantitatively assessed 5 domains: readability, organization, credibility and quality of information, navigability and usability, and content. **Results:** We found that the larger Canadian universities provide more mental health resources, alternatives and appropriate contact information; most universities scored at a university level on the readability criterion. Assessment of usability and navigability revealed that the average webpage length is 2.65 pages, and on average 3 clicks were required to access the service page. Whereas only a few universities scored high on the organization and content criteria, 6 universities failed to mention their fees, and all universities failed to mention their wait times. **Conclusion:** Overall, websites from larger universities are more organized and richer in content. With these findings, we hope to gain insight into how to improve accessibility to mental health resources by university students.

Expression of melanin-concentrating hormone receptor 1 in the ventral tegmental area. *C. Duncan Spencer, Alex J. Hebert, Bianca S. Bono, Melissa J. Chee.* From the **Department of**

Neuroscience, Carleton University, Ottawa, Ont., Canada (Spencer, Bono, Chee); and the Division of Endocrinology, Beth Israel Deaconess Medical Center, Boston, MA, USA (Hebert, Chee).

Background: Melanin-concentrating hormone (MCH) is an orexigenic neuropeptide. MCH or MCH receptor (MCHR1) deletion produces lean and hyperactive animals; a hyperdopaminergic state mediates this hyperactivity. We found that MCH can suppress dopamine release at the nucleus accumbens, which receives dopaminergic afferents primarily from the ventral tegmental area (VTA). To investigate possible mechanisms underlying the inhibitory effect of MCH on dopamine release, we determined if VTA neurons express *Mchr1*. **Methods:** We compared the expression of *Mchr1* mRNA in the VTA and hypothalamus using quantitative polymerase chain reaction. To determine the relative distribution of *Mchr1* within the VTA, we used RNAscope technology to perform in situ hybridization for *Mchr1* mRNA. This hybridization signal was labelled by tyramide signal amplification of cyanine 3 fluorescence, and we analyzed this signal by confocal microscopy to determine the coexpression of *Mchr1*, which appear as red “dots,” with nuclei labelled with 4',6-diamidino-2-phenylindole (DAPI). **Results:** *Mchr1* mRNA was easily detected, but relatively less abundant in the VTA (0.6 ± 0.1 , $n = 3$) than hypothalamus (1.0 ± 0.2 , $n = 3$). We thus performed in situ hybridization to determine VTA distribution. While not all VTA neurons expressed *Mchr1*, positively labelled cells contained high levels of *Mchr1* hybridization (> 5 dots per DAPI-labelled nucleus). Furthermore, the distribution of *Mchr1*-labelled neurons was more abundant toward the medial VTA. **Conclusion:** We provide molecular and neuroanatomical evidence that VTA neurons express *Mchr1* mRNA. As MCHR1 may accumulate at the nerve terminal, these findings suggest that MCH may directly inhibit dopamine release at VTA nerve terminals, such as in the nucleus accumbens.

Studying the effects of nuclear α -synuclein in a novel mouse model. *Haley M. Geertsma, Steve M. Callaghan, Maxime W.C. Rousseaux.* From the Department of Cellular and Molecular Medicine, University of Ottawa (Geertsma, Rousseaux); the University of Ottawa Brain and Mind Research Institute (Geertsma, Callaghan, Rousseaux); the Ottawa Institute of Systems Biology, University of Ottawa (Rousseaux); and the Centre for Neuromuscular Disease, University of Ottawa (Rousseaux), Ottawa, Ont., Canada.

Background: Parkinson disease and related synucleinopathies are devastating neurodegenerative disorders characterized by the accumulation of misfolded α -synuclein throughout the brain. While α -synuclein is natively found in the synapse and the nucleus (hence its name), data from our laboratory and others have shown that nuclear accumulation of α -synuclein is toxic and occurs in Parkinson disease. The toxic mechanism(s) of nuclear α -synuclein remain(s) elusive. To this end, we have created a mouse in which endogenous flag-tagged α -synuclein is localized to the nucleus via a nu-

clear localization signal (NLS) tag. Characterizing this novel α -synuclein NLS-flag mouse will provide insight into the potentially neurotoxic effects of endogenous nuclear-localized α -synuclein. **Methods:** We are characterizing this mouse line on behavioural, histological and biochemical levels to determine whether these mice phenocopy aspects of synucleinopathy over time. Motor and nonmotor tests will determine whether α -synuclein NLS-flag mice exhibit dysfunction as they age. We will describe the histological findings from a young cohort of mice to determine whether α -synuclein nuclear accumulation causes neurodegeneration in the nigrostriatal tract, which is a principal site of cell loss in Parkinson disease. We will present biochemical analyses to determine whether nuclear α -synuclein is pathologically phosphorylated and/or misfolded. **Results:** Pending. **Conclusion:** Determining the presence and extent of the neurotoxic effects of nuclear α -synuclein provides a meaningful step forward in elucidating the mechanisms of neurotoxicity that are involved in Parkinson disease and related synucleinopathies.

Pilot testing of the Integrated Parkinson's Disease Care Network: feasibility, efficacy outcomes, and cost description analysis. *Julia Shen, Dorothy Kessler, Ahmed Basndwah, Heba Shinawi, Coreen Nussey, Avery Orman, Diane Côté, Clare Liddy, Kednapa Thavorn, Monica Taljaard, David Grimes, Tiago A. Mestre.* From the Division of Neurology, Department of Medicine, University of Ottawa, Ottawa, Ont., Canada (Shen, Basndwah, Shinawi, Grimes, Mestre); the School of Rehabilitation Therapy, Queen's University, Kingston, Ont., Canada (Kessler); the Ottawa Hospital Research Institute, Ottawa, Ont., Canada (Nussey, Orman, Côté, Thavorn, Taljaard, Grimes, Mestre); the Department of Family Medicine, University of Ottawa, Ottawa, Ont., Canada (Liddy); the Bruyère Research Institute, Ottawa, Ont., Canada (Liddy); and the Brain and Mind Research Institute, University of Ottawa, Ottawa, Ont., Canada (Mestre).

Background: Multispecialty care is an attractive model in Parkinson disease, but there has been sparse evidence on health benefits and cost analyses. We developed a novel model of complex care delivery for people with Parkinson disease, the Integrated Parkinson's Disease Care Network (IPCN), based on care integration and self-management support and health technology. The objective of this study is to assess its feasibility while evaluating health-related outcomes and patient/caregiver experience, and describing associated costs. **Methods:** This is a single-centre pre-post study design. We included a group with newly diagnosed Parkinson disease (< 1 yr, $n = 25$) and a group with advanced Parkinson disease (> 8 yr, Hoehn and Yahr scale score of ≥ 3 , $n = 75$). Assessments included A) evaluation of IPCN implementation and study enrolment; and B) clinical assessments at baseline, 3, and 6 months to identify the most appropriate health outcomes that included the Parkinson's Disease Questionnaire-8 (PDQ-8), Geriatric Depression Scale and Zarit Caregiver Burden Questionnaire among others. **Results:** We recruited 100 people with Parkinson disease in 6 months. After the

IPCN program, there was a patient-reported improvement in chronic care experience (Patient Assessment of Chronic Illness Care [PACIC+]: 1.1, 95% confidence interval [CI] 0.9 to 1.3), and 72 (76.6%) caregivers were (much) satisfied. Only the advanced Parkinson disease group had an improvement in health outcomes (PDQ-8: 3.4 points, 95% CI 0.8 to 6.8). Nonsignificant differences were found for lower mean monthly societal costs (Can\$ -239.44; 95% CI Can\$ -549.53 to Can\$ 70.65). **Conclusion:** The data support and inform a future cluster randomized trial to evaluate the effectiveness of the IPCN. Preliminary evidence suggests a positive impact of IPCN on chronic care, quality of life and possibly societal costs.

Parental adverse childhood experiences and future family dysfunction: exploring the intergenerational transmission of trauma. *Kate Goheen, Michelle Conway, Nicole Instead, Floyd Wood.* From the Forensic Research Unit, Royal Ottawa Mental Health Centre (Goheen, Conway, Instead, Wood); and the Department of Psychiatry, University of Ottawa (Wood), Ottawa, Ont., Canada.

Background: Decades of research have shown that adverse childhood experiences (ACEs) have a negative, cumulative impact on physical and mental health in adulthood. However, there has been a paucity of research on how parental ACEs (PACEs) affect future parenting. We explored the association between ACE scores and current family dysfunction in the population of families involved with the Children's Aid Society (CAS) referred to the Family Court Clinic (FCC) for child welfare assessments. We hypothesized that the parents involved in the FCC assessments would have a higher level of ACEs than the original study population (Feletti and colleagues, 1998) and that higher ACE scores would positively correlate with degree of adulthood dysfunction, measured by total medical, mental health, addictions, and legal problems, as well as violence within relationships. **Methods:** This exploratory retrospective study was conducted using information obtained by psychiatry, psychology and social work during child welfare assessments conducted at the FCC. Collateral information was provided by schools, health care providers and health facilities. Additional results were obtained from psychological testing (Minnesota Multiphasic Personality Inventory, Millon Clinical Multiaxial Inventory-III, the Child Abuse Inventory). **Results:** In total, 85.9% of parents in this sample had at least 1 ACE (mean 3.59 ± 2.657), which was significantly higher than reported in the original study ($p < 0.0001$). Total ACE scores were positively correlated with current adulthood dysfunction ($r = 0.220$, $p = 0.002$). **Conclusion:** This study highlights the intergenerational impact of PACEs and underscores the importance of early intervention in vulnerable populations.

The association between suicidal ideation and perceived stress: a functional neuroimaging study. *Katie L. Vandelloo, Patricia Burhunduli, Adel Farah, Pierre Blier, Jennifer L. Phillips.* From the Mood Disorders Research Unit, The Royal's Institute of Mental Health Research, affiliated with the University of Ottawa (Vandelloo, Burhunduli, Farah, Blier,

Phillips); the Department of Neuroscience, Carleton University (Vandelloo, Phillips); the Department of Psychiatry, University of Ottawa (Farah, Blier, Phillips); and The Royal Ottawa Mental Health Centre (Blier), Ottawa, Ont., Canada.

Background: The significance of the progression from suicidal ideation (SI) to suicide attempts (SA) has been highlighted in individuals with treatment-resistant depression (TRD). Previous research has identified the need for more objective measures of SI, as self-report questionnaires are often inadequate for predicting SA. **Methods:** The present study included 25 individuals with TRD (14 male, 11 female; mean age 42.08 ± 12.7 yr), in which the association between varying severities of SI and alterations in resting-state functional networks was investigated. The association between various clinical constructs and imaging data was also explored, including that of perceived stress and depression severity, as well as both self-report and clinician-rated measures of SI. **Results:** Analysis of clinical data revealed a significant correlation between clinician and self-rated measures of SI ($p < 0.001$), SI and depression severity ($p = 0.005$), and perceived stress and SI ($p = 0.034$). Functional magnetic resonance imaging (fMRI) data were preprocessed and analyzed using the CONN Functional Connectivity SPM Toolbox (2017), with a focus on the anterior cingulate cortex (ACC), orbitofrontal cortex (OFC) and amygdala. Preliminary results suggest reduced connectivity between the left OFC and the ACC in association with greater SI severity ($p = 0.008$; uncorrected) as well as reduced connectivity between the ACC and the left amygdala in association with higher perceived stress ($p = 0.013$; uncorrected). **Conclusion:** These preliminary, uncorrected results suggest that inter-region connectivity between the OFC, ACC and amygdala may be associated with SI and perceived stress. Further analysis with a larger sample size is hypothesized to obtain a more robust effect with a corrected analysis.

Elucidating molecular changes during dopaminergic neuron regeneration in adult zebrafish. *Khang Hua, Rafael Godoy, Sandra Noble, Nayaar Islam, Marc Ekker.* From the Department of Biology, University of Ottawa (Hua, Noble, Islam, Ekker); and the Ottawa Hospital Research Institute (Godoy), Ottawa, Ont., Canada.

Background: Parkinson disease is a progressive and debilitating neurodegenerative disease in which patients suffer from motor impairments. Pathologically, motor symptoms in humans arise from the progressive loss of dopaminergic (DA) neurons within the substantia nigra. The study of neuronal regeneration and the molecular mechanisms that regulate this process in species that can regenerate cells of the central nervous system (CNS) could provide potential novel therapeutic targets. To study the process of neuronal regeneration, we used zebrafish because of their ability to regenerate cells within the CNS. Currently, little is known about the molecular mechanisms that regulate and drive neuronal regeneration in the adult zebrafish brain. **Methods:** To specifically ablate DA neurons, we used a chemogenetic approach. BrdU and EdU pulse-chase was done to determine when the

increase in DA neuron neurogenesis occurs following ablation of DA neurons. In addition, gene expression analysis was done on isolated telencephalon of control and metronidazole-treated fish using digital droplet polymerase chain reaction. **Results:** Following dopaminergic neuron ablation, adult transgenic zebrafish were able to regenerate dopaminergic neurons within the olfactory bulb after 45 days. In addition, BrdU and EdU pulse-chase experiments showed that there was a 3-fold increase in the number of newly generated dopaminergic neurons in the olfactory bulb. At 5 days following treatment, we observed an increase in the expression of *Shha* and *Her4*. **Conclusion:** Altogether, these data will help elucidate the molecular changes that take place during dopamine neuron regeneration in zebrafish.

Environmental enrichment protocol for laboratory mice. *Kevin Smith, Rajini Chandrasegaram, Alanah Yazbeck, Nafissa Ismail.* From the Department Psychology, University of Ottawa, Ottawa, Ont., Canada (Smith, Yazbeck, Ismail); and the Department of Neuroscience, Cardiff University, Cardiff, Wales (Chandrasegaram).

Background: Environmental enrichment (EE) is an experimental manipulation that provides animals with running wheels, toys and additional cage mates. EE facilitates socialization, physical activity and cognitive stimulation. Currently, using an EE design is challenging because there is no standardized protocol. The lack of standardization creates variable and potentially unreplicable data. Our housing protocol offers a standardized EE design. However, we must validate our EE design before attempting standardization. Comparing the immune response between housing groups can be used as a metric to examine EE housing protocol efficacy. **Methods:** Male and female mice ($n = 180$) were separated into 3 housing groups: deprived (DH), social (SH) and EE housing. At 6 weeks of age (during puberty), mice were injected with the bacterial endotoxin, lipopolysaccharide (LPS), and were monitored for sickness behaviour. Eight hours later, they were euthanized, and trunk blood was collected. **Results:** After LPS injection, EE male and female mice demonstrated a significantly greater sickness behaviour response than the SH and DH mice during the first 4 hours. Additionally, male mice experienced a significantly greater sickness response than females during the first 2 hours following LPS treatment. **Conclusion:** The difference in sickness response between housing conditions provides evidence that our EE protocol affects the immune system effectively. Given the success of our protocol, we intend to develop and distribute instructions for replicating our design.

A first glance at the presenting characteristics of inpatients admitted at risk of suicide. *Elizabeth Kamler, Patricia Burhunduli, Katerina Nikolitch, Robyn J. McQuaid, Jennifer L. Phillips.* From the Mood Disorders Research Unit, The Royal's Institute of Mental Health Research, affiliated with the University of Ottawa (Kamler, Burhunduli, Nikolitch, Phillips); and the Culture and Gender Research Unit, The Royal's Institute of Mental Health Research, affiliated with the University of Ottawa (McQuaid), Ottawa, Ont., Canada.

Background: The International Resident Assessment Instrument (interRAI) is a data collection tool completed by health care providers at the Royal Ottawa Mental Health Centre (ROMHC) for every inpatient admission. Although easily accessible, this data set has not yet been harnessed for research purposes at the ROMHC. The goal of this study was to perform an initial examination of the presenting demographic and psychosocial characteristics of patients admitted to the ROMHC deemed to be at risk of suicide. **Methods:** Data were derived from ROMHC admissions over a 9-year period, between Jan. 2, 2008, and Dec. 31, 2016, with "threat or danger to self" selected as one of the reasons for patient admission. Preliminary descriptive statistics were used to examine the demographic and psychosocial characteristics associated with these admissions. **Results:** In total, 1363 individuals (age 15–99 yr; 52.7% male) were admitted to the ROMHC and deemed to be at risk of harming themselves. Examining previously known suicide risk factors, we found that 34.2% did not complete high school, 53.0% did not have stable housing, and only 8.5% were employed at time of admission. Moreover, those admitted with a history of suicide attempt were more likely to have had a suicide plan in the 30 days preceding hospital admission ($p < 0.001$). **Conclusion:** Using the interRAI data at the ROMHC, we provide a preliminary look at the demographic and social factors among individuals at risk of suicide. Next steps include clarifying the specific risk factors that contribute to suicide attempts and incorporating those factors into predictive suicide risk assessments.

Transcranial direct current stimulation in pediatric neuropsychiatry: safety, tolerability, acceptability. *Derrick Matthew Buchanan, Amedeo D'Angiulli, André Samson, Philippe Robaey.* From the Department of Neuroscience, Carleton University (Buchanan, D'Angiulli, Robaey); the Neuroscience of Imagery Cognition Emotion Research Laboratory, Carleton University (Buchanan, D'Angiulli); the Neuropsychiatric Laboratory, Children's Hospital of Eastern Ontario Research Institute (Buchanan, Robaey); the Department of Education, University of Ottawa (Samson); and the Department of Psychiatry, University of Ottawa (Robaey), Ottawa, Ont., Canada.

Background: Transcranial direct current stimulation (tDCS) is a noninvasive brain-modulation technique widely used in adults, but disproportionately understudied in children. The aims of our 3 studies were to translate the safety/tolerability/acceptability evidence for tDCS into neuropsychiatric practice via a systematic review and a randomized, double-blind, placebo-controlled trial (RCT) in children and adults, and assess the acceptability of tDCS for treating atypical youth by interviewing parents whose children participated in the RCT. **Methods:** In the first study, a systematic review of tDCS safety in youth was conducted, focusing on adverse effects and cognitive/neuroimaging/neuropsychiatric outcomes. In the second study, 60 participants (30 children aged 6–17 yr and 30 adults aged 18–45 yr) received 10 minutes of tDCS twice, separated by a 1-hour interval. The stimulation amperage (sham, 0.5, 1, and 2 mA), and anode/cathode locations were

randomly selected. The researcher measuring physical/emotional adverse effects (at 7 time points) and the participant were blinded to the amperage. In the third study, parents of 14 children who participated in the RCT were interviewed about the acceptability/desirability/feasibility of tDCS as a treatment option for their child compared with current methods. **Results:** No participants reported any adverse effects. Children tolerated tDCS in a similar manner as adults. Adverse effects attenuate with a short break, but physical adverse effects mildly aggregate with multiple sessions. Given the safety of tDCS treatment in youth, parents prefer it as an alternative to stimulant medication. Education about the procedure was important for their comfort. **Conclusion:** There is demand for routinely available tDCS treatment in pediatric neuropsychiatry, especially in patients who are medication-resistant.

Dietary fructose induces synaptic plasticity at neuropeptide Y neurons. *Mikayla A. Payant, Jenny Campbell, Alex J. Hebert, Eleftheria Maratos-Flier, Melissa J. Chee.* From the Department of Neuroscience, Carleton University, Ottawa, Ont., Canada (Payant, Campbell, Hebert, Chee); and the Division of Endocrinology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA (Hebert, Maratos-Flier).

Background: Increased fructose consumption, such as from added sugars in processed foods, contributes to the prevalence of obesity. Fructose, though largely metabolized by the liver, is also absorbed by the brain to regulate energy balance. It can stimulate food intake via the brain, but the neuronal mechanisms underlying fructose-mediated obesity are not well defined. Interestingly, dietary fructose increases the gene expression of neuropeptide Y (NPY) in the hypothalamus, and activating NPY neurons promotes feeding and weight gain. We thus determined if dietary fructose leads to adaptations at NPY neurons in fructose-mediated obesity. **Methods:** As fructose is consumed with dextrose via table sugar, we fed male mice a 60% fructose diet (HFrD), 60% dextrose diet (HDxD), or standard chow for up to 4 weeks to compare differences in calorie intake, body weight and body fat. We then obtained ex-vivo patch-clamp recordings to determine if HFrD feeding (compared with HDxD or chow) alters synaptic activity at NPY neurons. **Results:** HFrD-fed mice were hyperphagic and gained more body fat than HDxD or chow controls. One week of HFrD feeding increased the frequency of glutamatergic inputs to NPY neurons. This synaptic plasticity persisted over 4 weeks of HFrD feeding and was not seen following HDxD or chow feeding. Interestingly, returning HFrD-fed mice to a chow diet also reversed the level of glutamatergic input at NPY neurons. **Conclusion:** Dietary fructose reversibly increases excitatory input to NPY neurons. This synaptic plasticity is fructose-specific and may underlie the neuronal maladaptations leading to fructose-mediated obesity.

Investigating locomotor defects in a neurotoxin-induced Parkinson disease zebrafish model. *Michael Kalyn, Khang Hua, Dung Ngo, Marc Ekker.* From the Department of Biology, University of Ottawa, Ottawa, Ont., Canada.

Background: Parkinson disease is the second most prevalent neurodegenerative disease. Clinical hallmarks of Parkinson disease are motor movement symptoms associated with a progressive and irreversible loss of dopaminergic (DA) neurons within the substantia nigra pars compacta of the mid-brain. In humans, locomotor impairing phenotypes are onset following a 60%–80% DA loss. To our knowledge, previous experimental models have yet to induce this degree of neuronal ablation and observe any critical motor defects. **Methods:** Our aim is to develop a Parkinson disease model in adult zebrafish. Here, we use cerebrotentorial microinjections (CVMI) for efficient delivery of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), a neurotoxin known to induce Parkinson-like symptoms. Injections are performed on a Tg(dat:eGFP) line of zebrafish. Imaging, gene expression analyses and behaviour assays are implemented to measure overall specificity, cell death and any motor-related phenotype. **Results:** Following injection, the treated zebrafish display a significant decrease in DA neurons where there was a correlated decrease in *Dat* and *Th* gene expression levels. This loss is observed to be localized to DA cells, as there are no observed effects on the serotonergic or GABAergic pathways. The increased DA cell loss is shown to translate into a locomotor defective phenotype in treated zebrafish assessed through total distance, freezing bout and average velocity proxies. These data suggest the efficiency of CVMI delivery and the specific cytotoxicity of MPTP on DA neurons to induce a motor deficiency. **Conclusion:** The results of this investigation serve as a novel platform for neurotoxin-induced Parkinsonism, while ameliorating current vertebrate models for Parkinson disease.

A novel mouse model of Dravet syndrome. *Minh Hieu Tran, Kerstin Ure, Sarah Schock, David Dymant.* From the Department of Chemistry and Biomolecular Sciences, University of Ottawa (Tran); the Animal Research Core, Faculty of Medicine, University of Ottawa (Ure); the Research Institute, Children's Hospital of Eastern Ontario (Schock, Dymant); and the Department of Genetics, Children's Hospital of Eastern Ontario (Dymant), Ottawa, Ont., Canada.

Background: Individuals with Dravet syndrome experience difficult-to-treat seizures and developmental delay. There is no definitive cure, and treatment options are limited. Children often require a combination of antiepileptic medications, but are rarely seizure-free. Most cases of Dravet syndrome are caused by variants in the *SCN1A* gene, which encodes the NaV1.1 sodium channel responsible for hyper-excitability neuronal networks. To date, only mouse models of *SCN1A* knockout or conditional knockout of loss-of-function variants have been studied. Substitution variants due to missense mutations have not been characterized, despite comprising one-third of the pathogenic variants seen in Dravet syndrome. Our animal studies will provide insight into how this type of variant alters behavioural, motor and cognitive functioning in Dravet syndrome. **Methods:** A novel Dravet syndrome mouse model harbouring the same missense mutation as a Canadian Dravet syndrome patient was created using CRISPR/Cas9 technology.

Survival, weight and seizure frequency in heterozygous mice were measured. In addition, mice were subjected to behavioural, cognitive and motor testing at 2 and 6 months of age. **Results:** Heterozygous mutant mice containing the novel missense variant display a recurrent seizure and early death phenotype. They also have poor contextual learning ability and exhibit abnormal anxiety behaviours compared with control mice. **Conclusion:** The missense variant in the *SCN1A* gene contributes to impaired learning ability and sociability in addition to seizures and early death. These findings support what has been previously reported in other mouse models of Dravet syndrome.

Cellular changes in dopaminergic neuron regeneration in zebrafish. *Nayaar Islam, Khang Hua, Hardy Ding, Marc Ekker.* From the Department of Biology, University of Ottawa, Ottawa, Ont., Canada.

Background: Parkinson disease is a neurodegenerative disorder marked by the loss of dopaminergic (DA) neurons in the midbrain. Previous studies have deemed adult zebrafish (*Danio rerio*) to be a successful model for DA neuron regeneration. However, there remains a lack of understanding regarding the mechanisms by which this DA neuron regeneration occurs. This study uses zebrafish as a model for Parkinson disease to investigate whether radial glia (RG) cells function as neuronal stem cells during DA neuron regeneration. **Methods:** Adult transgenic zebrafish expressing nitroreductase (NTR) enzyme in their DA neurons are treated with the pro-drug metronidazole (MTZ), which selectively ablates NTR-expressing DA neurons. Zebrafish brains from MTZ treatment and control conditions are then isolated at various time points, cross-sectioned and analyzed with immunohistochemistry. Proliferating cell nuclear antigen and brain lipid-binding protein antigens are labelled as markers for proliferating RG cells, and Sox2 transcription factor is labelled as a general stem cell marker. **Results:** Increased proliferation of RG cells and Sox2-positive stem cells was observed in the telencephalon at 5 days post DA neuron ablation. **Conclusion:** These results suggest a possible association between DA neuron regeneration and RG cell proliferation in the brain. This study will provide insight on the mechanisms by which DA neuron regeneration occurs in adult zebrafish and how the considerations of these mechanisms may play a role in the future of Parkinson disease therapeutics.

Prenatal stress modulates proinflammatory responses to an adult social stressor in male and female mouse offspring. *Natasha Osborne, Tryston Charlton, Chase Groulx, Kristin Connor, Marie-Claude Audet.* From the Department of Cellular and Molecular Medicine, University of Ottawa (Osborne, Audet); The Royal's Institute of Mental Health Research, affiliated with the University of Ottawa (Osborne, Audet); the Department of Neuroscience, Carleton University (Charlton, Groulx, Audet); the Department of Health Sciences, Carleton University (Connor); and the School of Nutrition Sciences, University of Ottawa (Audet), Ottawa, Ont., Canada.

Background: Early-life experiences may modulate responses to stressors encountered later in life. In adult rodents, social stressors known to promote depressive-like behaviours also damage the integrity of intestinal and brain membranes and activate proinflammatory signalling pathways. Our objective was to investigate the effects of a prenatal stressor on inflammatory cytokines and membrane permeability along the gut-brain axis in male and female offspring exposed to an adult social stressor. We hypothesized that prenatally stressed offspring would show exaggerated inflammatory activation and membrane disruption in response to adult stress. **Methods:** C57BL/6 mice in the second trimester of pregnancy experienced physical restraint (30 min, 3 times daily) or were left undisturbed. In adulthood, male and female offspring experienced a social stressor or were not manipulated. Plasma corticosterone levels as well as mRNA expression of the proinflammatory cytokine interleukin (IL)-6 and of the tight junction proteins claudin-5 and occludin in the prefrontal cortex and the jejunum were determined 90 minutes after stressor exposure. **Results:** Social stress increased plasma corticosterone in both males and females ($p < 0.005$), regardless of prenatal stressor experience. Upregulated prefrontal and jejunal expression of IL-6 in socially defeated offspring ($p < 0.05$ and $p < 0.0001$, respectively) was limited in prenatally stressed males, but not females. Curiously, prefrontal claudin-5 expression was upregulated in prenatally stressed males, irrespective of adult stressor experience ($p < 0.05$), but was reduced in socially stressed females ($p < 0.05$). **Conclusion:** Prenatal and adult stressor experiences may modulate proinflammatory activation and membrane permeability along the gut-brain axis in a sex-specific fashion.

The impact of social anxiety on the neural processing of emotional faces. *Nina Hedayati, Rachel McCaig, Kayleigh A. Abbott, Nichole Scheerer, Jeffery A. Jones.* From the Department of Psychology, Wilfrid Laurier University, Waterloo, Ont., Canada (Hedayati, McCaig, Jones); the Department of Social Work, Wilfrid Laurier University, Waterloo, Ont., Canada (Abbott); and the Department of Psychology, Simon Fraser University, Burnaby, BC, Canada (Scheerer).

Background: Individuals with social anxiety (SA) have an excessive fear of being negatively evaluated in social situations and, as a result, they tend to pay attention to negative facial expressions. This study examined the influence of emotional valence, social relevance and SA on face perception. **Methods:** Individuals with high ($n = 15$) and low ($n = 12$) SA viewed faces that displayed happy, angry and neutral expressions. Event-related potentials (ERPs) were measured during a passive task and a meet task. In both tasks, participants viewed the same face stimuli, but the difference was that between the passive task and the meet task, participants were instructed that they would have to give a speech after the ERP portion to 1 of 2 people they had just viewed. The P1, early posterior negativity (EPN), and late positive potential (LPP) ERP components were analyzed. The Social Interaction Anxiety Scale, Social Phobia Inventory, the State-Trait Anxiety Inventory (state anxiety only), and the Beck

Depression Inventory were administered. **Results:** A preliminary analysis of trends indicates that individuals with high SA relative to those with low SA appeared to have larger P1 amplitudes for angry and neutral faces for the passive and meet tasks and smaller EPN amplitudes for neutral faces in the passive task only. LPP amplitudes did not appear to differ between groups. P1 appears earlier for individuals with high SA when happy faces are displayed. Individuals with high SA scored higher than those with low SA on measures of SA, state anxiety and depression. **Conclusion:** Results suggest that SA may affect facial perception.

Profiling exosomes in the prefrontal cortex of individuals with major depressive disorder. *Pascal Ibrahim, Corina Nagy, Saumeh Saeedi, Jean-Francois Theroux, Gustavo Turecki.* From the Integrated Program in Neuroscience, McGill University (Ibrahim, Turecki); the McGill Group for Suicide Studies, Douglas Mental Health University Institute (Ibrahim, Nagy, Saeedi, Theroux); the Department of Human Genetics, McGill University (Saeedi); and the Department of Psychiatry, McGill University (Turecki), Montreal, Que., Canada.

Background: Major depressive disorder (MDD) is one of the leading causes of disability worldwide, affecting 20% of the population. The environment is thought to play a role in the disease development by altering epigenetic mechanisms. MicroRNAs (miRNA) are well-known epigenetic regulators that can be packaged into exosomes, which are small extracellular vesicles of endosomal origin. Exosomes have emerged as means of intercellular communication, a process that is also disrupted in the depressed brain. They are thought to transfer miRNA between cells, modifying gene expression in recipient cells. We hypothesize that exosomal cargo is altered in patients with MDD compared with healthy controls. Our aim is to extract exosomes from human postmortem prefrontal cortex, a region previously associated with depression, and profile and compare the exosomal cargo. **Methods:** Exosomes were extracted using size exclusion chromatography, and the quality was assessed using Western blots and transmission electron microscopy (TEM). A small RNA library was also constructed and sequenced using the Illumina Platform. **Results:** Western blots confirmed the presence of endosomal and exosomal markers (TSG101, CD9) and little to no contamination (ER, Golgi, mitochondria). TEM images showed typical cup-shaped morphology within the expected size range (30–150 nm). Sequencing results revealed miRNA previously implicated in exosomes and brain function. **Conclusion:** High-quality exosome extractions can be obtained from post-mortem brain tissue using our method. This will be the first study to profile brain-derived exosomes in the context of depression. This will provide novel mechanistic insights into the pathophysiology of MDD.

Examination of hippocampal subfield volume in treatment-resistant depression. *Patricia Burhunduli, Adel Farah, Katie Vandelloo, Pierre Blier, Jennifer L. Phillips.* From the Mood Disorders Research Unit, The Royal's Institute of Mental Health Research, affiliated with the University of Ottawa

(Burhunduli, Farah, Vandelloo, Blier, Phillips); the Department of Cellular and Molecular Medicine, University of Ottawa (Burhunduli, Blier); the Department of Psychiatry, University of Ottawa (Blier, Phillips); and The Royal Ottawa Mental Health Centre (Blier), Ottawa, Ont., Canada.

Background: Reduced hippocampal volume is one of the most widely replicated structural neuroimaging findings in major depressive disorder (MDD). Despite known associations between the hippocampus and depression, little is known about the unique contribution of specific hippocampal subfields to the volumetric changes associated with depression. This study explored the association between depression severity and hippocampal subfield volumes in a clinically well-defined sample of patients with treatment-resistant MDD. **Methods:** Hippocampal total and subfield volumes were assessed using magnetic resonance imaging (MRI) in 20 participants with treatment-resistant MDD. T_1 -weighted structural images were acquired at 3 T using a multi-echo magnetization-prepared rapid gradient echo (MPRAGE) protocol. Cortical reconstruction and segmentation were performed using FreeSurfer 6.0.0. Severity of depressive symptoms was assessed using the Montgomery-Åsberg Depression Rating Scale. **Results:** Controlling for age, sex and total intracranial volume, Pearson partial correlations revealed negative associations between depression severity and total left hippocampal volume ($r = -0.60$, $p = 0.011$) and left subfield regions CA1 ($r = -0.59$, $p = 0.013$), CA3 ($r = -0.57$, $p = 0.018$), CA4 ($r = -0.49$, $p = 0.045$), molecular layer ($r = -0.62$, $p = 0.008$) and hippocampal-amygdala transitional area (HATA) ($r = -0.58$, $p = 0.014$). There was no significant association between depression severity and volume of the remaining hippocampal subfields or total hippocampal volume in the right hemisphere. **Conclusion:** The hippocampus is a highly heterogeneous structure, and distinct subfields may be involved differentially in MDD. Preliminary results in our small sample suggest that specific hippocampal subfield volumetric changes are differentially associated with depression severity. Research focusing on hippocampal subfields may provide insight on the potential contributions of hippocampal volume loss to continuing depressive symptoms.

Identification of cell networks in the motor cortex activated when performing motor tasks. *Patricia B. de la Tremblaye, Damian Chwastek, Marc Vani, Yingben Xue, Diane Lagace.* From the Department of Cellular and Molecular Medicine, University of Ottawa (Tremblaye, Chwastek, Vani, Xue, Lagace); and the Brain and Mind Research Institute, University of Ottawa (Tremblaye, Chwastek, Vani, Xue, Lagace), Ottawa, Ont., Canada.

Background: Inducible transgenic mice models that express immediate early gene (IEG)-driven fluorophores in response to cellular activation provide high temporal and spatial specificity to identify cells activated when performing a behavioural task. We used the ARC IEG (ArcCreERT2:RosaYFPf/f) mouse model that allows for the conditional and permanent labelling of specific populations of cells activated when

performing motor tasks at 2 time points in vivo. **Methods:** Naïve ArcCreERT2:RosaYFPf/f mice were trained and tested at 2 time points in either a gross or a fine motor task, using the rotarod and string pull tests, respectively. The cells that were activated when first performing the motor task were identified by their permanent expression of yellow fluorescent protein (YFP). Reactivated cells were identified by their expression of YFP and protein expression for the endogenous immediate early gene (Arc or c-Fos) at the second time point performing the motor task. **Results:** Quantification of labelled cells in subregions of the motor cortex revealed increased density of activated cells at both the first (YFP+) and second time point (c-Fos+) in mice performing either the rotarod or string pull task compared with nonbehaving littermate control mice. Additionally, the percentage of cells that were reactivated (YFP+, c-Fos+) was 65% and 45% when performing either the rotarod task or string pull task, respectively. **Conclusion:** These results suggest that the ArcCreERT2 mouse is able to reliably label motor networks used to perform either a gross or fine motor task at 2 time points and provide the foundation for ongoing studies examining how the active network is modified during recovery from stroke.

Development of an assay for the collection and cellular characterization of rodent and human dorsal root ganglia. *Rikesh Raichura, Annemarie Dedek, Jeffrey Landrigan, Chaya Kandegedara, Eve C. Tsai, Michael E. Hildebrand.* From the Department of Neuroscience, Carleton University (Raichura, Dedek, Landrigan, Kandegedara, Hildebrand); the Neuroscience Program, Ottawa Hospital Research Institute (Dedek, Kandegedara, Tsai, Hildebrand); and the Brain and Mind Research Institute, University of Ottawa (Hildebrand), Ottawa, Ont., Canada.

Background: Chronic pain is a debilitating condition severely affecting quality of life. To develop safer and more effective treatments, the elements of pain-signalling processes that become dysfunctional need to be identified. The dorsal root ganglia (DRG), which house clusters of sensory neuron cell bodies between the spinal nerve and dorsal root, are a critical component of pain detection and modulation. Hyperactivity within DRG has been linked to disproportionate pain responses observed in chronic pain conditions, and yet the morphology of human DRG remains uncharacterized. Much of the current research in the field has been limited to animal models, given the difficult nature and limited availability of human tissue for analysis. Thus, a more thorough understanding of the neuronal and glial subpopulations mediating the activity of DRG is needed. This translational research project serves to develop an assay through which intact DRG from both rats and human organ donor tissue can be characterized to compare the neuronal and glial subpopulations that mediate pain processing within the DRG. **Methods:** We have developed a consistent and reproducible method for extracting DRG from rats and as well as sectioning and mounting techniques for both rat and human DRG. In addition, staining protocols for Cresyl Violet, NeuN, and Hoechst are being optimized to improve the quality of results specific to human

and rat tissue. **Results:** Pending. **Conclusion:** Our assay will allow for further analysis of DRG morphology and supporting cell types, improving our understanding of the DRG's role in pain signalling and chronic pain disorders.

Screening and identification of γ -aminobutyric acid-producing bacteria isolated from commercial starter cultures. *Rojaalsadat Mousavi, Walid Mottawea, Marie-Claude Audet, Riadh Hammami.* From the NuGut Research Platform, School of Nutrition Sciences, University of Ottawa, Ottawa, Ont., Canada.

Background: Appreciable evidence suggests that intestinal microbiota interact with the brain and play a key role in the pathogenesis of mental illnesses. Probiotics are seen as promising treatments for mental illnesses, but the mechanisms by which they exert their effects have yet to be established, thus preventing evidence-based microbiota-targeted interventions. Commensal bacteria produce a variety of neurotransmitters such as γ -aminobutyric acid (GABA) which, beyond interacting with intestinal physiology, can transit through neural pathways linking the enteric and central nervous systems and influence brain functioning. The contribution of the GABAergic system in the pathogenesis of mood disorders is now well recognized. Decreased glutamate catabolism potential was observed in depressed individuals, linking microbial glutamate pathways to depression. Lactic acid bacteria (LAB) are an important source for glutamate decarboxylase (GAD; enzyme converting L-glutamate to GABA), and thus can be regarded as promising GABA-producing psychobiotics. **Methods:** We screened LAB from starter cultures for their capacity to produce GABA in vitro. Several LAB were isolated and detected for presence of *Gad* using polymerase chain reaction. GAD enzymatic assay was then performed for positive strains. **Results:** The most active strains with high and fast production kinetics were identified and characterized, and included *Streptococcus thermophilus*, *Lactobacillus plantarum*, and *Lactobacillus delbrückii*. **Conclusion:** We have identified several psychobiotic candidates with a high capacity to produce GABA in vitro. The establishment of the psychobiotic impact of GABA-producing bacteria will inform and guide the development of next-generation probiotics or functional food products with psychobiotic properties with the potential to improve human mental health.

The effects of pubertal- and adult-onset oral contraceptives on brain structure. *Rupali Sharma, Samantha Smith, Aisa Dordari, Andra Smith, Nafissa Ismail.* From the Department of Psychology, University of Ottawa (Sharma, Smith, Smith, Ismail); and the Institute of Integrated Science, Carleton University (Dordari), Ottawa, Ont., Canada.

Background: Millions of women worldwide use oral contraceptives (OCs), often starting at a pubertal age when their brains are in a crucial developmental stage. For girls, puberty marks the transition to womanhood whereby the surge of ovarian hormones confers reproductive competence and initiates brain reorganization that gives rise to the social,

emotional and cognitive development across adolescence. The influx and fluctuations of ovarian hormones in women contribute to sex differences in mood disorders, as women are disproportionately affected. Given that OCs modulate internal hormone production and that the age of OC onset is decreasing toward early- to mid-puberty owing to their marketability as “regulators,” examining the influence of hormonal OCs on women’s brain structure, function and mood is warranted. The objective of the current study was to examine the effects of pubertal- and adult-onset OC use on grey matter and white matter volume. **Methods:** Undergraduate women ($n = 75$) underwent structural magnetic resonance imaging. **Results:** OC users displayed less grey matter volume in the putamen but showed larger regional white matter volume in the putamen, amygdala and hippocampus than naturally cycling women. Pubertal-onset OC users also show more white matter volume in the fusiform compared with their adult-onset counterparts. **Conclusion:** The current findings show that OC use alters brain structure, especially during puberty. These results advance our understanding of the impact of OC use on the brain, which is critical to women’s health.

An unrecognized “excitement” of epilepsy in Parkinson disease: evidence of systemic biomarkers and cognitive function. *Saba Rawjani, Alysia Ross, Hui Zhang, Shawn Hayley, Hongyu Sun.* From the Department of Neuroscience, Carleton University, Ottawa, Ont., Canada (Rawjani, Ross, Hayley, Sun); and the Department of Neurology, The State University of New York, New York, NY, USA (Zhang).

Background: Parkinson disease is a debilitating age-related neurodegenerative disorder. Its progression is associated with severe neuronal degeneration, cognitive decline, functional impairment and fluctuation in cerebrospinal fluid (CSF) biomarkers. Despite the vast amount of research being conducted to define the etiology of Parkinson disease, there are still numerous mechanisms yet to be uncovered. While epilepsy is frequently comorbid with various neurodegenerative diseases, it is a very uncommon comorbidity of Parkinson disease and has been considered not directly associated with the disease. Interestingly, single seizure episodes have been shown to decrease the magnitude of Parkinson disease motor symptoms. Thus, characterization of seizures in patients with Parkinson disease and epilepsy may allow for analysis of the association between these conditions. **Methods:** Here, we analyzed the clinical data from 198 patients with Parkinson disease, 99 healthy controls and 6 Parkinson disease patients with epilepsy to examine whether the co-existence of epilepsy and Parkinson disease will normalize motor and cognitive function and the level of CSF biomarkers. **Results:** We found that epilepsy significantly improved clinical motor symptoms in patients with Parkinson disease. Furthermore, CSF biomarkers in patients with Parkinson disease and epilepsy (i.e., α -synuclein, A β -142, t-Tau) and cognitive decline were rescued to levels similar to healthy controls. **Conclusion:** Our results support a potential interaction between epilepsy and Parkinson disease and suggest a novel therapeutic strategy for the treatment of motor and cognitive symptoms in patients with the disease.

Quality of life in children with epilepsy treated with the low glycemic index diet — a pilot study. *Sama Boles, Richard Webster, Sophie Parnel, Julie Murray, Erick Sell, Daniela Pohl.* From the Faculty of Medicine, University of Ottawa (Boles); the Clinical Research Unit, Children’s Hospital of Eastern Ontario (Webster); the Children’s Hospital of Eastern Ontario (Parnel, Murray); and the Division of Neurology, Children’s Hospital of Eastern Ontario, University of Ottawa (Pohl), Ottawa, Ont., Canada.

Background: About 30% of children with epilepsy respond insufficiently to first-line anticonvulsant drug treatment. The low glycemic index (LGID) and ketogenic diets may improve seizure control in those children. The LGID liberalizes the stricter ketogenic diet and is reported to be almost equally effective and associated with higher adherence and tolerability. However, little is known about the quality of life in children treated with LGID. **Methods:** We conducted a pilot trial to explore the quality of life and implications of the LGID among pediatric patients and their families. Patients with epilepsy treated with the LGID, ages 5–18 years, were enrolled. Participants and their parents were asked to fill out standardized, validated questionnaires (Pediatric Quality of Life Epilepsy Module). They fill 2 questionnaires: 1 retrospectively (i.e., answered in a manner as if it were before starting the LGID) and 1 in real time. An additional questionnaire was provided with 2 open-ended questions to gain a better understanding of personal experiences of patients with epilepsy on the LGID. Data were collected from 3 male and 2 female participants and their parents. Descriptive statistics will summarize the patient and parent self-reported quality of life, and the open-ended data will be analyzed using conventional content analysis to provide better understanding of personal experiences of patients with epilepsy on the LGID. **Results:** Pending. **Conclusion:** We expect that parental report of pediatric quality of life will increase because of lower frequency of epileptic seizures; however, pediatric quality of life, as reported by the children, will decrease because of limitations in dietary intake.

Cannabis treatment in children with epilepsy: practices and attitudes of neurologists in Canada. *Stephanie M. DeGasperi, Richard Webster, Daniela Pohl.* From the Faculty of Medicine, University of Ottawa (DeGasperi); the Clinical Research Unit, Children’s Hospital of Eastern Ontario (Webster); and the Division of Neurology, Children’s Hospital of Eastern Ontario, University of Ottawa (Pohl), Ottawa, Ont., Canada.

Background: Medical cannabis has recently emerged as a treatment option for children with drug-resistant epilepsy. Despite the fact that many pediatric epilepsy patients across Canada are currently being treated with cannabis, little is known about the attitudes of neurologists toward cannabinoid treatment of children with epilepsy. **Methods:** A 26-item online survey was distributed via email to 148 pediatric neurologists working in hospitals and community clinics across Canada. Questions were related to clinical practice,

and demographics. **Results:** This survey achieved a response rate of 38% (56 Canadian neurologists). These neurologists were treating 668 pediatric epilepsy patients with cannabinoids. While 29% of neurologists did not support cannabis treatment in their patients, 34% prescribed cannabis, and 38% referred to another authorizing physician, mostly to community-based non-neurologists. The majority of neurologists considered cannabis for patients with Dravet syndrome (68%) and Lennox–Gastaut syndrome (64%) after an average of 3 failed trials of anticonvulsants. Close to one-third (27%) considered it for patients with idiopathic generalized epilepsy, and 18% considered it for focal epilepsy. No neurologist used cannabis as a first-line treatment. All neurologists had at least 1 hesitation regarding cannabis treatment in pediatric epilepsy. The most common hesitation was poor evidence (66%), followed by poor quality control (52%), and high cost (50%). **Conclusion:** The majority of Canadian pediatric neurologists consider using cannabis as a treatment for epilepsy in children. With many gaps in evidence and high patient-driven demand for cannabis therapy, this survey provides immediate, pragmatic information to aid neurologists until further evidence is available.

Effects of maternal immune activation on estrogen receptors in the bed nucleus of stria terminalis of postpartum female rats. *Shreya Sarmah, Matt Lukasik, Amanda C. Kentner, Anne T.M. Konkle.* From the Department of Biology, University of Ottawa, Ottawa, Ont., Canada (Sarmah); the Interdisciplinary School of Health Sciences, University of Ottawa, Ottawa, Ont., Canada (Lukasik, Konkle); the School of Arts & Sciences, Massachusetts College of Pharmacy and Health Sciences, Boston, MA, USA (Kentner); the School of Psychology, University of Ottawa, Ottawa, Ont., Canada (Konkle); and the University of Ottawa Brain and Mind Research Institute, Ottawa, Ont., Canada (Konkle).

Background: Pregnancy and the postpartum period are vulnerable times for mammals, as considerable hormonal changes occur. While in utero perturbations are known to impact neurodevelopment, little is known about their effects on maternal brain and behaviour. The steroidogenic hormone, estrogen, via activation of estrogen receptors (ER α), plays an important role in regulating maternal behaviour. The objective of this project was to evaluate the effects of maternal immune activation during pregnancy on the number of ER α in the bed nucleus of stria terminalis (BNST) in rats, a brain area involved in maternal behaviour. It is hypothesized that immune activation will decrease the number of ER α in the BNST. **Methods:** Rat dams were randomly assigned to live in a standard or socially enriched environment. Dams received an injection of either vehicle (saline) or lipopolysaccharide (LPS) on gestational day 11. On postpartum day 22, the brains were extracted, sectioned at 40 μ m, and

processed for immunohistochemistry with an antibody for detection of ER α . Positive cell counts were performed with the software Image J. The effects of treatment and housing were assessed using a factorial analysis of variance. **Results:** Analysis ($n = 21$) revealed maternal immune activation during pregnancy significantly reduced the number of ER α in the BNST of postpartum female rats ($p < 0.001$), and there was no notable effect of housing on the number of ER α in this area ($p > 0.05$). **Conclusion:** These results speak to the consequences of maternal immune activation on the postpartum maternal brain and the need to further study the impact of environmental perturbations at this critical period.

Systems-based approach to uncover regulatory mechanisms of TDP-43 mislocalization in amyotrophic lateral sclerosis. *Terry R. Suk, Emily C. MacInnis, Jean-Louis A. Parmasad, Steve M. Callaghan, Stephen D. Baird, Maxime W.C. Rousseaux.* From the Department of Neuroscience, University of Ottawa (Suk); the University of Ottawa Brain and Mind Research Institute (Suk, Callaghan, Rousseaux); the Centre for Neuromuscular Disease, University of Ottawa (Suk, Rousseaux); the Department of Biology, University of Ottawa (MacInnis, Parmasad); the Children's Hospital of Eastern Ontario Research Institute (Baird); the Department of Cellular and Molecular Medicine, University of Ottawa (Rousseaux); and the Ottawa Institute of Systems Biology, University of Ottawa (Rousseaux), Ottawa, Ont., Canada.

Background: Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease of the motor neurons. Although the majority of ALS cases are sporadic, with no known cause or genetic inheritance, almost all cases display cytoplasmic mislocalization and aggregation of the RNA binding protein, TDP-43. What drives cytoplasmic accumulation of TDP-43 in ALS, however, remains unclear. Identifying the forces underlying cytoplasmic mislocalization of TDP-43 will not only provide insight into the modes of toxicity, but could also shed light onto novel ALS genes and potential avenues of interception. **Methods:** We generated cell lines that label endogenous TDP-43 (TARDBP locus) with green fluorescent protein (GFP) using a CRISPR/Cas9 knock-in approach. We ensured that the TDP-43–GFP fusion does not impact native TDP-43 function by looking at its localization, levels and downstream targets. Building on this new cell line, we are making additional clones containing ALS-linked mutations (Q331K, M337V, and G348C) by editing TARDBP in cis with the GFP tag. As a proof of principle, we are using a siRNA library against the human kinome coupled with high content imaging to identify modifiers of TDP-43 localization. **Results:** Pending. **Conclusion:** Further studies will validate our findings in cells with patient mutations and in animal models, and will cross-reference to genetically relevant ALS cases to identify putative ALS-driving genes.