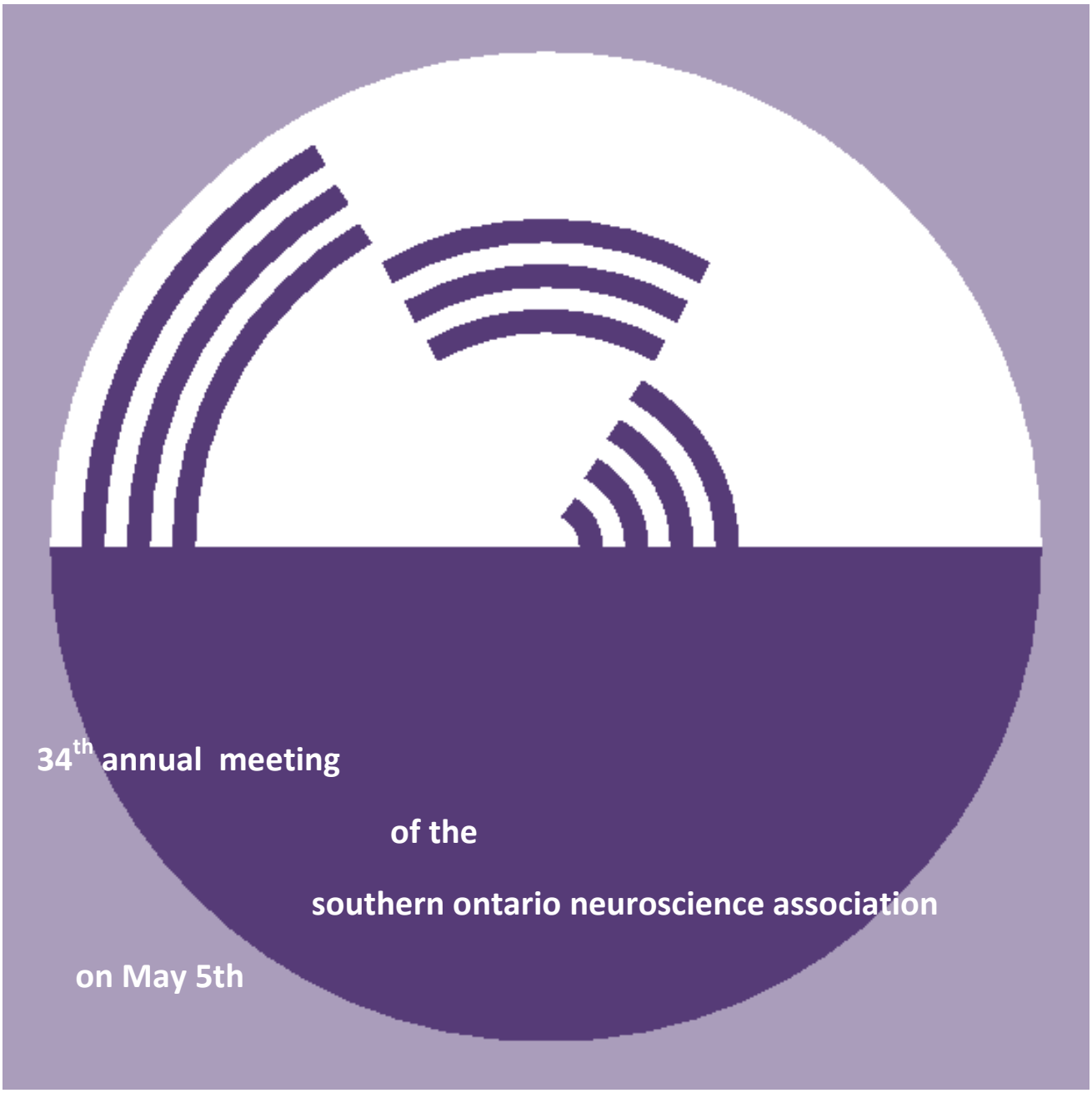
SONA

SOUTHERN ONTARIO NEUROSCIENCE ASSOCIATION



34th annual meeting

of the

southern ontario neuroscience association

on May 5th

Western

UNIVERSITY · CANADA

ORGANIZING COMMITTEE

Susanne Schmid, PhD
Brian Corneil, PhD
Steve Lomber, PhD
Brian Allman, PhD
Shawn Whitehead, PhD

VOLUNTEERS

Erin Azzopardi
Komal Shaikh
Mahabba Smoka
Dan Park
Ryan Wong
Jennifer Au
Li-Ann Leow
Ashley Schormans
Cleusa DeOliveira
Nicole MacLeod
Jordan Zunder

SPONSORS

Society for Neuroscience
Schulich School of Medicine & Dentistry, Western
Faculty for Social Sciences, Western
Faculty for Health Sciences, Western
Dept. of Anatomy & Cell Biology
Dept. of Physiology & Pharmacology
Dept. for Psychology
The Brain & Mind Institute
The Neuroscience Graduate Program

Special thanks to all volunteers and sponsors!

SOUTHERN ONTARIO NEUROSCIENCE ASSOCIATION

34th Annual Meeting
May 5th 2014

Western

Meeting Program

8:00	**Registration, Breakfast**
8:45	**Opening remarks: Susanne Schmid, President of SONA**
9:00 - 11:15	**Barbara Zielinski** (Univ. of Windsor) "Olfaction in the wild: the olfactory system in two invasive fish"
	Deda Gillespie (McMaster) "Exciting development at inhibitory synapses"
	Scott MacDougall-Shackleton (Western) "Stress and the brain: lessons from songbirds"
	Boyer Winters (U of Guelph) "Cholinergic regulation of object memory destabilization"
11:15 – 1:15	**Poster session I**
12:00	**Lunch (Business meeting for SONA delegates and interested people, Room 146)**
1:15 – 3:00	**Arthur Brown** (Western) "SOX after central nervous system injury"
	Kelly Shen (Baycrest) "Anatomical constraints on functional network organization and *dynamics*"
	James Danckert (U of Waterloo) "Playing games to understand the brain: building mental representations of statistical regularities."
3:00-4:30	**Poster session II**
4:30 -5:15	**Keynote: Marla Sokolowski** (Univ. of Toronto) "The *foraging* gene: Will that be for here or to go?" *Sponsored by the Western* ***Neuroscience Graduate Program***
5:15	**Closing remarks, Announcement of the poster awards**
5:20	**Post Meeting Reception the Wave (Finger food & Cash-Bar)**

A: Cognition and Behaviour

A1: THE EFFECTS OF MUSICAL MOOD AND MUSICAL AROUSAL ON VISUAL ATTENTION

Angela Marti Marca[1], Tram Nguyen[2], and Dr. Jessica Grahn[3]
Department of Psychology, University of Western Ontario, London, ON

The presence of music is a visceral part of the human experience and its influence on cognitive function is a growing area of research in psychology. In particular, perceptual properties of music (mood and arousal) have been shown to significantly affect performance. There has been minimal research in the field on the interaction of mood and arousal and their influence on attention, thus the purpose of this study. Fifty undergraduate students (University of Western Ontario) were recruited for this study. Given that music is a highly subjective experience, participants rated an assortment of music clips on their mood and arousal levels. The clips that participants rated highest and lowest on mood (positive and negative) and arousal (low and high) were used on the Posner cueing task. This visual attention task was either performed in silence or while listening to music as per their ratings. Results indicated that musical mood and musical arousal, independently of one another, had no significant effect on visual attention. Rather, a significant interaction between the two perceptual properties was observed. The fastest reaction times were recorded when participants listened to high arousal positive music and the longest reaction times were found when participants listened to high arousal negative music. Intermediate performance occurred when participants listened to low arousal negative music and low arousal positive music. Future studies should investigate whether the combined modulatory effects of musical mood and musical arousal generalize to other attentional paradigms.

A2: EFFECT OF CHRONIC ISOLATION ON SOCIAL PREFERENCE AND MONOAMINE SYSTEMS IN ZEBRAFISH

Soaleha Shams[1], Amanda Facciol[2], Diptendu Chatterjee[2], & Robert Gerlai[1,2]
[1]Department of Cell & Systems Biology, University of Toronto Mississauga
[2]Department of Psychology, University of Toronto Mississauga

The zebrafish serves as an excellent translational model for the analysis of vertebrate physiology and behaviour. Zebrafish is a social species with a wide range of quantifiable social and non-social behaviours. Similar to mammals, the social environment of zebrafish can alter brain function and expression of behaviour. However, beyond the larval stage, the effects of social deprivation on zebrafish behaviour remain relatively unknown. To investigate this, we compared social and isolated zebrafish in adulthood. We exposed groups of socially-deprived and control fish to social stimuli; either a live group of conspecifics or an animated moving image of zebrafish. These observations were recorded and tracked using custom in-house developed tracking software, the Real Fish Tracker. The coordinates for each fish were used to calculate behavioural variables, such as distance traveled, speed, bottom dwelling and distance to the social stimulus. For neurochemical profiles, whole brain dopamine, DOPAC (dopamine metabolite), serotonin, and 5-HIAA (serotonin metabolite) levels of socially deprived zebrafish were compared with control zebrafish using high precision liquid chromatography (HPLC) analysis. Here we report that social deprivation altered locomotor activity, anxiety-like behaviour, and social response to live vs. automated stimuli in adult zebrafish. Social deprivation also altered monoamine systems in the brain. Findings from this study establish zebrafish as an appropriate animal model for studying the behavioural and neurological consequences of social deprivation.

Acknowledgements: Supported by NSERC and NIH/NIAAA

A3: THE ROLE OF INTRA-VISCERAL INSULAR CORTEX ENDOCANNABINOIDS IN NAUSEA-INDUCED CONDITIONED GAPING IN RATS

Martin A. Sticht and Linda A. Parker
Department of Psychology and Collaborative Neuroscience Program, University of Guelph, Guelph, Ontario, Canada

Manipulations that elevate the endocannabinoids (eCBs), anandamide (AEA) and 2-arachidonoylglycerol (2AG), have previously been shown to interfere with the establishment of nausea-induced conditioned gaping in rats. The visceral insular cortex (VIC) has been found to play a critical role such that localized administration of the anti-emetic drug, ondansetron, or the cannabinoid agonist, HU210, disrupts the establishment of nausea-induced conditioned gaping. However, at present, the precise role of the VIC in mediating eCB-suppression of nausea remains unknown. Therefore, the current study investigated the potential of intra-VIC eCB manipulations to interfere with the establishment of conditioned gaping in rats. Rats received an intraoral infusion of saccharin, preceded or followed by an intra-VIC infusion of exogenous eCBs, URB597 (FAAH inhibitor), or MJN110 (MAGL inhibitor), and were subsequently administered nausea-inducing LiCl. It was found that bilateral intra-VIC infusions of 2AG or MJN110 dose-dependently suppressed conditioned gaping in rats, whereas anandamide and URB597 were without effect. Interestingly, the ability of intra-VIC 2AG to interfere with conditioned gaping does not appear to be mediated by CB_1 receptors, as pretreatment with a CB_1 antagonist (AM251) did not reverse the suppressive effects of 2AG. These findings suggest that manipulations that elevate 2AG within the visceral insular cortex may have anti-nausea potential, and furthermore that downstream metabolites of eCBs may play a role in these effects.

This research was supported by an NSERC grant to LAP and a CGS award to MAS.

A4: POTENTIAL ROLE OF THE STRESS-INDUCIBLE PHOSPHOPROTEIN 1 AND PRION PROTEIN COMPLEX IN RESPONSE TO STROKE

Flavio H. Beraldo, Daniela F. Goncalves, Benjamin Kolisnyk, Francis Nguyen-Do, Talal Masood, Robert Gros, Robert Bartha, Vania F. Prado, Marco A. M. Prado
University of Western Ontario, London, ON

Prion Protein (PrP^C) forms a complex with the Stress Inducible Phosphoprotein I (STI1) improving neuronal survival after distinct insults. To establish potential roles of STI1 in neuronal function after ischemia, we examined the response of neuronal cultures obtained from mice expressing different levels of STI1 (WT,$STI1^{-/+}$-50% less and $STI1^{TgA}$ – 4-fold compared to WT), to oxygen-glucose-deprivation (OGD). OGD induced an increase in neuronal death independently of the STI1 levels and extracellular STI1 protected against neuronal death induced by OGD via PrP^C. In order to uncover potential *in vivo* roles of STI1 in ischemia we submitted mice to unilateral middle cerebral artery occlusion (MCAO). There was no difference in survival or in the infarct volume after stroke between WT and $STI1^{TgA}$ mice however, $STI1^{-/+}$ displayed larger infarct volume and increased mortality. In order to evaluate the potential to use sustained attention as a marker for executive function in stroke we trained mice on the 5 choice serial reaction time task (5-CSRT) and submitted them to MCAO. Two weeks after surgery, sham-operated mice performed normally on the 5-CSRT, whereas control WT mice submitted MCAO could no longer complete this test. In contrast, $STI1^{TgA}$ mice show significant improvement compared to WT on the 5CSRTT after this mild stroke injury. Our results suggest that STI1 is able to protect neurons from OGD and decreased STI1 levels affect animal survival and brain injury after ischemia. In addition, increased STI1 levels improve deficits in sustained attention in experimental stroke.

A5: MATERNAL GENOTYPE OF THE M5 MUSCARINIC RECEPTOR IS CRITICAL FOR ULTRASONIC VOCALIZATIONS IN MOUSE PUPS

Pavel Tselichtchev [1], David I. Wasserman[2], and John S. Yeomans[1,2]
[1]Department of Cell & Systems Biology, University of Toronto, ON
[2]Department of Psychology, University of Toronto, ON

Rodent pups emit ultrasonic vocalizations (USVs) after maternal separation to convey distress and to promote maternal care. Dopamine plays a role in maternal behaviors, such as nest building, retrieval, nursing, and grooming. The M5 receptor (M5R) is important for activating dopamine neurons for reward and motivation functions. We examined the influence of the M5R on USV calling and pup-dam interaction with M5R knockout (KO) mice. M5R KO pups emitted fewer USVs than wild type (WT) pups on postnatal day 8. Using heterozygous (HET) crosses, however, KO, HET and WT pups showed similar isolation-induced USVs, indicating pup genotype is not critical. Using reciprocal M5R KO-WT crosses to determine how parental genotype affects pup USVs, HET pups from M5R KO dams produced 90% fewer USVs than HET pups from WT dams. Therefore, maternal M5R genotype controls how many calls M5 pups produce, while pup genotype has little effect. These results differ from dopamine D2R mice, where both pup and maternal genotype influence pup USVs (Curry et al., 2013). The importance of maternal hormones and anxiety is discussed.

A6: ANATOMICAL CONNECTIONS BETWEEN THE MESOPONTINE TEGMENTUM AND THE MIDBRAIN VTA AND RMT

Joel M.J. Tan[1], David I. Wasserman[1], and John S. Yeomans[1,2]
[1]Department of Cell & Systems Biology, University of Toronto, ON
[2]Department of Psychology, University of Toronto, ON

Opioids induce rewarding and locomotor effects mainly via rostromedial tegmental (RMTg) GABA neurons that express opioid receptors. Opioids inhibit RMTg GABA neurons that then strongly inhibit dopamine (DA) neurons. Opioid reward and DA release, however, depend on laterodorsal and pedunculopontine tegmentum (LDT/PPT) neurons that activate DA neurons via M5 muscarinic receptors. Here, the retrograde tracer, cholera toxin B, was injected into ventral tegmental area (VTA) and RMTg sites to identify LDT and PPT inputs. Many cholinergic neurons in LDT and PPT project to both the VTA and RMTg. Triple-labeling of RMTg neurons showed μ-opioid and muscarinic M4 receptors near the cell body, indicating a site of cholinergic innervation of RMTg GABA neurons. Therefore, opioids act on μ-opioid receptors on RMTg neurons, co-localized with inhibitory M4 receptors. LDT/PPT neurons facilitate opioid effects by inhibiting RMTg neurons via M4 receptors. LDT and PPT cholinergic neurons activate DA neurons via M5 muscarinic receptors and inhibit RMTg GABA neurons via M4 muscarinic receptors; Both these effects increase opioid reward and locomotion.

A7: MUSCARINIC CONTROL OF ROSTROMEDIAL TEGMENTAL NUCLEUS GABA NEURONS AND MORPHINE-INDUCED LOCOMOTION

David I. Wasserman[1], Joel M.J. Tan[2], Junchul C. Kim[1], and John S. Yeomans [1,2]
[1]Department of Psychology, University of Toronto, ON
[2]Department of Cell & Systems Biology, University of Toronto, ON

Opioids induce rewarding and locomotor effects mainly via rostromedial tegmental (RMTg) GABA neurons that express μ-opioid and nociceptin receptors. These GABA neurons then strongly inhibit midbrain dopamine neurons. Opioid rewards and locomotion also depend on dorsal tegmental cholinergic and glutamate neurons that project to and activate VTA dopamine neurons. Here we show that many pedunculopontine and lateral tegmental cholinergic neurons project to both RMTg and VTA, and that M4 muscarinic receptors are co-localized with μ-opioid receptors on RMTg GABA neurons. To inhibit or excite RMTg GABA neurons, we transfected designed muscarinic receptors (M4D or M3D) in GAD2-Cre mice with AAV vectors. In M4D-expressing mice, clozapine-N-oxide (CNO) administration increased morphine-induced, but not saline-induced locomotion. In M3D-expressing mice, CNO blocked morphine-induced locomotion, but not saline-induced locomotion. We propose a disinhibitory model of opioid-induced locomotion in which cholinergic inhibition of RMTg GABA neurons via M4 muscarinic receptors facilitates opioid inhibition of the same neurons. Collateral cholinergic activation of VTA dopamine neurons via M5

muscarinic receptors activates dopamine neurons and facilitates dopamine-dependent locomotion.

A8: WEBER'S LAW IN DELAYED TACTILE GRASPING AND MANUAL ESTIMATION

Shirin Davarpanah Jazi[1], Stephanie Hosang[1], Matthew Heath[1,2]
[1]*School of Kinesiology, The University of Western Ontario, London, ON*
[2]*Graduate Program in Neuroscience, The University of Western Ontario, London, ON*

The somatosensory processing model (SPM) asserts that ventral and dorsal cortical pathways support tactile perceptions (relative cues) and actions (absolute cues), respectively. In support of the SPM, recent work by our group showed that peak grip aperture associated with grasping a tactile object presented on the palm of the hand was refractory to Weber's law, whereas manual estimations elicited apertures that adhered to the law's psychophysical principles. This dissociation is evidence for the existence of separate streams of tactile processing as indicated by the SPM. In the present investigation, we sought to determine whether introducing a delay between target presentation and response initiation influences the tactile metrics supporting grasping control. To accomplish that object, we presented differently sized objects on the palm of participants left hand for a 4,000 ms tactile preview and subsequently asked participants to either grasp the object with their right hand immediately after the preview (i.e., closed-loop grasping) or following a 2,000 ms delay after removal of the target object (i.e., memory-guided grasping). Notably, we computed just-noticeable difference (JND) scores at the time of PGA. Preliminary results (N = 5) demonstrate a null scaling of JNDs to object size in the closed-loop condition and a linear scaling of JNDs to object size in the memory-guided conditions. These findings suggest that memory-guided grasping is mediated via a relative and perception-based target percept supported by the ventral tactile processing stream.

Acknowledgements: Supported by NSERC.

A9: MODELING FUNCTIONAL ORGANIZATIONS OF RESTING BRAINS USING THE ANATOMICAL STRUCTURE

Tushar K. Das[1], Pubuditha Abeyasinghe[1], Erik Ziegler[2], Steven Laureys[2,3], Adrian Owen[4], Andrea Soddu[1].
[1] *Brain & Mind Institute, Physics & Astronomy Department, Western University*[2] *Cyclotron Research Center and University Hospital of Liège, University of Liège, Liège, Belgium.*
[3] *Department of Neurology, CHU Sart Tilman Hospital, University of Liège, Liège, Belgium.*
[4] *Brain & Mind Institute, Social Science Department, Western University, London ON*

Recent advances in neuroimaging have enabled us to investigate the structure-function relationship in brain networks under rest, physiological (sleep), pharmacological (anesthesia) and pathological (disorder of consciousness) conditions. Growing research in these experimental findings of resting brain functional networks shed light on finding the unknown emergent properties of functional organizations in the healthy wake resting brain that may solely be governed from the structural connectivity network. Any disruption in the structural connectivity of brain networks may change the pattern of functional organizations, leading to explain brain mechanisms in different conditions. To study the relationship between structure-function in the large scale brain network, we present a computational model (based on the Ising spin model) that takes into account of spin configurations based on the human connectome structure. The numerical results at the critical temperature explain the emergent properties of self-organized criticality as well as the competing effect between modularity and integrity within spatio-temporal patterns of spontaneous spin dynamics. Later, our simulated results of functional self-organized criticality are compared with the organization properties of resting state spontaneous brain activity recorded with functional magnetic resonance imaging. Using graph theory we compare correlated network dynamics between the simulated and empirical results. These analyses explain the basis of optimized information processing in resting state brain networks.

A10: DIFFERENTIATING THE CONTRIBUTIONS OF FRIENDSHIP CHARACTERISTICS AND MENTAL HEALTH FACTORS TO THE FREQUENCY OF USE AND MOTIVATIONS TO USE MDMA, ALCOHOL AND MARIJUANA

Felicity A. Backhouse, Sarah L. Brekenridge, and Bruce E. McKay
Department of Psychology, Wilfrid Laurier University, ON

Friends can be integral to the avoidance of drug use, or the initiation and maintenance of drug use, and friends can contribute positively or negatively to mental health status; such decidedly different outcomes of friendship presumably depend on the specific characteristics of one's friendships. Here we have investigated the characteristics of close friendships, past-month frequency of alcohol, marijuana and MDMA use, motivations to use these drugs, and recent mental health status, in a sample (n=454) of undergraduate university students. Students with past-month MDMA or marijuana use had overall lower quality friendships than lifetime or non-users, a finding that was not apparent for recent alcohol users. Past-month MDMA, alcohol, or marijuana users scored poorly on several friendship characteristics that together suggest an unsupportive friendship dynamic mostly involving fun activities. Past-month MDMA users reported lower levels of perceived stress than lifetime or non-users, but did not differ on measures of anxiety or depression, whilst marijuana and alcohol use were not correlated with any mental health variables. Self-medicating with marijuana and alcohol, and using alcohol out of boredom, were correlated with depression, anxiety, and perceived stress scores, a finding that was not apparent for MDMA use. Anecdotally, these drugs may be used to facilitate social interactions; however our results suggest these social interactions may be within the context of low quality friendships.

A11: EXAMINING THE EFFECTS OF ROSTRAL AGRANULAR INSULAR CORTEX LESIONS ON ACQUISITION OF A RAT GAMBLING TASK

Abhiram Pushparaj[1], Martin Musiol[1], Catherine A. Winstanley[2] and Bernard Le Foll[1]
[1]*Translational Addiction Research Laboratory, Centre for Addiction and Mental Health, Toronto, ON*
[2]*Department of Psychology, University of British Columbia, Vancouver, BC*

Gambling disorder has recently been classified as an addictive disorder in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) due to research findings establishing its similarity to substance use disorders in terms of clinical expression, brain origin, comorbidity, physiology and treatment. The insular cortex, a brain region best known for integrating interoceptive information, has recently been identified as an important part of the neurocircuitry underlying drug addiction. The insular cortex has also been observed to be active during functional magnetic resonance imaging (fMRI) of the brains of individuals performing the Iowa Gambling Task (IGT), used clinically to measure gambling-like behaviour. Here we examined the effect of NMDA-induced excitotoxic lesions of the rostral agranular subregion of the insular cortex (RAIC) on a rat model of the IGT. Rats choose among four different options to earn as many sugar pellets as possible within 30 min. Each option is associated with the delivery of a different amount of reward, but also with a different probability and duration of punishing time-out periods during which reward cannot be earned. RAIC-lesioned animals demonstrated a greater preference for the choices resulting in smaller, more consistent rewards compared to sham-lesioned controls. These findings are in agreement with studies demonstrating that pharmacological inactivation of the RAIC decreases risky behaviour, thus suggesting that interoceptive information may be of importance to decision-making under risk.

Acknowledgements: Supported in part by a Level II grant awarded to Drs. Winstanley and Le Foll by the Ontario Problem Gambling Research Centre

A12: AGE DEVELOPMENT AND ACCESS INDUCED SUCROSE ESCALATION

Gehan Senthinathan and Roelof Eikelboom
Department of Psychology, Wilfrid Laurier University, Waterloo, ON

Adult rats (~65 days old) with ad lib food and water, given every day access (EDA) to 4 % sucrose, consume ~120 g of the solution in 24 h. When rats are restricted to 24 h of sucrose access once every third day (E3DA), these rats increase their sucrose intake, stabilizing at ~240 g of solution in 24 h. This twofold sucrose consumption difference (EDA/E3DA effect) is not evident among pre-pubertal pups. The typical EDA/E3DA effect becomes evident around the time of puberty (~37 days of age), a time associated with an increased susceptibility for addiction. Compared to younger, and older rats, it is unclear if pubertal rats are most sensitive to the access induced escalation of sucrose intake described above. The following design tests the effect of daily, and intermittent access, during different phases of development. Male Sprague-Dawley rats (N=72; 22 days old) were randomly assigned to access conditions (either daily access, single exposure, or one intermittent access cycle; all rats were also given sucrose 20 days after their initial exposure) that began sucrose exposure during different developmental phases (pre-puberty, puberty, and adulthood). The results suggest, compared to adult rats, pubertal rats are equally susceptible to the access induced escalation of sucrose intake. Consistent with previous work, pre-pubertal rats seem less susceptible to the access effect.

Acknowledgements: Supported by NSERC

A13: ESCALATED SUCROSE INTAKE IS ACCOMPANIED BY INCREASED VALUE

Adam Celejewski, Milan Valyear, Roelof Eikelboom
Wilfrid Laurier University, Waterloo, ON

With 24 h periods of Every 3rd Day Access (E3DA), rats markedly escalate their intake of a 4% sucrose solution, whereas with Every Day Access (EDA), the same solution is consumed at lower, stable levels. Importantly, if sucrose solution access is then switched to a common E2DA schedule, rats with E3DA experience continue to consume more solution than rats with EDA experience over an extended period of time. Here, we ask if the access-induced consumption increase reflects a change in sucrose solution value. Rats were first provided with a 4% sucrose solution paired with one flavour (the standard), for 12 E3DA exposures or 34 days of EDA. Rats with E3DA escalated their intake to consume almost twice as much sucrose solution as EDA rats. Next, a series 24h, 2 bottle preferences tests were conducted on an E2DA schedule. On each test day, preference was measured for the standard solution against ascending concentrations (2-32%) of a second sucrose flavour (the alternate). The point at which standard and alternate solutions were isohedonic was higher for the alternate concentration (rightward shift) for rats with E3DA relative to EDA experience. Further, both preference for the standard, as well as overall consumption of standard and alternate combined, were always higher after E3DA experience. Preference testing was followed by 12 E2DA exposures to the standard only. Again, rats with E3DA experience consumed more than rats with EDA experience. Together, these findings suggest that E3DA relative to EDA can increase the value of a sucrose solution over the relatively long term.

Acknowledgements: Supported by NSERC

A14: EFFECTS OF HEROIN DEPENDENCE ON YOHIMBINE-INDUCED REINSTATEMENT OF HEROIN SEEKING AND STARTLE REFLEX IN RATS

Meenu Minhas and Francesco Leri
Department of Psychology, University of Guelph, ON, Canada

It is known that heroin dependence alters responses to stressors, but it is not clear whether these effects can be observed also after dissipation of withdrawal symptoms. The current study explored whether heroin dependence alters the action of yohimbine (YOH), an α-2-adrenergic antagonist, on goal-directed and reflexive behaviors. Male Sprague-Dawley rats self-administered 0.05 mg/kg/infusion heroin for 10 sessions (1 session x day, each lasting 3h, on a continuous schedule of reinforcement). Four hours after each session, rats received 3 injections (SC) of vehicle or heroin, 2h

apart. The dose of these injections escalated from 3 mg/kg/day to 24 mg/kg/day. Withdrawal precipitated by a low dose of naloxone (0.1 mg/kg, SC) was measured after the last session of self-administration on a progressive ratio schedule. After a 4-day drug-free period and 9 sessions of extinction, animals were pre-treated with 0 or 0.5 mg/kg injection (IV) of YOH, and then tested for reinstatement of heroin seeking. In a separate experiment, rats received SC injections of heroin as described above. Following a 13-day drug-free period, two tests of startle were performed separated by 24 hours: one test following an injection of vehicle, and the other following an injection of 0 or 2.5 mg/kg YOH (IP). It was found that animals injected with heroin during the period of heroin self-administration displayed greater signs of naloxone-precipitated withdrawal, as well as greater YOH-induced reinstatement after extinction. YOH also amplified startle reactivity, but this effect was not affected by previous heroin dependence. These data suggest a possible dissociation between the actions of heroin dependence on stress-induced behaviors. More precisely, in the case of chemical stressors such as yohimbine, it appears that dependence and withdrawal amplify the action of stress on goal-directed behavior, without altering more reflexive stress responses.

Acknowledgments: Supported by NSERC

A15: ATRX HETEROZYGOSITY IN THE MOUSE BRAIN RESULTS IN MOTOR SKILLS DEFECTS, HYPERACTIVITY AND IMPAIRED SPATIAL LEARNING AND MEMORY

Renee Tamming[1,2], Yan Jiang[1,2], Marco Prado[3] and Nathalie Bérubé[1,2]
[1]*Children's Health Research Institute*
[2]*Departments of Biochemistry and Paediatrics, Western University, London, Canada*
[3]*Robarts Research Institute at Western University, London, Canada*

Alpha thalassemia mental retardation, X-linked (ATR-X syndrome) is caused by mutations in the *ATRX* gene and is characterized by abnormal development and intellectual disability. ATRX is a chromatin remodeling protein known to influence several cellular processes including gene expression. To study a role of ATRX in learning and memory processes, we generated a conditional deletion of *Atrx* in the brain using the Nestin-Cre / flox system. While the homozygous male mice died at birth, we were able to study behavioural outcomes in heterozygous female mice, where ATRX is deleted in ~50% of brain cells. We observed that $Atrx^{NestinCre}$ heterozygous female mice had decreased body weight and exhibit hindlimb clasping. Motor dysfunction was apparent in forelimb grip tests. They also exhibited hyperactivity compared to controls in the open field test, but no defects in depression or anxiety in the forced swim and elevated plus maze tests, respectively. Finally, spatial learning and memory was impaired in the mutant mice in the Morris Water Maze and the Barnes Maze paradigms. We conclude that loss of ATRX in a subset of brain cells causes several behavioural abnormalities, some of which phenocopy aspects of the ATR-X syndrome. These mutant mice will be useful to decipher the molecular and cellular underpinnings of the disease and to test therapeutic agents.

A16: THE ROLE OF ∆9-TETRAHYDROCANNABINOL AND URB597 IN THE WHEEL-INDUCED FEEDING-SUPPRESSION

Benjamin Peckham, Roelof Eikelboom, and Paul E. Mallet
Department of Psychology, Wilfrid Laurier University, Waterloo, ON

Anorexia nervosa is an enigmatic human condition typified by food-restriction that is often accompanied by extensive exercise. This has been modeled in rats in the wheel-induced feeding-suppression (WIFS) model. In this model, animals are given access to a running-wheel, which induces a volitional drop in food-consumption. This drop in feeding has been effectively reversed using chlorpromazine (Adams et al., 2009), suggesting that a neurological system governs this effect. In a similar animal model, it has been shown that ∆9-tetrahydrocannabinol (THC; the main psychoactive agent in cannabis sativa) similarly increases food-consumption and therefore slows weight-loss in rats (Verty et al., 2011). Pilot work suggested that URB597, a FAAH-inhibitor that indirectly increases levels of anandamide, might also be able to prevent the WIFS. The current research incorporated both THC (0, 0.125, and 0.25 mg/kg) and URB597 (0, 0.17, 0.5, and 1.0 mg/kg) into a WIFS paradigm, in which rats will gain 6 h of access to a locked or unlocked running-wheel every three days. Rats (n=30) were split into two groups: one receiving THC, the other URB597. Within these two groups, a Latin Square design was implemented. The no-drug (0 mg/kg), unlocked wheel condition should show a feeding suppression whereas this is not expected in the locked wheel conditions. This WIFS is predicted to be attenuated in a dose-dependent manner by THC and URB597, without these drugs having a direct effect on feeding in the locked wheel condition.

Acknowledgements: Support by NSERC funding to RE.

A17: DELINEATING THE ROLE OF THE DORSAL STRIATUM IN COGNITION: AN EVENT-RELATED FUNCTIONAL MRI STUDY

Brian D. Robertson[1], Nole M. Hiebert[1,2], Ken N. Seergobin[2], Penny A. MacDonald[1,2,3]
[1]*Department of Physiology and Pharmacology, University of Western Ontario*
[2]*The Brain and Mind Institute, University of Western Ontario, London, ON, Canada.*
[3]*Clinical Neurological Sciences, University of Western Ontario, London, ON, Canada*.

Cognitive flexibility—the mental ability to switch between thinking about two different concepts, and to shift response strategies dependent upon changes in the environment—is required for proper decision-making. Many studies have investigated which brain regions mediate cognitive flexibility. The dorsal striatum (DS) has been implicated, but a pervasive confound exists in many of these studies. Often, experimental trials designed to have greater cognitive flexibility demands also require more cognitive effort—the proportion of limited capacity central processing engaged, the number of elementary processes enacted, or the duration over which cognitive resources are expended. To test whether DS mediates cognitive flexibility, and not cognitive effort, we coupled functional magnetic resonance imaging (fMRI) with a number Stroop task that allows independent manipulation of cognitive flexibility and cognitive effort demands. This paradigm allowed us to directly compare DS blood-oxygenation-level-dependent (BOLD) signal between trials with high and low cognitive flexibility demands as well as trials with high and low cognitive effort demands. In 17 healthy young adults, longer response times (RTs) and increased DS BOLD signal occurred during trials with higher relative to lower cognitive flexibility demands. In contrast, longer RTs, but no change in DS BOLD signal, occurred during trials that differed only in terms of cognitive effort demands. These findings support the notion that DS mediates cognitive flexibility specifically and not cognitive effort.

Acknowledgments: This study was supported by a Canada Excellence Research Chair award to Dr. Adrian M. Owen, and by start-up funds and an Opportunity Grant from the Academic Medical Organization of Southwestern Ontario awarded to Dr. Penny A. MacDonald.

A18: MALE-INDUCED ESTROUS CYCLE SYNCHRONY: DOES IT OCCUR IN RATS?

Kathryn Leach[1], Angela Mastroianni[1] & Roelof Eikelboom[1]
[1]*Department of Psychology, Wilfrid Laurier University, Waterloo, ON*

Several variables can affect estrous cycle patterns in female rodents. 1) In rats, McClintock *et al* (1978) found that females housed in close proximity move into synchronous cycles. Work by Schank (2001) has failed to replicate this effect. 2) In mice, male pheromones can induce increased cycle synchrony among females (Whitten, 1956). Their absence results in disrupted cycles (Lee & Boot, 1956). It is not clear if males have this impact on female rats. Our experiments explored these two effects. In a pilot study, we relied on appetitive markers for the cycle phase -wheel running and feeding- since running is elevated and feeding is reduced on the night of estrus (Wang, 1923; Eckel *et al*., 2000). Accordingly, wheel turns and food intake were measured daily. This experiment suggested that male presence in the room affected synchrony. Females housed with males showed enhanced synchrony in running and feeding, showing an elevation and suppression respectively on the same night. Unisex-housed females showed less synchrony. A second experiment added estrous determination from vaginal smears with 32 females in two groups: males absent or present. Both groups showed evidence of synchrony, supporting a McClintock effect. The presence of 12 males in the room (in separate cages) did not increase synchrony or regularity, failing to support the Whitten or Lee-Boot effect in rats. Female pheromones may affect synchrony in the rat, whereas male pheromones may not. This may suggest that, in rats, there is a closer parallel with the human cycle more so than the mouse cycle.

Acknowledgements: Supported by NSERC.

A19: DETERMINING COGNITIVE DEFICITS IN MOUSE MODELS OF ALZHEIMER'S DISEASE USING TOUCHSCREEN TASKS: IMPLICATIONS FOR DRUG TREATMENTS

Talal S. Masood[1,2], Flavio H. Beraldo[1,3], Matthew Cowan[1], Vania F. Prado[1,2,3,4], Marco A. M. Prado[1,2,3,4]
[1]*Robarts Research Institute,* [2]*Graduate Department in Neuroscience,* [3]*Physiology and Pharmacology,* [4]*Anatomy and Cell Biology, Schulich School of Medicine, University of Western Ontario, London, ON*

Several approaches identified recently as promising treatments in pre-clinical trials for Alzheimer's disease (AD) have not met endpoints in clinical trials. The Cambridge Neuropsychological Test Automated Battery (CANTAB) provides a set of computerized methods used to assess cognitive dysfunction in human neurodegenerative disorders such as AD. A touchscreen system has been developed for mice based on the human CANTAB that can make behavioural cognitive tests more standardized, thus increasing the translational potential of research in mouse models. There are several cognitive dysfunctions that occur due to AD including deficits in attention, memory and executive control that can be tested using the touchscreen tasks. In this study, we will test three different mouse models of familial AD (5XFAD, 3XTG, APP-PS1) with mutations that lead to an accelerated rate of amyloidosis. Mice will be tested as they age (3, 6, 9 months old) in order to determine whether drugs have different effects during progression of AD pathology. In order to investigate hippocampal-dependent learning and memory deficits, we will use the Paired-Associate Learning task. Attention deficits will be evaluated using the 5-Choice Serial Reaction Time Task and behavioural flexibility will be tested using Pairwise Visual Discrimination with reversal learning. We expect to define baseline parameters in different mouse lines of familial AD to help accelerate drug screening in AD.

Acknowledgements: The Willard Garfield Weston Foundation.

A20: IS SPACE PERCEPTION DEPHT PERCEPTION? NO! A HISTORICAL ERROR.

Marta Wnuczko and John M. Kennedy
Department of Psychology, University of Toronto Scarborough, Toronto, ON

Space perception involves three dimensions: depth, width and height. The study of depth perception has been central to the study of vision for a thousand years. However, the problem of space perception has been often cast as judging depth, e.g., Alhazen (1039/1989) and Berkeley (Towards a new theory of vision, 1709). Also, empirical research on visual depth has typically measured depth, e.g., Gilinsky (1951); Wohlwill (1963); Ooi, Wu, & He (2001). This conception fails to account for width (Dopkins & Sargent, 2014). We point out depth could be underestimated more than width, less than width or treated just like width. We suggest the correct answer is that in the distance depth is underestimated more than width. Similarly, we suggest, depth is underestimated more than height.

Acknowledgments: Supported by APA Dissertation Research Award, DCA, and OGS.

A21: DISTRIBUTED NATURE OF FAMILIARITY-BASED MEMORY REPRESENTATIONS IN PERIRHINAL CORTEX

Chris B. Martin[1] and Stefan Köhler[1,2]
[1]Brain and Mind Institute, University of Western Ontario, London, ON
[2]Rotman Research Institute, Baycrest Centre, Toronto, ON

A prominent proposal concerning the functional organization of the medial temporal lobes stipulates that perirhinal cortex (PrC) supports familiarity-based recognition memory judgments. However, relatively little is known about the specific nature of familiarity signals in human PrC. Here, we used multivoxel pattern analyses (MVPA) of fMRI data to identify patterns of activity in right PrC that distinguished familiar from novel faces. We then examined these patterns of activity asking whether these memory representations are distributed and carry information that extends beyond what is present at the level of the individual voxels that make up the patterns. With respect to the spatial distribution, the diagnostic voxels in the patterns that allowed for successful classification were widely distributed across right PrC with limited regularities. Importantly, the mean difference in activity across all selected voxels did not differ between familiar and novel faces at the group level, nor in the large majority of individual participants. Moreover, we found that these mean differences showed no significant relationship to classification accuracy across participants, nor to the voxel weights that define the location and orientation of the classifier decision boundary. Finally, we found that while classification accuracy was significantly correlated with behavioural performance across participants, mean differences in activity were not. Taken together, the current findings suggest that a distributed population code in PrC may guide familiarity-based recognition decisions.

Acknowledgements: Supported by NSERC.

A22: EVENT-RELATED RESPONSES TO FEEDBACK REGARDING DECISIONS MADE USING RELEVANT AND IRRELEVANT INFORMATION

Vivian O. Cheng, Nichole E. Scheerer, Jeffery A. Jones
Department of Psychology, Laurier Centre for Cognitive Neuroscience, Wilfrid Laurier University, Waterloo, ON

When placing a bet, we often rely on statistical information to guide our decisions. Although gamblers often believe this information is strongly related to the outcome of their bets, research disproves this belief.Event related potential (ERP) studies have shown that both the feedback-related negativity (FRN) and the P300 (P3) can index neurological responses to feedback resulting from our decisions. However, it is unclear how the relevance of information influences the amplitudes of the FRN and the P3. For this study, participants completed a gambling task where they placed bets on horse races. Prior to each bet, participants were presented with information about the two horses, where the information was either relevant (i.e., horses' lifetime winning percentages) or irrelevant (i.e., colours of horses' coats) to the horses' future performance. Three experiments with different win/loss probabilities were conducted in order to examine whether probability interacts with the relevance of information to change how decision feedback is processed. For the relevant information condition, the win/ loss probability of each experiment was 75/25 win/loss probability in Experiment 1, 50/50 win/loss probability in Experiment 2, and 25/75 win/loss probability in Experiment 3. For the irrelevant information condition, the win/loss probability for Experiment 1 and 3 was 75/25, while it was 50/50 for Experiment 2. Results indicated that FRN amplitudes were modulated by individuals' perception of the relevance of information to a horse's future performance, while P3 amplitudes were modulated by the probabilities of the feedback outcomes.

Acknowledgements: Supported by NSERC

A23: MODIFIED CONCENTRATIONS OF ACETYLCHOLINE IN BRAIN CHANGE COCAINE RESPONSIVENESS IN MICE

Helena Janickova, Monica S. Guzman, Vania F. Prado, Marco A. M. Prado
Robarts Research Institute, Graduate Program in Neuroscience, Department of Physiology and Pharmacology, Department of Anatomy and Cell Biology, Schulich School of Medicine and Dentistry, University of Western Ontario, London, ON

Dopamine (DA) release in the nucleus accumbens (NAc) plays a crucial role in development of drug addiction in humans and rodents. It is well known that DA release in the NAc is modulated by acetylcholine (ACh) released by striatal cholinergic interneurons (CINs). Recent studies suggest that glutamate (Glu) co-released from CINs may also be important for the modulation of DA release. The aim of the present work is to investigate the importance of ACh released by CINs for the rewarding properties of cocaine in mice. To test that, we used 2 different genetically modified mouse lines: 1) Striatum selective Vesicular acetylcholine transporter (VAChT) knockout (VAChT$^{VGLUT3\text{-}cre;flox/flox}$); 2) VAChT overexpressor (ChAT-ChR2-EYFP). Sensitivity of the individual mouse lines to cocaine was measured (behavioral sensitization). Our data show that mice with increased release of ACh in different parts of brain (VAChT overexpressor), as well as mice with decreased release of ACh in the striatum (VAChT$^{VGLUT3\text{-}cre;flox/flox}$) are more sensitive to repeated administration of cocaine. These seemingly contradictory results can be explained by the influence of increased release of ACh in other parts of brain apart from striatum in ChAT-ChR2-EYFP mice. Alternatively, it is possible that a precise balance of ACh concentration is necessary for proper function of striatal reward-related system.

Acknowledgements: CIHR and Heart & Stroke Foundation

A24: INTRAORAL SELF-ADMINISTRATION OF SWEETENERS IN LABORATORY RATS

AnneMarie Levy , Gabrielle Colangelo , Mazen El-Baba , Dr. Cheryl Limebeer , Dr. Linda Parker , Dr. Francesco Leri
University of Guelph

The food addiction hypothesis predicts that some foods may share with drugs of abuse the ability to reinforce behaviours leading to their consumption. The current study in male Sprague-Dawley rats was designed to compare the reinforcing effect of sucrose (S) and high fructose corn syrup (HFCS) using procedures commonly used to study the reinforcing properties of drugs. To assess the palatability of these sweeteners, rats implanted with intraoral cannulas received taste reactivity (TR) tests with isocaloric solutions of S (20%) or HFCS (25%). Then, rats self-administered the same solutions (one 3 hour session/day) for 40 days. To this end, rats pressed a lever to receive an intraoral infusion (90µl/inf) of either S or HFCS on continuous and progressive ratio (PR) schedules of reinforcement. Preliminary data indicate that HFCS engendered greater hedonic reactions in tests of TR; however, palatability was not related to intake when lever pressing on a continuous schedule in self-administration (SA) as rats maintained higher intake of S while binge-like behaviour only emerged in rats that self-administered HFCS. Finally, group differences did not emerge when lever pressing on a PR schedule. Taken together, these data suggest that isocaloric solutions of S and HFCS do not have the same effect on mechanisms of reward and reinforcement as these sweeteners engendered differences in palatability, overall intake, and binge-like behaviour. Future studies will focus on replicating these results as well as identifying features of S and HFCS that may contribute to these notable effects.

A25: ONE POSSIBLE AND TWO IMPOSSIBLE RESPONSE ALTERNATIVES ON THE PIAGET 3-MOUNTAINS TASK

Hsin-Yi Chao, John M. Kennedy & Marta Wnuczko
Department of Psychology, University of Toronto Scarborough, Toronto, ON

In Piaget's 3-mountains task, participants assess a 2-D response option matching 3-D objects (a sphere, a cone and a cube) on a table. Possible vantage points are front, back, left, and right. Of interest is the difficulty of an impossible response order in which the order of the 2-D shapes does not match the order of the 3-D objects from any vantage point. An impossible response option may be assessed using one critical object – a corner object. Corner objects should not be in the middle of the response order. In an experiment with one possible order and two impossible orders for each of 24 participants, impossible orders were less accurate than front orders (which may be the standard) but more accurate than a side order. In reaction time, impossible orders were longer than front orders but shorter than a side order. Also, impossibles were judged more difficult than the possible orders. Participants may check the response order of the front vantage point first and then use the corner object criterion to assess impossibles.

Acknowledgements: supported by NSC & NSERC.

A26: DEFICITS IN COGNITIVE FUNCTION, DISRUPTION IN HIPPOCAMPAL NEUROGENESIS AND DE NOVO PLAQUE FORMATION DUE TO LONG-TERM DECREASE IN CHOLINERGIC FUNCTION

Mohammed A. Al-Onaizi[1,2], Benjamin Kolisnyk[1,4] , Gustavo M. Parfitt[1], Marco A. M. Prado[1,2,3,4] , Vania F. Prado[1,2,3,4]
[1]Robarts Research Institute, [2]Department of Anatomy and Cell Biology, [3]Department of Physiology and Pharmacology, [4]Graduate Program in Neuroscience.

Acetylcholine (ACh) plays a crucial role in controlling physiological processes in both the peripheral and central nervous system. In Alzheimer's disease (AD) there is pronounced degeneration in basal forebrain cholinergic neurons, increased number of amyloid plaques, and decreased neurogenesis. We hypothesized that deficits of cholinergic tone in the hippocampus leads to disruption in cognitive processes, characterized by changes in the molecular functionality of the hippocampus. To test this, we generated a mouse line with basal forebrain-specific deletion of the vesicular acetylcholine transporter (VAChT;VAChT$^{NK\text{-}Cre\text{-}flox/flox}$), a protein required for synaptic storage and release of ACh. To analyze cognitive ability, mice were tested in a novel hippocampal-dependent paired associated learning (PAL) task, a human version of which is currently utilized to identify individuals at high risk for developing AD. Robust deficits were seen in their performance in the PAL task compared to controls. Moreover, we investigated neurogenesis markers in the Subgranular Zone, which indicated vigorous alterations in adult neurogenesis in VAChT$^{NK\text{-}Cre\text{-}flox/flox}$ mice, similar to what is observed in AD. Interestingly, we found that plaque formation was considerably increased in aged VAChT$^{NK\text{-}Cre\text{-}flox/flox}$ mice compared to controls. These results indicate that this novel mouse model provides insight on how the basal forebrain cholinergic system modulates the functionality of the hippocampus at the cellular level and in controlling plaque formation, both of which are hallmarks of AD.

A27: AUDITORY EMOTIONAL CUES MODIFY THE EMOTIONAL INTENSITY, BUT NOT GAZE TOWARDS DIAGNOSTIC CUES DURING EMOTIONAL EXPRESSION IDENTIFICATION

James H. Kryklywy[b,c] & Derek G.V. Mitchell[a,b,c]*
[a]Departments of Psychiatry and Anatomy & Cell Biology, Schulich School of Medicine & Dentistry, [b]Graduate Program in Neuroscience, [c]Brain and Mind Institute, Department of Psychology.
University of Western Ontario, London, Ontario, N6A 5A5, Canada

There exists evidence that the recognition of fearful faces is largely determined by the capacity to attend to the eyes. According to this model, neurocognitive systems previously associated with emotional experience and encoding emotional intensity are instead involved in directing attention to crucial diagnostic facial features. This model raises the possibility that the neurocognitive systems crucial for emotional recognition are, at least in part, distinct from those dedicated to the assessment of emotional intensity. In the current study, we further examined the relationship between emotional expression recognition, attention to diagnostic facial features, and perceived emotional intensity. Participants viewed emotional facial expressions and performed an emotional expression recognition task, while task-irrelevant emotional auditory vocalizations were played. Emotional intensity ratings were acquired after the recognition task, while eye-behaviour was monitored throughout the experiment. Of particular interest, task-irrelevant emotional sounds modified the emotional intensity rating of the faces (fearful sounds increasing the intensity ratings of all faces). However, eye-tracking revealed that there were no significant effects of sound on the facial features used to assess the emotional category. These data are

consistent with the suggestion that neurocognitive processes involved in encoding emotional intensity are at least partially dissociable from those involved in facilitating emotional expression recognition by directing attention to critical facial features.
Acknowledgements: This work is supported by NSERC

A28: ASSESSING INVOLVEMENT OF MUSCARINIC CHOLINERGIC RECEPTORS IN MOUSE CROSSMODAL OBJECT RECOGNITION

Mike Varkovetski, Megan Hamilton, Daniel Palmer, & Boyer D. Winters
Department of Psychology and Collaborative Neuroscience Program, University of Guelph, Guelph, ON

Information about the world is often best processed through a combination of sensory modalities. The mechanisms responsible for the integration of unimodal sensory information in the brain are not well understood. The current study investigated the role of acetylcholine muscarinic receptors in sensory integration using a crossmodal object recognition (CMOR) task for mice. The CMOR task allows mice to explore a to-be-remembered object tactually in a sample phase that prevents visual access. Following a 30-min delay, the mice are exposed to the sample object and a novel object in a visual-only choice phase. As such, the mice must recognize the sample object across sensory modalities in order to display the novel object preference typical of such recognition tasks. Mice were administered muscarinic receptor antagonists prior to the choice phase to assess cholinergic involvement in this crossmodal recognition process. The non-selective muscarinic antagonist scopolamine disrupted CMOR task performance; this effect was specific to crossmodal object recognition, as pre-choice scopolamine did not impair unimodal (tactile- or visual-only) object recognition. Moreover, antagonism of the M1 receptor sub-type with dicyclomine produced a similar CMOR task impairment. These results highlight the important involvement of muscarinic receptors in crossmodal cognition. M1 receptors, which are particularly concentrated in forebrain structures associated with cognitive functions, may have a specific role in facilitating binding of object features across sensory modalities.
Acknowledgements: Supported by NSERC

A29: IMPACT OF PERSPECTIVE ON IMAGINED EVENTS

James Siklos-Whillans, Dr. Todd Ferretti, Jeffery Hong, Deanna Hall
Sir Wilfrid Laurier University

The current study uses electroencephalography to examine the impact of visual perspective on the imagination of events. Slow cortical potentials (SCPs) were recorded as an index of difficulty associated with event imagination. Participants imagined themselves participating in events from the first-person or third person perspective, or imagined other people participating in events, in response to verb-phrase cues (e.g., I skated/Katherine skated). SCPs at anterior and posterior regions demonstrated that imagining oneself from the third-person perspective required more cognitive effort than either the first-person perspective or imagining another person. Similarly, imagining from the first-person perspective demanded more cognitive effort than imaging another person, an effect that was most pronounced over central and posterior regions. These results provide novel neurocognitive insight for how mental representations of events are constrained by verb processing and varying visual perspectives.

A30: DELIVERY OF THE CB_1 ANTAGONIST, AM251, AND CB_1 AGONIST, HU210, BILATERALLY TO THE CENTRAL NUCLEUS OF THE AMYGDALA AND ITS EFFECTS ON MORPHINE WITHDRAWAL

Kiri L.Wills[1], Alana Kalmar[1], Kiran Vemuri[2], Cheryl L. Limebeer[1], Alexandros Makriyannis[2] and Linda A. Parker[1]
[1]*Department of Psychology and Collaborative Neuroscience Program, University of Guelph, Guelph, ON, N1G 2W1*
[2]*Center for Drug Discovery, Northeastern University, Boston, MA, USA*

Our lab has recently shown that CB_1 antagonists attenuate the establishment of a one trial naloxone-precipitated morphine withdrawal induced CPA, a sensitive measure of affective morphine withdrawal. The present study sought to determine the brain region responsible in mediating these effects.
The central nucleus of the amygdala (CeA) has been implicated in the establishment of a one trial naloxone-precipitated morphine withdrawal induced CPA. Consequently, we evaluated whether delivery of a CB_1 antagonist, AM251, or CB_1 agonist, HU210, bilaterally to the CeA would interfere with or potentiate establishment of the CPA, respectively.
Rats were surgically implanted with bilateral guide cannulas directly to the CeA. The naloxone-precipitated morphine withdrawal induced CPA was established using a three day conditioning cycle: Day 1) saline floor pairing, Day 2) morphine treatment (20 mg/kg ip), Day 3) naloxone (1 mg/kg ip) precipitated withdrawal floor pairing. To determine the effect of the cannabinoids on establishment of the CPA, AM251 (1 ug), HU210 (1 ug) or VEH was microinfused bilaterally into the CeA prior to Day 1 and 3 of conditioning. Physical symptoms of withdrawal (wet dog shakes, body weight, activity) were also measured. The amount of time spent on the saline floor or withdrawal paired floor at test revealed AM251 interfered with the establishment of the CPA, but did not modify physical symptoms of withdrawal during conditioning. HU210 was without effect. These findings suggest that CB1 antagonism is able to interfere with affective morphine withdrawal.
Acknowledgements: Funded by the Natural Sciences and Engineering Council of Canada.

A31: TYPICALITY, FAMILIARITY AND FEATURE PRODUCTION IN A CASE OF DEVELOPMENTAL AMNESIA

Devin Duke[1,2], Ben Bowles[3], Asaf Gilboa[4], Shayna R. Rosenbaum[4,5], Ken McRae[1,2], Stefan Köhler[1,2,4]
[1]*Department of Psychology, University of Western Ontario, London, Ontario*
[2]*The Brain and Mind Institute, University of Western Ontario, London, Ontario*
[3]*Department of Psychology, Stanford University, Palo Alto, California*
[4]*Rotman Research Institute, Baycrest, Toronto, Canada*
[5]*Department of Psychology, York University, Toronto, Canada*

Developmental Amnesia (DA) is one of the strongest sources of evidence for the notion that episodic and semantic memory are dissociable systems that develop independently, with hippocampal integrity necessary for episodic memories only. While it has been demonstrated that core semantics can be learned even without hippocampi, no research has addressed the structural relationships among semantic representations acquired in DA. Inasmuch as there are suggestions that re-organization processes known to support episodic memory play a role in general knowledge integration, it seems likely that semantic representations differ in their structure when acquired with impaired episodic memory. To examine this possibility, we tested a developmental amnesic (HC) using semantic memory tasks based on normative database of concrete concepts. Unlike typical neuropsychological tests that tap into discrete aspects of semantic memory, our tasks required comparisons among similar concepts in terms of their typicality for semantic categories, and also their familiarity. We probed relationships between concepts and their features, and between related concepts, in two generation tasks. Analyses suggest that HC's category structure (typicality rating) differs from that of controls. In DA, abnormalities in these structural relationships may be present even when concepts have apparently been acquired. These findings suggest that the hippocampus, a brain structure thought to be dedicated to episodic memory, may also play a role in the development of fine-grained structural semantic relationships.

A32: RECOVERY FROM ACUTE TOLUENE INTOXICATION IS FACILITATED BY THE NMDA RECEPTOR CO-AGONIST D-SERINE BUT NOT THE $GABA_A$ RECEPTOR ANTAGONIST PICROTOXIN

Susan R. Samuel-Herter, Bruce E. McKay
Wilfired Laurier University

Toluene is a volatile solvent found in many household products and can be intentionally inhaled for intoxication purposes. Acute inhalation of toluene results in impairments in rat behaviour including; increased ambulation, decreased vertical behaviour and increased neurological impairments. Previous research has shown that toluene may exert its cellular effects by inhibiting NMDA receptor function, or by activating GABA receptors. To test whether modulation of these receptor systems are also implicated in the motor behaviour and neurological impairments related to toluene vapour inhalation, rats were injected with the NMDA receptor co-agonist D-serine, the $GABA_A$ antagonist picrotoxin, or saline, and then exposed to either 15 or 30 minutes of toluene vapour (~5000 ppm). Open field behaviours including; locomotion, rearing, grooming and neurological impairment were quantified before and following toluene vapour inhalation. Our results indicate that D-serine increases the speed of recovery from ambulatory and neurological impairments following acute toluene exposures. Picrotoxin did not affect recovery, indicating that $GABA_A$ antagonism does not disrupt toluene vapour induced behavioural impairments

A33: OPIATE EXPOSURE STATE CONTROLS A MOLECULAR SWITCH IN OPIATE REWARD MEMORY FORMATION IN THE BASOLATERAL AMYGDALA-PREFRONTAL CORTICAL PATHWAY

Laura G. Rosen[1,2], Danika Lyons[1,2], Walter J. Rushlow[2,3], and Steven R. Laviolette[2,3]
[1]*Graduate Program in Neuroscience,* [2]*Department of Anatomy & Cell Biology,*[3]*Department of Psychiatry, Schulich School of Medicine & Dentistry, University of Western Ontario, London, ON*

The potent rewarding effects of opiate class drugs facilitate the formation of strong associative memories linked to the drug experience that play a key role in triggering relapse. These opiate reward memories are encoded and stored in the basolateral amygdala (BLA) and medial prefrontal cortex (mPFC) along a temporal gradient. Interestingly, intra-BLA processing of opiate-related reward memories is mediated by dopamine D1R and D2R signaling as a function of opiate exposure state, where D1R receptors are required for acute memory formation in the previously drug-naïve state, but D2R signaling is necessary for memory formation during opiate dependence and withdrawal. Links between D1R and ERK 1/2 and between D2R and CaMKIIα suggest these signaling molecules may underlie the state-dependent opiate memory formation switch. Using an unbiased place conditioning procedure with targeted microinfusions, we show that associative memories are processed in the BLA via an ERK-dependent mechanism in the naïve state, but via a CaMKIIα-dependent mechanism following the transition to dependence and withdrawal. Interestingly, intra-mPFC memory acquisition requires CaMKIIα signaling in the drug-naïve state, but not ERK1/2 in either opiate exposure state. Western blots revealed reduced ERK1/2 and CaMKIIα expression in BLA, but an increase in both CaMKIIα and ERK1/2 in the mPFC, thus demonstrating a functional interaction between BLA and mPFC during the processing of opiate-related associative memories, during the switch from the non-dependent, to dependent/withdrawn opiate exposure states.
Acknowledgements: Supported by CIHR

.

A34: IMMUNE SYSTEM STIMULATION AND CONDITIONED PLACE AVOIDANCE IN THE FEMALE RAT: LIPOPOLYSACCHARIDE TREATMENT IN ADOLESCENCE PRODUCES TOLERANCE TO AN ADULT HOMOTYPIC CHALLENGE

Caylen J. Cloutier[1], Martin Kavaliers[1,2], and Klaus-Peter Ossenkopp [1,2]
[1]*Department of Psychology, University of Western Ontario, London, ON*
[2] *Department of Neuroscience, University of Western Ontario, London,*

This study examined the effects of immune system stimulation, in adolescence and/or adulthood, on the acquisition of toxin (LiCl)-induced conditioned place avoidance (CPA). At 42 days old (adolescent), 64 female Long Evans rats were intraperitoneally (ip) injected with either the bacterial endotoxin lipopolysaccharide (LPS; 200 µg/kg), or 0.9% isotonic saline (NaCl; 1 ml/kg). At 60 days old (adult), subjects underwent a CPA procedure (2 cycles of 4 consecutive days, spaced 72 h apart). On drug-paired conditioning days, rats were treated with LPS or NaCl 90 minutes prior to a second injection of either 0.15M lithium chloride (LiCl; 15 ml/kg) or NaCl (15 ml/kg), immediately followed by a 30 minute exposure to a specific context (gray wall, rough floor) and limited to the right chamber. On control days, rats were treated with NaCl 90 minutes prior to a second injection NaCl, immediately followed by a 30 minute exposure to a different context (striped wall, wire floor) and limited to the left chamber. On a 20 minute drug-free test day, rats pre-treated with LPS 90 minutes prior to LiCl conditioning spent significantly more time in the drug-paired chamber relative to NaCl pre-treated rats that were conditioned with LiCl, showing that LPS impaired the acquisition of CPA. However, treatment with LPS in both adolescence and adulthood produced tolerance to the deleterious effects of LPS on learning and memory, evidenced by a significantly shorter period of time spent in the drug-paired chamber that was comparable to other LiCl-treated animals not treated with LPS.

Acknowledgements: Supported by NSERC.

A35: QUININE CONCENTRATION AND ACCESS CONDITIONS INTERACT TO DETERMINE SUCROSE SOLUTION INTAKE

Milan Valyear[1], Roelof Eikelboom[1]
[1]*Department of Psychology, Wilfrid Laurier University, Waterloo, ON*

Rats with *ad lib* access to food and water will consume significantly more 4% sucrose solution when it is available for 24h every 3rd day (E3DA) as opposed to 24h every day (EDA). This difference is maintained when all rats are switched to every 2nd day access (E2DA). The E3DA/EDA difference becomes smaller and, at times, unnoticeable with more concentrated (8% and 16%) sucrose solutions. When rats with a history of E3DA or EDA to 16% sucrose are given E2DA to 4% sucrose a significant consumption difference emerges immediately. The lack of an initial consumption difference may be attributed to the higher caloric consumption with 16% sucrose. In the current study four different concentrations of quinine (Q) were added to an 8% sucrose solution to reduce intake, and consequently calories consumed, and allow an E3DA/EDA difference to emerge. Sprague-Dawley rats (n=64) were given access to 8% sucrose adulterated with 0.0025%, 0.005%, 0.01%, or 0.02% Q continuously for three days and then assigned to E3DA or EDA based consumption during this 3-day preexposure. Quinine adulteration concentration-dependently decreased sucrose consumption and the E3DA/EDA consumption difference was most apparent at the highest quinine concentration. This suggests that reduced caloric intake as a result of quinine adulteration can allow for an EDA/E3DA consumption difference to emerge but only when caloric intake is substantially reduced.

Acknowledgements: Supported by NSERC grant to R.E.

A36: ANHEDONIC BEHAVIOR IN RATS: A CONTEXTUAL AVERSION PRECIPITATED BY HIGH FRUCTOSE CORN SYRUP WITHDRAWAL

Stephen Daniels[1], Francesco Leri[1]
[1]*Department of Psychology, University of Guelph, Guelph Ontario*

Blunted reward functioning known as anhedonia has devastating consequences on daily life functioning in a number of mental health disorders. Studying biological components of anhedonia requires an aversive stressor and a neurobehavioral endpoint representative of human conditions. Growing evidence suggests sugar can induce a withdrawal like state, which may provide an etiologically valid stressor for anhedonia. In order to determine the viability of this approach a conditioned place aversion procedure (CPA) was conducted. The mu-opioid receptor antagonist Naltrexone (3mg/kg) was administered SC in satiated (ad lib chow) and food restricted rats with ad-lib home cage liquid HFCS (50%). CPA was also conducted in rats that had never been exposed to HFCS as well as rats with chronic access prior to a washout period. Satiated rats with acute HFCS showed a significant reduction in time spent in the drug-paired box after one conditioning trial. After three additional pairings this aversion was not significantly changed. Food restricted rats with acute HFCS did not show an aversion after the first pairing but did after three additional sessions. Rats without exposure to HFCS or with previous exposure but no acute access did not show a significant aversion. These results indicate that when HFCS is in the system a withdrawal like state can be precipitated with a mu-opioid receptor antagonist. This research provides the basis for a neurobehavioral stressor targeting anhedonic behavior in rats.

Acknowledgments: Supported by the Ontario Brain Institute

B: Development

B1: CTCF LOSS RESULTS IN FATE CHANGE OF MGE-DERIVED INTERNEURONS

Adrienne Elbert[1,2], L. Ashley Watson[1,2], Emilie Brûlé[1,2], and Nathalie G. Bérubé[1,2]
[1]*Children's Health Research Institute, Victoria Research Laboratories, London, ON*
[2]*Departments of Paediatrics and Biochemistry, Western University, London, ON*

CCCTC binding factor (CTCF) is a chromatin-associated protein that influences chromatin topology and gene expression. Recently, *CTCF* mutations were identified in patients with intellectual disability, demonstrating the important role for CTCF in neural development. To study the role of CTCF in the developing brain, we generated mice with conditional deletion of *Ctcf* in the brain using the NestinCre mouse driver line. Transcriptional profiling of embryonic control and *Ctcf*-null forebrain reveals decreased expression of the GABAergic marker gene *Lhx6* as well as its downstream effector genes *Cxcr4* and *Cxcr7* in the medial ganglionic eminence (MGE). As this pathway was previously demonstrated to influence migration of interneurons from the MGE to the neocortex, we examined the outcome of CTCF deficiency on the migration of interneurons. *In* situ hybridization of another interneuron marker, Dlx1, revealed that fewer GABAergic interneurons reach the neocortex in the *Ctcf*-null compared to control. In transwell assays, CTCF-null MGE cells displayed reduced migration towards SDF-1, the main ligand for Cxcr4 and Cxcr7. Notably, we detected increased expression of *Lhx8* and *Gbx2*, markers of cholinergic interneurons fated to migrate to the striatum. Together, these results suggest that loss of CTCF in the basal forebrain causes a GABAergic to cholinergic interneuron fate switch.

Acknowledgements: Supported by CIHR

B2: TESTOSTERONE REGULATION OF HYPOTHALAMIC-PITUITARY-ADRENAL FUNCTION IN ADOLESCENT AND ADULT MALE RATS

Matthew R. Green[a], Travis Hodges[a], Jonathan Simone[b], & Cheryl M. McCormick[ab]
[a]*Department of Psychology,* [b]*Department of Biology, Brock University, St. Catharines,*

Previous studies have found that testosterone dampens hypothalamic-pituitary-adrenal (HPA) function in adulthood, but not before puberty. Nevertheless, these studies investigated age-differences and did not provide the appropriate comparisons to determine that testosterone does not suppress HPA function in pre-pubertal male rats. Therefore, we investigated HPA reactivity to restraint stress and to a lipopolysaccharide injection in pre-pubertal and adult males that underwent either (A) an orchiectomy, (B) an orchiectomy with testosterone replacement, (C) a sham surgery, or (D) no surgery, three days prior to testing. Blood samples were taken prior to and at various time points after stress exposure to determine the effects of surgery and of testosterone at different ages on corticosterone concentrations. The results of this study will further our limited understanding of the underlying basis for age-differences in HPA function and provide further insight into puberty, a critical period for neuroendocrine development.

Acknowledgments: Supported by NSERC

B3: MOLECULAR AND NEURAL CORRELATES OF ENVIRONMENTAL ENRICHMENT IN A MOUSE MODEL OF FETAL ALCOHOL SPECTRUM DISORDER

Aniruddho Chokroborty-Hoque[1]
[1] *Department of Biology, Western University, London, ON*

Maternal drinking during pregnancy leads to children with developmental and cognitive disabilities which are commonly referred to as Fetal Alcohol Spectrum Disorders (FASD). In mouse models of behavioural and cognitive disabilities, mice that are subjected to physically and cognitively challenging environments (enriched environments) are usually less stressed with improved memory performance. This project asks (i) if rehabilitative therapies can ameliorate behavioural and cognitive abnormalities of FASD mice and (ii) what are the molecular correlates of these changes? After alcohol exposure during synaptogenesis, mice will be kept in standard (S) or enriched conditions (E). The former (S) will characterize (behaviour and genetics) the effects of alcohol exposure during neurodevelopment. The latter (E) will (i) track behavioural changes of FASD mice that have undergone rehabilitation and (ii) assess any alterations in gene expression and protein levels in the hippocampus that are associated with behavioral rehabilitation. Results indicate that environmental enrichment ameliorates anxiety levels (Elevated Plus Maze, Light-Dark Box) and working and visuospatial deficits (Novel Object Recognition, Barnes Maze) of FASD mice. Further studies will attempt to explain these alterations in terms of gene expression and protein levels of the Brain Derived Neurotrophic Factor in the hippocampus. Ultimately, these processes might be targeted in specific rehabilitative therapies to treat behavioral and cognitive deficits associated with FASD.

B4: CHOLESTEROL AND ITS METABOLITES IN DROSOPHILA DEVELOPMENT

Kiel G. Ormerod[1], Sonia Aksamit[1], Jens R. Coorssen[2], Glenn J. Tattersall[1], and A.Joffre Mercier[1].
[1]*Department of Biological Sciences, Brock University, St. Catharines, ON, Canada.*
[2]*Department of Molecular Physiology, and the UWS Molecular Medicine Research Group, School of Medicine, University of Western Sydney, Australia*

High cholesterol levels are associated with cardiovascular disease and obesity. One strategy to reduce cholesterol is dietary substitution with analogous sterols. In mammals cholesterol is obtained from diet and endogenous biosynthesis, but in insects cholesterol must be obtained from diet. We examined the effects of replacing cholesterol with analogues and steroid hormones on development and morphology in *Drosophila melanogaster*. We prepared a lipid-depleted medium (LDM) by combining agarose, dextrose, yeast extract and an antifungal agent and then extracted lipids

with chloroform. We then added varying concentrations of either cholesterol, stigmasterol, ergosterol, 20-hydroxyecdysone or ecdysone. *Drosophila* were unable to develop on LDM beyond second instar. Supplementation with ergosterol did not improve development. Addition of cholesterol, stigmasterol, 20-hydroxyecdysone and ecdysone all resulted in complete development to adulthood. Surprisingly, cholesterol, stigmasterol, and 20-hydroxyecdysone only slightly increased survival (# of larvae and pupae) compared to LDM. Ecdysone greatly improved survival of larvae (~5x more larvae and pupae than cholesterol supplementation). The length, width and weight of larval and pupae reared on 20-hydroxyecdysone were significantly lower than in control medium. Larvae and pupae reared on cholesterol and stigmasterol were significantly reduced in weight compared to controls. Thus, while cholesterol and stigmasterol enable complete development of *Drosophila*, ecdysone has a more profound effect.

Work supported by Queen Elizabeth II scholarship in science and technology and NSERC PGS funding to KGO. Canadian Institutes of Health Research, and UWS School of Medicine funding to JRC. NSERC grants to AJM (46292) and GJT (262087). Brock University Chancellor's Chair funding to GJT.

C: Disorders of the Nervous System

C1: FEATURE SELECTION IN HIGH DIMENSION LOW SAMPLE SIZES (HDLSS) IN NEUROIMAGING

Diego Cantor-Rivera[1,3], Ali R. Khan[1,2], Terry M. Peters[1,2,3]
[1]*Imaging Research Lab, Robarts Research Institute, London, ON*
[2]*Dept. of Medical Biophysics, Western University, London, ON*
[3]*Biomedical Engineering Graduate Program, Western University, London, ON*

To make the most of small datasets researchers extract as much information as possible from each image. This creates high dimension low sample size (HDLSS) scenarios, where the number of features exceeds the number of observations by several orders of magnitude. The analysis of relevant features to identify patients in these spaces requires reducing the dimensionality to minimize the effect of the *Hughes effect*.

We explored 4 methods to identify informative features in a HDLSS context: correlation, ANOVA, correlation+PCA, ANOVA+PCA in the context of MRIs of patients with temporal lobe epilepsy, 936 features x 36 subjects (17 patients, 19 controls). A support vector machine (SVM) was trained to detect TLE using leave-one-out cross-validation. The accuracy of the classifier was used as a measure of the quality of the feature selection.

We observed that the feature set cardinalities where the SVM performed the best corresponded to the estimated *inherent dimensionality* of the problem (the number of features that discriminate well between patients and controls). This estimation was made using a cross-validated L1-penalized logistic regression model. We concluded that the ANOVA+PCA method renders features that are as informative as the correlation-based method. However, ANOVA method was computationally efficient, which is a deciding factor when analyzing large dimensional spaces.

C2: THE NEUROPROTECTIVE EFFECTS OF SIRT3 IN THE SUBSTANTIA NIGRA OF MPTP MOUSE MODEL FOR PARKINSON'S DISEASE

Mahin S. Semmen, Jacqueline Gleave, and Joanne Nash
Department of Biological Science, University of Toronto Scarborough, Toronto, ON

Parkinson's disease is a neurodegenerative disorder caused by degeneration of dopaminergic neurons in the substantia nigra pars compacta. Recent studies show that the mitochondria play a central role in the disease progression. For this study, the neuroprotective effects of SIRT3, a protein that plays critical role in the maintenance of mitochondrial homeostasis was investigated. Sirtuins are a family of highly conserved protein deacetylases that is linked to increased cell lifespan. SIRT3, a member of the sirtuin family is found within the mitochondria that can prevent cellular degradation due to oxidative stress. We examined the role of SIRT3 in saline VS MPTP treated mice. SIRT3 was delivered via AAV virus into the substantia nigra of the mice following surgery with either control saline solution or the neurotoxon MPTP. Motor performance of the mice were assessed using the Noldus program; immunostaining and stereology was performed in order to visualize and count the NeuN and TH cell in the substantia nigra. Motor assessment of the animals revealed that there were no significant differences between animals treated with SIRT3 in both saline and MPTP group. Sterelogy results showed that MPTP caused significant degeneration of dopaminergic cells. SIRT3 had no toxic effect on both saline and MPTP mice nor did it confer any significant neuroprotective effect on the total cell population including dopaminergic cells. The study is still ongoing and adding more animals to each group can yield significant results and shed light on a novel gene-based therapy using SIRT3 for PD.

Acknowledgments: Supported by NSERC

C3: THE NEUROPROTECTIVE ROLE OF SIRT3 IN A CELL MODEL OF PARKINSON'S DISEASE

Filip Stojic, Joanne E. Nash
Department of Biological Sciences, Centre for Neurobiology of Stress, University of Toronto Scarborough, Toronto, ON

Parkinson's disease (PD) is the second most common progressive neurodegenerative disease following Alzheimer's. Current treatment strategies are symptomatic and fail to slow the progression of PD. Although a small proportion of PD cases are genetic, the majority are sporadic. Despite this, roles for mitochondrial inhibition, a dysfunctional ubiquitin proteasome system (UPS) and oxidative stress in the cell have been implicated in its pathogenesis. With recent studies demonstrating that mitochondrial dysfunction precedes other aberrant cellular mechanisms, potential treatment strategies may be aimed at ameliorating mitochondrial health to halt PD development. The purpose of this study was to determine the effectiveness of ectopic overexpression of SIRT3, a protein known to enhance mitochondrial function, in attenuating cell death caused by PD. Three toxins that mimic PD on the cellular level – by mitochondrial inhibition (rotenone), oxidative stress (dopamine) and UPS impairment (proteasome inhibitor) – were administered to rat neuronal fibroblasts following SIRT3 ectopic overexpression. Absolute cell death was measured by propidium iodide staining. Cell death was significantly reduced in SIRT3 transfected cells for all three toxins when compared to controls. Additionally, cells exposed to two of these toxins; dopamine and rotenone, had levels of cell survival statistically equivalent to those of control cells not exposed to toxins. These results indicate that SIRT3 overexpression is sufficient to protect against toxins that induce PD-like abnormalities in cell mechanisms.

Acknowledgements: Supported by NSERC and the Michael J. Fox Foundation

C4: ELUCIDATING THE ADP-RIBOSYLATION FACTOR 6 MEDIATED PATHWAY FOR MACROPINOCYTOSIS OF THE AMYLOID PRECURSOR PROTEIN

Justin K. Chiu, Stephen H. Pasternak
Department of Physiology and Pharmacology, Western University, London, ON

Alzheimer's disease (AD) is the leading cause of adult dementia, currently without cure. Literature suggests that reducing production of amyloid-β (Aβ) is a therapeutic avenue for which to delay or halt the progression of AD. For Aβ to be produced, amyloid precursor protein (APP) must first undergo endocytosis. One of the pathways of endocytosis through which this occurs may be macropinocytosis, mediated by ADP-ribosylation factor 6 (Arf6), whereby surface-labelled APP is internalized rapidly into lysosomes for processing. Arf6 is part of the Arf family of proteins involved in vesicular transport, and has been implicated in the formation of macropinosomes. Using confocal microscopy to analyze images of SN56 and N2A cells, the pathway by which Arf6 initiates macropinocytosis was investigated. Cultured cells were co-transfected with HA-βAPP, LAMP1, and DN or CA mutants of downstream effectors of Arf6, such as RhoA. Cells were then later surface-labelled with an anti-HA antibody conjugated to an Alexa Fluor and allowed to internalize βAPP at 37ºC for 15 minutes. Confocal images of the cells were then analyzed for colocalization between the 2% brightest pixels between the surface-labelled APP channel and LAMP1 channel. Colocalization of the two channels suggests internalization of surface-labelled βAPP into lysosomes. RhoA dominant negative and constitutively active mutants were found to have no significant differences ($P>0.05$) from controls after 5 replicate experiments. These results suggest RhoA does not play a role in Arf6-mediated macropinocytosis of APP into lysosomes.

Acknowledgements: Supported by CIHR.

C5: PRION PROTEIN-DEPENDENT β-AMYLOID NEUROTOXICITY IS MODULATED BY STRESS-INDUCIBLE PHOSPHOPROTEIN 1 AND α7 NICOTINIC ACETYLCHOLINE RECEPTOR

Valeriy G. Ostapchenko[1,2], Flavio H. Beraldo[1,2], Giulia D.S. Ferretti[1], Amro H. Mohammad[1,3], Yu-Feng Xie[1,2], Ana C. Magalhaes[1,2], Pedro Hirata[1], Wing-Yiu Choy[4], Peter J. Nicholls[5], Marc G. Caron[5], Michael F. Jackson[1], John F. MacDonald[1], Vilma R. Martins[6], Vania F. Prado[1-3], Marco A.M. Prado[1-3]
[1]*Robarts Research Institute, the University of Western Ontario, London, Ontario*[2]*Department of Physiology and Pharmacology,*
[3]*Department of Anatomy and Cell Biology and*
[4]*Department of Biochemistry, Schulich School of Medicine, the University of Western Ontario, London, Ontario, N6A 5K8;*
[5]*Department of Cell Biology, Duke University Medical Center, Durham, NC 27710;*
[6]*International Center for Research and Education - Antonio Prudente Foundation, A. C. Camargo Hospital, São Paulo, SP, Brazil*

In Alzheimer's disease oligomeric β-amyloid peptide (AβO) binds to the prion protein (PrP^C) initiating neurotoxic signal. PrP^C can also trigger α7 nicotinic acetylcholine receptor (α7nAChR)-dependent neuroprotective signal when it binds stress-inducible phosphoprotein 1 (STI1). We investigated if STI1 would compete with AβO binding to PrP^C and alleviate AβO neurotoxicity. In surface plasmon resonance assay, STI1 inhibited formation of AβO/PrP^C complex with IC_{50} of 70 nM. Moreover, STI1 domain TPR2A, containing PrP^C binding site, also inhibited AβO binding to PrP^C. In experiments with HEK293T cells overexpressing PrP^C and primary neuronal cultures both STI1 and TPR2A significantly impaired binding of AβO to the cell membranes. Next we tested if STI1 levels would influence neuronal function and survival. Co-treatment with recombinant STI1 fully rescued AβO-induced inhibition of long-term potentiation in mouse hippocampal slices and prevented apoptosis and cell death in neuronal cultures. Absence of α7nAChRs compromised not only survival of AβO-treated neurons but also their rescuing with STI1. Moreover, levels of endogenous STI1 influenced susceptibility of neurons to AβO toxicity. Reduction in STI1 expression increased neuronal cell death, while its overexpression made neurons resistant to AβO. STI1 levels were increased in Alzheimer's human brains, suggesting that this could be a compensatory response. Our results reveal a protective role of STI1 in Alzheimer's disease which involves competition with toxic AβO for PrP^C binding and α7nAChR-dependent neuroprotection.

Acknowledgement: Supported by Alzheimer's Association, CIHR and PrioNET

C6: DETERMINING STRUCTURAL CORRELATES OF RESTING STATE FUNCTIONAL CONNECTIVITY CHANGES IN TEMPORAL LOBE EPILEPSY PATIENTS

Jonathan C. Lau[1], Sandrine de Ribaupierre[1,2], Brent Hayman-Abello[1], Seyed M. Mirsattari[1], Terry M. Peters[2,3,4], Ali R. Khan[2,4]
[1]*Department of Clinical Neurological Sciences, Western University, London Health Sciences Centre, London, ON*
[2]*Department of Medical Biophysics, Western University, London, ON, Canada*

[3]*Biomedical Engineering Graduate Program, Western University, London, ON,*
[4]*Robarts Research Institute, Western University, London, ON*

Several recent studies have examined changes in connectivity in epilepsy patients particularly using resting state/default mode functional magnetic resonance imaging (MRI) paradigms. The structural underpinnings for these connectivity changes have yet to be determined. High-resolution MRI 3T and 7T structural and resting state scans were performed in a series of 20 temporal lobe epilepsy patients prior to undergoing temporal lobectomy. Operatively, the specimens were removed en bloc in two separate pieces: neocortex and hippocampus. Post-operatively, the temporal lobes were scanned ex-vivo pre-and-post-fixation. Histological processing was then performed. Pre-operative functional resting-state connectivity was computed using FSL. Results are correlated with neuropsychological measures performed during work-up prior to operation. A series of control subjects also underwent the same pre-operative imaging protocol for comparison. The regions of high correlation with the presumed affected hippocampus were used as seed points for DTI tractography. We are in the process of investigating the existence of structural substrates for differences in functional connectivity using our DTI results as well as investigating any microstructural changes in our patient-specific high-resolution in-vivo, ex-vivo and histological datasets.

Acknowledgements: Supported by CIHR grant MOP 184807, Canada Foundation for Innovation (CFI) grant 20994, and Ontario Brain Institute EpLink Project.

C7: DEEP BRAIN STIMULATION PARAMETER OPTIMIZATION FOR SPEECH IN PARKINSON'S DISEASE

Dona Anita Abeyesekera[1,2], Scott Adams[1,2], Cynthia Mancinelli[1,2], Fariborz Rahimi[3], Mehdi Delrobaei[3], Mandar Jog[3]
[1]*Health and Rehabilitation Sciences Program, Western University, London, ON*
[2]*School of Communication Sciences and Disorders, Western University, London, ON*
[3]*Movement Disorders Centre, London Health Sciences Centre, London, ON*

Deep brain stimulation of the subthalamic nucleus (DBS-STN) is a standard neurosurgical treatment procedure for Parkinson's disease (PD). Although DBS-STN is an effective treatment for most major symptoms of PD, effects on speech have been inconsistent across studies. The current DBS-STN study involves a systematic evaluation of different amplitude, frequency and pulse width settings on speech production in PD. Individuals with PD who are receiving bilateral DBS-STN treatment will be seen for 2 baseline and 5 treatment visits. The 5 treatment visits will involve examination of 20 stimulation parameter settings. These will include all permutations of two voltage (medium, high), three frequency (low, medium, high), and three pulse width (low, medium, high) settings. The following measures of speech will be obtained at each DBS-STN setting: speech rate, speech intensity, vocal perturbation, vowel formant dynamics, voice quality, and speech intelligibility. Results are expected to provide new DBS-STN parameter optimization solutions for speech in PD.

C8: MECHANISMS OF Aß-INDUCED BDNF DOWN-REGULATION

Elyse Rosa[1,2] & Margaret Fahnestock[2]
[1] *McMaster Integrative Neuroscience Discover & Study (MiNDS) Program,*
[2]*Department of Psychiatry & Behavioural Neurosciences, McMaster University*

Accumulation of amyloid-β (Aβ) peptide, a characteristic of Alzheimer's disease, results in loss of brain-derived neurotrophic factor (BDNF), loss of functional synapses and subsequent neurodegeneration and memory loss. The specific mechanism by which amyloid-β down-regulates BDNF is unclear and is the main focus of this work. Aβ treatment has been shown to block activity-induced up-regulation of BDNF via the transcription factor CREB, but whether it also reduces basal levels of BDNF via the same mechanism is unclear. Aβ treatment inactivates PKA and activates GSK3β, which decrease activating phospho-CREB133 and increase inactivating phospho-CREB129, respectively. We hypothesized that Aβ would also down-regulate basal BDNF transcription via these pathways. In this study we demonstrate consistent down-regulation of BDNF mRNA in human neuroblastoma (SH-SY5Y) cells following treatment with oligomeric Aβ. If Aß down-regulates BDNF via activation of GSK3ß, we should be able to rescue BDNF levels by inactivating GSK3ß. However, we found that treatment of SH-SY5Y cells with the GSK3β inhibitor CT99021 had no effect on Aβ-induced BDNF down-regulation. Additionally, if Aß down-regulates BDNF via inactivation of PKA, we should be able to rescue BDNF levels by activating PKA. However, we found that treatment with the PKA activator Forskolin did not rescue BDNF levels down-regulated by Aβ. Further, we found no change in levels of activating pCREB-133 or inactivating pCREB-129 following Aß treatment. Thus, other mechanisms must be responsible for Aβ down-regulation of BDNF.

C9: NERVE GROWTH FACTOR RECEPTOR LEVELS IN SUBJECTS WITH TAUOPATHIES: PROGRESSIVE SUPRANUCLEAR PALSY, CORTICOBASAL DEGENERATION, AND PICK'S DISEASE

Brij Karmur[1], Bernadeta Michalski[2], Elyse Rosa[3], Chiara Nicolini[4], Margaret Fahnestock[2]
[1]*Honours Psychology, Neuroscience, and Behaviour, McMaster University*
[2]*Department of Psychiatry and Behavioural Neurosciences, McMaster University,*
[3]*MiNDS Graduate Program, McMaster University, Hamilton, ON*
[4]*Medical Sciences Graduate Program, McMaster University, Hamilton, ON*

The precursor of nerve growth factor (NGF), proNGF, is highly expressed in the brain and plays an important role in neuronal survival and regulation. NGF is essential for the survival of basal forebrain cholinergic neurons, which are important for learning and memory. These neurons express the receptors for proNGF, TrkA and p75NTR. In Alzheimer's disease, which is characterized by amyloid plaques and tau neurofibrillary tangles, TrkA is lost and proNGF accumulates in the parietal cortex, a basal forebrain target region. ProNGF also accumulates in Pick's disease, but not in other tauopathies, diseases that exhibit abnormal tau protein but no amyloid plaques. Thus we hypothesized that in Pick's disease, but not in other tauopathies, proNGF accumulation occurs due to decreased TrkA levels. We measured TrkA protein levels in the parietal cortex of three different human tauopathies by Western blotting: Pick's disease (PiD; n=9), Corticobasal degeneration (CBD; n=12), and Progressive Supranuclear Palsy (PSP; n=13) compared to Controls (n=10). Surprisingly, we found an increase in TrkA levels (normalized to ß-actin) in PSP ($p<0.001$), and CBD ($p=0.002$), but no change in TrkA levels in PiD ($p=0.428$) compared to controls. Accumulation of TrkA in target tissue implies a functional anterograde transport system in CBD and PSP. However, accumulation of proNGF in PiD in the absence of TrkA accumulation suggests a role for the low-affinity NGF receptor, p75NTR, in retrograde transport of proNGF in basal forebrain cholinergic neurons.

C10: UNIQUE METABOLIC AND FUNCTIONAL PROFILES IN MILD AND MODERATE CERVICAL MYELOPATHY

Izabela Kowalczyk[1,2], Todd K. Stevens[2], Sandy Goncalves[1,2], Neil Duggal[2,3], and Robert Bartha[1,2]
[1]*Department of Medical Biophysics, Western University, London, ON*
[2]*Centre for Functional and Metabolic Mapping, Robarts Research Institute, London,*
[3]*Department of Clinical Neurological Sciences, University Hospital, London Health Sciences Centre, London, ON*

Purpose: The goal of this study was to use proton magnetic resonance spectroscopy (^{1}H-MRS) and functional MRI (fMRI) to determine whether there are distinct metabolic and functional profiles in the mild and moderate CM groups. We also evaluated neurological recovery following surgery.

Methods: Fifteen mild and 13 moderate CM patients had 2 MRI scans that included MRS and fMRI on a 3.0 Tesla MRI before and 6 months following surgery. Ten healthy controls underwent 2 MRI scans 6 months apart. A spectroscopy voxel was localized on the greater deficit side in the patients and on each side of the motor cortex in controls. Patients and controls completed a right finger-tapping paradigm. Volumes of activation (VOA) maps were created and analyzed using BrainVoyager QX.

Findings: Mild CM had a lower pre-op NAA/Cr ratio compared to moderate CM suggesting neuronal death or mitochondrial dysfunction. Following surgery, NAA/Cr in the moderate group dropped to similar values as in the mild group. The metabolic profile of the motor cortex did not recover, despite significant clinical improvement. The mild group had a larger VOA than moderate CM prior to surgery. Post-op, the VOAs were in the sensory cortex and were not signfincalty different between the mild and moderate.

Conclusion: NAA and VOA in the motor cortex discriminate between mild and moderate CM patients. Together with clinical improvement following surgery, these results suggest brain reorganization and recruitment of surrounding cortex as the primary modality for clinical recovery.

Acknowledgments: Supported by CIHR and WGRS

C11: THR^{175} PHOSPHORYLAYION REGULATES GSK3β ACTIVITY AND TAU PATHOLOGY *IN VITRO*

Alexander J. Moszczynski[1,2], May Gohar[2], Kathryn Volkening[2,3], Michael J. Strong[1,2,3]
[1]*Department of Neuroscience Western University, London, ON.*
[2]*Molecular Medicine Research Group, Robarts Research Institute Western University,*
[3]*Department of Clinical Neurological Sciences, Schulich School of Medicine and Dentistry, Western University, London, ON.*

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease characterized by motor neuron death. Half of all ALS patients develop cognitive impairment (ALSci) characterized by pathological fibril formation of microtubule associated protein tau. Phosphorylation of Thr^{175} (pThr^{175}) occurs specifically in ALSci, and induces fibril formation and cell death *in vitro*. Thr^{175} phosphorylation has been linked to increased GSK3β activation *in vivo*. Neuro2A cells were transiently transfected with either wild-type (WT) or pseudophosphorylated (Thr^{175}Asp) GFP-tagged 2N4R tau, or with GFP-tagged 2N4R tau in which phosphorylation at Thr^{175} is inhibited (Thr^{175}Ala). Activation of GSK3β was examined by western blot for phospho-GSK3β (Tyr^{216}), compared to total GSK3β. Blinded live cell confocal imaging was used to assess fibril formation. GSK3β activation and tau fibril formation were increased in Thr^{175}Asp transfected cells relative to WT and Thr^{175}Ala tau 72 hrs post transfection. Treatment with any of 4 GSK3β inhibitors at their IC_{50} decreased aggregation to baseline levels. All Thr^{231}Ala mutants (prevents phosphorylation) exhibited baseline levels of fibril formation regardless of Thr^{175} state while Thr^{231}Asp (phosphomimic) mutants all showed increased fibril formation. pThr^{175} tau increases activation of GSK3β. pThr^{175} induced formation of fibrils in transfected cells is prevented by GSK3β inhibitors, indicating that further phosphorylation is required. Thr^{231} has been implicated as a critical site of downstream phosphorylation for fibril formation.

C12: THE ROLE OF RHO GUANINE NUCLEOTIDE EXCHANGE FACTOR, A NOVEL RNA-BINDING PROTEIN DISCOVERED IN AMYOTROPHIC LATERAL SCLEROSIS, IN THE CELLULAR STRESS RESPONSE

Kevin Cheung[1,2], Cristian Droppelmann[2], Kathryn Volkening[2,3], Michael J. Strong[2,3]
[1]*Department of Pathology, Schulich School of Medicine and Dentistry, Western University, London, ON*
[2]*Robarts Research Institute, Western University, London, ON*
[3]*Department of Clinical Neurological Sciences, Schulich School of Medicine and Dentistry, Western University, London, ON*

Amyotrophic Lateral Sclerosis (ALS) is a degenerative disorder of motor neurons causing death within 5 years of onset. A common pathology in ALS is aberrant aggregation of protein. Recent studies also implicate aberrant RNA metabolism in the disease, and show a role for oxidative stress in neurodegeneration. Stress granules (SG), a specific type of RNA granule, are of interest due to increased oxidative stress within ALS neurons. Our lab is examining a novel, ALS-related RNA-binding protein: Rho Guanine Nucleotide Exchange Factor (RGNEF). RGNEF co-localizes with

neuronal protein aggregates, and we identified a novel mutation in *ARHGEF28* (encodes RGNEF) in a familial ALS family. RGNEF is also upregulated in mouse neuronal injury, so we hypothesize that RGNEF is involved in stress response. We subjected HEK293T cells overexpressing myc-tagged RGNEF to oxidative or osmotic stress. Cell death was measured using MTT assay. For both stressors, RGNEF overexpression increased survival compared to controls. To define RGNEF's protective domain, truncated constructs were created and analyzed by MTT. We saw that RGNEF's N-terminal region, specifically its leucine-rich domain, is important to protect against osmotic stress. We then examined RGNEF by confocal microscopy under stress conditions and found that RGNEF did not co-localize with SG, but did co-localize with transport granules. Our findings show that RGNEF has a role in stress response and the N-terminal region is important for its protective effects.
Acknowledgements: ALS Society of Canada, McFeat Family Fund, Michael Halls Foundation.

C13: VIRAL VECTOR-MEDIATED *FMR1* GENE DELIVERY IN FRAGILE X KNOCKOUT MICE

Shervin Gholizadeh, Jason Arsenault, Ingrid Cong Yang Xuan, and Laura K. Pacey, and David R. Hampson
Department of Pharmaceutical Sciences, Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, Ontario, Canada

Fragile X syndrome is a neurodevelopmental disorder caused by a trinucleotide repeat expansion in the FMR1 gene that codes for fragile X Mental retardation Protein (FMRP). We used a single-stranded adeno-associated viral vector that contained a major isoform of murine Fmr1 gene, to determine if FMRP expression in the central nervous system could reverse phenotypic deficits in the Fmr1-knockout mouse model of fragile X syndrome. The vector was delivered to the brain via intra-cerebroventricular injection into neonatal Fmr1 knockout mice. Transgene expression and behavioral assessments were conducted 3-4 and 7-8 weeks post-injection. Western blotting and immunocytochemical analyses of AAV-FMRP injected knockout mice revealed FMRP expression in multiple structures in the forebrain. Cellular expression was selective for neurons and reached approximately 50% of wild-type levels in the hippocampus and cortex, which remained persistent for up to 7 months post-injection. The pathologically elevated repetitive behavior and the deficit in social dominance behavior observed in PBS-injected Fmr1 knockout mice, were reversed in AAV-FMRP injected mice. These results provide proof-of-principle that gene therapy can correct specific behavioral abnormalities in the mouse model of fragile X syndrome.

C14: Aberrant NEFL MRNA 3'UTR VARIANTS IN ALS SPINAL CORD TISSUE

Danae Campos-Melo[a], Kathryn Volkening[ab] and Michael J. Strong[ab].
[a]Molecular Brain Research Group, Robarts Research Institute, and [b]Department of Clinical Neurological Sciences, Schulich School of Medicine and Dentistry, Western University, London, Ontario, Canada.

Amyotrophic Lateral Sclerosis (ALS) is a progressive, adult onset neurodegenerative disease of motor neurons (MN). ALS can be viewed as a disorder of RNA metabolism. Evidence includes the observation that MN death is related to the selective suppression of low molecular weight neurofilament (NEFL) mRNA in spinal cord (SC) in ALS. Our main goal is to study stability determinants of the NEFL mRNA. Previously, we documented an expression profile alteration of a type of non-coding RNA that regulates the majority of the transcriptome, microRNAs. We showed that this profound microRNA dysregulation could be affecting NEFL mRNA levels in ALS. Now, we are interested in studying the main target of microRNAs, mRNA 3' untranslated region (UTR). mRNA UTRs, often neglected during genetic screening, play important roles in the pathogenesis of several diseases. Using RACE-PCR and sequencing we found different variants for NEFL mRNA 3'UTR in SC control samples. Interestingly, we also found mutations in NEFL mRNA 3'UTR of ALS patients; some of them possibly caused by the selection of alternative polyadenylation (APA) sites. Alterations in the mRNA 3'UTR length could influence the fate of the transcript in several ways, for example, by altering the availability of microRNA recognition elements. To build on these findings, we are characterizing NEFL mRNA 3'UTR variants and mutants. Ultimately, we are interested in determining whether there is a correlation between the alteration of NEFL mRNA 3'UTR in ALS and the selective vulnerability of MN in this neurodegenerative condition.

C15: AN ATYPICAL LEUCINE–RICH DOMAIN IN THE ALS–RELATED PROTEIN RGNEF IS CRITICAL FOR THE PROPER REGULATION OF ITS RNA DESTABILIZING ACTIVITY

Cristian A. Droppelmann[1], Kathryn Volkening[1,2] and Michael J. Strong[1,2]
[1]Molecular Brain Research Group, Robarts Research Institute, Western University, London, Ontario, Canada.
[2]Department of Clinical Neurological Sciences, Schulich School of Medicine and Dentistry, Western University, London, Ontario, Canada.

Amyotrophic lateral sclerosis (ALS) is an adult-onset progressive disorder characterized by death of motor neurons. Although the cause of the disease remains elusive, protein aggregate formation in motor neurons, including RNA binding proteins, is a neuropathological hallmark. Previously, we observed that Rho Guanine Nucleotide Exchange Factor (RGNEF) forms cytoplasmic inclusions in ALS spinal motor neurons. Also, we demonstrated that RGNEF is an RNA binding protein that destabilizes low molecular weight neurofilament (NFL) mRNA. To study this activity, we developed several RGNEF mutants lacking specific regions of the protein. Using luciferase reporter gene assays we observed that RGNEF's GEF domain is not relevant for its RNA destabilizing activity. Interestingly, we observed that a region containing an atypical Leucine-rich (L-rich) domain in the amino terminal domain of RGNEF is critical for proper regulation of its RNA destabilizing activity. Additionally, we determined the minimum region of the protein necessary to have RNA destabilizing activity. Finally, we observed that deleting the region containing the L-rich domain on mouse isoform of RGNEF (p190RhoGEF) its RNA stability activity is also greatly affected. Our results provide evidence that the amino terminal region of RGNEF, containing the L-rich domain, is critical for proper regulation of its RNA destabilizing activity across different species. Moreover, since L-rich domains participate in protein-protein interactions, this suggests participation of a protein complex in the RNA stability regulation by RGNEF.
Acknowledgements: Canadian Institute of Health Research (CIHR); The McFeat Family Fund; ALS Society of Canada.

C16: MOTOR ASSESSMENT OF PARKINSON DISEASE PATIENTS FOLLOWING DEEP BRAIN STIMULATION SURGERY USING KINEMATIC ANALYSIS TECHNOLOGY

Greydon Gilmore[1], Krisitna Ognjanovic[1], Mehdi Delrobaei[2], Dr. Mandar Jog[2]
[1]Department of Neuroscience, Western University, London, ON
[2]Clinical Neurosciences, University Hospital, London, ON

Background and Aim: Parkinson's disease (PD) motor assessment is commonly conducted using various clinical scales and clinician observation. While these avenues have proven useful they are often criticized for lacking sensitivity and objectivity, relying solely on the clinicians' judgement. Deep brain stimulation (DBS) is a new treatment approach for PD and its clinical efficacy is being investigated. Kinematic technologies would objectively measure movement, while programming, to allow the clinician to more easily determine efficacious DBS settings for each patient. This study combines these objective measures with standard clinical rating scales. Our goal is to systematically and objectively measure the clinical effects on the motor symptoms of PD patients over successive sessions of DBS programming. **Methods:** 24 PD participants alongside 24 healthy age-matched controls will be used. Patients were assessed one week pre-operatively and follow up visits were conducted up to 6 months post-operatively. During each programming visit, the participant was set to various pre-determined setting parameters (voltage, frequency, pulse width). Gait was captured using the PKMAS gait analysis carpet. The Animazoo motion capture suit assessed Parkinsonism motor symptoms. **Results and Conclusion:** Preliminary data analysis of the gait analysis suggested a setting of medium voltage (3V), low pulse width (60 μs) and medium frequency (120Hz) was most efficacious across each participant ($F(2,3)= 7.35$, $p=.070$). Motion data displayed tremor was reduced up to six months post-operatively. Further analysis, following future programming sessions, is needed to confirm these findings.
Acknowledgments: Supported by CIHR.

C17: HOW DOES AFFERENT REGULATION OF THE UPPER LIMB MOTOR CORTEX EXCITABILTY CHANGE AFTER AN INCOMPLETE SPINAL CORD INJURY?

Aaron Z. Bailey, Peter Mi, Philemon Tsang and Aimee J. Nelson
Department of Kinesiology, McMaster University, Hamilton, Ontario

Incomplete spinal cord injury to the cervical spine impairs the transmission of afferent and efferent volleys along the remaining neural pathways. An impairment of afferent volleys to the cortex can decrease the inhibitory effect on the motor cortex known as short latency afferent inhibition (SAI) and long latency afferent inhibition (LAI). In order to characterize how these inhibitory circuits are altered as a result of a spinal cord injury, stimulation of peripheral nerves innervating muscles of the forearm and transcranial magnetic stimulation (TMS) were used to probe the excitability of motor cortex. The Participants studied have an incomplete cervical spine injury between C3 and T1 and their data was compared against aged-matched uninjured controls. Motor evoked potentials were recorded from flexor carpi radialis (FCR) and excitability of the motor cortex was determined by calculating the area of the resulting MEP. Conditioning afferent volleys were evoked by electrical stimulation of the median nerve at the elbow. A wide range of interstimulus intervals (ISI) were used with nerve stimulation preceding the TMS pulse by 15, 20, 25, 35, 45, 55, 65 and 200 ms. Preliminary results from injured participants indicate a lack of inhibition or facilitation of MEPs at any ISI when the FCR muscle is active or at rest. In contrast, uninjured controls show an inhibition of MEPs in FCR at rest and during voluntary contraction. Characterization of these circuits in an SCI population is critical to the development of plasticity protocols to change their function.

C18: INCREASED STROKE INJURY AND WORSE OUTCOMES IN MICE WITH SELECTIVE ELIMINATION OF STRIATAL VESICULAR ACETYLCHOLINE TRANSPORTER

Goncalves D. F. (1, 2, 3), Guzman M. S. (2,3) , Gros, R. (2,3), Massensini A. R. (1), Bartha R. (2,5), V. F. Prado (2,3,4), M. A. M. Prado (2,3,4).
(1) Núcleo de Neurociências, Departamento de Fisiologia e Biofísica, Instituto de Ciências Biológicas, Universidade Federal de Minas Gerais, Brazil. (2) Robarts Research Institute (3) Department of Physiology and Pharmacology (4) Department of Anatomy & Cell Biology (5) Department of Medical Biophysics, The University of Western Ontario, London, ON, Canada.

The cholinergic system plays important roles in neuroprotection. Acetylcholine release is increased during and after ischemia and cholinergic neurons in the striatum, one of the main regions affected during stroke, are preserved. The specific contribution of striatal acetylcholine during ischemic lesion and functional recovery is poorly understood. To address this question, our group generated a striatal-selective vesicular acetylcholine transporter (VAChT) knockout mouse line using the Cre/loxP system. Mutant mice and littermate controls were subjected to unilateral middle cerebral artery occlusion (MCAO) and cerebral lesion was evaluated by MRI, while survival and functional recovery was evaluated using tape removal and gait analysis. Most wild-type mice survived unilateral MCAO stroke injury for 60 min (73% survival rate); however, striatal-selective VAChT-KO mice ($VAChT^{D2\text{-}Cre\text{-}flox/flox}$) presented higher mortality rate. Interestingly, $VAChT^{D2\text{-}Cre\text{-}flox/flox}$ showed increased brain injury volume ($13.68 \pm 1.005 mm^3$) when compared to control mice ($9.642 \pm 0.8647\ mm^3$).

Both genotypes lost weight following surgery, but recovered 14 days post-surgery. Behavioural analysis demonstrated that 7 days after ischemia, VAChT$^{D2\text{-}Cre\text{-}flox/flox}$ mice exhibited impaired dexterity to remove tape on the contralateral side and presented gait dysfunction when compared to littermate controls. Levels of apoptosis and edema were investigated as potential mechanisms contributing to increased lesion size in VAChT knockout mice. Our results show no difference in apoptosis between genotypes. However higher levels of pGSK3 (Tyr 279, 216) suggest increased cell death by edema in VAChT knockouts. This data indicates that acetylcholine released during and/or after stroke is important to limit injury facilitating functional recovery of mice.

Supported by: CNPq, CIHR and Heart & Stroke Foundation.

C19: THE ROLE OF SIRT3 AS A DISEASE MODIFYING AGENT IN PARKINSON'S DISEASE

Jacqueline A. Gleave[1], Krisitn Lizal[1], Chris Yong-Kee[1], Peter Perri[1], Jonathan Brotchie[2], James Koprich[2], James Eubanks[2], Joanne E. Nash[1]

[1]Department of Biological Sciences, Centre for the Neurobiology of Stress, University of Toronto Scarborough, Toronto, ON, M1C 1A4, Canada

[2]Toronto Western Research Institute, Toronto, ON M5T 2S8, Canada

Sirtuin 3 (SIRT3) is the main mitochondrial deacetylase regulating proteins involved in cellular respiration. In Parkinson's disease (PD), mitochondrial dysfunction is central to the pathogenic process. We hypothesized that SIRT3 may have a neuroprotective role in PD because it is beneficial to mitochondrial health. We utilized cellular and rodent models of PD to test this hypothesis. Recombinant adeno-associated virus (AAV) expressing a-synuclein was infused into the substantia nigra pars compacta (SNc) of rats followed by AAV expressing SIRT3 on day 18. Three and six weeks following □-synuclein administration, behavioural deficits were assessed using a cylinder test. To investigate the neuroprotective mechanism of SIRT3, SH-SY5Y cells stably overexpressing SIRT3-myc were used as a cellular model of PD. Toxins that mimic mechanisms of cell death in PD were used to induce cell stress. Cellular toxicity, reactive oxygen species (ROS), ATP production, and changes in mitochondrial membrane potential were assessed. Overexpression of SIRT3 in rats reversed behavioural abnormalities. Overexpression of SIRT3 in a cellular model of PD decreased cellular toxicity after toxin exposure. Overexpression of SIRT3 also decreased ROS production, and stabilized ATP production and mitochondrial membrane potential. These results suggest that SIRT3 has neuroprotective effects in a rat model of PD. These neuroprotective effects are likely due to SIRT3's ability to stabilize mitochondrial function by reducing ROS, and maintaining ATP production and mitochondrial membrane potential.

Acknowledgements: Supported by MJFF, PSC, and NSERC.

C20: INDUCTION OF HEAT SHOCK PROTEINS IN DIFFERENTIATED HUMAN NEURONS BY LOW DOSE CO-APPLICATION OF CELASTROL AND ARIMOCLOMOL: RELEVANCE TO THE TREATMENT OF NEURODEGENERATIVE DISEASES

Catherine Deane and Ian R. Brown

Centre for the Neurobiology of Stress and Department of Biological Science University of Toronto Scarborough, Toronto, Ontario M1C 2C2

Neurodegenerative diseases such as Alzheimer's, Parkinson's, and Amyotrophic Lateral Sclerosis (ALS) have been termed 'protein misfolding disorders' that are characterized by the accumulation of aggregation-prone, misfolded proteins which trigger pathogenic cascades that lead to cell death in specific populations of neurons. Heat shock proteins (Hsps) are protein repair agents which can detect and repair misfolded proteins. Accordingly, upregulation of Hsps has been suggested as a potential therapeutic strategy to combat neurodegenerative protein misfolding disorders. Celastrol induces Hsps by acting on heat shock transcription factor 1 (HSF1). Arimoclomol is a co-inducer of Hsps that potentiates their induction. *In vivo* administration of celastrol in a mouse model of Alzheimer's reduces a key neuropathological feature, namely aggregation of amyloid-beta protein, while *in vivo* administration of arimoclomol in a mouse model of ALS delays the time course of the disorder. Using differentiated SH-SY5Y human neuronal cells, we examined if co-application of celastrol and arimoclomol, at low dosages that do not affect cell viability or neuronal process morphology, triggered induction of Hsps in neurons that is greater than that obtained by their individual application. Low dosage co-application induced Hsps in the human neuronal cells whereas single application did not. Hence this may represent a promising strategy to upregulate a set of neuroprotective Hsps in the treatment of neurodegenerative diseases.

Acknowledgements: Supported by grants from NSERC and a Canada Research Chair (Tier I) to IRB.

C21: LIVE IMAGING AND FRAP OF HSP70 HEAT SHOCK PROTEINS TO DISCRETE CYTOPLASMIC AND NUCLEAR STRUCTURES OF DIFFERENTIATED HUMAN NEURONAL CELLS AFTER CELLULAR STRESS

Sadek Shorbagi and Ian R. Brown

Centre for the Neurobiology of Stress and Department of Biological Sciences University of Toronto Scarborough, Toronto, Ontario M1C 1A4

Heat shock proteins (Hsps) are protein repair agents that can detect and refold misfolded, aggregation-prone proteins that accumulate during neurodegenerative diseases, such as Alzheimer's, Parkinson's and ALS, triggering pathogenic cascades that result in cell death in specific populations of neurons. The localization of Hsps to particular cytoplasmic and nuclear sites was employed as an index to identify 'hot spots' in differentiated human neuronal SH-SY5Y cells that are particularly sensitive to cellular stress and require the recruitment of Hsps to refold misfolded, aggregation-prone neuronal proteins. Live imaging, using spinning disk microscopy, revealed that YFP-tagged members of the Hsp70 multigene family rapidly localized to discrete neuronal cytoplasmic structures (centrioles) after cellular stress and also to particular elements of the nucleus (nuclear speckles, rich in RNA splicing factors, and the nucleolus). The cytoplasmic and nuclear structures that were targeted by the YFP-tagged HSPA6 (Hsp70B' protein) and HSPA1A (Hsp70-1 protein) were subjected to FRAP (Fluorescence Recovery After Photobleaching). The recovery kinetics, after laser induced photobleaching, demonstrated that the stress-induced recruitment of the Hsp70 proteins into specific cytoplasmic and nuclear structures of human neuronal cells was highly dynamic.

Acknowledgements: Supported by grants from NSERC and a Canada Research Chair (Tier I) to IRB.

C22: CANNABINOID CB1 RECEPTOR TRANSMISSION IN THE BASOLATERAL AMYGDALA BI-DIRECTIONALLY CONTROLS THE MOTIVATIONAL PROPERTIES OF OPIATES VIA FUNCTIONAL EXCITATORY INPUTS TO THE NUCLEUS ACCUMBENS SHELL

Tasha Ahmad[1,2], and Steven R. Laviolette[2,3,4]

Graduate Program in Neuroscience[1], Dept. of Anatomy and Cell Biology[2], Dept. of Psychiatry[3], Dept. of Psychology[4], Schulich School of Medicine, Western University, London, Ontario

The basolateral amygdala (BLA) and nucleus accumbens (NAc) are involved critically in opiate-reward processing. The cannabinoid CB1 receptor is highly expressed in the BLA, and studies have shown its involvement in associative learning processes and memory during the drug addiction process. In the BLA, inhibitory GABAergic neurons are inhibited by CB1 receptor activation, removing inhibition on BLA efferents. Indeed, activation of CB1 receptors within the BLA has shown to reinforce the motivational effects of opiates. Furthermore, opiates activate mesolimbic DAergic inputs to the NAc, and modulate the motivational effects of opiates. Using an unbiased conditioned place preference (CPP) procedure, we administered either a CB1 agonist (WIN 55,212-2) or antagonist (AM 251) into the BLA of Sprague-Dawley rats, and examined how intra-BLA modulation of CB1 transmission within these neural regions may influence opiate-reward CPP, using either a sub-reward threshold (0.05 mg/kg; i.p.) or supra-reward threshold (5 mg/kg; i.p.) conditioning doses of morphine. Surprisingly, we found that CB1 receptor activation in the BLA made a normally sub-reward threshold dose of morphine, highly aversive, as rats demonstrated a strong aversion to morphine environments during recall testing. In contrast, intra-BLA blockade of CB1 transmission potentiated the rewarding properties of sub-reward threshold morphine, with rats demonstrating robust CPP. Thus, activation of CB1 transmission in the BLA produces bi-directional effects on opiate reward memory acquisition, switching morphine reward signaling into aversion, or potentiating normally non-rewarding doses of morphine. Our previous research has identified critical functional connections between the BLA and NAc during opiate reward memory processing (Lintas et al., 2012). Accordingly, we next examined if intra-BLA CB1 modulation of opiate reward signaling depends upon functional BLA>NAc projections by reversibly blocking excitatory BLA>NAc projections with the NMDA receptor antagonist, AP-5. We performed bilateral micro-infusions of AP-5 (1 µg/0.5 µl) directly into the NAc shell or NAc core, prior to intra-BLA administration of either AM 251 or WIN-55. Interestingly, blockade of NMDA transmission in the NAc shell, but not core, prevented both intra-BLA CB1 blockade-mediated opiate reward potentiation and CB1 activation-mediated aversion effects, demonstrating that intra-BLA CB1 receptor modulation controls opiate reward processing via functional inputs to the NAc shell. We are currently examining how intra-BLA CB1 transmission modulates in vivo neuronal network dynamics within the NAc.

Acknowledgement: Supported by NSERC

C23: CORRELATION OF QUANTITATIVE MRI AND HISTOLOGY OF SURGICAL SPECIMENS IN DRUG-RESISTANT FOCAL EPILEPSY

Maged Goubran[1], Robert R. Hammond[2], Sandrine de Ribaupierre[3], Terry M. Peters[1], and Ali R. Khan[1]

[1]Imaging Laboratories, Robarts Research Institute, London, Ontario, Canada,

[2]Department of Pathology, Western university, London, Ontario, Canada,

[3]Department of Clinical Neurological Sciences, Western university, London, Ontario, Canada

Clinical MRI protocols used for pre-operative assessment of focal epilepsy lack sensitivity, with greater than 30% of patients diagnosed as MR negative. The histology evaluation of the surgical tissue, nevertheless, often reveals gliosis or malformations of cortical development undetected pre-operatively. Such data have motivated the need for MRI-histology correlation, to validate improved pre-operative imaging for localizing epileptogenic foci. Our objective here is to correlate quantitative MRI and histology metrics of surgical specimens from temporal lobe epilepsy (TLE) patients. 10 TLE patients were recruited for this study. All patients underwent pre-operative imaging (relaxation mapping and diffusion-tensor imaging) on a 3T scanner. Field maps of NeuN and GFAP immunohistochemistry stains of surgically resected tissue were automatically computed. Regions of interest were subsequently delineated on histology slices. Using our previously reported histology to MRI registration protocol, the histology ROIs were warped to match corresponding regions on *in-vivo* quantitative maps (T1, T2, FA, MD). Spearman's rank correlation was employed to test for correlation between the MRI metrics: T1, T2, FA & MD, and field fractions of NeuN & GFAP. A negative correlation between NeuN field fraction and the T1 value in gray matter was found using both tests ($r = -0.617$, $p=0.001$). This study is the first to relate *in-vivo* T1 values to the proportion of neurons in the grey matter for focal epilepsy. These findings suggest that *in-vivo* T1 mapping may act as a predictor of neuronal density.

Acknowledgements: Supported by CIHR

C24:EFFECT OF GLUCOSE: FRUCTOSE RATIOS ON C-FOS EXPRESSION IN NEURAL AREAS ASSOCIATED WITH FEEDING AND REINFORCEMENT

Katrina Kent, Paul Marshall, Ari Shore, Tiana Downs, Stephen Daniels,Francesco Leri

University of Guelph, Guelph, ON

The increased consumption of sugars, particularly those high in fructose, has been associated with a rise in obesity. This association may be due to their ability to act as reinforcers, thus contributing to the overconsumption of food. We hypothesized that the ratio of glucose and fructose consumed differentially affects neuronal activation in areas associated with feeding and reinforcement. To test this, 48 male Sprague Dawely rats underwent 14 days of training in an operant task in which they nosepoked to receive either high ratio (HR; 45%-55%) or low ratio (LR; 70%-30%) glucose-fructose pellets (BioServ, Frenchtown NJ). Ninety minutes following the final session rats were sacrificed and their brains were extracted and processed for Fos immunohistochemistry. No significant correlations were found between pellets consumed and c-fos density (count/um^2) in the nucleus accumbens. In contrast, significant positive correlations were found in the dorsomedial hypothalamus (DMH), perifornical lateral hypothalamus (PeLH) and arcuate nucleus (ArcN). In both the ArcN and the PeLH the directions of these correlations differed between consumption groups, such that among the LR group density was positively correlated with pellets consumed, where as this relationship was slightly negative among the HR group, although the difference between the correlations was only significant in the ArcN. These results indicate that sugars containing a higher ratio of glucose as opposed to fructose increase activity in areas associated with feeding, but not reinforcement.

Acknowledgments: Supported by NSERC and OBI

C25: REGULATION OF HUMAN CHOLINE ACETYLTRANSFERASE PROTEIN STABILITY BY AN N-TERMINAL PROLINE-RICH MOTIF

Trevor M. Morey, R. Jane Rylett

Molecular Medicine Research Group, Robarts Research Institute, London ON

Department of Physiology and Pharmacology, Western University, London ON

Choline acetyltransferase (ChAT) is essential for the healthy function of cholinergic neurons through production of the neurotransmitter acetylcholine. ChAT contains a highly conserved N-terminal proline-rich motif at residues $_{14}$**P**KL**P**V**PP**$_{20}$ which shares homology with SH3-domain binding motifs. Early investigation into this motif revealed that mutation of both prolines-17/19 to alanine (P17A/P19A) dramatically reduced ChAT steady state protein levels in cholinergic SN56 cells. This reduction could be due to changes in protein stability, and using a novel fluorescent-biorthogonal pulse-chase protocol we have determined that the protein half-life of P17A/P19A-ChAT (2.2 hours) is substantially reduced when compared to wild-type (WT) ChAT (19.7 hours). By using heterologously-expressed HA-tagged ubiquitin and the proteasome inhibitor MG132 we have determined that both WT and P17A/P19A-ChAT are polyubiquitinated, and that polyubiquitination of P17A/P19A-ChAT appears to be enhanced. Lastly, we have determined that both WT and P17A/P19A-ChAT are targeted for proteasomal degradation by lysine-48-linked polyubiquitination. Overall, these results establish a novel form of ChAT protein regulation whereby ChAT protein stability is regulated by the ubiquitin-proteasome system. Furthermore, mutation of the conserved N-terminal proline-rich motif of ChAT reduces ChAT protein stability through enhanced polyubiquitination and proteasomal degradation, supporting future investigation into whether ChAT protein stability is regulated by protein-protein interactions mediated through this motif.

D: Neural Excitability, Synapses, and Glia: Cellular Mechanisms

D1: THE MODULATORY EFFECTS OF NON-AROMATIZABLE ANDROGENS ON GABA CURRENTS OF PYRAMIDAL CELLS IN THE MEDIAL PREFRONTAL CORTEX

Brandon Reid[1], Craig D.C. Bailey[1], and Neil J. MacLusky[1]

[1]*Department of Biomedical Sciences, University of Guelph, Guelph, ON*

The medial prefrontal cortex (mPFC) plays a critical role in working memory and the consolidation of short-term to long-term memory. The structure and function of this area is heavily influenced by gonadal steroid hormones, however precise mechanisms leading to these changes are not well defined. In the male, while testosterone has effects on dopaminergic input to the mPFC through an androgen-receptor-dependent mechanism, 5□-androstan-3□, 17□-diol (3□-diol), a 5□-reduced testosterone metabolite that is a positive allosteric modulator of the gamma-aminobutyric acid$_A$ (GABA$_A$) receptor, may also play a role. Here, we propose that the non-aromatizable androgen metabolite, 3□-diol, through modulation of the GABA$_A$ receptor on upstream GABAergic interneurons, decreases the influence of GABA, and has an overall permissive effect on pyramidal cells of the mPFC. Using pre-pubertal CD-1 male mice, we investigated the effects of 3□-diol on GABAergic currents within pyramidal cells of the mPFC using a whole-cell patch clamp technique in brain slices. We found that, compared to vehicle controls, there was a significant decrease in GABAergic currents in mPFC pyramidal cells following application of either 3□-diol, suggesting an overall disinhibitory effect on these cells.

Acknowledgements: Supported by NSERC.

D2: SALVIA VAPOR INHALATION DECREASES SYNAPTIC TRANSMISSION IN THE RAT DENTATE GYRUS IN VIVO

Mitchel P. Brewer and Bruce E. McKay

Department of Psychology, Wilfrid Laurier University, Waterloo, ON

Salvia is the only natural hallucinogen that we have found to date that has its effects mediated by kappa opioid receptors. Previous studies using synthetic kappa opioid agonists have shown that activation of these receptors cause short term depression in synaptic transmission, however this has yet to be investigated with a naturally occurring hallucinogen such as salvia. One of the unique effects of salvia is that it often causes resurgence of vivid memories. This effect could be mediated by the dentate gyrus as it has a large concentration of kappa opioid receptors and has a large role in memory storage and recollection. The purpose of this study was to examine the how salvia affects synaptic transmission in the dentate gyrus using field potential recordings in anesthetized rats. Specifically, we were looking for any changes in the slope, latency, and population spike amplitude of fEPSPs in the dentate gyrus after salvia exposure. We hypothesized that we would see short term depressive effects on synaptic transmission as seen with synthetic kappa opioid ligands. Our results approached significance,and with an increased sample size it likely would have reached significance indicating that the amplitude of the fEPSPs population spike was decreased. This decrease in synaptic transmission provides the grounds for vivid memory recollection associated with salvia use.

Acknowledgments: Supported by NSERC

D3: EFFECTS OF THE ESTROUS CYCLE ON NEURON MORPHOLOGY IN FEMALE RAT HIPPOCAMPI

Sarah Atwi[1], Ari Mendell[1] and Neil J. MacLusky[1]

[1]*Department of Biomedical Sciences, University of Guelph, Guelph ON*

Exploration of estrogenic effects on female rat hippocampi has increased in recent decades, however robust research on specific regional effects has yet to be established. Increased estrogen in female rats has been linked to significant trophic effects on dendritic spine density (DSD) and arborization of apical neurons of CA1, but not CA3 of the hippocampus. This study revisits the question of the effects of endogenous estrogen fluctuation by extensively observing changes in hippocampal neurons. Following estrous stage identification, 7 adult female rats (4 at proestrus, 3 at metestrus) were sacrificed and brains were extracted and processed for Golgi-Cox impregnation. 5 images from each field of the apical dendritic tree of pyramidal neurons in CA1 and CA3 were taken and analyzed for DSD and spine length. As in past literature, at proestrus, CA1 DSD was significantly higher than at metestrus ($P<0.05$). Surprisingly, significantly higher DSD was also found in CA3 ($P<0.05$). No significant difference was found in spine length. These results reiterate the trophic effects of higher estrogen levels on CA1 DSD, but also add new insight on CA3 dendritic response. Since each hippocampal field is connected to specific synaptic transmission pathways that lead to particular physiological function, it is necessary to further characterize the effects of the estrous cycle on these neurons and input pathways. This would provide incite into the consequences of naturally fluctuating hormones on hippocampal-related cognitive function and mechanisms behind certain neurological disorders.

Acknowledgements: Supported by NSERC 197293-2007

D4: INSULIN-INDEPENDENT INCREASE IN METABOLIC ACTIVITY BY TENEURIN C-TERMINAL ASSOCIATED PEPTIDE (TCAP)-1

Yani Chen[1], Andrea D'Aquila[1], and David A. Lovejoy[1]

[1]*Department of Cell and Systems Biology, University of Toronto, Toronto, ON*

The TCAP family is a unique energy regulation signalling system that evolved at the base of metazoan evolution. Since efficient regulation of energy production and utilization underlies the evolutionary success of multicellular animals, this peptide family could play a fundamental role in the regulation of cellular energy and glucose utilization of all metazoans. Previous in vitro data indicate that the primary role of TCAP may be to regulate metabolic optimization in the brain by increasing the efficiency of glucose transport and energy utilization. I hypothesize that TCAP-1 also plays a significant role in regulating energy metabolism of the organism by optimizing glucose usage. Preliminary results in vivo indicated that TCAP-1 results in a 15-20% decrease in plasma glucose levels in rats one week after administration. TCAP-1 also induced ^{3}H-deoxyglucose transport into neurons and skeletal muscle cells in vitro in an insulin-independent manner. To understand the mechanism by which this occurs, we used a previously deduced pathway by which TCAP-1 signals in vitro to establish a link between the MEK-ERK1/2 pathway and glucose uptake as well as a connection between the MEK-ERK1/2 and AMPK pathways. This is speculated to be underlying the changes observed in skeletal muscle tissue and myocytes that have been treated with TCAP-1 as well.

Acknowledgments: Supported by NSERC and Protagenic Therapeutics Inc.

D5: CHOLINERGIC REGULATION OF COGNITIVE FUNCTION AND UNDERLYING MOLECULAR MECHANISMS

Benjamin Kolisnyk[1,2], Mohammed Al-Onaizi[1,4], Gustavo M. Parfitt[1], Maxine T. Kish[1,3], Jason Xu[1,4], Geula Hanin[5], Hermona Soreq[5], Marco Prado[1,2,3,4], Vania F. Prado[1,2,3,4]

1 Robarts Research Institute, Schulich School of Medicine & Dentistry, University of Western Ontario, London, Ontario, Canada, N6A5K8 2 Graduate Program in Neuroscience, 3 Department of Physiology and Pharmacology, 4 Department of Anatomy & Cell Biology, 5 The Hebrew University of Jerusalem

Cholinergic vulnerability, characterized by loss of acetylcholine (ACh), is one of the hallmarks of Alzheimer's disease (AD). Recent work has suggested that decreased ACh activity in AD may contribute to pathological changes through global alterations in alternative splicing. This occurs via the regulation of the expression of a critical protein family in RNA processing, hnRNP A/B proteins. Changes in pre-mRNA processing may underlie dysfunction of neurons; impairing plasticity, metabolism, the inflammatory response and promoting neurodegeneration. To assess the role of ACh in cognitive function we targeted the expression of the Vesicular Acetylcholine Transporter (VAChT), the rate limiting step in ACh release. To test the hypothesis that cholinergic tone regulates alternative splicing in neurons by controlling the fate of hnRNPA2/B1 expression, thereby influencing cognition, we employed a combination of genetic in vivo and in vitro techniques to alter cholinergic tone and evaluate

expression of hnRNPA2/B1. Decreasing cholinergic tone reduced levels hnRNPA2/B1 and alternative splicing patterns mirroring those seen in Alzheimer's disease, while increasing cholinergic signalling *in vivo* increased expression of hnRNPA2/B1. This effect is not due to decreased hnRNP mRNA expression or increased degradation of the protein. Cell culture experiments demonstrated that muscarinic signalling may underlie cholinergic control of hnRNPA2/B1 expression. Finally we evaluated long term changes in APP processing and other key AD related transcripts in aged forebrain VAChT deficient mice

D6: ANDROGEN-MEDIATED REGULATION OF BRAIN-DERIVED NEUROTROPHIC FACTOR IN THE MALE MOUSE HIPPOCAMPUS

Sarah Atwi[1], Dallan McMahon[1] and Neil J. MacLusky[1]
[1]*Department of Biomedical Sciences, University of Guelph, Guelph ON*

The effects of androgens on hippocampal brain-derived neurotrophic factor (BDNF) and its precursor of opposing action, proBDNF, remain largely unknown. A recent study demonstrated that gonadectomy was linked with an increase in BDNF protein expression within the mossy fiber pathway as well as modifying synaptic transmission in male rats (Skucas et al. 2013). Considering androgens play a role in hippocampal dendritic morphology and spine density, this current study endeavors to determine how androgen might control BDNF expression. Male CD-1 mice underwent either bilateral gonadectomy (GDX) or sham surgery and were subsequently sacrificed after a short and long-time point post surgery. BDNF mRNA expression was studied by RT-qPCR at the short time point and no difference was seen between groups. BDNF levels assessed at both time points also showed no significant change in levels in the entire hippocampus, as well as microdissected regions. However, proBDNF, assessed through Western Blotting, was statistically lower in both GDX and sham mice sacrificed 27-30 days, versus 8-12 days post-surgery ($P<0.05$). These results suggest BDNF may not be regulating hippocampal morphology in mice; thus, androgens may play a different role in male mouse plasticity compared to rats. Furthermore, post-surgical stress may have led to the upregulation of proBDNF levels. Additional exploration of the mechanism of androgen action in male mice and the effects of surgical stress on neurotrophic factors and hippocampal morphology are needed.

Acknowledgements: Supported by NSERC 197293-2007

D7: DIFFERENTIAL INVOLVEMENT OF THE HISTONE ACETYLTRANSFERASES CBP, P300, AND PCAF IN THE HIPPOCAMPUS AND PERIRHINAL CORTEX OF RATS FOR OBJECT MEMORY PROCESSING

James B. Humble[1], Krista A. Mitchnick[1,3], Bethany Christen[1], Monika Van Tiggelen[2], Oleksiy Zaika[2,3], Samantha Creighton[1,3], Jacob Cloke[1,3], Bettina E. Kalisch[2,3]. and Boyer D.Winters[1,3]
[1]*Department of Psychology,* [2]*Department of Biological Sciences, and* [3]*Collaborative Neuroscience Program, University of Guelph, ON, Canada N1G 2W1*

Chromatin remodelling via epigenetic mechanisms, such as histone acetylation, is crucial for certain forms of long-term memory. The roles of specific histone acetyltransferases (HATs) in distinct brain regions, however, are only beginning to be revealed. For the present study, we used various HAT inhibitors (HATi) to examine the contributions of three prominent HATs, CBP, p300 and PCAF, to memory consolidation in the hippocampus (HPC) and perirhinal cortex (PRh) using the object-in-place (OiP) task, which requires both structures. Selective inhibition of CBP, p300 or PCAF in the HPC significantly impaired long-term OiP memory, whereas only CBP and PCAF were necessary in the PRh. qPCR analyses of HAT mRNA levels in PRh and HPC following OiP learning were consistent with these findings. Furthermore, only PCAF inhibition within the HPC caused impairments when short-term OiP memory was tested, suggesting that PCAF might also influence memory through non-histone targets. Finally, the CBP inhibitor/PCAF activator, SPV106, successfully facilitated long-term OiP memory in both brain regions, providing evidence that these HATs can compensate for one another. These results highlight the complexity of the 'histone code' for memory processing, and the dissociation between HAT contributions for object memory within the HPC and PRh emphasizes the importance of assessing epigenetic mechanisms of memory for different types of information and in different brain regions.

Acknowledgements: Supported by NSERC

D8: ROLE OF NEUREXIN-1A IN THE REGULATION OF NEURITE GROWTH

Adam Wang, Yun-Yan Xiang
Graduate Program in Neuroscience and Robarts Research Institute, University of Western Ontario, ON, Canada

During development, a neuron makes synaptic connections with other cells by growing its neurites, and the process of neurite growth is guided along specific pathways through attractive and repulsive cues in the extracellular environment. Neurexins, a group of transmembrane proteins abundantly expressed in axonal terminals of central neurons, play a critical role in the regulation of synaptogenesis by interacting with other proteins such as neuroligin. The goal of this study was to study the role of neurexin-1α in the control of neurite outgrowth. Transfecting a siRNA of neurexin-1α into cultured rat hippocampal neurons significantly increased the length of neurites in comparison to that of neurons transfected with a control siRNA sequence. The efficiency of neurexin-1α siRNA was demonstrated by its action on INS-1, a line of endocrine cells, in which this siRNA greatly reduced the protein level of neurexin-1α. In addition, treating the cultured hippocampal neurons with neurexin-1 antibody; or neurexin binding molecules such as α-latrotoxin and soluble peptide of neuroligin, significantly decreased the length of neuritis relative to controls. These findings indicate that neurexin-1α regulates neurite outgrowth by interacting with repulsive molecular cues.

E: Sensory and Motor Systems

E1: SEROTONERGIC MODULATION OF PHEROMONE AND AMINO ACID RESPONSES IN THE OLFACTORY BULB OF THE SEA LAMPREY (*PETROMYZON MARINUS*)

Karl C. Boyes[1], Warren W. Green[1], Zeenat Aurangzeb[1], Réjean Dubuc[2,3], Barbara Zielinski[1].
[1]*Department of Biological Sciences, University of Windsor, Windsor, ON*
[2]*Groupe de Recherche en Activité Physique Adaptée, Université du Québec à Montréal, Montreal, QC*
[3]*Université de Montréal Department of Neuroscience, Montreal, QC*

Responses to pheromones and food odours vary tremendously at the behavioural level. The generation of locomotor responses to olfactory signals in lampreys is one example of variability in behavioural responses. Modulatory mechanisms in the olfactory bulb will likely affect the magnitude of these responses. The dorsal and lateral bulbar regions in lampreys receive sensory inputs from the main olfactory epithelium and bulbar projection neurons extend their axons to the lateral pallium. The dorsal bulbar region responds predominantly to pheromones and bile acids and the lateral region responds to amino acids. While serotonergic (5-hydroxytryptamine, 5-HT) fibers are abundant in the lamprey olfactory bulb (Frontini et al., 2003 JCN 465: 27-37), it is unknown if 5HT modulates odour responses. In this study, we observed that upon local bulbar injection of the 5-HT1a and 5-HT2 receptor antagonist, spiperone, and of the specific blocker of the 5-HT1a receptor, s(-)-uh-301, the amplitude of local field potential responses to pheromones, bile acid and amino acids was enhanced in the dorsal and lateral bulbar regions. This modulation did not take place when 5-HT was applied along with the antagonists. Based on these findings, we conclude that 5-HT modulates responses in the olfactory bulb largely by attenuating the amplitude of pheromones, bile acid and amino acid odour responses and we propose that endogenous 5-HT modulates olfactory-mediated behaviours.

FUNDING ACKNOWLEDGMENTS: Supported by Great Lakes Fishery Commission, Natural Sciences and Engineering Research Council of Canada

E2: ANODAL TRANSCRANIAL DIRECT CURRENT STIMULATION OF THE SUPPLEMENTARY MOTOR AREA IMPROVES BEAT-BASED TIMING

Cricia Rinchon[1,2], Li-Ann Leow[2], and Jessica A. Grahn[2,3]
[1]*Schulich School of Medicine and Dentistry, Western University, London, ON*
[2]*Brain and Mind Institute, Western University, London, ON*
[3]*Department of Psychology, Western University, London, ON*

Effective motor control requires accurate timing. Timing performance is improved by representing time intervals with respect to a regular beat (i.e., via beat-based timing) compared to representing individual intervals independently. Neuroimaging studies suggest that the supplementary motor area (SMA) is involved in beat-based timing (Grahn & Brett, 2007). To investigate whether the SMA plays a causal role in beat perception, we delivered anodal transcranial direct current stimulation (tDCS) to increase SMA excitability when participants discriminated between pairs of rhythms. The premotor cortex (PMC) was used as a control area. Half the rhythms could be timed relative to a beat (beat-based rhythms), and half could not (non-beat-based rhythms). Increasing excitability of the SMA, but not the PMC, significantly improved rhythm discrimination performance for beat-based rhythms and not for non-beat rhythms. These results confirm that the SMA, but not the PMC, plays a causal role in beat-based timing.

E3: DUAL LABELING OF GLOMERULAR CHAINS IN THE OLFACTORY BULB OF CHINOOK SALMON FRY *(ONCORHYNCHUS TSHAWYTSCHA)*

Tina Suntres[1], Cory Ochs[1], Trevor Pitcher[1], Barbara Zielinski[1]
[1]*Department of Biology, University of Windsor, Windsor ON*

Vital to a Chinook salmon's success in life is its olfactory system. Olfactory sensory neurons (OSNs) project from the nasal epithelium, where odour molecules are detected, to the olfactory bulb (OB). OSNs stimulated by amino acid odours project to the lateral OB region where axon endings cluster forming glomerular chains. Chinook salmon use amino acids for feeding and possibly for imprinting and homing to natal waters to spawn. To develop an understanding of the organization of OSN axon endings in the OB of Chinook salmon fry, we applied immunohistochemistry to label serial OB sections. An antibody against keyhole limpet hemocyanin non-selectively labelled OSN axons and a calretinin antibody which labelled microvillous OSNs that extend to lateral OB glomeruli. An extended protocol was adapted to optimize the labelling and sections collected in three different planes created a multidimensional perspective of glomerular chain organization within the OB. We found large glomerular chains located dorsally, as well as a clustering of small chains ventrally. A large chain labeled with calretinin was found in the lateral portion of the OB. Our results showed consistent organization of glomerular chains in Chinook salmon fry. These techniques are now being used to test the effects of olfactory enrichment of the organization of OSN axons in these same glomerular chains.

Acknowledgments: Supported by NSERC.

E4: HEMIPLEGIC CEREBRAL PALSY PATIENTS TREATED WITH CONSTRAINT-INDUCED MOVEMENT THERAPY: RESTING STATE FUNCTIONAL MAGNETIC RESONANCE AND DIFFUSION IMAGING PREDICTORS AND NEUROPLASTIC REORGANIZATION

Kathryn Y. Manning[1], Darcy Fehlings[2], Lauren Switzer[2], Jan Willem Gorter[3], Ronit Mesterman[4], Ravi S. Menon[1]

[1]*Department of Medical Biophysics, Western University, London, ON*
[2]*Holland Bloorview Kids Rehabilitation Hospital, Toronto, ON*
[3]*Department of Pediatrics, McMaster University, Hamilton, ON*
[4]*McMaster Children's Hospital, Hamilton, ON*

Purpose: Evaluate children with hemiplegic cerebral palsy (CP) treated with constraint-induced movement therapy (CIMT) to (a) determine baseline resting state functional magnetic resonance imaging (RS-fMRI) and diffusion tensor imaging (DTI) measures that predict improvement after CIMT and to (b) better understand the relationship between functional changes and neuroplasticity.

Methodology: Twelve children with hemiplegic CP (5 control) from three facilities were evaluated at baseline, 1-month and 6-months after CIMT. Clinically assessed using Quality of Upper Extremity Skills Test (QUEST), Jebsen-Taylor Test of Hand Function (JTTHF) and Canadian Occupational Performance Measure (COPM). RS-fMRI and DTI images were acquired on a 3T MR scanner and the sensorimotor resting state network (RSN) was spatially characterized. DTI data was used to find the fractional anisotropy (FA) and mean diffusivity (MD) along the corticospinal tract (CST).

Findings: Baseline sensorimotor RSN organization was related to change in COPM score at 1-month (p=0.03). Higher MD in the ipsilesional CST was related to the 1-month change in JTTHF score (p=0.02). Sensorimotor RSN reorganization and QUEST scores 1-month post-CIMT were correlated, and at 6-months reorganization was significantly correlated with COPM change scores (p=0.04). Predictor relationships indicate that children with more unilateral sensorimotor RSN and further compromised tracts improved the most. The correlated changes between sensorimotor RSN reorganization and clinical measures provide further evidence of neuroplasticity.

Acknowledgements: Supported by the Ontario Brain Institute. The opinions, results and conclusions are those of the authors and no endorsement by the Ontario Brain Institute is intended or should be inferred.

E5: *NEFM* MRNA TARGETING MICRORNAS, A ROLE IN AMYOTROPHIC LATERAL SCLEROSIS

Muhammad Ishtiaq, Kathryn Volkening and Michael Strong

Robarts Research Institute, Western University, London ON

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease characterized by muscle weakness which leads to paralysis and ultimately death. Low, medium and high molecular weight neurofilament subunits (NFL, NFM, and NFH respectively, encoded by *NEFL*, *NEFM* and *NEFH* area n important structural and functional component of motor neurons. Stoichiometric imbalance of NFL, NFM and NFH subunits can lead to neurofilament aggregate formation, therefore regulation of neurofilament expression is vital for normal structure and function. We have previously reported that miRNAs regulate the expression of *NEFL* mRNA(levels of which are known to be reduced in degenerating motor neurons in ALS), and that the expression of these miRNAs are also altered in ALS in a manner than can result in a loss of *NEFL* mRNA. We hypothesize that miRNA might play a significant role in expression and stability of *NEFM* transcripts and thus aimed to identify miRNAs regulating *NEFM* expression. We first examined the *NEFM*3'UTR lengths expressed in sporadic ALS (sALS; n=7) and neuropathologically normal control samples (n=5) by using 3' Rapid Amplification of cDNA ends (3'RACE). Three *NEFM* 3'UTR lengths were detected: 487bases(found in all spinal cord samples from sALS patients and controls),and additional 300 bases and 853 bases forms(found in some control and some sALS samples). MiRNA binding sites were determined using Miranda and Targetscan, as well as manual screening (for novel microRNAs) for recognition sites of at least seven nucleotides for miRNAs we have identified to be altered in ALS. We found 60 miRNA binding sites in *NEFM* 3 UTR. Differentially expressed miRNAs as determined by Taqman array are being assessed for their functional relevance to *NEFM* stability by luciferase assay. This is the first report describing alternate 3'UTR lengths of *NEFM* in ALS and control spinal cords, and suggests that alternative 3'UTRs may be key in dictating miRNA regulation of expression of NF mRNA species.

E6: EFFECTS OF RAPID-RATE PAIRED ASSOCIATIVE STIMULATION ON SHORT LATENCY AFFERENT INHIBITION

Philemon Tsang[1], Tanner Mackenzie[1], Peter Mi[1], Aaron Z. Bailey[1], Michael J. Asmussen[1], Aimee J. Nelson[1]

[1]*Department of Kinesiology, McMaster University, Hamilton, ON*

Paired associative stimulation is a protocol involving peripheral nerve stimulation and TMS to non-invasively create long term potentiation (LTP) like effects using Hebbian principles of plasticity. Transient changes in primary motor cortex (M1) have been observed via increases in motor evoked potentials (MEPs). PAS can also be applied at high frequencies (5Hz) to create long lasting LTP like effects and is known as rapid-rate paired associative plasticity (rPAS). RPAS over M1 not only increases MEPs but decreases inhibition of a sensorimotor circuit known as short-latency afferent inhibition (SAI). The purpose of the present study was to investigate the effects of rPAS applied over primary somatosensory cortex (SI) and investigate its effects on SAI. This was done by repeated pairing of median nerve stimulation and TMS applied over SI at 5Hz. The interstimulus interval (ISI) between median nerve stimulation and the TMS pulse was set to each subject's N20 latency for SI and N20 + 5ms for M1. SAI was measured before and at 5-20 minutes, 25-40 minutes, and 45-60 minutes following rPAS over left M1 and SI. SAI was elicited in the abductor pollicus brevis (APB) muscle by median nerve stimulation. SAI was quantified by measuring MEPs in the presence of nerve stimulation normalized to MEPs without nerve stimulation. Preliminary results indicate minimal decreases in SAI following SI rPAS. In contrast, SAI is significantly decreased at all time points following M1 rPAS. These novel findings may provide future direction for developing neural plasticity paradigms for SI.

Acknowledgements: Supported by Natural Sciences and Engineering Research Council to AJN

E7: EFFECTS OF OBSTACLE MOTION AND REDUCED PLANNING TIME ON THE OBSTACLE AVOIDANCE STRATEGIES OF YOUNG ADULTS

Joshua J. Fisher[1], Michael P. Bijman[1], Maya K. Goldman[1], and Lori Ann Vallis[1,2]

[1]*Dept. of Human Health & Nutritional Sciences, University of Guelph, Guelph, ON*
[2]*Schlegel-University of Waterloo Research Institute for Aging, Kitchener, ON*

Modifying gait in order to successfully navigate through cluttered environments is a common task of daily living. There exists an abundance of research investigating the strategies used by humans to avoid stationary obstacles [e.g. 1,2]. However, the understanding of the visually guided locomotor adjustments associated with dynamic obstacle avoidance tasks is limited. The objective of this study was to characterize and quantify these dynamic obstacle avoidance behaviours among young adults (n=9, aged 20.9 ± 0.93 years) in order gain insight into how obstacle motion, as well as reduced planning time, may influence avoidance strategies. Kinematic data were collected as participants stepped over a dynamic obstacle located three steps after a light gate trigger. Participants completed 54 obstructed walking trials (dynamic without delay, dynamic with 333 ms delay and static obstacle positions). Toe clearances, toe off distance, landing distance, step durations, and velocities were used to analyze avoidance strategies. Neither obstacle motion nor delayed obstacle motion significantly affected any outcome measures. It appears that avoidance strategies for dynamic and static obstacles are similar in a young adult population, perhaps due to the ability to quickly integrate sensory information and change on-going locomotor behaviour. The results of this study provide the background information necessary for future studies investigating dynamic obstacle avoidance among older adults.

References: [1] Chen et al. (1991) J Gerontol 46:M196-M203 [2] Lu et al. (2006) Gait Posture 23:471-479

E8: SPATIAL SEPARATION BETWEEN A REPETITIVE BACKGROUND SOUND AND A DEVIANT SOUND ENHANCES NEURAL SENSITIVITY TO THE DEVIANT SOUND IN THE RAT AUDITORY MIDBRAIN

Chirag R. Patel, and Huiming Zhang

Department of Biological Sciences, University of Windsor, Windsor, ON, Canada

The acoustic world is constantly changing. The ability to recognize acoustic changes is critical for the behavioural needs of animals. Neural processing of acoustic changes has been studied by using an oddball paradigm, in which a deviant sound is occasionally interspersed in otherwise repetitively presented standard sounds. Previous research was conducted in an artificial listening condition in which sounds were delivered only to one ear. In a real world situation, a deviant sound typically has a spatial location different from repetitive background sounds. Therefore, in the present study we examined whether neural sensitivity to a deviant sound was affected by a spatial separation between deviant and standard sounds. Using single unit recordings, we found that neurons in the auditory midbrain had various degrees of sensitivity to a deviant sound when both standard and deviant sounds were presented directly in front of the animal (0°). For many neurons, the sensitivity to a deviant sound located at 0° was enhanced by moving a standard sound from 0° to a location ipsilateral to the side of the brain on which neurophysiological recordings were made. Furthermore, when a standard sound was located at 0°, neural sensitivity to a deviant sound was enhanced when the deviant sound was from an ipsilateral azimuth. Neurons sensitive to deviant sounds were located in the belt areas of the auditory midbrain. These results provide an insight into auditory deviance detection in a real world situation.

Acknowledgements: Supported by an NSERC DG to HZ and an NSERC PGS to CRP

E9: DYNAMIC NERVOUS SYSTEM OBJECTIVES

Joshua G. A. Cashaback[1], Tyler Cluff [2]

[1] *The Brain and Mind Institute, Western University, London, ON*
[2] *Center of Neuroscience Studies, Queen's University, Kingston, ON*.

Our nervous system selects motor commands that allow us to perform everyday tasks. Empirical evidence suggests that the nervous system considers many, sometimes competing objectives when choosing these motor commands. For example, during fatiguing contractions there are continual increases in muscular cocontraction and joint moment variability. Muscular cocontraction increases joint stability, but is energetically expensive and increases fatigue. Thus, the nervous system must compromise between energy efficiency and joint stability, and this balance seems to shift with fatigue. Here we investigate if the nervous system shifts the influence of its objectives during fatiguing task. Participants were instructed to maintain 40%, 70%, or 100% of their maximal elbow flexor moment, or as close to that level as possible, to exhaustion. We recorded the elbow moment and EMG of the biceps and triceps. We then predicted biceps and triceps activity by optimizing the trade-off between joint stiffness and energy efficiency. Interestingly, we found that fatigue shifted the relative influence of these competing objectives, and favoured joint stability at the expense of muscular energy efficiency. This change in strategy was highly correlated with measures of muscular contraction (R2 = 0.78) and joint moment variability (R2 = 0.57). A strong relationship also existed between our predicted and collected muscle activations (R2 = 0.94). These results show that the nervous system is able to dynamically control the balance between energy efficiency and joint stability in fatiguing tasks.

E10: INDIVIDUAL AND COMBINED INFLUENCES OF PRIMARY AUDITORY CORTEX AND THE POSTERIOR AUDITORY FIELD ON NEURONAL RESPONSES IN THE DORSAL ZONE OF AUDITORY CORTEX

Melanie A. Kok[1], Daniel Stolzberg[2], Trecia A. Brown[2], Stephen G. Lomber[1,2]
[1]*Schulich School of Medicine & Dentistry, University of Western Ontario*
[2]*Department of Physiology & Pharmacology, University of Western Ontario*

Hierarchical processing schemes for auditory cortex have been proposed based on anatomical connections; however, the functional nature of this network remains largely unexplored. Using cortical cooling deactivation, previous studies have addressed functional reciprocal connectivity between primary auditory cortex (A1), the anterior and posterior auditory fields (AAF and PAF), and second auditory cortex (A2). Thus, the purpose of the present study was to expand this functional assessment of inputs to a higher-order auditory area, the dorsal zone (DZ). Because they comprise the two largest auditory cortical inputs to DZ, cooling loops were placed over A1 and PAF based on electrophysiological mapping (A1) and known sulcal and gyral landmarks (A1 & PAF). Based on the current model of auditory cortical hierarchy, it was predicted that deactivation of these areas would significantly influence neuronal response rates in DZ. Neuronal responses in DZ were recorded in response to broadband noise stimuli, as well as pure tones, while A1 alone, PAF alone, or both A1 and PAF together were reversibly deactivated using cortical cooling. Cooling A1 alone significantly reduced neuronal responses in DZ, regardless of stimulus type. Deactivation of PAF alone had an effect on DZ neuronal responses, but these effects were not ubiquitous across stimulus sets. Together, these results support previous models of auditory cortical hierarchical organization, in that deactivation of the two largest auditory cortical inputs (A1 and PAF) resulted in declines in neuronal responses in DZ.

Acknowledgements: Supported by CIHR, NSERC and CFI.

E11: DELINIATION OF TONOTOPICALLY ORGANIZED CORE AND NON-PRIMARY AUDITORY CORTEX OF THE CAT USING HIGH FIELD FMRI

Amee J Hall and Stephen G Lomber
Schulich School of Medicine & Dentistry, University of Western Ontario

It has been theorized that the initial stages of cortical processing are tonotopically organized because this is one of the most basic elements of sound. In cats, there are four known tonotopically organized cortical areas: the anterior (AAF), posterior, and ventral posterior auditory fields and primary auditory cortex (A1). Electrophysiological and anatomical evidence have indicated that AAF and A1 form core auditory cortex. Using high-field functional magnetic resonance imaging (fMRI) this investigation defined the borders of all four tonotopically organized areas, identified core auditory cortex, and demonstrated tonotopy similar to that seen using more invasive techniques. Five adult cats were examined. Eight different pure tones or one broad-band noise (BBN) stimuli were presented in a block paradigm during continuous fMRI scanning. Analysis was performed on each animal individually using conservative familywise error thresholds. Group analysis was performed by extracting data from fMRI analysis software and performing a battery of statistical tests. A reflection of the tonotopic gradient is known to occur at borders between tonotopically organized areas. Therefore, high and low tones were used to delineate these borders. Activations in response to BBN as opposed to tonal stimulation demonstrated that core auditory cortex consists of both A1 and AAF. Finally, tonotopy was visualized in each of the four known tonotopically organized areas. In conclusion, fMRI is effective at defining all four tonotopically organized cortical areas and delineate core auditory cortex.

E12: DEVELOPMENT OF A RAT MODEL OF MULTISENSORY PROCESSING: INVESTIGATION OF THE ROLE OF CORTICAL INHIBITION ON MULTISENSORY INTEGRATION

Ashley Schormans[1], Marei Typlt[1] and Brian L. Allman[1]
[1]*Department of Anatomy and Cell Biology, Schulich School of Medicine and Dentistry, Western University, London, ON*

Throughout the mammalian cortex there are functionally-specialized regions that are largely populated by neurons capable of integrating information from more than one sensory modality (e.g., hearing and vision). However, not all neurons in a given multisensory cortical area are equally responsive to multisensory stimuli; some neurons respond overtly to both auditory and visual stimuli, whereas others only respond to a single modality. At present, it remains uncertain what anatomical and/or physiological factors contribute to each neuron's responsiveness to multisensory stimuli. Because it has been speculated that the level of local GABA-ergic inhibition influences cortical multisensory processing, we are developing a rat model in which we will compare the spiking responses of a population of neurons in the extrastriate visual cortex to auditory, visual and audiovisual stimuli that are presented before and after pharmacological blockage of local GABA-ergic inhibition. It is our working hypothesis that although the blockage of inhibition will cause more neurons to respond overtly to both auditory and visual stimuli, these "new" multisensory neurons will show impaired multisensory integration; i.e., they will fail to show a greater response when the audiovisual stimuli are combined compared to when either stimulus is presented alone. Such impaired multisensory integration could have significant implications for the performance of multisensory behaviours in circumstances where cortical inhibition has been compromised (e.g., psychiatric disorders or following hearing loss).

Acknowledgements: Supported by NSERC.

E13: DOES CHRONIC STRESS LEAD TO AUDITORY PROCESSING DYSFUNCTION AND EXACERBATE NOISE-INDUCED HEARING LOSS?

Marei Typlt[1], Julia M. Abitbol[1], Ashley Schormans[1] and Brian L. Allman[1]
[1]*Department of Anatomy and Cell Biology, Schulich School of Medicine and Dentistry, Western University, London, ON*

Hearing sensitivity can be influenced by environmental factors such as loud noise and psychological stressors. Excessive noise exposure can damage the sensory cells in the inner ear causing hearing loss, whereas acute stress can provide a protective function and hypersensitivity to the auditory system. Despite the prevalence of chronic stress in society, its impact on the auditory system is not fully understood. What is known is that the neurons in the auditory system are particularly vulnerable to chronic stress. In the present study, we are using a rat model to investigate whether 1) chronic stress leads to auditory processing dysfunction, including impairments in hearing sensitivity, and 2) if chronic stress prior to noise exposure exacerbates the level of noise-induced hearing loss. To induce chronic stress, rats are placed in a plastic restraint device that limits their ability to move for 6 hours/day for 21 consecutive days. To assess features of auditory processing, click- and tone (4 and 20 kHz) evoked auditory brainstem responses (ABRs) are performed under anesthesia at baseline, and the results will be compared to ABRs following chronic stress and/or noise exposure (12 kHz tone at 120 dB for 1 h). Hearing sensitivity at the different frequencies will be determined by the ABR thresholds. Finally, by comparing the relative amplitudes and latencies of the various waves of the ABR (which reflect the neural activity at successive relay nuclei in the central auditory system), we will identify whether chronic stress leads to auditory processing dysfunction.

Acknowledgements: Supported by Western Academic Development Fund.

E14: COMPARING NEUROMUSCULAR FUNCTION IN HEALTHY OLDER AND YOUNG ADULTS

Neal B. McKinnon[1] and Timothy J. Doherty[1,2]
[1]*School of Kinesiology, Western University, London, ON*
[2]*Department of Physical Medicine and Rehabilitation, Schulich School of Medicine and Dentistry, Western University, London, ON*

The reduced number of motor units (MU) in a given muscle and the associated loss of muscle mass and strength (termed sarcopenia) is a hallmark of normal human aging. This study investigated the relationship between MU properties and the strength and power of two lower limb muscles in healthy old and young adults. Twelve older adults (six male, six female; mean age, 77 ± 5 yrs) and twelve young adults (six male, six female; mean age, 24 ± 3 yrs) were studied. MU properties of the tibalis anterior (TA) and vastus medialis (VM) muscles were determined using decomposition-enhanced spike-triggered averaging (DE-STA). The maximal strength and peak power output of these two muscles were also measured using the Biodex Systems 3 dynamometer. Motor unit number estimates (MUNE) of the TA were significantly reduced ($P>0.05$) in older adults (102 ± 76) compared to young adults (234 ± 109), primarily as a result of significantly larger surface-detected motor unit potentials (S-MUP) in older adults (63 ± 29 μV) compared to young subjects (28 ± 14 μV). Although VM S-MUP values were larger in older adults compared to young, the difference was not significant. Maximal strength and power were normalized to subject's body weight and were significantly larger in both the TA and knee extensors of young adults compared to old. Results from this study indicate that changes in MU properties of the TA and VM occur with ageing, and this effect may be greater in the TA muscle. Further, power, especially in the knee extensors, may be a more sensitive measure of neuromuscular health than strength.

Acknowledgements: This study was supported by the Ontario Graduate Scholarship

A: Cognition and Behaviour

A37: RAT MODEL FOR AMYOTROPHIC LATERAL SCLEROSIS (ALS) WITH FRONTOTEMPORAL DYSFUNCTION (ALS-FTD)

Wencheng Yang(1), Kathryn Volkening(1), Rob Bartha(1), Susanne Schmid(2), Michael J. Strong(1)
(1)Robarts Research Institute and (2) Department of Anatomy & Cell Biology, Western University

Background: The presence of frontotemporal dysfunction in ALS patients (ALS-FTD) is a significant negative prognostic factor in survival. Its neuropathological hallmark is the presence of cortical and subcortical neuronal and glial phospho-Thr^{175} tau (pThr^{175}-tau) deposition initially in the entorhinal cortex, followed by hippocampus, anterior cingulate gyrus and frontal cortex. No in vivo model currently exists for this process.
Methods: Twelve adult female Sprague Dawley rats underwent bilateral hippocampal inoculations with a total dose of 1.32 x 10^{10} vector genomes (2 groups of 6 received either rAAV9-*wt*-tau or rAAV9-Thr^{175}Asp-tau (pseudophosphorylated tau) (AUP #2013-12)). All rats underwent Morris water maze testing and gait testing prior to receiving inoculations. At 1, 2, 3 and 6 month post inoculation, all rats underwent gait analysis and Morris water maze testing, with neuroimaging at months 1 and 6. Three rats from each group were killed at month 1 and 6. Immunohistochemical studies included anti-tau, pThr^{175}-tau, TDP43 and GSK3β.
Results: A significant decrease in leaning ability was observed at month 3 in rAAV9-Thr^{175}Asp-tau inoculated rats, whereas at 6 months, both groups were equally impaired. MR spectroscopy suggested neuronal loss only in rAAV9-Thr^{175}Asp-tau inoculated rats. Expression of pThr^{175}Asp-tau was associated with increased TDP43 and GSK3β immunoreactivity was observed. There was no locomotor dysfunction observed across time points.
Conclusion: Stereotaxic bilateral hippocampal inoculations of rAAV9-Thr^{175}Asp-tau is a potential *in vivo* model of ALS-FTD.
Research supported by a "Western Strategic support for CIHR" grant (2013)

A38: CHRONIC STRESS AND COGNITIVE FLEXIBILITY

Erika K. Lui, Manraj Chahal, Nikita Puri, Misbah Salim, Elham Satvat
School of Public Health & Health Systems, University of Waterloo, ON, Canada

Recent findings suggest that functional neurogenesis is required for learning novel changes or new strategies in a familiar environment. Chronic stress and corticosterone (CORT) treatment have been shown to inhibit adult hippocampal neurogenesis. The effects of chronic stress on cognitive performance are complex, task specific and reversible. We investigated the effects of chronic CORT treatment with and without a recovery period on cognitive flexibility using a water maze protocol that incorporated reversal training. We hypothesized that chronic CORT treatment, which has been shown to suppress hippocampal neurogenesis, would attenuate cognitive flexibility. New neurons were labeled by injecting rats with BrdU (4x50 mg/kg) on the first day after drug treatment (40 mg/kg CORT or vehicle). Drug treatment continued for either 14 or 22 days and spatial performance was assessed on days 18 to 20 in the water maze. CORT-treated rats with a recovery period showed improved spatial memory. Cognitive flexibility was assessed on days 21 and 22 by reversal task, in which the hidden platform was placed in a new location. Remarkably, the CORT-treated rats without a recovery period showed enhanced cognitive flexibility, measured by shorter latency to find the new location of the hidden platform. Retention was also assessed on day 23 and regardless of drug treatment and recovery period, rats spent more time in the target quadrant than in the opposite quadrant. Brain tissues were collected half an hour after the probe test and are currently being analyzed for BrdU labeling.
Acknowledgment: The Brain and Behavior Research Foundation

A39: DIFFERENTIAL CONTRIBUTIONS OF *DE NOVO* AND MAINTENANCE DNA METHYLTRANSFERASES TO OBJECT MEMORY PROCESSING IN THE RAT HIPPOCAMPUS AND PERIRHINAL CORTEX: A DOUBLE DISSOCIATION

Krista A. Mitchnick[1], Samantha Creighton[1], Matthew O'Hara[1], Bettina E. Kalisch[2] and Boyer D. Winters[1]
[1]Department of Psychology and Collaborative Neuroscience Program, [2]Department of Biomedical Sciences and Collaborative Neuroscience Program, University of Guelph, ON

Epigenetic mechanisms are crucial for certain types of memory formation. Specifically, DNA methylation is necessary for long-term memory (LTM) in various brain regions, including the hippocampus (HPC); however, its role in the perirhinal cortex (PRh), which is critical for object memory, has not been characterized. Moreover, the mnemonic effects of selective DNA methyltransferase (DNMT) inhibition have not been investigated, despite their distinct *de novo* (DNMT3a, 3b) and maintenance (DNMT1) roles. Consequently, we assessed the effects of various DNMT inhibitors (DNMTi) within the HPC and PRh of rats using the object-in-place paradigm. The cytidine analog 5-AZA impaired LTM when infused into the HPC, but not when administered into the PRh, whereas the non-nucleoside DNMTi RG-108 impaired LTM in both areas. Further, intra-cranial administration of siRNAs implicated DNMT3a and DNMT1 in the HPC and PRh effects, respectively. mRNA expression analyses revealed concordant results, as only *de novo DNMT3a* and *DNMT3b* mRNA was upregulated in the HPC (dentate gyrus; DG) post-learning, whereas *DNMT1* mRNA was selectively upregulated in the PRh. Preliminary data suggest heightened expression of memory-enhancing genes (*BDNF*) and a concomitant down-regulation of memory-suppressing genes (*PP1*) post-learning, as well as an increase in neurogenesis-related genes specifically in the DG (*Disc1, NeuroD1*). These results establish a functional double dissociation between the HPC and PRh, demonstrating differential involvement of DNMTs across brain regions for different types of mnemonic processes.
Acknowledgements: Supported by NSERC

A40: A NOVEL NEUROMODULATOR: ACTIONS OF TENEURIN C-TERMINAL ASSOCIATED PEPTIDE (TCAP-1) ON CORTICOTROPIN-RELEASING FACTOR (CRF)-MEDIATED STRESS-ASSOCIATED BEHAVIOURS

Rebecca Woelfle[1], Yani Chen[1], Dhan Chand[1], Laura Tan[1], Suzanne Erb[2] and David Lovejoy[1]
[1]Department of Cell and Systems Biology, University of Toronto, Toronto, Ontario [2]Department of Psychology, Centre for the Neurobiology of Stress, University of Toronto at Scarborough, Toronto, Ontario

On the last exon of the teneurin transmembrane protein, there is a cleavable bioactive peptide called the teneurin C-terminal associated peptide (TCAP). Out of the four TCAP isoforms, only TCAP-1 is independently transcribed from teneurin, and induces a number of morphological changes in neurons including neurite outgrowth, increased spine density, and cytoskeletal reorganization. TCAP-1 exerts its neuroprotective effects by binding to β-dystroglycan (β-DG) and activating the MEK-ERK1/2 pathway. Recent studies suggest that these neuroprotective mechanisms are associated with TCAP's modulatory effects on stress-related behaviours. Stress stimulates the release of corticotropin-releasing factor (CRF), activating the HPA axis and stress-associated behaviours. As seen in rodent models of anxiety, TCAP-1 inhibits the CRF-mediated stress response. In particular, TCAP-1-treated rodents show reduced anxiety-related behaviours and inhibited CRF-induced reinstatement of cocaine addiction. Also, TCAP-1-treated rats show altered behavioural responses in the elevated plus maze, open field test, and acoustic startle test. However, TCAP-1 has no effect on the HPA axis or on CRF receptor-binding activation. Thus, without affecting HPA axis components, TCAP-1 may be blocking downstream components of CRF receptor activity, thereby attenuating the physiological actions of CRF.
Acknowledgements: Supported by NSERC

A41: DIFFERENTIAL MODULATION OF UNCONDITIONED AND CONDITIONED FEAR BY CB1 RECEPTORS IN ADULT MALE RATS

Jonathan J. Simone[1], Matthew R. Green[2], Travis E. Hodges[2], & Cheryl M. McCormick[1,2]
[1]Department of Biological Sciences, Brock University, St. Catharines, ON [2]Department of Psychology, Brock University, St. Catharines, ON

Using the highly selective CB1 receptor agonist ACEA, and antagonist AM251, we compared the effects of CB1 receptor signalling on unconditioned and conditioned fear responses in adult male rats. CB1 receptor effects on unconditioned fear were assessed using elevated plus maze, and open field testing. Conditioned fear was analyzed using a classical auditory fear conditioning paradigm. As CB1 receptors are known to elicit changes in intracellular signalling cascades implicated in fear behaviours, we performed an additional study investigating the effects of ACEA on hippocampal ERK1/2 and Akt signalling. When tested on the elevated plus maze and the open field test, AM251 and ACEA treated rats displayed increased unconditioned fear relative to vehicle treated controls. Neither AM251 nor ACEA had any effect on cued-fear recall, however AM251 impaired, and ACEA enhanced, fear extinction. To determine the effects of ACEA on ERK1/2 and Akt signalling, rats were injected and brains harvested at various post-injection time points. ACEA was seen to decrease phospho-ERK1/2 expression in the dorsal hippocampus 30 minutes post-injection, and increase phospho-ERK1/2 expression in the ventral hippocampus 60 minutes post-injection. There was no effect of ACEA on phospho-Akt expression in either region at any of the time points examined. Taken together, these results demonstrate a differential regulation of unconditioned and conditioned fear by CB1 receptors in adult male rats, and suggest a possible role of ERK1/2 signalling in these behavioural effects.
Acknowledgements: Supported by NSERC and OGS

A42: THE ROLE OF NOREPINEPHRINE IN THE DENTATE GYRUS DURING A DELAYED-NON-MATCH-TO-POSITION TASK INVOLVING PATTERN SEPARATION

Rachel Lackie[1], Stephanie L. Grella[1], Sarah M. Gomes[1], and Diano F. Marrone[1,2]
[1]Wilfrid Laurier University, Waterloo, ON, Canada, [2]McKnight Brain Institute, Univ. of Arizona, Tucson, AZ, USA

Contextual information is represented in the dentate gyrus (DG) of the hippocampal formation through recruitment of distinct neurons. The phenomenon by which different contexts produce different activation patterns is termed "pattern separation", and is contingent on the integrity of the DG. Norepinephrine (NE), naturally released in the DG in response to novelty, forces memory systems to switch from retrieval to encoding to incorporate "novel" information by resetting activation patterns despite placement in the same context twice. Thus, we hypothesized that activation of β-adrenergic receptors prior to encoding would facilitate memory retrieval, while activation experienced after encoding and prior to retrieval would impair memory. In a radial 12-arm maze, rats learned to obtain a reward from one arm of the maze (sample phase, encoding) and 10 min later were given a choice, between the previously rewarded arm and a newly baited arm (choice phase, retrieval). As the distance between the arms narrowed during the choice phase, the task became more DG-dependent. The β-adrenergic agonist isoproterenol and the antagonist propranolol were infused bilaterally into the DG prior to encoding or retrieval and choice accuracy was measured.

A43: THE INFLUENCE OF CULTURE ON RHYTHM PROCESSING

Jocelyn Bentley[1], Daniel J. Cameron[2], Eric Moryoussef[2], Jessica A. Grahn[2,3]
[1]*University of Toronto, ON*
[2]*The Brain & Mind Institute, Western University, London, ON*
[3]*Dept. of Psychology, Western University, London, ON*

Does culture influence perception and neural processing of musical rhythm? In this study, we tested participants from East Africa and North America with musical rhythms from each culture's music, to identify the aspects of rhythm processing that are culturally influenced. Both groups completed three tasks: rhythm reproduction, rhythm discrimination, and beat tapping. We expected performance on all tasks to be influenced by the culture of both the rhythm and the participant. For the reproduction task, group and rhythm culture interacted such that East African participants were significantly better at reproducing East African rhythms, but North Americans did not significantly differ in reproduction accuracy between rhythm types. For the discrimination task, there was no effect of (or interaction with) rhythm type. For beat tapping, accuracy was greater for the rhythms from the home culture of the participant. Additionally, East African participants tapped to more metrical levels than North Americans for all rhythm types, and both groups tapped to a greater number of metrical levels for the East African rhythms. Additionally, we recorded electroencephalography (EEG) from East African participants while they listened to rhythms. They showed greater power of EEG frequencies to metrical frequencies while listening to East African compared to Western music rhythms. Overall, these results demonstrate an influence of culture on rhythm production, beat tapping, and potentially on entrainment in EEG. However, the discrimination task may not have been sufficiently sensitive to detect the influence of culture.

Acknowledgements: Supported by NSERC, Students for Development, Western International Research Fund, and CHRP (NSERC).

A44: IMMEDIATE EARLY GENE EXPRESSION IN THE PREFRONTAL CORTEX FOLLOWING CONTEXTUAL ALTERATIONS AND SHIFTS IN COGNITIVE STRATEGY.

Sarah M. Gomes[1], Stephanie L. Grella[1], Brandy J. Schmidt[2], Elham Satvat[1], Etan J. Markus[2], and Diano F. Marrone[1, 3]
[1]*Wilfrid Laurier University, Waterloo, ON, Canada,* [2]*University of Connecticut, Storrs, CT, USA,* [3]*McKnight Brain Institute, Univ. of Arizona, Tucson, AZ, USA*

Using the expression of the mRNA coding for activity-regulated cytoskeletal protein (Arc), we recently showed that when rats are trained to utilize two different cognitive strategies while traversing an identical trajectory, in the absence of external cues, strategy-specific remapping occurs in the hippocampus. That is, hippocampal place cells maintain multiple representations of contexts and can "remap" (i.e., switch flexibly between representations). Because this design allows the cellular activity linked to task strategy to be dissociated from that related to path travelled, it may also be insightful in examining the patterns of Arc expression within several regions of the prefrontal cortex. The prefrontal cortex has been implicated in decision making and response selection but the degree to which neurons in the infralimbic, prelimbic, and orbitofrontal cortices exhibit unique patterns of activity is unclear in a situation in which both the trajectory and reward obtained remain the same. These results will provide data on the degree to which these prefrontal regions provide response selection based on strategy, independent from changes in overt behaviour.

Acknowledgements: *Supported by NSERC, NARSAD, OMHF.*

A45: PHASIC AND TONIC ACTIVATION OF THE LOCUS COERULEUS INDUCES GLOBAL REMAPPING IN THE DENTATE GYRUS.

Stephanie L. Grella[1], Hilary T. Edison[3], Jonathan Neil[3], Irina V. Odintsova[1], Carolyn W. Harley[3], and Diano F. Marrone[1,2]
[1]*Wilfrid Laurier University, Waterloo, ON, Canada,* [2]*McKnight Brain Institute, Univ. of Arizona, Tucson, AZ, USA,* [3]*Memorial University of Newfoundland, St. John's, NL, Canada*

The role of norepinephrine (NE) in sculpting representations formed by the hippocampus remains poorly understood. Locus coeruleus (LC) neurons, (source of hippocampal NE input), are activated in response to novelty, producing brief phasic firing that induces transient potentiation of the perforant path input to the dentate gyrus (DG) enhancing DG throughput. These effects suggest novelty-associated phasic activation of the LC may induce a reset of representations in the DG (remapping), a possible mechanism for incorporating novel information into existing representations. The distribution dynamics of the mRNA of immediate early genes *Arc* and *zif268*, allow us to map the activity history of individual neurons activated within the hippocampus of animals engaged in spatial processing using fluorescence *in situ* hybridization and confocal microscopy. Rats were placed in either 1.) same context twice (A/A) or 2.) two different contexts (A/B). Following the first context exposure, rats were infused unilaterally, or bilaterally, with glutamate in the LC (phasic activation). In addition, separate groups of rats were infused bilaterally with Orexin A, Bethanechol, and CRF (substances previously shown to increase tonic LC discharge) and clonidine (decreases tonic LC discharge) to assess remapping effects in the DG, CA1 and CA3 regions of the hippocampus.

A46: EARLY LIFE REPETITIVE BINGE EXPOSURES TO TOLUENE LEADS TO LESS SEVERE TOLUENE INTOXICATION AS AN ADULT

Meghan N. McKay & Bruce E. McKay
Department of Psychology, Wilfrid Laurier University, Waterloo, Ontario, Canada

Toluene is an organic solvent and the psychoactive component of numerous industrial and household products including paint thinner, and cleaners. These products are commonly abused, as inhalation of toluene vapour induces euphoria which progresses to functional neurological and motor impairments. The highest abuse rate is for early adolescents, which has many neurodevelopmental implications for later life drug use. Here we investigated the effects of early life adolescent (PND17-20) exposures to repeated binge-like toluene inhalations (15 min; 5000 ppm) on behavioural (exploratory and anxiety-like behaviours) and neurological impairments (tremoring, myoclonus, falling) exhibited from a subsequent young adult (PND60-61) exposure to toluene. Impairments were measured during young adulthood using a combination of open field measurement, and a neurological assessment during and following toluene exposure. Repeated toluene use during adolescence resulted in delayed onset and a faster recovery time of neurological impairments, and more locomotion during the first 10 min of the recovery period in comparison to rats who had received only a single toluene exposure during adolescence. Our results suggest that repeated exposures to toluene during early life leads to a less severe toluene intoxication during subsequent use later in life.

Acknowledgements: Supported by a Discovery Grant from NSERC (B.E.M).

A47: GEOMETRICAL CONCEPTS IN THE BRAIN: AN FMRI STUDY ON FIGURE DEPENDENCY

Tzu-ching Chiang[1], Chao-Jung Wu[2]
[1] *Brain and Mind Institute, Department of Psychology, University of Western Ontario*
2 Department of Educational Psychology and Counseling, National Taiwan Normal University, Taiwan

What kinds of representations are stored in the brain for geometrical concepts we have learnt in the primary school? We can speak out without a second thought some geometrical concepts such as 'triangle inequity theorem'. However, some theorems require more time to respond, such as 'In a triangle, the longest side is across from the largest angle', or 'the opposite sides of a parallelogram are parallel'. To what extent of differences in the brain to deal with the two types of known concepts? Two experiments with different groups of subjects were executed to clarify the issue. The first experiment was a behavioral study to differentiate the two types of learnt concepts, With the control of background knowledge of subjects, reaction times and accuracy of each question, the k-mean cluster results showed 2 distinctive types of questions, one was primed by geometrical figures, called 'figure questions'; the other was immune from the influence of geometrical figures, called 'rule questions'. The fMRI study used parts of appropriate questions from the 1st experiment. The contrast, 'figure questions' vs 'rule questions', showed activation in the occipital cortices, parietal lobes and middle frontal lobe, and deactivation in the anterior cingulate cortex, precuneus/cuneus, and the angular gyrus/superior temporal lobe. Meanwhile, the questions with the accuracy above 0.75 activated amygdala/hippocampus, angular gyrus/lateral sulcus and anterior/mid/posterior cingulate cortex, compared to the questions with accuracy below 0.4. The results verifies 2 corespondent systems in the brain.

Acknowledgement: Supported by Ministry of Science and Technology, Taiwan.

A48: ELUCIDATING THE ROLE OF STRIATAL CHOLINERGIC TONE IN STRIATAL COGNITIVE FUNCTIONS.

Guzman MS[1,3], Rosborough K[2,3], Gonçalves DF[1,3], Lopes-Borges J[4], Arredondo A[2], Jacobsen J[5], Caron M[5], Prado MAM[1, 2,3], Prado VF[1,2,3].
1. Department of Physiology & Pharmacology, Schulich School of Medicine & Dentistry, 2. Department of Anatomy & Cell Biology, Schulich School of Medicine & Dentistry, 3. Robarts Research Institute;
4. Instituto de Ciências Biológicas, Universidade Federal de Minas Gerais 5. Duke University Medical Center.

The striatum has been implicated in learning and memory processes like appetitive learning, skill learning, goal-directed behaviour and executive function. However, the exact role of striatal cholinergic interneurons in these processes is not well understood. Recently it has been demonstrated that striatal cholinergic neurons are co-release acetylcholine (ACh) and glutamate and use these two neurotransmitters to differentially regulate functions controlled by the striatum. We generated two mouse lines, D2-Cre-fx/fx and VGluT3-Cre-fx/fx, in which ACh release was selectively eliminated in the striatum by deleting the vesicular acetylcholine transporter (VAChT) gene. Here we use these mutant mice to examine the importance of striatal ACh for cognitive functions directed by the striatum. Investigation of stimulus-response learning using Cued-Y maze and Cued-Water maze showed that cued-direct behaviour was disturbed in D2-Cre-fx/fx, while VGluT3-Cre-fx/fx animals did not show any deficits. In addition, spatial memory, as determined by the spatial version of the Morris Water maze, was preserved in both mouse lines. Furthermore, we also evaluated behaviour flexibility using the automated pairwise visual discrimination and reversal learning task. Both VAChT-deficient mouse lines were able to learn the task normally, but D2-Cre-fx/fx animals showed deficits in reversal learning while VGluT3-Cre-fx/fx mice did not show any deficits. These results suggest that striatal ACh might not have a role in the modulation of cued-directed learning and behaviour flexibility.

Supported by: CIHR, Heart & Stroke Foundation of Canada, NSERC.

A49: INVOLVEMENT OF THE HIPPOCAMPUS IN RAPID ENHANCING EFFECTS OF ESTRADIOL ON SOCIAL LEARNING

Kelsy Ervin, Amy Moore, Kathryn Sinclair, and Elena Choleris
Dept. of Psychology, University of Guelph, Guelph, ON N1G 2W1 Canada

Social learning is an adaptive learning strategy commonly assessed in rodents using the social transmission of food preferences (STFP), in which an observer interacts with a demonstrator who has recently eaten a novel food. The observer tends to prefer the food it smelled on the demonstrator's breath over other novel foods. Systemic 17β-estradiol (E2) enhances performance on the STFP within 45 min, acting through rapid mechanisms rather than genomic. The brain regions responsible for E2 enhancements of social learning are unknown. We focused on the hippocampus (HC) as systemic E2 increases spine density in the CA1 HC, intra-HC E2 rapidly enhances nonsocial learning, and HC lesions impair performance on the STFP. We infused E2 (vehicle, 25, 50, 100nM) into the CA1 HC of ovariectomized female observer mice 15min prior to a brief interaction with a same-sex demonstrator

mouse. We then tested the observers for food preference, taking measurements at the 30min, 2h, 4h, 6h and 8h intervals. The first measurement was therefore 45min after infusion, allowing us to assess rapid effects of estradiol. We used a difficult version of the STFP, in which control mice typically show no social learning, in order to see any enhancing effects. Our results show that intra-HC E2 did not rapidly improve learning on the STFP. This suggests that estrogens act in other regions to enhance social learning and that estrogens affect social and nonsocial learning through different pathways. These results help further our understanding of how estrogens act to rapidly enhance different types of learning.
Acknowledgements: Funded by NSERC.

A50: THE ROLE OF NMDA RECEPTORS IN CROSS MODAL OBJECT RECOGNITION IN MICE

Daniel Palmer[1], Emily Binsell[1], and Boyer D. Winters[1]
[1]Department of Psychology, University of Guelph, Guelph, ON

The N-Methyl-D-Aspartate (NMDA) receptor has been implicated in aspects of memory and cognition. Previous research with the spontaneous object recognition (SOR) task in rodents has revealed that NMDA receptor blockade in regions such as the perirhinal cortex disrupts long term memory if given prior to the acquisition of object information. Recently, a cross modal variation of the SOR task has been developed and adapted for mice. The present research project was interested in determining if NMDA activity is necessary for performance in this task. It was found that systemic administration of MK-801 (0.01mg/kg), an NMDA receptor antagonist, disrupted performance on the cross modal object recognition task when given prior to acquisition, but not when administered before retrieval. Interestingly, this effect was found with a relatively short retention delay of 30 minutes. This result suggests that NMDA receptors contribute to cross modal object representation beyond the requirements of long term memory acquisition, and may in fact be important for the process of multisensory integration.
Acknowledgements: Supported by NSERC.

A51: EFFECT OF SEROTONIN 1A AND 1B/D RECEPTOR ANTAGONISM ON ZEBRAFISH BEHAVIOUR

Steven Tran[1], Magda Nowicki[2], Stefan Markovic[2], Arrujyan Muraleetharan[2], and Robert Gerlai[1, 2]
[1]Department of Cell and Systems Biology, University of Toronto, Toronto, ON
[2]Department of Psychology, University of Toronto Mississauga, Mississauga, ON

The serotoninergic system is thought to be highly conserved across a number of vertebrate species including zebrafish. Activation of serotoninergic receptors mediates a large number of affective processes including anxiety and fear. In the current study we examined whether pharmacological blockade of serotonin (5HT) receptor subtypes in zebrafish alters measures of anxiety in a novel environment. To address this question, we initially exposed individual zebrafish to p-MPPF dihydrochloride (5HT1A antagonist) or GR55562 (5HT1B/D antagonist) for 30 minutes at different concentrations (0, 0.1, 0.5, and 1.0 mg/L) to examine baseline motor changes. Following the 30 minute drug exposure, zebrafish were placed in a novel tank to examine levels of anxiety. We report no significant impairments in motor patterns directly associated with serotonin receptor antagonism. However, blocking 5HT1A receptors decreased locomotor activity (total distance travelled) and increased erratic movements (angular velocity) in the novel environment, indicative of an anxiogenic effect. In addition, blocking 5HT1B/D receptors increased locomotor activity and decreased erratic movements, indicative of an anxiolytic effect. Overall, the results support behavioural and pharmacological approaches to investigate the function of serotoninergic receptors in zebrafish.
Acknowledgements: Supported by NSERC and OGS

A52: THE ROLE OF DNA METHYLATION IN OBJECT AND SPATIAL MEMORY IN THE RAT PERIRHINAL CORTEX AND HIPPOCAMPUS

Samantha D. Creighton, Krista A. Mitchnick, and Boyer D. Winters
Department of Psychology and Collaborative Neuroscience Program, University of Guelph, ON, Canada N1G 2W1

DNA methylation, an epigenetic mechanism catalyzed by DNA methyltransferases (DNMT), is crucial to the formation of various forms of long-term memory. Systematic inhibition of DNMT subtypes has revealed a dissociable contribution of DNMTs to object-in-place (OiP) memory in rats, such that maintenance DNMTs (DNMT1) in the perirhinal cortex and *de novo* DNMTs (DNMT3a) in the hippocampus are necessary for long-term but not short-term memory. As the OiP task is comprised of an object identity component, thought to be dependent on the perirhinal cortex, and a spatial component, thought to be dependent on the hippocampus, our recent findings suggest distinct epigenetic modifications may be required for object and spatial memory. The present study explored the differential role of DNMTs during tests of object identity (object recognition) and spatial memory (radial arm maze) via non-selective (RG108) and subtype specific (short-interference RNA specific to DNMT1 or DNMT3a) DNMT disruption in the perirhinal cortex and hippocampus. Preliminary findings are consistent with a requirement for DNMT involvement in PRh-mediated long-term object recognition memory consolidation, as rats were impaired with post-sample intra-PRh RG108 infusions when the retention delay was 24h, but not when it was 1h.
Acknowledgements: Supported by NSERC

A53: CAN SHORT-TERM DUAL-TASK TRAINING IMPROVE PERFORMANCE ON A SIMULTANEOUS OBSTACLE AVODIANCE AND AUDITORY STROOP TASK?

Timothy A. Worden[1], Codey Forrest[1], and Lori Ann Vallis[1]
[1] Department of Human Health and Nutritional Sciences, University of Guelph, Guelph

Current evidence on training protocols to improve dual-task performance is limited (Pellecchia, *J Motor Behavior*; 37(3): 239-246). The purpose of our project was to examine dual-task performance following a training protocol in healthy young adults (n=33). Two tests were used to examine dual-tasking ability; a computer based psychological refractory period test as well as a concurrent obstacle avoidance and auditory Stroop test. An initial baseline performance was collected on both tests before random assignment of subjects to a training group (no training, one week of training or four weeks of training). Training consisted of performing unobstructed overground walking and concurrent challenging cognitive tasks (e.g. auditory Stroop, backwards counting by 7). One week after the completion of training, subjects were re-tested on both dual-task tests as in Visit 1. Finally, participants were tested 5 weeks after Visit 2 to determine if training effects had been retained following a period of no training. Preliminary results from the Psychological Refractory Period test indicate that all groups significantly decreased response time ($p<0.05$) for stimuli two from Visit 1 to Visit 2, regardless of training group. Only the four week training group was able to decrease response time from Visit 2 (1.00 s) from to Visit 3 (0.94 s). For the concurrent walking and obstacle avoidance task a training effect was observed; the four week training group was significantly ($p<0.05$) more accurate at performing the auditory Stroop task compared to the one week trained group (95 % versus 89 %).
Acknowledgements: Project supported by NSERC

A54: THE EFFECTS OF BLOCKING DORSAL HIPPOCAMPAL DOPAMINE D1-TYPE RECEPTORS WITH SCH23390 ON SOCIAL LEARNING, FEEDING AND SOCIAL INTERACTIONS IN MALE AND FEMALE MICE

***Richard Matta,** Angela N. Tiessen, Michelle M. Kivlenieks, Angela M. Meersseman, Yaw O. Adjei-Afriyie, and Elena Choleris
Department of Psychology and Neuroscience Program, University of Guelph, Guelph, ON N1G 2W1 Canada

Dopamine (DA) is involved in drug abuse, feeding behavior and social learning. Our lab has previously found dopamine D1-type receptors to be involved in the social transmission of food preferences (Choleris et al., 2011), however, the brain site(s) of action remain unclear. The ventral tegmental area has direct dopaminergic projections to the hippocampus, which is well known for mediating learning and memory processes, and social learning. In this study, we micro-infused the DA D1-type antagonist SCH23390 (at 1, 2, 4 & 6 µg/µL) directly into the CA1 region of the dorsal hippocampus of adult male and female CD1 mice 15 minutes before a 30 minute social interaction where mice had the opportunity to acquire a food preference from a conspecific. In line with our systemic results, we found that the highest dose of SCH23390 blocked social learning, but had no effect on total food intake in both males and females. Video analysis of the social interactions also revealed that this social learning impairment could not be explained by a reduced exposure to the socially carried food odor, since SCH23390 treatment did not influence oronasal investigation. An olfactory discrimination control task using the effective dose of SCH23390 also revealed that both males and females could distinguish between the two food types used in the social learning test. These results suggest hippocampal DA D1-type receptors are involved in social learning and social interactions, but not food intake.
Acknowledgments: Supported by NSERC.

A55: THE RELATIONSHIP BETWEEN MENTAL ROTATIONS ABILITY, EYE MOVEMENT PATTERNS, AND SPATIAL TASK PERFORMANCE

Victoria A. Roach[1], Ngan T. Nguyen[2], James Krykylwy[3], Derek Mitchell[3], Sandrine de Ribaupierre[4], Roy Eagleson[2] and Tim D Wilson[1].
[1]Department of Anatomy and Cell Biology, Western University, London ON
[2]Department of Electrical & Computer Engineering, Western University, London ON
[3] Center for Brain and Mind, Western University, London, ON
[4]London Health Sciences Center, London, ON.

Mental rotations ability (MRA), a subset of spatial ability, is linked to success in anatomy and the STEMM disciplines. Like any ability, MRA differs in the general population. Some people can mentally rotate 2D and 3D objects with ease, while others have difficulty with these mental tasks. Previous research suggests that the cognitive processes underlying MRA are manifest in eye-movements. However, research has focused primarily on describing how individuals of high and low-MRA differ in eye-movement patterns rather than demonstrating how knowledge of these differences can be used to improve observational approaches and learning. This study aims to determine whether the eye-movement patterns (frequency of fixation, duration of fixation, salient features, and average visual scan path) of high-MRA individuals can be used to improve spatial task performance for low-MRA individuals. Undergraduate students at Western University will complete a standardized test of MRA (Shepard and Metzler Mental Rotations Test) while eye-movement metrics are collected. The eye-movement patterns of high-MRA individuals will then be used to train low-MRA individuals to improve performance on subsequent spatial tests. Results from these studies may be employed to guide the design and delivery of innovative eye-movement based approaches to improve instruction in anatomy and other STEMM disciplines.

A56: INHIBITION-RELATED DEVALUTION OF VISUAL STIMULI REPRESENTED IN SHORT- AND LONG-TERM MEMORY

David De Vito[1], Anne E. Ferrey[2], Katherine McArthur[1], and Mark J. Fenske[1]
[1]Department of Psychology, University of Guelph, Guelph, ON
[2]Child Study Center, Yale University School of Medicine, New Haven, CT

Cognitive inhibition triggers affective devaluation of environmental stimuli that are ignored or from which a response is withheld. Here we show that such 'inhibitory devaluation' also occurs for items represented in memory, even in the absence of external sensory stimulation. Participants in Experiment 1 were required to hold two different types of briefly-presented visual patterns in working memory until a cue indicated which pattern-type was the to-be-localized target for that trial. Affective evaluations made after each target-localization trial revealed significantly more

negative ratings for prior distractors within working-memory than for prior targets. To the extent that inhibition is critical for reducing potential distractor interference, this finding suggests that the negative affective consequences of inhibition are the same for items represented in short-term memory as they are for sensory stimuli. To assess whether such inhibitory-devaluation effects also occur for items represented in longer-term memory, affective ratings were obtained in Experiment 2 for previously-memorized words and line-drawn objects that were then presented in a Think/No-Think paradigm. Items whose retrieval was previously inhibited on No-Think trials subsequently received more negative ratings than non-inhibited baseline items. Taken together, our results suggest that inhibition within short- and longer-term memory may be critical, not only for prioritizing stimulus maintenance and retrieval, but also for determining subsequent affective value.

Acknowledgements: Supported by NSERC

A57: SELECTIVE ACTIVATION OF HIPPOCAMPAL G-PROTEIN COUPLED ESTROGEN RECEPTOR MAY IMPROVE OBJECT AND SOCIAL RECOGNITION IN THE ABSENCE OF SPATIAL CUES IN FEMALE MICE

Jennifer Lymer, Christopher Gabor, Anna Phan, Fiona Young-MacDonald, Heather Morris, Elena Choleris

Department of Psychology and Neuroscience Program, University of Guelph, Guelph

Learning and memory can be affected by estrogens on a rapid timescale (Phan et al., 2011, 2012). Estrogens act through at least 3 receptors, estrogen receptor (ER) α, ERβ, and the G-protein coupled estrogen receptor (GPER). Both systemic and intrahippocampal administration of 17β-estradiol, an ERα agonist and the GPER agonist, G-1 rapidly enhanced social recognition, object recognition and object placement, while administration of the ERβ agonist impaired social recognition, had no effect on object recognition and improved object placement. These paradigms were completed within 40min of treatment in the test mouse home cage which provides spatial cues that mice can use to assist in the recognition paradigms. The Y-maze can be used to eliminate most of these cues. Intrahippocampal administration of 17β-estradiol improved object recognition but not social recognition in the Y-maze. The current study investigates the role of GPER in the CA1 hippocampus on social and object recognition in the absence of spatial cues using a Y-maze. Mice were infused with the GPER agonist, G-1 (50, 100, 200, 300, 400nM). 15min later the mice were tested for social and object recognition using the Y-maze. All testing was completed within 40min of treatment, thus assessing rapid effects of GPER activation. Intrahippocampal infusion of G-1 improved both object (50, 200nM G-1) and social (100, 200, 300nM G-1) recognition in the Y-maze. This suggests that GPER in the hippocampus mediates rapid estrogenic improvements in object and social recognition learning even in the absence of spatial cues.

Acknowledgements: Supported by NSERC.

A58: HVC IS ACTIVATED BY THE PRODUCTION OF THE GARGLE CALL IN BLACK-CAPPED CHICKADEES (*POECILE ATRICAPILLUS*)

Shannon K. Mischler[1, 2]; Scott A. MacDougall Shackleton[1, 2]

Department of Psychology, University of Western Ontario, London, ON

Advanced Facility for Avian Research, London, ON

Black-capped chickadees are characterized by the production of a variety of highly complex vocalizations that they use in different contexts. One of these is the *fee-bee* song, which is most often produced by males during the breeding season in order to try and attract a mate, or to defend their territory. It has been shown that the neural song-control system is instrumental for the learning, production and maintenance of song (such as the *fee-bee*) in songbirds. This system includes brain regions such as HVC, the robust nucleus of the arcopallium (RA) and area X. Previous studies have found that the size of these brain regions vary significantly across seasons, being larger in volume during the breeding season. However in chickadees these seasonal changes are reduced. We hypothesized this is due to the production of complex learned non-song vocalizations throughout the year (e.g. the *gargle* and the *chick-a-dee* call). In this study, black-capped chickadees were subjected to behavioural manipulations in order to elicit the *fee-bee* song, *gargle*, *chick-a-dee* and *tseet* calls. The birds were then sacrificed and their brains were collected and processed by immunohistochemistry in order to examine motor-driven immediate-early gene (ZENK) expression in the song-control regions of the brain. The birds that produced the gargle call consistently, showed significantly more ZENK activation in HVC than birds that produced the *fee-bee* song, *chick-a-dee* and *tseet* calls. This suggests that HVC should be considered a vocal-control brain region rather than strictly a song-control region.

Acknowledgements: Supported by NSERC

A59: SYSTEMIC OR INTRAACCUMBENS APPLICATION OF AMPHETAMINE DIFFERENTIALLY ELICITS SUBTYPES OF 50 KHZ RAT VOCALIZATIONS

Kevin G. Mulvihill[1] and Stefan M. Brudzynski[1]

[1]*Department of Psychology, Brock University, St. Catharines, ON*

Ultrasonic vocalizations in rats serve as a behavioural index of their affective states. It has been established that production of 50 kHz calls, associated with appetitive states, involves activity of the ascending mesolimbic dopamine (DA) pathway from the VTA to the nucleus accumbens. The 50 kHz call category can be further subdivided into flat and frequency modulated subtypes based on sonographic characteristics. Little is known about the role of these subtypes and how they are generated. The purpose of the current study was to investigate whether the route of DA agonist application can have effect on parameters and subtypes of elicited 50 kHz calls. Injections of saline or the indirect DA agonist, amphetamine (AMPH) were made both systemically (1.5-2.0 mg/kg, subcutaneous) and directly to the brain (7 µg, intraaccumbens) with the resultant call profiles analyzed (N = 24). Systemically-induced AMPH calls were found to differ significantly in total number of generated calls, acoustic parameters, and subtype proportions when compared with those after saline (n = 12), as well as compared to intraaccumbens AMPH microinjections (n = 12). These results support the hypothesis that different routes of drug application differentially elicit 50 kHz call subtypes and modulate their acoustic parameters. Systemic application appears to more effectively induce affective signaling presumably by more complete activation of the mesolimbic DA system than local intraaccumbens injection.

Acknowledgements: Supported by NSERC.

A60: "BLINDSIGHT" AND SUBJECTIVE AWARENESS OF FEARFUL FACES: INVERSION REVERSES THE DEFICITS IN FEAR PERCEPTION ASSOCIATED WITH CORE PSYCHOPATHIC TRAITS

Lindsay D Oliver[4,5], Alexander Mao[3], and Derek GV Mitchell[1,2,4,5]

Departments of Psychiatry[1], Anatomy & Cell Biology[2], and Ophthalmology[3], Graduate Program in Neuroscience[4], Schulich School of Medicine & Dentistry, Department of Psychology, Brain and Mind Institute[5], University of Western Ontario, London, ON

Though emotional faces have been found to preferentially reach awareness, the present study utilized continuous flash suppression (CFS), and both objective and subjective indices of awareness, to determine whether they enhance subjective awareness and "blindsight". CFS induces potent perceptual rivalry via dichoptic presentations; one image is typically suppressed from awareness in favour of a dynamic noise image presented to the opposing eye. Under CFS, healthy adults localized a target disgusted, fearful, or neutral face (objective index), and rated their confidence in their response (subjective index) on each trial. Psychopathic traits were also measured to investigate their influence on emotion perception. As predicted, fear increased localization accuracy, subjective awareness, and "blindsight" of upright faces. Coldhearted traits were also inversely related to localization accuracy and subjective awareness, but not "blindsight", of upright fearful faces. In a follow-up experiment using inverted faces, increased localization accuracy and awareness, but not "blindsight", were observed for fear. Surprisingly, localization accuracy and subjective awareness of inverted fearful faces was positively correlated with coldheartedness. These results suggest that emotion enhances both pre-conscious processing and the qualitative experience of visual awareness. However, the distinct effects associated with "blindsight" and subjective awareness raise the possibility that pre-conscious and conscious processing of emotional faces rely on different cognitive mechanisms.

Acknowledgements: Supported by NSERC

A61: DETECTING EARLY NEURAL DYSFUNCTION IN FAMILY MEMBERS OF PATIENTS WITH FRONTOTEMPORAL DEMENTIA

Tamara P Tavares[4,5], Derek GV Mitchell[1,4,5], and Elizabeth Finger [3]

Departments of Psychiatry & Anatomy & Cell Biology, Psychology [1]

Clinical Neurological Sciences University of Western Ontario, London, ON [3]

Graduate Program in Neuroscience University of Western Ontario, London, ON [4]

Schulich School of Medicine & Dentistry, Brain and Mind Institute University of Western Ontario, London, ON[5]

Frontotemporal dementia (FTD) is a neurodegenerative disorder characterized by early behavioural impairments such as loss of empathy, emotional blunting and deficits in emotion recognition. Currently, the tools used to diagnose FTD are not sensitive to detect patients during the early course of the disorder. Thus, there is an urgent need to develop new diagnostic tools in order to detect patients early. Considering that deficits in emotional processing and protein levels occur early, related tasks may be valuable untapped tools that can facilitate earlier diagnosis in pre-symptomatic individuals. The present study will use the combination of functional neuroimaging during an emotional processing task and protein biomarkers to determine whether abnormalities are present in pre-symptomatic family members of patients with FTD. Participants will complete an fMRI scan during an emotional processing task, and undergo neuropsychological tests as well as blood and cerebrospinal fluid collection. We hypothesize that family members will show neural deficits during the emotional processing task and abnormal patterns of protein biomarkers that parallels the abnormalities in FTD. Currently, we are recruiting participants (current n = 19) and conducting preliminary analyses. Upon completion of this study, we will have determined abnormalities in neural activation and protein biomarkers prior to symptom onset. This approach may be applied to establish new tools for diagnosing and tracking disease progression.

Acknowledgements: Supported by Alzheimer's Society of Canada.

A62: DISSOCIATING THE PSYCHOACTIVE EFFECTS OF DISTINCT MARIJUANA COMPOUNDS IN THE MESOCORTICOLIMBIC CIRCUITRY

Jordan Zunder, Michael Loureiro & Steven R. Laviolette

Dept. of Anatomy & Cell Biology, Dept. of Psychiatry

University of Western Ontario. Schulich School of Medicine & Dentistry

London, Ontario, CANADA N6A 5C1

A growing body of evidence supports the link between heavy marijuana exposure and an increased risk of developing schizophrenia-related psychoses. However, marijuana smoke represents a complex mixture of chemical components, possessing dissociable psychoactive properties. Indeed, emerging clinical evidence suggests a functional dissociation between the two main pharmacological components of cannabis, cannabidiol (CBD) and Δ9- tetrahydrocannabinol (THC). Clinical imaging evidence suggests that THC and CBD may exert differential psychoactive effects in distinct mesocorticolimbic substrates. In the prefrontal cortical and amygdalar regions, CBD has been shown to be a weak antagonist of CB1 receptors. In contrast, THC acts as a partial CB1 agonist. Our previous work has shown that modulation of CB1 transmission in the BLA>mPFC pathway can mediate the emotional valence of an associative fear memory. Our current objective is to examine the roles of CBD vs. THC in mediating emotional learning and memory formation.

Our results suggest that CBD has rewarding properties in the nucleus accumbens shell (NASh) and blocks the formation of fear memory to a salient footshock, mediated by a serotonergic-dependent mechanism. In contrast, THC potentiates non-

salient fear memory formation to a sub-threshold footshock through a dopamine-dependent mechanism. We report evidence of a rostrocaudal hedonic gradient in the NASh that is sensitive to THC. *In vivo* electrophysiology results suggest a complex interplay between DAergic and GABAergic signaling in the VTA, which may account for our results.

A63: EVALUATING THE PATHOLOGICAL AND BEHAVIOURAL OUTCOMES OF AMYLOID BETA OLIGOMERS IN THE RAT

Ryan S. Wong, David F. Cechetto and Shawn N. Whitehead
Vulnerable Brain Laboratory, Dept. Anatomy and Cell Biology, Western University, London, ON, CANADA, N6A 5C1

Although Alzheimer's disease (AD) has been discovered well over a century ago, the field is still uncertain on how the disease progresses. Recently, significant amounts of research have begun to focus on a soluble oliogomeric form of amyloid beta (Aβ) peptide. *In vitro* studies have suggested that Aβ oligomers may play a significant role in the progression towards AD from a normal healthy brain. Human studies have also shown the correlation between clinical diagnoses of AD with elevated levels of Aβ oligomers. However, the field is lacking on the effects of amyloid beta oligomers in an *in vivo* model. The purpose of this project is to discover the spatial and temporal consequences of injecting Aβ oligomers into the rat brain by evaluating pathological and behavioural outcomes. We hypothesize that injecting Aβ oligomers into the rat brain will result in neurodegeneration, neuroinflammation and concomitant, behavioural and cognitive deficits. Aβ oligomers were injected either cortically or intracerebroventricularly into the rat brain. Survival time points were 1, 3, 7 or 21-days post surgery. Pathological and behavioural analyses were completed. Results demonstrate that low molecular weight Aβ oligomers crossed into the parenchyma of the rat brain caused neuroinflammatory responses. Overall our results indicate that injection of Aβ oligomers into the rat brain may be an alternative, non-transgenic strategy to investigate the effects of Aβ oligomers within the rat brain.

Acknowledgements: This work was funded by a CIHR-ETG to D.F.C and S.N.W along with Lawson-IRF, NSERC-DG and CIHR-OG support to S.N.W

A64: DEVELOPMENTAL STRESS AFFECTS AUDITORY LEARNING IN FEMALE, BUT NOT MALE, EUROPEAN STARLINGS (*STURNUS VULGARIS*)

Tara Farrell[1], Amanda Morgan[2], & Scott MacDougall-Shackleton[1,2]
[1]*Department of Psychology, Western University, London, ON*
[2]*Department of Biology, Western University, London, ON*

In songbirds, early-life environments are instrumental in shaping song development. As it is typically the male of the species that sings, most studies to date have been male-focused. However, song has evolved through signaler-receiver networks and the effect stress has on the ability to receive auditory signals is equally important, especially for females who use song as an indicator of mate quality. We subjected juvenile European starlings (*Sturnus vulgaris*) to either an *ad libitum* or unpredictable food-supply treatment from 35-115 days of age. In adulthood, we assessed learning in both auditory and visual dimensions. In an operant conditioning task, we found that females reared in control conditions acquired two auditory discriminations (absolute and relative frequency tasks) faster than females raised in our stressful conditions. There was no difference between treatment groups for males. However, there was a significant effect of treatment group on the number of errors committed per trial on a colour association task; food-restricted birds committed more errors than controls. Our results suggest the auditory system may be more robust to developmental stress in males than females. In conclusion, developmental stressors have sex-specific effects on cognition that could be the result of different selection pressures on each sex.

A65: REACHING THE LIMITS OF COGNITIVE RESOURCES: CONTROL STRATEGIES USED BY CHILDREN DURING A MULTI-TASK PARADIGM

Dorelle Hinton[1], Lori Ann Vallis[1]
[1]*Department of Human Health and Nutritional Sciences, University of Guelph, Guelph*

Dual motor tasks have been well studied in adults however little is known about strategies used by children during cognitive-motor multitasking paradigms. The current work increased cognitive load and motor tasks in a stepwise approach, and hypothesized that altered control strategies (e.g. slowing/stopping) would be used as attentional limit was reached. Healthy children aged 7 years (n=8) were asked to balance a ball on a Frisbee (non-dominant hand) and pick up a toy off the ground (dominant hand) in three postures: seated, standing and walking. The Auditory Stroop task was performed simultaneously during half of the trials. Preliminary findings suggest children age 7 partition concurrent motor-cognitive tasks. Walking speed was significantly slower for the pickup phase (0.47±0.052 m/s compared to 0.99±0.046 m/s for the toy approach phase; $F_{(1,17)}$ = 43.120, p<0.001) While walking, two answering patterns emerged: within pickup phase (64% of trials) or after (36%). Interestingly, trials where the child answered during pickup, the answer was correct only 65% of the time, no different than chance ($z_{(13)}$=1.069, *ns).* Conversely, trials where subjects answered after pickup were always correct, indicating that the ability to answer the cognitive task properly required a simplification of the overall motor task. Strategies to complete individual motor or cognitive tasks are well established in this age group however our findings highlight the use of compensation strategies in order to integrate a complex motor and cognitive task simultaneously.

Funding Support: NSERC Discovery Grant, University of Guelph College of Biological Sciences.

A66: SEX DIFFERENCES IN MYELINATION OF THE SONG CONTROL SYSTEM

Adam Piraino[1,2], David Sherry[1,2], Scott MacDougall-Shackleton[1,2]
[1]*Department of Psychology, The University of Western Ontario, London, ON*
[2]*Advanced Facility for Avian Research, The University of Western Ontario, London*

The song control system (SCS) is an intensively studied network in the songbird brain, responsible for the learning, production, and maintenance of song. Extreme sex differences exist within the SCS and in singing behaviour, making songbirds an excellent model to study sex differences in the brain. Previous work has examined volume, neural number and density of SCS nuclei, while other important components of brain nuclei have been relatively unexamined. Myelination of the SCS, vital to the function of the nuclei and network, is relatively unexamined. In the current study, we used adult male and female zebra finches to examine sex differences in myelination of the SCS, specifically because males sing while females do not. To measure myelination in the SCS, we used immunohistochemical labeling of myelin basic protein (MBP). Regions examined included nucleus HVC, RA, and LMAN, in addition to tract HVC to RA, and HVC to Area X contained within lamina mesopallium ventralis (LMV). We found a significant male-biased sex difference in MBP immunoreactivity within HVC, RA, and the HVC to RA tract, but not within LMAN or LMV. This suggests myelination of HVC, RA, and the HVC to RA tract is important to functional adult song, as males sing and females do not. Furthermore, results for LMAN and LMV suggest they are functionally important for females, potentially for the perception of song, and/or the production of non-song vocalizations. Determining how sex differences in myelination of the SCS are regulated will provide an important advance in basic neurobiology.

Acknowledgements: Supported by NSERC.

A67: DOPAMINERGIC MEDICATION IMPAIRS LEARNING BUT NOT DECISION MAKING IN PARKINSON'S DISEASE

Andrew Vo[1,2], Nole M. Hiebert[1,3], Ken N. Seergobin[1], Stephanie Solcz[4], Allison Partridge[1], Penny A. MacDonald[1,2,3,4,5]
[1]*Brain and Mind Institute, University of Western Ontario, London, ON*
[2]*Department of Psychology, University of Western Ontario, London, ON*
[3]*Department of Physiology and Pharmacology, University of Western Ontario*
[4]*Schulich School of Medicine and Dentistry, University of Western Ontario*
[5]*Department of Clinical Neurological Sciences, University of Western Ontario*

Cognitive dysfunction is now recognized in Parkinson's disease (PD). Further, some aspects of cognition are impaired by dopaminergic medications given to address movement symptoms that typify PD. This presumably owes to a dopamine overdose of relatively dopamine-replete brain regions. Learning is the cognitive function most frequently worsened by dopaminergic therapy. However, this result could reflect impaired learning per se versus deficits in how learning is measured (e.g., response selection). We sought to clarify the specific effects of dopaminergic medication on i) stimulus-response association learning from feedback and ii) response selection in PD. We tested 28 PD patients on and/or off dopaminergic medication along with 32 healthy, age- and education-matched control participants. In Session 1, participants learned to associate abstract images with specific key-press responses through trial-and-error via feedback. In Session 2, participants provided specific responses to abstract images learned in Session 1, without feedback, precluding new feedback-based learning. This tested response selection only. PD patients on medication learned stimulus-response associations more poorly than PD patients off medication and controls. Medication did not influence decision performance at test. We demonstrated non-confoundedly that dopaminergic therapy specifically impairs learning and not decision making in PD. This study directly investigated an alternative explanation for results of learning studies in PD, clarifying the effect of dopaminergic medication.

A68: HIPPOCAMPAL CANNABINOID TRANSMISSION MODULATES MESOLIMBIC DOPAMINERGIC NEURONS ACTIVITY: IMPACT ON NATURAL SOCIABILITY AND MEMORY FORMATION

Michael Loureiro, Justine Renard and Steven R. Laviolette
Department of Anatomy and Cell Biology, The Schulich School of Medicine & Dentistry of Western Ontario, London, Ontario, Canada N6A 5C1.

Cannabinoid type 1 (CB1) receptors are highly expressed in the mammalian nervous system, particularly in the hippocampus, a brain region involved in memory and emotional processes. The ventral hippocampal sub-region (vHip) is known to modulate the activity of dopaminergic (DA) neurons located in the ventral tegmental area. DA cells are implicated in cognitive processes critical for memory formation and social interaction behaviors, such as the detection of salient information. The control exerted by the vHip on DA cells is not direct but is made possible via modulation of nucleus accumbens neurons. However, it is not known whether activation of CB1 receptors in the vHip modulates nucleus accumbens neurons and DA cell activity. Therefore, we performed *in-vivo* recordings in anesthetized rats and found that activation of CB1 receptors in the vHip was able to modulate nucleus accumbens neuronal activity and significantly increase the firing frequency of DA cells. Furthermore, by using a conditioned place preference procedure and a social interaction test, our results showed that activation of CB1 receptors in the vHip promotes the learning of non-salient information and abolishes rats' natural sociability. Finally, these behavioral effects were prevented by blocking either glutamatergic or DA receptors in the nucleus accumbens before CB1 receptor activation in the vHip. Collectively, these results provide evidence for the role of hippocampal cannabinoid transmission in the modulation of the mesolimbic DA pathway and behavioral perturbations linked to schizophrenia pathophysiology.

Acknowledgements: supported by NSERC and CIHR grants.

A69: ASSESSING THE CONTRIBUTION OF THE ORBITOFRONTAL CORTEX TO CROSS-MODAL OBJECT RECOGNITION IN RATS

M.Moon, E. Boughner, D.L. Jacklin & B.D. Winters
University of Guelph

The neural mechanisms by which the brain amalgamates unimodal sensory features, such as tactile and visual information about objects multimodal representations are not well understood. In the present study, we assessed the specific contributions of the orbitofrontal cortex (OFC) to the recognition of objects across sensory modalities. In a series of experiments, we investigated the temporal involvement of OFC in cross-modal object recognition (CMOR) as well as its functional interaction with two other brain regions also implicated in CMOR: the posterior partial cortex (PPC) and the perirhinal cortex (PRh). The CMOR task required rats to compare a stored tactile object representation from a sample phase with visually-presented objects in the choice phase to discriminate between novel and familiar stimuli. Temporary inactivation of the OFC with lidocaine disrupted CMOR performance when administered prior to the sample phase, but not when given before the choice phase; this effect was also delay-dependent, being observed with a 1-h but not shorter retention interval. This impairment was abolished when rats were exposed to a sensory restriction condition to reduce the influence of potentially interfering stimulation during the retention delay. Temporary disconnections of the OFC and PPC, but not OFC and PRh, also resulted in CMOR impairment. These results imply that the OFC is important for CMOR task performance under highly specific conditions and that, under certain conditions, there is a functional interaction between the OFC and PPC. We suggest that the OFC facilitates CMOR via top-down processes required to help link tactile with visual information during the tactile object encoding stage.

Supported by NSERC

A70: THE ASSOCIATION BETWEEN CHRONIC PAIN AND RESPONSE TO METHADONE IN OPIOID DEPENDENT PATIENTS: A CROSS-SECTIONAL CLINICAL INVESTIGATION OF CONTINUED OPIOID ABUSE AND INFLAMMATORY PROFILE

Brittany B. Dennis[1], M. Constantine Samaan[2], Monica Bawor[3], James Paul[4], Carolyn Plater[5], Guillaume Pare[1], Andrew Worster[6], Michael Varenbut[7], Jeffery Daiter[7], David C. Marsh[7,8], Dipika Desai[9], Lehana Thabane[1, 10, 11], and Zainab Samaan [1,3, 9, 12]
[1] *Department of Clinical Epidemiology and Biostatistics, McMaster University*
[2] *Department of Pediatrics, Division of Pediatric Endocrinology, McMaster University*
[3] *McMaster Integrative Neuroscience Discovery and Study Program, McMaster University*
[4] *Department of Anesthesia, McMaster University*
[5] *Ontario Addiction Treatment Centre, Collingwood, Canada*
[6] *Department of Medicine, Hamilton General Hospital, Hamilton, Canada*
[7] *Ontario Addiction Treatment Centre, Richmond Hill, Canada*
[8] *Northern Ontario School of Medicine, Sudbury, Canada*
[9] *Population Genomics Program, Chanchlani Research Center, McMaster University*
[10] *Centre for Evaluation of Medicine, Hamilton, Canada*
[11] *System Linked Research Unit, Hamilton, Canada*
[12] Department of Psychiatry and Behavioural Neurosciences, McMaster University

Concomitant use of illicit opioids in combination with methadone maintenance treatment (MMT) poses a serious risk of abnormal cardiac conductivity, overdose and death. MMT patients with comorbid chronic pain are thought to be in the highest risk category for such adverse events. The objectives of this study were to explore the relationship between chronic pain and methadone response in opioid dependent patients as well as establish the inflammatory profile of MMT patients with chronic pain. This multi-center cross-sectional study enrolled patients (n=235) on MMT for the treatment of opioid dependence. Clinical history, blood and urine data were collected for the GENetics of Opioid Addiction (GENOA) study. Blood samples were obtained for inflammatory markers serum levels (TNF-α, IL-1ra, IL-6, IL-8, IL-10, IFN-γ and CCL2). Our primary outcome response to MMT was determined based on urine analysis. Our secondary outcome of inflammatory profile was determined through blood serum analysis. Multivariable regression models were constructed to address our objectives using STATA Version 12. Participants with chronic pain were less likely to respond to MMT compared to patients without chronic pain (Estimated coefficient: -8.58; 95%CI: -15.27, -1.90, p=0.01). In addition, IFN-γ was found to be significantly elevated among patients reporting chronic pain (Odds Ratio: 1.92 95%CI: 1.14, 3.25, p=0.01). Patients with chronic pain show poor response to MMT in addition to having elevated IFN-γ in comparison to patients without chronic pain. The ability to objectively distinguish between patients with chronic pain may help to improve the prediction of poor responders as well as identify treatment approaches such as anti-inflammatory medications as a safe alternative to opioid analgesics in patients with chronic pain.

Acknowledgements: This work was supported by CIHR Drug Safety and Effectiveness Network (DSEN) grant (grant number: 126639). The funders had no role in study design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

A71: α4β2 NICOTINIC RECEPTORS AMELIORATE THE CROSSMODAL OBJECT RECOGNITION DEFICIT IN KETAMINE-TREATED RATS THROUGH STIMULATION OF THE GABAERGIC SYSTEM

Jacob M. Cloke and Boyer D. Winters
Department of Psychology and Collaborative Neuroscience Program, University of Guelph, Guelph, ON

The neural bases of multisensory integration impairments in schizophrenia are not well understood. Rats treated sub-chronically with NMDA receptor antagonists (e.g. ketamine), which model symptoms of schizophrenia, are impaired on a tactile-to-visual crossmodal object recognition (CMOR) task; this deficit is reversed by systemic nicotine, which can also attenuate cognitive impairment in patients with schizophrenia. Furthermore, cortical gamma oscillations mediated by parvalbumin-containing GABAergic interneurons (PV-INs) may be deficient in schizophrenia, possibly contributing to aberrant multisensory processing. PV-INs contain nicotinic acetylcholine receptors (nAChR). This study assessed the receptor specificity of nicotine's ameliorative effect in the CMOR task and the interaction between nAChRs and GABA. Male Long-Evans rats were treated sub-chronically for 10 days with ketamine or saline and tested on the CMOR task after a 10-day washout. Systemic nicotine given before the sample phase of the CMOR task reversed the ketamine-induced impairment, but this effect was blocked by co-administration of the $GABA_A$ receptor antagonist bicuculline at a dosage that itself did not cause impairment. Selective α7 and α4β2 nAChR agonists were tested, with only the latter reversing the ketamine impairment; bicuculline blocked this effect. These results suggest that nicotine-induced agonism of α4β2 nAChRs ameliorates CMOR deficits in ketamine-treated rats via stimulation of the GABAergic system. These findings may have implications for understanding cognitive impairment in schizophrenia.

Acknowledgements: Supported by NSERC.

A72: The role of perspective-taking in event imagination

Jeffrey P. Hong, Todd R. Ferretti, Rachel Craven, Rachelle D. Hepburn, and Deanna C. Hall
Wilfrid Laurier University

During the linguistic processing of verbs, mental representations of the events described by these verbs are formed. A key factor in the formation of these event representation is the perspective from which they are viewed. The current study used electroencephalography to investigate the cognitive effort associated with forming imagined events from different perspectives. Slow-cortical potential negativity was used as an index of cognitive difficulty, associated with event representation. Participants were presented with verb phrases (e.g. I was acting) and asked to imagine themselves participating the described events from either the first-person or the third-person perspective. It was found that event representation was more difficult from the first-person perspective that from the third-person perspective. Further, these effects were found to differ in amplitude, based on topographical region. The study represents a novel investigation of the effects of perspective on event representation, based on verb cues.

B: Development

B5: SOCIAL BUFFERING OF ENDOCRINE AND BEHAVIOURAL RESPONSES TO REPEATED ISOLATION DIFFER BETWEEN ADOELSCENT AND ADULT MALE RATS

Travis E. Hodges, Julie C. Vasseur, Cheryl M. McCormick
Psychology Department, Neuroscience Program
Brock University, St Catharines, ON

Here, we investigated whether adolescents and adults respond differently to chronic social instability stress (daily isolation and return to an unfamiliar peer for 16 days) on the basis of endocrine and behavioural measures. In the repeated isolation condition, adolescent (postnatal (P) day 30) and adult (P70) rats were isolated daily for 16 days, after which they returned to either a familiar or unfamiliar cage partner. A control group of adolescents and adults underwent a first isolation on the last day of the isolations to investigate whether habituation to isolation had occurred, and half then returned to their original cage partner and half to a new cage partner. Behaviours of the animals after being returned to a familiar or unfamiliar peer were observed throughout the procedure. Both adolescent and adult rats had a similar pattern of increased testosterone in the recovery period regardless of partner familiarity and of corticosterone release immediately after a 16th exposure to isolation stress and a 16th exposure to a familiar peer during recovery. There was, however, a potentiated release of corticosterone after a 16th exposure to isolation and return to an unfamiliar peer in adolescent (p=0.03) and not adult (p>0.50) rats. Moreover, we demonstrate that isolation stress increases affliative behaviours in adolescent rats and decreases affliative behaviours in adult rats. Adolescent and adult rats respond to social interactions differently, and we are currently investigating the neural sites that may play a role in this age difference.

Acknowledgements: Supported by NSERC

B6: EFFECTS OF SOCIAL INSTABILITY STRESS IN ADOLESCENCE ON ADULT DOMINANCE BEHAVIOUR AND MATING BEHAVIOUR IN MALE RATS

Madison Thompson*, Mark J. Cumming*, Cheryl M. M.Cormick
*co-first authors, *Centre for Neuroscience, Brock University, St Catharines ON*

We investigated whether social instability stress in adolescence (SS; daily 1 h isolation + new cage partners postnatal days 30 – 45) alters dominance–submissive (DS) behaviour in a food competition test and whether sexually-receptive females would discriminate between SS and CTL males in a paced mating test. Pairs of SS and pairs of CTL male cagemates, housed together since postnatal day 45 (SS) or postnatal day 22 (CTL) rats competed for access to a preferred food (sweetened condensed milk) in 5 test sessions. A similar number of SS and CTL pairs displayed significant DS relationships (8 of 12 pairs each), but during the test session, SS pairs displayed more aggressive behaviour and were less likely to leave relinquish access to the food voluntary than CTL pairs. SS and CTL rats were then housed singly and underwent five 45 min sex behaviour test sessions in a paced mating chamber (3 compartments with an SS rat at one end and a CTL rat at the other end, with a receptive female in the middle, and with only the female able to visit all three compartments; DS status of opponents was controlled) to invest whether females would discriminate between CTL and SS males. In the 5th test session, preliminary analyses indicated females were sensitive to both DS status and stress history of the

males. These results add to our previous findings that social instability stress in adolescence modifies the adult social repertoire of rats.
Acknowledgements: Supported by NSERC

B7: DUAL EFFECT OF CTCF LOSS ON NEUROPROGENITOR DIFFERENTIATION AND SURVIVAL

L. Ashley Watson[1,2], Xu Wang[1,2], Adrienne Elbert[1,2], Kristin D. Kernohan[1,2], Niels Galjart[3], and Nathalie G. Bérubé[1,2]
[1]Departments of Paediatrics and Biochemistry, Western University
[2]Children's Health Research Institute, London, ON
[3]Medical Genetics Centre Department of Cell Biology and Genetics, Erasmus University, Rotterdam, The Netherlands

The CCCTC-binding factor (CTCF) is a zinc finger DNA binding protein involved in higher-order chromatin organization, and mutations in the human *CTCF* gene cause an intellectual disability (ID) syndrome associated with microcephaly. However, information on CTCF function *in vivo* in the developing brain is lacking. To address this gap, we conditionally inactivated the *Ctcf* gene at early stages of mouse brain development. Cre-mediated *Ctcf* deletion in the telencephalon and anterior retina at embryonic day 8.5 (E8.5) triggered upregulation of the p53 effector PUMA, resulting in massive apoptosis and profound ablation of telencephalic structures. Inactivation of *Ctcf* at E11 also resulted in PUMA upregulation and increased apoptosis, and the *Ctcf*-null forebrain was hypocellular and disorganized at birth. Although deletion of both *Ctcf* and *Puma* in the embryonic brain effectively rescued *Ctcf*-null progenitor cell death, it failed to improve neonatal hypocellularity due to decreased proliferative capacity of rescued apical and outer radial glia progenitor cells. This was exacerbated by an independent effect of CTCF loss that resulted in depletion of the progenitor pool due to premature neurogenesis earlier in development. Our findings demonstrate that CTCF activities are required for two distinct events in early cortex formation: first, to correctly regulate the balance between neuroprogenitor cell proliferation and differentiation, and second, for the survival of neuroprogenitor cells, providing new clues regarding the contributions of CTCF in microcephaly/ID syndrome pathologies.
Acknowledgements: This work was supported by a National Science and Engineering Research Council of Canada (NSERC) Canada Graduate Scholarship to L.A.W., a Canadian Institute for Health Research (CIHR) Vanier Scholarship to A.E., an NSERC Canada Graduate Scholarship to K.D.K., and an operating grant from the CIHR (MOP93697) to N.G.B.

B8: ELECTROPHYSIOLOGICAL EVIDENCE OF ALTERED VISUAL PROCESSING IN ADULTS WITH BLOCKED PATTERN VISION DURING INFANCY

Avital Sternin[a], Sidney J. Segalowitz[a], Terri L. Lewis[b], Jane Dywan[a] & Daphne Maurer[b]
[a] *Brock University*
[b] *McMaster University*

We examined the role that early visual input plays in the proper development of the visual system by testing adults who had been born with bilateral congenital cataracts. Cataracts blocked patterned visual input until they were removed surgically and the eyes fitted with compensatory contact lenses. All were treated within the first year after birth and had acuity good enough to easily differentiate the test stimuli. Stimulus Set 1 used simple and complex textures to explore early processing regions (V1, V2). Set 2 used a series of motion stimuli to explore higher-level processing regions responsible for global motion perception (V5). Set 3 used a series of Glass stimuli to examine global form processing (V4). Patients differed from controls in the texture task where N75 components were much smaller for all but the simplest stimuli. As well, patients' P100 and N170 amplitudes did not differentiate amongst texture stimuli, despite their N170s being much larger than those of controls. Further, patients' N170 and P200 response to motion and Glass pattern stimuli were smaller, respectively, and unlike those of controls did not differentiate among stimuli. These results indicate that early visual deprivation contributes to permanent abnormalities in mechanisms that underlie the processing of visual stimuli and are consistent with behavioural evidence of enduring deficits in the ability to process complex stimuli, global motion, and global form.

C: Disorders of the Nervous System

C26: DIFFERENTIAL REGULATION OF THE HIGH-AFFINITY CHOLINE TRANSPORTER BY WILD TYPE AND SWEDISH MUTANT AMYLOID PRECURSOR PROTEIN

Leah K. Cuddy, Claudia Seah and R. Jane Rylett
Department of Physiology and Pharmacology, Schulich School of Medicine & Dentistry and Robarts Research Institute, Western University, London, ON

Two hallmark features of Alzheimer's disease (AD) are the degeneration of cholinergic neurons and the processing of amyloid precursor protein (APP) to amyloid-beta (Aβ) peptides and the development of Aβ plaques. The uptake of choline into cholinergic nerve terminals by the choline transporter CHT is considered the rate-limiting step to acetylcholine synthesis. Internalization of CHT proteins from the plasma membrane limits the uptake of choline, and thus trafficking of CHT critically regulates its activity. It is known that APP interacts with CHT and regulates its presynaptic localization. The objective of this study is to investigate how wild-type APP (APP-WT) and APP containing the Swedish mutation (APP-Swe), which causes familial early-onset AD, affect CHT function. Our data reveal that APP-WT or APP-Swe expression decreases CHT activity and cell surface retention in SH-SY5Y neural cells. Confocal microscopy shows similar CHT co-localization with early endosomes between cells expressing APP-WT or APP-Swe. Importantly, co-immunoprecipitation and *in situ* proximity ligation assay experiments show that APP-Swe interacts with CHT significantly less than does APP-WT. Taken together, these results suggest that APP-WT and APP-Swe alter CHT function through different mechanisms. These studies will provide novel information that could aide design of independent therapeutic strategies for patients carrying wild-type or Swedish mutant *APP*. With the incidence of AD on the rise and the projected increases in our aging population, these studies are both timely and critical.
Acknowledgements: Alzheimer's Society of Canada

C27: NUCLEAR LOCALIZED 82 KDA CHOLINE ACETYLTRANSFERASE DRIVES AN EPIGENETIC RESPONSE TO AMYLOID BETA STRESS

Warren Winick-Ng[1], Shawn Albers[1] and R. Jane Rylett[1]
[1]Molecular Medicine Research Group, Robarts Research Institute, Department of Physiology and Pharmacology, Schulich School of Medicine and Dentistry, University of Western Ontario, London ON

82 kDa choline acetyltransferase (82-ChAT) localizes to the nucleus of cholinergic neurons, but is redistributed to the cytoplasm in individuals with Alzheimer's disease. The role of 82-ChAT is unknown, but has previously been shown to reduce Aβ secretion. In the current study, human SH-SY5Y cells expressing 82-ChAT were treated with Aβ oligomers for 4 h. 82-ChAT formed nuclear aggregations following Aβ exposure, as observed by confocal microscopy. Using super-resolution ground-state depletion microscopy, the aggregations were revealed to be organized rings that co-localized with special AT-rich binding protein 1 (SATB1). SATB1 anchors target DNA to the nuclear matrix to form matrix attachment regions (MARs) that becomes either activated or repressed chromatin regions. We determined that these aggregations peripherally expressed the transcriptionally active Histone H3 Lysine 4 tri-methylation marker, were enriched with these markers after 24 h of Aβ, and that 82-ChAT was associated with the chromatin. Treatment with DNA minor groove-binding competitors attenuated this association and displaced 82-ChAT from the aggregations. Taken together, 82-ChAT facilitated the formation of transcriptionally active MARs, and associated with these structures at the DNA minor groove. The role of 82-ChAT at MARs and the functional outcome of MAR formation requires further investigation. These experiments demonstrate that Aβ stress induces epigenetic changes in chromatin structure in human neurons, which has implications for understanding the etiology of neurodegenerative diseases.
Acknowledgments: These studies were supported by a CIHR operating grant to R. Jane Rylett, and a Dean's PhD Scholarship for Graduate Research to Warren WInick-Ng

C28: NON-CANONICAL ACTIVATION OF NRF2 AS A POTENTIAL THERAPY FOR HUNTINGTON'S DISEASE

Lauren Tindale, Kyle Dailey and Robert C. Cumming
Department of Biology, University of Western Ontario, London, ON

Mitochondrial dysfunction and elevated reactive oxygen species (ROS) levels are strongly implicated in various neurodegenerative disorders, including Huntington's disease (HD). We previously demonstrated that overexpression of mHtt in PC12 cells leads to elevated ROS production and a concomitant decrease in expression of the antioxidant protein peroxiredoxin1 (Prx1). Interestingly, treatment with the FDA-approved compound dimercaptopropanol (DMP) prevents mHtt-mediated inhibition of antioxidant gene expression and neurotoxicity. Nrf2 is a transcription factor responsible for regulating expression of a diverse array of antioxidant genes including Prx1. Nrf2 is normally maintained at very low levels by its negative regulator Keap1, which facilitates the sequential ubiquitination and degradation of Nrf2 by the proteasome. Electrophiles and oxidants can disrupt the Keap1-Nrf2 interaction, resulting in the stabilization and nuclear translocation of Nrf2. There is currently great interest in identifying Nrf2-activating compounds for the treatment of neurodegenerative diseases. Here we demonstrate that mHtt prevents Nrf2-mediated activation of antioxidant enzyme expression in PC12 cells and in an immortalized striatal cell line (STHdhQ111) which is rescued with DMP exposure. Preliminary findings indicate that DMP promotes the degradation of Keap1, possibly via an autophagic/lysosomal process which suggests that alternative modes of Nrf2 activation exist. This study indicates that DMP may have relevance for the treatment of HD and other neurodegenerative disorders.
Acknowledgements: Supported by the Huntington Society of Canada, NSERC and the Canadian Foundation for Innovation

C29: NEUROANATOMICAL ANALYSIS OF ZEBRAFISH EXPOSED TO LOW EMBRYONIC ALCOHOL

Keith Misquitta[1], Samantha Mahabir[2], Diptendu Chatterjee[1], Robert Gerlai[1,2]
[1]Department of Psychology, University of Toronto, Mississauga, ON
[2]Department of Cell and Systems Biology, University of Toronto, Toronto, ON

Fetal Alcohol Spectrum Disorder (FASD) is the umbrella term used to include a wide range of deficits shown in children with this disorder. Previous studies using zebrafish showed that high levels of embryonic alcohol exposure resulted in behavioural, neurochemical and physical abnormalities. Here we investigate the effects of lower ethanol doses which is more realistic from the perspective of FASD. No studies at present have shown neuronal and neuroanatomical differences in embryonic ethanol-induced zebrafish. In this study, the AB strain of zebrafish was exposed for two hours to two concentrations of ethanol (0.00% (control), and 1.00% vol/vol) at 24 hours post-fertilization. Four months following exposure, these zebrafish were analyzed using nissl staining methods. Analysis of the brain sections were performed to quantify differences in the number of cells within the Lateral Zone of the Dorsal Telencephalon (DT) and Glomerular layer of the Olfactory bulb (OB). Results showed that in the lateral zone of the DT there was no significant difference in the number of cells observed. However, the glomerular layer of the OB displayed a significant difference in the average number of cells between 0.00%, and 1.00% (vol/vol) embryonic ethanol exposed zebrafish. We are currently completing the analysis for 0.50% (vol/vol) in these areas. Reduction in neurons or cell population in

the central nervous system may be responsible for neurobehavioural effects associated with FASD in humans.
Acknowledgements: Supported by an NIH/NIAAA grant to RG.

C30: EFFECTS OF NEONATAL LESIONS OF PREFRONTAL CORTICAL SUBPLATE ON EXECUTIVE FUNCTION

Sagar J. Desai[1], Brian L. Allman[1] and Raj Rajakumar[1]
[1]*Department of Anatomy & Cell Biology, Western University, London, ON*

Rat pups injected with p75 receptor antibody conjugated to saporin into the developing prefrontal cortex to lesion subplate neurons manifest adult onset behavioral abnormalities reminiscent of positive and negative symptoms of schizophrenia. Also, these rats have neurochemical and structural abnormalities in GABA, glutamate and dopamine synapses. Thus, we hypothesize that subplate lesioned rats will show cognitive deficits which are thought to be dependent on GABAergic glutamatergic and dopaminergic neurotransmission in the prefrontal cortex. Cognitive deficits in schizophrenia affect 'executive functions' which involve working memory, reasoning and task flexibility. Executive function like 'set-shifting' refers to the ability to modify the ongoing behavior in response to a change in strategies to achieve the goal. Our set-shifting task requires rats to learn visual-cue discrimination, and then, shift to a response discrimination strategy to obtain a reinforcer (sucrose pellet). Our preliminary results show that control rats take ~75 trials to reach the successful performance criterion in the set-shifting task. We predict that subplate lesioned rats will require a greater number of trials than the control rats to reach the performance criterion. Additional studies, including novel object recognition and the Morris Water Maze, will be performed to investigate if working memory is impaired in the subplate lesioned rats. Collectively, our findings will characterize how the neonatal disruption of the subplate in the prefrontal cortex impairs executive functioning.
Acknowledgement: Supported by NSERC.

C31: ROLE OF PEDUNCULOPONTINE CHOLINERGIC NEURONS IN GAIT

Nahal Farhani, Nagalingam Rajakumar, Mandar Jog
Neuroscience Graduate Program, Western University

The pedunculopontine nucleus (PPN) is located in the midbrain and contains neurons possessing either acetylcholine or GABA dispersed throughout the nucleus. Post-mortem studies have shown a marked loss of cholinergic neurons in the PPN in Parkinson disease patients. Preliminary neuro-physiological studies have hinted at a role of the PPN in gait and posture control. Therefore in this study, It was hypothesized that cholinergic neurons of the PPN mediate certain aspects of gait. In this study, we will inject a specific cholinergic toxin, anti-p75 receptor antibody-conjugated to saporin (192-sap), directly in to two different areas of the PPN in separate groups of adult rats and their gait will be studied using a catwalk apparatus. Then, a neuronal tracer that labels the axonal projection sites of neurons will be microinjected into each of the topographical areas of the PPN identified previously, and target sites of cholinergic neurons that mediate different aspects of gait will be determined. Following this, specific cholinergic receptor (nicotinic and muscarinic) blockers will be microinjected in awake rats via pre-implanted indwelling cannulae at target zones and their gait patterns will be determined using catwalk apparatus. Expected results in this study will confirm the topographical location and target connection of cholinergic neurons of the PPN mediating different aspects of gait.

C32: A COMPARISON OF NEUROIMAGING-BASED ASSESSMENTS OF COVERT COGNITION IN PATIENTS WITH DISORDERS OF CONSCIOUSNESS

Raechelle M. Gibson, Davinia Fernández-Espejo, Adrian M. Owen, & Damian Cruse
Brain and Mind Institute, Department of Psychology, Western University, London,

Neuroimaging can be used to evaluate residual cognition in patients who are behaviourally non-responsive, including patients with Disorders of Consciousness (DOC). An important step for identifying the clinical utility of these types of neuroimaging-based evaluations is to compare the findings of these assessments across imaging methodologies. We report separate behavioural, fMRI, and EEG evaluations for six DOC patients. Behavioural evaluations consisted of the standardized Coma Recovery Scale - Revised. For the fMRI and EEG evaluations, patients were asked to perform validated mental imagery tasks. One patient produced appropriate, reliable brain responses for motor imagery in both the fMRI and EEG tasks. Two patients produced reliable, appropriate activation only in the fMRI study for mental imagery involving spatial navigation. Finally, one patient demonstrated command-following in both the behavioural assessment and in the EEG motor imagery task. The findings of this work demonstrated some convergence between imaging methodologies. The results emphasise the importance of utilizing multiple modalities (*i.e.*, behaviour, fMRI, and EEG) and tasks (*i.e.*, different types of imagery) in the evaluation of residual cognition in DOC patients.
Acknowledgements: Supported by the CERC program, CIHR, and OGS

C33: AGE-DEPENDENT DECLINE IN AEROBIC GLYCOLYSIS CORRELATES WITH MEMORY LOSS IN A TRANSGENIC MOUSE MODEL OF ALZHEIMER'S DISEASE

Richard Harris and Robert Cumming
Department of Biology, Western University, London, ON

The majority of glucose consumed by the adult brain is fully oxidized to carbon dioxide and water in the mitochondria of neurons to supply large amounts of ATP for functions related to synaptic transmission. However, a certain percentage of glucose in the brain can be metabolized by glycolysis, even in the presence of oxygen, and produce lactate as a by-product. This process is known as aerobic glycolysis. Emerging evidence now suggests that aerobic glycolysis in the brain plays a critical role in generating biosynthetic metabolites during early childhood development and persists in certain regions of the adult brain to support synaptic plasticity during learning and memory. However, aerobic glycolysis steadily declines with age and virtually disappears in the elderly. In this study, I demonstrate that the ageing process induces a progressive decline in aerobic glycolysis in the mouse brain and correlates with loss of memory in a transgenic mouse model of Alzheimer's disease (AD). Proton magnetic resonance spectroscopy revealed an age-dependent decline in cortical lactate levels in wild-type mice. Western blot analysis of cortical extracts revealed a decline in key regulatory proteins of aerobic glycolysis in both control and, to a greater extent, transgenic AD mice at 12 months of age; events which correlated with the onset of memory loss in transgenic AD mice as measured by the Morris water maze. These data indicate that aerobic glycolysis in the brain declines normally with age and may contribute to neurodegeneration and memory loss in the brains of transgenic AD mice.
Acknowledgments: Supported by the Scottish Rite Charitable Foundation

C34: DEVELOPING A HIERARCHY OF LANGUAGE PROCESSING: IMPLICATIONS FOR PATIENTS WITH DISORDERS OF CONSCIOUSNESS

Steve Beukema, Ken McRae, Adrian M. Owen, Damian Cruse
The Brain and Mind Institute, University of Western Ontario, London, ON

Functional neuroimaging assessments of residual cognitive capacities, including those that support language, can improve diagnostic and prognostic accuracy in patients with disorders of consciousness – i.e. the vegetative and minimally conscious states. Due to the portability and relative inexpensiveness of electroencephalography, language-sensitive event-related potential (ERP) components have been proposed as a clinically valid means to identify preserved linguistic function in these non-communicative patients. While the semantic-priming N400 effect meets these criteria, we have previously shown that its detection in a given subject is reliant on the preservation of a range of high-level cognitive abilities not necessarily limited to an ability to process meaning (semantics). This component may therefore not always be suitable for patients with heterogenous brain-injuries, such as patients with disorders of consciousness, who are 'unaware' by definition. As a follow-up, we investigated a two-stage hierarchy of ERP markers of language function – from low-level (speech vs. non-speech) to high-level (semantics) functions – and employed source localization techniques in order to identify their differential generators in healthy individuals. The identification of these ERP effects in patients with disorders of consciousness may allow us to characterize the extent to which a given patient possesses preserved function in their linguistic networks. Such evidence for preserved language processing and the cortical networks that support it may also provide positive prognostic value.
Acknowledgements: Supported by Canada Excellence Research Chair (CERC)

C35: METHOD OF AMYLOID BETA OLIGOMER DETECTION USING MALDI-TOF MASS SPECTROMETRY

J. S.-H. Wang[1, 2], K. Jurcic[1], S.N. Whitehead[2], and K. K.-C. Yeung[1]
[1]*Dept. Chemistry and Biochemistry, Western University, London, ON, Canada*
[2]*Vulnerable Brain Laboratory, Dept. Anatomy and Cell Biology, Western University, London, ON, Canada*

Accumulating evidence in the literature supports the correlation between amyloid beta (Aβ) oligomers and severity of Alzheimer's disease (AD). Numerous protocols have been reported for *in vitro* oligomeric $A\beta_{1-42}$ preparations, yet the effect of variations among protocols on the resulting composition is poorly understood. Methods that provide qualitative and quantitative characterization of the monomeric and oligomeric Aβ species are therefore extremely important to oligomeric $A\beta_{1-42}$ research in AD progression and severity. The most common means of Aβ oligomer quantification is gel electrophoresis. However, it has low sample throughput, and gel smearing poses as a significant resolution limitation. Alternatively, the use of electrospray ionization mass spectrometry (ESI-MS) in conjunction with ion mobility (IMS) has been applied to study the assembly of Aβ oligomers. IMS is critical in differentiating oligomers of different sizes with the same m/z; circumvent the issue of overlapping m/z from non-covalent homo oligomers with multiple charge states from ESI. The research described here focuses on a simpler mode of MS based on matrix-assisted laser desorption ionization (MALDI). MALDI produces predominantly singly-charged ions, allowing for oligomers of varying sizes to be resolved by a time-of-flight (TOF) mass analyzer. Our results demonstrate that MALDI-MS offers a fast and easy method to measure the extent of Aβ oligomerization. The method has been applied to determine the effect of protocol variations on the resulting composition of the Aβ assemblies.
Acknowledgements: Supported by NSERC, CIHR, and CFI.

C36: THE TARGETED ANTIOXIDANT, CAT-SKL, REDUCES BETA-AMYLOID TOXICITY IN THE RAT BRAIN

Hayley J. Nell[1], Jennifer L. Au[1], Courtney R. Giordano[2], Lin Wang[1], Stanley R. Terlecky[2], Paul A. Walton[1], Shawn N. Whitehead[1] and David F.Cechetto[1].
[1]*Department of Anatomy and Cell Biology, University of Western Ontario, London,*
[2]*Department of Pharmacology, Wayne State University School of Medicine, Detroit, Michigan*

Accumulation of beta-amyloid (Aβ) in the brain has been implicated as a major contributor to the cellular pathology and cognitive impairment observed in Alzheimer's disease. This study set out to investigate whether CAT-SKL, a genetically engineered derivative of the peroxisomal antioxidant enzyme catalase, is able to reduce the toxicity induced by Aβ in the mature rat brain. Bilateral intracerebroventricular (icv) injections of the $A\beta_{25-35}$ peptide was used to model Aβ toxicity in 6-month-old male Wistar rats with a subset of rats receiving intraperitoneal CAT-SKL injections. Spatial learning and reference memory were assessed using the Morris water maze (MWM); immunohistochemical analyses were used to evaluate neuroinflammation and catalase assays were used to assess catalase activity. $A\beta_{25-35}$ administration resulted in increased microglia activation and cholinergic neuronal loss in the basal forebrain, along with astrocytosis and reduced neuronal numbers in the hippocampus compared

to the control group. CAT-SKL treatment was able to reduce the pathology induced by $A\beta_{25-35}$ by significantly decreasing the number of activated microglia and reducing cholinergic neuronal loss in the basal forebrain, however no significant increases in catalase activity were detected. $A\beta_{25-35}$ animals showed deficits in long-term reference memory in the MWM, while those treated with CAT-SKL did not demonstrate long-term memory impairments. This preclinical data provides support for the use of CAT-SKL in reducing neuroinflammation and long-term reference memory deficits induced by $A\beta_{25-35}$.

Acknowledgements: Supported by CIHR

C37: THE EFFECTS OF ANTIOXIDANT CATALASE-SKL ON NEUROLOGICAL OXIDATIVE STRESS IN A CO-MORBID RAT MODEL OF STROKE AND ALZHEIMER'S DISEASE

Jennifer L. Au, Hayley J. Nell, John J.W. Shin, Paul A. Walton, Shawn N. Whitehead and David F. Cechetto

Department of Anatomy and Cell Biology, Schulich School of Medicine and Dentistry, Western University, London, ON

A major late-stage event in Alzheimer's disease (AD) is the accumulation of beta-amyloid protein (Aβ) into plaques, but it has been demonstrated that pathologic neuroinflammation and oxidative stress precede the formation of Aβ plaques. These pathologies are coincident in ischemic stroke, which has been shown to exacerbate AD pathology in clinical and experimental studies. This study aims to investigate oxidative stress in the interaction of stroke and AD and makes use of a unique, genetically engineered antioxidant catalase (CAT-SKL) to target oxidative stress in a co-morbid stroke and AD rat model. In 6-month-old male Westar rats, bilateral intracerebroventricular injections of $A\beta_{25-35}$ peptide (the neurotoxic fragment of $A\beta_{1-42}$) and unilateral striatal injections of endothelin-1 (a potent vasoconstrictor) were used to model AD and stroke, respectively. Rats were randomly assigned to a treatment of saline or CAT-SKL (1mg/kg) administered through intraperitoneal injection. Rats completed the asymmetrical forelimb use task and modified sticky tape task, which are both motor-related tasks and the Morris Water Maze task to assess cognitive function. Co-morbid rats showed prolonged gross motor deficits and cognitive behavioural deficits in comparison to controls. CAT-SKL delayed the appearance of gross motor deficits in co-morbid rats, but resulted in an increase in cognitive deficits.

Acknowledgements: Supported by CIHR

C38: INCREASED EXPRESSION OF SIMPLE GANGLIOSIDE SPECIES GM2 AND GM3 DETECTED BY MATRIX-ASSISTED LASER DESORPTION IONIZATION IMAGING MASS SPECTROMETRY IN A COMBINED RAT MODEL OF ABETA TOXICITY AND STROKE.

Sarah Caughlin[1], Jeff Hepburn[1], Dan Park[1], Kristina Jurcic[2], Ken Yeung[2], David F. Cechetto[1] and Shawn N. Whitehead[1,3]

[1] *Dept. Anatomy and Cell Biology, Western University, London, ON.*

[2] *Dept. Biochemistry, Western University, London, ON.*

[3] *Dept. Clinical Neurological Sciences, London Health Sciences Centre, Western University, London, ON.*

Gangliosides are membrane lipids enriched in the central nervous system. Their expression patterns have been found to be altered in a number of neurodegenerative disease and injury states but has yet to be explored in the context of comorbidity. The aging brain is often characterized by the presence of multiple comorbidities resulting in synergistic effects on brain degeneration as seen in the case of Alzheimer's disease (AD) and stroke. Matrix-Assisted Laser Desorption/Ionization (MALDI) Imaging Mass Spectrometry (IMS) was used to study the expression of A-series ganglioside species GD1a, GM1, GM2, and GM3 to determine how their expression profiles are altered in the presence of beta-amyloid (Aβ) toxicity in addition to ischemic injury. 3 month old male Wistar rats were given either a unilateral striatal injection of endothelin-1 (stroke group), a striatal injection of endothelin-1 and intracerebralventricular injections of Aβ (25-35) (combined Aβ/stroke group), or underwent sham surgery. A significant increase in the simple ganglioside species GM2 was observed 3 days after surgery, while both GM2 and GM3 were significantly elevated in the combined Aβ/stroke group. By 21 d after surgery, GM3 was elevated in the stroke alone group while GM2 returned to normal levels. In the combined Aβ/stroke group, both GM2 and GM3 remained elevated at 21 d after treatment. The accumulation and persistent expression of potentially toxic simple ganglioside species observed in the combined Aβ/stroke group may be indicative of a mechanism of synergism between AD and ischemic injury.

Acknowledgements: Supported by CIHR STP to S.C., NSERC-DG to K.Y, CIHR-ETG to D.F.C and S.N.W, and NSERC-DG, Lawson-IRF, CIHR-OG and CFI-LOF to S.N.W

C39: LOCALIZATION OF HUMAN 82-KDA CHAT IN BRAIN OF NEWLY DEVELOPED TRANSGENIC MOUSE MODEL

Silke M. Vanvaerenbergh[1,2], Daisy Wong[2], and Rebecca J. Rylett[1,2]

[1]*Department of Physiology and Pharmacology, University of Western Ontario, London*

[2]*Molecular Brain Research Group, Robarts Research Institute, London, ON*

Alzheimer's disease is characterized by cholinergic neuron dysfunction and β-amyloid (AB) plaque accumulation in the brain. AB decreases synthesis and release of acetylcholine (ACh). Choline acetyltransferase (ChAT), a key component of cholinergic neurons, is required for the synthesis of ACh. *In vitro* expression of 82-kDa ChAT in neuronal nuclei changes expression of APP processing genes, suggesting a protective role of 82-ChAT. We successfully generated transgenic mice that have neuron-specific expression of human 82-kDa ChAT through crossing with Nkx2.1 Cre-mice. It is necessary to examine the localization of human 82-ChAT in mice brains. Brains were bisected along the midline with one side processed for histology and the other for biochemical analysis. Fixed halves were stained using a custom primary antibody for the C-terminus of human 82-ChAT. IHC shows staining of 82-ChAT in neurons transgenic mice brains. Staining reveals the presence of human 82-ChAT in a number of cholinergic brain areas including the lateral and medial septa, the diagonal band of Broca and the cerebral cortex. As expected, it was found that human 82-ChAT is localized predominantly to neuronal nuclei. Expression of human 82-ChAT protein in these mice provides an *in vivo* model for the study of AD. These mice can be crossed with double transgenic APP-PSI AD-model mice to study changes in AB deposition and cholinergic neuron function. The human 82-ChAT-expressing mice will provide new data about APP metabolism and how its regulation is altered by the presence of nuclear ChAT.

Acknowledgements: Funding provided by CIHR and the Alzheimer's Association

C40: GLUTAMATE TOXICITY CHANGES EXPRESSION PROFILE OF GANGLIOSIDES IN NEURODEGENERATING RAT PRIMARY CORTICAL NEURONS

Daniel Park[1], Gilles A. Lajoie[2] and Shawn N. Whitehead[1]

[1]*Vulnerable Brain Laboratory, Department of Anatomy and Cell Biology, Western University, London, ON, Canada, N6A 5C1*

[2]*Deptartment of Biochemistry, Western University, London, ON, Canada*

Neurons within different brain regions have varying levels of vulnerability to external stress and therefore respond differently to injury. A potential reason to explain this may lie within a key lipid class of the cell's plasma membrane called gangliosides. These glycosphingolipid species have shown to play various roles in the maintenance of neuronal viability. The purpose of this study is to use electrospray ionization mass spectrometry (ESI-MS) technique and immunohistochemistry to evaluate the temporal and structural changes in the expression profiles of various ganglioside species during the course of neurodegeneration in rat primary cortical neurons exposed to glutamate toxicity. Primary embryonic (E18) rat cortical neurons were cultured to DIV14. Glutamate toxicity was induced for 1, 3, 6 and 24 hours and immunohistochemistry was used to stain for GM1 and GM3 species. ESI-MS was used to quantify the ganglioside species expressed within these injured neurons, which were compared to expression profiles of healthy neurons. Immunohistochemistry revealed that at early stages of glutamate toxicity, level of GM1 was highly expressed along the neuronal projection. At later time points, these levels decreased but still showed high expression relative to significant reduction in these projections. GM3 were undetectable in uninjured control neurons, but the expression was initiated by 1 h and remained elevated throughout neurodegeneration. ESI-MS data is still pending as its process is currently being optimized. These data suggests that different gangliosides play diverse roles in the process of neurodegeneration.

Acknowledgements: This work was supported by a CIHR-OG, NSERC-DG and a Lawson-IRF to S.N.W, an NSERC-DG to L.J and an NSERC-CGS-M to D.P

C41: LONG-TERM EFFECTS OF ADOLESCENT THC EXPOSURE ON ADULTHOOD PSYCHOPATHOLOGY

Justine Renard, Michael Loureiro, Walter J. Rushlow, Steven R. Laviolette

Dept. of Anatomy and Cell Biology & Dept. of Psychiatry, Schulich School of Medicine, University of Western Ontario, London, Ontario N6A 5C1

Marijuana is the most widely used illicit drug among adolescents. Adolescence is characterized by a brain in transition that differs anatomically and neurochemically from that of the adult. These modifications are thought to support the emergence of adult cerebral processes and behaviors.

The endocannabinoid system is a central component of these neurodevelopmental changes. This is mainly due to its involvement in the maintenance of the synaptic plasticity. Delta-9-tetrahydrocanabinol (THC), the main psychoactive component of marijuana, acts as a cannabinoid receptor agonist. Therefore, an over activation of the cannabinoid system by THC exposure during adolescence may dramatically alter brain maturation, thereby adult cerebral functions.

In the present study, we hypothesize that long-term adolescent chronic THC exposure will disrupt adult rat behaviors and the underlying neuronal functioning related to dysfunctions observed in schizophrenia.

To achieve this investigation, our protocol consists to expose adolescent rats (postnatal day (PND) 35 to 45) to THC (i.p. injections). At adulthood (PND75), behavioral tasks, *in-vivo* electrophysiological recordings and molecular analyses are performed.

Our results show that adolescent THC exposure induces long-term alterations in (1) social interactions/recognition; (2) sensorimotor gating; (3) locomotor activity and (4) neuronal DA activity in the ventral tegmental area (VTA). We are currently running molecular analyses in brain areas known to be disrupted in schizophrenia to correlate these changes with neuronal function alterations.

This animal model represents an interesting new framework for the study of the long-term consequences of marijuana exposure during adolescence. It might improve our understanding of the emergence of psychotic symptoms.

C42: DECREASED mTOR SIGNALING VIA p70S6K/eIF4B IS ASSOCIATED WITH LOSS OF THE EXCITATORY POSTSYNAPTIC MARKER PSD-95 IN AUTISM

Chiara Nicolini[1], Margaret Fahnestock[1]

[1]*Department of Psychiatry & Behavioural Neurosciences, McMaster University*

Defects in the establishment of neuronal networks are believed to be responsible for the clinical symptomatology of autism. However, the molecular mechanisms underlying the abnormal cortical circuitry seen in autistic brains remain to be elucidated. We previously found imbalances in TrkB isoforms and decreased upstream components of the mTOR pathway in postmortem brains of autism versus control subjects. mTOR downstream signaling pathways p70S6K/eIF4B and 4E-BP1/eIF4E are involved in regulation of dendritic spines which form excitatory postsynapses. Thus, we now aimed to examine whether mTOR-mediated signaling pathways are disrupted in autism and whether their disruption is associated with changes in PSD-95, a marker of excitatory synapses.

Phospho-mTOR, mTOR, p70S6K, eIF4B, 4E-BP1, eIF4E and PSD-95 were measured by Western blotting in postmortem fusiform gyrus of 11 autism and 13 control subjects.
Significantly decreased phospho-mTOR, mTOR, p70S6K, eIF4B and PSD-95 protein levels were observed in autism versus control fusiform gyrus. Surprisingly, no significant changes in 4E-BP1 and eIF4E protein expression were found.
Our findings show decreased mTOR expression and activation and down-regulation of mTOR downstream pathway p70S6K/eIF4B in autism which might result in reduced protein translation at spines. Spine protein translation deficits are likely to adversely affect spine density as suggested by decreased PSD-95 in autistic fusiform gyrus. Changes in spine density might perturb cortical circuitry and thus contribute to autism's cognitive and behavioural deficits.
Acknowledgements: Supported by a studentship from the Autism Research Training (ART) Program to Chiara Nicolini

C43: THALAMIC STROKE: MECHANISMS OF REMOTE DEGENERATION

N. Weishaupt[1], T. Dobbs[1], P. Riccio[2], V.C. Hachinski[2] and S.N. Whitehead[1,2]
[1]Vulnerable Brain Laboratory, Dept. Anatomy and Cell Biology, Western University
[2]Dept. Clinical Neurological Sciences, London Health Sciences Centre, Western University, London, ON

Individuals with a history of subcortical stroke (SS) often develop deficits in executive functions associated with frontal cortex regions. Cortical thinning in frontal regions remote from but connected with a SS has been reported, yet why these remote changes occur is poorly understood. The aim of this study is to elucidate the mechanisms that lead to remote cortical degeneration after SS in order to identify potential targets for a preventative strategy.
To investigate this, we induced a focal infarct in the dorsomedial thalamic nucleus (DMN) in rats by endothelin-1 injection (n=6). Control rats (n=6) received an injection of saline into the same region. All animals were allowed to survive for 4 weeks post-surgery.
Evidence of degenerating cells (FluoroJadeB) in the frontal cortex was found exclusively in stroke animals. To characterize pathological processes along the thalamocortical pathway, we screened key regions of axonal projections between the DMN and the frontal cortex with markers for reactive astrocytes (GFAP+) and for microglia (Iba-1+, OX-6+). No difference in any of these markers was detectable between stroke and control animals.
Our results indicate that damage to remote cortical areas is initiated earlier than 4 weeks after SS in rats. Further, our observations suggest that factors other than inflammation are likely initiating frontal cortex pathology. Whether inflammation accompanying axonal degeneration may exacerbate this process needs to be determined at different survival times.
Acknowledgements: This work was supported by a CIHR-STIHR Fellowship to N.W, the Premier's Discovery Award to V.C.H and a Lawson-IRF, CIHR-OG, NSERC, DG and CFI-LOF to S.N.W.

C44: NEUROPROTECTION BY STRESS-INDUCIBLE PHOSPHOPROTEIN-1 AGAINST ISCHEMIC INSULT AND APOPTOSIS

Jason Z. Xu[1,3], Flavio H. Beraldo[2,3], Valeriy G. Ostapchenko[2,3], Jue Fan[3], Vania F. Prado[1,2,3], Marco A. M. Prado[1,2,3,]
[1]Dept. of Anatomy and Cell Biology, University of Western Ontario, London, ON,
[2]Dept. of Physiology and Pharmacology, University of Western Ontario, London, ON
[3]Robarts Research Institute, London, ON,

Stroke, the disturbance of blood flow in the brain, is the third leading cause of death in Canada and is estimated to have a societal burden of $3-5 billion annually. The current treatment for stroke patients is thrombolytic therapy, a treatment only effective if administered immediately following the onset of stroke thus limiting its efficacy. Previous literature data indicated that the cellular prion protein (PrP^c) plays a role in regulating neuronal death after stroke. However, the mechanisms involved are poorly understood. In our current study, we tested the role of stress-inducible phosphoprotein-1 (STI1) in the response of mouse neurons to oxygen-glucose deprivation, a model of ischemic insult *in vitro*. STI1 is a co-chaperone protein that is also released by astrocytes to act as an activator of PrP^c. Mouse hippocampal neurons obtained at E17 were cultured for 7 days and treated with recombinant STI1 before and after depriving the cells of oxygen and glucose. The cells were given 24 hours to recover from ischemia. Our results demonstrate that pre-treatment with recombinant STI1 significantly decreased the level of apoptosis in mouse hippocampal neurons subject to oxygen-glucose deprivation. Furthermore, our results also show that the neuroprotective effect of STI1 pre-treatment is dependent on the α7 nicotinic acetylcholine receptor and the ALK2 receptor. We conclude that PrP^c activation by STI1 and its subsequent downstream signalling cascades may play a neuroprotective role in stroke.
Acknowledgments: Supported by CIHR

C45: EXAMINATION OF THE MELATONERGIC SYSTEM IN A 6-HYDROXYDOPAMINE RAT MODEL OF PARKINSON'S DISEASE

Na Hyea Kang[1], Candace Carriere[1], Lennard P. Niles[2]
[1]Graduate Student, McMaster integrative Neuroscience Discovery & Study (MiNDS) Program, McMaster University, Hamilton, ON,
[2]Department of Psychiatry and Behavioural Neurosciences, McMaster University, Hamilton, ON

The neuroprotective function of melatonin is mediated via G-protein-coupled MT_1 and MT_2 receptors, which trigger cell protection and survival pathways. By utilizing this function of melatonin, studies have shown positive effects in animal models Parkinson's disease (PD). Chronic treatment with a physiological dose of melatonin showed neuroprotective effects in the nigrostriatal pathway, as indicated by preservation of tyrosine hydroxylase (TH) in a 6-hydroxydopamine (6-OHDA) model of PD. Moreover, an increase in striatal melatonin levels was observed in 6-OHDA lesioned rats. Based on these implications of a close relationship between the dopaminergic and melatonergic systems, we hypothesize that degeneration of dopaminergic neurons induced by 6-OHDA will alter the melatonergic system in the nigrostriatal pathway. In this study, 6-OHDA was unilaterally injected into the rat striatum or substantia nigra. At 3 weeks post-surgery, an apomorphine rotation test was performed to select effectively lesioned animals. Loss of TH immunoreactivity in striatum and substantia nigra of the lesioned groups confirmed 6-OHDA-induced degeneration of dopaminergic neurons in the nigrostriatal pathway. Anticipated changes in melatonin MT_1 and/or MT_2 receptor expression in 6-OHDA lesioned rats, will help to clarify the neuroprotective interaction between the melatonergic and dopaminergic systems and perhaps reveal novel therapeutic strategies for Parkinson's disease.
Acknowledgements: Supported by CIHR.

C46: STEREOLOGICAL CONFIRMATION OF NEUROPROTECTION BY VALPROIC ACID IN A MODEL OF PARKINSON'S DISEASE

Candace H. Carriere[1], Na Hyea Kang[1], Lennard P. Niles[2]
[1]Graduate Student, MiNDS Program, McMaster University, Hamilton, ON
[2]Department of Psychiatry & Behavioural Neurosciences, McMaster University

Rotenone, a pesticide/insecticide, causes systemic inhibition of mitochondrial complex I activity, with consequent degeneration of dopaminergic (DA) neurons within the substantia nigra (SN) and striatum (STR), as observed in Parkinson's disease (PD). A novel intrastriatal rotenone model of PD was used to examine the neuroprotective effects of valproic acid (VPA), which upregulates neurotrophic factors in the brain. Sham or lesioned rats were treated with either vehicle or VPA (4 mg/mL) in drinking water. The right STR was lesioned by infusion at 3 points along its rostro-caudal axis (total of 6 µg of rotenone or vehicle). Motor function was assessed using a forelimb asymmetry test. Animals were sacrificed, 6 weeks post-surgery, by transcardial perfusion and brains were harvested for immunohistochemical examination of tyrosine hydroxylase (TH) within the STR and SN. Forelimb asymmetry data indicated a significant ($p<0.01$) decrease in contralateral forelimb use in lesioned animals (3rd week of testing), which was abolished by VPA treatment. A significant ($p<0.01$) increase in ipsilateral forelimb use in lesioned animals was not seen in animals treated with VPA. Stereological cell counting indicated a significant ($p<0.05$) decrease in TH+-DA neurons in the SN of lesioned animals. Importantly, this loss was blocked by chronic VPA treatment. Treatment with VPA abolished motor dysfunction and retrograde degeneration of the nigrostriatal pathway, with preservation of TH-immunoreactivity in the STR and TH+-DA neurons in the SN, indicating its therapeutic potential in PD.
Acknowledgements: Supported by CIHR Canada

C47: ROLE OF INSULIN IN THE REGULATION OF CHT-1 IN ALZHEIMER'S DISEASE

Katherine Fishwick & R. Jane Rylett
Department of Physiology and Pharmacology; Robarts Research Institute, University of Western Ontario

Alzheimer's Disease (AD) is a neurodegenerative disease characterized by memory loss, impaired learning ability and changes in mood or personality. It is the most common form of dementia in older people, currently affecting 1 in 13 Canadians over the age of 65 and numbers are rapidly increasing worldwide. There is no known cure and the cause is incompletely understood; however increasing attention is being drawn to the fact that insulin resistance or type 2 diabetes is a major risk factor in developing AD. One of the earliest deviations in the brains of AD victims away from healthy aging is the loss of activity of basal forebrain cholinergic neurons. Availability of acetylcholine, the neurotransmitter, is limited by how fast it can be recycled from the synaptic cleft by the cholinergic transporter protein CHT-1. Using a neuronal cell line, we are examining the regulation of CHT by insulin using an extended period of insulin treatment to replicate the changes occurring with insulin resistance. We demonstrate alterations in the regulation of cell surface transporter protein levels following insulin treatment which are only revealed when cells are stimulated, such as by depolarisation. We show that whilst insulin treatment decreases choline uptake at saturating concentrations of choline, at lower concentrations, insulin treatment increases cell surface CHT and choline uptake. Understanding the mechanism by which this occurs may offer a way of persevering neuronal function in early stage AD patients.

C48: INVESTIGATING THE MULTIPLE HIT HYPOTHESIS OF PARKINSON DISEASE

Komal Shaikh, Alvin Yang, Kate Youshin, Jeremy Kwok, Susanne Schmid
Anatomy & Cell Biology, University of Western Ontario, ON

Parkinson disease (PD), characterized by degeneration of dopaminergic neurons in the substantia nigra, is the most common movement disorder. While the cause of this disease is largely unknown, the Multiple Hit Hypothesis suggests that the combination of several risk factors, including aging, genetics and exposure to environmental toxins leads to the development of PD. Here, we explore the interaction between two potential causes of PD; a genetic mutation in the Lrrk2 gene and exposure to the neurotoxin, Paraquat. Genetic mutations in the leucine-rich-repeat kinase 2 gene cause autosomal dominant familial PD. This project characterizes transgenic BAC rats expressing human LRRK2 bearing the familial PD mutation, R1441G. Transgenic animals and wildtype littermates undergo a battery of motor and cognitive tests in order to determine if the genetic mutation alone is sufficient to cause PD related phenotypes. At 12 months of age, all rats are then further exposed to I.P injections of Paraquat or saline in order to determine if $LRRK2^{R1441G}$ rats have an increased susceptibility to environmental toxins. We hypothesize that LRRK2 transgenic rats will show vulnerability to Paraquat as compared to their wildtype counterparts. Preliminary testing indicates that LRRK2 transgenic rats are not significantly different from their wildtype counterparts by the 12 month stage, suggesting that the genetic

mutation alone is insufficient for PD symptoms. The interaction between the LRRK2 mutation and exposure to Paraquat is currently being tested

C49: VALIDATING LRRK2^{R1441G} RATS AS AN ANIMAL MODEL FOR PARKINSON DISEASE

Alvin Yang, Komal T. Shaikh, Jeremy Kwok, Kate Youshin, Charles Walewski, and Susanne Schmid

Department of Anatomy and Cell Biology, University of Western Ontario, ON

Parkinson Disease (PD) is a neurodegenerative disorder that impairs motor and cognitive functions. While most cases are sporadic, a small percentage is caused by genetic defects, such as mutations in the Lrrk2 (Leucine-rich repeat kinase 2) gene. There are currently no treatments to inhibit or slow down PD progression due to the absence of an ideal animal model on which new therapeutic strategies can be tested. However, rats recently became a viable alternative as overexpression and knock-in models have been developed. This study subjected cognitive tests to Lrrk2^{R1441G} transgenic rats, to determine if they show deficits characteristic of PD. The acoustic startle response (ASR) was used to examine impairments in short-term habituation (STH) and pre-pulse inhibition (PPI), as deficits in these areas have been observed in PD patients. STH and PPI assessments were performed every 3 months for a year to detect progressive deteriorations in cognitive function. At the end of 12 months, both WT and Lrrk2 rats showed normal STH and PPI, with no significant difference. The results suggest that Lrrk2 rats do not yet adequately reflect key PD features. However, given that PD is an age-dependent disease, it may be beneficial to continue STH and PPI assessments to allow more time for the defective gene to show its phenotype. In conclusion, the lack of cognitive deterioration suggests that Lrrk2^{R1441G} rats cannot yet be used as an animal model for PD.

C50: NEUROPROTECTION AGAINST B-AMYLOID MEDIATED BY A TARGETED ANTIOXIDANT

Courtney R. Giordano[1], Laura J. Terlecky[1], Aliccia Bollig-Fischer[2], **Paul A. Walton[3]**, and Stanley R. Terlecky[1]

Departments of [1]Pharmacology and [2]Oncology, Wayne State School of Medicine, Detroit, MI, USA. and [3]Department of Anatomy and Cell Biology, Western University, London, Ontario, Canada

Alzheimer's disease is a progressive neurodegenerative disorder characterized, in part, by accumulation of amyloid β-protein (Aβ) in the brain. Aβ either assembles extracellularly into fibrils or remains as soluble globular oligomers. How fibrillar or soluble oligomeric amyloid induces neuronal toxicity remains an area of intense investigation. Affected neurons experience oxidative stress, generate a number of pro-inflammatory cytokines, and appear to activate the endoplasmic reticulum-mediated unfolded protein response. Synaptic circuitry is compromised and neurological loss results.

The goal of this work was to document the neuroprotective effects of a cell-penetrating enzyme with powerful antioxidant and anti-inflammatory properties. To accomplish this, soluble amyloid β-derived diffusible ligands (ADDL) were generated *in vitro* and used to treat primary rat hippocampal/cortical neuron co-cultures. We show that soluble forms of Aβ induces production of reactive oxygen species (ROS) in these cells, viability is compromised, as well as neuronal degeneration. We also demonstrate that our targeted antioxidant, catalase-SKL dramatically protects cells, reducing ROS levels, enhancing their survival and preventing neurite loss. In addition, the decrease in GSTΠ observed following ADDL treatment could be prevented by treatment with catalase-SKL, either before or after ADDL exposure.

These results constitute the preliminary observations/proof-of-concept validation necessary for follow-up studies with appropriate Alzheimer's disease/aging animal models in a preclinical setting.

C51: DO DIFFERENCES IN FRUCTOSE/GLUCOSE RATIOS MATTER? A SUGAR-SEEKING AND SUGAR CONSUMPTION BEHAVIOUR STUDY VIA SELF-ADMINISTRATION.

[1]Paul Marshall, [1]Katrina Kent, [1]Stephen Daniels, [1]Ari Shore, [1]Tiana Downs, [1]Francesco Leri

[1]Department of Psychology, University of Guelph, Guelph, ON

Many have suggested that food additives like HFCS and sucrose may be a major factor in driving the obesity epidemic. However, the literature is split on this issue as to whether ratios of glucose (G) and fructose (F) play different roles in consumption behaviour, and if they do what mechanisms they may do this by. Therefore, the current study explored the hypothesis that ratio of F/G will influence sugar-seeking and consumption behaviours. Using a radial arm maze, non-food restricted male Sprague-Dawley rats self-administered high ratio (HR; 55%F-45%G, typical ratio used in the food industry) or low ratio (LR; 30%F-70%G, typical commercial sucrose pellets employed in animal research, Bio-Serv, Frenchtown, NJ) fructose-glucose pellets for 10 minutes daily, over 14 days. It was predicted that higher ratios of fructose toglucose would increase intake and sugar-seeking behaviour. However, what was found was that LR rats consumed at least one pellet on significantly more days than HR rats. Mechanisms of differential reinforcement and satiety were explored. From results it is suggested that LR and HR may not differ on ability to induce satiety, but instead on reinforcing ability driven by the higher proportion of glucose. Overall, this may have potential applications on policy and practices of weight management helping to continue to frame overeating as a problem of learning maladaptive habits, and that successful adherence to better habits may be dependent on avoidance of strong and unhealthy reinforcers such as glucose.

Acknowledgements: Supported by NSERC and Ontario Brain Institute.

D: Neural Excitability, Synapses, and Glia: Cellular Mechanisms

D9: MEMORY OR ATTENTION? THE EFFECT OF EARLY AUDITORY EXPERIENCE ON NEURAL IMMEDIATE-EARLY GENE EXPRESSION IN FEMALE ZEBRA FINCH (*TAENIOPYGIA GUTTATA*) AUDITORY FOREBRAIN AREAS.

Adriana Diez [1,2], Scott MacDougall-Shackleton [1,2,3]

[1]Advance Facility for Avian Research, London, ON

[2] Neuroscience Graduate Program, University of Western Ontario, London, ON

[3] Department of Psychology, University of Western Ontario, London, ON

The auditory forebrain regions caudo-medial nidopallium (NCM) and caudo-medial mesopallium (CMM) of songbirds are associated with auditory perception and complex auditory processing. Neural activation measure through the expression of the immediate-early gene ZENK in these areas varies in response to different sounds. Two hypotheses are proposed for this variation. First, ZENK may reflect access to a representation of song memories created early in life. Second, ZENK may reflect attentional processes. We tested these hypotheses by measuring ZENK in response to tutored heterospecific or isolate songs compared to non-tutored wild-type song. Young zebra finch females were exposed during development to one of three different tutoring conditions; 1. Conspecifics that sang an isolate song, 2. Heterospecific, Bengalese finches (*Lonchura striata domestica*), 3. Conspecifics that sang a wild-type song. After maturity females were exposed to one of five different playback types; wild type song, isolate song, their own tutor song, heterospecific song (Bengalese finch song), or white noise. Subsequently, the expression of ZENK in CMM and NCM was measured. We found that ZENK responses varied across playback stimuli in CMM and NCM, and this variation seemed to interact with early auditory tutoring conditions. Females tutored by wild type conspecifics or heterospecific showed more activation in response to conspecific or isolated song, but isolate females did not. In conclusion, these results do not support the hypothesis that ZENK activation reflects early auditory memories.

Acknowledgements: Supported by NSERC.

D10: ATRX IS REQUIRED FOR MYELINATION IN THE MOUSE CNS

Matthew W. Edwards[1,2,3], Yan Jiang[1], and Nathalie G. Bérubé[1,2,3]

[1]Children's Health Research Institute, London, ON

[2]Departments of Biochemistry and Paediatrics University of Western Ontario, London, [3]Lawson Health Research Institute, London, ON

ATRX is a close homolog of the Rad54 ATPase translocase and emerging studies implicate ATRX in the regulation of chromatin structure and gene expression and in the maintenance of genomic stability. Microarray analysis revealed that ATRX loss in the mouse forebrain results in decreased expression of many genes implicated in myelination. Myelin is a specialized membrane that encompasses axons of neurons and is necessary for efficient firing of action potentials. In the CNS, myelin arises via a differentiation event of oligodendrocyte precursor cells into myelinating oligodendrocytes, which then extend and wrap around axonal fibres. This is a tightly regulated process, however the mechanisms involved have yet to be fully elucidated. Here, we show that loss of ATRX in the brain of mice results in severe hypomyelination. We demonstrate that decreased myelination is not due to a reduction of the precursor cell population, nor to their proliferation or differentiation capacity. Rather, ATRX appears to be required for the final steps of oligodendrocyte maturation. These findings indicate that ATRX is required for maturation of oligodendrocytes, possibly by promoting the expression of myelin genes and proteins. Elucidating the role of ATRX in the myelination process may lead to novel therapeutic avenues for dysmyelination disorders.

D11: ACTIVATION OF THE ERK/MAPK PATHWAY BY DIMETHYL SULFOXIDE IS PREVENTED BY THE 5α-REDUCED TESTOSTERONE METABOLITE 3α-ANDROSTANEDIOL VIA GABA-ERGIC MODULATION IN SH-SY5Y NEUROBLASTOMA CELLS

Ari L. Mendell, Bettina Kalisch, Neil J. MacLusky

Department of Biomedical Sciences, University of Guelph, Guelph, ON

The mechanisms by which androgens regulate synaptic plasticity in the brain are largely uncharacterized. It has recently been demonstrated that hippocampal synaptic responses to fluctuating androgen levels are more complicated than previously believed, and it is becoming increasingly important to understand the signaling pathways involved. Additionally, it has been suggested that the cognitive effects of testosterone may be largely mediated by conversion to its 5α-reduced metabolites. Therefore, we investigated the effects of the testosterone metabolites dihydrotestosterone (DHT) and 5α-androstane-3α,17β-diol (3α-diol) on extracellular signal-regulated/mitogen-activated protein kinase (ERK/MAPK) activation in SH-SY5Y human neuroblastoma cells. During our investigation, we found a substantial activation of ERK/MAPK by the dimethyl sulfoxide (DMSO) vehicle, which, even at a final concentration of 0.001%, interfered with any observable androgenic effects of DHT. However, the reduced metabolite of DHT, 3α-diol, significantly reduced this activation via modulation of gamma-aminobutyric acid $(GABA)_A$ receptor signaling. The importance of these findings is two-fold. First, it appears that the commonly used vehicle DMSO induces activation of ERK phosphorylation, which may interfere with studies of rapid steroid signaling responses. Second, 3α-diol has the ability to inhibit ERK/MAPK activation through GABAergic modulation. The interaction between GABA signaling and ERK/MAPK activation may have a role in synaptic remodelling.

Acknowledgements: Supported by NSERC and the Government of Ontario (through an Ontario Graduate Scholarship).

D12: CHOLESTEROL REMOVAL ELICITS CONTRACTION IN DROSOPHILA MUSCLES

Andrea Krahn-Roldan[1], Lianne Esmores[1], Sonia Aksamit[1], Kiel Ormerod[1], Jens Coorssen[2], A. Joffre Mercier[1]
[1]*Department of Biological Sciences, Brock University, St. Catharines, ON*
[2]*Department of Biochemistry & Molecular Biology, University of Western Sydney, Australia*

We examine physiological functions of cholesterol, an integral component of cellular membranes. Methyl-beta-cyclodextrin (MßCD), which removes cholesterol from membranes, is reported to alter neuronal excitability, transmitter release and responsiveness to neurotransmitters in muscle cells. Some of these effects were unrelated to cholesterol removal. We report that bath application of 10 mM MßCD elicits slow contractions in body wall muscle fibres of 3rd instar *Drosophila* larvae. These contractions increase muscle tonus over 5-7 min and then subside in the continued presence of MßCD. Contraction amplitude is 2-5% of maximal contraction elicited by depolarization with 300 mM KCl. Following washout of MßCD, muscle force drops below the initial resting value. Pre-loading MßCD with cholesterol dramatically reduces contractions without altering the loss of force upon washout, suggesting that the contractions are related to cholesterol removal but the loss of force during washout is not. MßCD induces contractions in calcium-free saline, even though 300 mM KCl does not, suggesting that MßCD elicits release of calcium from the sarcoplasmic reticulum (SR) independently of membrane depolarization. Application of caffeine in calcium-free saline elicits strong contractions and prevents subsequent application of MßCD from eliciting contractions. Thus, depletion of SR calcium truncates the effect of MßCD on contractions. These results suggest that MßCD removes cholesterol from the plasma membrane and SR, and that the latter effect increases permeability to calcium.

Acknowledgements: Supported by NSERC.

D13: EPIGENETIC MECHANISMS UNDERLYING UPREGULATION OF MELATONIN RECEPTORS BY VALPROIC ACID

Sarra Bahna[1], Jane Foster[2], Lennard P. Niles[2]
[1]*Neuroscience Graduate Program, McMaster University, Hamilton, ON, Canada*
[2]*Department of Psychiatry & Behavioural Neurosciences, McMaster University*

Accruing evidence supports a neuroprotective role for valproic acid (VPA), a common anticonvulsant and mood stabilizer, in the CNS. While the exact mechanism of neuroprotection by VPA is not yet characterized, there are several targets implicated to contribute to this role. For example, VPA enhances pro-survival molecules pErk1/2 and pAkt, and inhibits caspase-3 activity through ERK and AKT signaling pathways. Recently, VPA was characterized as an activator for AMP-activated protein kinase. VPA is also known to be a potent histone deacetylase (HDAC) inhibitor. In the past, we have shown an induction of melatonin receptor mRNA and protein by VPA in C6 cells, as well as the adult rat hippocampus. Preliminary evidence from our lab indicates that VPA also induces melatonin receptor mRNA expression in the rat striatum and midbrain. While blockade of ERK signaling results in an attenuation of neuroprotection by VPA, we have reported that this inhibition does not affect the upregulation of melatonin receptor expression by VPA. This suggests another mechanism of neuroprotection by VPA, via the melatonergic system. The robust upregulation of melatonin receptors by VPA begs the question as to the mechanism underlying this induction. Other HDAC inhibitors, which are structurally distinct from VPA, have shown a similar induction of these receptors. These findings suggest an epigenetic mechanism involving melatonin receptor promoter hyperacetylation associated with an increase in receptor gene expression. In this study, we use chromatin immunoprecipitation to examine this possibility.

Acknowledgements: Supported by NSERC.

D14: THE EFFECTS OF GONADECTOMY ON HIPPOCAMPAL DENDRITIC SPINE DENSITY AND BRANCHING IN ADULT MALE MICE

Dallan McMahon[1], Sarah Atwi[1], Craig Bailey[1] and Neil J MacLusky[1]
[1]*Department of Biomedical Sciences, University of Guelph, Guelph, ON*

The effects of androgens on hippocampal morphology and function are poorly understood. Gonadectomy (GDX) induces a small decline in dendritic spine density in CA1 and CA3 in adult male rats, accompanied by an outgrowth and increase in branching of apical dendrites of neurons located in the CA3 pyramidal cell layer. In mice, by contrast, previous work has suggested that androgen may have trophic effects on hippocampal dendrites, suggesting a possible species difference. To test this hypothesis, we examined the effects of GDX on dendritic branching patterns and dendritic spine density in CA1 and CA3 pyramidal neurons of adult male mice. The brains of CD-1 mice were removed and stained using the Golgi-Cox method 21 days after either GDX or sham-operation. Sholl analysis was used to assess dendritic branching of 3-dimensionally traced pyramidal neurons from 300um thick coronal sections. These same sections were used to measure dendritic spine density in the proximal, medial, and distal regions of the apical dendrites of CA1 and CA3. Results show a small overall decline in dendritic spine density in CA1 and CA3 following GDX, similar to what has been observed in the rat. However, Sholl analysis revealed a decline in dendritic branching in both CA1 and CA3, without an effect on dendritic length. This result is consistent with previously observed effects of manipulating androgen levels in mice, supporting the view that mice and rats may show very different hippocampal responses to changes in circulating androgen levels.

Acknowledgements: Supported by NSERC and CFI.

D15: INCREASED EXPRESSION OF THE IMMEDIATE EARLY GENE *ARC* IN BRAINS OF MICE RESISTANT TO ETHANOL SENSITIZATION

Christina N. Nona, José N. Nobrega
Behavioural Neurobiology Research Section, Centre for Addiction and Mental Health, Toronto, Ontario

Repeated exposure to ethanol (EtOH) in mice results in behavioural sensitization, a progressive increase in locomotor activity. Not all mice treated with EtOH will sensitize and the underlying neuroadaptations mediating this variable response are unclear. Abused drugs have been shown to induce the expression of immediate early genes (IEGs), markers of neuronal activity, throughout the brain. The IEG *arc* plays a critical role in activity-dependent synaptic plasticity given that its synthesis requires NMDA receptor activation. Examining *arc* expression between sensitized and non-sensitized mice may reveal brain areas in which EtOH-induced neuroplasticity contributes to the development of sensitization. To do this, male DBA mice received 5 biweekly EtOH (2.2g/kg, i.p.) or saline injections. Two weeks later, mice were challenged with either EtOH (1.8g/kg) or saline and brains were immediately removed 30mins later for examination of *arc*. Results showed that an EtOH challenge suppressed *arc* expression in many brain areas. However, it increased *arc* expression in the lateral accumbal shell in non-sensitized mice compared to controls. When challenged with saline, *arc* expression was higher in the ventral tegmental area (VTA) compared to sensitized animals. These findings suggest that EtOH differentially regulates neuronal activity in sensitized and non-sensitized mice. The fact that non-sensitized mice have increased basal activity in the VTA raises the possibility that this population may have overactive NMDA receptors as a consequence of withdrawal from repeated EtOH exposure.

Acknowledgments: Funded by NSERC

D16: ABNORMAL HIPPOCAMPAL ACTIVATION IN FREELY BEHAVING MICE DEFICIENT FOR VESICULAR ACETYLCHOLINE TRANSPORTER

Shahin Moallem [1], Marco Prado[1,2], Vania Prado[1,2] and L. Stan Leung[1,3]
[1] *Neuroscience Graduate Program, [2]Dept. Anatomy and Cell Biology, [3]Dept. Physiology and Pharmacology, University of Western Ontario, London ON*

Acetylcholine has a fundamental role in cortical activation. The activation of the hippocampus, a cortex implicated in cognitive and sensorimotor functions, is characterized by an increase in power and frequency of oscillations in the theta (4-10 Hz) and gamma (30-100 Hz) frequency range. We studied hippocampal activation in mice with deficiency in cholinergic functionality due to heterozygous knockdown (KD^{Het}) of the vesicular acetylcholine transporter gene. We hypothesized that the mutant KD^{Het} mice, relative to wild type (WT) mice, will manifest abnormal theta and gamma oscillations during different behaviors, and in response to muscarinic cholinergic antagonist scopolamine hydrochloride (5 mg/kg i.p.). Hippocampal electroencephalogram (EEG) was recorded from CA1 electrodes in 6 WT and 3 mutant KD^{Het} freely behaving mice. We found that mutant mice manifested higher frequency theta but weaker gamma oscillations during walking or awake-immobility, as compared to WT mice. Injection of scopolamine abolished the immobility-associated theta oscillations of 4-7 Hz in all WT but not in 3 mutant mice. Scopolamine attenuated the immobility-associated gamma power in both WT and mutant mice. After scopolamine injection, theta and gamma power during walking were increased in the mutant mice but attenuated in the WT mice. In conclusion, mutant mice showed increased scopolamine-resistant hippocampal activation during walking and awake-immobility, which may occur in compensation of the low cholinergic function.

Acknowledgements: Supported by CIHR grants to MP, VP and LSL

E: Sensory and Motor Systems

E15: HOW DOES VISUAL MANIPULATION AFFECT OBSTACLE AVOIDANCE STRATEGIES USED BY ATHLETES AND NON-ATHLETES?

Michael P. Bijman[1], Joshua J. Fisher[1], and Lori A. Vallis[1]
Human Health & Nutritional Sciences, University of Guelph, Guelph, ON, CANADA[1]

Past research examining our ability to react to, and avoid static [1,2] and dynamic [3] obstacles in our travel path has stressed the importance of lower limb and obstacle visual input during obstacle clearance [4]. The aim of this study was to determine if athletes playing varsity level field sports are more proficient than recreationally active individuals when using visual information to guide the foot over a moving obstacle [5]. Ten varsity level athletes and ten age matched control subjects (age 18-25) walked along a 7-meter walkway and stepped over a stationary (high position scaled to 30% lower leg length) or dynamic obstacle (motion along a 180° arc). Visual input was manipulated using PLATO visual occlusion goggles one and two steps pre-obstacle. Kinematic data (N=4; Optotrak 3020 system, NDI, Waterloo) demonstrated a significant main effect between athletes and non-athletes in landing distance (location of right foot after obstacle cross) and max lead toe at obstacle (height of right toe at obstacle cross). Preliminary results suggest athletes are more comfortable on a single-limb (larger landing distance) and are more efficient (smaller max lead toe at obstacle cross) during obstacle cross. Further investigation aims to strengthen these findings with the analysis of more subjects.

References: [1] Patla & Greig (2006) Neuroscience Letters.397:110-114. [2] Patla &Vickers (1997) NeuroReport. 8:3661-3665. [3] Santos, Moraes, Patla (2010) Motor Control 14(4): 424-39. [4] Rietdyk (2006) Exp Brain Research 169: 272-278. [5] Weast (2011) Exp Psychology (Hove) 64(4): 689-706.

E16: SYNAPTIC ARCHITECTURE OF THE ACOUSTIC STARTLE RESPONSE PATHWAY

Mahabba Smoka, Nagalingam Rajakumar, Cleusa deOliveira, Susanne Schmid
Department of Anatomy and Cell Biology, Western University, London, ON

The acoustic startle reflex (ASR) is an important tool used to measure sensorimotor gating. The primary ASR pathway involves auditory hair cells and secondary neurons in the cochlear root nucleus. The latter then synapse onto giant neurons of the caudate pontine reticular nucleus (PnC) which directly innervate cranial and spinal motor neurons. Based on physiological and behavioral data, habituation of startle is thought to occur due to hyperpolarizing BK channels localized at glutamatergic terminals in PnC auditory afferents. Pre-pulse inhibition also modulates startle and is predicted to be mediated by cholinergic innervation of PnC giant neurons; glutamate or GABA may play a role. The purpose of this project is to describe the synaptic architecture of the ASR pathway and its modulatory afferents in order to better understand the neurotransmitter(s) involved and the effect of drugs on sensory gating. Fluorogold is injected into the cervical spine of rats to label a subpopulation of PnC giant neurons. KCa1.1, VGLUT1, GAD67, and CHT1 antibodies are used to stain for BK channels, glutamatergic, GABAergic, and cholinergic terminals, respectively, to clarify the synaptic inputs modulating startle. Dual staining shows some BK channel expression on glutamatergic terminals. Co-localization of either glutamate or GABA in a subpopulation of cholinergic terminals is also seen and this is consistent with studies done in basal forebrain cholinergic neurons. These results indicate that BK channels implicated in habituation are localized on auditory glutamatergic afferents as predicted.

Acknowledgments: Supported by NSERC.

E17: CHOLINERGIC MECHANISMS OF SENSORY FILTERING

Erin Azzopardi and Susanne Schmid
Department of Anatomy and Cell Biology, Western University, London, ON

Sensory filtering is a basic cognitive process. It refers to the brain's ability to remove extraneous sensory information from awareness. Many disorders are associated with deficits in sensory filtering, particularly habituation and prepulse inhibition (PPI). Both habituation and PPI reflect a decrease of behaviour in response to a stimulus. Habituation refers to a decrease after repeated exposure to that stimulus. PPI occurs when a subthreshold stimulus precedes a strong behaviour-eliciting stimulus, causing a reduction in behavioural responding.

The role of acetylcholine in sensory filtering is not fully understood. To investigate this, we used a transgenic mouseline (B6.Cg-Tg(ChAT-COP4*H134R/EYFP)6Gfng/J)$^{+/+}$). This mouse has a modified channel rhodopsin2 (ChR2)-gene inserted into a cholinergic promoter. The hChR2 protein is a light-sensitive cation channel; insertion allows us to excite cholinergic cells using light.

It has been shown that this mouse has increased cholinergic tone, resulting in impaired cognition. However, we found these mice exhibit normal sensory filtering of the startle reflex. Startle ability, habituation and PPI were not statistically different in transgenic mice.

We are further investigating this transgenic model by validating that the ChR2 protein is expressed in midbrain cholinergic cells using immunohistochemistry. We aim to establish these mice as a model to study cholinergic mechanisms of sensory filtering using optogenetics. Specifically, my next step will be to implant light cannula targeting the midbrain during sensory filtering tasks.

Acknowledgments: Supported by OMHF

E18: VISUAL RESPONSE ON HUMAN UPPER LIMB MUSCLES CAN BE INDPEDENT OF THE ENSUING REACH MOVEMENT

Chao Gu, Daniel K. Wood, Paul L. Gribble, Timothy J. Doherty, Melvyn A. Goodale, Brian D. Corneil
Western University, London, ON

Presentation of a bright visual stimulus can evoke a brief recruitment of the proximal limbs in both humans and non-human primates (NHPs) at reflexive-like latencies. In the upper limb of humans such a stimulus-locked response (SLR) appears within 80-100 ms after visual stimulus onset during a reaching task, increasing/decreasing muscle activity when the muscle functions as an agonist/ antagonist for the reaching movement, respectively (Pruszynski et al., 2010). SLRs have also been reported in neck muscles in NHP before saccadic gaze shifts (Corneil et al., 2004). To further investigate the SLR phenomenon in human limb muscles, we studied upper limb muscle recruitment during two reaching tasks modified from classical oculomotor tasks; these tasks separate visual sensory events from either the time or direction of the ensuing movement. We recorded intra-muscular EMG activity from the right pectoralis major (PM) muscle while human subjects performed two tasks. In the first task, subjects performed center-out delayed or immediate reaches to stimuli placed either in or opposite to the PM's preferred direction. Subjects were instructed to wait until a central fixation point (FP) disappeared before moving. FP disappeared either immediately or 1 sec later. In the second task, the color of the central FP instructed subjects to either reach towards (pro-trials) or in the diametrically opposite direction (anti-trials) of the peripheral target. In both of these tasks SLR was reliably evoked in PM and were in the direction of visual stimuli regardless of the ensuing movement.

E19: DISSOCIATION OF PARIETAL CORTEX CONTRIBUTIONS TO OBSTACLE MEMORY IN LOCOMOTING CATS

Carmen Wong[1], Keir G. Pearson[3], Stephen G. Lomber[2]
[1]*Graduate Program in Neuroscience, The University of Western Ontario, London, ON*
[2]*Brain and Mind Institute, The University of Western Ontario, London, ON*
[3]*Department of Physiology, University of Alberta, Edmonton, AB*

A working memory of environmental obstacles is essential for avoidance in walking animals. In quadrupeds, vision is not available to guide hindleg stepping over an obstacle previously cleared by its forelegs. Instead, memory of the obstacle is used to modify hind limb movements. Previous studies suggest that this obstacle memory system is reliant on regions of parietal cortex associated with visually-guided movements. To investigate the role of parietal cortex in obstacle memory, cortical cooling was used to reversibly deactivate areas 5 or 7 in cats trained to step over a barrier. Hindleg step height and trajectory over the barrier were measured to assess memory of the obstacle. Bilateral cooling of area 5 resulted in significantly lower steps and altered trajectories, demonstrating a disregard for the obstacle. However, hindleg stepping was unaffected when area 7 was bilaterally cooled. The laterality of the memory system was then assessed with selective unilateral deactivations. Cooling of area 5 in one hemisphere produced deficits in step height and trajectory in the contralateral hindleg only. Unilateral area 7 cooling did not affect hind limb steps over the remembered barrier. These findings suggest that while area 7 may not contribute to obstacle memory, area 5 of parietal cortex is involved in the working memory of an obstacle encountered in the contralateral hemispace.

Acknowledgements: Supported by the Natural Sciences and Engineering Research Council of Canada.

E20: THE INFLUENCE OF CUTANEOUS VIBRATION APPLIED TO THE FOOT SOLE AND FOOT DORSUM ON ANKLE PROPRIOCEPTION

Robyn L. Mildren[1] and Leah R. Bent[1]
Department of Human Health and Nutritional Sciences, University of Guelph, Guelph

Cutaneous afferents from the foot dorsum code for the direction and velocity of ankle rotation[1]. Meanwhile, afferents from the foot sole provide information about ground contact and pressure distribution[2]. In the hand, it has been shown that high-frequency cutaneous vibration applied to adjacent areas can interfere with proprioception[3]. Interactions between cutaneous afferents from adjacent regions and proprioceptive signals have not been investigated in the lower limb. The purpose of this experiment is to determine if cutaneous afferents from the foot sole and foot dorsum influence ankle proprioception, assessed through an ankle-matching task. The left ankle (target) will be passively rotated by a motor and held at a target angle (7^o dorsiflexion, 7^o plantarflexion, or 17^o plantarflexion). The right ankle (matching) will then be passively rotated until the subject perceives that the two angles are aligned. During the ramp-up and hold, vibration will be applied to the target foot (heel, metatarsals, or foot dorsum) at 3 frequencies (8, 40, or 250 Hz). Outcome measures include directional error (DE), absolute error (AE), and variability (VAR) in ankle matching. Preliminary results (n=4) of high frequency vibration applied to the foot dorsum showed no significant changes in DE, AE, or VAR compared to control trials. However, 2 subjects showed a consistent trend of increased variability with cutaneous vibration across all angles.

1. Aimonetti et al. (2007) J Physiol 580:649-658
2. Inglis et al. (2002) Adv Exp Med Biol 508:111-117
3. Weerakkody et al. (2007) J Physiol 581:971-980

Acknowledgements: Supported by NSERC

E21: MUSIC-INDUCED MOOD IMPROVES RETENTION IN VISUOMOTOR ADAPTATION

Kristina Waclawik[1] and Li-Ann Leow[2]
[1]*Huron University College, University of Western Ontario*
[2]*Brain and Mind Institute, University of Western Ontario*

Learning to adapt motor outputs to distortions in sensory feedback, or sensorimotor adaptation, is crucial to rehabilitation following injury or disease. Reinforcement increases persistence of adapted movements after removing the distortion, suggesting improved retention. Music is a strong modulator of dopamine reward responses, and might influence reinforcement mechanisms in adaptation. Striatal responses are evoked by music-induced positive mood but not music-induced negative mood. Here, we compared the effects of music-induced positive and negative mood on a sensorimotor adaptation task. In Experiment 1, music-induced positive mood increased persistence of adapted movements upon removing the distortion, indicating improved retention. In Experiment 2, reinforcing the adapted motor output with pictorial reward decreased retention when combined with positively-valenced music but not silence or negative music. We suggest that the rewarding properties of the music present during both pre-distortion baseline and adaptation phase overrode the rewarding properties of the pictures in the post-adaptation period. Music has a similar effect on retention of adaptation as other rewards and can even override the effects of direct pictorial reinforcement when competing movements have been reinforced.

E22: REDUCED *N*-ACETYLASPARTATE IN THE MOTOR AND SENSORY CORTICES DUE TO CERVICAL SPONDYLOTIC MYELOPATHY: A LONGITUDINAL STUDY

Sandy Goncalves[1-3], Todd Stevens[2], Robert Bartha[1, 2], Neil Duggal[1, 3]
[1] *Department of Medical Biophysics,*
[2] *Centre for Functional and Metabolic Mapping, Robarts Research Institute*
[3] *Department of Clinical Neurological Sciences, University Hospital - London Health Sciences Centre, University of Western Ontario, London, Ontario, Canada*

CSM is the most common type of spinal cord dysfunction in people over the age of 55. Surgeons are unable to accurately predict when and for whom operative management is absolutely indicated. Magnetic resonance spectroscopy (MRS) is a non-invasive *in-vivo* technique used to acquire metabolic information from specific volumes of tissue. Kowalczyk et al (2011) previously demonstrated a significant (p=0.008) decrease in the *N*-acetylaspartate (NAA) / creatine (Cr) ratio in the motor cortex in people with CSM indicating reduced neuronal integrity/function. We hypothesize that NAA recovery following surgery will lag in the sensory cortex compared to the motor cortex emulating the time course of functional recovery. 24 patients with CSM underwent proton-MRS on a 3.0T Siemens MRI. Long echo-time (TE=135, TR=2000) ^{1}H spectroscopy data were acquired to measure absolute levels of NAA from the motor and sensory cortices in each subject on the side of greater motor deficit at baseline and then at 6 weeks and 6 months following surgery. At

baseline, patients had significantly lower NAA compared to controls in both the motor ($p<0.05$) and sensory cortices ($p<0.05$). In patients, there was a trend toward decreased NAA 6-weeks post-surgery ($p<0.1$) in the sensory cortex and a significant NAA decrease at 6 months post surgery ($p<0.05$). A decrease was also found in the motor cortex at 6-months post-surgery ($p=0.05$). These results suggest a progressive decline in neuronal integrity/function in both motor and sensory cortices from six weeks to six months following surgery.

E23: CORTICAL REORGANIZATION IN CERVICAL SPONDYLOTIC MYELOPATHY BEFORE AND AFTER DECOMPRESSION SURGERY

Kayla Ryan[1,2], Sandy Goncalves[1,2], Robert Bartha[1,2] & Neil Duggal[1,3]
[1] Department of Medical Biophysics,[2] Centre for Functional and Metabolic Mapping, Robarts Research Institute, University of Western Ontario, London, Ontario, Canada
[3] Department of Clinical Neurological Sciences, University Hospital, London Health Sciences Centre, London, Ontario, Canada

Cervical spondylotic myelopathy (CSM) is characterized by the compression of the spinal cord causing a wide range of debilitating symptoms as well as differences in brain activity measured by functional magnetic resonance imaging (fMRI). We have previously shown an increase in the volume of activation (VOA) in the primary motor cortex (M1), and a decrease in VOA in the somatosensory area (S1) in people with CSM. After decompression surgery, an observed increase in the VOA in both M1 and S1 suggested functional reorganization within the brain. The purpose of this study is to characterize the reorganization that occurs within the sensorimotor cortices following spinal decompression in people with CSM. 13 CSM patients with right hand deficit underwent blood oxygenation level dependent fMRI in a 3.0 Tesla Siemens MRI prior to as well as 6 weeks and 6 months following spinal decompression surgery. Subjects performed a finger tapping paradigm with the right hand. 10 right handed control subjects were also studied with the same paradigm. Preoperatively, control subjects exhibited a larger VOA in the primary somatosensory cortex compared to CSM patients (8.8 cm^3 and 0.2 cm^3 respectively, p-corrected=0.0001). Six weeks post decompression surgery, the VOA of S1 decreased (0.017cm^3) however, 6 months following decompression surgery, the VOA increased to 1.1 cm^3. Changes in cortical activation following surgery indicated that patients recruited the ipsilateral premotor cortex. In addition, patient data at 6 weeks and 6 months after surgery showed recruitment of the supramarginal gyrus ($p < 0.05$). Reorganization of brain function within the primary somatosensory region was observed as early as six weeks post decompression surgery. Recruitment of the supramarginal gyrus and ipsilateral premotor cortex may compensate for the decrease in activity of S1.

Acknowledgments: Supported by CIHR

E24: INVESTIGATING THE ROLE OF REPEATED EXPOSURE TO ALTERATIONS OF VOCAL AUDITORY FEEDBACK

Arden R. DeMarco[1], Nichole E. Scheerer[1], and Jeffery A. Jones[1]
[1]Department of Psychology & Laurier Centre for Cognitive Neuroscience, Wilfrid Laurier University, Waterloo, ON

When speakers hear auditory feedback regarding their vocal pitch (F0) shifted upward or downward, a compensatory response is elicited that opposes the perceived shift. This "pitch shift reflex" is typically labelled as automatic. The present study was designed to determine whether repeated exposure to altered auditory feedback (AAF) would modify this compensatory response. Participants heard their F0 shifted downward over multiple sessions on the same day, or over several days. In each session participants were exposed to multiple, brief pitch perturbations while event related potentials (ERP) were recorded. Based on previous research, we hypothesized that repeated exposure to AAF across several days would result in memory consolidation, and produce larger changes in responses across sessions, relative to multiple sessions on the same day. While consolidation effects were not observed, we did find that repeated exposure to AAF resulted in a decrease in vocal compensation magnitude. ERP responses were also found to change as a function of exposure. Over time, exposure to AAF decreased N100 latency, increased P200 amplitude, and decreased P200 latency. All these findings occurred as a result of repeated exposure to AAF. Timing (i.e., same day testing compared to testing over multiple days) did not affect ERP or vocal responses. These results suggest that more prolonged exposure to AAF may be necessary to determine what role, if any, consolidation of memory plays in responses to AAF.

Acknowledgements: Supported by NSERC.

E25: DO REAL TOOLS PRIME HAND ACTIONS MORE THAN PHOTOGRAPHS OF TOOLS?

Scott D. Squires[1], Scott N. Macdonald[1], Derek J. Quinlan[1], Joey U. Paccioco[1,] Jody C. Culham[1], and Jacqueline C. Snow[2],
[1]The Brain and Mind Institute, Department of Psychology, University of Western Ontario, London, ON
[2]Cognitive and Brain Sciences Program, University of Nevada Reno, Reno, NV

Past work from our lab found that participants are faster to use a real tool if they have been primed by a visual preview of that same real tool compared to a different real tool (Valyear et al., 2011, Exp Brain Res). Moreover the priming effect was larger when the task was to use the tool – which requires associating the visual form of the tool with the appropriate action – than when the task was to simply move the tool. Here we wondered how priming would be affected when the prime was a 2D photo of the tool instead of a real tool. Participants saw a 1-s preview of either a photo of a tool or the real tool itself and then grasped a real tool (the probe) to either move it to the side during "grasp-to-move" (GTM) trials or demonstrate its everyday use during "grasp-to-use" (GTU) trials. Reaction times (RTs) to initiate the actions were measured. The identity of prime and probe could be the same (congruent trials; e.g., spatula-spatula) or different (incongruent trials; e.g., whisk-spatula).
Main effects revealed that subjects were faster to respond when the prime was congruent vs. incongruent, when the prime was a real tool vs. a photo, and when the task was GTM vs. GTU. In addition there was a trend toward an interaction in which the priming effect (incongruent – congruent RT) was larger for GTU than GTM tasks. Taken together, these results indicate that although a glimpse of either a real tool or a photo are equally effective at invoking the appropriate action association, viewing a real tools facilitates a faster overall action response.

Acknowledgements: Supported by NSERC Discovery Grant to JCC

E26: EFFECTS OF CATHODAL AND ANODAL TRANSCRANIAL DIRECT CURRENT STIMULATION (tDCS) OF THE SUPPLEMENTARY MOTOR AREA (SMA) ON BEAT PERCEPTION

Ruxanda A. Rusu, Li-Ann Leow, Jessica A. Grahn
Brain and Mind Institute, University of Western Ontario, ON

Perception of the beat in music appears intrinsically linked to movement, as functional neuroimaging studies show that perception of the beat engages motor areas of the brain, including the supplementary motor area (SMA) and the basal ganglia. Here, we examined whether the SMA plays a causal role in beat perception by altering SMA excitability using transcranial direct current stimulation (tDCS) in a polarity-dependent fashion. Beat perception was estimated by performance on a rhythm discrimination task, in which subjects discriminated changes in either beat rhythms or non-beat rhythms. Increasing SMA excitability with anodal tDCS selectively improved perception of beat rhythms. Decreasing SMA excitability with cathodal stimulation worsened perception of beat rhythms. Neither anodal nor cathodal stimulation altered perception of non-beat rhythms. These polarity-dependent effects suggest a causal link between SMA function and the ability to perceive the beat.

E27: ANODAL TDCS STIMULATION OF THE CEREBELLUM AND SMA ALTERS RELATIVE TIMING PERFORMANCE

David Prete[1,2], Li-Ann Leow[1,2], Jessica Grahn[1,2]
[1]Brain and Mind institute, University of Western Ontario, London, ON
[2]Department of Psychology, Western University London, ON

The supplementary motor area (SMA) and the cerebellum are involved in timing mechanisms that allow synchronized movements to musical beats. The supplementary motor area appears to be involved in encoding multiple time intervals relative to a beat (i.e., beat-based timing). The cerebellum appears to be involved in encoding time intervals independently (i.e., non-beat based timing). Here, we examined how enhancing SMA and cerebellar excitability using anodal transcranial direct current stimulation (tDCS) affected the ability to discriminate changes in beat-based and non-beat based rhythms. Consistent with a hypothesized role in beat-based timing, anodal SMA stimulation significantly improved discrimination of beat-based rhythms without significantly altering performance for non-beat rhythms. However, counter to previous work, anodal cerebellar stimulation *decreased* discrimination performance for beat-based rhythms without significantly altering discrimination performance of non-beat rhythms.

Last minute submission:

CUT ADULT MAMMALIAN BRAIN HEALS VIGOROUSLY WITH ITS HEART

Foerster A1, Holmes M1
1Department of Psychiatry & Behavioural Neurosciences, McMaster University

Cut CNS is considered to be inert and toxic without interventions because its axons do not elongate spontaneously, looking disorderly, like those of regenerating peripheral nerves. Orderly--seeming structures near its lesions are assumed to have been spared, and not cut and regenerated, although there is histological, physiological and HRP-tracing evidence that cut brain can heal itself routinely, accurately and functionally (1) when its cuts are permanently defined so that could be detected if it had happened. To explain that, so that new experiments can be designed to promote the recovery of its functions that were compromised immediately post-lesion, we have analyzing the results of making vertical cuts through rat brain with a wire device that was immediately implanted or withdrawn. Their series of sections is comprehensively stained with a technique that provides a detailed view of its architecture and fine details which allows a three dimensional tracing of the effects of a cut on its components including blood vessels*. Images are captured with a microscope and software (Nikon) for automatic high-resolution image stitching. All cut regions can heal appropriately. Cuts marked by implanted devices are easiest to study because they generate the most dramatic histological images of its topologically correct healing which takes the form of locally reoriented, tract-specific, axonal detours re-connected around the marked incision. Massive and appropriate scar-less re-connection can also occur across the marked incision. Withdrawing the device immediately does not trigger the formation such detours, but produces evidence that the cut has knitted together progressively from axon fusion at its ends, in an orderly way that can obliterate evidence of scarring and which is reminiscent of second intention healing in other cut tissues, e.g. skin. The new view that the CNS is a cooperative neurovascular system in which blood vessels, covered by astrocytes with processes that connect them to neuronal elements and trigger impulses, and the finding that they have stable locations after lesion (2), suggest that cutting its neurovascular network triggers the immediate healing ability of the circulatory system, which is specialized for rapid re-connection, and also facilitates a rapid and appropriate re-connection of cut axons and of their astrocytic nourishment systems. That would be evidenced by new axonal growth patterns which mimic those of new blood vessel patterns.

**We thank Dr. Thomas Hawke, Department of Pathology, McMaster, for recognizing this.Foerster AP, Holmes MJ. Cut adult mammalian CNS routinely regenerates. Program No. 229.13/A54 Neuroscience Meeting Planner. Washington DC: Society for Neuroscience, 2011. Online.*

Tsai H-H, Li H, Fuentealba LC, Molofsky AV, Taveira-Marques R, Zhuang H, Tenney A, Fancy SPJ, Merkel F, Kessaris N, Alvarez-Buylla A, Richardson WD & Rowitch DH. Regional astrocyte allocation regulates CNS synaptogenesis and repair.Science, 2012; 337:358-362.

Author Index

Morning session:
A1-A36, B1-B4, C1-C25, D1-D8, E1-E14

Afteroon session:
A37-A72, B5-B8, C26-C51, D9-D16, E15-E27

Fisher Scientific

Thermo SCIENTIFIC

Receive **33% off** Nunc and Nalgene Products **FOR 1 YEAR!!** with purchase of a Thermo Scientific Freezer, AND Incubator, AND Centrifuge!!

Valid Until August 30th 2014.

Fisher Scientific

Receive a **FREE Additional Year of Warranty** on Any Qualifying piece of equipment from Fisher! Ask your local Fisher rep for more information and to see if your instrument qualifies!!

Valid until June 30th 2014.

HyClone

CORNING

GE Healthcare

R&D SYSTEMS

Thermo SCIENTIFIC

Fisher Chemical

sartorius

Fermentas
Part of Thermo Fisher Scientific

FINNZYMES
Part of Thermo Fisher Scientific

MILLIPORE

Fisher BioReagents®