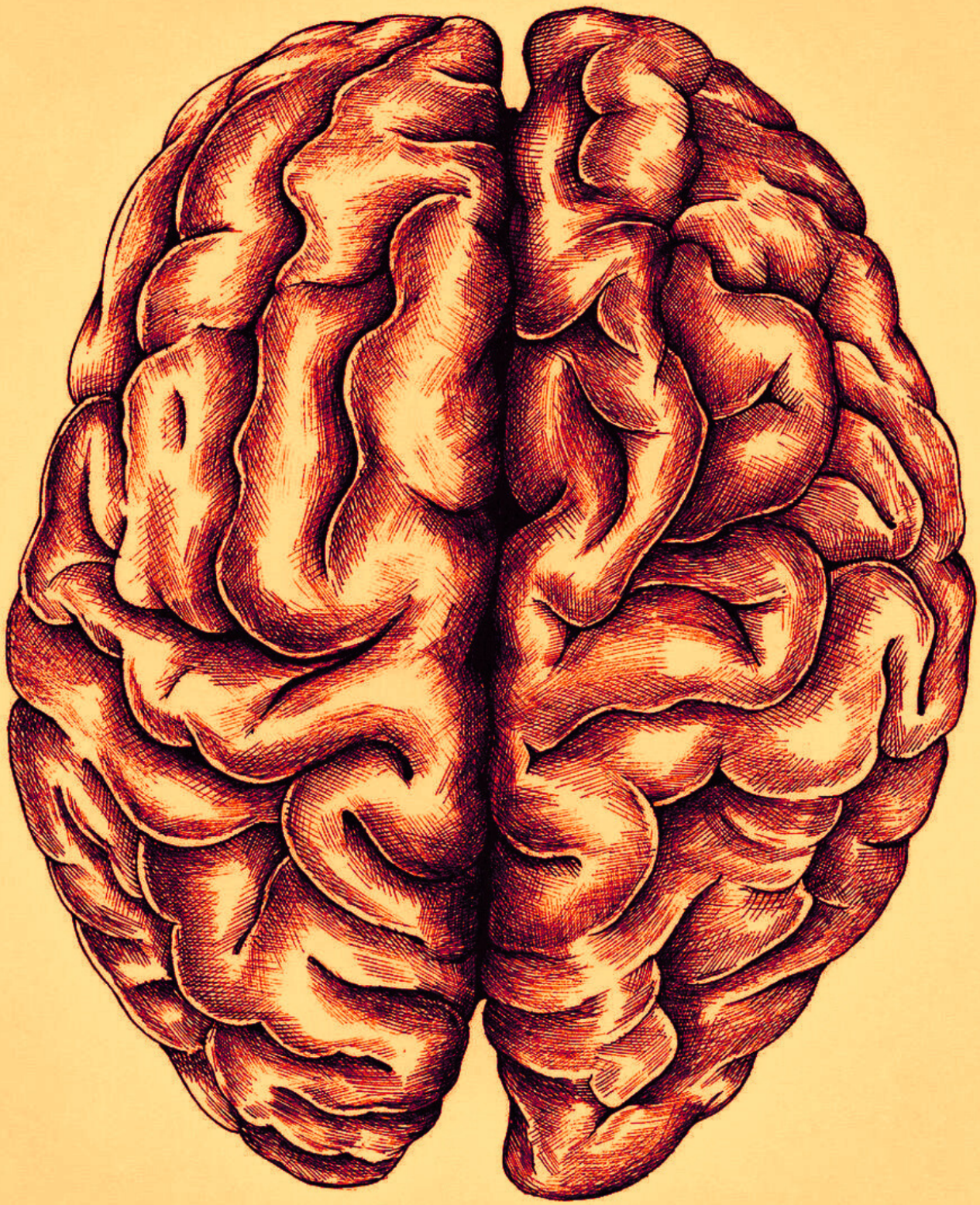

University of Guelph's 17th Annual
Neuroscience Day

May 10th, 2024
Summerlee Science complex

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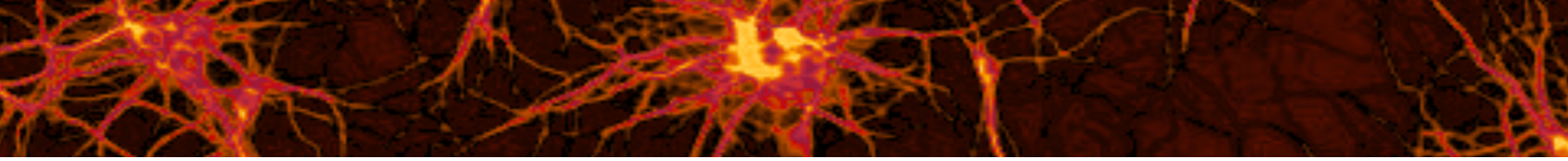
Welcome to University of Guelph's Neuroscience Day

Hello and welcome to the University of Guelph's 17th annual Neuroscience Day! This conference is a unique opportunity for trainees to present some of the amazing neuroscience research that is happening on the U of G campus! Neuroscience Day hosts a series of trainee talks and a diverse collection of poster presentations to foster connections across research groups on campus. To ensure the success of today's conference, we ask everyone to be respectful during presentations, Q&A periods, and poster session interactions.

U of G's Neuroscience Day also hosts keynote speakers from outside of Guelph to share remarkable research conducted at universities in Canada and other countries. This year, we are excited to have Dr. Jaideep Bains, from the Hotchkiss Brain Institute at the University of Calgary, present the keynote talk.

Keynote Speaker
Dr. Jaideep Bains
Director of the Krembil Research Institute, University Health Network

A stress response is essential for survival. But when stress is intense, unpredictable or pervasive, it can have lasting, negative consequences on behaviour and physiology. How stress changes the brain to affect behaviour is still largely unresolved. We propose that stress imprints the brain, causing biochemical and molecular changes that alter synaptic, cellular and circuit function. Here I will present data linking stress-induced synaptic changes to behavioural changes and discuss distinct ways to erase these synaptic memories of stress.



Schedule of Events

9:00-9:30am	SSC Atrium	Coffee & light breakfast
9:40am – 12:00pm	Richards lecture halls	Student Talks Concurrent sessions Session 1 - RICH2520 Session 2 - RICH2529
12:00pm - 2:00pm	SSC Atrium	Poster session Lunch served during poster session
2:00pm - 2:30pm	SSC Atrium	Coffee break
2:30pm - 4:00pm	SSC Atrium	Keynote Speaker Dr. Jaideep Bains Director of the Krembil Research Institute University Health Network, Toronto

Link for Oral/Poster Presentation Judges:

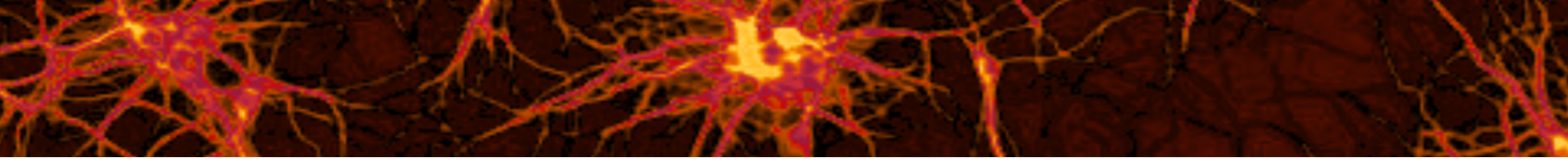
https://qualtricsxmmwzyktpnt.qualtrics.com/jfe/form/SV_20m5JHwbG7bNks6

Sponsors

Neuroscience Day organizing committee members

Jenna Penney
Boyer Winters
Jayson Capistrano
Ethan Huff
Henrietta Locke
Olivia O'Neill
Hannah Robeson
Tushar Sharma

If you have questions about the event, please contact Jenna at penneyj@uoguelph.ca



Student Talks (9:40am – 12pm)
Session 1 & 2 run in parallel

Session 1 – RICH2520

9:40am

Adiia Stone

UNDERSTANDING THE INFLUENCE OF SWEET ADDITIVES IN AN ORAL MORPHINE SELF-ADMINISTRATION TASK

A.P. Stone, E.V. Claridge, D. Peart, R. El Azali, J. Zheng, M. Rumas, K. Habib, S.T. Barrett, J.E. Murray

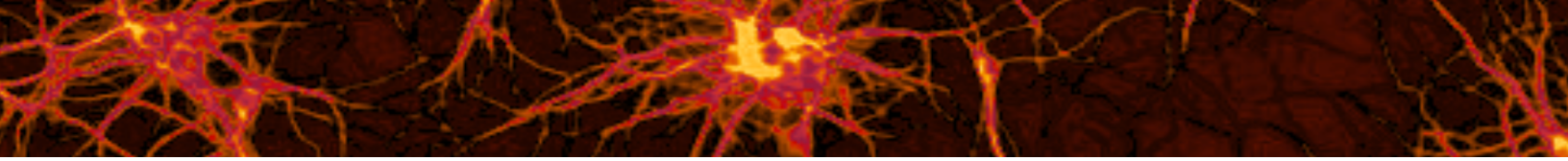
Morphine is predominantly consumed orally, but rarely administered via this route in preclinical literature. To increase translatability, we use a two-lever oral morphine self-administration (SA) model with a reinforcer solution containing grapefruit juice (GFJ) – thought to increase morphine's bioavailability – and varying sucrose (SUC) concentrations to overcome morphine's bitter taste. However, conclusions on morphine's reinforcing properties in our model are obfuscated by these sweet additives and the lack of knowledge of GFJ's pharmacokinetic impact on morphine in rats.
Exp 1: Rats were trained to lever press for a morphine solution using a SUC fading procedure (20%, 10%, 5%); half with GFJ solution during training and half without. Seven 10-session phases followed, each manipulating a component of the reinforcer solution to discern additive-dependent differences in consumption. Exp 2: Rats were trained to lever press for a morphine solution containing 5% SUC with or without GFJ. Two 3-day testing cycles followed, during which a normal SA session was followed by high or low dose naloxone administration and an additional SA session.
Stable consumption across phases does not seem sex-dependent but likely influenced by vehicle sweetness and modulation of morphine pharmacokinetics by GFJ. Consummatory behaviour after naloxone administration indicates additive- and sex-dependent differences. Conclusions: Further understanding of the reinforcing effects of the sweet additives used in oral morphine SA reinforcer is imperative to elucidate morphine-seeking behaviours.

Funding Acknowledgement: Support for the research was provided by the Canadian Foundation for Innovation John R. Evans Leader's Fund #38866 and Canadian Institutes of Health Research Project Grant PA: Sex and Gender in Health Research Bridge fund Project #488582.

10:00am

Aimee Dawe

THE EFFECT OF MYOCARDIAL INFARCTION ON BEHAVIOUR AND THE BRAIN: A PILOT STUDY IN MICE



A. Dawe, A. King, B. Gupta, J. Simpson, M. Alpaugh
The development of neurological disease is associated with a variety of risk factors, including cardiovascular dysfunction. To investigate this relationship, we used a surgical model of myocardial infarction (MI) in CD-1 wild-type mice. Specifically, after undergoing either the MI or sham surgical procedure, mice were followed post-surgically at 3,7 and 14 days to gain a comprehensive understanding of how the brain and behaviour changed across the beginning stages of heart failure. General differences in behaviour and cognition were measured using the Open Field test, and alterations in brain volume were observed through structural analysis of sectioned tissue. Preliminary results show motor impairment and increased anxiety-like behaviour in the MI mice at 3- and 7-days post-surgery, with the effects most notably observed at 3 days. Interestingly, cognition was reduced only at the 14-day time point in the MI mice when compared to sham and non-surgery control mice. These behavioural differences at the early versus late time points suggest a variety of underlying mechanisms; currently, we hypothesize there will be an increase in inflammation at early time points and reduced cerebral blood flow at later time points, which will be investigated moving forward. Initial analysis of brain structure yielded an overall decrease in total and lateral ventricle volume between 3- and 7-days post-surgery; further analysis is necessary to parse out specific differences between the MI mice and controls.

10:20am

Dante Cantini

INTERPLAY BETWEEN ESTROGEN RECEPTORS AND THE OXYTOCIN RECEPTOR IN SOCIAL RECOGNITION PROCESSING WITHIN THE MEDIAL AMYGDALA OF FEMALE MICE

D. Cantini, M. Cha, C. Schmidt, E. Choleris

Social recognition is the ability to recognize previously encountered conspecifics and is crucial for adaptive behaviour in social groups. The potent and most abundant estrogen, 17β-estradiol (E2), has been shown to facilitate social recognition of conspecifics in mice on a rapid time scale in various brain regions within the social-brain-network. The medial amygdala is heavily involved in olfactory processing of social odours in mice and expresses the three known estrogen receptors (ER): ERα, ERβ, and G Protein-Coupled ER (GPER). Selective agonists for each of the three ERs rapidly facilitate social recognition in the medial amygdala of female CD1 mice. The neuropeptide oxytocin is also crucial for the processing of social information. Fully functional oxytocin receptors (OTR) within the medial amygdala are necessary for the rapid effects of 17β-estradiol on social recognition, suggesting an E2/OTR interplay. The objective of this study is to elucidate how the three ERs interplay with OTRs in the medial amygdala of female mice to elicit rapid facilitation of social recognition. Female mice were ovariectomized and had bilateral cannulae implanted into the medial amygdala. A sub-effective dose of OTR antagonist (meaning the highest dose of the antagonist that will impair OTR function without fully inhibiting oxytocin signalling) was infused into the medial amygdala before the infusion of one of the respective ER agonists (ERα agonist PPT; ERβ agonist DPN; GPER agonist G1). A difficult social recognition paradigm designed to measure the

rapid facilitating effects of treatment was administered. If the facilitating effect of the ER agonist is impaired by the administration of the OTRA, we can infer that the specific ER is implicated in the interplay with OTR. The results demonstrated that a sub-effective dose of OTR antagonist administered before each respective ER agonist caused impairment to social recognition. This shows that ERα, ERβ, and GPER require fully functional OTRs to rapidly facilitate social recognition in the medial amygdala of female mice and suggests an interplay between ERs and OTRs in this process.

10:40am

Jessie Cait

IMPLICATIONS OF CONVENTIONAL LABORATORY HOUSING FOR RODENT WELFARE AND DATA REPLICABILITY

J. Cait, C. Winder, G. Mason

Over 120 million research rodents are used annually, most housed in small, barren “shoeboxes” that are poor for welfare. But are these cages so chronically stressful that they impact rodent health? And if so, could these health effects impact experimental results? To find out, we conducted two meta-analyses. First, we tested the hypothesis that, compared to rats and mice in cages ‘enriched’ with resources to better met their needs, conventional housing increases stress-related morbidity and all-cause mortality. Second, we tested the hypothesis that the stressful nature of rodent housing reduces data replicability. After a comprehensive literature search, 214 studies were included in the review containing data on all-cause mortality plus five experimentally induced stress-sensitive diseases: anxiety, cancer, cardiovascular disease, depression, and stroke. Random-effects meta-analyses supported both hypotheses. Conventional housing significantly exacerbated disease severity and increased mortality rates. Thus, conventional housing negatively impacts rodent health. Furthermore, by looking for statistical interactions between housing conditions and “disease modifiers” being studied (e.g. therapeutic drugs) we found that rodent housing can change experimental results, influencing replicability. These findings suggest that welfare is important for scientific rigour as well as improved animal welfare.

11:00am

Heather Collett

DISRUPTING PERIRHINAL GABAERGIC PARVALBUMIN INTERNEURONS IMPAIRS LEARNING ON A MOUSE OBJECT CATEGORY RECOGNITION TASK

H.A. Collett, K.H. Jardine, S.D. Creighton, J.H. Fournier, R.A. Pandit, C.E. Wideman, B.D. Winters

Object category recognition (OCR) may rely on generalized category representations which could be refined with inhibitory GABAergic signaling. Parvalbumin-containing GABAergic interneurons (PVINs) have been implicated in cortical representation

refinement and provide inhibitory control in the perirhinal cortex (PRh), an area which is necessary for object recognition. To determine the role of GABAergic transmission in the refinement of object category representations, male C57/BL6 mice were administered a GABAA receptor antagonist (bicuculline) prior to exposure to category exemplars. When tested on an OCR task, mice administered bicuculline failed with a 1-h retention delay, which requires pre-exposure to category objects. Additional exposure to learned categories 1h prior to sacrifice revealed greater c-fos activation vs control mice in the PRh of mice administered bicuculline. This suggests that OCR task performance may be supported by sparser representations in the PRh. Chemogenically disrupting PRh PVINs, prior to object category exposure through inhibition or excitation impaired OCR task performance with a 1-h, but not a 30-min, retention delay. With a 30-min delay, performance was also disrupted by pre-sample PVIN inhibition or stimulation. Previous object category familiarity ameliorated this deficit. Interestingly, neither pre-sample PVIN PRh inhibition nor stimulation produced a deficit on the spontaneous object recognition task with a 30-min or 24-h retention delay. The pre-sample deficit may be due to the PRh role in complex perceptual processes such as object feature conjunction or binding. To assess whether GABAergic transmission is involved in discriminating between objects with overlapping features we administered bicuculline prior to a configural simultaneous object oddity discrimination task. Bicuculline administration impaired oddity discrimination when objects where highly ambiguous and all had overlapping features. These findings suggest that GABAergic signalling and PVINs in the PRh may play an essential role in refinement of object category representations and may support the binding and generalizing of object features.

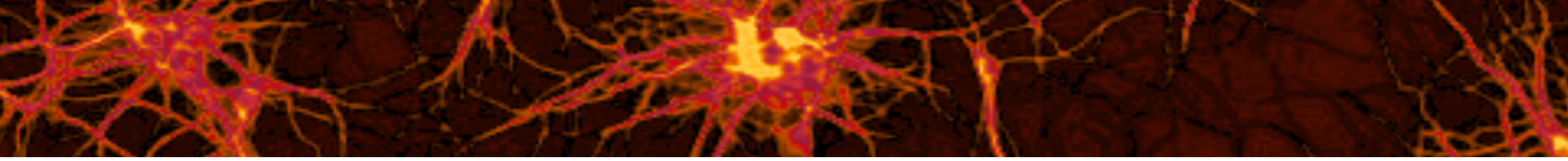
11:20am

Brooke Ginson

MODULATION OF THE OPIOID SYSTEM IN ASSOCIATIVE DRUG MEMORIES

B. Ginson, G. Grandison, F. Leri

It has been demonstrated that acute opioid intoxication, as well as precipitated opioid withdrawal, have effects on memory. Specifically, post-training administration of opiates or precipitated opioid withdrawal enhances memory in object recognition (OR) tasks. As such, we aimed to investigate if the memory-enhancing effect of opiates and opioid withdrawal can be observed in the context of drug memories. To test this, the conditioned place preference paradigm was used to establish a drug memory. 4 pairings with alternating 0 mg/kg and 1 mg/kg heroin over 30-minute conditioning sessions have been shown to sufficiently produce a drug memory, such that animals associate the drug-paired compartment with heroin availability and will approach this environment preferentially in a drug-free state. To test whether the strength of this drug memory could be modulated, post-training treatments were employed, and animals were monitored for 1 hour following administration. Immediately following drug conditioning sessions, animals received either: 1 mg/kg heroin + 3 mg/kg naloxone (post-training withdrawal), 1 mg/kg heroin (post-training heroin), or 0 mg/kg heroin (post-training vehicle). On saline conditioning, all animals received saline post-training.



Animals were tested after the first pairing (test 1), at the end of conditioning (test 2), and again 1 week later (test 3). Animals in the post-training heroin condition demonstrated an enhancement of memory, as demonstrated by a significant increase in time spent in the drug compartment at test 1, however, this effect was ameliorated by test 2. Both the post-training withdrawal and post-training vehicle groups displayed no difference in time spent in the drug compartment by test 1, but a significant increase by test 2. Locomotion data during conditioning and post-training observation lend support to the hypothesis that the rapid development of tolerance occurred in post-training heroin-treated animals. This suggests that the memory-enhancing effects of opioids may also display tolerance.

11:40am

Siobhon Weber

THE EFFECT OF EARLY LIFE ENVIRONMENTAL ENRICHMENT IN THE 3XTG-AD MOUSE MODEL

S.E. Weber, B.D. Winters

Lower-limb prostheses can restore mobility, however, individuals with amputations face challenges in postural control due to the lack of somatosensory feedback. Sensory substitution is a non-invasive approach that provides artificial sensory feedback by using patterns of vibration on a grid located at the thigh to represent relevant cues such as limb flexion. For this technique to be effective, careful consideration must be given to the spacing between vibratory actuators and vibration frequency to ensure that the cues are correctly interpreted. The study recruited fifteen female students from the University of Guelph. A mini shaker with probes spaced at 20, 25, and 30 mm, and vibrating at either 30 or 150 Hz was used to deliver a 1s vibration on the middle of the participants' thigh. The probes were positioned either vertically or horizontally and the participants were asked to report the orientation of the probes, and the % of correct response was used as an outcome measure. The effects of distance and frequency were tested using a 2x3 repeated-measures ANOVA, and a simple linear regression of distance/thigh length and accuracy was also conducted. Significant main effects were found for frequency ($p < .05$) but not for distance ($p = .132$) when using thigh length as a covariate. We found that vibrating at 150 Hz resulted in greater orientation discrimination accuracy at smaller distances and vibrating at 30 Hz resulted in accuracy at larger distance. This contradicts assumptions about the receptors targeted by 30Hz in non-hairy skin that can distinguish cues at closer distances. These findings underscore the importance of considering both frequency and relative actuator spacing when selecting the spacing of vibratory actuators.

Session 2 – RICH2529

9:40am

Laura Marrelli

FATIGUE-INDUCED IMPAIRMENTS IN VOLUNTARY RATE OF TORQUE DEVELOPMENT OF THE PLANTAR FLEXORS IS ATTENUATED WITH FOOT SOLE STIMULATION

L.C. Marrelli, T. Sharma, G.A. Power, L.R. Bent

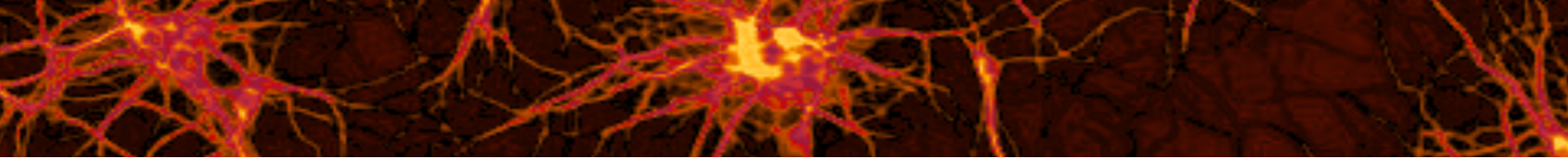
Rate of torque development (RTD), how quickly one can generate torque, is important in balance. Reduced RTD, due to fatigue or aging, is associated with an increased fall risk, thus improving RTD may prevent injury and improve motor outcomes. Foot sole cutaneous stimulation generates location dependent muscle responses in the leg: heel stimulation provides excitation, while metatarsal stimulation elicits inhibition. Further, cutaneous stimulation has been shown to preferentially increase the excitability of high threshold motor units (MUs), potentially facilitating faster force production. Thus, cutaneous stimulation of the foot sole may alter RTD in a location dependent manner during voluntary contractions. This study aimed to investigate if cutaneous stimulation could mitigate the fatigue-induced decline in RTD.
Eight young, healthy males performed isometric plantarflexions “as fast and hard as possible” in the rested and fatigued state, under three conditions: No stimulation (CON), heel stimulation (HEEL), and metatarsal stimulation (MET). RTD was measured as the slope of torque over time from contraction onset to 200ms, in continuous 25ms epochs. Fatigue was induced via a sustained maximum voluntary plantarflexion. All cutaneous stimulation was set to 2x perceptual threshold. We compared the percent decrease in RTD from rest to fatigue in HEEL, MET and CON.
On average, HEEL reduced the effects of fatigue on RTD over all 200ms. Overall, MET was also found to benefit RTD in the fatigued state. However, interestingly, early in the contractions, MET was shown to exacerbate the effects of fatigue on RTD, further reducing the rate at which force can be generated.
Our findings suggest foot sole cutaneous stimulation may attenuate fatigue-induced reductions in RTD in a non-location dependent manner. We speculate this effect may be due to changes in MU recruitment gain induced by cutaneous stimulation. Maintenance of RTD during fatigue may inform clinical interventions aimed to improve motor outcomes.

10:00am

Niyatee Narkar

OCULOMOTOR-CONTROL MECHANISMS HAVE AFFECTIVE CONSEQUENCES FOR ASSOCIATED STIMULI

N. Narkar, K. Barlewski, M. Fenske



Mechanisms of selective attention and motor-response control can determine emotional responses for visual stimuli. Items that are inhibited or from which a motor-response is withheld on a previous trial, for example, receive more negative affective ratings than the targets of attention/response, an effect termed as the affective devaluation by inhibition. Utilizing head-stabilized screen-based eye-tracking, we explored whether this form of affective devaluation can also be replicated for oculomotor inhibition captured through saccadic eye-movements. In a selective-looking task (Exp. 1), shifting gaze away from individual stimuli led to their affective devaluation relative to looked-at stimuli. To test whether the affective status of visual stimuli is specifically altered by oculomotor inhibition, beyond any fluency-related affective enhancement from foveal processing, we examined the affective consequences of suppressing the urge to make an eye-movement toward an abrupt-onset stimulus (Exp. 2: anti-saccade task). Taken together, our results suggest the mechanisms underlying the 'distractor devaluation' effect in other selective attention may be similar to those determining emotional responses in the oculomotor domain. We discuss the next steps in extending this work to explore whether oculomotor inhibition also shares the same mechanisms with the 'No-go devaluation' effect in the motor-response control domain.

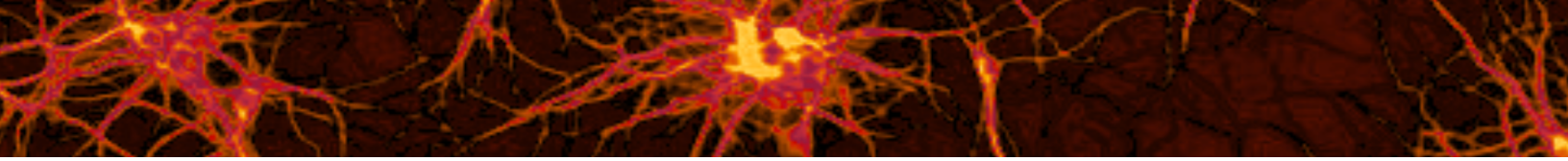
10:20am

Olivia Williams

EXPLORING SEX CONSIDERATIONS IN TRANSLATIONAL ASD RESEARCH

O. Williams, M. Coppolino, J. Manduca, R. McCallum, P. Henry-Duru, C. Micelli, M. Perreault

Autism Spectrum Disorders (ASD) exhibit sex differences in age of onset, prevalence, etiology, and presentation, yet the molecular and cellular underpinnings of these differences remain unexplored. In this study, sex differences in cortical neuronal architecture, neuronal activity, oscillatory function, and behaviour, and possible molecular and cellular mechanisms were determined.
In the valproic acid (VPA) model of ASD, dendritic morphology, protein abundance assays, transcriptomics and neuron function assays in vitro and in vivo were used. In vitro studies showed that VPA-derived cortical neurons from sexed pups were less complex and showed elevated neuronal activity with greater effect in the female-derived neurons. Behavioural testing in adolescence revealed sex-specific differences in the VPA group. VPA-exposed female rats displayed greater anxiety, showed deficits in recognition memory, as well as in social index scores, whereas VPA males exhibited difficulties in location memory and lower sociality. Female VPA rats displayed alterations in cortical low frequency power, however male VPA rats displayed elevated high frequency power and lower high frequency coherence between the cingulate cortex and the hippocampus. Sex differences in gene expression were also observed. In female VPA rats, gene transcripts involved in vascular permeability, such as gpr116, cldn5, flt1, rgs5, angptl4, esam, and decorin showed the greatest fold reduction in expression. In male rats, genes that showed the greatest changes were those involved in neurotransmitter/ neuropeptide signalling and included an upregulation of drd2,



cartpt, adora2a, and pdyn, and a downregulation of nxph4 and several solute carrier genes. In both sexes, genes associated with myelination, rxrg, opalin and mog, were downregulated.
These findings identify key sex differences in behaviour, and neuronal structure and function, upon exposure to VPA. This suggests that sex differences in the VPA model may have relevance to the sex-specific symptoms observed in ASD and emphasizes the inclusion of both sexes in biological research.

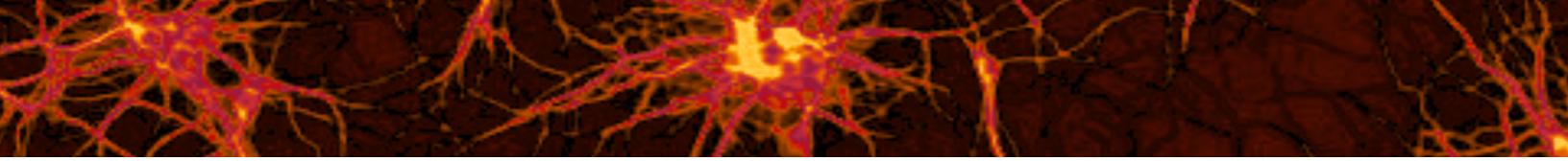
10:40am

Jayson Capistrano

STUDYING THE EFFECTS OF GUT-DERIVED METABOLITES IN BRAIN DEVELOPMENT TO UNDERSTAND ITS ROLE IN THE ETIOLOGY OF AUTISM SPECTRUM DISORDER (ASD)

J. Capistrano, V. Rea, P.N.G. Tran, T. Ball, T. Van Raay

Autism spectrum disorder (ASD) is a group of neurodevelopmental disorders caused by genetic and environmental factors. Due to its complex and often pleiotropic nature, its etiology has been difficult to elucidate—ultimately, hampering the identification of definitive diagnostic markers and development of potential therapies/treatments. Interestingly, most individuals with ASD suffer from gastrointestinal problems, which underscores a potential connection between ASD and the gut. Metabolites produced from the gut have been reported to impact the brain; however, the mechanisms of how these metabolites influence the brain or vice-versa remain poorly understood. Here, we hypothesize that distinct metabolites derived from different diets and/or mental health profiles result in unique phenotypic effects in the developing brain. In the first study, metabolites from naïve fecal samples that were grown in a robogut in the presence of different diets (high fiber Western, low fiber Western, Mediterranean, and Yanomami) were isolated. In the second study, age- and gender-matched fecal samples from neurotypical (NT) and children with ASD were used to isolate metabolites. We then evaluated the effects of these gut-derived metabolites on neurodevelopment by looking into changes in gene and protein expression, sensory organ development, and behavioral responses using germ-free zebrafish as our model. Thus far, our results suggest that the zebrafish model may not be sensitive enough to detect the effects of metabolites derived from different diets. However, we found that zebrafish neurodevelopment seems to be sensitive enough to detect the different effects of ASD and NT metabolites, where we see unique behaviors and distinct alterations in sensory organ development and gene expression profiles. Our goal is to eventually uncover the molecular mechanisms underlying the contributions of gut-derived metabolites on the development of the brain, which has implications for ASD and other relevant diseases and disorders.



11:00am

Amelia Doerksen

REGULATION OF AXONAL TRANSPORT IN NEURONS BY PROTEIN PALMITOYLATION OF P150GLUED

A. Doerksen, A. Leekha, S. Sanders

Neurons are large, complex cells requiring efficient trafficking and delivery of proteins and organelles to specific subcellular locations. Fast, continuous, anterograde and retrograde transport of cargo along axonal microtubules by dynein and kinesin motors is critical for neuronal function. The activity of motor proteins is tightly regulated, and aberrant activity can result in neurodegeneration or neurodevelopmental deficits. One important mechanism to regulate neuronal protein trafficking is the covalent addition of fatty acids to cysteine residues, a process known as palmitoylation. Several kinesin and dynein motor subunits and their activators have been identified in high throughput palmitoyl-proteomic studies as being potentially palmitoylated. Indeed, we recently demonstrated palmitoylation of the dynein activating complex dynactin subunit p150Glued. Dynactin is critical for dynein activation and processivity. P150Glued is palmitoylated predominantly in nervous system tissues on cysteines 617 and 1252 by the ZDHHC12 palmitoyl acyltransferase. p150Glued is the largest dynactin subunit that mediates dynein-dynactin microtubule binding and processive motility. The functional role of p150Glued palmitoylation is unknown, but due to the importance of p150Glued in dynein-mediated fast axonal transport, p150Glued palmitoylation likely regulates transport. Interestingly, when palmitoylation-resistant (C617/1252A; CCAA) p150Glued-GFP is expressed in neurons, less GFP signal is present in distal axons and in the vesicular fraction compared to wild type expressing neurons. This suggests that palmitoylation may regulate association of p150Glued with vesicular cargos. This study will be the first to investigate the function of p150Glued palmitoylation. Our findings will provide novel insights into how palmitoylation can regulate neuronal transport, contributing to the foundational knowledge within the field of palmitoylation with potential for understanding how trafficking can be altered in various neuropathies.

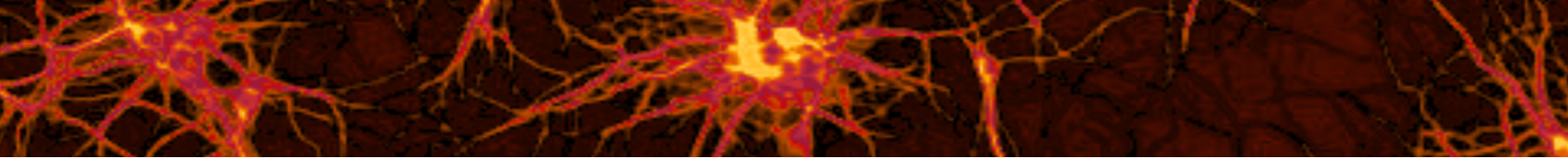
11:20am

Ana Leticia Simal

SEX DIFFERENCES IN ASTROCYTE-NEURON DYNAMICS IN CHRONIC NEUROPATHIC PAIN IN THE ANTERIOR CINGULATE CORTEX

A.L. Simal, J. Tuling, G. Descalzi

Chronic pain impacts 25% of Canadians aged fifteen and above, especially marginalized groups, with women making up 67% of those affected. Despite this, pre-clinical research has predominantly prioritized male rodent models, leaving a knowledge gap regarding female chronic pain mechanisms.



Mounting evidence indicates neuroplastic changes within the anterior cingulate cortex (ACC) as pivotal in chronic pain development. Responding to neuronal activity, the astrocyte-neuronal lactate shuttling (ANLS) can rapidly provide lactate to neurons, meeting metabolic demands required for neuroplasticity. However, its role in chronic pain-induced neuroplasticity remains unknown.
This study investigates ANLS in the ACC of female and male mice, exploring its involvement in chronic neuropathic pain development. Using the spared nerve injury (SNI) model in adult female and male C57BL/6 mice, we assessed gene expression in the ACC of ANLS pathways at 5-, 14-, 30-, and 60-days post-surgery using RT-qPCR. We also confirmed mechanical allodynia for each timepoint using the Von Frey Test. Despite similar patterns of SNI-induced pain hypersensitivity in both sexes, we found that long-term SNI increased ANLS-related gene expression in the ACC of male but not female mice. We thus conclude that neuropathic pain affects ANLS in the mouse ACC in a sexually dimorphic manner. Furthermore, these sex differences highlight the need to include both females and males in research on molecular targets for chronic pain treatment, deepening our knowledge of pain chronification.

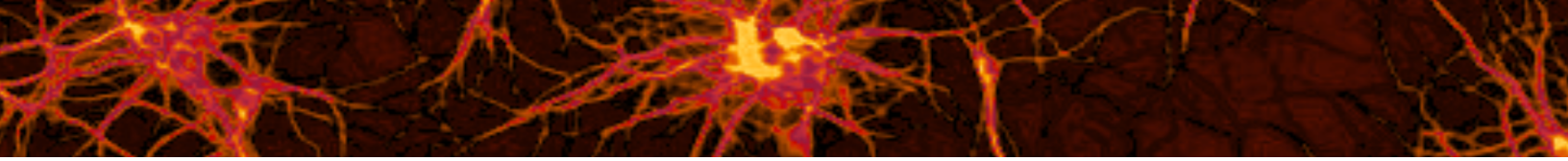
11:35AM

Jennifer Holborn

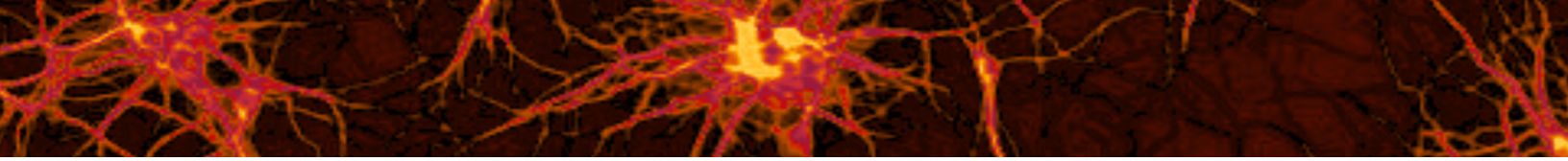
INVESTIGATING THE ANTICANCER POTENTIAL OF CANNFLAVIN A AND CANNFLAVIN B AGAINST GLIOBLASTOMA MULTIFORME

J. Holborn, T. Gluscevic, A. Borenstein, A. Carter, A. Gardner, J. Lalonde

Multiple object tracking is the ability to keep track of the positions of a subset of identical Glioblastoma multiforme (GBM) is a highly aggressive and invasive brain tumor associated with poor prognosis and limited treatment options. Previous studies have shown that cannflavin A and cannflavin B, flavones that accumulate uniquely in C. sativa, produce promising anticancer effects in bladder and pancreatic cancer models. In this study, we explored the therapeutic potential of cannflavins against GBM utilizing a comprehensive approach involving cell viability, migration, and invasion assays to delineate the impact of these compounds against various aspects of GBM biology. Our investigation revealed a dose-dependent decrease in GBM cell viability following exposure to increasing concentrations of cannflavin B (0.5 to 20 μM), with no discernible cytotoxic effects observed. Remarkably, low doses of both cannflavin A and cannflavin B exhibited significant inhibition of GBM cell migration in timelapse scratch assays, indicating their potential to impede tumor dissemination. Of particular interest, cannflavin B demonstrated robust anti-migratory and anti-invasive properties, as evidenced by transwell migration and spheroid invasion assays. Cannflavin B at low concentrations not only suppressed the migration of GBM cells but also attenuated their ability to invade surrounding tissues, highlighting its multifaceted therapeutic effects. Together, our findings underscore the promising anticancer attributes of cannflavins in the context of GBM. Their ability to modulate critical cellular processes implicated in tumor progression suggests a potential role in GBM therapy. Further studies elucidating the underlying molecular mechanisms and in vivo efficacy of cannflavin A and



cannflavin B are warranted to validate their utility as novel therapeutic agents for GBM treatment.



Poster Session (12pm – 2:00pm)

Poster 1

Abina Thomas

MORPHINE DISCRIMINATION ACROSS THE RAT ESTROUS CYCLE

A. Thomas, D.R. Peart, J.M. Karlovcec, E.V. Claridge, R. El Azali, A. Sikic, A.P. Stone, J.E. Murray

Interceptive drug cues, like those sensed internally, can acquire conditioned properties similar to external reward cues, influencing behavior. We used a Pavlovian drug discrimination task, training rats to associate an interceptive drug cue (morphine) with an external cue (white noise) followed by access to sucrose. Previous studies showed that females are less sensitive to generalization of a morphine cue than males, so we studied the role of gonadal hormones in this difference. Male and female rats were given daily injections of morphine or saline before training sessions. Training involved presenting a white noise cue followed by access to sucrose only in morphine sessions. After training, rats were tested for generalization of the morphine cue to different doses of morphine. Females were monitored for estrous cycle phase. Results suggest that both male and female rats similarly learned the discrimination task, which was maintained across the estrous cycle. A gradient of generalization was measured across morphine doses and this behaviour did not differ by sex, nor did it differ across the estrous cycle in females. Therefore, we conclude that morphine generalization is independent of fluctuations in levels of sex and endogenous gonadal hormones in females under these experimental conditions.

Poster 2

Adina Borenstein

ASSESSING THE INFLUENCE OF CANNFLAVINS ON GLIOMA CELL MOTILITY USING A SPHEROID MODEL

A. Borenstein, J. Holborn, B. Alural, J. Lalonde

Glioblastoma multiforme (GBM) is the most common and aggressive type of adult brain cancer. These tumors can occur in any region of the central nervous system, and the average survival time of patients after diagnosis is less than two years. The poor prognosis associated with GBM is attributable to the fact that these cancer cells have high motility and can rapidly invade normal brain tissue. This feature is difficult to attack with current treatment options; therefore, novel agents that can limit the invasion of surrounding healthy brain tissue by GBM cells are critically needed. Signaling downstream of the Tropomyosin receptor kinase B (TrkB) receptor contributes to cell proliferation, growth, and survival. Evidence suggests that the TrkB pathway can be hyperactive and dysregulated in GBM, resulting in increased invasion. Our group recently found that cannflavins A and B, two metabolites of the Cannabis sativa plant, can interfere with TrkB receptor activity. Here, we studied the effects of cannflavins

against GBM cell invasion. First, we completed a western blot analysis to determine whether cannflavins A and B interfere with TrkB activation and downstream signaling pathways in the GBM cell line U87. Second, we used a 3D spheroid assay to identify that low concentrations of cannflavins can prevent U87 cell invasion. Our results suggest that cannflavins could be an effective treatment against this aggressive hallmark of GBM cells.

Poster 3

Allison Carter

INVESTIGATING THE INTERFERENCE OF CHRYSOERIOL ON NEURONAL TRKB SIGNALLING IN GLIOBLASTOMA MULTIFORME CELLS

A. Carter, T. Gluscevic, J. Holborn, J. Lalonde

Glioblastoma Multiforme (GBM) is one of the most aggressive types of human cancers to exist. Characterized by uncontrolled cell proliferation, invasion and angiogenesis, GBM has a very poor prognosis as it shows limited response or even resistance to current treatments. Although the pathophysiology of GBM is multifactorial, the dysregulation of neuronal Tropomyosin Receptor Kinase B (TrkB) signaling cascade is a therapeutic target. TrkB is a Receptor Tyrosine Kinase (RTK) that has high binding affinity for brain derived neurotrophic factor (BDNF). The binding of BDNF to TrkB regulates cellular survival, motility and proliferation. The overactivation of TrkB/BDNF cascade in GBM contributes to the aggressive oncogenic phenotype in GBM. Cannflavins derived from Cannabis sativa are a subclass of flavonoids that are highly lipophilic and prenylated, permitting their binding to extracellular receptors such as TrkB. In a previous study cannflavins A and B were found to interfere with TrkB signaling in GBM. The present study aims to investigate the interference on neuronal TrkB in GBM A172 and U87 cell lines by chrysoeriol, the metabolic precursor of cannflavins A and B. The findings were that chrysoeriol did not cause a significant decrease in cell viability in GBM cells compared to the DMSO control. Further studies should explore the effects of ligand prenylation on TrkB modulation in GBM. This area of research has exciting potential to expand the use of cannflavins, delivering a new way to use cannabis as a therapeutic agent for neurodegenerative diseases.

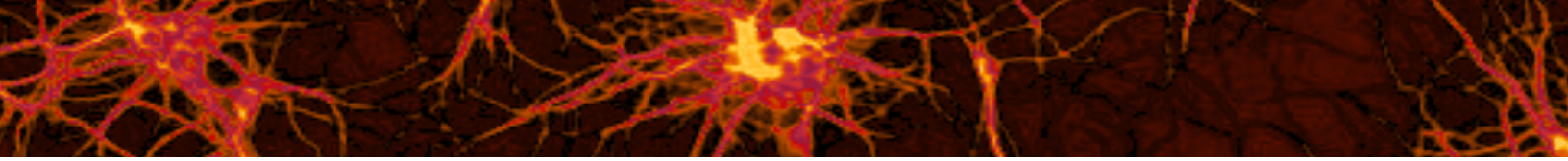
Poster 4

Ana-Maria Mercu

M1 mAChR ACTIVATION DURING MEMORY REACTIVATION RESTORES OBJECT MEMORY MODIFIABILITY IN THE 3xTG MOUSE MODEL OF ALZHEIMER'S DISEASE

A.M. Mercu, K.H. Jardine, C.E. Wideman, W.S. Messer, B.D. Winters

Along with the hallmark amyloid and tau pathology, cholinergic system dysfunction contributes to the cognitive deterioration observed in patients with Alzheimer's disease



(AD). While AD deficits in new learning are well established, there is limited research on the effect of AD pathology on long-term memory flexibility. Reactivation-induced memory destabilization, which is likely important for long-term memory updating, relies on cholinergic transmission. Currently, there is limited research on reconsolidation and memory updating in AD. We hypothesize that long-term memory flexibility is impaired by AD-like pathology and that this deficit can be reversed by pro-cholinergic interventions. In the present study, we tested this hypothesis using the triple transgenic (3xTG) mouse model of AD, in which we have previously observed object memory updating impairments in the absence of basic learning and memory disruption. We predicted that pharmacologically activating M1 muscarinic cholinergic receptors (mAChRs) during memory reactivation would facilitate object memory destabilization in male 3xTG mice. Behavioural experiments for male 3xTG mice subjects commenced at 3-months-old with the selective M1 agonist CDD-0102A (0.3 mg/kg, ip) before memory reactivation in an object memory reconsolidation task. Our findings indicated that systemic M1 receptor activation during object memory reactivation promotes memory destabilization and renders the memory modifiable. Furthermore, we used western blots to compare cholinergic protein expression changes in the perirhinal cortex of 3xTG mice compared to age-matched wildtype counterparts. Interestingly, we found reduced expression of vesicular acetylcholine transporter (VAChT) protein and M1 mAChRs in the perirhinal cortex of 6-month-old 3xTG AD mice, suggesting that early AD pathology targets cholinergic neurons, possibly inducing memory inflexibility. The significance of our research lies in the potential therapeutic benefits of targeting M1 receptors to improve memory flexibility in AD. Treating these nuanced memory deficits associated with AD could possibly extend the period of neurotypical cognitive abilities in patients.

Poster 5

Anita Sikic

INTEROCEPTIVE AND PRELIMINARY PROTEOMIC EFFECTS OF NICOTINE VS CIGARETTE SMOKE EXTRACT IN MALE AND FEMALE RATS

A. Sikic, M.A. Williams, D.R. Peart, A. R. Cameron, J.M. Karlovcec, B.W. Florek, J.A. Frie, J.Y. Khokhar, R.A. Bevins, B. Muselius, J.A. McAlister, J. Geddes-McAlister, J.E. Murray

Although nicotine (NIC) is generally the primary alkaloid investigated for tobacco use disorder, the other ~8000 constituents in cigarette smoke are thought to interact with NIC to affect its etiology. The primary study used a Pavlovian drug discrimination task; we hypothesized that rats could discriminate between NIC and cigarette smoke extract (CSE) of the same NIC concentration based on the presence of constituent chemicals. We have also begun investigation of brain proteomic changes resulting from long-term exposure to CSE, NIC, or vehicle (VEH).
Behaviour is assessed using three types of occasion setting training: NIC discriminating from VEH, CSE discriminating from VEH, and CSE discriminating from NIC. Separate rats were injected daily for 28d with CSE, NIC, or VEH, and brains were excised for proteomic processing. Subjects readily discriminate between NIC and VEH and

between CSE and VEH; however, they are unable to discriminate between CSE and NIC after 72 sessions with 8 trials of each. Preliminary results suggest differential proteomic changes evoked by CSE vs NIC.
Our results confirm that CSE is a successful occasion setter and adds to previous NIC literature. Interestingly, we demonstrate that CSE and NIC do not create distinct interoceptive environments under current training conditions and differences evoked by each substance may be occurring at the cellular level instead. Significance: This has important implications for ongoing discussions regarding nicotine as a proxy for tobacco in animal models.

Poster 6

Anjana Varatharajah

THE ROLE OF LOCALLY SYNTHESIZED ESTROGENS IN SOCIAL RECOGNITION WITHIN THE BED NUCLEUS OF THE STRIA TERMINALIS (BNST) OF MALE MICE

A. Varatharajah, D. Aspesi, E. Choleris

Social recognition (SR) is essential for differentiation between familiar and novel conspecifics allowing for appropriate behavioural responses. Sex steroids, including testosterone (T) and 17□-estradiol (E2), can rapidly influence SR. These sex steroids are locally synthesized within the brain and gonads to modulate SR. Previous research has established that hippocampally produced E2 within ovariectomized female mice is necessary for encoding and initial consolidation of short-term SR memory. In male mice, hippocampal E2 is required for long-term memory and consolidation in gonadectomized (GDX) male mice, but not in intact mice, implying a protective role of circulating androgens against diminished local E2. Exogenous administration of E2 within the bed nucleus of the stria terminalis (BNST) of GDX male mice can rapidly facilitate SR, however, the vitality of locally synthesized E2 in SR within the BNST of males remains unclear. The current study investigates the role of local E2 production within the BNST, which is heavily involved in male social behaviour, of GDX and intact male mice. A range of inhibiting doses of letrozole, an aromatase inhibitor blocking T to E2 conversion, is being determined within both GDX and intact male mice. Subjects will be infused with these doses or the vehicle treatment targetting the BNST. A rapid SR paradigm will assess the impairing effects of attenuated local E2 production on SR. It is hypothesized that intact mice will require higher doses of letrozole to impair SR in comparison to GDX mice due to circulating androgens. This research will elucidate the role of locally synthesized E2 in isolation from circulating androgens, highlighting the differing role of local E2 production within both GDX and intact male mice. This may provide insights into whether the brain is a target of peripheral endocrine glands or if local synthesis of E2 within the BNST is required for SR.

Poster 7

Ashley Geremia

MUSCARINIC RECEPTORS MODULATE NEURON EXCITABILITY WITHIN THE MOUSE ENTORHINAL CORTEX IN A SEX-DEPENDENT MANNER

A.A. Geremia, C.D.C. Bailey

The entorhinal cortex (EC) comprises part of the hippocampal formation. This brain region plays a central role in the cognitive functions of spatial learning and memory, which show sex differences in humans and rodents. Acetylcholine (ACh) is an important modulatory neurotransmitter that facilitates EC-dependent cognitive functions by acting upon its muscarinic receptor (mAChR) within the EC. The EC is stratified into six cellular layers, with each layer containing layer-specific subtypes of pyramidal neurons. The mAChR is expressed throughout the EC with a particularly high expression density within cellular layer V (ECV), which contains the major output pyramidal neurons from this brain region. Given the known sex differences in spatial learning and memory, and the importance of mAChRs to facilitate these cognitive functions, we sought to determine whether a sex difference exists for the mAChR-mediated modulation of ECV pyramidal neurons. Using whole-cell electrophysiology in acute brain slices from juvenile mice, we found that mAChR activation led to a greater excitability response in neurons from females when neurons sat at a subthreshold membrane potential, but not when neurons were already active above their threshold membrane potential. Further investigation showed that input resistance was greater at a subthreshold membrane potential for neurons from females. Of the primary contributors to input resistance at subthreshold potentials, we found a striking sex difference in the subthreshold current-voltage relationship for hyperpolarization-activated cyclic nucleotide-gated (HCN) channels, but not for voltage-gated sodium or potassium channels. These findings suggests that HCN channels may underly a general sex difference in the excitability response to positive neuron modulation. This research identifies a novel sex difference in the general and muscarinic-specific excitatory modulation of output signals from the EC, adding to our fundamental knowledge of EC physiology and potential mechanisms underlying sex differences in cognitive functions that this brain region supports.

Poster 8

Ashley Vanderhaeghe

SITE-DEPENDENT SKIN DISPLACEMENT ACROSS THE FOOT SOLE IN RESPONSE TO LOAD AND RATE OF FORCE

A.V. Vanderhaeghe, E.E. Howe, L.C. Marrelli, L.R. Bent

The foot sole displays mechanical, morphological, anatomical, and sensory differences, which are unique across different foot sole regions which may influence skin displacement. The region-specific differences of skin displacement in relation to these factors is unknown and essential to facilitate a complete understand of the mechanics of

the skin. The aim of this work was to examine: 1) How the magnitude and rate of force affect skin displacement across the foot sole 2) If the hardness of the foot sole alters this displacement. We measured hardness and displacement at eight sites across the foot sole: Great toe (GT), 1st metatarsal (1MT), 3rd metatarsal (3MT), 5th metatarsal (5MT), medial arch (MA), intermediate arch (IA), lateral arch (IA) and heel. Displacement was measured using a linear encoder mounted to a custom build orthogonal loading device. Six magnitudes of load (10-125% body weight) were blocked randomized and applied at four rates of 5, 10, 15, and 20 N/s to each site. Ten young, healthy participants (7 F; 21.7 mean ± SD=2.87) were tested. Hardness at the heel was significantly different than the MA, IA, and LA (p<0.01, p<0.01, and p=0.02, respectively) but not different than any other sites (p>0.05). Magnitude of load predicted skin displacement (R2 =0.45, p<0.001). An interaction exists in which displacement was most influenced by rate when load was applied at 10% of body weight (R2 =0.030, p<0.001). Displacement at the heel was significantly different from all sites (p<0.001) except the GT, and 1MT (p=1.0). Our results suggest that skin displacement is dependent on the magnitude of the applied load and is site dependent. The site dependency of skin displacement is also related to hardness at that site. These data have implications for understanding foot sole biomechanics and mechanoreceptor firing in response to skin displacement.

Poster 9

Brittany D'Agostin

INVESTIGATING THE IMPACT OF SPINAL REGION VARIABILITY ON NERVE-DEPENDENT FIBROBLAST ACTIVATION

B.L. D'Agostin, S.L. Payne

The default response to skin injury is the formation of a non-functional, fibrotic scar which can severely impact tissue morphology and function. Upon injury, resident dermal fibroblasts become activated, migrating into the wound area where they proliferate and secrete collagen I to form a matrix-rich scar. The skin is densely innervated by peripheral sensory nerves which are important for successful wound healing. Previous work in our lab using an in vitro co-culture model of dorsal root ganglia (DRG) and human dermal fibroblasts (HDFs) demonstrated that culture with DRG enhances HDF activation (i.e., increased proliferation and collagen I expression). However, it is unknown whether active DRG sprouting is required for this effect. Furthermore, DRG from different regions of the spine (i.e., cervical, thoracic, and lumbar) vary in their ability to sprout neurites in vitro, with lumbar-derived DRG typically exhibiting more sprouting than other regions. Based on these observations, I hypothesize that actively sprouting lumbar DRG will induce greater activation of fibroblasts compared to DRG from other spinal regions. This project has three objectives: First, to characterize sprouting DRG from cervical, thoracic, and lumbar regions. Second, to compare regional variability of DRG to elicit activation of HDFs in direct co-culture. Third, to evaluate if DRG-induced HDF activation requires neurite sprouting. I have optimized the DRG-HDF co-culture system and am currently evaluating HDF activation and DRG sprouting at key time points using immunocytochemical staining for HDF proliferation

(Ki67), collagen I expression, and neurite sprouting (GAP43). Ongoing investigation will determine if spinal region impacts the ability of DRG to elicit HDF activation, and if axonal sprouting plays a role in this effect. Completion of this project will further our understanding of nerve-mediated HDF activation, advancing the development of technologies for utilizing nerve-derived factors to reduce scarring and promote regeneration of cutaneous wounds.

Poster 10

Carson Rumble-Tricker

PHYSICAL EXERTION: A NOVEL INDEX OF LISTENING EFFORT AND MOTIVATION TO HEAR

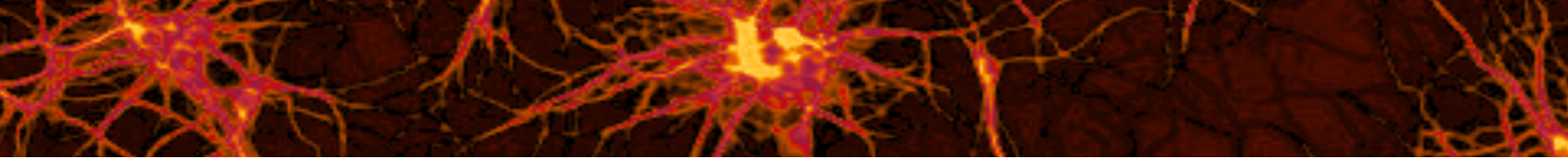
C. Rumble-Tricker, G. Singh, M.J. Fenske

Attending to and understanding speech in noisy environments can be challenging. Measuring the corresponding increases in listening effort is therefore important for investigating the cognitive mechanisms involved in speech perception, and for assessing the effectiveness of interventions that address hearing impairments. Here we examined a novel index of listening effort based on prior evidence in the visual domain that individuals readily exert physical effort to secure easier perceptual conditions. Participants (total N = 189) exerted physical effort through repeated button-pressing before each trial to reduce levels of background noise in a subsequent speech-identification task. In Experiment 1, key-pressing was greatest for unpredictable sentences and those with higher initial levels of background noise, and it consistently increased with the progressive-ratio requirement for ever-greater numbers of key presses to obtain easy listening conditions. These findings were also evident in Experiment 2, despite employing roughly half as many total trials. Importantly, this physical-exertion index was indicative of both motivation and effort, given that participants made more key presses to achieve easier perceptual conditions following both incorrect trials; and following trials reported as more subjectively effortful, despite equal performance. Moreover, our index of effort was significantly correlated to both subjective ratings of effort and task performance. Finally, the incorporation of individual measures in Experiment 2 revealed that our index of listening effort is not significantly affected by age, self-reported hearing ability, or trait boredom, distractibility, and absorption.
These findings provide converging evidence that understanding speech in noise is effortful, and that this can motivate participants to invest physical effort in order to make listening easier. Measures of physical exertion may therefore provide a path towards a useful objective index of listening effort.

Poster 11

Cassandra Clausen

INVESTIGATING THE ROLE OF SHCD IN THE OLIGODENDROCYTE LINEAGE



C. Clausen, B. Alural, G. Smith, S. Hawley, M. Wills, V. Spreuer, G. Harauz, N. Jones

Oligodendrocytes are the myelinating cells of the central nervous system; with the myelin they produce facilitating rapid action potential propagation and providing metabolic support to energy demanding neurons. Myelinating oligodendrocytes are derived from their precursors, oligodendrocyte progenitor cells (OPCs), through a complex differentiation process that is regulated by various growth factors and neurotrophins. Crosstalk between intracellular signaling cascades are at the helm of coordinating this differentiation process and the function of the cells at each stage of differentiation.
The Shc family of adaptor proteins are well established modulators of many intracellular signaling pathways and have been noted to be expressed within the central nervous system. ShcD, the most recently identified and least well characterized Shc, has been found to be uniquely expressed within the oligodendrocyte lineage, particularly in OPCs; however, an understanding of the role ShcD plays within these cells has yet to be elucidated.
We aim to investigate ShcD in the oligodendrocyte lineage with the use of ShcD knockout and ShcD wildtype mouse derived primary OPCs. Probing differences in OPC proliferation and migration, as well as comparing their differentiation capacity, will allow for a better understanding of the importance of ShcD within these cells. In parallel, we aim to investigate differences between ShcD KO and WT mouse myelination profiles in vivo using immunofluorescence, to identify the significance of this protein in oligodendrocytes within the neural environment. The culmination of these efforts allows for a more comprehensive understanding of ShcD and the role it plays within the oligodendrocyte lineage, while also allowing insight into various intracellular pathways that may be involved in regulating oligodendrocyte dynamics and function.

Poster 12

Charlotte Townsend

CLTD INDUCES CHANGES IN KV1.4 PALMITOYLATION AND AIS LOCALIZATION

C. Townsend, E. Sellar, S. Sanders

The axon initial segment (AIS) serves as a pivotal site for action potential initiation within neurons, housing a diverse array of ion channels, notably the voltage-gated potassium ion channels (Kv1). Disruption of Kv1 channel trafficking has been implicated in various channelopathies, including episodic ataxia type-I and epilepsy, emphasizing their fundamental role in neuronal function. Still, the molecular mechanisms governing the precise AIS distribution of Kv1 channels remain poorly understood. The AIS is dynamic and plastic, such that there are alterations in morphology and ion channel composition in response to neuronal activity. The post translational lipid modification, palmitoylation is critical for the clustering of Kv1 channels at the AIS. Palmitoylation involves the covalent attachment of long-chain fatty acids to cysteine residues via a thioester linkage. Importantly, palmitoylation is critical for the clustering of Kv1 channels at the AIS and the reversible nature of palmitoylation makes it well suited to dynamically

regulate Kv1 channel localization in response to changes in neuronal activity. Preliminary data following cLTD treatment reveal alterations in the AIS localization of Kv1 channel subtypes and changes in Kv1 channel palmitoylation. These findings could suggest interplay of dynamic palmitoylation and Kv1 channel localization, shedding light on the molecular mechanisms underlying synaptic plasticity and neuronal excitability. Furthermore, this research holds promise for uncovering novel therapeutic targets for Kv1-related channelopathies.

Poster 13

Dan Ambrochi

DEVELOPING A MOUSE OBJECT CATEGORIZATION WITH AUTOMATED TOUCHSCREENS (CAT) TASK

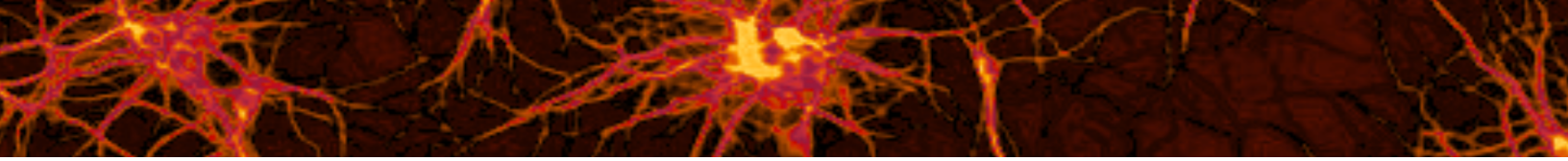
D. Ambrochi, S. Catania, H.A. Collett, K. Pabbi, B.D. Winters

Despite categorization being a fundamental perceptual process, the underlying neurobiological mechanisms are not well understood. Mice have poor visual acuity but can use visual features for complex object-based tasks. To determine if mice are capable of visual object categorization, we developed an operant categorization with automated touchscreens (CAT) task. For the CAT task, 24 male C57BL/6J mice learned to discriminate between images from two object categories (i.e., balls, nail polish bottles, locks, scissors). Mice are first presented with one of six possible exemplars from one of two categories as a sample image. Upon interacting with this image, choice exemplars from each of the two categories appear flanking the sample image. To receive a milkshake reward, mice must select the choice exemplar from the same category as the sample image. Training continues until a performance criterion of at least 70% accuracy 3 days in a row is reached, which was achieved after ~35 days. Mice were later able to generalize their performance to novel exemplar images from the learned categories, showing significantly higher accuracy over 12 days of additional training when images were swapped for new object exemplars from previously studied categories compared with when new images were from completely novel categories. To confirm that mice can visually distinguish between category exemplar images, we trained mice to perform a pairwise discrimination task with two different images from the same category. Mice achieved a criterion of 80% accuracy two days in a row after ~25 days of training. Our findings suggest that mice can acquire a touchscreen-based visual categorization task that requires generalization within categories despite being able to distinguish between category exemplars. The CAT task is a novel tool which can be used to further our understanding of the neurobiological processes underlying category learning.

Poster 14

D. MacDonald

THE INFLUENCES OF TASK DEMANDS AND OBJECT FEATURE DIMENSIONS ON SACCADIC TARGET SELECTION TRAJECTORIES



D. MacDonald, M. Fallah, H. Jordan

In the presence of competing distractors, saccadic trajectories to visual targets have been shown to curve away from the distractors after the resolution of target-distractor competition. Whether this inhibition of the distractor is independent-feature-based or object-based is currently unknown. It is also unknown if top-down attentional influence can modulate saccade trajectories based on different object featural goals during visual search tasks. To answer both of these questions, we designed a delay-match-to-sample task based on a modified version of the Wisconsin Card Sorting Task that had target-distractor pairs vary in the number of overlapping object features. We hypothesized that as the number of unattended features shared between the target-distractor pair increased, the level of inhibition would increase, demonstrated by a greater degree of sum curvature away from the distractor. We also hypothesized that saccades made in colour search trials would be significantly different than trials made in shape or numerosity search trials due to differences in the processing speeds of the visual cortical hierarchy. 57 participants underwent our experiment using head-mounted eye-tracking at 500 Hz. Our results supported both of our hypotheses, demonstrating that the inhibition of distractors observed during saccades is independent feature-based and can be modulated by top-down attentional influences. We propose a modified version of a diagram from Treisman and Gormican's 1988 study displaying how independent features on featural maps throughout the ventral stream are inhibited if a target-distractor pair shares that specific feature.

Poster 15

Donna Wood

GESTATIONAL NICOTINE AND CIGARETTE SMOKE EXTRACT EFFECTS ON HIPPOCAMPAL DEVELOPMENT

D.R. Wood, A. Thomas, E.V. Claridge, A.P. Stone, A. Sikic, A. Geremia, C.D.C. Bailey, J.E. Murray

Tobacco and e-cigarette using during pregnancy and adolescence has become more prevalent in recent years, increasing the risk of cardiovascular disease and neurological dysfunction. Previous studies have found that smoking during pregnancy leads to deficits in learning and memory in offspring, but the neurological underpinnings of these deficits across development remain poorly understood. This project aims to understand the interactions between nicotine and tobacco and morphological changes in the hippocampus across the lifespan. Further, this research aims to examine the relationship between these morphological changes, protein expression, and behavior. We exposed pregnant dams to one of three drinking water exposure conditions: standard tap water, nicotine, cigarette smoke extract (CSE), or vehicle. Following parturition, offspring were exposed via breastmilk until PND21 and then euthanized for brain extraction. Currently, we are imaging pyramidal neurons within the CA1 and CA3 regions of the hippocampus to measure dendritic spine morphology, and we plan to conduct Western blot analysis to measure cAMP response element binding protein (CREB) and brain derived neurotropic factor (BDNF) expression. Due to uneven

consumption across dams, follow-up cohorts will have their assigned compound experimenter administered. Brains will be collected at set developmental stages to establish a time-course of neural outcomes of gestational nicotine and tobacco smoke exposure.

Poster 16

Ella Claridge

ASSESSING THE ROLE OF DOPAMINERGIC AGONISM AND ANTAGONISM ON MORPHINE DRUG DISCRIMINATION IN MALE AND FEMALE RATS

E.V. Claridge, D.R. Peart, C.J. Nolan, A.P. Stone, M.A. Williams, J.M. Karlovcec, J.E. Murray

One aspect of opioid use disorder is the elicitation of behaviours by drug cues. Interoceptive drug cues may modulate behavioural responsivity to exteroceptive drug cues through Pavlovian conditioning. To model this effect in rats, a drug state may be trained as a feature positive (FP) or feature negative (FN) occasion setter (OS) to disambiguate the relationship between a discrete conditioned stimulus (CS) and an unconditioned stimulus. Dopamine has been implicated in cued reward seeking, so we aimed to investigate its role in the functioning of a morphine drug state as a FP or FN OS. Methods: Male and female rats were assigned to FP or FN training groups and received daily intermixed morphine or saline injections before training sessions. Training sessions consisted of presentations of a white noise CS followed by access to sucrose on morphine, but not saline sessions, for FP rats. FN rats learned the reverse contingency. Following acquisition, rats were tested for morphine discrimination after systemic pretreatment with the non-selective dopamine receptor antagonist flupenthixol, the non-selective dopamine receptor agonist apomorphine, or saline vehicle. Results: Male and female FP and FN rats acquired the discrimination. Flupenthixol and apomorphine inhibited sucrose seeking on test trials in all rats, likely through distinct mechanisms. Conclusion: Our findings lend support to a mechanism of OS involving gating of CS-induced dopamine release by FP or FN drug states.

Poster 17

Ellis Chartley

CHARACTERIZING THE INTERACTION OF ARC AND STK38/STK38L IN NEURONS

E. Chartley, B. Alural, H. Robeson, J.A. Steen, S.J. Haggarty, J. Lalonde

Activity-regulated cytoskeleton-associated protein (Arc) is rapidly expressed following neuronal activity and plays a crucial role in altering the strength of neuronal connections, a process called synaptic plasticity, which is important for learning and memory. Arc coordinates a variety of plasticity-related functions through interactions with different effector proteins. A mass spectrometry screen identified a previously

unreported interaction of Arc with two proteins, Serine/Threonine Kinase 38 (Stk38) and Stk38-Like (Stk38L). These kinases have been linked to receptor trafficking, dendritic spine morphology, and actin cytoskeleton rearrangement, processes that are consistent with known functions of Arc at synapses. This research aims to characterize the interaction between Arc and Stk38/Stk38L in neurons. After verifying the interaction by co-immunoprecipitating Arc-GFP with Stk38, preliminary results suggest that stimulation of mouse primary cortical neurons with brain-derived neurotrophic factor (BDNF) may increase expression of Stk38L in mature neurons. Further, compartmentalization of Arc and Stk38 was observed in dendritic spines, and in F-actin-rich areas of Arc-GFP overexpressing Neuro2a cells. This work provides evidence of two novel interactors of Arc which could lead to new insight into the role Arc plays in synaptic plasticity.

Poster 18

Isaac Sullivan

PURINERGIC REGULATION OF THE ZEBRAFISH SPINAL-CORD-INJURY RESPONSE

I. Sullivan, E. Stefanova, M. Chinn, A. Scott

In contrast to mammals, adult zebrafish (Danio rerio) undergo successful neural regeneration following spinal cord injury (SCI). Radial glia lining the zebrafish central canal function as neural progenitors that undergo a massive injury-induced proliferative response before differentiating into both neurons and glial cells. However, the molecular mechanisms that underlie these processes remain elusive. Among the signaling pathways that are dysregulated following mammalian SCI is the purinergic signaling system. While purines such as ATP and its metabolites mediate diverse cellular processes within the mammalian central nervous system (CNS), their roles have not been explored within the zebrafish CNS. Given that the purinergic system is evolutionarily conserved among vertebrates, we sought to characterize potential roles for P2Y2 receptor signaling in neurogenesis following SCI in adult zebrafish. Our findings demonstrated that expression of P2Y2 receptors were upregulated following injury, and activation of P2Y2 signaling enhanced injury-induced neurogenesis in this species. Further work will elucidate the roles of more receptors in these natural regenerators following SCI.

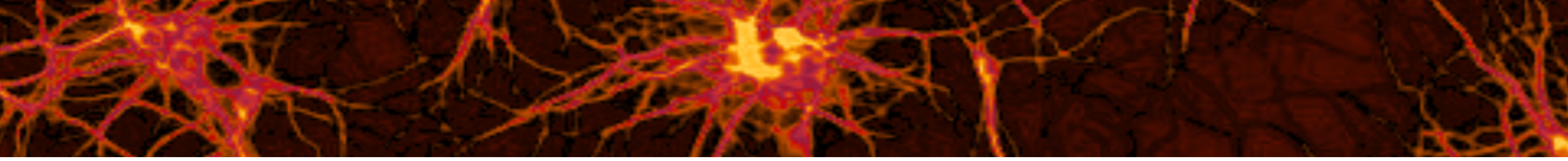
Poster 19

Jaime Tuling

ASTROCYTE-NEURONAL LACTATE SHUTTLING IN THE ANTERIOR CINGULATE CORTEX IN A MURINE MODEL OF CHRONIC NEUROPATHIC PAIN

J. Tuling, D. Halasz, A. Simal, G. Descalzi

Chronic pain impacts 1 in 4 Canadians over the age of 15, with less than half reporting any pain relief with current treatment options. Our current lack of understanding



regarding the molecular mechanisms involved in chronic pain development has contributed to this lack in effective treatments available. Current research points towards neuroplasticity in the anterior cingulate cortex (ACC) as a critical mechanism for long-term brain changes associated with chronic pain. We previously found that astrocyte-neuronal lactate shuttling (ANLS) is fundamental for hippocampal neuroplastic changes associated with pain-induced fear learning. Here, we used a neuropathic model of chronic pain, the spared nerve injury (SNI) model, to investigate nerve injury induced changes in lactate transport in the ACC of female and male mice to better understand the neural origins of chronic neuropathic pain. Various timepoints were chosen to assess lactate shuttling over time post-injury, and mechanical thresholds of injury were assessed using the Von Frey Test. After completing behavioural assessments, samples were collected from specific brain regions including the ACC and assessed using a lactate colorimetric assay. We found that both sexes showed a robust increase in SNI-induced nociceptive hypersensitivity, but observed a sex-specific increase of lactate in the ACC. These findings suggest that nerve injury engages ANLS in the ACC in a sex dependent manner, indicating sexual dimorphism of the ANLS in chronic pain development.

Poster 20

Jason Cousineau

ASSESSING THE RELATIONSHIP BETWEEN HYPERTENSION, BLOOD-BRAIN BARRIER BREAKDOWN, AND NEUROLOGICAL DYSFUNCTION

J. Cousineau, P. Marquez, P. Sellar, M. Alpaugh

Hypertension is highly associated with physiological changes to the body, such as altered blood flow to the brain and damage to the blood-brain barrier (BBB). These changes are known to influence the development and progression of dementia in general and Alzheimer's disease in particular. However, little is known about how hypertension may interact with other neurological disorders. Therefore, we aim to assess the effect of hypertension on the blood vessels of the cortex and the glial cells of the surrounding area, within the context of Huntington's disease (HD) and Schizophrenia. HD, a dominantly inherited protein-misfolding neurodegenerative disease, and Schizophrenia, a neuropsychiatric disorder with strong genetic ties to cardiovascular health, have both been found to have decreased tight-junction (TJ) expression and have been linked to earlier onset of disease when comorbid with hypertension. Hypothesis. Hypertension will reduce BBB integrity and enhance neuropathology in a disease-specific manner within cellular models of HD and Schizophrenia. Methods. A 3D microfluidic cellular model of the BBB will be used to examine the effects of inducing hypertensive-like pathology (HLP) in vessels produced using human control, HD, or Schizophrenia induced pluripotent stem cells. Specifically, BBB integrity, TJ protein expression, and disease-specific indicators will be measured after the induction of HLP. This will be accomplished by way of BBB integrity assays, western blots, and immunofluorescence respectively. We anticipate variations between disease groups in vessel integrity, TJ protein expression, endothelial cell size, and glial

behavior, showing an exacerbated effect when HLP is present. Results. Preliminary data shows that there is increased permeability of the BBB after the induction of HLP (high salt diet) in control vessels, but this effect is modulated in disease conditions. Conclusion. Our current results suggest that disease status has a modulatory effect on the response of the BBB to hypertension-related stressors.

Poster 21

Jessica Karlovcec

GENERALIZATION OF THE STIMULUS EFFECTS OF MORPHINE TO OTHER OPIOIDS IN RATS

J.M. Karlovcec, E.V. Claridge, D.R. Peart, J.E. Murray

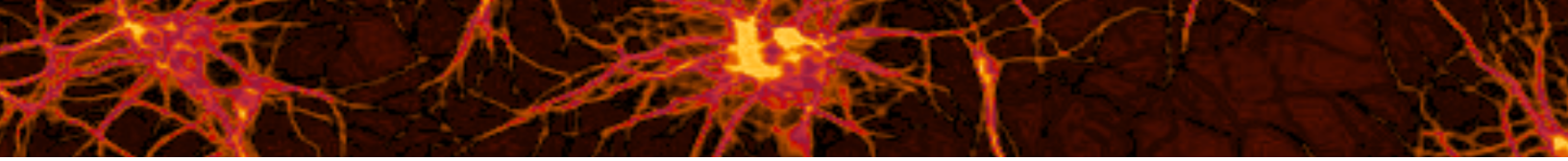
Interoceptive effects elicited by opioids can guide behaviours through Pavlovian associations with drug-related stimuli. Following the acquisition of appropriate conditioned sucrose-seeking guided by a morphine stimulus, stimulus specificity can be determined by assessing different opioid receptor agonists and comparing results to baseline discrimination behaviour.
Male and female rats received daily injections of either morphine or saline before chamber placement. Training sessions consisted of 8 presentations of a white noise conditioned stimulus (CS) each followed by sucrose delivery on morphine, but not on intermixed saline sessions. Following stable discrimination, rats completed generalization cycles consisting of two qualification sessions identical to training, followed by a test session if sufficient discrimination between the qualification sessions was demonstrated. On tests, responding to a single CS presentation was recorded after rats were pre-treated with one of four doses of either morphine, oxycodone, hydromorphone, fentanyl, naloxone, or saline. All rats were tested on all drugs.
Male and female rats acquired the discrimination replicating previous work. Though the study is still ongoing, preliminary results indicate the morphine generalization curve appears to plateau at doses higher than that of training. Curves for oxycodone, hydromorphone, and fentanyl appear to follow an inverted-u pattern. Naloxone blocks agonist-appropriate responding.
Our findings demonstrate that the stimulus effects of morphine can generalize to alternative doses of other opioid agonists and are blocked by antagonism, confirming that the mechanisms driving the behavioural stimulus effects of morphine overlap with other agonists with subtly different opioid receptor activity.

Poster 22

Jiayu Zheng

INVESTIGATING THE ROLE OF AMPAR TRANSIENT EXCHANGE IN THE PERIRHINAL CORTEX FOR OBJECT MEMORY DESTABILIZATION IN A RODENT MODEL

J. Zheng, E. Minard, K. Jardine, B. Winters



Consolidated memory can be manipulated through reactivation-induced memory destabilization and subsequent reconsolidation. Prior studies have shown that the transient exchange of α-amino-hydroxy-5-methyl-4-isoxazolepropionic acid receptors (AMPAR) from calcium-impermeable to calcium-permeable in the lateral amygdala is required for destabilizing auditory-induced fear memory in rodents. Yet, no research has investigated the AMPAR exchange on other forms of memory. Here we present the findings examining the role of AMPAR exchange in the perirhinal cortex (PRh) for object memory destabilization. Using a standard spontaneous object recognition (SOR) task, bilateral PRh infusions of a transient exchange blocker, GluA23y (100μg/μl), were administered prior to memory reactivation (RA). Following RA, rats received an infusion of a reconsolidation blocker, anisomycin. Our results indicate that AMPAR exchange in the PRh is required for object memory destabilization. Some memories are more resistant to destabilization upon reactivation due to boundary conditions such as remoteness. Previous research reveals that remote memories can destabilize when a salient change, such as a novel floor insert, is present during RA. We then tested whether AMPAR exchange in the PRh is required for remote object memory destabilization using a remote SOR task. Similar to the standard SOR protocol, with the exception of a 48h delay between sample and RA, along with a novel floor insert during RA. Our results indicate that AMPAR exchange in the PRh is required for remote object memory destabilization. The findings from this study will expand our current understanding of the neurobiological mechanisms involved in memory updating.

Poster 23

Julia Heidel

SEX DIFFERENCES IN NEURON MORPHOLOGY WITHIN THE DEVELOPING MOUSE ENTORHINAL CORTEX

J.M. Heidel, A.A. Geremia, C.D.C. Bailey

Sex differences in spatial learning and memory have been observed in mammals, yet the mechanisms underlying these differences remain elusive. While extensive research has focused on various components of the hippocampus, the entorhinal cortex, a pivotal communication hub between the neocortex and hippocampus, remains relatively understudied in this context. Pyramidal neurons within layer V of the entorhinal cortex are the primary recipients of hippocampal output and are hypothesized to exhibit sex differences during critical developmental periods. This study tested whether a sex difference exists for entorhinal cortex layer V neurons sampled from mice at postnatal day 20, which is a juvenile stage of development. Neurons were labelled using Golgi-Cox staining and dendrite morphology was analyzed using Sholl and branch structure analyses. Results revealed no sex difference for many parameters including dendrite surface area, diameter, volume, number of terminals, and distance of terminals for both apical and basal dendrites. However, females exhibited a greater length for apical dendrites overall and for basal dendrites within 75-150 microns from the cell body. Potential mechanisms underlying these sex differences include different developmental timing for neurogenesis, for dendrite growth and pruning, and for synaptic spine development. There also may be sex differences in the neuromodulatory input received

by these neurons. Future research by our laboratory will employ neurophysiological and behavioural measures to determine the means by which sex differences within the entorhinal cortex impact spatial learning and memory. Results from this current study contribute to the characterization of neuron morphology within the entorhinal cortex and highlight the importance of considering sex as a variable in neuroscience research.

Poster 24

Kashaf Gilani

DYSREGULATION OF ASTROCYTE-MEDIATED PURINERGIC SIGNALLING IN FRAGILE X SYNDROME

K. Gilani, C. Atkinson, S. Kang, M. Napier, A. Scott

Fragile X Syndrome (FXS) is a neurodevelopmental disorder and the leading genetic cause for inherited intellectual disability and autism spectrum disorders. While the underlying genetic cause is known, the subsequent cellular and molecular mechanisms of the disorder remain unclear. Recent work has identified significant changes to the evolutionarily conserved purinergic signalling system within the FXS brain. Specifically, activation of the purinergic receptor P2X7 may contribute to the aberrant calcium activity and oxidative stress responses reported in astrocytes, a primary glial cell population in the brain. Our findings to date indicate that P2X7 is upregulated within the cortex of the FXS animal model, Fmr1 knockout (KO) mouse, compared to wild-type (WT) mice early in development. We also found that the elevations in spontaneous calcium activity found in cortical astrocytes isolated from KO mice over that of WT astrocytes can be normalized with P2X7 antagonism (JNJ). In addition, P2X7 antagonism can prevent upregulation of active STAT3, a transcription factor involved in inflammation and cellular stress, as well as an isoform of NOX2-beta that works to elevate the emission of reactive oxygen species. Taken together, P2X7 dysregulation in FXS astrocytes appears to have a detrimental effect on both activation levels as well as stress responses.

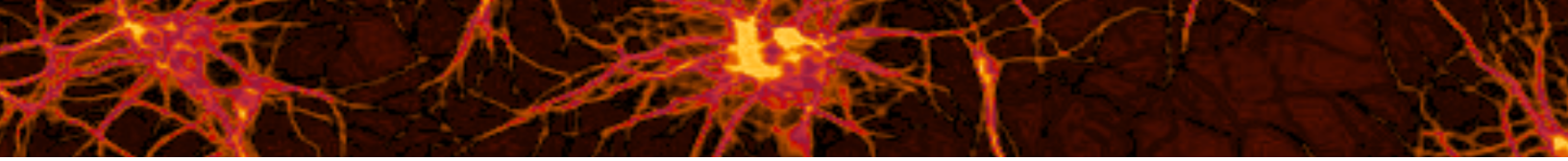
Poster 25

Mallory Terry

SOMETIMES MORE (OVERLAP) IS BETTER! ACTION PLAN OVERLAP IMPACTS THE INTERFERENCE BETWEEN VISUALLY-GUIDED TOUCH AND MULTIPLE-OBJECT TRACKING (MOT)

M.E. Terry, V. Amelio, L.M. Trick

When two tasks are performed simultaneously their action plans can overlap with one another. Past findings suggest that the overlap can either improve or degrade performance, depending on the relatedness of the required actions (e.g., Fournier et al. 2015). In this study we assessed the impact of overlapping action plans in a multiple-object tracking (MOT) task. Participants tracked 1-4 MOT targets while also touching moving items in MOT that changed colour. To determine the effects of action plan



overlap between the MOT and touch task, we manipulated the way that participants reported the identity of the targets at the end of the trial (untimed). In the touch task participants always used the index finger of their dominant hand. To report the targets participants either typed in the letters corresponding to the targets with their non-dominant hand (minimal overlap) or touched MOT targets with the index finger of their dominant hand (maximal overlap). Target report method had no effect on single-task MOT performance. However, when participants had to touch moving items that changed colour during tracking (dual-task), MOT performance was significantly worse when overlap was minimized. It also took participants longer to touch moving items that changed colour - even though target report occurred 7-8 seconds later. Nonetheless, MOT performance was always better and touch latencies lower when the touched items were targets as compared to distractors in MOT; report technique had no effect. This shows a dissociation between the effects of attentional selection in MOT and overlapping action plans.

Poster 26

Natalina Becke

CREB IS ACTIVATED BY STORE-OPERATED CALCIUM ENTRY VIA CALMODULIN-DEPENDENT SIGNALLING PATHWAYS IN IPSC-DERIVED HUMAN NEURAL PROGENITOR CELLS

N. Becke, T. Hewitt, E. Proud, E. Anderson, S.D. Sheridan, R.H. Perlis, J. Brind'Amour, J. Lalonde

cAMP Response Element-Binding Protein (CREB) is a calcium (Ca2+)-sensitive transcription factor that has been implicated in multiple neuronal processes. CREB becomes active when it is phosphorylated at serine 133 by signaling pathway kinases, many of which are Ca2+-dependent. In neural progenitor cells (NPCs), intracellular Ca2+ is regulated by storage-operated Ca2+ entry (SOCE)—a mechanism that promotes Ca2+ influx through ORAI channels when Ca2+ stores are empty. Evidence shows that SOCE in mature neurons influences synaptic growth and plasticity while in NPCs, this pathway contributes to the proliferation and differentiation of NPCs. Interestingly, no direct connection has been made between SOCE and CREB activity in NPCs to date. Therefore, we tested whether CREB phosphorylation is influenced by SOCE-facilitated Ca2+ influx and seek to understand how this interaction could affect downstream gene expression using human induced pluripotent stem cell (iPSC)-derived NPCs. Indeed, our efforts suggest that SOCE activation promotes the phosphorylation of CREB and significant changes in neurodevelopment-related gene expression. Further testing with a pharmacological inhibitor suggests that CREB phosphorylation appears to be dependent on calmodulin signaling. Downstream effectors of calmodulin include Ca2+ /calmodulin-dependent protein kinase II (CaMKII) and Ca2+ /calmodulin-dependent protein kinase IV (CaMKIV), both of which can directly interact with and phosphorylate CREB. However, protein expression tends to vary at different stages of neuron development, as shown with a completely diminished expression of CaMKII in NPCs when compared to neurons who were differentiated for 8-weeks or primary mouse cortical neurons. In contrast, CaMKIV is expressed at a similar level to the 8-

week neurons, making it our kinase of interest for the activation of CREB following SOCE events. Taken together, these findings begin to piece together the signaling mechanism that connects SOCE to its effect on the early stages of neuron growth and differentiation.

Poster 27

Olga Burenkova

EFFECTS OF ENVIRONMENTAL 'ENRICHMENT' ON ZEBRAFISH BRAIN CELL PROLIFERATION

O.V. Burenkova, R.D. Lippert, J.M. Lavery, G.J. Mason

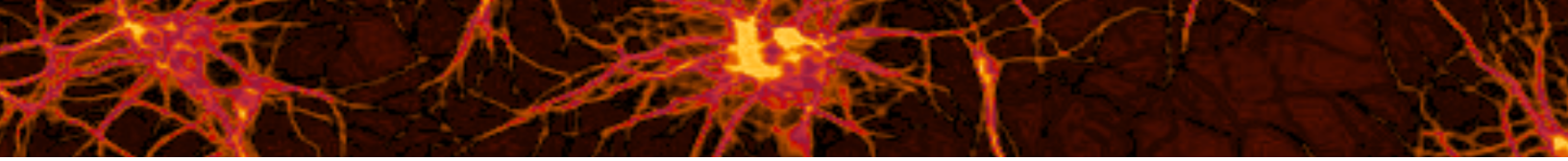
Zebrafish are commonly employed as a model organism in neuroscience research, during which small barren tanks are the default housing. However, they exhibit intriguing improvements in cognitive abilities if their housing conditions are improved, according to previous research from our lab. Specifically, so-called 'enriched' (i.e., non-barren) housing emerged as the preferred choice for fish, also facilitating faster learning rates in a T-maze compared to barren housing conditions. Furthermore, this learning improvement occurs gradually: more preferred housing conditions are accompanied by better learning. The present pilot study examines the neurobiological mechanisms underlying these effects by investigating brain cell proliferation and vasculature in zebrafish subjected to ‘enriched’ versus barren environments. The brains of 10 fish (6 barren and 4 ‘enriched’) were harvested after approximately 20 months of differential housing. Brains were sectioned and stained for Nissl bodies using cresyl violet. Brain cell density and vessel density were measured manually in two brain regions, the telencephalon and optic tectum. Our findings revealed significantly greater brain cell density in the dorsomedial telencephalon of ‘enriched’ fish. No differences were revealed in the optic tectum, both for brain cell density and vasculature. These preliminary results underscore the influence of environmental factors on neurobiological outcomes and provide new insights into the intricate interplay between environmental ‘enrichment’ and zebrafish brain function. In our further research, we are planning to increase statistical power, explore additional variables such as sex differences, and broaden the biological markers to include markers of proliferation, neuronal plasticity, and of metabolic activity. This will contribute to advancing our understanding of the nuanced neurobiological mechanisms of environmental impacts on cognitive abilities, with potential implications for animal welfare, basic science, and translational applications in neurodevelopmental disorders.

Poster 28

Olivia O’Neill

DOPAMINE AT D1 RECEPTORS WITHIN THE DORSAL HIPPOCAMPUS IS INVOLVED IN OVERCOMING BOUNDARY CONDITIONS FOR SPATIAL OBJECT LOCATION MEMORY MALLEABILITY

O.S. O’Neill, K.V. George, B.D. Winters



Consolidated long-term memories become modifiable in strength or content via memory reconsolidation. This is the process by which a reminder cue initiates reactivation of the memory trace and triggers destabilization. There are biological boundary conditions that are believed to gate this process, such that older and more strongly encoded memories do not readily undergo destabilization. The present study investigated the role of dopamine at D1-receptors in object location memory destabilization, with focus on overcoming boundary conditions for older ("remote") memory destabilization. Using male rats in a modified object location task, D1-receptor antagonist SCH23390 was administered systemically (0.1mg/kg) prior to reactivation of recent or relatively remote object location memories. Subsequent injection of NMDA receptor antagonist MK801 was used to impair reconsolidation. Remote memories do not destabilize unless a salient novel cue is presented at reactivation. SCH23390 blocked destabilization of recent memories, as well as relatively remote object memories when a novel floor insert was presented at reactivation. Using the same paradigm, we administered D1-receptor agonist SKF38393 (5mg/kg; systemic) to induce destabilization of remote memories in the absence of salient novelty. The results revealed that SKF38393 promoted destabilization of the relatively remote trace, supporting a potentially important role for dopamine in this "boundary condition override" process. The dorsal hippocampus (dHPC) has consistently been implicated in the storage and maintenance of spatial object memories; as such, we found that using the aforementioned behavioural paradigms, intra-hippocampal administration of SCH23390 (2µg/µL) similarly blocked destabilization for recent and relatively remote object location memories, negating the amnesic effects of post-reactivation protein synthesis inhibitor anisomycin (100µg/µL). Consistent with previous findings implicating dopamine in memory destabilization, this study shows evidence for the role of D1-receptors within the dHPC in destabilization of boundary condition protected-object location memories and a potentially critical role in adaptive modification of newly encoded and relatively remote spatial memories.

Poster 29

Rachel Eng

INVESTIGATING CONTINGENT CAPTURE IN DRIVING SCENES

R. Eng, N. Al-Aidroos, L. Trick

Contingent capture theory predicts that a stimulus will capture attention only if it is consistent with the observer's internal goals. For example, when an observer's goal is to find a red target, a red stimulus should capture attention but not other coloured stimuli. While this has been demonstrated numerous times using basic stimuli (e.g., simple colours and shapes, few items in a display), it is unclear whether contingent capture occurs in complex real-world scenes. Arexis et al. (2017) investigated this using a search task where participants viewed photographed driving scenes with a single red letter embedded at random locations. Their task was to report whether the red letter was a T or an L. A GPS navigation system image was also shown in the bottom right corner of the display. The GPS either had a blank screen, a red-coloured route (goal-relevant distractor colour) or a green-coloured route (goal-irrelevant distractor colour). The GPS appeared 1 second in advance of the driving scene and letter, acting as a pre-

search display. If contingent capture occurs, participants should be slower to respond when the GPS showed a red route (goal-relevant distractor colour). However, goal-relevance had no effect, perhaps because the GPS pre-search display appeared so far in advance of the search display (1 s). In the present study, we manipulated the presentation duration of the pre-search display (0 ms, 100 ms, 1 s) and instructed participants to ignore the GPS. We predicted that goal-relevance would have an effect, but only when there was insufficient time to disengage attention from the GPS distractor before search display onset (the 0 and 100 ms conditions). Results call into question the contingent capture hypothesis within the context of real-world scenes.

Poster 30

Rebecca McCabe

HOW DO INTERNAL GOALS AND THE EXTERNAL ENVIRONMENT SUPPORT ATTENTIONAL CONTROL SETTINGS?

R. McCabe, S. Joubran, N. Al-Aidroos

Attentional control settings (ACSs) are known as being reflective of current attentional goals that are determined by the nature of the task being performed. The present study aims to identify the role of the external environment in solidifying attentional control settings in episodic long-term memory. In the present study, participants memorized a set of 16 objects. Unbeknownst to the participant, these images were then separated into two sets: Target Full and Target Half, which were used to complete a spatial blink task. In the first block of the experiment, the Target Full images were presented as distractors and targets and the Target Half images were presented only as distractors, along with non-studied images which are images that are not part of the studied set. In the second block, Target Half images began being presented as targets as well, and all other conditions remained the same. Due to the amount of time participants took to learn the task, only the second half of each block was investigated. The results demonstrate that the images that are presented as targets capture more attention as distractors (Target Full) then images that are only presented as distractors (Target Half). However, when the Target Half images begin being shown as distractors, they begin capturing attention similarly to Target Full. This provides evidence that interacting with the external environment solidifies our attentional control settings, leading to higher levels of attentional capture.

Poster 31

Rita El Azali

INDIVIDUAL DIFFERENCES IN ORAL MORPHINE SEEKING BEHAVIOR IN RATS: COMPARING THE EFFECTS OF CONTINGENT AND NON-CONTINGENT FOOT SHOCK

R. El Azali, A.R. Noon, A.P. Stone, S. Latremouille, A.McGinn, E.M. Rock, S.T. Barrett, J.E. Murray

Altering opioid circuitry through uncontrollable stress could expose an overlap in analgesic and reinforcement systems. The present study investigates the effects of contingent and non-contingent punishment on oral morphine (OM) intake. Male and female rats were randomly assigned to one of five groups: Morphine Control (MC); Punishment (P); Yoked (Y); Shock Control (SC); and Chamber Control (CC). Following OM acquisition, groups transitioned to the punishment phase. MC rats continued self-administration with no foot shocks (FS). P rats received FS at a 15% probability, contingent on active lever pressing for OM. Y rats were matched with P to receive time-matched non-contingent FS during SA sessions. SC rats received matched FS, but never had access to OM; CC rats never experienced FS or had access to OM.
Male and female morphine controls are consuming similar amounts of drug in mg/kg, and this stabilizes across time. Contingent FS reduces drug intake in high and low consumers, but there appear to be strong individual differences between animals more resistant versus more sensitive to FS when it is linked with morphine seeking. High or low levels of non-contingent FS does not appear to decrease consumption in neither high nor low consumers. Notably, both sexes show equivalent pain sensitivity in the tail-flick test. These results have an impact on theoretical notions of the role of compulsivity in substance use disorders as well as provide insight into individual differences between those sensitive and resistant to punished drug-seeking behaviour.

Poster 32

Brooke Ginson

MODULATION OF THE OPIOID SYSTEM IN ASSOCIATIVE DRUG MEMORIES

B. Ginson, G. Grandison, F. Leri

It has been demonstrated that acute opioid intoxication, as well as precipitated opioid withdrawal, have effects on memory. Specifically, post-training administration of opiates or precipitated opioid withdrawal enhances memory in object recognition (OR) tasks. As such, we aimed to investigate if the memory-enhancing effect of opiates and opioid withdrawal can be observed in the context of drug memories. To test this, the conditioned place preference paradigm was used to establish a drug memory. 4 pairings with alternating 0 mg/kg and 1 mg/kg heroin over 30-minute conditioning sessions have been shown to sufficiently produce a drug memory, such that animals associate the drug-paired compartment with heroin availability and will approach this environment preferentially in a drug-free state. To test whether the strength of this drug memory could be modulated, post-training treatments were employed, and animals were monitored for 1 hour following administration. Immediately following drug conditioning sessions, animals received either: 1 mg/kg heroin + 3 mg/kg naloxone (post-training withdrawal), 1 mg/kg heroin (post-training heroin), or 0 mg/kg heroin (post-training vehicle). On saline conditioning, all animals received saline post-training. Animals were tested after the first pairing (test 1), at the end of conditioning (test 2), and again 1 week later (test 3). Animals in the post-training heroin condition demonstrated an enhancement of memory, as demonstrated by a significant increase in time spent in the drug compartment at test 1, however, this effect was ameliorated by test 2. Both the

post-training withdrawal and post-training vehicle groups displayed no difference in time spent in the drug compartment by test 1, but a significant increase by test 2. Locomotion data during conditioning and post-training observation lend support to the hypothesis that the rapid development of tolerance occurred in post-training heroin-treated animals. This suggests that the memory-enhancing effects of opioids may also display tolerance.

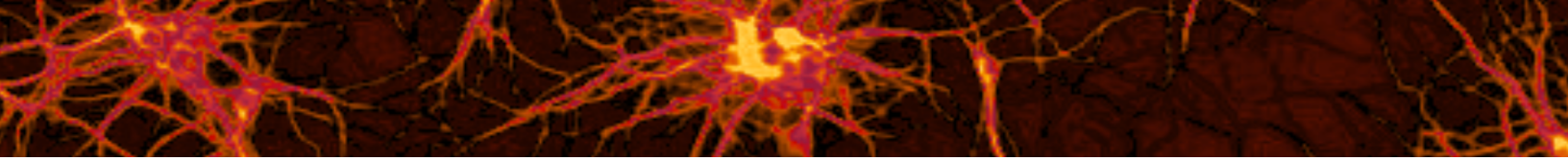
Poster 33

Heather Collett

DISRUPTING PERIRHINAL GABAERGIC PARVALBUMIN INTERNEURONS IMPAIRS LEARNING ON A MOUSE OBJECT CATEGORY RECOGNITION TASK

H.A. Collett, K.H. Jardine, S.D. Creighton, J.H. Fournier, R.A. Pandit, C.E. Wideman, B.D. Winters

Object category recognition (OCR) may rely on generalized category representations which could be refined with inhibitory GABAergic signaling. Parvalbumin-containing GABAergic interneurons (PVINs) have been implicated in cortical representation refinement and provide inhibitory control in the perirhinal cortex (PRh), an area which is necessary for object recognition. To determine the role of GABAergic transmission in the refinement of object category representations, male C57/BL6 mice were administered a GABAA receptor antagonist (bicuculline) prior to exposure to category exemplars. When tested on an OCR task, mice administered bicuculline failed with a 1-h retention delay, which requires pre-exposure to category objects. Additional exposure to learned categories 1h prior to sacrifice revealed greater c-fos activation vs control mice in the PRh of mice administered bicuculline. This suggests that OCR task performance may be supported by sparser representations in the PRh. Chemogenically disrupting PRh PVINs, prior to object category exposure through inhibition or excitation impaired OCR task performance with a 1-h, but not a 30-min, retention delay. With a 30-min delay, performance was also disrupted by pre-sample PVIN inhibition or stimulation. Previous object category familiarity ameliorated this deficit. Interestingly, neither pre-sample PVIN PRh inhibition nor stimulation produced a deficit on the spontaneous object recognition task with a 30-min or 24-h retention delay. The pre-sample deficit may be due to the PRh role in complex perceptual processes such as object feature conjunction or binding. To assess whether GABAergic transmission is involved in discriminating between objects with overlapping features we administered bicuculline prior to a configural simultaneous object oddity discrimination task. Bicuculline administration impaired oddity discrimination when objects where highly ambiguous and all had overlapping features. These findings suggest that GABAergic signalling and PVINs in the PRh may play an essential role in refinement of object category representations and may support the binding and generalizing of object features.



Poster 34

Jayson Capistrano

STUDYING THE EFFECTS OF GUT-DERIVED METABOLITES IN BRAIN DEVELOPMENT TO UNDERSTAND ITS ROLE IN THE ETIOLOGY OF AUTISM SPECTRUM DISORDER (ASD)

J. Capistrano, V. Rea, P.N.G. Tran, T. Ball, T. Van Raay

Autism spectrum disorder (ASD) is a group of neurodevelopmental disorders caused by genetic and environmental factors. Due to its complex and often pleiotropic nature, its etiology has been difficult to elucidate—ultimately, hampering the identification of definitive diagnostic markers and development of potential therapies/treatments. Interestingly, most individuals with ASD suffer from gastrointestinal problems, which underscores a potential connection between ASD and the gut. Metabolites produced from the gut have been reported to impact the brain; however, the mechanisms of how these metabolites influence the brain or vice-versa remain poorly understood. Here, we hypothesize that distinct metabolites derived from different diets and/or mental health profiles result in unique phenotypic effects in the developing brain. In the first study, metabolites from naïve fecal samples that were grown in a robogut in the presence of different diets (high fiber Western, low fiber Western, Mediterranean, and Yanomami) were isolated. In the second study, age- and gender-matched fecal samples from neurotypical (NT) and children with ASD were used to isolate metabolites. We then evaluated the effects of these gut-derived metabolites on neurodevelopment by looking into changes in gene and protein expression, sensory organ development, and behavioral responses using germ-free zebrafish as our model. Thus far, our results suggest that the zebrafish model may not be sensitive enough to detect the effects of metabolites derived from different diets. However, we found that zebrafish neurodevelopment seems to be sensitive enough to detect the different effects of ASD and NT metabolites, where we see unique behaviors and distinct alterations in sensory organ development and gene expression profiles. Our goal is to eventually uncover the molecular mechanisms underlying the contributions of gut-derived metabolites on the development of the brain, which has implications for ASD and other relevant diseases and disorders.

Poster 35

Amelia Doerksen

REGULATION OF AXONAL TRANSPORT IN NEURONS BY PROTEIN PALMITOYLATION OF P150GLUED

A. Doerksen, A. Leekha, S. Sanders

Neurons are large, complex cells requiring efficient trafficking and delivery of proteins and organelles to specific subcellular locations. Fast, continuous, anterograde and retrograde transport of cargo along axonal microtubules by dynein and kinesin motors is critical for neuronal function. The activity of motor proteins is tightly regulated, and

aberrant activity can result in neurodegeneration or neurodevelopmental deficits. One important mechanism to regulate neuronal protein trafficking is the covalent addition of fatty acids to cysteine residues, a process known as palmitoylation. Several kinesin and dynein motor subunits and their activators have been identified in high throughput palmitoyl-proteomic studies as being potentially palmitoylated. Indeed, we recently demonstrated palmitoylation of the dynein activating complex dynactin subunit p150Glued. Dynactin is critical for dynein activation and processivity. P150Glued is palmitoylated predominantly in nervous system tissues on cysteines 617 and 1252 by the ZDHHC12 palmitoyl acyltransferase. p150Glued is the largest dynactin subunit that mediates dynein-dynactin microtubule binding and processive motility. The functional role of p150Glued palmitoylation is unknown, but due to the importance of p150Glued in dynein-mediated fast axonal transport, p150Glued palmitoylation likely regulates transport. Interestingly, when palmitoylation-resistant (C617/1252A; CCAA) p150Glued-GFP is expressed in neurons, less GFP signal is present in distal axons and in the vesicular fraction compared to wild type expressing neurons. This suggests that palmitoylation may regulate association of p150Glued with vesicular cargos. This study will be the first to investigate the function of p150Glued palmitoylation. Our findings will provide novel insights into how palmitoylation can regulate neuronal transport, contributing to the foundational knowledge within the field of palmitoylation with potential for understanding how trafficking can be altered in various neuropathies.

Poster 36

Ana Leticia Simal

SEX DIFFERENCES IN ASTROCYTE-NEURON DYNAMICS IN CHRONIC NEUROPATHIC PAIN IN THE ANTERIOR CINGULATE CORTEX

A.L. Simal, J. Tuling, G. Descalzi

Chronic pain impacts 25% of Canadians aged fifteen and above, especially marginalized groups, with women making up 67% of those affected. Despite this, pre-clinical research has predominantly prioritized male rodent models, leaving a knowledge gap regarding female chronic pain mechanisms.
Mounting evidence indicates neuroplastic changes within the anterior cingulate cortex (ACC) as pivotal in chronic pain development. Responding to neuronal activity, the astrocyte-neuronal lactate shuttling (ANLS) can rapidly provide lactate to neurons, meeting metabolic demands required for neuroplasticity. However, its role in chronic pain-induced neuroplasticity remains unknown.
This study investigates ANLS in the ACC of female and male mice, exploring its involvement in chronic neuropathic pain development. Using the spared nerve injury (SNI) model in adult female and male C57BL/6 mice, we assessed gene expression in the ACC of ANLS pathways at 5-, 14-, 30-, and 60-days post-surgery using RT-qPCR. We also confirmed mechanical allodynia for each timepoint using the Von Frey Test. Despite similar patterns of SNI-induced pain hypersensitivity in both sexes, we found that long-term SNI increased ANLS-related gene expression in the ACC of male but not female mice. We thus conclude that neuropathic pain affects ANLS in the mouse ACC

in a sexually dimorphic manner. Furthermore, these sex differences highlight the need to include both females and males in research on molecular targets for chronic pain treatment, deepening our knowledge of pain chronification.

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Jennifer Holborn

INVESTIGATING THE ANTICANCER POTENTIAL OF CANNFLAVIN A AND CANNFLAVIN B AGAINST GLIOBLASTOMA MULTIFORME

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Multiple object tracking is the ability to keep track of the positions of a subset of identical Glioblastoma multiforme (GBM) is a highly aggressive and invasive brain tumor associated with poor prognosis and limited treatment options. Previous studies have shown that cannflavin A and cannflavin B, flavones that accumulate uniquely in C. sativa, produce promising anticancer effects in bladder and pancreatic cancer models. In this study, we explored the therapeutic potential of cannflavins against GBM utilizing a comprehensive approach involving cell viability, migration, and invasion assays to delineate the impact of these compounds against various aspects of GBM biology. Our investigation revealed a dose-dependent decrease in GBM cell viability following exposure to increasing concentrations of cannflavin B (0.5 to 20 μM), with no discernible cytotoxic effects observed. Remarkably, low doses of both cannflavin A and cannflavin B exhibited significant inhibition of GBM cell migration in timelapse scratch assays, indicating their potential to impede tumor dissemination. Of particular interest, cannflavin B demonstrated robust anti-migratory and anti-invasive properties, as evidenced by transwell migration and spheroid invasion assays. Cannflavin B at low concentrations not only suppressed the migration of GBM cells but also attenuated their ability to invade surrounding tissues, highlighting its multifaceted therapeutic effects. Together, our findings underscore the promising anticancer attributes of cannflavins in the context of GBM. Their ability to modulate critical cellular processes implicated in tumor progression suggests a potential role in GBM therapy. Further studies elucidating the underlying molecular mechanisms and in vivo efficacy of cannflavin A and cannflavin B are warranted to validate their utility as novel therapeutic agents for GBM treatment.

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Alexandra Law

P1 RECEPTOR DYSREGULATION WITHIN THE FMR1 KO CORTEX LEADS TO ABERRANT SYNAPTIC ACTIVITY AND CIRCUITRY DEVELOPMENT

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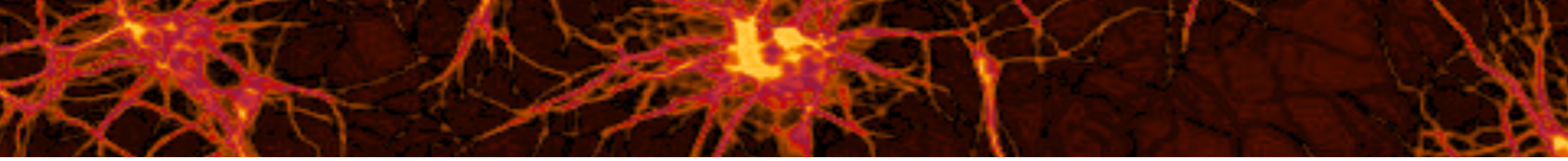
Fragile X Syndrome (FXS) is an X-linked genetic disorder that results in cognitive impairments such as mental retardation and hyperactive behaviours. FXS arises from



reduced expression of Fragile X mental retardation protein (FMRP), which has established roles in synaptogenesis. Thus, the absence of FMRP in FXS has various repercussions on synaptic development and maturation. Alternative factors that may contribute to the abnormal synapse formation in FXS include astrocytes, which display various regulatory roles in the central nervous system, and adenosine, which acts through purinergic signalling. This study examined the effects of adenosine signalling in co-cultures of astrocytes and neurons on synaptogenesis and network circuitry. While synaptogenesis and neuronal excitability was both elevated in Fmr1 KO cultures, inhibition of the P1 receptor A2A lead to normalization of both back to levels similar to WT cultures. These findings demonstrate that dysregulation of adenosine signalling in Fmr1 KO astrocytes and neurons may play an important role in network development and pathology of FXS.