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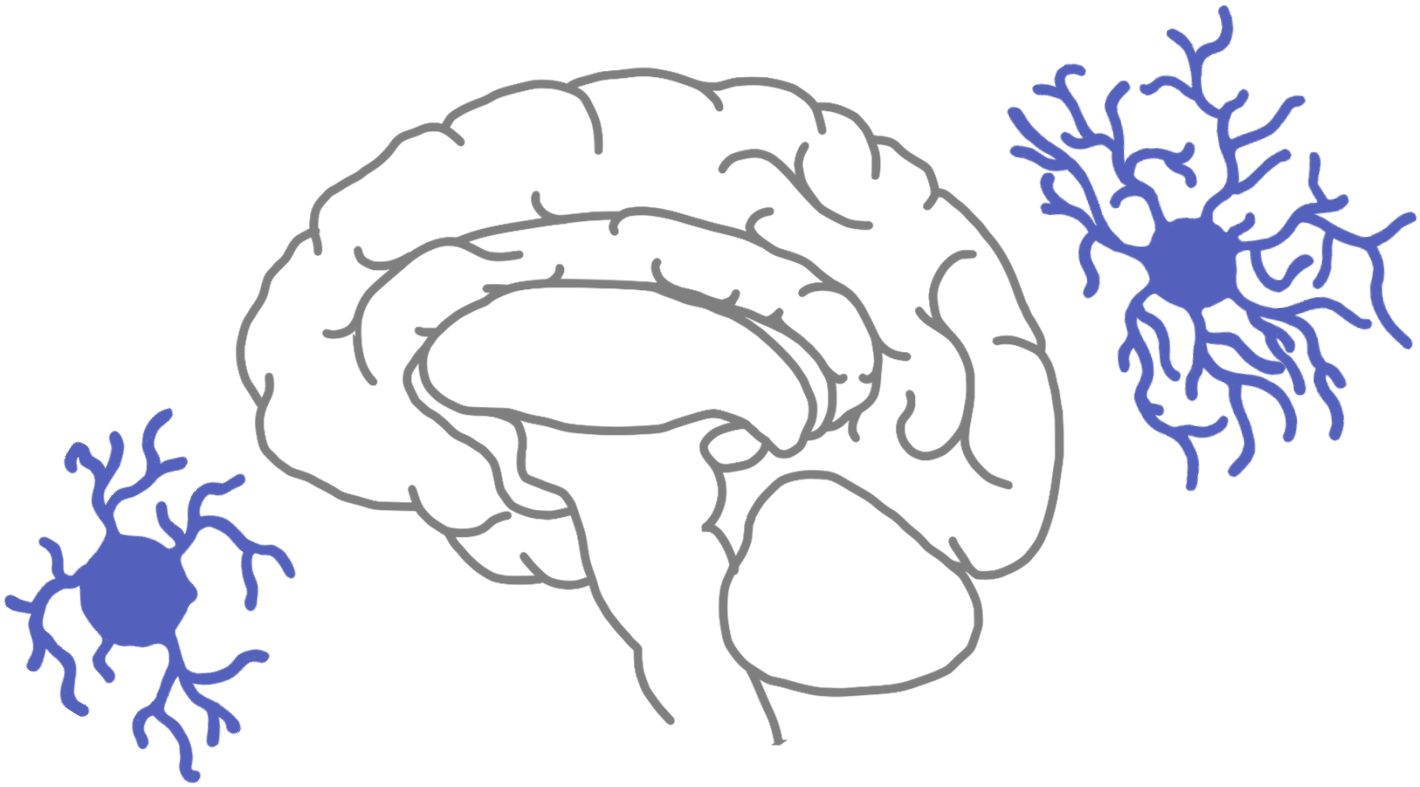
Poster Abstracts



2021 Society for Behavioral Neuroendocrinology Annual Meeting

Poster presentations

Three poster sessions will be held during the meeting to provide an informal exchange of information and allow trainees to network with established scientists.

Poster Session I

Tuesday, June 29, 2021 from 12:00pm to 1:30pm (ET)

P1.1 GENDER POLYMORPHISMS, VISUAL PATHWAY, AND COLOR PERCEPTION IN CHINESE WOMEN

Diana Derval
DervalResearch, Shanghai

Introduction: The objective of this research was to study the impact of prenatal hormones on eye specialization and color perception among Chinese women.
Method: The experimental group comprised of 81 Chinese women aged 25-45 years with no reported health disorders. Physiological information like lower-order aberrations (nearsightedness or farsightedness) and the influence of prenatal hormones were collected (digit ratio measurement). Subjects were presented a color strip containing 39 color nuances with separation lines between the different colors, and in four locations, an extra line separating a repetition of the same color. Subjects indicated how many and which ones of the colors nuances they were able to see, as well as their color preferences.
Results: Some subjects were able to distinguish 17 color nuances and others 44. Women influenced by prenatal testosterone tended to see more than 39 color nuances as they counted the separation lines - their eye being attracted to contrast. Women influenced by prenatal estrogen tended to count 39 colors nuances or less - their eye being attracted to the actual colors.
Discussion: Individuals perceive more or less color nuances depending on the number, range, and distribution of their color cones. Some individuals are more attracted to contrast than to colors with a visual pathway dominated by rods. Prenatal hormones seem to act as a predictor of an individual's visual pathway. These findings could help explain variations in color preferences (black and white vs colors) and adapt the sensory experience to different gender polymorphisms.

P1.2 INVESTIGATING IN UTERO EXPOSURE TO AN ENVIRONMENTALLY RELEVANT PHTHALATE MIXTURE ON THE ANXIETY-LIKE BEHAVIOR IN ADULT MALE AND FEMALE MICE

Stephanie Soriano[1], Leia Jones[2], and Megan Mahoney[1,3]
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Endocrine-disrupting chemicals (EDCs) are pervasive in the environment. These chemicals interfere with hormone synthesis, metabolism, and actions. Specifically, gonadal hormones participate in the modulation of emotional behaviors including anxiety and depression. Herein, we tested the hypothesis that developmental exposure to an environmentally relevant phthalate mixture impacts anxiety-like behaviors differently in male and female mice. In this study, pregnant CD-1 dams were

orally dosed with vehicle (tocopherol-stripped corn oil) or a phthalate mixture (20, 200 µg/kg/day, and 200 mg/kg/day) daily from gestational day 10.5 to birth. The phthalate mixture was derived from levels of phthalate metabolites measured in urine samples from pregnant women in the Illinois Kids Development Study. Animals were tested at post-natal day 62 -76 in the light-dark box (LDB) and the elevated plus maze (EPM). In the LDB test, 200µg phthalate mixture exposed females spent more time in the light zone compared to control females, suggesting an anxiolytic effect. Circling stereotypic behavior was observed in 200mg phthalate mixture exposed females but not in other groups reflecting a negative affective state. Additionally, prenatal exposure to the phthalate mixture had no effect on anogenital distance (AGD) in males. However, AGD increased in 200mg phthalate mixture exposed females compared to 200µg females. AGD is determined by prenatal androgen levels. Therefore, it is possible that the phthalate mixture increased androgen levels leading to an increase in AGD. Collectively, our data suggest that prenatal exposure to an environmentally relevant phthalate mixture disrupts aspects of reproduction and anxiety-like behavior.

P1.3 ANDROGEN RESPONSIVENESS TO SIMULATED TERRITORIAL INTRUSIONS IN ALLOBATES FEMORALIS MALES: EVIDENCE SUPPORTING THE CHALLENGE HYPOTHESIS IN A TERRITORIAL FROG

Camilo Rodríguez[1], Leonida Fusani[1], Gaëlle Raboisson[1], Walter Hödl[1], Eva Ringler[2], and Virginie Canoine[1]

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Territorial behaviour has been widely described across many animal taxa, where the acquisition and defence of a territory are critical for the fitness of an individual. Extensive evidence suggests that androgens (e.g. testosterone) are involved in the modulation of territorial behaviour in male vertebrates. Short-term increase of androgen following a territorial encounter appears to favour the outcome of a challenge. The "Challenge Hypothesis" proposed by Wingfield and colleagues outlines the existence of a positive feedback relationship between androgen and social challenges (e.g. territorial intrusions) in male vertebrates. Here we tested the challenge hypothesis in the highly territorial poison frog, Allobates femoralis, in its natural habitat by exposing males to simulated territorial intrusions in the form of acoustic playbacks. We quantified repeatedly androgen concentrations of individual males via a non-invasive water-borne sampling approach. Our results show that A. femoralis males exhibited a positive behavioural and androgenic response after being confronted to simulated territorial intrusions, providing support for the Challenge Hypothesis in a territorial frog.

P1.4 GUT MICROBIOTA DEPLETION IN EARLY DEVELOPMENT AND ADULTHOOD ALTERS SOCIOSEXUAL BEHAVIORS IN MALE MICE

Stephanie Salia, Yellow Martin, Lauren Jackman, Francine F. Burke, Leah A. Myles, Francis Bambico, Ashlyn Swift-Gallant

Memorial University of Newfoundland

The gut microbiome is host to trillions of microorganisms that influence the brain and behaviour via the gut-brain axis. Gonadal hormones drive sex differences in the gut microbiota composition that

translates into sex-dependent effects on behaviour when depleted. To date, these studies have only examined the gut's depletion on psychiatric disorders, including anxiety and depressive-like behaviours in rodents. The current study explored the role of gut microbiota on sociosexual behaviours in male and female mice. Broad-spectrum antibiotic (ABX) in drinking water was used to deplete the microbiota in either early development (embryonic day 16 to postnatal day 21) or adulthood (day 60 to 81) while the control group received normal drinking water. Compared to control males, early and adult ABX decreased male territorial aggression, while adulthood ABX also decreased sexual odor preferences among males. Next, we examined whether these decreases in sociosexual behaviour among males following ABX resulted from the depletion of the gut microbiota, rather than other non-specific effects of antibiotics, and/or whether these behavioural deficits could be due to decreases in androgens. To do so, cecal microbiota transplantation with same and opposite-sex control cecum contents or testosterone treatment was provided to adult antibiotic-treated males. Microbiota transplant with male cecum restored both olfactory preference and male aggression among adult ABX males. Female microbiota partially restored olfactory preference but not aggression among ABX males, while testosterone treatment was insufficient to rescue any of these behaviours. In adult ABX females, male microbiota transplant did not alter sociosexual behaviours, but testosterone treatment increased male-typical sexual behaviours. Together, the results suggest a sex-dependent role for the gut microbiome in the display of sex-typical behaviours in mice that is independent of androgen.

P1.5 VALPROIC ACID ALTERS SOCIOSEXUAL SIGNALLING IN MALE NAKED MOLE-RATS DURING THEIR PUBERTAL TRANSITION

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Adult neuroplasticity is an adaptive process by which animals can alter behavior in response to shifting environmental stimuli. The naked mole-rat (NMR) presents a fascinating opportunity to examine the interplay between epigenomics and social environment. NMRs exhibit the most extreme form of socially-mediated reproductive suppression (eusociality). They reside in large colonies where breeding is restricted to one breeding female and 1-3 male consorts; all other animals are pre-pubertal and socially subordinate. Most NMRs will never go through puberty unless removed from suppressive in-colony cues. Valproic acid (VPA) is a histone deacetylase inhibitor that alters social behavior in diverse species. Drugs of a similar class are also implicated in control of pubertal onset in rodents. To test whether DNA acetylation is involved in NMR reproductive/neural plasticity, we removed animals from their home colony for one week to trigger puberty and, simultaneously treated them with peripheral VPA injections or vehicle control. Animals were scored for sociosexual behaviors with unfamiliar opposite-sex conspecifics prior to/following colony separation and VPA manipulation. VPA-treated males received increased body/genital investigation from their stimulus females compared to saline-treated males; investigatory behaviors in females was not altered. Preliminary protein quantification of histone acetylation marks revealed increased H3K18-acetylation in VPA-treated males, but not females. Finally, VPA treated males had increased genital size compared to control males. Collectively, these data demonstrate altered sociosexual signalling in male NMRs treated with VPA during their pubertal transition, suggesting a key role for acetylation in at least some components of socially-induced plasticity observed in this species.

P1.6 OXYTOCIN MODULATION OF SOCIALLY DRIVEN ADULT NEUROGENESIS IN ZEBRAFISH

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Adult neurogenesis, the formation of new neurons from precursors cells, is regulated by both intrinsic and extrinsic factors. The social context is a key environmental factor that can modulate positively or negatively the formation of new neurons. Preliminary work from our lab shows that social isolation has a negative impact on cell proliferation in zebrafish, which can be rescued by the exposure to a social stimulus (a sex-mixed shoal). Moreover, in rats, adult neurogenesis can be modulated by the action of oxytocin receptors present in the hippocampus, an area belonging to the social decision-making network (SDMN). The SDMN is a network that regulates social behaviour and is influenced by the action of hormones and neuromodulators, like oxytocin. Here, we used a zebrafish mutant line for oxytocin receptor, to test if oxytocin mediates the effects of the social environment on adult neurogenesis in the brain nuclei belonging to the SDMN. The results indicate an effect of oxytocin on brain cell proliferation in Dm, Vc, PPa, PPp, Vd and the pretectum. Thus, this study can be considered a steppingstone to clarify the role of oxytocin on the social modulation of adult neurogenesis in vertebrates.

P1.7 USING VERY-HIGH FREQUENCY PROXIMITY-TRACKING COLLARS TO QUANTIFY MONOGAMOUS BEHAVIOR IN CAPTIVE COYOTES

Alexandra Turano[1], Julie K. Young[2], Sara M. Freeman[1]
[1]Utah State University, Logan, UT, USA, [2]USDA-WS-National Wildlife Research Center, Predator Research Facility, Millville, UT, USA

Social monogamy is a unique social system exhibited by only 3-5% of mammalian taxa; however, all wild canid species studied to date exhibit this mating system. Social monogamy extends beyond sexual fidelity between two unrelated adults; monogamous adults defend a shared territory, they share resources and parenting duties, they guard one another from opposite-sex conspecifics, and they show distress upon separation. Accordingly, the amount of time that two adults spend in close proximity may provide an index for the degree to which monogamous behaviors occur. Thus, we first validated the use of very-high frequency (VHF) proximity-tracking collars in quantifying proximity in a ubiquitous canid species, the coyote (Canis latrans). We fitted adult, coyote pair-mates, which were housed at a USDA predator research facility, with VHF collars. We determined that the collars accurately quantified pair-mate proximity, without the intrusion of a human observer and without coding extensive video files. These collars may now be deployed to non-intrusively investigate questions such as: 1) does season (breeding vs. nonbreeding) impact coyote pair-mate proximity and does that match predictions about the monogamous behaviors taking place (e.g., copulation and mate-guarding) and their hormonal status, 2) does pair-bond duration (newly paired vs. 1-2 years vs. 5 plus years) impact pair-mate proximity, and finally 3) do coyotes exhibit a significant partner preference, whereby they spend significantly more time near a pair-mate than near an opposite-sex stranger. This project will provide much needed comparative data to complement the existing behavioral and biological research in monogamous rodents and primates.

P1.8 CHRONIC INTRANASAL OXYTOCIN PROMOTES ADULT NEUROGENESIS AND SOCIAL APPROACH

Patrick Monari, Jessica Bymers, Zach Herro, Catherine Marler
University of Wisconsin-Madison

Social avoidance is a common symptom underlying several psychiatric illnesses and neurodevelopmental disorders, and intranasal oxytocin is of potential therapeutic value to mitigating social avoidance due to its ability to promote affiliative behaviors. Moreover, oxytocin is known to regulate adult neurogenesis, which in turn is likely involved in anxiety regulation and social behavior. To examine how chronic intranasal oxytocin influences adult neurogenesis and social approach, we administered intranasal oxytocin to unpaired male and female California mice for seven days, and subsequently assessed their approach to a simulated unfamiliar intruder using an aggressive vocal playback test (no-delay cohort). A separate cohort of males and females was also administered a seven-day series of intranasal infusions but received the approach test three weeks later (3-week delay cohort). In both cohorts we assessed the number of doublecortin positive cells in the dorsal and ventral hippocampus as well as the volume of the dentate gyrus. Intranasal oxytocin did not impact the amount of time males or females in the no-delay cohort spent near the playback stimulus and did not increase the doublecortin-positive cell density in either the dorsal or ventral hippocampus for either sex. However, intranasal oxytocin increased the amount of time both males and females in the 3-week delay cohort spent near the playback stimulus, and also increased the doublecortin-positive cell density in both the ventral hippocampus of both sexes. Our results suggest that in California mice chronic intranasal oxytocin treatment regulates social approach, but only after an extended delay. Additionally, this change in behavior is associated with a change in immature neuron density in the hippocampus, suggesting that adult neurogenesis may play a role in the oxytocin-mediated regulation of social approach.

P1.9 USING A PARTNER PREFERENCE TEST TO QUANTIFY MONOGAMOUS BEHAVIOR IN A CAPTIVE COYOTE COLONY

Sara M. Freeman[1], Alexandra Turano[1], Julie K. Young[2]
[1]Utah State University, Logan, UT, USA, [2]USDA-WS-National Wildlife Research Center, Predator Research Facility, Millville, UT, USA

Social monogamy is a unique mating system exhibited by only 3-5% of mammalian taxa; however, all canid species studied to date exhibit this social system. Despite the prevalence of social monogamy among canids, little is known about their ability to form selective social attachment relationships among non-kin. Thus, we aimed to quantify monogamous behavior in a highly ubiquitous canid species, the coyote (Canis latrans). We adapted a three-chambered partner preference test that was developed for quantifying preference for a pair-mate versus a stranger in monogamous rodents to test coyotes that are maintained as mated pairs at a captive research colony in Millville, Utah. We quantified whether monogamy-related behaviors, such as proximity, synchronous vocalizations, and visual seeking, were exhibited toward a pair-mate versus toward a stranger. Our results indicate that captive coyotes spent more time spatially and behaviorally interacting with their pair-mate than a stranger. This study provides much needed comparative work to complement the existing behavioral research in monogamous rodents and primates. These results also warrant the opportunistic examination of the coyote brain to better understand the biological underpinnings of these monogamy-related behaviors.

P1.10 THE NEUROGENOMIC CHANGES ASSOCIATED WITH THE TRANSITION FROM A NON-PARENTAL TO A PARENTAL STATE IN NON-REPRODUCTIVE JAPANESE QUAIL

Patricia C. Lopes
Chapman University

For the vast majority of bird species, parental care is essential for offspring survival. However, the neural molecular changes that are associated with the onset of young-directed care in birds (and in other non-placental species) are still mostly unknown. We took advantage of a domesticated bird species, the Japanese quail, for which parental behavior towards chicks can be readily induced through an overnight sensitization procedure. This procedure works for animals of both sexes and can induce care in virgin non-reproductive animals, permitting the study of the onset of care in the absence of pregnancy, copulation or other forms of hormonal priming. We used the variation in parental responses to study neural transcriptomic changes associated with the sensitization procedure itself and with the outcome of the procedure (i.e., presence of parental behaviors). Out of the brain regions studied, we found that most differences in gene expression were located in the hypothalamus. Two genes identified are of particular interest, as no role in avian parental care was known for those genes. One is neurotensin, previously only demonstrated to be causally associated with maternal care in mammals. The other one is urocortin 3, causally demonstrated to affect young-directed neglect and aggression in mammals. Our work opens new avenues of research into understanding the neural basis of parental care in non-placental species.

P1.11 BIASED AGONIST OF OXYTOCIN RECEPTOR IN THE BED NUCLEUS OF STRIA TERMINALIS FACILITATES SOCIAL ANXIETY-LIKE BEHAVIORS

Pei X. Luo, Lisette Y. Torres, Roberto A. Rios, Christine K. Xu, Vanessa A. Minie, Amy M. Tran, Brian C. Trainor
Department of Psychology, University of California, Davis

Oxytocin is a neuropeptide that can produce anxiolytic and prosocial effects. However, emerging evidence shows that under some condition oxytocin can instead induce anxiety-related behaviors. These diverse effects of oxytocin appear to be mediated by circuit-specific actions. Recent data show that activation of oxytocin receptors (OTR) in the bed nucleus of stria terminalis (BNST) facilitates social anxiety-like behaviors. As a member of the G-protein coupled receptor family, oxytocin receptors can induce distinct downstream pathways by coupling to different G-protein isoforms. In this study, we show that infusion of Carbetocin, a biased OTR-Gq agonist, in the BNST reduced social approach in both male and female California mice. In both males and females, Carbetocin also increased social vigilance, a behavior in which individuals orient towards an unfamiliar individual while simultaneously avoiding it. The results suggest that the anxiogenic effects of OTR in the BNST are mediated by Gq-coupled signaling.

P1.12 ORGANIZATIONAL EFFECTS OF PUBERTAL TESTOSTERONE DRIVE SEX DIFFERENCES IN SOCIAL ANXIETY BEHAVIOR IN CALIFORNIA MICE

Emily C. Wright, Hannah I. Culkin, Shwetha Sekar, Brian C. Trainor
UC Davis

About 20% of US adults will be diagnosed with an anxiety disorder in their lifetime. Women in particular face higher risks and are 2 times more likely to be diagnosed with an anxiety disorder then men. Interestingly, this sex difference does not extend to childhood anxiety which only emerges at puberty. Work in rodents has also found larger social anxiety response in adult females vs. males. However, adult castration does not eliminate this sex difference indicating that any hormonal effects across puberty may be organizational instead of activational. Here I present original, unpublished data on the origin of major sex differences in social anxiety behavior in California mice (Peromyscus californicus). Male and female California mice exhibit aggression toward conspecifics, allowing for a social defeat model in both sexes. Juvenile California mice do not show sex differences in social anxiety behavior, and it is only after exposure to pubertal testosterone that males exhibit species-characteristic lower levels of anxiety behavior. This mirrors trends seen in humans where there are no sex differences in rates of childhood anxiety but higher rates of diagnosed anxiety disorders in adolescent and adult women. Dihydrotestosterone manipulations indicate activation of androgen receptors to be pathway through which this change occurs. Oxytocin receptor antagonist manipulation in juveniles shows that oxytocin plays an important role in prepubertal social anxiety behavior, matching results from adult California mice. I also present original data characterizing pubertal development in California mice, which has a later onset and protracted course than comparable rodents.

P1.13 CHRONIC PHASE ADVANCE IN MICE INDUCES DEPRESSIVE-LIKE RESPONSES AND SUPPRESSES NEUROIMMUNE ACTIVATION POTENTIALLY VIA REGULATION OF CORTICOSTERONE

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Shifted working and sleeping schedules during the COVID-19 pandemic likely impact our circadian systems. At the molecular level, clock genes form feedback inhibition loops that control 24 h oscillations throughout the body. Importantly, core clock genes also regulate the brain resident immune cell, microglia, suggesting circadian regulation of neuroimmune function. To assess whether circadian-disruption induces neuroimmune and associated behavioral changes, we mimicked chronic jetlag with a chronic phase advance (CPA) model. 32 adult male C57BL/6J mice underwent 6hr light phase advance shifts every 3 light/dark cycles (CPA) 14 times or were maintained in standard light/dark cycles (control). CPA mice showed higher behavioral despair but not anhedonia in forced swim and sucrose preferences tests, respectively. Changes in behavior were accompanied by desynchronization of hippocampal circadian genes in CPA mice. Further, CPA suppressed expression of brain-derived neurotrophic factor (BDNF) and proinflammatory cytokine interleukin-1 beta in the hippocampus. Plasma corticosterone concentrations were elevated by CPA, suggesting that CPA may suppress neuroimmune pathways via glucocorticoids. These results demonstrate that chronic circadian disruption alters mood and neuroimmune function, which may have implications for shift working populations such as frontline health workers.

P1.14 THE EFFECTS OF HORMONE CONTRACEPTIVES AND MENSTRUATION ON OBJECT MEMORY AND SPATIAL ABILITY IN YOUNG WOMEN

Lauren Harburger, Christina Thrasher, Lily Otto
Purchase College

This study investigated the effects of hormone contraceptives and menstruation on cognitive performance in young women. The object array task assessed object memory and a mental rotations test assessed spatial ability in women taking hormone contraceptives and naturally cycling women. Subjects first completed an object array task where they were shown a series of multiple objects on an array and then asked to mark objects that had moved locations from the original array to test object location memory. Next, women were given a 24 question mental rotations task to assess spatial ability. Lastly, women completed the final object array task where they were asked to identify objects that were new to the array to test memory for object identity. Results demonstrated that women taking hormone contraceptives were significantly better at identifying novel objects on an object array than naturally cycling women. However, there were no significant differences in spatial ability performance on the mental rotations test or object location memory on the object array task in women taking hormone contraceptives and natural cycling women. There were also no significant differences on either task between naturally cycling women who were menstruating and those who were not menstruating during testing. The results of this study suggest that women taking hormone contraceptives outperformed naturally cycling women in recalling the identities of objects. The findings from this study help to further demonstrate the relationship between ovarian hormones and cognitive performance, as well as add to the understanding of how hormone contraceptives affect cognition.

P1.15 MECHANISMS OF MATERNAL HIGH-FAT DIET-INDUCED BRAIN AND BEHAVIOR CHANGES

Alexis M Ceasrine, Ben A Devlin, Young Chan Jo, Carolyn Huynh, Bailey Patrick, Susan Murphy, Staci Bilbo
Duke University

Over 50% of women in the United States are overweight when they become pregnant. Maternal high-fat diet (mHFD) creates an environment of chronic inflammation and is associated with detrimental outcomes for offspring, including increased susceptibility to psychiatric disorders. Despite these observations, many studies are correlative and do not propose a mechanism through which mHFD contributes to offspring psychiatric disorder development. The placenta is a critical interface between maternal environment and the developing fetal brain, and is poised to translate maternal insults into offspring neural outcomes. Further, the placenta is the primary source of fetal forebrain serotonin, and decreased serotonin signaling is correlated with increased vulnerability to stress in rodents. Serotonin levels are decreased in the context of inflammation; thus, we hypothesize mHFD-induced inflammation reduces prenatal serotonin levels, altering the development of the central serotonin system and causing anxiety-/depressive-like behaviors in mice.
We see that mHFD increases inflammation in offspring placenta and fetal brain, but results in decreased serotonin in placenta and brain in males only. Moreover, mHFD increases anxiety/depressive-like behaviors in male offspring only. To investigate whether high maternal weight has sex-specific effects on human serotonin system development, we assessed serotonin levels in fetal brain tissue in conjunction with maternal triglyceride levels as a proxy for maternal weight. Serotonin levels were decreased in male human fetal brain tissue in samples where maternal triglyceride levels were elevated (high maternal weight). Together, our data suggest that mHFD and resulting high maternal weight negatively impact the development of the central serotonin system in males, contributing to sex-biased psychiatric disorder susceptibility.

P1.16 PRENATAL ALLERGIC INFLAMMATION PROGRAMS THE DEVELOPMENTAL TRAJECTORY OF DENDRITIC SPINE PATTERNING AND OXYTOCIN FIBER DENSITY IN BRAIN REGIONS ASSOCIATED WITH JUVENILE SOCIAL PLAY

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Social behavior is an adaptive, conserved behavior that ensures reproductive success. Juvenile social play is important for social, cognitive, and neural development, and males engage in rough and tumble play more than females. We have shown that prenatal allergic inflammation impaired juvenile social play and reduced neonatal microglia colonization in brain regions relevant to play. Hypothesis: Given that microglia regulate developmental synaptic patterning, dendritic spine density may be altered in offspring exposed to prenatal allergic inflammation. Additionally, as oxytocin and vasopressin signaling in the lateral septum (LS) contribute to social behavior, prenatal inflammation may alter nonapeptide fiber density in the juvenile LS. Methods: Female rats were sensitized to ovalbumin, bred, and allergically challenged on gestational day 15. For dendritic spine density analyses, brain tissue was collected from offspring on postnatal days (P)5, 15, 30, and ~80-90 and processed for Golgi-Cox staining. For nonapeptide analysis, brains were collected on P28 and processed for immunohistochemistry. Results: Prenatal allergic inflammation persistently reduced spine density in the prefrontal cortex and amygdala. Allergic inflammation-induced reductions in spines were also found in the female striatum at P15 and nucleus accumbens at P30. In the P30 septum, allergic inflammation reduced spine density in females but increased it in males. Allergic inflammation also decreased oxytocin fiber density in the male, but not female, LS. Ongoing analyses are focused on vasopressin fiber density in LS and nonapeptide fibers in other brain regions. Conclusions: Early life perturbations may shape sex-specific social behavior via underlying effects on microglia-mediated neural circuit development.

P1.17 PHOTOPERIODIC CONTROL OF SINGING BEHAVIOR AND REPRODUCTIVE PHYSIOLOGY IN MALE FIFE FANCY CANARIES

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Temperate-zone birds often display marked seasonal changes in reproductive behaviors and in the underlying hormonal and neural mechanisms. These changes have been extensively studied in canaries (Serinus canaria) and there is emerging evidence of variation among strains in physiological responses to seasonal cues. Fife fancy male canaries were previously shown to change their reproductive physiology in response to variations in day length but it remained unclear whether they display absolute refractoriness, as Border canaries do, or only display relative refractoriness or simply track day length to control gonadal activity, singing behavior and the associated neural plasticity. Male birds maintained on 8L:16D (SD) for 6 months that had become reproductively competent (high song output and large testes) were divided into two groups: control birds remained on SD and experimental birds were switched to long days (16L:8D). During the following 11 weeks, singing behavior (recorded and quantitatively analyzed for 3X2 hours every

week) and gonadal size (repeatedly measured by CT X-ray scans) remained similar for birds in both groups except for trill numbers that increased in the experimental group. Prolonged exposure to SD had thus induced a nearly full activation of reproductive physiology and behavior. Day length was then decreased back to 8L:16D for experimental birds which immediately induced a cessation of song, a decrease in testes size and a decrease in the volume of song control nuclei (Area X, HVC, RA). These data demonstrate that Fife fancy canaries sharply respond to changes in photoperiod but only display relative photorefractoriness.

P1.18 DAILY LEUPROLIDE TREATMENT DURING PERIADOLESCENCE DELAYS PUBERTY AND ALTERS SEXUAL BEHAVIOR IN FEMALE RATS

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The present study was designed to examine the long-term effects of suppressing puberty with the GnRH agonist, leuprolide acetate, in female rats. Few studies have examined the effects of daily leuprolide exposure when given prior to puberty and continuing until early adulthood in animal subjects. Our previous work found that leuprolide administration for 25 days (postnatal day (PD) 25-50) delayed puberty and disrupted the development of copulatory behavior and sexual motivation in male rats. However, it was unclear what effect leuprolide would have in female subjects. Therefore, we injected female Long-Evans rats with either leuprolide acetate (Experiment 1: 25 µg/kg; Experiment 2: 50 µg/kg) or 0.9% sterile saline daily for 25 days, starting on PD 25 and ending on PD 50. Vaginal opening was observed daily starting on PD 30 for signs of pubertal onset and first estrous cycle. Approximately one month later, sexual motivation was measured for the first time on the afternoon of proestrus using the partner preference paradigm, with and without physical contact. In Experiment 1, we found that the low dose of leuprolide did not delay puberty in female rats. However, sexual motivation was affected. Female rats who had been exposed to leuprolide during the periadolescent period, spent less time with the male partner, made fewer visits to the male, and took longer to return after receiving an ejaculation than the vehicle controls. In experiment 2, we found that doubling the dose of leuprolide significantly delayed pubertal onset. However, the behavioral tests have not been conducted yet. Together with our findings in male rats, these results add to understanding of the developmental effects of chemically suppressing puberty.

P1.19 PROTECTIVE EFFECTS OF ESTROGENS DURING DORSAL HIPPOCAMPAL D2-TYPE DOPAMINE RECEPTOR MEDIATED SOCIAL LEARNING IN MICE

Noah Bass, Maura Hickey, Sarah Van Den Berghe, Elena Choleris
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Social learning is a critical form of learning that may be defined as learning that occurs via social interaction and/or social observation (Galef, 1998). Regulatory mechanisms of social learning are poorly understood, but in animals may be tested using the social transmission of food preference (STFP). During the STFP, social learning was blocked by dorsal hippocampus (HPC) infusions of the

D2-type dopamine receptor antagonist raclopride in female but not male mice suggesting that hormonal mechanisms may be at play (Matta et al., 2017). Later studies found that intra-HPC raclopride blocked social learning in gonadectomized males and females, but not gonadally intact mice, further suggesting an interaction with sex hormones. Here, we aim to elucidate the specific hormone(s) that may be interacting with dorsal HPC D2-type dopamine receptors during social learning in mice. In the male brain, androgens may be aromatized to estrogens. Starting with estradiol benzoate (EB), we implanted subcutaneous slow releasing silastic capsules of EB or sesame oil in castrated (CAS) "observer" (OBS) mice in study 1 and in ovariectomized (OVX) OBSs in study 2. OBSs received dorsal HPC infusions of raclopride or saline 10-minutes prior to a 30-minute social interaction with a recently fed, same-sex, familiar DEM, followed by an 8-hour OBS choice test. If social learning occurs, OBSs prefer the novel flavored food diet previously consumed by their DEMs. Preliminary findings revealed that long term EB treatment protects against the impairing effects of intra-HPC raclopride on social learning in CAS and OVX mice.

P1.20 SEX DIFFERENCES IN GLUCOCORTICOID RECEPTOR-REGULATED GENE PROGRAMS

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Dysregulation of stress response is associated with several mental health conditions including major depression, schizophrenia, and bipolar disorder. Moreover, both human and pre-clinical studies have demonstrated that there are sex differences in stress responses that may underlie susceptibility to developing such conditions. The hypothalamic-pituitary-adrenal (HPA) axis is more active in females, resulting in a greater release of CORT (corticosterone in rodents, cortisol in humans) from the adrenal glands into circulation. CORT binds glucocorticoid receptor (GR) throughout the body, which then activates or represses gene expression to facilitate behavioral adaptation and homeostasis. Although there have been significant advances in understanding the hypothalamic circuitry that mediates the HPA axis, how differential activation of GR-regulated genes in the brain impacts the two sexes remains an open question. Therefore, the goal of this project is to define the neural targets of GR in both sexes and to explore how sex steroids, and particularly testosterone, impact GR targets. Using the state-of-the-art molecular genomics techniques established in the lab, we profiled GR targets in brain regions of GR expression after acute stress in both sexes. Combining this data with RNAseq in these brain regions in acutely stressed and control mice of both sexes, we define a sex-specific GR-regulated gene program responsive to stress. These studies will provide a molecular mechanism for sex differences in stress response, and may show a protective role of testosterone signaling in stress.

P1.21 ESTRADIOL MITIGATION OF LIGHT-INDUCED ANXIETY BEHAVIOR IN FEMALE RATS REQUIRES MGLU5

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Anxiety-related behaviors are influenced by steroid hormones such as 17β-estradiol and environmental stimuli including acute stressors. For example, rats exhibit increased anxiety-related behaviors in the presence of light. In females, estradiol potentially mitigates these anxiety-related behaviors. Experiments across behavioral paradigms and brain regions indicate that estradiol action can be mediated via activation of metabotropic glutamate receptors, including Group I

subtype five (mGlu5). Here we test if mGlu5 is necessary for estradiol mitigation of light-induced acute anxiety and locomotor behaviors.

P1.22 DEVELOPMENTAL EXPOSURE TO THE SYNTHETIC PROGESTIN, 17A-HYDROXYPROGESTERONE, ALTERS THE ONTOGENY OF DOPAMINERGIC INNERVATION OF MEDIAL PREFRONTAL CORTEX IN MALES AND FEMALES

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Pregnant women with a history of preterm delivery are often prescribed the synthetic progestin, 17-α-hydroxyprogesterone caproate (17-OHPC), despite little evidence of efficacy. Treatment with 17-OHPC coincides with the development of the fetal mesocortical dopamine pathway, a neural pathway regulating complex cognitive behaviors. In rodent models, the developing mesocortical dopamine pathway is sensitive to progestins, as progesterone receptors are transiently expressed in the ventral tegmental area and medial prefrontal cortex (mPFC) during postnatal life. Neonatal exposure to 17-OHPC produces deficits in cognitive flexibility, decision-making, and attention in adulthood. These behavioral deficits are likely related to the aberrant dopaminergic innervation of the mPFC, which has been observed separately in both the neonatal and preadolescent periods. Here, we tested the hypothesis that 17-OHPC exposure during development alters the ontogeny of dopaminergic innervation of the mPFC in males and females at postnatal day 7 (P7), P14, P21, and P40. Indeed, 17-OHPC treatment abolished a sex difference in dopaminergic fiber distribution at P7, and significantly increased fiber density and distribution at P21 in the prelimbic (PL) mPFC. Further analysis revealed that 17-OHPC treated animals also have more synaptophysin-immunoreactive boutons in the PL mPFC than controls at P7 and P21. Together, these findings strongly suggest that 17-OHPC treatment changes functional connectivity over the course of development, resulting in the behavioral deficits previously observed in adulthood. These findings may inform potential risks associated with 17-OHPC treatment in humans.

P1.23 ACTIVATIONAL EFFECTS OF ANDROGENS AND ESTROGENS CAN NOT REVERSE SEX DIFFERENCES IN SONG BEHAVIOR AND THE SONG CONTROL NUCLEI IN ADULT MALE AND FEMALE CANARIES.

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Treatments with testosterone (T) do not activate singing behavior nor promote growth of song control nuclei to the same extend in male and female canaries (Serinus canaria). Because T acts in part via aromatization into an estrogen and brain aromatase activity is lower in females than in males, we hypothesized that this enzymatic difference explains the differential response to T in the two sexes. To test this idea, three groups of castrated males and 3 groups of photoregressed females received either 2 empty 10 mm Silastic implants or one empty implant and one implant filled with T or one implant filled with T plus one with estradiol (E2). Songs were recorded and analyzed for 3 hours each week for 6 weeks before brains were collected and song control nuclei volumes were measured in Nissl-stained sections. We confirmed that multiple measures of song were induced more efficiently by T in males than in females. Co-administration of E2 did not

improve these measures and even inhibited some measures such as song rate and song duration. Similarly, the volume of three main song control nuclei (HVC, RA, and Area X) was increased by the two steroid treatments but they remained significantly smaller in females than in males irrespective of the endocrine condition. The lower response of females to T is thus not caused by a lower aromatization of the steroid; sex differences in canaries are probably organized either by early steroid action or by sex-specific gene regulation directly in the brain.

P1.24 THE IMPACT OF ESTROUS CYCLE AND SEX ON DENDRITIC SPINE SIZE AND SPINE DENSITY IN RAT NUCLEUS ACCUMBENS SHELL, CORE, AND CAUDATE-PUTAMEN

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An important natural factor that modulates neuron properties are sex-specific hormone fluctuations including the human menstrual cycle and rat estrous cycle in adult females. Our laboratory has detected estrous cycle-dependent changes in medium spiny neuron (MSN) electrophysiological properties in rat striatal regions: the nucleus accumbens core, shell, and caudate-putamen. In select striatal regions, these changing properties encompass those related to glutamatergic synapse function, such as miniature excitatory post-synaptic current (mEPSC) frequency, amplitude, and decay. Other brain regions exhibit similar estrous cycle-associated changes in mEPSC properties concomitant with changes in dendritic spine attributes. Dendritic spines are a key site for glutamatergic input. Thus, we hypothesized that rat striatal MSN dendritic spine attributes would differ by estrous cycle stage and sex. To test this hypothesis, brains from adult male rats and female rats in diestrus, proestrus, and estrus phases were processed using the Rapid Golgi Stain Kit (FD Neurotechnologies). Dendritic spines on MSNs in the nucleus accumbens core, shell, and caudate-putamen were analyzed. Our tentative results indicate dendritic spine length/width ratio and spine density did not differ across estrous cycle phase or sex. These preliminary results suggest global MSN dendritic spine size and spine density may not be concomitant with nor contribute to sex- or estrous cycle-associated changes in neuron electrophysiological properties in the rat striatum while inspiring further investigation into other dendritic spine attributes and glutamatergic synapse properties.

P1.25 HIPPOCAMPAL CA2 DEVELOPMENT UNDER THE INFLUENCE OF PRENATAL SPIRONOLACTONE

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Mineralocorticoid receptors (MRs; Nr3c2) are highly expressed in hippocampal area CA2, where they regulate CA2 gene expression and social memory. In addition, mutations in Nr3c2 can cause a syndromic form of autism in humans. Although our previous studies using conditional MR knockout (KO) mice provided valuable information relevant to genetic disruption of MRs, pharmacological blockade of MRs could provide a clinically and translationally relevant model of stress-related

disorders, given that MRs bind corticosterone/cortisol. Thus, we set out to test our hypothesis that chronic, prenatal exposure to the MR antagonist spironolactone would disrupt CA2 gene expression and social behavior similar to what we observed using conditional MR KO mice. To do this, we implanted subcutaneous 21-day release pellets in two dam groups—Vehicle and Spironolactone—at approximately gestational day 12 (+/- 3 days), alongside a no-surgery Control dam group. Using immunofluorescence, we examined CA2 marker development in the resulting litters at postnatal days (PNDs) 12, 14, and 21. A separate subset of pups was allowed to grow until adulthood (PND 60 or PND 170) to investigate the impact of prenatal MR blockade on behavior. We tested mice in the open field, novel object exposure, novel social interaction, and social discrimination. In summary, we find that prenatal MR antagonism with spironolactone does not cause overt effects on the development of CA2, however, does display some disruptions comparable to that of the embryonic MR KO model in the measurement of anxiety and novel object exposure, but with no disruptions seen in social memory.

P1.26 COMPOSITIONAL VARIATION IN EARLY LIFE PARENTING STRUCTURES ALTERS OXYTOCIN AND VASOPRESSIN 1A RECEPTOR DEVELOPMENT IN PRAIRIE VOLES (MICROTUS OCHROGASTER)

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In the socially monogamous prairie vole (Microtus ochrogaster), the experience of paternal absence during development inhibits partner preference formation in adulthood. This effect has generally been demonstrated by comparing the development of offspring reared under biparental care with those reared by a single mother. However, studies employing this design conflate two significant modifications: removal of paternal qualities and the general reduction of parental care. Employing alloparents as substitutes for fathers, we previously demonstrated that paternal absence affects pair bond formation in female offspring via reduced quantity of care; but it affects pair bond formation in males by means of a missing paternal quality (or qualities). Here, we present evidence that paternal absence (with and without alloparental substitution) alters the ontogeny of neural oxytocin receptor (OXTR) and vasopressin 1a receptor (AVPR1a) distribution in male and female prairie voles. Compared to biparentally reared controls (BPC), male offspring reared in mother only (MON) and maternal-plus-alloparental (MPA) conditions show lower densities of OXTR in the central amygdala; and MPA males show lower densities of OXTR in the caudate putamen and nucleus accumbens. MON and MPA females show greater densities of AVPR1a in the medial amygdala than BPC; and MPA females show greater densities of AVPR1a in the ventromedial nucleus of the hypothalamus. Demonstrated with corticosterone concentrations, MON and MPA offspring are not more susceptible to social isolation. We conclude that paternal absence, while likely not a salient early life stressor, has neuroendocrine consequences for offspring, some of which may affect partner preference formation.

P1.27 ON THE RELATIONSHIP OF SEXUAL EXPERIENCE AND PROGESTERONE IN PACED MATING BEHAVIOR OF FEMALE RATS

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Sexually experienced, ovariectomized, female rats treated with 10μg estradiol benzoate (EB) and 1mg progesterone (P) return to the male more quickly after intromissions and spend more time with the male during paced mating tests compared to sexually naïve females with the same hormone priming. However, rats that became sexually experienced under EB+P that were then injected with 2μg EB for 6 days (EB Alone) to induce receptivity displayed longer latencies to return to the male after mounts, intromissions, and ejaculations and spent less time with the male. The present experiment tested whether paced mating behavior changes over multiple mating tests in rats primed only with EB. Ovariectomized, sexually naïve, female Long-Evans rats were assigned to receive one of two hormone regimens: 1) EB+P, or 2) EB Alone prior to four paced mating tests, each lasting 15 intromissions. We hypothesized that paced mating experience functions independently of P, such that rats in both hormone groups would show shorter latencies to return to the male after intromission and spend more time with the male when sexually experienced relative to when they were sexually naïve. Further, we hypothesized that on the fourth test, paced mating behavior would be comparable between EB+P- and EB Alone-treated rats. Results augment our understanding of the role of hormones and sexual experience in mating behavior.

P1.28 THE EFFECT OF EARLY LIFE STRESS ON CHROMATIN ARCHITECTURE IN EXPERIENCE-SENSITIVE CELLS OF THE NUCLEUS ACCUMBENS

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Early life stress (ELS) includes any form of negative childhood experience or trauma (such as maternal separation and/or physical, sexual, and/or emotional abuse). As such, ELS has been found to be one of the strongest predictors for development of mood and/or anxiety disorders in adulthood. While evidence suggests epigenetics may be involved in driving this correlation between ELS and disorder risk, the specific mechanisms contributing to this process are still poorly understood. The work aims to understand how ELS changes the dynamic epigenetic mechanism of chromatin architecture in the nucleus accumbens (NAc), and how these changes mediate increased risk for altered behavior in adulthood. This work will contribute to the growing field of discovering underlying mechanisms mediating the priming of susceptibility to altered behavioral phenotypes in individuals with a history of ELS.

P1.29 EFFECTS OF SEX EXPERIENCE ON VAGINAL EPITHELIAL THICKNESS

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Female sexual dysfunction (FSD) affects up to 65% of women and available treatments are mostly ineffective with substantial negative side effects. Female rats have similar vaginal morphology and sex hormone release to humans, making them a useful model organism for understanding genital morphology and sensitivity. Prior work has shown that sexually experienced female rats return more quickly to male rats after intromissions than sexually naïve rats. This may indicate a decreased sensitivity to stimulations in sexually experienced female rats compared to sexually naïve rats, as female rats return to the male more quickly following less intense stimulations (mount < intromission < ejaculation). We measured vaginal epithelial thickness in naïve and experienced females administered estradiol benzoate (EB) and progesterone (P) or oil vehicle. Our

study tests the hypothesis that the thickness of the vaginal epithelium is a mediating factor in paced mating differences observed between naïve and sexually experienced rats. We aim to evaluate whether sensitivity-related changes in paced mating behavior can be linked with differences in vaginal epithelial thickness. Our results will shed light on the contribution of vaginal epithelial thickness to sensitivity and pain in FSD.

P1.30 PACED MATING BEHAVIOR IS INFLUENCED BY THE DURATION OF DELAY BETWEEN MATING BOUTS.

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Paced mating behavior varies under different test parameters, but the specific factors affecting female rat response to mating stimulation is unclear. For example, we have shown that female Long-Evans rats display longer contact-return latencies to ejaculation when paced mating tests end after 30 minutes elapse relative to ending after receipt of 15 intromissions. Previous studies from our lab show that contact-return to ejaculation progressively increases under a single-male 30-minute test-end criterion paradigm, whereas contact-return to ejaculation only increases during individual, but not across successive, 15-intromission tests. A number of factors differ between 30-minute and 15-intromission tests that could explain the longer contact-return to ejaculation in the 30-minute tests. Therefore, the present study systematically investigated the role of mating with one or multiple males (Experiment 1), a long or short delay between receipt of ejaculation and initiation of next mating bout (Experiment 2), and ejaculation intensity (Experiment 3) on the display of paced mating behavior. Only manipulating the delay between ejaculation and more mating led to differences in paced mating behavior. Female rats in the long delay condition exhibited shorter exit latency after intromission, longer contact-return latency to ejaculation, and longer withdrawal duration after ejaculation. The present findings illustrate that providing access to another rested, sexually vigorous male rat after receipt of an ejaculation enables the female to regulate re-initiation of mating. Affording the female rat control of the interval between an ejaculation and a subsequent intromission is critical for accurate neuroethological investigation of female sexual behavior in the laboratory.

P1.31 ENVIRONMENTAL ENRICHMENT PROTECTS AGAINST HEIGHTENED HPA-ACTIVATION IN AN ANIMAL MODEL OF MATERNAL IMMUNE ACTIVATION

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Maternal immune activation (MIA) during pregnancy is associated with neurodevelopmental disorders and long-term gene dysregulation in offspring. Animal models of MIA offer mechanistic ways to explore these changes and opportunities to mitigate them. Environmental enrichment (EE) has demonstrated benefit in a lipopolysaccharide (LPS)-induced rat model of MIA. Using a polyinosinic-polycytidylic acid (poly (I:C)) MIA model of schizophrenia, the study explored whether the benefits of a supportive environment could generalize across immunogens and species. In the current study female C57BL/6J mice were randomized into standard or EE housing and bred in these conditions. On gestational day 15, mice were challenged with either 20 mg/kg (i.p) of the viral mimetic poly (I:C) or pyrogen-free saline. After birth, quality of maternal nesting behavior was evaluated. Male and female adult offspring (n = 8-14) were assessed on measures of social

behavior and neural markers of stress. We show that poly (I:C) challenge led to disrupted maternal care in the form of poorer nest quality. In offspring, poly (I:C) induced MIA resulted in repetitive behavior, reduced social interest, and sex-specific mRNA expression of neural stress markers. MIA males had delayed recovery of plasma corticosterone in response to a novel social encounter. Enrichment housing protected against these MIA-induced effects. These data demonstrate that the benefits of EE on social behavior and HPA regulation can generalize across immunogens and species. Our findings provide further evidence for the viability of EE interventions in maternal and pediatric settings.

P1.32 MATERNAL POSTPARTUM CORTICOSTERONE AND FLUOXETINE TREATMENT HAVE LONG-TERM EFFECTS ON ADULT HIPPOCAMPAL NEUROGENESIS AND NEUROINFLAMMATION IN OFFSPRING

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Perinatal depression (PND) affects 15% of mothers and selective serotonin reuptake inhibitors (SSRIs) are the first-line treatment for PND. However, SSRI efficacy for mood alleviation in mothers and safety to SSRI-exposed infants have been questioned. We previously reported that maternal SSRI exposure in the postpartum period increased hippocampal IL-1b levels, which may be tied to the limited efficacy of SSRIs in the late postpartum period. However, it is not yet known whether maternal postpartum SSRIs affect the neuroinflammatory profile of adult offspring. We hypothesize that maternal corticosterone (CORT) treatment used to induce depressive-like endophenotypes in dams, and postpartum SSRI treatment will alter offspring puberty development, neurogenesis, and neuroinflammation in adulthood. CORT (40mg/kg, s.c) was given to dams in the postpartum to model de novo postpartum depression, with or without the SSRI, fluoxetine (FLX; 10mg/kg, s.c.) for 21 days. We found maternal FLX treatment decreased hippocampal IFN-□, IL-10, and IL-13 in adult offspring regardless of sex. Using a principal component analysis, we found maternal FLX treatment decreased the overall neuroinflammatory profile in adult offspring regardless of sex. Maternal FLX treatment reduced adult hippocampal neurogenesis in the ventral dentate gyrus in both sexes. Moreover, maternal CORT treatment delayed puberty development in female offspring only. These data underscore that postpartum depression and SSRI treatment in dams can have long-term effects on offspring, some of which are dependent on sex.

P1.33 ULTRA-SENSITIVE QUANTIFICATION OF MULTIPLE ESTROGENS IN THE BLOOD AND BRAIN OF SONGBIRDS

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Estrogens affect many aspects of brain function, including neuroprotection, cognition, and social behavior. Estrogens are synthesized in the ovaries, as well as in the brain. Importantly, estrogens are active in the brain at low levels. Current methods lack the necessary sensitivity and/or specificity to measure endogenous estrogens in small plasma and brain samples. Further, most assays focus on 17β-estradiol and disregard other estrogens. Here, we developed a method to measure several estrogens simultaneously, with high specificity and sensitivity. We derivatized estrogens using 1,2-dimethylimidazole-5-sulfonyl-chloride (DMIS). We used liquid chromatography tandem mass spectrometry to examine a panel of eight estrogens: 17β-estradiol, 17α-estradiol, estriol, estrone, 2-hydroxyestradiol, 4-hydroxyestradiol, 2-methoxyestradiol, and 4-methoxyestradiol. Our method can detect as little as 0.02 pg of 17β-estradiol per sample (approx. 50X better than most assays). We can quantify 17β-estradiol and estrone in song sparrow plasma (20 µl) and microdissected brain (1-1.5 mg). In breeding male song sparrows, 17β-estradiol and estrone levels varied across brain regions and were highest in the caudomedial nidopallium, which has high aromatase expression. Circulating levels of estrogens were extremely low and did not correlate with brain levels. Future work will examine the effects of an aggressive encounter and season. This assay will also be useful in studies of other small animals (e.g., rats and mice), as well as studies of humans that include saliva samples or subjects with very low estrogen levels (e.g., post-menopausal women, men, and children).

P1.34 SEX-SPECIFIC EFFECTS OF DEVELOPMENT ON SOCIAL RECOGNITION IN RATS

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The ability to recognize previously encountered conspecifics is crucial for social interaction. This social recognition ability is well characterized in adults of both sexes but remains unexplored in juveniles. We first found that, unlike juvenile and adult male rats or adult females, juvenile female rats do not display a difference in investigation directed toward a novel vs. familiar stimulus rat. We then determined that social recognition is established by the time of adolescence in female rats. Based on these findings, we hypothesized that social recognition is dependent on the initiation of ovarian hormone release during puberty. To test this, we ovariectomized females prior to puberty and found that prepubertal ovariectomy prevented the development of social recognition ability in adulthood. Interestingly, administration of estradiol benzoate, 48 hours prior to testing, to juvenile females or prepubertally ovariectomized adult females did not restore social recognition, suggesting that ovarian hormones organize the neural circuitry regulating this behavior during adolescence. This may include the bed nucleus of the stria terminalis (BNST), a sexually differentiated brain area implicated in adult social recognition. Indeed, the BNST shows social stimulus-induced activation in juvenile females, but not in males. These findings provide the first evidence of a development-specific sex difference in social recognition ability. Ongoing work seeks to tease apart the role of the BNST in regulating ovarian hormone dependent differences in adult female social recognition, as well as to determine the role of the BNST oxytocin receptor system in regulating sex differences in the development of social recognition.

P1.35 INCREASING CENTRAL SEROTONIN WITH 5-HTP DISRUPTS THE INHIBITION OF SOCIAL GAZE IN NON-HUMAN PRIMATES

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To competently navigate the world, individuals must flexibly balance distinct aspects of social gaze, orienting toward others and inhibiting orienting responses, depending on the context. These behaviors are often disrupted in patient populations treated with serotonergic drugs. However, the field lacks a clear understanding of how the serotonergic system mediates social orienting and inhibiting behaviors. Here, we tested how increasing central concentrations of serotonin with the direct precursor 5- Hydroxytryptophan (5-HTP) would modulate the ability of rhesus macaques to use eye movements to flexibly orient to, or inhibit orienting to, faces. Systemic administrations of 5-HTP effectively increased central serotonin levels and impaired flexible orientation and inhibition. Critically, 5-HTP selectively impaired the ability of monkeys to inhibit orienting to face images, whereas it similarly impaired orienting to face and control images. 5-HTP also caused monkeys to perseverate on their gaze responses, making them worse at flexibly switching between orientating and inhibiting behaviors. Furthermore, the effects of 5-HTP on performance correlated with a constriction of the pupil, an increased time to initiate trials, and an increased reaction time, suggesting that the disruptive effects of 5-HTP on social gaze behaviors are likely driven by a downregulation of arousal and motivational states. Taken together, these findings provide causal evidence for a modulatory relationship between 5-HTP and social gaze behaviors in non-human primates and offer translational insights for the role of the serotonergic system in social gaze.

P1.36 DIFFERENTIAL RESPONSES TOWARD AVERSIVE STIMULI AND DECREASED HPA AXIS RESPONSIVENESS IN NEONATAL HIPPOCAMPAL LESIONED MONKEYS.

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The hippocampus is important for long-term memory storage, but it also plays a key role in the regulation of the hypothalamic-pituitary-adrenal (HPA) axis and emotional behaviors. We have previously reported that neonatal hippocampal (Neo-Hibo) lesions result in increased anxious expression and blunted cortisol stress response. In this model, animals develop across their lifespan without, or with a severely degraded, hippocampus, which helps to answer questions about the effects of early damage, as well as the development and function of the hippocampus in general. Here we further probe their responses toward aversive stimuli and evaluate HPA axis dysfunction. Responses toward social, innate, and learned aversive stimuli and pituitary-adrenal function were investigated in 13 adult rhesus monkeys with and without neonatal hippocampal lesions (Neo-Hibo = 6 and controls = 7). Neo-Hibo monkeys responses varied depending on stimulus type, such that increased anxiety behaviors were detected toward social and learned, but decreased reactivity was found toward innate stimuli. In response to HPA axis stimulation, Neo-Hibo monkeys exhibited less cortisol response, potentially suggesting adrenal fatigue. Current findings suggest that the hippocampus plays a large role in regulating not only anxiety behaviors, but also the HPA-axis, a neurological system crucial for how we respond to the world around us. These data have important clinical significance considering that many developmental neuropsychiatric disorders exhibit altered hippocampal structure and function, emotional and HPA axis dysregulation.

P1.37 MEASUREMENT OF STEROID FATTY ACYL ESTERS IN SONGBIRD PLASMA WITH LC-MS/MS

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Steroid fatty acyl esters (FAEs) consist of a steroid molecule conjugated to a fatty acid. These steroid metabolites are abundant in circulation and can be converted to active unconjugated steroids. Their functions are unknown. Steroid-FAEs have long half-lives and are stored in lipid-rich tissues, and thus they may act as a long-term steroid reservoir. Dehydroepiandrosterone (DHEA) is an androgen precursor that can be conjugated to fatty acids. DHEA modulates aggression in several species, including songbirds, rodents and humans. DHEA-FAEs might be present in songbird blood and/or brain, in part, to regulate aggression. We (1) quantified multiple fatty acids in songbird plasma and (2) developed an indirect method to measure steroid-FAEs in blood and brain. First, preliminary work demonstrated high circulating levels of total (esterified and non-esterified) fatty acids, especially oleic, linoleic, and palmitic acids, in song sparrows. These 3 abundant fatty acids are likely candidates to be conjugated to steroids. Second, we developed a saponification technique to indirectly measure DHEA-FAEs using liquid chromatography-tandem mass spectrometry (LC-MS/MS). Saponification cleaves the bond between the steroid and the fatty acid; we then measure unconjugated steroids using LC-MS/MS. After saponification, recovery of unconjugated DHEA was 83-86% using DHEA-FAE reference standards in neat solution. We validated this method in song sparrow, chicken, and human serum, obtaining recoveries of 83-104%. Furthermore, we measured putative endogenous steroid-FAEs in human serum after saponification. This work will elucidate possible roles of steroid-FAEs in the regulation of steroid-dependent social behavior, such as aggression, and offer novel insights into steroid signaling.

P1.38 SOCIAL BOLDNESS CORRELATES WITH BRAIN GENE EXPRESSION IN MALE GREEN ANOLES

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Within populations, some individuals tend to exhibit a bold or shy social behavior phenotype relative to the mean. The neural underpinnings of these differing phenotypes – also described as syndromes, personalities, and coping styles – is an area of ongoing investigation. Although a social decision-making network has been described across vertebrate taxa, most studies examining activity within this network do so in relation to exhibited differences in behavioral expression. Our study instead focuses on constitutive gene expression in bold and shy individuals by isolating baseline gene expression profiles that influence social boldness predisposition, rather than those reflecting the results of social interaction and behavioral execution. We performed this study on male green anole lizards (Anolis carolinensis), an established model organism for behavioral research, which provides a crucial comparison group to investigations of birds and mammals. After identifying subjects as bold or shy through repeated reproductive and agonistic behavior testing, we used RNA sequencing to compare gene expression profiles between these groups within various forebrain, midbrain, and hindbrain regions. The ventromedial hypothalamus had the largest group

differences in gene expression, with bold males having increased expression of neuroendocrine and neurotransmitter receptor and calcium channel genes compared to shy males. Conversely, shy males express more integrin alpha-10 in the majority of examined regions. There were no significant group differences in physiology or hormone levels. Our results highlight the ventromedial hypothalamus as an important center of behavioral differences across individuals and provide novel candidates for investigations into the regulation of individual variation in social behavior phenotype.

P1.39 ACUTE INHIBITION OF DOPAMINE B-HYDROXYLASE ATTENUATES BEHAVIORAL RESPONSES TO PUPS IN ADULT VIRGIN CALIFORNIA MICE (PEROMYSCUS CALIFORNICUS)

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In biparental species, in which both parents care for their offspring, the neural and endocrine mediators of paternal behavior appear to overlap substantially with those underlying maternal behavior. Little is known, however, about the roles of classical neurotransmitters, such as norepinephrine (NE), in paternal care and whether they resemble those in maternal care. We tested the hypothesis that NE facilitates the initiation of nurturant behavior toward pups in virgin male and female California mice (Peromyscus californicus), a biparental rodent. Virtually all parents in this species are attracted to familiar and unfamiliar pups, while virgins either attack, avoid, or nurture pups, suggesting that the neurochemical control of pup-related behavior changes as mice transition into parenthood. We injected virgin males and females with nepicastat, a selective dopamine β-hydroxylase inhibitor that blocks NE synthesis (75 mg/kg, i.p.), or vehicle 2 hours before exposing them to a novel pup, estrous female (males only), or pup-sized novel object for 60 min. Nepicastat significantly reduced the number of males and females that approached the pup and that displayed parental behavior. In contrast, nepicastat did not alter virgins' interactions with an estrous female or a novel object, suggesting that nepicastat-induced inhibition of interactions with pups was not mediated by changes in generalized neophobia, arousal, or activity. Nepicastat also significantly reduced NE levels in the amygdala and prefrontal cortex and increased the ratio of dopamine to NE in the hypothalamus. Our results suggest that NE may facilitate the initiation of parental behavior in male and female California mice.

P1.40 CHEMOGENETIC ACTIVATION OF THE LATERAL SEPTUM ALTERS SOCIALITY BUT NOT PAIR BONDING BEHAVIORS IN MALE PRAIRIE VOLES

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The lateral septum (LS) mediates social behaviors, emotional processes, and stress responses. The LS is particularly important in sociability and monogamy but its role in how these two behavioral domains interact is unclear. Therefore, the aim of this study was to investigate the effects of DREADD-mediated LS activation on social behavioral responses in male prairie voles when they are 1) sex naïve and generally affiliative and when they become 2) pair bonded and display selective

aggression. We show that amplifying neural activity in the LS augments social approach behaviors in sex naïve males compared to controls. Despite partner preference formation remaining unaltered, LS activation in pair bonded males leads to reduced levels of selective aggression and increased social affiliative behaviors. Collectively, this study suggests that LS activation alters behavior within certain social contexts, by increasing sex naive affiliative behaviors and reducing mating-induced aggression with same-sex conspecifics, but does not alter behavior within other social domains, such as partner preferences with opposite sex individuals.

P1.41 *Withdrawn*

P1.42 ANDROGEN ACTION WITHIN THE VOMERONASAL ORGAN CONTRIBUTES TO THE SEXUAL DIFFERENTIATION OF THE BRAIN AND BEHAVIOR

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The vomeronasal organ (VNO) is responsible for pheromone processing and plays a critical role in mediating socio-sexual behaviors in mice. Testosterone (T) masculinizes and defeminizes the brain and socio-sexual behavior during early development by acting directly on androgen receptors (AR) or indirectly via estrogen receptors (ER). In Experiment 1, we asked whether androgens can act via the VNO in early development to affect the display of socio-sexual behaviors in adulthood by administering a microinjection of T locally to the VNO on the day of birth (PND1) in mice. In Experiment 2, we asked whether T acts on AR or ER by injecting the VNO with a vehicle, estradiol or the non-aromatizable androgen, dihydrotestosterone (DHT) on PND1. In Experiment 3, we assessed the necessity of androgen action by blocking AR and ER in the VNO with the aromatase inhibitor letrozole and AR antagonist flutamide on PND1. In Experiment 1, we found that a single microinjection of T on PND1 was sufficient to increase territorial aggression in males but did not affect female behavior. In Experiment 2, we found that a single microinjection of DHT on PND1 was sufficient to increase male territorial aggression, increasing boxing, biting, and attacking behavior towards males. In Experiment 3, we found that a single microinjection of letrozole on PND1 was sufficient to increase sexual behaviour with males displaying increased thrusts per mount towards a female intruder. Our findings suggest that androgens act via the VNO in early critical periods in development to affect adult socio-sexual behaviours.

P1.43 CO-EXPRESSION OF ANDROGEN RECEPTOR AND ESTROGEN RECEPTOR ALPHA WITH CORTICOTROPIN-RELEASING FACTOR EXPRESSING NEURONS IN MALE AND FEMALE MICE

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Anxiety and depression are nearly twice as prevalent in women when compared to men, with potential contributing factors involving sex-dependent exposure to gonadal hormones and dysregulation of HPA axis function. Gonadal hormone actions through androgen receptor (AR) and estrogen receptor alpha (ERα) have been shown to regulate hypothalamic-pituitary-adrenal (HPA) axis responsiveness and anxiety behaviors. Corticotropin-releasing factor (CRF) is known to

regulate the HPA axis, anxiety and depression. We first tested whether CRF neurons co-localize AR in mice and if this differed by sex. We found high co-localization of AR in CRF neurons within the medial preoptic area (MPOA), bed nucleus of the stria terminalis (BNST), medial amygdala (MeA), and ventromedial hypothalamus (VMH). Moderate CRF/AR co-expression was found in the central amygdala (CeA) while low co-expression was found in the paraventricular hypothalamus (PVN). Sex differences in CRF/AR co-expression were found in numerous brain regions, including the BNST, CeA, and VMH where males showed higher levels of co-expression. We next investigated CRF co-localization with ERα, finding generally less CRF/ERα co-localization relative to CRF/AR co-localization. However, regions including the MPOA and VMH showed high co-expression, with moderate co-expression found in the arcuate nucleus, and low co-expression in the PVN and CeA. Females showed higher CRF/ERα co-localization in the MPOA and PVN compared to males. Given the role of CRF in the regulation of anxiety, depression and the HPA axis, the presence of AR and ERα in these neurons indicate a mechanism through which androgens and estrogens might mediate sex differences in these functions.

P1.44 CESAREAN BIRTH ELICITS LONG-TERM EFFECTS ON VASOPRESSIN AND OXYTOCIN NEURONS IN THE PARAVENTRICULAR NUCLEUS OF THE HYPOTHALAMUS

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Birth is a dramatic event for placental mammals and occurs at a time when the brain is undergoing key developmental processes. Remarkably, little is known about the contributions of birth to brain development and whether birth mode (vaginal vs. Cesarean) alters neurodevelopmental trajectories. We previously reported that Cesarean birth is associated with decreased vasopressin (VP) neuron number in the hypothalamic paraventricular nucleus (PVN) at weaning in mice. In this study, we investigated whether this effect extends to adulthood and whether oxytocin (OT) neurons, another prominent population in the PVN, are also affected by birth mode. We found that Cesarean-born adult mice had fewer VP neurons in the PVN, and this effect was localized to magnocellular regions. The PVN of Cesarean-born adults also had smaller VP neuron somas and reduced VP efferent projections. In addition, Cesarean-born mice showed a trend for reduced OT neuron number and a significant reduction in OT soma size in the PVN. We also examined VP and OT neuron number in the supraoptic and suprachiasmatic nuclei but no effect of birth mode was found in these regions. Thus, there are long-term effects of birth mode on the VP and OT systems in the PVN, suggesting that this region is particularly sensitive to the effects of birth mode. Given that VP and OT mediate social behavior, our findings may help explain the social deficits reported for Cesarean-born mice. Our results are also of significance to humans, given the widespread practice of Cesarean section deliveries across the world.

P1.45 SOCIAL EXPERIENCE CONDITIONS OXYTOCINERGIC MODULATION IN THE NUCLEUS ACCUMBENS OF FEMALE PRAIRIE VOLE

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Social relationships are dynamic and evolve with shared and personal experiences. Nevertheless, whether the function of social neuromodulators also evolves with social experience and whether this impacts the trajectory of social relationships is unknown. We used pair bonding in the socially monogamous prairie vole as an example of socio-sexual experience dramatically altering behaviors displayed toward a partner and novel individuals. Using slice electrophysiology, we investigated the oxytocin-dependent modulation of excitatory synaptic transmission in the nucleus accumbens of pair bonded and control, sister-housed females. We found that oxytocin receptor agonist decreases the amplitude of spontaneous EPSCs in control but not paired voles (pair bonding: $p=0.009$) and increases the amplitude of electrically evoked EPSCs in paired but not control voles (pair bonding x time: $p=0.0001$). The oxytocin-dependent potentiation of synaptic transmission observed in paired animals depends on oxytocin receptors located on nucleus accumbens neurons, since this effect was abolished by viral-mediated CRISPR Oxtr knockdown (KD x time: $p=0.023$). The oxytocin-dependent potentiation requires endocannabinoid receptors CB1 signaling since CB1 antagonist blocks the potentiation (treatment x time: $p=0.013$). Behaviorally, blocking CB1 receptors after the pair bond is established increases the occurrence of defensive behaviors displayed toward the partner ($p=0.009$) but not toward a novel individual ($p=0.862$). Altogether, our study shows that oxytocin action on the nucleus accumbens is modulated by social experience, and that the oxytocin receptor-dependent CB1 receptor activation observed in pair bonded voles plays a role in the trajectory of social interactions with the partner as the relationship unfolds.

P1.46 THE ROLES OF OXYTOCIN AND ARGININE-VASOPRESSIN IN ATTACHMENT BEHAVIORS IN CAPTIVE COPPERY TITI MONKEYS

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Neuropeptides such as arginine-vasopressin (AVP) and oxytocin (OT) have been hypothesized to be important mechanisms underlying selective attachment relationships in monogamous species. The present study investigates the roles of OT and AVP in attachment behaviors (separation distress, stress buffering, proximity maintenance) in juvenile female coppery titi monkeys (Plecturocebus cupreus), a socially monogamous New World monkey. Subjects received intranasal treatments of saline, low/medium/high OT, low/high AVP, or OT antagonist (OTA) prior to a social separation or parent preference test. We hypothesized that OT treatments would reduce separation distress and enhance parent preference, and AVP treatments would do the opposite. Results from our preliminary general linear mixed-effects models show the while fathers are significant stress buffers ($p<.001$), none of our treatments reduced female separation distress ($n=12$). Our preliminary parent preference test results ($n=10$) suggest that low OT, medium OT, and OTA increase parent proximity maintenance ($p<.001$), low AVP increases stranger proximity maintenance ($p=.01$), and high AVP increases time subjects spend alone during tests ($p=.01$). This study suggests that while manipulations of the OT and AVP systems during a social separation challenge are not able to compensate for the distress experienced upon separation from the attachment figure, these intranasal treatments do impact social behaviors. Manipulations of the OT system generally increase proximity maintenance with the parents, while manipulations of the AVP system lead to abnormal socialization behaviors, such as spending more time alone or interacting with an unfamiliar stimulus pair.

P1.47 HYPOTHYROIDISM THROUGHOUT THE PERINATAL PERIOD IS NECESSARY TO INCREASE JUVENILE PLAY BEHAVIOR

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Thyroid hormones (THs) play an instrumental role in the perinatal development of most, if not all, brain areas and neurochemical systems. THs are entirely maternally derived until 16–20 weeks gestation in humans and embryonic day 17.5–18 in rats; afterwards, the fetal thyroid secretes additional THs. Maternal hypothyroidism rates vary among countries but can be as high as 40%, and children born to these mothers have higher rates of ADHD-like behaviors and possibly autism spectrum disorder, although these results are contradictory. The mechanisms through which maternal hypothyroidism might alter social behavior are unknown. In a previous study, we found that the induction of maternal hypothyroidism throughout perinatal development (E12–P23) drastically increased juvenile play behavior in male and female rats. In this experiment, we hoped to determine whether a shorter critical period exists by inducing maternal hypothyroidism during the prenatal (E12–birth), postnatal (birth–P23), or perinatal (E12–P23) period using methimazole in the drinking water. Offspring were then tested for juvenile play behavior with a same-sex sibling at P30–33. Interestingly, only subjects with hypothyroidism for the entire perinatal period showed increases in play behavior compared to control rats. For some behaviors (chasing), postnatal hypothyroidism alone even decreased play. We saw no sex differences in any of the behaviors or the effects of treatment. Therefore, it appears that prolonged reduction in THs can increase social behaviors, perhaps because of impulsivity, but that normal TH levels in pre- or postnatal life can compensate and may even suppress some behaviors.

P1.48 MU OPIOID RECEPTOR STIMULATION IN THE NUCLEUS ACCUMBENS INCREASES VOCAL-SOCIAL INTERACTIONS IN FLOCKING EUROPEAN STARLINGS, STURNUS VULGARIS

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Social connections in gregarious species are vital for safety and survival. Many bird species form large flocks outside the breeding season. It has been proposed that such large social groups may be maintained by reward induced by positive interactions with conspecifics and by the reduction of a negative affective state caused by social separation. Moreover, within a flock optimal social spacing between conspecific is important. Mu opioid receptors (MORs) in the nucleus accumbens (NAc) are well known for their role in both reward and the reduction of negative affective states, suggesting that MOR stimulation in NAc may play a critical role in flock cohesion. To begin to test this hypothesis, social and non-social behaviors were examined in male and female European starlings (Sturnus vulgaris) in non-breeding flocks after intra-NAc infusion of saline and three doses of the selective MOR agonist D-Ala2, N-Me-Phe4, glycinol5-ENK (DAMGO). DAMGO in NAc dose-dependently increased singing behavior and facilitated social approach while at the same time promoting mild agonistic behaviors used to maintain social distance. These findings support the hypothesis that MORs in NAc promote social interactions important for group cohesion in non-sexual contexts and suggest the possibility that MOR in the NAc play a role in optimizing the pull of joining a flock with the push of potential agonistic encounters.

P1.49 FURTHER INVESTIGATION OF THE RAPID CONTROL OF MALE SEXUAL BEHAVIOR BY NEUROESTROGENS IN MICE

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Neuroestrogens play a key role in the activation of male sexual behavior by testosterone through their nuclear- and membrane-initiated actions. Studies conducted in birds suggested that membrane vs. nuclear actions of neuroestrogens differentially control sexual motivation and performance. In mice, estrogen receptor alpha (ERα) plays a major role in the control of male sexual behavior. However, whether the translocation ERα and its activation at the membrane rapidly affect male sexual behavior remains unclear. Recently, a mouse model (C451A-ERα) carrying a mutated ERα unable to traffic to and signal from the membrane was generated. Moreover, the natural estrogen estetrol (E4) has been described to act as an agonist of nuclear estrogen receptors but as an antagonist on their membrane-associated fraction. Here, we used the complementary properties of estetrol and C451A-ERα mice to investigate the role of membrane ERα (mERα) on male sexual motivation and performance. Regardless of the genotype, systemic aromatase blockade decreased within 10 min sexual performance and motivation, measured by the time spent close to an estrous female. E4 rapidly decreased sexual performance only in wild-type males and had no effect on sexual motivation. Together, these data confirmed the key role of aromatization in the rapid control of male sexual performance and extended this conclusion to sexual motivation. Moreover, E4, likely acting on mERα rapidly inhibits sexual performance, but not sexual motivation. Finally, the inhibitory effect of aromatase blockade in C451A-ERα mice suggests that another estrogen receptor than mERα also regulates both aspects of male sexual behavior.

P1.50 DIFFERENTIAL EGR1 AND CRHR1 GENE EXPRESSION IN BRAINS OF PROACTIVE AND REACTIVE ZEBRAFISH IN RESPONSE TO A STRESSOR

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An animal's response to a stressor can have important ramifications for its continued survival. Two consistent and distinct ways of responding to stress have been characterized: proactive and reactive stress coping styles. Along with differences in behavioral response to stressors, there are cognitive and genetic differences between the coping styles. The specific neural mechanisms involved in this variation, however, are still largely unknown. Here we exposed zebrafish selectively bred to display the proactive or reactive stress coping style to a novelty stressor and measured expression of molecular markers of neural activity (immediate early gene, egr1), and stress response (corticotropin releasing hormone receptor, crhr1). Using in situ hybridization we quantified egr1 and crhr1 expression in eight brain areas that are part of the aversive brain system and compared them to levels in individuals at rest and between the coping styles. As expected, the proactive line of zebrafish showed significantly less stress-related behaviors such as decreased freezing time and wider use of the water column compared to the reactive line when exposed to the novelty stressor. Overall, our results suggest that the differing behavioral responses between the coping styles may be facilitated in part by neural activity patterns within and between select brain regions.

P1.51 INTERMITTENT FASTING ALTERS BEHAVIORAL OUTCOMES AND GENE EXPRESSION IN THE CENTRAL NERVOUS SYSTEM

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Intermittent fasting (IMF) is associated with many health benefits, yet little is known if an IMF diet affects mood and cognitive processing. We have previously identified that IMF in young, diet-induced obese males increased hypothalamic norepinephrine (NE) and arcuate neuropeptide Y (NPY) expression. This suggests that IMF may improve cognition through activation of the hindbrain NE network and reverse the age-dependent decline in NPY expression. Here, we address the impact of IMF on the Y-maze, spatial object recognition (SOR), novel object recognition (NOR), the open field task (OFT), and gene expression in the arcuate nucleus (ARC), lateral hypothalamus (LH), and locus coeruleus (LC) in middle-aged male (12 mos.) and aged female (18 mos.) mice. Our cognitive results suggest that, in middle-aged males, IMF results in deficits in hippocampal-dependent tasks, yet an enhancement in hippocampal-independent tasks. In aged females, only the hippocampal-dependent task of SOR was affected, suggesting IMF disrupts spatial object configuration. In the OFT, IMF male and female displayed an anxiolytic phenotype. IMF treatment did not affect expression in the ARC in aged females but did decrease expression of Orexin and Adr1b in the LH and Slc6a2, Dbh, and Hypo1r in the LC. Our research suggests that IMF is enough to produce both an impairment and enhancement in memory dependent upon sex and age, potentially through modulation of the LH orexin-to-LC NE neuronal circuit. Current studies examining the effects of IMF on cognition and memory and gene expression in middle-aged females and aged males are currently underway.

P1.52 SEX- AND EXPERIENCE-DEPENDENT PROGRAMMING OF GENE EXPRESSION IN A MONOGAMOUS RODENT

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Early life experience can alter developmental trajectories and behaviors later in life, although the precise mechanisms underlying this phenomenon is unknown. In prairie voles, a model organism for human social behaviors, increased parental care early in life is associated with increased sociality as juveniles and adults. We used this model to investigate how early life experience affects gene expression in the nucleus accumbens, a region of the brain involved in regulating social behaviors. Parents were experimentally manipulated to increase pup-directed behavior. Using RNA-seq, we identified 259 significantly differentially expressed genes in male offspring that had been raised by high care parents compared to those raised by low care parents. Surprisingly, only two differentially expressed genes were identified in female offspring, indicating an important sex difference in the response to early nurture. We then performed several gene ontology analyses in order to understand the functions of differentially expressed genes, finding that upregulated genes in male offspring of high care parents are involved in synaptic transmission and neurodevelopment, while downregulated genes in these males are involved in metabolism and microglia function. In addition, differentially expressed genes in males are significantly enriched for autism risk genes, monogamy-related genes, and androgen responsive genes. These results provide evidence that gene expression programs in the developing brain, including those of autism risk genes, are

experience-dependent in a sex-specific manner. Furthermore, these results suggest that early nurture alters microglia-dependent pruning of synapses in the developing male brain.

P1.53 INFLUENCE OF MENSTRUAL CYCLE ON ELECTROENCEPHALOGRAPHY RHYTHMS DURING MOTOR IMAGERY

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Female sex hormones influence brain activity and promote plastic changes in the motor cortex, as well as the performance of motor skills. The electrical activity of the motor cortex is facilitated in the follicular phase and inhibited in the luteal phase of the menstrual cycle, probably associated with the levels of estradiol and progesterone, respectively. The aims of this study were to verify the effect of the phases of the menstrual cycle (CM) on mu and beta electroencephalography (EEG) rhythms and on interhemispheric inhibition (IHI= a mechanism present in unilateral motor performance) during the practice of motor imagery. Twenty-one right-handed women were submitted to blood collection and EEG recording during the practice of motor imaging of the right hand in the menstrual, follicular and luteal phases of the CM. The Freedman test was used to compare the IHI and EEG rhythms between the different phases. The FSS profile of the participants showed variations compatible with the fluctuations of a normal cycle. It was possible to find significant differences between the phases of the MC for the amplitude of the beta rhythm on the C3 electrode ($\chi 2$ (2) = 10.67; p = 0.005). The follicular phase shows greater attenuation of beta when compared to the menstrual (p = 0.006) and luteal phases (p = 0.041). There was no alteration in mu rhythm and IHI. To our knowledge it is the first report in the literature showing the association between sexual steroids and cognitive motor processing.

P1.54 LIFELONG ENHANCEMENT OF BODY MASS FROM ADOLESCENT STRESS

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In hamsters, exposure to stress in adulthood causes increased body weight. We addressed how social stress during puberty would impact food intake and body weight (n=21/group). Stressed hamsters started gaining significantly more weight than controls after only two days of stress exposure. Over a two-week period, stressed subjects gained 10% more weight and consumed more food than controls. At the end of the stress period, stressed hamsters collected nearly twice as many palatable sugar pellets from an arena than controls. Stressed subjects presented 15-20% more body fat in mesenteric, inguinal, and retroperitoneal fat pads. In order to assess the duration of these effects, we analyzed data from previous studies keeping hamsters for over two months past the stress period in puberty (nearly 100 animals per group). Our analysis shows that stressed hamsters stopped gaining more weight after the stress period, but their body weights remained elevated for over two months, consistently weighing 10% more than their non-stressed counterparts. We also analyzed conditioning training data collected after the period of stress in late puberty and early adulthood (P56 to P70) that was part of the original studies. Training consisted of lever pressing for palatable food rewards. At these times, previously stressed hamsters retrieved similar numbers of food pellets from the conditioning chambers, suggesting no difference in

appetite after the stress period. These data showing a long-lasting effect of stress on body weight may be relevant to studies on the ontogeny of lifelong obesity.

P1.55 MACHINE LEARNING WITH DEEP NEURAL NETWORKS IDENTIFY LINEAGE-SPECIFIC CHANGES IN RAT SOCIAL BEHAVIOR DUE TO ANCESTRAL EDC EXPOSURE

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Exposure to endocrine-disrupting chemicals during gestation can change behavior in exposed rats, and lead to behavioral alterations across generations. We conducted an extensive behavioral assessment of two common EDCs; Vinclozolin (an anti-androgenic fungicide) and A1221 (an industrial polychlorinated biphenyl with estrogenic action). Gestating F0 dams were treated with Vinclozolin (1 mg/kg), A1221 (1 mg/kg), or vehicle between embryonic day 8 – 18. Further breeding was done to generate lineage specific (paternal or maternal) F2 and F3 individuals. A subset of pregnant F3 dams were exposed to a second hit of the same or the other EDC followed by breeding to the F6 generation. Approximately 1600 rats were tested in a social novelty paradigm in which a rat was given a choice between a novel or familiar same-sex stimulus animal. Behaviors were manually scored for nose-touches, a sensitive index of choice. This data was used to train deep neural networks using Deeplabcut and the results were optimized to be consistent with manually-scored results. In the F6 generation, only males from the vinclozolin paternal exposure lineage spent more time nose-touching than control individuals, an effect that was limited to the two-hit vinclozolin treatment lineage and not observed in other EDC combinations. These results indicate 1) anti-androgenic EDCs may impair social recognition, 2) parental lineage of EDC exposure matters, and 3) hits of EDCs across generations can lead to emergent behavioral abnormalities.

P1.56 ACUTE EFFECTS OF PUBERTAL MICROBIAL DYSBIOSIS ON LPS-INDUCED NEUROINFLAMMATION

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Stressors experienced during puberty can have a significant impact on brain development and behavior. Exposure to the bacterial endotoxin lipopolysaccharide (LPS) significantly increases cytokine mRNA expression (e.g. IL-6, IL-1β, TNF-α) in the hippocampus and prefrontal cortex (PFC) and alters the gut microbiome more in pubertal mice compared to adult counterparts. Moreover, probiotic supplementation has been shown to influence immunomodulation and have positive effects on immune responsivity. However, it is unknown whether probiotic supplementation could reverse the effects of microbial dysbiosis on LPS-induced neuroinflammation. The objective of the current research project was to examine whether the adverse effects of pubertal microbial dysbiosis on LPS-induced immune response can be mitigated by probiotic supplementation in male and female mice. At 5 weeks of age, male and female CD1 mice received either broad spectrum antibiotics or water through gavage, twice a day, for seven days. During the same period, mice received either a probiotic supplement or placebo in their drinking water. At 6 weeks of age, mice received either an intraperitoneal injection (i.p.) of LPS or

saline. Eight hours following the injection, mice were euthanized and brains were collected. The hypothalamus, hippocampus, and PFC were extracted and processed with a real-time quantitative PCR (RT-qPCR) to examine central cytokine mRNA expression (i.e. IL-1β, TNF- α, IL-6). It is hypothesized that pubertal antibiotic treatment will potentiate the LPS-induced immune response in the hypothalamus, hippocampus, and PFC and that probiotic supplementation will mitigate these effects in a sex-specific manner.

P1.57 IMMEDIATE EARLY GENE LABELING SUGGESTS A CONTEXT-DEPENDENT ROLE FOR THE NUCLEUS ACCUMBENS IN SONG IN MALE EUROPEAN STARLINGS

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Birdsong is well known for its role in mate attraction during the breeding season. However, many birds, including European starlings (Sturnus vulgaris), also sing outside the breeding season as part of large flocks. Song in a breeding context can be extrinsically rewarded by mate attraction; however, song in flocks, referred to here as gregarious song, results in no obvious extrinsic reward and is proposed to be intrinsically rewarded. The nucleus accumbens (NAc) is a brain region well-known to mediate reward and motivation, which suggests it is an ideal candidate to regulate reward associated with gregarious song. The goal of this study was to provide new histochemical information on the songbird NAc and its subregions (rostral pole, core, and shell), and begin to determine their individual contributions to regulating gregarious song in male starlings. We examined immunolabeling for tyrosine hydroxylase, neurotensin, dopamine and cAMP regulated phosphoprotein, and enkephalin in NAc. We then examined the extent to which gregarious and sexually-motivated song differentially correlated with immunolabeling for the immediate early genes Fos and ZENK. We found that the starling NAc, particularly the core and shell, matched closely with the immunolabeling patterns seen in the core and shell of NAc in mammals and galliforms. Additionally, we found that gregarious song, but not sexually-motivated song, positively correlated with Fos in all NAc subregions. Our observations provide further evidence for three distinct regions within the songbird NAc, and our data suggest the NAc may play an important role in regulating gregarious song in songbirds.

P1.58 HISTORY OF PREVIOUS MIDLIFE ESTRADIOL TREATMENT PERMANENTLY ALTERS BRAIN ESTROGEN RECEPTOR SIGNALING TO ENHANCE COGNITIVE AGING IN A RAT MODEL OF MENOPAUSE

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Loss of ovarian hormones during menopause coincides with cognitive decline and increased risk of dementia. Due to health risks associated with prolonged estrogen exposure, current guidelines recommend using postmenopausal estrogen for as short a time possible. Our work in rodent models demonstrates long-lasting benefits of short-term estradiol treatment on hippocampal function and memory through sustained activation of estrogen receptor (ER) α. Previous midlife estradiol treatment enhances radial-arm maze performance and increases hippocampal ERα in aging ovariectomized rodents, an effect dependent on insulin-like growth factor-1 receptor (IGF-1R). Results of current experiments demonstrate mechanisms through which hippocampal ERα

enhances memory following long periods without ovarian hormones. First, we showed the necessary role of brain-derived neuroestrogens in IGF-1-mediated activation of ERα via MAPK and subsequent memory enhancements in aging ovariectomized rats. Then we tested the interactive relationship between neuroestrogens and IGF-1R in activating hippocampal ERα using two models of menopause: one in which long-term ovariectomized aging females received no estradiol treatment and one in which long-term ovariectomized aging females received midlife estradiol treatment terminated after 40 days. Following long-term ovariectomy without estradiol exposure, IGF-1R and neuroestrogens were no longer able to activate ERα and impact memory. However, previous midlife estradiol treatment maintained interactions between IGF-1R and neuroestrogens, resulting in sustained increases in ERα and enhanced memory. Together, results provide a strategy for combatting postmenopausal cognitive decline where short-term estradiol treatment following ovariectomy sustains hippocampal function and memory by permanently altering the relationship between IGF-1R and neuroestrogens, allowing for long-term activation of hippocampal ERα.

P1.59 OXYTOCIN ANTAGONIST DURING SONG TUTORING IN ZEBRA FINCHES REDUCES PREFERENCE FOR AND LEARNING OF THE TUTOR'S SONG

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In humans, language development is a highly social process requiring attention towards and motivation to engage with caregivers. Similarly, dynamic social interactions with a song "tutor" are necessary for juvenile zebra finches (Taeniopygia guttata) to learn song. The oxytocin system plays a central role in social behaviors across species, yet it is unknown whether this system is involved in the attentional and motivational processes that support vocal learning. We used a within-subjects design to test whether manipulating oxytocin receptor availability during exposure to tutors would impact learning from those tutors. Juvenile, song-naïve males were each tutored by two unfamiliar adult males. During exposure to one tutor, the juvenile was treated with oxytocin receptor antagonist (OTA) and during exposure to the other, saline (control). We found that OTA significantly reduced behaviors associated with attention and approach during tutoring sessions. Second, using an operant assay in which exposure to the control-paired and OTA-paired songs was balanced, we found that the juveniles preferred the control song over the OTA song. The developmental time course of song preference mirrored that of oxytocin receptor abundance in the brain as shown in other studies. Finally, when the song of these juveniles crystallized in adulthood, it more closely resembled control song than OTA song. The magnitude of this difference was significantly predicted by the preference for the control song. Together, these results suggest that oxytocin receptors play a role in socially-guided vocal learning in juvenile zebra finches, perhaps through effects on attention and motivation during tutoring.

P1.60 THE BRAIN CLOCK'S PORTAL SYSTEM: SUPRACHIASMATIC NUCLEUS AND ORGANUM VASCULOSUM OF THE LAMINA TERMINALIS

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Vascular portal systems are structures necessary for transporting products directly from the capillary bed of one region to the capillary bed of another region in high concentrations, without dilution in the systemic vasculature. The only known portal system in the brain is the hypophyseal-pituitary portal system, a communication system that is necessary for reproduction and survival. Secretions from specialized hypothalamic neurons travel in portal vessels to their targets. Neurons of the hypothalamic suprachiasmatic nucleus (SCN), locus of the brain's master clock, also produce secretions deeply implicated in health and survival. The grafted SCN, when encapsulated in a polymer material, can restore behavior rhythmicity. Thus diffusible signal from the SCN sustain circadian rhythms. Although the neural network of between the brain clock and has been extensively studied, its pathway to transport diffusible signals to surrounding brain regions, including the vasculature, has not been studied. In this study, we obtained the whole-mount vasculature image of mouse anterior hypothalamus without slicing the brain by combining tissue clearing and light sheet microscopy. We identified a portal system connecting the SCN and organum vasculosum of the lamina terminalis (OVLT). The OVLT is a circumventricular organ (CVO) lacking a blood-brain barrier, enabling communication between the blood, brain, and cerebrospinal fluid. This "clock portal system" points to entirely new routes and targets for secreted signals, restructuring our understanding of brain communication pathways. Whether any of the remaining six CVOs in the mammalian brain bear portal systems is yet to be determined.

P1.61 INDIVIDUAL DIFFERENCES IN TASKS THAT RECRUIT THE FRONTAL LOBE

Christopher Purkis, Dr. Elizabeth Hampson
University of Western Ontario.

The presence of potential sex differences in specific domains of cognition is an actively debated subject, with differences being well-established in certain domains and poorly established in others. Specifically, mixed or limited findings have been obtained from studying potential sex differences in working memory and reversal learning. As such, this study attempted to clarify the presence of sex differences in both aspects of cognition, and whether differences in reversal learning performance were related to differential androgen concentrations. It was hypothesized that female participants would display a significant advantage on an executive working memory task; that male participants would display a significant advantage on a reversal learning task; and that participants with higher endogenous testosterone levels would show superior reversal learning performance. Participants completed computerized versions of the n-back task, a measure of executive working memory, and probabilistic reversal learning (PRL), a measure of reversal learning. Saliva samples were collected before and after the testing session. A sex difference in task performance failed to be detected on both the n-back task and the PRL. Furthermore, analysis of participants' salivary testosterone was inconclusive due to difficulties in obtaining the necessary reagents required for the immunoassay. Therefore, the findings of the current study support the notion that specific cognitive functions mediated by the prefrontal cortex may not be sexually differentiated. While the findings fail to provide support for the initial hypotheses of a sex difference in both the n-back task and the PRL, they serve as further evidence to the ongoing debate regarding the existence of sex differences in working memory and reversal learning.

Poster Session II

Wednesday, June 30, 2021 from 12:00pm to 1:30pm (ET)

P2.1 BEHAVIORAL RESPONSE TO CHRONIC VARIABLE MILD STRESS IN MALE AND FEMALE MICE

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Chronic stress leads to the development of mood disorders such as major depressive disorder and post-traumatic stress disorder. Women are more susceptible to developing these disorders, suggesting a sex-related difference in the neurological circuits that process stress. An important area in the central stress response is the bed nucleus of the stria terminalis (BNST). The BNST is sexually dimorphic and expresses both aromatase and estrogen receptors, suggesting that these sex differences are dependent on the BNST. We assigned male and female mice to either six weeks of chronic variable mild stress (CVMS) or control conditions. To assess approach/avoidance behaviors, we tested mice in the open field test (OFT), elevated plus maze (EPM), light/dark box (LDB), and novelty suppressed feeding (NSF). In the OFT, stressed mice spent a decreased percentage of time in the center zone, an anxiety phenotype, regardless of sex. In the EPM, mice did spent more time in the closed arms, supporting a stress-induced anxiogenic effect. Outcomes from the LDB support our findings such that CVMS reduced the time spent in the transition zone. Lastly, in the NSF parameter of pre- and post- food depravation weight loss, stressed mice lost less weight than their control counterparts. Collectively, our preliminary studies indicate that CVMS resulted in an anxiety-like phenotype. Present analysis consists of examining the relationship between these outcomes and estrous cyclicity. Our current follow-up studies include assessing the transcriptomic effects of CVMS in the BNST and the neurophysiological consequences of CVMS in the BNST across the sexes.

P2.2 THE NEURAL CORRELATES OF TICKLING MAY DIFFER FROM THOSE INVOLVED IN PRO-SOCIAL BEHAVIOURS

Emma Tivey[1], Jessica Martin[1], V Poon[1], Sarah Brown[1], Valerie Bishop[1], Alistair Lawrence[1,2], Simone Meddle[2]

[1]The Roslin Institute; [2]SRUC

'Tickling' is a widely used technique used to model social play and positive affective states in rats. The behavioural response to tickling is associated with the ascending mesolimbic dopamine system and the somatosensory cortex, however, any hormonal regulation of tickling has yet to be explored. We aimed to test the hypothesis that oxytocin and vasopressin neurons in the paraventricular nucleus of the hypothalamus (PVN) are involved in regulating the behavioural response to tickling in female and male juvenile Wistar rats. Rats (n=32/sex) received either tickling (Tickled, n=16/sex) or no hand contact (Controls, n=16/sex). Rats were culled and their brains taken: double-labelled immunohistochemistry was used to quantify c-fos expression in multiple brain regions, including oxytocinergic and vasopressinergic neurons of the PVN; these neurons project to the reward circuitry and are thought to play a vital role in coding the rewarding nature of prosocial behaviours. Tickled rats, regardless of sex, had lower numbers of c-Fos positive

oxytocin (p=0.02) and vasopressin (p=0.03) neurons in the PVN. Similarly, we found that correlations in neural activation in connected regions of the social behaviour network are disrupted in tickled, compared to control, rats, for example, BNST-Nucleus Accumbens (Control, p= 0.006; Tickled, p= 0.607), Amygdala-VTA (Control, p= 0.01; Tickled, p= 0.38), Lateral Septum-Amygdala (Control, p= 0.004; Tickled, p= 0.245). This suggests that tickled rats had lower neural activity in regions associated with social behaviours. Therefore, tickling, while rewarding, may not be perceived as a social behaviour for rats, which may affect how we interpret rat tickling studies.

P2.3 ORGANOPHOSPHATE FLAME RETARDANTS AND THE DEVELOPING DOPAMINERGIC SYSTEM

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The use of organophosphate flame retardants (OPFRs) in commercial and consumer goods is widespread despite their persistence in human and wild environments, and structural similarity to known toxicants. Our previous research has identified that OPFRs can disrupt prenatal neurodevelopment and adult behaviors including socioemotional behaviors. Additionally, we have shown that OPFRs accumulate in the fetal portion of the rat placenta and perturb placental function including the production of serotonin and other tryptophan metabolites. This has broad implications for fetal brain development as the placenta is a critical transitionary organ that regulates neuroendocrine function, and is the main source of serotonin and other factors to the growing fetus. We sought to extend these findings by investigating the potential for OPFRs to alter the development of a second monoaminergic neurotransmitter system, the midbrain dopaminergic system. Pregnant Wistar rats were orally administered an OPFR mixture used as flame retardants and in other applications (triphenyl phosphate and isopropylated triarylphosphate isomers (ITPs)) at 0, 500, 1000, or 2000 µg/day for 14 days during pregnancy. The developing mesodiencephalic dopaminergic pathway of the fetuses was then analyzed. Significant changes were observed in the morphology of the mesodiencephalic dopamine neuron nuclei (putative VTA and SNc) in OPFR treated fetuses compared to controls. Tyrosine hydroxylase immunoreactive (THir) fibers in OPFR males and females were significantly longer than in controls. Taken together, these results suggest prenatal OPFR exposure may interfere with foundational biological mechanisms directing development of the midbrain dopaminergic system, and alter the developmental trajectory of mesodiencephalic dopaminergic projections.

P2.4 TRACKING RAPID CHANGES IN PLASMA CORTICOSTERONE AND NEURAL GENE EXPRESSION DURING SOCIAL ASCENSION AND DESCENSION IN MOUSE SOCIAL HIERARCHIES

Tyler Marie Milewski, Won Lee, James P. Curley
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Social hierarchies are a common form of social organization across species, with conspecifics establishing social ranks through competitive social interactions. Although rank order in most hierarchies is relatively stable over time, animals need to flexibly change their behavior and physiology according to ongoing environmental changes. This study investigated how mice plastically change their behavior, physiology, and brain gene expression at 70min and 25hr during

a social challenge. Groups of four outbred CD-1 male mice formed stable social hierarchies with unique ranks for 10 days. After, mice were either left in their stable social hierarchies or reorganized into novel social groups with unfamiliar animals of identical social ranks. We found that all reorganized groups rapidly reformed social hierarchies within minutes. Consequently, this rearrangement led mice to either socially ascend, descend, or remain at the same rank in new groups. Reorganized mice had significantly higher plasma corticosterone levels than controls 70min post-reorganization, but no differences were found at 25hr post-reorganization. Animals who held dominant status prior to reorganization showed a higher rise in plasma corticosterone levels at 70min post-reorganization than their subordinate counterparts. Differential expression (TagSeq) indicated higher neurogenomic responses in the MeA than the mPFC at 70min following the manipulation. Enrichment analysis revealed alterations in brain gene expression are dependent on the direction of social status change. Overall, these findings suggest that mice are able to rapidly modify how they process social cues following a social challenge, and transcriptional changes in the MeA may be particularly significant for such dynamic responses.

P2.5 SEASONAL AND SEX-SPECIFIC REGULATION OF 3B-HYDROXYSTEROID DEHYDROGENASE (3B-HSD) ACTIVITY AND AGGRESSIVE BEHAVIOR IN SIBERIAN HAMSTERS

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Numerous studies have shown that circulating gonadal steroids are positively correlated with aggression during the breeding season. It is becoming increasingly clear, however, that alternative neuroendocrine mechanisms are critical in modulating aggressive behavior, particularly for animals that are more aggressive during the short-day (SD) photoperiods of the non-breeding season. Our previous work suggests that the pineal hormone melatonin, the adrenal androgen dehydroepiandrosterone (DHEA), and neurosteroids are important in regulating non-breeding aggression in Siberian hamsters (Phodopus sungorus); it is unclear, however, what the relative roles of adrenal and neural steroids are in contributing to aggressive behavior and if the importance of these pathways differs between males and females. In this study, we housed male and female hamsters in long days (LDs, characteristic of breeding season) or SDs, treated them with timed melatonin or saline injections, and quantified aggression after 10 weeks of treatment. Following behavioral testing, we measured the activity of 3β-hydroxysteroid dehydrogenase (3β-HSD), an enzyme that catalyzes the conversions of pregnenolone to progesterone and DHEA to androstenedione, in the adrenal glands and two brain regions associated with aggressive behavior (the anterior hypothalamus and periaqueductal gray). We predict that SD hamsters and LD hamsters given timed melatonin injections will display higher levels of aggression than LD hamsters, and that this increase in aggression will be associated with elevated adrenal and neural 3β-HSD activity. Collectively, our results will provide insight into how adrenal and neural steroid synthesis mediate aggressive behavior in seasonally breeding animals.

P2.6 PRIMING OF ENSEMBLES BY EARLY LIFE STRESS IN THE NUCLEUS ACCUMBENS

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Early life stress (ELS) increases the risk of developing psychiatric disorders such as anxiety and depression. One potential mechanism mediating this increased susceptibility is through a sensitization of responses to future stress. However, little is known about the level at which this sensitization might be occurring in the brain. We postulated that ELS-induced stress sensitization may be evident at the level of neuronal ensembles, such that cells activated by ELS might be more reactive to adult stress. To study this, we used a stress model in mice and a transgenic mouse line to tag and track experience-activated cells. We found an increased neuronal activation in the nucleus accumbens (NAc) in mice with an ELS history. We then hypothesized that the reactivation of ELS-responsive microcircuits in the NAc is a necessary component of the sensitized behavioral response to additional stress. We causally tested this hypothesis by overexpressing an inhibitory DREADD (Designer Receptors Exclusively Activated by Designer Drugs) in experience-responsive cells in the NAc of mice during an ELS-specific time-sensitive period. During adult chronic social defeat stress (CSDS), we inhibited experience-responsive microcircuits with olanzapine, a ligand specific to inhibitory DREADDs, and studied the effect on subsequent depression- and anxiety-like behavior, in both male and female mice. We found interactions between inhibition of early-life-responsive cells and response to adult stress, which suggests that inhibitory DREADDs were expressed in distinct ensembles in the NAc, responsive to either ELS or reward, and inhibition of these circuits during CSDS dampened or enhanced the stress experience, respectively.

P2.7 DEHYDROEPIANDROSTERONE (DHEA)-SULFATE CORRELATES WITH THE DYSPHORIC DOMAIN OF THE PREMENSTRUAL DYSPHORIC DISORDER (PMDD)

Nhan Dang, Ajna Hamidovic
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Dehydroepiandrosterone-sulfate (DHEA-sulfate) is the most abundant neuroactive steroid hormone in the peripheral circulation. Its importance in Premenstrual Dysphoric Disorder (PMDD) was recently shown in a pharmacometabolomic study, involving ovarian suppression and metabolic processing of exogenous estradiol and progesterone. The purpose of the present study was to highlight the importance of DHEA-sulfate in PMDD using a naturalistic, instead of pharmacologic, study design. Fifteen non-prescription and non-illicit drug using women, who self-reported premenstrual symptomatology, were recruited from the community. They provided ratings of DSM-5 defined PMDD symptoms for three menstrual cycles. In the third menstrual cycle, they were scheduled to come to the clinic and provide blood samples at 8 different time points: early follicular (EF), mid-follicular (MF), periovulatory (PO) (urinary luteinizing hormone (LH)-guided 3 visits), early luteal (EL), mid luteal (ML), and late luteal (LL). Study visits were realigned posthoc, considering menstrual cycle duration and serum LH levels. The premenstrual symptomatology data was analyzed using correlation structure at the 6 different timepoints across the menstrual cycle. Only DHEA-sulfate emerged as significant neuroactive steroid, with negative correlations for mood swings (LL, EF), depression (LL, EF), and feeling overwhelmed/inability to cope (EL, ML, LL, EF). None of the remaining affective, psychological, behavioral, and physical symptoms were correlated with DRSP-sulfate. PMDD diagnosis is particularly burdensome, requiring prospective symptom rating. Our study highlights the importance of luteal DHEA-sulfate, specifically for the dysphoric

symptom domain. Future work should expand the area of research evaluating luteal DHEA-sulfate in PMDD for diagnostic and therapeutic purposes.

P2.8 PROXIMATE MECHANISMS FOR VARIATION IN TITI MONKEY (PLECTUROCEBUS CUPREUS) VOCAL DUETS

Allison Lau[1], Dena Clink[2], Karen Bales[1]
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Many social primates use vocal communication when interacting with conspecifics. Intra-specific variation in vocalization signals is presumably due to a combination of proximate mechanisms, including genetics, learning, and environment. Disentangling the mechanisms that lead to vocal variation can broaden our understanding of the evolutionary forces that shape behavioral variation more broadly. Here, we provide a synthesis of work done thus far on coppery titi monkeys (Plecturocebus cupreus) at the California National Primate Research Center to investigate the mechanisms of vocal variance in a pair-bonded species. We present three complementary analyses assessing: 1) the potential for vocal individuality, 2) the relationship between acoustic and genetic distance, and 3) evidence for vocal convergence among pair mates. We recorded duets from adult monkeys and estimated call features from spectrograms. We classified individuals with 83% accuracy and found limited evidence for kin signatures. Call features were predicted by individual age and pair bond duration. Further, we found the first evidence of vocal convergence among pair mates. Combined, these three analyses reveal that no one proximate mechanism alone can predict variation in call features and contribute to the growing evidence that—contrary to the traditional view that they are innate and inflexible––primate vocalizations exhibit a high degree of plasticity.

P2.9 OXYTOCIN RECEPTORS IN THE MIDBRAIN DORSAL RAPHE REGULATE PERINEURONAL NET EXPRESSION IN THE PRIMARY SOMATOSENSORY CORTEX

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We recently found that viral vector-mediated knockdown of oxytocin receptors (OTRs) in the serotonergic dorsal raphe (DR) of mother rats impaired nearly all aspects of postpartum behavior. For instance, OTR knockdown resulted in high pup loss soon after parturition, decreased nursing, increased maternal aggression, and increased depressive-like behavior. All of these behaviors are mediated, in part, by the somatosensory inputs that mothers receive from their pups. Thus, we hypothesized that the behavioral effects of OTR knockdown in the DR may be due to disrupted neuroplasticity in the barrel field of the primary somatosensory cortex that represents the mystacial pad vibrissae. Compared to scrambled virus-injected controls, OTR-knockdown mothers had significantly more plasticity-restricting perineuronal nets (PNNs) in the rostral barrel field, but fewer PNNs in the caudal barrel field. Given that the rostral barrel field is essential for textural object recognition, and that snout inputs that dams receive from pups are critical for many maternal behaviors, reduced plasticity in the rostral barrel field may have particularly contributed to the impaired caregiving and affective behaviors in our OTR-knockdown mothers. These results

extend our mechanistic understanding of motherhood-associated neuroplasticity to include dorsal raphe OTRs and their influence on PNN expression in the primary somatosensory cortex.

P2.10 DIFFERENTIAL CHANGES IN SONG PRODUCTION FOLLOWING ACTIVATION OF DOPAMINE D1 RECEPTORS AND DOPAMINE D2 RECEPTORS IN THE SONG CONTROL SYSTEM

Chelsea M. Haakenson, Gregory F. Ball
University of Maryland, College Park

In order to investigate the neural mechanisms underlying the social and motivational aspects of communication, we examined a species that uses vocal communication to relay social information, the canary (Serinus canaria), and a potential modulator of the motivation to sing - the neurotransmitter dopamine. Dopamine in some song nuclei can influence the amount of singing directed at potential mates. However, the activation of dopamine type 1 receptors (D1R) results in contrasting physiological effects compared to dopamine type 2 receptors (D2R). In order to investigate the effects of dopamine receptor activation on song, we implanted guide cannula targeting the song control nucleus HVC. Each bird received injections of a D1R agonist, a D1R antagonist, a D2R agonist, a D2R antagonist, and saline with a 48-hour washout period between treatments. Following injections, we quantified the amount of time individuals took to sing and the quality of songs produced. In addition, we applied a novel computational approach to identify changes in song structure following treatment – utilizing dimensionality reduction techniques, density-based spatial clustering, and network diagrams. This experiment indicates that D1 receptor activation in HVC increases the latency to sing. Furthermore, song following D1 receptor agonist treatment had a reduction in three particular syllable types, while these syllable types were increased in song following D2 receptor agonist and antagonist treatment. These results indicate that activation of dopamine receptor types have profoundly different effects on song production, potentially modulating the type of vocalization produced to be appropriate for the social context.

P2.11 PERINEURONAL NETS IN SYRIAN HAMSTERS

Emma Shaughnessy, Alisa Norvelle, Kim Huhman
Neuroscience Institute GSU

Perineuronal nets (PNNs), extracellular matrix proteoglycans that primarily surround GABAergic interneurons, can also be found around glia and glutamatergic neurons, as well. These PNNs, recently thought to act only as structural support in the nervous system, are now thought to serve a variety of purposes in neuronal function and synapse maintenance. PNN expression is increased in response to stress and inflammation. Recently, it has also been shown that PNN expression exhibit a circadian rhythm in their expression. Our lab uses a social defeat model of stress using Syrian hamsters and has recently shown a stark difference in response to defeat stress across the circadian cycle. We hypothesized that PNNs would be increased in response to acute and repeated social defeat stress and that these changes would be different depending on the time of day the defeat took place. Instead, we found that there are no changes in number of PNN-positive cells following acute or repeated social defeat or between two timepoints at the beginning of the dark or light phase of the circadian cycle. Thus, we did not support our hypothesis that changes in PNNs modulate either nervous system responses to social defeat stress or the circadian differences in these responses.

P2.12 NEURAL CIRCUITRY OF GREGARIOUSNESS IN SPINY MICE (ACOMYS CAHIRINUS)

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The spiny mouse (Acomys cahirinus) is a large-group living, cooperatively breeding rodent that holds great potential for studying a range of social behaviors in both reproductive and non-reproductive contexts. A propensity for one of these social behaviors, gregariousness (i.e., a preference to affiliate with large groups), may be a precursor for other complex, group-based social behaviors. However, the neural circuitry underlying gregariousness in spiny mice, or any mammal, remains unknown. Here we present data demonstrating the high degree of gregariousness exhibited by male and female spiny mice using social interaction tests and a group size preference test. Spiny mice exhibit significantly more prosocial behavior than aggression with novel same- and opposite-sex conspecifics when freely interacting, and they also display a strong preference for affiliating with and investigating larger groups of novel, same-sex conspecifics over smaller groups during a group-size preference test. Additionally, an immediate early gene (IEG) study revealed that the dorsal, but not ventral, lateral septum (LS) displayed greater Fos responses when exposed to larger groups compared to smaller ones, identifying this subdivision of the LS as potentially playing an important role in promoting gregariousness. Further, we discuss preliminary data on DREADD inhibition of the LS during group size preference tests as well as viral tracing combined with an IEG study identifying inputs and outputs of the LS that suggest potential circuits underlying gregariousness. Together, these results begin to reveal the neural mechanisms of gregariousness in spiny mice and provide insight into how other grouping behaviors may be regulated.

P2.13 THE EFFECT OF EARLY LIFE STRESS ON CHROMATIN ARCHITECTURE IN EXPERIENCE-SENSITIVE CELLS OF THE NUCLEUS ACCUMBENS

Rebekah Rashford, Dr. Catherine Peña
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Early life stress (ELS) is one of the strongest predictors for development of mood and anxiety disorders. ELS can include trauma (neglect, and/or physical, sexual, and/or emotional abuse) or other negative childhood experiences. However, the increased risk for depression following ELS is not well understood. Previous work in a mouse model of stress across the lifespan has shown unique gene expression patterns in the nucleus accumbens (NAc), a key region of the reward pathway implicated in stress response, after ELS and adult stress. The three-dimensional structure of chromatin, as well as transcription factors, determine how genes are regulated and expressed, with more open chromatin being permissive for gene expression and more closed chromatin repressing expression. We hypothesize that ELS changes chromatin accessibility within stress-responsive neuronal cells in the NAc. To determine how chromatin architecture is altered within ELS-activated neurons, we generated a novel double-transgenic mouse that allowed us to label and capture both activated and non-activated neurons, then performed ATAC-sequencing (a modern method of cleaving and indexing the DNA of open chromatin regions) within these cells. Interestingly, we find ELS decreases open chromatin (permissive for gene expression) in both activated and non-activated cells in juvenile mice. This result confirms previous findings which show decreased marks of primed chromatin following ELS, with ongoing work aimed at investigating how these patterns change into adulthood. This work contributes to our

understanding of the epigenetic mechanisms driving heightened risk of mood disorders following ELS.

P2.14 SOCIAL STRESS REDUCES SOCIAL REWARD AND MESOLIMBIC ACTIVATION IN SYRIAN HAMSTERS (MESOCRICETUS AURATUS)

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Social stress plays an important role in the etiology of many neuropsychiatric disorders and can lead to a variety of behavioral deficits such as social withdrawal. Despite the potent effects of social stress on the development of psychiatric disorders, little is known about the underlying mechanisms responsible for these effects. One way that social stress may contribute to psychiatric disorders is by altering the rewarding properties of social interactions thereby reducing social motivation. We investigated the impact of varying types of social encounters on social reward by comparing the rewarding properties of social interactions in dominant, subordinate, and socially defeated Syrian hamsters. Using an Operant Social Preference (OSP) task, we found that socially defeated hamsters made significantly fewer entries and had longer latencies to enter chambers containing novel, same-sex conspecifics compared to dominant and subordinate hamsters. Surprisingly, there was no difference in entries into the social chamber by hamsters with a stable dominant versus subordinate status. We also examined the resulting neural activation using cFos immunohistochemistry in brain regions associated with motivated behavior and reward, including medial prefrontal cortex (mPFC), nucleus accumbens (NAc), and ventral tegmental area (VTA). While mPFC activation was similar across all three groups, defeated hamsters had less activation in the VTA and NAc compared to dominant and subordinate hamsters. This difference in neural activation following social conditioning mirrors the behavioral differences seen in the OSP task. Thus, social defeat stress, but not stress associated with a stable subordinate status, reduces social reward and mesolimbic activation.

P2.15 ETHOLOGICALLY RELEVANT REPEATED ACUTE SOCIAL STRESS INDUCES MATERNAL NEGLECT IN THE LACTATING FEMALE MOUSE.

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Social stress is a top predictor of peripartum mood disorders (PMD) in human mothers. In the present study we developed a novel model to examine the effects of direct and vicarious social stress on maternal and mood-related behaviors in mice. We examined the extent to which postpartum dams actively withdraw from their litters following repeated social stress. Repeated social stress consisted of daily 7-minute (or mock) exposure to a sexually naïve male mouse from postpartum days 5-7 during a 15-minute mother-pup separation. To isolate the effects of purely psychosocial or vicarious social stress, a separate group of dams were housed next to socially stressed females. The vicarious dams were otherwise the same as controls, who were housed in a separate vivarium. Direct and vicarious social stress both induced significant deficits in maternal care and increased maternal anxiety relative to controls. Vicarious stress effects were more likely to occur in response to the acute stress exposure during intruder test days, while direct stress sustained maternal deficits 24 hours after the final intruder exposure. Finally, female offspring of

stressed dams weighed less at weaning than female offspring reared by any other group. In adulthood these mice displayed anhedonia. Overall, these data suggest that social stress induces a PMD-like phenotype in mice and negatively affect offspring outcomes.

P2.16 A COMPARATIVE SPECIES APPROACH DETERMINES TESTIS SYMMETRY AND TESTOSTERONE CONCENTRATIONS WITHIN TESTES AND THE HYPOTHALAMUS OF MALE BIRDS

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Most bird species exhibit bilateral asymmetry in their reproductive tracts. In male birds, the trend is for the right testis to be smaller in mass and volume than the left testis, although both testes perform steroidogenesis. Gonadally synthesized testosterone (T) is regulated by the hypothalamus-pituitary-gonadal axis. We used a comparative species approach to investigate the degree of bilateral asymmetry in T concentrations between right and left testes. We compared T concentration between right and left testes of male cinnamon teal (Spatula cyanoptera), mallards (Anas platyrhynchos), European starlings (Sturnus vulgaris), and Eurasian collard-doves (Steptopelia decaocto) collected from the wild in southeastern Idaho during the breeding season. Additionally, we quantified the difference in T concentration between testicular and hypothalamic tissues. We prepared and purified tissue samples through solid phase extraction and quantified T using an enzyme immunoassay. We found no difference in T concentrations between the left and right testes within any of these species. Testosterone concentrations were significantly lower within hypothalamic than testicular tissue in cinnamon teal, mallards, and starlings. Eurasian collard-doves had low T concentrations relative to the other species but had equal T concentrations between testicular and hypothalamic tissues. The match between testicular and hypothalamic T concentration of Eurasian collard-doves may be related to the long breeding season and life history strategies of nonnative Eurasian collard-doves. Conversely, the high T concentrations within the testis tissue of cinnamon teal, mallards, and European starlings may facilitate high spermatogenesis for sperm competition and extra pair mating.

P2.17 SEX DIFFERENCES IN COGNITIVE AGING: A 4-YEAR LONGITUDINAL STUDY IN MARMOSETS (CALLITHRIX JACCHUS).

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Longitudinal studies are essential to understand healthy and pathological neurocognitive aging such as Alzheimer's Disease, but longitudinal designs are rare in both humans and non-human primate models of aging because of the difficulty of tracking cognitive change in long-lived primates. Common marmosets (Callithrix jacchus) are uniquely suited for aging studies due to their naturally short lifespan (10-12 years), sophisticated cognitive and social abilities and Alzheimer Disease-like neuropathology. We report the first longitudinal study of cognitive aging in marmosets (N=28) as they transitioned from middle- (~ 5 years) to old age (~ 9 years). We characterized aging trajectories using reversal learning with different stimuli each year. Marmosets initially improved on cognitive performance due to practice, but worsened in the final year, suggesting the onset of age-related decline. Cognitive impairment emerged earlier in females than males and was more prominent for discrimination than for reversal learning. Sex differences in cognitive aging could not

be explained by differences in motivation or motor abilities, which improved or remained stable across aging. Likewise, males and females did not differ in aging trajectories of overall behavior or reactivity to a social stressor, with the exception of a progressive decline in the initiation of social behavior in females. Patterns of cognitive aging were highly variable across marmosets of both sexes, suggesting the potential for pathological aging for some individuals. Future work will link individual cognitive trajectories to neuropathology in order to better understand the relationships between neuropathologic burden and vulnerability to age-related cognitive decline in each sex.

P2.18 EFFECTS OF PREGNANCY STRESS AND PROBIOTIC TREATMENT ON POSTPARTUM CAREGIVING AND AFFECTIVE BEHAVIORS

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At least 15% of peripartum women experience high depression and/or anxiety, with stress during pregnancy a strong predictor of these mental health issues as well as disrupted caregiving. A recent study reported that peripartum probiotic treatment reduced postpartum depression and anxiety symptoms in women. The current study determined the effects of probiotic treatment on caregiving and affective behaviors in a laboratory rat model of chronic variable stress during pregnancy. Female rats were provided overnight with a commonly studied probiotic in their drinking water, or untreated water, from the first day of pregnancy through postpartum day 10. Females underwent a chronic variable stress paradigm involving two mild-to-moderate stressors daily from the first week of pregnancy until the day before parturition, or were left undisturbed. Mothers' undisturbed caregiving behaviors were observed twice daily through the first week postpartum, anxiety tested in an EPM, and depression-like behaviors assessed with forced swim and saccharin preference tests. Fecal samples were collected in pregnancy and mid-lactation for gut microbiome analysis. Blood samples were taken in mid-lactation to measure circulating corticosterone. Preliminary analyses reveal that pregnancy stress reduced later maternal nest scores, increased non-maternal behaviors in the home cage, and reduced total time spent with pups. Probiotic treatment alleviated some, but not all, of these effects of pregnancy stress. Maternal gut microbiota species abundance and diversity are being determined. This work will provide valuable information about stress-induced disruptions of postpartum behaviors and the ability of probiotic supplementation to ameliorate these negative effects on the mother.

P2.19 THE IMPACT OF PERINATAL EXPOSURE TO A FLAME RETARDANT MIXTURE ON MICROGLIAL DENSITY AND REACTIVITY IN ADULT PRAIRIE VOLE BRAIN

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Microglia are known to shape brain sex differences critical for social behaviors. Chemicals, including flame retardants, can disrupt brain sexual differentiation but there is limited data regarding how they may impact microglia distribution and function. We focused on the prevalent flame retardant mixture Firemaster 550 (FM550) which is used in foam-based furniture and infant products including strollers and nursing pillows. We hypothesized FM550 exposure would disrupt microglial distribution and reactivity in brain regions known to be highly sexually dimorphic or associated with social disorders in humans. We used prairie voles (Microtus ochrogaster) because

they display spontaneous prosocial behaviors not seen in rats or mice, and thus are a powerful model for studying chemical exposure-related impacts on social behavior and the underlying neurobiological systems. We have previously demonstrated that perinatal FM 550 exposure sex-specifically impacts socioemotional behaviors in prairie voles. Vole dams were exposed to FM550 (0, 500, 1000, 2000 µg/day) via subcutaneous injections through gestation, and pups were directly exposed beginning the day after birth until postnatal day 21. Adult offspring's brains were assessed for ionized calcium-binding adapter molecule 1 (Iba-1)-positive microglia using unbiased stereology in the medial prefrontal cortex (mPFC) and the cerebellum (lobules VI-VII) and thresholding method in the amygdala. For stereology, microglia were classified based on morphology (ramified, intermediate, ameboid). Effects were sex- and dose-specific in the regions of interest. Our studies demonstrate the utility of the prairie vole for investigating the impact of chemical exposures on the developing brain, particularly regions essential for prosocial behavior.

P2.20 TITI MONKEY PARENTS HAVE LOWER HIPPOCAMPAL AVPR1A BINDING THAN NON-PARENTS

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Across mammalian species, parenthood brings many changes in social behavior, cognitive functioning, and neurophysiology, especially in nonapeptide regulators in the hippocampus. Studies in prairie voles suggest that central vasopressin receptor 1a (AVPR1a) expression and regulation is altered by parenthood and pair-bonding; however, this relationship is unexplored in primates and in the hippocampus specifically. We hypothesized that in biparental titi monkeys (Plecturocebus cupreus) AVPR1a binding would differ between male and female parents and non-parents in the hippocampus and other opportunistically-measured nearby brain regions. We further hypothesized that AVPR1a binding would predict affiliative behavior between pair mates and, among parents, the frequency of infant carrying. Brain tissue was obtained from 10 monkeys, and AVPR1a binding was determined using receptor autoradiography for 73 brain tissue sections (1-10 per subject). Affiliation between pair mates (Proximity, Contact, and Tail Twining behavior) and the frequency of infant carrying were determined from longitudinal observations (5-6 per day). Across all 17 regions assessed, parents had lower AVPR1a binding than nonparents, with the strongest effect sizes observed in hippocampal subregions (MANOVA: $F(1, 8) = 11.62$, $p = .017$, Pillai's trace = 0.94; Cohen's d for subregions ranged from 1.92 – 2.89). There were no sex differences and no associations with pair mate affiliation in any brain region. Infant carrying was negatively correlated with AVPR1a binding in the caudate head ($r = -0.94$, $p = .018$) and caudate tail ($r = -0.91$, $p = .031$). Our findings suggest that parenthood systematically decreases AVPR1a binding in titi monkeys, particularly in the hippocampus.

P2.21 USING NEXT-GENERATION SEQUENCING AND AAV-CRISPR/CAS9 TO IDENTIFY NON-CODING REGULATORY ELEMENTS IN THE PRAIRIE VOLE GENOME THAT INFLUENCE OXTR EXPRESSION

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Natural variation in oxytocin receptor (Oxtr) expression increases diversity in social behaviors within and across species. In the socially monogamous prairie vole (Microtus ochrogaster), variation in Oxtr expression in the nucleus accumbens (NAC) is associated with variation in pair bonding, alloparental behavior and resilience to neonatal social neglect. Previously, we found a set of intronic SNPs that largely explain individual variation of Oxtr expression in the NAC ($r2>0.7$). We are using ATAC-seq, RNA-seq and nanopore-seq to investigate if and how this SNP set affects the regulatory landscape of the Oxtr locus in the NAC. So far, we developed a bio-informatics pipeline to analyze genome-wide sequencing data in the prairie vole and found that ATAC peaks are highly enriched in the transcription start site of expressed genes ($P<0.00001$). We also identified multiple ATAC-peaks in the Oxtr locus in tissue taken from NAC and insular cortex, a brain area where the SNP set does not explain Oxtr expression. We are investigating if differential chromatin accessibility relates to variation in Oxtr expression. In addition, we have developed an AAV-CRISPR/Cas9 approach that disrupts the Oxtr coding sequence by introducing indels and significantly reduces OXTR binding (>80%). We are adapting this tool to displace putative transcription factors from their binding sites. By combining AAV-CRISPR/Cas9 and sequencing strategies, this project aims to identify and disrupt candidate regulatory regions of Oxtr expression and provide mechanistic insight in the individual variation of Oxtr expression and social behaviors.

P2.22 PROSTAGLANDIN F2A DRIVES REPRODUCTIVE FEMALE PHEROMONE SIGNALING THROUGH ITS METABOLIZATION

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Pheromones play essential roles in communication and reproduction in many species. In most fishes, prostaglandin F2α (PGF2α) acts as a female reproductive hormone, eliciting mating behavior in response to ovulation. Additionally, PGF2α acts as a sex pheromone to induce males' courtship in some species. Here, we use the African cichlid, Astatotilapia burtoni, to investigate the role of PGF2α in mediating female attractiveness and molecular mechanisms underlying pheromonal signaling between sexes. Our data reveal that adult males can distinguish gravid versus non-gravid females solely by olfactory cues. Interestingly, injection of the prostaglandin synthesis inhibitor, indomethacin, abolishes attractivity of gravid females. Though males are insensitive to PGF2α and three common metabolites, they exhibit strong preference for females injected with PGF2α. This attractiveness is independent of the PGF2α hormonal receptor Ptgfr, indicating this pheromone signaling derives from PGF2α metabolization, rather than acting as a hormone. We further discovered that only adult males, but not adult females or juveniles, showing preference for gravid female cues, and the gravid-female and PGF-injected female odors induce significantly more activation in male's olfactory epithelium, particularly in ciliated olfactory sensory neurons. These results show that PGF2α is necessary and sufficient to attract males. However, unlike zebrafish, PGF2α itself is not a pheromone to directly induce male preference in cichlids, but it plays a vital role in initiating physiological responses to prime females to become attractive. Further work to identify the pheromone candidates and the olfactory receptor(s) will highlight how an essential hormone activates an evolutionarily divergent pheromone signaling pathway.

P2.23 SEX DIFFERENCES IN THE TRANSCRIPTIONAL NETWORKS UNDERLYING PLAYFULNESS SUGGEST A DISTINCT FUNCTION FOR PLAY IN MALES COMPARED TO FEMALES

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Social play is a dynamic, well-conserved behavior known to be sexually differentiated; in most species, males play more than females, a sex difference driven by the medial amygdala (MeA). To investigate whether the transcriptional signatures underlying play also differ by sex, we performed RNA-sequencing of MeA samples from high- and low-playing juvenile rats of both sexes. Using Weighted Gene Co-expression Network Analysis (WGCNA), we identified 22 co-expression modules, or networks of genes highly correlated in expression. Of the 12 modules (for $p<0.05$) associated with play, almost all (~92%) are sex-specific in expression, correlating with expression of play in one sex only. These data suggest there is a distinct transcriptomic profile associated with playfulness in the MeA of males compared to females, a noteworthy finding given the MeA regulates many sex-typical adult behaviors. We propose this is no coincidence: play-associated gene networks in the MeA are sex-specific because play modulates circuitry driving different adult behaviors depending on sex. We created Plexiglass cage dividers to separate juvenile cagemates, hypothesizing that preventing play would result in sex-specific impairments in later-life behavior. Supporting our hypothesis, preventing juvenile play impaired object memory and copulatory behavior and resulted in a hypersocial phenotype in adulthood in males only. Surprisingly, we observed no effects in females. Future experiments will examine the effects of modulating expression of our identified sex-specific modules on juvenile playfulness and later-life behavior. Together, these analyses will provide novel insight into the ultimate function of play and how and why this may differ by sex.

P2.24 THE IMPACT OF PERIPARTUM ESTROGEN FLUCTUATIONS ON SLEEP ACTIGRAPHY AND NEUROPLASTICITY IN THE DORSAL RAPHE NUCLEUS IN SYRIAN HAMSTERS

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Pregnant and postpartum people report clinically-significant disruptions in sleep, but the role of peripartum hormone fluctuations in this sleep dysregulation is poorly understood. We used a hormone-simulated pseudopregnancy model in Syrian hamsters to test the role of peripartum estrogen fluctuations on sleep actigraphy and neuroplasticity in the dorsal raphe nucleus (DRN). Adult female hamsters were ovariectomized and then given daily hormone injections that approximate estrogen levels during and after pregnancy. 24-hour homecage video recordings were collected at 7 timepoints: twice before the initiation of hormone injections, twice during "early pregnancy," twice during "late pregnancy," and once during the "postpartum" period. At the conclusion of the experiment, subjects were sacrificed and their brains were processed for immunohistochemical localization of tryptophan hydroxylase (TPH), a marker of serotonergic

neurons, and FosB, a marker of long-term plasticity, in the DRN. High levels of estrogen during "late pregnancy" decreased cumulative duration of sleep and sleep efficiency, and increased locomotor behavior during the white light period. These differences persisted into the postpartum period for females who continued to receive estrogen, but not in estrogen-withdrawn females. In the DRN, FosB immunoreactivity was increased in estrogen-sustained females compared to oil-treated females, but did not differ from estrogen-withdrawn females. Interestingly, the total number of TPH/FosB double-labeled neurons was increased in estrogen-sustained females compared to both estrogen-withdrawn and oil-treated females. Together, these results suggest that high estrogen levels in late pregnancy disrupt sleep, but postpartum estrogen withdrawal may ameliorate these disruptions, possibly via plasticity in DRN serotonin neurons.

P2.25 DIFFERENCES IN FENTANYL-INDUCED BEHAVIORS AND GENE EXPRESSION IN C57BL/6J AND A/J MICE

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Drug overdoses are on the rise in America, particularly due to drugs like the synthetic opioid fentanyl. These changes in drug-related deaths on a national scale demonstrates the complex nature of addictive behaviors- there is significant contribution by environmental conditions, as well as a significant contribution by one's genes. The current study looks at the genetic factors associated with drug abuse by using two mouse strains- C57BL/6J and A/J. These mice were tested for the formation of conditioned place preference and locomotor activity in response to fentanyl. As expected, C57 mice displayed heightened conditioned locomotor activity after fentanyl injection, and formed a stronger conditioned place preference than A/J after four days of conditioning with fentanyl. Gene expression in response to either fentanyl or saline injection was examined with qPCR and RNA-seq. At least 5,000 genes were differentially expressed between the two strains in the Nucleus Accumbens, and a large number of these genes showed differences in expression depending on whether an animal was injected with fentanyl or saline. The expression of these genes, Glo1 and Sapcd1, was examined in the Nucleus Accumbens and the Prefrontal Cortex with qPCR. A/J mice showed higher expression of both of these genes in both regions, and mice treated with fentanyl showed reduced expression of Glo1 in the prefrontal cortex. These gene expression data suggest that drugs of abuse may significantly alter gene expression, and that these differences are dependent on other genetic factors.

P2.26 PRENATAL EXPOSURE TO BISPHENOL A, S, AND F EFFECTS ON MATERNAL CARE AND GENE EXPRESSION IN FIVE BRAIN REGIONS IN DAMS AND PUPS

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Gestational exposure to the endocrine disruptor bisphenol (BP) A alters offspring cognitive, emotional, and neural development. However, little research has investigated whether BPA alternatives (i.e. BPS and BPF) have similar effects despite wide and growing use in BPA-free products. We tested whether daily exposure to vehicle (corn oil; n=4), BPA (50ug/kg; n=3) or a mixture of BPs (BPA, BPS, and BPF 150ug/kg; n=4) from gestational day 8 through parturition affects maternal care and gene expression. BPA-exposure, but not mixed BPs, reduced nest attendance and time spent nursing on P1-10 ($p < .05$). Dams and pups were sacrificed at weaning

and tissue from five brain regions (prelimbic cortex, nucleus accumbens, hypothalamus, hippocampus, and amygdala) were laser-dissected for RNA-seq analysis. DESeq2 analysis identified seven differentially expressed gene (DEGs) across the five regions for the dam (adjusted $p<.05$). In pups, there were 2175 DEGs across five regions, including 1896 DEGs in the amygdala (adjusted $p<.05$). The top two factors from principal component analysis of the pup amygdala accounted for 24% and 51% of the variance respectively, with clear separation of the vehicle-exposed and bisphenol-exposed pups. Of the 1896 DEGs in the pup amygdala, 350 DEGs were identified in both the BPA and mixed BP groups, with complete agreement in directionality (80 genes upregulated, 270 down regulated). These findings show that gestational exposure to bisphenols affects postnatal maternal care and is accompanied by changes in gene expression, particularly in the pup amygdala, at least three weeks after BP exposure has ended.

P2.27 PREPUBERTAL OVARIECTOMY ALTERS DMS INDIRECT PATHWAY NEURON EXCITABILITY AND EXPLORE/EXPLOIT BALANCE IN FEMALE MICE

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Ovarian hormones are a potential mechanism by which decision-making circuits are modulated across life stage transitions and within reproductive cycles to meet changing environmental and physiological demands. Here we examined the influence of prepubertal ovariectomy (OVX) versus sham surgery on performance in an odor-guided multiple choice reversal task. We observed that compared to sham females, OVX females had a reduced tendency to perseverate during reversal learning that was reflected in a lower explore/exploit reinforcement learning parameter. To seek a neural correlate of this behavioral difference, we performed whole-cell patch clamp recordings within the dorsomedial striatum (DMS), a region implicated in regulating action selection and explore/exploit choice policy. We found that the intrinsic excitability of dopamine receptor type 2 (D2R) expressing indirect pathway spiny projection neurons (iSPNs) was significantly higher in OVX females compared to both unmanipulated and sham surgery females. Finally, to test whether mimicking this increase in iSPN excitability could recapitulate the pattern of reversal task behavior of OVX females, we chemogenetically activated DMS D2R+ neurons within intact female mice. We found that chemogenetic activation increased exploratory choice during reversal, similar to the pattern we observed in OVX females. Together, these data suggest that pubertal status may influence explore/exploit balance via the modulation of SPN intrinsic excitability within the DMS.

P2.28 INVESTIGATING THE ROLE OF CORTICOTROPIN-RELEASING HORMONE NEURONS OF THE BED NUCLEUS OF THE STRIA TERMINALIS IN THE REGULATION OF PAIR BOND FORMATION IN MALE AND FEMALE PRAIRIE VOLES

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Corticotropin-releasing hormone (CRH) is known for its function in stress neuroendocrinology, but it also influences motivated behaviors such as reward-seeking and social preference. In the prairie vole (Microtus ochrogaster), a socially monogamous rodent species, pharmacological manipulation of CRH receptor function in the brain can alter pair bond formation. Prior research has also reported increased levels of CRH mRNA expression in the bed nucleus of the stria terminalis (BNST)

in pair-bonded vs. sexually-naïve prairie voles. Since the BNST is a center for limbic information and valence monitoring, there may be a causative link between BNST CRHergic activity and pair bond formation. Here, we explore a direct link between BNST CRHergic activity and pair bond formation in male and female prairie voles. First, CRH protein content in the BNST was found to be significantly increased in both sexes following a 24-hour cohabitation with an opposite-sex mate, but not after a 6-hour cohabitation. This is intriguing as 24-hours of male-female cohabitation, but not 6-hours, is known to promote partner preference, an early indicator of pair bond formation in prairie voles. Furthermore, chemogenetic activation of BNST CRHergic neurons induced partner preference in males after only a 6-hour cohabitation with a female. Conversely, inhibition of BNST CRHergic activity led to a lack of partner preference in males after 24-hour cohabitation. Comparable chemogenetic experiments in females are still underway. These results provide more insight into the role of CRH in pair bond formation and add to the growing knowledge of the complex neurobiology underlying social connection.

P2.29 MEASURING MOTIVATION FOR JUVENILE SOCIAL INTERACTION IN A RAT MODEL OF NEUROPSYCHIATRIC DEVELOPMENTAL DISORDERS

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Rough-and-tumble play is conserved across mammalian juveniles, including humans, and is impaired in children with male-biased neuropsychiatric developmental disorders (NDDs) such as autism spectrum disorder. Because play is thought to be important to development of later life social skills, it is plausible that the disrupted play in NDDs contributes to the lasting social impairments common in these disorders. Our lab has employed a "two-hit" rat model of NDDs by combining two established risk factors: haploinsufficiency of the candidate gene Nrxn1a (Sprague Dawley-Nrxn1tm1sage) and early life inflammation induced by postnatal PolyI:C injection. Interestingly, previous work in the lab has demonstrated that the "two-hit" model results in impaired playfulness in juvenile males but not females. We hypothesize that these deficits arise from reduced motivation for social interaction. We have recently optimized a novel assay for assessing social motivation in juvenile rats and found no sex differences in the willingness to push through a door for access to a playmate, even though males play more intensely than females. However, there was a positive correlation between the number of door entries and the number of play behaviors in males but not females, suggesting motivation for social interaction may be more closely related to playfulness in males. Thus, we predict that the "two-hit" model of NDDs will reduce the motivation for social interaction in juvenile males but not females. This work provides insights into the origin of the lasting social deficits central to male-biased NDDs and was supported by R01DA039062 to MMM.

P2.30 HIGH ESTRADIOL REDUCES ADULT NEUROGENESIS AND ALTERS FUNCTIONAL CONNECTIVITY WITHIN THE HIPPOCAMPUS DURING SPATIAL PATTERN SEPARATION

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Adult neurogenesis in the dentate gyrus (DG) plays an important role for pattern separation, the process of separating similar input and forming distinct neural representations. Our previous work demonstrated that there were sex differences in the ability for spatial pattern separation favouring male rats, which corresponded to greater adult neurogenesis in the DG of males. Here, we examined estrogenic regulation of adult neurogenesis and functional connectivity in the hippocampus after spatial pattern separation task in female rats. Ovariectomized Sprague-Dawley rats received daily injections (vehicle, low and high dose of estradiol benzoate) for 28 consecutive days (From day 0). A single bromodeoxyuridine (BrdU) was injected on day 1 and rats were tested in the spatial pattern separation paradigm for 14 days beginning on day 14 after BrdU. Rats were tested in a delayed nonmatching to place with radial 8-arm maze (RAM). Rats were perfused 90 minutes after the final trial and brain sections were immunohistochemically stained for BrdU, the mature neuronal marker, NeuN and the immediate early gene, zif268. High estradiol reduced the density of BrdU/NeuN double-labelled neurons compared to oil treated female rats, whereas there was no significant effect on the ability for separating similar patterns in RAM between groups. Furthermore, high estradiol altered the inter-regional correlations of zif268 expression between DG and CA1, and between CA3 and CA1. In conclusion, chronic administration of estradiol benzoate reduced adult neurogenesis in a dose dependent manner in the dentate gyrus, and altered functional connectivity in the hippocampus during pattern separation.

P2.31 COMPARING THE EFFICIENCY OF CELL-TYPE SPECIFIC AND UBIQUITOUS PROMOTERS IN TRANSDUCING OXYTOCIN AND VASOPRESSIN NEURONS

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Recent technological advances in viral vectors and the development of transgenic rodent models have allowed for targeted gene expression to study the functions of specific cell populations and brain circuits. Studies concerning the hypothalamic oxytocin (OXT) and arginine-vasopressin (AVP) systems have begun to utilize these advanced methods to further characterize their roles across a range of physiological and behavioral functions. However, the efficacy of widely used viral constructs has not yet been systematically evaluated in these neural populations. Here, we injected viral vectors of different promoter and serotype combinations into the paraventricular nucleus of the hypothalamus in rats and mice then performed immunohistochemistry to determine specificity. We found that (1) ubiquitous promoters were not, on their own, effective at driving expression of a down-stream fluorescent protein in OXT or AVP neurons, (2) the OXT promoter efficiently drove gene expression in OXT neurons and this efficiency was attributable to the promoter and not the viral serotype, and (3) using a Cre recombinase-dependent system, in combination with a virus that expresses Cre recombinase under the control of OXT promoter, significantly improved the efficiency of viral transduction in OXT neurons. Finally, we demonstrate the utility of the OXT promoter for conducting circuit tracing studies to identify inputs to OXT neurons in mice by using a novel modified rabies virus system with specificity to OXT neurons. We conclude that extreme caution is needed when employing non-neuron-specific viral approaches/promoters to study neural populations within the hypothalamus.

P2.32 LIPOPOLYSACCHARIDE STIMULATES REGION-SPECIFIC GLUCOCORTICOID PRODUCTION IN THE NEONATAL MOUSE

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Altricial species, such as mice, rats, and some birds, exhibit a stress hyporesponsive period (SHRP) in early life, characterized by low circulating glucocorticoids (GCs) and a greatly reduced response to stressors. In mice, during the SHRP, specific brain regions have higher corticosterone levels than blood, suggesting local production. Lipopolysaccharide (LPS) (i.e., endotoxin) elicits an adrenal GC response during the SHRP, but it is not known how LPS affects local GC levels in specific brain regions. We administered LPS (50µg/kg, i.p.) or vehicle (n=12/group) to C57Bl/6J mice within the SHRP (day 5) and collected blood and brain microdissected brain (prefrontal cortex, hippocampus, hypothalamus, amygdala) after 4hr. We measured a panel of GCs in the blood and brain regions via liquid chromatography tandem mass spectrometry (LC-MS/MS). In the same animals, we quantified brain mRNA levels of key steroidogenic enzymes via RT-qPCR. LPS increased GC levels in blood and brain. However, corticosterone levels were lower and dehydrocorticosterone levels were higher in the prefrontal cortex compared to blood. Alternatively, corticosterone levels were higher and dehydrocorticosterone levels were lower in the amygdala compared to blood. Accordingly, LPS animals had greater Hsd11b2 transcript levels in the prefrontal cortex, and greater Hsd11b1 transcript levels in the amygdala, compared to controls. These data suggest that specific brain regions actively modulate local GC levels independently of each other, rather than simply being passive recipients of systemic corticosterone. Local GC production may provide a mechanism by which endotoxins can exert region-specific effects on brain development.

P2.33 CHANGES IN PUP-INDUCED NEURAL ACTIVATION WITHIN THE MATERNAL NEURAL CIRCUIT ACROSS EXPERIENCE

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Although naïve virgin female B6 mice spontaneously respond to pups in a familiar environment, they are not motivated enough to care for pups in a challenging environment. However, experienced (2hours/4days) virgin mice even under challenge come to display postpartum-like maternal motivation that persists one month later. We have reported that experience-dependent increases in maternal motivation are associated with higher relative immediate early gene (IEG) expression in a neural region that regulates maternal motivation (ventral tegmental area) and lower expression in regions that regulate pup avoidance (anterior hypothalamus/ventromedial nucleus). We hypothesize that the maintenance of care is mediated by stable alterations of neural activity patterns within circuits regulating care or avoidance. Here, we use the Fos Targeted Recombination in Active Populations 2 (FosTRAP2) model to investigate whether the same cells within regions across the maternal neural circuit are activated in response to pups as female mice transition from pup-naïve to pup-experienced. In this model, a tamoxifen-inducible Cre recombinase downstream from a cFos promoter drives red fluorescent reporter expression. Thus, cells that are activated around the time that tamoxifen is present are permanently labelled with a

red signal. Naïve virgin female mice were injected with tamoxifen following a brief exposure to pups to label cells initially responsive to pups. Females were then euthanized following repeated experience with pups and a cFos assay was used to examine experience-dependent cell activation in response to pups. Colocalization analyses were performed to determine the overlap in cellular activity associated with maternal experience.

P2.34 LPS INDUCES ENDURING HYPOTHALAMIC KISS1 AND KISS1R DOWNREGULATION IN PUBERTAL, BUT NOT ADULT MALE AND FEMALE MICE

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Pubertal stress causes enduring impairments in sexual behavior in males and females, but the underlying mechanism remains unknown. Previous findings show that stress exposure downregulates the HPG axis, particularly by inhibiting the production and release of the neuropeptide kisspeptin (Kiss1) and by downregulating its receptor (Kiss1R). While acute changes in Kiss1 and Kiss1R have been observed following stress, it is unclear whether these changes are still present beyond the pubertal period. The current study investigated the sex-specific acute and enduring consequences of the bacterial endotoxin lipopolysaccharide (LPS) on Kiss1 and Kiss1R mRNA expression in pubertal and adult mice. Six-week (pubertal) and 10-week old (adult) male and female mice were treated with either saline or LPS. Mice were euthanized either at 8 hours or at 4 weeks following treatment. Pubertal and adult male and female mice treated with LPS displayed a decrease in hypothalamic Kiss1 and Kiss1R mRNA expression 8 hours following treatment. However, only male and female mice treated with LPS during puberty displayed a decrease in hypothalamic Kiss1 expression 4 weeks following treatment. Males treated with LPS during puberty also displayed a decrease in in hypothalamic Kiss1R expression 4 weeks following treatment. Our findings suggest that exposure to stress during puberty can cause enduring impairments in sexual behavior by permanently inhibiting specific components of the HPG axis. Furthermore, this work highlights the importance of considering sex- and age-related differences in the investigation of the long-term effects of stress.

P2.35 GENITAL PAPILLA MORPHOGENESIS IN GRAVID FEMALE BLUEBANDED GOBIES, LYTHRYPNUS DALLI

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Female genitalia have been largely neglected in studies of genital evolution, perhaps due to the long-standing assumption that they are relatively invariable and therefore taxonomically and evolutionarily uninformative in comparison with male genitalia. Here, we investigated this idea in Lythrypnus dalli, a bidirectionally hermaphroditic fish, that exhibits complex and sexually dimorphic reproductive behaviors. The external genital papilla (GP) undergoes dramatic morphogenesis concurrent with physiological changes associated with sex change. Males have a longer, tapered GP with length:width ratio (L:W) >1.6, female to male transitioning fish have a conical GP with L:W 1.4-1.6, and females have a L:W <1.4. In this study, we hypothesized that the variation in female GP shape is associated with the gravidity state of females. We investigated the GP L:W of sexually

mature female L. dalli of variable sizes (N=250). The standard length of fish was not related with gravidity; thus smaller fish were gravid as larger fish. There was an inverse relationship between GP L:W and gravidity, such that a wider GP was associated with more gravid females. We categorized the shape of GP as 'rounded' if they were not gravid versus 'rectangular' for gravid fish. It is possible that a wider morphology allows for a more efficient release of mature vitellogenic eggs. Interestingly, we also discovered females whose GP had a 'tubular' appearance; these could be fish that have recently transitioned from male to female. Differences in steroid hormone sensitivity via receptor expression might underlie morphological changes in GP in gravid females.

P2.36 TESTOSTERONE AND ITS METABOLITES RAPID MODULATE SOCIAL RECOGNITION AND AGGRESSION IN MALE MICE, POSSIBLY IN INTERACTION WITH VASOPRESSIN IN THE BED NUCLEUS OF THE STRIA TERMINALIS

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Androgens are involved in the regulation of social recognition (SR) and aggression. The effects of testosterone (T) on SR are often mediated by estrogenic action, including those mediated by rapid mechanisms. T regulates the vasopressin (AVP) system which includes highly sexually differentiated brain regions, such as the bed nucleus of the stria terminalis (BNST) which shows more AVP neurons in males than in females. The AVP/androgen (and estrogen) interplay impacts social behaviors with mechanisms currently poorly understood. To elucidate the rapid, non-genomic, effects of androgens and estrogens on AVP neurons in the BNST, adult castrated male mice were intracerebrally infused with T, or its metabolites 17β-estradiol (E) or dihydrotestosterone (DHT). Mice were then exposed to a 'difficult' SR paradigm, in which castrated mice showed an impairment, and to a resident-intruder (RI) paradigm to assess aggression at either 35- or 120-min post-infusion to evaluate rapid and long-lasting effects. Results revealed that infusing T, E, or DHT facilitates SR, with male mice spending more time investigating a novel over a familiar castrated mouse, with an inverted U-shaped dose-response. In addition, T infusions did not elicit overt aggression towards the intruders, but mice receiving the highest doses of T showed a higher dominance score with long-lasting effects after 120 min. Intriguingly, also E and DHT increased the dominance score at 35 min and 120 min too. Elucidating the AVP-sex hormones interaction could lead to new therapeutic approaches for psychopathologies of social behavior with strong sex difference as autism spectrum disorder.

P2.37 THE INTERPLAY OF ESTROGEN AND OXYTOCIN RECEPTORS RAPIDLY MEDIATES SOCIAL RECOGNITION

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Estrogens and oxytocin (OT) have been found to affect social behaviours, such as social recognition (SR). For example, 17b-estradiol (E2), estrogen receptor (ER) agonists, or OT administered systemically or into various brain regions facilitates SR, whereas gene knock outs in mice of ERs, OT, or the OT receptor block SR. These findings suggest both estrogens and OT are needed for SR and therefore could be interacting. We have shown this interaction, finding E2 infused into the paraventricular nucleus of the hypothalamus (PVN), a region of OT production, rapidly facilitates SR

and a subeffective dose of an OTRA in the MeA blocks this facilitation. We currently aim to determine which ER is mediating the interplay with the OTR. Both the G-protein coupled ER (GPER) and ER beta (ERb) are highly expressed in the PVN, so one or both ERs could be mediating this interplay. We infused agonists for GPER (G1) or ERb (DPN), and found that both were able to rapidly facilitate SR. Currently, we are infusing G1 or DPN into the PVN as well as the subeffective dose of the OTRA into the MeA to see if the rapid facilitation SR caused by either is blocked. Preliminary results show that the OTRA blocks the rapid facilitation of SR by G1 but not DPN. This would suggest that the interplay between estrogens and OT is mediated by GPER and not ERb.

P2.38 IDENTIFYING A ROLE FOR LACTOGENIC HORMONES IN MATERNAL MOTIVATION IN MICE

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Maternal behaviour is essential for offspring survival in mammals. Lactogenic hormones are important regulators of this behaviour, acting through prolactin receptors (PRLR) in the medial preoptic area (MPOA) in the brain. The mechanism by which lactogenic action in this region induces maternal behaviour is unclear. Since MPOA neurons project to and activate reward-processing regions, we hypothesised that lactogenic hormones promote maternal behaviour by activating the reward circuitry to lead to pup-induced motivational and reward behaviour. To study this, we first characterised these behaviours in female mice of different reproductive states, using three testing paradigms. Virgin and pregnant, but not lactating mice developed a preference for pup-associated contexts in a conditioned place preference (CPP) test. In contrast, in a T-maze or barrier climbing test, only lactating females showed full motivation to retrieve pups. In reproductively experienced females, maternal motivation declined over time after weaning of pups. Reproductive state thus differentially affects pup-related reward learning and motivation, with specific behavioural tests distinguishing maternal from non-maternal mice.
Subsequently, we tested whether conditional deletion of PRLR from GABA neurons disrupted pup-related reward and motivation behaviours. While both knockout and control animals developed a preference for pup-associated contexts in the CPP, GABA neuron specific PRLR knockout mice showed incomplete and slower pup retrieval behaviour in the T-maze compared to controls. Together, these findings imply that pup-related reward learning in the CPP test appears independent of the action of lactogenic hormones, while lactogenic action specifically on GABA neurons is required for full maternal motivation.

P2.39 SOCIAL BEHAVIOR IN GROUPS OF CATS AND THE EFFECTS OF ENVIRONMENTAL TEMPERATURE.

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Cats are naturally solitary animals, but nowadays they have come to live in groups with humans. We have reported the negative correlations between cortisol, food sharing, and contact behavior, and between oxytocin and contact behavior in group-living cats. Thermoregulation by social contact is one of the basic functions of group formation, and both cortisol and oxytocin have a thermogenic function. Therefore, we hypothesized that environmental temperature changes hormone secretion

and social behavior in group-living cats. Under two temperature conditions, 20 and 26°C, we collected cats' urine in the morning and analyzed urinary oxytocin and cortisol levels along with their behavior, and body weight and temperature were measured as well. Under 26℃ condition, urinary cortisol concentration was higher and there were positive correlations between oxytocin and sniff, and between cortisol and play, and negative correlations between body weight and both grooming and entering bed. On the other hand, under 20℃ condition, food sharing, entering bed, and following behavior increased and there were positive correlations between oxytocin and sniff, and between body temperature and follow, entering bed, and food sharing. These results suggested that social behavior was more susceptible to temperature changes than endocrine changes. The social behaviors that increased with decreasing environmental temperature were considered to be a response to temperature changes. Since these behaviors correlated with body temperature, it was suggested that body temperature was one of the causal factors for behavioral changes related to maintaining the body temperature.

P2.40 CONTRIBUTIONS OF PERIPUBERTAL GONADAL STEROIDS ON THE DEVELOPMENT OF STEROID-INDEPENDENT SOCIOSEXUAL BEHAVIOR IN THE B6D2F1 HYBRID MALE MOUSE

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In rodents, gonadal steroids during the perinatal and peripubertal periods play both organizational and activational roles in adult sociosexual behavior. Adult sexual behavior is generally contingent on steroidal activation, as castration typically causes a reduction or cessation of male sexual behavior. However, approximately one third of B6D2F1 hybrid male mice retain sexual behavior long term after castration ("maters"). We investigated the organizational role of pubertal steroids in this model of steroid-independent activation. On the day of weaning, animals were prepubertally castrated or underwent sham surgery and implanted with testosterone-filled or empty Silastic capsules. Capsules were removed and sham males were castrated in adulthood. Exposure to gonadal steroids during puberty was necessary for steroid-independent male sexual behavior, but there were no differences in mater phenotype between animals that underwent puberty intact or with replacement testosterone ($p = 0.43$). Next, males were tested in a 3-chamber arena. Neither treatment group nor mater status predicted steroid-independent sexual partner preference ($p > 0.2$). Finally, we measured c-Fos activation in the mPOA and MeA following home cage exposure to an estrous female. There were no differences among groups in the mPOA ($p > 0.3$). In the anterior medial amygdala, prepubertally castrated males had significantly more c-Fos positive cells compared to males that underwent puberty intact ($p = 0.04$). Our data suggest that pubertal exposure to testosterone may be necessary for the mater phenotype to emerge. We hypothesize that both mater phenotype and pre-castration sexual experience may be necessary for steroid-independent sexual partner preference.

P2.41 CONSERVED ABILITY FOR EMOTION RECOGNITION

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The recognition of emotional states enables their sharing, which forms the basis of human empathy. Yet the neurocognitive origins of this ability remain unknown. This question regards a crucial shift in social cognition from the perception to the interpretation of behaviour in others. We tested the conservation of this ability using a zebrafish model. We identified the transmission of fear behaviour and reveal that, similar to humans, it is modulated by oxytocin-like projections to the forebrain. We also demonstrate that this process is regulated by the recognition of the fearful state and followed by preferred interaction towards fearful others. This evidence provides face, construct and content validity to a model of fear recognition in an evolutionarily distant vertebrate.

P2.42 ACUTE ADMINISTRATION OF SEROTONIN-ACTIVE DRUGS MODULATES SOCIAL AVOIDANCE IN MALE AND FEMALE SYRIAN HAMSTERS

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Social stress is the most common stressor experienced by humans and is associated with many neuropsychiatric disorders, such as post-traumatic stress disorder (PTSD) and depression. Recently, it has been hypothesized that agonistic behaviors related to dominance (e.g., aggression) are associated with stress resistance. Because serotonin increases dominant behaviors in females and decreases them in males, we hypothesized that serotonin signaling would increase social avoidance in socially defeated males and decrease avoidance in defeated females. Using a conditioned defeat model in Syrian hamsters, we found, as predicted, that an acute dose of the selective serotonin reuptake inhibitor (SSRI), fluoxetine (20 mg/kg), increased social avoidance in defeated males, while an acute dose of the tryptophan hydroxylase (rate limiting enzyme in serotonin synthesis) inhibitor, para-chlorophenylalanine (PCPA; 100 mg/kg), increased social avoidance in defeated females. However, contrary to our hypothesis, the acute dose of fluoxetine also increased social avoidance in defeated females, while the acute dose of PCPA did not impact avoidance in defeated males. These data indicate that there may be a sex difference in the effects of endogenous serotonin activity on behavioral responses to social stress, and suggest that treatment with an SSRI immediately following trauma exposure in humans could contribute to PTSD symptomology in both males and females.

P2.43 SOCIAL STATUS MEDIATED VARIATION IN HYPOTHALAMIC TRANSCRIPTIONAL PROFILES OF MALE MICE

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The establishment and maintenance of social dominance relationships requires individuals to integrate external social information with internal states to adapt their behavior and physiology to the current social context. Here we present the effect of social status and corticosterone levels on the global transcriptome expression of alpha, beta and subordinate male mice living in large social hierarchies using tag-based RNA sequencing. Specifically, we analyzed the transcriptomes of two brain regions involved in hormonal signaling and the regulation of social behavior - the ventromedial region and arcuate nucleus of the hypothalamus (VMH/ARC) and medial preoptic area

(mPOA). In VMH/ARC, we observed significant downregulation of genes involved in food intake and energy expenditure regulation in dominants. Interestingly, not only orexinergic genes (Npy and Agrp) but also anorexic genes (Pomc) were downregulated. Additionally, Npy expression showed a positive association with plasma corticosterone in subordinate mice. We further identify the Galanin (Gal) gene as a hub gene driving status-specific gene expression in the hypothalamus. In mPOA, beta males showed distinct up- or down-regulation compared to alpha and subordinate males in genes known to modulate social behaviors (e.g. Oxt, Npy, Nos1). Coupled with our previous behavioral findings, these results suggest that animals plastically shift the expression of neuroendocrine-related genes to support their status-specific physiological and behavioral needs.

P2.44 OVARIECTOMIZED MICE EXHIBIT AMPLIFIED EXPRESSION OF HIPPOCAMPAL IL6 AND SICKNESS BEHAVIORS AFTER AN IMMUNE CHALLENGE

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Estrogen deficiency in women is linked to a heightened susceptibility to the development of mood disorders. Estrogens may exert neuroprotective effects by inhibiting the inflammatory responses caused by microglia, the primary immune cell in the brain. Our objective is to determine the neuroimmune mechanisms through which estrogen deficiency heightens neuroinflammatory responses. C57BL/6 mice underwent either a bilateral ovariectomy (OVX) or sham operation and received estradiol (E2) replacement or vehicle of sesame oil. After a month, mice were injected with saline or lipopolysaccharide (LPS) to stimulate an immune response. Our results indicate that OVX mice displayed amplified sickness responses in the sucrose preference test that were rescued by E2 replacement. OVX mice also had exacerbated expression of the pro-inflammatory cytokine interleukin 6 in the hippocampus after an immune challenge. Microglia morphological analyses demonstrated an increase in soma perimeter and decrease in circularity following LPS, but these features were not regulated by estrogens. These results suggest that estrogen loss may contribute to exaggerated neuroimmune responses, raising vulnerability to adverse affective-related behavioral changes.

P2.45 THE EFFECTS OF ETHINYL ESTRADIOL AND LEVONORGESTREL ON DENDRITIC SPINE DENSITY IN THE HIPPOCAMPUS OF FEMALE RATS.

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Hormonal contraceptives are widely used but little is known about their effects on the brain. Two compounds frequently used in hormonal contraception are ethinyl estradiol (EE), levonorgestrel (LNG), or a combination of the two. Although some studies have looked at the cognitive effects of these compounds in female rats, very few have examined their effect on neuroplasticity. Over the course of 21 days, 13 intact Long-Evans Female rats received daily subcutaneous injections of either 10ug/kg EE alone, 20ug/kg LNG alone, combined EE and LNG, or sesame oil control. The brains of these rats were cryosectioned and stained using a Golgi-Cox stain. Hippocampal sections were then analysed under a microscope using Neurolucida software to count dendritic spine density. Spines were categorized as being either mature (>0.6 μm in diameter) or immature (< 0.6 μm) . Preliminary results (n = 3/group) show that EE increased total spine density (both alone and in combination with LNG). LNG alone (but not in combination with EE) increased only mature

spine density. Both EE alone and LNG alone (but not in combination) increased the proportion of mature spines to total spines. These data show that EE and LNG affect dendritic spine density in the hippocampus of female rats and have implications for the effects of hormonal contraceptives on learning and memory.

P2.46 THE EFFECTS OF THE CONTRACEPTIVE HORMONES ETHINYL-ESTRADIOL AND LEVONORGESTREL ON MAZE ACQUISITION AND NAVIGATION STRATEGY IN FEMALE RATS.

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Synthetic hormones, such as ethinyl estradiol (EE) and levonorgestrel (LNG), have been used for over half a century alone or in combination as hormonal contraceptives. Yet, despite their widespread use, very few studies have examined their effects on cognition using animal models. During 21 days of maze training, a total of fifty-three Long-Evans female rats received daily subcutaneous injections of either 10ug/kg EE alone (n=14), 20ug/kg LNG alone (n=13), or both (EE+LNG; n=14) and tested on day 21. Rats in the control condition (NC; n=12) received daily subcutaneous sesame oil injections and were tested during diestrus (confirmed by vaginal lavages) after at least 21 days of training. Maze acquisition speed and navigation strategies were assessed using a dual-solution plus-maze task. Rats treated with EE+LNG reached testing criterion in significantly fewer days than those in any other condition. Rats treated with EE or LNG alone showed a bias for the hippocampal-based place memory, while those receiving EE+LNG in combination were biased toward the used of response memory which is mediated by the dorsal striatum. This finding is another indication that EE and LNG taken together may act differently than when either is administered on its own. Overall, we have shown that the effects of EE and LNG when combined on maze acquisition and navigation strategy that are different from what is observed when each hormone was administered on its own.

P2.47 SEX DIFFERENCES IN AGE-RELATED MEMORY DEFICITS AND INFLAMMATORY PROFILE FOLLOWING A LIPOPOLYSACCHARIDE INDUCED IMMUNE CHALLENGE.

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Aging is a major risk factor for cognitive decline. Neuroinflammation, which can contribute to cognitive decline, is modulated in aged individuals. Biological sex is shown to impact the onset and severity of various neurodegenerative diseases that involve neuroinflammation. Here we determined the impact of aging and sex on cognitive function and inflammatory profile in rats following a lipopolysaccharide (LPS) immune challenge. Young adult (3 month) and aged (24 month) male and female F344xBN rats received an intraperitoneal injection of 40µg of LPS or vehicle (saline) and then were trained and tested in a contextual fear conditioning paradigm 2 and 4 days later, respectively. LPS exposure led to a reduction in freezing in aged male rats as compared to young LPS males and age matched saline controls, indicating an immune challenge induced sustained impairments in contextual memory. In contrast, no significant change in freezing behavior occurred in aged females relative to age matched saline controls nor young adults.

Differences in cognitive function may relate to neuroinflammatory changes induced by microglia: microglia isolated from the hippocampus of aged male but not female rats exhibit exaggerated pro-inflammatory cytokine responses to ex vivo LPS challenge. Moreover, aged male but not female rats exhibit potentiated hippocampal IL-1β mRNA 6, 24, and 48h following LPS exposure. These results suggest aged male rats are at higher risk for cognitive dysfunction following neuroimmune challenge versus females. Ongoing investigation will further determine the mediating mechanisms underlying this age-related sex difference in behavior.

P2.48 CHARACTERISING THE NEUROENDOCRINE AND MOLECULAR BASIS OF SEASONAL VARIATION IN ENERGY REGULATION IN MALE SIBERIAN HAMSTERS.

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Seasonal animals exhibit robust, regulated changes in energy stability. An endogenous annual timer functions to optimize seasonal programs in energetic state to survive harsh winters and anticipate the future breeding climates. This study investigated the molecular, neuroendocrine and behavioral programs that control seasonal rhythms in energy regulation. Using male Siberian Hamsters, locomotor activity, food intake, body and adipose tissue mass, plasma insulin and the pituitary transcriptome was examined monthly across a photoperiod-induced seasonal cycle. Short winter-like photoperiods decreased food intake (23%), body mass (20%), epididymal adipose tissue mass (67%) and plasma insulin (71%). After 20 weeks of short days, these behavioral and physiological measures initiated a return to the long summer-like day conditions. A transient increase in locomotor activity occurred 8 weeks of short days. Plasma insulin concentrations were significantly reduced after 16 and 20 weeks of short days compared to the long day controls. RNA-sequencing of pituitary tissue identified 1343 differentially expressed genes. Gene ontology analysis revealed diverse functions of these transcripts, including axonogenesis and GTPase mediated signaling. Prolactin and insulin receptor were two genes that preceded the endogenous circannual programmed change in body mass, food intake and plasma insulin. These findings suggest that pituitary prolactin may be a neuroendocrine marker for seasonal programs in energy regulation. Future work aims to characterize the link between prolactin signaling and the well characterized neuroendocrine peptides involved in short term energy regulation.

P2.49 DIFFERENTIAL EXPRESSION OF PNNS AND OTX2 FOLLOWING TRAUMATIC BRAIN INJURY IN ADULT ZEBRA FINCHES

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Following TBI, a wide array of neurodegenerative symptoms occur including increased prevalence of mood disorders, post-traumatic epilepsy, and memory problems. Some of these can be attributed to disruption of regulatory pathways involving parvalbumin (PV), perineuronal nets (PNNs), and Orthodenticle Homeobox 2 (Otx2), all of which work together to maintain neuronal health and play a role in structure development and critical learning periods. Chondroitin sulfate proteoglycans (CSPGs) are key components to PNNs and play an important role in axon growth inhibition. Thus understanding their expression following injury, may play a role in discovering

therapies that may enhance axon repair. Additionally, Otx-2's presence during sensory learning periods, specifically auditory and ocular development, has been shown to be more effective in forming complex patterns of sensory reception and output due to their protection of PV+ neurons. Studies have also shown a loss of Otx2 following TBI results in loss of cortical inhibition associated with the neurodegenerative symptoms mentioned prior. This study serves to evaluate the more acute response of specific CSPGs (neurocan, brevican, aggrecan) and OTx2 following injury in adult Zebra Finches (ZF). Adult ZFs underwent an unilateral hemispheric brain injury and using qPCR, mRNA expression was measured at 2 time-points following injury (24 h and 1 week) in males and females. The results showed a significant decrease in OTx2 at 24 hours, and in neurocan at 1 week following TBI, but no change in aggrecan. Interestingly, brevican had an overall sex difference, but was not altered by injury.

P2.50 PRENATAL ANDROGEN TREATMENT DOES NOT ALTER THE FIRING ACTIVITY OF ARCUATE KISSPEPTIN NEURONS

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Neuroendocrine control of reproduction is disrupted in many individuals with polycystic ovary syndrome, manifested as increased luteinizing hormone (LH), and presumably gonadotropin-releasing hormone (GnRH), release frequency, and high androgen levels. Prenatal androgenization (PNA) recapitulates these phenotypes in primates and rodents. Offspring of mice injected with dihydrotestosterone (DHT) on gestational d16-18 exhibit disrupted estrous cyclicity, increased LH and testosterone, and increased GnRH neuron firing rate as adults. PNA also alters the developmental trajectory of GnRH neuron firing rates, markedly blunting the prepubertal peak in firing that occurs in 3wk-old controls. GnRH neurons do not express detectable androgen receptors and are thus probably not the direct target of DHT. Rather, PNA likely alters GnRH neuronal activity by modulating upstream neurons, such as hypothalamic arcuate neurons expressing kisspeptin, neurokinin B, and dynorphin, aka KNDy neurons. We hypothesized PNA treatment changes firing rates of KNDy neurons in a similar age-dependent manner as GnRH neurons. We conducted targeted extracellular recordings (0.5-2h) of Tac2-identified KNDy neurons from control and PNA mice at 3wks of age and in adulthood. About half (53%) of neurons were quiescent (<0.005Hz). Firing rates of active cells varied, suggestive of episodic firing, but rates were not different among groups. Based on our findings, we reject the hypothesis that PNA alters the firing rate of KNDy neurons. This does not preclude changes in gene expression leading to altered neurosecretory output of KNDy neurons, involvement of other neuronal populations, or in-vivo networks as critical drivers of altered GnRH firing rates in PNA mice. P50HD028394

P2.51 STRUCTURAL SEX DIFFERENCES IN THE VENTRAL PALLIDAL VASOPRESSIN SYSTEM MAY BE ASSOCIATED WITH THE SEX-SPECIFIC REGULATION OF SOCIAL PLAY BEHAVIOR IN JUVENILE RATS

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Vasopressin (AVP) signaling in the ventral pallidum (VP) regulates adult social behaviors such as pair-bonding and sociosexual motivation. However, the role of intra-VP AVP signaling in regulating juvenile social behaviors, such as social play behavior, is unknown. In this study, we first examined the structure of the intra-VP AVP system in juvenile rats and found multiple sex differences, with denser AVP-immunoreactive fibers and vasopressin 1a receptor (V1aR) binding in males compared to females, but a greater number of v1aR+ cells in females compared to males. However, when we examined AVP inputs to the VP originating from the bed nucleus of the stria terminalis (BNST), we found no sex differences in the number of avp+ cells in the BNST or in the proportion of VP-projecting BNST avp+ cells. Next, in order to determine the functional role of intra-VP AVP signaling in regulating social play behavior, we first investigated whether exposure to social play altered recruitment of VP v1aR+ cells and then we tested the causal involvement of intra-VP AVP signaling by infusing a specific V1aR antagonist into the VP prior to social play exposure. We found that exposure to social play enhanced recruitment of VP v1aR+ cells in males only. However, V1aR blockade in the VP increased social play duration in males but decreased social play duration in females compared to same-sex control groups. Together, these findings suggest that structural sex differences in the VP-AVP system are associated with the sex-specific regulation of social play behavior.

P2.52 CHRONIC STRESS & METABOLISM IN FEMALES: EVALUATING TWO NOVEL MODELS OF FEMALE SOCIAL DEFEAT STRESS

Andrea Smith, Lindsay Hyland, Bethany Watts, Hiyam Al Ansari, Miski Dahir, Aleyna Akgun, Zachary Silver, Alfonso Abizaid
Department of Neuroscience Carleton University

Social defeat is a preclinical model to study the effects of chronic psychosocial stress in rodents, as it recapitulates many stress-induced pathologies observed in humans, including metabolic changes. This model, however, is based off male territorial aggression that is not applicable to female rodents. To investigate how females respond to psychosocial stress, we tested two adaptations to the social defeat paradigm to study the effect of chronic stress on metabolism in females. In the first paradigm, fighting females, a female and castrated male CD-1 are cohoused for several days, priming the CD-1 female to display territorial behaviors towards an intruding C57 female mouse. In the second paradigm, non-discriminatory social defeat, we introduced a C57 male and female simultaneously to a CD-1 male mouse. The intruding male provokes territorial aggression towards both the male and female mice. We tested both paradigms for 21-days and gave mice access to chow and a high fat diet, ad lib. Females in the non-discriminatory model displayed changes to hormone levels and metabolism commonly associated with chronic stress. These mice increased their consumption of the standard chow diet, high in carbohydrates, when stressed and had elevated ghrelin and corticosterone levels. Females from the fighting female's paradigm, however, did not display the same markers of chronic stress. Our results highlight discrepancies in the magnitude of stress elicited by each paradigm, with the second paradigm inducing metabolic changes in females commonly observed in males following social defeat.

P2.53 EFFECTS OF THE ESTROUS CYCLE ON VALUE-BASED DECISION-MAKING AND DOPAMINERGIC SIGNALING

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Center for Neural Science, New York University

Value-based decision-making behavior varies across the reproductive cycle in women, but the underlying neural mechanisms of these effects are not well-understood. In reinforcement learning models of decision-making, a subject learns the value of an option from experience and updates that value based on reward prediction errors (RPE), or the difference between what was expected and what actually happened. Dopamine released in the nucleus accumbens core (NAcc) represents RPEs. Estradiol and progesterone activate dopaminergic signaling, suggesting that this modulation may be responsible for the influence of the reproductive cycle on value-based decision-making. We examined value-based decision-making in female rats over their estrous cycle with a novel task wherein they deliberate between waiting for an unspecified amount of time for a reward or moving on to the next trial. The length of time they wait provides an analog readout of subjective value. We manipulated rats' reward expectations over trials by varying the magnitude of rewards they recently received (local reward context). During estrus, rats' subjective value is more sensitive to local reward context. Using a behavioral model, we also found that they have greater learning rates, where they update their estimate of the local reward context from RPEs faster. Mass spectrometry identified the downregulation of two proteins related to dopamine reuptake in the NAcc during estrus. Using fiber photometry and a dopamine sensor, we further observed enhanced dopamine availability aligned to reward-predictive cues. Altogether, these findings suggest that dopamine reuptake is reduced during estrus, leading to enhanced phasic dopamine responses and learning.

P2.54 PARKINSON'S DISEASE-LINKED LRRK2 MUTATION ALTERS SYNAPTIC AND INTRINSIC MEMBRANE PROPERTIES FOLLOWING STRESS

Christopher A. Guevara, Swati Gupta, Ajay Tupil, Kumayl Alloo, Emily Dodd, Kyomi Blake, Alexander Tielemans, Kirstie A. Cummings, Roger L. Clem, Scott J. Russo, Deanna L. Benson, George W. Huntley

Nash Family Department of Neuroscience, Friedman Brain Institute, Graduate School of Biomedical Sciences, Icahn School of Medicine at Mount Sinai, New York, NY

Parkinson's disease (PD) is associated with cognitive and psychiatric (anxiety, depression) non-motor symptoms that appear early, are initially independent of dopamine neuron loss and are poorly understood. The G2019S mutation in LRRK2 is the most common genetic cause of late-onset Parkinson's Disease (PD). The risk for both PD and depression is increased by stress. To probe relationships between PD mutation, stress, and neural circuit modifications, we subjected young adult (2-3 mo) male wildtype (WT) and G2019S knockin mice to acute social defeat stress followed by whole-cell recordings to interrogate synaptic function and intrinsic membrane properties in striatal projection neurons in the nucleus accumbens, an area enriched in LRRK2 and known to regulate stress and depression-like responses. Behaviorally, acutely stressed G2019S-mice were significantly more socially avoidant in comparison with stressed WT mice, and displayed underlying synaptic and intrinsic excitability changes that were distinct from those in stressed WT mice or unstressed controls. These data suggest that mice expressing G2019S mount entirely distinct behavioral and adaptive cellular plasticity responses to stress. Ongoing experiments are utilizing a variable stressor paradigm to further probe circuit-specific differences driven by behavioral stress, and to compare whether responses vary by sex, as female patients exhibit a lower prevalence of PD overall but a higher risk for stress-induced depression compared to males. Understanding these interactions would provide insight into the differential adaptations between male and female mice

harboring the G2019S mutation. Ultimately the data may reveal novel targets for ameliorating mood-related and cognitive symptoms associated with PD.

P2.55 THE EFFECTS OF PERINATAL PCBS AND SCAR ON THE BEHAVIOR OF FEMALE RATS

M. Nicole Kunkel[1], Isabella Barnes[2], Ximena de la Cruz[1], Maria Portillo[2], Mandee Bell[1], Andrea C. Gore[1]
[1]University of Texas at Austin; [2]St. Edward's University

Individuals experience multiple stressors across the lifetime. This experiment investigated the independent and interdependent effects of two relevant stressors: exposure to environmental endocrine-disrupting chemicals (EDCs) and sociosexual stress, on anxiety, cognition, and sociosexual behaviors of female rats. Rats were developmentally exposed to an ecologically-relevant polychlorinated biphenyls (PCB) mix or vehicle. In adolescence, they either underwent the stress of sexual conspecific aggression response (SCAR) to an adult male, or no SCAR. SCAR males had diluted limonene applied to their fur. SCAR trials began on the day of vaginal opening of the experimental females, and took place once daily for 15 minutes for eight consecutive days. These females were subsequently tested on an open field test of anxiety, followed by a test of conditioned mate preference for a limonene-scented (evocative of the SCAR male) or unscented male. There were no significant main effects of PCBs on time spent inside of the open field, and SCAR significantly enhanced time spent inside of the open field ($p = 0.005$). A two-way ANOVA suggested no significant interaction of treatments on time spent inside the open field. These results suggest that SCAR, but not PCBs, decrease subsequent anxiety in female rats. Scoring of conditioned mate preference tests is currently underway. Animals who underwent SCAR are expected to show less of a preference for limonene-scented animals compared to controls, and PCBs are expected to disrupt odor preference in female rats. The findings of this experiment will help improve our modeling of stress/trauma in female animals and women.

P2.56 ROLE OF THE VENTRAL PALLIDUM IN THE REGULATION OF SOCIAL PLAY BEHAVIOR IN JUVENILE MALE AND FEMALE RATS

Elie D.M. Huez, Jessica D.A. Lee, Christina J. Reppucci, Samantha M. Bowden, Remco Bredewold, Alexa H. Veenema
Michigan State University

Social play is a rewarding behavior that is displayed by juveniles of many mammalian species. Engagement in social play behavior is important for the development of social competencies throughout life. Children diagnosed with neurodevelopmental disorders such as autism spectrum disorder (ASD) show deficits in social play, which may contribute to their life-long impairments. Therefore, it is essential to understand how the brain modulates the expression of typical and impaired social play behavior. In the present study, we aimed to determine the role of the ventral pallidum (VP) in modulating social play behavior in juvenile male and female rats. The VP regulates adult social behaviors such as maternal behavior and pair-bonding, but its role in regulating juvenile social behaviors, such as social play, is unknown. We first determined whether activation of the VP is required for the expression of social play behavior by temporarily inactivating the VP via local infusions of the GABA-A receptor agonist muscimol. We found that pharmacological inactivation of the VP decreased social play behaviors in males and females compared to their vehicle-treated counterparts. Next, we determined whether exposure to social play altered

neuronal activation of the VP. We observed that exposure to social play increased the number of fos+ cells in the VP of males only. Together, these findings provide the first evidence that activation of the VP is required for the typical expression of social play in both sexes but that exposure to social play recruits VP cells in a sex-specific manner.

P2.57 ACTIVATION OF HYPOTHALAMIC NEURONS DURING ODOR-STIMULATED SCENT MARKING IN SYRIAN HAMSTERS

Jacob W Vander Velden, Jack H Taylor, Kim L Huhman, H Elliott Albers
Georgia State University

Social Communication plays a critical role in social interactions that are essential for reproductive success. Many mammalian species communicate through chemosensation. Chemosensation allows animals to communicate indirectly; odor markings can last for days and can be used to mark territory and indicate reproductive or social status. For solitary species, chemosensation is critical for social interactions. Syrian hamsters engage in a scent marking behavior called flank marking during social interactions and in response to the odors of other hamsters. In the present study, we investigated whether odor-induced flank marking results in the activation of neurons in key hypothalamic structures that are important for social behavior in hamsters, such as the anterior hypothalamus (AH), paraventricular nucleus (PVN), and supraoptic nucleus (SON). Hamsters were exposed to either a clean cage (control) or a cage that was previously marked by a conspecific. The number of flank marks observed in hamsters exposed to conspecific odors (26.27±3.35; Mean□SEM) was significantly greater than in controls (13.31±3.35) ($p=0.01$). Ninety minutes after behavioral testing, the brains were taken and processed for immunohistochemical localization of cFos. In hamsters exposed to conspecific odors, expression of cFos in the AH ($p=0.044$) and the PVN ($p=0.036$) was significantly greater than in controls. We also observed a trend in the SON ($p=0.073$) for less neuronal activation in odor-exposed hamsters compared to controls. These data support the hypothesis that activation of neuronal activity in the AH and PVN along with inhibition of neuronal activity in the SON occurs during odor-stimulated flank marking.

P2.58 FOREBRAIN OXYTOCIN AND VASOPRESSIN 1A RECEPTOR DISTRIBUTIONS IN THE MONOGAMOUS COYOTE (CANIS LATRANS)

Sara Freeman[1], Julie K. Young[1,2]
[1]Utah State University; [2]USDA-National Wildlife Research Center

Studies in monogamous animals have yielded a large body of scientific evidence that the oxytocin and vasopressin systems of the brain are key mediators of social bonding. However, this work has been primarily conducted in monogamous rodents and primates, so the applicability of these discoveries to other classes of animals is limited. Canidae is one class of highly social mammals that has been understudied with respect to the neurobiological basis of social attachment. While monogamy is relatively rare in mammals, all canid species studied to date exhibit monogamy. In no other group of mammals is the pair bond this prevalent. The goal of the current study was to characterize the oxytocin receptor (OXTR) and vasopressin 1a receptor (AVPR1a) distributions in the coyote forebrain using postmortem brain tissue collected opportunistically. We performed OXTR and AVPR1a receptor autoradiography in 20 um sections of unfixed, frozen coyote brain tissue (n= 6; 3 males, 3 females). AVPR1a binding was prominent in the lateral septum, diagonal band, and throughout the cortex, especially the cingulate cortex, straight gyrus, and rhinal cortex. We

detected OXTR in the hippocampus, amygdala, nucleus accumbens, caudate, and putamen. We also found prominent OXTR binding in several areas important for olfactory processing: the olfactory bulbs, accessory olfactory nucleus, piriform cortex, and olfactory tubercle. This is the first study to localize OXTR/AVPR1a in the brain of a canid, and it establishes the neurobiological foundation for future studies of the function of oxytocin and vasopressin in the coyote brain.

P2.59 THE EFFECTS OF INTERACTIVE OBJECT PROVISIONING ON CORTICOSTERONE, STRESS-RELATED BEHAVIORS, AND COGNITION IN JUVENILE AND ADULT ZEBRA FINCHES (TAENIOPYGIA GUTATTA)

Laura West
University of Mississippi

My work compares adult and juvenile zebra finches in basic housing those in a more interactive environment. I will test behavior in a novel object test; open-field test; and spatial maze; and quantify corticosterone; body weight; and stereotypies.

Poster Session III

Thursday, July 1, 2021 from 1:00pm to 2:30pm (ET)

P3.1 THE ROLE OF EGR1 IN REGULATING AN ESTROUS CYCLE-DEPENDENT BEHAVIORAL PHENOTYPE AND VENTRAL HIPPOCAMPAL TRANSCRIPTIONAL SIGNATURE

Devin Rocks[1], Ivana Jaric[1], Eric Purisic[1], Eduardo Gallo[1], John M. Greally[2], Masako Suzuki[2], Marija Kundakovic[1]
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Compared to men, women have a two-fold increase in risk for anxiety and depression disorders. Due to the exclusion of female subjects from animal studies of the brain and behavior, however, the biological basis of this sex difference is unknown. In humans, clinical and epidemiological data indicate fluctuating ovarian hormones contribute to this sex-gap in risk. Previously, we found that anxiety-like behavior in female mice varies across the estrous cycle, and we demonstrated, for the first time, changes in neuronal chromatin organization and gene expression in the ventral hippocampus, a brain region critical for emotion regulation in rodents, underlying this behavioral phenotype. Analysis of these data indicated that Egr1, an estrogen-responsive immediate early gene product, is a potential regulator of the observed changes in chromatin accessibility and gene expression over the estrous cycle. In the work presented here, we determine whether ventral hippocampal Egr1 expression drives estrous cycle-dependent changes in behavior. To address this, we leveraged AAV-mediated overexpression of Egr1 in the ventral hippocampus of intact male and OVX female mice followed by a series of tests measuring anxiety- and depression-related behavior. These experiments established a mechanistic role of Egr1 in regulating cyclical changes in anxiety- and depression-related behavior in females. We found overexpression of Egr1 has no effect on behavior in male animals, indicating the effect in females is sex-specific. By linking Egr1 to estrous cycle-driven behavioral changes and gene regulation, our results establish a foundation for the development of sex-specific treatments for anxiety and depression disorders.

P3.2 CONDUCTING HUMAN SOCIAL NEUROENDOCRINOLOGY RESEARCH DURING A GLOBAL PANDEMIC

Tracy-Lynn Reside, Francesca R. Luberti, Justin M. Carré
Nipissing University

The COVID-19 pandemic has had a significant negative impact on the ability to carry out face-to-face research in laboratory settings. Here, we describe a novel approach to collecting human social neuroendocrinology data during this pandemic. The aim of the study was to investigate the extent to which previously observed positive correlations between competition-induced testosterone dynamics and human aggression (see Geniole et al., 2020 for meta-analysis) would extend beyond the laboratory setting. Participants (n = 300, 50% women) were recruited through online social media ads (Facebook, Instagram) and upon signing up, underwent a brief intake interview via Zoom. A testing day was scheduled using an online scheduling platform, following which saliva sample collection packages were mailed to participants. On their scheduled testing time, participants completed online surveys assessing demographic and personality traits, and provided saliva samples before and after completing the Point-Subtraction Aggression Paradigm (PSAP), a well-validated behavioural measure of aggression. We hypothesized that changes in testosterone during the PSAP would be positively correlated with aggressive behaviour in men, but not women. Data collection will be completed prior to the conference and results of preliminary analyses will be discussed.

P3.3 DEVELOPMENT OF A SINGLE-DOSE INTRANASAL TESTOSTERONE ADMINISTRATION PARADIGM FOR USE IN MEN AND WOMEN

Francesca R. Luberti[1], Tracy-Lynn Reside[1], Pierre L. Bonin[2], Justin M. Carré[1]
[1]Nipissing University; [2]Northern Ontario School of Medicine

For over two decades, researchers in the field of human social neuroendocrinology have been using single-dose pharmacological challenge protocols to determine the causal effects of testosterone on psychological, behavioural, and neural processes. Most of these single-dose administration studies have so far used (1) single-sex samples and (2) varying modes of testosterone administration (intramuscular, transdermal, sublingual, and intranasal) that produced vastly different dose-response curves. Moreover, whereas studies with male participants increased men's testosterone concentrations within the high normal physiological range, studies with women typically increased testosterone concentrations to supraphysiological levels. The purpose of this study was to develop a single-dose administration protocol using intranasal testosterone that would produce a proportionally similar rise in testosterone for both sexes. We found that an 11 mg intranasal testosterone dose in men and a 0.3 mg dose in women raised testosterone concentrations to the high normal physiological range for each sex, producing similar dose-response dynamics in both sexes. This paradigm will allow researchers to design studies with mixed-sex samples that test physiologically plausible sex differences/similarities in the causal effects of testosterone. It will also provide a replicable protocol to examine the possible adaptive functions of acute increases in testosterone in both sexes.

P3.4 EFFECTS OF DOPAMINE SIGNALING IN FEMALES ON THE VOCAL DYNAMICS OF PAIRED AND COURTING DYADS

Nora H. Prior[1], Chelsea M. Haakenson[1], Karan J. Odom[1], Jane A. Brown[2], Gregory F. Ball[1]

[1]Department of Psychology University of Maryland College Park; [2]School of Communication Sciences and Disorders University of Memphis

Across a range of social contexts, zebra finches employ interactive vocal exchanges, composed of both male song as well as male and female calls. These vocal exchanges are socially modulated: prior experience shapes overall vocal activity and the extent of coordination between callers. Additionally, the vocal exchanges between mates change over the first few days of pairing. However, the neuroendocrine mechanisms that regulate vocal dynamics and mediate the effect of experience on these interactions remain largely unknown. Here, we conducted two experiments testing the effect of DA signaling on female calling in isolation and with a male. We first quantified the effect of D1 and D2 receptor agonists on paired and courting females (Exp1). Additionally, we tested the effect of D1 and D2 receptor antagonists and agonists on courting females (Exp2). Pharmacological doses were administered via subcutaneous injection. Each female received all manipulations: D1 agonist (SKF-38393 hydrochloride), D2 agonist (quinpirole dihydrochloride), D1 receptor antagonist (SCH-23390), D2 receptor antagonist (raclopride), and vehicle (physiological saline). In both experiments, female calling during isolation was highest following peripheral administration of D2 agonist. Additionally, D2 agonist treatment had striking effects on courting females, including increasing female calling in response to male song. In contrast, only rarely did paired males and females engage in song-call exchanges. In Exp 2, D1 and D2 receptor antagonists decreased calling during social contexts. Combined, these experiments provide insight into the differential role of D1 and D2 signaling in the regulation of calling activity and the nature of dynamic communication.

P3.5 STRESS BEHAVIORS AND THE GUT MICROBIOME IN RHESUS MONKEYS IN A PRIMATE SANCTUARY

Sarah Jane Alger[1], Michael Steury[1], Hilary Hemmes-Kavanaugh[2], Julia Adkins[1], Breanne Cyr[2]
[1]University of Wisconsin-Stevens Point; [2]Primates Incorporated

Retired research primates are increasingly sent to sanctuaries that aim to maximize their health and happiness. These primates commonly receive probiotic supplements to reduce stress and improve well-being. However, the exact impact of these probiotics on behavior is poorly understood. We used noninvasive methods of behavioral observation and opportunistic fecal collection of five rhesus macaques (Macaca mulatta) sent from two different research labs to a primate sanctuary to explore relationships between the gut microbiome and behavior. We collected behavior and fecal samples both before and after probiotic administration and during different cohabitation pairings. We found abundances of several bacterial classes to correlate with stress and positive behaviors. Although probiotic administration increased microbial class richness, it did not significantly impact behavior. Also, gut microbiomes differed between animals that came from different labs. Sample sizes were insufficient to adequately test for effects of subsequent repairing of cagemates on microbial communities. Overall, noninvasive behavior and fecal data collection can provide valuable information to sanctuaries.

P3.6 ACETAMINOPHEN INTERACTS WITH HORMONAL MILIEU EARLY IN LIFE TO INFLUENCE SOCIAL BEHAVIOR, MATE PREFERENCE, AND ANXIETY IN LONG-EVANS RATS (RATTUS NORVEGICUS)

Anna G. Warner, Christopher Harshaw
University of New Orleans

Epidemiological studies have reported an association between early-life Acetaminophen (EL-APAP) exposure and risk of Autism Spectrum Disorder (ASD). Rodent studies have also found differences in social and emotional behaviors after EL-APAP. A study from our lab, for example, found that EL-APAP mice showed a number of social abnormalities, with effects being more pronounced in males. APAP can alter sex steroids vital for brain sexual differentiation, but no study to date has examined whether social, anxiety, and mate preference behavioral alterations occur as a function of interactions between APAP and the sex steroid milieu during the neonatal sensitive period of brain sexual differentiation (SPBSD). Here, we examined the effects of APAP in the presence of 17β-Estradiol (E2), Letrozole (LTZ), or corn oil vehicle during the SPBSD on play, social conditioned place preference (SCPP), and mate preference. From postnatal day 1 (P1) to P11, pups received subcutaneous injections (s.c) of either E2 (.05 µg; masculinized), LTZ (1 mg/kg; feminized), or corn oil vehicle (50 µl). On P5, P8, and P11, pups were administered s.c. injections of APAP (5 cc/kg) or saline 45 min after the first injection. Assays of play, social conditioned place preference, mate preference, and anxiety were conducted. We used linear mixed effects modeling, controlling for litter as a random effect. Analyses revealed significant interactions between sex, APAP, and E2 on rough-and-tumble play, SCPP, mate preference, and anxiety behaviors (ps < .05). These preliminary data show that sex steroid x APAP interactions influence development of sex-specific behaviors relevant to ASD.

P3.7 DISTRIBUTION OF NONAPEPTIDE RECEPTORS IN THE FOREBRAIN AND MIDBRAIN OF SPINY MICE (ACOMYS CAHIRINUS)

Jeanne M. Powell, Kiyoshi Inoue, Larry J. Young, Aubrey M. Kelly
Emory University

The nonapeptides oxytocin (OT) and vasopressin (AVP) play key roles in modulating social behaviors across taxa via the activation of the OT receptor (OTR) and AVP V1a receptor (V1aR). Differences in the distributions and densities of these receptors have been linked to differences in social phenotype both within and across species. However, much of what we know about these systems have been learned using rodent models that primarily display prosocial behaviors in reproductive contexts, such as pair bonding and parental care. The gregarious and communally breeding spiny mouse (Acomys cahirinus) presents a unique opportunity to explore nonapeptide-mediated social behavior because they exhibit high degrees of prosociality in both reproductive and non-reproductive contexts. Here, we provide a basic characterization of neuronal OTR and V1aR binding in spiny mice using receptor binding autoradiography. We observed similar binding distributions throughout the basal forebrain and midbrain as has been found in many rodents. However, there are some notable discrepancies in the spiny mouse brain, such as a lack of OTRs in the lateral septum. Additionally, we explore effects of sex on nonapeptide receptor densities, and present complimentary data mapping V1aR and OTR mRNA using fluorescent in situ hybridization. This characterization lays a basic foundation for future studies that seek to examine the relationship between nonapeptide receptor density and phenotypic differences in behavior and identifies target regions for causal manipulation to determine direct contributions of nonapeptide circuitry to social behavior in spiny mice.

P3.8 A VOCAL SIGNATURE OF PAIR-BONDING IN PRAIRIE VOLES

Morgan L. Gustison, Steven M. Phelps
University of Texas at Austin

Prairie voles (Microtus ochrogaster) are one of the few mammalian species to form stable pair bonds, and they have become an excellent model for the neuroendocrine basis of attachment. A wide range of conspicuous behaviors (e.g., mating, side-by-side contact) are known to facilitate the physiological transition from an unbonded to bonded state. The potential contribution of inconspicuous social behaviors like ultrasonic vocalizations (USVs) remains a mystery. Here, we test the hypothesis that vocal communication is critical part of the pair-bonding process. Subjects were paired with either a familiar same-sex sibling or a novel mating partner for one day while we continuously tracked individuals and vocalizations. Specific social behaviors were manually recorded during 10 min focal observations at each hour of cohabitation. We quantified the time courses of vocal activity for mating and sibling pairs, and mapped these trajectories onto social interactions. Supporting our hypothesis, mates produced higher USV rates than siblings, especially during the early stages of pair-bonding. The trajectories of mates' vocal activity also predicted subsequent social interactions such as courtship and reunion after separation. Moreover, the acoustic structure of USVs differed based on partner type and social context. Mating pair USVs tended to be long, high frequency, and modulated, especially during courtship. Taken together, our results suggest that a unique vocalization repertoire functions to maintain close proximity between partners and promote mating interactions that are critical for bond formation. A promising area for future study will be to explore the neuroendocrine mechanisms that drive vocal communication during pair-bonding.

P3.9 BRAIN-WIDE SYNAPTIC INPUTS TO AROMATASE-EXPRESSING NEURONS IN THE MEDIAL AMYGDALA SUGGEST COMPLEX CIRCUITRY FOR MODULATING SOCIAL BEHAVIOR

Joseph FD Dwyer, Diane A Kelly, Joseph F Bergan
Neuroscience and Behavior Program, University of Massachusetts

Aromatase-expressing neurons in the medial amygdala are critical for social behaviors but the synaptic inputs to these cells remained unknown. We used rabies tracing and light-sheet microscopy to reveal an unbiased view of the brain regions that provide specific inputs to these cells, and observe both well-established connections (e.g., bed nucleus of the stria terminalis and accessory olfactory bulb), as well as regions with reciprocal inputs and several entirely novel and surprising inputs from areas involved in parenting and aggression, metabolism, fear and anxiety, and memory and cognition. These results confirm the central role of the medial amygdala in social recognition behavior and point to an expanded role for its aromatase-expressing neurons in the integration of multiple sensory and homeostatic factors, which can be used to modulate many other social behaviors.

P3.10 AN INVERTED U RELATIONSHIP BETWEEN THE "DOSE" OF SOCIAL INTERACTION (E.G., DURATION AND/OR INTENSITY) AND THE REWARDING PROPERTIES OF THOSE INTERACTIONS

Jack H Taylor, Soliyana A Fekadesellasie, Erica Browne, Nazanin Pourshiravi, Margaret Welch, Kim L Huhman, H Elliott Albers

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Although the rewarding properties of social interactions are well known, the relationship between the "dose" of social interaction (e.g., duration and/or intensity) and the rewarding properties of those interactions has not been systematically evaluated. In the present study, we tested the hypothesis that there is an inverted U-shaped relationship between the dose of social interaction and its rewarding properties. More specifically, we propose that as the dose of social interaction increases, the rewarding properties of those interactions initially increase, then level off, and then eventually decline. Using both an operant social preference test (OSP) and a conditioned place preference test (CPP), we exposed male and female Syrian hamsters to increasing doses of social interaction. In both the OSP and CPP, a robust inverted U-shaped dose response curve was observed as a function of social dose in males and females. Previously, we have shown that activation of OT receptors in the ventral tegmental area (VTA) is necessary for the rewarding properties of social interactions. In the present study, we found that OT injected into the VTA prior to each of three social interactions with same-sex conspecifics significantly increased the rewarding properties of those social interactions in females but not in males. These data support the hypothesis that there is an inverted U-shaped dose response curve between the dose of social interaction and its rewarding properties in males and females, and that this dose response curve is modulated by OT in the VTA in a sex-dependent manner.

P3.11 INVESTIGATING THE ROLE OF HYPOTHALAMIC OXT IN SOCIAL PLAY BEHAVIOR OF JUVENILE FEMALE RATS

Samantha M. Bowden, Anna M. Luxhoj, Adelina R. Tatone, Valery Grinevich, Remco Bredewold, Alexa H. Veenema,
Michigan State University

Juvenile social play is a highly motivated and rewarding behavior displayed across a variety of mammalian species, and deficits in social play is a hallmark symptom of Autism Spectrum Disorder (ASD). Although the oxytocin (OXT) system has been implicated as a potential therapeutic in ASD, little is known about its role in social play. We recently found that administration of an OXT receptor antagonist into the nucleus accumbens (NAc) decreases social play in juvenile rats, but the origin of these OXT projections to the NAc is unknown. Here, we used anterograde and retrograde tracing techniques and identified both the paraventricular nucleus of the hypothalamus (PVN) and supraoptic nucleus (SON) as origins of OXT neurons innervating the NAc. Next, we determined the involvement of PVNOXT and SONOXT populations in the modulation of social play behavior using an excitatory DREADD construct under the control of the OXT promoter that was infused into either the PVN or SON of juvenile female rats. We found that chemogenetic activation of PVNOXT cells significantly increased the duration of social play with no effect on social or non-social investigation. Current studies are underway to determine the effects of chemogenetic activation of SONOXT cells on social play behavior. Future experiments will then determine the involvement of the PVNOXT and SONOXT projections to the NAc in modulating social play behavior. Together, these experiments demonstrate the involvement of PVNOXT cells in the modulation of juvenile social play behavior and its potential to alleviate social play deficits in children with ASD.

P3.12 INVESTIGATING THE ROLE OF PROSTAGLANDINS IN PRENATAL BRAIN DEVELOPMENT AND BEHAVIOR IN MICE

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Prostaglandins (PGs) are fatty acid metabolites which influence cellular developmental processes and play essential roles in immune response. Knockout or pharmacological inhibition of upstream synthesizing enzymes of PGs, Cyclooxygenases 1 and 2, in-utero or in the early postnatal brain impacts dendritic outgrowth, neurogenesis, brain-wide transcription of genes which regulate development, or social and locomotor behaviors in adulthood. These enzymes produce at least four types of bioactive PGs, but it is still unclear whether and which PGs are endogenous to the fetal brain. Here we use LC-MS/MS for a lipidomic assessment of PGs and other fatty acid metabolites present in the mouse brain over the course of fetal development. We show that Prostaglandin D2 (PGD2) is the most abundant PG in the fetal brain. To identify potential cell signalling pathways of PGD2, we quantified cell type specific gene expression of synthesizing enzymes and receptors in the PGD2 pathway across fetal brain development. We found that brain myeloid-lineage cells have higher expression of enzymes for PGD2 synthesis than non-myeloid cells, such as neural progenitors. These non-myeloid cells, however, express the receptors for PGD2 more highly than myeloid cells. This evidence may suggest that PGD2 produced by myeloid cells could impact the development of neural cells. We are testing in detail the role of myeloid derived PGD2 in neural development and adult behaviors. Lastly, we introduce a method in behavioral tracking and computational modelling to screen social and non-social behaviors in mice with disruptions in the PGD2 pathway.

P3.13 SEVERITY OF MATERNAL BEHAVIOR DEFICITS IS ASSOCIATED WITH ALTERED POSTPARTUM ACTIVITY OF ESTRADIOL IN A RAT MODEL OF POSTPARTUM DEPRESSION

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Mothers who experience depression during the postpartum period often exhibit impairments in maternal behavior. Prior research has suggested altered gestational profiles of estradiol and progesterone as predicting risk for postpartum depression (PPD), especially its associated impairments in maternal behavior. However, it is unclear whether differences in postpartum estradiol signaling also contribute to ongoing depression-related maternal behavior deficits. Considering that postpartum depression is a highly prevalent disorder that impacts maternal health and well-being as well as child socio-emotional development, determining the role postpartum estradiol may play in ongoing maternal behavior is critical to bettering diagnostic measures and treatments for depression-related disturbances in parenting. The goal of the current study was to investigate the association between estradiol signaling and maternal behavior. To this aim, we used Wistar-Kyoto (WKY) rats, who display a depression-like phenotype and deficient maternal caregiving behaviors relative to control Sprague-Dawley (SD) rats, that recapitulates many features of depression in human mothers. Estradiol serum concentrations were measured in SD and WKY mothers via an ELISA, and estrogen receptor alpha (ERα) expression via qPCR and

immunohistochemistry (IHC) was evaluated in the maternal medial preoptic area (mPOA). Serum estradiol and brain receptor expression and activity (via cFOS IHC expression in the mPOA) were then correlated with maternal behavior phenotype. Together, our data suggest that estradiol activity in the mPOA mediates the severity of depression-related maternal behavior deficits. Ongoing analyses are evaluating the interaction between estradiol activity and oxytocinergic activity between the mPOA and the periventricular nucleus as a possible neurobiological mechanism that, when disrupted, drives the severity of depression-related caregiving deficits in WKY mothers.

P3.14 DOES TESTOSTERONE MODULATE SICKNESS BEHAVIOR IN JAPANESE QUAIL?

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An immune response not only elicits physiological changes, but also a suite of behavioral changes including decreased activity, and decreased food and water intake. Some studies have shown that the expression of these sickness behaviors can change depending on the social context. There is some evidence that suggests that testosterone may be responsible for this modulation. Here, we assessed how GnRH, a regulator of the reproductive axis, influences the expression of sickness behaviors in male Japanese quail before and after they are presented with mating opportunities. Sickness behaviors were elicited by injection of lipopolysaccharide (LPS) and male quail were in the following treatment groups: saline/sham, saline/GnRH; LPS/sham; or LPS/GnRH. Behavior was monitored before and after female presence and blood samples were taken to quantify testosterone. We found that, as expected, LPS injection increased crouching and generally reduced activity (drinking, eating, crowing). When males were presented with mating opportunities, they readily attempted to mount, regardless of treatment. Additionally, males in all treatment groups tended to rest more when in the presence of females. Although LPS caused an increase in immobility, when in the presence of females that immobility included less crouching and more standing (upright) relative to isolated males. Finally, we found that GnRH treatment increased testosterone, however LPS appeared to prevent this. Together, these results suggest that male Japanese quail modulate the expression of some sickness behaviors depending on social context; however, we were unable to provide support for the hypothesis that testosterone is responsible for this.

P3.15 UNDERSTANDING THE PROGRAMMING EFFECTS OF MATERNAL METABOLIC AND INFLAMMATORY STATE ON OFFSPRING CENTRAL AND PERIPHERAL INFLAMMATORY OUTCOMES

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Obesity is an epidemic that effects 40% of adults in the US. About one-third of pregnant women are classified as obese. Previous research suggests that children born to obese mothers are at increased risk for developing neurodevelopmental and neuropsychiatric disorders. The mechanisms behind this increased risk are poorly understood. Increased exposure to inflammation in-utero

induced by maternal obesity is a proposed mechanism for neurodevelopmental alterations in offspring. Utilizing a non-human primate model of maternal obesity, we hypothesized that maternal consumption of an obesogenic diet will predict offspring peripheral (e.g. cytokines and chemokines) and central (microglia density) inflammatory outcomes through measures of maternal metabolic and inflammatory state (e.g. adiposity, insulin response, and maternal peripheral inflammatory measures). To understand the complex interactions of metabolic state and inflammation we employed structural equation modeling (SEM). Latent variables were created for maternal chemokines, and offspring cytokine and chemokines. Model results showed that neither maternal pre-pregnant adiposity (β=0.433, p=0.251) or maternal 3rd trimester insulin area under the curve (IAUC) (β=-0.364, p=0.150) predicted offspring peripheral cytokine or chemokine levels. However, maternal chemokines were associated with offspring chemokine (β=0.292, $p<0.05$) and cytokine (β=-0.390, $p<0.05$) measures. In contrast, maternal diet had an indirect effect on offspring amygdala microglia cell counts through both maternal adiposity (β=0.536, $p<0.05$) and 3rd trimester IAUC (β=-0.487, $p<0.05$) but was not influenced by maternal inflammatory state. In summary, these data suggest that maternal metabolic state appears to predict offspring amygdala microglial counts while maternal inflammatory state influences offspring peripheral inflammatory outcomes.

P3.16 VASOACTIVE-INTESTINAL POLYPEPTIDE(VIP)-EXPRESSING NEURONS IN THE SUPRACHIASMATIC NUCLEUS COORDINATE PERI-OVULATORY REPRODUCTIVE AXIS ACTIVITY

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Just prior to ovulation, the master brain clock in the suprachiasmatic nucleus (SCN) integrates with high estradiol concentrations to stimulate GnRH secretion and pre-ovulatory luteinizing hormone (LH) surge. Kisspeptin- and gonadotropin inhibitory hormone (GnIH)-expressing neurons that lie upstream of the GnRH system positively and negatively drive GnRH release, respectively. Although VIP-expressing SCN neurons have been implicated in the regulation of the LH surge in rodents, no studies to date have specifically manipulated their activity in vivo to examine downstream impact on the HPG axis. In the present study we used a VIP-Cre mouse driver line and chemogenetics to isolate the functional role of this SCN neuropeptidergic cell phenotype. Specifically, VIP neurons in the SCN were stimulated in the morning prior to the LH surge or inhibited in the afternoon around the time of the LH surge using AAV-hM3Dq and hM4Di, respectively. Brains were collected and analyzed for GnRH, kisspeptin, and GnIH cellular activity using FOS immunofluorescence. Morning stimulation of SCN VIP cells suppressed GnIH cellular activity, whereas kisspeptin and GnRH cells were unresponsive at this time, suggesting temporal gating of responsiveness to prevent premature ovulation. In contrast, afternoon inhibition of SCN VIP cells increased GnIH cellular activity with concomitant inhibition of kisspeptin and GnRH cellular activity. Together, these findings suggest that VIP communication to the HPG axis is suppressed prior to the surge, with increased signaling at the time of the surge to coordinate removal of GnIH inhibition with kisspeptin and GnRH cell activation.

P3.17 THE EFFECTS OF INTERMITTENT HIGH FAT DIET CONSUMPTION ON HYPOTHALAMIC INFLAMMATION

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Recent studies using animal models demonstrate that chronic consumption of a high fat diet (HFD) promotes neuroinflammation. Our lab is interested in elucidating the mechanisms underlying intermittent overconsumption of HFD (i.e., binge-like eating), and whether this also promotes neuroinflammation. Here, we used a model of binge-like eating in female rats to determine whether intermittent consumption of large (binge-like) meals promotes inflammation in brain regions that control food intake, including the arcuate nucleus (ARC) of the hypothalamus. We hypothesized that intermittent overconsumption of HFD is sufficient to induce a neuroinflammatory response that is similar, and possibly greater, than that observed in rats consuming HFD daily. Female rats were assigned to one of three groups: INT binge eating (daily chow plus intermittent access to HFD every 3 days), CONT control group (daily access to chow and HFD), and CHOW control group (daily access to chow only). Food intake and body weight were measured daily for 3 weeks (i.e., 3 binge cycles), after which rats were perfused and brain tissue was processed via immunohistochemistry to identify microglia, the resident immune cells in the brain. On days in which binge-like eating was assessed, INT rats consumed significantly more calories than CONT or CHOW rats (e.g., 34.8 vs. 9.0 vs 10.6 kcal/2h, respectively, $p < 0.05$). Quantification of Iba-1, a cytoskeletal protein specific to microglia, was assessed across groups. This analysis revealed an increase in the number of microglia in the ARC of CONT and INT rats, compared to CHOW rats ($p < 0.05$). We conclude that intermittent overconsumption of a HFD induces inflammation, as shown by greater Iba-1 expression, in the ARC compared to control groups.

P3.18 COGNITION IN A SOCIAL WORLD: ASSESSING COGNITIVE VARIATION BY SEX AND DOMINANCE STATUS IN THE SOCIAL CICHLID FISH ASTATOTILAPIA BURTONI

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Animals use cognitive processes to navigate their social worlds. While cognition in social contexts has been investigated in detail, this research rarely integrates cognition in nonsocial contexts. Understanding how the social environment shapes, or is shaped by, cognition in nonsocial contexts is essential to identifying relationships, constraints, and trade-offs between social and nonsocial realms.

Here, we used the highly social cichlid fish, Astatotilapia burtoni, to compare males and females in a novel object recognition task and a spatial task, hypothesizing that males would outperform females in a spatial learning task and exhibit more neophilic/exploratory behavior across both tasks. However, there were no sex differences in performance, suggesting that cognitive flexibility may be beneficial in A. burtoni's dynamic social environment. The sexes did diverge in their cognitive style (how they learned), differing in decision latencies, preference timing, space use, and error correction.

When male A. burtoni ascend in social status, they undergo a suite of behavioral, physiological, and neuromolecular changes. Despite extensive characterizations of these changes, we know little about their influence on cognition. Before and after territory acquisition, we assessed male A. burtoni in three tasks and assayed cortisol and testosterone levels. We found that ascending males changed their physiology and novel object preference, and they subsequently differed in social competence from subordinate males. We also identified a multivariate profile that was predictive of

social ascent even before the perturbation. Our results underscore the importance of integrating cognition with social behavior and physiology and provide surprising insights into this relationship.

P3.19 LONG TERM EFFECTS OF CHRONIC INTRANASAL OXYTOCIN ON ADULT PAIR BONDING BEHAVIOR AND BRAIN GLUCOSE UPTAKE IN TITI MONKEYS (PLECTUROCEBUS CUPREUS)

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Intranasal oxytocin (IN OXT) administration has been proposed as a potential pharmacological treatment for the social deficits of autism spectrum disorder (ASD). However, studies evaluating the potential long-lasting effects of chronic IN OXT during development have not been addressed in humans or non-human primates. Here we conducted a follow-up study of a cohort of adult titi monkeys that received intranasal oxytocin 0.8 IU/kg (n=15) or saline (n=14) daily for six months during their juvenile period (12 to 18 months of age), with the goal of evaluating the potential long-lasting behavioral and neural effects one-year post-treatment. Subjects were paired at 30 months of age (one-year post-treatment) and tested for behavioral components of pair-bonding at one week and four months post-pairing. We assessed long-term changes in brain activity using 18FDG positron emission tomography (PET) scans; subjects were scanned at 23 months old (pre-pairing) and 33 months old (3 months post-pairing). Our results showed no significant differences in pair-bonding-related behavior between SAL and OXT-treated animals at one-week post-pairing during behavioral tests. At four months post-pairing, both SAL ($F_{1,24}=8.35$, $p=.008$) and OXT ($F_{1,26}=15.63$, $p<.001$) treated animals showed a significant preference for their pair-mate over a stranger animal during the Partner Preference Test (PPT). During the Sequential Partner Preference Test OXT-treated males touched the partner condition more than SAL-treated males ($t=3.298$, $p=0.008$). OXT-treated animals were also less likely to be aggressive towards an unfamiliar stimulus animal presented in their home cage compared to SAL-treated animals.

P3.20 MEASURING EXPLORATORY BEHAVIOR ACROSS DEVELOPMENT IN A WILD-DERIVED SPECIES: CAN WE STUDY ADOLESCENT DISPERSAL IN THE LAB?

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Adolescence is a time of increased risk taking, novelty seeking, and exploration in a wide variety of species. These behaviors have an adaptive function to facilitate dispersal from the natal nest but may also have relevance to addiction and morbidity in human adolescence. We examined exploratory behavior during development in Mus spicilegus as a putative model of dispersal behavior with potential for seasonal regulation in the lab. To measure exploratory behavior across development, we tested different long day (12h:12h) reared cohorts in a standard open field test, and then measured their exploration of a novel object. We found that open field distance traveled, time in center, and novel object approach were significantly greater in long day reared M. spicilegus tested at postnatal day (P) P60-70 compared to younger ages. We next tested if rearing on a short photoperiod (10h:14h), M. spicilegus could reduce the higher level of exploratory behaviors seen at P60 on long days. This was based on the fact that in the wild, dispersal is delayed when M. spicilegus overwinter in a mound. We found that rearing in a short photoperiod

did not affect P60 open field measures, but did reduce novel object approach behavior in male M. spicilegus compared to long day reared counterparts. The data raise our confidence that we can model multiple aspects of dispersal behavior in wild-derived mice in a lab environment and possibly regulate some aspects with light. Future work will include gonadal hormonal measures and a more ethological burrow leaving test for which we will show pilot data.

P3.21 ESTROGEN RECEPTOR ALPHA IN THE BRAIN MEDIATES TAMOXIFEN-INDUCED CHANGES IN TEMPERATURE AND METABOLISM IN MICE

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Selective Estrogen Receptor Modulators (SERMs) are among the world's most prescribed drugs. The SERM tamoxifen is used to treat ER positive breast cancer and significantly improves survival in breast cancer patients. Unfortunately, long-term tamoxifen therapy comes with side effects that impact health and quality of life, including hot flashes, changes in bone density, and fatigue. Partly due to a lack of proven animal models, the tissues and cells that mediate these negative side effects are unclear. Here, we show that female mice undergoing long-term tamoxifen treatment exhibit lower core body temperature, higher heat dissipation, higher bone density, and lower movement compared to vehicle-treated controls. Single-cell RNA sequencing reveals that tamoxifen treatment induces widespread gene expression changes in the hypothalamus and preoptic area (hypothalamus-POA). These expression changes are dependent on estrogen receptor alpha (ERa), as conditional knockout of ERa in the hypothalamus-POA ablates or reverses tamoxifen-induced gene expression. Accordingly, conditional knockout mice lacking ERa in the hypothalamus-POA do not exhibit tamoxifen-induced changes in temperature, bone density, or movement. These findings provide mechanistic insight into the effects of tamoxifen on the hypothalamus-POA and indicate that ERa mediates the principal physiological effects of tamoxifen treatment in mice.

P3.22 SEX DIFFERENCES IN NEGATIVE COGNITIVE BIAS ACROSS THE LIFESPAN: RELATION TO NEUROINFLAMMATION

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Negative cognitive bias is a perception of neutral situations or objects as negative, and is increased in depression. Negative cognitive bias can predict the onset of future depressive episodes. However, the underlying neural mechanisms of cognitive bias have seldom been investigated. Here, adolescent, young adult, and middle-aged adult male and female rats underwent a fear-based cognitive bias task. Rats were trained for 16 days to distinguish between two contexts: a context paired with foot-shock and a context paired with no foot-shock. Positive (low freezing) or negative (high freezing) was determined (on Day 18) in response to an ambiguous context. Adolescent rats displayed a positive bias, whereas young adult rats displayed a negative bias in response to the ambiguous context, regardless of sex. Curiously, in middle-aged adults, females

displayed a more positive bias in response to the ambiguous context whereas males displayed a negative cognitive bias. When examining neuroinflammation and freezing in response to the ambiguous context, middle-aged males had positive correlations between freezing and the levels of the cytokines IFN-y, IL-6, and IL-13 in the ventral hippocampus, but not in females. Moreover, while males had negative correlations between freezing and cytokine levels in the basolateral amygdala females had positive correlations. Our data suggest a more optimistic cognitive bias in females than in males that emerges in older adulthood, and that negative cognitive bias is related to neuroinflammation in the ventral hippocampus of males but in the basolateral amygdala of females.

P3.23 THE EFFECT OF ENERGY PRIMING AND SUCROSE OR SWEETENER CONSUMPTION ON SYMPATHETIC AND PARASYMPATHETIC RESPONSES TO ACUTE STRESS IN FASTED WOMEN

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The consumption of sugary, but not sweetener-containing drinks before stress exaggerates the cortisol stress response in males, yet sympathetic responses remain unaffected. In females, also sweetener might increase cortisol stress responses. So far, the underlying mechanisms are unknown. Information about a sweet drink's energy content, e.g., based on verbal descriptions, could trigger implicit or explicit expectations towards drink content and influence behavioral and physiological responses. While information of whether a drink contains calories independent of its actual content (energy prime) does not seem to affect cortisol stress responses in females, its effect on sympathetic and parasympathetic responses has so far not been investigated. Thus, we studied the effects of energy priming in conjunction with sugar and sweetener consumption on sympathetic (indexed by salivary alpha amylase [sAA], and heart rate [HR]) and parasympathetic (indexed by respiratory sinus arrythmia [RSA]) responses to stress.
Eighty-three fasted women (meanage=21.29, sdage=2.55, meanfasting_durtation=12.00h) participated in the Trier-Social-Stress-Test for groups in the morning hours. Beforehand, they received an energy prime, deceptive in 50% of the cases, and consumed a drink containing sucrose (n=42), or sweetener (n=41). We repeatedly measured sAA and continuously monitored cardiac activity. We calculated stress-induced changes from baseline to peak for each marker.
Linear regressions indicated that sweetener consumption (independent of energy prime) led to significantly higher stress-induced sAA increases as compared with sugar. HR and RSA changes did not differ between conditions. Further analyses focusing on sAA, HR and RSA trajectories over time will be presented and discussed at the poster.

P3.24 OPIOID USE DURING PREGNANCY: IMPACT OF CONTINUED OR DISCONTINUED GESTATIONAL MORPHINE OR BUPRENORPHINE EXPOSURE ON MATERNAL CARE AND OFFSPRING SURVIVAL IN A TRANSLATIONAL RODENT MODEL

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The opioid crisis in the United States has grown to epidemic proportions with opioid dependence among pregnant women quadrupling from 1999-2014. Opioid-dependent pregnant women are commonly given opioid maintenance therapies (e.g., buprenorphine), but the behavioral and neurological effects of these drugs on maternal caregiving behaviors and offspring development are poorly understood. Our study is using a translational rodent model to characterize the behavioral and neurochemical consequences of gestational morphine (mimicking opioid use disorder) and buprenorphine (mimicking opioid maintenance therapy) exposure on the dam and on the neural network of the offspring. Female rats started opioid exposure before pregnancy and either continued exposure until the postpartum or discontinued shortly before parturition (gestational day (GD) 19). Dams were evaluated for appropriate maternal behaviors and neonatal male and female pups were assessed for weight, temperature, body length, milk bands, and severity of withdrawal symptoms. Our preliminary results revealed that buprenorphine exposure resulted in more maternal care deficits, impaired offspring development, increased offspring withdrawal symptoms, and lower offspring survival compared to our control group. On the other hand, morphine exposure seemed to result in a high number of spontaneous abortions, resulting in fewer successful pregnancies compared to other groups, but fewer deficits in maternal care compared to buprenorphine dams. More research is needed to understand how buprenorphine interacts with the maternal brain during the transition to motherhood to help avoid negative consequences in human mothers undergoing treatment with this opioid maintenance drug.

P3.25 NEURAL CORRELATES OF MATING SYSTEM DIVERSITY: OXYTOCIN AND VASOPRESSIN RECEPTOR DISTRIBUTIONS IN MONOGAMOUS AND NON-MONOGAMOUS EULEMUR

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Contemporary theory that emphasizes the roles of oxytocin and vasopressin in mammalian sociality has been shaped by seminal vole research that revealed interspecific variation in neuroendocrine circuitry by mating system. However, substantial challenges exist in interpreting and translating these rodent findings to other mammalian groups, including humans, making research on nonhuman primates crucial. Both monogamous and non-monogamous species exist within Eulemur, a genus of strepsirrhine primate, offering a rare opportunity to broaden a comparative perspective on oxytocin and vasopressin neurocircuitry with increased evolutionary relevance to humans. We performed oxytocin and arginine vasopressin 1a receptor autoradiography across the entire brains of 12 Eulemur individuals from seven closely related species to (1) characterize receptor distributions across the genus, and (2) examine differences between monogamous and non-monogamous species in regions part of putative "pair-bonding circuits". We find some binding patterns across Eulemur reminiscent of olfactory-guided rodents, but others congruent with more visually oriented anthropoids, consistent with lemurs occupying an 'intermediary' evolutionary niche between haplorhine primates and other mammalian groups. We find little evidence of a "pair-bonding circuit" in Eulemur akin to those proposed in previous rodent or primate research. Mapping

neuropeptide receptors in these nontraditional species questions existing assumptions and informs proposed evolutionary explanations about the biological bases of monogamy.

P3.26 SEASONALITY IN THE CONTROL OF AGONISTIC BEHAVIOR BY ESTROGENS IN A YEAR-ROUND AGGRESSIVE TELEOST

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Agonistic behavior is an adaptive social behavior that emerges from the competition among conspecifics for limited resources. Sex steroids are key factors regulating this behavior. Their role as modulators has been primarily studied within the reproductive season, when circulating sex steroid levels are high. Interestingly, in animals that display agonistic encounters uncoupled from the breeding season, these hormones are still essential. In the electric fish Gymnotus omarorum, a territorial seasonal breeder, non-breeding aggression is expressed in males and females, is independent of gonadal hormones, but depends on rapid estrogen synthesis. Our aim was to fully characterize this year-round aggression and analyze potential seasonality in its underlying hormonal mechanisms.

Intrasexual dyads (n=16) showed short, robust agonistic encounters during the breeding season. Aggression in females was lower during the breeding season than the non-breeding season. The rapid inhibition of aromatase (Fadrozole 20ug/g) had no effect on breeding aggression in either sex, whereas it diminished non-breeding aggression in both sexes (n=28 dyads). Circulating sex hormones in wild-caught fish (n=61) were quantified by LC-MS/MS and showed seasonal and sex differences in androgen levels. Interestingly, in the non-breeding season, plasma estrogens were non-detectable in both sexes. Preliminary results from qRT-PCR in the preoptic area show year-round aromatase expression and an upregulation of estrogen receptor expression in non-breeding males and females. In sum, our results show that G. omarorum displays year-round aggressive behavior that depends on rapid modulatory effects of neuroestrogens with seasonal variation. This seems to be a shared strategy with birds and mammals.

P3.27 TRANSCRIPTOMIC PREDICTION OF ANTIDEPRESSANT TREATMENT RESPONSE

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Early-life stress (ELS) affects nearly one billion children across the world. ELS increases the risk for depression and predicts poor response to standard antidepressant treatments among patients with major depression. However, the relation between ELS and antidepressant non-response remains understudied. Previous studies implicate the nucleus accumbens (NAc) in depression and in antidepressant treatment response. In the NAc of mice, ELS has been shown to sensitize individuals to additional stress in adulthood at the level of gene expression. We hypothesize that ELS produces lasting transcriptional changes in the NAc that predict non-response to antidepressant treatment. To test this, we leverage existing RNA-sequencing datasets from mouse models for ELS and for response to the antidepressants imipramine and ketamine. In mice assigned female at birth, exposure to stress in only adulthood induces gene expression patterns in the NAc similar to those of mice that respond favorably to imipramine and ketamine treatment. However, female mice exposed to ELS prior to adult stress exhibit significant transcriptomic overlap with mice that fail to respond to antidepressant treatment. In male mice, ELS experience before adult stress predicts response to either treatment, reflecting known sex differences in the prevalence of major depression. Ongoing analyses are comparing transcriptional profiles of ELS in our mouse model with antidepressant treatment efficacy in human patients with major depression. Our cross-species computational approach will have translational significance by improving our understanding of the unique transcriptional mechanisms that mediate response to antidepressant treatment among patients that experienced early adversity.

P3.28 PARTNER PREFERENCE FORMATION IN THE LINED SEAHORSE (HIPPOCAMPUS ERECTUS)

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Social monogamy is a reproductive strategy characterized by the tendency for an animal to show a preference for a familiar partner relative to a stranger. While this behavioral pattern is exhibited by less than 5% of mammalian species, it is much more common in other animals, including fish. Seahorses have long been thought to exhibit monogamous behavior, although this has never been thoroughly studied in a laboratory setting. Here we examined behaviors of male and female lined seahorses (Hippocampus erectus) during and after the process of pair bond formation. We observed several types of courtship behaviors, including hitching, swaying, and pumping, and found considerable variation across pairs and sexes. Five days after initial pairing, we performed a partner preference test. Male seahorses exhibited a significant preference for their partner over an opposite-sex stranger. In females, however, this preference was less apparent. At the conclusion of testing, subjects were euthanized, and RNA was extracted from whole brains. These data show that lined seahorses display species-typical courtship behaviors in a laboratory setting and that males form a strong partner preference. Future studies will expand upon these findings, investigate the neuroendocrine and genetic basis of these behaviors, and compare them to behaviors seen in monogamous mammals. Ultimately this research will elucidate the evolutionary history of these complex social behaviors.

P3.29 UNCOVERING THE CIRCUIT CONFIGURATIONS OF AVP-EXPRESSING NEURONS

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The neuropeptide Arginine Vasopressin (AVP) plays a critical role in mammalian homeostatic stress response as well as social behavior. AVP produced in the hypothalamus regulates water osmolality and vasoconstriction in the body and through connections made within the brain it is involved in social regulation, aggression, and anxiety. However, the AVP-dependent links between social behavior, homeostatic function, and disease are not well understood. AVP-expressing neurons are found in only a few areas in the brain but are thought to receive synaptic input from brain regions distributed throughout the nervous system. This study investigates the circuit configurations of AVP expressing neurons in the rodent hypothalamus. We targeted one of the main AVP producing populations, the paraventricular nucleus (PVN) using retrograde tracing techniques to identify afferent and efferent synaptic connections made by these populations of AVP-expressing neurons. AVP neurons in the PVN display region-specific anatomical configurations that reflect their unique contributions to social behavior and homeostatic function. This includes differing inputs from thalamic, hypothalamic and cerebral nuclei areas. This proposed work reveals new insights into the organization of social behavior circuits in the brain, and how neuropeptides act centrally to modulate social behaviors.

P3.30 SEX-SPECIFIC LATERAL SEPTUM CIRCUITS FOR THREAT MEMORY ACQUISITION

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Dysregulation of emotional learning and memory is a core feature of anxiety disorders. Women disproportionately experience anxiety disorders, leading us to hypothesize that emotional memory circuits may differ between the sexes. Using cued threat conditioning as a model for emotional memory, we found robust lateral septum (LS) activation after training in females but not males. Since the LS does not receive input from primary sensory regions, we next questioned which upstream regions recruit the female LS during threat memory acquisition. We bilaterally infused the retrograde tracer cholera toxin subunit B (CTb) into the LS of male and female animals followed by threat conditioning one week later. In ongoing analysis, we are quantifying regional expression of CTb+ as well as CTb/FOS+ neurons throughout the brain. Thusfar, we have not observed any sex differences in input to the LS. We found that the ventral hippocampus (vHC) is the primary source of input to the LS, but vHC→LS projections are robustly activated during training in both sexes. However, we found that LS-projecting neurons in the lateral orbital cortex (LO) are activated by training in males but not in females, whereas LS-projecting neurons in the infralimbic cortex (IL) are activated by training in females but not in males. These data suggest that hardwiring of LS circuitry does not differ between the sexes, but sex-specific activation of upstream regions may drive sex-specific LS activation during threat memory acquisition. Future experiments will determine the causal relationship of LS circuitry on threat memory formation.

P3.31 INFLUENCE OF SPECIES-TYPICAL GROUP SIZE ON SOCIAL PREFERENCES AND REWARD CIRCUITRY RESPONSES TO SOCIAL NOVELTY

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Responses to social novelty and the degree of gregariousness (i.e., a preference to affiliate with large groups) exhibited in a non-reproductive, social context may be influenced by species-typical group size. Using the large-group living, highly social African spiny mouse (Acomys cahirinus) and the closely related, small-group living, moderately social Mongolian gerbil (Meriones unguiculatus), we explore how species-typical group size influences behavioral and neural responses to social novelty in non-reproductive contexts. We hypothesized that high levels of gregariousness may correlate with a tendency to seek social novelty, and that more gregarious animals may exhibit higher activation of reward circuitry. To do this we ran gerbils and spiny mice through a series of behavioral tests to measure preferences for group size, interest in social novelty, and prosocial and aggressive behavior during social interactions with novel, same-sex conspecific. We then conducted an immediate early gene study to examine neural activation of social (i.e., oxytocin) and reward (i.e., dopaminergic) circuitry in response to interactions with a novel, same-sex conspecific. We found that spiny mice preferred affiliating with large groups, were more prosocial, and spent significantly more time investigating a novel, same-sex conspecific compared to gerbils. Additionally, correlations revealed that more aggressive gerbils exhibited greater neophobia, suggesting a relationship between gregariousness and a preference for social novelty. However, no significant correlations were found for spiny mice. Interestingly, PCA analyses yielded distinct components for each species, suggesting that behavioral phenotypes are differentially regulated in gerbils and spiny mice; gerbils also exhibit a more consistent phenotype.

P3.32 EFFECT OF SEASONAL CHANGES AND THERMAL STRESS ON CORTISOL AND GLUCOSE LEVELS IN WILD REDBAND TROUT

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Poikilothermic organisms cope with thermal fluctuations in their environments through physiological and behavioral plasticity. Maintenance of homeostasis due to chronically high thermal stress increases energetic costs. The gluconeogenic hormone, cortisol, circulates at higher levels to provide organisms with the required energy to survive their stressful circumstance. Redband trout (Oncorhynchus mykiss gairdnerii) are a cold-water species that have adapted to survive in warm, arid, desert streams, under environmental conditions that are outside of the optimal temperature ranges of many other salmonids. Here, we measured plasma cortisol and glucose among redband trout (N=480, >2 y) from two cold montane and three hot desert sites in South West Idaho from June through October. Across fish from all streams, cortisol levels were highly variable in June and dramatically decreased in October. The fluctuations in cortisol could be related to relatively rapidly changing water temperatures associated with seasonal transitions during these months. There was also a weak, yet significantly non-zero positive relationship between water temperature and cortisol concentrations ($R2 = 0.17$, $p < 0.001$). Although the trout in desert environments generally faced higher temperatures than that of the montane trout, morphometric data indicates that the body conditions of these two groups are similar. This suggests that desert trout are able to cope with increased temperatures, typically thought to be harmful to salmonids. Circulating glucose levels will be quantified and we hypothesize a positive correlation between cortisol and glucose levels,

because higher glucose levels are known to compensate for the increased energetic demand during stressful periods.

P3.33 THE POSITIVE EFFECT OF ESTRADIOL ON COGNITION IN MIDDLE-AGED FEMALE RATS DEPENDS ON REPRODUCTIVE EXPERIENCE.

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Female-specific characteristics, such as pregnancy, can influence disease risk later in life. Estrogens can improve cognition in postmenopausal women and women with AD, but their effects vary dramatically across studies. This is in part due to different types (primarily estradiol and estrone) and doses of estrogens. However, other factors such as pregnancy and motherhood (parity), can have long-term effects on cognition and brain plasticity in both humans and rodents. Previous research from our lab indicates that reproductive experience influences the neuroplastic ability of the hippocampus to respond to estrogens in middle age. Acute estrogens increase cell proliferation in the hippocampus in middle age in multiparous, but not in nulliparous rats. In the present study, we examined whether maternal age (age of first pregnancy) and 17β-estradiol treatment differentially affected hippocampal neurogenesis and cognition in middle-age. Female rats were either bred at 3 months, 6 months, or were nulliparous (never bred). At 13 months, rats received daily injections of 0.03ug 17β-estradiol (or sesame oil vehicle) for 16 days. From day 12-15, rats were trained on the standard reference memory version of the Morris water maze, and on day 16 they performed a probe trial and reversal training paradigm. We found that that younger maternal age coupled with 17β-estradiol was associated with impaired reference memory performance compared to controls. However, advanced maternal age showed greater cognitive flexibility with 17β-estradiol treatment. Our findings suggest that maternal age and 17β-estradiol influence cognitive performance in middle age.

P3.34 OXYTOCIN/OXYTOCIN RECEPTOR MODULATION OF SOCIAL ODOR INVESTIGATION IN JUVENILE MICE

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For species-typical social development, juvenile mice must strike a balance between motivated approach behaviors and vigilant threat assessment. In adults, the oxytocin receptor (OXTR) increases motivation to explore and threat discrimination. Here, we tested the genetic contribution of Oxtr in male and female juvenile mice behavior toward same-sex adult social odor stimuli. Juvenile (P40-41; N = 70) mice (Oxtr+/+, Oxtr+/-, Oxtr-/-) were exposed to the soiled bedding of same-sex adults with (OXTWT) and without (OXTKO) oxytocin in a three-chamber social-odor interaction test. Repeated measures ANOVAs determined effects of sex and genotype on frequency and duration of behaviors toward OXTWT- and OXTKO-soiled bedding, including olfactory investigation and orienting at a distance (i.e., vigilance). Between-subjects main effects demonstrated that juvenile male mice show heightened frequency and duration of total investigation of the bedding stimuli, while female mice displayed greater frequency of total

vigilance behavior toward the bedding stimuli. An interaction of sex and genotype was evident with duration of orienting, with Oxtr+/- females displaying the highest and Oxtr+/- males showing the lowest total orienting durations. Within-subjects analysis demonstrated a main effect of bedding type, with all juveniles spending more time investigating the OXTWT bedding than the OXTKO bedding, regardless of the Oxtr genotype or sex of the juvenile. In contrast, there was a significant bedding type x genotype x sex interaction for frequency of investigation, with Oxtr+/- males showing more frequent visits to OXTWT bedding. These data begin to show oxytocin's modulatory role in approach-avoidance and sex-specific effects on juvenile behavior.

P3.35 *Withdrawn*

P3.36 PROLACTIN MODULATES THE FEMALE ACCESSORY OLFACTORY BULB RESPONSE TO MALE STIMULI

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Olfactory cues from the opposite sex can induce neuroendocrine and behavioral changes towards reproduction by its processing via the accessory olfactory bulb (AOB). Prolactin (PRL) is one of the hormones regulated by some of these cues and participate in neuroendocrine responses mediated by olfaction. Additionally, there is evidence on the expression of the PRL receptor in the olfactory bulb (OB) during embryonic development. In the present study we aimed to determine the expression of mRNA of PRL and long isoform of PRL receptor (Prl and Prlr-l) in the OB from puberty onset to adult females in C57BL6J mice. We found that the expression of both, Prl and Prlr-l remain stable at all sexual maturation stages. Then, we evaluated the participation of PRL on the response of AOB after sexual relevant odor stimulation. Adult female mice were exposed to bedding from a sexually experienced male after an acute PRL administration. Females exposed to the stimuli that received the PRL treatment showed increased activation of mitral cells in the anterior region of the AOB. Also, PRL promoted an increased exploration of sexual stimuli. In conclusion, our results suggest that PRL is participating on perception and behavioral response to pheromones.

P3.37 MALE-TO-FEMALE SEX CHANGE IN THE COMMON CLOWNFISH AMPHIPRION OCELLARIS IS ASSOCIATED WITH PERSISTENT MALE-LIKE BEHAVIOR AND A UNIQUE SEX HORMONE PROFILE

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Some sex-changing vertebrate species, like the common clownfish Amphiprion ocellaris, display stark social behavioral sex differences, providing a unique opportunity to study sexual plasticity of behavior. When two male A. ocellaris are paired together, the larger fish establishes dominance and changes sex to female. Previous work in this species has established that feminization of the preoptic area of the hypothalamus is complete by six months and precedes gonadal sex change, which can take much longer. Males of this species are precocious parents, and females are highly aggressive toward other females. However, it is not known how these behaviors are expressed in

fish that are actively changing sex. In this study we paired off 60 male A. ocellaris to initiate sex change in the larger fish of each pair. We assessed parental effort, aggression with novel males and females, and circulating androgen (11-ketotestosterone) and estrogen (estradiol) throughout six months of sex change. Results were compared to those from control males and females. We found that sex-changing fish were behaviorally male-like and aggressive until gonadal sex change occurred. Sex-changing fish displayed greater parental effort and greater aggression with novel males and females. In sex-changing fish, both hormones were between control male and female levels, and 11-ketotestosterone was higher compared to non-changing partners. These findings indicate that sex change is not associated with immediate behavioral feminization, but rather with persistent dominant male behavior, until gonadal sex change is completed. This stands in contrast to rapid behavioral sex change reported in other sex-changing fish.

P3.38 REGULATION OF PERINEURONAL NET EXPRESSION IN PRIMARY SOMATOSENSORY CORTEX DURING MATERNAL BEHAVIOR

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Nulliparous adult female mice provide alloparental care after cohousing with the dam and her pups, in a hormone-independent manner. Such non-hormonal factors are thought to be important in mediating plasticity, likely through chromatin remodeling of specific neural circuitry. Previously, we showed that adult female mice deficient in the gene, methyl CpG-binding protein 2 (MECP2), displayed inefficient pup gathering behavior. In addition, the inefficiency correlated with abnormal increased expression of specialized extracellular matrix structures called perineuronal nets (PNNs) in the auditory cortex. PNNs are thought to restrict synaptic plasticity in adult brains. Pharmacological reduction of auditory cortical PNNs in Mecp2-deficient female mice partially rescued efficiency of pup retrieval. This suggests other sensory system(s) related to maternal behavior is affected. Here, we analyzed PNN expression in the whole primary somatosensory cortex (SS1), a brain region for processing tactile information. We found that subregions of the SS1 of adult wild type female exhibited dynamic changes in PNN expression after alloparental experience. Mecp2-deficient female mice exhibited atypical SS1 PNN expression before and after this experience, resulted in inefficient pup gathering behavior. Finally, pharmacological bilateral reduction of SS1 PNNs in Mecp2-deficient female mice rescued pup gathering behavior. Taken together, our data suggest critical roles for both primary somatosensory cortex and PNNs in this multisensory pup gathering behavior.

P3.39 REGULATION OF SOCIAL BEHAVIOR BY NONCANONICAL GENOMIC IMPRINTING IN THE BRAIN MONOAMINE SYSTEM

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Genomic imprinting is a form of epigenetic regulation in which one of a gene's alleles, either of maternal or paternal inheritance, is silenced and the opposite parental allele is exclusively expressed. Some genes are considered to be noncanonically imprinted, meaning they exhibit a bias towards higher expression of either parental allele. Noncanonically imprinted genes have been identified at the tissue level by RNAseq analyses and follow-up studies indicate that noncanonical

imprinting effects may involve highly cell-type specific imprinting. Tyrosine hydroxylase (Th) and Dopa decarboxylase (Ddc) encode monoamine synthesis enzymes and preferentially express their maternal allele in particular brain regions. Genomic imprinting in the brain is theorized to regulate social behaviors in offspring. TH and DDC enzymes are in the catecholamine synthesize pathway of dopamine, norepinephrine, and epinephrine; DDC is also in the pathway of serotonin. Monoamine neurotransmitters are critical regulators of social behavior and are implicated in human mental illnesses. Here we investigated the functional effects of noncanonical imprinting of Th and Ddc on social behavior in mice. By using reciprocal maternal and paternal allele mutant mice we tested the impacts of Th and Ddc heterozygosity on social preference, recognition, and dominance behaviors. We found that Th and Ddc heterozygous mutations impact certain aspects of social preference behavior. Furthermore, some heterozygous mutation effects are dependent on whether the mutation is inherited from the mom compared to the dad. These results imply that maternal biased allelic expression in the monoamine system in the brain functions to regulate social behavior phenotypes.

P3.40 SOCIAL STATUS AND ITS EFFECTS ON CORTISOL IN THE BRAIN OF THE BLUEBANDED GOBY

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Cortisol, a hormone that controls stress-induced responses in all vertebrates, may be an important mediator of changes in behavioral phenotype due to changes in social structure. Bluebanded gobies, Lythrupnus dalli, are bidirectionally hermaphroditic fish that live in complex social structures comprised of a linear dominance hierarchy. Sex change occurs due to a change in social structure, such that upon male removal (MR), the most dominant female exhibits rapid increases in rates of aggression and territoriality. We investigated the water-borne and brain cortisol levels in fish living in a stable social structure and rapidly following a disruption in status. For fish living in stable groups, status had no effect on water-borne cortisol levels. Within 30 min of MR, there were no changes in water-borne cortisol levels. However, 24 h after MR, subordinate females had significantly higher water-borne cortisol than transitioning fish. We then focused on microsections of brain (rostral, middle, and caudal) tissue collected 30 minutes after MR. There was no significant difference in cortisol levels across any brain region for dominant or subordinate fish. We will compare cortisol levels in brains of fish in stable and transitional groups. Additionally, we will analyze cortisol levels within the context of agonistic and subordinate behavior exhibited by these fish during hierarchy resolution. Future studies will include measuring levels of glucocorticoid receptor mRNA levels within these regions. Measuring localized glucocorticoid signaling within region specific brain areas will provide insight into the mechanisms that facilitate behavioral interactions in stressful social environments.

P3.41 A TIMELY REMINDER: WITHIN-SEX INDIVIDUAL DIFFERENCES IN TESTOSTERONE ARE NOT A PROXY FOR MASCULINITY (AND MOST OTHER THINGS PEOPLE THINK)

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The role of steroid hormone testosterone (T) in masculinizing anatomy and behavior during critical developmental windows is well understood. However, this organizational effect of T produces

misunderstandings in the role of circulating basal T in adulthood. Unsubstantiated folk wisdom about T – that individual differences in endogenous levels, within-sex, predict factors like strength, body size, athleticism, competitive and dominant personalities, and an eternal sense of "masculinity" - remain evasive in society and popular media despite contradictory evidence in the scientific literature. Consequences of this folk wisdom have led to entire pseudoscientific medical and pharmacological industries and even discriminatory practices for dealing with "high T" women athletes. In a correlational study of 418 college students, I show that within-sex variability in basal T levels are unrelated to all physical and psychological factors traditionally thought to be T mediated. Specifically, among the 270 females and 149 males tested, baseline T and T averaged across the study period did not correlate with body size, self-reported masculinity and femininity in body and personality, competitiveness, dominance motivation, or persistence in a behavioral task of competitive will. Furthermore, there was no difference in T levels between those who identified an athlete compared to those who did not and those who reported regular strength-based exercise (e.g., weightlifting) compared to those who did not. These results will be discussed both in terms of the behavioral function of circulating T and the social-political role of T in informing the classification of "biological sex."

P3.42 MATERNAL WESTERN-STYLE DIET INCREASES HIPPOCAMPAL VOLUME AND ALTERS PROSOCIAL ENGAGEMENT AND IDIOSYNCRATIC BEHAVIOR IN JAPANESE MACAQUES

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The chronic complications associated with obesity place a heavy burden on our public health system. Oxidative stress induced by obesity and the overconsumption of obesogenic diets, such as the Western-Style Diet (WSD), lead to hypertrophic environments throughout the body. These hypertrophic environments stimulate the production of inflammatory cytokines and increase the overall systemic inflammatory profile. During pregnancy, these changes are reflected in the placental inflammatory profile. It is well established that changes to the placental immune milieu are associated with alterations to fetal neurodevelopment and postnatal behavioral outcomes. Epidemiological studies have associated higher prepregnancy body mass index with an increased risk of neuropsychiatric diagnoses such as Attention Deficit Hyperactivity Disorder (ADHD) and Autism Spectrum Disorder (ASD) in children. Using an established non-human primate model (macaca fuscatta) of maternal western-style diet (mWSD), we assessed differences in offspring behavioral phenotypes during the Novel Peer Introductions (NPI, n= 39) at six months of age. Results show that mWSD offspring display decreased social engagement behavior (initiated proximity,$p = .02$; affiliative contact,$p = .048$) and increased idiosyncratic behavior ($p=.03$). Structural MRI results show differences in hippocampal volume may underlie behavioral observations, where mWSD offspring exhibit increased hippocampal volumes at four (left, $p=.032$; right, $p=.018$) and six (left, $p=.002$; right, $p=.01$) months. Both behavioral and volumetric results suggest mWSD macaque offspring display phenotypes similar to those described in individuals diagnosed with an ASD. These findings support and expand on previous hypotheses that mWSD alters postnatal behavioral outcomes.

P3.43 DAYTIME LIGHT INTENSITY MODULATES NEUROINFLAMMATION IN A DIURNAL RODENT

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Microglia-induced neuroinflammation has been implicated in human depression and dementia. The objective of the present study was to evaluate the effects of daytime light intensity on neuroinflammation in a diurnal rodent, the Nile grass rat (Arvicanthis niloticus). Previous studies have found that compared to grass rats housed in bright light (bright-L, 1000 lux) during the day, those housed in dim-L (50 lux) showed increased depression- and anxiety-like behaviors and impaired spatial memory. The present study examined the effects of bright or dim daylight on neuroinflammation using immunohistochemistry or qPCR for the microglia markers Iba-1and CD11b, as well as proinflammatory cytokines TNF-α and IL-6, in the dorsal hippocampus (dHipp), basolateral amygdala (BLA), and anterior cingulate cortex (ACC). Iba-1 immunostaining revealed that dim-L animals had higher numbers of microglia in the dHipp, and more branching in the dHipp, BLA, and ACC compared to animals in bright-L. A sex difference of more microglia in females was found in the BLA. For the expression of CD11b, TNF-α and IL-6, significant interactions between light and sex was found in the dHipp and BLA, but no significant effects were found in the ACC. In the dHipp, TNF-α and CD11b expression was higher in dim-L in females, but not different in males; whereas in the BLA, TNF-α and IL-6 expression was higher in females but lower in males in bright-L than in dim-L. These findings suggest that neuroinflammation could play a role in the depression-like behaviors and cognitive impairments induced by daytime light deficiency.

P3.44 EXERCISE PLASMA BOOSTS MEMORY AND DAMPENS BRAIN INFLAMMATION VIA CLUSTERIN

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Physical exercise seems universally beneficial to human and animal health, slowing cognitive aging and neurodegeneration . Cognitive benefits are tied to increased plasticity and reduced inflammation within the hippocampus, yet little is known about the factors and mechanisms mediating these effects. We discovered that "runner" plasma, collected from voluntarily running mice and infused into sedentary mice, reduces baseline neuroinflammatory gene expression and experimentally induced brain inflammation. Plasma proteomic analysis revealed a striking increase in complement cascade inhibitors including clusterin (CLU), a central protein for the anti-inflammatory effects of runner plasma. Intravenously injected CLU strongly binds to brain endothelial cells reducing their inflammatory gene expression in an acute model of brain inflammation and in an Alzheimer's disease mouse model. Cognitively impaired patients participating in structured exercise for 6 months had higher plasma clusterin levels. These findings demonstrate the existence of anti-inflammatory "exercise factors" that are transferrable, target the cerebrovasculature and benefit the brain, and are present in humans engaging in exercise.

P3.45 BRAIN REGION-SPECIFIC CONCENTRATIONS OF SEX STEROIDS DURING AGGRESSIVE ENCOUNTERS IN A HERMAPHRODITIC FISH

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In vertebrates, rapid responses during conspecific aggressive encounters are mediated by neural steroid synthesis that precedes changes in systemic steroids. In teleost fishes, brain region-specific regulation of steroids in response to aggression is not fully understood. Whole brain levels of a potent teleost fish androgen, 11-ketotestosterone (KT) and the estrogen, 17β-estradiol (E2) change 24 h into hierarchy resolution in bluebanded gobies, Lythrypnus dalli. These fish are bidirectional hermaphrodites that live in linear hierarchies with a nesting male and multiple subordinate females. Here, we investigated dynamic hormone-behavior relationships associated with disruption of hierarchy. We made social groups of L. dalli comprising of one male and two females and verified stable status via behavioral observations. We found baseline differences in water-borne KT and E2 between dominant and subordinate fish. We then disrupted hierarchy via male removal (MR) or male addition (MA). Within 30 min of instability, there were differences between the aggressive intensity displayed by two males versus two females, but systemic steroids were not affected. To gain insights into spatial specificity of hormone signaling, we next measured differences across multiple regions of the brain. After MR or MA, we quantified dynamic encounters between fish for 30 min and collected brain tissue. Across all fish, rostral areas of the brain, that contain the medial preoptic areas had highest levels of KT and E2. Identification of discrete areas and/or neural connective pathways involved in steroid signaling will help understand mechanisms for rapid regulation of motivated behaviors such as aggression.

P3.46 THE INFLUENCE OF MATERNAL ADIPOSITY AND NUTRITION ON CHILD RISK FOR PSYCHOPATHOLOGY

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Epidemiological studies demonstrate an association between developmental exposure to maternal obesity and increased incidence of neurodevelopmental disorders; however, the mechanisms for this association remain largely unknown. Our work, using non-human primate models, demonstrates causal effects of maternal obesity and poor nutrition on offspring negative affect, specifically increased anxious behaviors. Here we present data from a longitudinal, prospective human study designed to examine the influence of maternal metabolic state and nutrition on child risk for psychopathology. We hypothesized that developmental exposure to maternal obesity and/or poor maternal nutrition increases infant negative affect. In this study participants (N=300) completed 3 unannounced 24-hour dietary recalls and had their body composition measured using a BodPod during the second and third trimesters of pregnancy. At 1, 6, and 12 months postpartum, participants complete the Infant Behavior Questionnaire to track infant temperament. Our data support an interaction between maternal adiposity and dietary omega-6/omega-3 fatty acid ratio and infant negative affect. We observed an association between greater adiposity during the second trimester and increased infant negative affect and sadness at 1 months of age and sadness

at 12 months of age when mothers consumed a diet with a high omega-6/omega-3 ratio during pregnancy (ps<0.04). This data suggest that focusing on increasing consumption of foods rich in omega-3 fatty acids in pregnancies complicated by obesity is important in improving child neurobehavioral outcomes. It is critical that future studies further isolate the potential mechanisms that underlie the complex relationships between maternal metabolic state and nutrition and child behavioral outcomes.

P3.47 ESTRADIOL IN THE MEDIAL PREFRONTAL CORTEX OF FEMALE MICE RAPIDLY FACILITATES SOCIAL RECOGNITION BUT NOT OBJECT RECOGNITION.

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An important component of social cognition is Social Recognition (SR) the ability to differentiate between conspecifics. SR has been found to be mediated in several brain regions and by various neurohormones, including estrogens such as estradiol (E2). For instance, within minutes of infusing E2 into the hippocampus and medial amygdala, SR is facilitated in female mice. Another brain region likely to mediate SR is the medial prefrontal cortex (mPFC) since it has a role in social cognition and E2 rapidly mediates other forms of memory in this region. Therefore, we hypothesize that E2 in the mPFC rapidly facilitates SR. In this project, sexually mature female mice were ovariectomized (ovx) and had a cannula implanted above their mPFC. Mice received an infusion of either E2, at 25nM, 50nM or 100nM, or a control of 0.02% ethanol in aCSF into the mPFC, 15 minutes before taking part in a social recognition paradigm too difficult for ovx control mice to demonstrate SR. The entire paradigm was completed within 40 minutes, to observe the rapid effects of E2 on SR. Results demonstrated that E2 infused into the mPFC rapidly facilitates SR. A second experiment was conducted to assess if the role of E2 in the mPFC is selective for SR, or if it extended to other forms of recognition memory. Mice were run through a difficult object recognition (OR) paradigm. Preliminary results suggest that E2 does not rapidly facilitate OR in the mPFC, suggesting it may facilitate SR specifically. Overall, this research will provide us with novel information on the rapid effects of estrogens on social cognition within the social brain.

P3.48 THE RIPPLE EFFECT OF A SINGLE NUCLEOTIDE POLYMORPHISM IN THE BDNF GENE ON ESTRADIOL-MEDIATED COGNITION IN MIDDLE-AGED FEMALE RATS

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A common human single nucleotide polymorphism in the brain-derived neurotrophic factor (BDNF) gene (Val66Met), shown to modulate BDNF signaling, is associated with greater risk for neural disorders, including anxiety and age-related cognitive decline in Met-carriers. Estrogen and stress status regulate and are regulated by BDNF. These states also interact to modulate learning and memory. Thus, cascading effects of impaired BDNF release in Met-carriers on the hypothalamic-pituitary-gonadal and hypothalamic-pituitary-adrenal axes may produce cognitive impairments, with Met-carriers being insensitive to estrogenic modulation. We tested this using female homozygous CRISPR/cas9 rats that model the human Val66Met. Ovariectomized, middle-aged rats received a daily injection of vehicle or 17beta-estradiol-benzoate (EB) 48 and 24 hours prior to

testing on an object recognition task. There was a genotype by treatment interaction, with recognition scores increasing in EB-treated Val/Val rats but decreasing in EB-treated Met/Met rats. Remarkably, adrenal weights were 3-fold heavier in Met/Met rats compared to Val/Val rats, matching their elevated anxiety-like and stress-related behaviors. Moreover, compared to Val/Val rats, Met/Met rats exhibited considerably accelerated reproductive senescence, with earlier onset of irregular cycles and acyclicity by ~3 months and less time spent in proestrus. These results suggest a lifelong deprivation of estradiol in female Met-carriers that might magnify the effects of BDNF deficiency. The Val66Met appears to produce a ripple effect in female Met-carriers such that impaired BDNF signaling in the brain, ovaries, and adrenals alter hypothalamic-pituitary-gonadal and hypothalamic-pituitary-adrenal function, yielding reduced hormone neuroprotection and elevated vulnerability to stress that culminates in increased risk for neural disorders.

P3.49 PAIR BONDING IS ASSOCIATED WITH THE REGULATION OF OXYTOCIN RECEPTOR AND PARTNER-SEEKING DURING LOSS IN PRAIRIE VOLES

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In social species such as humans and the socially monogamous prairie vole, the dissolving of social bonds is disruptive, leading to increased stress responsiveness and a strong desire for reunion with the lost loved one. Epigenetic regulation of the oxytocin receptor (OTR) has been implicated in the formation of pair bonds in prairie voles, with pair-bonded animals showing increased histone acetylation at the OTR promotor region, leading to increased OTR mRNA expression in the nucleus accumbens (NAc). While epigenetic mechanisms appear to contribute to oxytocin's facilitation of pair bonding, it is still unknown how long these changes in the oxytocin system are maintained. Additionally, some prairie voles never form a pair bond with an opposite sex animal, and little is known about the neurochemical phenotype underlying this lack of bond formation. Here we hypothesize that pair bonding is associated with epigenetic regulation of OTR expression in the NAc, and that these markers are maintained after loss of a partner and promote partner-seeking behavior. We used social conditioned place preference to assess the rewarding properties of the subjects' partner in pair-bonded animals that remained in an intact pair, pair-bonded animals that lost their partner, and non-bonded animals that lost their partner. We found that pair-bonded animals that lost their partner spent more time in the chamber associated with their partner than pair-bonded intact animals and non-bonded animals that lost their companion. We also assessed histone acetylation at the OTR promotor region, OTR mRNA expression, and OTR binding in the NAc.

P3.50 OROFACIAL STIMULATION IN NEONATAL MICE

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Oxytocin (OXT) is an essential neuropeptide involved in social behaviors such as mother-infant attachment. Milk and saliva contain OXT produced by the mother that may be shared with the infant. We have previously identified oxytocin receptor (OXTR) in the orofacial region of neonatal mice. We propose that exogenous OXT may cue the infants' oxytocin receptors (OXTR) to label maternal touch as a social interaction. We hypothesize that OXT co-applied with sensory stimulation will modulate infant behavior. Neonatal male and female C57/BL6j wildtype mice were

observed in a socially isolated environment for two hours on the day of birth (P0). After two hours of habituation to social isolation, tactile stimulation was applied to the whisker pads and mouth of neonates for 30 seconds with a paintbrush coated in either saline, a low dose (1.56pg/uL) of OXT in saline, or a high dose (1.25ng/uL) of OXT in saline. Neonates were observed for an additional 60 seconds after stimulation. Our results demonstrate temporal changes in neonatal behavior in response to the presentation of tactile orofacial stimulation paired with exogenous OXT exposure in a socially isolated setting. Exogenous OXT paired with somatosensory stimulation may facilitate optimal nursing and infant attachment in early social development.

P3.51 OXYTOCIN MODULATES SENSITIVITY TO ACCULTURATION AND DISCRIMINATION STRESS IN PREGNANCY

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Latinas in the United States suffer disproportionately high levels of pre- and postnatal depression. However, little is understood regarding biopsychosocial mechanisms linking socio-environmental factors and increased in mental health risk. The oxytocinergic system may be an important modulator of this sensitivity. We have previously reported prenatal discrimination to be a predictor of postnatal depression in Latinas; here we tested whether sensitivity to discrimination stress depends on oxytocinergic system activity. A sample of 148 Latina women residing in the US were assessed prenatally at 24-32 weeks' gestation and 4-6 weeks postnatally for perceived discrimination exposure, acculturation and depression and anxiety symptoms. Plasma oxytocin (OXT) levels and DNA methylation of the oxytocin receptor (OXTR) were measured prenatally together with genotyping for the OXTR SNP, rs53576. In mothers with low OXT levels and low OXTR methylation, acculturation level was associated with postnatal depression and anxiety symptoms. No such associations were found in those with higher OXT levels and higher OXTR methylation. We also found a significant relationship between prenatal discrimination and acculturation and postnatal depression and anxiety in carriers of the G-allele at rs53576. OXTR methylation positively correlated with a mother's reported exposure to affiliative social touch, and social touch mediated the relationship between discrimination and postnatal depression in those with low OXTR methylation. These results support the hypothesis that the oxytocinergic system modulates sensitivity to prenatal stress in the development of postnatal mood and anxiety disorders in Latina mothers.

P3.52 NEUROPROTECTIVE EFFECTS OF ESTRADIOL AND GENISTEIN IN THE ZEBRA FINCH (TAENIOPYGIA GUTTATA) CEREBELLUM POST-LESION

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The estradiol (E2) synthetic pathway converts testosterone to E2 via aromatase (AROM), and plays an important role in neuroplasticity. However, exogenous E2 increases cancer risk and interferes with gonadal function. Phytoestrogens, plant-based estrogens, may provide neuroprotection without negative E2 effects. Genistein (GEN), a soy phytoestrogen, binds to estrogen receptor beta in the cerebellum. The songbird cerebellum is an ideal model for steroid-mediated plasticity. Songbird brains are highly plastic and contain all steroidogenic synthetic enzymes. Previous studies in zebra finches have shown that AROM and E2 prevent post-injury secondary neurodegeneration. In this study, adult male ZFs (n=6/group) were implanted with either E2, GEN, or silastic vehicle, and injected with either saline or an AROM inhibitor, letrozole (LET), during delivery of cerebellar puncture lesions. We tracked body mass changes and examined testes morphology. We found E2 compared to GEN and control birds, reduced testes mass, spermatozoa presence, sperm density, and testes laminarity. Body mass, which often decreases in handled birds, decreased in E2 and control, but not GEN birds, suggesting additional GEN benefits. Preliminary measures of TUNEL reactive necrosis (n=3/group) indicate LET versus saline increases apoptosis, but neither GEN nor E2 decreased apoptosis compared to controls with E2 trending upward and GEN trending downward compared to controls. Results confirm local AROM is neuroprotective post-cerebellar-lesion in zebra finches. Contrary to other results, systemic estrogens did not provide neuroprotection. Analyses are ongoing; final TUNEL and Fluoro-Jade reactive lesion volumes and circulating levels of estrogens will refine conclusions.

P3.53 PROJECTIONS FROM PROLACTIN-RESPONSIVE NEURONS IN THE MEDIAL PREOPTIC AREA ARE WIDE-SPREAD IN THE MALE MOUSE BRAIN

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Parental care is a critical component of successful reproduction in mammals. In comparison to maternal care, however, the underlying neuroendocrine mechanisms supporting paternal behavior are less well-studied. Laboratory mice show a mating-induced onset of paternal care and suppression of infanticide (normally observed in virgins). Using this model, we have recently shown that prolactin responsive (Prlr) neurons in the medial preoptic area (MPOA) of the hypothalamus are required for the display of pup retrieval behavior in father mice. However, how prolactin action in the MPOA of fathers leads to a change in behavior is currently unknown. To determine where in the brain these prolactin-sensitive MPOA neurons are projecting to, we unilaterally injected a cre-dependent YFP-labeled anterograde tracer AAV into the MPOA of Prlr-cre-IRES-tdtomato males (n=4). The highest level of YFP fiber labelling was observed within the MPOA itself, bilaterally in the bed nucleus of the stria terminalis and in the premamillary nucleus. YFP-labelled fibers were also detected bilaterally throughout the forebrain including the subfornical organ, paraventricular and periventricular nuclei, retrochiamatic area, and the fasciculus retroflexus. Ipsilateral projections were detected in the anterior and lateral hypothalamus, caudal arcuate nucleus, ventromedial hypothalamus, and the medial, basolateral, and central amygdaloid nucleus, with contralateral projections in the dorsomedial hypothalamic nucleus. In the brainstem, fibers were detected bilaterally in the periaqueductal grey, parabrachial pigmented nucleus and superior and medial

vestibular nuclei. Overall, Prlr-expressing MPOA neurons project widely throughout the brain, and prolactin may influence multiple facets of paternal care through these different projections.

P3.54 DIRECT AND INDIRECT PRIOR STRESS EXPOSURE MODULATES PREFERENCE FOR STRESSED CONSPECIFICS IN MALE RATS.

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Empathy is the ability to perceive, understand, and share others' emotional states, which is thought to be conserved across many mammalian species. It has been reported that rats approach a juvenile conspecific in distress while avoiding a stressed adult, representing social affective processes including empathy. Prior stress experience and thereby obtained own internal states notably modulate empathic-like behaviors. Here, we examined whether prior stress experience modulated rats' social preference behaviors based on others' distress states, especially focusing on the nature of the prior experienced stress.

Male Wistar-Imamichi rats (8 weeks old) were assigned to one of 5 experimental groups (Naive (n=7), Housed with shock-experienced cagemates (n=15), Low (n=15), Middle (n=14), and High shock-experienced (n=14)). Except for the naive and housed with stressed mates groups, they were subjected to a contextual fear conditioning with two foot-shocks (5s for each; 0.1, 0.5, or 1.0 mA, respectively). Twenty-four hours after the contextual fear conditioning, they were exposed to two stimulus conspecifics and allowed to explore them for 10 min freely. One of the two stimulus conspecifics was naive; the other was in distress due to acute two foot-shocks (5s for each; 1.0 mA). The exploration time toward each stimulus conspecific was measured. After this procedure, rats were introduced to the fear conditioning chamber, and conditioned freezing responses were observed.

In the fear memory test, rats in the high and middle shock-experienced groups showed significantly higher freezing rates than those in the naive, housed with stressed mates, and low shock-experienced groups did. The freezing rate of the low shock-experienced group was significantly higher than those of the naive and housed with stressed mates groups. To evaluate their preference for the stressed conspecific, we calculated a preference index (=Exploration time to the stressed conspecific/Total exploration time). One-sample t tests revealed that the preference indices were significantly higher than the chance level (=50%) in the housed with stressed mates ($t(14)=3.1281$, $p=.007$) and high shock-experienced groups ($t(13)=2.5658$, $p=.023$). In any other groups, on the other hand, the preference indices were not significantly different from the chance level.

The high shock-experienced rats exhibited preference for the conspecific in distress while the low and middle shock-experienced rats did not. These findings suggest that stress experience itself is not sufficient to trigger the preference for the stressed conspecific, but the severity of experienced stressor is critical for the preference for the conspecific in distress. Additionally, rats that were not directly exposed to shocks but housed with shock-experienced conspecifics approached the distressed conspecific. Stress-related signals are indirectly transmitted from shock-experienced rats to their cage-mates due to social interactions with each other, and then modulate cage-mates' preference for the distressed conspecific. Our study shows that prior stress experiences through both direct shock exposure and social transmission modulate the social preference based on others' affective states, suggesting the importance of prior experience on empathic-like behaviors in rats.

P3.55 IMPACT OF PERIGESTATIONAL OPIOID EXPOSURE ON JUVENILE PLAY BEHAVIOR AND OXYTOCIN RECEPTOR BINDING IN RATS

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Social behavior is an essential component of individual survival and reproductive success in rodents. Proper development of social behavior in adulthood can occur only when rodents experience rewarding social play during adolescence. Juvenile play behavior is mediated by several neurotransmitter systems, including endogenous opioids. Clinically, children exposed to opioids in utero have a harder time making friends and tend to spend more time alone, suggesting that social behavior is less rewarding. To elucidate the underlying neural mechanisms whereby opioids modulate social behavior, we developed a preclinical model in which female rats are exposed to clinically relevant levels of morphine prior to and throughout gestation, ending when pups are postnatal day 6. Juvenile play behavior of adolescent pups was observed at 25, 35, and 45 days of age. Our data show that females exposed to opioids perigestationally showed a significant reduction in social play, with a corresponding increase in time spent alone. Morphine-exposed females also initiated fewer pins and nape attacks. Together, this data suggests that females perigestationally exposed to morphine are less motivated to participate in social play, potentially due to an alteration in the reward circuitry due to developmental exposure to morphine. As oxytocin has been previously implicated in social bonding, studies are underway to assess for changes in OT expression and signaling in social reward associated brain regions, including the NAcc and VTA.

P3.56 PAIR BOND FORMATION IN THE CALIFORNIA MOUSE

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The California mouse demonstrates strict monogamy, characterized by the formation of pair-bonds. Pair-bonds are quantified using partner-preference-tests and are defined as a significant social preference for the mate over a stimulus. There is disagreement on how long pairs must cohabitate for this criterion to be met. Additionally, few studies test for sex differences in pair-bond formation. The aim of this study was to test for sex differences on the effect of cohabitation length on pair-bond formation. Estrus females were used to create male-female pairs. After the 1, 3, 5, or 7 days of cohabitation, one member of the pair was assigned as the focal, the other and an opposite-sex stranger mouse were tethered in an opposing chambers of a 3-chambered cage. Focal animals were able to move freely throughout the cage. Affiliation, time in and entrance to each chamber, attack frequency and duration were scored for both the mate and stimulus. Focal animals spent significantly more time in and entering the mate's chamber. Focal animals attacked the stimulus more often and for longer. Focal males were more aggressive toward the stimulus than mate, females showed no difference. Analyses revealed no effect of length of cohabitation on the dependent measures indicating that California mice pairs can form bonds after 24 hours of cohabitation. Since previous studies, that did not examine estrus, found no evidence of bond formation following 24 hours of cohabitation, our work highlights the need for future research on the impact of estrus cycle and/or copulation on pair-bond formation.

P3.57 OVARIAN HORMONES TUNE AMYGDALA INHIBITION TO DRIVE ANXIETY-LIKE BEHAVIOR ACROSS THE ESTROUS CYCLE

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Ovarian hormone fluctuations influence emotional processing. In the context of anxiety disorders, high levels of ovarian hormone concentrations relieve anxiety symptoms compared to low levels. Similarly, female rodents experience decreased anxiety-like behavior during proestrus compared to low levels during diestrus. However, the cellular mechanisms driving the anxiolytic effect of proestrus remain unknown. The basolateral amygdala's (BLA) activity is tightly regulated by GABAergic parvalbumin-expressing interneurons (PVIs). Studies indicate that PVIs express hormone receptors. We hypothesized that ovarian hormones regulate BLA PVI activity to drive anxiety-like behavior across the estrous cycle (EC). We performed electrophysiology on BLA PVIs and found that BLA PVIs in proestrus had hyperpolarized resting membrane potential and reduced frequency of miniature excitatory postsynaptic currents, indicating reduced function. We thus hypothesized that increasing BLA PVI activity would eliminate the anxiolytic effect of proestrus. We injected excitatory DREADDs into the BLA of male and female PV-IRES-Cre mice and validated that CNO administration induced equivalent c-fos expression. We activated BLA PVIs prior to the elevated plus maze (EPM), open field (OF), and social interaction (SI) tests. Activation reversed the anxiolytic effects of proestrus while having no effect on males or diestrus females in the EPM or OF. During the SI test, activation decreased social preference in females only. Our data suggests PVI activity is decreased in proestrus females, indicating a shift in the regulation of BLA inhibition across the EC, and that increased BLA PVI activity promotes, rather than inhibits, anxiety-like behavior, opposing current models of BLA inhibition.

P3.58 USING DEEP LEARNING APPROACHES TO QUANTIFY GOAL DIRECTED MOVEMENTS DURING PUP RETRIEVAL BEHAVIOR OVER DAY

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Maternal behavior is a well-studied complex social behavior paradigm involving care and retrieval of pups to the nest. Previous studies report on qualitative observations and quantitative endpoint measurements of retrieval, but little is known about the dynamic sequences and trajectories of this behavior. Systematic analysis of the dynamic sequences of goal-related movements and their corresponding trajectories are essential for understanding the underlying neural circuits involved. Manual systematic frame by frame analysis using DataVyu coding software revealed crystallization of search-approach-retrieval behavior in surrogate WT (SurWT), but not in a female Mecp2-heterozygous (SurHet) mouse model of Rett Syndrome. Little is known about the goal directed trajectories of these mice which is critical for understanding the neural circuits required for crystallizing this behavior. Recent advances in marker-less pose estimation techniques, such as DeepLabCut, allow for extraction of goal directed trajectories. Here we use DeepLabCut to generate trajectories of SurWT and SurHet across 6 days of maternal behavior. We find distinct differences in orientation angles, time spent in ROIs, and trajectories of surrogates during pup retrieval. In our future analysis, we will use supervised machine learning to predict behavioral sequences, and unsupervised machine learning to identify novel behavioral motifs of goal-related movements during pup retrieval. These findings will facilitate studies investigating the underlying circuits of these behaviors.

P3.59 NEURAL MECHANISMS OF SOCIAL BONDING ACROSS CONTEXTS

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It has been postulated that the neural mechanisms underlying maternal-offspring bonds in mammals may have been co-opted for monogamous pair bonding. But the interrelatedness of these two phenotypes is still poorly understood. Prairie voles (Microtus ochrogaster) are a socially monogamous species in which females form social bonds with both offspring and mating partners. Within shared neural mechanisms, the nucleus accumbens (NAc) is central to the outlined "pair bonding" and "maternal" neural circuits and has a significant role in controlling the reward and motivation to engage in these social phenotypes. To assess the role of the NAc in social bonding across contexts, we chemogenetically inactivated the NAc in a series of within-subject behavioral tests. A partner preference test (PPT) was performed during pregnancy and again after parturition, with an own-pup retrieval test performed in between PPTs. Inactivating the NAc did not abolish partner preference before parturition but it did significantly decrease time spent with the partner between conditions. NAc inactivation also did not abolish maternal care but did increase latency to retrieve all pups. Independent of NAc inactivation, time spent with partner was decreased after parturition, but NAc inactivation fully abolished the post-birth partner preference. We interpret these results as support for the hypothesis that in females, NAc activity modulates the motivational salience of social stimuli (i.e., pups and partners) in general, and that salience of a mating partner is specifically weakened after bonding with offspring.

P3.60 CHARACTERIZATION OF MICE PUP ULTRASONIC VOCALIZATIONS DURING RETRIEVAL USING DEEPSQUEAK, A DEEP LEARNING PROGRAM

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During pup retrieval task, an experienced adult female (surrogate, Sur) mouse is tasked with retrieving scattered pups to the nest. Studies from the 1960s showed that rat dams use a combination of olfactory, tactile, and auditory information to locate, identify and retrieve pups. Isolated pups emit ultrasonic vocalizations (USVs), thought to act as 'distress calls' which prompt retrieval from adults. However, retrievals are fast, and can occur without USVs. This prompted us to inquire if pup USVs are indeed 'distress calls' and broadly, if they communicate socially relevant information useful for retrieval.
As a first step, we analyzed ~10,000 calls emitted by pups, (days 0-5), in isolation and during retrieval, after manual curation and using DeepSqueak analysis. Though pup calls in isolation have been reported for decades, fewer studies have reported characteristics of pup calls during physical interactions with adults. Changes in call frequency from lower (~70 kHz) to higher (~110 kHz) occurred around pup age day 3. We found significant developmental changes in spectral and temporal properties of pup calls, regardless of different conditions (isolation/retrieval phase, genotype of retrieving adults and successful or failed retrievals). Furthermore, we identified ~13 single call types using two different hierarchical clustering analysis. From these initial analysis, we do not see significant differences in spectral and temporal call characteristics produced during

retrieval interaction or isolation, suggesting that these features may not be important for pup retrieval by adult mice.

P3.61 VIDEOPLAYBACKS ELICIT ENDOCRINE RESPONSES IN MALES OF THE SIAMESE FIGHTING FISH BETTA SPLENDENS

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Hormones have been associated with the modulation of aggressive behavior in fish. Earlier studies have shown that androgens and corticosteroids increase in response to mirror images and interacting conspecifics in males of the Siamese fighting fish Betta splendens. However, it is still not clear which components of the interaction trigger the endocrine response and whether animals secrete these hormones to regulate behavior during ongoing fights, future fights or both. The presentation of controlled stimuli in videos, a.k.a. videoplaybacks, could provide an alternate method for aggression studies, allowing better control of the fight components. However, videoplaybacks have produced conflicting results in animal behavior studies and need to be carefully validated. Here, we compared the behavioral and endocrine response of male B. splendens to non-interactive fights by presenting them with matched for size conspecific fighting behind a one-way mirror or a videoplayback of a similar fight. The aggressive response started with stereotypical threat displays and progressed to overt attacks, which were overall similar in frequency and duration towards both types of stimuli. There was a marked and comparable increase in plasma androgen (11-ketotestosterone) to both types of stimuli while videoplaybacks also induced a corticosteroid (cortisol) response. The endocrine responses seemed to be reduced when compared to interactive mirror or live-conspecific fights, suggesting that fight dynamics is an important component of the interaction. Overall, the study shows for the first time in a fish a robust endocrine response to video stimuli and supports its use for the investigation of behavior in B. splendens.

P3.62 EFFECT OF ENRICHMENT ON CORTICOSTERONE, STRESS-RELATED BEHAVIORS, AND COGNITION IN THE ZEBRA FINCH

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In lab rats, environmental enrichment has been found to reduce baseline and reactive stress and anxiety, and enhance cognition. While there is evidence that enrichment is similarly effective in birds, no rigorous studies have been done using the zebra finch (Taeniopygia guttata), a common avian lab model. Although there are basic enrichment guidelines established by local IACUCs, it is unclear if such provisions eliminate stress-related behaviors and provide a buffer for stressful events as they do in rats. I will compare zebra finches living in basic housing to those provided an interactive environment, which includes natural perches, swinging perches, rings, a bell, and bedding. To determine whether birds in the latter environment have lower baseline and acute stress hormone levels; fewer stress-associated behaviors; less neophobia; and enhanced cognition, I will measure baseline and stress-induced levels of corticosterone; monitor body weight; count stereotypies; and assay behavior in a novel object test; open-field test; and spatial maze. These results will be compared to birds in basic conditions in both juveniles and adults of both sexes.

P3.63 A BRAIN CIRCUIT CONTROLS A GENERAL AGGRESSIVE BEHAVIOR

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While aggressive behaviors are universal and essential for survival, 'uncontrollable' and abnormal aggressive behaviors in animals or humans may have severe adverse consequences or social costs. Neural circuits regulating specific forms of aggression under defined conditions have been described, but how brain circuits govern a general aggressive response remains unknown. Here, we found that posterior substantia innominata (pSI) neurons responded to several aggression-provoking cues with the graded activity of differential dynamics, predicting the aggressive state and the topography of aggression in mice. Activation of pSI neurons projecting to the periaqueductal gray (PAG) increased aggressive arousal and robustly initiated/promoted all the types of aggressive behavior examined in an activity level-dependent manner. Inactivation of the pSI circuit largely blocked diverse aggressive behaviors but not mating. By encoding a general aggressive response, the pSI-PAG circuit universally drives multiple aggressive behaviors and may provide a potential target for alleviating human pathological aggression.

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