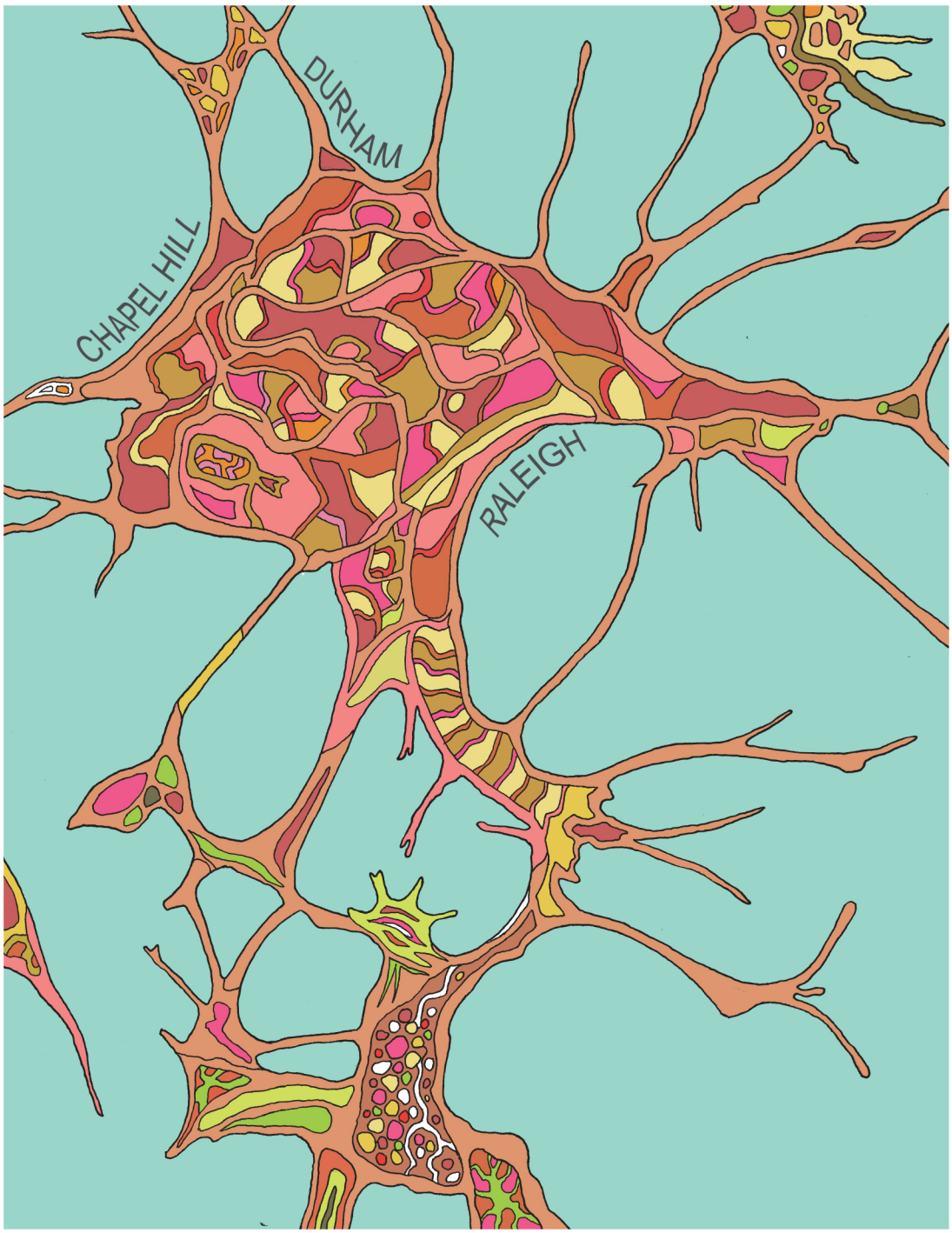
TRIANGLE CHAPTER
SOCIETY FOR NEUROSCIENCE

2019

5th Annual Spring Neuroscience Meeting



Program and Abstracts

April 4th, 2019

Embassy Suites, RTP

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Triangle_SfN

TriangleSfN

Presidential Remarks

Welcome message from the President:

Dear Colleagues and Friends,

It is an honor to welcome you to our 5th Annual Triangle SfN Spring Meeting. Over the past few years, our annual conference has provided a venue to highlight the outstanding research of our diverse neuroscience community. We are pleased by your continued interest and support, and are happy that we can again offer a full day of new and exciting research presentations.

This year, we have invited four distinguished neuroscientists to speak at our meeting. It is with great pleasure that we welcome Drs. Kevin LaBar of Duke University, Gregory Cole of NC Central, Jerry Yakel of NIEHS, and our keynote speaker Dr. Staci Bilbo of Harvard. We are also pleased to offer poster sessions and a special lunch networking session to allow students and trainees to explore a variety of career opportunities with prominent neuroscientists in the area.

This meeting depends on the hard work of our talented councilors, and committee members. I would like to personally thank our many graduate students and postdoctoral fellows who are the driving force of our chapter. Through their hard work and commitment, we have made great strides in our outreach and advocacy programs. As our membership continues to grow, I would encourage all members, at all stages of your career, to commit to service to our chapter. Please be sure to visit our committee interest tables throughout the day to explore opportunities in outreach and policy within our chapter.

I want to thank all of our members and sponsors for joining us today. I look forward to your continued participation in our neuroscience communities' vibrant, scientific exchange.

John Meitzen, Ph.D.
Triangle SfN Chapter President
Associate Professor
Department of Biological Sciences
North Carolina State University

Congressional Letter

Senator Thom Tillis
North Carolina

U.S. Senate
Washington D.C. 20510

April 4, 2019

Dear Friends,

I am happy to welcome everyone gathered for the Triangle Society for Neuroscience's Spring Neuroscience meeting. While the Senate schedule prevents me from attending today's event, I would like to acknowledge special keynote speaker Dr. Staci Bilbo, as well as other top scientists from around the Triangle area for their leadership and commitment to the health of our communities.

Scientific research in medicine, information technology, and energy is critical in keeping our nation's economy competitive and its citizens and environment healthy. I applaud the mission of the Triangle Society of Neuroscience to promote and foster collaboration between neuroscientists, the public, and legislators. I encourage you to continue contributing to neuroscience research and interacting with our community leaders as part of our nationwide effort to advance scientific research.

I wish you all the best for a collaborative event.

Sincerely,

Thom Tillis
U.S. Senator

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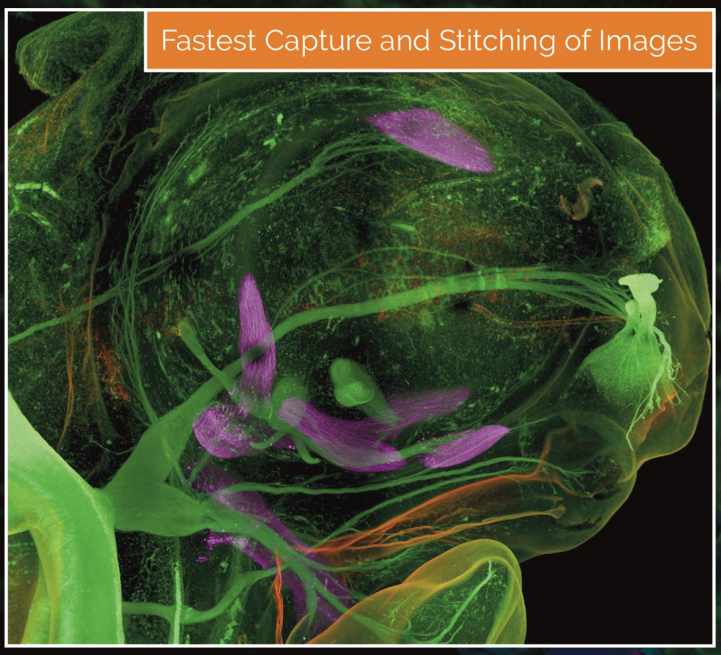

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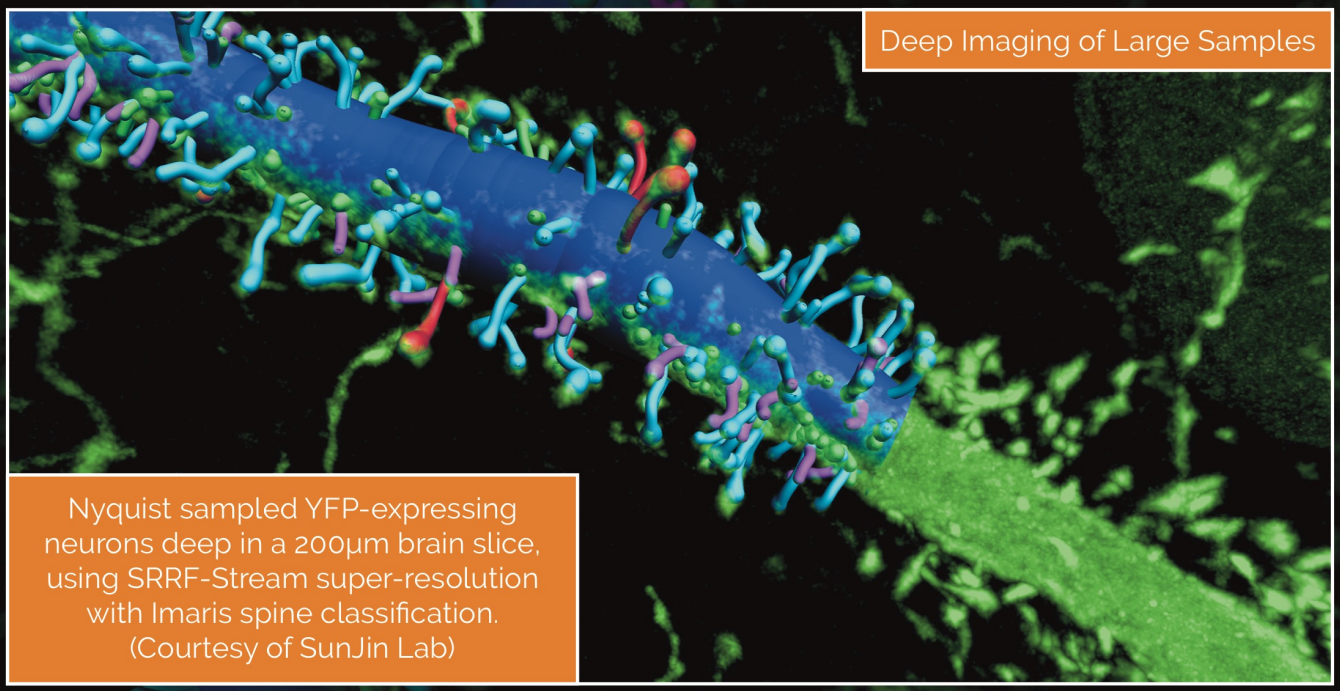
Chick embryo head labelled with 3 fluorophores, imaged to a depth of 1.2mm across 7x5 tiles, captured and stitched in just 2 hours!
(Courtesy of Tajbakhsh Lab)



Deep Imaging of Large Samples

Nyquist sampled YFP-expressing neurons deep in a 200µm brain slice, using SRRF-Stream super-resolution with Imaris spine classification.
(Courtesy of SunJin Lab)

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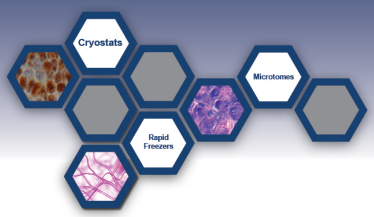

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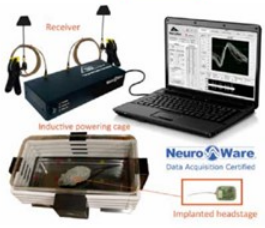

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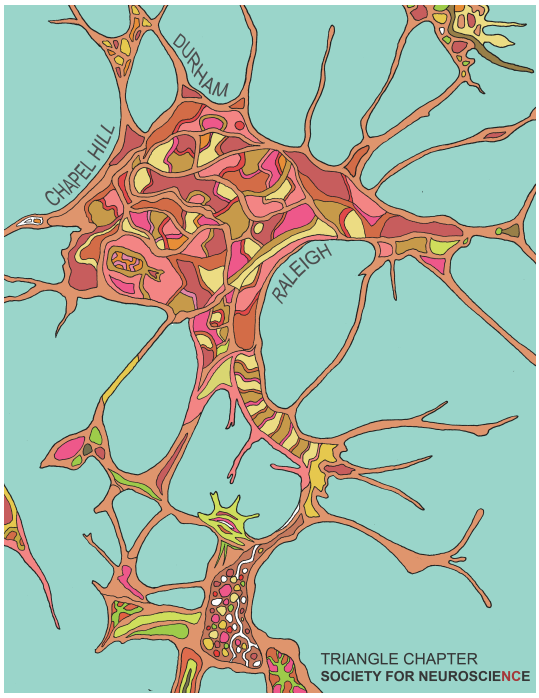
Cover Art Competition



Hannah Sage Yoder is the illustrator/artist featured on our abstract booklet cover.

She received first place in the Triangle SfN inaugural Cover Art Competition in 2018. Hannah has conducted scientific research at North Carolina State University and the National Institute of Environmental Health Sciences, is a published author, and is an accomplished artist.

Check out this image and others in her published coloring book: **Cellfies: A Cell Biology Coloring Book**!

If you would like to have an image or artwork featured on the Triangle SfN abstract booklet cover next year, please look for the

2019 Cover Art Competition

announcement in the Spring/Summer issue of the Triangle Transmitter newsletter.

Speakers

Staci Bilbo, PhD

Staci Bilbo, Ph.D., is an associate professor of pediatrics and neuroscience at Harvard Medical School and the director of research for the Lurie Center for Autism at Massachusetts General Hospital for Children. Her research is broadly focused on the mechanisms by which the immune and endocrine systems interact with the brain to impact health and behavior. Bilbo was the recipient of the Robert Ader New Investigator Award from the Psychoneuroimmunology Research Society (PNIRS) in 2010 and the Frank Beach Young Investigator Award from the Society for Behavioral Neuro-endocrinology (SBN) in 2011. Bilbo has served on the board of directors for the PNIRS, and was the Invited Mini-Review Editor for Brain, Behavior and Immunity from 2012-15. She has served on the editorial board since 2010. Bilbo received her B.A. in psychology and biology from the University of Texas at Austin and her Ph.D. in neuroendocrinology at Johns Hopkins University. She was on the faculty at Duke University from 2007-2016 before she joined the faculty at Harvard in 2017. Dr. Bilbo will return to Duke University in 2019 and will serve as the Haley Family Professor of Psychology & Neuroscience.

The broad goal of Dr. Bilbo's research is to understand the important role of the immune system during brain development, and how influences during this critical period can shape health throughout the lifespan. Current research seeks to understand the consequences of early life events, including infection, social and environmental toxins, drugs of abuse, and others, on neural-glial, gut-brain, and immune system development, and the consequences for health throughout the lifespan. A particular focus of the work is on the resident immune cells of the brain, microglia, including their development and function in response to early life inflammatory signals, neural-glial interactions, and their role in shaping neural circuits.

Jerry Yakel, PhD

Gregory Cole, PhD

Kevin LaBar, PhD

Program

10:00 A.M. **Presidential Welcome: Dr. John Meitzen**

Local Speaker Presentations:

10:10 A.M. **Dr. Jerry Yakel**

Neurobiology Laboratory Chief and Principal Investigator,
National Institute of Environmental Health Sciences

"Cholinergic regulation of hippocampal excitability and plasticity: role of interneurons."

10:45 A.M. **Data Blitz: Dr. Chris Mazzone - NIEHS**

11:00 A.M. **Dr. Gregory Cole**

Professor and Chair of Biological Science,
North Carolina Central University

"Modeling fetal alcohol spectrum disorder in zebrafish: from morphology to genes and behavior."

11:35 A.M. **Data Blitz: Regina Fernandez - ECU**

11:50 A.M. **Dr. Kevin LaBar**

Professor of Psychology and Neuroscience,
Duke University

"The neuroscience of virtual fear learning."

Poster Sessions, Lunch, & Networking:

12:30 P.M. Lunch / Networking Topic Tables
1:30 P.M. Poster Session I and Vendor Exhibits
2:30 P.M. Poster Session II and Vendor Exhibits

Keynote Address & Awards Ceremony:

3:30 P.M. **Dr. Staci Bilbo**

Director of Research, Lurie Center for Autism
Harvard Program in Neuroscience

"Neuroimmune interactions in neurodevelopment: implications for life-long health."

4:15 P.M. Poster Awards & Reception
5:00 P.M. Closing Remarks and Adjourn

SESSION 1; ABSTRACT NO. 1

FUNCTIONS OF RHO GTPASES AND THEIR IMPLICATIONS IN NEURODEGENERATIVE DISEASES

BJ Aguilar, Y Zhu, and Q Lu
Department of Anatomy and Cell Biology; The Harriet and John Wooten Laboratory for Alzheimer's and Neurodegenerative Diseases Research; Brody School of Medicine at East Carolina University, Greenville, NC, 27834

BACKGROUND: The roles of Rho GTPases in neural development have been well documented, but their exact functions in neurodegenerative diseases are still under study. The three major classes of Rho GTPases are RhoA, Rac1, and Cdc42. These proteins play an active role in synapse structure, function, and plasticity. The general consensus is that RhoA acts in opposition of Rac1 and Cdc42. In several neurodegenerative diseases, such as Alzheimer's disease, this balance has been disrupted. Therefore, attempts have been made to restore the balance with several small molecule regulators.

METHODS: Herein, we describe the use of these regulators in restoring proper synapse function as well as summarize their use in several Alzheimer's disease mouse models. Initial studies focused on utilizing nonspecific pharmacological tools such as NSAIDs. More recent studies evaluate ROCK and Rho GTPase inhibitors.

RESULTS: Rho GTPase regulation alters synapse structure, function, and plasticity. Rho GTPase regulators showed a beneficial effect on restoring behavioral and/or learning deficits observed in Alzheimer's disease mouse models. Improvements in learning and/or behavior was observed in Morris water maze, elevated plus maze, and novel objection recognition.

CONCLUSIONS: The recent development of specific Rho GTPase regulators allows for the evaluation of the therapeutic potential Rho GTPases for Alzheimer's disease. Additionally, evaluation of other behavior/learning assessment such as Activities of daily living (e.g. burrowing and nesting) may provide some additional insight. Altogether, a unified approach is necessary to increase our understanding of targeting specific Rho GTPases in various stages of Alzheimer's disease pathogenesis.

SESSION 1; ABSTRACT NO. 2

ASSOCIATIVE FEAR LEARNING ENGAGES A NOVEL SEX-SPECIFIC LS CIRCUIT FOR MEMORY ENCODING

S Basu, A Jegarl and E Lucas
North Carolina State University, CVM, 1060 William Moore Dr, Raleigh, NC 27606

Fear-based psychiatric conditions, such as post-traumatic stress and anxiety disorders, are the most prevalent mental illnesses worldwide, affecting 18% of the population annually. These illnesses are thought to arise from enhanced encoding of cues associated with aversive outcomes, leading to maladaptive fear responses that persist in the absence of threat. Women are twice as likely as men to be diagnosed with fear-based mental illness, suggesting that the underlying mechanisms of associative fear memory might differ between the sexes. However, to date the majority of studies elucidating the neural circuits underlying associative fear memory have been conducted solely in male subjects. To determine if associative fear memory engages similar neural circuits in males and females, we quantified expression of the neural activity marker c-fos throughout selected forebrain regions after auditory fear conditioning. We found a robust female-specific increase in the neural activity in the lateral septum (LS). We next used designer receptors exclusively activated by designer drugs (DREADDs) to determine if sex-specific LS activation is causally related to sex-specific memory encoding. In females, activating the LS during fear conditioning with the excitatory DREADD hM3D enhanced fear memory encoding, whereas LS silencing with the inhibitory DREADD hM4D rendered

fear memories more pervious to extinction. In males, on the other hand, LS activation impaired memory encoding. Activating or silencing the LS before an open field test did not alter locomotor activity in either sexes, suggesting that the LS does not illicit freezing behavior in the absence of threatening cues. To determine the projection targets of the LS fear memory ensemble, we used time-limited, activity-dependent tagging to label fear-active LS neurons with eYFP. We observed more tagged neurons in fear-conditioned females in comparison to fear-conditioned males or naïve animals of either sex. Dense axon accumulation of female fear-active LS neurons was observed in lateral hypothalamus, ventral hippocampus, and periaqueductal gray - canonical mediators of the fear response. These data suggest that the female LS memory ensemble may directly drive fear expression in females. To our knowledge, this is the first demonstration of a sex-specific circuit for associative fear memory.

SESSION 1; ABSTRACT NO. 3

QUANTIFYING HEAD IMPACT EXPOSURE IN HIGH SCHOOL FOOTBALL USING A NOVEL WEEKLY ATHLETIC EXPOSURE FORM: A PILOT STUDY

B Blass, V Nukala, W Pritzlaff, A Putka, L Smeltz, J Zhou, C Bass, J Luck
Dept. of Biomedical Engr; Duke University; Durham, NC 27708

Introduction: Brain injury is a common occurrence in youth football and obtaining accurate measurements of head impact exposure is of great importance. A wide array of devices have been implemented for tracking hits sustained during football, but these devices face significant limitations in reliability and interpretation of the data. Other methods use postseason self-report data, but these are limited in detail and often performed long after a season has ended. An acute assessment of head impact exposure is desired for a more nuanced characterization of hits sustained during football.

Objective: This study used weekly self-reported athletic activity and contact to assess head impact exposure in a team of high school football players during one season of play.

Methods: Weekly exposure data was collected from varsity football players during the 2017-2018 season (n=31) through completion of athletic activity/contact exposure questionnaires (AACEQs). The following questions were analyzed: 1. Did you participate in football-related athletic activities on this day?, 2.Did you participate in football-related athletic activities on this day that involved body-to-body contact?, and 3.Did you participate in football-related athletic activities on this day that involved body-to-body contact where your helmeted head contacted another player or the ground? Weekly activity, body-to-body contact, and head contact rates were computed for each participant.

Results: AACEQ data was available for the first 13 of 15 weeks of documented activity, with an average form return rate of 80.4%. Six players had data for each of these 13 weeks, and 22 of 31 total players had 10 or more weeks of data available. Overall, players participated in football practices/games (question 1) an average 4.69 days each week (SD = 1.11). Players had an average body-to-body contact rate (question 2) of 3.74 days/week (SD = 1.12) and an average head contact rate (question 3) of 3.08 days/week (SD = 1.41).

Conclusions: This season-long investigation provided useful insight into the day-to-day activities of a high school football team and yielded a more nuanced characterization of head impact exposure than other studies of this type. The favorable response rate indicates that this is a viable approach to quantifying head impact exposure and the data made available from this study can be paired with observable outcomes to investigate the potential implications of subconcussive hits.

SESSION 1; ABSTRACT NO. 4

DYSREGULATION OF THE M1/M2 RESPONSES OF MICROGLIA WITH INORGANIC ARSENIC EXPOSURE

C Bowen, C McPherson, G Harry
Division of the National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC 27709

The contribution of microglia and their associated inflammatory response to multiple aspects of nervous system function is a growing field of inquiry. To maintain homeostasis, microglia clear aberrant cellular debris and coordinate the response to infection or sterile activators. This well-regulated system can be compromised in neurodegenerative diseases and neurodevelopmental disorders. While many studies suggest a role for environmental exposures in the induction of a neuroinflammatory response, their ability to dysregulate the normal functioning of the system has not been well examined. Inorganic arsenic (iAs) is a known immunotoxicant associated with autoimmune disorders in humans and inhibition of cultured macrophages to mount an effective inflammatory response. We show that iAs (1μL) exposure to BV-2 cells or primary murine microglia, at dose levels relevant to those in human brain tissue, downregulated the pro-inflammatory response to LPS and the anti-inflammatory response to IL-4/IL-13. This downregulation was not associated with an inhibition of NF-kB nuclear translocation. The cytokine pattern was reproduced in the hippocampus of mice with in vivo exposure (42 ppm, 3 weeks). With prolonged in vitro exposure, the downregulation of *TNFa* mRNA levels was no longer present, while *IL1b* mRNA levels remained downregulated. The shift over time in culture was not related to microglia senescence as demonstrated by telomere length nor in changes in mitochondria bioenergetics. These results demonstrate that exposure to low levels of iAs can dysregulate the inflammatory responses of microglia. This data raises the concern that low-level exposures of environmental factors can shift the underlying biology, and by a dysregulation of the neuroimmune system, represent an increased susceptibility to a subsequent injury or disease progression.

SESSION 1; ABSTRACT NO. 5

LONG-LASTING IMPACT OF EMBRYONIC ALCOHOL EXPOSURE: CELLULAR AND BEHAVIORAL STUDIES IN ZEBRAFISH

A Brown, G Anthony, S Howell, J Lee
jLC-BBRI, NCCU, Durham, NC 27707

Prenatal alcohol exposure (PAE)-induced developmental abnormalities have long-lasting impacts on the quality of affected individuals' life, including structural defects such as craniofacial malformations, and cognitive deficits. Previous studies from our laboratory show that an acute ethanol exposure to zebrafish embryos at the onset of CNS migration of microglia precursors induces an increase in early microglia population resulting from increased proliferation mediated by the notch signaling pathway.

To test if this developmental increase in microglia is maintained into the later juvenile stages, we conducted whole mount in situ hybridization to detect microglia in the surgically removed juvenile zebrafish brains. Our new data indicates that the early ethanol exposure-induced microglial population may in fact persist into the juvenile stage.

Encouraged by the long-lasting microglia population increase by embryonic alcohol exposure, we tested our hypothesis that the developmentally alcohol-exposed brains may react differently to cellular stressors encountered later in life. We used an acute alcohol exposure during juvenile stage as a 'second hit' stimulus. Using in situ hybridization, we show that upon a juvenile binge alcohol exposure, a higher level of a pro-inflammatory cytokine TNF alpha mRNA is detected in the brains of juvenile zebrafish that had previously received an acute alcohol exposure in the embryonic stage. Next, counting the number of 'aileron rolls' (stereotypical rotatory swimming along the AP axis observed under alcohol intoxication)

as a behavioral measure of disrupted body balance during alcohol exposure, we show that a second hit of EtOH at juvenile stage causes significant differences in the number of inversion in a manner dependent on the embryonic exposure doses.

Our results suggest that an early embryonic alcohol exposure may not only be associated with long term changes in microglia population and the regulation of inflammatory cytokine expression in the juvenile stage brain, but also changes in behavioral responses to cellular stresses (in our case, an acute alcohol exposure) encountered at a later stage of life. The use of acute alcohol exposure as a second hit stressor and the counts of aileron rolls as a quantifiable behavioral parameter for the level of intoxication in zebrafish may facilitate FASD research in the zebrafish model system.

SESSION 1; ABSTRACT NO. 6

CHARACTERIZING THE ROLE OF PGC1α TRANSCRIPTS AND ITS EFFECTS ON MITOCHONDRIAL FUNCTION AND RETINAL AGING

A Castillo, D Hodorovich, ML Foster, R Woychik, FM Mowat
Department of Biological Sciences, NC State University, College of Sciences, Raleigh, NC, 27606

A leading cause of retinal degeneration and permanent vision loss in adult humans over the age of 65 is age-related macular degeneration (AMD). Mitochondrial dysfunction is considered a primary contributor to retinal aging, a key risk-factor for AMD. We hypothesized that the dysregulation of the mitochondrial coregulator pathway of peroxisome proliferator activated receptor gamma coactivator 1-alpha (PGC1α) would cause premature retinal aging. Dark- and light-adapted electroretinography was used to investigate retinal function with aging in two transgenic mouse models lacking isoforms of PGC1α. One model lacks all isoforms of PGC1α (PGC1α-KO) and the other lacks only a novel fusion transcript of PGC1α, formed from splicing of an upstream region to exon 2 of PGC1α (PGC1α-FT-KO). We compared electroretinographic responses to littermate wild-type controls. PGC1α-KO mice at 30 weeks showed significant reductions in the amplitude of rod and cone-derived responses compared with controls. Particularly large reduction in responses was noted at high light intensity and to flickering light. At the same age, PGC1α-FT-KO mice had no significant differences in ERG responses compared with controls. Absence of PGC1α contributes to early retinal dysfunction in mice. We hypothesize that ATP deficiency occurs due to mitochondrial dysfunction in these mice. This deficiency contributes to a prolonged recovery from cell membrane hyperpolarization following the initiation of phototransduction. Future directions include the study of the process of dark adaptation in these mice, and the effect of prolonged aging on retinal structure.

SESSION 1; ABSTRACT NO. 7

ASSESSING RISK FACTORS FOR AFRICAN AMERICAN OF ALZHEIMER'S DISEASE IN CULTURED HIPPOCAMPAL NEURONS

Q Cheng
Biomedical/Biotechnology Research Institute, NCCU, Durham, NC 27707

Alzheimer's disease (AD) is a progressive neurodegeneration disease affecting more than 5.7 million people in US. The prevalence of AD in African American is significant higher that of non-Hispanic whites; and AD is a major health disparity for people over 65 years of age. Both biologic (genetic variants, metabolic diseases, stress hormones) and non-biologic (social-economic status, stress, environmental exposures, and health care access) factors are suggested to render the susceptibility to AD, however, the biological basis for AD disparity in African American remains poorly understood. The prevalence of the APOE ε4 alleles is consistently higher in African American than non-Hispanic whites, which

makes it a potential genetic candidate for race-dependent disparity. Previous studies have identified hyperlipidemia as a potential risk factor for dementia and Alzheimer's disease as well. Therefore, we would like to assess the impact of APOE4 with consideration of lipid levels. We will exam the synaptic development of dentate granule cells and GABAergic interneurons of hippocampus. In addition, we will investigate the regulation of cholesterol and APOE4 on nicotinic receptors function in these two populations of hippocampal neurons. We will combine both patch-clamp electrophysiology and confocal imaging with fluorescent sensors to investigate cholesterol and APOE4's impact on nAChR functions, and subsequent modulation of synaptic transmission. Our study will provide new insight in the biological mechanisms of APOE4 and cholesterol on nAChR function and cognition, and important data for developing potential treatment to reduce health disparity.

SESSION 1; ABSTRACT NO. 8

NLRP3 INFLAMMASOME ACTIVATION: A MODE OF ACTION UNDERLYING MITOCHONDRIAL TOXICANTS

G Childers, C Perry, M Roberts, M Fessler, and GJ Harry
National Toxicology Program Laboratory; National Institute of Environmental Health Sciences; RTP, NC 27709

Mitochondria act as important regulators of the immune response both through changes in energy dynamics upon immune cell activation and through release of damage associated molecular patterns (DAMPs). Recent literature has identified the NLRP3 inflammasome as having a pivotal role in recognizing and acting upon mitochondria-linked DAMPs, suggesting a mechanism that links mitochondrial dysfunction to the inflammatory response. Activation of NLRP3 results in the formation of aggregates ('specks') of the NLRP3-associated protein, apoptosis-associated speck-like protein containing a CARD (ASC), and downstream cleavage and release of active pro-inflammatory cytokine interleukin-1 beta (IL-1b). ASC specks are released from activated cells along with IL-1b and have been implicated in propagating the pro-inflammatory state to neighboring immune cells. We hypothesized that two organometals that are known mitochondrial toxicants, trimethyltin (TMT) and triethyltin (TET), might trigger NLRP3 inflammasome activation. Using RAW 264.7 macrophages and BV-2 murine microglia-like cells virally transfected to create ASC reporter cells and then primed with lipopolysaccharide, we found that low concentrations of TMT (1.25 uM) and TET (10 uM) indeed activate the NLRP3 inflammasome. Both compounds reduced mitochondrial oxidative phosphorylation (OCR) in RAW 264.7 cells but only TET did so in BV-2 cells. Fluorescently labelled ASC specks isolated from LPS/ATP-dosed BV-2 cells stimulated phagocytosis and upregulated mRNA levels of *TNFa*, *IL1a*, and *IL1b* in naïve BV-2 cells. Overall, this study demonstrates that low dose levels of mitochondrial toxicants can trigger an innate immune response in microglia in a manner that may be propagated to neighboring cells, thereby leading to a chronic inflammatory state.

SESSION 1; ABSTRACT NO. 9

NEUROGENETIC ANALYSIS OF CYFIP2'S ROLE IN ESTABLISHING THE ACOUSTIC STARTLE THRESHOLD

J Deslauriers, D Burton, K Marsden
Department of Biological Sciences, North Carolina State University, Raleigh, NC, 27607

Animals experience a constant stream of sensory stimuli, and to effectively navigate their environments they must filter out irrelevant stimuli and respond to important ones. For example, a sudden loud sound triggers a startle response that enables animals to escape from danger. An appropriate threshold for this behavior must be established such that threats are detected while innocuous stimuli are ignored. Startle threshold dysregulation can produce

hypersensitivity associated with autism and anxiety-related disorders, yet the genetic regulation of this threshold is poorly understood. Previously, a forward genetic screen using a high-throughput system to analyze larval zebrafish responses to acoustic stimuli isolated five hypersensitive mutant lines. A causal nonsense mutation was identified in one line in Cytoplasmic Fragile X Mental Retardation Protein Interacting Protein (FMRP) 2 (cyfip2), but the molecular and cellular pathways by which cyfip2 regulates the startle threshold remain unknown. Cyfip2 binds Rac1 to promote actin polymerization and may regulate local RNA translation through its interaction with FMRP. To identify the molecular pathway(s) Cyfip2 engages to regulate the startle threshold we acutely treated wild-type (WT) larvae with the actin polymerization inhibitor, CK-869. Treated larvae phenocopy cyfip2 mutant hypersensitivity, suggesting that Cyfip2 may act by modulating actin polymerization to maintain the startle threshold. To validate these results, we created mutant cyfip2 constructs with specifically altered residues required for interaction with Rac1 or FMRP. By expressing these constructs in cyfip2 mutants we will determine if mutants are rescued or retain their hypersensitivity. If these transgenes fail to restore normal startle sensitivity, then Cyfip2 interaction with Rac1 and/or FMRP is required. To determine the cellular context in which Cyfip2 acts, we will use two approaches to test whether it 1) controls auditory sensation or 2) filters auditory information in the brain. First, we will optogenetically activate the auditory (VIII) nerve neurons with increasing intensities of blue light. If cyfip2 mutants retain hypersensitivity in response to optogenetic light stimulation, then we will know Cyfip2 likely regulates processing of auditory information in the brain, but if no difference in sensitivity to optogenetic stimulation is observed, Cyfip2 likely acts to regulate sensation in auditory hair cells. Based on these results, we will determine where Cyfip2 acts using a transgenic approach so specifically express wild-type cyfip2 in either hair cells, or candidate populations of downstream hindbrain neurons in cyfip2 mutants. Together, our results will define a specific cellular and molecular pathway for how a single gene directly impacts a critical, disease-associated behavior.

SESSION 1; ABSTRACT NO. 10

ACYL-COA SYNTHETASE 6-MEDIATES BRAIN DOCOSAHEXAENOIC ACID (DHA) ENRICHMENT AND NEUROPROTECTION

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The omega-3 fatty acid, docosahexaenoic acid (DHA), is enriched in the central nervous system and thought to protect against neurological dysfunction. Yet, studying the role of brain DHA metabolism in the development of neurological dysfunction has remained limited because the biochemical mechanisms regulating DHA enrichment in the brain remain unclear. To define a critical regulatory node in brain DHA biochemistry we targeted long chain acyl-CoA synthetase 6 (Acsl6) because this enzyme initiates cellular fatty acid metabolism, is enriched in the brain and prefers DHA as its substrate. Genetically deleting Acsl6 in mice resulted in large and specific reductions (35-72%) in DHA-containing phospholipids across tissues that highly express Acsl6 (i.e. the central nervous system). Acsl6-/-mice develop age-related deleterious neurological pathology characterized by increased astrogliosis and microglia. Surprisingly, this pathology develops in the absence of alterations in pro- and anti-inflammatory lipid mediators, suggesting alternative mechanisms mediating neuroinflammation in Acsl6-induced DHA deficiency. Together our findings demonstrate a novel central nervous system DHA-deficient model susceptible to aging-induced neuroinflammatory pathology.

SESSION 1; ABSTRACT NO. 11

IN SITU DETECTION OF NEUROENERGETIC SUBSTRATES IN THE RAT STRIATUM WITH FAST-SCAN CYCLIC VOLTAMMETRY: EXTRACELLULAR AVAILABILITY OF LACTATE AND GLUCOSE SCALES WITH ELECTRICAL STIMULATION OF THE DOPAMINERGIC MIDBRAIN

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Real-time detection of energy substrates, such as glucose and lactate, is essential to advance understanding of energy availability in normal and pathophysiological brain function. Although glucose has been believed to be the principle energy source for the brain, lactate has also been implicated in neuroprotection, long-term memory formation, and cortical spreading depression. We have developed and characterized glucose oxidase (GOx)- and lactate oxidase (LaOx)-modified carbon-fiber microelectrodes for the detection of these neuroenergetic substrates. When coupled with fast-scan cyclic voltammetry (FSCV), these tools are effective for detection of rapid glucose and lactate fluctuations in real-time. In this work, we demonstrate the precise timescale over which extracellular glucose and lactate availability increases in response to electrical stimulation of dopamine release in the anesthetized rat. In most cases, a bimodal response was evident over the seconds timescale. Careful evaluation of these chemical dynamics promises to shed light on the role of cerebral blood flow in delivering these molecules to the recording site, vs local sourcing via the astrocyte to neuron lactate shuttle. An improved understanding of the molecular mechanisms in place to fuel neuronal activation will lead to improved pharmacological strategies to treat a wide range of metabolic disorders.

SESSION 1; ABSTRACT NO. 12

DEVELOPMENT AND BEHAVIOR OF LARVAL ZEBRAFISH IS INFLUENCED BY EMBRYO MEDIA

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A central goal in neuroscience is to understand the genetic and neural circuit basis of behavior. Although genetics play a role in the neural circuit basis of behavior, environmental factors also affect the formation and function of these circuits. Researchers use zebrafish as a model for studying both environmental and genetic influences on behavior because they have a high degree of developmental, structural, and genetic similarity to higher vertebrates. Despite the broad adoption of the zebrafish model system, there is not a standardized medium for raising zebrafish larvae and researchers use a variety of embryo media. In order to address this and directly examine how the contents of embryo media affect neural development, we raised zebrafish larvae in ten commonly used laboratory media and analyzed both their spontaneous and evoked behaviors at six days of age. We looked at the fish's acoustic startle sensitivity, pre-pulse inhibition, short-term habituation, and overall locomotion because these are standard assays used to examine innate motivation, sensory and motor function, as well as behavioral plasticity. Here we show that methylene blue, high calcium levels, and HEPES decrease spontaneous movement. Sensorimotor function and plasticity were also impacted by the embryo medium. Methylene blue and high calcium levels significantly reduce startle sensitivity while increasing pre-pulse inhibition and short-term habituation. Since we saw that methylene blue has significant effects on the neural development of larval zebrafish, we are currently examining how methylene blue affects the development of neurons within the startle circuit. This knowledge may help researchers choose the most appropriate medium for their developmental or behavioral studies. Furthermore, by illuminating which

media are suitable for detecting increases or decreases in movement and sensation, this work establishes a foundation for future high-throughput screens to identify genetic, chemical, and toxicological pathways implicated in disease.

SESSION 1; ABSTRACT NO. 13

SOCIAL BEHAVIORAL EFFECTS IN PRAIRIE VOLES PERINATALLY EXPOSED TO FIREMASTER 550

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The prairie vole (Microtus ochrogaster) is a uniquely valuable model organism used to study complex social behavior. This species readily forms social bonds and spontaneously displays social monogamy, bi-parental care, and partner preference; behaviors not seen more traditional laboratory rodent models such as rats or mice. Our studies demonstrate the utility of the prairie vole for investigating the impact of chemical exposures on social behavior. Healthy social interactions and the ability to form stable social attachments are important for mental health and impairments are common characteristics of some mental health disorders. The incidence of neurodevelopmental disorders in children is rapidly rising raising speculation that developmental exposure to environmental contaminants may be contributory. Firemaster 550 (FM550) is one of the most prevalent flame retardant mixtures used in foam-based furniture and baby products. We and others have published evidence of developmental neurotoxicity and sex specific effects of FM550 on anxiety-like and exploratory behaviors in rats and zebrafish suggesting impacts on social behavior. To test this hypothesis, we investigated the impact of perinatal FM550 exposure on a range of social behaviors in prairie voles. Dams were exposed to 0, 500, 1000, or 2000 µg of FM500 via subcutaneous injections throughout gestation, and pups were directly exposed to the same dose beginning the day after birth until weaning at three weeks of age. Tasks performed on the offspring of both sexes were open field, novel social, social preference, social recognition, novel object recognition, and partner preference. Effects were dose responsive and sex specific, with females more affected than males. Behavioral effects included elevated anxiety, decreased social interaction, decreased exploratory motivation, and altered social preference for novel versus partner animals. Future studies will probe the possible mechanisms by which these effects arise. These data support the hypothesis that developmental FR exposure impacts the social brain and demonstrate the value of the prairie vole for assessing chemical effects on sociability and attachment.

SESSION 1; ABSTRACT NO. 14

RAPID AND NON-RAPID EFFECTS OF ESTRADIOL ON VOLUNTARY WHEEL RUNNING BEHAVIORS IN ADULT FEMALE AND MALE RATS

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Sex differences in locomotion and motivation have been measured in several species, including humans and rats, as well as in the neurological diseases that affect these behaviors. The sex steroid hormone estradiol has been shown to mediate aspects of these sex differences including increasing overall locomotion and motivated behaviors. A key brain region implicated in controlling these behaviors is the nucleus accumbens, which in adult rats exclusively expresses membrane estrogen receptors that enable rapid estradiol action. Thus, we tested whether estradiol can rapidly change motivated locomotion by assessing voluntary wheel running. Gonadectomized adult female and male adult rats were placed in running wheel cages and separated into an estradiol priming group, where rats received 3 days of estradiol benzoate (EB) injections, or a

vehicle group. This EB priming protocol mimics the repeated estradiol exposure generated by the natural adult female hormone cycle. On the fourth day, all rats received an injection of EB to assess rapid effects of estradiol on voluntary running. EB-primed males and females both elevated running over the course of the 4 days of EB injections. However, EB-primed females significantly decreased running between 15-45 minutes after EB injection on Day 4, and this decrease in running was much larger than EB-primed males. These findings suggest that: 1) males and females have non-rapid responses to estradiol for motivated locomotion; however, females are more sensitive to rapid responses; 2) different brain circuits may be recruited to control these rapid and non-rapid effects; 3) estradiol neuromodulation is influenced by hormone state and should be considered as a significant biological variable.

SESSION 1; ABSTRACT NO. 15

MONITORING ELECTRICALLY-EVOKED DOPAMINE AND H2O2 IN THE RAT STRIATUM WITH FAST-SCAN CYCLIC VOLTAMMETRY

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Hydrogen peroxide (H_2O_2) is a reactive oxygen species that participates in normal cell function and can modulate release of striatal dopamine (DA); however, it can also contribute to oxidative stress, neuronal dysfunction, and cell death. Indeed, reactive oxygen species are critically implicated in the neurodegeneration evident in Parkinson's disease, a condition characterized by reduced, maladaptive dopaminergic transmission. H_2O_2 is membrane permeable, allowing for it to diffuse through cells and into the extracellular space following its formation. There is a critical gap in understanding the unique role H_2O_2 plays within the brain, as previous analytical strategies for monitoring dynamic changes in H_2O_2 concentrations in situ have been hindered by insufficient sensitivity and selectivity. Fast-scan cyclic voltammetry (FSCV) allows for reliable detection of rapid fluctuations in H_2O_2 on a sub-second timescale. This experiment utilizes FSCV coupled with carbon-fiber microelectrodes in intact brain tissue to investigate striatal H_2O_2 fluctuations evident upon electrical stimulation of DA release. A novel 'double' voltammetric waveform was employed to facilitate removal of interference from shifts in pH. Stimulations were delivered at varying frequencies (30, 60, and 90 Hz) using increasing pulse numbers, to vary the length of the stimulation and the magnitude of DA release. The data demonstrate that the H_2O_2 signal scales with the duration of the stimulation, and that this occurs predictably following evoked DA release. The dynamic relationship between H_2O_2 and DA in the striatum, defined in this work, is important for an increased understanding of the role H_2O_2 in normal striatal function, and ultimately in the dysfunction of this circuit in Parkinson's disease.

SESSION 1; ABSTRACT NO. 16

AGE-DEPENDENT STUDY OF PATHOLOGICAL PROGRESSION OF ALZHEIMER'S DISEASE IN HIPPOCAMPAL AND CORTICAL TISSUE OF HUMAN AND AD MOUSE MODEL

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BACKGROUND: Degeneration of synaptic plasticity plays a critical role in Alzheimer's disease (AD) pathogenesis. Recent studies have suggested that neuroinflammation may contribute to this degeneration by disrupting the amyloid metabolism and by microglial overgrowth. This study aims to investigate the pathological progression of AD hippocampal and cortical tissues of human and an AD mouse model.

METHODS: To examine the amyloid and microglial activity in the human brain, we acquired brain tissues from clinically diagnosed AD and non-dementia (ND) patients. To examine this activity in the mouse model, we acquired brain tissues from age-matched wild type (WT) and AD affected (3xTg-AD) mice in 4, 6, and 8-month age groups. Immunohistochemical (IHC) analysis was utilized to determine the characteristics of pathological AD hallmarks.

RESULTS: Analysis of the human brain tissue showed an alteration in amyloid precursor protein (APP) in the hippocampus of AD patients as compared to the ND patients. The activation of microglial cells in the AD patients was increased, which indicates neuroinflammation. Results of mouse brain tissue analysis indicated a heightened proliferation of microglial cells in the CA3 region (*$p<0.05$) of the hippocampus in the 6-month-old 3xTg-AD male mice. Additionally, results indicated hyper-proliferation of microglial cells in multiple regions of the hippocampus in 8-month-old 3xTg-AD female mice, (*$p<0.05$). Moreover, increased presence of amyloid burdened neurons was observed in both the cortical and amygdala regions of 4, 6, and 8-month age groups of 3xTg-AD mice as compared to their age-matched WT.

CONCLUSIONS: Neuroinflammation and aberrant activity of microglial proliferation contribute to the progression of AD. Future directions of this study aim to further illuminate the regulation of microglial activation in AD and the potential roles of Rho GTPase activity through quantification and analysis of the age-matched animal brain tissue. The ability to understand, and therefore modulate, neuroinflammation may be a promising approach for prevention of progression in AD.

SESSION 1; ABSTRACT NO. 17

STRAIN- AND SEX-SPECIFIC DIFFERENCES IN ANXIETY-LIKE BEHAVIOR AND EMOTIONAL MEMORY DYNAMICS ACROSS FOUR INBRED MOUSE STRAINS

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Dysregulation of emotional memory features prominently in psychiatric conditions such as post-traumatic stress and anxiety disorders. Women have twice the lifetime incidence of emotional memory disorders, suggesting that biological sex contributes to susceptibility and resilience to these diseases. Despite this clinical reality, females are vastly underrepresented in emotional learning studies, contributing to a lack in understanding of the biological mechanisms underlying these differences. In an attempt to find an adequate preclinical model for studying these mechanisms, we assayed anxiety-like behavior and emotional memory dynamics with the open field test, elevated plus maze, and auditory fear conditioning and extinction training in adult male and female mice across four inbred mouse strains: C57Bl/6J, 129S1/SVlmJ, DBA/2J, and BalB/cByJ. Independent of sex, BalB/cByJ and 129S1/SVlmJ mice exhibited more anxiety-like behavior, spending less time in the center of the open field and the open arms of the elevated plus maze, compared to DBA/2J and C57BL/6J. Enhanced fear memory encoding and persistence was observed for the 129S1/SVlmJ and C57Bl/6J lines. However, throughout fear conditioning, extinction, and recall assays, DBA/2J mice had very low levels of freezing, suggesting that freezing may not be an accurate measure of cued fear expression in this strain. Within strains, no sex differences in anxiety-like behavior were observed. However, opposing sex differences on fear memory encoding and persistence were found for the C57Bl/6J and 129S1/SVlmJ lines. Compared to males, female C57Bl/6J mice exhibited lower fear memory recall and enhanced extinction. Meanwhile, 129S1/SVlmJ females exhibited increased fear memory recall and persistence. Our data demonstrate that

individual differences emotional memory dynamics and innate anxiety-like behaviors are genetically driven. Furthermore, the 129S1/SV1mJ mouse strain may be the best model for investigations of the genetic and biological underpinnings of sex differences in emotional learning.

SESSION 1; ABSTRACT NO. 18

ETHANOL CHALLENGE FOLLOWING ALCOHOL DEPENDENCE AND WITHDRAWAL ALTERS BRAIN ALLOPREGNANOLONE LEVELS IN MALE C57BL/6J MICE

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In rodents, primates, and humans, chronic alcohol exposure and withdrawal changes neurosteroid levels, including (3α,5α-THP, allopregnanolone) in many brain regions. 3α,5α-THP is an inhibitory neuroactive steroid that influences various behaviors, including stress responsivity, anxiety, and alcohol self-administration and consumption. In the present study we assessed the impact of acute alcohol (ethanol) administration following chronic intermittent ethanol (CIE) exposure on cellular 3α,5α-THP levels in various amygdala sub-regions, the prefrontal cortex, and in the paraventricular nucleus of the hypothalamus (PVN). We predicted alcohol administration following alcohol dependence and withdrawal would increase brain 3α,5α-THP immunoreactivity in the amygdala and prefrontal cortex. Briefly, mice were exposed to four cycles of CIE or air (16 hr/day x 4 days) in vapor inhalation chambers followed by 72 hr withdrawal periods over four consecutive weeks. Following the final 72 hr withdrawal phase, mice were administered saline or alcohol (2 g/kg). This resulted in an experimental design of four groups [Air-Saline, Air-Ethanol, Ethanol-Saline, and Ethanol-Ethanol]. Sixty minutes later, blood was collected for blood ethanol concentration (BEC) analysis, and mice were administered an overdose of pentobarbital, perfused, and brains collected for immunohistochemical analysis. Brain sections (40 microns; 4-6 sections/region) were immunostained and analyzed by pixel cell density in each brain region for each animal. CIE exposure does not alter BECs in response to the alcohol injection. In the prefrontal cortex, 3α,5α-THP levels were increased following alcohol administration in both the Air-Ethanol and Ethanol-Ethanol groups, as supported by a main effect of post-treatment ($p<0.05$). In the lateral amygdala, 3α,5α-THP levels were decreased in the Ethanol-Saline and the Ethanol-Ethanol groups, as supported by a main effect of post-treatment ($p<0.05$). In the basolateral amygdala, 3α,5α-THP levels were decreased (38.6%) in the Ethanol-Ethanol group. There were no statistically significant differences in 3α,5α-THP immunoreactivity in the central nucleus of the amygdala or in PVN between any of the groups. Together, these data indicate that the basolateral amygdala, lateral amygdala, and the prefrontal cortex may be affected by re-exposure to alcohol following alcohol dependence and a brief withdrawal period. All these data suggest that re-exposure to alcohol following alcohol dependence and withdrawal could serve as a useful model for alcohol relapse for alcohol use disorders and elucidate local brain changes that are important for alcohol drinking behaviors.

SESSION 1; ABSTRACT NO. 19

ADULT EXPOSURE TO THE PESTICIDE CHLORPYRIFOS CAUSES SHORT-TERM BEHAVIORAL EFFECTS IN THE ZEBRAFISH

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Organophosphate pesticides (OP), such as chlorpyrifos (CPF), were introduced as alternatives to organochlorine pesticides such as DDT, which was banned due to toxicity and environmental hazards in the

early 1970s. Since then, many American farm workers have been chronically exposed to OP throughout their adult lives. Recent evidence suggests that farm workers chronically exposed to pesticides as younger adults face greater risk for adverse cognitive effects and neurodegenerative diseases. Our lab has recently observed that chronic adult exposure to DDT can produce short and long term effects on behavior in the zebrafish, including increased anxiety-like behaviors. The aim of the present study is to demonstrate whether adult exposure to CPF carries similar risks. Na√Øve adult zebrafish (6-8 months of age) were separated into tanks of 10 mixed-sex fish and exposed to CPF concentrations of 0.3, 1 or 3uM in 0.001% DMSO or to the vehicle alone over the course of two weeks. These doses were selected to fall below the threshold for overt toxicity. This relatively brief exposure models the consequences of chronic CPF exposure during a short period in early-mid adulthood, rather than over a career. Following a 1 week recovery period, the fish were assessed in a behavioral test battery with assays for anxiety-related behavior, sensorimotor response and habituation, social interaction, predator avoidance. Fish were then tested again at 14-months of age, to assess the persistence of these effects and/or the emergence of aging related behavioral deficits. Assessment at the 1-week time point showed that a relatively brief exposure time of two weeks can dose-dependently impact multiple behavioral outcomes, although these effects were not persistent into late adulthood. The highest dose of CPF reduced anxiety-like responding in the novel tank test at 1-week post-exposure and enhanced social approach behaviors in the shoaling test ($p<.05$). Similar trends in the middle dose group approached significance ($0.05<p<0.06$). The low dose of CPF did not produce these effects, but rather impaired the habituation of acoustic startle in the tap test ($p<0.05$). These data show that adults are vulnerable to CPF-induced neurotoxicity, although the brief exposure used here did not produce effects which persisted into adulthood. Further testing with longer exposure periods will be necessary.

SESSION 2; ABSTRACT NO. 1

INTEGRATION OF GENOMIC AND METABOLOMIC DATA STREAMS IN AN IN VITRO NEURONAL DEVELOPMENT MODEL

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A microelectrode array-based assay (MEA) has been developed in rat primary cortical cultures for screening and prioritization of chemical effects on neural network formation. In this study, pathway-based transcriptomic and metabolomic methods were utilized to complement this assay and identify molecular key events involved in adverse outcome pathways leading to neural network disruption. Gene expression and metabolic alterations were determined after exposure to two DNA synthesis inhibitors (Cytosine Arabinoside and 5-Fluorouracil), two voltage-gated sodium channel (VGSC) modulators (Deltamethrin and Cypermethrin), a dopamine receptor antagonist (Haloperidol), and a glutamate receptor agonist (Domoic Acid). Doses (0.1-3μM) were selected based on critical concentrations at which the neural networks switched from recovery to non-recovery trajectories based on the MEA results. Global transcriptomic response for the DNA synthesis inhibitors repressed gene response, consistent with robust impacts on DNA synthesis, while the dopamine receptor antagonist slightly repressed gene activation. By contrast, exposure to VGSC modulators and the glutamate receptor agonist tended to increase gene expression. Regardless of chemical class, “Axonal Guidance Signaling” was a significantly altered transcriptomic pathway identified for all chemicals excluding Haloperidol, highlighting a shared disruption in neural development. Metabolomic analysis indicated twelve altered metabolites common

to all tested chemicals related to neuronal, developmental, and psychological disease. Further, “Activation of tRNA charging” was the most significantly perturbed metabolomic pathway with all chemicals, indicating an impact on a general translational response in rat cortical neurons. Overall, our combined findings across MEA, transcriptomic, and metabolomic responses consistently reinforce each other, suggesting that the molecular endpoints may serve as a complement to the functional MEA assay. Importantly, these results provide data to build an adverse outcome pathway network based on neural development disruption. This abstract does not necessarily reflect EPA policy.

SESSION 1; ABSTRACT NO. 2

HIGH FAT DIET IMPAIRS HYPOTHALAMIC RESPONSES TO FOOD AND HUNGER

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Obesity is a worldwide epidemic believed to be due, in part, to the increasing availability of calorically dense foods, such as those rich in fats. Our motivations to eat are regulated by complex interactions between hormonal signals from the gut and neural circuits that govern the sensation of hunger and consummatory behaviors. However, the effects of a high fat diet (HFD) on the neural circuits underlying feeding remain poorly understood. The arcuate nucleus of the hypothalamus (ARC) contains a population of neurons known to be critically involved in regulating food intake and are marked by expression of agouti-related peptide (AgRP). Previous work provides evidence that HFD alters the response of AgRP neurons to the hunger hormone ghrelin, however, the in vivo effects of HFD on AgRP neurons remain unknown. We aimed to determine how HFD access alters the responses of AgRP neurons to chow, HFD, and ghrelin throughout the transition to HFD-induced obesity. To accomplish this, we injected a virus encoding a cre-inducible fluorescent calcium sensor GCaMP6 to the arcuate nucleus of AgRP-Cre transgenic mice. We then implanted an optical fiber above the arcuate nucleus to allow for in vivo fiber photometry recordings of arcuate AgRP neuron activity before, during, and after ad libitum access to HFD. In agreement with previous reports, we observed that under conditions of food deprivation, subsequent chow availability decreased AgRP neuron activity. Following one week of HFD access, this inhibitory response to chow presentation was greatly reduced. Availability of HFD, however, was able to further reduce AgRP neuron activity under fasted conditions. This diminished response remained across 8 weeks of HFD access. The weakened ability of chow to inhibit AgRP neuron activity during fasting may contribute to a selective feeding of HFD. In separate recordings assessing AgRP neuron responses to the hunger hormone ghrelin, we observed that eight weeks of HFD led to a roughly 50% reduction in ghrelin-evoked AgRP neuron activity. These findings highlight how chronic consumption of high fat foods alters the AgRP neuron responses to food during physiological hunger, and to the hormonal signals of hunger itself, which may contribute to the dietary choices and consummatory behaviors that lead to the development of obesity.

SESSION 2; ABSTRACT NO. 3

THE IMPACT OF HORMONE STATUS AND NOVELTY ON FEMALE RAT BEHAVIOR IN THE OPEN FIELD TEST

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Many natural factors impact animal behavior. In females, one important consideration is hormone status due to the presence of cyclic hormone changes such as the menstrual cycle in humans and the estrous cycle in rats. These behaviors include those related to anxiety, depression, and motivation, which are often assessed in rodents using the open field test. It has been well established that in female rats within the

open field test, exploratory behaviors such as locomotion and propensity to enter areas perceived as dangerous fluctuate naturally across the estrous cycle. However, it is not well-explored as to how behavioral differences induced by hormone cycles interact with other factors such as exploration in a novel environment. Thus, hormone-induced behavioral differences may be masked by novelty-induced behavioral changes. Here, we aim to disassociate differences in exploratory behaviors in the context of the estrous cycle from differences resulting from a novelty effect. We hypothesized that behaviors in the open field such as total distance traveled and time spent in the center would be increased both during initial exposure to the open field as well as in the estrus stage compared to diestrus stage, when hormone effects are limited. We found that both the estrous cycle stage and day of exposure to the open field influenced exploratory behavior. This is important to note when studying behaviors in the context of the open field test, as hormone-induced behavioral differences may not be detected as robustly due to the presence of the novelty effect. This approach to open field testing should be considered when exploring mechanisms of hormone-induced behavioral changes across the natural cycle.

SESSION 2; ABSTRACT NO. 4

TARGETING NEUROINFLAMMATION WITH HUMAN UMBILICAL CORD TISSUE DERIVED MESENCHYMAL STROMAL CELLS

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Neuroinflammation is common in many demyelinating diseases, such as multiple sclerosis (MS), Krabbe disease, and cerebral palsy. Mesenchymal stromal cells (MSCs) can modulate immune cells and potentially limit neuroinflammation. Human umbilical cord tissue is readily available and a rich source of rapidly proliferating MSCs. In this study, we hypothesized that human cord tissue-derived MSCs (hCT-MSCs) can promote remyelination by suppressing inflammation. Multiple lines of hCT-MSCs were developed, which are currently being tested in a phase I clinical trial for autism spectrum disorder (ASD). We first tested if hCT-MSCs could suppress inflammation in experimental autoimmune encephalomyelitis (EAE). hCT-MSCs injected into the cerebral spinal fluid prevented the progression of clinical scores in EAE. Further, in an acute demyelination model, hCT-MSCs promoted remyelination in spinal cord white matter after focal lesions. To study the mechanism underlying the protective effects of hCT-MSC in EAE, we tested if hCT-MSC could directly suppress T cells or if they indirectly suppressed T cells by modulating other immune cells. We determined that hCT-MSCs suppressed T cells from proliferating when they were in peripheral blood or spleen mononuclear cells yet failed to suppress isolated T cells. hCT-MSC indirectly suppressed T cells by interacting with macrophages and this interaction dependent on direct cell contact. hCT-MSCs were engulfed by macrophages and led to long-term programing of macrophages which maintained their ability to suppress T cells when hCT-MSCs were removed. Overall, hCT-MSCs program macrophage to suppress T cell and prevent the progression of EAE.

SESSION 2; ABSTRACT NO. 5

BENEFITS OF COLLABORATIVE LEARNING IN UNDERGRADUATE NEUROSCIENCE EDUCATION

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Collaborative learning is an evidence-based instructional strategy that facilitates rich discussions between students to deepen student engagement and learning. This

pedagogical approach increases learning gains and reduces failure rates among undergraduate students in STEM courses. In addition, student participation, motivation, and self-efficacy can all be increased with these structured learning environments. One such structured, active learning environment is Team-Based Learning (TBL). In TBL, students spend the majority of classroom time applying course content, analyzing data, synthesizing new ideas, and evaluating hypotheses. Importantly, previous studies have shown that learning outcomes and student course satisfaction are higher in courses that use TBL, compared to lecture-based classrooms. To better understand how TBL improves student learning and course satisfaction, we collected end of semester course evaluations and measured student-perceived classroom dynamics, as well as learning of lower and higher order levels of Bloom's taxonomy. Our results suggest that implementation of TBL in an undergraduate neuroscience classroom improves student-perceived learning in both lower order (gaining knowledge, understanding concepts) and higher order (learning to apply and synthesize) levels of Bloom's taxonomy. These increases are consistent with the strong emphasis placed on application and synthesis within a TBL classroom.

SESSION 2; ABSTRACT NO. 6

USE OF 3D PRINTED CAPACITIVE TOUCH OBJECTS FOR OBJECT RECOGNITION TASKS

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Object recognition is a critical behavioral assay in evaluating and understanding cognition especially learning and memory. Object recognition typically involves familiarizing mice with a set of objects and then presenting a novel object or displacing an object to a novel location. Learning and memory is inferred by the amount of object investigation of the novel/displaced object. These tasks are in widespread use, but unfortunately there are large discrepancies in findings between labs. Two major contributors to these discrepancies are the lack of consistency in the method of measuring object investigation and the lack of standardization of the objects that are used. Current video-based automated algorithms can often be unreliable, lack temporal precision and can be costly, whereas manually scoring object investigation is time consuming, tedious and more subjective. To resolve these issues, we sought to design and implement 3D printed objects, so that objects can be standardized across labs and we utilize capacitive sensing to better measure object investigation. Utilizing a 3D printer with conductive filament and low cost off-the-shelf components we demonstrate that 3D printed capacitive touch objects are a reliable and precise way to perform object recognition tasks. Ultimately, this approach will lead to better standardization, greater consistency and thus prove invaluable to evaluating and understanding cognition in a variety of diseases including mental illnesses, drug addiction, and neurodegenerative diseases.

SESSION 2; ABSTRACT NO. 7

DEFINE: A METHOD FOR ENHANCEMENT AND QUANTIFICATION OF FLUORESCENTLY LABELED AXONS

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Visualization and quantification of fluorescently labeled axonal fibers are widely employed in studies of neuronal connectivity in the brain. However, accurate analysis of axon density is often confounded by autofluorescence and other fluorescent artifacts. By the time these problems are detected in labeled tissue sections, significant time and resources have been invested, and the tissue may not be easy to

replace. In response to these difficulties, we have developed Digital Enhancement of Fibers with Noise Elimination (DEFiNE), a method for eliminating fluorescent artifacts from digital images based on their morphology and fluorescence spectrum, thus permitting enhanced visualization and quantification of axonal fibers. Application of this method is facilitated by a DEFiNE macro, written using ImageJ Macro Language (IJM), which includes an automated and customizable procedure for image processing and a semi-automated quantification method that accounts for any remaining local variation in background intensity. The DEFiNE macro is open-source and used with the widely available FIJI software for maximum accessibility.

SESSION 2; ABSTRACT NO. 8

EYE-TRACKING AND SUBCONCUSSIVE LOADING: CHANGES IN OBJECTIVE OCULOMOTOR TASK METRICS FOLLOWING HEAD IMPACT EXPOSURE IN A HIGH SCHOOL FOOTBALL SEASON

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Introduction: An accurate and objective diagnostic tool does not yet exist for mild traumatic brain injury (mTBI) resulting from sub-concussive loading – described as the cumulative effects of sustained low-magnitude head impact exposure (HIE) – in adolescent football players. However, previous studies have shown that performance on the anti-saccade eye-tracking task is sensitive to neurological damage resulting from mTBI.

Objective: The objective of this pilot study was to examine the relationship between HIE and eye-tracking performance in varsity high school football athletes. It was hypothesized that varsity football athletes who experienced a high level of HIE would demonstrate significant differences in several anti-saccade metrics from beginning-of-season (BOS) to end-of-season (EOS), while the low level HIE group would show no significant differences.

Methods: Participating varsity football athletes during the 2017-2018 season (n = 31) were grouped into HIE percentiles based on weekly self-report HIE questionnaires. An independent samples t-test (alpha level of 0.05) was performed for anti-saccade latency, initial gain, end gain, and correct direction saccade for each eye between BOS (control) and EOS assessment for both the 10th percentile (n = 4) and 90th percentile (n = 4) of HIE.

Results: The independent t-test result indicated a significant decrease in both left eye and right eye latency from BOS (μ = 327.8, SD = 155.4 and μ = 317.5, SD= 21.3, respectively) to EOS (μ = 227.8, SD = 76.1 and μ = 256.6, SD = 92.6, respectively) in the 10th percentile of HIE (BOS—$p < 0.001$; EOS—$p = 0.017$). No other anti-saccade metric demonstrated statistically significant differences from BOS to EOS in the 10th percentile nor in the 90th percentile of HIE.

Conclusions: These pilot results suggest that anti-saccade latency, initial gain, end gain, and correct direction saccade do not yield overall significant changes from BOS to EOS in both high and low frequency HIE groups of varsity football athletes across a season. However, some limitations may have impacted the results, which include the assumptions that the AACEQ accurately stratifies HIE, the small samples are representative of true 90th and 10th percentile exposure, and there was no learning effect. A further investigation controlling for these limitations is necessary to further our understanding of the potential role of anti-saccade metrics as objective mTBI indicators.

SESSION 2; ABSTRACT NO. 9

STANDARDIZED ASSESSMENT OF CONCUSSION (SAC) SCORE STABILITY: COMPARING ACROSS A HIGH SCHOOL FOOTBALL SEASON: A PILOT STUDY

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Introduction: Mild traumatic brain injury is a potential injury for adolescent football players but remains a challenge to objectively diagnose. The Standardized Assessment of Concussion (SAC) is a five-minute neurophysiological evaluation testing attention and memory. By means of comparing a player's baseline score with his score on an assessment when he is suspected of having a head injury, a rapid assessment of the player's severity of head injury may be established.

Objective: The objective was to examine the change in SAC score over the course of a season of play, from BOS (baseline-before the start of the season) to EOS (end-of-season). This information provides insight into the utility of the SAC for concussion purposes and for understanding possible relationships between SAC scores and seasonal exposure data (days of practice and head contact per week).

Methods: The pilot study included high school varsity football players (n = 42) during the 2017-2018 season who had BOS and EOS testing conducted. To analyze the stability of SAC scores for a single player over the course of the season, t-tests for two related samples were conducted (alpha level of 0.05) for the player's overall SAC scores at BOS and EOS as well as the player's scores on the SAC subsections: immediate memory, orientation, concentration, and delayed recall.

Results: The mean BOS total SAC score was 27 (SD = 1.8) and the mean EOS total SAC score was 28 (SD = 1.6), demonstrating a statistically significant increase from BOS to EOS ($p < 0.05$). Similarly, the concentration ($p = 0.032$) and delayed recall ($p = 0.028$) subsets of the SAC demonstrated a statistically significant increase from BOS to EOS. The immediate memory and orientation score subsets of the SAC did not demonstrate significant differences from BOS to EOS.

Conclusion: These pilot results suggest that over the course of one season of high school football, the total SAC score and the score on the subsets of concentration and delayed recall increase from BOS to EOS. This suggests that a learning effect on the SAC tasks should be investigated. Additionally, quantified individual head impact exposure should be included in future analyses to further differentiate exposure groups, as 'season-of-play' alone may not be sufficient to relate exposure to changes in SAC score.

SESSION 2; ABSTRACT NO. 10

BIOORTHOGONAL REFILLABLE DRUG DEPOTS FOR LOCALIZED BRAIN TUMOR TREATMENT

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Local presentation of cancer drugs by drug eluting depots can reduce off-target systemic side effects. However, local depots rapidly deplete their drug stores, have a less than ideal volume, and cannot be refilled, reducing their utility in treating disease. I have developed an intradermal, intratumoral, and intracranially injectable drug-eluting depot that can be noninvasively refilled from the blood. These refillable depots utilize bioorthogonal click chemistry, a fast and highly specific reaction, to capture systemically-delivered inactive drugs. The depot is established by injecting a liquid PBS solution containing click motif conjugated sulfo-NHS esters which react with proteins (that have primary amines) and become anchored extracellularly at a disease site. We have shown specific capture of small molecules modified with click chemistry motifs and refilling to intradermal depots for

up to 6 months, within pancreatic tumors, and to intracranially injected depots in mice. We are moving on the brain tumors models and combining this technology with a blood brain barrier disruption technique for therapeutic efficacy. The system has not been shown to illicit any noticeable immune response. Further, I will present results from in silico simulations to model drug depot diffusion concentrated around the site of depot injection. This technology is useful for tumors requiring prolonged chemotherapy administration and may even be applied to other diseases that would benefit from repeated dosing.

SESSION 2; ABSTRACT NO. 11

DISRUPTION OF STRIATAL FUNCTION IMPAIRS TEMPORAL PROCESSING ACROSS DURATION RANGES

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The contributions of cerebellar, and striatal circuits to time perception has often been a point of contention. Dissociations between these two systems have been based on a variety of factors, but recently more attention has been given to their contribution to sub- vs supra-second duration ranges. In order to further investigate these dissociations we used a two alternative forced choice task that required estimating durations across two interval ranges (i.e. sub- and supra- second). We then used muscimol, a GABAA receptor agonist, to disrupt ongoing striatal activity, and assess if timing performance was impaired. We found that injection of muscimol into the dorsolateral striatum affected animals' ability to time across both duration ranges. While the muscimol injections increased response time, the disruption of timing could not be explained by motor deficits. Overall, we find that the striatum plays an essential role in timing durations both above, and below a second.

SESSION 2; ABSTRACT NO. 12

CENTRAL AMYGDALA SOMATOSTATIN (SST) SELECTIVELY REDUCES BINGE-LIKE ETHANOL INTAKE

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Somatostatin (SST) is a polypeptide widely expressed throughout the brain. Multiple lines of evidence support a role of the SST system in regulating emotional states closely associated with the initiation and perpetuation of alcohol use disorders, such as stress, anxiety, and depressive behaviors. Notably, SST-positive (SST+) cells represent a significant portion of GABAergic cells within the central nucleus of the amygdala (CeA), an area known to be critically involved in emotional processing and alcohol use disorders. However, the role of CeA SST in alcohol consumption remains essentially unexplored. Here we began to address this gap and evaluated the role of CeA SST signaling in a rodent model for binge-like alcohol consumption in non-dependent animals, the "drinking in the dark" (DID) model. We cannulated the CeA of singly housed male and female mice on a C57BL/6J background prior to DID alcohol or sucrose exposure. Three hours following lights off on day 1-3 of each week water bottles were removed and mice exposed to sipper tubes containing 20% ethanol or 3% sucrose solution for 2h. On day 4, ~30 minutes prior to the beginning of the DID session, animals received a microinjection of 3 µg/0.5 µl/side SST or a 0.5 µl/side of 5% DMSO in saline vehicle. A Latin Square design was used to evaluate SST impact on drinking. Intra-CeA injection of SST significantly reduced alcohol consumption without altering sucrose intake. Further, CeA microinjection of SST increased time spent in the open arm of an elevated plus maze without impacting total movement, suggesting an anxiolytic effect. These results extend our previous work examining the role of CeA neuropeptide involvement in binge-like ethanol intake and provide, to our knowledge, the first evidence of a role of CeA

SST in modulating binge-like ethanol consumption. This work was supported by NIH grants AA022048, AA013573 & F32AA02581.

SESSION 2; ABSTRACT NO. 13

NOVEL ROLE FOR MINERALOCORTICOID RECEPTORS IN HIPPOCAMPAL DEPENDENT BEHAVIORS

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Exposure to chronic stress at virtually any stage of life is a well-known risk factor for the development of neuropsychiatric disorders, including depression, schizophrenia, and post-traumatic stress disorder. In the brain, the response to stress is mediated by hypothalamic-pituitary-adrenal (HPA) axis activation and the subsequent release of glucocorticoids that bind to either glucocorticoid receptors (GRs) or mineralocorticoid receptors (MRs). GRs are expressed in neurons throughout the brain, while the higher-affinity MRs are restricted to neurons in the limbic system. In both mice and humans, the distribution of GRs and MRs within the hippocampus is subregion specific, with area CA2 having the highest expression of MRs and lower expression of GRs compared with other hippocampal subregions. In addition to this striking MR:GR ratio, CA2 has a distinct molecular profile and is critical for several behaviors, including social recognition. Using 2 conditional knockout models to delete MRs embryonically or postnatally, we previously found that MRs are required for the development and maintenance of the unique CA2 protein and mRNA expression profile. Thus, the goal of this study was to investigate the behavioral consequences of the compromised CA2 molecular phenotype in our MR knockout mice. We tested both conditional knockout lines for anxiety-like behavior in the elevated plus maze and open field assays and for their reactivity to novelty in both social and nonsocial contexts. We found that deleting MRs in CA2 led to a loss of social recognition memory, but not sociability: both wildtype and knockout animals showed had normal social investigation ($p<0.0001$) but knockouts had impaired social memory ($p>0.05$). Animals with MR knocked out either embryonically or postnatally show a hyperreactivity to both novel context and novel objects ($p<0.05$). Anxiety-like behavior varied depending on when MRs were deleted. In summary, CA2-targeted deletion of MRs is sufficient for behavioral deficits observed with global neuronal deletions of MR or silencing of CA2, suggesting that MRs in CA2 may be critical in facilitating these behavioral responses.

SESSION 2; ABSTRACT NO. 14

ANTERIOR CINGULATE CORTEX ENCODES VISUAL INFORMATION AND ADAPTS TO VISUAL EXPERIENCE

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The mouse visual system provides a model to study how experience modifies the brain. Mechanisms of experience-dependent plasticity have been well characterized in primary visual cortex (V1), including a form of potentiation driven by repeated presentations of a familiar visual sequence ("sequence plasticity"). The prefrontal anterior cingulate cortex (ACC) receives input from visual cortex, yet little is known about how visual experience modifies ACC circuits. We found that ACC exhibits sequence plasticity, but the plasticity expresses as a change in response latency, rather than a change in response magnitude (as in V1). Sequence plasticity was absent in ACC, but not V1, in a mouse model of a neurodevelopmental disorder associated with intellectual disability and autism-like features. Our results demonstrate that relatively simple sensory stimuli can be used to reveal how experience functionally (or dysfunctionally) modifies higher-order prefrontal circuits, and suggest

a divergence in how ACC and V1 encode familiarity.

SESSION 2; ABSTRACT NO. 15

VOLUNTARY ETHANOL DRINKING BEHAVIOR IN AN ALZHEIMER'S MOUSE MODEL FOLLOWING REPEATED MILD TRAUMATIC BRAIN INJURY

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Traumatic brain injury (TBI) has been recognized as the "signature injury" of the military, especially in recent military campaigns. Furthermore, evidence suggests that ethanol consumption following injury is associated with poor health outcomes, including increased PTSD symptoms and decreased cognitive processing. Despite this, it is not uncommon for individuals to continue ethanol consumption even after sustaining a TBI, and there is evidence to suggest that TBI may even increase an individual's risk for ethanol misuse. A sub-population that may be particularly vulnerable to the effects of ethanol on recovery from TBI include carriers of the epsilon 4 allele of the apolipoprotein E (APOE) gene. APOE4 is associated with increased tau pathology characteristic of not only Alzheimer's disease but also of chronic traumatic encephalopathy (CTE), a neurodegenerative disease resulting from repetitive TBI. Furthermore, evidence suggests that the APOE4 allele confers increased risk of poor cognitive outcomes as a result of ethanol use.

To understand the relevance of the APOE4 allele in drinking behavior in the context of TBI, we aimed to establish a model of pre- and post-TBI ethanol consumption in mice expressing either the human APOE3 or APOE4 genotype. We examined voluntary drinking behavior before and after a repeated moderate TBI (rmTBI) paradigm consisting of three closed cortical impacts spaced 24 hours apart. The mice were housed in the automated IntelliCage system, which allow the continuous recording of discrete drinking behaviors in a social context. We report drinking behavior as the percentage of licks each mouse made for ethanol (12%) prior to ethanol withdrawal and when access to ethanol was reintroduced one week post-TBI.

We observed that there was a difference in baseline drinking behavior between the genotypes ($F(1,22)=15.3$, $p=.0007$) with higher consumption in the APOE4 mice ($m=28\pm2.4\%$,) than in APOE3 ($m=6\pm2.2\%$). However, there was no main effect of TBI or genotype on drinking behavior ($F(3,20)=0.7$, $p=0.56$), nor was there any interaction of these two variables either before or after TBI.

This preliminary data suggests that there may be underlying alcohol preferences in the APOE4 genotype, but that withdrawal from alcohol may more robustly affect future alcohol preferences than rmTBI. Future behavioral tests are planned to further determine the effect of post-TBI recovery on alcohol seeking behaviors such as motivation and impulsivity.

SESSION 2; ABSTRACT NO. 16

LACK OF ADAP-1/CENTA1 RESCUES COGNITIVE AND SYNAPTIC IMPAIRMENT IN A MOUSE MODEL OF ALZHEIMER'S DISEASE

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Alzheimer's disease (AD) is a progressive neurodegenerative disorder that starts as a failure of synapses in brain regions important for memory formation, including the hippocampus and the entorhinal cortex. Dysfunction of synapses in AD thought to be caused by accumulation in the brain of a toxic peptide, called beta-amyloid (Aβ42). Previous studies from our lab found that a brain-specific Ras-anchoring protein, called ADAP-1/Centaurin α1

(CentA1), is involved in the cellular mechanisms by which Aβ42 induces neuronal dysfunctions. To test this finding in vivo, we created mice that lack CentA1 protein (CentA1 knockout, KO). Using these mice, we wanted to understand first the precise role of CentA1 in normal brain function. For this we performed a battery of memory tests followed by biochemical assays to investigate signaling pathways activated in the brain of the CentA1 KO mice. To our surprise, the mice lacking CentA1 exhibited a significant improvement in a hippocampus-dependent location memory task (OPT-object in place task). These mice also have increased density and plasticity of dendritic spines in the hippocampus compared to their non-transgenic litter mates. To test the role of CentA1 in development of AD, we crossed the mice lacking CentA1 with the J20 mouse model of AD. Lack of CentA1, significantly reduced AD like phenotype, including loss of synapses, deposit of amyloid plaques, neuroinflammation and spatial memory impairment. Therefore, our work indicates for the first time that CentA1 functions as a negative regulator of learning and memory formation and targeting CentA1 signaling might have therapeutic potential for AD prevention or treatment.

SESSION 2; ABSTRACT NO. 17

NMDA RECEPTOR AGONISTS AND ANTAGONISTS MICROINJECTED INTO THE DORSOLATERAL STRIATUM MODULATE THE SPEED OF INTERVAL TIMING MECHANISMS

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The ability of the brain to perceive and reproduce durations in the seconds-to-minutes range, also known as interval timing, is an essential component of cognitive control and complex behaviors such as movement, foraging, and decision making. Interval timing is mediated through the dopamine-glutamate pathways in the basal ganglia, specifically the cortico-striatal-thalamic loops. It has been shown that medium spiny neurons (MSNs) in the dorsal striatum receive glutamatergic and dopaminergic input from various regions of the brain including the prefrontal cortex and substantia nigra pars compacta, and are one of the key components for encoding/decoding signal durations. In this study, we investigated the role of NMDA receptors on MSNs in modifying timing accuracy and precision. Using a bi-peak timing procedure, rats were trained to reproduce two target durations (12 and 36 s). The training phase was followed by bilateral infusions of NMDA (agonist), AP5 (antagonist), or vehicle into the dorsolateral striatum 30 min prior to start of the 2-hr testing sessions. Our results indicated that the activation of NMDA receptors produces a rightward shift in the psychometric functions consistent with a decrease in clock speed, whereas the deactivation of NMDA receptors produces a leftward shift consistent with an increase in clock speed. These findings suggest that the glutamatergic input received by MSNs through NMDA receptors has a regulatory effect on their firing pattern, thereby leading to alterations in time perception.

Keywords: Interval timing; Cortico-striatal-thalamic loops; Medium spiny neurons; NMDA receptors.

SESSION 2; ABSTRACT NO. 18

ALTERNATIVE APPROACHES TO REVEAL BEHAVIORAL ABNORMALITIES IN AN ALZHEIMER'S DISEASE ANIMAL MODEL

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BACKGROUND: Alzheimer's disease (AD) is commonly characterized as a progressive decline in cognitive function; therefore, the majority of current behavioral

assessments are also focused on testing for disruptions in cognition. However, research data and clinical observations indicate that deterioration in performing activities of daily living (ADL) and alterations in emotional state are early signs of AD. Therefore, new approaches that could assess the ADL performance and emotional state of humans or animals may serve as valuable tools in AD research. Fortunately, several behavioral assays have recently been developed to assess ADL.

METHODS: In the current study, we employed burrowing and nesting experiments, which are well-characterized and sensitive assays for the ADL of rodents. These were used to evaluate the differences in performance between age-matched wild type (WT) and triple-transgenic AD (3xTg-AD) mice. Furthermore, a 5-score system was designed to evaluate the emotional state of each mouse. Lastly, learning and memory abilities of each mouse were assessed by Morris water maze (for spatial) and trace eyeblink conditioning (for non-spatial).

RESULTS: Results of our ADL assessment showed that 3xTg-AD mice not only demonstrated a significant deficit in burrowing food when compared to WT mice, but also performed poorly in the construction of nests. Furthermore, evaluation of emotional state revealed a striking change in the 3xTg-AD mice over the course of experiment, which was mainly manifested as aggressive and agitated behaviors during routine handling. Last, spatial and non-spatial learning and memory abilities were also compromised in the 3xTg-AD mice.

CONCLUSIONS: Prior to the development of severe cognitive deficits, disruption of normal ADL and emotional state are signals of early onset of AD. Unfortunately, these valuable signals are often ignored or unnoticed by care-givers of AD patients. Therefore, establishing a system to monitor subtle changes of ADs and emotional state may serve as a power tool for early diagnosis of AD as well as AD prevention. Future directions aim to apply small molecule modulators, such as Rho GTPase regulators, to modify the aberrant ADL behaviors and emotional state in the 3xTg-AD mice.

SESSION 2; ABSTRACT NO. 19

WIRELESS STIMULATION FOR IN-VIVO ELECROPHYSIOLOGY ON FREELY MOVING ANIMALS

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One of five people will be affected by a neurological disease which inspires the need for improved life science research equipment to understand the many mysteries of the nervous system. Rodent and primate experiments include in-vivo electrophysiology and behavior equipment play a significant role in diagnosing and understanding these neurological diseases. Over the last two decades Triangle BioSystems International (TBSI) has developed wireless technology for neural recording and stimulation used with in-vivo electrophysiology applications on freely moving mice, rats and non-human primates. Novel integrated telemetric headstage systems can now replace cumbersome tethered recording equipment to record local field potentials as EEG, ECOG and EMG along with single unit (or spikes) signals. This same is true for electrical and optogenetic stimulation. These head mounted and implantable headstage systems are used with research experiments investigating Alzheimer's, Dementia, Parkinson, Epilepsy, ALS and many other neurological disorders in academic or pharmaceutical laboratories all around the world. System level concepts for telemetric recording on 128 simultaneous channels and bipolar constant current electrical stimulation and optogenetic stimulation on 16 channels will be described. Key design challenges and tradeoffs of these wireless technologies used with behavior equipment will be explained for head mounted and implantable systems.

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