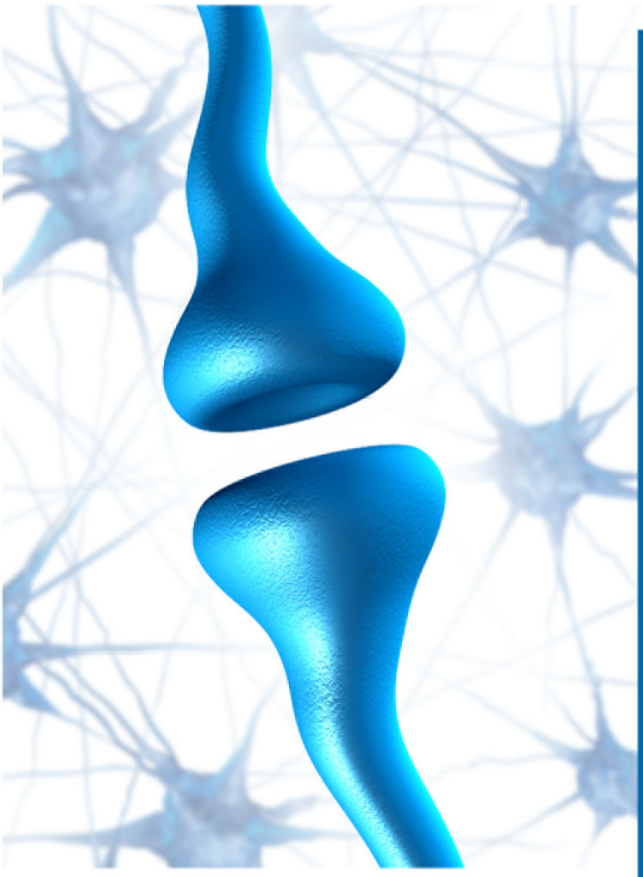

NATIONAL ENHANCEMENT
OF UNDERREPRESENTED
ACADEMIC LEADERS

NEURAL Conference 2023

June 14-16

University of Alabama at Birmingham
Birmingham, AL

UAB Neuroscience Roadmap Scholars

Our mission is to enhance engagement and retention of underrepresented trainees in the neuroscience workforce.

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Welcome

Dear Attendee:

Welcome to the 9th Annual NEURAL Conference! The **N**ational **E**nhancement of **U**nder**R**epresented **A**cademic **L**eaders (NEURAL) Conference is an extension of the UAB Neuroscience Roadmap Scholars Program. Our goal is to enhance engagement and retention of underrepresented in neuroscience (URiN) graduate trainees (as defined in the Notice of NIH's Interest in Diversity) in the neuroscience workforce.

We have put together an exciting scientific and professional program. We hope you will take every opportunity to network with other trainees and neuroscience faculty and discuss your work and individual challenges.

Farah D. Lubin, Ph.D.
Professor of Neurobiology & Triton Endowed Professor
Director, UAB Neuroscience Roadmap Scholars Program
Co-Director for Research, IRACDA-MERIT Program
Co-Chair, SoM Black/African-American Faculty Association
SoM Office for Diversity and Inclusion, Faculty Liaison

Michelle Gray, Ph.D.
Associate Professor of Neurology & Neurobiology
Jarman F. Lowder Endowed Professorship in Neuroscience
Associate Director for Professional Development,
UAB Neuroscience Roadmap Scholars Program

Jane Allendorfer, Ph.D., FAES
Associate Professor of Neurology & Neurobiology
Associate Director for Academic Development,
UAB Neuroscience Roadmap Scholars Program

Brian Sims, M.D., Ph.D.
Professor of Pediatrics, Division of Neonatology
Director, Brain Hemorrhage Prevention Program and Community Program for Reduction of Perinatal Mortality
Consultant, UAB Neuroscience Roadmap Scholars Program

Agenda

Wednesday, June 14, 2023

12:00-5:00 pm	Arrivals & Check In at McMahon Hall
5:45 pm	Shuttle from Hilton and McMahon Hall to Welcome Reception
6-7:30 pm	Welcome Reception Abroms-Engel Institute for the Visual Arts (1221 10th Ave. S.)
7:30 pm	Shuttle from AEIVA to McMahon Hall and UAB Hilton

Thursday, June 15, 2023 - UAB Alumni House - Alumni Hall (1301 10th Ave. S.)

7:15 am	Shuttle from Hilton and McMahon Hall to Alumni Hall
7:30 am	Breakfast
8:00 am	Opening Remarks & Ice Breaker: Farah Lubin, Ph.D. Director, NEURAL Conference and UAB Roadmap Scholars Program
8:15 am	Oral Session I
9:30 am	Break
9:45 am	Oral Session II
11:00 am	Break
11:15 am	Keynote Speaker I: Alicia D. Guemez-Gamboa, Ph.D. “Cell-type Specific Alterations Underpinning PACS1 Neurodevelopmental Disorder: Uncovering Novel Therapy Avenues”
12:30 pm	Lunch Break
1:15 pm	Oral Session III
2:15 pm	Break
2:30 pm	Keynote Speaker II: André Fenton, Ph.D. “Learning to Learn - What We Think, We Become”
3:45 pm	Break
4:00 pm	Professional Development Session I: Postdoctoral Q&A Panel

Thursday, June 15, 2023 - UAB Hilton - Hamilton Ballroom (808 20th St. S.)

5:15 pm	Shuttle to Hilton
5:30 pm	Dinner Reception
6:30 pm	Poster Hanging
7:00 pm	Poster Session (hors d'ouevres served)
9:15 pm	Shuttle to McMahon Hall

Friday, June 16, 2023 - UAB Alumni House - Alumni Hall (1301 10th Ave. S.)

7:15 am	Shuttle from Hilton and McMahon Hall to Alumni House
7:30 am	Breakfast
8:00 am	Special Guest Speaker: Angeline Dukes, Ph.D. "Making Time for What Matters: Balancing Research with Your Goals and Passions"
9:15 am	Break
9:30 am	Oral Session IV
10:30 am	Break
10:45 am	Shark Tank
11:45 pm	Lunch
12:30 pm	Professional Development Session II: Matthew C. Madison, Ph.D. "Networking: Increasing your Professional Visibility"
1:30 pm	Awards & Closing Remarks
2:00 pm	Adjourn & Lab Tours

Keynote Speaker

Alicia D. Guemez-Gamboa, Ph.D.
Assistant Professor of Neuroscience
Feinberg School of Medicine, Northwestern University

Biography:

Dr. Alicia Guemez-Gamboa earned her BS in Biology and her PhD in Biomedical Sciences from the Universidad Nacional Autonoma de Mexico. She then completed postdoctoral training at the University of California, San Diego and at The Rockefeller University. Her research aimed to understand how neural circuits assemble during development and disease by uncovering fundamental means of neural differentiation, synaptic formation, cell death and their functional interaction. Dr. Guemez-Gamboa is currently an Assistant Professor at the Department of Neuroscience at the Feinberg School of Medicine in Northwestern University. Dr. Guemez-Gamboa's laboratory is focused on investigating the molecular and cellular pathways that orchestrates neural circuit assembly dysfunction leads to neurodevelopmental disorders. She aims to uncover the mechanisms by which cell-surface recognition molecules and somatic mosaicism determine cellular identity to ensure proper neuronal connectivity by coupling human genetics, next generation sequencing, and disease modeling using animal and stem cells. Particularly, she uses induced pluripotent stem cells (iPSCs) from patients as well as CRISPR edited iPSC to generate neural progenitors, neurons, and forebrain organoids predisposed to neurodevelopmental disorders. Characterization of these models helps elucidating the mechanisms of disease of a variety of brain connectivity defects and lays the groundwork for the development of new therapeutic approaches and personalized medicine. Dr. Guemez-Gamboa is a 2022 Mentoring Institute for Neuroscience Diversity Scholars (MINDS) Fellow.

Talk Title & Description:

"Cell-type Specific Alterations Underpinning PACS1 Neurodevelopmental Disorder: Uncovering Novel Therapy Avenues"

PACS1 syndrome is a neurodevelopmental disorder characterized by intellectual disability and craniofacial abnormalities resulting from a *de novo* p.R203W variant in phosphofurin acidic cluster sorting protein 1 (PACS1). PACS1 plays roles in the endosomal pathway and nucleus, but little is known about how this variant affects developing neurons and patients have few therapeutic options. Here, we used stem cellderived models to show that PACS1$^{(+/R203W)}$ neurons have impaired expression of genes enriched for synaptic signaling processes. We assessed the functional impact of this differential expression and find that PACS1$^{(+/R203W)}$ neurons have a striking prolongation of network burst duration resulting from an increased inter-spike interval. These results suggest that an aberrant regulation of ionic flux affecting spike frequency underlies the neurological phenotypes experienced by patients. This work is the first to investigate the impact of the PACS1 p.R203W variant on developing neural tissue, revealing electrophysiological mechanisms of disease and putative targets for pharmacological intervention.

Keynote Speaker

André Fenton, Ph.D.
Professor
Neurobiology of Cognition Laboratory
Director, Center for Neural Science and Neuroscience Institute
New York University Langone Medical Center

Biography:

Dr. André Fenton is the PI of the Neurobiology of Cognition Laboratory at NYU. He investigates the molecular, neural, behavioral, and computational aspects of memory. He studies how brains store experiences as memories, how they learn to learn, and how knowing activates relevant information without activating what is irrelevant. His investigations and understanding integrates across levels of biological organization; his research uses genetic, molecular, electrophysiological, imaging, behavioral, engineering, and theoretical methods. This computational psychiatry research is helping to elucidate and understand mental dysfunction in diverse conditions like schizophrenia, autism, and depression. Dr. Fenton and his colleagues identified PKMzeta as the first molecule that maintains the persistence of memories in the brain, a discovery recognized by Science Magazine as one of the 10 most important breakthroughs in all of science and technology published in 2006. Dr. Fenton founded Bio-Signal Group Corp., which commercialized an FDA-approved portable, wireless, and easy-to-use platform for recording EEGs in novel medical applications. He also implemented a CPAP-Oxygen helmet treatment for COVID-19 in Nigeria and other LMICs and founded Med2.0 to use information technology for the patient-centric coordination of behavioral health services that is desperately needed to equitably deliver care for mental health. Additionally, Dr. Fenton co-hosted the PBS series NOVA Wonders. Currently, Dr. Fenton hosts “The Data Set”, a new web series on how data and analytics are being used to solve some of humanity’s biggest problems.

Talk Title:

“Learning to Learn - What We Think, We Become”

Special Guest Speaker

Angeline Dukes, Ph.D.

Assistant Professor of Neuroscience, University of Minnesota
Co-Director of MN Inclusive Neuroscience Development Scholars (MINDS) Post-Baccalaureate Program
President & Founder, Black In Neuro

Biography:

Dr. Angeline Dukes is a daughter of Haitian and Trinidadian immigrants and a first-generation college graduate. She earned her Bachelor's degree in biology from the Historically Black College/University (HBCU) Fisk University in 2017. She then earned her Masters and Ph.D. degrees in neuroscience from the University of California, Irvine. Upon completing her Ph.D. in June 2022, Dr. Dukes began a teaching faculty position in the Department of Neuroscience at the University of Minnesota. As an assistant professor, her unique role includes teaching neuroscience courses, co-directing a post-baccalaureate program for historically marginalized students, and leading her own diversity, equity, and inclusion initiatives. She aims to foster a community at UMN that welcomes, supports, and empowers all students, but especially those with historically marginalized identities, both in and out of the classroom. Her research seeks to assess the long-term effects of adolescent nicotine and cannabinoid exposure. In addition to these responsibilities, Dr. Dukes also serves as the current President of Black In Neuro, a non-profit organization that supports Black scholars in neuroscience-related fields worldwide.

Talk Title & Description:

"Making Time for What Matters: Balancing Research with Your Goals and Passions"

In this talk, Dr. Dukes will share her journey through academia as a Black woman and first-generation college graduate. She will discuss findings from her dissertation research on the long-term effects of adolescent nicotine and cannabinoid exposure as well as her tips on surviving and thriving in graduate school. Finally, she will share how she leveraged social media to cultivate a community as the Founder of Black In Neuro and how this led to her current unique career path.

Professional Development Sessions

Thursday, June 15
Professional Development Session I 4:00 - 5:00 pm

A moderated Q&A session with a panel of postdoctoral scholars who can speak to their experiences with finding their career pathway.

Rodrigo Campos-Cardoso, Ph.D.
Dr. Campos-Cardoso is currently a Postdoctoral Fellow in the Department of Neurobiology at UAB under the mentorship of Kirstie Cummings, Ph.D., studying the effects of the HPA-axis responses on memory and behavior in adolescent and adult rodents. He received his Ph.D. in Neuroscience from University of São Paulo at Ribeirão Preto in 2022.

Mariana DuPont, Ph.D.
Dr. DuPont is a 1st year IRACDA-MERIT Postdoctoral Scholar at UAB. She received her Ph.D. in Vision Science from UAB in 2022 and is a former Roadmap Scholar. Currently, she is performing her postdoctoral research under the mentorship of Burel Goodin, Ph.D., Associate Professor of Psychology, conducting laboratory-based pain research in patient cohorts.

Annesha King, Ph.D.
Dr. King is a 2nd year IRACDA-MERIT Postdoctoral Scholar at UAB. She received her Ph.D. in Neuroscience from UAB in 2021 and is a former Roadmap Scholar. Currently, she is a postdoctoral fellow under the mentorship of Nicole Riddle, Ph.D., Associate Professor of Biology, performing research on elucidating chromatin structure in Drosophila.

Richard Sanchez, Ph.D.
Dr. Sanchez is currently a Postdoctoral Scholar in the Department of Neurobiology at the University of California San Diego, performing research on the relationship between mitochondrial and neuronal metabolism under the mentorship of Gülçin Pekkurnaz, Ph.D. He received his Ph.D. in Neuroscience from UAB in 2021 and is a former Roadmap Scholar.

Andre B. Toussaint, Ph.D.
Dr. Toussaint is currently a Simons Junior Fellow and BWF PDEP Fellow at the Zuckerman Mind Brain Behavior Institute at Columbia University, investigating how a genetic predisposition to chronic pain affects the likelihood of opioid abuse under the mentorship of Ishmail Abdus-Saboor, Ph.D. He received his Ph.D. in Psychology and Neuroscience from Temple University in 2022.

Professional Development Sessions

Friday, June 16
Professional Development Session II 12:30 - 1:30 pm

"Networking: Increasing your Professional Visibility" featuring Matthew C. Madison, Ph.D.

Matthew C. Madison, Ph.D.
Dr. Madison is currently an Assistant Professor in the Department of Clinical and Diagnostic Sciences in the UAB School of Health Professions and a faculty of the Biomedical and Health Sciences MS Program. Dr. Madison completed the UAB IRACDA-MERIT Program in 2022, and received his Ph.D. in Translational Biology and Molecular Medicine from Baylor College of Medicine in 2019. His educational interests include Professional & Career Development and STEM success of first-generation college students.

Poster Presentation Session

Thursday, June 15
Poster Hanging 6:30 pm
Poster Session 7:00 - 9:00 pm

Poster presentations are open to ALL neuroscience trainees. Abstracts must be neuroscience-related. Abstract bodies should be no longer than 250 words and include: Title; Author list; Introduction; Materials & Methods; Results; Conclusion. Use Microsoft Word; Arial 11pt; single spaced. Posters should fit on a 4-ft high by 8-ft wide poster board. If you have questions, please email roadmap@uab.edu.

Shark Tank

Friday, June 16
10:45 am

The "Shark Tank" is a platform to allow participants to present their work in the most grandiose way to attract attention to their work. Modeled after the reality television show where would-be entrepreneurs pitch their business ideas to a panel of investors, it is one of the highlights of the NEURAL Conference. "Shark Tank" gives the students freedom to think about how their project could have a big impact in neuroscience and to highlight the importance of their work. Students who want to participate will be randomly assigned an order of presentation the day of the event. The "Shark Tank" presenters will be allowed 3 minutes each to sell their project to the conference attendees and a panel of judges. Cash prizes ($100 - $250) will be awarded to the top 3 presenters. Winners will be announced at 1:30 pm.

Oral Presentation Session I
Thursday, June 15, 8:15 - 9:30am

8:15 am	Indonesia Jordan “Brain Glutamate-Glutamine after Endotoxin Challenge in Fibromyalgia”
8:30 am	Barbara Marin “Characterization of Conformally Coated Spinal Progenitor Cells”
8:45 am	Maria Fernanda Juarez Anaya “A subpopulation of inhibitory neurons may regulate blood flow throughout brain states”
9:00 am	Adrianna Milton “Recovery of forearm and fine digit function after chronic spinal cord injury by si multaneous blockade of inhibitory matrix CSPG production and the receptor PTPσ”
9:15 am	L. Sofia Gonzalez “Ventral striatal dopamine encodes unique properties of visual stimuli in mice”

Oral Presentation Session II
Thursday, June 15, 9:45 - 10:45am

9:45 am	Emma Jones “Nanopore long-read RNA sequencing reveals region-specific sex differences in wildtype mouse brain mRNA isoforms”
10:00 am	Melody Iacino “Diurnal Variation in Acetylcholine Modulation of Dopamine Dynamics Following Chronic Cocaine Intake”
10:15 am	Charlie Rodriguez Deliz “Behavioral and neural analysis of global form sensitivity in developing macaques”
10:30 am	Rachel Frazer “Mechanosensory neurons responsible for dopaminergic activity and social-touch-like behaviors”

Oral Presentation Session III
Thursday, June 15, 1:15 - 2:15pm

1:15 pm	Preston Siegler “Identification of Hippocampal Area CA2 in Hamster and Vole Brain”
1:30 pm	Gabriella Perez “Excitatory and inhibitory neurons produce distinct amyloid structures in mouse models of Alzheimer’s disease”
1:45 pm	Joanna Hobson “Discrimination Hurts: A Sequential Mediation Examining Associations Between Discrimination, Stress, Sleep, Depression and Pain”
2:00 pm	Oluwatomi Akinduro “Breast milk derived exosomes attenuate Lipopolysaccharide-induced activation of Microglia via CD9 interference with the Toll-like Receptor 4 Complex”

Oral Presentation Session IV
Friday, June 16, 9:30 - 10:30am

9:30 am	Ana Almeida Rojo “Sleep Deprivation Engages the Hypocretin/Orexin System to Regulate Reward Seeking”
9:45 am	Asia Wiggins “A Low-Carbohydrate Diet to Reduce Self-Reported Pain in Non-Hispanic Black Women with Knee Osteoarthritis”
10:00 am	Dana May “Evaluating Toxoplasma gondii Colonization in the Murine Brain Using a Cellular Bar coding Approach”
10:15 am	Samantha Thompson “Molecular Mechanism of T-Type Calcium Current Elevation in Childhood Absence Epilepsy”

Oral Presentation Abstracts

Oral Presentation Session I: Thursday, June 15, 8:15 - 9:30am

1	Brain Glutamate-Glutamine after Endotoxin Challenge in Fibromyalgia	Indonesia Jordan
2	Characterization of Conformally Coated Spinal Progenitor Cells	Barbara Marin
3	A subpopulation of inhibitory neurons may regulate blood flow throughout brain states	Maria Fernanda Juarez Anaya
4	Recovery of forearm and fine digit function after chronic spinal cord injury by simultaneous blockade of inhibitory matrix CSPG production and the receptor PTPσ	Adrianna Milton
5	Ventral striatal dopamine encodes unique properties of visual stimuli in mice	L. Sofia Gonzalez

Oral Presentation Session II: Thursday, June 15, 9:45 - 11:00am

6	Nanopore long-read RNA sequencing reveals region-specific sex differences in wildtype mouse brain mRNA isoforms	Emma Jones
7	Diurnal Variation in Acetylcholine Modulation of Dopamine Dynamics Following Chronic Cocaine Intake	Melody Iacino
8	Behavioral and neural analysis of global form sensitivity in developing macaques	Charlie Rodriguez-Deliz
9	Mechanosensory neurons responsible for dopaminergic activity and social-touch-like behaviors	Rachel Frazer

Oral Presentation Session III: Thursday, June 15, 1:15 - 2:15pm

10	Identification of Hippocampal Area CA2 in Hamster and Vole Brain	Preston Siegler
11	Excitatory and inhibitory neurons produce distinct amyloid structures in mouse models of Alzheimer's disease	Gabriella Perez
12	Discrimination Hurts: A Sequential Mediation Examining Associations Between Discrimination, Stress, Sleep, Depression and Pain	Joanna Hobson
13	Breast milk derived exosomes attenuate Lipopolysaccharide-induced activation of Microglia via CD9 interfer-ence with the Toll-like Receptor 4 Complex	Oluwatomi Akinduro

Oral Presentation Session I: Friday, June 16, 9:30 - 10:30am

14	Sleep Deprivation Engages the Hypocretin/Orexin System to Regulate Reward Seeking	Ana Almeida Rojo
15	A Low-Carbohydrate Diet to Reduce Self-Reported Pain in Non-Hispanic Black Women with Knee Osteoarthritis	Asia Wiggins
16	Evaluating Toxoplasma gondii Colonization in the Murine Brain Using a Cellular Barcoding Approach	Dana May
17	Molecular Mechanism of T-Type Calcium Current Elevation in Childhood Absence Epilepsy	Samantha Thompson

Presentation 1

Brain Glutamate-Glutamine after Endotoxin Challenge in Fibromyalgia

Indonesia Jordan[1], Christina Mueller Ph.D.[2], Matthew McDaniel[1], Sophia Fox[1], Jarred Younger Ph.D.[1]
[1]Department of Psychology, University of Alabama at Birmingham, Birmingham, AL,
[2]Department of Neurology, Heersink School of Medicine, University of Alabama at Birmingham, Birmingham, AL

Fibromyalgia (FM) is a chronic musculoskeletal pain condition with an unknown cause. The central aim of this current study was to determine whether there is a relationship between the immune system and the brain concentrations of Glx (Glutamate + Glutamine) in FM patients using magnetic resonance spectroscopy after an endotoxin-driven immune challenge.

Twelve women with FM and 13 age-matched healthy controls completed the study. Participants underwent an MRI 1.5 hours before receiving 0.3ng/kg versus 0.4ng/kg endotoxin and 4 hours after. Glx was measured in 47 brain regions. We conducted a mixed analysis of variance (ANOVA) with time as the within-subjects factor (pre-LPS, post-LPS) and the study group as the between-subject factor (FM, healthy control); additionally, we looked at dosage as another between-subjects factor. A $p < 0.05$ was set as the statistical significance threshold for all analyses.

We found significant time-by-group interactions in the right precentral gyrus, the right supplementary motor area, and the left anterior cingulate cortex. We found no significant time-by-dosage interactions. There were also significant main effects of time in several regions. Before receiving LPS, FM patients reported lower Glx compared to healthy controls. After receiving LPS, we found no significant differences between groups. Lastly, we found several regions that significantly increase Glx pre- to post- LPS.

These preliminary findings suggest that FM patients have increased Glx after receiving LPS. Increased Glx is believed to be involved in common symptoms associated with FM. These findings warrant further study in a larger sample and look at separated Glu and Gln to see which is the catalyst for these changes.

Presentation 2

Characterization of Conformally Coated Spinal Progenitor Cells

Marin, B, BS [1], Gonzalez, G, BS [1], Al-Hanoosh, F, BS [1], Tomei, A, Ph.D. [1], Dumont, C, Ph.D. [1]; [1]Biomedical Engineering, University of Miami, Miami, FL 33136.

Traumatic spinal cord injury (SCI) is a devastating condition that disrupts autonomic, sensory, and motor function. Spinal progenitor cells (SPCs) can modulate the site into a more pro-regenerative milieu, but poor SPC survival due to inflammation can hamper transplant potential. Thin layered biomaterial encapsulation, termed conformal coating, is a technique that shields transplants from immune attack while allowing diffusion of nutrients and waste. Conformal coating reduces diffusion distances and minimizes transplant volume size compared to traditional encapsulations. Conformal coating has not been applied to SPCs as an SCI therapy, however, the objective of this study is to engineer a conformal coating capable of maintaining SPC survival and potency in inflammatory models. SPCs were expanded as neurospheres and encapsulated in a polyethylene glycol (PEG) capsule using a microfluidic platform. SPC viability, proliferation, SPC phenotype, and capsule integrity were evaluated over 14 days in vitro. Immunostaining and qRT-PCR were used to evaluate SPC outcomes. RNA was isolated from cell cultures to identify and quantify expression of specific marker proteins. Conformally coated neurospheres can be encapsulated without negatively impacting cell viability and sustained over a 2-week period. Future experiments will interrogate SPC secretory anti-inflammatory potential.

Presentation 3

A subpopulation of inhibitory neurons may regulate blood flow throughout brain states

Fernanda Juarez Anaya, Catherine F. Ruff, Benjamin O. Brandeis, Sarah E. Ross, Alberto L. Vazquez

Cerebral blood flow (CBF) and neuronal activity vary across brain states. CBF increases during high gamma-band, related to arousal, and during delta-band, related to non-rapid eye movement (NREM) sleep. Inhibitory neurons, which are crucial for mediating brain states, are associated with the changes in CBF across brain states. However, whether the same populations of neurons regulate changes in CBF across brain states is unknown. Previous studies suggest that a subpopulation of somatostatin neurons that are depolarized by Tac1 (known as substance P), co-express Tachykinin Receptor 1 (Tacr1) and neuronal nitric oxide synthase (nNOS), and show Fos induction during NREM sleep, regulate CBF. Here, we characterize the activity of Tacr1 neurons across brain states and identify possible sources of Tac1 inputs to Tacr1 neurons. To measure changes in Tacr1 neuron activity during different brain states, we performed two-photon calcium imaging and pharmacological manipulations in Tacr1CreER mice expressing GCaMP, while simultaneously measuring EEG and EMG. During periods of NREM sleep and following whisker stimulation, Tacr1 neuron activity increased. Administration of an antihistamine, which increases the probability of the animal sleeping, also increased Tacr1 neuron activity. Furthermore, to identify possible sources of Tac1 that could depolarize Tacr1 neurons, we used viral transfection mapping. This revealed that besides local projections of Tac1+ neurons, a population of Tac1+ neurons in the perirhinal cortex may be a source of Tac1. These results indicate that Tacr1 neuron activity varies across brain states and that the perirhinal cortex could be a source of Tac1 during NREM sleep.

Presentation 4

Recovery of forearm and fine digit function after chronic spinal cord injury by simultaneous blockade of inhibitory matrix CSPG production and the receptor PTPσ

Milton, Adrianna J.[1], Kwok, Jessica[2], McClellan, Jacob[1], Randall, Sabre G.[3], Lathia, Justin D.[3,4], Warren, Philippa M.[1,5], Silver, Daniel J.[1,3,4,§], Silver, Jerry[1,§]

[1]Department of Neurosciences, Case Western Reserve University, Cleveland, Ohio. [2]School of Biomedical Sciences, Faculty of Biological Sciences, University of Leeds, Leeds, UK. [3]Cleveland Clinic Lerner Research Institute, Department of Cardiovascular and Metabolic Sciences, Cleveland, Ohio. [4]Cleveland Clinic Lerner College of Medicine at Case Western Reserve University, Department of Molecular Medicine, Cleveland, Ohio. [5]Wolfson Centre for Age-Related Diseases, King's College London, London, UK. [§] Denotes equal contribution

Spinal cord injuries, for exists limited effective treatments, result in enduring paralysis and hypoesthesia due, in part, to the inhibitory microenvironment that develops and limits regeneration/sprouting, especially during chronic stages. Recently, we discovered that targeted enzymatic modulation of the inhibitory chondroitin sulfate proteoglycan (CSPG) component of the extracellular and perineuronal net (PNN) matrix via Chondroitinase ABC (ChABC) rapidly restores robust respiratory function to the previously paralyzed hemi-diaphragm up to 1.5 years following a cervical level 2 hemi-transection. Importantly, ChABC treatment at cervical level 4 in this chronic model also elicited rapid improvements in gross upper arm function. In the present study, we sought to further optimize and elucidate the capacity for nerve sprouting/regeneration to restore crude as well as fine motor control of the forearm and digits at lengthy chronic stages post-injury. However, instead of using ChABC, we utilized a novel and more clinically relevant systemic combinatorial treatment strategy designed to both reduce and overcome inhibitory CSPGs simultaneously and spatially extensively. Following a three-month upper cervical spinal hemi-lesion using adult female Sprague Dawley rats, we show that the combined treatment had a profound effect on functional recovery of the chronically paralyzed forelimb and paw, specifically during walking as well as precision movements of the digits. The regenerative and immune system related events that we describe deepen our basic understanding of the crucial role of CSPG mediated inhibition via the PTPσ receptor in constraining functional synaptic plasticity at lengthy time-points following SCI, hopefully leading to clinically relevant translational benefits.

Presentation 5

Ventral striatal dopamine encodes unique properties of visual stimuli in mice

L. Sofía González[1,2], Austen Fisher[1], and J. Elliott Robinson[1]

[1]Rasopathy Program, Division of Experimental Hematology and Cancer Biology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 45229, USA
[2]Neuroscience Graduate Program, University of Cincinnati, Cincinnati, OH, 45229, USA

The mesolimbic dopamine (DA) system is an evolutionarily conserved set of brain circuits that plays a role in attention, appetitive behavior, and reward processing. In this circuitry, ascending dopaminergic projections from the ventral midbrain innervate targets throughout the limbic forebrain, such as the ventral striatum/nucleus accumbens (NAc). Dopaminergic signaling in the NAc has been widely studied for its role in behavioral reinforcement, reward prediction error encoding, and motivational salience. Less well characterized is the role of dopaminergic neurotransmission in the response to surprising or alerting sensory events. To address this, we used the genetically encoded dopamine sensor dLight.2 and fiber photometry to explore the ability of striatal dopamine release in to encode the properties of salient visual stimuli in mice, such as threatening looming discs. We report that lateral NAc dopamine release encodes the rate and magnitude of environmental luminance changes rather than visual stimulus threat level. This encoding is highly sensitive, as lateral NAc dopamine could be evoked by light intensities that were imperceptible to human experimenters. We also found that light-evoked dopamine responses are wavelength-dependent at low irradiances, independent of the circadian cycle, robust despite previous exposure history, and involve multiple phototransduction pathways. Thus, we have further elaborated the mesolimbic dopamine system's ability to encode visual information in mice, potentially relevant to studies/pathologies involving light and downstream dopamine circuitry.

Presentation 6

Nanopore long-read RNA sequencing reveals region-specific sex differences in wildtype mouse brain mRNA isoforms

Emma F. Jones, Timothy C. Howton, Victoria L. Flanary, Brittany N. Lasseigne
University of Alabama at Birmingham

Introduction: The human brain has the most complex RNA splicing profile out of all tissues, and many neurological and psychiatric disorders are associated with defects in alternative splicing (AS). AS is specific to a given biological condition, such as sex or brain region, similar to how diseases typically display a bias toward a condition. Unlike previous short-read technologies, long-read sequencing can capture full-length mRNA transcripts, essential for confidently determining the consequences of AS.

Materials & Methods: We first extracted RNA from wildtype C57BL/6J mouse (n = 5 male and 5 female, age = 20 weeks) hippocampus, striatum, cerebellum, and cortex. We then prepared and sequenced long-read RNA-Seq libraries with the Oxford Nanopore GRIDion. We processed the resulting data with the nf-core nextflow nanoseq pipeline and performed differential transcript usage (DTU) analyses with IsoformSwitchAnalyzeR.

Results: We identified significant region-specific transcript expression across all four mouse brain regions. Cerebellum had 438 genes with DTU, the most region-specific transcript expression across brain regions, followed by the striatum, cortex, and then hippocampus. We did not identify shared sex-specific DTU across all four brain regions but did identify 13 genes with sex-specfic DTU within brain regions. Interestingly, the striatum exhibited the most sex-specific splicing with 6 DTU genes, including Dhrs4. Finally, we determined 21 brain region-specific DTU genes that are known to be psychiatric disorder risk genes.

Conclusion: Overall, with long-read RNA sequencing we identified different patterns of AS across wild-type mouse brain regions, including in genes known to be relevant to human disease.

Presentation 7

Diurnal Variation in Acetylcholine Modulation of Dopamine Dynamics Following Chronic Cocaine Intake

Melody C. Iacino and Mark J. Ferris, Ph.D.

Wake Forest University School of Medicine

Despite decades of research into its neurobiological mechanisms, cocaine use disorder (CUD) remains a major worldwide health problem. One variable that is often overlooked in CUD research is cocaine-induced disruption of diurnal (night/day) rhythms. Acetylcholine (ACh) from striatal cholinergic interneurons (CINs) modulates mesolimbic dopamine (DA) release in the nucleus accumbens (NAc) core via nicotinic acetylcholine receptors (nAChRs) on DA terminals. Thus, ACh plays a critical role in motivated and reward-associated behaviors. Though the effect of chronic cocaine on DA signaling has been studied at single time points, cocaine-induced diurnal disruptions of DA release and their mechanisms have not been investigated. Here, we utilized fast scan cyclic voltammetry in a rodent model of cocaine self-administration following various access schedules [(Short continuous access (ShA), long continuous access (LgA), or intermittent access (IntA)] to test the hypothesis that diurnal variation and the CIN ACh influence on DA release will vary based on the pattern of cocaine availability. Consistent with the literature, we found that IntA resulted in cocaine intake that was comparable to ShA, but significantly less compared to LgA. Interestingly, IntA significantly increased DA release midway through the dark cycle while LgA increased DA release midway through the light cycle compared to other groups. Furthermore, the CIN ACh influence on DA release is greatest following IntA and LgA schedules versus ShA and relative to naïve controls across time points. Understanding the influence of rhythms underlying NAc neurochemistry will provide a rationale for targeting these receptor systems as a mechanism for cocaine-induced disruptions.

Presentation 8

Behavioral and neural analysis of global form sensitivity in developing macaques

C. L. Rodríguez Deliz, Gerick M. Lee, Najib J. Majaj, J. Anthony Movshon and Lynne Kiorpes

New York University Center for Neural Science

Postnatal changes in shape discrimination cannot be entirely explained by maturation of the early visual pathway. We propose that development of extrastriate areas enables our ability to integrate lower-level contour information into global shape percepts. We studied neural signals in V1, V2, V4 and IT–areas known to respond selectively to textures, intermediate shapes and objects, respectively. It is unknown when selectivity for shapes emerges in early life, so we studied the development of form sensitivity in 4 macaques, ages 5 to 12 mo. We used radial frequency stimuli (RFS), circular targets whose radii are modulated sinusoidally. We tested monkeys' ability to discriminate RFS from circles as a function of the depth and frequency of modulation using a 4-alternative oddity task. Behavioral performance was best for higher radial frequencies and improved both longitudinally and cross-sectionally across our subjects. We placed 96-channel "Utah" arrays in V1/V2, V4 and IT, and recorded multi-unit neuronal responses to RFS from the same subjects during development. We used a maximum correlation coefficient classifier to measure neural decoding performance. V2, V4 and IT populations showed shape-selective responses even at the earliest ages tested. V4 and IT reliably signaled the presence of modulations near the behavioral threshold. Neural decoding was optimal for shorter time windows in older animals than in younger ones. However, we found no age-dependent differences in neural performance. Response changes in V4 and IT therefore do not account for the development of behavioral form sensitivity.

Presentation 9

Mechanosensory neurons responsible for dopaminergic activity and social-touch-like behaviors

Rachel E. Frazer[1], Dr. Leah J. Elias[2,3], Dr. Melanie Shaffler[2], Alexis A. Knight[1], Sarah Sorensen Ogata[1], Ziad Eltabakh[4] & Dr. Ishmail Abdus-Saboor[1]. [1] Columbia University [2] University of Pennsylvania [3] Johns Hopkins University [4] LaGuardia High School.

Social touch is known to elicit oxytocinergic and dopaminergic activity in the brain promoting stress relief, reward, and even analgesia. However, the molecular identity of the mechanosensory neurons responsible for transducing pleasurable touch and promoting bonding and social encounters has previously been unknown. Here, we aimed to determine if a candidate population of mechanosensory neurons that express mas-related g-coupled protein receptor B4 (Mrgprb4-lineage neurons) are necessary and sufficient for social-touch-like behaviors as well as activation of dopaminergic neurons in the ventral tegmental area (VTA) and dopamine release in the nucleus accumbens (NAc) - areas important for determining reward. In order to test this, we used Cre-lox genetics to produce mice in which we could optogenetically activate these neurons (B4-ChR2) as well as mice that had these neurons ablated (B4-DTA) and recorded behavioral and neuronal responses to touch and Mrgprb4-lineage neuron stimulation. We found that mice with these neurons intact show normal sexual receptivity and release of dopamine into the NAc and that optogenetic activation of Mrgprb4-lineage neurons alone was sufficient to be rewarding shown by conditioned place preference and increased dopamine release. However, mice with these neurons ablated showed decreased sexual receptivity and decreased dopaminergic release during social encounters. Therefore, signaling between these neurons and the brain is necessary and sufficient for mediating social-touch-like behaviors. Additionally, because oxytocinergic signaling from the hypothalamus to the VTA is important for mediating social reward, we are currently delineating whether Mrgprb4-lineage neuron activation is necessary and sufficient for oxytocinergic activity.

Presentation 10

Identification of Hippocampal Area CA2 in Hamster and Vole Brain

Preston Siegler

University of North Carolina (UNC)/National Institute of Environmental Health Sciences (NIEHS)

Prairie voles (Microtus ochrogaster) and Syrian hamsters (Mesocricetus auratus), closely related to mice (Mus musculus) and rats (Rattus norvegicus), are commonly used in studies of social behavior, including social interaction, social memory, and aggression. The CA2 region of the hippocampus is a critical node that is known to play a key role in social memory and aggression in mice, likely owing to its high expression of oxytocin and vasopressin 1b receptors there. However, CA2 has yet to be characterized in hamsters and voles. In this study, we sought to determine whether we could identify CA2 in vole and hamster. To do this, we stained free-floating tissue slices using primary antibodies raised against known markers of CA2 typically used in mice and rats and fluorescently labeled secondary antibodies. Imaging was performed on an epifluorescence microscope and images were processed using Fiji software. Here we report that immunofluorescent staining for CA2 markers in vole and hamster brains, like in mice and rats, reveals a population of neurons that includes both neurons receiving mossy fiber input and those without, extending just beyond the end of the stratum lucidum. Antibodies raised against RGS14, commonly used to label neurons in area CA2, stained this population of neurons and colocalized with immunostaining for two other CA2 markers, STEP and PCP4. These cells were located at the tail end of the mossy fiber projections, marked by the presence of calbindin stain in all three species. In addition to staining the mossy fibers, antibodies raised against calbindin also labeled the superficial layer of CA1 pyramidal cells in mouse and hamster but not vole. However, a WFS1 stain marked CA1 neurons in all three species. These results demonstrate that CA2 can be distinguished within the hippocampus from neighboring CA1 and CA3 areas in voles and hamsters, which should facilitate the future study of CA2's role in social behavior in these species.

Presentation 11

Excitatory and inhibitory neurons produce distinct amyloid structures in mouse models of Alzheimer's disease

Gabriella A. Perez, Rong Zhao, M. Danish Uddin, Jonathan C. Bean, Joanna L. Jankowsky

Baylor College of Medicine

Alzheimer's disease (AD) is the most common form of dementia and characterized by the formation of extracellular amyloid plaques in the brain. Although plaques are diagnostic of AD, they can look qualitatively different between subjects and it is not known how these differences arise. Clinical symptoms also vary among patients, leading to the hypothesis that distinct plaque conformations contribute to clinical heterogeneity. To study this issue in the laboratory, plaque formation has been modeled in mice by overexpressing the amyloid precursor protein (APP). All neurons express APP in the human cortex, however, many of the existing AD mouse models overexpress APP largely from excitatory neurons. Inhibitory neurons serve a different function in the brain and often do not express APP in many AD mouse models. We hypothesized that the neuronal source of APP may contribute to plaque and clinical diversity found in patients. To test this, we generated two mouse models expressing APP in either excitatory or inhibitory neurons. We used immunofluorescence and histological staining to examine plaque structure in the brains of our mice. Although both models produced amyloid plaques, their structures were completely different. Excitatory plaques stained for both amyloid peptide and thioflavin dye, which is a diagnostic standard for human AD. In contrast, the inhibitory model stained for amyloid peptide but lacked thioflavin staining. Our findings suggest that inhibitory and excitatory neurons produce distinct amyloid structures that may contribute to variation in AD pathology, presentation, and progression.

Presentation 12

Discrimination Hurts: A Sequential Mediation Examining Associations Between Discrimination, Stress, Sleep, Depression and Pain

Joanna Hobson[1]; Burel R. Goodin, PhD[1]; Calia A. Morais, PhD[2]

[1]Department of Psychology, College of Arts and Sciences, University of Alabama at Birmingham, Birmingham, AL, USA
[2]Division of Hematology and Oncology, Department of Medicine, School of Medicine, University of Alabama at Birmingham; Birmingham, AL, USA

People living with chronic pain (CP) experience stigma and discrimination in their daily lives due to their health condition. These experiences of stigma and discrimination can be harmful for their state of mind, health behav-iors (e.g. sleep) and could possibly exacerbate their CP condition. Studies have shown that experiences of dis-crimination can worsen stress in the brain and body, and lead to poor health related quality of life, especially for minoritized groups. However, few studies have elucidated the causal impact of discrimination on pain. We exam-ined this impact in 208 individuals with CP. Participants were recruited from the UAB pain clinic, and asked to complete the Everyday Discrimination scale, the Perceived Stress Scale, the Center for Epidemiological Studies Depression Scale, the Insomnia Severity Index, and the Brief Pain Inventory – Short Form. Results show that there was a significant indirect effect of discrimination on pain severity through stress, depressive symptoms and insomnia symptoms with a point estimate of .009 and a 95% confidence interval of .003 to .018. Specifically, experiences of discrimination predicted greater perceived stress ($t = 8.308$, $p = .000$), greater perceived stress predicted greater symptoms of depression ($t = 5.737$, $p = .000$), greater depressive symptoms predicted greater symptoms of insomnia ($t = 8.643$, $p = .000$) and greater insomnia symptoms predicted greater pain severity ($t = 4.082$, $p = .000$). Similar results were shown for pain interference. These findings highlight a causal pathway of discrimination on pain severity, and serve as potential targets for treatment recommendations.

Presentation 13

Breast milk derived exosomes attenuate Lipopolysaccharide-induced activation of Microglia via CD9 inter-ference with the Toll-like Receptor 4 Complex

Oluwatomi Akinduro[1], Thomas Van Groen[1], Quamarul Hassan[2], Brian Sims[1]
[1]Department of Pediatrics/Division of Neonatology and Center of Glial Biology in Medicine at the University of Alabama School of Medicine, University of Alabama, Birmingham, Alabama 35294; [2]RNA Biology and Epigenetics Laboratory, Department of Oral and Maxillofacial Surgery, School of Dentistry, University of Alabama at Birmingham, Alabama 35233

Exosomes are nanosized vesicles (30-120 nm) involved in intercellular communication and implicated in numer-ous pathophysiological processes. Human breast milk is vital for neonatal immune system maturation and adap-tation, which may be due in part to its abundant supply of exosomes. Microglia are intrinsic mediators of the CNS immune response and may become pathogenic depending on the magnitude of environmental insults. In our previous work, we have demonstrated the therapeutic potential of human breast milk derived exosomes (HBMDE) in attenuating lipopolysaccharide (LPS)-induced microglial activation as evidenced by the suppression of CD40, an immune cell marker important in microglial activation, and associated proinflammatory markers such as p38, NFkB, and IL-1β. In the current study, we look to elucidate the mechanism by which HBMDEs cause this effect. Exosomes carry and transport DNA, lipids, mRNA, microRNA, and proteins that may act as effectors in target cells. CD9 is a membrane bound tetraspanin protein well recognized as a specific biomarker for exosomes and for its role in cell signaling, motility, and growth. CD9 can inhibit the CD14 (TLR4 cofactor) interaction with Toll-like receptor 4 (TLR4), which is required for LPS to bind and activate microglia. Our preliminary data suggests that breast milk from some mothers has decreased expression of CD9 in its exosomes. This may translate as differential neuroprotective potential in neonates. We hypothesize that HBMDEs attenuate LPS-induced activa-tion of microglial proinflammatory markers by transporting CD9 to microglia and attenuating their activation. Our future investigations will elucidate the validity of this mechanism.

Presentation 14

Sleep Deprivation Engages the Hypocretin/Orexin System to Regulate Reward Seeking

Almeida Rojo AL, Heim B, Cai L, and Huang YH
University of Pittsburgh

Introduction: Sleep disruptions alter reward processing in the brain, but the mechanisms are not clearly understood. The hypocretin/orexin system presents a candidate mechanism in sleep deprivation (SD)-modulation of reward. Orexin 1 and orexin 2 receptors (OX1R and OX2R) are differentially expressed in the brain with sexual dimorphism. Functionally, OXRs regulate sleep and wakefulness, promote arousal, and regulate reward seeking. Thus, we hypothesize that SD recruits the orexin system to modulate natural reward-seeking in a sex- and receptor subtype-dependent manner.

Methods: Male and female mice were trained for sucrose self-administration (SA). Following acute SD for 6 hours (ZT0-6) by gentle-handling, mice received systemic administration of OX1R or OX2R antagonist prior to the SA test. Changes in c-Fos expression in reward circuitry were quantified 90 min from entering the SA chamber. To further understand c-Fos changes, fiber photometry was applied to measure neuronal activities in relation to orexin release following SD.

Results: Following normal sleep, OX1R or OX2R signaling did not modulate sucrose SA in males or females. After SD in females, OX2R but not OX1R antagonism reduced sucrose SA; no reductions were observed in males. C-Fos quantifications suggested a trend of SD-induced, OX2R-modulated changes in the nucleus accumbens (NAc) and paraventricular nucleus of the hypothalamus (PVN). On-going fiber photometry experiments in the NAc suggested that there were SD-induced changes in calcium and orexin activity.

Conclusion: In female mice, SD preferentially engages OX2R signaling to increase sucrose reward seeking. This effect may be mediated by OX2Rs in the NAc and/or PVN.

Presentation 15

A Low-Carbohydrate Diet to Reduce Self-Reported Pain in Non-Hispanic Black Women with Knee Osteoarthritis

Asia M. Wiggins, Larissa J. Strath, Gray E. McPherson, & Robert E. Sorge
University of Alabama at Birmingham

Introduction: It has been well known that diet plays a role on chronic pain states and chronic pain diseases. There has also been an acknowledgement of potential sex differences in pain outcomes. However, the link between a low-carbohydrate diet (LCD) on knee osteoarthritis (OA) pain in women has not been well-established. The purpose of this study is to investigate the impact that a low carbohydrate diet has on chronic pain states and the quality of life of women living with knee OA.

Materials & Methods: 14 chronic knee osteoarthritis female participants enrolled in a low carbohydrate dietary intervention for the course of 6 weeks. Baseline, 3-week, and 6-week measures of pain sensitivity, quality of life, dietary habits, and overall chronic pain, disability, and physical functioning was obtained using questionnaires, functional performance tasks, and pain sensitivity tests.

Results: The LCD significantly reduced body weight. The LCD reduced pain severity and interference. The LCD reduced pain, stiffness, and functional impairment. The LCD improved function, energy, pain, general health, and health change. The LCD reduced pain intensity in the temporal summation and chair stand tasks and unpleasantness in the temporal summation task.

Conclusion: The utilization of a low-carbohydrate diet for knee OA is a modifiable and simplistic alternative to current chronic pain treatments, like opioids.

Presentation 16

Evaluating Toxoplasma gondii Colonization in the Murine Brain Using a Cellular Barcoding Approach

Dana A. May[1, 2], Ceire J. Wincott[3], Matthew A. Child[3], Sarah E. Ewald[1]

[1]Department of Microbiology, Immunology and Cancer Biology at the Carter Immunology Center, University of Virginia School of Medicine, [2]Department of Neuroscience, Neuroscience Graduate Program, University of Virginia School of Medicine, [3]Department of Life Sciences, Imperial College London, South Kensington Campus

Cellular barcoding techniques are powerful tools to understand microbial pathogenesis. However, barcoding strategies have not been broadly applied to protozoan parasites, which have unique genomic structures and virulence strategies compared with viral and bacterial pathogens. Here, we present a CRISPR-based method to barcode protozoa, which we successfully apply to Toxoplasma gondii. Using libraries of barcoded T. gondii, we evaluate shifts in the population structure from acute to chronic infection of mice. Contrary to expectation, most barcodes were present in the brain one-month post-intraperitoneal infection in both inbred CBA/J and outbred Swiss mice. Although parasite cyst number and barcode diversity declined over time, barcodes representing a minor fraction of the inoculum could become a dominant population in the brain by three months post-infection. These data establish a cellular barcoding approach for protozoa and evidence that the blood-brain barrier is not a major bottleneck to colonization by T. gondii. However, our results examine the bottleneck capacity of the blood-brain barrier across the whole brain and lacks the resolution of the bottleneck effect within distinct brain regions. Therefore, my future work will utilize our barcoding approach in conjunction with brain microdissection to probe the within-host population dynamics of T. gondii brain colonization at various time points of chronic infection.

Presentation 17

Molecular Mechanism of T-Type Calcium Current Elevation in Childhood Absence Epilepsy

Samantha J. Thompson, Anika Sonig, and Jeffrey Noebels M.D. Ph.D.
Baylor College of Medicine

Childhood absence epilepsy (CAE) is the most common form of pediatric epilepsy where spike-wave seizures accompanied by lapses in consciousness occur hundreds of times per day. Known mutations in Cacna1a that cause CAE disrupt P/Q type calcium channels that are expressed broadly throughout the brain and are involved in synaptic transmission. Consequently, cortical loss of Cacna1a lead to elevated thalamic T-type calcium currents and evoke burst firing in the thalamocortical circuit that drive spike-wave seizures. Cav3.1 T-type calcium channels are encoded exclusively by Cacna1g alpha-subunits expressed in layer VI cortical neurons and thalamic relay cells. Elevated thalamic T-currents precede the onset of spike-wave seizures have been identified in 3 CAE mouse models. Transgenic Cacna1g overexpression produces spike-wave seizures while Cacna1g deletion and ethosuximide, a T-type channel blocker, suppress seizures. The mechanism underlying downstream Cav3.1 thalamic T-current elevation in these models is unknown. To test if Cacna1g is transcriptionally upregulated in Cacna1a mutant mouse tottering, we analyzed pre- and post-seizure tottering mice and wildtype littermates using fluorescent in situ hybridization technique RNAscope. We found a significant difference in thalamic relay Cacna1g transcription in tottering mutants that may explain elevated T-channel currents driving spike-wave seizures. Transcriptional upregulation is present prior to the onset of seizures and persists after seizure onset in adult tottering mice, suggesting Cacna1g upregulation may play a role in epileptogenesis and maintaining seizure activity in tottering mice.

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Poster 1

Hierarchical social ranks are altered in Rett syndrome mice

Cesar Acevedo-Triana

Atypical social behaviors are prevalent in neurodevelopmental disorders, and a mouse model of Rett syndrome shows impaired social memory caused by heightened activity of the monosynaptic projection from the ventral hippocampus to the mPFC. We performed the 'tube' test over 6 consecutive days to establish the social hierarchy within groups of 3 age-matched male mice of the same genotype. We found that Mecp2 KO mice failed to form stable social ranks, displaying fewer dominant behaviors than WT mice. We followed the 'tube' test with a novel 'warm' spot test, where the same 3 age-matched mice compete to stand on a single warm spot in a cage with a cooled floor. As expected, the 'dominant' WT mouse occupied the 'warm' spot far longer than the other 2 mice, while Mecp2 KO mice equally shared the 'warm' spot regardless of their social rank, showing fewer dominant behaviors than WT mice. In vivo Ca2+ imaging with head-mounted miniscopes to follow neuronal activity in unrestricted mice poses a significant challenge to study Mecp2 KO mice because they begin to have neurological impairments around P50. To overcome this, we performed a single surgery to inject AAVs expressing GCaMP6 and implant a GRIN lens in the mPFC of WT mice at P25. After 2 weeks, WT mice displayed stable social ranks in the 'tube' and 'warm spot' tests. We are currently using this shortened and simplified procedure in Mecp2 KO mice to compare the activity patterns of mPFC neuronal ensembles in mice performing the 'warm' spot test.

Poster 2

Common and Distinct Associations between Baseline Impulsivity and Longitudinal Development of Positive and Negative Alcohol Expectancies in Alcohol Naïve Youth in the Adolescent Brain Cognitive Development (ABCD) Cohort

Faith Adams[1], Iliyan Ivanov[2], MD, Muhammad Parvaz, PhD[1,2]
1. Department of Neuroscience and 2. Psychiatry, Icahn School of Medicine at Mount Sinai, New York, NY

Background: Both impulsivity and longitudinal development of positive and negative alcohol expectancies (PAE and NAE, respectively) are implicated in alcohol initiation and escalation in youth. However, for precise phenotyping of at-risk youth, it is imperative to determine whether PAE and NAE are fully complementary to each other and how different facets of impulsivity (i.e., impulsive action, impulsive choice, and impulsive personality traits) at baseline map on to the longitudinal development of PAE and NAE in youth.
Methods: From the ABCD sample, we identified alcohol naïve participants at Year 1 (n = 8328, ages 10-11), Year 2 (n = 7,782; ages 11-12) and Year 3 (n = 4,776, ages 12-13). Stop signal reaction time from the Stop Signal Task (SST) paradigm, reaction time difference between high and low reward from the Monetary Incentive Delay (MID) task, and subscale scores from the UPPS-P Impulsive Behavior Scale were used to quantify impulsive action, impulsive choice, and impulsive personality traits, respectively. Bootstrapped linear mixed regression models were used.
Results: At baseline, higher lack of planning and higher sensation seeking predicted higher PAE at Year 1(pYear 1<0.001), whereas lower impulsive choice, higher lack of planning and higher sensation seeking predicted higher PAE at Years 2 and 3 (pYear 2 <0.001, pYear 3 < 0.022). Moreover, lower impulsive choice and lower positive urgency predicted higher NAE at Year 1 (pYear 1<0.004), higher impulsive action, lower impulsive choice, lower positive urgency and lower lack of perseverance predicted higher NAE at Year 2 (pYear 2<0.036), and lower impulsive choice, and lower positive urgency predicted higher NAE at Year 3 (pYear 3<0.001).
Conclusions: Results indicate that although some facets of impulsivity consistently predict the longitudinal development of both PAE and NAE, there are some distinct associations as well, suggesting that PAE and NAE may not be fully complementary. These results identify different facets of impulsivity as targets for modulating alcohol expectancies for prevention efforts.

Poster 3

Altered DNA Hydroxymethylation and Neuronal Activity Gene Expression in the Dorsal Hippocampus of a Temporal Lobe Epilepsy Model Following Sequential Behavioral Testing

Rudhab Bahabry, Jonathan Harmon, Leah Dinah Sheppard, Bellafaith Oyassan, Farah D. Lubin
The University of Alabama at Birmingham, Department of Neurobiology

Temporal lobe epilepsy (TLE) is a prevalent form of focal epilepsy that is extremely difficult to manage, often leading to cognitive deficits that significantly impair the quality of life of affected individuals. Impaired hippocampal-dependent memory is one of the most common cognitive deficits in TLE. While the kainic acid (KA) model of TLE is widely used to study memory dysfunction in epilepsy, it remains unclear whether the underlying transcriptional and epigenetic mechanisms of chronic epilepsy following prolonged behavioral testing are applicable. This study aimed to characterize the epilepsy-related memory deficits in the KA model of TLE, examine the effect of prolonged behavior training on hippocampal immediate early gene (IEG) expression and DNA methylation marks, and determine whether traditional behavioral testing methods can be used to study memory function in chronic epilepsy.

Here, we injected male Sprague Dawley rats (125-150g) with either saline (vehicle) or 10mg/kg of KA to induce TLE, and measured behavioral seizure severity using the Racine scale. Six weeks following the injections, we conducted a battery of experiments to evaluate the effects of chronic epilepsy on locomotor activity, anxiety, hippocampus-dependent memory, and working memory. To accomplish this, we employed two experimental cohorts, each consisting of control and epileptic animals. One group underwent behavioral testing, while the other was housed under standard homecage conditions. The animals underwent the following tests: elevated plus maze (EPM), open-field test (OF), object location recognition (OLR), Y-Maze, Barnes Maze, and Fear Conditioning. Following the last test, we sacrificed the animals and extracted their hippocampi for Quantitative RT-PCR and Immunohistochemistry.

Our findings indicate that epileptic animals exhibited enhanced locomotor activity in the EPM, elevated levels of anxiety-like behavior in the OF, and deficits in hippocampus-dependent memory in the OLR, Barnes Maze, and Fear Conditioning tasks compared to controls. Conversely, no significant difference in working memory performance was observed in the Y-maze. Furthermore, following the prolonged behavioral testing, epileptic animals exhibited alterations in experience-dependent IEG expression and DNA hydroxymethylation levels, which were more pronounced than those observed in homecaged controls.

While our study confirms previous findings showing a strong relationship between hippocampus-dependent memory impairment and chronic epilepsy, our results also suggest that the traditional sequential behavioral testing paradigm may not be the most appropriate approach for studying the underlying transcriptional and epigenetic mechanisms. Specifically, our results demonstrate that prolonged behavioral testing induces significant changes in hippocampal gene expression, which may confound the interpretation of the underlying mechanisms of memory dysfunction. Therefore, caution should be exercised in the design and interpretation of prolonged behavioral experiments to study underlying molecular mechanisms involved in memory impairment in chronic epilepsy. Nonetheless, our findings provide a valuable roadmap for future studies investigating the impact of seizures and behavior testing on memory-associated mechanisms in chronic epilepsy.

Poster 4

Temperature-related increases in epileptic activity are captured by machine learning in a mouse model of epilepsy

Asad I. Beck, Glorianna I. Gutierrez, Hannah Zaini, Horacio O. de la Iglesia

Introduction: Presence of excessively synchronized neural activity (seizures) and epileptiform discharge (interictal spikes; IS) characterized epilepsy. Epileptic activity frequency may increase in relation to core body temperature, with both seizures and IS occurring more frequently as the individual's body becomes hotter. We examined whether increases in IS frequency could be indicative of imminent seizure onset by inducing temperature-related seizures in a mouse model of Dravet Syndrome (DS; heterozygous Scn1a gene deletion).
Materials & Methods: Neural activity was via two electrocorticography electrodes and one electromyography electrode with a sampling rate of 400 Hz, while core body temperature was captured every three minutes via a sensor implanted in the peritoneal cavity. To induce temperature-related seizures, animal core body temperature was gradually increased by 0.5 °C every two minutes until a seizure was observed or core body temperature reached 42.5 °C. Finally, a previously trained machine learning model was used post-hoc to autonomously detect IS in collected data.
Results: As core body temperature was increased, both seizure and ML-predicted IS frequency increased, with there being significant correlation between IS frequency and temperature ($r = 0.27$, $p = 3.53e\text{-}17$). Both temperature-induced and spontaneous seizures tended to be preceded and followed by increases in IS frequency, but not all increases in IS frequency evolved into seizures.
Conclusions: These results suggest our model can capture epileptic activity – both spontaneous and temperature-induced. Due to the low computational power needed, this ML-based method may be a potential avenue for real-time seizure forecasting and prevention for humans with epilepsy.

Poster 5

Analysis of Spectral Responses to SPES to Localize the Epileptogenic Network

Helen E. Brinyark, Soondos Kamel, Erin C. Conrad, Rachel J. Smith

Introduction: Resection or ablation of the seizure onset zone (SOZ) has been proven to reduce or eliminate seizures that are not controlled with medication in patients with epilepsy. However, 30-80% of patients undergoing this invasive surgery do not become seizure free. This is partly because no biomarker of the seizure onset zone (SOZ) exists. Intracranial EEG recorded during single-pulse electrical stimulation (SPES) can be analyzed to localize the SOZ. It has been shown that cortico-cortical evoked potentials (CCEPs) and cortico-cortical spectral responses (CCSRs) evoked during SPES hold promise for SOZ localization.
Methods: In this preliminary study, we analyzed CCEPs and CCSRs in two epilepsy patients. CCEP amplitudes were calculated from the EEG data as the root mean square values 15-50 ms after the stimulus onset for each response channel. CCSR amplitudes were calculated as the average power across 30 trials for each response in four canonical frequency bands: theta (4-7 Hz), alpha (8-12 Hz), beta (13-30 Hz), low gamma (30-60 Hz). We then identified significant peak CCEP amplitudes and CCSR frequencies using the nonparametric Wilcoxon rank-sum test and corrected for multiple comparison using the Benjamini-Hochberg procedure.
Results and Conclusions: Our preliminary results suggest that channels with significant spectral responses in the beta band correlated with the clinician identified SOZ. We also found that the significant spectral responses co-localize with "delayed responses" which have been shown to be significantly associated with the SOZ. This overlap corroborates the use of CCSRs as a candidate biomarker for the SOZ.

Poster 6

Tau Induced Alterations in Amyloid Precursor Protein Proteolysis Promotes Alzheimer's Disease

Andy Delgado, Danitra Parker, Andrew M. Pickering
University of Alabama at Birmingham, Department of Neurology

The amyloid precursor protein (APP) undergoes sequential protease cleavage to generate metabolites of itself with biological effects relevant to Alzheimer's disease (AD). Literature shows that in AD, non-amyloidogenic processing of APP is diminished and amyloidogenic processing is enhanced. How this shift in APP processing occurs is unknown. Literature shows the tau protein binds to APP, an interaction that may influence protease cleavage. In this study, we investigate the effects pathological forms of tau have on APP proteolysis. We will measure ADAM10, BACE1, and gamma secretase activity from lysates and membrane fractions of the SH-SY5Y cell line to compare treatment with tau oligomers and fibrils with untreated cells. We will also measure APP, sAPP-alpha, C99 and amyloid beta 42/40 ratio from lysates, membrane fractions and cell culture media to assess how tau pathology influenced production of APP derivatives. Our expected result is that tau will reduce ADAM10 cleavage of APP and increase BACE1 cleavage of APP, thus reducing production of the neuroprotective sAPP-alpha fragment and increasing the production of the neurotoxic C99 and amyloid-beta fragments. We further anticipate tau to alter gamma secretase cleavage of C99 such that it generates longer, more pathogenic variants of amyloid-beta. This finding would implicate APP tau binding as an interaction that alters APP processing to promote AD.

Poster 7

Emotional Stress regulates Endocannabinoid signaling in cerebellar cortex

Mohamed Sayed, Jessica Fawcett-Patel, Muhammad Farooq, June Liu.
Cell Biology and Anatomy department, Louisiana State University Health Sciences Center, New Orleans, LA 70112, USA.

Background: A growing set of evidence emphasizes cerebellum's major role in regulation of emotional memory. For instance, the endocannabinoid system in the cerebellum is involved in fear memory formation through retrogradely regulating synaptic transmission. A pilot study from our lab showed that predator odor stress reduces endocannabinoid signaling in the cerebellar cortex. This can be due to 1) increased degradation of endocannabinoids by monoacylglycerol lipase, 2) decreased endocannabinoid receptor signaling, or 3) decreased production of endocannabinoids by diacylglycerol lipase. We have shown that predator odor stress did not alter the activity of MAGL compared to naive mice. In this study we determined the effects of predator odor stress on endocannabinoid receptor signaling.

Methods: P21 to P35 male C57BL/6 mice were divided into 2 groups: a control naive group and fox urine exposed group. The latter was exposed to fox urine for 5 minutes, three hours before cerebellum was isolated. Sagittal slices (300 µm) were cut from the cerebellar vermis. All recordings were obtained in lobules V and VI of the cerebellar vermis. miniature IPSCs (mIPSCs) were recorded in the presence of a non-NMDAR inhibitor (5 µM NBQX) and TTX (0.5 µM) and after stable baseline, a synthetic CB1R agonist WIN55212-2 (5 µM) is bath applied.

Results: In naïve mice, application of WIN55212-2 reduced the frequency of mIPSCs in stellate cells, which indicates that the activation of CB1R reduces the spontaneous GABA release. In fox urine exposed mice, WIN55212-2 reduced mIPSCs frequency by ~30% ,comparable to naive mice, suggesting that fox urine exposure did not disrupt the CB1R signaling.

Conclusions: This study suggests that predator odor stress does not decrease endocannabinoid receptor signaling in the cerebellar cortex. (Supported NIH R01 NS106915 ,VA I01 BX003893-01A1)

Poster 8

Early-life status epilepticus on postnatal day 7 alters ultrasonic vocalizations in a sex-specific manner

Leighton Douglas, John M. Reinhart, Katherine J. Blandin, Danielle Santana-Coelho, and Joaquin N. Lugo

Introduction: Early-life status epilepticus (SE) is known to cause long-term deficits in learning, memory, social behavior, and communication. In order to better understand the acute effects of SE, our laboratory has used ultrasonic vocalizations (USV) to investigate early communication deficits in mice. We have previously found that male mice that had experienced SE on postnatal day (PD) 10 present a decreased number of 50KHz USVs on PD12. In the current study, we aimed to investigate the effects of SE on communication at an earlier timepoint in development that has not previously been investigated. Also, we assessed if there were any dimorphic effects of SE in communication.
Methods: Neural activity was via two electrocorticography electrodes and one electromyography electrode with a sampling rMale and female C57BL/6 mice were housed and monitored at Baylor University for this experiment. We induced SE using an intraperitoneal injection of 0.5% KA (2.5mg/kg) on PD7. Age-matched control male and female pups were administered 0.9% physiological saline. After the injection, the mice were placed into an individual container with clean bedding and monitored through the duration of SE, which is characterized by continuous tonic-clonic seizures lasting 1-2 h. Control pups were also monitored during this time. On PD8 mice were placed individually into containers where they were separated from the dam and sire. Their vocalizations were recorded for a total of two minutes through the Avisoft software. The files were analyzed in Matlab DeepSqueak where the calls were quantified and characterized. Vocalizations were then individually characterized based on established categories. A measure of total number of calls; total number of complex, two-component, upward, downward, chevron, short, composite, frequency steps, and flat calls; total duration of calls; Percentage of complex, two-component, upward, downward, chevron, short, composite, frequency steps, and flat calls; total duration of call; Average call duration; Average Median Frequency of calls; Average Amplitude of calls; and first call latency.
Results: Analysis of USVs showed that the total number of calls did not differ between the groups. A two-way Anova revealed Mean amplitude was not affected by SEs ($F_{1, 52}=0.59$, $p=0.44$)), but a trend to a main effect of sex was identified ($F_{1, 52}=4.04$, $p=0.05$) suggesting that females present a lower call amplitude than males.). A main effect was observed in short calls (SE: $F_{1, 52}=5.78$, $p=0.02$; sex: $F_{1, 52}=0.03$, $p=0.85$), and flat calls (SE: $F_{1, 52}=4.35$, $p=0.04$; sex: $F_{1, 52}=0.01$, $p=0.89$). A chi squared analysis revealed select alterations to call repertoire which is consistent with similarly observed findings at the 24-hour timepoint. We observed a significant difference between female pups after SE, $x2(9) = 2914$, $p<0.001$. Z-tests for column proportions revealed select differences in various calls types of significance $p < 0.05$. There was an observed increase in the complex, upward, and chevron calls; decrease in two component, short, and frequency steps calls; and no change to the unstructured, downward, composite, and flat calls. We observed a significant difference between seized and control male pups, $X2(9) = 57.609$, $p < 0.001$. Z-tests for column proportions revealed select differences in various calls types of significance $p < 0.05$. There was an observed increase in two-component, chevron, and frequency steps calls; decrease in upward, downward, and flat calls; and no change in the complex, unstructured, short, and composite calls.
Conclusions: Preliminary data show that SE at PD7 alters USVs amplitude at PD8 in a sex-specific manner. Most of the findings in our study revealed the female pups were the main sex affected by SE. As seen in previous studies differences to specific call types were also observed. These findings support the need for additional research to explore the dimorphic effects that early life seizures can have on development.

Poster 9

Medial Prefrontal Cortex Subregion-Specific Activity and Plasticity in Fear Memory Consolidation and Extinction

Brianna Fitzgerald

The prefrontal cortex is very important for cognitive activity including working memory, emotions, thoughts, and behaviors as they relate to environmental conditions. Deficits of prefrontal circuitry and plasticity during neurodevelopment contribute to the onset and progression of neuropsychiatric disorders such as post-traumatic stress disorder (PTSD), anxiety, depression, schizophrenia, and autism spectrum disorder. The rodent functional analogue, the medial prefrontal cortex (mPFC), has been demonstrated to be involved with fear processing and extinction. Many studies have demonstrated the role of the prelimbic (PL) subregion of the dorsal mPFC in fear promotion and the infralimbic (IL) subregion of the ventral mPFC in fear inhibition. However, the dorsal pedunculus (DP), another ventral subregion of the mPFC, has not been vastly studied. Preliminary data from our lab suggest that the circuitry within the mPFC is, to a great extent, dependent upon the activity of the GABAergic interneuron populations, mostly the somatostatin-expressing interneurons (SST-INs) or the parvalbumin-containing interneurons (PV-INs). My research centers around the investigation of the functional connectivity of interneuron populations involved in fear memory encoding and expression within the mPFC with a particular emphasis on prefrontal GABAergic microcircuits. Overall, we have observed subregion-specific plasticity changes in both SST-INs and PV-INs with fear processing in multiple regions of the mPFC.

Poster 10

Striatal Somatostatin Interneuron Involvement in the Pathogenesis of Huntington's Disease

Jahmel A. Fowler, MHA, Michelle Gray, PhD
Department of Neurology, The University of Alabama at Birmingham Heersink School of Medicine

Huntington's disease (HD) is an autosomal dominant disease caused by an expansion of a CAG repeat in the gene encoding the Huntingtin protein. The resulting abnormal polyglutamine containing protein is expressed throughout the brain in neuronal and non-neuronal cell types. HD patients exhibit motor, psychiatric, and cognitive deficits. Neuropathologically, this disease is characterized by significant degeneration of medium spiny neurons (MSNs) in the striatum. These cells are very important members of the basal ganglia circuit and are critically involved in controlling motor coordination. The function of striatal MSNs is regulated by extrastriatal glutamatergic input from cortex and thalamus as well as intrastriatal and extrastriatal GABAergic input. One population of GABAergic interneurons express the neuropeptide somatostatin (SST)– and are also defined as persistent low-threshold spiking interneurons. In multiple mutant Huntingtin (mHTT) expressing mice, including the conditional human mutant Huntingtin expressing BACHD model, the SST-positive interneurons have increased spontaneous firing that likely impinges on the activity of MSNs. The increase in SST-positive interneuron firing in these mice could be contributing critically to the abnormal function of MSNs in HD. Thus, understanding the role mHTT expression plays in these cells is important and can provide insight into the dysfunction observed in the striatum of HD patients. In this study, we will use a genetic approach to knockdown mHTT expression in SST cells, by crossing BACHD mice to SST-Cre mice, to determine if mHTT expression in SST is contributing to the behavioral, neuropathological, and electrophysiological changes observed in BACHD mice. We hypothesize that expression of mHTT in SST cells influences the increased GABAergic changes observed in MSNs. Here, we report the initial characterization of the animal model for specificity of mHTT knockdown and preliminary behavioral data on BACHD/SST-Cre.

Poster 11

Differences in Spinal Neuronal Recruitment during Pelvic Floor Stimulation in the Context of Early In Life Stress

Anastasiia Gryshyna, MS; Cary DeWitte, BS; Alan Randich, PhD; Jennifer DeBerry, PhD
The University of Alabama at Birmingham

The exact etiology of chronic pelvic pain in unknown and that introduces several challenges for a correct diagnosis and proper treatment of this disorder. Multiple causes of chronic pelvic pain have been recognized, including abnormalities in the immune system and in central and peripheral nervous system processing. Adverse life events have been shown to contribute to the development of chronic pelvic pain, however, the exact differences in neuronal activation and classifications have not been described in the affected population. In the following study, mice were subject to chronic neonatal maternal separation (NMS) for three weeks (postnatal days 1-21). In vivo spinal electrophysiological recordings were made once mice reached 8 weeks of age. The evoked responses of spinal neurons to descending presentation of von Frey hairs to the perigenital region were recorded. Neurons were classified as either wide-dynamic range (WDR) or nociceptive specific (NS), based on their response to non-noxious cutaneous mechanical stimulation. A significant main effect of sex was observed in the evoked activity of WDR neurons during mechanical stimulation. Additionally, male mice who have been exposed to maternal separation demonstrated increased pelvic hypersensitivity. The findings suggest that exposure to chronic early life stress not only contributes to the development of chronic pelvic pain, but also to spinal neuronal phenotype and could be sex dependent. The identification of pathways that contribute to the neuronal changes in chronic pelvic pain, provides a better understanding about etiology of pain and creates potential avenues for prevention research.

Poster 12

How Concussive-like Injury Affects Levels of Serotonin in Rats

Natasha M. Jiménez-Rivera, Laura C. Vicente-Rodríguez, Mauricio Cáceres-Chacón, M.D./Ph.D.; Alexdiel Figueroa-Pérez; Sian Rodríguez-Rosado; Gabriela Hernández-Busot; Héctor Haddock-Martínez; Melissa Rivera-López, Ph.D.; Osmarie Martínez-Guzmán, Ph.D.; and Demetrio Sierra-Mercado, Ph.D. University of Puerto Rico, School of Medicine, San Juan, PR

Concussive brain injury is closely linked to anxiety. According to Collins SM et al., 2022, anxiety is associated with alterations in serotonin. A site of interest for serotonergic activity is a brain region called dorsal raphe (DR) located in the midbrain. Furthermore, a recent study revealed a correlation between serotonin activity and anxiety. The purpose of this investigation is to determine if concussion influences behaviors related to anxiety, and neuronal activity in the raphe nuclei. We hypothesize that concussive brain injury would increase signals of serotonin activity, given that neurons in the dorsal raphe are where most serotonin in the brain is produced. The experimental design consists of three phases: closed head injury via weight drop, as a model of concussion, behavioral analysis and tissue analysis. First a group of anesthetized rats will sustain a closed head injury via a weight drop to the closed head. Next, they will be video recorded for measurement of anxiety-like behaviors such as grooming and rearing, and lastly euthanized for the recollection of brains to undergo tissue staining through the technique of immunohistochemistry to measure signals of serotonin transporter in the dorsal raphe. Preliminary results for behavior analysis of grooming suggest that concussive-like injury (n=6) versus sham (n=6) does not affect the amount of grooming bouts ($p=0.08$). We will next be quantifying amount of rearing and cellular activity using c-Fos in the dorsal raphe nuclei. Future directions include performing double staining immunohistochemistry using c-Fos and a serotonin antibody (Anti-Tph2).

Poster 13

The effects of a concussion on behaviors associated with anxiety in male rats

Taysha M. Jiménez-Rivera; Natasha M. Jiménez-Rivera; Marcel González-Pedraza; Héctor G. Haddock-Martínez; Osmarie Martínez-Guzmán, Ph.D.; Mauricio Cáceres-Chacón, M.D./Ph.D.; Melissa Rivera-López, Ph.D.; and Demetrio Sierra-Mercado, Ph.D. University of Puerto Rico, School of Medicine, San Juan, Puerto Rico

The relationship between concussions and behaviors related to emotional stress remains unclear. Recent reports suggest that concussion increases fear-behaviors in paradigms of Pavlovian fear conditioning. Here, freezing behavior is used as an index of fear. Of note, other ethologically relevant behaviors such as grooming and rearing can also be utilized as indicators of emotional stress. Studies have introduced them as an index of anxiety. For this reason, we hypothesized that a closed head injury would alter rearing and grooming. To help us determine this, rats were anesthetized and delivered either closed head injury via weight drop, or sham injury for controls. After recovery, rats were exposed to an open field space. Spontaneous activity was recorded to quantify rearing and grooming behaviors in the open field. Data collection was performed by observers blind to experimental manipulations. Specifically, the number of rears, time spent rearing, grooming bouts, and time spent grooming were quantified manually. Preliminary results suggest that closed head injury (n=10) versus sham (n=9) does not affect either the number of rears (p=0.16), time spent rearing (p=0.32), the number of grooming bouts (p=0.96), nor the time spent grooming (p=0.75). Next, we will assess rearing and grooming in other contexts. Together, these data suggest that concussive brain injury does not affect these specific behaviors related to anxiety. Currently, activity in brain regions involved in anxiety, namely the ventral hippocampus, is being quantified using cFos immunohistochemistry.

Poster 14

Establishing a Novel Mouse Model of Cancer-Related Cognitive Impairment to Assess Neural and Circuit Mechanisms

Briana Machen, Alan Umfress PhD., James Bibb PhD., Sofia Beas PhD.

Cancer-Related Cognitive Impairment (CRCI) is a common neuropsychological side effect many cancer patients experience before, during, and after treatment. The cognitive deficits associated with CRCI (e.g., difficulty concentrating, short attention span, stress, and lacking motivation) can negatively impact a patient's quality of life. As cancer survival rates increase, addressing CRCI is urgently needed to enhance survivor's well-being. However, the underlying mechanisms of CRCI are unknown, posing barriers to developing CRCI treatments. Current CRCI animal models lack consistency and clinical translatability. As such, standardized pre-clinical models are needed. Here, we aim to establish a clinically-relevant mouse model of CRCI that can then help us assess the neural and circuit mechanisms underlying CRCI. For this, mice will be orthotopically injected with E0771 breast cancer cells to induce breast cancer. Mice will then be treated with a chemotherapeutic regimen that mimics clinical treatments (cyclophosphamide, methotrexate, and 5-fluorouracil (CMF) 3times/week for 3weeks). Thereafter, the independent or synergistic effects of breast cancer paired with CMF on anxiety-like behaviors, motivated responses, and PFC-mediated cognition will be characterized. Since altered dopamine (DA) signaling is a hallmark of CRCI and results in cognitive deficits similar to those experienced by CRCI patients, we will next assess how cancer and/or chemotherapy treatment affects DA release in-vivo. We expect both cancer and chemotherapy alone and combined will impair cognition, motivation, and emotional regulation. We also expect DA signaling to be dysregulated. Altogether, the results from this project will reveal substantial insight into how chemotherapy treatment leads to neurological and neuropathological effects.

Poster 15

Amphetamine-mediated changes in midbrain neurons firing underline changes in striatal dopamine release

Emily A. Makowicz, Mahalakshmi Somayaji, Shashaank N, Eugene V. Mosharov and David Sulzer

Amphetamine (AMPH) and its derivatives are highly addictive substances that elicit their response by increasing striatal extracellular dopamine (DA) levels. Mechanisms that have been suggested to account for this include depletion of DA vesicular stores and blockade and reversal of dopamine uptake transporters (DAT) thus promoting non-exocytotic DA efflux from striatal DA terminals. Additionally, in vivo studies suggest that AMPH augments action potential-mediated presynaptic DA release (Ramsson et al., 2011). Here, we studied the relationship between the firing activity of SNpc dopaminergic neurons and DA release in the dorsal striatum evoked by midbrain electrical stimulation in vivo in anesthetized animals. We found a ~5-fod increase in evoked striatal DA release accompanied by a ~50% decrease in DA neurons spontaneous firing following 10 mg/kg i.p. AMPH injection. The effect of AMPH on striatal DA release appears to be calcium-independent. Furthermore, deficiency of alpha-synuclein - a protein implicated in Parkinson's Disease - diminishes AMPH-mediated increase in striatal evoked DA release. Although still preliminary, these results suggest that both inhibition of DAT and a decrease in tonic neuronal firing mediate the effect of the psychostimulant on striatal DA release. Further evaluation of the relationship between DA neuron tonic activity and DA release from their striatal terminals will help to better understand the mechanisms of AMPH and alpha-synuclein involvement in these processes.

Poster 16

Characterization of Conformally Coated Spinal Progenitor Cells

Marin, B, BS [1], Gonzalez, G, BS [1], Al-Hanoosh, F, BS [1], Tomei, A, Ph.D. [1], Dumont, C, Ph.D. [1]; [1]Biomedical Engineering, University of Miami, Miami, FL 33136.

Traumatic spinal cord injury (SCI) is a devastating condition that disrupts autonomic, sensory, and motor function. Spinal progenitor cells (SPCs) can modulate the site into a more pro-regenerative milieu, but poor SPC survival due to inflammation can hamper transplant potential. Thin layered biomaterial encapsulation, termed conformal coating, is a technique that shields transplants from immune attack while allowing diffusion of nutrients and waste. Conformal coating reduces diffusion distances and minimizes transplant volume size compared to traditional encapsulations. Conformal coating has not been applied to SPCs as an SCI therapy, however, the objective of this study is to engineer a conformal coating capable of maintaining SPC survival and potency in inflammatory models. SPCs were expanded as neurospheres and encapsulated in a polyethylene glycol (PEG) capsule using a microfluidic platform. SPC viability, proliferation, SPC phenotype, and capsule integrity were evaluated over 14 days in vitro. Immunostaining and qRT-PCR were used to evaluate SPC outcomes. RNA was isolated from cell cultures to identify and quantify expression of specific marker proteins. Conformally coated neurospheres can be encapsulated without negatively impacting cell viability and sustained over a 2-week period. Future experiments will interrogate SPC secretory anti-inflammatory potential.

Poster 17

The small-molecule TrkB ligand LM22A-4 improves dendritic spine phenotypes in male and female Rett mice

Destynie Medeiros, Karen Ayala-Baylon, Hailey Edigo-Betancourt, Eric C Miller, Christopher Chapleau, Holly Robinson, Mary Phillips, Tao Yang, Frank Longo, Wei Li, Lucas Pozzo-Miller

Rett syndrome (RTT) is a neurodevelopmental disorder caused by loss-of-function mutations in the X-linked MECP2 gene, affecting specifically females with a prevalence of 1:10,000 births and the manifestation of neuropsychiatric symptoms. MeCP2 is a transcriptional regulator of multiple genes, including brain-derived neurotrophic factor (Bdnf), whose levels are lower in postmortem RTT brains and Mecp2-deficient mice. As BDNF has very low blood-brain barrier permeability, a brain-penetrant small molecule ligand of the BDNF receptor TrkB has become a potential therapeutic to improve impaired BDNF signaling in RTT. LM22A-4 improves breathing irregularities and restores spatial learning in female Mecp2 heterozygous (HET) mice. To evaluate LM22A-4's effects in vivo, we used 4-6 month old Mecp2 HET mice that express GFP-tagged MeCP2 in cells that had silenced the mutant allele by X-chromosome inactivation in their 'mosaic' brain. We dye-loaded CA1 pyramidal neurons of known 'genotypes' (based on MeCP-GFP expression) in ex vivo slices during whole-cell recordings, followed by fixation and confocal microscopy. Surprisingly, mutant neurons lacking MeCP2-GFP showed dendritic spine volume comparable to that in controls, while MeCP2-GFP-expressing neurons show smaller spines, opposite to the phenotype observed in Mecp2 KO. Consistently, LM22A-4 (i.p. 60 days in vivo) had an effect only in MeCP2-GFP-expressing neurons, which improved dendritic spine volumes to control levels. These data revealed unexpected differences in dendritic spine phenotypes in female Mecp2 HET mice, while providing support to the potential usefulness of BDNF-related therapeutic approaches such as the partial TrkB agonist LM22A-4.

Poster 18

Early life stress in adults with hoarding disorder: A mixed methods study

Paula Andrea Muñoz Rodríguez [a e] Catherine Sanchez [a b 1], Omer Linkovski [a c 1], Peter van Roessel [a d], Naomy Steinberg [c], Elizabeth McCarthy [a], Tatevik Avanesyan [a], Pavithra Mukunda [a], Randy O. Frost [f], Carolyn I. Rodriguez [a g]

[a] Department of Psychiatry and Behavioral Sciences, Stanford University, Stanford, CA, USA; [b] Department of Sociology, Stanford University, Stanford, CA, USA; [c] Department of Psychology & The Gonda Multidisciplinary Brain Research Center, Bar-Ilan University, Ramat-Gan, Israel; [d] Sierra Pacific Mental Illness Research, Education, and Clinical Center (MIRECC), Veterans Affairs Palo Alto Health Care System, Palo Alto, CA, USA; [e] Department of Neuroscience, Stanford University, Stanford, CA, USA; [f] Department of Psychology, Smith College, Northampton, MA, USA; [g] Veterans Affairs Palo Alto Health Care System, Palo Alto, CA, USA.

Traumatic life events are common among individuals with hoarding disorder (HD), though rates of posttraumatic stress disorder are no higher than in other groups. HD symptoms typically begin to appear in mid-childhood, and early life stress (ELS) is a known associated feature of negative mental health outcomes. The specifics of this relationship are still unclear. We obtained Early Life Stress Questionnaire (ELSQ) responses from 35 participants with HD, 22 participants with obsessive-compulsive disorder (OCD), and 23 non-clinical control participants. We combined these quantitative data with qualitative interviews exploring what role ELS experiences play in HD. Per the ELSQ, individuals with HD reported significantly more ELS events than the nonclinical control participants. In qualitative interviews, HD participants described the ELS events that were most impactful in shaping their relationship to material possessions; these events tended to be long in duration and elicited feelings of scarcity of emotional support. Participants described relying on possessions in place of relationships and viewed possessions as potential sources of connection to peers. Our qualitative and quantitative results build on the cognitive behavioral model of HD, emphasizing early experiences of prolonged stress or scarcity of emotional support as a key contributing vulnerability factor. Specific differences are consistent with earlier research that people with HD experience absence of early warmth. They further suggest that screening for ELS experiences is important when working with individuals with HD, and that HD treatments may benefit from increased focus on social and emotional connection building.

Poster 19

Unique protein degradation profiles in the anterior cingulate cortex during the formation of a directly vs indirectly acquired auditory fear memory

Morgan B. Patrick[1], Shaghayegh Navabpour [2], Timothy J. Jarome [1,3]

[1] School of Neuroscience, Virginia Polytechnic Institute and State University, Blacksburg, VA, USA; [2] Department of Translational Biology, Medicine and Health, Virginia Polytechnic Institute and State University, Roanoke, VA, USA; [3] School of Animal Sciences, Virginia Polytechnic Institute and State University, Blacksburg, VA, USA.

Post-traumatic stress disorder (PTSD) is a major anxiety disorder that affects 6% of the world population with females being 2-3 times more likely than males to develop it. Recent progress has been made in elucidating the brain molecular mechanisms supporting the formation of fear memories that underlie PTSD, with these studies primarily examining individuals that directly experience traumatic events. However, some individuals acquired PTSD from witnessing a traumatic event happen to someone else in close proximity, though the molecular mechanisms supporting the formation of indirectly acquired fear memories has yet to be explored. Here, we tested whether the molecular signature for directly and indirectly acquired fear was the same, specifically focusing on the anterior cingulate cortex (ACC) because prior research suggests that this area plays a crucial role in indirect fear learning. As a marker of the molecular signature for fear memory formation, we used an unbiased proteomic analysis of K48 polyubiquitination, a marker for protein degradation that we have consistently shown is critical for fear memory formation in several brain regions. We found that in the ACC male observer rats had a smaller, but largely distinct protein degradation profile from the demonstrator rat that they watched undergo auditory fear conditioning. K48 polyubiquitin proteomic analysis of female rats is currently being conducted to determine if any sex differences exist in these protein degradation profiles. These data suggest that indirectly and directly acquired fear memories have distinct molecular signatures, which has important implications for the development of treatments for “bystander” PTSD.

Poster 20

NtsR1 β-arrestin biased positive allosteric modulation of body weight in mice

Jariel Ramirez-Virella[1,2], Netanya Dennis[3], Dipankar Roy[3], Pooja Menon[3], Raluca Bugescu[3], Gina Leinninger[1,3]

[1]Graduate Neuroscience Program, [2]Pharmacology & Toxicology Dept., [3]Physiology Dept., Michigan State University East Lansing.

With obesity rates increasing, there is a need to identify safe treatments for weight loss. The neuropeptide Neurotensin (Nts) supports weight loss via Neurotensin Receptor-1 (NtsR1). However, systemic Nts or NtsR1 agonists also invoke hypothermia and hypotension, thought to occur via NtsR1-mediated Gq-coupled signaling, which reduced enthusiasm for NtsR1-based treatments. Recently, a blood-brain permeable NtsR1 positive allosteric modulator was developed (SBI-553) that biases for NtsR1 β-arrestin signaling while antagonizing Gq-coupled signaling. An independent group showed that SBI-553 reduced stimulant intake in mice via modulating mesolimbic dopamine signaling without eliciting hypotension or hypothermia. Since natural reward (food) intake also engages the dopamine system, **we hypothesized that SBI-553 could suppress feeding and promote weight loss in obese mice.** To examine this, we treated normal weight and diet-induced obese C57/Bl6 mice with vehicle or SBI-553 via a cross-over design and assessed the impact on feeding, metabolism, and body weight. SBI-553 treatment did not promote weight loss in normal weight mice. In contrast, SBI-553 treated obese male mice lost weight, which they regained after discontinuing treatment. Curiously, SBI-553 did not alter ad libitum water or food intake, nor locomotor activity, though it modestly decreased O2 and CO2 production. However. SBI-553 treatment suppressed fasting-induced refeeding in obese male mice over 24 hr, suggesting it may influence hunger. Together, these findings suggest that systemic approaches to modulate Nts-NtsR1 may have promise to modulate body weight, and point to further investigation of the central and peripheral mechanisms by which it may do so.

Poster 21

The effects of short term EtOH exposure withdrawal on mPFC neurons

Sierra Rodriguez, University of Dallas

Introduction: Alcohol use disorder (AUD) is linked to prefrontal cortex (PFC) impairments that compromise executive functions, leading to increased alcohol intake and heightened risk of relapse. In rodent models of AUD, activation of the prelimbic (PL) or infralimbic (IL) regions of the PFC promote or extinguish alcohol intake, respectively. However, even within these regions neurons may show heterogeneous responses to alcohol or other reinforcers. Using a transgenic mouse line (TRAP2/Ai9) which permits fluorescent tagging of active populations, we identified PL and IL neurons that were active during withdrawal in groups of mice that self-administered alcohol or sucrose, respectively.
Methods: We conducted whole-cell patch-clamp current-clamp recordings in PL and IL neurons that were either active (Ai9+) or inactive (Ai-) during withdrawal from alcohol or sucrose self-administration. We compared intrinsic membrane properties, including resting membrane potential and properties of evoked action potentials, including rheobase current, threshold, and firing frequency.
Results: Our results demonstrate that the intrinsic excitability of withdrawal-activated PFC neurons differs between the PL and IL regions, and that these neurons exhibit distinct action potential firing properties following acute application of alcohol (20mM) ex vivo. In PL-Ai9+ neurons, acute application of EtOH increases the excitability of cells from EtOH drinking animals. However, in sucrose-drinking mice acute EtOH application decreases excitability.
Conclusions: These findings support the existence of a PL/IL dichotomy in the context of reward-seeking and suggest that alcohol exposure indues changes in the intrinsic excitability of specific PL and IL ensembles, shaping PFC network activity and modulating control over drug-seeking behavior.

Poster 22

Closed Loop Brain Computer Interface for Real-time Pre-motor Potential Recognition Background

Ashton Weber, Caila Coyne, Hero Liu, **Caleb Rowe**, Macy McCuiston
University of Alabama at Birmingham Neuroengineering PhD

Background: This semester our cohort was challenged with the task of “creating a model that predicts what a person will do before they do it”. We sought to accomplish this task using pre-motor potentials to predict a button press before it happens. Prior to motor actions, EEG signal amplitude from electrodes placed on the scalp outside the pre-motor cortex have been shown to increase. We empirically found that electrode placements Cz, C3, F2, and F3 are most contributive to pre-motor potentials as is seen in the literature by measuring the pre-motor cortex.
Methods: We utilized gold-cup electrodes wired to a 4-channel ganglion board from OpenBCI to stream our data into MATLAB over Bluetooth. Data streaming and synchronization was accomplished using Lab Streaming Layer (LSL). Our model is trained on 20 time-locked trials that are epoched (2 to 0.5 seconds) and low-pass filtered in MATLAB before being fed into machine learning. The machine learning process of K nearest neighbor (KNN) allowed us to generate our model in MATLAB. Partitioned data was used to test the model prior to single-trial demonstrations revealing an over 80% accuracy on average.
Conclusions: Open Brain-Computer-Interface successfully records pre-motor potentials with single-trial reliability. This study has important implications for developing BCI systems that can be used for clinical and research purposes, such as in the development of prosthetics or rehabilitation for individuals with motor disabilities.

Poster 23

Regulation of mitochondria and endoplasmic reticulum dynamics via O-GlcNAcylation

Richard Sánchez[1], Gülcin Pekkurnaz[1]

[1]School of Biological Sciences, Department of Neurobiology, University of California San Diego

The endoplasmic reticulum (ER) is a vast network of tubules and sheets that span from the nucleus to the plasma membrane. The ER plays a major role in protein secretion, Ca^{2+} homeostasis and lipid synthesis, the latter two functioning synergistically with mitochondria. It is known that the mitochondria and the ER can form mitochondrial-ER contact sites (MERCS) that facilitate lipid, and Ca^{2+} homeostasis. Loss of MERCS have been observed in neurodegenerative disorders, with promotion of MERCS relieving neurodegeneration disorders. However, the mechanism behind the formation and dynamics of MERCS is not well understood. Here we propose that the post-translational modification O-GlcNAcylation, a major nutrient sensor that couples metabolism with cellular function and signaling, is altering mitochondrial and ER dynamics to favor MERCS. We show that increased O-GlcNAcylation decreases mitochondrial and ER motility in COS7 cells. Both the mitochondria and ER demonstrate a perinuclear clustering when O-GlcNAc is increased. In addition, ER analysis reveals decreased tubular length and width primarily affecting the perinuclear region of the cell. Using Split-green fluorescent Protein based Contact site. Sensor (SPLICS) associated with the ER and mitochondrial outer membranes we identified MERCS motility and localization differences influenced by O-GlcNAc. We propose that co-regulation of ER and mitochondria via MERCS is essential for cellular morphological alterations in response to cellular stress.

Poster 24

Identification of Hippocampal Area CA2 in Hamster and Vole Brain

Preston Siegler, UNC/NIEHS

Prairie voles (Microtus ochrogaster) and Syrian hamsters (Mesocricetus auratus), closely related to mice (Mus musculus) and rats (Rattus norvegicus), are commonly used in studies of social behavior, including social interaction, social memory, and aggression. The CA2 region of the hippocampus is a critical node that is known to play a key role in social memory and aggression in mice, likely owing to its high expression of oxytocin and vasopressin 1b receptors there. However, CA2 has yet to be characterized in hamsters and voles. In this study, we sought to determine whether we could identify CA2 in vole and hamster. To do this, we stained free-floating tissue slices using primary antibodies raised against known markers of CA2 typically used in mice and rats and fluorescently labeled secondary antibodies. Imaging was performed on an epifluorescence microscope and images were processed using Fiji software. Here we report that immunofluorescent staining for CA2 markers in vole and hamster brains, like in mice and rats, reveals a population of neurons that includes both neurons receiving mossy fiber input and those without, extending just beyond the end of the stratum lucidum. Antibodies raised against RGS14, commonly used to label neurons in area CA2, stained this population of neurons and colocalized with immunostaining for two other CA2 markers, STEP and PCP4. These cells were located at the tail end of the mossy fiber projections, marked by the presence of calbindin stain in all three species. In addition to staining the mossy fibers, antibodies raised against calbindin also labeled the superficial layer of CA1 pyramidal cells in mouse and hamster but not vole. However, a WFS1 stain marked CA1 neurons in all three species. These results demonstrate that CA2 can be distinguished within the hippocampus from neighboring CA1 and CA3 areas in voles and hamsters, which should facilitate the future study of CA2's role in social behavior in these species.

Poster 25

Aerobic Chronic Exercise alters hippocampal DNA methylation in the Kainate experimental rodent model of Temporal Lobe Epilepsy

Silvienne C Sint Jago, Tram Nguyen, Fernando Mejia, Julia Homola, Jane Allendorfer, Farah D. Lubin.
The University of Alabama at Birmingham, Department of Neurobiology

Temporal lobe epilepsy (TLE) and its associated comorbidities have a substantial impact on the quality of life for many who are affected. Currently, there are no pharmacological treatments that alleviate seizure occurrence or the associated comorbidities. Recently, clinical, and pre-clinical studies have begun to show positive effects of exercise on seizure control and cognitive function for people with epilepsy. Previous studies have indicated that epigenetic mechanisms such as DNA methylation (DNAme) are altered with epilepsy leading to abnormal gene expression regulation. However, it is unknown whether epigenetic regulations like DNAme are impacted by exercise leading to the subsequent positive effects on seizure control and memory. Here we investigated, in the epileptic hippocampus, 2 major forms of DNAme contributing to gene expression in the brain, 5-methylcytosine (5-mC) and 5-hydroxymethycytosine(5-hmC), in response to exercise. We used a Kainic Acid (KA) induced model of TLE and investigated the effects of acute versus chronic aerobic exercise in epilepsy. While one bout of acute aerobic exercise was not sufficient to induce any whole blood bulk DNAme in either 5-mC or 5-hmC, 5-hmC levels were significantly altered in response to chronic 4-week aerobic exercise. We further explored the effects of chronic exercise in the hippocampus area CA3 of the epileptic hippocampus, showing a significant decrease of 5-hmC levels with epilepsy, whereas the chronic exercise intervention leads to significant increases in 5-hmC similar to the levels of non-epileptic controls. Gene expression analysis of methylation enzymes indicate that these bulk 5-hmC changes are primarily mediated by TET1 and TET3.

Poster 26

State-Dependent Modulation of Paraventricular Thalamus Activity

Alexa J. Tellez, Carine Lampert PhD., and Sofia Beas PhD.

Interoception refers to the ability to sense, integrate, and track signals originating from within our body. Interoception is critical for survival, and dysfunction in this ability can lead to mental health disorders. Interoception awareness has three main features: 1. Detection, 2. Magnitude, and 3. Discrimination of physiological needs. The paraventricular thalamus (PVT) has emerged as a brain region important for interoception since we previously showed that it integrates homeostatic signals and promotes adaptive behavioral responses. Moreover, we recently discovered that a significant neuronal subpopulation in the PVT, Type1PVT neurons, and not another subpopulation, Type2PVT, are responsible for the detecting and tracking of physiological needs. However, whether Type1PVT neurons can discriminate between two physiological needs is still unknown. Here, we set out to investigate whether Type1PVT neurons can discriminate between different physiological states (e.g., hunger vs. thirst) and promote specific behavioral responses (e.g., food-seeking vs. water-seeking behavior) needed to re-establish homeostasis. First, to confirm that Type1PVT neurons can sense and track hunger levels, we tested whether providing non-caloric food would prevent the satiety-induced modulation of these neurons. Next, we used chemogenetic approaches to test whether silencing Type1PVT neurons in hungry mice reduced food-seeking behavior. Lastly, we used c-Fos tagging in combination with c-Fos immuno to investigate whether different physiological deficits (hunger vs. water) produce differential recruitment of Type1PVT neurons. Altogether, the results from these experiments shed light on the neural mechanisms mediating interoceptive response. Future studies will investigate how addiction can hijack these systems resulting in interoception deficits.

Poster 27

Activation of Calcium-Activated Chloride Channels Suppresses Inherited Seizure Susceptibility in Genetically Epilepsy-Prone Rats

Miracle Thomas, Mark Simms and Prosper N'Gouemo
Howard University

Introduction: Inherited seizure susceptibility in genetically epilepsy-prone rats (GEPR-3s) is associated with increased voltage-gated calcium channel currents suggesting a massive calcium influx resulting in increased levels of intraneuronal calcium. Cytosolic calcium, in turn, activates many processes, including chloride channels, to restore normal membrane excitability and limit repetitive firing of the neurons.
Materials and Methods: EACT and T16Ainh-A01, potent activator and inhibitor of calcium-activated channels transmembrane protein 16A (TMEM16A), respectively, were used to probe the role of these channels in the pathophysiology of acoustically evoked seizures in the GEPR-3s. Adult male and female GEPR-3s were used in this study. Acoustically evoked seizures consisted of wild running seizures (WRSs) that evolved into generalized tonic-clonic seizures (GTCSs) and eventually culminated into forelimb extension (partial tonic seizures).
Results: Acute EACT treatment at relatively higher tested doses significantly reduced the incidences of WRSs and GTCSs, and the seizure severity in male GEPR-3s. Furthermore, these antiseizure effects were associated with delayed seizure onset and reduced seizure duration. Interestingly, the inhibition of TMEM16A channels reversed EACT's antiseizure effects on seizure latency and seizure duration. No notable antiseizure effects were observed in female GEPR-3s.
Conclusion: Together, these findings suggest that activation of TMEM16A channels may represent a putative novel cellular mechanism for suppressing GTCSs.

Poster 28

Chemogenetic interrogation of Crh+ amygdala neurons in aggressive mice

Emily L. Newman[1], **Khalil J. Threadgill**[1], Kerry J. Ressler[1]
[1]Psychiatry, McLean Hosp., Belmont, MA; Harvard Med. Sch., Boston, MA

Introduction: Exposure to trauma can lead to posttraumatic stress disorder which can be accompanied by increases in emotional reactivity and aggression. The central amygdala (CeA) is a point of intersection for threat and aggression neurocircuitry and corticotropin releasing hormone(Crh)-expressing CeA cells are necessary for adaptive active threat responding. The present study uses chemogenetics in mice to examine the role of Crh+ CeA neurons in territorial inter-male aggression.
Materials and Methods: Male CRH-ires-Cre mice were tested for aggression every other day for two weeks. During these 5-min resident-intruder confrontations, a submissive intruder male was placed into the territory of the aggressive resident CRH-ires-Cre male and agonist behavior was quantified as latency to the first bite and total bite frequency. Aggressive resident males received intra-CeA adeno-associated virus for Cre-dependent expression of inhibitory designer receptors activated exclusively by designer drugs (DREADD; hM4Di) in Crh+ CeA neurons. After recovering from surgeries, mice were tested for aggression after receiving systemic vehicle or deschloroclozapine (DCZ) for chemogenetic inhibition of Crh+ CeA neurons.
Results: Chemogenetic inhibition of Crh+ CeA cells blocked aggression.
Conclusion: Crh+ CeA cell activity is necessary for aggressive behavior onset in mice. Crh+ CeA neurons may serve as a therapeutic target to treat aberrant, offensive aggression with improved behavioral selectivity.

Poster 29

Investigating the spectrum of Brain Tumors associated with Adgrb3 and Tp53 loss in a mouse model of Li-Fraumeni Syndrome

Alex Torrelli-Diljohn[1,2], Svetlana Komarova[2], Benjamin Lin[3], Vipul Sheth[4], Paran Goel[4], Robert Welner[4], Ryan Miller[2,3], and Erwin G. Van Meir[2]

[1]Pharmacology, Physiology, & Pathobiology Theme, [2] Department of Neurosurgery, University of Alabama at Birmingham, [3] Department of Neuropathology, University of Alabama at Birmingham, [4] Hematology-Oncology, University of Alabama at Birmingham

Introduction: Li-Fraumeni syndrome (LFS) is a rare inherited autosomal dominant disorder caused by a germline mutation in one TP53 allele, predisposing patients to the development of a variety of tumors from a pediatric age, including gliomas and medulloblastoma. Adhesion G protein-coupled receptor 3 (ADGRB3), also known as brain specific angiogenesis inhibitor (BAI3) are highly expressed in the cerebellum and hippocampal neurons. Loss of ADGRB3 expression has been observed in brain tumors, but the significance of this observation has not been investigated. Moreover, no mouse models to understand the role of ADGRB3 in brain tumor susceptibility and pathobiology have been developed thus far.
Materials & Methods: To investigate the molecular mechanisms underlying brain tumor formation in LFS patients and the role of p53 and ADGRB3 in the process, we have generated an LFS mouse model. The mice harbor a germline Tp53 deleted allele and a second floxed allele. These mice also express Nestin-Cre and are Adgrb3-/-.
Results: About 20% of the mice developed hind leg paralysis and harbored large gliomas, which likely caused their demise. The remaining mice lacked brain tumors, but had other malignancies (sarcomas, etc.) as observed in patients. Remarkably, the addition of Adgrb3 deletion led to a dramatic increase (from 20% to 60%) in the number of brain tumors.
Conclusion: The Adgrb3-/- p53+/- Nestin-Cre mouse model constitutes a useful tool to understand the tumorigenic landscape caused by the loss of Adgrb3. We are now performing genomic analyses on the excised tumors and derived neurosphere cultures to further study the transformation process and the molecular changes induced by Adgrb3 loss.

Poster 30

Genes, molecules, and mechanisms associated with heightened pain sensitivity and opioid abuse vulnerability

Andre B. Toussaint, Mathieu E. Wimmer, Ishmail Abdus-Saboor

Opioid abuse and chronic pain are co-occurring disorders with a complicated relationship. Furthermore, parental history of opioid exposure is seldom considered when prescribing opioids for pain relief. To explore whether parental opioid exposure may affect sensitivity to morphine in offspring, we developed a “rat pain scale” with high-speed imaging, machine learning, and mathematical modeling in a multigenerational model of paternal morphine self-administration. For the multigenerational rodent model, we exposed adult male rats (sires) to morphine (0.75mg/kg/infusion) for 60 days (the duration of rat spermatogenesis) using a self-administration paradigm; controls received saline. Following chronic morphine self-administration, each sire was bred with a drug-naïve female to produce F1 offspring (morphine-sired or saline-sired). Adult male and female F1 progeny of morphine-exposed and saline-treated sires were allowed to self-administer morphine (0.25mg/kg/infusion) for 10-days on a FR1 reinforcement schedule. We found that male, but not female, offspring took more morphine than their respective controls. F1 morphine-sired male offspring also worked harder to receive infusions of morphine, under a progressive ratio schedule. We also find that male progeny of morphine-treated sires had no baseline changes in mechanical pain sensitivity but were more sensitive to the pain-relieving effects of morphine. Lastly, the male offspring of morphine-exposed sires also had increased expression of mu-opioid receptors in the ventral tegmental area but not in the nucleus accumbens. Together, this rat pain scale revealed that paternal opioid exposure increased sensitivity to morphine’s reinforcing and pain-relieving effects in male offspring.

Poster 31

Influence of negative emotional states in pain processing

Paulette Vázquez-Martínez[1,2], Laura Vicente-Rodríguez, PhD[1,2], Osmarie Martínez-Guzmán, PhD[2], Yarimar Carrasquillo-García, PhD[3], Demetrio Sierra-Mercado, PhD[2]

University of Puerto Rico at Cayey, Department of Biology[1], University of Puerto Rico, Medical Sciences Campus, Department of Anatomy and Neurobiology[2], National Center for Complementary and Integrative Health, National Institutes of Health, Bethesda, Maryland[3]

Concussive brain injury has received increased interest as a public health concern in the United States. Concussion results in axonal damage that disrupts communication between brain regions, inducing negative emotional states, such as increased anxiety-like behaviors. Moreover, concussion leads to the development of somatosensory impairments, namely pathological pain that occurs distant from the site of injury. The periaqueductal gray (PAG) and the dorsal raphe nucleus (DRN) are adjacent midbrain structures necessary for the processing of emotions and pain. We hypothesized that neuronal activity in these two brain regions will be affected by concussive brain injury, thus influencing both emotional and pain states. To test this idea, we used a closed head injury (CHI) model that simulates concussive brain injury in male rats. We performed platform mediated avoidance to evaluate anxiety-like behaviors. Then, we measured neuronal activity in the PAG and DRN using cFos immunohistochemistry. CHI rats showed increased time on the platform, suggesting that concussive injury increases anxiety-like behaviors. Immunohistochemistry results revealed an increased neuronal activity in the DRN, supporting the idea that concussive injury influences both anxiety and pain. To further test this possibility, we are now examining the influence of CHI on pain-related responses. Preliminary results suggest that CHI causes mechanical hypersensitivity. In conclusion, brain injury induces anxiety-like behaviors, and this negative emotional state might affect both emotional and pain processing.

Poster 32

Transgenic expression of the hypermorphic SERT Gly56 Ala substitution induces tonic innate immune activation in the CNS in vivo

Allison E. Walsh*[1], Rania M. Katamish*[1], Hideki Iwamoto[1,2], Paula A. Gajewski-Kurdziel[1], Matthew J. Robson[3], Kally C. O'Reilly[4], Jeremy Veenstra-VanderWeele[4], Ning Quan[1,2], and Randy D. Blakely[1, 2]
*co-first authors

[1]Department of Biomedical Science, Charles E. Schmidt College of Medicine and [2]Stiles-Nicholson Brain Institute, Florida Atlantic University, Jupiter, FL, 33458
[3] Division of Pharmaceutical Sciences, James L. Winkle College of Pharmacy, University of Cincinnati, Cincinnati, Ohio, 45229
[4] Department of Psychiatry, New York State Psychiatric Institute, Columbia University, 1051 Riverside Dr., Unit 78, New York, NY, 10032, USA

Altered serotonin (5-HT) signaling, as indicated by hyperserotonemia in a significant number of Autism Spectrum Disorder (ASD) patients, has been proposed to contribute to ASD traits. A major regulator of 5-HT is the 5-HT transporter (SERT). Therefore, we generated mice expressing the ASD-patient derived SERT coding substitution Gly56Ala (SERT Ala56 mice). In this model, we observed hyperserotonemia, increased rates of CNS 5-HT clearance, alterations in 5-HT signaling, deficits in social behavior and juvenile communication, as well as repetitive behavior. The constitutive hyperfunction of SERT Ala56 is mirrored acutely by the ability of IL-1b to enhance SERT activity through a p38a MAPK pathway. Moreover, both genetic elimination of p38a MAPK in 5-HT neurons and pharmacological treatment of MW150, a specific, brain p38a MAPK inhibitor, can normalize disrupted behavioral traits. As 5-HT has been reported to diminish microglial reactivity, we hypothesize that excess 5-HT clearance of SERT Ala56 could lead to tonic inflammation and ASD-like traits. Inflammatory cytokine mRNA levels were found by qPCR to have significant IL-1b elevation in the midbrain of SERT Ala56 mice. Our findings indicate that our model displays evidence of region-specific, chronic inflammation. The latter finding is particularly interesting given the high level of IL-1b receptors on serotonergic raphe neurons. Ongoing studies seek to evaluate further the sex-specificity of these findings, explore additional molecular and cellular markers of immune and glial activation, as well as determine whether basal inflammatory changes support altered responses to challenge with environmental stressors.

Poster 33

Understanding Primate Amygdala Development: The Microglia's Perspective

Dennisha King
University of Rochester

Background: The amygdala of nonhuman primates is remarkably similar to that of humans, developing over a lengthy postnatal period. This long development means that environmental events may influence neuronal growth and connectivity during early life. Our group and others including those working with human postmortem tissue have shown that throughout life, the primate amygdala has a repository of immature post-mitotic neurons (the paralaminar nucleus, PL) that surrounds and interdigitates with the main basal nucleus (Bpc). While most PL neurons are immature at birth, by adolescence a proportion have developed mature profiles suggesting ongoing differentiation. The Bpc in contrast is largely populated by mature neurons based on immunocytochemical markers. While we are beginning to understand normal neural maturation in the PL, the role of microglia, the brain's immune cells, in PL development is unknown. However, microglia are critical for differentiation of precursor cells to neurons, clearing excess neuroblasts and pruning synaptic contacts. Each of these functions is associated with different morphological and molecular signatures. Microglia phagocytose unneeded neural precursors (large microglia soma, short thick processes, clustered), prune neural synapses (small microglia soma, ramified processes, relatively dispersed), and release growth factors that assist in neural differentiation.

Methods: As a first step in characterizing the role of microglia in the developing PL, we assessed microglia in 3-month-old (infant) and 4-year-old (adolescent) macaques (n=4/group) in both the PL and adjacent Bpc. We immunostained 1:12 sections through the amygdala for Iba1 (ionized calcium-binding adaptor molecule 1), which is a marker for microglia. The region of the PL and Bpc were identified using adjacent sections stained for mature and immature neurons. High-power photomicrographs were then taken at similar levels across cases, in a blinded fashion. We then analyzed morphologic features (microglia density, 'clustering', and soma size/shape) using FIJI/Image J. Studies of microglia branching (Sholl) and immunostaining for chemical markers for synaptogenesis are ongoing.

Results: The average density of microglia in the PL was 37% greater in adolescents (390 microglia/mm2) compared to infants (267 microglia/mm2; p=0.0143), with no differences in density across medial, central, and lateral PL. The Bpc microglia density was also greater in adolescents (341 microglia/mm2) compared to infants (290 microglia/mm2), although by a lesser percentage:16% (p=0.0143). The clustering (spacing) index, which measures microglial distribution while accounting for density (calculated as: (average nearest neighbor distance)2 *microglia density) was similar between the infant and adolescent groups in the PL (p=0.395). In contrast, in adolescent Bpc the spacing index (0.473) was 10% less relative to infants (0.530), indicating closer spacing (p=0.0277).

Conclusions: These preliminary data show an increase in microglia numbers from infancy to adolescence in both the PL and Bpc. There is also increased clustering of Bpc microglia in adolescence, suggesting potential increased microglia interactions with neurons. Ongoing data analyses will determine whether differences in increasing microglia densities in each region are associated evidence of regional synaptogenesis.

Poster 34

Nanopore long-read RNA sequencing reveals region-specific sex differences in wildtype mouse brain mRNA isoforms

Emma F. Jones, Timothy C. Howton, Victoria L. Flanary, Brittany N. Lasseigne
University of Alabama at Birmingham

Introduction: The human brain has the most complex RNA splicing profile out of all tissues, and many neurological and psychiatric disorders are associated with defects in alternative splicing (AS). AS is specific to a given biological condition, such as sex or brain region, similar to how diseases typically display a bias toward a condition. Unlike previous short-read technologies, long-read sequencing can capture full-length mRNA transcripts, essential for confidently determining the consequences of AS.

Materials & Methods: We first extracted RNA from wildtype C57BL/6J mouse (n = 5 male and 5 female, age = 20 weeks) hippocampus, striatum, cerebellum, and cortex. We then prepared and sequenced long-read RNA-Seq libraries with the Oxford Nanopore GRIDion. We processed the resulting data with the nf-core nextflow nanoseq pipeline and performed differential transcript usage (DTU) analyses with IsoformSwitchAnalyzeR.

Results: We identified significant region-specific transcript expression across all four mouse brain regions. Cerebellum had 438 genes with DTU, the most region-specific transcript expression across brain regions, followed by the striatum, cortex, and then hippocampus. We did not identify shared sex-specific DTU across all four brain regions but did identify 13 genes with sex-specfic DTU within brain regions. Interestingly, the striatum exhibited the most sex-specific splicing with 6 DTU genes, including Dhrs4. Finally, we determined 21 brain region-specific DTU genes that are known to be psychiatric disorder risk genes.

Conclusion: Overall, with long-read RNA sequencing we identified different patterns of AS across wild-type mouse brain regions, including in genes known to be relevant to human disease.

Poster 35

Ventral striatal dopamine encodes unique properties of visual stimuli in mice

L. Sofía González[1,2], Austen Fisher[1], and J. Elliott Robinson[1]

[1]Rasopathy Program, Division of Experimental Hematology and Cancer Biology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 45229, USA
[2]Neuroscience Graduate Program, University of Cincinnati, Cincinnati, OH, 45229, USA

The mesolimbic dopamine (DA) system is an evolutionarily conserved set of brain circuits that plays a role in attention, appetitive behavior, and reward processing. In this circuitry, ascending dopaminergic projections from the ventral midbrain innervate targets throughout the limbic forebrain, such as the ventral striatum/nucleus accumbens (NAc). Dopaminergic signaling in the NAc has been widely studied for its role in behavioral reinforcement, reward prediction error encoding, and motivational salience. Less well characterized is the role of dopaminergic neurotransmission in the response to surprising or alerting sensory events. To address this, we used the genetically encoded dopamine sensor dLight.2 and fiber photometry to explore the ability of striatal dopamine release in to encode the properties of salient visual stimuli in mice, such as threatening looming discs. We report that lateral NAc dopamine release encodes the rate and magnitude of environmental luminance changes rather than visual stimulus threat level. This encoding is highly sensitive, as lateral NAc dopamine could be evoked by light intensities that were imperceptible to human experimenters. We also found that light-evoked dopamine responses are wavelength-dependent at low irradiances, independent of the circadian cycle, robust despite previous exposure history, and involve multiple phototransduction pathways. Thus, we have further elaborated the mesolimbic dopamine system's ability to encode visual information in mice, potentially relevant to studies/pathologies involving light and downstream dopamine circuitry.

Poster 36

Microglia play beneficial roles in multiple experimental seizure models.

Synphane Gibbs-Shelton, Jordan Benderoth, Ronald P. Gaykema, Justyna Straub, Kenneth A. Okojie, Joseph O. Uweru, Dennis H. Lentferink, Binita Rajbanshi, Maureen N. Cowan, Brij Patel, Anthony Brayan Campos-Salazar, Edward Perez-Reyes, Ukpong B. Eyo
University of Virginia

Seizure disorders are common, affecting both the young and the old. Currently available antiseizure drugs are ineffective in a third of patients and have been developed with a focus on known neurocentric mechanisms, raising the need for investigations into alternative and complementary mechanisms that contribute to seizure generation or its containment. Neuroinflammation, broadly defined as the activation of immune cells and molecules in the central nervous system (CNS), has been proposed to facilitate seizure generation, although the specific cells involved in these processes remain inadequately understood. The role of microglia, the primary inflammation-competent cells of the brain, is debated since previous studies were conducted using approaches that were less specific to microglia or had inherent confounds. Using a selective approach to target microglia without such side effects, we show a broadly beneficial role for microglia in limiting chemoconvulsive, electrical, and hyperthermic seizures and argue for a further understanding of microglial contributions to contain seizures.

Poster 37

Is Blood Brain Barrier permeability increased 24 hours following Pregnancy related Acute Kidney Injury?

Ashley Griffin, Brittany Berry, Shauna-Kay Spencer, Teylor Bowles, Kedra Wallace
University of Mississippi Medical Center

Pregnancy related acute kidney injury (PR-AKI) is associated with increased risk of cognitive changes while the cause of these changes is still unknown. In nonpregnant individuals, following AKI, Indoxyl Sulfate (I.S.), a uremic toxin, accumulates in circulation and is associated with blood brain barrier (BBB) disruption. Whether there is an increase in BBB permeability following PR-AKI is unknown. The purpose of these experiments was to test the hypothesis that 24 hours following PR-AKI there is evidence of increased BBB permeability.

Sprague Dawley rats arrived on gestational day (GD)10 and were grouped into the following: normal pregnant (NP; n=4), AKI (n=4), 100 I.S. mg/kg (n=4), and 200 I.S. mg/kg (n=4). On GD11-19, I.S was administered via drinking water. On GD18, AKI rats received a 45-min bilateral renal ischemic reperfusion surgery. On GD19 animals were infused with 4% Evan's Blue (EB) via jugular vein followed by saline flush. Data was analyzed via one-way ANOVA followed by multiple comparisons via GraphPad Prism with significance as $p<0.05$.

In the frontal cortex, there were no differences between groups ($p= 0.97$). Similarly, with the posterior cortex ($p=0.24$) and cerebellum ($p=0.48$), there were no significant differences between groups. In the brain stem region, the 200 I.S group had significantly more EB than NP ($p=0.0003$), NP+AKI ($p=0.0008$), and 100 I.S ($p=0.0001$) groups.

These results suggest that there are no changes in BBB permeability after PR-AKI, and that treatment of I.S. at a higher dose during pregnancy leads to a disruption of the BBB in the brain stem.

Poster 38

Apparently high-dimensional spontaneous neural activity is locally low-dimensional in time

Pranjal Gupta, **Trevor Alston,** John Pearson

Introduction: It is commonly reported across species and brain regions that neural population dynamics are low-dimensional, leading to a broad range of theories on the significance of this structure [1, 2]. However, several recent studies have reported that spontaneous activity in rodent sensory regions is high-dimensional [3], presenting a challenge to explanations which posit low-dimensional dynamics as integral to neural computations. Here we hypothesized that the observation of high-dimensional population dynamics in these datasets results from neural activity progressing through a series of low-dimensional manifolds. That is, dynamics which seem to explore a high-dimensional subspace over a long period of time may be better described as dynamics which explore many low-dimensional subspaces over many short periods of time, where the high-dimensional space is composed of the union of the low-dimensional subspaces.

Materials and Methods: We developed a novel statistical model and algorithm termed SPLAT to quantify the time-local dimensionality of neural population activity, defined as the number of active latent neural patterns during a small segment of time.

Results: We tested its validity in both synthetic and real mouse V1 data [4] , where in each case evidence for establishing meaningful locally low-dimensional latent variables in a high dimensional dataset was uncovered. Specifically for the real data, PCA estimates that 32 dimensions capture 85% of the variance, while SPLAT infers no more than 6 patterns are active during any given 10ms bin.

Conclusion: Together, these results suggest that apparently high dimensional activity may represent passage through a sequence of low-dimensional neural computations.

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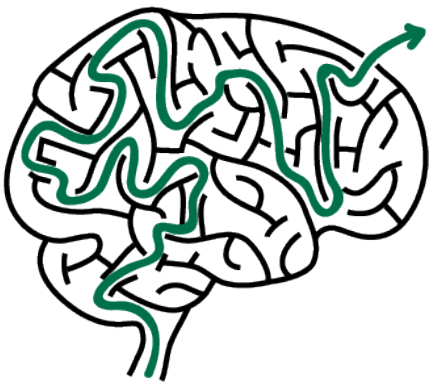

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