10th Annual NEURAL Conference 2024

National **E**nhancement of **U**nder**R**epresented **A**cademic **L**eaders

June 12-14

University of Alabama at Birmingham
Birmingham, AL

UAB Neuroscience Roadmap Scholars

UAB HEERSINK SCHOOL OF MEDICINE
The University of Alabama at Birmingham

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

Use hashtag #NEURAL2024 on your social media posts!

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Table of Contents

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Welcome

Dear Attendee:

Welcome to the 10th Annual **N**ational **E**nhancement of **U**nder**R**epresented **A**cademic **L**eaders (NEURAL) Conference! The NEURAL Conference is an extension of the UAB Neuroscience Roadmap Scholars (RMS) Program. Our goal is to enhance engagement and retention of historically underrepresented graduate trainees (as defined in the Notice of NIH's Interest in Diversity) in the neuroscience workforce.

This year marks the 10th anniversary of the UAB Neuroscience Roadmap Scholars Program and the NEURAL Conference. Resolved to address the lack of diversity in the neurosciences, in 2014 we launched the Neuroscience Roadmap Scholars (RMS) Program at UAB, the first program of its kind in the country, along with the NEURAL Conference. NEURAL is an annual regional conference - the only one of its kind - specifically designed to capture and engage the broader community of underrepresented neuroscience graduate trainees.

For the past 10 years, the NEURAL Conference has annually hosted neuroscience trainees from underrepresented groups from across the country to participate in professional development workshops, poster and oral presentations, and has featured numerous world-renowned keynote speakers sharing their science and speaking on the challenges they've endured in their professional growth.

This year, we are seeing our efforts come full circle. Alumni from our earliest RMS and NEURAL cohorts are now faculty and are mentoring the next generation of diverse neuroscientists. For NEURAL 2024, we intend to spotlight our outstanding RMS and NEURAL alumni, giving them a platform to share their science, highlight their journeys as neuroscientists, and address how they overcome challenges faced on their journeys.

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. We are here to help the next generation of diverse neuroscientists reach their full potential. Never forget - **YOU BELONG.**(period)

Best regards,

Farah D. Lubin, PhD, FAES
Professor & Vice Chair of Trainee Engagement and Development
Director, R25 NINDS Graduate Neuroscience Roadmap Scholars Program
Director, T32 NINDS Cognition & Cognitive Disorders Training Program
Triton Endowed Professorship in Neurobiology
Department of Neurobiology, Heersink School of Medicine
University of Alabama at Birmingham (UAB)

Leadership

Farah D. Lubin, Ph.D.
Professor & Vice Chair of Trainee Engagement and Development
Triton Endowed Professorship in Neurobiology
Director, R25 NINDS Neuroscience Roadmap Scholars Program
Director, T32 NINDS Cognition & Cognitive Disorders Training 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

Keri Dickens, MPA
Program Administrator, UAB Neuroscience Roadmap Scholars Program and NEURAL Conference
SOM Office for Diversity and Inclusion Staff Liaison
Department of Neurobiology

Agenda

Wednesday, June 12, 2024 - Welcome Reception at Birmingham Civil Rights Institute

12:00-5:00 pm	Arrivals & Check In at McMahon Hall (for non-UAB guests only) (1600 10th Ave S, Birmingham, AL 35205)
5:45 pm	Shuttle from Hilton and McMahon Hall (for non-UAB guests only) to Welcome Reception
6-7:30 pm	Welcome Reception Birmingham Civil Rights Institute (BCRI) 520 16th St N, Birmingham, AL 35203
7:30 pm	Shuttle from BCRI to McMahon Hall and UAB Hilton (for non-UAB guests only)

Thursday, June 13, 2024 - UAB Cudworth Building - Room 102 (1919 University Blvd.)

7:15 am	Shuttle from Hilton and McMahon Hall to Cudworth Building (for non-UAB guests only)
7:30 am	Breakfast
8:00 am	Opening Remarks & Ice Breaker: Farah Lubin, Ph.D. Director, NEURAL Conference and UAB Roadmap Scholars Program
8:30 am	Special Guest Speaker I: Laura Vicente Rodríguez, Ph.D.
9:00 am	Oral Session I
10:00 am	Break
10:15 am	Special Guest Speaker II: Lillian Brady, Ph.D.
10:45 am	Oral Session II
11:45 am	Lunch and Networking
1:15 pm	Special Guest Speaker III: Nathaniel Harnett, Ph.D.
1:45 pm	Break
2:00 pm	Panel Discussion: The Future of Neuroscience Training Panelists: Rita Cowell, Ph.D. David Knight, Ph.D. Michelle Gray, Ph.D. Rajesh Kana, Ph.D.

Thursday, June 13, 2024 - UAB Hilton - Hamilton Ballroom (808 20th St. S.)

3:00 pm	Break
3:15 pm	Keynote Speaker I: Dr. Ukpong Eyo “Assessing roles for microglia in seizure disorders”
4:30 pm	Walk to the UAB Hilton - Hamilton Ballroom (808 20th St. S.)
4:45 pm	Poster Hanging Begins
5:00 pm	Dinner Reception for NEURAL Guests
6:00 pm	Poster Session (hors d’ouevres served)
8:15 pm	Shuttle to McMahon Hall (for non-UAB guests only) (1600 10th Ave S, Birmingham, AL 35205)

Friday, June 14, 2024 - UAB Hill Student Center - 3rd Floor Ballrooms (1400 University Blvd.)

7:15 am	Shuttle from Hilton and McMahon Hall to Hill Student Center (for non-UAB guests only)
7:30 am	Breakfast
8:00 am	Special Guest Speaker IV: Shahzad Khan, Ph.D.
8:30 am	Oral Session III
9:30 am	Break
9:45 am	Special Guest Speaker V: Kirsten Schoonover, Ph.D.
10:15 am	Shark Tank
11:30 am	Lunch
12:30 pm	Keynote Speaker II: Dr. Michael Burton
1:45 pm	Awards & Closing Remarks - Presenting Awards for Best Oral Presentation, Best Poster, and Shark Tank - Presenting RMS Outstanding Faculty Awards
2:00 pm	Adjourn

Keynote Speaker

Michael D. Burton, Ph.D.
Associate Professor
Eugene McDermott Distinguished Professor
Rita Allen Foundation Scholar
University of Texas at Dallas

Biography:

Dr. Burton is the Principal Investigator of the Neuroimmunology and Behavior (NIB) Lab in the Department of Neuroscience, Center for Advanced Pain Studies (CAPS) at the University of Texas at Dallas. His lab studies how the immune system communicates with the peripheral nervous system to regulate pain, reproductive physiology and energy homeostasis. His Neuroimmunology and Behavior Lab at The University of Texas at Dallas uses translational molecular and integrative neurobiology to learn how lifestyle factors like diet, alcohol and surgery influence neuroimmune interactions across age and gender. He has investigated the effects of cell-specific toll-like receptor 4 signaling on neuropathic pain, inflammatory pain and metabolic stress, as well as the impact of peripheral lipid signaling on diet-induced diabetes and energy homeostasis, and glucose metabolism on neuroinflammation and feeding. Dr. Burton received his B.S. and Ph.D. at the University of Illinois at Urbana-Champaign. He moved to Dallas, TX to begin his postdoctoral fellowship at both UT Southwestern Medical Center and UT Dallas. In 2016 he received the only K22 grant that year from the National Institute of Neurological Disorders and Stroke intended to help a postdoc transition to a faculty position. In 2019 he received the National Institute of Health Pain Consortium Mitchell Max Award for Research Excellence. He was honored with Congressional recognition for science research and leadership in 2021, and he was chosen as a Society for Neuroscience Rising Star/SFNova Lecturer. He also has been selected for honors from the Rita Allen Foundation, the Endocrine Society, the American Pain Society and the American Society for Cell Biology. His lab strives to traverse the gap between basic research and clinical application to patients. His goal is to continue developing his leading research program studying neuroimmune interactions and mentor highly motivated trainees at all levels.

Talk Title:

“Cell and Sex-specific Neuroimmune mechanisms in pain sensitization”

Keynote Speaker

Ukpong Eyo, Ph.D.

Assistant Professor
University of Virginia

Biography:

Eyo (pronounced “A”-“Yo”) was born in Nigeria and grew up in several different countries. He immigrated to the US in 2003 to pursue undergraduate studies at Northwest Missouri State University. He then went on to graduate school at the University of Iowa where he developed a keen interest in real-time imaging of microglia during development under the mentorship of Dr. Michael Dailey. During his time in the Dailey Lab, Eyo reported remarkable migratory capacities for neonatal microglia and elucidated purinergic mechanisms in microglial demise under simulated ischemic conditions. Following his Ph.D studies, Eyo joined the lab of Dr. Long-Jun Wu, first at Rutgers University in New Jersey, then at Mayo Clinic in Minnesota to study microglial-neuronal communications. His postdoctoral research in the Wu Lab uncovered novel physical interaction phenomena between microglia and neurons including microglial process extensions (Eyo et al., 2014), microglial process convergence (Eyo et al., 2015; Eyo et al., 2017) and microglial process pouches (Eyo et. al., 2021). Moreover, he showed that microglial neuronal communication was beneficial following experimentally-induced seizures. Through these studies, Dr. Eyo became interested in microglial P2RY12 receptors which he continues to study. In August 2018. Since then, Eyo started his independent lab in the Department of Neuroscience and the Center for Brain Immunology and Glia (BIG) to continue his research on microglia in (i) neural injury (especially seizure disorders); (ii) neurovascular interactions and function and (iii) sex differences.

Talk Title:

“Assessing roles for microglia in seizure disorders”

Special Guest Speaker

Laura Vicente Rodríguez, Ph.D.

Assistant Professor
University of Puerto Rico at Cayey

Dr. Vicente is a NEURAL Conference alumna; she attended and presented at the 2016, 2017, and 2019 NEURAL Conferences.

Biography:

Dr. Vicente received her Ph.D. in Anatomy and Neurobiology from the University of Puerto Rico Medical Sciences Campus. Dr. Vicente's graduate work yielded the comprehensive characterization of the FMRF-gated Na+ channel (FaNaC) from Biomphalaria glabrata—the intermediate host in the life cycle of schistosome parasites. Employing varied techniques, including immunohistochemistry and in situ hybridization, she elucidated the effect of parasitic infection on the FMRF-amide dynamics within the central nervous system of the snail. After obtaining her PhD, she transitioned towards a research endeavor harmonizing more closely with her core interests—namely, the understanding of pathological pain. Her current focus centers on a rat model of traumatic brain injury, where her primary objective resides in understanding the mechanisms through which concussive events impact neural circuits implicated in pain processing, ultimately leading to the manifestation of pathological pain states.

Talk Title & Description:

"Effect of a concussion in pain-like behaviors in rats"

Special Guest Speaker

Lillian J. Brady, Ph.D.
Assistant Professor
Department of Psychiatry and Behavioral Neurobiology
Heersink School of Medicine
University of Alabama at Birmingham

Dr. Brady was a Roadmap Scholar from 2015 until her graduation in 2017.

Biography:

Dr. Brady is a native of Jackson, MS and is a two-time graduate of HBCU, Alcorn State University, where she received a B.S. in Chemistry in 2009 and M.S. degree in Biotechnology in 2011. In 2017, she received her Ph.D. in Neurobiology at the University of Alabama at Birmingham, where her dissertation research focused on outlining the effects of antipsychotic medications and other pharmacological agents targeting the dopamine system, on the local circuitry of the hippocampus, which controls learning, memory, and cognition. Dr. Brady joined the Vanderbilt University Department of Pharmacology and Vanderbilt Center for Addiction Research as a Postdoctoral Fellow as part of the 1st cohort of Academic Pathways Postdoctoral Research Fellows, where her research on sex differences in nicotinic receptor regulation of dopamine release mechanisms underlying reward circuitry in addition is funded by an NIH MOSAIC K99/R00 Career Transition Award through the National Institute on Drug Abuse. In 2023, Dr. Brady returned to UAB to establish her independent lab in the Department of Psychiatry and Behavioral Neurobiology. Her lab investigates sex differences and hormonal regulation of neural circuit activity underlying environmental context-reward associations in substance use disorder.

Talk Title:

“Sex-specific regulation of dopamine release mechanisms through nicotinic receptors underlying substance use disorder”

Special Guest Speaker

Nathaniel G. Harnett, Ph.D.

Director, Neurobiology of Affective and Traumatic Experiences (NATE) Laboratory, McLean Hospital
Assistant Professor of Psychiatry, Harvard Medical School

Dr. Harnett was a member of the first cohort of Roadmap Scholars; he was a Roadmap Scholar from 2014 until his graduation in 2018.

Biography:

Dr. Harnett earned his PhD in Psychology at the University of Alabama at Birmingham under the mentorship of David C. Knight, PhD. He then completed postdoctoral training at McLean Hospital/Harvard Medical School with Kerry J. Ressler, MD/PhD. His research primarily focuses on the neurobiological mechanisms of susceptibility to trauma and stress-related disorders. In addition to his research activities, he is currently a co-editor of Mental Health Science. Dr. Harnett's work has been funded by the National Institute of Neurological Disorders and Stroke, the National Institute of Mental Health, the Ford Foundation, and the Brain Behavior Research Foundation.

Talk Title & Description:

"Moving towards (hopefully) generalizable neural signatures of trauma and stress-related disorders"

Special Guest Speaker

Shahzad S. Khan, Ph.D.

Assistant Professor
University of North Carolina School of Medicine
Departments of Cell Biology & Physiology and Neurology

Dr. Khan is a NEURAL Conference alumnus; he attended and presented at the 2015 and 2016 NEURAL Conferences.

Biography:

Dr. Khan received his B.Sc. in Chemical Sciences from The Florida State University in 2011, and his Ph.D. in Neuroscience from The University of Virginia in 2018 under the mentorship of Dr. George Bloom, where he investigated how small clumps of proteins called oligomers initiate cellular dysfunction in Alzheimer's disease and related dementias. He completed his postdoctoral training at Stanford University from 2018-2023 under the mentorship of Dr. Suzanne Pfeffer, where his research focused on inherited forms of Parkinson's disease. Dr. Khan's research program at UNC Chapel Hill will utilize cutting-edge approaches to identify the causes and consequences of primary cilia dysfunction in neurodegenerative diseases. His future work aims to expand knowledge of neural signaling and to uncover novel targets for disease intervention.

Dr. Khan has received several awards and honors, including a Jump Start Award from Stanford University and a 2022 Rising Star Award from UNC Chapel Hill. Dr. Khan received a Stanford JEDI Champion Award in 2021, awarded to postdoctoral scholars who have served as champions of initiatives, activities, or efforts that advance justice, equity, diversity, and inclusion at Stanford and beyond. Dr. Khan also received a BRAINS Fellowship, a Stanford PRISM Postdoctoral Fellowship, and a Ruth L. Kirschstein Predoctoral Fellowship.

Talk Title:

"Primary cilia dysfunction in neurodegenerative diseases"

Special Guest Speaker

Kirsten Schoonover, Ph.D.
Assistant Professor
Department of Psychiatry and Behavioral Neurobiology
Heersink School of Medicine
University of Alabama at Birmingham

Dr. Schoonover was a Roadmap Scholar from 2015 until her graduation in 2019.

Biography:

In 2017, she received her Ph.D. in Behavioral Neurobiology at the University of Alabama at Birmingham under the mentorship of Dr. Rosalinda Roberts, where her dissertation research focused on “Mechanisms of dysbindin abnormalities in schizophrenia”. In 2023, she joined the Department of Psychiatry and Behavioral Neurobiology at UAB as an Assistant Professor. Her current research primarily focuses on synaptic dysfunction and how it relates to cognition in schizophrenia. Dr. Schoonover is the Associate Director of the Alabama Brain Collection. Additionally, Dr. Schoonover is a Benjamin-Carver FIRST Scientist, committed to advancing diversity, equity, and inclusion in research areas pertaining to health disparities. Dr. Schoonover’s long-term goals include diversifying brain donation samples, in an effort to create a bank of samples for researchers that accurately represents the whole population. Dr. Schoonover also strives to become a mentor for underrepresented trainees in science, and is currently a Career Coach for the Roadmap Scholars Program.

Talk Title & Description:

“Identifying the neural substrate of working memory impairments in schizophrenia: multi-faceted approaches in human postmortem tissue”

Panel Discussion: The Future of Neuroscience Training

Thursday, June 13
2:00 - 3:00 pm
UAB Cudworth Building - Room 102 (1919 University Blvd.)

Panelists:

Rita Cowell, Ph.D.
Professor, Department of Neurology
Director, T32 Training Program in Neurodegeneration (TPiN)
University of Alabama at Birmingham (UAB)

Michelle Gray, Ph.D.
Associate Professor of Neurology & Neurobiology
Jarman F. Lowder Endowed Professorship in Neuroscience
Director, Graduate Biomedical Sciences Neuroscience Theme
University of Alabama at Birmingham (UAB)

Rajesh Kana, Ph.D.
Professor, Department of Psychology
Associate Dean for Graduate & Continuing Education
University of Alabama at Birmingham (UAB)

David Knight, Ph.D.
Professor, Department of Psychology
Director, Behavioral Neuroscience Ph.D. Program
University of Alabama at Birmingham (UAB)

Adrienne Lahti, MD
Professor and Chair
Department of Psychiatry & Behavioral Neurobiology
PI, NIMH T32 Predoctoral Training in Multifaceted Translational Approach to Mental Illness (AMI) Program
University of Alabama at Birmingham (UAB)

Poster Presentation Session

Thursday, June 13
Poster Hanging 4:45 pm
Poster Session 6:00 - 8:00 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 14
10:15 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 13, 8:45 - 9:45am

8:45 am — Derian Pugh - University of Alabama at Birmingham
"Regional brain co-expression network analysis identifies NRN1 as a mediator of cognitive resilience to Alzheimer's disease"

9:00 am — Manessa Riser - Wayne State University
"Sex-Specific Associations Between Brain Activity and Future PTSD Symptoms in Trauma-Exposed Youth"

9:15 am — Elam Cutts - University of Alabama at Birmingham
"Toward comparing scotomas: Using microperimetry paired with cortical magnification factor to quantify retinal functional health in patients with central vision loss"

9:30 am — Lindsay Ejoh - University of Pennsylvania
"Opioidergic control of a thalamic pain circuit during placebo analgesia"

Oral Presentation Session II: Thursday, June 13, 10:30 - 11:30am

10:30 am — Brianna Fitzgerald - University of Alabama at Birmingham
"Development of an ethologically relevant rodent model of social stress"

10:45 am — Jenelle Collier - University of Pittsburgh
"Reactive Astrocyte Na+/H+ exchanger upregulation in Alzheimer's Disease"

11:00 am — Matheus Teles de Araujo - University of Alabama at Birmingham
"Clinical and neurobiological heterogeneity in first-episode psychosis patients: A normative modeling approach"

11:15 am — Khalil Threadgill - Harvard Medical School/McLean Hospital
"Amygdala Crh cell activity required for territorial aggression"

Oral Presentation Session III: Friday, June 14, 8:30 - 9:30am

8:30 am — McKenna Somerville - University of Alabama at Birmingham
"Early Inflammaging and Senescence Transcriptional Response to Ocular Hypertension in Living Human Retina"

8:45 am — Kaejaren Caldwell - University of Cincinnati
"The Characterization and validation of an ex vivo ischemia model for neurochemical analysis"

9:00 am — Jhodi Webster - University of Alabama at Birmingham
"Co-pathologies and immune cell activation in a model of Parkinson's Disease"

9:15 am — Deanna Ross - University of Texas at Austin
"Differential DNA methylation related to trauma type in the PTSD brain"

Oral Presentation Abstracts

Oral Presentation Session I: Thursday, June 13, 9:00 - 10:00am

1	“Regional brain co-expression network analysis identifies NRN1 as a mediator of cognitive resilience to Alzheimer’s disease”	Derian Pugh
2	Sex-Specific Associations Between Brain Activity and Future PTSD Symptoms in Trauma-Exposed Youth”	Manessa Riser
3	“Toward comparing scotomas: Using microperimetry paired with cortical magnification factor to quantify retinal functional health in patients with central vision loss”	Elam Cutts
4	“Opioidergic control of a thalamic pain circuit during placebo analgesia”	Lindsay Ejoh

Oral Presentation Session II: Thursday, June 13, 10:45 - 11:45am

5	“Development of an ethologically relevant rodent model of social stress”	Brianna Fitzgerald
6	“Reactive Astrocyte Na+/H+ exchanger upregulation in Alzheimer’s Disease”	Jenelle Collier
7	“Clinical and neurobiological heterogeneity in first-episode psychosis patients: A normative modeling approach”	Matheus Teles de Araujo
8	“Amygdala Crh cell activity required for territorial aggression”	Khalil Threadgill

Oral Presentation Session III: Friday, June 14, 8:30 - 9:30am

9	“Early Inflammaging and Senescence Transcriptional Response to Ocular Hypertension in Living Human Retina”	McKenna Somerville
10	“The Characterization and validation of an ex vivo ischemia model for neurochemical analysis”	Kaejaren Caldwell
11	“Co-pathologies and immune cell activation in a model of Parkinson’s Disease”	Jhodi Webster
12	“Differential DNA methylation related to trauma type in the PTSD brain”	Deanna Ross

Oral Presentation 1

"Regional brain co-expression network analysis identifies NRN1 as a mediator of cognitive resilience to Alzheimer's disease"

Derian A. Pugh[1], Cheyenne Hurst[2], Measho H. Abreha[2], Duc M. Duong[2], Eric B. Dammer[2], David A. Bennett[3], Nicholas T. Seyfried[2], and Jeremy H. Herskowitz[1]

[1]University of Alabama at Birmingham School of Medicine, Center for Neurodegeneration and Experimental Therapeutics, Department of Neurology, Birmingham, AL, USA
[2]Emory School of Medicine, Department of Biochemistry, Emory Goizueta Alzheimer's Disease Research Center, Atlanta GA, USA
[3]Rush Alzheimer's Disease Center, Rush University Medical Center, Chicago, IL, USA

The molecular mechanisms and pathways enabling certain individuals to remain cognitively normal despite high levels of Alzheimer's disease (AD) pathology remain incompletely understood. These cognitively normal people with AD pathology are described as preclinical or asymptomatic AD (AsymAD) and appear to exhibit cognitive resilience to the clinical manifestations of AD dementia. Multiplex tandem mass tag mass spectrometry (TMT-MS) proteomic data (n=7,787 proteins) was generated on brain tissue from Brodmann area 6 and Brodmann area 37 (n=109 cases, n=218 total samples) and evaluated by consensus weighted gene correlation network analysis. Notably, neuritin (NRN1), a neurotrophic factor previously linked to cognitive resilience, was identified as a hub protein in a module associated with synaptic biology. To validate the function of NRN1 with regard to neurobiology to AD, we conducted microscopy and physiology experiments in a cellular model of AD. NRN1 provided dendritic spine resilience against amyloid-β (Aβ) and blocked Aβ-induced neuronal hyperexcitability in cultured neurons. To better understand the molecular mechanisms of resilience to Aβ provided by NRN1, we assessed how exogenous NRN1 alters the proteome by TMT-MS (n=8,238 proteins) of cultured neurons and integrated the results with the AD brain network. This revealed over-lapping synapse-related biology that linked NRN1-induced changes in cultured neurons with human pathways associated with cognitive resilience. Collectively, this highlights the utility of integrating the proteome from human brain and model systems to advance our understanding of resilience-promoting mechanisms and prioritize therapeutic targets that mediate resilience to AD.

Oral Presentation 2

"Sex-Specific Associations Between Brain Activity and Future PTSD Symptoms in Trauma-Exposed Youth"

Manessa Riser, BS[1], Charis N. Wiltshire, BS, William M. Davie, BS, Mariam H. Reda, BS, John M. France, BS, Sattvik Basarkod, BS, Sterling Winters, BS, Anais F. Stenson, PhD, & Tanja Jovanovic, PhD

[1]Wayne State University

Introduction: Trauma exposure during childhood may alter brain activity associated with inhibitory control, leading to an increased vulnerability to post-traumatic stress disorder (PTSD). Furthermore, there may be developmental sex differences related to this susceptibility. We used longitudinal data in trauma-exposed children to investigate inhibitory control and future PTSD symptomatology. We hypothesized that a) brain activation at Visit 1 would be associated with increased PTSD symptoms 2 years later (Visit 2), and b) that these patterns would differ between sexes.
Methods: Children (N=35, 20 Female, Age = 9 years at Visit 1) in the Detroit, MI area participated during two separate visits, 2 years apart. PTSD symptoms were assessed using the UCLA PTSD Reaction Index. A change in PTSD symptoms was calculated as Visit 2 minus Visit 1. Participants completed an inhibition task during fMRI at Visit 1. ROI analysis was performed on the ventromedial prefrontal cortex (vmPFC), amygdala and hippocampus.
Results: Activation in the vmPFC at Visit 1 was positively correlated with PTSD symptoms at Visit 2 ($r = 0.47$, $p = 0.01$). When we stratified by sex, we found that in females, but not males, vmPFC activation predicted greater increase in PTSD symptoms ($r=0.59$, $p=0.02$). No significant findings with other ROIs.
Conclusions: Our findings suggest that increased activation of the vmPFC may predict higher future PTSD symptoms in adolescent females, but not males, indicating a sex-specific vulnerability. Future longitudinal studies with larger sample sizes are needed to explore other contributing factors in the early emergence of PTSD symptoms.

Oral Presentation 3

"Toward comparing scotomas: Using microperimetry paired with cortical magnification factor to quantify retinal functional health in patients with central vision loss"

Elam Cutts[1] (ecutts99@uab.edu), Marcello Maniglia[2], Matthew Defenderfer[1], Pinar Demirayak[1], Dawn DeCarlo[1], Kristina Visscher[1]

[1]University of Alabama at Birmingham, [2]University of California, Riverside

In macular degeneration, the primary cause of vision loss among older adults, photoreceptor death in the retina results in vision impairment. Complex visual tasks such as reading or navigation require both basic visual sensation ('low level vision') as well as neural processes beyond this ('high-level vision'). Patients with similar retinal damage can differ widely in their performance on complex visual tasks, suggesting that compensation for this impairment varies between patients. Quantification of this compensation is a necessary step to understanding the neural mechanisms involved in compensation. Traditional tests like visual acuity and contrast sensitivity gauge do not explain the entire visual experience. To bridge this gap, we developed a method using outcomes from the Macular Integrity Assessment (MAIA), a microperimetry method that evaluates sensitivity across the retina. Comparison of these results is difficult, given that lesions in central vision lead to worse impairment than peripheral vision. Here we introduce a method that uses the concept of the "Cortical Magnification Factor" (CMF). Different parts of visual cortex correspond to parts of vision, and the CMF describes how much more cortex is devoted to each portion of the visual field. By weighting MAIA scores with CMF, we derived a measure called macular functional health (MFH). MFH reliably reflects the clinical impression of the severity of a scotoma. MFH was significantly correlated to contrast sensitivity, as well as acuity. Further, models incorporating MFH were better predictors of high-level visual processing. These results validate our measure of MFH to compare scotoma severity across participants.

Oral Presentation 4

"Opioidergic control of a thalamic pain circuit during placebo analgesia"

Ejoh, L.[1], Kimmey B., Sandoval Ortega, R.A., Mahmood M., Deisseroth, K., Corder, G.

[1]University of Pennsylvania

Introduction:
Placebo analgesia is an expectation-driven reduction in pain perception. There is diminished activity and endogenous opioid release onto medial thalamic neurons during placebo analgesia. A subset of these neurons, rostral intralaminar thalamus (rILN), receive inputs from the ventrolateral periaqueductal gray (vlPAG), activate in response to nociceptive stimuli and densely express mu-opioid receptors (MORs), indicating potential modulation of pain signals by endogenous opioid release at this site.
Materials & Methods:
To model placebo, we utilize a drug-free instrumental conditioning assay to drive expectation-driven analgesia. Here, mice are conditioned to expect pain relief when escaping to avoid a noxious temperature floor plate on one side of a two-chamber maze. After conditioning, both plates are set to noxious temperatures while cameras record exploration and nocifensive behaviors. We employ this paradigm to investigate the population-level calcium activity of MOR+ vlPAG and rILN ($vlPAG^{MOR}$ and $rILN^{MOR}$) neurons during nociception and endogenous analgesia.
Results:
After conditioning, placebo-conditioned mice learn to avoid the noxious-associated chamber, while also displaying reduced nocifensive responses to the inescapable heat stimulus during the initial ~90 second placebo response period. We observed increased calcium activity in $vlPAG^{MOR}$ neurons in response to nociceptive stimuli and reduced activity during the placebo response period. rILN neurons exhibit increased activity in response to nociceptive stimuli, and inhibition leads to reduced nocifensive behavioral responses to noxious heat stimuli. We are investigating $rILN^{MOR}$ activity dynamics during this placebo analgesia response.
Conclusions:
Placebo analgesia conditioning induces a transient endogenous pain relief response that modulates pain-active neural populations like $vlPAG^{MOR}$ and potentially $rILN^{MOR}$.

Oral Presentation 5

"Development of an ethologically relevant rodent model of social stress"

Fitzgerald, B.L.[1] and Cummings, K.A.[1]

[1]University of Alabama at Birmingham

About 1 in 11 people in America are diagnosed with posttraumatic stress disorder (PTSD) within their lifetime. PTSD develops with exposure to life-threatening or highly traumatic events. Most of these cases are socially derived, involving child neglect, domestic violence, sexual abuse, or bullying. Some common symptoms of PTSD include persistent fear and the inability to extinguish this fear. There is no cure for PTSD and the most effective treatment is exposure therapy, which is only effective in 50% of patients.

Rodents are a great model to study fear and trauma due to their numerous circuit parallels with humans. However, current rodent models of PTSD utilize components such as foot shocks or other artificial forced aversive stimuli, which could produce PTSD-like phenotypes, but which are not ethologically relevant and difficult to translate to natural rodent behaviors. Here, we developed an ethologically relevant rodent model for social trauma that mimics persistent fear and extinction deficits by using stimuli that a rodent may naturally encounter. In this model, we combine the previously established social defeat stress paradigm, predator odor exposure, and social housing instability.

Recent evidence suggests that inhibitory GABAergic neurons are centrally involved in fear promotion and suppression within the rodent medial prefrontal cortex (mPFC). Additionally, GABAergic dysfunction is common in humans with PTSD, but the mechanisms are unknown. Thus, by using this paradigm, we will characterize the alterations in GABAergic microcircuitry and plasticity within the rodent mPFC that allows for the persistent promotion of fear and fear extinction deficits following trauma.

Oral Presentation 6

"Reactive Astrocyte Na^+/H^+ exchanger upregulation in Alzheimer's Disease"

Jenelle Collier[1], S. Metwally, M. McFarland, V. Fiesler, S. Krishna, M. Stauffer, G. Begum, J. Kofler, D. Sun

[1]University of Pittsburgh

Introduction: Astrocytes undergo functional transformations throughout Alzheimer's Disease (AD) pathogenesis. Here, we characterized Na+/H+ exchanger (NHE1) upregulation and association with AD astrogliosis.

Methods: Immunohistochemistry was used for assessing astrogliosis in post-mortem AD patient brain tissues and APP/PS1dE9 mouse brains (APP mice). Wild-type (WT) and APP mice were administered with either vehicle (Veh) or NHE1 inhibitor HOE642 to determine effects on astrogliosis and neurological behavioral changes.

Results: Post-mortem AD cortical brain showed elevated NHE1 protein in GFAP+ astrocytes. APP mouse brains also displayed significantly elevated NHE1 expression in hippocampal GFAP+ astrocytes, especially in proximity to amyloid-beta plaques. At 4-months-old (prior to drug treatment), compared to WT mice, APP mice displayed longer travel distance (Open Field Test) and spent significantly more time in the dark zone (Light Dark Test). However, at 7-months-old, APP-Veh mice failed to show locomotor hyperactivity but remained more in the dark zone. This was in contrast to the APP-HOE group. In testing Y maze short-term memory, both WT and APP mice spent significantly more time in the novel arm at 4 and 7 months of age. This trend remained unchanged in the WT-Veh, APP-Veh or APP-HOE treated mice. However, the WT-HOE mice displayed short-term memory deficit.

Conclusions: We detected NHE1 protein upregulation in reactive astrocytes in AD brains. Inhibition of NHE1 in APP mice attenuated anxiety-like behavior but sustained the locomotor activity.

Oral Presentation 7

"Clinical and neurobiological heterogeneity in first-episode psychosis patients: A normative modeling approach."

Teles M[1], Remiszewski N, Rutherford S, Marquand A, Kraguljac NV[2]

[1]University of Alabama at Birmingham, [2]Ohio State College of Medicine

Introduction: Normative modeling is a novel approach to investigate heterogeneity in structural brain pathology. The deficit syndrome (DS) is a subtype of schizophrenia characterized by primary and enduring negative symptoms and thought to be clinically more homogeneous than non-deficit schizophrenia (NDS). We employed a normative model of cortical thickness to investigate differences in neurobiological heterogeneity between DS and NDS first-episode psychosis patients. We hypothesized that DS patients would present reduced variance and mean in the number of cortical thickness deviations than NDS.
Materials and Methods: We applied a normative modeling approach to T1-weighted MRI data. We quantified individual region-level structural deviations from a reference cohort (defined as >±2SD) in cortical thickness in DS and NDS patients. Patient groups were contrasted on variance and mean.
Results: Twenty-nine antipsychotic medication-naïve first-episode psychosis patients included in the analysis displayed features of DS, while 72 patients did not. DS patients had lower variance in the number of cortical negative deviations than NDS ($F=6.27$, $p=.01$). DS patients had a lower mean number of cortical negative deviations (2.58 ± 2.96) than NDS (4.77 ± 6.36), ($t(84.16)=2.32$, $p=.02$). There were no patient group differences in variance and mean number of cortical positive deviations. Patient groups presented few shared abnormalities in regional cortical deviations.
Conclusion: We observed reduced neurobiological heterogeneity in DS patients, supporting the idea that DS is a more homogeneous and distinct subtype of schizophrenia. Normative modeling effectively captured individual-level cortical brain pathology and evidenced inter-individual variability. This contributes to our understanding of the pathophysiology of DS.

Oral Presentation 8

"Amygdala Crh cell activity required for territorial aggression"

Emily L. Newman[1], **Khalil J. Threadgill**[1], Kerry J. Ressler[1]

[1]Psychiatry, McLean Hosp., Belmont, MA; Harvard Med. Sch., Boston, MA

Introduction: 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 and self-defensive inter-male aggression.
Materials and Methods: During 5-min resident-intruder confrontations, a submissive intruder male was placed into the territory of the aggressive resident CRH-ires-Cre male and aggressive behavior was quantified as latency to the first bite and total bite frequency. Aggressive resident males received intra-CeA adeno-associated virus (AAV) for Cre-dependent expression of designer receptors activated exclusively by designer drugs (DREADDs; hM3Dq, hM4Di) or control virus in Crh+ CeA neurons. After recovering from surgeries, mice were tested for aggression after receiving systemic vehicle or deschloroclozapine (DCZ) for chemogenetic manipulation of *Crh*+ CeA neurons. Territorial aggression tests were conducted using submissive intruders and self-defensive aggression tests using aggressive intruders.
Results: Chemogenetic inhibition of *Crh*+ CeA cells blocked aggression in territorial aggression tests but did not block self-defensive retaliation during self-defensive aggression tests. Chemogenetic activation of Crh+ CeA cells increased 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.

Oral Presentation 9

"Early Inflammaging and Senescence Transcriptional Response to Ocular Hypertension in Living Human Retina"

[1]McKenna M. Somerville, [1]Ryan G. Strickland, [1]Mary Anne Garner, [1]Christopher A. Girkin, [1]Alecia K. Gross

[1]Department of Neurobiology; Ophthalmology and Visual Sciences; Heersink School of Medicine, University of Alabama at Birmingham, Birmingham, AL, USA

Purpose: Aging and elevated intraocular pressure are primary risk factors for glaucomatous optic neuropathy, a blinding neurodegenerative disease. The acute immune response to elevation in IOP in animal models has been described, however, the exact molecular pathways that trigger these response remains unknown in the human eye. This study evaluates the impact of acute elevation in IOP in the living human eye on transcriptional genes responsible for immune recruitment, inflammaging, and senescence seen with early injury in the retina.
Methods: Research-consented brain-dead organ donors underwent screening for inclusion criteria. Blood pressure was monitored via an arterial line and tonometry was performed using an applanation tonometer. The experimental eye received one hour of manometric pressure elevation at 50 mmHg via pars plana cannulation while the fellow eye served as a control. Electroretinography was performed in regular intervals. Ocular tissues were subsequently procured, dissected, formalin-fixed and paraffin embedded. Peripheral and macular retina was sliced in 5 µm sections, deparaffinized and RNA fluorescent in-situ hybridization was performed according to RNAScope (Advanced Cell Diagnostics) protocol for FFPE tissues.
Results: Acute, 1-hour increase in IOP results in a change in retinal transcripts involved in innate immune activation, recruitment of peripheral immune effector cells, inflammaging and senescence. To date, we have analyzed 2 donors of 2 different ages and found an increase in chemokine ligand 2 (CCL2), FasR, cluster of differentiation 44 (CD44), and transforming growth factor beta 1 (TGF-β1), which differ between retinal regions. Analysis is ongoing.
Conclusions: Brief, acute increases in IOP results in alteration in the transcription of genes involved in early immune and senescent pathways in the living human retina. Further studies of this acute response within the living human eye could further elucidate early injurious pathways at the onset of ocular hypertension.

Oral Presentation 10

"The Characterization and validation of an ex vivo ischemia model for neurochemical analysis"

[1]Kaejaren Caldwell

[1]University of Cincinnati

Disruption of the ability to exchange glucose and oxygen in the brain leads to one of the most common forms of brain damage, ischemic stroke. The increases in inflammation, glutamatergic excitotoxicity, and oxidative stress compound to the detrimental outcomes of this disease. Work on understanding various important biomarkers during stroke is useful for the development of therapeutics; however, there remains a lack of understanding of the neuropathological impact of ischemic events. Guanosine is a signaling molecule and is an emerging biomarker of interest for neuroprotection. Many have shown the ameliorating effects of exogenous guanosine treatment in ischemic stroke yet the molecular mechanism of how endogenous guanosine aids in recovery of stroke events has not been elucidated. Previously, our lab has shown an increase in rapid, endogenous guanosine signaling during severe ischemic events using fast-scan cyclic voltammetry (FSCV). Despite this finding, an understanding of how this subsecond signaling changes as a function of ischemic severity is not well understood, therefore it is advantageous to interrogate the brain's immediate neuroprotective response during varying severities of injury. In this work, we use an optical oxygen sensor to characterize a tunable ex vivo oxygen-glucose deprivation (OGD) model (normoxia, mild, and severe). In doing so, we have cultivated a standard for ex vivo slice ischemic studies that better correlate to the varying ischemic severity models that exist for in vivo analysis. Immunohistochemistry and 2,3,5-Triphenyltetrazolium chloride (TTC), and ELISA assays were used to help further correlate the changes observed as a function of OGD model to the changes measured in guanosine signaling as a function of ischemic severity. Overall, this work provides the first method to specifically control ischemic severity ex vivo with correlations to how these changes influence neural signaling.

Oral Presentation 11

“Co-pathologies and immune cell activation in a model of Parkinson’s Disease”

Jhodi M Webster[1], Gabrielle M Childers[1], Nicole J Corbin Stein[1], Vickie Yang[1], Asta Zane[1], Rajesh Gupta[1], Lucas Hampton[2], Warren D Hirst[2], Fredric P Manfredsson[3], Ivette M Sandoval[3], Jeffrey H Kordower[4], Ashley S Harms[1]

[1]University of Alabama at Birmingham, Department of Neurology, Center for Neurodegeneration and Experimental Therapeutics; [2]Neurodegenerative Diseases Research Unit, Biogen, Cambridge; [3]Barrow Neurological Institute, Department of Translational Neuroscience, Phoenix, AZ, [4]ASU-Banner Neurodegenerative Disease Research Center, Bio-design Institute, Arizona State University

Along with Lewy body formation due to α-synuclein (α-syn) inclusions, β-amyloid (Aβ) and tau aggregates are also implicated in the clinical progression of Parkinson’s Disease (PD). Aβ plaques and tau fibers constitute over 50% of PD cases with pathology found in the cortex and hippocampus of post-mortem patient brains. Studies show that these three pathologies synergistically interact and may promote the aggregation of each other. As animal models for the disease lack representation of these co-pathologies, the importance for comprehensive models to further understand mechanisms underlying PD is necessary. Neuroinflammation in PD, includes T cell infiltration, gliosis and an increase in pro-inflammatory cytokines, and significantly contribute to neurodegeneration.

We aim to test whether co-pathologies enhance neuroinflammation and neuropathology in a novel model of PD. We developed a co-pathology model of PD by inducing tau and α-syn pathologies into the brains of J20 mice, a transgenic line that overexpresses mutant Aβ protein.

Our co-pathology model mice exhibit Aβ, tau and α-syn pathology as well as a robust neuroinflammatory response. This includes increased microglia cell number, changes in activation markers, CD68 and TLR2 and robust infiltration of CD4 and CD8 T cells into brain regions specific to pathology. Co-pathology mice also show increased protein pathology load. This is compared to Aβ, tau and α-syn single pathology mice, which show no changes in T cell infiltration or myeloid populations. This clinically relevant co-pathology model highlights neuroinflammation and changes in neuropathology, indicating that the presence of these pathologies may be driving the progression of disease.

Oral Presentation 12

“Differential DNA methylation related to trauma type in the PTSD brain”

Deanna Ross[1], Dhivya Arasappan, Dennis Wylie, Aarti Jajoo, Nikolaos Daskalakis, Joel Kleinman, Kerry James Ressler, Charles Nemeroff, Frances Champagne[1]. [1]University of Texas at Austin.

Introduction: Understanding the molecular basis of post-traumatic stress disorder (PTSD) is challenging due to significant variation in the type and chronicity of trauma experience and other life history variables that may impact the brain. Profiling of unique DNA methylation patterns within the PTSD brain may provide insights into the pathophysiology of this disorder. In addition to examining differentially methylated regions and genes, this profiling can give insight into biological aging that may have implications for disease pathways.

Materials & Methods: We conducted genome-wide DNA methylation analyses using Infinium MethylationEPIC arrays of dissected postmortem brain tissue. The current sample includes brains from subjects with post-traumatic stress disorder (PTSD, n=101). Our analyses include DNA extracted from the central nucleus of the amygdala, hippocampus and medial prefrontal cortex (mPFC). Analysis was done on differentially methylated regions (DMRs) and differentially methylated probes (DMPs) as well as epigenetic age utilizing three epigenetic clocks (Horvath, Levine, and Hannum). Using medical records, we grouped individuals based on trauma history.

Results: Analyses of DNA methylation profiles indicate that there is significant variation in the ratio of neuronal/non-neuronal cells across different trauma categories, such as assaultive vs. non-assaultive trauma and the presence and absence of childhood trauma. We find differentially methylated CpG sites within the PTSD brain when comparing those experienced assaultive vs non-assaultive trauma. A notable gene found differentially methylated in the amygdala between the assaultive vs non-assaultive trauma groups is protein kinase M zeta (PKMζ). This gene plays a critical role in memory and is involved in the stress response. Several DMRs and DMPs were found when comparing the those with and without childhood trauma. The hippocampus had the highest number of DMRs and DMPs ($p<0.001$). A notable gene found differentially methylated in the hippocampus between those with and without childhood trauma is SLC6A4, a gene that encodes for a serotonin transporter responsible for serotonin reuptake. No epigenetic age deceleration or acceleration were detected within individuals grouped by the trauma characteristics.

Conclusion: Our analyses suggest that there are unique DNA methylation signatures of PTSD that vary by types of trauma and implicate neurotrophin, cellular physiology and transcriptional pathways. Stress-sensitive genes have been hypothesized to play a critical role in psychiatric risk and here we find differential methylation in these genes within the amygdala. Epigenetic aging appears to vary by brain region and may be responsive to within-subject variation in life experience.

Poster Presentation Abstracts

Poster #	Title	Presenter
1	Neural Mechanisms mediating Interoception	Karen Aikhionbare
2	Oscillatory Sparse Pattern Learning Across Time (O-SPLAT): A novel streaming model for decoding latent sources in oscillatory data	Trevor Alston
3	Transcriptional regulation of PI3K-AKT-mTOR axis and consequences in metabolism	Margaret Bell, PhD
4	The effects of opioids on PACAP modulation of vlPAG neurons	Bethany Boston
5	Time-Frequency Analysis of Spectral Responses to SPES to Localize the Epileptogenic Network	Helen Brinyark
6	The Impact of Early Life Pain on Social and Impulsive Behaviors	Nadja Brown
7	Diffusion magnetic resonance imaging analysis after sports-related concussion in adolescents	Elizabeth Castro
8	Bed nucleus of the stria terminalis GLP-1R neuron effects on feeding behavior	Isabel Coiduras
9	IFNγ drives neuroinflammation, demyelination, and neurodegeneration in the Olig001-SYN mouse model of multiple system atrophy (MSA).	Nicole Corbin-Stein
10	Calcium signaling in Schwann cells development and myelination.	Jazmin Corral
11	Dynamics of Default Mode Network Activity Linked to Processing Speed in Cognitively Healthy Oldest-Old	Hannah Cowart
12	Comparing Resting State and Stimulation Evoked Network Connectivity Using Dynamical Systems Modeling	Caila Coyne
13	Toward comparing scotomas: Using microperimetry paired with cortical magnification factor to quantify retinal functional health in patients with central vision loss	Elam Cutts
14	Overexpression of Neuronal PSMB5 protects against age-related cognitive decline	Kanisa Davidson
15	Examining Protein Translation Alterations in Alzheimer's disease using Drosophila	Andy Delgado
16	A Pilot Feasibility and Efficacy Study of Transdermal Auricular Vagus Nerve Stimulation for Treating Insomnia in Breast Cancer Patients Receiving Palliative Care	Melissa Do
17	Glucagon-like peptide 1 receptors (GLP-1Rs) regulate the activity of central amygdala neurons.	Miguel Duran
18	Long-term ketogenic and time restricted diets impact mitochondrial function in a tissue-specific manner in aged rats	Brea Ford
19	Somatostatin Interneuron Involvement in the Pathogenesis of Huntington's Disease	Jahmel Fowler
20	The role of prelimbic interneurons in reward learning	Hunter Franks
21	Investigating the effects of increased O-GlcNAcylation on glial cell morphology and noradrenergic innervation in TgF344-AD rats	Melissa Garcia
22	Exploring Odor-evoked Activity in Diagonal Band Cholinergic Neurons in Awake Mice	Kelsey Glasper
23	Assessment of orofacial pain in mice by an artificial intelligence-based method	Saurav Gupta
24	Relationships Between HIV Status, Racism-Related Vigilance, and Mental Health	Joanna Hobson-Bell

Poster Presentation Abstracts

Poster #	Title	Presenter
25	The Role of Apha-Actinin-2 in the Pathogenesis of Huntington's Disease	Jordynn Hunter
26	Diurnal variation in reciprocal modulation of dopamine and acetylcholine dynamics by differential cocaine access	Melody Iacino
27	LRRK2 inhibition protects against mitochondrial damage from environmental toxicants associated with Parkinson's Disease	Neda Ilieva
28	Cerebral cortex cell-type specific alternative splicing in a Schinzel-Giedion Syndrome patient variant mouse model	Emma Jones
29	Loss of estradiol promotes greater body weight dysregulation than exposure to high fat diet in female rats.	Savoya Joyner
30	Influence of Biological Sex and Age on Alcohol Modulation of Synaptic Gating in Nucleus Core Medium Spiny Neurons.	Timmy Le
31	Heterozygosity of the GBA1 L444P mutation impairs synaptic degeneration through lysosomal dysfunction.	Casey Mahoney-Crane
32	Dopamine in the Tail of the Striatum Enhances Safety Learning	Emily Makowicz
33	Overview of the Progress of Factors in Learning and Plasticity (FLAP) at UAB	Elliot Maxwell
34	Alzheimer's Disease and Normative Aging Neuropathology in the Basolateral Amygdala of the TgF344 Rat	Macy McCuiston
35	Defining the Role of Huntingtin and Mutant Huntingtin in Stress Granule Dynamics	Jharrayne McKnight
36	Ventral Pallidal Regulation of Motivated and Consummatory Behaviors	Aisha Mesco
37	Identifying a novel role for meninges-derived retinoic acid in regulating neocortical neurogenesis	Danae Mitchell
38	Ventral Tegmental Area Oxytocin Receptor-Expressing Neurons Suppress Chow Intake in Mice	Patience Moseley
39	Investigating the impact of C. amycolatum colonization on Parkinson's Disease pathology and neuroinflammation in the Thy1-SNCA PD mouse model	Nikhita Mudium
40	Imaging as a biomarker of activity in Cerebral Cavernous Malformations	Ogechukwu, Ngwu-Hyacinth
41	Forskolin reverses the O-GlcNAcylation dependent decrease in GABAAR current amplitude at hippocampal synapses possibly through action at the neurosteroid site on GABAARs.	Shekinah Phillips
42	Investigating the Genetic Vulnerability of Adolescents to Nicotine Exposure	Roshae Roberts
43	Changes in intrinsic excitability in a population of withdrawal-activated neurons in the medial prefrontal cortex of alcohol self-administering mice	Sierra Rodriguez
44	Hand and eye movements during object categorization discriminate between younger and older adults	Valerie Sainterant
45	Prolonged ocular hypertension in the living human eye causes a selective loss of the PhNR	Ryan Strickland
46	Clinical and neurobiological heterogeneity in first-episode psychosis patients: A normative modeling approach.	Matheus Teles de Araujo
47	Amygdala Crh cell activity required for territorial aggression	Khalil Threadgill

Poster Presentation Abstracts

Poster #	Title	Presenter
48	Investigating the role of ADGRB3 loss of expression in brain tumor formation in Li-Fraumeni Syndrome	Alex Torrelli-Diljohn
49	Effects of the β2 nAChR on acquisition and motivation for nicotine self-administration	Noah Walker
50	Exploring the role of serotonergic and inflammatory signaling in a model of Autism Spectrum Disorder	Allison Walsh
51	Closed-Loop Approaches to Cognitive Training for Enhancing Processing Speed	Ashton Weber
52	Striatal Astrocyte and Interneuron Activity Revelations from a Mutant Huntingtin Mouse Model	Jewel Hairston
53	Human Breast Milk-Derived Exosomes Attenuate Lipopolysaccharide-induced Activation of CD40 and NLRP3 through CD9 Mediated Regulation of Microglia	Oluwatomi Akinduro
54	Depletion of Hemopexin Is a Predisposing Factor in Bladder Hypersensitivity Induced by Acute, but not Repeated, Psychological Stress Exposure	Anastasiia Gryshyna

Poster 1

Neural Mechanisms mediating Interoception

Karen Aikhionbare[1], Hunter Franks[1], Morris Jackson, Briana Machen[1], Carine Lampert, Lauren Assaf, Julia Tucker, Dr. Kirstie Cummings[1], Dr. Sofia Beas[1]

[1]University of Alabama at Birmingham

Introduction: 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 PVT neurons can detect and track the magnitude of physiological needs. However, whether PVT neurons can discriminate between two physiological needs is still unknown.
Materials and Methods: Here, we sought to investigate whether PVT 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. For this, we used combinatory approaches to confirm that PVT neurons can sense and track hunger levels and to investigate whether different physiological deficits (hunger vs. water) produce differential recruitment of PVT neurons.
Results: We found that PVT neurons are critical for interoception; as such, they can detect physiological needs, sense, and track the magnitude of these needs, and discriminate between different needs.
Conclusion: Altogether, the results from these experiments shed light on the neural mechanisms mediating interoception. Future studies will investigate how addiction can hijack these systems, resulting in interoception deficits.

Poster 2

Oscillatory Sparse Pattern Learning Across Time (O-SPLAT): A novel streaming model for decoding latent sources in oscillatory data

Trevor Alston[1], Pranjal Gupta, John Pearson

[1]Duke University

Introduction: While sophisticated neural recording technologies have made it increasingly easy to collect large, rich neural data sets comprising activity from many brain regions during natural behaviors, much of this data has yet to produce interpretable neural patterns. Typical studies look for structure by averaging neural signals over many repeats of the same behavior, but naturalistic behavior lacks this structure. Thus, what is needed are methods to effectively analyze large-scale brain responses without averaging across trials, especially in cases where the relevant patterns of brain activity change over time. Because streaming algorithms process data only once, they are ideal for both large datasets and for online/closed-loop applications [1][2]. Prior work from our lab has demonstrated that such algorithms can learn stable, informative data patterns and function at high input rates, but these methods do not translate readily to oscillatory signals like Local Field Potentials (LFPs), the most common data type collected by brain implants.
Materials and Methods: To address these challenges, we introduce O-SPLAT (oscillatory sparse pattern learning across time), a novel streaming approach that models multichannel oscillatory data driven by a collection of latent sources, each with its own power spectrum, that are sparsely active in time.
Results: Using synthetic experiments, we show that O-SPLAT can recover multichannel activity patterns under noisy conditions, can learn the latent frequency information embedded in each source, and can operate in real time speeds of up to 25 times data acquisition.
Conclusion: These results, along with preliminary experiments on real data, suggest that O-SPLAT is suitable for online analysis in future closed-loop experiments.

References:
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Poster 3

Transcriptional regulation of PI3K-AKT-mTOR axis and consequences in metabolism

Margaret Bell[1], Joshua Kramer[1], Mariame S Kane[1], John C Chatham[1], Martin E Young[3], Matthew Ryan Smith[4,5], Victor Darley-Usmar[1, 2], Jianhua Zhang[1, 2]
[1]Department of Pathology, University of Alabama at Birmingham, Birmingham, AL, USA
[2]Birmingham VA Medical Center, Birmingham, AL, USA
[3]Department of Medicine, University of Alabama at Birmingham, Birmingham, AL, USA
[4]VA Atlanta Healthcare System; Emory University, Atlanta, GA, USA
[5]Department of Medicine; Division of Pulmonary, Allergy, Critical Care, and Sleep Medicine; Emory University, Atlanta GA

O-GlcNAc, a post-translational modification added to Ser/Thr residues, is significantly changed in Alzheimer's disease (AD) brains. O-GlcNAc is added to protein by O-GlcNAc transferase (OGT) and removed by O-GlcNAcase (OGA). OGA inhibitors have been tested in AD clinical trials, however the mechanisms through which they impact AD pathology are not understood. Previous research showed that pharmacologically inhibiting OGA using Thiamet-G (TG) for 3 hours increased O-GlcNAcylation of 85 peptides >1.5 fold. This modification affected networks linked to O-GlcNAcylation enzymes/ activities, impacting mitochondrial function, autophagy-related proteins, and proteins associated with neurodegeneration, with variations observed between sexes, dependent on TG treatment. Because OGA and OGT tend to localize in the nucleus, we investigated the effect of TG on transcriptomics and metabolism in the mouse brain and discovered that 1,234 genes are differentially expressed after 3 hr of TG versus saline. Of these, 24 genes encode mitochondrial oxidative phosphorylation proteins. Pathway analysis revealed downregulated PI3K-AKT signaling. After 2.5 months of chronic TG treatment, we found 4,145 differentially expressed transcripts with p <0.05, 98 of them are related to mitochondrial oxidative phosphorylation and 5 related to mTOR signaling, with some in common and some different from those genes regulated by 3 hr TG. Pathway analysis showed upregulated learning and cognition. In addition, metabolomics analysis identified metabolites in the TCA cycle exhibiting decreased levels comparing chronic TG to saline. This study will provide better understanding of the downstream signaling and metabolic regulation mechanisms of OGA inhibition, and potential of targeting these pathways in AD treatment.

Poster 4

The effects of opioids on PACAP modulation of vlPAG neurons

B. Boston[1], KB. McPherson, B., Coutens, CM., De Anda Gamboa, LC. Patti, SL. Ingram
[1]Department of Anesthesiology and Neuroscience Graduate Program, University of Colorado, Anschutz Medical Campus, Aurora CO

The ventrolateral periaqueductal gray (vlPAG) is a key brain area within the descending pain modulatory pathway and an important region in opioid-mediated analgesia. The neuropeptide pituitary adenylate cyclase-activating polypeptide (PACAP) promotes migraine via the PACAP receptor (PAC1) that is densely expressed in the vlPAG. The goal of this project is to determine the effects of PACAP on activity and intrinsic membrane properties of vlPAG neurons and GABAergic synaptic transmission within the vlPAG. Whole cell patch clamp recordings from ex vivo brain slices containing the vlPAG from C57/B6 male and female mice were performed. PACAP 1-38 (10 nM) depolarized most neurons and increased spontaneous firing. The PAC1 specific inhibitor M65 (100 nM) did not reverse this effect of PACAP suggesting non-PAC1-mediated effects, possibly via VPAC receptors.

The effects of PACAP 1-38 on GABAergic synaptic transmission were determined using bipolar stimulating electrodes and NBQX (5 µM) to block glutamatergic synaptic transmission. PACAP 1-38 enhances evoked GABA release which is reversed in the presence of M65 (100 nM). In addition, PACAP 1-38 significantly increased spontaneous inhibitory postsynaptic currents and miniature inhibitory postsynaptic current frequency in the vlPAG in a PAC1-dependent manner. Increased GABA release in the vlPAG is consistent with promoting hyperalgesia. Given that delta-opioid agonists reverse behavioral effects of PACAP (Mangutov, et al., 2023), we are currently testing the ability of delta opioid agonists to reverse PACAP-mediated potentiation of GABAergic inhibitory postsynaptic currents in the vlPAG. Understanding PACAP signaling in the descending pain modulatory circuit may identify new therapeutic targets for migraine.

Poster 5

Time-Frequency Analysis of Spectral Responses to SPES to Localize the Epileptogenic Network

Helen E. Brinyark[1], Ben Cox, Joshua LaRocque, Erin C. Conrad, Rachel J. Smith[1]

[1]University of Alabama at Birmingham

Introduction: Resection or ablation of the seizure onset zone (SOZ) has been proven to reduce or eliminate seizures in patients with epilepsy. Intracranial EEG recorded during single-pulse electrical stimulation (SPES) can be analyzed to localize the SOZ. It has been shown that cortico-cortical spectral responses (CCSRs) that are evoked during SPES hold promise for SOZ localization.
Methods: In this preliminary study, we analyzed CCSRs in seven epilepsy patients. The convolution result for each SPES evoked response was calculated using a continuous Morse wavelet transform. CCSRs were calculated by taking the square of the absolute value of this result and converting to decibels. P-values were calculated for each time-frequency value and corrected for multiple comparisons using the Benjamini-Hochberg procedure. CCSRs were segmented into eight time-frequency zones (TFZs) across four frequency bands theta (4-7 Hz), alpha (8-12 Hz), beta (13-30 Hz), low gamma (30-60 Hz) and spanning the N1 and N2 peak time intervals (15-50 ms and 50-250 ms post-stimulus, respectively). The fraction of significant time-frequency values in each TFZ and over the whole evoked response (all frequency bands, 15-500 ms post-stimulus) was calculated for each electrode. Electrodes with the greatest fractions were compared to the clinician identified SOZ for each TFZ.
Results: In five of seven patients, electrodes that were significantly responsive to SPES across the whole response and in the low gamma-N2 TFZ correlated with the clinician identified SOZ.
Conclusions: This preliminary analysis suggests that CCSRs can be used to improve SOZ localization and increase success rates for those seeking surgical treatment for epilepsy.

Poster 6

The Impact of Early Life Pain on Social and Impulsive Behaviors

Nadja Brown[1], Anne Murphy[1]

[1]Georgia State University

About 10% of births in the United States are premature and often require a stay in the neonatal intensive care unit (NICU), where neonates experience painful procedures from heel pricks to surgeries and endotracheal intubation. Babies born 24-34 weeks gestation have an increased risk of developing psychiatric and neurodevelopmental disorders. Clinical research has shown that infants exposed to early-life pain have an increased risk of cortical thinning, particularly in the frontal cortex - a brain region that mediates executive functions including social behavior and impulsivity. However, few studies have examined the behavioral outcomes of early-life pain during adolescence, a critical time point that predicts adult behavioral phenotypes. Research in our lab aims to characterize how early-life pain impacts juvenile social play and impulsive behavior. We have developed a clinically relevant model of early-life pain that recapitulates an infant experience in the NICU. On the day of birth, rat pups receive an intraplantar injection of 1% carrageenan to induce inflammation and pain. Maternal behavior and juvenile social play were analyzed at key developmental timepoints. Pilot studies measuring impulsivity via an operant-conditioning task are underway. This work will provide the basis for identifying potential mechanisms by which early life pain influences social behaviors and impulsivity in adolescents. Many people begin experimenting with drugs during adolescence with tetrahydrocannabinol (THC). Because impulsivity predicts substance use, this work will also contribute to early life pain and THC self-administration studies to provide critical insight on the impact of early-life pain on adolescent development of cannabis-use disorders.

Poster 7

Diffusion magnetic resonance imaging analysis after sports-related concussion in adolescents

E. Castro[1], F. Schweser[2], S. E. Muldoon[3], J. Leddy[4], M. N. Haider[4]

[1]Neuroscience Program, Univ. at Buffalo, The State Univ of New York Buffalo, NY; [2]Department of Neurology, Univ. at Buffalo, The State Univ. of New York, Buffalo, NY; [3]Department of Mathematics, State Univ. of New York, Univ. at Buffalo, Buffalo, NY; [4]Department of Orthopedics, Univ. at Buffalo, Buffalo, NY

Sport-related concussions (SRC) are a public health concern, prompting their investigation using advanced neuroimaging techniques such as diffusion magnetic resonance imaging (dMRI). Autonomic nervous system (ANS) dysfunction during SRC is a cause of exercise intolerance, defined as symptom exacerbation that limits exercise performance. Crucial ANS centers are in the brainstem, which are often excluded from analyses, therefore currently not much is known about exercise intolerance in adolescent athletes. SRC symptoms, like exercise intolerance, are heterogenous, so symptom subtypes have been developed, but are not well-studied yet. This study characterizes SRC neurological profiles by integrating structural brain analyses and their association with ANS dysfunction and symptom subtypes. We collected dMRI, cognitive, physiological, and clinical data from 13–18-year-old adolescent athletes within 10 days of experiencing an SRC (baseline) and after recovery (follow-up). Controls had the same data collected at baseline and follow-up visits. A total of 35 SRC and 34 controls with dMRI data were collected. The dMRI data was preprocessed, a population specific atlas was applied, and generalized q-sample imaging (GQI) was used for reconstruction and tractography. We find structural brain differences between the SRC group and healthy controls, specifically in the brainstem regions. Further, these differences correlate with injury symptoms experienced by the adolescents. By incorporating the brainstem, examining exercise intolerance and ANS dysfunction, and leveraging advanced dMRI methodologies, this study offers a novel approach to address gaps in current literature.

Poster 8

Bed nucleus of the stria terminalis GLP-1R neuron effects on feeding behavior.

Isabel I. Coiduras[1], Lisa R. Anderson, Stefan Trapp, Frank Reimann, Fiona M. Gribble, Diana L. Williams

[1]Department of Psychology & Program in Neuroscience, Florida State University, Tallahassee, FL 32306, United States of America. (IIC, LRA, DLW)
[2]Centre for Cardiovascular and Metabolic Neuroscience, Department of Neuroscience, Physiology & Pharmacology, University College London, London WC1E 6BT, UK. (ST)
[3]Institute of Metabolic Science & MRC Metabolic Diseases Unit, University of Cambridge, Addenbrooke's Hospital, Hills Road, Cambridge CB2 0QQ, UK (FM, FMG)

Glucagon-like peptide 1 (GLP-1) is a neuropeptide made in hindbrain cells that project widely throughout the brain, and GLP-1 receptor (GLP-1R) activation in many nuclei, including the bed nucleus of the stria terminalis (BNST), suppresses food intake suppresses food intake. Here, we chemogenetically manipulated GLP-1R-expressing BNST neurons to investigate the mechanisms for this effect. GLP-1R-Cre mice received intra-BNST AAV injections to introduce hM3Dq-mCherry or control mCherry into GLP-1R neurons, and were then housed in a continuous food intake monitoring system. They were injected with vehicle or CNO before dark onset, in counterbalanced order separated by 48 h. Chow intake was significantly suppressed by CNO for the first 6 hours of dark in hM3Dq mice, with no effect in control mice and no sex differences observed. We previously showed that BNST GLP-1R neurons project to the lateral hypothalamus (LH), and that GLP-1R stimulation directly inhibits 60% of GLP-1R-expressing BNST neurons. Because the BNST GLP-1R neuron population is heterogeneous, we hypothesized that those that project to LH affect food intake differently than those that project elsewhere. To test this, we implanted bilateral cannulas into the LH for site-specific vehicle or CNO delivery as described above. Intra-LH CNO had no effect on chow intake, but when mice were maintained on 60% fat diet, CNO significantly increased intake in the hM3Dq mice. We conclude that the GLP-1R BNST-to-LH neuron projection influences food intake under some circumstances, and the anorexic effects of BNST GLP-1R neuron activation are mediated by neurons that project elsewhere.

Poster 9

IFNγ drives neuroinflammation, demyelination, and neurodegeneration in the Olig001-SYN mouse model of multiple system atrophy (MSA).

Nicole Corbin-Stein[1]

[1]University of Alabama at Birmingham

Multiple system atrophy (MSA) is a fatal, progressive neurodegenerative disease that is characterized by demyelination in the corpus callosum and putamen and accumulation of alpha synuclein (α-syn) in glial cytoplasmic inclusions (GCI) within the oligodendrocytes. Previous data has shown in post-mortem MSA brain, α-syn pathology is accompanied by MHCII expression and increased infiltration of peripheral T cells (CD4). IFNγ released from CD4 T cells enhances inflammation by binding to its receptor (IFNγR1), and through the JAK/STAT pathway, activates MHCII antigen presentation. *It is unknown if IFNγ drives the neuroinflammation and demyelination known to be in MSA pathology.* Using a novel rodent model transduced with a modified AAV, Olig001-SYN that displays high tropism (>95%) for oligodendrocytes, we assayed for inflammation and demyelination with immunohistochemistry and flow cytometry. Moreover, the Oligo001-SYN rodent model of MSA shows a similar robust CD4 T cell response due to the oligodendrocyte α-syn expression. My results indicated there was a significant neuroinflammation shown by the increase in IFNɣ producing CD4 T cells and MHCII expression within the striatum of Olig001-SYN mouse model. Additionally, at 4 weeks post Olig001-SYN transduction the genetic deletion of Tbet (a transcription factor required for IFNɣ production) showed reduced MHCII expression and reduced immune cell infiltration into the striatum. T cell infiltration into the striatum was decreased in the Tbet -/- mouse when α-syn was present. At 6 months post Olig001-SYN injection the genetic deletion of Tbet attenuated neurodegeneration 6 months post Olig001-SYN transduction. Additionally, when IFNɣ was knocked down via a neutralization antibody (XMG1.2) there was a significant reduction in overall MHCII expression and general neuroinflammation and demyelination. The summary of these results indicates that IFNɣ is required for neuroinflammation, demyelination, neurodegeneration observed in the Olig001 mouse model of MSA.

Poster 10

Calcium signaling in Schwann cells development and myelination.

Jazmin Corral, Karissa Garbarini, Veronica T. Cheli, Pablo M. Paez.

Institute for Myelin and Glia Exploration, Department of Pharmacology and Toxicology, Jacobs School of Medicine and Biomedical Sciences, The State University of New York, University at Buffalo, Buffalo, New York.

Schwann cells are the major glial cells in the peripheral nervous system (PNS), and they are essential for the maintenance and myelination of peripheral nerves. In the central nervous system, the importance of G-Protein coupled receptors (GPCRs) modulating Ca2+ signaling in oligodendrocytes and neurons has previously been shown. However, there is a lack of information of how the modulation of Ca2+ signaling by GPCRs in Schwann cells affect myelination of the PNS. Using Cre-mediated recombination we specifically expressed the excitatory hM3Dq and the inhibitory hM4Di GPCRs in Schwann cells. These receptors were created from different subtypes of human muscarinic receptors and are exclusively activated by clozapine N-oxide (CNO). We performed Ca2+ imaging, immunocytochemistry, and electron microscopy experiments to assess Schwann cell development and function after hM3Dq and hM4Di activation in vitro as well as in vivo. Our results show that hM3Dq activation during early development significantly delays the myelination of the sciatic nerve and the maturation of Schwann cells. Furthermore, hM3Dq activity in mature Schwann cells disrupts the myelin sheath and induces a severe demyelination in the adult sciatic nerve. In contrast stimulation of hM4Di increases myelin synthesis and Schwann cell proliferation in adult peripheral nerves. We have conducted Ca2+ imaging experiments to determine how hM3Dq and hM4Di affects the activity of Ca2+ channels and receptors in Schwann cells and we have also performed behavioral test, such as Rotarod and Catwalk, to study how changes in myelination induced by hM3Dq and hM4Di impact motor coordination in young and adult mice.

Poster 11

Dynamics of Default Mode Network Activity Linked to Processing Speed in Cognitively Healthy Oldest-Old

Ling, G[1], **Cowart, H[1]**, Nolin SA[1], Stewart, P[1], Fleming, L[1], Faulkner ME[1], Merritt S[2], Rezaei RF[3], Bharadwaj PK[4], Franchetti MK[4], Raichlen DA[5], Jessup CJ[4], Edwards, L[1], Hishaw GA[4], Van Etten EJ[4], Trouard TP[4], Geldmacher D[1], Wadley VG[1], Alperin N[2], Porges EC[3], Woods AJ[3], Cohen RA[3], Levin BE[2], Rundek T[2], Alexander GE[4], Visscher KM*[1]

[1]UAB School of Medicine/Evelyn F. McKnight Brain Institute, Birmingham, AL; [2]University of Miami Miller School of Medicine/Evelyn F. McKnight Brain Institute, Miami, FL; [3]University of Florida/Evelyn F./William L. McKnight Brain Institute, Gainesville, FL; [4]University of Arizona/Evelyn F. McKnight Brain Institute, Tucson, AZ; [5]University of Southern California, Los les, CA

Background: "Oldest-old" individuals differ significantly regarding cognition. Dynamic brain activity can be clustered frame-by-frame, producing "brain states" (Coordinated Activity Patterns) which offer temporal information used to explore correlations between dynamics and cognition.
Methods: Across 4 sites, 146 cognitively intact participants aged 85+ underwent 8-minutes of functional MRI during rest as well as extensive neurocognitive assessments as part of the McKnight Brain Aging Registry. K-means clustering was used to calculate CAPs. Persistence/fraction of occurrence/transitions defined dynamics.
Results: Most stable CAP (r=0.92) has active DMN and ventral attention network (DMN/VAN, z= 2.2/1.0) and otherwise low activation (z<-0.6). In comparison between cognition and dynamics, processing speed was positively associated with transition entropy/fraction of occurrence/persistence.
Conclusions: DMN was identified as stable/common measure in this population across models. Processing speed was correlated to dominant/persistent DMN activity. This analysis adds dynamic dimension to fMRI.

Poster 12

Comparing Resting State and Stimulation Evoked Network Connectivity Using Dynamical Systems Modeling

Caila Coyne,[1] Helen Brinyark,[2] Ben Cox,[3] Sridevi V. Sarma,[4] Arie Nakhmani[5] and Rachel J. Smith.[5]

[1]Neuroengineering, University of Alabama at Birmingham, Birmingham, AL
[2]Department of Biomedical Engineering, University of Alabama at Birmingham, Birmingham, AL
[3]Department of Neurology, University of Alabama at Birmingham, Birmingham, AL
[4]Department of Biomedical Engineering, Johns Hopkins University, Baltimore, MD
[5]Department of Electrical and Computer Engineering, University of Alabama at Birmingham, Birmingham, AL

The aim of this study is to develop a framework for comparing resting state connectivity networks to stimulation evoked networks in drug resistant epilepsy patients. Single-pulse electrical stimulation has become increasingly used to investigate functional and pathological connectivity in epilepsy and to probe cortical excitability. However, the procedure is still not a part of routine clinical care. Consequently, by mapping resting to stimulation evoked networks, we can investigate whether similar information about epileptogenic connectivity can be obtained from resting state intracranial EEG data alone.

To compare the two states, linear time invariant (LTI) state-spaces models are constructed from short windows of interictal recordings and from trial averaged cortico-cortical evoked potentials (CCEPs). The interictal models take the form: $\boldsymbol{x}[t+1]=\boldsymbol{A}_{\mathbf{RS}}\boldsymbol{x}[t]$, where $\boldsymbol{x}[t]\in\mathbb{R}^{n\mathrm{x}1}$ represents the state vector describing the neuronal activity recorded from the n contacts, and $\boldsymbol{A}_{\mathrm{RS}}\in\mathbb{R}^{n\mathrm{x}n}$ is the state transition matrix which maps one state in time to the next. The models for the stimulated state are calculated similarly but have an additional exogenous perturbation term to account for the electrical input into the system: $\boldsymbol{x}[t+1]=\boldsymbol{A}_{\mathrm{CCEP}}\boldsymbol{x}[t]+\boldsymbol{B}\mathrm{u}[t]$.

Then, to quantify similarity in connectivity between resting and stimulated networks, we calculate the L2 norm of the transformation matrix $\boldsymbol{T}$ which maps $\boldsymbol{A}_{\mathrm{RS}}$ to $\boldsymbol{A}_{\mathrm{CCEP}}$ ($\mathrm{T}=\boldsymbol{A}_{\mathrm{CCEP}}*\boldsymbol{A}_{\mathrm{RS}}{}^{-1}$). We found that this metric can highlight different subnetworks such as the seizure onset zone and the early propagation zone, as distributions formed from comparisons of 100 observations of ARS with unique stim evoked transition matrices show separation that reflects the hypothesized differences in cortical excitability.

Poster 13

Toward comparing scotomas: Using microperimetry paired with cortical magnification factor to quantify retinal functional health in patients with central vision loss

Elam Cutts[1] (ecutts99@uab.edu), Marcello Maniglia[2], Matthew Defenderfer[1], Pinar Demirayak[1], Dawn DeCarlo[1], Kristina Visscher[1]

[1]University of Alabama at Birmingham, [2]University of California, Riverside

In macular degeneration, the primary cause of vision loss among older adults, photoreceptor death in the retina results in vision impairment. Complex visual tasks such as reading or navigation require both basic visual sensation ('low level vision') as well as neural processes beyond this ('high-level vision'). Patients with similar retinal damage can differ widely in their performance on complex visual tasks, suggesting that compensation for this impairment varies between patients. Quantification of this compensation is a necessary step to understanding the neural mechanisms involved in compensation. Traditional tests like visual acuity and contrast sensitivity gauge do not explain the entire visual experience. To bridge this gap, we developed a method using outcomes from the Macular Integrity Assessment (MAIA), a microperimetry method that evaluates sensitivity across the retina. Comparison of these results is difficult, given that lesions in central vision lead to worse impairment than peripheral vision. Here we introduce a method that uses the concept of the "Cortical Magnification Factor" (CMF). Different parts of visual cortex correspond to parts of vision, and the CMF describes how much more cortex is devoted to each portion of the visual field. By weighting MAIA scores with CMF, we derived a measure called macular functional health (MFH). MFH reliably reflects the clinical impression of the severity of a scotoma. MFH was significantly correlated to contrast sensitivity, as well as acuity. Further, models incorporating MFH were better predictors of high-level visual processing. These results validate our measure of MFH to compare scotoma severity across participants.

Poster 14

Overexpression of Neuronal PSMB5 protects against age-related cognitive decline

Kanisa Davidson[1]

[1]University of Alabama at Birmingham

The proteasome is a critical driver of protein turnover that is necessary for learning and memory. The proteasome function decreases throughout age. This decline results in protein toxicity and contributes to age-related cognitive declines. Astrocytes are necessary for maintaining neuronal health and synaptic activity. Astrocytes reactivity increase with aging. Our study investigated whether neuronal targeted augmentation of proteasome function via overexpression of the rate-limiting proteasome subunit PSMB5 could alleviate age-related declines in cognitive function and astrocyte expression.

We investigated whether augmentation of proteasome function via over-expression of the rate-limiting proteasome subunit PSMB5 could alleviate age-related declines in cognition and astrocyte expression. Three cohorts were created and aged to 11-12 Mo (Young), 18-19 Mo (Middle aged) and 22-26 Mo (Old). Behavioral tests were performed to access memory, balance, and coordination. Immunohistochemistry was performed to analyze glial reactivity in the hippocampus.

We demonstrated that neuronal proteasome overexpression reduced age-related deficits in measures of coordination and balance (rotarod), along with reduced deficits in spatial learning and memory (Morris Water Maze, and closed arm Y-maze) in our middle and older overexpression PSMB5 male mouse model at $p<.05$. Our investigation further demonstrated proteasome augmentation drives changes in glial cell prevalence including an increase in GFAP in our younger transgenic cohort $p<.05$.

We developed a novel mouse model with neuronal proteasome overexpression and investigated the capacity of enhanced proteasome function to slow age-related cognitive decline. These findings could be used access proteasome augmentation in neurodegenerative diseases.

Poster 15

Examining Protein Translation Alterations in Alzheimer's disease using *Drosophila*

Andy Delgado, Danitra Parker, & Andrew Pickering[1]

[1]University of Texas Health Houston at the Medical Center

Age-related neurodegenerative diseases are characterized by excess deposition of misfolded protein aggregates. Dysregulations in protein translation through the mTOR translation pathway is reported in Alzheimer's disease (AD) and tau interference with ribosomal function is reported in AD and other tauopathies. This study investigates how repressing protein translation at the ribosome through cycloheximide (CHX) feeding modulates longevity in a Drosophila tauopathy model as measured by the lifespan assay. This study finds that CHX has a protective effect on lifespan in both male and female flies overexpressing human wildtype tau in neurons. Further investigation is warranted to determine if this protective effect is due specifically to reduction in global protein translation or interference with tau ribosome interaction. We developed a novel mouse model with neuronal proteasome overexpression and investigated the capacity of enhanced proteasome function to slow age-related cognitive decline. These findings could be used access proteasome augmentation in neurodegenerative diseases.

Poster 16

A Pilot Feasibility and Efficacy Study of Transdermal Auricular Vagus Nerve Stimulation for Treating Insomnia in Breast Cancer Patients Receiving Palliative Care

Melissa Do[1]

[1]University of Alabama at Birmingham

Background: While the purpose of sleep is heavily debated, it is widely accepted that quality sleep is essential to the well-being of every individual. It has been shown to decrease stress, improve depressive moods, enhance memory consolidation, reduce inflammation, and improve one's overall health. Insomnia is a common problem experienced by patients with breast cancer, affecting about 40% of cancer survivors. This is a critical concern with cancer clinicians as it can affect the overall health of those with breast cancer or those recovering from breast cancer. Benzodiazepines are commonly prescribed to treat insomnia in breast cancer patients, but these drugs come with negative side effects and a high risk of abuse. Transauricular Vagus Nerve Stimulation (taVNS) is a non-invasive and non-pharmacologic intervention that could potentially be used as an alternative to treat insomnia. taVNS is safe and well-studied neuromodulation device that delivers low-intensity pulsed electrical currents to the vagus nerve through the external ear. This neuromodulation device has demonstrated efficacy in treating insomnia, stress, anxiety, pain, depression, inflammation reduction, and other diseases. Therefore, this intervention could serve as a safe, critical intervention to aid in breast cancer recovery and issues associated with breast cancer diagnosis.
Methods: In this study, we aim to investigate the influence of taVNS to address insomnia in breast cancer patients receiving palliative and supportive care services. Specifically, we aim to evaluate the feasibility of using taVNS to treat insomnia in patients with breast cancer. We also aim to evaluate the efficacy of repeated, nightly taVNS on sleep quality, anxiety, and cancer-related fatigue. Additionally, we aim to evaluate the effect of taVNS on blood inflammation markers, IL-6, IL-10, CRP, and fibrinogen, and the effect of taVNS on cortisol levels.
Results: We expect that 30 patients with breast cancer and insomnia will be enrolled and undergo taVNS to address insomnia, quantified by various sleep related outcome measures, with an estimated recruitment rate of 70%, eligibility rate of 70%, completion rate of 80%, and follow up rate of 80%. We hypothesize that patients will report significantly improved sleep (minimally clinically significant change of 6 points on the Insomnia Severity Index (ISI)), with possible improvements in anxiety, depression, and cancer related fatigue after two weeks of taVNS.
Conclusion: This study is ongoing and recruitment strategies include recruiting breast cancer patients who have an active diagnosis or have had a diagnosis of Stage I-IV breast cancer and have cancer-related insomnia, as defined by having a Insomnia Severity Index of >8.

Poster 17

Glucagon-like peptide 1 receptors (GLP-1Rs) regulate the activity of central amygdala neurons.

Miguel Duran[1], Elam Cutts[1], Christian Lopez[1], Ningxiang Zeng[1], Eshita S. Yadav[1], Sonja A. Virkus[1], J. Andrew Hardaway[1]

[1]Department of Psychiatry and Behavioral Neurobiology, University of Alabama at Birmingham

Obesity and type 2 diabetes are serious health concerns affecting 13% and 6.28% of the global population, respectively. Glucagon-like peptide-1 receptor (GLP-1R) agonists are prescribed for weight management and treatment of type 2 diabetes. In the brain, GLP-1R activation reduces food intake via multiple brain sites, i.e., hypothalamus, hindbrain, and limbic systems. Multiple studies have shown that systemic administration of GLP-1R agonists activates the central nucleus of the amygdala (CeA), yet the mechanisms mediating this action is understudied. In mice, we observed that Glp1r is diffusely expressed among neuronal subpopulation within CeA, Prkcd, Sst, and Tac2 neurons, and that GLP-1Rs are enriched in the medial subdivision of the CeA. In the present study, we used in vivo fiber photometry and GCaMP in the CeA in freely behaving mice to determine the role of GLP-1Rs in modulating neural activity in response to peripheral administration of GLP1R agonists. We found that Exendin-4 activates CeA neurons, and this effect can be blocked. These novel measurements from freely behaving mice suggest that CeA GLP-1Rs are potentially mediating changes in neuronal activity when activated by its agonists. Currently, we are assessing the requirement of CeA neuron activation in food-seeking.

Poster 18

Long-term ketogenic and time restricted diets impact mitochondrial function in a tissue-specific manner in aged rats

Brea J. Ford[1], Sarah Ding[1], Sara N. Burke[2], Abbi R. Hernandez[1]

[1]Department of Medicine, Division of Gerontology, Geriatrics, and Palliative Care, Heersink School of Medicine, The University of Alabama at Birmingham
[2]Department of Neuroscience, College of Medicine, The University of Florida

Mitochondria play a crucial role in cellular energy production through oxidative phosphorylation facilitated by the four complexes of the electron chain transport. However, as organisms age, mitochondria are subjected to many stressors, such as mitochondrial DNA damage, resulting in impaired energy production across multiple organ tissues. Recent studies indicate the potential benefits of dietary interventions to alleviate mitochondrial dysfunction in aged organisms. Ketogenic diets (KD) and time restricted feeding (TRF; aka intermittent fasting) improve cognitive and physical outcomes in aged subjects. Thus, the current study investigates the effects of a long-term (~18 months) KD in conjunction with TRF on mitochondrial function in aged rats. Mitochondrial assays were conducted on several tissues associated with mitochondrial dysfunction in aging: muscle, liver, prefrontal cortex (PFC), and hippocampus (HPC). While there were no differences in activity across diet groups within the PFC, complex IV activity within the HPC was significantly lower in TRF-fed rats. Complex IV activity within the muscle followed the same pattern as the HPC, along with a significant reduction in complex II activity in KD-TRF rats. Interestingly, there was an increase in complex II activity within the liver of KD-TRF rats, despite the liver's inability to utilize ketone bodies as an alternative fuel source. The differential effects of complex II activity across these tissues may reflect the different functions and energetic demands of these organ systems. These data are helping to further understand the mechanisms by which KDs improve cellular, and thereby cognitive, functions.

Poster 19

Somatostatin Interneuron Involvement in the Pathogenesis of Huntington's Disease

Jahmel A.R. Fowler, MHA[1], Mariangela Scarduzio, Ph.D. Michelle Gray, Ph.D.[1]

[1]Department of Neurology, University of Alabama at Birmingham

Huntington's disease (HD) is a fatal neurodegenerative disease that is caused by expansion of the CAG tract in exon 1 of the gene encoding the Huntingtin protein. The resulting abnormal polyglutamine-containing protein is ubiquitously expressed, primarily causing striatal degeneration. HD patients have motor, cognitive and psychiatric abnormalities. Striatal degeneration is accompanied by electrophysiological dysfunction of specific cell types. Striatal medium spiny neurons (MSNs) are the primary cell types lost. These cells are modulated by various interneuron populations, one of which is the somatostatin-expressing interneuron (SST+). To study cellular contributions to HD, we utilize conditional BACHD mice, which express a full-length human mutant huntingtin gene (mHTT). Interestingly, these cells are not lost in HD patients as well as in BACHD mice but have increased spontaneous firing. In BACHD mice we also see increased striatal extracellular GABA (e[GABA]) via in vivo microdialysis. It is possible that increased SST+ cell firing contributes to the increase in striatal e[GABA]. Understanding the role mHTT expression plays in these cells can provide insight into the dysfunction observed in the striatum of HD patients. We will use a genetic approach to decrease mHTT expression in SST+ cells by crossing BACHD mice to SST-Cre mice, and will assess neuropathological, behavioral, and electrophysiological abnormalities. We hypothesize that expression of mHTT in SST+ influences the increased GABAergic changes observed in MSNs, motor and psychiatric abnormalities and the e[GABA]. Motor dysfunction is not improved in BACHD/SST-Cre mice. Additionally, we prove that the increased spontaneous firing of SST+ cells is cell autonomous.

Poster 20

The role of prelimbic interneurons in reward learning

Franks, H.[1], Gonzalez, J., Campos-Cardoso[1], R., Cummings, K.[1]

[1]Department of Neurology, University of Alabama at Birmingham

Dysfunction in reward learning is a central feature of addiction. Most addiction studies focus on the role of dopamine and glutamate; however, dysfunction of cortical GABAergic signaling is also central to this pathology. In rodents, among other regions, the prelimbic cortex (PL) is a critical reward-encoding region. While the two most abundant PL interneuron subtypes, somatostatin (SST-INs) and parvalbumin (PV-INs) interneurons, are central to other types of learning, whether they participate in reward learning is unstudied. I hypothesize that dynamic activity/plasticity of PL interneurons underlies reward encoding. To test this hypothesis, we subjected mice to fixed ratio 1 operant sucrose conditioning. 24 hours post-training, we performed ex-vivo slice electrophysiology and observed that SST-INs exhibit increased excitability following reward conditioning compared to naïve animals. In line with increased excitability, c-fos quantification after reward conditioning revealed a significantly higher proportion of c-fos+ SST-INs in animals learning the task compared to those that did not. Finally, in-vivo calcium imaging of PL SST-INs and PV-INs during reward conditioning revealed that both SST-INs and PV-INs exhibit increased activity during cue presentation. When pressing lever to receive reward, however, we observed that SST-INs and PV-INs exhibit increased and decreased activity, respectively. Intriguingly, both SST-INs and PV-INs exhibit session-dependent activity alterations during cue presentation and lever press, indicating a novel role for PL interneurons in reward learning. Aside from underscoring the significant role of PL interneurons in reward learning, our results lay the foundation to study how PL interneuron dysfunction contributes to maladaptive reward states, like addiction.

Poster 21

Investigating the effects of increased O-GlcNAcylation on glial cell morphology and noradrenergic innervation in TgF344-AD rats

Melissa Garcia[1], Lori McMahon[2]

[1]University of Alabama at Birmingham, [2]The Medical University of South Carolina

Alzheimer's disease (AD) pathology accumulates 20-30 years before cognitive symptoms appear. During this time, there are increases in inflammation, amyloid-β (Aβ), and hyperphosphorylated Tau. Previous preclinical studies have shown that the post-translational modification, O-GlcNAcylation, which involves the addition of a single N-acetyl-glucosamine moiety to serine or threonine residues, can decrease amyloidogenic processing of amyloid precursor protein (APP) and compete with phosphorylation of specific serines on Tau, thereby decreasing its accumulation. In addition, protein O-GlcNAcylation has anti-inflammatory effects. This study is designed to evaluate how pharmacologically increasing O-GlcNAcylation via inhibition of O-GlcNAcase (OGA), the enzyme that removes O-GlcNAc moieties, impacts the progression of AD pathology using the TgF344-AD rat model, the most comprehensive AD rat model to date. This work is significant since OGA inhibitors are currently in AD clinical trials. To increase O-GlcNAcylation we used the highly selective OGA inhibitor thiamet-G (TMG; 10mg/kg s.c) administered 3x/wk for 3 months (n=8-10/gp). We chose 6-month-old TgF344-AD (Tg) rats and non-transgenic (non-Tg) littermates since pathology is already significant at this age. Preliminary results confirm significant increases in GFAP, Iba1, and amyloid-β in Tg+saline compared to non-Tg+saline rats. Importantly, GFAP and Iba1 protein levels in Tg+TMG are not significantly different from non-Tg+saline rats. Using tyrosine hydroxylase (TH) immunohistochemistry and confocal imaging we examined the density of noradrenergic innervation in the dentate gyrus and found a significant decrease in TH+ axons in Tg+saline rats compared to non-Tg+saline, confirming our previous findings. Unexpectedly, we found that increasing O-GlcNAcylation led to an increase in TH+ axon density in non-Tg+TMG compared to non-Tg+saline, with no significant differences observed in either Tg treatment groups. Tg animals did have an increase in abnormal TH innervation in the hilus of the dentate gyrus compared to non-Tg rats. These studies shed light on how increasing O-GlcNAc in non-Tg and Tg animals affects noradrenergic innervation and amyloid pathology, which could give further insights into the current clinical trials.
Keywords: O-GlcNAc, Neuroinflammation, TgF344-AD

Poster 22

Exploring Odor-evoked Activity in Diagonal Band Cholinergic Neurons in Awake Mice

KR Glasper[1], MB Fox, and ML Fletcher[1]

[1]University of Tennessee Health Science Center

Introduction: Cholinergic neurons in the horizontal limb of the diagonal band of Broca (HDB) project to olfactory pathway areas, including the olfactory bulb and piriform cortex. Cholinergic modulation impacts odor responses, olfactory learning, and odor discrimination, but the circumstances driving cholinergic activity in awake animals are unclear. We investigated how HDB cholinergic neurons respond under baseline conditions, following olfactory and non-olfactory stimuli, and during olfactory-guided exploration. We expressed the calcium indicator GCaMP8f in cholinergic neurons of ChAT-cre mice and used head-mounted microendoscope recordings to characterize cholinergic activity in awake, head-fixed mice. We found that these neurons display both homogenous and heterogeneous activity patterns, likely indicative of differing projection patterns. Current work focuses on correlating cholinergic activity with behavioral events in awake, freely moving mice and evaluating the activity patterns of olfactory-projecting HDB neurons.
Materials & Methods: 500 nl of AAV1.Syn.GCaMP8f virus was injected unilaterally into the HDB of ChAT-cre mice. A microendoscope was attached over a 0.5mm diameter GRIN lens implanted at the injection site, with a metal baseplate cemented to the skull for scope attachment. Animals underwent a series of odor, light, and clean air stimulus trials in an olfactometer setup.

Poster 23

Assessment of orofacial pain in mice by an artificial intelligence-based method

Saurav Gupta[1], Akihiro Yamada, Jennifer Ling, Jianguo G. Gu

[1]Dept. of Anesthesiology and Perioperative Medicine, University of Alabama at Birmingham – Birmingham, AL USA

Orofacial pain is difficult to reliably assess in experimental animals, hamper the preclinical studies of orofacial pain. In the present study, we aimed to develop an artificial intelligence-based (AI-based) method using DeepLabCut to assess orofacial pain in mice quantitatively. Mouse Grimace scale (MGS) is used to study changes in facial expression for assessing spontaneous pain in mice. Since one of the prominent MGS behaviors of orofacial pain is orbital tightening, in our experiments we video-recorded orofacial and orbital regions of animals and then quantified orbital tightening of animals using an AI-based method. In one set of experiments, $Nav1.8^{ChR2}$ mice were tested. We applied blue laser light to their orofacial regions, we found that $Nav1.8^{ChR2}$ mice also showed a reduction of orbital dimension over an extended time following the blue light stimulation. In a separate set of experiments, animals received subcutaneous injections of 10µl saline (control group) or 5-10µl capsaicin (inflammatory pain group) in the cheek regions and hindpaw regions (separately). The mean orbital dimension in the capsaicin-induced inflammatory pain group was significantly smaller in comparison with the control group. Orbital dimension histogram also showed an overall reduction of orbital dimension, i.e., orbital tightening, following capsaicin-induced orofacial inflammation both in cheek regions and hindpaw regions. Collectively, the present study has established an AI-based method to quantify orofacial pain in mice, which will help us in the future to better understand orofacial pain and identify therapeutic targets for the relief of orofacial pain.

Poster 24

Relationships Between HIV Status, Racism-Related Vigilance, and Mental Health

Joanna Hobson-Bell[1]

[1]University of Alabama at Birmingham

Objective: People living with HIV (PLWH) experience discrimination daily. These experiences of discrimination are related to their health status, racialized identity, gender, and education levels as well. African Americans with HIV are at increased risk of experiencing racism and discrimination due to their health-status. These experiences can contribute to further vigilance, rumination (via depression), and insomnia symptoms.
Methods: Participants (N = 121) completed the Heightened Vigilance Scale, the Centers for Epidemiological Studies Depression Scale, and the Insomnia Severity Index. We administered oraQuick tests to all participants to determine HIV status, and a demographic questionnaire to determine age, gender, race, and education levels.
Results: PLWH had greater depressive symptoms ($p = .027$) and insomnia symptoms ($p = .022$) than people without HIV. Additionally, in PLWH, there was an indirect effect of vigilance on insomnia symptoms via depressive symptoms [95% Bootstrap CI = .028 - .414]. Specifically, greater racism-related vigilance contributed to greater depressive symptoms ($b = .528$, $p = .033$), and greater depressive symptoms predicted greater insomnia symptoms ($b = .377$, $p = .000$).
Discussion: Racism may be a precursor for the development of depression and insomnia in PLWH. Interventions geared towards building resilience and easing anxiety among PLWH may counteract this relationship. Future work will incorporate exercise, spirituality, and community-work to improve the health-related quality of life of PLWH.

Poster 25

The Role of Apha-Actinin-2 in the Pathogenesis of Huntington's Disease

Jordynn Hunter[1], Michelle Gray, Ph.D.[1]

[1]Dept. of Neurology, University of Alabama at Birmingham

Huntington's Disease is a fatal genetic and progressive neurodegenerative disorder caused by a polyglutamine expansion in the huntingtin protein. HD patients exhibit motor, psychiatric, and cognitive deficits. There is significant degeneration of striatal medium spiny neurons. The MSNs show abnormal electrophysiology in mutant huntingtin expressing mouse models. Decreased α-actinin-2 expression is observed in striatal tissue from HD patients and mutant huntingtin expressing mouse models. Studies in hippocampus show that α-actn2 is important for localization of neurotransmitter receptors in the post synaptic density, suggesting an important role for α-actinin-2 in proper synaptic function.
The MSNs express dopamine receptor D1 (Drd1) or dopamine receptor D2 (Drd2). The Drd2 MSNs degenerate most prominently at early stages of HD. These MSNs are also characterized by their location in patch or matrix compartments. The MSNs in the patch receive limbic input and the matrix MSNs receive sensorimotor input. While it is known that α-actn2 is decreased in the striatum, it remains unclear which cell type has altered expression and whether patch or matrix show a difference in α-actn2 levels. To determine whether specific MSNs show a reduction of α-actn2 and if this alteration is patch or matrix specific, we use mutant huntingtin BACHD mice. We performed immunofluorescence staining and RNAscope to determine cell type specific protein and RNA expression, respectively in MSNs in patch and matrix. We hypothesized that since Drd2-expressing MSNs are affected earliest in HD, alterations of α-actinin-2 will be observed most prominently in Drd2-expressing MSNs.

Poster 26

Diurnal variation in reciprocal modulation of dopamine and acetylcholine dynamics by differential cocaine access

Melody C. Iacino and Mark J. Ferris, Ph.D.[1]

[1]Wake Forest University

Despite decades of research, 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) in the nucleus accumbens (NAc) core via nicotinic acetylcholine receptors (nAChRs) on DA varicosities. Mesolimbic DA modulates NAc ACh via D2-like receptors (D2Rs) on CINs. However, cocaine-induced dysregulation of rhythms in NAc DA-ACh interactions have not been investigated. Here, we used 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 rhythms of DA release and CIN control will vary based on the pattern of cocaine availability. Despite consuming less cocaine than LgA, we show that IntA significantly increases DA release across the light/dark cycle as compared to other groups. While ShA and cocaine-naïve rats show higher DA release mid-light versus mid-dark cycle, IntA and LgA show an absence of diurnal rhythmicity. Interestingly, IntA induced rhythmicity in cholinergic modulation of DA release with greater ACh control mid-light versus mid-dark cycle. Additionally, IntA exhibits greater CIN D2R control mid-dark versus mid-light cycle compared to other groups. Targeting DA-ACh interactions via CIN D2Rs may provide a mechanism for restoring cocaine-induced disruptions in drug-taking behavior.

Poster 27

LRRK2 inhibition protects against mitochondrial damage from environmental toxicants associated with Parkinson's Disease

N. M. ILIEVA[1], B. R. DE MIRANDA[1]

[1]Univ. of Alabama at Birmingham, Birmingham, AL

Environmental pollutants like pesticides rotenone (ROT) and paraquat (PQ) and solvents trichloroethylene (TCE) and tetrachloroethylene (PERC) cause mitochondrial damage and are linked to a higher risk of Parkinson's disease (PD). TCE exposure in rats increased LRRK2 activity, commonly associated with PD. TCE also caused similar neuronal pathology as seen in LRRK2 mutations. We suggest inhibiting LRRK2 activity to reduce toxicant damage to DA neurons and be protective.

Our study aimed to evaluate the effectiveness of MLi2, an LRRK2 kinase inhibitor, against ROT, PQ, TCE, and PERC in 293-T cells. We observed that MLi2 decreased ROS levels in WT and CRISPR-edited LRRK2 cells when exposed to toxicants; however, this effect was not observed in LRRK2 KO cells. Toxicant-exposed and CRISPR-edited cells had mitophagy deficits, improved by MLi2. LRRK2 KO cells were protected. We exposed aged female rats to 200 mg/kg TCE or olive oil via oral gavage for 6 weeks and tested the effects of a post-lesion intervention of 10 mg/kg MLi2 at 3 weeks, when elevated LRRK2 kinase activity was observed in the basal ganglia. TCE exposure induced elevated ROS in DA neurons in the substantia nigra (SN), measured with 3-nitrotyrosine (3-NT) and 4-hydroxynonenal (4-HNE), paralleled by TCE-induced mitochondrial damage (pS65-Ub) and neuroinflammation (CD68), as well as TCE-induced DA neuronal loss. These were all significantly rescued by post-lesion treatment with MLi2 (***p=<0.001, ****p<0.0001). Our findings suggest that LRRK2 kinase activity has a role in PD-linked neurotoxicity. Inhibition of LRRK2 kinase activity through medication can protect against dopamine neurotoxicity by reducing oxidative stress, mitochondrial damage, mitophagy deficits, and neuroinflammation.

Poster 28

Cerebral cortex cell-type specific alternative splicing in a Schinzel-Giedion Syndrome patient variant mouse model

Emma F. Jones[1], Timothy C. Howton[1], Tabea M. Soelter[1], Brittany N. Lasseigne[1]

[1]Department of Cell, Developmental and Integrative Biology, Heersink School of Medicine, The University of Alabama at Birmingham

Introduction: Schinzel-Giedion Syndrome (SGS) is an ultra-rare Mendelian disorder caused by gain-of-function mutations in the SETBP1 gene. SGS symptoms include neurodegeneration, intellectual disability, and seizures and begin early in neurodevelopment. Alternative splicing (AS) is essential for neurodevelopment and neural cell type differentiation. While previous studies determined multiple roles for how SETBP1 and associated pathways may cause disease manifestation, they have not assessed whether AS plays a role in SGS.
Materials & Methods: We used STARsolo (v.2.7.10b) to quantify gene and splice junction expression for 51,465 cells previously generated from Setbp1S858R+/- SGS patient variant (n=3) and wildtype control (n=3) mouse snRNA-Seq cerebral cortex tissue. We annotated cell types with Seurat (v.5.0.0). We then performed pseudobulk differential gene expression and splice junction usage (SJU) analyses using DESeq2 (v.1.40.2) and MARVEL (v.2.0.5), respectively, across patient variant mice and wildtype controls.
Results: We found 34 cell-type-specific and shared genes with statistically significant (permutation test, $p<0.05$) alterations in SJU between patient variant and wildtype control mice. Oligodendrocytes had the most genes with changes in SJU (n=10), followed by astrocytes (n=9), excitatory (n=9), and inhibitory neurons (n=9). One gene, Son, a splicing cofactor known to cause the neurodevelopmental disorder ZTTK Syndrome, had SJU changes in all six non-vascular cell types in the Setbp1S858R+/ variant mice compared to controls.
Conclusion: This is the first research to report neural changes in AS in SGS and the first study to link SGS to changes in Son, which may help explain SGS's severe neurological phenotype.

Poster 29

Loss of estradiol promotes greater body weight dysregulation than exposure to high fat diet in female rats.

Savoya Simone Joyner, Lisa Eckel, Ph.D.[1]

[1]Florida State University

Introduction: Diet-induced obesity is studied primarily in male rodents despite well-documented sex differences in the neural control of energy balance. A small literature suggests that females are less susceptible to diet-induced obesity than males. This protection may arise from estradiol's (E2's) neuroprotective and anti-inflammatory effects.
Materials/ Methods: We examined how loss of E2 affects caloric intake, weight gain, and hedonic eating. Food intake and body weight were monitored for 4 weeks in ovariectomized (OVX) rats maintained on a standard chow diet with or without E2 replacement (OVX-veh, OVX-EB). Control (ovarian intact) rats were fed chow or 45% high-fat diet (HFD) (INT-chow, INT-HFD). Hedonic eating was also assessed in a 30-min chocolate Ensure "dessert" test administered immediately after the consumption of a satiating meal.
Results: Access to HFD led to a temporary increase in food intake in INT-HFD rats compared to INT-chow rats. OVX-veh rats, lacking E2, exhibited higher food intake and weight gain than OVX-EB rats. Interestingly, OVX-veh, chow-fed rats gained significantly more weight than INT-HFD rats (63.7±2.4 g vs. 35.2±3.2 g over 4 weeks). During the dessert test, OVX-oil rats consumed more chocolate Ensure than INT-HFD rats (23.1 ± 1.3 kcal vs. 12.4 ± 1.3 kcal).
Conclusion: Loss of E2 promotes greater weight dysregulation than exposure to an obesogenic diet. Ongoing studies are assessing whether loss of E2's anti-inflammatory effects mediates OVX-induced weight gain.

Poster 30

Influence of Biological Sex and Age on Alcohol Modulation of Synaptic Gating in Nucleus Core Medium Spiny Neurons.

Timmy Le,[1,2] Pablo Gimenez-Gomez,[1], Gilles E. Martin,[1]

[1]Department of Neurobiology, The Brudnick Neuropsychiatric Research Institute, University of Massachusetts Chan Medical School, Worcester, MA 01605
[2]Graduate Program in Neuroscience, Morningside Graduate School of Biomedical Sciences, University of Massachusetts Chan Medical School, Worcester, MA 01605

Binge alcohol drinking is a drinking pattern typically associated with adolescents and young adults. Bechara and Damasio postulated that alcohol exposure during adolescence weakens the frontocortial-reflective system, a system involved in decision-making and the ability to assess one's actions. Conversely, it strengthens the amygdala-impulsive system, which links pleasant or aversive stimuli to their emotional attributes. These two systems projects onto the nucleus accumbens (NAc), a brain region that plays a pivotal role in the reward circuit and addictive behavior. We recently reported that these competing cognitive and emotional inputs primarily converge onto NAc medium spiny neurons (MSN's), where they are processed, integrated, and translated into behavior through a phenomenon known as "synaptic gating." We also found that synaptic gating, defined as the ability of the neural circuit to facilitate or suppress specific inputs (i.e., emotional or cognitive), is sensitive to binge alcohol drinking. However, little is known about how sexes and age affect synaptic gating. Such an understanding can help elucidate the biological propensity as to why girls and young women from the ages of 12-20 years old are more likely to drink more alcohol than 12-20 years old boys and young men. To address this key biological question regarding sex and age differences, we expressed channelrhodopsin and chrimson in the medial prefrontal cortex (mPFC) and anterior basolateral amygdala (BLAa), respectively, of male and female C57BL/6 mice through stereotaxic surgery at four weeks old. Afterward, we performed NAc MSNs whole-cell recordings after independent light stimulation of BLAa and mPFC afferents at 6-, 8-, and 12-weeks old. We found that, in males, the ability of cortical inputs to inhibit the transmission of information from the BLAa region increases significantly in 8 weeks old mice compared to younger animals (i.e., 6-week-old). Interestingly, mPFC inhibition of BLAa transmission is strongest at 12-weeks old in females relative to 6- and 8-weeks old. Moreover, 20% ethanol negates the mPFC inhibition of the BLAa in both sexes. Our work suggests that the control of emotional and cognitive information in the NAc is a phenomenon that depends on age and sex.

Poster 31

Heterozygosity of the GBA1 L444P mutation impairs synaptic degeneration through lysosomal dysfunction.

Casey Mahoney-Crane[1], Sumedha Bobba[1], Eli Berry[1], and Laura A. Volpicelli-Daley Ph.D.[1]

[1]University of Alabama at Birmingham, AL, USA

Heterozygous mutations, in the GBA1 gene, are a common genetic risk factor for both Parkinson's disease (PD) and Dementia with Lewy Bodies (DLB). Clinically, heterozygosity of the GBA1 L444P mutation ($GBA1^{+/L444P}$) leads to a 5.6-fold increased risk of cognitive impairments, including dementia and spatial working memory impairments. However, the underlying mechanism behind cognitive impairment in GBA1-associated PD is not fully understood. In this study, we used $GBA1^{+/L444P}$ knock-in mice of both sexes and their wildtype littermates ($GBA1^{+/+}$) as controls, to determine the deleterious effects of this severe GBA1 mutation on nonmotor function and synaptic morphology. By 12-months of age, both cortical and hippocampal regions in $GBA1^{+/L444P}$ mice show a selective ~50% increase in inhibitory loci, yet no changes in excitatory loci count compared to wildtype ($GBA1^{+/+}$) mice. This excitatory and inhibitory imbalance may contribute to spatial memory deficits observed concurrently at 12-months of age, as determined by the Y maze behavioral tasks. To investigate overall lysosomal function, a DQ-BSA activity assay was used and determined that lysosomal function in hippocampal primary neurons was significantly reduced. Furthermore, *in vivo* analysis of immature and mature GCase will also be assessed in cortical brain regions. Collectively, lysosomal dysfunction may contribute to the increased memory deficits observed in mice expressing the GBA1L444P mutation. Significantly, elucidating the molecular mechanism behind cognitive impairments and synaptic changes will likely aid in the development of novel therapies that can efficiently slow the progression of Parkinson's disease.

Poster 32

Dopamine in the Tail of the Striatum Enhances Safety Learning

Emily Makowicz[1]**,** Adrien Stanley, Maria Concetta-Miniaci, Se Joon Choi, Anika Frank, Stefano Cataldi, Clay Lacefield, N Shashaank, and David Sulzer

[1]Columbia University

Associative learning is important for survival as it allows for identification of cues that signal rewards and punishments. Impairments in the associative learning can potentially lead to excessive reward seeking as occurs in drug addiction or excessive avoidance as in conditions such as post traumatic stress disorder (PTSD). Understanding how the brain forms associations is critical for identifying therapeutic targets for these disorders. One target shown to be important for associative learning is the striatum. The striatum is composed of distinct subregions, each contributing to different aspects of learning. Recently, the overall activity in the tail of the striatum (TS) has been shown to correlate with the association of auditory cues with safety. However, it was not known which striatal cell type shows this response or the causal role of this activity in safety learning. Here, using fiber photometry, I show that D1 spiny projection neurons (D1 SPNs) and D2 spiny projection neurons (D2 SPNs) exhibit distinct responses when cues are associated with safety versus threat. I also demonstrate using ex vivo electrophysiological approaches that this enhanced response is driven by reduced intrinsic excitability concomitant with enhanced postsynaptic plasticity at auditory thalamostriatal synapses.

Poster 33

Overview of the Progress of Factors in Learning and Plasticity (FLAP) at UAB

Elliot Maxwell[1],*, Madeline Ragland[1], Elam Cutts[1], Pinar Demiyarak[1,2], Hannah Cowart[1], Marcello Maniglia[3], Samyukta Jayakumar[3], and Kristina Visscher[1,2]

[1]Civitan International Research Center, University of Alabama at Birmingham, Birmingham, AL, [2]Department of Neurobiology, Heersink School of Medicine, University of Alabama at Birmingham, Birmingham, AL, [3]University of California Riverside, Riverside, CA

Factors in Learning and Plasticity (FLAP) is a multisite clinical research study that seeks to understand how the brain changes with increased peripheral vision use, in the hopes of developing alternative rehabilitation strategies for patients with Macular Degeneration (MD). MD is a retinal degenerative disorder caused by damage to the macula, which leads to progressive central vision loss. This study aims to gain insight into the most effective potential training strategies for patients with central vision loss. With improved training of remaining peripheral vision, MD patient may regain autonomy in day to day tasks that ordinarily require central vision.
This study analyzes the outcomes of multiple training types with each training type assessing a specific aspect of visual processing. By implementing a gaze-contingent display paradigm, participants are required to complete the task by using peripheral vision in the assigned training location instead of their central vision. To assess both behavioral effects and neural effects of training, participants in this study undergo a battery of visual assessments in addition to anatomical and functional MRI scans before and after training.
With an anticipated enrollment of around 60 individuals with MD and 100 healthy controls across the multiple sites, the study has currently enrolled nearly 25 participants at UAB with almost 10 completing the entire protocol. This study is expected to contribute to both the field of perceptual learning and the field of visual rehabilitation.
Key words: perceptual learning, central vision loss, peripheral vision

Poster 34

Alzheimer's Disease and Normative Aging Neuropathology in the Basolateral Amygdala of the TgF344 Rat

Macy A. McCuiston[1], Nateka L. Jackson[2], Lori L. McMahon[2], Lynn E. Dobrunz[3], Caesar M. Hernandez[1]

[1]Department of Medicine, Division of Gerontology, Geriatrics, and Palliative Care, The University of Alabama at Birmingham , [2]Department of Neuroscience, Medical University of South Carolina, [3]Department of Neurobiology, The University of Alabama at Birmingham

Fear impairments appear in non-pathologic aging in conjunction with impaired executive functions. There is a greater prevalence of fear-based disorders in older populations and even more so in those with Alzheimer's disease (AD). The basal amygdaloid nucleus is a part of central medial lobe structures that are involved in fear-based circuitry. We've seen an impairment in fear conditioning extinction in those with AD, who also have a higher prevalence of PTSD. This extinction impairment has been demonstrated in TgF344AD (AD) rats. To elucidate the change in BLA functionality during fear conditioning correlated with age and AD progression, we use in-vivo electrophysiology in-vivo fiber photometry in the BLA of wild-type (WT) and AD during fear conditioning at old and young adult ages. We hypothesize that being supplemented a daily keto diet can rescue fear extinction deficits through targeting mechanisms related to hyperexcitability and/or neuroinflammation in AD rats.

Poster 35

Defining the Role of Huntingtin and Mutant Huntingtin in Stress Granule Dynamics

Jharrayne McKnight[1], Keona Wang[1], Amber Keith[1],Thai Nguyen[1], Joan S. Steffan[1], Leslie M. Thompson[1]

[1]University of California Irvine, Irvine, CA 92697

Introduction: Huntington's disease (HD) is a genetic neurodegenerative disease caused by a CAG repeat expansion in the huntingtin gene (HTT)and translated into a mutant huntingtin (mHTT) protein. Expansion of ≥40 repeats is fully penetrant. There are no disease modifying treatments for HD and an effective treatment depends on understanding HTT's normal function and dysregulation caused by the mutation. Several processes mHTT dysregulates, including RNA binding protein dynamics and autophagy, are implicated in Stress Granule (SG) dynamics as part of cellular stress responses. SGs are a subtype of messenger ribonucleoprotein (mRNP) membrane-less complexes formed in response to various cellular stressors. The stress response and SGs have been linked to neurodegenerative diseases and we identified SG persistence in the HD brain. Data linking HTT and SG-related processes suggests a role for HTT and mHTT in regulation/dysregulation of SG dynamics via a role as an RBP.
Methods: This study utilizes immunofluorescence and confocal microscopy to identify how mHTT expression alters SG dynamics in isogenic pluripotent cell lines differentiated into medium spiny neurons (MSNs).
Results: Treating with acute sodium arsenite caused significant decreases in SG presence and related morphological parameters in ES-MSNs expressing mHTT compared to controls. Currently, I am investigating how changes in SGs are affected during dynamic stages of formation and clearance.
Conclusion: Understanding the role, whether direct or indirect, of both HTT and mHTT in SG dynamics may provide insights into mechanisms by which mHTT dysfunction contributes to disease pathology and inform future therapeutic strategies.

Poster 36

Ventral Pallidal Regulation of Motivated and Consummatory Behaviors

Mesco, A.[1], Fayette, N., Guaderrama S.D., Giannotti, G., Heinsbroek, J.A.

[1]University of Alabama at Birmingham

Introduction: The ventral pallidum (VP) is a central node within the ventral basal ganglia circuit that regulates motivated behavior and reward processing. While the VP has long been known for its role in modulating reward seeking behavior and food consumption, the comprehensive circuit mechanisms underpinning these effects remains largely unknown. Recent investigations, both from our lab and others, have notably implicated inhibitory (GABAergic) VP projection neurons in motivation and reward. However, GABAergic neurons of the VP comprise multiple subclasses, including fast-spiking neurons that produce parvalbumin (PV), and regular spiking neurons that produce the opioid neuropeptide enkephalin (Penk).

Methods: In this study, we interrogate the contributions of the overall population of VP_{GABA}, as well as the distinct VP_{Penk} and VP_{PV} subpopulations in mediating reward-seeking behaviors, employing optogenetic self-stimulation (SS) and real-time place preference (RTPP) assays. Furthermore, we probe the regulation of food consumption by these neurons in ad libitum fed mice.

Results: Optogenetic stimulation of VP_{GABA} neurons emerges as highly reinforcing, as it produces prominent SS, and RTPP. Concurrently, activating VP_{GABA} neurons also produces voracious consummatory behavior, with mice consuming up to 30% of their daily food intake (~1g) within a 30-minute interval. These effects are mediated by VP_{GABA} projections to the lateral hypothalamus (LH) and ventral tegmental area (VTA). Stimulating VP_{Penk} neurons partially recapitulates these effects, albeit VP_{Penk}-LH stimulation specifically elicits feeding behavior. Lastly, VP_{PV} stimulation fails to exert reinforcing effects and instead induces suppression of food consumption.

Conclusion: Collectively, these data indicate a differential regulation of motivated behaviors and food consumption by distinct subpopulations of VP neurons.

Poster 37

Identifying a novel role for meninges-derived retinoic acid in regulating neocortical neurogenesis

Danae Mitchell[1]

[1]University of Colorado Anschutz Medical Campus

Development of the central nervous system (CNS) requires precise intercellular 'crosstalk' between neural cells and non-neural cells. Fibroblasts in the meninges are an important regulator of neocortical development by secreting factors for neural progenitor differentiation and migration. Meningeal-derived retinoic acid (RA) is an important factor in neocortical development, underscored by significant defects in CNS development observed in mice and humans with mutations in FOXC1, a transcription factor expressed by meningeal fibroblasts but not any neural cells. Foxc1 mutants do not have normal meningeal fibroblasts over the forebrain, have increased apical progenitor self-renewal and reduced neuron production leading to neocortical lengthening, linked in part to lack of meninges derived retinoic acid. However, it is not known what aberrant signaling pathways in Foxc1 mutant apical progenitors promote increased self-renewal and how this is connected to a reduction of meninges derived factors like retinoic acid. Using spatial transcriptomics, CUT&RUN, ATAC-seq, and RNAscope on embryonic control and Foxc1-KO tissue sections, I identified that there is elevated Notch signaling, a pathway known to promote stem cell self-renewal, in Foxc1-KO neocortical progenitors that correlates with the emergence of meningeal-derived RA. Further, my work investigates how meningeal derived RA binds to its nuclear receptor in neural progenitors to transcriptionally modulate Notch signaling and Sox2 via Sox2ot to promote neurogenesis. Overall, the results from this project provide important insight into molecular mechanisms for meninges-brain signaling that is required for normal development.

Poster 38

Ventral Tegmental Area Oxytocin Receptor-Expressing Neurons Suppress Chow Intake in Mice

Patience E. Moseley, Lisa R. Anderson, Daniel O. Campos, Diana L. Williams[1]

[1]Florida State University

Pharmacologic treatment with oxytocin (OXT) suppresses food intake in multiple species. Ventral tegmental area (VTA) OXT receptors (OXTR) may play a role, because intra-VTA OXT suppresses intake and motivation for food. The OXTR is an excitatory receptor, therefore, we hypothesized that chemogenetic activation of VTA Oxtr neurons suppresses food intake. In a preliminary study, male and female OxtrCre mice received bilateral intra-VTA injections of AAV for Cre-inducible hM3Dq or mCherry. After recovery, they received intraperitoneal injections of either CNO or vehicle 20 minutes before dark onset, and CNO suppressed chow intake in male hM3Dq mice within 2 hours of dark onset. Tracing with an AAV for Cre-inducible synaptophysin-mCherry identified the nucleus accumbens (NAc) as a target of dense innervation by VTA Oxtr neurons. Therefore, we hypothesized that activation of VTA Oxtr neurons projecting to NAc mediate intake suppression. To test this, we induced hM3Dq expression only in VTA Oxtr neurons that project to NAc by bilaterally injecting rgAAV for Cre-inducible Flp into NAc and AAV for Flp-inducible hM3Dq or control mCherry into the VTA of male and female OxtrCre mice. The experiment proceeded as described above, and CNO significantly reduced dark phase chow intake in hM3Dq mice by 18-28% at timepoints from 4-12 h. There were no apparent sex differences. Taken together, our results suggest that VTA Oxtr neurons, particularly those projecting to NAc, control food intake.

Poster 39

Investigating the impact of C. amycolatum colonization on Parkinson's Disease pathology and neuroinflammation in the Thy1-SNCA PD mouse model

Nikhita Mudium[1], Woong-jai Won[2], and Ashley Harms[2]

[1]Department of Neurobiology, University of Alabama at Birmingham (UAB), Birmingham, Alabama [2]Department of Neurology, UAB Heersink School of Medicine, Birmingham, Alabama

Parkinson's Disease (PD) is a progressive movement disorder characterized by alpha-synuclein (a-syn) accumulation and the loss of dopaminergic neurons in the substantia nigra, a region responsible for regulating movement. Recent research suggests that the early pathology of PD is influenced by gut barrier deterioration or dysbiosis. Distinct gut microbial profiles have been shown to increase circulating inflammatory molecules and a-syn aggregates thus leading to neurodegeneration. A potential pathway through which gut bacteria can act is by modulating neuroinflammation, a key driver of neurodegeneration in PD. A recent study identified *Corynebacterium amycolatum*, an opportunistic pathogen, as disproportionately increased in human PD patients' gut. We hypothesized that *C. amycolatum* would enhance the PD behavioral phenotype, increase a-syn aggregation, and increase glial dysregulation in the Thy1-SNCA mouse model. Germ-Free Thy1-SNCA transgenic mice overexpressing human a-syn and non-transgenic controls either received or did not receive *C. amycolatum* transplants. The 6-month post-transfe cohort underwent two behavioral assays while brain tissue from both 1-month and 6-month cohorts were immunolabeled for misfolded a-syn, astrocytes, microglia, and MHCII, for neuroinflammation. Image J was utilized to assess microglial cell body area and branch number. 1-month post-transfer, the transgenic *C. amycolatum* transplant group demonstrated a significant decrease in microgliosis in the ventral midbrain (vmb) and striatum and a significant decrease in MHCII in the vmb. The 6-month cohort demonstrated fewer motor deficits and a decrease in a-syn aggregates. Interestingly, our study provides evidence that the *C. amycolatum* condition attenuates PD pathology and neuroinflammation, suggesting an early protective role of gut bacteria in the Thy1-SNCA mouse model.

Poster 40

Ventral Pallidal Regulation of Motivated and Consummatory Behaviors

O.P. Ngwu-Hyacinth[1], W.R. Willoughby[1] & M. Bolding[1]

[1]The University of Alabama at Birmingham, Birmingham, AL.

Introduction: The evolution of magnetic resonance imaging (MRI) has permitted the detection of angiographically occult vascular malformations, including cerebral cavernous malformations (CCMs). CCMs are vascular lesions found predominantly in the brain that may cause severe neurological symptoms and stroke. CCMs repeatedly hemorrhage and are permeated by iron-rich blood breakdown products (BBPs) whose compositions change in characteristic ways over time. Iron in BBPs is believed to have a strong positive correlation with CCM disease severity; however, iron disrupts the inhomogeneity of the MRI magnetic field, generating susceptibility artifacts that make these lesions difficult to interrogate with MRI. We propose *FerroQuant*, a novel multi-modal MRI technique, for detecting recent hemorrhage within a CCM lesion by measuring the concentration and ratio of BBPs and characteristic changes over time. We hypothesize that combining quantitative susceptibility mapping (QSM) with T1 and T2 mapping will allow simultaneous independent measurement of multiple BBPs.
Methods: Preliminary work was done on a CCM phantom (jelly beads containing 2g of Iron (III) citrate). MRI images were acquired at 3.0T. The mean susceptibility values of the CCM phantoms were correlated with the QSM-derived iron measurements in human patients.
Results: The CCM mimics appeared hyperintense on QSM, with susceptibility of iron averaging 2ppm, similar to the iron content of human CCM lesions (Tan et al., 2014).
Conclusion: In this experiment, we successfully estimated the iron concentration using QSM. Future experiments will apply T1 and T2 mapping to validate *FerroQuant*.

Poster 41

Forskolin reverses the O-GlcNAcylation dependent decrease in GABAAR current amplitude at hippocampal synapses possibly through action at the neurosteroid site on GABAARs.

Shekinah Phillips[1,2], John C Chatham[2], Lori McMahon[1]

Medical University of South Carolina[1], Department of Neuroscience Charleston, SC, University of Alabama at Birmingham[2], Cell, Department of Developmental, and Integrative Biology and Pathology, Birmingham, AL

Serine phosphorylation and O-GlcNAcylation are fundamental modulators of GABAARs, yet no study has examined whether they interact to control GABAAR function. Using forskolin to activate adenylyl cyclase and drive protein kinase A (PKA) dependent phosphorylation, we determined whether phosphorylation before and after increasing O-GlcNAcylation effects GABAAR function. Using whole-cell recordings of evoked IPSCs (eIPSCS) from CA1 pyramidal cells and dentate granule cells in acute slices from 3-5 week old male and female rats, we bath applied forskolin, either before or after bath application of glucosamine and the O-GlcNAcase inhibitor, thiamet-G. In CA1 pyramidal cells and dentate granule cells, prior forskolin had no effect on the magnitude of the O-GlcNAc dependent depression of eIPSC amplitude. However, in both CA1 and dentate, a prior increase in O-GlcNAcylation elicits a forskolin-dependent increase in IPSC amplitude, reversing the O-GlcNAc-induced depression. To confirm forskolin was working via PKA, we used the PKA inhibitor, KT5720 and adenylyl cyclase inhibitor SQ22536, separately. Surprisingly, neither inhibitor prevented the forskolin dependent increase in GABAAR current amplitude following a prior increase in O-GlcNAcylation, indicating this potentiation occurs through another mechanism. Interestingly, the inactive forskolin analog, 1,9-dideoxyforskolin, also elicited a significant potentiation of eIPSC amplitude, consistent with a non-PKA dependent mechanism. A previous study in carp amacrine-like cells (Li& Yang, 2001) found that forskolin can act directly at the neurosteroid site on GABAARs. We found that following a prior increase in O-GlcNAcylation, 5α-pregnane-3α,21-diol-20-one (THDOC) and progesterone application mimics forskolin, indicating O-GlcNAcylation enhances access to the neurosteroid site on GABAARs.

Poster 42

Investigating the Genetic Vulnerability of Adolescents to Nicotine Exposure

Roshae Roberts[1], Shahrdad Lotfipour[1]

[1]University of California Irvine

Introduction: In 2023 over 6.2 million middle and high schoolers reported having tried a tobacco product in the US. Adolescents are vulnerable targets of the tobacco industry and experience increased susceptibility to long-lasting changes induced by nicotine on the brain. Clinical studies highlighted a mutation in the CHRNA6 gene that results in a 'C' to 'G' allele change that correlates with higher levels of nicotine use and dependence. This mutation impacts the alpha (α) 6 subunit of the nicotinic acetylcholine receptor (nAChR). Nicotine directly activates α6 nAChRs in dopamine (DA) neurons. To assess the role of this mutation in adolescent nicotine use, our lab engineered a rat line containing this genetic variant. Studies in this line demonstrate sex- and genotype-dependent effects in brain neurotransmitter levels, and nicotine-induced anxiolytic and locomotor behavior. My central hypothesis is that nicotine induces neurotransmitter level changes in brain reward regions and underlies the sex and genotype-dependent behavior observed.
Materials & Methods: Using High-Performance Liquid Chromatography- Electrochemical Detection (HPLC), I will assess brain neurotransmitter level alterations in the human CHRNA6 3'- UTR SNP animals after an initiation dose of nicotine, modeling a 2-4 cigarette first exposure.
Results: Preliminary results indicate a continued sex and genotype-dependent phenotype in addiction-related behaviors. Neurotransmitter profiles should mirror this pattern of expression.
Conclusion: This will provide novel mechanistic insight into understanding nicotine addiction in adolescence and contribute to screening biomarkers for risk prevention and intervention.

Poster 43

Changes in intrinsic excitability in a population of withdrawal-activated neurons in the medial prefrontal cortex of alcohol self-administering mice

Sierra Rodriguez[1], John O'Brien, Yi Luo, Sanjana Tata, Jonathan James, Aaron John, Tanav Chachad, Giana Abraham, Abigial Nguyen, Amaan Khan, Sophia Jalilvand, Aamna Khan, Neha Suji, Sven Kroener

University of Texas Dallas[1]

Introduction: Alcohol use disorder (AUD) impairs the prefrontal cortex (PFC) and compromises cognitive and executive functions, leading to heightened risk of relapse. In rodent models, activation of the prelimbic (PL) or infralimbic (IL) regions of the PFC are thought to promote alcohol intake or aid the extinction of drug memories. Within these regions, neurons may show heterogeneous responses to alcohol (EtOH).
Materials & Methods: Using a transgenic mouse line (TRAP2/Ai9) which tags active populations with fluorescence, we identified mPFC neurons that were active during withdrawal in mice self-administering EtOH or sucrose. We conducted whole-cell patch-clamp current-clamp recordings in PL and IL neurons that were either active (Ai9+) or inactive (Ai9-) following an18-hour withdrawal.
Results: Sucrose initially had higher response rates, but during cue-induced reinstatement, EtOH mice showed similar responses, suggesting EtOH's reinforcing properties. Neurons in mPFC of EtOH mice exhibited increased excitability compared to sucrose controls. Withdrawal activated neurons Ai9+ in IL and PL fired more action potentials, while no intrinsic excitability differences were observed in Ai9- cells between groups. Lower rheobase currents and AHP amplitude in EtOH Ai9+ cells reflected increased excitability. Acute alcohol application (20 mM) reduced activity in EtOH Ai9+ neurons without affecting Ai9- neurons in both PL and IL cortices.
Conclusion: Overall, our results highlight a potential withdrawal neuron population in the mPFC. Ongoing experiments are identifying the role of withdrawal neurons during cue-induced reinstatement using immunohistochemistry. Further research is essential to understand the precise neurophysiological mechanisms of alcohol withdrawal, leading to more targeted treatments for AUD.

Poster 44

Hand and eye movements during object categorization discriminate between younger and older adults

Valerie Sainterant[1], Ryan A. Kretschmar[2], Emma Stovall[2], Jonathan E. Chisolm[2], Patrick Tootle[2], Valery Sastoque[2], Sophie Allen[2], Jessica Moser[3], Chris B. Martin[1,2]

[1]Program in Neuroscience, Florida State University
[2]Department of Psychology, Florida State University
[3]Department of Neuroscience, Wayne State University

The ability to flexibly categorize objects is an essential aspect of adaptive behavior. In complex environments with rapidly changing task demands, accurate categorization requires the resolution of feature-based interference. Recent neuroimaging and neuropsychological evidence suggest that perirhinal cortex allows us to group objects based on either their semantic or visual features when faced with cross-modal interference. We build on these findings by asking whether hand and eye movements made in the context of categorization tasks with cross-modal interference discriminate between younger and older adults. We additionally examined whether these behavioral indices track overall cognitive status in older adults. Three objects were presented on each trial: a referent, a target, and a distractor. Targets in the visual categorization task were visually similar to the referent, whereas distractors were semantically similar to the referent. Targets in the semantic categorization task were semantically similar to the referent, whereas distractors were visually similar to the referent. Categorization decisions were made by touching targets in our motion-tracking experiment and with a button press in our eye-tracking experiment. We found that reach trajectory and gaze, which are continuous measures of decision making, reliably discriminated between younger and older adults. In both cases, older adults were influenced by the distractors to a greater degree than were younger adults. Most interestingly, reach and gaze were significant predictors of overall cognitive function in the older adult group. These findings suggest that hand and eye movements may reveal subtle age-related changes in cognitive functions supported by perirhinal cortex.

Poster 45

Prolonged ocular hypertension in the living human eye causes a selective loss of the PhNR

Ryan G. Strickland[1,2], Mary Anne Garner[1,2], McKenna M. Somerville[1,2], Thomas A. Swain[2], Massimo A. Fazio[2], Alecia K. Gross[1], Christopher A. Girkin[2]

Departments of Neurobiology[1] and Ophthalmology and Visual Sciences[2], Heersink School of Medicine, University of Alabama at Birmingham, Birmingham, AL, USA

Introduction: We have previously demonstrated that transient elevation of intraocular pressure (IOP) in the living eye of brain-dead organ donors resulted in a selective reduction of the photopic negative response (PhNR) amplitude and that this loss is dependent on ocular perfusion pressure (OPP). To investigate the initial cellular responses to elevated IOP, we have developed an approach to elevate IOP in the living human eye targeting 8-10 hours of elevation. We aim to determine if there is selective diminishment of the PhNR amplitude, or if there is a more generalized inner retinal dysfunction seen over the course of many hours.
Methods: Thirteen research-consented brain-dead organ donors underwent screening. Blood pressure was measured via an arterial line, and IOP was measured using a tonometer. PhNR was measured using modified full-field electroretinography with DTL Plus electrodes. The experimental eye received an injection of viscoelastic to achieve an IOP of 30 – 40 mmHg while the fellow eye served as a control. Blood pressure, IOP, and PhNR were recorded every 2 hours until organ procurement.
Results: IOP was significantly elevated, and OPP was significantly diminished post-injection. For up to 8 hours post-injection, the PhNR amplitude was significantly diminished relative to baseline. Generalized estimating equations demonstrated a significant association between PhNR amplitude and OPP.
Conclusions: Prolonged IOP elevation persistently diminishes the PhNR response without substantially altering photoreceptor function. Some donors also demonstrated diminished b-wave responses at later timepoints which will allow us to elucidate mechanisms of biomechanical versus ischemic injuries of the retina and optic nerve head.

Poster 46

Clinical and neurobiological heterogeneity in first-episode psychosis patients: A normative modeling approach.

Teles M[1], Remiszewski N, Rutherford S, Marquand A, Kraguljac NV[2]

[1]University of Alabama at Birmingham, [2]Ohio State College of Medicine

Introduction: Normative modeling is a novel approach to investigate heterogeneity in structural brain pathology. The deficit syndrome (DS) is a subtype of schizophrenia characterized by primary and enduring negative symptoms and thought to be clinically more homogeneous than non-deficit schizophrenia (NDS). We employed a normative model of cortical thickness to investigate differences in neurobiological heterogeneity between DS and NDS first-episode psychosis patients. We hypothesized that DS patients would present reduced variance and mean in the number of cortical thickness deviations than NDS.
Materials and Methods: We applied a normative modeling approach to T1-weighted MRI data. We quantified individual region-level structural deviations from a reference cohort (defined as >±2SD) in cortical thickness in DS and NDS patients. Patient groups were contrasted on variance and mean.
Results: Twenty-nine antipsychotic medication-naïve first-episode psychosis patients included in the analysis displayed features of DS, while 72 patients did not. DS patients had lower variance in the number of cortical negative deviations than NDS ($F=6.27$, $p=.01$). DS patients had a lower mean number of cortical negative deviations (2.58 ± 2.96) than NDS (4.77 ± 6.36), ($t(84.16)=2.32$, $p=.02$). There were no patient group differences in variance and mean number of cortical positive deviations. Patient groups presented few shared abnormalities in regional cortical deviations.
Conclusion: We observed reduced neurobiological heterogeneity in DS patients, supporting the idea that DS is a more homogeneous and distinct subtype of schizophrenia. Normative modeling effectively captured individual-level cortical brain pathology and evidenced inter-individual variability. This contributes to our understanding of the pathophysiology of DS.

Poster 47

Amygdala Crh cell activity required for territorial aggression

Emily L. Newman[1], **Khalil J. Threadgill[1]**, Kerry J. Ressler[1]

[1]Psychiatry, McLean Hosp., Belmont, MA; Harvard Med. Sch., Boston, MA

Introduction: 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 and self-defensive inter-male aggression.
Materials and Methods: During 5-min resident-intruder confrontations, a submissive intruder male was placed into the territory of the aggressive resident CRH-ires-Cre male and aggressive behavior was quantified as latency to the first bite and total bite frequency. Aggressive resident males received intra-CeA adeno-associated virus (AAV) for Cre-dependent expression of designer receptors activated exclusively by designer drugs (DREADDs; hM3Dq, hM4Di) or control virus in Crh+ CeA neurons. After recovering from surgeries, mice were tested for aggression after receiving systemic vehicle or deschloroclozapine (DCZ) for chemogenetic manipulation of *Crh*+ CeA neurons. Territorial aggression tests were conducted using submissive intruders and self-defensive aggression tests using aggressive intruders.
Results: Chemogenetic inhibition of *Crh*+ CeA cells blocked aggression in territorial aggression tests but did not block self-defensive retaliation during self-defensive aggression tests. Chemogenetic activation of Crh+ CeA cells increased 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 48

Investigating the role of ADGRB3 loss of expression in brain tumor formation in Li-Fraumeni Syndrome

Alex Torrelli-Diljohn[1,2], Svetlana Komarova[2], Benjamin Lin[3], Vipul Sheth[4], Abigail Shelton[3], Ryan Bash[3], Paran Goel[4], Jeremy Foote[5], 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, [5]Comparative Pathology Lab

Introduction: Li-Fraumeni syndrome (LFS) is a rare cancer predisposition syndrome caused by a germline mutation in the TP53 tumor suppressor gene. Glioblastoma (GBM) is the most prevalent central nervous system (CNS) tumor in LFS, with TP53 mutations detected in 30% of all GBMs. GBM is the most aggressive primary neoplasm of the brain that affects adults, and the prognosis for this condition remain dismal with a median survival of 12-15 months post-diagnosis. In recent studies, the dysregulation of adhesion G-protein coupled receptors (GPCRs), have been implicated in GBM development. Brain angiogenesis inhibitor 3 (BAI3), is a member of the BAI1-3 subfamily of adhesion GPCRS and is known to have heightened expression in neuronal and glial cells. Loss of ADGRB3 expression has been observed in brain tumors, but the significance of this observation has not been investigated.
Materials & Methods: To investigate the molecular mechanisms underlying brain tumor formation in LFS patients and the role of Tp53 and BAI3, we developed an LFS mouse model and isolated GBM stem cells (GSCs) for further analysis. These mice carry a germline Tp53 deletion and a second floxed allele under the control of Nestin-Cre. Additionally, these mice were crossed to Bai3-/- mice.
Results: Preliminary findings indicate that the simultaneous loss of Bai3 and Tp53 expression in our mouse model increased the incidence of spontaneous brain tumor formation from 36% to 71%, in contrast to the loss of p53 alone. The remaining mice lacked brain tumors, but had other malignancies (sarcomas, etc.) as observed in patients.
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 49

Effects of the β2 nAChR on acquisition and motivation for nicotine self-administration

Walker, N., Tucker, B. R., Thomas, L. N., Tapp, A.E. & Drenan, R. M[1]

[1]Wake Forest University School of Medicine

Despite nicotine's status as a weak reinforcer, cigarette smoking is the leading cause of preventable death worldwide highlighting a disparity between the 70% of smokers who desire to quit and the 8% of successful quit attempts persisting 6-12 months. The β2 nicotinic acetylcholine receptor (nAChR), a subunit highly expressed in the mesolimbic dopamine pathway and throughout the CNS, has been shown to play a key role in several nicotine related processes including but not limited to nicotine-elicited firing of dopaminergic neurons, dopamine release in the nucleus accumbens, nicotine-stimulated locomotor activation, and maintenance of nicotine self-administration. In this study, we tested the hypothesis that ventral tegmental area (VTA) β2 nAChR activation increases motivation to self-administer nicotine. We expressed a virus containing a hypersensitive mutation of the β2 nAChR (β2L9S) which allows for selective activation of β2* nAChRs using low doses of nicotine and have shown VTA β2 activation to be sufficient for nicotine reinforcement in rats. However, the role of this subunit in motivation is unclear. Cohorts of rats self-administered different doses of nicotine each separated by a 2.7-fold increase ranging from 1.5 µg/kg to 30 µg/kg in Sprague-Dawley rats and from 0.08 µg/kg to 30 µg/kg in β2L9S rats. Rats then underwent 17 self-administration sessions on a fixed-ratio 1 (FR1) schedule followed by 5 progressive ratio (PR) sessions. These results, in addition to providing a behavioral dose-response curve for Sprague-Dawley and β2L9S rats, also provide novel insights on the role of VTA β2 nAChR activation on motivation.

Poster 50

Exploring the role of serotonergic and inflammatory signaling in a model of Autism Spectrum Disorder

Allison E. Walsh[1], Natalie Souza[2], Rania M. Katamish[1], Hideki Iwamoto[1,3], Paula A. Gajewski-Kurdziel[1], and Randy D. Blakely[1,3]

[1]Department of Biomedical Science, Charles E. Schmidt College of Medicine and [2]Wilkes Honors College
[3]Stiles-Nicholson Brain Institute, Florida Atlantic University, Jupiter, FL, 33458

Autism Spectrum Disorder (ASD), a neurodevelopmental disorder with complex etiology affects 1 out of every 36 children in the US, with a ~4-1 male diagnostic bias. ASD is characterized by rigid repetitive behaviors and social and communication deficits, and has been linked to varied aspects of immune dysfunction. Up to 25% of ASD patients display an elevation of whole blood 5-HT levels, known as hyperserotonemia. Additionally, the connection between 5-HT and immune dysfunction are of significant interest in relation to disease etiology and possible treatment. 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, inhibiting p38a MAPK in 5-HT neurons 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 changes in a sex-specific and region-specific manner. Ongoing studies seek to 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 51

Closed-Loop Approaches to Cognitive Training for Enhancing Processing Speed

Weber AM, Visscher KM, McGregor KM[1]

[1]The University of Alabama at Birmingham

Processing speed can be defined as the amount of time it takes to extract, synthesize, and respond to presented information. Processing speed, along with other cognitive domains, declines as a function of age. Aging-related decline in cognitive functioning, including working memory, may be explained by a general slowing of this information processing, although it is not fully understood. Specifically, older adults tend to report difficulties in everyday tasks that rely on the ability to suppress irrelevant, or distracting, visual information, which may interfere with processing efficiency. A proposed mechanism by which the brain selectively inhibits irrelevant visual processing is by alpha oscillations (8-12 Hz) in the occipitoparietal cortex. Alpha activity, as measured by electroencephalography (EEG), can be thought of as a "sensory gate" to incoming stimuli, with increases in activity to suppress distractors and decreases in activity to enhance targets in visual attention tasks. Older adults do not modulate alpha as younger adults; however, limited research to date has reported stronger overall alpha modulation when people are better at suppressing irrelevant information. The goal of this study is to evaluate the effects of occipitoparietal alpha band EEG neurofeedback on cognitive performance, including processing speed, across age groups. The first session will consist of cognitive and behavioral assessments in which the primary outcome measure is DSST. The second session will consist of a visual attention assessment utilizing EEG. Participants will return for three subsequent neurofeedback training sessions involving alpha modulation using EEG. Participants will then repeat the behavioral and visual attention assessments at their sixth and final session. Our Study Aim 1 will determine the relationship between alpha modulation and cognitive performance, including processing speed. We hypothesize that participants who better modulate alpha will have better measures of cognitive performance. Further, we hypothesize that younger adults will exhibit better alpha modulation and have better cognitive performance compared to older adults. Our Study Aim 2 will evaluate the effects of alpha modulation neurofeedback training on cognitive performance, including processing speed. We hypothesize that neurofeedback training will improve cognitive performance, including processing speed, and we expect older adults to show greater changes in alpha modulation and cognitive measures compared to younger adults.

Poster 52

Striatal Astrocyte and Interneuron Activity Revelations from a Mutant Huntingtin Mouse Model

Jewel Hairston[1], Michelle Gray[1]

[1]The University of Alabama at Birmingham

Huntington's disease (HD) is a rare neurodegenerative disease caused by a CAG trinucleotide repeat expansion in the Huntingtin gene resulting in an expansion of a polyglutamine repeat in the Huntingtin protein. HD results in degeneration of striatal medium spiny neurons (MSNs). The MSNs are controlled by extrinsic glutamatergic input from cortex and thalamus, extrinsic GABAergic input, and intrinsic inhibitory input from striatal GABAergic interneurons, particularly somatostatin-expressing interneurons (SST-INs) and parvalbumin-expressing interneurons (PV-INs). The balance of input onto the striatal MSNs ensures their proper function which impacts the various striatal circuits that contribute to motor, limbic, and cognitive activities.

Astrocytes are also important contributors to the striatal circuit. Striatal astrocytes respond to GABA application as well as endogenous GABAergic activity with Ca2+ elevations. In cortex, astrocytes are more sensitive to SST-IN activity than PV-IN activity. Astrocytic Ca2+ responses strengthened when evoked by SST-IN stimulation and weakened when evoked by PV-IN stimulation. In hippocampus, astrocyte activity was shown to enhance SST-IN inhibition of pyramidal neurons. This response was not seen in PV-INs. However, the interactions of PV-Ins and SST-INs and astrocytes have yet to be studied in striatum.

In this work we will use aged BACHD mutant huntingtin expressing mouse model displaying motor abnormalities, and wildtype mice to explore spontaneous astrocytic Ca2+ elevations in the striatum. We have injected these mice with AAV5-gfaABC1D-cyto-GCaMP6f to measure spontaneous Ca2+ signals in preliminary experiments and carried out successful data collection from these astrocytes in slice. Furthermore, we have bred SST-Cre and PVB-Cre mice with Ai32 Cre-dependent Channelrhodopsin (ChR) expressing mice and will inject them with AAV5-gfaABC1D-cyto-GCaMP6f to explore responses of astrocytes to SST and PVB interneuron activation. We show cell type specificity of expression of ChR in SST and PVB interneurons. Together, these experiments will be used to reveal fundamental interactions of striatal astrocytes and interneuron populations and striatal astrocytic Ca2+ activity in the aged BACHD mutant huntingtin expressing mouse model.

Poster 53

Human Breast Milk-Derived Exosomes Attenuate Lipopolysaccharide-induced Activation of CD40 and NLRP3 through CD9 Mediated Regulation of Microglia

Oluwatomi Akinduro[1], Sanjay Kumar[1], Yuechuan Chen[2], Quamarul Hassan[2] and 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

Microglia are intrinsic mediators of the CNS immune response, which can be induced by a variety of insults including lipopolysaccharide (LPS), a bacterial endotoxin that is a common instigator of neuroinflammation in the neonatal population, especially preterm infants. Both CD40 and NLRP3 are products of the canonical NF-ĸB cascade as they are transcribed by the phosphorylated NF-ĸB p50⁄p65 heterodimer in LPS-induced microglia. Exosomes are nano-sized vesicles (40-150 nm) involved in intercellular communication and implicated in numerous pathophysiological processes. Human breast milk is rich in exosomes and plays a vital role in neonatal immune system maturation and adaptation through the proteins, lipids, and genetic material they carry. Activated microglia are a potential cause of brain-associated injuries⁄disorders; therefore, we hypothesized that human breast milk derived exosomes (HBMDE) attenuate LPS-induced activation of CD40, NLRP3, and IL-1β by decreasing p38 MAPK and NF-ĸB p65⁄p50 activation⁄phosphorylation downstream of TLR4 in microglia. Furthermore, we suggest this occurs, at least partially, due to the exosome marker CD9 and its interference with the functionality of the TLR4 complex. To test our hypothesis, HBMDEs were isolated, purified, and characterized. BV2 and HMC3 microglia were exposed to LPS (1 µg⁄mL), HBMDEs (10 µg⁄mL), and a CD9 blocking antibody. Our findings suggest that HBMDEs significantly modulate the expression of CD40, NLRP3, cytokines IL-1β and IL-10, nitric oxide, and signaling molecules in the canonical NF-ĸB pathway, including p38 MAPK which has input both within this pathway and independently. These changes were reversed in LPS-induced HMC3 cells that were also exposed to anti-CD9. In brief, HBM-derived exosomes exhibit great potential in attenuating CD40 and the NLPR3 inflammasome expression in the microglial response to LPS through CD9 and thus decreasing the exaggerated neuroinflammatory response.
Key words: Lipopolysaccharide; Neonatal Neuroinflammation; Breast milk; Exosomes; CD9; BV2 microglia; HMC3 microglia; NF-ĸB; p38 MAPK; CD40; NLRP3; IL-1β; IL-10

Poster 54

Depletion of Hemopexin Is a Predisposing Factor in Bladder Hypersensitivity Induced by Acute, but not Repeated, Psychological Stress Exposure

Gryshyna, A. E., Vendrame, F., Ricart, K., Patel, R. P., DeBerry, J. J.
University of Alabama at Birmingham

Introduction: Psychological stress is known to contribute to pelvic hypersensitivity; however, the exact relationship between pelvic hypersensitivity and stress is unknown. Hemopexin (Hpx) is an anti-inflammatory protein with high binding affinity for heme. In patients with urological hypersensitivity, Hpx is shown to be depleted suggesting a possible contribution to nociception.
Methods: Female Hpx knockout (KO) and wildtype (WT) mice were exposed to acute or repeated water avoidance stress (WAS) to induce psychological stress. Bladder hypersensitivity was assessed via visceromotor response (VMR) to urinary bladder distensions (UBDs). Spinal neuronal activity was also measured at baseline. Plasma heme levels were measured to explore hemolytic changes in these animals.
Results: No baseline differences were found in VMRs or spinal neuron activity ($p>.05$). However, acute WAS significantly increased UBD-evoked VMRs in Hpx KO mice ($p<.01$), with no noted changes after repeated WAS ($p>.05$). Baseline plasma heme concentrations were higher in Hpx KO than WT ($p<.05$), with no change post-stress.
Conclusions: Hpx depletion is associated with urologic pain induced specifically by acute psychological stress. This effect, which is not explained by total circulating heme levels, does not appear to be elicited under repeated stress conditions indicating the potential for adaptation over time. Further research into Hpx may identify therapeutic targets for stress-related bladder pain in chronic pelvic pain syndromes.

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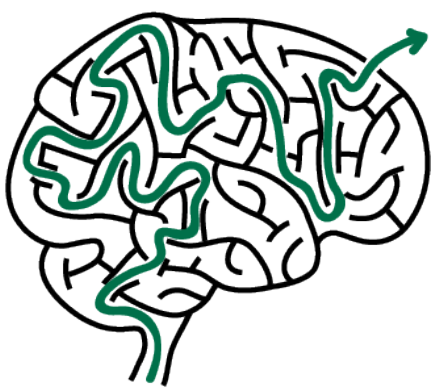

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