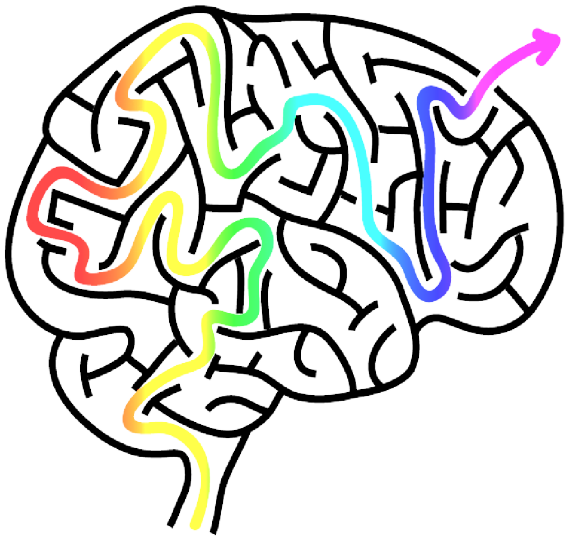
11th Annual NEURAL Conference 2025



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

June 11-13

University of Alabama at Birmingham
Birmingham, AL

UAB The University of Alabama at Birmingham

Neuroscience Roadmap Scholars

Our mission is to enhance engagement and retention of graduate trainees with diverse life experiences, perspectives and viewpoints in the neurosciences.

Use hashtag #NEURAL2025 on your social media posts!

@UAB_NeuroRMS

UAB_NeuroRMS

UAB.Neuroscience.Roadmap.Scholars

@uabneurorms.bsky.social

Table of Contents

Welcome

Dear Attendee:

Welcome to the 11th 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 graduate trainees with diverse life experiences, perspectives and viewpoints in the neuroscience workforce.

This year marks the 11th anniversary of the UAB Neuroscience Roadmap Scholars (RMS) Program and the NEURAL Conference. Launched in 2014, RMS was 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 neuroscience graduate trainees with diverse life experiences, perspectives and viewpoints.

For the past 11 years, the NEURAL Conference has annually hosted neuroscience trainees 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. The conference gives UAB Roadmap Scholars the opportunity to develop leadership skills by helping to determine the conference agenda.

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 neuroscientists reach their full potential.

Best regards,

Farah D. Lubin, PhD, FAES
Distinguished 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., FAES
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

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 Manager I, UAB Neuroscience Roadmap Scholars Program and NEURAL Conference
Department of Neurobiology

Agenda

Wednesday, June 11, 2025 - Birmingham Museum of Art

12:00-5:00 pm	Arrivals & Check In at McMahon Hall (for NEURAL Travel Award recipients only) (1600 10th Ave S, Birmingham, AL 35205)
5:30 pm	Shuttle begins from McMahon Hall (5:30 pm) and UAB Hilton (5:45 pm) to Welcome Reception (shuttle has limited capacity and is for NEURAL Travel Award recipients and Keynote Speakers only)
6-7:30 pm	Welcome Reception (all NEURAL registrants are welcome to attend) Birmingham Museum of Art 2000 Reverend Abraham Woods Jr Blvd, Birmingham, AL 35203
7:30 pm	Shuttle from BMA to McMahon Hall and UAB Hilton (for non-UAB guests only)

Thursday, June 12, 2025 - UAB Alumni House (1301 10th Ave S)

8:00 am	Shuttle begins from McMahon Hall (8:00 am) and UAB Hilton (8:15 am) to Alumni House (for non-UAB guests only)
8:30 am	Breakfast
8:45 am	Opening Remarks & Ice Breaker: Farah Lubin, Ph.D. Director, NEURAL Conference and UAB Roadmap Scholars Program
9:00-10:20am	**Oral Session I**
9:00-9:20	Katherine Canada: "DLG4-GRIN2B Complex: A Critical Convergence Point Between Autism Genetics and Functional Connectivity"
9:20-9:40	Kanisa Davidson: "Proteasome activator mitigates amyloid induced toxicity and cognitive deficits"
9:40-10:00	Alexander Foden-Pérez: "Glia control experience-dependent plasticity in an olfactory critical period"
10:00-10:20	Helen Brinyark: "Resonance-guided Stimulation to Evoke Seizure Activity in Epileptogenic Brain Networks"
10:20-10:30 am	Break
10:30-11:15 am	**Professional Development Session I: "**Overcoming Imposter Syndrome" Dr. Laurence Boitet, Assistant Professor and Director of Trainee Wellness, Department of Medical Education
11:15-11:25 am	Break
11:25 am-12:10 pm	**Panel: New Pathways to Enhance Neuroscience Training**
12:15-1:00 pm	Lunch and Networking
1:00-2:00 pm	**Keynote Speaker I:** Jennifer Tudor, Ph.D. "Sleep is where memories and metabolism meet"
2:00-2:10 pm	Break

Thursday, June 12, 2025 - UAB Hilton - Hamilton Ballroom (808 20th St. S.)

2:10-3:30 pm	**Oral Session II**
2:10-2:30	Elizabeth Castro: "Adolescent Structural Whole-Brain Changes After Sport-Related Concussion"
2:30-2:50	Cydney Martin: "Limbic neuropeptides may mediate sex differences in affective behavior changes following repetitive mild traumatic brain injury in adolescent rats"
2:50-3:10	Bryana Whitaker Hardin: "Ovarian hormone regulation of basolateral amygdala activity during valence processing"
3:10-3:30	Melissa Do: "A Pilot Study of Transdermal Auricular Vagus Nerve Stimulation for Treating Insomnia in Breast Cancer Patients"
3:30-3:40 pm	Break
3:40-4:40pm	**Keynote Speaker II:** Corey Harwell, Ph.D. "Development and Functional Diversity of Neural Cell Types in the Septum"
4:50 pm	Shuttle departs from the UAB Alumni House to the UAB Hilton - Hamilton Ballroom (808 20th St. S.)
5:00 pm	Dinner Reception for NEURAL Guests & Speakers, Poster Hanging
6:00 pm	Poster Session (hors d'ouevres served)
8:15 pm	Shuttle departs from UAB Hilton to McMahon Hall (for non-UAB guests only) (1600 10th Ave S, Birmingham, AL 35205)

Friday, June 13, 2025 - UAB Alumni House (1301 10th Ave S)

8:00 am	Shuttle begins from McMahon Hall (8:00 am) and UAB Hilton (8:15 am) to Alumni House (for non-UAB guests only)
8:30 am	Breakfast
9:00-10:00 am	**Keynote Speaker III:** Matia Solomon, Ph.D. "Neurons and Networks: My Journey as a Neuroscientist in Academia, Industry, and in the Community"
10:00-10:10 am	Break
10:10-11:30 am	**Oral Session III**
10:10-10:30	Princess Felix: "Knockdown of the glucocorticoid receptor (GR) in a corticostriatal pathway increases the propensity to attribute incentive salience to a reward cue"
10:30-10:50	Saurav Gupta: "Nociceptive Aβ-Afferent Neurons Mediate Mechanical Allodynia in Oxaliplatin-Induced Neuropathy"
10:50-11:10	Jazmin Corral: "Calcium signaling in Schwann cells development and myelination"
11:10-11:30	Gabrielle Blahusiak: "Investigating a Link Between Cytomegalovirus Infection and Cognitive Decline in a Mouse Model of Alzheimer's Disease"
11:30 am-12:30 pm	Lunch and Networking
12:30-1:15 pm	Shark Tank

Friday, June 13, 2025 - UAB Alumni House (1301 10th Ave S)

1:15-2:00 pm	**Professional Development Session II:** "Conflict Resolution between mentors and trainees" Michelle R. Horvath, University Ombudsperson Office of the Ombuds, University of Alabama at Birmingham
2:00 pm	Awards & Closing Remarks - Presenting Awards for Best Oral Presentation, Best Poster, and Shark Tank - Presenting RMS Outstanding Faculty Awards
2:30 pm	Adjourn Shuttle bus from UAB Alumni House to McMahon Hall

Keynote Speaker

Corey Harwell, Ph.D.
Associate Professor, Neurology
University of California San Francisco

Biography:
Corey Harwell is an associate professor in the Department of Neurology at the University of California, San Francisco. Dr. Harwell had originally planned to go to medical school, and initially began doing research to set himself up as a competitive applicant. However, his participation in a UCSF summer research program set him on the path to graduate school in neuroscience. He obtained his Ph.D. at the Massachusetts Institute of Technology in the laboratory of Elly Nedivi, where he studied the role of CPG15 and its protein product in neural development and plasticity. His experience in the Nedivi lab sparked his desire to become an independent investigator. He completed a postdoctoral fellowship in Arnold Kriegstein's laboratory at the University of California, San Francisco, studying the development and formation of cortical circuits. After completing his postdoctoral training, Dr. Harwell accepted a tenure-track position in the Department of Neurobiology at Harvard Medical School, where he was awarded a K01 and R01 by NINDS. In 2021, his laboratory moved to UCSF.

The Harwell lab is focused on understanding how the extensive morphological, molecular and functional diversity of neural cell types is achieved during development of the central nervous system. They focus their studies on the forebrain, with particular attention to the cortex and the septal nucleus of the basal forebrain. Their long-term goal is to understand how genetic and epigenetic programs associated with a progenitor cells spatial and temporal identity dictates their fate choice. They are also interested in understanding how these diverse groups of neurons and glia coordinate to assemble the precise circuitry of the mammalian forebrain.

Dr. Harwell has emphasized the impact of mentorship along his scientific career journey: "Choosing your mentors wisely to addresses the multiple aspects of your careerdevelopment, is very important. We all get into this career path because we're passionate about science, so that part tends to come relatively easy. Forging relationships with people who can help you develop all the other skills necessary to be an independent investigator—that is critical for success."

Talk Title:
"Development and Functional Diversity of Neural Cell Types in the Septum"

Keynote Speaker

Matia B. Solomon, Ph.D.
Associate Professor of Neuroscience and Psychology
University of Cincinnati

Biography:
Dr. Solomon's passion for research began as an undergraduate student at Georgia State University under the mentorship of Dr. Kim L. Huhman. Her research experience studying behavior in male and female Syrian hamsters shaped her interests in studying sex differences in stress-related diseases. She received her B.A., M.A., and Ph.D. in Psychology (Behavioral Neuroscience) from Georgia State University. As a postdoctoral research fellow, she worked under the tutelage of Dr. James P. Herman in the Department of Psychiatry and Behavioral Neuroscience at the University of Cincinnati, studying the neurobiological underpinnings of sex differences in behavioral and hormonal stress responses using various genetic mouse models and rats. She later became a faculty member at the University of Cincinnati, where she is currently an Associate Professor of Neuroscience and Psychology.

Dr. Solomon's research program is dedicated towards understanding sex differences in the neurobiology of depression, and more recently, Alzheimer's disease. Her research team is particularly interested in determining whether various factors including chronic stress renders the female brain especially vulnerable to these conditions. Her research endeavors have been supported by various entities including NIH, private foundations, and pharmaceutical companies. In addition to leading her research team, Dr. Solomon holds several leadership roles, including Director of Undergraduate Research Education in the Department of Psychology and Co-Director of the NIH R25-funded RISE UP Program, a neuroscience research training program for undergraduate students. She has mentored and advised approximately 100 undergraduate, graduate, and postdoctoral trainees. Mentoring is her greatest joy, and she routinely speaks on the importance of effective mentorship for the emotional, academic, and scientific success of the next generation of behavioral neuroscientists.

In 2022, Dr. Solomon took a brief sabbatical from academia to work in industry at Supernus Pharmaceuticals Company in the Department of Medical Affairs. She returned to academia in 2024, to continue her research, mentoring, and leadership efforts. She now combines her expertise from both academia and industry to train her mentees for multiple career opportunities in the biomedical research pipeline. Outside of work, Dr. Solomon enjoys spending time with family and friends, cooking, traveling, reading, and using the infrared sauna.

Talk Title:
"Neurons and Networks: My Journey as a Neuroscientist in Academia, Industry, and in the Community"

Keynote Speaker

Jennifer C. Tudor, Ph.D.
Associate Professor of Biology
Dirk Warren ’50 Sesquicentennial Chair
Saint Joseph's University

Biography:
Dr. Jennifer Tudor is an Associate Professor in the Biology Department of Saint Joseph's University in Philadelphia, Pennsylvania. Originally from New York, she obtained her undergraduate degree in Psychology from Stony Brook University, her MS and Ph.D. in Physiology and Neuroscience from New York University, and conducted her postdoctoral training at the University of Pennsylvania. Outside the lab, she enjoys mono-skiing and SCUBA diving. She also sings and plays several musical instruments for various organizations.

Molecular and cellular signaling pathways in the brain affect all facets of life. The Tudor lab is interested in how sleep and disease affects these pathways critical for memory and behavior.

Talk Title:
“Sleep is where memories and metabolism meet”

Professional Development Session I

Laurence Boitet, Ph.D.
Assistant Professor and Director of Trainee Wellness
Department of Medical Education
Heersink School of Medicine
University of Alabama at Birmingham

Biography:
Laurence Boitet, PhD is an Assistant Professor in the Department of Medical Education in the University of Alabama at Birmingham (UAB) Heersink School of Medicine and the Director of Biomedical Scientist Trainee Wellness in the UAB Medicine Office of Wellness. She earned her PhD in Cell Biology from UAB in 2019, after which she completed a postdoctoral fellowship mentored by Dr. Katherine Meese. Dr. Boitet's research focuses on biomedical scientist engagement within the academic medical center. Her work has been published in the Journal of Healthcare Management, Journal of Healthcare Risk Management, and Journal of Multidisciplinary Healthcare, among other journals.

Talk Title:
"Overcoming Imposter Syndrome"

Professional Development Session II

Michelle R. Horvath, J.D.
University Ombudsperson
Office of the Provost
University of Alabama at Birmingham

Biography:

Michelle Horvath is the University Ombudsperson for the University of Alabama at Birmingham. She has more than ten years of experience in planning, training, adjudication and alternative dispute resolution in a higher education setting. Prior to joining UAB in 2023, she was Assistant Dean of Students responsible for Student Conduct and Academic Integrity and Deputy Title IX Coordinator at Florida International University in Miami, Florida. Her previous roles in higher education have included judicial administrator and deputy Title IX coordinator at Cornell University in New York and director of the Office of Citizenship and Community Standards at Truman State University in Missouri. Prior to entering higher education, she was a solo practitioner in Metro Detroit.

Originally from Michigan, Horvath holds a Bachelor of Science in history from Grand Valley State University, a juris doctorate from Thomas M. Cooley Law School (now Western Michigan Cooley Law School), and a Master of Arts degree in higher education/student personnel from the University of Mississippi.

The UAB Ombuds Office is a confidental, neutral resource available to all university faculty, staff, and mentored graduate and postdoctoral students to discuss workplace issues, academic concerns, issues relating to administrative paperwork and processes, and explanations and interpretations of policies and procedures, among other issues.

Talk Title & Description:

“Conflict Resolution between Mentors and Trainees”

Panel Discussion

"New Pathways to Enhance Neuroscience Training"
Thursday, June 12
11:25 am - 12:10 pm

Panel Moderator:

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)

Panelists:

Lillian Brady, Ph.D.
Assistant Professor
Department of Psychiatry & Behavioral Neurobiology
University of Alabama at Birmingham (UAB)

Brianna Fitzgerald
Graduate Trainee, Graduate Biomedical Sciences Neuroscience Theme
UAB Neuroscience Roadmap Scholars Program
President, Neuroscience Roadmap Scholars Program Student Executive Board

Abigail L. Hernandez, Ph.D.
Assistant Professor
Department of Medicine
Division of Gerontology/Geriatrics/Palliative Care

Caesar Hernandez, Ph.D.
Assistant Professor
Department of Medicine
Division of Gerontology/Geriatrics/Palliative Care

Eric Randolph, Ph.D.
Postdoctoral Researcher, UAB Department of Biology
Integration Initiative: Sex, Aging, Genomics, and Evolution (IISAGE)

Kirsten Schoonover, Ph.D.
Assistant Professor
Department of Psychiatry & Behavioral Neurobiology
University of Alabama at Birmingham (UAB)
Associate Director, Alabama Brain Collection

Poster Presentation Session

Thursday, June 12
Poster Hanging: Begins at 5:00 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 13
11:30 am - 12:30 pm

Shark Tank Moderator:

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

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. Cash prizes ($100 - $250) will be awarded to the top 3 presenters. Winners will be announced at 2:00 pm.

Oral Presentation Session I: Thursday, June 12, 9:00 - 10:20am

9:00 am	Katherine Canada - University of Virginia "DLG4-GRIN2B Complex: A Critical Convergence Point Between Autism Genetics and Functional Connectivity"
9:20 am	Kanisa Davidson - University of Alabama at Birmingham “Proteasome activator mitigates amyloid induced toxicity and cognitive deficits”
9:40 am	Alexander Foden-Pérez - Case Western Reserve University “Glia control experience-dependent plasticity in an olfactory critical period”
10:00 am	Helen Brinyark - University of Alabama at Birmingham “Resonance-guided Stimulation to Evoke Seizure Activity in Epileptogenic Brain Networks”

Oral Presentation Session II: Thursday, June 12, 2:10 - 3:30pm

2:10 pm	Elizabeth Castro - State University of New York at Buffalo “Adolescent Structural Whole-Brain Changes After Sport-Related Concussion”
2:30 pm	Cydney Martin - Drexel University “Limbic neuropeptides may mediate sex differences in affective behavior changes following repetitive mild traumatic brain injury in adolescent rats”
2:50 pm	Bryana Whitaker Hardin - University of Alabama at Birmingham “Ovarian hormone regulation of basolateral amygdala activity during valence processing”
3:10 pm	Melissa Do - University of Alabama at Birmingham “A Pilot Study of Transdermal Auricular Vagus Nerve Stimulation for Treating Insomnia in Breast Cancer Patients”

Oral Presentation Session III: Friday, June 13, 10:10 - 11:30am

10:10 am	Princess Felix - University of Michigan “Knockdown of the glucocorticoid receptor (GR) in a corticostriatal pathway increases the propensity to attribute incentive salience to a reward cue”
10:30 am	Saurav Gupta - University of Alabama at Birmingham “Nociceptive Aβ-Afferent Neurons Mediate Mechanical Allodynia in Oxaliplatin-Induced Neuropathy”
10:50 am	Jazmin Corral - State University of New York at Buffalo “Calcium signaling in Schwann cells development and myelination”
11:10 am	Gabrielle Blahusiak - Tulane University “Investigating a Link Between Cytomegalovirus Infection and Cognitive Decline in a Mouse Model of Alzheimer’s Disease”

Oral Presentation Abstracts

Oral Presentation Session I: Thursday, June 12, 9:00 - 10:20am

1	“DLG4-GRIN2B Complex: A Critical Convergence Point Between Autism Genetics and Functional Connectivity”	Katherine Canada
2	“Proteasome activator mitigates amyloid induced toxicity and cognitive deficits”	Kanisa Davidson
3	“Glia control experience-dependent plasticity in an olfactory critical period”	Alexander Foden-Pérez
4	“Resonance-guided Stimulation to Evoke Seizure Activity in Epileptogenic Brain Networks”	Helen Brinyark

Oral Presentation Session II: Thursday, June 12, 2:10 - 3:30pm

5	“Adolescent Structural Whole-Brain Changes After Sport-Related Concussion”	Elizabeth Castro
6	“Limbic neuropeptides may mediate sex differences in affective behavior changes following repetitive mild traumatic brain injury in adolescent rats”	Cydney Martin
7	“Ovarian hormone regulation of basolateral amygdala activity during valence processing”	Bryana Whitaker Hardin
8	“A Pilot Study of Transdermal Auricular Vagus Nerve Stimulation for Treating Insomnia in Breast Cancer Patients”	Melissa Do

Oral Presentation Session III: Friday, June 13, 10:10 - 11:30am

9	“Knockdown of the glucocorticoid receptor (GR) in a corticostriatal pathway increases the propensity to attribute incentive salience to a reward cue”	Princess Felix
10	“Nociceptive Aβ-Afferent Neurons Mediate Mechanical Allodynia in Oxaliplatin-Induced Neuropathy”	Saurav Gupta
11	"Calcium signaling in Schwann cells development and myelination”	Jazmin Corral
12	“Investigating a Link Between Cytomegalovirus Infection and Cognitive Decline in a Mouse Model of Alzheimer’s Disease”	Gabrielle Blahusiak

Oral Presentation 1

“DLG4-GRIN2B Complex: A Critical Convergence Point Between Autism Genetics and Functional Connectivity”

Katherine Canada[1]

[1]University of Virginia

White matter abnormalities are consistent neuroimaging findings in Autism Spectrum Disorder (ASD), showing initial hypermyelination followed by reduced myelination compared to typically developing peers. After stratifying ASD-associated genes by cell type, we investigated proteins preferentially expressed in inhibitory neurons, including TCF4, ARX, SLC6A1, AUTS2, AFF2, GRIN2B, and NRXN3. Using STRING protein interaction database and Louvain community detection, we identified functional clusters with DLG4 emerging as a convergent protein that is vital for coordinating one clusters function with another. Permutation testing (1000×) confirmed that DLG4 removal significantly disrupts inter-cluster connectivity ($p<0.001$) and reduces cross-cluster protein interactions. Notably, DLG4 directly interacts with GRIN2B, forming a complex critical for glutamatergic transmission and excitatory/inhibitory balance. This finding aligns with recent work by Rasero et al. (2023), which identified distinct ASD subtypes based on spatial transcriptomics mapped onto brain connectivity patterns, where only a hyperconnected subtype (43% of patients) showed significant enrichment for excitation/inhibition imbalance genes, including DLG4 and GRIN2B. Biologically, this suggests that genetic variations affecting the DLG4-GRIN2B complex could lead to excitatory/inhibitory imbalance, altered functional connectivity, and the white matter abnormalities observed in neuroimaging studies. Our computational analyses reveal a potential mechanistic pathway connecting genetic variations to the functional connectivity alterations characteristic of a specific ASD subtype, providing a foundation for stratified diagnostic and therapeutic approaches.

Oral Presentation 2

“Proteasome activator mitigates amyloid induced toxicity and cognitive deficits”

Kanisa Davidson[1], Mehar Bano[1], Danitra Parker[2], Pawel Osmulski[3], Maria Gaczynska[3], Andrew M. Pickering[2]

[1]University of Alabama at Birmingham, Behavioral Neuroscience Graduate Program; [2]The University of Texas Health Science Center at Houston, Department of Integrative Biology and Pharmacology; [3]The University of Texas Health Science Center at San Antonio

Alzheimer’s Disease (AD) is a neurodegenerative disease that affects around 50 million people. The pathological hallmarks of this diseases are marked by cognitive decline and the accumulation of β-amyloid plaques and hyperphosphorylated tau. AD treatment options are limited highlighting the need for novel approaches. Proteasomal activity is decreased across human and animal models of AD. We hypothesize that β-amyloid and/or hyperphosphorylated tau impair proteasome function in AD by disrupting critical neuronal processes such as memory formation and synaptic plasticity. We investigated the role of Aβ in the modulation of proteasomal function, the capacity of two proteasome-activating compounds to rescue Aβ-induced survival deficits in cell culture, and Aβ-induced cognitive deficits in *Drosophila and mice*. We demonstrate β-amyloid inhibits 20S proteasome function while simultaneously driving disassembly of 26S proteasome into free 20S proteasome. Treatment with proteasome activators enhances 20S and 26S proteasome function and reduces cell death caused by Aβ42 toxicity in SK-N-SH cells. In our AD *Drosophila* models, our proteasome agonist delayed mortality and restored cognitive function. Chronic treatment with the activator protected against deficits in working memory caused by Aβ42 in mice and in hAPP(J20) mice with established deficits, acute drug treatment significantly improved spatial learning deficits, with treated mice performing comparably to controls. Our proteasome activator shows promise in mitigating AD-like deficits by protecting against amyloid toxicity and enhancing proteasome function. These findings suggest that targeting proteasome activity could be a viable therapeutic approach for AD, warranting further investigation into the broader impacts of proteasome modulation on AD pathology.

Oral Presentation 3

"Glia control experience-dependent plasticity in an olfactory critical period"

Hans C Leier[1], **Alexander J Foden[1]** Darren A Jindal[1], Abigail J Wilkov[1], Paola Van der Linden Costello[1], Pamela J Vanderzalm[2], Jaeda Coutinho-Budd[3], Masashi Tabuchi[1], Heather T Broihier[1]

[1]Department of Neurosciences, Case Western Reserve University School of Medicine, United States; [2]Department of Biology, John Carroll University, United States; [3]Department of Neuroscience, University of Virginia School of Medicine, United States

Sensory experience during developmental critical periods has lifelong consequences for circuit function and behavior, but the molecular and cellular mechanisms through which experience causes these changes are not well understood. The *Drosophila* antennal lobe houses synapses between olfactory sensory neurons (OSNs) and downstream projection neurons (PNs) in stereotyped glomeruli. Many glomeruli exhibit structural plasticity in response to early-life odor exposure, indicating a general sensitivity of the fly olfactory circuitry to early sensory experience. We recently found that glia shape antennal lobe development in young adults, leading us to ask if glia also drive experience-dependent plasticity during this period. Here, we define a critical period for structural and functional plasticity of OSN-PN synapses in the ethyl butyrate (EB)-sensitive glomerulus VM7. EB exposure for the first 2 days post-eclosion drives large-scale reductions in glomerular volume, presynapse number, and post- synaptic activity. Crucially, pruning during the critical period has long-term consequences for circuit function since both OSN-PN synapse number and spontaneous activity of PNs remain persistently decreased following early-life odor exposure. The highly conserved engulfment receptor Draper is required for this critical period plasticity as ensheathing glia upregulate Draper, invade the VM7 glomerulus, and phagocytose OSN presynaptic terminals in response to critical-period EB exposure. Loss of Draper fully suppresses the morphological and physiological consequences of critical period odor exposure, arguing that phagocytic glia engulf intact synaptic terminals. These data demonstrate experience-dependent pruning of synapses and argue that *Drosophila* olfactory circuitry is a powerful model for defining the function of glia in critical period plasticity.

Oral Presentation 4

"Resonance-guided Stimulation to Evoke Seizure Activity in Epileptogenic Brain Networks"

Helen E. Brinyark[1], Rebekah Chatfield, Arie Nakhmani, Benjamin C. Cox, Rachel J. Smith

[1]University of Alabama at Birmingham

Introduction: Localization of the seizure onset zone (SOZ) is critical to surgically treat drug-resistant epilepsy. Seizures evoked during single-pulse electrical stimulation (SPES) can be localizing and have inspired the development of frequency-specific stimulation protocols to reliably evoke seizures. Dynamical network models built from SPES-evoked responses can be used to model neural resonance and predict "resonant frequencies" at which electrical stimulation can induce an epileptic seizure.
Materials & Methods: In 10 patients who consented to undergo stimulation to induce seizures (SIS) at UAB, we stimulated at resonant frequencies and at standard frequencies (5, 10, 15, 20 Hz) and elicited seizures at both resonant and standard frequencies. In 5 patients who experienced stimulation-induced seizures at a standard frequency, we recalculated our models to investigate local rather than global resonant frequencies, particularly for brain regions in the SOZ. In a single patient, we prospectively stimulated at local SOZ resonant frequencies in addition to global resonant frequencies and standard frequencies to elicit seizures.
Results: Our retrospective analysis showed that the standard event-inducing stimulation frequency in 16 of 18 seizures were local resonant frequencies for SOZ brain regions. Our prospective analysis found that local SOZ resonant frequencies more effectively elicited epileptic events (8/17 stimulations) than when stimulating at global resonant frequencies (5/17 stimulations).
Conclusions: These findings suggest that local resonant frequencies calculated using our neural resonance models more reliably elicit epileptic activity during SIS, particularly when targeting the suspected SOZ network, which could lead to improved epileptogenic network localization and overall surgical outcomes.

Oral Presentation 5

"Adolescent Structural Whole-Brain Changes After Sport-Related Concussion"

Elizabeth V. Castro[1], Ferdinand Schweser[2,3], Sarah Muldoon[1,4,5], John J. Leddy[6], and Mohammad N. Haider[6]

[1]Neuroscience Program, University at Buffalo, Jacobs School of Medicine and Biomedical Sciences, SUNY Buffalo; [2]Buffalo Neuroimaging Analysis Center, Department of Neurology, Jacobs School of Medicine and Biomedical Sciences SUNY Buffalo; [3]Center for Biomedical Imaging, Clinical and Translational Science Institute at the University at Buffalo; [4]Mathematics Department, SUNY Buffalo; [5]Institute for Artificial Intelligence and Data Science, SUNY Buffalo; [6]UBMD Orthopaedics and Sports Medicine, Jacobs School of Medicine and Biomedical Sciences, SUNY Buffalo

Introduction: After sport-related concussion (SRC), conventional neuroimaging typically reveals no brain abnormalities. Diffusion magnetic resonance imaging (dMRI) allows the investigation of SRC-associated microstructural brain changes and has provided evidence of microstructural changes and associations with SRC symptoms. However, these analyses are limited by focusing on one aspect of the injury, such as structural connectivity or integrity. Few studies combined analyses for a complete picture of the microstructural changes after SRC. Here, we performed three analyses to understand white matter changes, structural connectivity, and individual variability in SRC. We hypothesized that adolescents with SRC and controls will show structural whole-brain differences.
Materials and Methods: Whole-brain dMRI scans were collected from 13–18-year-old adolescent athletes (n= 35) within 10 days of SRC (V1) and after clinical recovery (~4-6 weeks, V2). Age and sex-matched controls (n= 34) had dMRI scans collected at baseline and 4-6 weeks later. Structural network and diffusion measures were calculated. Differential tractography was computed to assess individual variability. Statistical analysis was performed using linear mixed effect models and differential tractography was qualitatively assessed.
Results: There were no overall network or diffusion differences between groups or visits. Stratification by sex revealed that females had greater clustering coefficients, global dissimilarity, mean diffusivity, and radial diffusivity than males, regardless of injury status. Differential tractography showed differences in the cerebellum, corpus callosum, and brainstem between groups.
Conclusion: These results suggest that focused investigations into sex-specific differences and tract-specific analyses are needed in future research.

Oral Presentation 6

"Limbic neuropeptides may mediate sex differences in affective behavior changes following repetitive mild traumatic brain injury in adolescent rats"

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Mild traumatic brain injury (mTBI) is common among adolescents and often occurs repetitively because of participation in contact sports. Growing evidence suggests that girls are more likely to sustain sports-related concussions and to report deficits in affect like depression, which often persists for years following injury. This study used adolescent-age rats, to determine if changes in depression-like and motivated behaviors are accompanied by changes in expression of limbic neuropeptides after repetitive mTBI. Adolescent male and female Long-Evans rats were anesthetized and subjected to 3 closed-skull impacts over 7 days (brain-injured males n=21, females n=27) or anesthetized without injury (sham-injured males n=20, females n=26). At 5 weeks, but not 2 weeks following injury, injured females displayed increased immobility in the forced swim test compared to shams (p<0.05), indicating increased depression-like behavior. Injured females trended towards drinking less 20% ethanol in the home cage and less lever pressing for saccharin reward in operant chambers compared to shams, indicating reduced motivation. In the nucleus accumbens shell (NAcSh), mRNA expression was decreased for dynorphin (-38%) and enkephalin (-33%, p<0.05) in injured females at 5 weeks. In the posterior paraventricular thalamic nucleus (pPVT), pituitary adenylate cyclase-activating polypeptide (PACAP) mRNA was increased in injured females but not males at 2 (+215%, p<0.05) and 5 weeks (+162%, p<0.05) compared to shams. These data suggest that depression-like behavior emerges in the chronic phase following repetitive mTBI in adolescent females. Moreover, pPVT PACAP may contribute to behavior differences by regulating neuropeptide expression in the NAcSh in a sex-dependent manner.

Oral Presentation 7

"Ovarian hormone regulation of basolateral amygdala activity during valence processing"

Bryana Whitaker Hardin[1] & Elizabeth K. Lucas[1]

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Valence refers to the intrinsic emotional value, both positive (or appetitive) and negative (or aversive), associated with a specific environmental stimulus. Valence processing is orchestrated by the basolateral amygdala and varies in a predictable manner across the menstrual cycle in humans as well as the estrous cycle of rodents. Current research regarding the cellular mechanisms underlying this dynamic process suggests a model of disinhibition through inhibitory microcircuits. Specifically, we propose that principal neurons expressing the protein R-spondin 2 (Rspo2) and interneurons expressing parvalbumin (PV) or somatostatin (SST) comprise this microcircuit. This prediction is further supported by preliminary research demonstrating the exclusive expression of estrogen receptor beta in Rspo2 and SST neurons. To test this hypothesis, we assessed the responses of these three distinct neuronal populations to aversive and appetitive stimuli presented through social, gustatory, olfactory, and somatosensory assays in mice. Neuronal responses were measured using bulk calcium transients with fiber photometry. While data analysis is ongoing, we expect to see divergent responses regarding the activation of these neuronal populations that are dependent on the estrous cycle stage of the mouse. Together, these data will allow us to examine the estradiol regulation of a novel, sex-specific amygdala microcircuit responsible for valence processing.

Oral Presentation 8

"A Pilot Study of Transdermal Auricular Vagus Nerve Stimulation for Treating Insomnia in Breast Cancer Patients"

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Introduction: Insomnia affects about 40%-70% of breast cancer patients and contributes to cancer-related fatigue (CRF), which can increase the risk of disease progression, decrease survival, increase systematic inflammation, and cause physical, emotional, and mental distress. Transcutaneous-auricular Vagus Nerve Stimulation (taVNS) is a non-invasive intervention that has gained attention due to its implications to modulate autonomic nervous system activity, inflammation, and affect brain regions associated with cognition, arousal, and mood. It is a well-studied neuromodulation device that delivers mild electrical current to the auricular branches of the vagus nerve. This intervention could serve as a safe, effective intervention to improve the overall well-being in breast cancer patients.
Methods: We investigate the influence of taVNS to address insomnia in breast cancer patients. We examine the efficacy of 2 week, at-home use of taVNS as a treatment for insomnia by looking at measurements of sleep, CRF, and mental health. Additionally, we aim to evaluate the effect of taVNS on pro-inflammatory biomarkers in the blood.
Results: We hypothesize that patients will report significantly improvements in sleep, inflammation, anxiety, depression, and CRF after two weeks of taVNS. Current results show significant decreases in sleep and fatigue ($p =< 0.005$). Additionally, there has been no reported adverse effects.
Conclusion: This study is ongoing with active participants and ongoing recruitment. Results so far indicate significant improvements in sleep and fatigue.

Oral Presentation 9

"Knockdown of the glucocorticoid receptor (GR) in a corticostriatal pathway increases the propensity to attribute incentive salience to a reward cue"

Princess Felix[1,2], Stephen E. Chang[2], James P. Herman[4], Shelly B. Flagel[2,5]

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Glucocorticoid receptors (GRs) are critical modulators of the stress response, yet their role in behavioral regulation outside of stress remains unclear. Given that stress-related psychopathologies, such as substance use disorder (SUD) and impulse control disorders, are characterized by deficits in inhibitory control, we investigated the role of GR within a top-down cortico-striatal pathway in governing incentive motivation. Specifically, we used transgenic Sprague-Dawley rats with conditional GR knockdown to selectively reduce GR expression in glutamatergic projections from the prelimbic cortex (PrL) to the nucleus accumbens core (NAcC)—a pathway implicated in reward-seeking behavior and the regulation of dopamine signaling. To assess the effects of GR knockdown on incentive salience attribution, rats underwent a Pavlovian conditioned approach (PavCA) paradigm, in which a neutral cue was repeatedly paired with a food reward. Our results indicate that rats with GR knockdown in the PrL-NAcC pathway were significantly more likely to sign-track—attribute heightened motivational value to the reward cue—compared to wildtype controls. Additionally, the degree of GR knockdown positively correlated with the magnitude of this behavior, further implicating GR in the regulation of incentive motivation. Notably, these effects were observed irrespective of sex. Since sign-tracking behavior is associated with increased impulsivity, attentional deficits, and susceptibility to cue-induced reinstatement of drug-seeking behavior, our findings suggest that GR signaling within the PrL-NAcC pathway plays a crucial role in inhibitory control and maladaptive behaviors. These results provide insight into the neuromolecular mechanisms underlying stress-induced vulnerabilities to compulsive reward-seeking and may have implications for stress-related psychiatric disorders.

Oral Presentation 10

"Nociceptive Aβ-Afferent Neurons Mediate Mechanical Allodynia in Oxaliplatin-Induced Neuropathy"

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Chemotherapy-induced peripheral neuropathy (CIPN) remains a major dose-limiting side effect of oxaliplatin treatment, often manifesting as debilitating mechanical allodynia. While C- and Aδ-fibers are well-studied in neuropathic pain, the contribution of nociceptive Aβ-afferent neurons remains poorly understood. Here, we provide compelling evidence that nociceptive Aβ-afferent neurons play a critical role in mechanical hypersensitivity following oxaliplatin treatment, utilizing an integrative approach combining electrophysiology, behavior, and molecular analysis.
Behavioral assessments revealed significant increases in mechanical, cold, and pain sensitivity, and heightened orbital tightening responses to evoked mechanical pain in oxaliplatin-treated mice. Electrophysiological characterization of nociceptive Aβ-afferent neurons demonstrated a significant decrease in soma diameter, AP rheobase, AP threshold, AP amplitude, and AP width, indicative of increased excitability. Furthermore, voltage-clamp recordings revealed enhanced voltage-activated inward and outward currents, alongside increased action potential firing at 100Hz and 500Hz stimulation, further supporting a hyperexcitable state. Mechanistically, we observed a significant increase in pH-5, 5-HT, GABA, and Piezo-mediated currents, suggesting amplified chemical and mechanical sensitivity in nociceptive Aβ-afferent neurons. Notably, TTX-resistant sodium currents were significantly elevated, as confirmed by both electrophysiology and PCR, implicating Nav1.8 upregulation in the hyperexcitability of these neurons. Additionally, Piezo-mediated mechanically activated currents were markedly increased, correlating with upregulated Piezo gene expression post-oxaliplatin treatment. Importantly, these effects were absent in non-nociceptive Aβ-afferent neurons, underscoring a selective effect on nociceptive subtypes.
Our findings establish nociceptive Aβ-afferent neurons as key contributors to oxaliplatin-induced mechanical allodynia, providing novel mechanistic insights into CIPN pathophysiology. These results highlight potential therapeutic targets for mitigating chemotherapy-induced neuropathic pain.

Oral Presentation 11

"Calcium signaling in Schwann cells development and myelination"

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Schwann cells are the primary glial cells of the peripheral nervous system (PNS), playing a crucial role in the maintenance and myelination of peripheral nerves. While G-protein coupled receptors (GPCRs) have been shown to modulate Ca^{2+} signaling in oligodendrocytes and neurons in the central nervous system (CNS), their role in Schwann cells and how they influence PNS myelination remains poorly understood. To investigate this, we used Cre-mediated recombination to selectively express the excitatory hM3Dq and inhibitory hM4Di GPCRs in Schwann cells. These receptors, derived from human muscarinic receptor subtypes, are exclusively activated by clozapine N-oxide (CNO). We performed a combination of Ca^{2+} imaging, immunocytochemistry, and electron microscopy to assess Schwann cell development and function following hM3Dq and hM4Di activation both in vitro and in vivo. Our findings reveal that hM3Dq activation during early development significantly delays sciatic nerve myelination and Schwann cell maturation. Moreover, hM3Dq activation in mature Schwann cells disrupts the myelin sheath, leading to severe demyelination in the adult sciatic nerve. To further explore the mechanisms underlying these effects, we conducted Ca^{2+} imaging experiments to examine how hM3Dq influences Ca^{2+} channel and receptor activity in Schwann cells. Additionally, we performed behavioral tests, including Rotarod and Catwalk assays, to evaluate how hM3Dq-induced myelination changes impact motor coordination in both young and adult mice.

Oral Presentation 12

"Investigating a Link Between Cytomegalovirus Infection and Cognitive Decline in a Mouse Model of Alzheimer's Disease"

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Alzheimer's Disease (AD) affects over 55 million people worldwide and is projected to double by 2050. Numerous risk factors–including pathogen exposure across the lifetime–have been associated with accelerated age-related cognitive decline. Cytomegalovirus (CMV) is a herpesvirus with few detectable symptoms and seroprevalence between 60–90% globally. Due to a lack of treatment options, CMV persists throughout life, cycling between latent and reactivation phases. Our previous data show lifetime CMV reactivation induces dysfunctional neurometabolic profiles associated with altered transcriptional and epigenetic profiles in metabolic pathways, impaired blood-brain barrier integrity, neuroinflammation, and cognitive decline in both wild-type and AD mouse models despite absence of CMV infection in the brain. This suggests a potential link between peripheral CMV infection and neurodegeneration. We aimed to investigate this link and determine the timepoint of accelerated cognitive decline with peripheral CMV reactivation across the lifespan in the 3xTg-AD mouse model. 3xTg-AD mice received initial mock or MCMV IP injections at 2 months of age; regimen was then repeated every 3 months. Y maze, passive avoidance, and hot plate assays assessed cognitive performance at 2-, 4-, and 6-months post-infection (MPI). We found no cognitive changes prior to 6MPI. At 6MPI, MCMV-infected mice had significantly reduced total alterations and correct alterations on the Y maze. Overall, mild locomotor deficits emerge at 6MPI with CMV reactivation every 2 months. Additional timepoints, more sensitive behavioral assays, and characterization of peripheral immune profiles and transcriptional changes in the CNS will aid in linking peripheral infection with AD-associated cognitive decline.

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Poster Presentation Abstracts

Poster #	Title	Presenter
1	Ionic Mechanism Underlying Burst-Firing in Pten KO neurons	Asan Abdulkareem
2	Reduced ASIC2a Expression is Associated with Cerebral Hypoperfusion in the Prefrontal Cortex and Olfactory area of Aging Mice	Goodness Adegbola
3	Disentangling Conscious Auditory Perception from Report: A Machine Learning and fMRI Framework for Identifying Covert Awareness	Shanae Aerts
4	Neural Risk Markers of Depression and Mania in Three Independent Young Adult Samples During Working Memory and Emotional Regulation	Yvette Afryie-Agyemang
5	Diurnal Rhythm Analysis of Stress Response Markers in the Paraventricular Nucleus of Subjects with Bipolar Disorder	Obie Allen IV
6	Age-Dependent Neutrophil Accumulation in the Thalamus Following Traumatic Brain Injury: Insights from Single-Cell RNA Sequencing	Frida Anguiano
7	Characterization of neurodegeneration in Familial Dysautonomia peripheral sympathetic neurons using an induced pluripotent stem cell model	Jennifer Art
8	Implications of lncRNA Neat1 in Seizure and Memory Responses in Temporal Lobe Epilepsy	Rudhab Bahabry
9	Discovering the genetic link of cognitive dysfunction with insomnia and cardiovascular disease	Morgan Barkley
10	Conservation and Diversification of Olfactory Receptor Function	Erin Beck
11	Resonance-guided Stimulation to Evoke Seizure Activity in Epileptogenic Brain Networks	Helen Brinyark
12	The Impact of Neonatal Adversity on Endocannabinoid Signaling and Adolescent Behavior	Nadja Brown
13	Pannexin-1 regulates neural cell fate and brain size	Trenton Buckner
14	Complex Spinal Mechanisms Underlying Stress-Induced Bladder Hypersensitivity in Hemopexin Depleted Mice	Anastasiia Caangay
15	Phase-Contrast Adaptive Optics Scanning Laser Ophthalmoscopy (AOSLO) Reveals Diverse Cellular-Scale Immune Activity in the Non-Human Primate Retina In Vivo	Andrea Campbell
16	Autism Genetic Pathways Affect Oligodendrogenesis	Katherine Canada
17	The Role of Estradiol in Hippocampus Function in Control and High Fat Diet-fed Ovariectomized Mice	Kierstin Cousin
18	KCNT1 Influences Cocaine-Seeking Behavior in Female Rats on Day 1 of Extinction	Ariel Cox
19	Toward comparing scotomas: Using microperimetry paired with cortical magnification factor to quantify retinal functional health in patients with central vision loss	Elam Cutts
20	Neural Dynamics of Event Model Maintenance Across Age During Naturalistic Viewing	Mohsen Davoudkhani
21	GABAergic mechanisms of fear encoding in the dorsal peduncular cortex	Zephyr Desa
22	A Pilot Study of Transdermal Auricular Vagus Nerve Stimulation for Treating Insomnia in Breast Cancer Patients	Melissa Do
23	Chemogenetic inhibition of Central Amygdala neurons acutely attenuates the anorexigenic effects of exogenous GLP-1 signaling	Miguel Duran
24	Knockdown of the glucocorticoid receptor (GR) in a corticostriatal pathway increases the propensity to attribute incentive salience to a reward cue	Princess Felix
25	Development of an ethologically relevant rodent model of social stress	Brianna Fitzgerald
26	Glia control experience-dependent plasticity in an olfactory critical period	Alexander Foden-Pérez
27	Cell Autonomous Effects of Mutant Huntingtin Expression in Somatostatin Cells	Jahmel Fowler

Poster Presentation Abstracts

Poster #	Title	Presenter
28	Sex-specific aging in brain tissue gene expression in the genus Drosophila	Abigail Fox
29	The role of prelimbic interneurons in reward learning	Hunter Franks
30	Orexin/Hypocretin Modulation of Cholinergic Signaling within the Prefrontal Cortex in Response to an Immune Challenge	Marla Frick
31	C. elegans as a Model Organism to Study the Neuronal Effects of Cocaine Exposure	Audrey Gilbert
32	Synaptic activity in a neurodevelopmental mouse model of GAT1 haploinsufficiency	William Gilbert
33	Uncovering the Role of the Astrocyte Secretome in Blood-Brain Barrier Integrity and Repair	Samantha Golf
34	Assessing NMDA receptor distribution by cortical layer in human postmortem dorsolateral prefrontal cortex	Cheyenne Griffin
35	The Role of Salivary Sodium in the Gustatory Responses to Salt and Water in Humans	Catalina Guzman
36	Striatal Astrocyte and Interneuron Activity Revelations from a Mutant Huntingtin Expressing Mouse Model	Jewel Hairston
37	Dissecting Genetic Drivers of Cardiometabolic, Circadian, and Cognitive Dysfunction	Sajal Kumar Halder
38	Investigating whether lysosome-targeted progranulin prevents FTD-like pathology	Jakub Hel
39	HIV-Tat disrupts amphetamine-induced non-vesicular dopamine release	Cesar Hernandez
40	Relationship between default mode network activity and mood disturbances in idiopathic generalized epilepsies	Crager Hester
41	Inflammation Induces Deficits in Neurotransmission in Female iPSC-derived Dopaminergic Neurons	Yiqi Huang
42	The Role of Apha-Actinin-2 in the Pathogenesis of Huntington's Disease	Jordynn Hunter
43	Spatial Transcriptomics and Magnetic Resonance Imaging Reveal the Genetic and Cytoarchitectonic Determinants of Alzheimer's Disease	Tamara Jafar
44	Exploring the contribution of increased SCN8A activity to Alzheimer's disease	Katie James
45	Modelling the "group project" – the emergence of worker/parasite relationships	Jarildy Javier
46	Dorsal Hippocampus to Cortex Projections Drive Sex-Differences in Cocaine Seeking Persistence	Savannah Julian
47	Progranulin acts in astrocytic lysosomes to promote neuronal outgrowth	Azariah Kaplelach
48	Beta frequency activity reflects sensorimotor processing in the human subthalamic nucleus	Autum Key
49	Microglia and Synaptic Pruning in the Primate Amygdala: Effects of Early Life Stress	Dennisha King
50	Characterizing NTSR1-Expressing Medial Prefrontal Cortex Afferents into the Nucleus Accumbens in Opioid-Seeking Behavior	Crystal Lemchi
51	Traumatic brain injury induced Cx43 phosphorylation enhances seizure susceptibility	Owen Lietzel
52	Applying spatial transcriptomics and mouse molecular genetics to understand the mechanisms of fibrotic scarring for promoting neural repair after spinal cord injury	Camilo Londono
53	Effect of Oxytocin on Hyperalgesia in Alcohol-Dependent Rats	John Marendes Jr.
54	Cognition and Mood Changes in Recently Diagnosed De Novo Persons With Parkinson's Disease	Caelia Marshall
55	Overview of the Progress of Factors in Learning and Plasticity (FLAP) at UAB	Elliot Maxwell
56	Cell-Specific Ventral Pallidal Regulation of Reward-Seeking	Aisha Mesco
57	Investigating Extrinsic and Intrinsic Mechanisms of Meningeal Fibroblast Development	Danae Mitchell

Poster Presentation Abstracts

Poster #	Title	Presenter
58	Blood-Brain Barrier Repair Following Focal Traumatic Brain Injury	Amitis Moradkhani
59	Characterization of the dCA1-LS-VTA pathway and its role in novelty-induced locomotor hyperactivity	Meaghan Navarrette-Mathews
60	T1 Relaxivity of Ferritin: Implications for Quantitative Magnetic Resonance Imaging in Cerebral Hemorrhage	Oge Ngwu-Hyacinth
61	Speech-Derived Linguistic Markers as Predictors of Cognitive Impairment in Older Adults	Cynthia Nyongesa
62	AKT is Necessary for Neuronal Hypertrophy and Excitatory Synaptogenesis Caused by Pten Knockout	Mackenzi Prina
63	Weight Regulation by GLP1R agonists via a non-canonical hypothalamic PKA-mTORC1 mediated Pathway	Ritika Raghavan
64	Early-life correlates of AD-vulnerable relational memory in the structure and function of hippocampal subfields: Findings from the PRANK study	Meghan Ramirez
65	Modelling Hallmarks of Amphetamine Use Disorder in Drosophila using the Fly Liquid-food Interaction Extinction Assay (FLIXA)	Caleb Rowe
66	Genipin's ECM cross-linking property to prevent developmental and degenerative phenotypes in Familial Dysautonomia	Tripti Saini
67	Characterization of a mouse model of infant traumatic brain injury	Nishell Savory
68	Advancing TMS for PTSD– from networks to individuals	Patlapa Sompolpong
69	Development of a new, in vivo, screenable, split-luciferase based model of huntingtin multimerization	Morgan Thomas
70	Investigating the role of BAI3 loss of expression in glioblastoma formation	Alex Torrelli-Diljohn
71	Co-Pathologies and Immune Cell Activation in a Model of Neurodegeneration	Jhodi Webster
72	Exercise mitigates obesity-induced cognitive dysfunction, lipid accumulation, and neuro-inflammation	Archana Yadav

Poster 1

Ionic Mechanism Underlying Burst-Firing in Pten KO neurons

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Pten is tumor suppressor and regulatory antagonist of PI3K/Akt/mTOR pathway that is involved in cellular differentiation and growth. Loss of function mutation in Pten is one of the most common genetic aberrations associated with autism spectrum disorder (ASD), which is an increasingly diagnosed neurodevelopmental disorder. Pten depleted neurons have shown an increase in soma size, dendritic arborization, migration, and increased hyperexcitation. Knocking out Pten in granule neurons of dentate gyrus in mice has resulted in an increased burst-firing phenotype as well as a smaller fast AHP (after hyperpolarization) of the action potentials. While burst-firing accomplishes numerous functions in the brain such as emotional regulation, release of neurotransmitters and other peptides, abnormal bursting has been detected in various neuropathies. Furthermore, over 20% of ASD patients have epilepsy and seizures, and the link between seizures and burst-firing is still very ambiguous. Through genetic manipulation and pharmacological targeted inhibition, we evaluate changes in the ionic activities and determine possible signaling pathways involved in burst-firing. Therefore, identifying the underlying cause of neuronal hyperexcitability in these neurons. Findings from genetic inhibition of downstream signaling intermediates of Pten indicated the possibility of Akt/mTORC2 involvement in producing excessive burst-firing rather than mTORC1. This is based on the decrease in bursting probability seen in Pten/Akt/Akt3 triple knockout and Pten/Rictor (mTORC2) double knockout neurons compared to Pten/Raptor (mTORC1) double knockout where there is no significant change in the burst probability. Also, electrophysiological evaluations suggest possible underlying voltage-gated ion channel alterations. Altogether, our data thus far suggests an ionic dysregulation governed by players downstream of Pten in the formation of burst-firing. Understanding the ionic mechanism will allow a deeper insight into the electrical activity of the brain and it will also help in identifying better therapeutic targets to halt seizures in inflicted patients.

Poster 2

Reduced ASIC2a Expression is Associated with Cerebral Hypoperfusion in the Prefrontal Cortex and Olfactory area of Aging Mice

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Acid sensing ion channels (ASICs) are proton-gated ion channels expressed in neural and peripheral tissue that are activated by drops in extracellular pH. Previous studies have shown that reduced expression of ASIC2a is implicated in seizure-susceptibility and severity in preclinical models of eclampsia. The specific mechanisms underlying this effect are not fully elucidated. Furthermore, ASIC2a plays a key role in mediating vascular myogenic tone. **Methods:** Male and female wild-type (WT) and heterozygous (HET, knock-down) ASIC2a mice between 12-14 months of age were used in this study. All female mice were nulliparous. Mice were anesthetized using isoflurane and cerebral perfusion was measured using Laser Speckle Imager. **Results:** There was no significant difference in regional brain water content between the genotypes. There was a significant main effect of sex on baseline perfusion of the whole brain ($p=0.02$), with males having lower perfusion. There was a main effect of genotype on perfusion of the left prefrontal cortex ($p=0.006$) and olfactory area ($p=0.002$), with HET having reduced perfusion. **Conclusion:** Reduced perfusion to the PFC and olfactory lobe observed in heterozygous mice could be indicative of a function of ASIC2a in coupling sensory information with cognitive responses. Future studies will determine the effects of multiparity on cerebral perfusion and brain water content in response to reduced ASIC2a expression.

Poster 3

Disentangling Conscious Auditory Perception from Report: A Machine Learning and fMRI Framework for Identifying Covert Awareness

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Ayushe Sharma, PhD, Taruna Yadav, PhD, Kate L. Christison-Lagay, PhD, Al Powers, PhD, Hal Blumenfeld, MD, PhD

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Introduction: Patients with disorders of consciousness (DoC) often retain some level of awareness, but current diagnostic tools rely on subjective reports or motor output. As a result, up to 40% of DoC patients are misdiagnosed, impacting prognosis and care. Traditional consciousness paradigms confound perceptual awareness with report. We introduce a novel no-report auditory paradigm integrating eye-tracking, machine learning, and fMRI to identify conscious perception without report—advancing the detection covert consciousness. **Materials & Methods:** Auditory stimuli (whistle, laser, or water-drop) were presented to each ear at perceptual threshold. Participants (n=35) reported perception in one ear while asynchronous stimuli played in the contralateral "no-report" ear. Reflexive eye metrics (pupil size, blink rate, microsaccades) were recorded during fMRI. Eye metrics from report trials trained an SVM classifier to predict perception in no-report trials. fMRI analyses compared network activity between perceived and nonperceived trials. **Results:** Threshold-level sounds were perceived in 55% of report trials; 89% were correctly identified, with 10% false-positives in blank trials. Eye metrics significantly diverged between perceived and nonperceived trials: pupil dilation at 200–2500ms, blink rate at 1130–1880ms, microsaccades at 153–510ms. The classifier currently achieves ROC AUC = 0.79. In fMRI, perceived trials significantly increased activation in detection/arousal/salience networks (FEF, ACC) at 3s post-stimulus, followed by task-positive network increases (dlPL, aMFG) and DMN suppression at 6s. **Conclusion:** We provide the first evidence that eye metrics can classify auditory perception without behavioral report. This multimodal approach isolates perceptual awareness from report confounds, with direct relevance for detecting covert consciousness. These findings lay the groundwork for developing objective, report-independent biomarkers and neuromodulatory interventions to restore consciousness.

Poster 4

Neural Risk Markers of Depression and Mania in Three Independent Young Adult Samples During Working Memory and Emotional Regulation

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Objective markers of pathophysiological processes underlying lifetime depression and mania/hypomania risk can provide biologically informed targets for novel interventions to help prevent the onset of affective disorders in individuals with subsyndromal symptoms. Greater activity within and functional connectivity (FC) between the central executive network (CEN), the default mode network (DMN), and the salience network (SN), is thought to interfere with cognitive functioning and predispose to depressive disorders. Using an emotional n-back paradigm designed to examine working memory (WM) and emotional regulation (ER) capacity, we examined relationships among activity and FC in these networks and lifetime depression and mania/hypomania risk, and whether findings in a Discovery sample could be replicated in a two independent Test samples of young adults. The Mood Spectrum Self-Report (MOODS-SR-L) assessed lifetime mania/hypomania risk and depression risk. We showed significant clusters of activity to each contrast in similar locations in the anatomic mask in each Test sample as in the Discovery sample, and, using extracted mean BOLD signal from these clusters as IVs, we showed similar patterns of IV-DV relationships in each Test sample as in the Discovery sample. Specifically, greater DMN activity during WM was associated with greater lifetime depression risk in all three samples, and greater CEN activity during ER was associated with increased lifetime depression risk and lifetime mania/hypomania risk in all three samples (all ps< 0.05 qFDR). These replicated findings provide promising objective, neural markers to better identify, and guide and monitor early interventions for, depression and mania/hypomania risk in young adults.

Poster 5

Diurnal Rhythm Analysis of Stress Response Markers in the Paraventricular Nucleus of Subjects with Bipolar Disorder

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Introduction: Many patients suffering from bipolar disorder (BD) display circadian rhythm and stress response disturbances. Animal models suggest that altered day length disrupts expression of neurotransmitters in the paraventricular nucleus (PVN) that regulate stress response, including somatostatin (SST), dopamine, and corticotropin releasing hormone (CRH). We tested the hypothesis that expression of these neurotransmitters is altered in the PVN of subjects with BD. **Methods & Materials:** We used a cohort of 68 control subjects and 67 subjects with BD. Time of death of each subject was used to examine diurnal rhythm relationships. Triple immunofluorescence for SST, tyrosine hydroxylase (TH) and CRH was conducted, and sections were quantified using stereology-based microscopy. Data analysis was conducted using analysis of covariance testing for the main effect of diagnosis and potential effects of covariates including medication treatments **Results:** We observed decreased densities of CRH, SST, and TH neurons in subjects with BD. Furthermore, diurnal expression rhythms were altered in subjects with BD, including greater densities of SST-TH neurons during the day in subjects with BD. **Conclusion:** Our findings provide insight regarding diurnal rhythm neurocircuitry abnormalities involved in stress response in subjects with BD and provide a foundation for designing chronobiology based therapeutic strategies.

Poster 6

Age-Dependent Neutrophil Accumulation in the Thalamus Following Traumatic Brain Injury: Insights from Single-Cell RNA Sequencing

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Aging exacerbates neuroinflammation and cognitive decline following traumatic brain injury (TBI), yet the role of neutrophils in this process remains poorly understood. Using single-cell RNA sequencing (scRNA-seq), we examine neutrophil heterogeneity in young and aged TBI mice, identifying distinct neutrophil subpopulations enriched in the thalamus with age. Our preliminary analysis suggests that aged TBI mice exhibit a greater accumulation of pro-inflammatory neutrophils expressing markers, which may contribute to chronic neuroinflammation and synaptic dysfunction. As we continue characterizing these subpopulations, we hypothesize that age-related neutrophil infiltration in the thalamus may drive long-term cognitive impairments. To test this, we will perform neutrophil depletion experiments and assess the impact on neuroinflammation and neuronal integrity. We predict that depletion will mitigate inflammation and rescue cognitive deficits, as measured by Novel Object Recognition (NOR) behavior. These findings will provide critical insights into neutrophil-driven pathology in aging TBI and inform potential therapeutic strategies targeting neutrophil activity.

Poster 7

Characterization of neurodegeneration in Familial Dysautonomia peripheral sympathetic neurons using an induced pluripotent stem cell model

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The peripheral sympathetic nervous system is responsible for the fight-or-flight response that primes the body to respond to environmental stimuli. Dysfunction of the sympathetic nervous system can result in patient pathologies such as familial dysautonomia (FD). FD is a rare autosomal recessive disorder that results in significant neurodevelopmental and neurodegenerative phenotypes in sensory and sympathetic neurons (symNs). FD patients struggle to regulate body temperature and blood pressure and experience a heightened stress response called dysautonomic crisis, which can be life threatening. Currently, there is no cure for FD and treatment options do not effectively treat sympathetic symptoms.

FD is known to be degenerative in patients and in mouse models, yet, FD symN degeneration has not been fully characterized, and thus the mechanism of FD degeneration remains unknown. Here, we utilize induced pluripotent

stem cell (iPSC) technology to begin to comprehensively characterize neurodegenerative phenotypes in FD patient specific symNs to gain better insights into FD disease mechanisms.

Here, we show that FD symNs exhibit neurodegenerative hallmarks, including abnormal mitochondrial function, abnormal axon outgrowth and branching, and signs of impaired viability and general neurodegeneration. Additionally, we have investigated the effects of drug treatments on neurodegeneration in FD symNs. Our results demonstrate that FD symNs degenerate in accordance with typical neurodegenerative disorders, and that characterization of this neurodegeneration can be a useful tool for novel drug and treatment discovery.

Poster 8

Implications of lncRNA Neat1 in Seizure and Memory Responses in Temporal Lobe Epilepsy

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Aberrant expression of the long non-coding RNA (lncRNA) *Neat1* has been implicated in both human intractable epilepsy and animal models. We have previously shown that epigenetic mediated chromatin remodeling by non-coding RNAs like *Neat1*, play a crucial role in hippocampus-dependent memory formation. Given these findings, we investigated the role of *Neat1* in Temporal Lobe Epilepsy (TLE) to better understand its contribution to associated seizures and memory deficits. Using the Kainic Acid (KA) intraperitoneally (IP;10 mg/kg) rat model of TLE, siRNA *Neat1* knockdown (KD) was administered in the dorsal hippocampus five days prior to the assessment of prolonged seizure activity or status epilepticus (SE). SE was induced in male Sprague Dawley rats (125–150 g) that underwent *Neat1* KD. Rats without *Neat1* manipulation or KA injection was included as a control group. Behavioral seizures were assessed using the Racine scale. We found that hippocampal *Neat1* KD resulted in a significant delay in forelimb clonus seizures in KA-SE animals *Neat1* siRNA exhibited compared to scrambled RNA controls, indicating a protective effect against KA-induced prolonged seizures.
Additionally, *Neat1* KD attenuated seizure severity, as reflected by delayed progression to SE. Next, hippocampus-dependent long-term memory formation was assessed to determine the effect of *Neat1* KD on memory deficits. Fear conditioning was administered four weeks post-KA injections when animals were epileptic or experiencing chronic seizures. Preliminary analysis indicates a neuroprotective role of *Neat1* during memory formation. Together, these findings suggest that loss of *Neat1* modulates seizures, potentially by altering the neuro plasticity mechanisms involved in excitatory-inhibitory imbalance in the epileptic hippocampus. Moreover, these results indicate that *Neat1* suppression mitigates epilepsy, highlighting its potential role as a therapeutic target for TLE and associated memory impairments.

Poster 9

Discovering the genetic link of cognitive dysfunction with insomnia and cardiovascular disease

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Insomnia, the most prevalent sleep disorder affects 10 to 30% of the population, which at a conservative estimate equates to around 770 million worldwide. Studies have shown that insomnia is associated to cardiovascular disease (CVD) where insomnia confers more than a 2-fold increased risk of incident CVD. Population-based studies demonstrate that insomnia and CVD patients report experiencing cognitive dysfunction. **Purpose:** Understanding the specific genetic pathways and mechanism connecting memory impairment with CVD and insomnia are currently unexplored the genetic and pathophysiological basis. **Methods:** Our collaborators identified 75 human candidate genes along with Drosophila orthologs at the insomnia genetic loci. Out of the 75 genes, 20 human candidate genes were identified as positive hits for CVD and insomnia phenotype by knockdown of these genes in cardiac using UAS GAL4 expression approach. To identify if these 20 candidate genes are also positive hits for cognitive dysfunction, we will use Drosophila melanogaster models, which are well-established model systems for learning and memory

studies. To test genetic susceptibility towards insomnia and/or CVD is vulnerable to cognitive dysfunction we knocked down these genes by using mushroom body specific OK-107-Gal4 (memory-related) driver. 3-week-old Drosophila progeny was subjected to olfaction aversive training to evaluate memory and learning performance. **Results:** Our results show 14 of the 20 positive hit genes led to memory dysfunction. Additionally, 6-week-old Drosophila progeny exhibited a pronounced decline in memory performance compared to 3-week-old progeny. **Conclusion:** Disruption of insomnia-associated genes in cardiac and neuronal tissues significantly impacted heart function and sleep patterns, respectively. Targeted gene knock-down within the mushroom bodies, which are crucial for learning and memory, resulted in decline learning. These findings underscore a genetic connection between learning impairments and genes related to insomnia and CVD. Overall, the data provide valuable insights into potential predictive markers for early identification of insomnia or CVD. **Future Direction:** Investigate whether knockdown of the mushroom body-specific driver influences sleep or cardiac phenotypes. Further, assess the impact of knockdown in circadian rhythm related specific drivers on short- and long-term memory. **Acknowledgements:** Drosophila stocks were obtained from Bloomington and VDRC. This work was supported by NIH grant MPIR01 HL146751 to J.W., R.S. and G.C.M.

Poster 10

Conservation and Diversification of Olfactory Receptor Function

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Olfaction, the oldest known sense, enables organisms to detect and respond to environmental cues critical for survival. Olfactory receptors (ORs), encoded by a diverse gene family, mediate odor detection and are shaped by evolutionary mechanisms. A major driver of OR gene family expansion are tandem gene duplications, where duplicated genes are located adjacent to the original. While these duplications have the potential to alter ligand specificity, the extent to whether these duplications preserve or introduce novel receptor functions remains unclear. Ants as a model organism provide a unique opportunity to measure minute differences in OR function, given their diverse OR gene repertoire and ability to detect extremely subtle differences in hydrocarbons, even just a single carbon length. Previous functional studies in *Harpegnathos saltator* ants have identified an OR that responds specifically to hydrocarbon C31. To investigate whether this function is conserved, we identified and characterized the function of two phylogenetically similar ORs in *Camponotus floridanus* ants. We assessed OR function through transgenic *Drosophila* models expressing ORs and recorded electrophysiological responses to C31 and related hydrocarbons. Our findings reveal that the candidate ORs respond to hydrocarbon C31, indicating that this function has been conserved through evolution. However, divergence in receptor function was also observed between a tandem gene duplication pair, highlighting how closely related ORs can evolve distinct specificities. By linking receptor function to evolutionary mechanisms, this work demonstrates how tandem gene duplications contribute to both the maintenance and diversification of OR function, ultimately shaping the neural processing of complex odors.

Poster 11

Resonance-guided Stimulation to Evoke Seizure Activity in Epileptogenic Brain Networks

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Introduction: Localization of the seizure onset zone (SOZ) is critical to surgically treat drug-resistant epilepsy. Seizures evoked during single-pulse electrical stimulation (SPES) can be localizing and have inspired the development of frequency-specific stimulation protocols to reliably evoke seizures. Dynamical network models built from SPES-evoked responses can be used to model neural resonance and predict “resonant frequencies” at which electrical stimulation can induce an epileptic seizure. **Methods:** In 10 patients who consented to undergo stimulation to induce seizures (SIS) at UAB, we stimulated at resonant frequencies and at standard frequencies (5, 10, 15, 20 Hz) and elicited seizures at both resonant and standard frequencies. In 5 patients who experienced stimulation-induced seizures at a standard frequency, we recalculated our models to investigate local rather than global resonant frequencies, particularly for brain regions in the SOZ. In a single patient, we prospectively stimulated at local SOZ resonant

frequencies in addition to global resonant frequencies and standard frequencies to elicit seizures. **Results:** Our retrospective analysis showed that the standard event-inducing stimulation frequency in 16 of 18 seizures were local resonant frequencies for SOZ brain regions. Our prospective analysis found that local SOZ resonant frequencies more effectively elicited epileptic events (8/17 stimulations) than when stimulating at global resonant frequencies (5/17 stimulations). **Conclusions:** These findings suggest that local resonant frequencies calculated using our neural resonance models more reliably elicit epileptic activity during SIS, particularly when targeting the suspected SOZ network, which could lead to improved epileptogenic network localization and overall surgical outcomes.

Poster 12

The Impact of Neonatal Adversity on Endocannabinoid Signaling and Adolescent Behavior

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Pre-term infants in the Neonatal Intensive Care Unit (NICU) may experience upwards of 15 painful and invasive procedures each day, including gastric suctioning and endotracheal intubation, often performed without analgesia. In addition to unresolved pain, NICU infants are housed in incubators and isolated from their caregivers. Further, over 45% of infants born prematurely are from low socioeconomic status (SES) households, presenting the additional stressor of limited resources to their early-life environment. While the neurodevelopmental impacts in adulthood have been explored independently, no studies have investigated the combined impact of early life pain (ELP), low SES, and isolation, recapitulating the NICU. Premature birth is a risk factor for substance use disorders (SUD); however, the mechanisms remain unknown. Early life adversity (ELA)-sensitive behaviors include social play and impulsivity, both hallmarks of adolescence, which may increase the risk of developing a SUD. The endocannabinoid system, particularly CB1 receptors, modulates these behaviors. We hypothesize that ELA results in the dysregulation of the endocannabinoid system, altering adolescent behaviors, and contributing to SUD. Our novel rat model incorporates ELP, limited bedding and nesting, and maternal separation to mimic the NICU. Social play is observed throughout the juvenile and adolescent periods while impulsivity is measured using a delay-discounting task employed throughout adolescence. CB1 expression will be quantified and correlated with observed behaviors. Additional studies will examine the effect of ELA on adolescent THC self-administration to investigate a causal role of the NICU experience in the increased risk of SUD development.

Poster 13

Pannexin-1 regulates neural cell fate and brain size

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Polymicrogyria (PMG) is a brain malformation characterized by excessive folding in the cortex, often associated with neurodevelopmental disorders like epilepsy. PMG is heterogeneous with diverse presentations and etiology, obscuring its genetic mechanisms. Recent whole exome sequencing of PMG patients identified ion-channelopathies as significant contributors to PMG, including mutations in the ATP-releasing channel gene *PANX1* found in individuals with PMG and microcephaly. PANX1 is expressed in early brain development in neural progenitor cells (NPCs), with studies indicating its role in their migration. However, whether PANX1 activity regulates NPC proliferation, influencing brain size and cell fate, is poorly understood. This project investigated the effects of PMG-associated mutations in *PANX1* on NPCs. Using crispant mice, we quantified SOX2+ and PAX6+ progenitors across genotypes. Additionally, we generated human induced pluripotent stem cells (hiPSC)-derived NPCs using dual SMAD inhibition and evaluated cell replication based on EdU incorporation during the S phase. Our findings revealed that *PANX1* disruption did not change the proportion of SOX2+ and PAX6+ progenitors between WT and knock-in mice. We also observed no difference in the proportion of EdU+ cells between WT and mutant lines. Together, these findings suggest that PMG-associated mutations in PANX1 may affect other neural stem cell populations within the cortex as a possible mechanism of dysfunction in the context of disease. Therefore, this study begins to characterize the nature of PMG-associated mutations in PANX1 on NPC behavior and highlights how ion channels regulate neural stem cell fate beyond the progenitor level and alter the structure of the brain.

Poster 14

Complex Spinal Mechanisms Underlying Stress-Induced Bladder Hypersensitivity in Hemopexin Depleted Mice

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Urologic Chronic Pelvic Pain Syndrome (UCPPS) is a chronic pain condition with a high prevalence in females (~3-8 million in the US), characterized by increased voiding frequency and urgency. Prior studies link stress to UCPPS development, but the mechanisms remain poorly understood. This study investigates the role of hemopexin (Hpx), an anti-inflammatory protein, in stress-induced bladder hypersensitivity. Hpx knockout (KO) and wild-type (WT) female mice were exposed to acute water avoidance stress (aWAS) for 1 hour. After 24 hours, bladder nociception was assessed via visceromotor response (n=12). A separate cohort of mice was used to conduct *in-vivo* spinal electrophysiology during urinary bladder distensions (n_{mice}=8-12; $N_{neurons}$=199). aWAS increased visceromotor response only in Hpx KO mice ($p<.05$). Spinal electrophysiology revealed reduced activity of wide dynamic range (WDR) neurons in both genotypes after aWAS ($p<.001$). Spontaneous nociceptive-specific neuron activity was highest in WT controls compared to other groups ($p<.01$). Hpx KO mice exposed to aWAS showed a phenotypic shift, with more non-inhibitory Type II neurons than inhibitory Type I neurons ($p<.05$). Overall, the data demonstrated that exposure to aWAS increased bladder hypersensitivity. This could be explained by the phenotypic switch in the quantity of Type I to Type II neurons. However, other spontaneous activity measures do point to the fact that stress-induced analgesia is also present. This highlights the complexity of spinal neuronal recruitment during noxious stimuli. Further studies will examine the activity of higher order structures to better understand the effect of hemopexin depletion and stress exposure on descending modulatory systems.

Poster 15

Phase-Contrast Adaptive Optics Scanning Laser Ophthalmoscopy (AOSLO) Reveals Diverse Cellular-Scale Immune Activity in the Non-Human Primate Retina In Vivo

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Understanding immune responses in the retina is crucial for neuroscience research, as inflammation plays a dual role—protecting against injury and infection while also contributing to retinal damage and vision loss when excessive. Conventional imaging lacks the resolution to capture individual immune cells in the living eye, necessitating advanced imaging techniques. Adaptive Optics Scanning Laser Ophthalmoscopy (AOSLO) combined with phase-contrast imaging enables high-resolution, non-invasive visualization of retinal immune cells, offering new insights into inflammatory processes.

This study employs AOSLO with phase-contrast imaging to investigate immune cell dynamics in the non-human primate (NHP) retina. Using three inflammation models—(1) infection via intravenous Adeno-Associated Virus (AAV) delivery, (2) sterile injury induced by inner limiting membrane (ILM) peel surgery, and (3) a case study of an NHP with chronic autoimmune dermatitis—we longitudinally tracked immune activity. The results revealed distinct immune responses across models, with cellular structures emerging in the retinal parenchyma post-ILM peel. These structures peaked at 1–2 weeks post-surgery before gradually declining, yet remained elevated above baseline. Additionally, immune cell motility and morphology varied between sterile and infectious models, suggesting different activation mechanisms.

The autoimmune dermatitis case study further illustrated systemic immune modulation. The affected NHP exhibited an amplified response to ILM peel compared to controls, yet systemic immunosuppression mitigated retinal inflammation, reducing cellular activity. This underscores the potential of immune-targeted therapies in controlling retinal inflammation. Our findings highlight the advantages of label-free AOSLO imaging for tracking immune responses in vivo. By bridging the gap between mouse and human studies, these advancements could enhance diagnostic and therapeutic strategies in ophthalmology and neuroscience.

Poster 16

Autism Genetic Pathways Affect Oligodendrogenesis

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Neuroimaging has consistently shown white matter abnormalities in Autism Spectrum Disorder (ASD), that suggest disrupted myelination processes. Our analysis of top SFARI ASD-associated genes reveals enrichment in oligodendrocyte precursor cells (OPCs), which are the cell types required for myelination. Using protein interaction analysis and community detection algorithms, we identified distinct functional clusters of ASD-associated proteins involved in transcription, chromatin organization, and cell-cell communication pathways within OPCs. While individual cluster functions remain partially intact when ASD-associated genes are disrupted, our findings suggest that reduced expression of inter-cluster connector proteins significantly impairs coordination between functional modules. Participation coefficient analysis identified super elongation complex subunit MLLT3, a component of the DOT1L complex involved in SOX2 transcriptional regulation, as a crucial connector protein that bridges multiple functional clusters. Permutation testing confirmed that MLLT3 disruption significantly reduces cross-cluster connectivity ($p<0.001$). The role of MLLT3 in oligodendrogenesis is particularly relevant, as it helps coordinate the transition between proliferation and differentiation stages of OPC development through SOX2 regulation. SOX2 functions as a key transcriptional regulator that maintains OPC proliferation and self-renewal capacity, and its downregulation is essential for initiating the differentiation program toward mature myelinating oligodendrocytes. A reduction in OPC turnover is associated with white matter dysregulation. This suggests a plausible mechanism by which genetic variations in ASD disrupt the sequential coordination of cellular functions: reduced connector protein expression impairs communication between functional clusters, ultimately leading to the white matter abnormalities observed in ASD neuroimaging studies.

Poster 17

The Role of Estradiol in Hippocampus Function in Control and High Fat Diet-fed Ovariectomized Mice

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Introduction: Menopause has been correlated to cognitive impairment and memory loss. Studies involving postmenopausal healthy women indicate that hormone therapy enhances cognitive function. However, contrasting clinical data across various health conditions present divergent effects of hormone treatment. To elucidate the mechanisms behind these effects, we hypothesize that E2 improves spatial memory and cognitive functions in control diet-fed mice but is less effective in high fat diet-fed animals.

Materials & Methods: Female C57BL/6J mice aged seven months were fed either a high-fat diet or a control diet for 10 to 14 weeks, followed by ovariectomy (OVX). Mice randomly received an implant that administered either 17β-estradiol (E2) or vehicle. The novel object location test (NOL) assessed memory performance. To investigate potential synaptic mechanisms underlying the effects of E2 on memory, we analyzed long-term potentiation (LTP) in the hippocampus. We evaluated the protein levels and phosphorylation status of the phosphoinositide 3-kinase (PI3K) pathway in the hippocampus using western blotting due to its crucial role in various physiological brain functions.

Results: The NOL test revealed that E2 significantly enhanced memory regardless of diet, but less in HFD mice. Extracellular field recordings in hippocampus slices indicated that E2 treatment enhanced LTP in CTD but not in HFD-fed mice. Diet and E2 showed no significant effect on either total or phosphorylated PI3K individually, analysis of the pPI3K/PI3K ratio suggests a potential augmentation in phosphorylation attributed to E2.
Conclusion: Our findings show that E2 treatment enhances cognitive processes in CTD- and HFD-fed mice and directly enhances synaptic plasticity in CTD but not in HFD-fed mice.

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Poster 18

KCNT1 Influences Cocaine-Seeking Behavior in Female Rats on Day 1 of Extinction

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The inability to maintain abstinence is a hallmark of addiction, with cravings during initial abstinence predicting long-term relapse outcomes in both humans and rodents. Promoting successful abstinence may be particularly complex in women, as their psychological and biological responses to drugs of abuse differ from those in men. Several measures of cocaine dependence are greater in women, a pattern reflected in female rodents, yet the biological mechanisms underlying these sex differences remain unclear. Extinction day 1 (ED1) marks the onset of abstinence when the expected drug is unavailable, representing a stressful time point associated with increased drug cravings. We have previously demonstrated that the dorsal hippocampus plays a significant role in driving sex-specific engagement in cocaine-seeking behavior on ED1. Using whole-transcriptome sequencing (RNA-Seq) analysis, we identified sex-specific gene expression patterns in the dorsal hippocampus elicited by exposure to the cocaine self-administration context on ED1, which correlate with cocaine-seeking behavior. In females, we identified 101 transcripts with fold-change differences on withdrawal day 1 (WD1) compared to naïve rats, and 22 transcripts with fold-change differences on ED1 compared to WD1 controls. Notably, only three targets overlapped between the sexes. Furthermore, five genes identified in females significantly correlated with cocaine-seeking behavior on ED1, showing R^2 values greater than 0.70. One of these targets, KCNT1, a potassium channel, negatively predicted cocaine-seeking behavior on ED1 in females. Inhibition of KCNT1 by PRX20 decreased cocaine-seeking behavior on ED1 when admitted systemically and intrahippocampally, while agonism of KCNT1 with Niclosamide increased cocaine-seeking behavior on ED1 specifically in females. These findings suggest that sex-specific transcriptomic signatures in the dorsal hippocampus, particularly KCNT1, may play a crucial role in driving cocaine-seeking persistence during early abstinence. Targeting these molecular pathways could enhance the maintenance of abstinence, with implications for sex-specific addiction treatment strategies. This work was supported by R00-045758 to ASK.

Poster 19

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

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In macular degeneration, the primary cause of vision loss among older adults, photoreceptor death in the retina can result 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 (damage to low-level vision) can differ widely in their performance on complex visual tasks (which involve high-level vision), 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. However, this quantification has been difficult in the past, as there is no reliable measure of the severity of the scotoma. Traditional tests like visual acuity and contrast sensitivity can be misleading, as people with small islands of spared vision can do very well on those tasks. Comparing scotoma sizes across participants 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". Different parts of visual cortex correspond to parts of vision, and the cortical magnification factor describes how much cortex is devoted to each portion of the visual field. We use the Macular Integrity Assessment (MAIA), a microperimetry method to evaluate sensitivity at many points across the retina. By weighting MAIA scores with the cortical magnification factor, we derived a measure called macular functional health (MFH). We found that the 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 20

Neural Dynamics of Event Model Maintenance Across Age During Naturalistic Viewing

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Background: Older adults segment and remember everyday activities less effectively than young adults. Previous fMRI studies (Kurby et al., 2013) indicate that both age groups recruit similar brain regions at event boundaries, suggesting intact event model updating. In the current study, we evaluated whether age-related declines in event memory are due to age-related changes in event model maintenance, which was operationalized as EEG pattern similarity. **Method:** We recorded EEG brain activity from 42 young and 42 older adults while they watched an episode of BBC's Sherlock. Afterward, they completed event memory and cognitive tasks. EEG pattern similarity was used to measure how consistently brain activity remained within events versus across different events. **Results:** Both groups showed higher EEG similarity within events than across events, suggesting stable event models. However, no significant age-related differences were observed in pattern similarity, meaning older adults maintained event models as well as young adults. Additionally, pattern similarity was not correlated with memory performance. **Conclusion:** Despite difficulties in event segmentation, older adults appear to maintain event models as effectively as younger adults. This suggests that other factors, such as attention or working memory, may play a larger role in age-related memory decline. Understanding how we process and store events can help improve strategies to support memory in aging populations.

Poster 21

GABAergic mechanisms of fear encoding in the dorsal peduncular cortex

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Fear learning is a necessary survival adaptation that better prepares organisms to appropriately respond to threatening stimuli. However, intensely traumatic events can negatively impact an organism's cognition, a feature central to various neuropsychiatric disorders. The rodent medial prefrontal cortex (mPFC) is a locus for processing fear, where dorsal and ventral areas are thought to promote and suppress fear, respectively. The role of fear encoding has been ascribed to excitatory glutamatergic principal neurons (PNs). Conversely, GABAergic interneurons (INs), of which the two main cortical sub-types are parvalbumin (PV-INs) and somatostatin-expressing (SST-INs) interneurons, are thought to strictly inhibit PNs to fine-tune fear circuits. In contrast, our lab discovered that prelimbic SST-INs have the capacity to encode and store fear memory. Our additional recent study has revealed a new role for the dorsal peduncular cortex (DP) in fear memory encoding. We provided evidence that DP is unexpectedly involved in fear encoding and expression, but not suppression -- a finding at odds with its presumed function. As this is the first study to examine fear memory encoding in the DP, how GABAergic INs in this region contribute to fear encoding remains unknown. Preliminary evidence via c-Fos labeling showed increases in DP interneurons following fear learning. Here, we aim to demonstrate that experience-dependent alterations in DP GABAergic activity and plasticity are required for fear memory encoding.

Poster 22

A Pilot Study of Transdermal Auricular Vagus Nerve Stimulation for Treating Insomnia in Breast Cancer Patients

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Introduction: Insomnia affects about 40%-70% of breast cancer patients and contributes to cancer-related fatigue

(CRF), which can increase the risk of disease progression, decrease survival, increase systematic inflammation, and cause physical, emotional, and mental distress. Transcutaneous-auricular Vagus Nerve Stimulation (taVNS) is a non-invasive intervention that has gained attention due to its implications to modulate autonomic nervous system activity, inflammation, and affect brain regions associated with cognition, arousal, and mood. It is a well-studied neuromodulation device that delivers mild electrical current to the auricular branches of the vagus nerve. This intervention could serve as a safe, effective intervention to improve the overall well-being in breast cancer patients.
Methods: We investigate the influence of taVNS to address insomnia in breast cancer patients. We examine the efficacy of 2 week, at-home use of taVNS as a treatment for insomnia by looking at measurements of sleep, CRF, and mental health. Additionally, we aim to evaluate the effect of taVNS on pro-inflammatory biomarkers in the blood. **Results:** We hypothesize that patients will report significantly improvements in sleep, inflammation, anxiety, depression, and CRF after two weeks of taVNS. Current results show significant decreases in sleep and fatigue ($p =< 0.005$). Additionally, there has been no reported adverse effects. **Conclusion:** This study is ongoing with active participants and ongoing recruitment. Results so far indicate significant improvements in sleep and fatigue.

Poster 23

Chemogenetic inhibition of Central Amygdala neurons acutely attenuates the anorexigenic effects of exogenous GLP-1 signaling

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Glucagon-like peptide-1 receptor (GLP-1R) activation reduces food intake via multiple brain regions, including the hypothalamus, hindbrain, and limbic system. Peripheral and central administration of GLP-1R agonists activate the central nucleus of the amygdala (CeA), but the underlying mechanisms remain unclear. Our lab has shown that Glp1r is broadly expressed in CeA neuronal subpopulations, including Prkcd, Sst, and Tac2 neurons, with enrichment in the medial CeA. Given this, we aimed to determine the CeA's role in mediating feeding behavior in response to systemic GLP-1 signaling. We hypothesized that CeA activation is required for the anorexigenic effects of peripheral GLP-1R activation. To test this, we chemogenetically inhibited CeA GABAergic or Pkcδ neurons using an inhibitory DREADD (hM4d (Gi)) and assessed feeding behavior following peripheral deschloroclozapine (DCZ) and Exendin-4 (Ex4) administration. Sixteen cre-positive male and female mice per group received bilateral injections of either cre-dependent mCherry or hM4d(Gi) into the CeA and were individually housed with their own FED under a fixed-ratio 1 feeding paradigm. Following food-deprivation, repeated-measures two-way ANOVA analysis of pellets retrieved within the first hour revealed that inhibition of CeA neurons with DCZ significantly attenuated food-seeking behavior despite Ex4 treatment in the hM4d(Gi) group, but not mCherry. These findings suggest that the CeA can also mediate the effects of exogenous GLP-1 signaling like other key feeding-regulatory brain regions. To what extent, warrants further investigation.

Poster 24

Knockdown of the glucocorticoid receptor (GR) in a corticostriatal pathway increases the propensity to attribute incentive salience to a reward cue

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Glucocorticoid receptors (GRs) are critical modulators of the stress response, yet their role in behavioral regulation outside of stress remains unclear. Given that stress-related psychopathologies, such as substance use disorder (SUD) and impulse control disorders, are characterized by deficits in inhibitory control, we investigated the role of GR within a top-down cortico-striatal pathway in governing incentive motivation. Specifically, we used transgenic Sprague-Dawley rats with conditional GR knockdown to selectively reduce GR expression in glutamatergic projections from the prelimbic cortex (PrL) to the nucleus accumbens core (NAcC)—a pathway implicated in reward-seeking behavior and the regulation of dopamine signaling. To assess the effects of GR knockdown on incentive salience attribution, rats underwent a Pavlovian conditioned approach (PavCA) paradigm, in which a neutral cue was repeat-

edly paired with a food reward. Our results indicate that rats with GR knockdown in the PrL-NAcC pathway were significantly more likely to sign-track—attribute heightened motivational value to the reward cue—compared to wild-type controls. Additionally, the degree of GR knockdown positively correlated with the magnitude of this behavior, further implicating GR in the regulation of incentive motivation. Notably, these effects were observed irrespective of sex. Since sign-tracking behavior is associated with increased impulsivity, attentional deficits, and susceptibility to cue-induced reinstatement of drug-seeking behavior, our findings suggest that GR signaling within the PrL-NAcC pathway plays a crucial role in inhibitory control and maladaptive behaviors. These results provide insight into the neuromolecular mechanisms underlying stress-induced vulnerabilities to compulsive reward-seeking and may have implications for stress-related psychiatric disorders.

Poster 25

Development of an ethologically relevant rodent model of social stress

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Posttraumatic stress disorder (PTSD) is a psychiatric disorder that develops with exposure to life-threatening or highly traumatic events. Most of these cases are socially derived, involving child neglect, domestic violence, sexual abuse, etc. Common symptoms of PTSD include persistent fear and the inability to suppress this fear. Currently, the most effective treatment is exposure therapy, which is only effective in 50% of patients. Additionally, GABAergic dysfunction is common in humans with PTSD, but the mechanisms are unknown.
Rodents are a great model to study fear and trauma due to their numerous circuit parallels with humans including analogs to the human brain. Recent evidence suggests that inhibitory GABAergic neurons are centrally involved in fear promotion and suppression within the rodent medial prefrontal cortex (mPFC). 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 such as the previously established social defeat stress paradigm, predator odor exposure, and social housing instability.
Using this paradigm, we can now identify GABAergic dysfunctions following social trauma. We will characterize the alterations in GABAergic microcircuitry and plasticity within the rodent dmPFC that allows for the persistent promotion of fear and fear extinction deficits following trauma using various in vivo cell manipulations and recordings.

Poster 26

Glia control experience-dependent plasticity in an olfactory critical period

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Sensory experience during developmental critical periods has lifelong consequences for circuit function and behavior, but the molecular and cellular mechanisms through which experience causes these changes are not well understood. The *Drosophila* antennal lobe houses synapses between olfactory sensory neurons (OSNs) and downstream projection neurons (PNs) in stereotyped glomeruli. Many glomeruli exhibit structural plasticity in response to early-life odor exposure, indicating a general sensitivity of the fly olfactory circuitry to early sensory experience. We recently found that glia shape antennal lobe development in young adults, leading us to ask if glia also drive experience-dependent plasticity during this period. Here, we define a critical period for structural and functional plasticity of OSN-PN synapses in the ethyl butyrate (EB)-sensitive glomerulus VM7. EB exposure for the first 2 days post-eclosion drives large-scale reductions in glomerular volume, presynapse number, and post- synaptic activity. Crucially, pruning during the critical period has long-term consequences for circuit function since both OSN-PN synapse number and spontaneous activity of PNs remain persistently decreased following early-life odor exposure. The highly conserved

engulfment receptor Draper is required for this critical period plasticity as ensheathing glia upregulate Draper, invade the VM7 glomerulus, and phagocytose OSN presynaptic terminals in response to critical-period EB exposure. Loss of Draper fully suppresses the morphological and physiological consequences of critical period odor exposure, arguing that phagocytic glia engulf intact synaptic terminals. These data demonstrate experience-dependent pruning of synapses and argue that *Drosophila* olfactory circuitry is a powerful model for defining the function of glia in critical period plasticity.

Poster 27

Cell Autonomous Effects of Mutant Huntingtin Expression in Somatostatin Cells

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Huntington's disease (HD) is a fatal autosomal dominant disease caused by an expansion of a CAG repeat in the gene encoding the Huntingtin protein. The resulting abnormal polyglutamine-containing protein is ubiquitously expressed. HD patients exhibit progressive motor cognitive and psychiatric abnormalities. HD is characterized by degeneration of striatal medium spiny neurons (MSNs) and is accompanied by dysfunction of other cell types. MSNs are regulated by extrastriatal glutamatergic and dopaminergic input as well as intrastriatal and extrastriatal GABAergic input. One population of GABAergic interneurons express the neuropeptide somatostatin (SST+). Interestingly, these cells are not lost in HD. In multiple mutant Huntingtin (mHTT) expressing mice, including the conditional human mHTT-expressing BACHD model, the striatal SST+ cells have increased spontaneous firing. The increase in SST+ cell firing in these mice could be contributing to abnormal behavior observed in HD. Thus, understanding the role mHTT expression plays in these cells is important and can provide insight into electrophysiological and behavioral deficits. In this study, we will use a genetic approach to knockdown mHTT expression in SST+ cells, by crossing BACHD mice to SST-Cre mice, to determine if mHTT expression in SST+ cells contributes to the behavioral and electrophysiological changes observed in BACHD mice. We hypothesize that expression of mHTT in SST+ cells influences the altered behavioral output in BACHD mice. Motor dysfunction is not improved in BACHD/SST-Cre mice. Additionally, we prove that the increased spontaneous firing of SST+ cells is cell autonomous, based on normalization of the firing rate in BACHD/SST-Cre mice.

Poster 28

Sex-specific aging in brain tissue gene expression in the genus Drosophila

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Sex-specific aging is common in animals across many taxa. However, little is known about the molecular basis of this phenomenon. This aging is associated with sex-specific changes in gene expression, including in the brain. Genome size and repeat content are potential molecular factors influencing sex-specific aging. The size and content of an organism's genome vary considerably across species, and the potential effects of this variation on lifespan are not well-studied. Drosophila melanogaster and its relative Drosophila virilis are useful model organisms to study aging and the effect of genome size due to their short lifespans, high yield of progeny, and varying genome sizes. Therefore, we present an experimental design for studying differential gene expression across sex and age in the brain tissue of D. melanogaster and D. virilis, the latter of which has a larger genome and higher percentage of non-coding satellite DNA. We use Kaplan-Meier survival curves to identify equivalent time points across sex and species; flies will be aged to these time points and then brains will be collected for RNA sequencing. RNA-seq data will be analyzed to identify differentially expressed genes across sex, species, and age. Additionally, RNA-seq reads will be aligned to de novo repetitive element libraries to assess the relationship between age and repeat transcription across groups. By studying sex differences in gene and repetitive element expression in brain tissue across Drosophila species with varying genome size and repeat content, we aim to improve our understanding of the molecular basis of sex-specific aging.

Poster 29

The role of prelimbic interneurons in reward learning

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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 30

Orexin/Hypocretin Modulation of Cholinergic Signaling within the Prefrontal Cortex in Response to an Immune Challenge

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Background: There has been limited progress in understanding the vulnerability of the basal forebrain cholinergic system (BFCS) in aging and disease states, suggesting that there are other factors at play, such as altered afferent regulation. We have previously shown that the orexin/hypocretin system modulates cholinergic signaling and neuroinflammation in key regions implicated in Alzheimer's Disease, such as the basal forebrain and prefrontal cortex (PFC). Therefore, we hypothesize that orexin downregulation will impair PFC cholinergic response following an immune challenge. **Methods:** We utilized lentiviral mediated gene transfer to downregulation orexin expression in young female rats and implanted a microdialysis guide cannula into the PFC. Following an intraperitoneal injection of lipopolysaccharide, in-vivo microdialysis with a food-paired stimulus was performed and brain dialysates were measured for acetylcholine using high-performance liquid chromatography. **Results:** We hypothesize that cholinergic response in the PFC of control females will be significantly increased following a food-paired stimulus, as we have previously shown in the insular cortex. This effect will be disrupted following orexin downregulation and LPS injection when compared to control females. **Conclusion:** Downregulation of orexin impairs the appropriate neuroimmune and neurochemical responses in the PFC to an immune challenge. Thus, the well-documented age- and AD-associated reduction of orexin signaling may be linked to BFCS degeneration via neuroinflammatory mechanisms.

Poster 31

C. elegans as a Model Organism to Study the Neuronal Effects of Cocaine Exposure

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Cocaine Use Disorder (CUD) is a prevalent issue affecting more than 1 million people in America. CUD's biological

mechanisms are of particular interest due to the lack of therapeutics and effective clinical interventions for cocaine addiction or overdose. We are working to establish *C. elegans* as a model organism to leverage a higher throughput due to the worms' short developmental time frame, extensively studied genome, and conserved neurotransmitter pathways. To analyze the neurotransmitter pathways cocaine targets, we are observing the easily quantifiable behavior, pharynx pumping. We hypothesize that the characterization of pharynx behavior after cocaine exposure will provide a platform to identify neurons of interest for future cocaine studies. Preliminary data show a decrease in the pharynx pumping rate of worms after acute cocaine exposure. Exploring the mechanism underlying this decrease with mutant strains will allow us to determine the neurotransmitter pathways cocaine is affecting in *C. elegans*. The long-term goal of the study is to establish a novel platform where we can readily identify and causally implicate conserved genetic susceptibility loci and molecular regulators that underlie cocaine-induced neuronal plasticity, eventually leading to an improved mechanistic understanding of CUD neurobiology and the identification of novel avenues of therapeutic targets.

Poster 32

Synaptic activity in a neurodevelopmental mouse model of GAT1 haploinsufficiency

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Many developmental epilepsies and neurodevelopmental disorders are associated with abnormal GABAergic signaling. *SLC6A1*-neurodevelopmental disorders (*SLC6A1*-NDDs) are caused by loss-of-function variants in the gene that encodes GAT1, the primary neuronal GABA transporter. Pathological variants in *SLC6A1* cause developmental delay and behavior disorders and are among the top 10 most common monogenic causes of epilepsy and autism spectrum disorders. To address whether altered GABAergic signaling in the developing hippocampus can contribute to *SLC6A1*-NDDs, we are investigating GABA-dependent synaptic activity in WT and mouse models of *SLC6A1*-NDDs using whole-cell electrophysiology in acute hippocampal slices from P4-6 mice. First, we found that total charge of synaptic currents mediated by GABAA receptors in response to spontaneous oscillations known as "giant depolarizing potentials" (GDPs) are enhanced by the selective GAT1 blocker, NO711. Thus, in the normal brain, GAT1 contributes to GDPs that are thought to be important for driving hippocampal circuit development. In ongoing experiments, we are comparing GDPs in a mouse model of *SLC6A1*-NDDs, a GAT1 heterozygous knockout mouse. Preliminary results do not show differences in GDPs between GAT1 KO and controls, however, the peak amplitude and area of GDPs in GAT1 KOs appear to be differentially enhanced by a GABAB antagonist. The observed differences in GABA-dependent activity in developing mice suggest that altered GABA homeostasis in *SLC6A1* models may influence GABA-dependent mechanisms of neurodevelopment within the hippocampus.

Poster 33

Uncovering the Role of the Astrocyte Secretome in Blood-Brain Barrier Integrity and Repair

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Blood-brain barrier (BBB) impairment is a hallmark of various neurodegenerative diseases, traumatic brain injury (TBI), and aging, yet the molecular mechanisms underlying BBB maintenance and repair remain poorly understood. Although *in vitro* studies have provided evidence for BBB regulation by astrocyte-secreted factors, a lack of available tools for identifying and manipulating astrocyte-secreted factors *in vivo* has precluded a mechanistic understanding of these processes. Thus, I designed tools to address this technical gap. The first tool facilitates *in vivo* labeling and identification of secreted proteins in a cell type-specific manner within the brain: Cell type-specific Neuroscretome (CeNSe-) labeling. The second tool, CeNSe-block, prevents one method of astrocyte secretion *in vivo* by cleaving specific molecular machinery required for exocytosis. In the present study, I demonstrated the feasibility of these tools *in vitro* and *in vivo*. First, western blot analysis of astrocyte cultures and mice transfected with the CeNSe-labeling and CeNSe-block tools indicates efficient expression of the viruses as reflected by detection of the construct tags. Further, analysis by immunohistochemistry shows correct localization of the CeNSe-labeling construct to the endoplasmic reticulum. Additionally, a reduction in protein content of media from cultured astrocytes treated with CeNSe-block suggests effective reduction of astrocyte secretion. I will utilize these tools in future studies to investi-

gate whether age- and injury-related BBB impairment correlates with changes in astrocyte-secreted proteins, as well as to test the necessity of astrocyte-secreted factors for BBB maintenance and repair.

Poster 34

Assessing NMDA receptor distribution by cortical layer in human postmortem dorsolateral prefrontal cortex

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Visuospatial working memory (vsWM) is associated with activity of the dorsal lateral prefrontal cortex (DLPFC) at gamma (30–80 Hz) frequency. Gamma oscillatory power increases with vsWM load and fails to increase corresponding with vsWM load in individuals with schizophrenia. The neural substrate responsible for gamma oscillatory power is believed to be, in part, somatostatin interneurons (SSTs) and pyramidal neurons (PNs). PNs stimulate other PNs through recurrent excitation, as well as SST interneurons, which in turn temporally tune the excitatory firing of PNs. Such PN-to-PN and PN-SST stimulations utilize, in part, N-methyl-D aspartic acid receptors (NMDARs). To validate new methodology and assess NMDAR-based neurotransmission among PNs and SSTs, we utilized combined fluorescent *in situ* hybridization (FISH) and immunohistochemistry in human postmortem DLPFC in 3 subjects unaffected by mental illness (UC) to characterize the mRNA expression of two primary NMDAR subunits, GRIN2A and GRIN2B, within PNs (labeled by VGLUT1) and SSTs (labeled by SST). Additionally, we used DAPI and NeuN to identify both the nuclei and somal bodies of neurons. SST neurons were observed throughout the tissue, with a higher density in layer 2. L3PNs were identified by labeling of VGLUT1 mRNA and presence within layer 3. We observed both GRIN2A and GRIN2B mRNA in VGLUT1+ L3PNs and SST+ interneurons across all three UC tissue samples. The combined FISH/Immunohistochemical procedure used successfully delineated the somal border of PNs and SSTs throughout the entire tissue, with expected clustering in specific cortical layers, and allowing cell-type specific quantitative analysis of NMDAR subunit mRNAs.

Poster 35

The Role of Salivary Sodium in the Gustatory Responses to Salt and Water in Humans

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The mechanisms by which salt and water are sensed in the mouth remain incompletely understood. Emerging evidence suggests that salivary sodium (Na^+) plays a key role in the gustatory perception of both. This study aimed to test the hypothesis that the gustatory brain response to water depends on the rinsing of Na^+ from the tongue. Using functional magnetic resonance imaging (fMRI), we measured cortical responses to deionized water and NaCl solutions at 5, 10, 15, and 30 mM in healthy adults. Equimolar concentrations of KCl were included to determine whether the effects were sodium-specific or related to osmolarity. Unstimulated salivary Na^+ concentrations were also measured to explore individual differences in baseline ionic levels. Contrary to the hypothesis, low NaCl concentrations did not attenuate the brain's response to water. Instead, 30 mM NaCl elicited the strongest activation in the anterior insula, indicating a concentration-dependent response. KCl elicited similar, but weaker, activations. Water itself produced a robust and consistent response in the gustatory cortex, although of lower amplitude than 30 mM NaCl. These findings confirm that water is a bona fide gustatory stimulus and that the neural encoding of salt in the insula is concentration-dependent. Our results challenge previous assumptions about the role of low sodium concentrations in modulating taste and expand current understanding of cortical representations of salt and water in humans.

Poster 36

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

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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, regulation from astrocytes, 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. However, interactions of astrocytes and GABAergic interneurons has not previously been studied in striatum. Abnormal activity of both astrocytes and interneurons has been shown in some mouse models of HD.
In this work, we used aged BACHD full length mutant huntingtin expressing mice and wildtype mice to explore astrocytic Ca^{2+} elevations in the striatum. We use GCaMP6f to measure Ca^{2+} signals and in preliminary experiments we observe alterations in Ca^{2+} signals in BACHD astrocytes. Furthermore, we have expressed ChrimsonR in SST-INs or PV-INs in SST-Cre and PVB-Cre mice, respectively, and expressed GCaMP6f in astrocytes to explore responses of astrocytes to SST-IN and PVB-IN activation. We present preliminary data demonstrating astrocytic responsiveness to SST and PVB interneuron stimulation. Together, these experiments reveal fundamental interactions of striatal astrocytes and interneuron populations and striatal astrocytic Ca^{2+} changes in the aged BACHD mutant huntingtin expressing mouse model.

Poster 37

Dissecting Genetic Drivers of Cardiometabolic, Circadian, and Cognitive Dysfunction

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Introduction: Obesity is a significant risk factor for cardiovascular disease (CVD), cognitive decline, sleep and circadian disruption. However, the molecular mechanisms linking genetic predisposition to multi-organ impairment remain poorly understood. Multiple genome-wide association studies (GWAS) have identified obesity-linked loci, including PSMC3 (an ATPase subunit) and Sec16B (an endoplasmic reticulum export factor), which exhibit dynamic, tissue-specific expression in cardiac and neuronal systems. These genes are strong candidates for investigating heart-brain axis dysfunction through both cell-autonomous and non-cell-autonomous mechanisms, with a focus on mitochondrial dynamics, proteostasis, and circadian regulation. **Materials & Methods:** Using an innovative Drosophila model, we performed RNAi knockdowns of Rpt5 and Sec16, the fly orthologs of human PSMC3 and Sec16B, in cardiomyocytes (Hand-Gal4), panneurons (Elav-Gal4), and circadian neurons (Pdf-Gal4). **Results:** By three weeks of age (middle-aged), knockdown of both genes led to compromised heart function, fragmented sleep and memory impairment in a cell-autonomous manner. Notably, cardiac-specific knockdown impaired both sleep and memory, while pan-neuronal knockdown disrupted cardiac function, highlighting heart-brain axis communication. Circadian neuron-specific knockdown also impaired sleep, further implicating circadian regulation. **Conclusion:** To elucidate underlying mechanisms, we are analyzing gene expressions in dissected heart and brain tissues, focusing on mitochondrial regulation (Pink1, Drp1), ER stress (Bip, Xbp1), and inflammation (upd3, eiger). Additionally, cytological assessments of myofibrillar integrity (phalloidin), extracellular matrix (Pericardin), mitochondria (Mito-GFP), and synaptic integrity (Synapsin) are underway. These findings will provide critical insights into the genetic and molecular basis of obesity-associated heart-brain axis dysfunction.

Poster 38

Investigating whether lysosome-targeted progranulin prevents FTD-like pathology

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Introduction: Progranulin (PGRN) is a secreted protein that supports lysosomal function and exerts neurotrophic and

anti-inflammatory effects. Loss-of-function mutations, which usually cause haploinsufficiency of the progranulin protein, are an autosomal dominant cause of Frontotemporal Dementia (FTD). Mutations in both copies of the GRN gene lead to neuronal ceroid lipofuscinosis (NCL), an early-onset lysosomal storage disorder characterized by lipofuscin buildup. While progranulin has been shown to act both extracellularly and inside lysosomes, the extent to which intracellular progranulin alone is sufficient to protect against FTD-like pathology remains unclear. **Materials & Methods:** To investigate progranulin's site of action, we developed constructs in which the transmembrane domain and cytosolic tail of LAMP-1 was fused to the C-terminus domain of progranulin. This resulted in a lysosome-targeted version of progranulin (L-PGRN), which undergoes minimal secretion. A new mouse line (GrnL) was generated through the knock-in of L-PGRN to the endogenous Grn locus, resulting in replacement of Grn with L-PGRN. GrnL mice express PGRN in normal patterns but exhibit minimal secretion of PGRN into the extracellular space. Grn knockout mice display markers of lysosomal dysfunction, microgliosis, and astrogliosis. We sought to determine whether GrnL mice would be protected from developing this FTD-like pathology by utilizing lysosome-targeted PGRN only. **Results/Conclusion:** Staining of 12-month–old GrnL mice brain tissue slices revealed that the levels of markers for lysosomal dysfunction, microgliosis, and astrogliosis were similar to those of the wild type. From this, we can conclude that the absence of extracellular progranulin does not lead to FTD-like pathology.

Poster 39

HIV-Tat disrupts amphetamine-induced non-vesicular dopamine release

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The use of amphetamine (AMPH) has been linked to human immunodeficiency virus (HIV) transmission, as HIV can spread through heightened unprotected sexual activity that is associated with AMPH use disorder (AUD). For these reasons, AUD and HIV infection have been termed a double epidemic. In this relationship, the role played by AUD in HIV dependent neurodegeneration is well documented. Furthermore, in humans, HIV infection increases AMPH frequency of use, frequency and duration of binging, as well as amount. This is important since the DSM-5 criteria for addiction includes a progressive intensification in drug use (*i.e.* escalation). *To date, no examples exist of verified mechanisms of how HIV/HIV proteins alter AMPH actions and/or behavioral expressions.*
AMPH behaviors stem from its ability to reverse the function of the DA transporter (DAT), causing non-vesicular DA release (NVDR), resulting in an increase in extracellular DA levels. To gain a deeper understanding of NVDR, we provided the first evidence that specific domains of human DAT (hDAT) engage in direct association with the plasma membrane lipid phosphatidylinositol 4,5-bisphosphate (PIP_2). These interactions are essential for AMPH to promote NVDR and specific behaviors. The HIV trans-activator of transcription regulatory protein Tat_{1-86} (Tat) is a protein that binds PIP_2 with high affinity through its basic domains. Consistent with Tat high affinity for PIP_2, we demonstrated that Tat impairs NVDR. We also demonstrated that Tat, by blunting AMPH-induced DA release (*i.e.* NVDR), promotes AMPH escalation.

Poster 40

Relationship between default mode network activity and mood disturbances in idiopathic generalized epilepsies

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Introduction: Epilepsy is a neurological disorder in which neuronal hyperexcitability and seizure activity alter functional brain networks. People with idiopathic generalized epilepsies (IGEs), unlike those with focal seizures, experience seizures originating from within and rapidly spreading to both brain hemispheres, which makes them a good population for investigating brain wide functional networks. People with IGEs suffer from comorbid mood disorders including depression and anxiety, which may be linked to functional brain network alterations; however, these relationships remain unclear. In this study, we examined if mood disturbances in people with IGEs, as measured by the

Profile of Mood States (POMS), would correlate with Default Mode Network (DMN) resting state functional connectivity. **Methods:** Adults with IGEs (ages 18-55; n=40) underwent neurocognitive and physiological examinations. Following examinations, 3T MRI was performed to collect anatomical and resting state functional MRI scans. Apriori seed-based analysis utilized posterior cingulate cortex (PCC) and bilateral inferior parietal lobules (bIPL), which are part of the DMN, for regions of interest. AFNI software was used to analyze MRI data and conduct statistical analyses of functional connectivity for the seed regions. **Results:** The covariate analysis revealed non-significant bidirectional trends in associations between POMS scores and functional connectivity of the PCC and bIPL. **Conclusion:** Our hypothesis was that epilepsy and mood disturbance are mediated by common network connectivity alterations associated with both conditions. While this study was inconclusive in determining a relationship, our preliminary results suggest that DMN connectivity as a potential mechanism for mood disturbance in IGEs warrants further investigation.

Poster 41

Inflammation Induces Deficits in Neurotransmission in Female iPSC-derived Dopaminergic Neurons

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Introduction: High inflammation is associated with impaired motivation in many neuropsychiatric disorders. Studies in human subjects and animal models have shown that immune challenges could lead to motivational deficits and reduced dopamine (DA) release in the brain, however, the underlying mechanisms are largely unknown. Furthermore, motivational deficits are more common in females with high levels of peripheral inflammatory markers, compared to males. However, the role of inflammation in shaping this disparity remains unclear. In this study, we examined how proinflammatory cytokine interleukin (IL)-6 affects neurotransmission differentially in healthy female and male human iPSC-derived DA neurons. **Materials & Methods:** Eight-week-old healthy female and male iPSC-derived DA neurons were treated with vehicle or 5ng⁄mL IL-6 for 24hrs. Changes in extracellular DA concentration, network neuronal activities, transcriptomic profiles, synaptic vesicle (SV) transport, density, size and docking at synaptic terminals were measured in treated and vehicle control neurons. **Results:** IL-6 treatment significantly reduces DA release, neuronal activity, SV velocity, and density of docked SVs only in female DA neurons. Moreover, female and male DA neurons show transcriptomic differences in inflammatory response and synaptic signaling-related genes. **Conclusion:** IL-6 treatment affects neurotransmission differentially in female and male DA neurons. Specifically, female DA neurons are more vulnerable to inflammation and show more IL-6-induced deficits in synaptic transmission, while the changes in male DA neurons largely remain insignificant. This study is the first to use a human-specific cellular model to investigate the mechanisms of inflammation-induced deficits in neurotransmission in female and male DA neurons.

Poster 42

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

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Huntington's Disease (HD) is a fatal, genetic, and progressive neurodegenerative disorder caused by a polyglutamine expansion in the huntingtin protein, leading to significant degeneration of striatal medium spiny neurons (MSNs). MSNs account for >95% of striatal cells. The MSNs express either dopamine receptor D1 (Drd1) or dopamine receptor D2 (Drd2). Drd2-expressing MSNs degenerate most prominently at early stages of HD. MSNs are also characterized by their location in patch or matrix compartments of the striatum, with patch MSNs receiving limbic input and matrix MSNs receiving sensorimotor input. In HD, MSNs exhibit abnormal synaptic plasticity, suggesting changes in neuroreceptors at the post-synaptic density.
Studies in hippocampus suggest that ACTN2 is crucial for the localization of neurotransmitter receptors and PSD-95 to the post synaptic density. A decrease in this protein could lead to synaptic dysfunction and affect neurotransmission. While it is known that ACTN2 is decreased in the striatum in HD patients and in mHTT expressing mice, it remains unclear whether MSNs contribute to this decrease, and whether patch or matrix show a difference in ACTN2 levels. To assess whether reduction of ACTN2 is MSN subtype-specific and if it is localized spatially within the patch

and matrix of the striatum, we used the mHTT-expressing BACHD mouse model. We performed indirect immunofluorescence and fluorescence *in situ* hybridization to determine cell type contribution to changes in ACTN2 expression. This study aims to provide insight into the role of ACTN2 in the pathogenesis of HD and to identify potential targets for restoring synaptic function.

Poster 43

Spatial Transcriptomics and Magnetic Resonance Imaging Reveal the Genetic and Cytoarchitectonic Determinants of Alzheimer's Disease

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Introduction: The World Health Organization estimates around 55 million people globally have dementia, with Alzheimer's disease (AD) accounting for 60–70% of cases[1]. Heritability estimates of 58–79% highlight a strong genetic contribution to AD risk, yet the molecular mechanisms underlying its characteristic cortical neurodegeneration remain poorly understood[11]. Advances in imaging transcriptomics provide a framework to uncover molecular pathways by integrating spatial gene expression data with neuroimaging phenotypes[3,4]. This study leverages transcriptomic data from the Allen Human Brain Atlas (AHBA) and MRI-derived gray-white contrast (GWC), a measure gray and white matter intensity differences at the cortical boundary, to identify genes and pathways associated with AD risk across two large cohorts. **Methods:** Participants included 2,286 individuals from the National Alzheimer's Coordinating Center (NACC) and 608 from the Alzheimer's Disease Neuroimaging Initiative (ADNI), comprising age- and sex-matched cognitively normal (CN) and AD groups[5-7]. T1-weighted MRI data were processed using FreeSurfer (v6.0) to extract cortical thickness and compute GWC as a normalized ratio of gray-to-white matter intensities at each vertex. Gene expression data from six postmortem brains from the AHBA were re-annotated using the hg38 genome reference[3,4].Expression values were averaged across probes and mapped onto the cortical surface by aligning sample locations to vertices on a mid-thickness mesh with z-score standardization[9]. Spatial autocorrelation was addressed with spin tests using 30,000 null distributions. Statistical significance was determined via Benjamini-Hochberg FDR correction ($q < 0.05$). Cell-type enrichment was performed using single-cell RNA sequencing data, and gene ontology (GO) analysis was conducted to identify functional pathways[23]. **Results:** Analyses revealed significant associations between MRI-derived GWC and spatial gene expression patterns, with both shared and cohort-specific findings. Genes enriched in regions of altered GWC were linked to processes such as neuroinflammation, synaptic signaling, and neurovascular integrity, with notable differences between AD and CN participants. GO analysis highlighted immune response pathways in AD participants, particularly in the NACC cohort, while ADNI-specific genes were associated with synaptic plasticity and neurovascular processes. CN-specific genes were enriched in synaptic maintenance pathways, reflecting potential mechanisms of cognitive resilience. Differential correlations between gene expression and GWC were observed across cortical regions, particularly in temporal and parietal lobes vulnerable to AD-related neurodegeneration. Astrocytic and endothelial markers showed correlations with GWC in AD participants. Cell-type enrichment analyses underscored glial and vascular contributions to cortical changes, with astrocytic and endothelial markers enriched in regions exhibiting significant GWC reductions. These findings emphasize the spatial specificity of neurovascular and glial dysfunction in AD. Regional analyses further revealed expression variability across AD-associated cortical areas, with chromosomal mapping identifying gene clusters in gene-dense regions implicated in neurodegenerative processes. **Conclusion:** Using an integrative imaging transcriptomics approach, we identified spatial associations between MRI-derived GWC gene expression, identifying molecular drivers of cortical features in AD. This study revealed specific genes with distinct GWC correlations and pathways. These findings highlight the utility of GWC as a biomarker bridging structural and molecular insights, advancing our understanding of neurodegeneration and providing a foundation for targeted interventions.

Poster 44

Exploring the contribution of increased SCN8A activity to Alzheimer's disease

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Introduction: SCN8A encodes the voltage-gated sodium channel (VGSC) Na$_v$1.6, which regulates neuronal excitability and action potential initiation. Patients with *SCN8A* mutations exhibit a range of clinical presentation, including epileptic encephalopathy and numerous behavioral comorbidities. Interestingly, *SCN8A* is differentially expressed in brain tissue from patients with Alzheimer's disease (AD), and *SCN8A* has been identified in a locus of genetic risk for AD. Both amyloid precursor protein (APP) and amyloid-β have been shown to increase expression of Na$_v$1.6, a mechanism which is thought to underlie neuronal hyperexcitability in AD models. In contrast, knockdown of Na$_v$1.6 has been shown to rescue cognitive function and reduce hippocampal plaque burden in APP/PS1 mutant mice. Given these observations, we hypothesize that *SCN8A* may be a genetic modifier for multiple AD phenotypes, such that increasing *SCN8A* activity would exacerbate disease progression and reducing *SCN8A* expression might be therapeutic. **Materials & Methods:** We generated AD mice with increased *SCN8A* activity by crossing mice expressing the human *SCN8A* R1620L mutation (RL/+) to 5xFAD mice, a mouse model of amyloid pathology. **Results:** Mice that harbor both the 5xFAD/+ and RL/+ mutations (5xFAD/RL) exhibit learning and memory deficits, hyperactivity, increased seizure susceptibility, and premature mortality, with most females dying by 4 months of age. We also observed greater AD neuropathology in male 5xFAD/RL mutants. **Conclusion:** These results support our hypothesis that *SCN8A* might be a genetic modifier for AD and provide the foundation for exploring *SCN8A* as a potential therapeutic target for AD and other neurological disorders.

Poster 45

Modelling the "group project" – the emergence of worker/parasite relationships

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Much of our knowledge of how workload assignment emerges within social groups has been limited to non-mammal species, like ants, honeybees, and cichlid fish, making it challenging to understand the neurobiological basis of this complex behavior in humans. Recent studies have found increased activation of the anterior cingulate cortex (ACC) in rats more likely to take on a disproportionate workload in a group setting. While these studies provide some insight, modelling this behavior in a more genetically tractable species would provide more opportunity to clarify the role of the ACC in determining or supporting a worker or parasite phenotype. In this project, we 1) behaviorally model the worker/parasite dynamic in mice, and 2) compare neuronal activation in the ACC between workers and parasites using in vivo one photon calcium imaging. In this pilot, we successfully modelled the worker/parasite dynamic in mice for the first time using groups of three within an operant behavioral task. Additionally, we established a quantitative method of defining "worker" and "parasite", which in past studies had been more qualitatively assigned. Finally, we provide preliminary calcium imaging data from the ACC of male mice, demonstrating a pathway for analysis of this data in this paradigm. This project not only introduces a new assay to probe aspects of labor division, but also, by modelling this behavior in mice, allows for the application of cutting-edge neuroscience techniques allowing for the expansion of the current understanding of complex group dynamics and strategies.

Poster 46

Dorsal Hippocampus to Cortex Projections Drive Sex-Differences in Cocaine Seeking Persistence

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Background: Extensive research shows clear sex differences in the progression of substance use disorders. Women tend to develop these disorders faster, escalate use more quickly, need treatment sooner, and experience shorter periods of abstinence. We and others have observed similar patterns in rodents, with female rats exhibiting stronger cocaine-seeking behaviors at the start of abstinence (extinction day 1, ED1) and showing greater persistence than males. Our previous studies highlighted the dorsal hippocampus's key role in recent cocaine memories, influencing these sex differences in context-driven seeking behavior. Recent studies suggest that hippocampal projections to the prelimbic cortex (PL) are involved in memory strengthening, while those to the infralimbic cortex (IL) facilitate

memory weakening. **Objective:** We hypothesize that on ED1, sex differences in the strength of these projections lead to enhanced memory strengthening in females, resulting in greater cocaine-seeking behavior, and memory weakening in males, promoting extinction. **Methods:** We first examined Fos+ neuron expression in the dorsal hippocampus, prelimbic, and infralimbic cortex on extinction day 1 to determine sex differences in neural activity. In a separate group of rats, we implanted retrogradely-transported mCherry-hM3Dq-DREADDSs or mCherry-hM4Di-DREADDS viruses to the PL or IL and guide cannula to the dorsal hippocampus. We infused CNO (1mM) 10m before testing in ED1 to determine the effects of exciting or inhibiting the dorsal hippocampus – PL or IL pathways on ED1 cocaine seeking behaviors and cocaine-seeking persistence. **Results:** Female rats showed greater Fos+ neuron reactivity in dorsal hippocampus (dHPC) and PL cortex during ED1 that correlated to greater ED1 cocaine seeking. Males showed greater IL cortex activity on ED1 that predicted decreased cocaine-seeking behavior. These findings support the hypotheses that dHPC signaling to different regions of the mPFC (medial prefrontal cortex) has different specific effects to promote or attenuate contextual cocaine seeking. In female rats, we show that activating dHPC to PL projections increased cocaine-seeking behaviors long-term but had minimal effects on retrieval of cocaine memories. Activation of dHPC to IL decreased cocaine-seeking behaviors persistently in females. **Conclusions:** Going forward, we hypothesize that reactivating the females during ED1 strengthens contextual memories of drug-seeking behavior. Oppositely, reactivating males during ED1 facilitates extinction of drug-seeking behavior shown by the presence of IL projections, however, future experiments will further investigate these effects in males. Overall, we aim to understand how sex differences in cortical activity drive continuous cocaine-seeking behavior, as insights into dHPC downstream pathways are essential for developing sex-specific therapies.

Poster 47

Progranulin acts in astrocytic lysosomes to promote neuronal outgrowth

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Introduction: Loss-of-function GRN mutations are a major autosomal dominant cause of frontotemporal dementia (FTD). Progranulin is a secreted pro-protein that is necessary for maintaining lysosomal function and exerts neurotrophic and anti-inflammatory effects in the brain. Progranulin is constitutively secreted and may interact with signaling receptors before being taken up and trafficked to lysosomes. It is not clear if progranulin's neurotrophic and anti-inflammatory effects are mediated through extracellular signaling or through lysosomes. **Materials & Methods:** To elucidate progranulin's site of action, we developed lentiviral vectors expressing human progranulin (PGRN) fused to the transmembrane domain and cytosolic tail of LAMP-1 (L-PGRN). L-PGRN is not secreted, but was trafficked to lysosomes, cleaved into granulins, and normalized lysosomal enzyme activity in $Grn^{-/-}$ neurons. We therefore used these vectors in mixed primary neuron/astrocyte cultures from Sprague-Dawley rats to test the hypothesis that progranulin's neurotrophic effects are mediated in lysosomes. **Results:** In primary hippocampal neurons, L-PGRN expressed with a non-specific lentiviral vector maintained PGRN's neurotrophic effects on dendritic outgrowth. Further experiments expressing L-PGRN with neuron- or astrocyte-specific vectors revealed that L-PGRN only promoted dendritic outgrowth when expressed with an astrocyte-specific vector. L-PGRN-expressing astrocytes were also able to promote dendritic growth of untransduced neurons when co-cultured using transwell inserts. GSEA analysis of bulk RNA sequencing of primary hippocampal astrocytes transduced with L-PGRN suggested that L-PGRN may reduce reactive phenotypes in astrocytes. **Conclusion:** Progranulin may promote dendritic outgrowth through a non-cell-autonomous mechanism involving astrocytes.

Poster 48

Beta frequency activity reflects sensorimotor processing in the human subthalamic nucleus

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Background: Parkinson's disease (PD) is a progressive neurodegenerative disorder primarily known for its motor

impairments. Sensory dysfunction, emerging before motor symptoms, is another key but often overlooked aspect of PD. The basal ganglia, critical for motor control, also process sensory information through the subthalamic nucleus (STN), suggesting a role in sensorimotor integration. However, the precise function of the STN in these circuits and its relevance to PD remain unclear. Here, we investigated STN activity during sensory and motor behavior to shed light on the involvement of the basal ganglia in these functions. **Methods:** We recorded intracranially from the dorsolateral STN and sensorimotor cortex of PD patients undergoing deep brain stimulation (DBS) surgery. Patients received vibratory stimuli (100 Hz) on the wrist and performed hand opening-closing tasks in separate blocks. We analyzed local field potentials in STN and cortex, focusing on event-related activity. **Results:** For the current analysis: Both the subthalamic nucleus (STN) and cortex exhibited beta responses that were time-locked to motor and sensory activity. The beta activity related to sensory stimuli was stronger than that related to motor activity in both the STN and cortex. The beta activity in the STN was significantly correlated with the clinical features of bradykinesia and rigidity. **Conclusions:** Our findings suggest that STN and cortical beta synchronization play a role in both motor intention and sensory processing, providing insight into beta-band activity in sensorimotor circuits. While beta-band neural oscillations have been implicated in PD pathophysiology, conflicting evidence challenges their role. Notably, one study found that increased beta activity correlated with increased movement, suggesting that the role of beta oscillations in PD pathophysiology remains unclear. This has implications for DBS, where beta is used as a control signal despite its unclear role. Additionally, interference between multiple signals may contribute to the variability of beta-band correlations with PD symptoms such as rigidity.

Poster 49

Microglia and Synaptic Pruning in the Primate Amygdala: Effects of Early Life Stress

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Background: The paralaminar nucleus (PL) of the amygdala contains a unique population of immature, post-mitotic glutamatergic neurons that mature between infancy and adolescence. Microglia are interspersed amongst these neurons and mature, likely supporting neuronal maturation and synapse formation. Early life stress (maternal separation) dramatically alters microglial morphology resulting in a hyper-ramified phenotype. We hypothesized that this altered microglial phenotype results in changes in pre- and post-synaptic elements in the PL. **Methods:** We compared tissue from infant and adolescent macaques that were maternally reared or separated from their mother at 1 week (1-WS) or 1 month (1-MS) of age. We used immunocytochemistry, confocal microscopy and Imaris analysis to quantify Syn1+ boutons, PSD95+ puncta, and 'putative excitatory synapses' (Syn1⁄PSD95 colocalized) in the PL. **Results:** In infancy, maternally separated animals showed significant reduction in all synaptic elements (Syn1 p=0.0006, PSD95 p= 0.0005), including putative synapses (p= =0.0028), compared to controls. In contrast, we reported no effects in the adolescents. Syn1+ boutons ($p<0.0001$), PSD95+ puncta ($p<0.0001$) and putative synaptic contacts (Syn1⁄PSD95 colocalization; $p<0.0001$) all decreased between infancy to adolescence across all groups. However, when putative synapses were normalized by available Syn1 and PSD95 puncta, the expected decrease between infants and adolescents was only observed in the maternally reared controls. **Conclusions:** We conclude that following typical rearing, putative synaptic contacts decrease in adolescence consistent with normal microglial morphology. Maternal separation disrupts this trajectory, suggesting that a hyper-ramified microglial phenotype in infancy may reflect excessive or premature synaptic pruning.

Poster 50

Characterizing NTSR[1]-Expressing Medial Prefrontal Cortex Afferents into the Nucleus Accumbens in Opioid-Seeking Behavior

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Relapse following abstinence occurs frequently in opioid use disorder (OUD) and significantly increases the risk of fatal overdose. Relapse episodes can arise spontaneously or be triggered by drug-associated environmental or contextual cues. However, the neural circuits driving opioid relapse remain incompletely understood. Emerging evidence suggests that relapse behaviors, analogous to stimulant-seeking relapse, involve glutamatergic neurons in

the medial prefrontal cortex (mPFC) projecting to the nucleus accumbens core (NAcC). Activation of this mPFC-NAcC circuit mediates cue-induced stimulant relapse in rodents, suggesting it as a potential therapeutic target. Nevertheless, precise mechanisms through which this circuitry influences opioid relapse remain unclear. Neurotensin receptor 1 (NTSR1), a Gq-coupled neuropeptide receptor, has been implicated in regulating drug-seeking behaviors. NTSR1 agonists induce, whereas antagonists attenuate, the reinstatement of stimulant-seeking. Our preliminary data indicate that an allosteric NTSR1 antagonist reduces cue-induced reinstatement of opioid-seeking behavior for remifentanil. Using retrograde tracing, we identified a subpopulation of mPFC neurons that project to NAcC and express NTSR1. However, the structural and functional roles of this specific circuit in opioid relapse remain unexplored. Employing RNAscope in situ hybridization, we characterized NTSR1-expressing neurons in the mPFC in mice, identifying substantial co-expression with glutamatergic markers. Furthermore, using intersectional genetics and inhibitory Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) in NTSR1-Cre mice, we selectively inhibited the mPFC-NAcC NTSR1 circuit. Our findings highlight this neuronal population as a promising therapeutic target, providing critical insights into the mechanisms underlying opioid relapse and potential intervention strategies for OUD.

Poster 51

Traumatic brain injury induced Cx43 phosphorylation enhances seizure susceptibility

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Astrocytes couple into networks of cells via gap junctions (GJs). These GJs, composed of connexins, gate the passage of ions, messengers, and metabolites between astrocytes. This gating is regulated by the phosphorylation state of the connexins. Dysregulation of Connexin 43 (Cx43), the primary GJ-forming protein in the astrocyte network, and astrocyte uncoupling have both been implicated in traumatic brain injury (TBI) and subsequent post traumatic epilepsy. Here, I investigated the relationship between astrocyte coupling and seizure susceptibility in the context of TBI. I find that after mild⁄concussive TBI, Cx43 is heterogeneously regulated with subsets of astrocytes lacking Cx43 being fully uncoupled from the astrocyte network. Other astrocyte populations expressed increased or unchanged Cx43 protein levels but also exhibited an increase in the phosphorylation of Cx43 at serine residue 368 (S368). It is known that Cx43 S368 phosphorylation functionally closes Cx43 gap junctions in cardiomyocytes, which has informed my hypothesis that TBI causes neuronal hyperexcitability due to Cx43 S368 phosphorylation-mediated astrocyte uncoupling. To test this hypothesis, I used a mouse model where Cx43 S368 is converted to an alanine (S368A mice), preventing phosphorylation at this site. After administering TBI to these S368A mice, which I have previously shown causes Cx43 S368 phosphorylation, I administered subthreshold doses of pentylenetetrazol (PTZ) to excite neuronal networks. I found a significant reduction in PTZ-induced seizure susceptibility. These findings suggest Cx43 S368 phosphorylation plays a role in driving seizure susceptibility post TBI.

Poster 52

Applying spatial transcriptomics and mouse molecular genetics to understand the mechanisms of fibrotic scarring for promoting neural repair after spinal cord injury

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Introduction: After spinal cord injury (SCI), fibroblasts drive fibrotic scarring-a process critical for acute tissue repair but detrimental when chronic, impairing CNS regeneration. While transforming growth factor-β (TGF-β) signaling is a known mediator of fibrosis in peripheral organs, its regulation in SCI fibrotic scarring remains unclear. **Materials & Methods:** We employed Col1a2-CreER^{T2}; TGFBR2$^{fl/fl}$; tdtomato$^{fl/fl}$ mice subjected to a T9 SCI, with tamoxifen administered either pre-injury or 4-8 days post-injury (dpi) to temporally control TGFBR2 deletion in fibroblasts. Lesion sites were analyzed at 2 weeks post-injury using quantitative immunohistochemistry for PDGFRβ+, collagen I, and collagen VI deposition, and tdTomato+ cell distribution. **Results:** Delayed TGF-β receptor 2 (TGFBR2) deletion in Col1a2-expressing fibroblasts caused a significant reduction in injury site PDGFRβ+, collagen I, and collagen VI expression compared to tamoxifen-treated controls. However, pre-injury TGFBR2 deletion showed no significant

differences. Intriguingly, delayed deletion also showed increased tdTomato+ cells at the lesion, suggesting time-dependent Col1a2 fibroblast expression after SCI. **Conclusion:** Our results demonstrate that: (1) TGF-β signaling regulates fibrotic scarring and extracellular matrix remodeling, and (2) Col1a2 expression in fibroblasts is temporally regulated after SCI. These findings suggest an optimal therapeutic window for targeting TGFBR2 to modulate fibrotic scarring. Future spatial transcriptomics (Visium⁄Stereo-seq) of scar-attenuated versus control SCI tissue will elucidate how these fibroblast-specific changes alter the capacity for SCI neural repair in the context of other injury site cell types.

Poster 53

Effect of Oxytocin on Hyperalgesia in Alcohol-Dependent Rats

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Introduction: Chronic alcohol exposure in humans and rodents causes tolerance to the analgesic effects of alcohol, and enhances pain sensitivity during alcohol withdrawal (i.e., hyperalgesia). We hypothesize that oxytocin, known to produce analgesic action in the central nervous system, could ameliorate hyperalgesia induced by alcohol-dependence. To test this hypothesis, we assessed the ability of central and peripheral oxytocin administration to alter thermal and mechanical pain sensitivity, in rats made alcohol dependent through alcohol-vapor exposure. **Methods:** Male Wistar rats were surgerized with ICV cannula, tested in the Hargreaves assay, and assigned to matching groups (alcohol nondependent, n = 10; alcohol dependent, n= 8). Groups were monitored via weekly Hargreaves assay to determine alcohol-dependence-induced hyperalgesia. Next, rats were ICV administered oxytocin (0, 0.5, or 5 µg in 2.5 µL saline) prior to Hargreaves testing (Experiment 1) or Von Frey testing (Experiment 2). Finally, rats were IP administered oxytocin (0, 0.1, or 1 mg⁄kg) prior to Hargreaves testing (Experiment 3) or Von Frey testing (Experiment 4). **Results:** Alcohol-dependent rats developed thermal hyperalgesia, observed in the Hargreaves assay (Experiment 1 & 3), however, mechanical hyperalgesia was not observed when the same rats were tested in the Von Frey assay (Experiments 2 & 4). In both assays, alcohol-dependent and nondependent rats demonstrated an analgesic effect of ICV or IP administered oxytocin. **Conclusion:** These data indicate that oxytocin can produce analgesic action in the CNS of alcohol-dependent, hyperalgesic rats.

Poster 54

Cognition and Mood Changes in Recently Diagnosed De Novo Persons With Parkinson's Disease

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Parkinson's disease (PD) is a neurodegenerative disorder that affects the substantia nigra region of the basal ganglia, impacting over ten million individuals worldwide. One of the leading challenges in managing PD is addressing a wide array of symptoms. While motor impairments are the most widely recognizable symptom of PD, mood disturbances are also common, particularly early in disease progression. In addition, cognitive changes including difficulties with attention, memory, and executive function, also are frequently comorbid with mood changes. Both mood changes and cognitive dysfunction are overlooked but can affect quality of life and complicate daily functioning in persons with PD. Identifying and addressing mood changes and cognitive dysfunction early during PD is cardinal for developing effective care strategies. The current study evaluates mood and cognition in recently diagnosed, de novo persons with PD (PD-off) compared to healthy older adults (HOA) using the Geriatric Depression Scale (GDS), Geriatric Anxiety Scale (GAS), Apathy Evaluation Scale (AES), and the Montreal Cognitive Assessment (MoCA). Demographic information including age, race, gender, years of education, and handedness was also collected. Data collection is currently ongoing. Preliminary results suggest that the GDS and MoCA are the most promising measures to distinguish between PD-off and HOA groups. Cohen's d was calculated for MoCA (d = 1.23) and GDS (d = -1.00) assessments, suggesting large effects. However, as participant recruitment continues, it is anticipated that an increased sample size will clarify the observed group differences, which may have important implications for pervasive intervention strategies in PD.

Poster 55

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

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Macular Degeneration (MD) is the number one cause of blindness in the western world. MD is a retinal degenerative disorder caused by damage to the macula which leads to progressive central vision loss. Improved understanding of the factors associated with training of spared peripheral vision may aid in the development of rehabilitative strategies that could help MD participants regain autonomy in daily tasks. 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 oculomotor rehabilitation strategies for patients with MD. This study analyzes the outcomes of four training types, each of which are designed to train a specific aspect of visual processing. By implementing a gaze contingent display paradigm with a simulated scotoma, participants are obligated to complete their assigned training task using their peripheral vision. 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 about 60 individuals with MD and 100 healthy controls across multiple sites, the study has currently enrolled nearly 50 participants at UAB with nearly 30 completing the entire protocol at UAB and nearly 45 completing the protocol across all sites. This study is expected to contribute to both the field of perceptual learning and the field of visual rehabilitation. This poster will describe the scientific and translational goals of the project, as well as preliminary results.

Poster 56

Cell-Specific Ventral Pallidal Regulation of Reward Seeking

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The ventral pallidum (VP) is a central node in the neural circuits that regulate motivated behavior. Recent studies show complex cellular heterogeneity in the VP and largely opposing functional roles in reinforcement and motivated behaviors between glutamatergic (VP_{Glu}) and GABAergic (VP_{GABA}) projection neurons. The primary goal of this study was to test the differential contributions of these cell types to motivated behavior, measured in sucrose self-administering mice during a progressive ratio test. VP neurons were virally transduced with the excitatory Gq-coupled receptor hM3D in Cre-driver mice. Bath application of the selective chemogenetic receptor ligand JHU37160 dihydrochloride (J60; 1uM) recruited Gq signaling, as evidenced by an increase in spontaneous neuronal firing. Mice received an injection (i.p.) of the chemogenetic receptor ligand J60 (1mg⁄kg) 30 min prior to a 6h progressive ratio test with a 1h time limit between two ratios. Activating VP_{GABA} neurons decreased break points for sucrose, whereas activating VP_{Glu} neurons increased break points. Cell-specific chemogenetic manipulations reveal a nuanced regulation of motivated behavior by VP_{Glu} and VP_{GABA} neurons. Behavioral effects seen after prolonged chemogenetic activation of VP_{Glu} and VP_{GABA} neurons are congruent with work from our lab and others showing opposing roles of these cells in the regulation of motivated behavior. Ongoing studies are recording calcium activity in these neurons and are separately manipulating VP_{GABA} and VP_{Glu} neurons to examine potential differences between these populations.

Poster 57

Investigating Extrinsic and Intrinsic Mechanisms of Meningeal Fibroblast Development

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Brain development is a highly coordinated process of multiple stages that includes cell birth, migration, and synaptogenesis. In order for proper brain function, neurodevelopment must proceed without issue. The meninges have emerged as having a vital role in neurodevelopment. The meninges are comprised of immune cells, vasculature, and meningeal fibroblasts that make up three distinct membrane layers: the dura, the arachnoid, and the pia. The meninges, specifically layer specific meningeal fibroblasts, produce factors that are necessary for proper neurodevelopment. However, despite their importance, the meninges remain understudied. One question that remains unanswered is what are the mechanisms that drive meningeal fibroblasts to differentiate and specify into their layer specific identities? To investigate whether neuronal derived signaling is also required for meningeal fibroblast development, we used a transgenic mouse model to disrupt neurogenesis in the dorsal forebrain and then used immunostaining to look at meninges' specific markers. The results show that proper neurogenesis is not necessary for the development of the meninges. Preliminary data from the lab suggests that the pia and dura layers begin to develop first, followed by the arachnoid layer. To investigate the hypothesis that the pia and dura are the source of factors necessary for the development of the arachnoid layer, we utilized our lab's single-cell RNA sequencing dataset and performed cellchat, an intercellular communication analysis, to identify these potential signals. The results from the analysis have identified multiple signaling pathways, including Wnt signaling and BMP signaling, that could be contributing to arachnoid fibroblast development.

Poster 58

Blood-Brain Barrier Repair Following Focal Traumatic Brain Injury

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The blood-brain barrier (BBB) is essential for maintaining homeostasis of the central nervous system (CNS) by restricting cells, factors, and ions in the blood from passing into the neural tissue. A traumatic brain injury (TBI) results in acute impairment of this barrier, allowing blood-borne factors to enter healthy brain tissue. This can exacerbate damage from the initial impact and can even contribute to long-term cognitive decline. We have previously demonstrated that after a diffuse TBI, BBB impairment is sustained. However, it is not known whether BBB repair occurs after a focal TBI. Thus, in the present study, we aimed to test whether the BBB is repaired in a mouse model of focal TBI and to establish a timeline for this potential repair. To do so, we performed stabwound TBIs on mice and assessed BBB properties at 5, 7, and 14 days post injury (dpi). Using retroorbital injections of cadaverine, a small fluorescent molecule which cannot cross the BBB under physiological conditions, we found increased BBB integrity at the later timepoints after injury. Further, we performed immunohistochemistry to quantify expression of the tight junction protein zona-occludens 1 and found increased expression levels along vasculature at the injury sight at 7 and 14 dpi compared to 5 dpi. Finally, we assessed perfusion of the vasculature at the injury sight at each of these timepoints using retroorbital injection of biotin. These findings provide a valuable model system to study the mechanisms underlying BBB repair and to identify potential therapeutic targets.

Poster 59

Characterization of the dCA[1]-LS-VTA pathway and its role in novelty-induced locomotor hyperactivity

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Psychosis is a mental disorder characterized by hallucinations and delusions. While an estimated 3% of the population will experience psychosis in their lifetime, we know little about its underlying neural circuitry. To address this knowledge gap, our lab created the 14-3-3 functional knockout (FKO) mouse model in which the 14-3-3 proteins are functionally inhibited in the forebrain. These mice display several phenotypes that are thought to correlate to symptoms of psychosis, including novelty-induced locomotor hyperactivity. We recently determined that this phenotype is mediated by hippocampal hyperactivity and overactive dopamine signaling, leading to the discovery of a dorsal hippocampus CA1 (dCA1) – lateral septum (LS) - ventral tegmental area (VTA) pathway. We are using the viral-genetic tracing methods known as Tracing the Relationship between Inputs and Outputs (TRIO) and the cell type specific cTRIO to visualize the cell type specific synaptic connections within the dCA1-LS-VTA neural circuit. In addition, we are utilizing chemogenetic approaches to manipulate neuronal excitability in both a cell-type- and pathway-specific

fashion within the dCA1-LS-VTA circuit in both wildtype and 14-3-3 FKO mice. By measuring the effects of neuronal activity manipulations on psychomotor behavior and dopaminergic signaling, we will gain insight into how the three brain regions within the dCA1-LS-VTA pathway functionally influence each other and affect psychosis-related behavior. These studies allow for the deeper understanding of neural circuitry involved in the pathophysiology of psychosis, contributing valuable knowledge to the field that may be used in the development of more targeted treatments and earlier diagnosis.

Poster 60

T1 Relaxivity of Ferritin: Implications for Quantitative Magnetic Resonance Imaging in Cerebral Hemorrhage

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Introduction: Iron accumulation after cerebral hemorrhage contributes to secondary injury, including oxidative stress and inflammation. Ferritin, the primary intracellular iron-storage protein, plays a crucial role in brain iron homeostasis, and influences Magnetic Resonance Imaging (MRI) contrast through its paramagnetic properties. While traditionally linked to T2 and T2* maps, ferritin's T1 relaxivity offers an alternative for iron quantification in hemorrhagic cerebrovascular diseases. This study evaluates the T1 relaxivity of ferritin at 3T to enhance MRI-based assessment of iron deposition following cerebral hemorrhage. **Materials & Methods:** Ferritin phantoms were prepared in 0.9% saline with serial dilutions ranging from 5mg to 0.0195mg concentrations. MRI scans were conducted on a Siemens Prisma 3T scanner using an inversion recovery spin-echo sequence with 12 inversion times (TIs), 50ms – 5000ms to achieve precise T1 mapping. Data analysis was performed using MATLAB to extract T1 values. Inter-observer variability and reproducibility were assessed between two independent analysts. **Results:** The extended range of TIs improved T1 fitting accuracy, mitigating errors seen in prior studies. Additionally, T1 measurements were reproducible across independent assessments, reinforcing the reliability of the methodology. **Conclusion:** These results suggest T1 mapping could be a sensitive metric for detecting iron accumulation in hemorrhagic cerebrovascular conditions. The findings support ferritin as a potential endogenous contrast agent for assessing brain iron deposition in neurological disorders. Future studies will examine temperature and field strength effects to optimize ferritin-based imaging biomarkers for cerebrovascular diseases.

Poster 61

Speech-Derived Linguistic Markers as Predictors of Cognitive Impairment in Older Adults

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Introduction: Preventing the progression of neurodegenerative disorders depends on early detection of mild cognitive impairment (MCI). Changes in spontaneous speech are becoming an increasingly sensitive and non-invasive indicator of cognitive impairment. **Methods:** We examined speech samples from 135 community-dwelling older adults tasked with describing a modern day version of the classic Cookie Theft illustration. Linguistic elements such lexical diversity, syntactic complexity, semantic coherence, and information content units (ICUs) were extracted and used to train supervised machine learning classifiers to predict MCI status. **Results:** Among the models evaluated, random forest achieved the highest classification accuracy (86%), followed by extreme gradient boosting (81%) and logistic regression (76%). Traditional linguistic feature-based regression yielded a modest $R^2 = 0.32$, whereas transformer-based embeddings significantly improved prediction to $R^2 = 0.68$ ($p < 0.001$). Among individual predictors, reduced use of low-frequency words (hapax dislegomenon; $p < 0.001$), diminished reference to spatial features (spatial deixis; $p = 0.001$), and failure to describe visually salient details like color (chromatic salience; $p = 0.001$) were strongly associated with lower cognitive performance. **Conclusion:** Our results demonstrate that speech can provide a highly sensitive and clinically relevant basis for early cognitive impairment. Transformer-based embeddings and ensemble machine learning models like random forest can significantly enhance predictive accuracy, achieving up to 86%. This study stresses the possibility of naturalistic, low-burden speech assessments as a promising basis for improving early detection and intervention plans in neurodegenerative diseases.

Poster 62

AKT is Necessary for Neuronal Hypertrophy and Excitatory Synaptogenesis Caused by Pten Knockout

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Mutations to phosphatase and tensin homolog deleted on chromosome 10 (PTEN) are a known contributor to Autism Spectrum Disorder (ASD), macrocephaly, and epilepsy. PTEN negatively regulates the mTOR signaling pathway. *Pten* knockout (KO) mouse models exhibit neuronal hypertrophy, hyperexcitability, seizures, and ASD-like behaviors. Using transgenic mouse lines and retroviral-mediated genetic alterations, we can analyze pathway outputs in response to the manipulation of various genes. In doing so, we have identified Akt as the specific downstream signaling intermediate mediating the robust neuronal hypertrophy caused by *Pten* loss. We are investigating isoform-specific roles and their contributions to this phenotype. Understanding the interactions of the downstream effectors within the mTOR pathway and how these go awry in patients with ASD, macrocephaly, and epilepsy will broaden the knowledge of these disease pathologies and identifies potential therapeutic targets.

Poster 63

Weight Regulation by GLP1R agonists via a non-canonical hypothalamic PKA-mTORC1 mediated Pathway

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The molecular mechanisms contributing to the anorectic effects of Glucagon-like Peptide-1 Receptor agonists (GLP1Ra) are unknown. GLP1Ra increase PKA-mediated phosphorylation of the mechanistic Target of Rapamycin Complex-1 (mTORC1) subunit Raptor at S791 and whole-body mutation of Raptor (S791A) attenuates the anorectic effect of GLP1Ra, yet the cell-type which contributes to this anorectic effect via this pathway is unknown. We hypothesize that proopiomelanocortin (POMC) neurons contribute to this anorectic effect. To test this, we developed two Cre-inducible mouse-lines that either knock-down (KD) Raptor in POMC neurons (iPOMC-Raptor KD) or that knock-in S791A in Raptor in POMC neurons (iPOMC-Raptor KI). Cre induction in both mouse lines also labels POMC neurons with tdTomato with an ~84% efficiency. We observed a ~45% KD of Raptor in iPOMC-Raptor KD vs. control mice in tdTomato+ cells and no difference in Raptor expression between iPOMC-Raptor KD and control mice in tdTomato- cells (n=3-4⁄group). To test whether Raptor and S791A in Raptor in POMC neurons contribute to the anorectic effects of GLP1Ras, iPOMC-Raptor KD and iPOMC-Raptor KI mice were fed a 60% high fat diet (HFD) and weights were measured during a 14-day GLP1Ra treatment period. There was no difference in GLP1Ra-induced weight loss between control and iPOMC-Raptor KD and a trend for iPOMC-Raptor KI mice to be less sensitive to the anorectic effects of GLP1Ra (n=7-9⁄group) in both male and female mice. Although preliminary, our results suggest that the Raptor Ser^{791} residue in POMC neurons partially contributes to the anorectic effect of GLP1Ra.

Poster 64

Early-life correlates of AD-vulnerable relational memory in the structure and function of hippocampal subfields: Findings from the PRANK study

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Alzheimer's disease (AD) involves progressive neurodegeneration, particularly in the hippocampus, with early atrophy of the cornu ammonis 1 (CA1) subfield. Although AD typically manifests in late life, vulnerability may be linked to

early-life differences in hippocampal structure and function. Additionally, factors such as physical activity and socio-economic status, which influence brain development, can modulate AD risk. The periadolescent period, marked by heightened brain plasticity, may be especially sensitive to these influences, shaping long-term cognitive outcomes and increasing vulnerability to AD. Participants (age 8-13 years) studied pairs of objects while fMRI-BOLD data were collected. The task measured study-time activation in brain regions linked to relational subsequent memory (RSM). The MRI protocol included a T2-weighted quasi-coronal slab orthogonal to the long axis of the hippocampus for sub-field segmentation. Data were preprocessed using the HCP minimal pipeline, and subfield volumes were measured with ASHS software. Task-related RSM activity was interpreted using subfield masks. Participants also completed the KIDSCREEN-52 questionnaire. Successful RSM was associated with increased activity in right anterior CA1. Additionally, right CA1 volume was positively correlated with RSM. We also examined the impact of self-reported physical and financial well-being on CA1 volume. Physical and financial well-being were both negatively associated with bilateral CA1 volume. These findings suggest that the CA1 is important for successful RSM. Additionally, early-life factors, such as physical and financial well-being may be associated with development of the AD-vulnerable CA1. Further investigation into these relationships could offer valuable insights into the role of brain development in shaping late-life AD risk.

Poster 65

Modelling Hallmarks of Amphetamine Use Disorder in Drosophila using the Fly Liquid-food Interaction Extinction Assay (FLIXA)

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This study introduces a novel circuit engineered to quantify interactions of *Drosophila melanogaster* with liquid food, providing precise measurement of amphetamine self-administration through voluntary drinking behavior over multiple days. Initially, flies were fed amphetamine-laced liquid food and compared to controls consuming a sucrose solution, revealing an escalation in self-administration behavior indicative of an addictive phenotype. Subsequently, the circuit was adapted to administer aversive shocks contingent upon liquid consumption, thereby incorporating punishment into the paradigm to model the negative consequences associated with drug procurement. Remarkably, flies consuming amphetamine continued to seek the drug despite experiencing punishment—a behavior attenuated in sucrose-consuming control flies. These data demonstrate that core behavioral hallmarks of addiction—including escalation, persistence despite negative consequences, and drug preference—can be effectively modeled within the neural circuitry of *Drosophila*. Importantly, the results challenge the prevailing paradigm that addiction-like behaviors depend upon complex mesolimbic dopaminergic or amygdalar-ventral striatal pathways characterized in mammals. This invertebrate model thus establishes a genetically tractable platform for dissecting the conserved molecular and cellular mechanisms underpinning addiction.

Poster 66

Genipin's ECM cross-linking property to prevent developmental and degenerative phenotypes in Familial Dysautonomia

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The peripheral nervous system (**PNS**) serves as a vital bridge between the brain and spinal cord (**CNS**) and the rest of the body. It comprises a network of nerves arranged in ganglia outside the CNS that enable sensory perception (pain, touch, temperature) and autonomic regulation (heart rate, blood pressure, respiratory rate, digestion). Familial Dysautonomia (**FD**) is a devastating disorder caused by a homozygous point mutation in the gene *ELP1* that

predominantly affects the PNS. In our previous studies, we have found that FD patients, along with ELP1 mutation, also have modifier mutations in genes related to the cytoskeleton and the extracellular matrix. Clinical studies also suggest that FD patients are born with fewer neurons (developmental defect) and experience a severe and progressive loss of neurons with age (degeneration defect). Despite knowing the cause of FD (*ELP1* mutation) for more than two decades there is no cure for FD, and patients are treated symptomatically. We have previously employed FD patient-derived induced pluripotent stem cells (iPSC) to generate sensory neurons, recapitulating the developmental and degenerative defects of FD. We then conducted a chemical drug screen to identify a drug⁄compound that could rescue the FD phenotype in our stem cell model. We discovered genipin, a compound with neurogenic and neuroprotective properties that is prescribed as a Traditional Chinese Medicine (TCM) for neurodegenerative disorders. We found that genipin rescues neural crest and SN development deficiencies and prevents neurodegeneration observed in FD. Additionally, genipin has activity *in vivo*, promoting the development of SNs in FD mouse models. Finally, we found that these effects are exerted via ECM crosslinking. Our results suggest genipin as a promising drug candidate for FD and potentially for other, common PNS neuropathies.

Poster 67

Characterization of a mouse model of infant traumatic brain injury

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Traumatic brain injury (TBI) is a leading cause of mortality and morbidity in children below the age of 4 and can lead to psychosocial and cognitive deficits well into adulthood. The progression of pathophysiologic alterations and behavioral deficits may differ between adult and pediatric TBI patients and, therefore, therapies that are effective in adults may be ineffective or danger in children. While multiple animal models of pediatric TBI exist, few specifically correlate to infant TBI, the highest risk group. A mouse model of infant TBI presents certain advantages with respect to examining mechanisms underlying acute and chronic functional deficits that follow TBI in this group. Infant (11-day-old) C57BL⁄6 mice (n=26) underwent closed head injury with a silicone-tipped indenter on the exposed intact skull above the left parietal cortex. At 3 days post-injury, histological analysis revealed significant glial activation and axonal injury in white matter tracts and the thalamus of the injured hemisphere. Behavioral assessments at 4-5 weeks post-injury indicated significant impairments in spatial learning and increased risk-taking behaviors, with no signs of depressive-like behaviors. By 6 weeks, while axonal injury and microglia activation were no longer detectable, reactive astrocytes persisted. No gross morphological alterations were noted due to the injury. These findings support the use of this infant mouse model to investigate the cellular and circuit mechanisms underlying long-term deficits from pediatric TBI.

Poster 68

Advancing TMS for PTSD– from networks to individuals

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Transcranial magnetic stimulation (TMS) has emerged as a promising non-invasive intervention for posttraumatic stress disorder (PTSD) that can directly modulate underlying neural circuitry involved in symptom maintenance and development. A major challenge is determining how to identify the optimal TMS target for better outcomes. Though network mapping approaches have paved the way for defining targeting based on neural circuitry, neuroimaging is recently being used to personalize targets based on each individual's unique brain connectivity. Based on strong evidence of heightened right amygdala activity driving hyperarousal symptoms, we propose a connectivity-guided targeting approach using real-time neuronavigation and resting-state functional connectivity (FC) in order to individualize targets in the dorsolateral prefrontal cortex most strongly connected with the right amygdala. The aim is to indirectly modulate amygdala activity by stimulating functionally-connected cortical regions accessible via TMS. In the first FC-guided personalized TMS clinical trial, we defined individual targets using Brainsight TMS Navigation system and stimulated with 1Hz TMS (10 days, 2 sessions⁄day) using a MagPro X100 machine. Participants meeting criteria for PTSD were recruited through the infrastructure of the Grady Trauma Project (GTP) and randomized to an active

or sham treatment group (N=50). Neuroimaging data were collected a week prior and after the treatment using a 3T Siemens PrismaFit scanner with a 64-channel head coil. Individualized TMS targeting for PTSD showed significant variability between subjects ($F(1,34)=5,929$, $p<0.001$, $\eta p2=0.99$), suggesting there is relevance in using a personalized approach to defining the target.

Poster 69

Development of a new, *in vivo*, screenable, split-luciferase based model of huntingtin multimerization

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Huntington's disease (HD) is a genetic neurodegenerative disorder caused by a polyglutamine (polyQ) expansion in the huntingtin gene, leading to the accumulation of mutant huntingtin protein aggregates. These aggregates range from soluble oligomers to insoluble fibrillar inclusion bodies. Huntingtin multimerization involves transition of the conformationally-flexible polyQ stretch to a beta-sheet rich structure, monomers of which interact with one another to form multimeric species. The precise molecular mechanisms that regulate huntingtin aggregation and the potential strategies for clearing these aggregates remain poorly understood. Traditional approaches to studying huntingtin aggregation rely on *in vitro* assays or cultured cell models, which fail to recapitulate the complexity of cellular processes in a living organism. To better understand the cellular factors facilitating huntingtin aggregation in a living, aging, screenable model organism over time, we have developed htt^{LUM}, a split-luciferase-based detector of huntingtin-huntingtin interaction in adult neurons of the *Drosophila melanogaster* brain. This system allows for real-time quantification of huntingtin multimerization within the brain of live flies, providing a novel and aging-compatible tool to study protein aggregation dynamics in vivo. Our model system is optimized for high-throughput screening in a 96-well plate format, enabling large-scale identification of genetic and pharmacological modifiers that influence huntingtin aggregation and toxicity. Using the htt^{LUM} system, we found Fosfosal, an FDA approved drug, reduces huntingtin multimerization and neurodegeneration. We also identified DNAJB6 as a potential genetic modifier of huntingtin multimerization. Using this approach, we aim to uncover genetic factors and explore potential pharmacological interventions that could mitigate protein aggregation and neurotoxicity.

Poster 70

Investigating the role of BAI3 loss of expression in glioblastoma formation

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Glioblastoma (GBM) is the most prevalent central nervous system (CNS) tumor, and TP53 mutations are detected in ~30% of sporadic GBMs. The prognosis for GBM remains dismal, with a median survival of 12-15 months post-diagnosis. Li-Fraumeni syndrome (LFS) is a rare cancer predisposition syndrome caused by a germline mutation in the TP53 tumor suppressor gene, and these patients are predisposed to gliomas. Recent studies suggest that the dysregulation of adhesion G-protein coupled receptors (GPCRs) may play a role in GBM development. Brain angiogenesis inhibitor 3 (BAI3) is a member of the BAI1-3 subfamily of adhesion GPCRs and exhibits high expression in neuronal and glial cells. BAI3 regulates synaptic plasticity, dendritic morphogenesis, and apoptotic cell clearance. Contrary to the high expression in normal brain tissue, BAI3 mRNA is strongly reduced in GBM, according to TCGA data. To evaluate the significance of this observation, I aged constitutive BAI3 knockout mice made in our lab, but I did not find any tumors, suggesting that loss of BAI3 is insufficient to trigger brain tumor formation per se. I, therefore, hypothesized that BAI3 loss needs to occur in the context of other genetic alterations to reveal its pro-tumorigenic potential. To test this, I selected p53 loss due to its well-established role in the formation of sporadic and hereditary GBM. I established an animal model by crossing *Bai3*$^{-/-}$ mice with p53f/d Nestin-Cre mice to induce the simultaneous loss of Bai3 and Tp53 in brain progenitor cells, the putative cells of origin of GBM. The *p53f/d Nestin-Cre* mice have one constitu-

tively deleted p53 allele (d), which mimics hemizygous loss of p53 function in LFS. The second allele is floxed (f) and is conditionally deleted by Cre in Nestin-expressing neuronal and glial progenitor cells. My preliminary findings revealed that the combined loss of *Bai3* and *Tp53* significantly increased the frequency of GBM development (71%) compared to the loss of Tp53 alone (34%). PCR confirmed the tumors had lost the second Tp53 allele. RNA-sequencing analysis identified the most upregulated differentially expressed gene in *Bai3*$^{-/-}$ *p53*$^{d/d}$ GBM formed in my mice was transcription factor activator protein-2B (Tfap2B). High expression of TFAP2B was reported in lung cancer to promote tumor proliferation, survival, and stemness. The expression of TFAP2B is high in GBM; however, the molecular consequences of this expression have not been explored in GBM. Therefore, in this proposal, I will further test the hypothesis that BAI3 suppresses tumorigenesis in GBM by downregulating Tfap2B and its oncogenic downstream targets.

Poster 71

Co-Pathologies and Immune Cell Activation in a Model of Neurodegeneration

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Lewy pathology due to alpha-synuclein (α-syn) inclusions is one of the major hallmarks of Parkinson's Disease (PD). β-Amyloid (Aβ) and phosphorylated-tau, pathologies usually found in Alzheimer's Disease (AD), have also been implicated in PD, with over 50% of patients exhibited the co-expression of these proteins (co-pathologies). In PD postmortem tissue, neuroinflammation – the activation of microglia and the infiltration of immune cells from the periphery, including T cells– are hypothesized to be drivers of neurodegeneration. In AD cases, with Aβ and tau pathologies, microglial activation and infiltration of immune cells from the periphery have also been observed. However, how the co-expression of these pathologies contribute to the inflammatory response and overall disease phenotype remains unknown. To test the hypothesis that the co-expression of pathologies drives neuroinflammation, pathology load and neurodegeneration, we developed a co-pathology model by stereotaxically injecting α-syn pre-formed fibrils (PFFs) into the striatum, and AAV-double^{mut} tau virus into the entorhinal cortex, of J20 transgenic mice with Aβ pathology. The effect of these co-pathologies on inflammation, progression of pathology and neuronal loss was analyzed.
The co-pathology mouse model exhibits Aβ, tau and a-syn pathology, with an increased protein pathology load and neuronal loss compared to the single pathology animals. CO-pathologies induced robust inflammatory responses, including increased microglial cell number and elevated MHCII expression, a complex important for antigen presentation. Additionally, there was significant infiltration of CD4 and CD8 T cells, with effector and tissue resident memory phenotypes, which were dependent on pathology load and brain region. This was synergistic effects in the co-pathology model, compared to the single pathologies, supporting the hypothesis that α-syn, Aβ and tau collectively may drive the progression of neurodegenerative disease via immune activation. Our model highlights an adaptive and innate immune response that may be promoting neurodegeneration and enhanced neuropathology in a co-pathology environment.

Poster 72

Exercise mitigates obesity-induced cognitive dysfunction, lipid accumulation, and neuro-inflammation

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Introduction: Obesity, influenced by factors like sedentary lifestyle, poor diet, and genetics, is a global health issue

linked to metabolic syndrome, cardiovascular problems, and neurodegenerative diseases. Midlife obesity raises dementia risk, though mechanisms remain unclear. Chronic inflammation from fat tissue contributes to metabolic and cognitive dysfunctions. Exercise helps improve health and may delay neurodegeneration. This study used Drosophila models to investigate the effects of genetic obesity on cognitive decline, neuro-inflammation, lipid accumulation, and the potential benefits of exercise. **Aim:** This study aimed to explore the impact of how genetic obesity on cognitive dysfunction, lipid dysregulation, and neuro-inflammation, and to evaluate how exercise can help to suppress these effects. **Material and methods:** We used Canton-S (CS) and *Sphingosine kinase 2 (Sk2)* mutant *Drosophila* to study obesity. Flies were exercised at one week and tested for memory impairments at three weeks. Lipid accumulation in the brain was assessed with Nile Red staining, while qPCR analyzed inflammatory cytokines, JAK/STAT genes, and pro-apoptotic markers to explore exercise's effects on inflammation and apoptosis. **Results:** Obese *Sk2* flies exhibited increased body weight, elevated triglyceride levels, and impaired locomotor abilities in middle age. These flies shows significant cognitive dysfunction compared to age-matched controls, resembling studies linking midlife obesity to cognitive decline. Increased lipid buildup in obese *Sk2* flies brain further supported the cognitive impairments, as abnormal lipid accumulation is associated with Alzheimer's disease. Exercise markedly reduced these effects, improving cognition and decreasing pro-apoptotic markers, suggesting that exercise mitigate neuro-inflammation and cognitive dysfunction related to obesity. **Conclusion:** Our study links midlife obesity to dementia risk, neuro-inflammation, and lipid buildup; exercise helps reduce cognitive impairments and inflammation.

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