2024

WINTER CONFERENCE ON BRAIN RESEARCH

56TH ANNUAL WINTER CONFERENCE ON BRAIN RESEARCH

2024 PROGRAM BOOK

BEAVER RUN RESORT

BRECKENRIDGE, CO

JANUARY 27 - FEBRUARY 1, 2024

WWW.WINTERBRAIN.ORG

We are pleased to return to Breckenridge, Colorado for the 56th meeting of WCBR. WCBR has a rich history of combining an outstanding scientific program with professional camaraderie, productive networking, and the enjoyment of alpine activities. Since its inception in 1968 by scientists from the Brain Research Institute of the University of California, Los Angeles (UCLA), WCBR has been dedicated to facilitating the free exchange of information and ideas between clinical and laboratory-based neuroscientists. Over the years, WCBR has continued to be a premier conference, providing a space for individuals to easily stay current on the latest advancements in all areas of neuroscientific research.

WCBR emphasizes a relaxed and inclusive atmosphere, encouraging scientific discourse and networking among scientists from various neuroscience fields, both within the conference center and across the mountain. The conference begins on Saturday, January 27th with a Welcome Reception and concludes on Thursday, February Ist with the Annual Banquet. In addition to the scientific program, Breckenridge offers an array of exciting winter activities, including skiing, snowboarding, and the International Snow Sculpture Championship. We are confident that the 56th WCBR meeting will be an exceptional experience for all attendees.

The conference begins Saturday evening with a Welcome Reception, where everyone is encouraged to welcome and network with friends, colleagues, travel fellows, and new attendees. The scientific program will commence on Sunday, January 28th with our Plenary Breakfast, featuring Dr. Gina Poe, Eleanor Leslie Professor of Innovative Brain Research at UCLA. Dr. Poe is an internationally recognized scientist on sleep, memory consolidation, monoamines, and cognition. Her talk, "Sleep to change your mind," will address memory difficulties in the sleep-dependent memory consolidation process of post-traumatic stress disorder, Schizophrenia, and Alzheimer's disease. The scientific program also includes sessions highlighting WCBR Pioneers on Sunday (Anil Malhotra, M.D. "Dissecting the Heterogeneity of Psychotropic Treatment Response") and Tuesday (Thomas Hyde, M.D., Ph.D. "How to Study the Human Brain: from Autopsy to Assay – Truth is Stranger than Fiction"). We also encourage participation in the Diversity and Inclusion sessions, Professional Development sessions, and the Outreach Program. Our Outreach Program involves presenting neuroscience research at local schools to inspire young students and enrich the communities hosting the WCBR meetings.

A traditional component of WCBR Outreach is the Brain Talk Town Meeting on Monday when Dr. Poe will present her work to the public audience. Afternoons offer opportunities for après-ski, exploring the exhibitor showcase, and attending poster sessions highlighting innovative research. The Special Poster Session on Wednesday recognizes the best posters from young investigators with competitive awards. The Smitty Stevens Ski Slalom, a fun race open to skiers and snowboarders of all skill levels, is followed by the Mountain Lunch on Wednesday. Finally, please join us for the WCBR Business Meeting on Wednesday, January 31st at 6:30 PM, where we discuss future sites for the meeting, the program, budget, and hold elections for Conference Chair-elect and board members and discuss conference budget decisions and future site selections. We will conclude the 56th WCBR meeting with the Annual Banquet on Thursday evening, where we will present awards for best posters and winners of the Ski Slalom, followed by dancing and music.

WCBR is an independent and all-volunteer organization, made possible by the dedicated efforts of the Executive Committee, Board of Directors, Program Committee, and Fellowship Committee. The Fellowship Program, supported by generous donations from attendees and sponsors, provides travel funds to outstanding young neuroscientists. We thank you all for your generous contributions of time and donations.

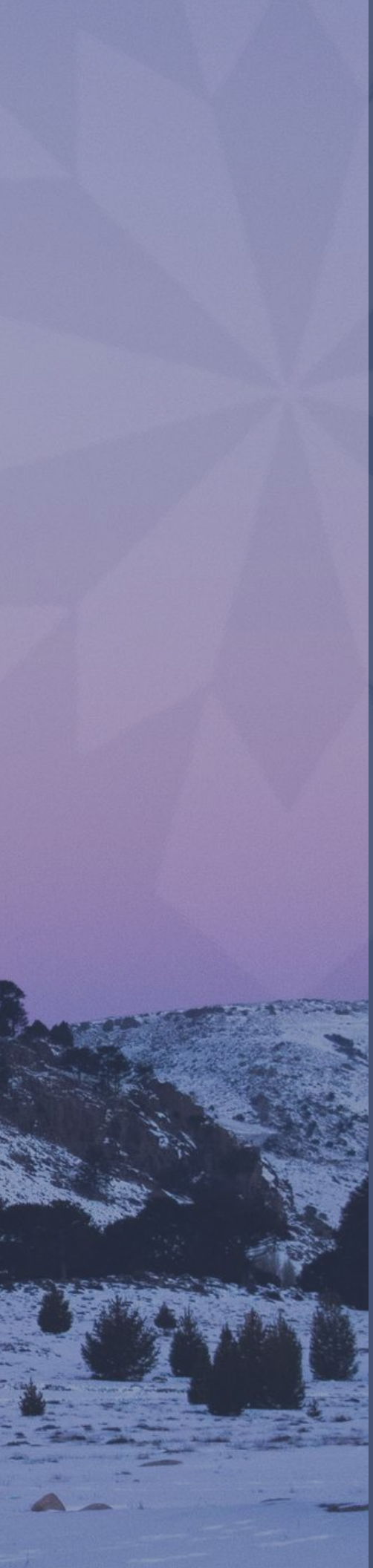
Finally, the success and future of WCBR depends on you. Please consider nominating yourself or your colleagues for election to the Board of Directors for an open board position in clinical, cellular/molecular, or systems/behavioral neuroscience or for the Program Committee. We also encourage you to make a meaningful contribution to the WCBR Fellowship Program, as it plays a vital role in nurturing and supporting the next generation of neuroscientists.

Welcome, thank you, and we look forward to sharing this outstanding experience with you!

David M. Devilbiss, Conference Chair

56th Winter Conference on Brain Research

Breckenridge, Colorado, January 27 – February 1, 2024



CONTENTS

REGISTRATION

Winter Brain Registration Desk and Message Center are located in the Beaver Run Resort in the Third Floor Foyer.

The Registration Desk hours are as follows:

Saturday, January 27, 2024	12:00 p.m. - 7:00 p.m.
Sunday, January 28, 2024	7:00 a.m. - 12:00 p.m., 2:00 p.m. - 7:00 p.m.
Monday, January 29, 2024	7:00 a.m. - 11:00 a.m., 2:30 p.m. - 7:00 p.m.
Tuesday, January 30, 2024	7:00 a.m. - 11:30 a.m., 2:00 p.m. - 7:00 p.m.
Wednesday, January 31, 2024	7:00 a.m. - 10:00 a.m., 2:00 p.m. - 6:00 p.m.
Thursday, February 1, 2024	7:00 a.m. - 10:00 a.m., 3:00 p.m. - 6:00 p.m.

Pick up your badge at the Winter Brain Registration Desk in the Third Floor Foyer at Beaver Run Resort. If you have purchased guest meal tickets, these will also be available at registration.

EXHIBITS AND POSTER SESSIONS

Exhibits and Poster Sessions are in Peak 4-5, Floor 3. Light refreshments are provided from 3:30 p.m. – 4:30 p.m., Sunday, January 28th through Wednesday, January 31st. Exhibitor setup is Sunday, January 28th, from 1:00 p.m. – 3:00 p.m. All exhibitors should have their materials removed by 10:00 p.m. on Wednesday, January 31.

POSTER SESSION I, SUNDAY, JANUARY 28TH
Posters can be set up after 1:00 p.m. on Sunday.

Posters will be available for viewing from 3:00 p.m. – 7:00 p.m. on Sunday. Presenters will be at their posters from 3:30 p.m. – 4:30 p.m. Posters must be removed by 7:00 p.m. on Sunday.

Continued on next page.

EXHIBITS AND POSTER SESSIONS CONTINUED...

POSTER SESSION 2, MONDAY, JANUARY 29TH
Posters must be set up between 8:00 a.m. – 11:30 a.m. on Monday.

Posters will be available for viewing from 12:00 p.m. – 7:00 p.m. on Sunday. Presenters will be at their posters from 3:30 p.m. – 4:30 p.m. Posters must be removed by 7:00 p.m. on Monday.

POSTER SESSION 3, TUESDAY, JANUARY 30TH
Posters must be set up between 8:00 a.m. – 11:30 a.m. on Tuesday.

Posters will be available for viewing from 12:00 p.m. – 7:00 p.m. on Monday. Presenters will be at their posters from 3:30 p.m. – 4:30 p.m. Posters must be removed by 7:00 p.m. on Tuesday.

POSTER SESSION 4, WEDNESDAY, JANUARY 31ST
Posters must be set up between 8:00 a.m. – 11:30 a.m. on Wednesday.

This is a special session displaying the highest-ranked posters by young investigators. Award certificates will be presented to the best posters. Presenters will be at their posters from 3:30 p.m. – 4:30 p.m. and return for the special session from 7:30 p.m. – 9:30 p.m. Posters must be removed by 10:00 p.m. on Wednesday. Please refer to pages 29-49 for a listing of poster sessions.

BREAKFAST

Breakfast is served to all conference delegates during the keynote presentation on Sunday, January 28th from 7:00 a.m. – 8:30 a.m. in Colorado Ballroom, Floor 3. Tickets are not required for the Sunday breakfast. Just ensure you are wearing your name badge!

Monday through Thursday, breakfast will be available in the Floor 3 Foyer. Tickets are not required. Please ensure you are wearing your name badge!

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SATISFACTORY COMPLETION

Learners must complete an evaluation form to receive a certificate of completion. Your chosen sessions must be attended in their entirety. Partial credit of individual sessions is not available. If you are seeking continuing education credit for a specialty not listed below, it is your responsibility to contact your licensing/certification board to determine course eligibility for your licensing/certification requirement.

PHYSICIANS

In support of improving patient care, this activity has been planned and implemented by Amedco LLC and the Winter Conference on Brain Research (WCBR). Amedco LLC is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team. Amedco Joint Accreditation #4008163

Credit Designation Statement – Amedco LLC designates this live activity for a maximum of 30 AMA PRA Category I Credits™ for physicians. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

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Each year Winter Brain offers travel fellowships to young investigators to encourage outstanding new investigator participation in the meeting. This has been a very successful program. Unrestricted donations to the fellowship program can be made at any value.

FELLOWSHIP COMMITTEE

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Thank you to the individuals and organizations that generously support the Travel Fellowship Program. The gift you make is used exclusively to introduce young neuroscientists to the Winter Brain meeting.

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EXHIBITORS

Thank you to the Winter Conference on Brain Research exhibitors.

WCBR CODE OF CONDUCT

I. Introduction

The Winter Conference on Brain Research (WCBR) is dedicated to providing a safe, productive and discrimination-free experience for all participants during the Annual Meeting regardless of race, color, national origin, religion, creed, age, sex (including pregnancy), gender, gender identity, physical or mental disability, perceived disability, ancestry, marital status, genetic information, sexual orientation, citizenship, past, current or prospective service in the uniformed services, or any other basis protected by federal, state or local laws. WCBR does not tolerate discrimination or any form of harassment and is committed to enforcing this Code of Conduct Policy. As a professional society, the WCBR is committed to providing an atmosphere that encourages the free expression and exchange of scientific and educational ideas. Furthermore, WCBR upholds the philosophy of equality of opportunity for, and treatment of, all meeting participants, including but not limited to, attendees, guests, speakers, exhibitors, contractors, staff, and volunteers at all venues and events, including all ancillary and unofficial social events held in conjunction with the Annual Meeting (collectively "Annual Meeting").

2. Scope of Code of Conduct

WCBR seeks to create a diverse, inclusive and respectful environment for the exchange of scientific information.

WCBR requires compliance with this Policy by all meeting participants throughout the period of the Annual Meeting, whether in public or private facilities. This policy is an expression of WCBR's values and commitment to a safe and productive experience for all participants at the Annual Meeting. This policy is not an acknowledgement, admission, or description of WCBR's
legal obligations with respect to any of the subject matters addressed herein, nor does it create any such legal obligations on WCBR, its Board Members, and committee members.

3. Prohibited Conduct

Prohibited conduct at the WCBR Annual Meetings include, but is not limited to:
I. harassment and discrimination based on race, color, national origin, religion, creed, age, sex (including pregnancy), gender, gender identity, physical or mental disability, perceived disability, ancestry, marital status, genetic information, sexual orientation, citizenship, past, current or prospective service in the uniformed services, or any other basis protected by federal, state or local laws;

WCBR CODE OF CONDUCT CONTINUED...

discrimination and all forms of harassment. WCBR reserves the right to discipline meeting participants who engage in any inappropriate conduct, even if it is not specifically referred to or defined in this Code of Conduct, or is not legally actionable as sexual or any other form of harassment.

5. Filing a Formal Complaint

If you feel you have been subject to or have witnessed a violation of this Code of Conduct, a formal complaint can be filed with an authorized representative from our meeting management company, Parthenon Management Group, LLC. This individual can be contacted through the registration desk, or if after the Annual Meeting, at 615-324-2365. No participant will be retaliated against for making a good faith claim of harassment or discrimination, for opposing harassment or discrimination, or for participating in, or cooperating with, the investigation of a complaint. A designated member of the Parthenon team will gather information and put together a summary report, which will then be forwarded to the Conduct Subcommittee of the Executive Board of WCBR for a decision. If the decision of the Subcommittee is contested, it can be appealed to the full Executive Board. The decision following appeal is final and not subject to further appeal. We will strive to keep the identity of the complainant and any witnesses, as well as the accused individual, confidential throughout this process. All participants of the Annual Meeting are bound by the decisions of the Conduct Subcommittee of the Executive Board. If it is determined that an individual has engaged in conduct constituting harassment or discrimination, discipline may be imposed, up to and including exclusion from participating in the WCBR Annual Meeting, and/or future meetings.

Code of Conduct Attestation:

The WCBR Annual Meeting is committed to supporting discovery and scientific dialogue, and providing an atmosphere that is safe, respectful and welcoming to all those present in order to encourage the free expression and exchange of scientific and educational ideas. This commitment applies to the WCBR Annual Meeting, at all venues and events, including all ancillary and unofficial social events held in conjunction with the Annual Meeting (collectively "Annual Meeting") and anyone present, including but not limited to, attendees, guests, speakers, exhibitors, contractors, staff, and volunteers.

To that end, the WCBR Annual Meeting strictly prohibits and does not tolerate unlawful harassment or discrimination on the basis of race, color, religion, creed,

WCBR CODE OF CONDUCT CONTINUED...

national origin, ancestry, sex (including pregnancy), sexual orientation, gender (including nonconformity and status as a transgender or transsexual individual), gender identity, age, physical or mental disability, perceived disability, citizenship, marital status, genetic information, past, current or prospective service in the uniformed services, or any other basis recognized by applicable federal, state, or local laws. WCBR upholds the philosophy of equality of opportunity for, and treatment of, all individuals present at the Annual Meeting and thus, does not tolerate any form of discrimination, harassment, and/or retaliation. We expect all those present at the Annual Meeting of the WCBR to help us in ensuring a productive, safe and positive environment for all.

By registering and attending the meeting, I confirm that I have read the Code of Conduct for the WCBR, and agree that it is my responsibility to be familiar with, and to abide by, its terms. I also attest that I will cooperate with any formal or informal inquiry into my behavior and/or actions at the Annual Meeting. I agree to be bound by the decisions of the Executive Subcommittee on Meeting Conduct, which may take any action that it deems appropriate, including but not limited to exclusion from a current Annual Meeting (without refund) or from future meetings.

PHOTOGRAPHY AND VIDEOGRAPHY POLICY

WCBR does not allow photography or videography of oral presentations, slides and/or posters without permission from the presenter. At the beginning of the presentation, the presenter must either grant permission to the audience and/or include an icon on the first slide or poster signifying photos or videos are allowed.

CONGRATS TO WINTER BRAIN'S 2024 PIONEER AWARDEES!

Each year, Winter Brain solicits nominations for the annual Pioneer Awards. This tradition serves to recognize and honor pioneering scientists who demonstrate excellence in the field of neuroscience and have made invaluable contributions to Winter Brain over the years. Many worthy candidates were nominated this year and the Winter Brain Board of Directors and Executive Committee had the difficult task to select two candidates for recognition.

THOMAS M. HYDE, M.D., PH.D.

2024 Winter Brain Pioneer Awardee

Dr. Hyde received his combined MD-PhD degrees in 1984, and then completed a general medical internship at Presbyterian-University of Pennsylvania Medical Center. Following his internship, Dr. Hyde completed a residency in Neurology at Stanford University Hospital from 1985-1988, serving as chief resident of Neurology his last year of residency. He completed his board certification in General Neurology in 1990.

In 2010, Dr. Hyde left the NIMH to become the Chief Operating Officer of the Lieber Institute for Brain Development on the Johns Hopkins Medical Campus in Baltimore. The Lieber Institute is a non-profit biomedical research organization dedicated to finding the causes and cures for complex behavioral disorders including schizophrenia, bipolar disorder, and depression. He served as Chief Operating Officer from 2010-2016 before transitioning to Chief Medical Officer. While at the institute in 2012 he established the Lieber Institute Human Brain and Tissue Repository. In addition to his administrative work, Dr. Hyde has had an active research career in neuropsychiatry. He has published over 230 peer reviewed original scientific articles with a focus on the biology of mental illness and post-mortem human brain.

ANIL MALHOTRA, M.D.

2024 Winter Brain Pioneer Awardee

Dr. Anil Malhotra is the Co-Director of the Institute of Behavioral Science at the Feinstein Institutes for Medical Research in Manhasset, NY, Director of Psychiatry Research at the Zucker Hillside Hospital in Glen Oaks, NY, and Professor and Vice Chair of Research, Department of Psychiatry, The Zucker School of Medicine at Hofstra/Northwell in Hempstead, NY.

Dr. Malhotra completed his undergraduate studies at Cornell University in 1985 and received his M.D. from Wake Forest University in 1989. After residency training in psychiatry at Georgetown University, he completed a research fellowship at the National Institute of Mental Health (NIMH) of the National Institutes of Health (NIH), where he initiated a research program in pharmacogenetics. Following his tenure at NIMH, Dr. Malhotra moved to the Zucker Hillside Hospital and developed an internationally recognized molecular genetics program focused on the major neuropsychiatric disorders.

Dr. Malhotra's group has identified a number of genes associated with increased risk for schizophrenia, determined their relationship with important clinical manifestations of illness, including cognitive impairment, and examined the role of genetic factors in predicting individual responses to pharmacological treatment. His group published the first genome-wide association study (GWAS) of schizophrenia and found evidence for a role of specific genetic factors in vulnerability to antipsychotic drug-induced weight gain, a common yet potentially serious side effect of treatment.

PIONEER AWARDS

WINTER CONFERENCE ON BRAIN RESEARCH

JANUARY 27 - FEBRUARY 1, 2024 • BRECKENRIDGE, CO

Brain Talk Town Hall: *Optimal Sleep for an Optimal You*
Brain Talk Town Hall presentation by:

Gina Poe

Gina Poe is the Eleanor Leslie Professor of Innovative Brain Research at UCLA. Her laboratory resides in the Department of Integrative Biology and Physiology with joint appointments in the Department of Psychiatry and Department of Neurobiology. Her internationally renown research investigates the role of sleep in memory consolidation, focusing on the different electrophysiological and neurochemical features characteristic of different states of consciousness and the actions of catecholamines, anesthesia, etc. on learning and unlearning. Her keynote, titled "Sleep to change your mind", will explore the conditions of sleep-dependent neural plasticity necessary to update one's cognitive schema. Updates are necessary during learning, when recovering from addiction or post-traumatic stress disorder, or any other condition when one changes one's mind. She will later give a Brain Talk Town Hall engaging clinicians, basic scientists, and the public in discussion around the various functions of sleep, how sleep can go wrong in mental health disorders, and how sleep can be optimized.

Brain Talk Town Hall: "Optimal sleep for an optimal you"

Monday, January 29th, 2024 - 7:00 pm - 8:30 pm - Beaver Run Resort

SATURDAY, JANUARY 27TH

6:00 p.m. - 6:30 p.m.
Welcome Reception for Newcomers, Travel Fellows and Mentors
Peak 1-3. Floor 3

6:30 p.m. - 7:30 p.m.
Welcome Reception
Peak 4-5. Floor 3

SUNDAY, JANUARY 28TH

7:00 a.m. - 8:00 a.m.
Plenary Breakfast
Floor 3 Foyer

8:00 a.m. - 9:30 a.m.
Conference Welcome
and Plenary Address
Colorado Ballroom Floor 3

Keynote: Sleep to Change Your Mind
Gina Poe

9:45 a.m. - 11:15 a.m.
Pioneer Session #1: Anil Malhotra, M.D.
Peak 11-12, Floor 2

Dissecting the Heterogeneity of Psychotropic Treatment Response
Pioneer: Anil Malhotra
Chair: Katherine Burdick
Investigators: Miklos Argyelan, Caitlin Millett

11:15 a.m. - 11:45 a.m.
Panel Chair Training Session
Peak 9-10, Floor 2

SUNDAY, JANUARY 28TH

2:00 p.m. - 3:30 p.m.
Professional Development
Session #1
Peak 6-8, Floor 2

Non-Academic Pathways in Neuroscience after PhD
Chair: Elora Williams
Erik Carlson, Rachel Herder, Patricio O'Donnell, Gretchen Snyder, Lyric Jorgenson

3:30 p.m. - 4:30 p.m.
Poster Session I
Peak 4-5, Floor 3

4:30 p.m. - 6:30 p.m.

Panel
Imperial Ballroom, Floor 4
Advanced Sensing Strategies to Take on the Double Diamonds of Brain Dynamics
Chair: Tod Kippin
Co-chairs: Yen-Yu Ian Shih & Nicole Emmons, Julian Gerson, Tatiana Shnitko, Arnab Mukherjee, Hojin Shin

Panel
Peak 1-3, Floor 3
Ion Channel Mechanisms of a Functional and Dysfunctional Mesolimbic System
Chair: Emily Teichman
Co-chair: Elyssa Margolis
Emily Jorgensen, Allyson Friedman
Peak 1-3, Floor 3

Panel
Peak 11-12, Floor 2
Delirium: "There's Too Much Confusion"
Chair: Robert Pearce
Richard Lennertz, Niccolo Terrando, Rob Sanders, Christina Boncyk

Panel
Peak 14, Floor 1
Translational Developments in Cannabis-Based Therapeutics*
Chair: Ryan Vandrey
Co-Chair: Marcel Bonn-Miller
Elise Weerts, Patrick Finan, Ziva Cooper, Brian Thomas

Panel
Peak 15-16, Floor 1
Interplay Between Traumatic Brain Injury and Gut Microbiome Composition: Implications for Neuroinflammation and Recovery
Chair: David Devilbiss
Cole Vonder Haar, Abigail Schindler, Mashkoor Choudhry, Susannah Nicholson

Panel
Peak 17, Floor 1
Stress and Addiction: New Insights From Animal Models and Human Studies
Chair: Yavin Shaham
John Mantsch, Marie Eikemo, Rajita Sinha

*Not eligible for CME credit.

SUNDAY, JANUARY 28TH

Panel
Peak 6-8, Floor 2
Visual Processing and Behavior in the Mouse
Chair: Cristopher Niell
Huizhong Tao, Jason Samonds, , Jennifer Hoy

Panel
Peak 9-10, Floor 2
The Influence of Sights, Smells, Sounds, and Rewards on Hippocampal Dynamics and Representations
Chair: Kamran Diba
Lara Rangel, Gideon Rothschild, Marielena Sosa, Sebastien Royer

6:30 p.m. - 7:00 p.m.
Evening Refreshment Break
Floor 1 Foyer & Floor 2 Foyer

7:00 p.m. - 8:30 p.m.

Short Course
Imperial Ballroom, Floor 4
Current Trends in Clinical Phytocannabinoid Molecule Development*
Chair: Thomas Swanson
Carl Lupica, Jacci Bainbridge, Hunter Land

Panel
Peak 1-3, Floor 3
Ion Channels and Excitability: Culprits Impairing Neuronal Activity in Disease?
Chair: Joshua Garcia
Darrin Brager, Nidia Quillinan

Panel
Peak 11-12, Floor 2
Neural Circuits and Cortical Plasticity for Innate and Learned Auditory Behaviors
Chair: Li Zhang
Alfonso Junior Apicella Michele Insanally, David Schneider, Robert Froemke, Robert Liu

Panel
Peak 14, Floor 1
Molecular Mechanisms Supporting Addiction Development and Relapse
Chair: Katherine Savell
Co-chair: Caleb Browne
Jennifer Tuscher, Bowen Tan,

Panel
Peak 15-16, Floor 1
Sex Differences in Aversive Processing
Chair: Julia Mitchell
Laura O'Dell, Edita Navratilova, Tiffany Wills

Short Course
Peak 17, Floor 1
Transcriptomic Studies in Neuroscience Research
Chair: Laura Ferguson
Laura Saba, R. Dayne Mayfield

Panel
Peak 6-8, Floor 2
Neuromodulatory Systems in the Control of Breathing
Chair: Adrienn Varga
Co-ChairErica Levitt
Gaspard Montandon, Jessica Whitaker-Fornek, Natalie Johnson

*Not eligible for CME credit.

SUNDAY, JANUARY 28TH

Panel
Peak 9-10, Floor 2
Emerging Routes to Modify Epileptogenesis and Neuropathology After Traumatic Brain Injury
Chair: Bret Smith
Mark Shapiro, Naomi Sayre

MONDAY, JANUARY 29TH

6:30 a.m. - 8:30 a.m.
Breakfast at Leisure (Provided)
Floor 3 Foyer

6:30 a.m. - 8:30 a.m.
Board of Director's Meeting (Invitation Only)
Base Nine, Floor 1

7:30 a.m. - 9:30 a.m.

Panel
Imperial Ballroom, Floor 4
Unlocking the Brain's Reward System: Insights Into the Striatal and Dopaminergic Mechanisms of Learning and Decision Making
Chair: Robin Magnard
Co-Chair: Sharlen Moore
Mai-Anh Vu, Alex Legaria

Panel
Peak 1-3, Floor 3
Novel Therapeutics for Treating Substance Use Disorders*
Chair: Alan Budney
Aron Lichtman, Margaret Haney, Sterling McPherson, Crystal Smith

Panel
Peak 11-12, Floor 2
Connectomic Neuromodulation in Psychiatry: Perspectives From Multi-Modal and Cross-Species Studies
Chair: Lucas Trambaiolli
Shan Siddiqi, Marina Celestine, Darin Dougherty

Panel
Peak 14, Floor 1
Metabolic Switches Required for Development of Normal Neuronal Excitability and Synaptic Plasticity
Chair: Elizabeth Jonas
Ryann Fame, Leonard Kaczmarek, Gulcin Pekkurnaz

*Not eligible for CME credit.

MONDAY JANUARY 29TH

Panel
Peak 15-16, Floor 1
Neuron-Glial Interactions: Mechanisms Underlying Development and Repair of Peripheral Nerves
Chair: Monique Lillis
Matthew Rasband, Lydia Daboussi, Yannick Poitelon

Panel
Peak 17, Floor 1
Dissection of Brain Circuitry Driving Pain Induced Nociceptive Behavior and Drug Seeking Behavior
Chair: Jose Moron-Concepcion
Rebecca Lorsung, Catherine Cahill

Panel
Peak 6-8, Floor 2
Development and Plasticity of the Visual System
Chair: Sandra Kuhlman
Chinfei Chen, Aaron McGee, Jianhua Cang

Panel
Peak 9-10, Floor 2
Defining the Molecular and Environmental Context Where Genes for Schizophrenia Work
Chair: Gianluca Ursini
Laura Wortinger, Bart Rutten, Martin Beaulieu

9:45 a.m. - 10:45 a.m.
Diversity and Inclusion Power Hour
Peak 15-16, Floor 1

11:00 a.m. - 12:00 p.m.
Inclusive Networking Coffee Hour
Peak 14, Floor 1

3:30 p.m. - 4:30 p.m.
Poster Session II
Peak 4-5, Floor 3

4:30 p.m. - 6:30 p.m.

Panel
Imperial Ballroom, Floor 4
Cortical Dysfunction in Parkinson's Disease
Chair: Hong-yuan Chu
Co-chair: Adriana Galvan
Colum MacKinnon & Robert Chen

Panel
Peak 1-3, Floor 3
Recent Advances in Understanding the Orbitofrontal Cortex
Chair: Ido Maor
Peter Rudebeck, Alessandro Livi, Joni Wallis

Panel
Peak 11-12, Floor 2
Synapse Plasticity in Health and Disease
Chair: Matthew Kennedy
Stephen Smith, Graham Diering, Serena Dudek

Panel
Peak 14, Floor 1
Neural Regulation of Appetitive and Aversive Learning
Chair: Merridee Lefner
Co-chair: Matthew Wanat
Alexey Ostroumov, Morgan Johnston, Stephanie Cajigas

MONDAY, JANUARY 29TH

Panel
Peak 15-16, Floor 1
Computational Methods for Investigating the Cognitive Processes Involved in Addictions and Brain Injury
Chair: Claire Hales
Co-chair: Peyton Mueller
Stephanie Groman & Nicholas Harp

Panel
Peak 17, Floor 1
Striatal Circuit and Synaptic Mechanisms of Cocaine and Opiate Addiction
Chair: Lauren Dobbs
David Barker, Flavia Barbano, Emilia Lefevre

Panel
Peak 6-8, Floor 2
Cellular and Network Dynamics of Sound Driven Behavior and Dysfunction
Chair: Ramnarayan Ramachandran
Co-chair: Patrick Kanold
Jun Kim, Maria Geffen, Shaowen Bao, Liberty Hamilton

Panel
Peak 9-10, Floor 2
Multi-Cellular Interactions Impacting Repair and Recovery After Traumatic Injury in the Central and Peripheral Nervous System
Chair: Yimin Zou
Mayssa Mokalled, Dario Bonanomi, Peter Galie

7:00 p.m. - 8:30 p.m.
Brain Talk Town Meeting: Optimal Sleep for an Optimal You
Peak 17, Floor 1

9:00 p.m. - 11:00 p.m.
Karaoke
Base Nine, Floor 1

TUESDAY, JANUARY 30TH

6:30 a.m. - 8:00 a.m.
Travel Fellow & Mentor Breakfast
Base Nine, Floor 1

6:30 a.m. - 8:30 a.m.
Breakfast at Leisure (Provided)
Floor 3 Foyer

7:30 a.m. - 9:30 a.m.

Panel
Imperial Ballroom, Floor 4
Delta Opioid Receptor Function in Pain and Reward Circuits
Chair: William Birdsong
Co-chair: Marie Walicki
Louis Gendron, Elizaveta Mangutov, Emily Jutkiewicz,

Panel
Peak 1-3, Floor 3
Monitoring and Manipulating the cAMP Signaling Pathway
Chair: Andrew Lutas
Yao Chen, Alfred Kaye, Haining Zhong

Panel
Peak 11-12, Floor 2
Behavioral and Molecular Mechanisms Underlying Fentanyl Intake
Chair: David Barker
Renata Marchette, Emily Prevost,Anthony Downs

Panel
Peak 14, Floor 1
Distributed and Local Circuits for Encoding Aversive Emotions
Chair: Joshua Johansen
Jan Grundemann , Sabine Krabbe, Hugo Tejeda

Panel
Peak 15-16, Floor 1
Astrocytes: A Flurry of Roles in Development and Disease
Chair: Justin Trotter
Co-chair: Stacey Glasgow , Sarah Ackerman & Nicola Allen

Panel
Peak 17, Floor 1
Striatal Mechanisms of Adaptive and Maladaptive Behavioral Control Strategy
Chair: Kate Wassum
Co-chair: Jacqueline Giovanniello
Melissa Malvaez, Kyle Smith, Mary Torregrossa,

Panel
Peak 6-8, Floor 2
Circuit Disruptions as a Common Consequence of Heterogeneous Types of Traumatic Brain Injury
Chair: Olga Kokiko-Cochran
Corina Bondi, Cole Vonder Haar, Akiva Cohen

Panel
Peak 9-10, Floor 2
Skiing Through the Molecular Landscape of Psychiatric Disorders in Postmortem Human Brains
Chair: Ryan Logan
Kirsten Schoonover, Michael Totty, Shelby Ruiz

TUESDAY, JANUARY 30TH

9:45 a.m. - 11:15 a.m.
Pioneer Session #2: Thomas Hyde, M.D., Ph.D.
Peak 11-12, Floor 2

How to Study the Human Brain: From Autopsy to Assay – Truth is Stranger Than Fiction
Pioneer: Thomas Hyde
Chair: Elizabeth Tunbridge
Investigators: Elizabeth Tunbridge, Gregory Carr

2:00 p.m. - 3:30 p.m.
Professional Development Session #2: Insider Tips for NIH Grant Success
Peak 6-8, Floor 2

Insider Tips for NIH Grant Success
Chair: Erik Carlson
Sunila Nair, DeAnna Adkins, Kathryn Reissner, Alison Hall

3:30 p.m. - 4:30 p.m.
Poster Session III
Peak 4-5, Floor 3

4:30 p.m. - 6:30 p.m.

Panel
Imperial Ballroom, Floor 4
Tools to Traverse the Slopes of D2-like Receptor Activation in Health and Disease
Chair: Kim Neve
Co-Chair: Amy Newman
Javier Garcia-Nafria, Veronica Alvarez

Panel
Peak 1-3, Floor 3
Reconsidering Parkinson's Disease From a Multi-System Perspective
Chair: Louis-Eric Trudeau
Co-Chair: Freja Herborg
Ulrik Gether, Per Borghammer, Michela Deleidi

Panel
Peak 11-12, Floor 2
Systematic Investigation Into the Effects of Substance Use
Chair: Yifeng Cheng
Co-Chair: Robin Magnard
Yvan Vachez, Miguel Lujan, Qiaowei Xie

Panel
Peak 14, Floor 1
AMPA Receptors and Their Auxiliaries in Health, Disease and Synaptic Plasticity
Chair: Ingo Greger
Johannes Hell, David Bredt, Roger Nicoll

Panel
Peak 15-16, Floor 1
Sex Differences in Pain and Negative Affect and Implications for Alcohol and Opioid Use Disorder Risk
Chair: Scott Edwards
Co-Chair: Dayna Averitt
Khalin Nisbett, Amanda Pahng

TUESDAY, JANUARY 30TH

Panel
Peak 17, Floor 1
Cell-Type Specific Striatal Control of Motivation and Decision–Making in Health and Disease
Chair: Matthew Hearing
Co-chair: Erin Calipari
Brad Grueter, Constanza Garcia Keller

Panel
Peak 6-8, Floor 2
Investigations Into Sleep Circuitry and Plasticity in Physiological and Pathological Conditions
Chair: Ada Eban-Rothschild
Franz Weber, Ashley Ingiosi, Shinjae Chung

Panel
Peak 9-10, Floor 2
Fostering Successful Partnerships Between Academia and Industry*
Chair: Elizabeth Tunbridge
Thomas Hyde, Wilfried Haerty, Gregory Carr

6:30 p.m. - 7:00 p.m.
Evening Refreshment Break
Floor 1 Foyer & Floor 2 Foyer

7:00 p.m. - 8:30 p.m.

Short Course
Imperial Ballroom, Floor 4
Optimizing Use of Neuroimaging Tools for Evaluation and Management of Cognitive Decline
Chair: Daniel Silverman
Co-chair: Cyrus Raji
John Seibyl, Sarah Banks

Panel
Peak 1-3, Floor 3
Interneuron Circuitry at the Intersection of Opioids and Reward
Chair: Emilia Lefevre
Co-chair: Carlee Toddes
Elysia Gauthier, James Otis

Panel
Peak 6-8, Floor 2
Moguls, Models, and Markers: Tackling the Mountain of Post-Traumatic Epilepsy
Chair: Dominique Duncan
John Huguenard, John Wolf

Panel
Peak 9-10, Floor 2
Immune-Sympathetic Effects of Spinal Cord Injury
Chair: Patricia Ward
Co-chair: Dylan McCreedy
Veronica Tom, Andrew Gaudet

Panel
Peak 11-12, Floor 2
Consequences of Neurodevelopmental Insults and Dysfunction
Chair: Miranda Reed
Nathaniel Robinson, Zijun Wang

Panel
Peak 14, Floor 1
Brain Mechanisms of Social Interactions to Modulate Pain and Empathy - New Tools and Methods
Chair: Vitaly Napadow
Co-chair: Monique Smith
Weizhe Hong, Fadel Zeidan

*Not eligible for CME credit.

TUESDAY JANUARY 30TH

Panel
Peak 15-16, Floor 1
Promoting Student Engagement: A Neuroscience Education Workshop
Chair: Kirsten Porter-Stransky
Lloyd Fricker, Sybil Stacpoole, Michael Stefanik

Short Course
Peak 17, Floor 1
Machine Learning Methods to Study Animal Behavior
Chair: Amelia Gallitano
Talmo Pereira, Jessica Verpeut, Ann Kennedy, Caleb Weinreb

WEDNESDAY, JANUARY 31ST

6:30 a.m. - 8:30 a.m.
Breakfast at Leisure (Provided)
Floor 3 Foyer

7:30 a.m. - 9:30 a.m.

Panel
Imperial Ballroom, Floor 4
Using Preclinical Models to Study the Neurobiological Mechanisms of Psychedelics in Anxiety and Depressive Disorders
Chair: Katherine Nautiyal
Co-chair: Sixtine Fleury
Charles Nichols, Cody Wenthur, Boris Heifets

Panel
Peak 1-3, Floor 3
Interactions Between Immune Signaling, Mesolimbic Circuitry and Behavior
Chair: Jordan Yorgason
Co-chair: Drew Kiraly
Ashley Ross, Philipp Mews

Panel
Peak 11-12, Floor 2
Disease-Specific Responses of Reactive Astroglial Cells – Concepts, Molecular Signatures and Opportunities for Intervention
Chair: Milos Pekny
Jan Mulder, Florence Perrin, Rachel Kim

Panel
Peak 14, Floor 1
Shifting Moguls: Lives of Dendritic Spines
Chair: Yi Zuo
Kristen Harris, Karen Zito, Yoshiyuki Kubota

Panel
Peak 15-16, Floor 1
Lifelong Oligodendroglial Dynamics in Brain Health and Disease
Chair: Wendy Xin
Tsai-Yi Lu, Pablo Paez, , Tobias Merson

WEDNESDAY, JANUARY 31ST

Panel
Peak 17, Floor 1
Double Diamond: The Pursuit of Reward Despite Consequence
Chair: Donna Calu
Laura Corbit, Rachel Smith, Sean Ostlund

Panel
Peak 6-8, Floor 2
Progressing From Green to Blue to Black: Experience, Choice, and Sex Differences Across the Lifespan Influence Drug Use and Behavior
Chair: Devin Mueller
Co-chair: Tod Kippin
Matthew Hearing & Zijun Wang,

Panel
Peak 9-10, Floor 2
Applying Visual Ethology and Virtual Reality in Emotion and Cognitive Circuits
Chair: Alfred Kaye
Matthew Isaacson, Stephanie Staszko, Yuta Senzai, Cristopher Niell

10:00 a.m. - 11:30 a.m.
Smitty Stevens Ski Slalom (Extra Fee)
Swinger Race Course, Mountain Peak 8

11:30 a.m. - 1:30 p.m.
Mountain Lunch
Coppertop Patio

3:30 p.m. - 4:30 p.m.
Poster Session IV
Peak 4-5, Floor 3

4:30 p.m. - 6:30 p.m.

Panel
Imperial Ballroom, Floor 4
Shredding Sex Differences in Opioid Reward Systems From Transcript to Circuit
Chair: Elizabeth Doncheck
Co-chair: Jessica Higginbotham
Jesse Niehaus, Yanaira Alonso-Caraballo,

Panel
Peak 1-3, Floor 3
Impact of Stress and Social Isolation on Behaviors Critical for Survival
Chair: Tara Raam
Reesha Patel, Holly Hunsberger, Asha Caslin

Panel
Peak 11-12, Floor 2
Synaptic and Electrophysiological Correlates of Different Forms of Associative Learning
Chair: Jonathan Morrow
Ankit Sood, Sara Morrison, Bryan Singer

Panel
Peak 14, Floor 1
Dopamine Neuromodulation in Hippocampus and Amygdala
Chair: Arthur Godino
Co-chair: Andrew Lutas
Avi Matarasso, Hye Sun (Sunny) Choi, Damien Kerspern

WEDNESDAY, JANUARY 31ST

Panel
Peak 15-16, Floor 1
Regulation of Diverse Motivated Behaviors by the Hypothalamus
Chair: Adam Gordon-Fennell
Co-chair: Flavia Barbano
Ada Eban-Rothschild, Edita Navratilova

Panel
Peak 17, Floor 1
Psychedelics for Neuropsychiatry: From Bench to Bedside
Chair: Praachi Tiwari
Co-chair: Alaina Jaster
Alexander Smith & Neil Savalia

Panel
Peak 6-8, Floor 2
Exercise Your Myelin: Interventions That Enhance Myelin Plasticity After Injury or Disease
Chair: Emily Petrus
Anne Wells, Christina Marion, Timothy Faw

Panel
Peak 9-10, Floor 2
Targeting the Complement System in Neurodegeneration
Chair: Marcela Pekna
Co-Chair: Jan Mulder
John Lee, Milos Pekny

6:30 p.m. - 7:30 p.m.
Winter Brain Business Meeting
Peak 17, Floor 1

7:30 p.m. - 9:30 p.m.
Special Poster Session and Reception
Peak 4-5, Floor 3

THURSDAY, FEBRUARY 1ST

6:30 a.m. - 8:30 a.m.
Breakfast at Leisure (Provided)
Floor 3 Foyer

6:30 a.m. - 8:30 a.m.
Board of Directors Meeting (Invitation Only)
Base Nine, Floor 1

7:30 a.m. - 9:30 a.m.

Panel
Imperial Ballroom, Floor 4
Ensemble-Specific Approaches to Identify Cell-types, Circuits and Molecular Alterations Underlying Reward-Related Behaviors
Chair: Marine Salery,
Co-Chair: Rajtarun Madangopal
Elizabeth Doncheck, Ana Clara Bobadilla

THURSDAY, FEBRUARY 1ST

Panel
Peak 6-8, Floor 2
Behavioral, Neural and Neurochemical Differences in Decision Making: Let's Talk About Sex
Chair: Catharine Winstanley
Andrew Wikenheiser, Valeria Gonzalez, Julia Cox

Panel
Peak 9-10, Floor 2
Repairing the CNS by Targeting the Gut and Enteric Nervous System
Chair: Warren Alilain
Alexandra Byrne, Cedric Geoffroy, Kristina Kigerl

Panel
Peak 14, Floor 1
Slippery Slope: Complex Biology of Synapses and its Implication for Synaptic Function and Disease
Chair: Martin Hruska
Co-chair: Matthew Dalva
Joris De Wit, Elva Diaz

Panel
Peak 15-16, Floor 1
A Bed of Nails: The Challenge of Disentangling the Circuits and Functions of the Bed Nuclei of the Stria Terminalis (BNST)
Chair: Samuel Centanni
Co-chair: Jason Radley
Zoe McElligott, Amelia Douglass

Panel
Peak 17, Floor 1
Neural Systems Regulating the Competition for Control over Motivated Behavior
Chair: Catharine Winstanley
Jacqueline Barker, Aqilah McCane, Catharine Winstanley, Jamie Peters

Panel
Peak 11, Floor 2
Short Tandem Repeats in Neuronal Function and Neurological Disease
Chair: Peter Todd
Co-chair: Andy Berglund
Eric Wang, Gary Bassell, Hannah Shorrock

Panel
Peak 12, Floor 2
Bridging the Gap: Exploring Brain Biomechanics and Neuroscience Synergy
Chair: Rouzbeh Amini
Turner Jennings, Mahsa Karamzadeh, Pirouz Kavehpour, Aditi Deshpande

4:30 p.m. - 6:30 p.m.

Panel
Imperial Ballroom, Floor 4
Dopaminergic Signals for Predictive Learning and Flexible Behavior
Chair: Sean Ostlund
Kate Wassum, David Martin, Mihaela Iordanova, David Bortz

THURSDAY, FEBRUARY 1ST

Panel
Peak 6-8, Floor 2
New Insight into Neuropeptide Dynamics - From Individual Exocytosis Events to Volume Transmission
Chair: Leslie Sombers
Co-chair: Elyssa Margolis
Paul Slesinger, Stephen Weber, Marta Soden

Panel
Peak 9-10, Floor 2
Deciphering the Neural Code for High-Level Vision
Chair: Mark Eldridge
Co-chair: Barry Richmond
Chris Baker, Hamidreza Ramezanpour

Panel
Peak 14, Floor 1
In Vivo Brain Recordings Reveal Calorie Dense Food Items Reshape Reward Circuitry Driving Maladaptive Behavior
Chair: Richard O'Connor
Co-chair: Bridget Matikainen-Ankney
Matt Howe, Kyle Burger

Panel
Peak 15-16, Floor 1
Breaking New Trails: New Molecular and Viral Technologies for Systems Neuroscience
Chair: Ofer Yizhar
Christina Kim, Lief Fenno, Raajaram Gowrishankar

Panel
Peak 17, Floor 1
Aprés-See: Visualizing Drug Effects With in Vivo Imaging to Advance Therapeutic Development*
Chair: Benjamin Hall
Co-chair: Jones Parker
Oliver Miller, Paolo Botta, Lisa Beutler

Panel
Peak 11, Floor 2
Expectations, Contextual and Placebo Effects: Brain Mechanisms
Chair: Luana Colloca
Matthew Banghart, Philip Corlett, Liane Schmidt,

Panel
Peak 12, Floor 2
Emerging Brain Metabolism Paradigms in Mood Disorders: Brain Transcriptomics, Diurnal Expression Rhythms, and Relationship to Cognition
Chair: Harry Pantazopoulos
Co-chair: Rammohan Shukla
Kateryna Maksyutynska, Barbara Gisabella,

6:30 p.m. - 7:30 p.m.
Cocktail Hour
Floor 3 Foyer

7:30 p.m. - 11:00 p.m.
Awards Banquet and Dance
Colorado Ballroom, Floor 3

*Not eligible for CME credit.

SUNDAY, JANUARY 28TH

POSTER SESSION I

3:30 P.M. - 4:30 P.M.

PEAK 4-5, FLOOR 3

S1. "TRANQ-DOPE" OVERDOSE AND LETHALITY: SYNERGISTIC INTERACTIONS BETWEEN FENTANYL AND XYLAZINE
MARK SMITH

S2. ASTROCYTIC REGULATION OF COCAINE LOCOMOTOR SENSITIZATION IN ECOHIV INFECTED MICE
QIAOWEI XIE

S3. THE ROLE OF ENDOCANNABINOIDS WITHIN CORTICOLIMBIC REGIONS IN ADAPTIVE STRESS COPING BEHAVIOR AND IMPLICATIONS FOR SUBSEQUENT ALCOHOL DRINKING
LAURA ORNELAS

S4. CASE SERIES: MICRODOSE INDUCTIONS FROM FULL OPIOID AGONIST TO PARTIAL OPIOID AGONIST
TOMMASO TOSINI

S5. MOLECULAR CHARACTERIZATION OF OPIOID SENSITIVE GABAERGIC AND GLUTAMATERGIC AFFERENTS TO THE VENTRAL TEGMENTAL AREA
OLIVER CULVER

S6. ELECTROCHEMICAL APTAMER BASED SENSORS FOR THE DETECTION OF IN BRAIN COCAINE
NICOLE EMMONS

S7. EXERCISE BLOCKS THE INCUBATION OF CRAVING FOR HIGH-FAT FOODS AND RECOVERS DIET-INDUCED CHANGES IN PERINEURONAL NETS
LYDIA BAILEY

S8. INVESTIGATING THE ROLE OF THE SEROTONIN IB RECEPTOR IN THE THERAPEUTIC EFFECTS AND NEUROBIOLOGICAL MECHANISMS OF ACTIONS OF PSILOCYBIN IN MICE
SIXTINE FLEURY

S9. A NETWORK APPROACH TO PSYCHOPATHOLOGY: BRIDGING NEUROIMAGING AND PSYCHOMETRICS
FREDERICK GOODSON-GREGG

SUNDAY, JANUARY 28TH

POSTER SESSION I CONTINUED

3:30 P.M. - 4:30 P.M.

PEAK 4-5, FLOOR 3

SI0. THE ROLE OF DORSAL STRIATUM D1 RECEPTOR SIGNALING IN FEAR EXTINCTION AND RELAPSE
BENJAMIN GREENWOOD

SI1. TONIC EXCITATORY SIGNALING IN THE BED NUCLEUS OF THE STRIA TERMINALIS
SARA CONLEY

SI2. GM-1020: AN ORAL NMDA ANTAGONIST DEMONSTRATES TARGET ENGAGEMENT AT DOSES THAT DO NOT CAUSE DISSOCIATION, ATAXIA OR SEDATION IN A PHASE I SAD STUDY
LASZLO KISS

SI3. DORSAL HIPPOCAMPUS UNDERPINS DISSOCIABLE PATTERNS OF DEFENSIVE BEHAVIOR IN MALE AND FEMALE RATS
MATTHEW ALWOOD

SI4. ELDERLY A9/10 NICOTINIC ACETYLCHOLINE RECEPTOR KNOCKOUT MICE DEMONSTRATE CONSERVED GAZE STABILITY
TOBIAS NIEBUR

SI5. HIGH FREQUENCY SIGNALS IN FRONTAL CORTEX AT LOSS OF CONSCIOUSNESS
M MACIVER

SI6. PRENATAL CANNABINOID EXPOSURE: EMERGING EVIDENCE OF MEDIAL PREFRONTAL CORTEX ABNORMALITIES
ADRIAN COURVILLE

SI7. SPECTRAL POWER AND PHASE-AMPLITUDE COUPLING IN HUMAN INTRACRANIAL RECORDINGS DURING MULTI-ATTRIBUTE DECISION MAKING
ERNST NIEBUR

SI8. TARGETING SPHINGOSINE-1-PHOSPHATE RECEPTOR 1 ATTENUATES THE DEVELOPMENT OF COGNITIVE DYSFUNCTIONS AFTER PACLITAXEL TREATMENT
SILVIA SQUILLACE

SI9. COMPARING MECHANISTICALLY DISTINCT INTERVENTIONS THAT ALTER INTER-TEMPORAL CHOICE BEHAVIOR USING CORTICAL-STRIATAL LOCAL FIELD POTENTIALS
WILDER DOUCETTE

SUNDAY, JANUARY 28TH

POSTER SESSION I CONTINUED

3:30 P.M. - 4:30 P.M.

PEAK 4-5, FLOOR 3

S20. MANIPULATING HDAC3 FUNCTION IN THE AUDITORY CORTEX DURING MEMORY FORMATION RESULTS IN DISTINCT CORTICAL TRANSCRIPTIONAL CHANGES
GUAN-EN GRAHAM

S21. MODULATION OF ROSTRAL TEGMENTAL EFFERENTS TO THE VENTRAL TEGMENTAL AREA INDUCES LONG-LASTING AVOIDANCE BEHAVIOR
JACOB WATSON

S22. WHO NEEDS FRIENDS? HYPOTHALAMIC-TO-VENTRAL TEGMENTAL AREA PROJECTIONS REGULATE MOTIVATION FOR FOOD BUT NOT SOCIAL REWARDS
JON CAVANAUGH

S23. THE EFFECTS OF TRAUMATIC EXPERIENCES ON BRAIN AGING IN ADOLESCENTS: A PRELIMINARY NEUROIMAGING STUDY
SHRAVYA CHANAMOLU

S24. CORRELATION BETWEEN SUBCUTANEOUS ADIPOSE TISSUE OF THE HEAD AND BODY MASS INDEX IN CHILDREN AND YOUNG ADULTS AGED 8-19 YEARS: IMPLICATIONS FOR FUNCTIONAL NEUROIMAGING
STACEY GORNIAK

S25. UNITARY STRIATOPALLIDAL CONNECTIONS IN THE MOUSE
JAMES JONES

S26. THE NANOSCALE ORGANIZATION OF DIVERSE GABAERGIC INHIBITORY SYNAPSES
KATHARINE SMITH

S27. DECODING THE MOLECULAR COMPUTATION BY CAMKII HOLOENZYMES THAT DIRECTS SYNAPTIC PLASTICITY
CAROLYN BROWN

S28. REGULATION OF LUTEINIZING HORMONE TO PREVENT COGNITIVE DECLINE OF ALZHEIMER'S DISEASE
EMMA REDMON

S29. DISSOCIATION OF STRUCTURAL AND FUNCTIONAL CHANGES IN ALZHEIMER'S DISEASE AND MILD COGNITIVE IMPAIRMENT
ANNIE DANG

SUNDAY, JANUARY 28TH

POSTER SESSION I CONTINUED
3:30 P.M. - 4:30 P.M.
PEAK 4-5, FLOOR 3

SS30. NEUROTOXIN MEDIATED NEURONAL DYSFUNCTION REGULATED BY LYSOSOMAL FUNCTION
JINHONG WIE

S31. RESIDENT-PERIPHERAL IMMUNE INTERPLAY: THE POTENTIAL ROLE OF IL-IB IN DOPAMINERGIC NEURON VULNERABILITY AFTER INJURY
COLIN KELLY

S32. SUCROSE OVERCONSUMPTION IMPAIRS FEEDING CIRCUIT DYNAMICS AND PROMOTES PALATABLE FOOD INTAKE
CAROLYN LORCH

S33. THE ROLE OF PHASIC INHIBITION ONTO BDNF+ NEURONS IN THE VENTROMEDIAL HYPOTHALAMUS REGULATING METABOLIC FUNCTION
THERESA HARVEY

S34. LOCALIZATION AND CHARACTERIZATION OF TRANSPLANTED NEURAL STEM CELL POPULATIONS FOLLOWING CENTRAL NERVOUS SYSTEM INJURY
JEFFERY PLUNKETT

S35. GLOBAL CEREBRAL ISCHEMIA DECREASES DENDRITIC SPINE DENSITY, ENHANCES MICROGLIAL REACTIVITY, AND INCREASES MICROGLIAL/SYNAPSE CO-LOCALIZATION IN A MOUSE MODEL OF CARDIAC ARREST
JACOB BASAK

S36. IMPROVING THE REGIONAL SPECIFICITY OF GLUTAMATE RECEPTOR MODULATION BY TARGETING ACCESSORY PROTEINS
MICHAEL MAHER

S37. TOWARD META-CONNECTOMIC ERGODICITY IN NEUROIMAGING: GRAPH THEORY MODELING EVIDENCE IN TEMPORAL LOBE EPILEPSY
JONATHAN TOWNE

S38. PRENATAL CANNABINOID EXPOSURE AFFECTS MEMORY THROUGH ALTERATIONS IN GLUTAMATERGIC RECEPTOR EXPRESSION
KATIE MOERSCHEL

S39. SYMPTOM-NETWORK DISRUPTION: A MECHANISM OF ACTION FOR INTENSIVE PSYCHIATRIC POLYTHERAPY
PETER FOX

SUNDAY, JANUARY 28TH

POSTER SESSION I CONTINUED

3:30 P.M. - 4:30 P.M.

PEAK 4-5, FLOOR 3

S40. LATERAL VENTRICLES OF THE BRAIN: ANATOMIC VARIABILITY DEPENDING ON THE AGE
IULIIA ZHURAVLOVA

S41. MECHANISTIC INSIGHTS INTO NMDA RECEPTOR POSITIVE ALLOSTERIC MODULATORS THAT ALTER EFFICACY, POTENCY, AND PERMEATION PROPERTIES
ELIJAH ULLMAN

S42. THERMOREGULATORY ROLES OF PREOPTIC AREA HISTAMINE RECEPTOR H1 NEURONS
ARIANNA VALERI

S43. ALTERATIONS IN INTRINSIC PROPERTIES OF CORTICAL PARVALBUMIN CELLS FOLLOWING CHRONIC MORPHINE, INFLAMMATORY PAIN AND DOR AGONIST TREATMENT
MARIE WALICKI

S44. NEURONAL ACTIVITY REVEALS PARADOXICAL CORTICAL STATE DURING DESFLURANE ANESTHESIA
ANTHONY HUDETZ

S45. ANALGESIC EFFICACY OF ALCOHOL IN THE CONTEXT OF HIV-ASSOCIATED PAIN
TAYLOR FITZPATRICK-SCHMIDT

S46. INFLAMMATORY STATUS SCHIZOPHRENIC PATIENTS AND CLASSIFICATION BASED ON BRAIN TRANSCRIPTOMICS IDENTIFY THE SAME GROUPS OF PATIENTS
C. HARKER RHODES

MONDAY, JANUARY 29TH

DATA BLITZ

3:00 P.M. - 3:30 P.M.

PEAK 17, FLOOR 1

1. HOW THE CLAUSTRUM INSTANTIATES COGNITIVE NETWORK ACTIVITY IN ACUTE AND CHRONIC PAIN
DAVID SEMINOWICZ

2. DEVELOPMENT OF WIRELESS EQUIPMENT FOR AUTONOMOUS RODENT INFUSION TASKS
NICOLAS MASSALY

3. ALCOHOL AFTER INJURY: UNCOVERING THE SYNERGISTIC EFFECTS OF CHRONIC ALCOHOL USE AFTER BLAST-INDUCED MTBI
MAKENZIE PATARINO

4. EAATS FOR STROKE: TO MODULATE OR NOT TO MODULATE
KATELYN REEB

5. PRENATAL CANNABINOID EXPOSURE ALTERS MEMORY BY MODULATING GLUTAMATERGIC NEUROTRANSMISSION
KAWSAR CHOWDHURY

6. CORTICAL TASTE PROCESSING CHANGES WITH TASTE EXPERIENCE ACROSS TRIALS AND DAYS
DANIEL SVEDBERG

MONDAY, JANUARY 29TH

POSTER SESSION II

3:30 P.M. - 4:30 P.M.

PEAK 4-5, FLOOR 3

MI. MODULATING LEVELS OF ΔFOSB ALTERS NUCLEUS ACCUMBENS MEDIUM SPINY NEURONS ACTIVITY TO SALIENT STIMULI
TAMARA MARKOVIC

M2. VTA GLUTAMATERGIC AND GABAERGIC INPUTS FROM THE PEDUNCULOPONTINE TEGMENTAL NUCLEUS AND THEIR ROLE IN MOTIVATED BEHAVIOR AND ON COCAINE-INDUCED CPP BEHAVIOR
HUILING WANG

M3. GLUTAMATERGIC AND GABAERGIC M-OPIOID RECEPTOR VTA NEURONS DIFFERENTIALLY MODULATE MOTIVATIONAL AND PHYSIOLOGICAL CONSEQUENCES OF FENTANYL USE
EMILY PREVOST

M4. INVESTIGATION OF WITHIN-SESSION COCAINE VS. SUCROSE CHOICE BEHAVIOR USING A DRUG-BIASED PROGRESSIVE EFFORT PARADIGM IN RATS
DAVID NOWAK

M5. PRESYNAPTIC KAPPA OPIOID CONTROL OF A GABAERGIC STRESS-SENSITIVE CIRCUIT INVOLVED IN REINSTATEMENT
VALENTINA MARTINEZ DAMONTE

M6. SCREENING FOR NOVEL ALLOSTERIC MODULATORS OF THE HUMAN DOPAMINE TRANSPORTER
FUYU YANG

M7. A RANDOMIZED TRIAL OF THE EFFECTS OF COMT INHIBITION ON SUBJECTIVE RESPONSE TO ALCOHOL: MODERATION BY BASELINE COMT ACTIVITY AND MEDIATION OF ALCOHOL SELF-ADMINISTRATION
JOSEPH SCHACHT

M8. GENDER DIFFERENCES IN ACUTE COCAINE RESPONSE: EXPLORING DAT REGULATION THROUGH MKP3 OVEREXPRESSION IN RATS
RASHMI TANTRI

M9. DEVELOPMENT OF WIRELESS EQUIPMENT FOR AUTONOMOUS RODENT INFUSION TASKS
NICOLAS MASSALY

MI0. CHRONIC ALCOHOL ALTERS ENDOCANNABINOID MODULATION OF ORBITOSTRIATAL ACTIVITY DURING GOAL-DIRECTED BEHAVIOR
NATALIE PAREDES

MONDAY, JANUARY 29TH

POSTER SESSION II

3:30 P.M. - 4:30 P.M.

PEAK 4-5, FLOOR 3

MI1. RIBOSOMAL HETEROGENEITY AND SYNAPTIC DYSREGULATION: NEW INSIGHTS INTO MOOD DISORDER MECHANISMS AND TREATMENT
RAMMOHAN SHUKLA

MI2. SUBJECTIVE AND PHARMACODYNAMIC EFFECTS OF THE NOVEL 5-HT2A RECEPTOR AGONIST GM-2505 IN HEALTHY VOLUNTEERS SHOW HIGH TRANSLATABILITY FROM RODENT DATA AND HOLD PROMISE FOR FUTURE DEVELOPMENT IN PATIENTS WITH DEPRESSION
ZOË HUGHES

MI3. A SUBSTANTIA NIGRA TO DORSOLATERAL STRIATUM PATHWAY MEDIATES THE EFFECTS OF FEMALE ESTROUS CYCLE ON FEAR EXTINCTION AND IS A NOVEL TARGET FOR THE PREVENTION OF RELAPSE
ALYSSA HOHORST

MI4. MECHANISMS BEHIND WORRY AND THEIR ROLE IN ANXIETY
AN YEE LOW

MI5. POST-TRAUMATIC STRESS DISORDER AND MAJOR DEPRESSIVE DISORDER SHOW SIGNIFICANT NEUROBIOLOGICAL OVERLAP
ANNIE DANG

MI6. SHORT AND LONG-TERM BEHAVIORAL AND DOPAMINE CIRCUIT ADAPTATIONS TO CHRONIC STRESS
CAROLE MOREL

MI7. DISCOVERY AND CHARACTERIZATION OF A SPECIFIC INHIBITOR OF SERINE-THREONINE KINASE CYCLIN DEPENDENT KINASE-LIKE 5 (CDKL5) DEMONSTRATES ROLE IN HIPPOCAMPAL CAI PHYSIOLOGY
TIM BENKE

MI8. CORTICAL TASTE PROCESSING CHANGES WITH TASTE EXPERIENCE ACROSS TRIALS AND DAYS
DANIEL SVEDBERG

MI9. NEUROPEPTIDES IN THE PARABRACHIAL NUCLEUS OF PRIMATES
SONSOLES DE LACALLE

M20. HOW DO INTERAURAL TIME AND INTERAURAL LEVEL DIFFERENCES INTERACT IN SPATIAL HEARING WITH COCHLEAR IMPLANTS?
JAN SCHNUPP

MONDAY, JANUARY 29TH

POSTER SESSION II

3:30 P.M. - 4:30 P.M.

PEAK 4-5, FLOOR 3

M21. ROLE OF NUCLEUS ACCUMBENS DOPAMINE RECEPTORS SIGNALING IN PUNISHED REWARD SEEKING
ANNA TOBUREN

M22. PRENATAL CANNABINOID EXPOSURE LEADS TO ENHANCED GABAERGIC SIGNALING RESULTING IN LEARNING AND MEMORY DEFICITS IN ADOLESCENT RAT OFFSPRING
MILES WILEY

M23. MESOSCOPIC DYNAMICS IN LARGE NEURONAL POPULATIONS: INSIGHTS FROM SIMULATIONS AND STATISTICAL PHYSICS
ALEX SHEREMET

M24. SUBREGION ENCODING OF DECISION VARIABLES AND UNDERLYING COMMUNICATION WITHIN MACAQUE VENTRAL FRONTAL CORTEX
FREDERIC STOLL

M25. TARGETING DOPAMINERGIC NEURONS IN RHESUS MONKEY: A COMPARISON OF RETROGRADE VIRAL VECTORS
ANNA PLOTNIKOVA

M26. PERIPUBERTAL SOCIAL DISRUPTION PERSISTENTLY ALTERS MOTIVATED BEHAVIORS IN ADULTHOOD
STUTI AGRAWAL

M27. DOXORUBICIN-INDUCED COGNITIVE IMPAIRMENT AND SYNAPTIC PLASTICITY
IVA DURDANOVIC

M28. LATERAL HABENULA CO-RELEASE OF GLUTAMATE AND GABA FROM THE VENTRAL TEGMENTAL AREA OR ENTOPEDUNCULAR NUCLEUS NEURONS: SYNAPTIC PROPERTIES AND THEIR ROLE IN BEHAVIOR
SUYUN HAHN

M29. ROLE OF INTRACELLULAR TRAFFICKING OF AMPAR DURING LTP
FRANÇOISE COUSSEN-CHOQUET

M30. LTP INDUCTION BY STRUCTURAL RATHER THAN ENZYMATIC FUNCTIONS OF CAMKII
ULLI BAYER

MONDAY, JANUARY 29TH

POSTER SESSION II

3:30 P.M. - 4:30 P.M.

PEAK 4-5, FLOOR 3

M31. UNVEILING SYNAPTIC DYNAMICS: SYNAPTOJANINEI REGULATION OF DOPAMINE D2 RECEPTOR SHORT ISOFORM MEMBRANE AVAILABILITY REVEALED BY A NOVEL PH-SENSITIVE OPTICAL REPORTER
ELNAZ KHEZERLOU

M32. GENOME-WIDE ASSOCIATION STUDY IDENTIFIES APOE AND ZMIZI VARIANTS AS MITOPHAGY MODIFIERS IN LEWY BODY DISEASE
WOLFDIETER SPRINGER

M33. BEHAVIORAL AND NEURONAL CHARACTERIZATION, ACROSS AGES, OF THE TGSWDI MOUSE MODEL OF ALZHEIMER'S DISEASE
NATALIE TAN

M34. MECHANISMS OF EAAT2 REGULATION FOLLOWING ISCHEMIC INSULT
SIMRAN GILL

M35. RESOLUTION OF HYPERGLYCEMIA AND DISEASE-RELATED CENTRAL AUTONOMIC NEUROPLASTICITY BY VERTICAL SLEEVE GASTRECTOMY IN A MURINE MODEL OF TYPE I DIABETES
KATALIN SMITH

M36. OPEN BOARD

M37. EAATS FOR STROKE: TO MODULATE OR NOT TO MODULATE
KATELYN REEB

M38. TRPM2-CAMKII SIGNALING DRIVE EXCESSIVE GABAERGIC SYNAPTIC INHIBITION AFTER ISCHEMIA
AMELIA BURCH

M39. ALCOHOL AFTER INJURY: UNCOVERING THE SYNERGISTIC EFFECTS OF CHRONIC ALCOHOL USE AFTER BLAST-INDUCED MTBI
MAKENZIE PATARINO

M40. REFINED GENE ANNOTATIONS INCREASE THE ACCURACY OF QUANTIFYING MU OPIOID RECEPTOR RNAS AND OTHER NEURONAL GENES IN SINGLE-CELL RNA-SEQUENCING DATA
JESSE NIEHAUS

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5, FLOOR 3

M41. THE HISTORY OF DANISH NEUROSCIENCE
OLAF PAULSON

M42. BIDIRECTIONAL ERK1/2 MODULATION IN DOPAMINERGIC NEURONS REGULATES DAT TRAFFICKING AND FUNCTION
CHRISTINA BESADA

M43. PRENATAL CANNABINOID EXPOSURE ALTERS MEMORY BY MODULATING GLUTAMATERGIC NEUROTRANSMISSION
KAWSAR CHOWDHURY

M44. ASSESSING THE FUNCTIONAL PROFILE AND CONTRIBUTION OF SENESCENT DRG NEURONS TO OSTEOARTHRITIS PAIN
CHELSIE BREWER

M45. HOW THE CLAUSTRUM INSTANTIATES COGNITIVE NETWORK ACTIVITY IN ACUTE AND CHRONIC PAIN
DAVID SEMINOWICZ

M46. THE SUICIDAL BRAIN: BIOLOGICAL INSIGHT FROM POSTMORTEM HUMAN TISSUE
GIOVANNA PUNZI

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5, FLOOR 3

T1. RESPONSES OF DOPAMINE NEURONS TO DISCRIMINATIVE AND PAVLOVIAN-CONDITIONED CUES ASSOCIATED WITH OPIOID VS. NATURAL REWARDS
NORA MILLER

T2. METHAMPHETAMINE-INDUCED NEUROINFLAMMATION IN THE PREFRONTAL CORTEX CORRESPONDS WITH COGNITIVE FLEXIBILITY DEFICITS THAT ARE ATTENUATED BY COX-2 INHIBITION
AMANDA ACUNA

T3. ALLOSTERIC DOPAMINE TRANSPORTER MODULATOR INHIBITS COCAINE-INDUCED BEHAVIORS
YIBIN XU

T4. ADOLESCENT BINGE DRINKING CAUSES FOREBRAIN CHOLINERGIC NEURON GENE SILENCING THROUGH HMGBI-TLR AND REST-G9A SIGNALING, IMPACTING REVERSAL LEARNING
FULTON CREWS

T5. EVALUATING THE EFFECTS OF PSYCHEDELIC DOI TREATMENT ON COGNITIVE FLEXIBILITY AFTER PROLONGED COCAINE EXPOSURE
ARTIN ASADIPOOYA

T6. ELEVATED DNA DAMAGE AND NEUROINFLAMMATORY MARKERS IN SPECIFIC STRIATAL CELL TYPES ASSOCIATED WITH OPIOID USE DISORDER USING SINGLE NUCLEI RNASEQ OF HUMAN POSTMORTEM BRAIN
RYAN LOGAN

T7. FURANYLFENTANYL DECREASES RESPIRATION BUT NOT OXYGEN SATURATION IN MICE
CATHERINE DEMERY-POULOS

T8. DEVELOPING TOOLS FOR STUDYING NEURONAL ENSEMBLES THAT ENCODE VOLITIONAL SOCIAL REWARD IN MICE
SAMANTHA LEE

T9. MODULATION OF PRELIMBIC CORTEX TO ROSTROMEDIAL TEGMENTAL NUCLEUS PATHWAY ELICITS DIFFERENTIAL RESPONDING IN CONDITIONED SUPPRESSION
EMMA CARLSON

TUESDAY, JANUARY 30TH

POSTER SESSION III

3:30 P.M. - 4:30 P.M.

PEAK 4-5, FLOOR 3

TI0. N-ACETYLCYSTEINE EFFECTS ON NEUROMETABOLITES, FUNCTIONAL CONNECTIVITY AND CUE REACTIVITY: A NEUROIMAGING STUDY OF TREATMENT-SEEKING INDIVIDUALS WITH ALCOHOL USE DISORDER
KIRSTEN MORLEY

TI1. DOPAMINE RELEASE IN RESPONSE TO CUES PREDICTING AVOIDABLE AVERSIVE STIMULI DIFFERENTIATES BEHAVIORAL RESPONSES: ESCAPE VERSUS HELPLESSNESS
STEPHANIE CAJIGAS

TI2. DISCOVERY AND CHARACTERIZATION OF ITI-1549, A NOVEL NON-HALLUCINOGENIC PSYCHEDELIC FOR THE TREATMENT OF NEUROPSYCHIATRIC DISORDERS
GRETCHEN SNYDER

TI3. VALIDATION OF INTERSECTIONAL CHEMOGENETIC APPROACHES FOR IN-VIVO MANIPULATION OF PROJECTION-DEFINED SUBSTANTIA NIGRA CIRCUITS
MARGARET TANNER

TI4. DOPAMINE PATHWAYS MEDIATING AFFECTIVE STATE TRANSITIONS AFTER SLEEP LOSS
MINGZHENG WU

TI5. COMPARING PLASTICITY EFFECTS OF ITBS AND 10-HZ RTMS WITH NMDA AND GABA RECEPTOR MODULATION
JOSHUA BROWN

TI6. LATERAL HYPOTHALAMIC GLUTAMATERGIC INPUTS TO VTA GLUTAMATERGIC NEURONS MEDIATE PRIORITIZATION OF INNATE DEFENSIVE BEHAVIOR OVER FEEDING
FLAVIA BARBANO

TI7. CHARACTERIZING THE KINEMATICS OF SKILLED ACTION IN A MOUSE MODEL OF DYT1 DYSTONIA
TIFFANY LIN

TI8. NUCLEUS ACCUMBENS DOPAMINE DYNAMICS UNDERLYING FLEXIBLE SIGN-TRACKING DURING A REWARD CONTINGENCY CHANGE
ERICA TOWNSEND

TUESDAY, JANUARY 30TH

POSTER SESSION III

3:30 P.M. - 4:30 P.M.

PEAK 4-5, FLOOR 3

T19. IDENTIFYING A DOWNSTREAM TARGET OF TBX1, A GENE ENCODED IN THE 22Q11.2 LOCUS, FOR OLIGODENDROGENESIS AND COGNITIVE FUNCTION
ANNE WELLS

T20. SUFFERING IN SILENCE OR SATISFIED IN SOLITUDE? PERIPUBERTAL SOCIAL DISRUPTION DIFFERENTIALLY ALTERS MOTIVATED BEHAVIORS IN JUVENILES
CATHERINE NEMESKAL

T21. TRAINING, CAREER DEVELOPMENT AND FUNDING OPPORTUNITIES VIA THE NATIONAL INSTITUTE ON AGING
DANA PLUDE

T22. TRANSIENT CAMP PRODUCTION DRIVES RAPID AND SUSTAINED SPIKING IN BRAINSTEM PARABRACHIAL NEURONS TO SUPPRESS FEEDING
JEREMIAH ISAAC

T23. AKAP-SCAFFOLDING OF CALCINEURIN IN AMYLOID Β-MEDIATED SYNAPTIC DYSFUNCTION
MARK DELL'ACQUA

T24. BRAIN-WIDE IN VIVO DOPAMINE DYNAMICS REVEALED WITH THE NEXT GENERATION OF DLIGHT SENSORS
JACOB ROSHGADOL

T25. RIT2 REGULATES INDUCTION OF THE AUTOPHAGY LYSOSOMAL PATHWAY AND PROTECTS AGAINST Α-SYNUCLEIN PATHOLOGY IN A CELLULAR MODEL OF PARKINSON'S DISEASE
WARREN HIRST

T26. OPEN BOARD

T27. THE UFMI PATHWAY IS DYSREGULATED IN ALZHEIMER'S DISEASE
FABIENNE FIESEL

T28. DISSECTING INCRETIN-MEDIATED MODULATION OF HYPOTHALAMIC FEEDING CIRCUIT
HAYLEY MCMORROW

TUESDAY, JANUARY 30TH

POSTER SESSION III

3:30 P.M. - 4:30 P.M.

PEAK 4-5, FLOOR 3

T29. OXYTOCIN RECEPTOR CO-LOCALIZATION IN BRAINSTEM PARASYMPATHETIC NEURONS
DAVID MENDELOWITZ

T30. STROKE-RELATED BLOOD-BRAIN BARRIER DISRUPTION IS HIGHER IN POSTERIOR CEREBRAL ARTERY INFARCTS WHEN COMPARED WITH OTHER VASCULAR TERRITORIES
RICHARD LEIGH

T31. METAGENOMIC SEQUENCING TO BETTER UNDERSTAND GUT MICROBIOME CONTRIBUTIONS TO TBI
KRIS MARTENS

T32. NOVEL A3 ADENOSINE RECEPTOR AGONIST MRS5980 PREVENTS TRAUMATIC BRAIN INJURY INDUCED COGNITIVE IMPAIRMENT
SUSAN FARR

T33. SEIZURE AVALANCHE AFTER SUPPRESSION WITH MTOR INHIBITION IN A MOUSE MODEL OF TSC
ANNE ANDERSON

T34. COMPARISON OF FIVE SECOND-LINE DRUGS IN THE TREATMENT OF EXPERIMENTAL STATUS EPILEPTICUS
CLAUDE WASTERLAIN

T35. DIHEXA RESCUES COGNITIVE IMPAIRMENTS FOLLOWING REPEATED MILD TRAUMATIC BRAIN INJURY
DAVID DEVILBISS

T36. EFFECTS OF COMPLEX I DEFICIENCY AND PINKI/ PARKIN MEDIATED MITOPHAGY ON NEUROGENESIS OF THE SUBVENTRICULAR ZONE IN NDUFS4 KO MOUSE MODEL OF LEIGH SYNDROME
SAHITYA RANJAN BISWAS

T37. TRANSCRIPTIONAL AND TOPOGRAPHICAL CHARACTERIZATION AND COMPARISON OF ROSTRAL MEDIAL TEGMENTAL NUCLEUS AND VENTRAL TEGMENTAL AREA GABA NEURONS AND ASSOCIATED SUBTYPES
ZACHARY HOUGH

T38. ASSESSMENT OF FUNCTIONAL AND CLINICAL CHARACTERISTICS OF GRIN VARIANTS IN A PUBLIC DATABASE: THE GRIN PORTAL
STEPHEN TRAYNELIS

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5, FLOOR 3

T39. THE EFFECTS OF NEURAL ACTIVITY AND INCREASED CAMP LEVELS IN PERIFORNICAL NUCLEUS OF HYPOTHALAMUS ON FOOD INTAKE
AMIN ATTARI

T40. INVESTIGATING THE ROLE OF SOMATOSTATIN INTERNEURONS IN ENDOGENOUS OPIOID SIGNALING WITHIN THE ANTERIOR CINGULATE CORTEX
JACOB REEVES

T4I. ADAPTATIONS OF THE ENDOCANNABINOID SYSTEM DURING PERSISTENT INFLAMMATION ARE DRIVEN BY CORTICOSTERONE WITHIN THE VLPAG
BASILE COUTENS

T42. COMPARISON OF SPECTRAL ANALYSIS, MULTIFRACTAL DETRENDED FLUCTUATION ANALYSIS, AND INFORMATION TRANSFER MODELING APPLIED TO EEG IN SCHIZOPHRENIA
TODD ZORICK

T43. REGIONAL- AND CELL TYPE-SPECIFIC ALTERATIONS IN A UNIQUE SUBTYPE OF SOMATOSTATIN-EXPRESSING NEURONS IN SCHIZOPHRENIA
KENNETH FISH

T44. CHANGES IN NEUROPEPTIDE LARGE DENSE CORE VESICLE TRAFFICKING DYNAMICS CONTRIBUTE TO ADAPTIVE RESPONSES TO A SYSTEMIC HOMEOSTATIC CHALLENGE
JAVIER STERN

T45. EXPLORING COLLECTIVE NEURAL ACTIVITY: MESOSCOPIC DYNAMICS AND IMPLICATIONS FOR NEUROLOGICAL PHENOMENA
YU QIN

T46. ISOLATING THE ROLE OF LC-NORADRENERGIC DOPAMINE RELEASE DURING AVERSIVE AND APPETITIVE BEHAVIORS
AVI MATARASSO

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV

3:30 P.M. - 4:30 P.M.

PEAK 4-5, FLOOR 3

W1. KAPPA OPIOID RECEPTOR SYSTEM IN THE NUCLEUS ACCUMBENS MEDIATES ESCALATION OF COCAINE CONSUMPTION
LYDIA GORDON-FENNELL

W2. ROLE OF DORSAL RAPHE GLUTAMATERGIC NEURONS IN COCAINE PREFERENCE
ORLANDO ESPINOZA

W3. LATERAL HABENULA INHIBITION SUPPRESSES FUTURE FENTANYL SEEKING
CHRISTOPHER O'BRIEN

W4. NUCLEUS ACCUMBENS NITRERGIC INTERNEURONS ARE REQUIRED FOR THE CELL TYPE-SPECIFIC PLASTICITY IN MEDIUM SPINY NEURONS UNDERLYING CUED COCAINE SEEKING
ADAM DENTON

W5. VTA GLUTAMATERGIC INPUTS FROM THE PARABRACHIAL NUCLEUS REGULATE LONG-LASTING FEAR MEMORY
RODRIGO OSNAYA

W6. SEROTONIN, PSYCHEDELICS, AND CLAUSTRUM SIGNALING TO THE ANTERIOR CINGULATE CORTEX
TANNER ANDERSON

W7. EXPLORING THE ASSOCIATION BETWEEN SEX STEROIDS AND NICOTINIC ACETYLCHOLINE RECEPTORS IN HETEROGENEOUS STOCK (HS) RATS THAT ARE RESISTANT OR SUSCEPTIBLE TO COCAINE ADDICTION-LIKE BEHAVIORS
ELIZABETH SNEDDON

W8. DEVELOPMENT OF MULTIPLEXED POPULATION SELECTION AND ENRICHMENT SINGLE NUCLEI RNA SEQUENCING TO CHARACTERIZE NEURONAL ENSEMBLES IN COCAINE RELAPSE
KAREEM WOODS

W9. SEX DIFFERENCES IN THE NEURAL CIRCUITS THAT PREDICT ALCOHOL DEPENDENCE DEVELOPMENT
KELLY HEWITT

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5, FLOOR 3

WI0. OPTOGENETIC MANIPULATION OF PRELIMBIC CORTICAL ENSEMBLES DISRUPTS CUED REWARD SEEKING
ROGER GRANT

WI1. TRANSCRIPTOME-GUIDED DIAGNOSIS AND DRUG REPURPOSING FOR ALCOHOL USE DISORDER: A TALE OF MICE AND HUMANS
LAURA FERGUSON

WI2. HEROIN-MEDIATED DISRUPTION OF THALAMO-ACCUMBAL BEHAVIORAL SUPPRESSION IS REQUIRED FOR REINSTATEMENT OF HEROIN SEEKING
JACQUELINE PANICCIA

WI3. CORTICOSTRIATAL NEURONAL ENSEMBLES REGULATE CUE-INDUCED HEROIN SEEKING
RACHEL CLARKE

WI4. XYLAZINE ACTS ON THE KAPPA OPIOID RECEPTOR AND WORSENS OPIOID WITHDRAWAL IN FEMALE BUT NOT MALE MICE
MADIGAN BEDARD

WI5. NICOTINE AND THE NODOSE GANGLIA: EVIDENCE FOR BRAIN-BODY INTERACTIONS IN SUBSTANCE USE DISORDERS
KEVIN BRAUNSCHEIDEL

WI6. ELUCIDATING THE ROLE OF MEDIAL SEPTUM GLUTAMATE NEURONS IN REWARD SEEKING BEHAVIORS
ANDREW KESNER

WI7. RESILIENT SPECIFIC SEX-CONSERVED TRANSCRIPTOMIC CHANGES IN THE NUCLEUS ACCUMBENS FOLLOWING CHRONIC SOCIAL DEFEAT STRESS IN MICE
TREVONN GYLES

WI8. STRESS-INDUCED NEUROIMMUNE MECHANISMS UNDERLYING REWARD DEFICITS
RACHEL FISHER-FOYE

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV

3:30 P.M. - 4:30 P.M.

PEAK 4-5, FLOOR 3

W19. DOES ACUTE PSYCHEDELIC "THERAPY" IN RATS PERSISTENTLY REVERSE STRESS-INDUCED BEHAVIORAL ABNORMALITIES?
KATE LAWSON

W20. EXPLORING THE SNOWBALL EFFECTS OF POSTTRAUMATIC STRESS SYMPTOMS ON ATTENTION-RELATED BRAIN AND BEHAVIORAL RESPONSES IN ADOLESCENTS
SAMANTHA ELY

W21. CELL TYPE-SPECIFIC ROLES OF H3 SEROTONYLATION IN NORMAL AND DISRUPTED POSTNATAL BRAIN DEVELOPMENT
ASHLEY CUNNINGHAM

W22. SEX-SPECIFIC EFFECTS OF PSYCHEDELIC DRUG ADMINISTRATION ON THREAT RESPONDING AND REACTIVITY WITHIN THE PARAVENTRICULAR NUCLEUS OF THE HYPOTHALAMUS
DEVIN EFFINGER

W23. NEURAL MECHANISMS OF AFFECTIVE STATES IN THE PRIMATE BRAIN
DAVIDE FOLLONI

W24. INTERPEDUNCULAR NUCLEUS CIRCUITRY IN INNATE AND ADAPTIVE DEFENSIVE LEARNING
ELORA WILLIAMS

W25. PERIRHINAL CORTEX HYPOACTIVITY UNDERLIES SPATIAL LEARNING DEFICITS IN THE SCN2A AUTISM MOUSE MODEL
RACHEL KEITH

W26. VALENCE-SPECIFIC GATING OF BEHAVIORAL FLEXIBILITY BY MEDIAL PREFRONTAL CORTEX PROJECTIONS TO THE VENTRAL TEGMENTAL AREA
MERRIDEE LEFNER

W27. THALAMIC INTERACTION OF BASAL GANGLIA AND CEREBELLAR CIRCUITS DURING MOTOR LEARNING
RICHARD ROTH

W28. CORTICOFUGAL CONTROL OVER REFLEXIVE VISUOMOTOR BEHAVIOR IN MICE
GAL ATLAN

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV

3:30 P.M. - 4:30 P.M.

PEAK 4-5, FLOOR 3

W29. CHOLINERGIC VENTRAL PALLIDUM CELLS AND THEIR ROLE IN CUE- AND REWARD- RELATED MOTIVATION
ELIZABETH BIEN

W30. VTA GABA NEURON ACTIVITY ENCODES SALIENCE, REINFORCES ACTIONS, AND SHAPES STRIATAL DOPAMINE SIGNALING
MARGARET STELZNER

W31. SCHEMA CELL FORMATION IN ORBITOFRONTAL CORTEX IS SUPPRESSED BY HIPPOCAMPAL OUTPUT
WENHUI ZONG

W32. A SPECIAL ROLE FOR ANTERIOR CINGULATE CORTEX, BUT NOT ORBITOFRONTAL CORTEX OR BASOLATERAL AMYGDALA, IN CHOICES INVOLVING INFORMATION
VALERIA GONZALEZ

W33. ROLE OF MEDIODORSAL THALAMIC INPUT TO DORSAL STRIATUM IN ACTION CONTROL
EMILY BALTZ

W34. ORBITOFRONTAL ENSEMBLES INTEGRATE TASTE, MOVEMENT, AND REWARD PREDICTIONS DURING LEARNING
EVAN HART

W35. MESOCORTICAL DOPAMINE ACTIVITY ENCODES TIMING-RELATED COGNITIVE PROCESSING
MACKENZIE (SPICER) RYSTED

W36. THE COMPARATIVE ORGANIZATION OF SINGLE AMYGDALA NEURON PROJECTION PATTERNS TO FRONTAL CORTEX AND STRIATUM IN MACAQUES AND MICE
ZACHARY ZEISLER

W37. DYNAMIC NEUROMODULATION BY THE ENDOGENOUS OPIOID DYNORPHIN PROMOTES REWARD-WEEKING
RAAJARAM GOWRISHANKAR

W38. OLIGODENDROCYTES AND MYELIN RESTRICT CORTICAL EXPERIENCE-DEPENDENT NEURONAL PLASTICITY
WENDY XIN

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV

3:30 P.M. - 4:30 P.M.

PEAK 4-5, FLOOR 3

W39. MICE WITH SYNAPTOJANINI DELETION IN DOPAMINERGIC NEURONS EXHIBIT SEX AND AGE DEPENDENT MOTOR FUNCTION ABNORMALITY
JACQUELINE SAENZ

W40. CHARACTERIZING THE ROLE OF MS4AS IN ALZHEIMER'S DISEASE
THUYVAN LUU

W41. IMPACT OF TAU EXPRESSION ON THE DEVELOPMENT OF ACQUIRED TEMPORAL LOBE EPILEPSY
MADELEINE MOSELEY

W42. ENLARGED PERIVASCULAR SPACES CHARACTERIZE SEIZURE OUTCOME AFTER TRAUMATIC BRAIN INJURY
CELINA ALBA

W43. SEX AND CIRCUIT SPECIFIC AMYGDALA DYSFUNCTION AFTER GLOBAL CEREBRAL ISCHEMIA
JOSE VIGIL

W44. THE TANDEM ROLE OF LATERAL HYPOTHALAMIC GABA AND GLUTAMATE NEURONS IN REGULATING STRIATAL DOPAMINE RELEASE AND MOTIVATED BEHAVIOR
ADAM GORDON-FENNELL

W45. DISSECTING THE ACCUMBAL DYNORPHINERGIC OUTPUTS UNDERLYING AFFECTIVE PAIN
FLORA D'OLIVEIRA DA SILVA

W46. NEUROPATHIC PAIN INCREASES BASOLATERAL AMYGDALA KAPPA OPIOID RECEPTOR EXPRESSION AND FUNCTION IN MALE BUT NOT FEMALE MICE
JAMIE MONDELLO

W47. THE ROLE OF NIGROSTRIATAL AND STRIATAL CELL SUBTYPE SIGNALING IN BEHAVIORAL IMPAIRMENTS RELATED TO SCHIZOPHRENIA
NICOLETTE MOYA

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

SI. "TRANQ-DOPE" OVERDOSE AND LETHALITY: SYNERGISTIC INTERACTIONS BETWEEN FENTANYL AND XYLAZINE

MARK SMITH*, SAMANTHA BIANCOROSSO, JACOB CAMP, SALOME HAILU, ALEXANDRA JOHANSEN, MACKENZIE MORRIS, HANNAH CARLSON

THE RECREATIONAL USE OF FENTANYL IN COMBINATION WITH XYLAZINE (I.E., "TRANQ-DOPE") REPRESENTS A RAPIDLY EMERGING PUBLIC HEALTH THREAT CHARACTERIZED BY SIGNIFICANT TOXICITY AND MORTALITY. THIS STUDY QUANTIFIED THE INTERACTIONS BETWEEN THESE DRUGS ON LETHALITY AND EXAMINED THE EFFECTIVENESS OF POTENTIAL RESCUE MEDICATIONS TO PREVENT A LETHAL OVERDOSE. MALE AND FEMALE MICE WERE ADMINISTERED ACUTE DOSES OF FENTANYL, XYLAZINE, OR THEIR COMBINATION VIA INTRAPERITONEAL INJECTION, AND LETHALITY WAS DETERMINED 0.5, 1.0, 1.5, 2.0, AND 24 HR AFTER ADMINISTRATION. BOTH FENTANYL AND XYLAZINE PRODUCED DOSE-DEPENDENT INCREASES IN LETHALITY WHEN ADMINISTERED ALONE. A NONLETHAL DOSE OF FENTANYL (56 MG/KG) PRODUCED AN APPROXIMATELY 5-FOLD DECREASE IN THE ESTIMATED LD50 FOR XYLAZINE (I.E., THE DOSE ESTIMATED TO PRODUCE LETHALITY IN 50% OF THE POPULATION). NOTABLY, A NONLETHAL DOSE OF XYLAZINE (100 MG/KG) PRODUCED AN APPROXIMATELY 100-FOLD DECREASE IN THE ESTIMATED LD50 FOR FENTANYL. BOTH DRUG COMBINATIONS PRODUCED A SYNERGISTIC INTERACTION AS DETERMINED VIA ISOBOLOGRAPHIC ANALYSIS. THE OPIOID RECEPTOR ANTAGONIST, NALOXONE (3 MG/KG), BUT NOT THE ALPHA-2 ADRENERGIC RECEPTOR ANTAGONIST, YOHIMBINE (3 MG/KG), SIGNIFICANTLY DECREASED THE LETHALITY OF A FENTANYL-XYLAZINE COMBINATION. LETHALITY WAS RAPID, WITH DEATH OCCURRING WITHIN 10 MIN AFTER A HIGH DOSE COMBINATION AND GENERALLY WITHIN 30 MIN AT LOWER DOSE COMBINATIONS. MALES WERE MORE SENSITIVE TO THE LETHAL EFFECTS OF FENTANYL-XYLAZINE COMBINATIONS UNDER SOME CONDITIONS SUGGESTING BIOLOGICALLY RELEVANT SEX DIFFERENCES IN SENSITIVITY TO FENTANYL-XYLAZINE LETHALITY. THESE DATA PROVIDE THE FIRST QUANTIFICATION OF THE LETHAL EFFECTS OF "TRANQ-DOPE" AND SUGGEST THAT RAPID ADMINISTRATION OF NALOXONE MAY BE EFFECTIVE AT PREVENTING DEATH FOLLOWING OVERDOSE.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S2. ASTROCYTIC REGULATION OF COCAINE LOCOMOTOR SENSITIZATION IN ECOHIV INFECTED MICE

QIAOWEI XIE*, ROHAN DASARI, JOSHUA JACKSON, JACQUELINE BARKER

COCAINE USE DISORDERS (CUDS) ARE HIGHLY COMORBID WITH HIV INFECTION. PRECLINICAL RESEARCH ON THE NEUROBEHAVIORAL OUTCOMES OF HIV INFECTIONS MAY YIELD CRUCIAL INFORMATION TO IMPROVE CUD PROGNOSIS IN PEOPLE LIVING WITH HIV (PLWH). COCAINE EXPOSURE INCREASES LOCOMOTION. REPEATED EXPOSURE TO THE SAME DOSE OF COCAINE PRODUCES GREATER LOCOMOTOR RESPONSE. THIS LOCOMOTOR SENSITIZATION REFLECTS CHANGES IN NEURAL PLASTICITY AND ASTROCYTE FUNCTION IN THE NUCLEUS ACCUMBENS (NAC) WHICH MAY BE ALTERED BY HIV. ASTROCYTES REGULATE EXCITATORY NEUROTRANSMISSION AND MAINTAIN HOMEOSTASIS. HOWEVER, ASTROCYTE FUNCTION CAN BE DIRECTLY IMPAIRED BY COCAINE USE AND HIV-RELATED NEUROINFLAMMATION. WE CHARACTERIZED CHANGES IN COCAINE LOCOMOTOR SENSITIZATION BY ASSESSING LOCOMOTION AFTER 5 DAILY REPEATED COCAINE EXPOSURE (10MG/KG) IN THE ECOHIV (A CHIMERIC HIV-1 WHICH INFECTS RODENTS) MOUSE MODEL. WE FOUND THAT ECOHIV INFECTION POTENTIATED COCAINE LOCOMOTOR SENSITIZATION VS SHAM CONTROLS. TO DETERMINE WHETHER MODULATING ASTROCYTE ACTIVITY COULD REVERSE ECOHIV-POTENTIATED COCAINE SENSITIZATION, WE CHEMOGENETICALLY ACTIVATED ASTROCYTES IN THE NAC VIA GFAP-GQ-DREADD. THIS ACTIVATION REVERSED ECOHIV-ENHANCED COCAINE SENSITIZATION, AND WAS SELECTIVE TO ECOHIV-INFECTED MICE. THIS MAY SUGGEST THAT ECOHIV INDUCED ADAPTATIONS IN NAC ASTROCYTE THAT DYSREGULATE THE ABILITY OF ASTROCYTES TO MODULATE COCAINE-RELATED BEHAVIORS. WE CONCLUDE THAT ECOHIV INTERACTS WITH COCAINE TO INCREASE LOCOMOTOR SENSITIZATION, AND PROMOTING NAC ASTROCYTIC ACTIVITY CAN RECOVER ECOHIV-INDUCED BEHAVIORAL CHANGES. ONGOING WORK IS INVESTIGATING HOW ECOHIV IMPACTS REACTIVE ASTROGLIOSIS IN THE NAC BY ASSESSING EXPRESSION ASTROCYTIC NUCLEAR MARKER SOX-9, AND CORRELATION BETWEEN SOX-9 EXPRESSION AND NEURONAL EXPRESSION OF THE PUTATIVE ACTIVITY MARKER, CFOS. THESE FINDINGS WILL IDENTIFY NEURAL FACTORS PRECIPITATING RISK FOR COCAINE USE IN PLWH AND OFFER INSIGHTS INTO DEVELOPING TARGETED THERAPEUTICS AGAINST CUDS FOR PLWH IN WHICH THE NEUROBEHAVIORAL ETIOLOGY OF CUD MAY BE DISTINCT.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S3. THE ROLE OF ENDOCANNABINOIDS WITHIN CORTICOLIMBIC REGIONS IN ADAPTIVE STRESS COPING BEHAVIOR AND IMPLICATIONS FOR SUBSEQUENT ALCOHOL DRINKING

LAURA ORNELAS*, JOYCE BESHEER

INDIVIDUAL DIFFERENCES IN RESPONSE TO STRESS SUGGEST RESILIENT AND SUSCEPTIBLE POPULATIONS, WHICH MAY BE IMPORTANT FOR UNDERSTANDING THE HIGH COMORBIDITY OF POST-TRAUMATIC STRESS DISORDER (PTSD) AND ALCOHOL USE DISORDER (AUD). WE HAVE PREVIOUSLY SHOWN THAT FEMALE RATS THAT ENGAGED IN GREATER ACTIVE COPING BEHAVIORS (DIGGING) DURING EXPOSURE TO THE SYNTHETICALLY PRODUCED PREDATOR ODOR 2,5-DIHYDRO-2,4,5-TRIMETHYLTHIAZOLINE (TMT) SHOWED INCREASES IN ALCOHOL SELF-ADMINISTRATION. IN CONTRAST, MALES AND FEMALES THAT ENGAGED IN GREATER PASSIVE COPING BEHAVIOR (IMMOBILITY) DURING THE TMT EXPOSURE SHOWED DECREASED OR NO INCREASES IN ALCOHOL DRINKING. THE PRESENT WORK EXAMINES THE ROLE OF ENDOCANNABINOIDS (ECB) IN MODULATING STRESS-REACTIVE BEHAVIORS USING PHARMACOLOGICAL AND LIQUID CHROMATOGRAPHY/MASS SPECTROMETRY (LCMS) APPROACHES.

FIRST, WE EXAMINED THE ROLE OF ECBS IN THE PRELIMBIC (PRL). FEMALE LONG-EVANS RATS WERE IMPLANTED WITH BILATERAL CANNULAE AIMED AT THE PRL. PRIOR TO WATER/TMT EXPOSURE, RATS RECEIVED INTRA-PRL INJECTION OF 0 OR 2.5 MG/ML JZL-184 (MAGL INHIBITOR) (N=13/VEH; N=9/JZL). ALL RATS TREATED WITH JZL-184 ENGAGED IN GREATER IMMOBILITY BEHAVIOR AND LESS DIGGING BEHAVIOR, SUGGESTING THAT INCREASING 2-AG PROMOTES PASSIVE COPING RESPONSES TO TMT AND CAN PREVENT ENGAGEMENT IN ACTIVE COPING RESPONSES.

NEXT, WE UTILIZED LCMS TO MEASURE DIFFERENCES IN ECB, GABA AND GLUTAMATERGIC LEVELS IN RATS THAT ENGAGE IN ACTIVE OR PASSIVE COPING BEHAVIORS DURING TMT. FEMALE LONG-EVANS RATS WERE EXPOSED TO WATER (N=8) AND TMT (N=20). BRAINS WERE COLLECTED AND TISSUE SAMPLES WERE PUNCHED FROM PRL, BASOLATERAL AMYGDALA (BLA) AND CENTRAL AMYGDALA (CEA). FEMALE RATS THAT ENGAGED IN GREATER DIGGING BEHAVIOR SHOWED INCREASES IN GABA BUT DECREASES FOR GLUTAMINE LEVELS WITHIN THE PRL AND A REDUCTION IN 2-AG LEVELS IN THE BLA. FEMALE RATS THAT ENGAGED IN GREATER IMMOBILITY BEHAVIOR SHOWED REDUCTION IN 2-AG LEVELS IN THE CEA. THEREFORE, AN INVERSE RELATIONSHIP BETWEEN EXCITATORY AND INHIBITORY SYSTEMS WITHIN THE PRL AND REDUCTION IN 2-AG IN THE BLA MAY BE DRIVING ACTIVE COPING BEHAVIOR.

OVERALL, THESE DATA IMPLICATE AN IMPORTANT ROLE OF THE ECB SYSTEM WITHIN CORTICOLIMBIC REGIONS IN MODULATING STRESS-REACTIVE BEHAVIORS DURING TMT AND POTENTIALLY MITIGATE AGAINST LATER INCREASES IN ALCOHOL SELF-ADMINISTRATION.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S4. CASE SERIES: MICRODOSE INDUCTIONS FROM FULL OPIOID AGONIST TO PARTIAL OPIOID AGONIST

TOMMASO TOSINI*

MY POSTER WILL PLAN TO PRESENT A CASE SERIES OF NOVEL INDUCTION PROTOCOLS ONTO BUPRENORPHINE FOR TREATMENT OF OPIOID USE DISORDER. TRADITIONALLY, PATIENTS ON FULL OPIOIDS AGONIST (SUCH AS METHADONE, OXYCODONE, HEROINE, FENTANYL, ETC.) WOULD NEED TO EXPERIENCE AT LEAST MODERATE WITHDRAWAL SYMPTOMS PRIOR TO BEING ABLE TO START BUPRENORPHINE TREATMENT. DUE TO BUPRENORPHINE'S HIGH AFFINITY TO THE MU-OPIOID RECEPTOR, THOUGH ONLY PARTIAL AGONIST ACTIVITY, IT IS AN IDEAL MAINTENANCE TREATMENT OPTION FOR THOSE STRUGGLING WITH ADDICTION. UNFORTUNATELY, BECAUSE OF THESE PHARMACODYNAMIC PROPERTIES IT CAN LEAD TO "PRECIPITATED WITHDRAWAL" WHEN STARTED TOO EARLY AND THIS BECOMES A MAJOR BARRIER TO PATIENT'S INITIATING TREATMENT. WITHDRAWAL SYMPTOMS, AND EVEN JUST FEAR OF WITHDRAWAL, PREVENTS MANY PATIENTS FROM ACCESSING MAT AND ULTIMATELY TO SIGNIFICANT MORBIDITY AND MORTALITY.
IN MY CLINICAL PRACTICE AS AN ADDITION SPECIALIST AT VENTURA COUNTY MEDICAL CENTER WE HAVE BEEN USING MICRO-DOSE INDUCTIONS TO START PATIENTS ONTO BUPRENORPHINE WITH MINIMAL TO NO WITHDRAWAL SYMPTOMS. USING BUPRENORPHINE'S HIGH AFFINITY AND SLOW DISSOCIATION FROM THE MU OPIOID RECEPTOR WE ARE ABLE TO USE REPEATED, VERY LOW DOSES TO SLOWLY DISPLACE THE FULL OPIOID AGONIST THAT PATIENT IS DEPENDENT WITH BUPRENORPHINE WHILE PATIENT CONTINUE TO MAINTAIN THEIR USE. MY POSTER WILL PRESENT THIS "BERNESE" TECHNIQUE IN VARIOUS SITUATIONS INCLUDING HIGH DOSE METHADONE, ILICIT FENTANYL USE AND PRESCRIBED OXYCODONE USE WITH DISCUSSIONS OF THE SUCCESSES AND CHALLENGES SPECIFIC TO EACH SUBSTANCE.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S5. MOLECULAR CHARACTERIZATION OF OPIOID SENSITIVE GABAERGIC AND GLUTAMATERGIC AFFERENTS TO THE VENTRAL TEGMENTAL AREA

OLIVER CULVER*, THOMAS JHOU

THE MOTIVATIONAL EFFECTS OF OPIOIDS HAVE LONG BEEN THOUGHT TO BE MEDIATED BY MU OPIOID RECEPTORS RESIDING ON LOCAL GABAERGIC NEURONS WITHIN THE VENTRAL TEGMENTAL AREA (VTA). HOWEVER, BEHAVIORAL AND ELECTROPHYSIOLOGICAL STUDIES FROM OUR LAB AND OTHERS HAVE FOUND THAT GABA NEURONS IN THE ADJACENT ROSTROMEDIAL TEGMENTAL NUCLEUS (RMTG) EXERT STRONGER INFLUENCES ON MIDBRAIN DOPAMINE NEURON FIRING AND OPIOID-SEEKING BEHAVIOR THAN LOCAL CIRCUITS WITHIN THE VTA ITSELF. WHILE MANY OF THOSE STUDIES WERE IN RATS, WE NOW SHOW IN MICE USING A COMBINATION OF RETROGRADE TRACING AND RNASCOPE THAT RMTG GABA NEURONS PROJECTING TO THE VTA EXHIBIT HIGH LEVELS OF THE MU OPIOID RECEPTOR GENE OPRM1. IN CONTRAST, LOCAL GABA NEURONS WITHIN THE VTA ARE LESS LIKELY TO EXPRESS OPRM1, ESPECIALLY IN MORE CAUDAL AND LATERAL REGIONS OF THE VTA. WE ALSO SURVEYED THE ENTIRE BRAIN FOR GABAERGIC OPRM1 EXPRESSING AFFERENTS TO THE VTA AND FOUND A POPULATION OF GABAERGIC NEURONS IN THE LATERAL PREOPTIC AREA (LPOA) OF THE HYPOTHALAMUS THAT ALSO EXPRESS SIMILARLY HIGH LEVELS OF OPRM1. OTHER GABAERGIC INPUTS TO THE VTA WERE LESS LIKELY TO EXPRESS OPRM1. ADDITIONAL STUDIES ARE UNDERWAY TO EXAMINE GLUTAMATERGIC NEURONS, WHICH MAY ALSO INFLUENCE OPIOID-SEEKING. COLLECTIVELY, THESE STUDIES POINT TO THE EXISTENCE OF LONG-RANGE INPUTS TO THE VTA THAT MAY EXERT PREVIOUSLY UNRECOGNIZED INFLUENCES ON OPIOID-SEEKING IN MICE.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S6. ELECTROCHEMICAL APTAMER BASED SENSORS FOR THE DETECTION OF IN BRAIN COCAINE

NICOLE EMMONS*, KEVIN HONEYWELL, YUTING (KAYLA) WANG, KEVIN PLAXCO, TOD KIPPIN

GIVEN THE UBIQUITY OF COCAINE ABUSE AND ITS MASSIVE IMPACT ON PUBLIC HEALTH, THE ABILITY TO DETECT THIS DRUG CONVENIENTLY, SENSITIVELY AND RAPIDLY ACROSS BIOLOGICAL MATRICES IN REAL TIME WOULD BE EXTREMELY VALUABLE. A PLATFORM TECHNOLOGY GENERALIZABLE TO THE DETECTION OF MANY MOLECULAR ANALYTES, EAB SENSORS SUPPORT THE SECONDS, OR EVEN SUB-SECONDS, RESOLVED MEASUREMENT OF SPECIFIC DRUGS, METABOLITES, AND BIOMARKERS IN SITU IN THE BRAIN, BLOOD, AND INTERSTITIAL FLUID OF THE SOLID TISSUES. COMPRISED OF A TARGET-BINDING APTAMER THAT HAS BEEN MODIFIED WITH A REDOX REPORTER, REENGINEERED TO UNDERGO BINDING-INDUCED FOLDING, AND ATTACHED TO AN INTERROGATING ELECTRODE, EAB SENSORS PRODUCE AN ELECTROCHEMICAL SIGNAL THAT IS MONOTONICALLY RELATED TO TARGET CONCENTRATION. HERE, WE UTILIZE EAB SENSORS TO DETECT PHYSIOLOGICALLY RELEVANT CONCENTRATIONS OF COCAINE IN BOTH BLOOD PLASMA AND IN DISTINCT BRAIN COMPARTMENTS WITH HIGH TEMPORAL RESOLUTION, GENERATING A COMPLETE PICTURE OF ITS COMPARTMENTAL PHARMACOKINETICS. WE ARE ALSO ABLE TO CORRELATE DYNAMIC IN BRAIN CONCENTRATIONS WITH BEHAVIORAL PARADIGMS, SPECIFICALLY LOCOMOTION, TO UNDERSTAND HOW CONCENTRATION DRIVES BEHAVIORAL CHANGES. FINALLY, WE EVALUATE THIS SENSORS SPECIFICITY TOWARDS COCAINE TO ENSURE A LACK OF CROSS-REACTIVITY.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S7. EXERCISE BLOCKS THE INCUBATION OF CRAVING FOR HIGH-FAT FOODS AND RECOVERS DIET-INDUCED CHANGES IN PERINEURONAL NETS

LYDIA BAILEY*, GEORGIA KIRKPATRICK, TRAVIS BROWN

AS OBESITY BECOMES INCREASINGLY PREVALENT, MANY DIETING STRATEGIES REMAIN INEFFECTIVE DUE TO THEIR INABILITY TO CURB CRAVINGS. A PHENOMENON CALLED "INCUBATION OF CRAVING" REVEALS THAT CRAVINGS FOR REWARDING STIMULI LIKE FOOD OR DRUGS INTENSIFY OVER TIME DURING PERIODS OF ABSTINENCE. OUR LAB HAS PREVIOUSLY DEMONSTRATED THAT FORCED, HIGH-INTENSITY EXERCISE CAN PREVENT THE INCUBATION OF CRAVING FOR HIGH-FAT FOODS IN MALE SPRAGUE-DAWLEY RATS (KIRKPATRICK ET AL., 2022). MOREOVER, WE'VE DISCOVERED THAT THIS SAME EXERCISE REGIMEN CAN REVERSE THE HIGH-FAT DIET-INDUCED REDUCTION IN PERINEURONAL NET (PNN) INTENSITY IN THE PRELIMBIC PREFRONTAL CORTEX (PFC; CH:100.0±6.3, HF: 74.0±6.9, HF+EX: 104.3±3.6; $F(1,26)=18.94$, $P < 0.05$). PNNS ENSHEATHE FAST-SPIKING INTERNEURONS IN PFC AND CAN MODULATE NEURONAL FUNCTION BY STABILIZING SYNAPSES AND RESTRICTING SYNAPTIC PLASTICITY, INFLUENCING THE OVERALL EXCITABILITY AND ACTIVITY OF NEURONS. THESE FINDINGS SUGGEST THAT ALTERATIONS IN PNNS COULD HAVE SIGNIFICANT IMPLICATIONS FOR NEURONAL FIRING PATTERNS. HOWEVER, IT REMAINS UNCERTAIN WHETHER THESE PATTERNS HOLD TRUE FOR FEMALES. IN RESPONSE TO HIGH-FAT DIETS, FEMALE RATS DISPLAY DISTINCTIVE CHANGES IN PNNS COMPARED TO MALES, EXPERIENCING AN INCREASE IN PNN INTENSITY IN THE INFRALIMBIC PFC (DINGESS ET AL., 2020). WHILE THE ULTIMATE BEHAVIORAL OUTCOME MAY BE SIMILAR, WITH FEMALES POTENTIALLY HAVING A REDUCED ABILITY TO INHIBIT OR SUPPRESS REWARD-SEEKING BEHAVIORS DUE TO PFC ACTIVITY DIFFERENCES, MALES MIGHT EXHIBIT AN ENHANCED PROPENSITY FOR INITIATING AND PLANNING SUCH BEHAVIORS. OUR RESEARCH AIMS TO UNCOVER HOW THESE ALTERATIONS AFFECT FEMALES AND WHETHER EXERCISE HAS SIMILAR EFFECTS, EXAMINING PNN-DRIVEN CHANGES IN THE PFC TO NAC CIRCUIT, A KEY REWARD PATHWAY, TO UNDERSTAND FOOD CRAVINGS, ADDRESSING OBESITY AND OVEREATING.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S8. INVESTIGATING THE ROLE OF THE SEROTONIN IB RECEPTOR IN THE THERAPEUTIC EFFECTS AND NEUROBIOLOGICAL MECHANISMS OF ACTIONS OF PSILOCYBIN IN MICE

SIXTINE FLEURY*, KATHERINE NAUTIYAL

RECENT STUDIES HAVE DEMONSTRATED STRONG POTENTIAL OF PSYCHEDELIC THERAPIES FOR THE TREATMENT OF PSYCHIATRIC DISORDERS, WITH ONGOING CLINICAL TRIALS AIMED AT SHOWING THAT PSILOCYBIN IS EFFECTIVE IN TREATING MAJOR DEPRESSIVE DISORDER. WHILE THE MECHANISMS OF ACTION ARE UNKNOWN, THE CLINICAL EFFECTS ARE MOST COMMONLY ATTRIBUTED TO ACTIVATION OF THE SEROTONIN 2A RECEPTOR (5-HT2A R).
HOWEVER, PSILOCIN, THE ACTIVE METABOLITE OF PSILOCYBIN, BINDS TO MANY SEROTONIN SUBTYPES. RECENT STUDIES IN RODENTS SUGGEST THAT THESE THERAPEUTIC EFFECTS MAY BE INDEPENDENT OF THE 5-HT2AR. INVESTIGATING OTHER 5-HTRS IS CRUCIAL TO COMPREHEND PSILOCYBIN'S LASTING CLINICAL EFFECTS.
WE HYPOTHESIZED THAT PSILOCYBIN MAY INFLUENCE ANTIDEPRESSIVE-LIKE BEHAVIORS VIA 5-HTIBRS ACTIVATION, A NON-HALLUCINATORY SUBTYPE OF SEROTONIN RECEPTORS PREVIOUSLY IMPLICATED IN MEDIATING DEPRESSIVE PHENOTYPES AND NEURAL PLASTICITY. WE FIRST ESTABLISHED A PROTOCOL TO TEST PSILOCYBIN'S EFFECTS ON ANXIETY-LIKE BEHAVIOR AND ANHEDONIA IN MICE. OUR RESULTS SHOW THAT PSILOCYBIN REDUCES ANXIETY AND DECREASES ANHEDONIA IN FEMALES TREATED WITH CHRONIC CORTICOSTERONE. NEXT, WE ASSESSED THE ROLE OF 5-HTIBR IN MEDIATING THESE BEHAVIORAL RESPONSES USING TETOIB TRANSGENIC MICE. INTERESTINGLY, FEMALE MICE LACKING 5-HTIB LACKED THE BEHAVIORAL CHANGES SEEN FOLLOWING PSILOCYBIN INJECTION IN CONTROL MICE. SPECIFICALLY, PSILOCYBIN-TREATED KNOCK-OUT FEMALES SHOWED NO REVERSAL IN CORT-INDUCED ANHEDONIA, NO INCREASED EXPLORATION IN THE ELEVATED PLUS MAZE, AND NO DECREASED ANXIETY IN THE NOVELTY-SUPPRESSED FEEDING TEST COMPARED TO SALINE-TREATED KNOCK-OUTS. FINALLY, WE USED C-FOS LABELING FOR QUANTIFICATION OF WHOLE BRAIN NEURAL ACTIVITY FOLLOWING PSILOCYBIN INJECTION TO COMPARE THE NEURAL ACTIVATION IN CONTROLS AND MICE LACKING 5-HTIBR. OVERALL, THIS RESEARCH SUGGESTS THAT PSILOCYBIN INDUCES THERAPEUTIC EFFECTS IN FEMALE MICE AT HIGH DOSES, WHICH MAY BE PARTIALLY MODULATED BY THE ACTIVATION OF THE NON-HALLUCINATORY SEROTONIN IB RECEPTOR.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S9. A NETWORK APPROACH TO PSYCHOPATHOLOGY: BRIDGING NEUROIMAGING AND PSYCHOMETRICS

FREDERICK GOODSON-GREGG*, JONATHAN TOWNE, ANNIE DANG, LARRY PRICE, PETER FOX

MENTAL ILLNESS IS AN ENORMOUS AND GROWING PUBLIC HEALTH BURDEN. DUE TO DECADES OF SLOW PROGRESS IN MENTAL HEALTH RESEARCH, THE NIMH HAS DEVELOPED STRATEGIES TO PROMOTE GROUNDBREAKING RESEARCH. TWO PILLARS OF THIS STRATEGY ARE 1) LEVERAGING ADVANCES IN HUMAN NEUROIMAGING – ESPECIALLY CONNECTOMICS – TO IMPROVE OUR UNDERSTANDING OF THESE DISORDERS, 2) PROMOTING ALTERNATIVE TAXONOMIES OF MENTAL DISORDERS, TO BETTER CLASSIFY PSYCHIATRIC PATIENTS. PSYCHOMETRIC META-ANALYSES HAVE MADE SUBSTANTIAL PROGRESS APPLYING FACTOR ANALYSIS AND NETWORK MODELING TO DEVELOP ALTERNATIVE TAXONOMIES, TOGETHER INFORMING THE CREATION OF THE HIERARCHICAL TAXONOMY OF PSYCHOPATHOLOGY (HITOP), A DATA-DRIVEN NOSOLOGY OF MENTAL DISORDERS, WHICH HAS SOLICITED NEUROBIOLOGICAL EVIDENCE IN SUPPORT OF ITS THEORETIC CONSTRUCTS. NEUROIMAGING STUDIES HAVE ALSO MADE SUBSTANTIAL PROGRESS ADVANCING OUR UNDERSTANDING OF MENTAL DISORDERS THROUGH NETWORK ANALYSIS. THIS ANALYSIS ADDRESSES THE HYPOTHESIS THAT NEUROBIOLOGY AND PSYCHOPATHOLOGY EXHIBIT COMPARABLE DATA STRUCTURES (FACTORS AND NETWORKS) THAT CAN BE EXPLOITED TO BRIDGE SYMPTOMS WITH BRAIN NETWORKS AND INFORM DATA-DRIVEN MENTAL DISORDER TAXONOMIES. THIS ANALYSIS RELIES ON NEUROIMAGING META-ANALYTIC METHODS, APPLYING BOTH STRUCTURAL VOXEL-BASED MORPHOMETRY (VBM) AND FUNCTIONAL VOXEL-BASED PHYSIOLOGY (VBP) BRAINMAP DATABASES TO COMPUTE NEUROBIOLOGICAL "SIGNATURES" OF MENTAL DISORDERS CAPABLE OF DEFINING RELATIONSHIPS BETWEEN DISORDERS. TO ENSURE ALIGNMENT OF STATISTICAL METHODS TO PSYCHOMETRICS, FACTOR ANALYSIS WAS UTILIZED TO CHARACTERIZE DISORDER RELATIONSHIPS. THIS ANALYSIS PROVIDES NEUROBIOLOGICAL EVIDENCE IN SUPPORT OF THE HITOP INTERNALIZING PSYCHOMETRIC CONSTRUCT BY REVEALING NEUROBIOLOGICALLY DRIVEN FACTOR LOADINGS FOR SEVERAL INTERNALIZING DISORDERS IN LINE WITH SYMPTOM DRIVEN FACTOR LOADINGS. GIVEN THE PROMISE OF THIS APPROACH, FURTHER ANALYSES AIM TO CONSTRUCT A NEUROIMAGING MODEL OF INTERNALIZING. THIS WILL ENABLE A DESCRIPTION OF INVOLVED REGIONS AND CONNECTIVITY, AS WELL AS THE APPLICATION OF THE MODEL TO PRIMARY PATIENT DATA WHERE PATIENT SYMPTOM SCORES WILL BE ALIGNED TO MODEL FIT INDICES.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S10. THE ROLE OF DORSAL STRIATUM D1 RECEPTOR SIGNALING IN FEAR EXTINCTION AND RELAPSE

BENJAMIN GREENWOOD*, MARGARET TANNER, ALYSSA HOHORST, JESSICA WESTERMAN, CAROLINA SANCHEZ MENDOZA, REBECCA HAN, LAREINA ALVAREZ, MILES DRYDEN, NICOLETTE MOYA, ALEEZAH BALOLIA, JENNIFER JAIME, ESTEBAN LOETZ

SYSTEMIC MANIPULATIONS THAT ENHANCE DOPAMINE (DA) TRANSMISSION AT THE TIME OF FEAR EXTINCTION CAN STRENGTHEN FEAR EXTINCTION AND REDUCE CONDITIONED FEAR RELAPSE. PRIOR STUDIES INVESTIGATING THE BRAIN REGIONS WHERE DA AUGMENTS FEAR EXTINCTION FOCUS ON TARGETS OF MESOLIMBIC AND MESOCORTICAL DA SYSTEMS ORIGINATING IN THE VENTRAL TEGMENTAL AREA, GIVEN THE ROLE OF THESE DA NEURONS IN PREDICTION ERROR. THE DORSAL STRIATUM (DS), THE PRIMARY TARGET OF THE NIGROSTRIATAL DA SYSTEM ORIGINATING IN THE SUBSTANTIA NIGRA (SN), IS IMPLICATED IN BEHAVIORS BEYOND ITS CANONICAL ROLE IN MOVEMENT, SUCH AS REWARD AND PUNISHMENT, GOAL-DIRECTED ACTION, AND STIMULUS-RESPONSE ASSOCIATIONS, BUT WHETHER DS DA CONTRIBUTES TO FEAR EXTINCTION IS UNKNOWN. WE HAVE OBSERVED THAT CHEMOGENETIC STIMULATION OF SN DA NEURONS DURING FEAR EXTINCTION PREVENTS THE RETURN OF FEAR IN CONTEXTS DIFFERENT FROM THE EXTINCTION CONTEXT, A FORM OF RELAPSE CALLED RENEWAL. THIS EFFECT OF SN DA STIMULATION IS MIMICKED BY A D1 AGONIST INJECTED INTO THE DS, THUS IMPLICATING DS DA IN FEAR EXTINCTION. DIFFERENT DS SUBREGIONS SUBSERVE UNIQUE FUNCTIONS OF THE DS, BUT IT IS UNCLEAR WHERE IN THE DS D1 SIGNALING MODULATES FEAR EXTINCTION. HERE, WE SOUGHT TO DETERMINE THE ROLE OF DS SUBREGIONS AND D1 SIGNALING WITHIN DS SUBREGIONS IN FEAR EXTINCTION AND RELAPSE. DORSOMEDIAL (DMS) AND DORSOLATERAL (DLS) DS SUBREGIONS OF MALE, LONG-EVANS RATS WERE PHARMACOLOGICALLY INACTIVATED DURING FEAR EXTINCTION TO DETERMINE THEIR CAUSAL ROLE IN EXTINCTION. THE INVOLVEMENT OF D1 RECEPTOR SIGNALING WAS INVESTIGATED WITH INTRA-DMS OR -DLS INFUSIONS OF THE D1 ANTAGONIST SCH23390 OR THE D1 AGONIST SKF38393. RESULTS SUGGEST THAT NEITHER DS SUBREGION CONTRIBUTES APPRECIATIVELY TO FEAR EXTINCTION, BUT AUGMENTING D1 SIGNALING IN THE DLS DURING FEAR EXTINCTION REDUCES RENEWAL. WE HYPOTHESIZE THAT INCREASING DLS D1 SIGNALING DURING FEAR EXTINCTION IMPAIRS HIPPOCAMPAL PROCESSING OF THE EXTINCTION CONTEXT, THEREBY FREEING EXTINCTION MEMORY FROM CONTEXTUAL MODULATION AND REDUCING RENEWAL. THE CONCEPT OF DUAL MEMORY SYSTEMS INVOLVING COMPETING CONTRIBUTIONS OF THE DS AND HIPPOCAMPUS SUPPORTS THIS HYPOTHESIS. THESE DATA SUGGEST THAT DS DA IS A NOVEL TARGET FOR THE REDUCTION OF FEAR RELAPSE AFTER EXTINCTION.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

SII. TONIC EXCITATORY SIGNALING IN THE BED NUCLEUS OF THE STRIA TERMINALIS

SARA CONLEY*, SARAH SIZER, MADIGAN BEDARD, KATHLEEN GRANT, ZOE MCELLIGOTT

WHILE MUCH WORK HAS BEEN DONE ON VARIOUS ASPECTS OF THE GLUTAMATERGIC SYSTEM AND THE PERTURBATIONS INDUCED BY STRESS AND DRUG EXPOSURE, ONE AREA THAT REMAINS UNEXPLORED IS THE ROLE OF DELTA GLUTAMATE RECEPTORS (GLUD1 AND GLUD2). RATHER THAN FUNCTION AS CANONICAL LIGAND-GATED IONOTROPIC RECEPTORS, THE GLUD FAMILY IS KNOWN TO ACT AS EFFECTORS FOR GQ-COUPLED RECEPTORS TO MEDIATE SLOW EXCITATORY TRANSMISSION AS WELL AS INDUCTION OF LONG-TERM DEPRESSION (LTD) THROUGH THE INTERNALIZATION OF CALCIUM-PERMEABLE AMPARS (CP-AMPARS). RECENTLY, GLUD1 HAS ALSO BEEN SHOWN TO BE CONSTITUTIVELY ACTIVE IN THE DORSAL RAPHE, PROVIDING A TONIC EXCITATORY CURRENT THAT IS BLOCKED BY 1-NAPHTHYLACETYL SPERMINE TRIHYDROCHLORIDE (NASPM). IN ADDITION, SEVERAL GENOME-WIDE ASSOCIATION STUDIES HAVE LINKED GLUD1 TO ALCOHOL USE DISORDER, DEPRESSION, AND SCHIZOPHRENIA. THE BED NUCLEUS OF THE STRIA TERMINALIS (BNST) IS A FOREBRAIN NUCLEUS RECIPROCALLY CONNECTED TO MANY IMPORTANT STRESS AND REWARD-RELATED STRUCTURES, POSITIONING IT AS A CRITICAL NEXUS THROUGH WHICH THE NEGATIVE AFFECTIVE SYMPTOMS COMMON TO MANY PSYCHIATRIC- AND SUBSTANCE USE-DISORDERS ARE MEDIATED. STUDIES HAVE SHOWN ALTERATIONS IN BNST PLASTICITY AND FUNCTION FOLLOWING STRESS AND DRUG AND ALCOHOL EXPOSURE. WE REPORT THAT THE ANTEROLATERAL (AL) BNST EXPRESSES A NASPM-SENSITIVE, GLUD1-MEDIATED TONIC EXCITATORY CONDUCTANCE WHICH INFLUENCES CELL EXCITABILITY. FURTHER, THIS IS CONSERVED ACROSS MICE AND RHESUS MACAQUES. LASTLY, WE SHOW PRELIMINARY EVIDENCE SUGGESTING THAT ACUTE WITHDRAWAL FROM CHRONIC INTERMITTENT ETHANOL VAPOR (CIE) DECREASES BOTH CP-AMPAR SYNAPTIC CURRENT AND ATTENUATES THE GLUD1 TONIC CURRENT, SUGGESTING THAT ALCOHOL EXPOSURE CAUSES A LOSS OF EXCITABILITY IN ALBNST NEURONS THROUGH MULTIPLE CONVERGING MECHANISMS.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

SI2. GM-1020: AN ORAL NMDA ANTAGONIST DEMONSTRATES TARGET ENGAGEMENT AT DOSES THAT DO NOT CAUSE DISSOCIATION, ATAXIA OR SEDATION IN A PHASE I SAD STUDY

JONATHAN SPORN, EDWARD CHRISTIAN, DINO DVORAK, ZOË HUGHES, GABRIEL JACOBS, LASZLO KISS*, ANDREW KRUEGEL, SOMA MAKAI-BÖLÖNI, SHANE RAINES, DANIEL UMBRICHT, JASON WINTERS, GERARD MAREK

THE RAPID ANTIDEPRESSANT EFFICACY OF THE NMDAR ANTAGONIST KETAMINE SPARKED EFFORTS TO IDENTIFY MOLECULES THAT ACHIEVE RAPID AND ROBUST EFFICACY BUT WITH REDUCED DISSOCIATION AND SEDATION. PRECLINICAL DATA SHOW THAT GM-1020, AN ORALLY ACTIVE NMDAR ANTAGONIST, HAS ROBUST AND DURABLE ANTIDEPRESSANT EFFECTS IN RODENTS AT DOSES THAT DO NOT AFFECT MOTOR ACTIVITY.
IN A STUDY IN HEALTHY VOLUNTEERS, SINGLE ORAL DOSES OF GM-1020 (20-360MG) WERE GENERALLY SAFE AND WELL-TOLERATED. DRUG EXPOSURE WAS DOSE PROPORTIONAL, SHOWED LOW VARIABILITY AND WAS CONSISTENT WITH %F > 60. TEAES WERE DOSE-DEPENDENT BUT NO SAES OR SEVERE TEAES WERE OBSERVED.
PHARMACODYNAMIC MEASUREMENTS INCLUDED ELECTROENCEPHALOGRAPHY (EEG) AND NEUROCART® TO ASSESS SEDATION, COGNITION AND ATAXIA. SUBJECTIVE EFFECTS WERE MEASURED USING QUESTIONNAIRES INCLUDING THE MEQ-30, 5D-ASC, AND CADSS, WHICH WAS SPECIFICALLY USED TO ASSESS DISSOCIATION.
GM-1020 PRODUCED DOSE-DEPENDENT EFFECTS ON EEG CONSISTENT WITH NMDAR ANTAGONISM; A REDUCTION IN ALPHA (8-13HZ) EEG POWER AT DOSES ≥60MG AND AN INCREASE IN GAMMA (30-90HZ) POWER OBSERVED AT DOSES ≥100MG INDICATED TARGET ENGAGEMENT.
GM-1020 WAS ORALLY BIOAVAILABLE AND PRODUCED SIGNIFICANT QUANTITATIVE AND SUBJECTIVE PD EFFECTS WITHOUT CAUSING DISSOCIATION, SEDATION OR ATAXIA AT EXPOSURES EXPECTED TO HAVE ANTIDEPRESSANT EFFECTS. THIS DISTINGUISHES GM-1020 FROM EXISTING KETAMINE-BASED THERAPIES. CONSISTENT WITH ITS PRECLINICAL PROFILE, GM-1020 PRODUCED SIGNIFICANT CHANGES IN LOW AND HIGH FREQUENCY EEG POWER AT DOSES BELOW THOSE ASSOCIATED WITH ATAXIA OR SEDATION. IN RODENTS, EXPOSURES ~2-FOLD BELOW THOSE ACHIEVED AT THE 140MG DOSE OF GM-1020 IN HUMANS RESULTED IN ROBUST AND DURABLE EFFICACY IN THE CHRONIC MILD STRESS PARADIGM SUGGESTIVE OF A GREATER THERAPEUTIC INDEX THAN KETAMINE. COLLECTIVELY, THESE DATA SUPPORT THE POTENTIAL OF GM-1020 AS A NOVEL, DIFFERENTIATED TREATMENT FOR DEPRESSION, WHICH MAY BE MORE ACCESSIBLE TO PATIENTS THAN EXISTING RAPID ACTING ANTIDEPRESSANTS.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

SI3. DORSAL HIPPOCAMPUS UNDERPINS DISSOCIABLE PATTERNS OF DEFENSIVE BEHAVIOR IN MALE AND FEMALE RATS

MATTHEW ALWOOD*, JUSTIN MOSCARELLO

COMPULSIVE AVOIDANCE BEHAVIOR IS A HALLMARK SYMPTOM OF ANXIETY DISORDERS, INCLUDING SPECIFIC PHOBIA AND PTSD. TO MODEL AVOIDANCE BEHAVIOR IN RODENTS, TWO-WAY SHUTTLE BOX AVOIDANCE TASKS ARE USED. UNSIGNALED (SIDMAN) ACTIVE AVOIDANCE (USAA) IS A COMPLEX ASSOCIATIVE CONDITIONING PARADIGM IN WHICH SUBJECTS ACQUIRE ESCAPE AND AVOIDANCE RESPONSES TO EARN AND PROLONG, RESPECTIVELY, PERIODS OF SAFETY FROM A SHOCK US DELIVERED AT REGULAR INTERVALS. UNLIKE OTHER ACTIVE AVOIDANCE TASKS, RESPONSES IN USAA ARE NOT TRIGGERED BY A CONDITIONED CUE, SUGGESTING THE HYPOTHESIS THAT THIS 'FREE OPERANT' FORM OF DEFENSIVE BEHAVIOR MAY INDEED BE UNDER THE CONTROL OF HIPPOCAMPALLY MEDIATED CONTEXTUAL PROCESSES. TO TEST THIS IDEA, WE EXPRESSED THE EXCITATORY HM3DQ DREADD IN DLX + INHIBITORY INTERNEURONS IN THE DORSAL HIPPOCAMPUS (DHPC) OF MALE AND FEMALE RATS WITH THE GOAL OF BROAD DHPC INHIBITION. DREADD-EXPRESSING INTERNEURONS WERE THEN ACTIVATED WITH SYSTEMIC CNO ON THE SECOND AND EIGHTH DAY OF TRAINING TO EXPLORE THE ROLE OF DHPC DURING ACQUISITION AND EXPRESSION OF USAA BEHAVIOR, RESPECTIVELY. DHPC INHIBITION WAS FOUND TO FACILITATE THE ACQUISITION OF AVOIDANCE IN FEMALE, BUT NOT MALE RATS. IN CONTRAST, DHPC INACTIVATION IN MALE RATS PRODUCED A PERMANENT INCREASE IN ESCAPE LATENCY, THOUGH THE OVERALL NUMBER OF ESCAPES WAS UNCHANGED. THESE DATA SUGGEST SEX-SPECIFIC ROLES FOR THE HIPPOCAMPUS IN BOTH REACTIVE AND PROACTIVE DEFENSIVE BEHAVIORS. IN A FOLLOW-UP EXPERIMENT, WE QUANTIFIED CFOS EXPRESSION FOLLOWING DHPC INACTIVATION DURING USAA ACQUISITION, IN ORDER TO CONFIRM THE EFFECT OF DREADD ACTIVATION OF INTERNEURONS ON NEURAL ACTIVITY IN DHPC ITSELF, AS WELL AS TO EXPLORE THE DOWNSTREAM EFFECTS IN THE BROADER SYSTEM OF AVOIDANCE-RELEVANT BRAIN REGIONS (I.E. MEDIAL FRONTAL CORTEX, MIDLINE THALAMIC NUCLEI, AMYGDALA, NUCLEUS ACCUMBENS).

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

SI4. ELDERLY A9/10 NICOTINIC ACETYLCHOLINE RECEPTOR KNOCKOUT MICE DEMONSTRATE CONSERVED GAZE STABILITY

TOBIAS NIEBUR*, KATHLEEN CULLEN

THE VESTIBULAR SYSTEM PLAYS A CRUCIAL ROLE IN ENSURING GAZE AND POSTURAL STABILITY IN DAILY LIFE. THE SIGNALS TRANSMITTED FROM THE VESTIBULAR SENSORY ORGANS TO THE BRAIN HAVE BEEN WELL CHARACTERIZED VIA NEUROPHYSIOLOGICAL RECORDING EXPERIMENTS FOCUSED ON SINGLE AFFERENTS WITHIN THE VIII NERVE. HOWEVER, THE VIII NERVE ALSO COMPRISES EFFERENT FIBERS, OF WHICH OUR UNDERSTANDING REMAINS LIMITED IN MAMMALS. ONE PROPOSAL IS THAT THE MAMMALIAN EFFERENT VESTIBULAR SYSTEM PLAYS A ROLE IN THE LONG-TERM CALIBRATION OF CENTRAL VESTIBULAR PATHWAYS, SUCH AS MAINTENANCE DURING AGEING. TO TEST THIS POSSIBILITY, WE STUDIED VESTIBULAR FUNCTION IN ELDERLY MICE (17-19 MONTHS) LACKING THE FUNCTIONAL A9 AND A10 SUBUNITS OF THE NICOTINIC ACETYLCHOLINE RECEPTOR (NACHR) GENE FAMILY AND COMPARED THEIR PERFORMANCE TO CONTROL MICE (18-20 MONTHS). PRIOR IN-VITRO STUDIES HAVE SHOWN THAT THESE NACHR RECEPTOR SUBUNITS MEDIATE EFFERENT ACTIVATION OF THE VESTIBULAR PERIPHERY AND ARE ALSO LARGELY ISOLATED TO THE INNER EAR. WE ASSESSED VESTIBULAR FUNCTION THROUGH QUANTIFICATION OF THE VESTIBULAR-OCULAR REFLEX (VOR), AND QUANTIFICATION OF SELF-PERCEPTION DURING CHALLENGING SELF-MOTION TASKS. THE VOR WAS TESTED BY PLACING HEAD-FIXED MICE WITHIN A BODYTUBE ON A MOTION PLATFORM. THE DEGREE OF GAZE STABILITY PROVIDED BY THE CANAL-DRIVEN ANGULAR VOR WAS MEASURED VIA VIDEO RECORDING EYE MOVEMENTS DURING SINUSOIDAL ROTATION (0.2-2 HZ, 16 DEG/S), IN BOTH LIGHT AND DARK CONDITIONS. THE VISUAL SURROUND WAS THEN SIMILARLY ROTATED SEPARATELY TO ASSESS CORRESPONDING OPTOKINETIC RESPONSES. FINALLY, TO QUANTIFY BALANCE, WE PERFORMED SWIM TESTING. THE SWIM TEST WAS CONDUCTED WITH MICE BEING LOWERED INTO A POOL OF WATER AND ALLOWED TO SWIM FOR 1 MINUTE, WHILE HEAD DYNAMICS WERE RECORDED WITH A HEAD-MOUNTED INERTIAL MEASUREMENT UNIT. IN LINE WITH PREVIOUS WORK ON YOUNGER DOUBLE KNOCKOUT MICE, PRELIMINARY RESULTS INDICATE THAT GAZE STABILITY IS PRESERVED IN ELDERLY KNOCKOUT MICE.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

SI5. HIGH FREQUENCY SIGNALS IN FRONTAL CORTEX AT LOSS OF CONSCIOUSNESS

M. MACIVER*

BRAIN OSCILLATIONS HAVE RARELY BEEN STUDIED AT FREQUENCIES BEYOND 200 HZ, AND IT REMAINS UNKNOWN WHAT THE HIGHEST FREQUENCY OF BRAIN BIOELECTRIC ACTIVITY IS. WE USED THE VOLATILE ANESTHETIC, ISOFLURANE, TO DEPRESS ACTIVITY AT BEHAVIORAL ENDPOINTS OF LOSS OF RIGHTING REFLEX (LORR) AND LOSS TAIL CLAMP RESPONSES (LOTC). THESE ENDPOINTS PROVIDE SURROGATE MEASURES OF LOSS OF CONSCIOUSNESS (LORR) AND SURGICAL ANESTHESIA (LOTC) IN RATS. WE RECORDED SIGNALS FROM DC TO 20 KHZ; EXTENDING ANALYSIS OF OSCILLATORY CORTICAL ACTIVITY WELL BEYOND TRADITIONAL RANGES. FOLLOWING IRB APPROVAL, LOCAL FIELD POTENTIALS WERE RECORDED FROM LAYER 2/3 OF FRONTAL CORTEX IN RATS USING CHRONICALLY IMPLANTED ELECTRODES. RATS WERE PLACED IN AN AIR-TIGHT CHAMBER WITH A CONTROLLED ATMOSPHERE OF ROOM AIR THAT WAS SLOWLY REPLACED WITH INCREASING CONCENTRATIONS OF ISOFLURANE IN OXYGEN, DELIVERED FROM A CALIBRATED VAPORIZER. BODY TEMPERATURE WAS MAINTAINED USING A HEAT LAMP. ANIMAL BEHAVIOR WAS CAREFULLY MONITORED TO DETERMINE LORR AND LOTC RESPONSES. RATS RECOVERED FOLLOWING EACH EXPERIMENT AFTER REPLACING ISOFLURANE WITH ROOM AIR.

ISOFLURANE PRODUCED A CHARACTERISTIC PROFILE OF EFFECTS, CONSISTENT WITH PREVIOUS REPORTS. AT LORR HIGH AMPLITUDE SLOW WAVE ACTIVITY WAS EVIDENT THAT TRANSITIONED TO A BURST SUPPRESSION PATTERN AT LOTC. SPECTRAL ANALYSIS REVEALED THAT INCREASED SLOW WAVE ACTIVITY WAS ACCOMPANIED BY DECREASED HIGHER FREQUENCIES IN THE GAMMA AND HIGH-GAMMA BANDS, AND EXTENDING BEYOND 1.0 KHZ AT LORR. THIS HIGH FREQUENCY ACTIVITY WAS NOT DUE TO MULTIUNIT ACTION POTENTIAL DISCHARGE, NOR TO HARMONICS FROM LOWER FREQUENCIES.

ISOFLURANE DEPRESSED HIGH FREQUENCY CORTICAL ACTIVITY WELL BEYOND THE TRADITIONAL EEG FREQUENCY RANGE OF 200 HZ. FUTURE RESEARCH SHOULD INVESTIGATE BRAIN PROCESSES THAT ARE ASSOCIATED WITH THIS VERY HIGH FREQUENCY BRAIN ACTIVITY, BETWEEN 500 TO > 1000 HZ.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S16. PRENATAL CANNABINOID EXPOSURE: EMERGING EVIDENCE OF MEDIAL PREFRONTAL CORTEX ABNORMALITIES

ADRIAN COURVILLE*, MILES WILEY, EMMA REDMON, TIA DANIELS, KAWSAR CHOWDHURY, VISHNU SUPPIRAMANIAM, MIRANDA REED

CANNABIS IS CURRENTLY ONE OF THE MOST OFTEN USED ILLICIT DRUGS BY PREGNANT WOMEN, WITH A 62% INCREASE IN USAGE FROM 2002 TO 2014. ADDITIONALLY, WHILE THERE IS A GROWING BELIEF THAT USING CANNABIS WHILE PREGNANT IS SAFE, THE PRECLINICAL RESEARCH EXAMINING THESE UNDERLYING NEUROCOGNITIVE CHANGES IS LIMITED. THIS IS ESPECIALLY CONCERNING BECAUSE CLINICAL STUDIES HAVE SHOWN THAT CANNABIS EXPOSURE THROUGHOUT DEVELOPMENT CAUSES LONG-LASTING CHANGES IN NEURO-FUNCTIONING AND COGNITION. AN AREA OF CONCERN FOR THESE CHANGES LIES IN THE MEDIAL PREFRONTAL CORTEX (MPFC) DUE TO ITS ABILITY TO FACILITATE DECISION-MAKING AND MEMORY CONNECTIONS. WE HYPOTHESIZE THAT PRENATAL CANNABINOID EXPOSURE (PCE) DECREASES GLUTAMATERGIC SIGNALING IN THE MPFC, LEADING TO ALTERATIONS IN THE HIPPOCAMPUS MPFC PATHWAY AND ULTIMATELY TO DEFICITS IN MPFC-MEDIATED BEHAVIOR. TO ADDRESS THIS, WE EXAMINED OFFSPRING EXPOSED PRENATALLY TO THC USING THE SPONTANEOUS ALTERNATION Y-MAZE TASK AND TRACE FEAR CONDITIONING WITH EXTINCTION. WE ALSO ANALYZED GLUTAMATE RECEPTOR LEVELS AND SIGNALING IN THE MPFC USING IMMUNOBLOTTING. RESULTS FROM THIS PROJECT WILL FURTHER OUR UNDERSTANDING OF PCE MECHANISMS THAT RESULT IN NEUROCOGNITIVE ALTERATIONS, SPECIFICALLY AS THEY RELATE TO THE MPFC, AND WILL ADD TO THE GROWING LITERATURE ON SOME OF THE OVERALL DANGERS THAT SHOULD BE CONSIDERED WITH CANNABIS USE DURING PREGNANCY.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

SI7. SPECTRAL POWER AND PHASE-AMPLITUDE COUPLING IN HUMAN INTRACRANIAL RECORDINGS DURING MULTI-ATTRIBUTE DECISION MAKING

SAMPSON SAMPSON, VICTORIA LIU, CHAD OLIVER, VICTORIA SUBRITZKY-KATZ, JESSICA KUO, NANDITA BALAJI, ERIC EMERIC, WITOLD LIPSKI, SOPHIA MOREIRA GONZALEZ, ARIANNA DAMIANI, JORGE GONZÁLEZ-MARTÍNEZ, SRIDEVI SARMA, VEIT STUPHORN, ERNST NIEBUR*

REAL-WORLD DECISIONS TYPICALLY REQUIRE THE CONSIDERATION OF MULTIPLE OPTIONS, EACH WITH MULTIPLE ATTRIBUTES. TO STUDY SUCH MULTI-ATTRIBUTE DECISIONS, WE IMPLEMENTED A TASK IN WHICH PARTICIPANTS CHOSE BETWEEN TWO OPTIONS. ON TRIALS IN THE 'WIN DOMAIN', BOTH OPTIONS OFFER CASH REWARDS WITH DIFFERENT AMOUNTS AND PROBABILITIES. FOR TRIALS IN THE 'LOSS DOMAIN' BOTH OPTIONS RESULT IN LOSING MONEY, AGAIN WITH SPECIFIED AMOUNTS AND PROBABILITIES. ATTRIBUTES ARE REPRESENTED BY DISTINCT SYMBOLS ON AN ELECTRONIC TABLET. WHEN TAPPED, THESE SYMBOLS ARE TEMPORARILY REMOVED TO REVEAL THE CORRESPONDING ATTRIBUTE VALUE. PARTICIPANTS CAN VIEW ATTRIBUTES ONE AT A TIME AND THEN INDICATE THEIR DECISION BY TAPPING 'SELECT' FOR THEIR CHOSEN OPTION, ALLOWING US TO PRECISELY OBSERVE WHEN EACH PIECE OF DECISION-RELEVANT INFORMATION IS BEING COLLECTED. TO STUDY THE NEURAL CORRELATES OF THIS PROCESS, WE COLLECTED STEREOELECTROENCEPHALOGRAM (SEEG) RECORDINGS FROM PATIENTS UNDERGOING TREATMENT FOR EPILEPSY WHILE THEY PERFORMED THE TASK. SPECTRAL POWER ACROSS FREQUENCY AND TIME ADJACENT TO KEY TRIAL EVENTS WAS TESTED WITH A NONPARAMETRIC CLUSTER-BASED TEST FOR SIGNIFICANT DIFFERENCES DEPENDING ON TASK CONDITION, E.G. WIN VS. LOSS, LIKELY VS. UNLIKELY OUTCOME ETC. SPECTRAL POWER WAS ALSO TESTED FOR CORRELATION WITH TASK-DEFINED VARIABLES, SUCH AS EXPECTED OR SUBJECTIVE VALUE, INSPECTED AND CHOSEN OPTIONS, WIN OR LOSS AMOUNT ETC. SIGNIFICANTLY TASK-RELATED ACTIVITY WAS IDENTIFIED IN A RANGE OF BRAIN REGIONS, INCLUDING ORBITOFRONTAL CORTEX, DORSOLATERAL AND MESIAL FRONTAL CORTEX, INSULA, AMYGDALA, AND HIPPOCAMPUS. ADDITIONALLY, SPECIFIC FREQUENCY BANDS THAT SHOWED SIGNIFICANT TASK CONDITION-DEPENDENCE AT THE SAME KEY TRIAL EVENT TIMES WERE ANALYZED FOR PHASE-AMPLITUDE COUPLING. IN MANY CASES WHERE HIGH (≥40 HZ) AND LOW (≤20 HZ) FREQUENCIES BOTH SHOWED TASK-RELATED DIFFERENCES, THE AMPLITUDE OF THE HIGHER FREQUENCY WAS SIGNIFICANTLY MODULATED BY THE PHASE OF THE LOWER FREQUENCY.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

SI8. TARGETING SPHINGOSINE-1-PHOSPHATE RECEPTOR 1 ATTENUATES THE DEVELOPMENT OF COGNITIVE DYSFUNCTIONS AFTER PACLITAXEL TREATMENT

SILVIA SQUILLACE*, KAREN GALEN, SARAH SPIEGEL, SUSAN FARR, DANIELA SALVEMINI

PERSISTENT COGNITIVE IMPAIRMENT HAS BEEN REPORTED IN MORE THAN 50% OF PATIENTS UNDERGOING CHEMOTHERAPY TREATMENT. NO FDA APPROVED DRUGS ARE AVAILABLE TO ADDRESS THIS MAJOR NEUROTOXICITY, AND UNDERLYING MECHANISMS ARE STILL LARGELY UNKNOWN. PACLITAXEL, STANDARD-OF-CARE FIRST-LINE CHEMOTHERAPY FOR EPITHELIAL OVARIAN CANCER AND TRIPLE NEGATIVE BREAST CANCER, HAS BEEN REPORTED TO CAUSE LONG LASTING MEMORY DEFICITS IN PATIENTS. WE DEVELOPED A MOUSE MODEL OF PACLITAXEL-INDUCED COGNITIVE IMPAIRMENT WHOSE CUMULATIVE DOSE IS COMPARABLE TO THE TOTAL DOSE PER CYCLE USED IN BREAST CANCER PATIENTS. THROUGH SPHINGOLIPIDOMIC ANALYSIS WE SHOWED THAT PACLITAXEL TREATMENT INCREASED THE EXPRESSION OF THE POTENT BIOACTIVE LIPID SPHINGOSINE-1-PHOSPHATE (SIP) AND ITS PRECURSORS IN MOUSE PREFRONTAL CORTEX AND HIPPOCAMPUS, LEADING TO COGNITIVE IMPAIRMENT. CO-TREATMENT WITH OZANIMOD (RPC1063/ZEPOSIA®), AN FDA APPROVED SIP RECEPTOR 1 FUNCTIONAL ANTAGONIST FOR THE TREATMENT OF MULTIPLE SCLEROSIS, PREVENTED THE DEVELOPMENT OF PACLITAXEL-INDUCED COGNITIVE DYSFUNCTION IN DIFFERENT HIPPOCAMPAL TESTS (T-MAZE, NOVEL OBJECT PLACE RECOGNITION TEST, NOPRT), WITHOUT ADVERSELY AFFECTING LOCOMOTOR ACTIVITY OR INDUCING ANXIETY-LIKE BEHAVIORS. MOREOVER, USING THE SYNGENEIC BREAST CANCER MODEL EMPLOYING EO771 MOUSE MAMMARY CARCINOMA CELLS IN C57BL/6J MICE, WE SHOWED THAT OZANIMOD DOES NOT INTERFERE WITH THE ANTICANCER ACTIVITY OF PACLITAXEL, AND SIGNIFICANTLY REDUCE TUMOR SIZE WHEN ADMINISTERED ALONE. THESE FINDINGS ESTABLISH SIPR1 AS A THERAPEUTIC TARGET IN PACLITAXEL-INDUCED COGNITIVE IMPAIRMENT AND COULD EXPEDITE PROOF-OF-CONCEPT CLINICAL STUDIES WITH OZANIMOD AS ADJUNCT TO CHEMOTHERAPY. THIS RESEARCH WAS SUPPORTED BY RO1CA261979 (2022-2027, DANIELA SALVEMINI, SUSAN FARR) AND SAINT LOUIS UNIVERSITY STARTUP FUNDS (DANIELA SALVEMINI).

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

SI9. COMPARING MECHANISTICALLY DISTINCT INTERVENTIONS THAT ALTER INTER-TEMPORAL CHOICE BEHAVIOR USING CORTICAL-STRIATAL LOCAL FIELD POTENTIALS

LUCAS DWIEL, MORIAH MCGUIER, MATTHEW COMPANY, WILDER DOUCETTE*

MALADAPTIVE DECISION MAKING (E.G., TOO IMPULSIVE) IS LINKED TO POOR OUTCOMES IN MANY PSYCHIATRIC CONDITIONS AND IS A SIGNIFICANT RISK FACTOR FOR SUICIDE, VIOLENCE, AND RISKY SUBSTANCE USE. ANIMAL MODELS USED TO STUDY THIS IMPORTANT TRANS-DIAGNOSTIC DOMAIN OF FUNCTION, ITS NEURAL UNDERPINNINGS, AND EVALUATE POTENTIAL INTERVENTIONS RELY ON BEHAVIORAL READOUTS THAT MAY NOT ALWAYS CAPTURE THE OVERARCHING DOMAIN OF INTEREST OR PERTINENT SUBDOMAINS. WE SIMULTANEOUSLY RECORDED LOCAL FIELD POTENTIALS (LFPS) FROM CORTICAL STRIATAL REGIONS AND USED MACHINE LEARNING TO DETERMINE IF CHANGES IN LFPS INDUCED BY AN INTERVENTION WERE PREDICTIVE OF INTERVENTION OUTCOMES, GENERALIZED ACROSS INTERVENTION TYPES (IDENTIFYING MECHANISTIC SIMILARITIES) OR DISTINGUISHED BETWEEN INTERVENTIONS THAT CAUSED THE SAME OUTCOME (IDENTIFYING MECHANISTIC DIFFERENCES). SPRAGUE-DAWLEY RATS (N=89, 44 MALE, 45 FEMALE) WERE TRAINED IN A DELAY DISCOUNTING TASK (DDT) USING EITHER AN ASCENDING (N=64) OR DESCENDING (N=25) DELAY ORDER. RATS WERE IMPLANTED BILATERALLY WITH ELECTRODES TARGETING THE NUCLEUS ACCUMBENS (NAC) SHELL AND CORE AS WELL AS THE INFRALIMBIC (IL) AND ORBITOFRONTAL CORTEX (OFC). ONCE DDT PERFORMANCE WAS STABLE, INTERVENTIONS WERE TESTED (BRAIN STIMULATION [7 SESSIONS] TARGETED TO THE IL, NAC CORE OR OFC; PHARMACOLOGICAL MANIPULATIONS [3 SESSIONS] WITH 1 OR 3 MG/KG OF METHYLPHENIDATE). AS REPORTED BY OTHERS, WE FOUND THAT METHYLPHENIDATE INCREASED RAT CHOICES FOR THE DELAYED LEVER WHEN DELAYS ASCENDED IN THE SESSION AND REDUCED CHOICES FOR THE DELAY LEVER WHEN THE DELAYS DESCENDED THROUGH THE SESSION. WE FOUND THAT NAC (AUROC = 0.92, $P < 0.05$); IL (AUROC = 0.97, $P < 0.05$), AND METHYLPHENIDATE (AUROC = 0.94, $P < 0.05$) OUTCOMES COULD BE PREDICTED BASED ON LFP FEATURE CHANGES. THESE DATA SUGGEST THAT NEURAL OSCILLATIONS HOLD POTENTIAL AS BIOMARKERS TO GUIDE THE DEVELOPMENT AND IMPLEMENTATION OF THERAPEUTIC APPROACHES TO CHANGE MALADAPTIVE DECISION MAKING.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S20. MANIPULATING HDAC3 FUNCTION IN THE AUDITORY CORTEX DURING MEMORY FORMATION RESULTS IN DISTINCT CORTICAL TRANSCRIPTIONAL CHANGES

GUAN-EN GRAHAM*, LIESL CO, ABHIRAM KANDUKURI, MADELYN SUMNER, DEVIN GRENARD, GABRIELLE POLIAK, MICHAEL CHIMENTI, KEVIN KNUDTSON, KASIA BIESZCZAD

EXPERIENCE-DEPENDENT MECHANISMS UNDERLYING NEUROPHYSIOLOGICAL PLASTICITY ARE REQUIRED FOR THE FORMATION OF LONG-TERM MEMORIES (LTMS). EPIGENETIC MECHANISMS ARE POWERFUL EXPERIENCE-DEPENDENT REGULATORS OF GENE EXPRESSION NEEDED FOR THE PROCESSING OF LTMS. ONE SUCH EPIGENETIC REGULATOR, HISTONE DEACETYLASE 3 (HDAC3) WORKS WITH TRANSCRIPTIONAL MACHINERY TO INFLUENCE ACTIVITY-DEPENDENT DE NOVO DNA TRANSCRIPTION. FIRST, WE BUILT UPON PREVIOUS STUDIES DETAILING INCREASED AUDITORY CORTICAL PLASTICITY AND SOUND-SPECIFIC BEHAVIOR WITH PHARMACOLOGICAL HDAC3 INHIBITION (HDAC3I) BY PROVIDING INSIGHT TO MOLECULAR MECHANISMS UNDERLYING THESE CHANGES. OUR RESULTS REVEAL THE AUDITORY CORTICAL EFFECTS OF SYSTEMICALLY INHIBITING HDAC3 IN ADULT MALE RATS DURING EARLY ACQUISITION OF AN AUDITORY ASSOCIATIVE TASK (SOUND-REWARD LEARNING) AT THE TRANSCRIPTOMIC LEVEL. ON A GENOME-WIDE SCALE, WE FOUND THAT HDAC3I PRODUCED LARGE CHANGES IN LEARNING-DEPENDENT TRANSCRIPTION BY FURTHER UP- OR DOWN-REGULATING UNIQUE SUBSETS OF INDUCED GENES (RELATIVE TO VEHICLE AND SOUND-NAÏVE GROUPS). QRT-PCR PERFORMED ON A SEPARATE COHORT OF ANIMALS THAT PERFORMED THE SAME BEHAVIORAL TASK VERIFIED EFFECTS SEEN IN IDENTIFIED GENES OF INTEREST (GOIS). WHILE THIS WORK ACHIEVED BULK ANALYSIS OF THE AUDITORY CORTICAL TRANSCRIPTOME DURING LEARNING, FURTHER INVESTIGATION WAS NEEDED TO RELATE THESE PROFILES TO CELLULAR IDENTITY. TO ACHIEVE ANATOMICAL SPECIFICITY OF GENE EXPRESSION EVENTS, WE VISUALIZED GOI MRNA TRANSCRIPTS, EGR1, PER2, AND CHRNA7, FROM A THIRD COHORT OF ANIMALS THAT EXPERIENCED THE SAME SOUND-REWARD LEARNING PARADIGM. TO CHARACTERIZE SUBPOPULATIONS OF CELLS, GOI TRANSCRIPTS WERE COLOCALIZED WITH CAMKIIA AND RORB TRANSCRIPTS TO IDENTIFY TRANSCRIPTIONAL CHANGES WITHIN EXCITATORY PYRAMIDAL CELLS AND DIFFERENT CORTICAL LAYERS. OUR FINDINGS CHARACTERIZE HOW HDAC3 REGULATES GENES WITHIN SUBPOPULATIONS OF CELLS TO BEGIN TO UNDERSTAND HOW CHANGES IN LOCAL CORTICAL MICROCIRCUITRY CAN SUPPORT HIGHLY PRECISE AND LASTING ASSOCIATIVE MEMORIES.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S21. MODULATION OF ROSTRAL TEGMENTAL EFFERENTS TO THE VENTRAL TEGMENTAL AREA INDUCES LONG-LASTING AVOIDANCE BEHAVIOR

JACOB WATSON*, MADDY LOPEZ DE LEON, EMMA CARLSON, PETER VENTO

IT IS WELL KNOWN THAT APPROACH BEHAVIOR AND REINFORCEMENT LEARNING ARE MEDIATED BY DOPAMINE (DA) SIGNALING ARISING FROM THE VENTRAL TEGMENTAL AREA (VTA); HOWEVER, FAR LESS IS KNOWN REGARDING HOW REDUCTIONS IN VTA DA ACTIVITY CONTRIBUTE TO AVOIDANCE AND BEHAVIORAL INHIBITION. THE ROSTROMEDIAL TEGMENTAL NUCLEUS (RMTG) ENCODES AVERSIVE STIMULI AND PROVIDES DENSE INHIBITORY PROJECTIONS TO DA NEURONS IN THE VTA, AND WE HAVE PREVIOUSLY FOUND THAT INACTIVATION OF THE RMTG > VTA PATHWAY IN RATS CAUSES PERSISTENT REWARD SEEKING UNDER PUNISHMENT. TO TEST WHETHER ACTIVATION OF THIS CIRCUIT IS SUFFICIENT TO SUPPRESS REWARD-SEEKING AND INDUCE AVOIDANCE, WE FIRST EMPLOYED A SINGLE LEVER REWARD-SEEKING TASK WHERE LEVER PRESSING (FR5) FOR FOOD REWARD WAS ACCOMPANIED BY BRIEF MILD FOOTSHOCK (0.5MA, 500MS), WHICH WE FOUND TO ROBUSTLY SUPPRESS FOOD SEEKING. TO MIMIC THE AVERSIVE EXPERIENCE OF FOOTSHOCK WITHOUT DELIVERING AN OVERTLY AVERSIVE STIMULUS, WE THEN ADMINISTERED HIGH FREQUENCY (50HZ) OPTOGENETIC STIMULATED THE RMTG > VTA PATHWAY EITHER FOR A DURATION EQUAL TO THE PREVIOUSLY TESTED FOOTSHOCK (500MS) OR CONSIDERABLY LONGER 30SEC OPTICAL STIMULATION. WHILE BRIEF 500MS RMTG > VTA STIMULATION WAS INEFFECTIVE AT REDUCING FOOD SEEKING, THE LONGER 30SEC STIMULATION ROBUSTLY SUPPRESSED LEVER PRESSING FOR FOOD. NOTABLY, IN SUBSEQUENT TESTING WHERE LIGHT DELIVERY OR FOOTSHOCK PUNISHMENT WAS REMOVED, RATS RAPIDLY RESUMED TYPICAL FOOD SEEKING WITHIN 1-2 SESSIONS. TO TEST FOR MORE SUBTLE ENDURING CONSEQUENCES OF OPTOGENETIC RMTG > VTA STIMULATION, WE NEXT TESTED A SEPARATE GROUP OF RATS IN A TWO-FLAVOR CHOICE PARADIGM IN WHICH TWO REWARD OPTIONS WERE AVAILABLE (VANILLA- OR CHOCOLATE-FLAVORED PELLETS). HERE, WE SHOW THAT PAIRING EITHER PATHWAY-SPECIFIC CHEMOGENETIC ACTIVATION OR TIMING- AND PATHWAY-SPECIFIC OPTOGENETIC STIMULATION OF THE RMTG > VTA PATHWAY WITH ONE OF THE TWO FLAVOR OPTIONS RESULTED IN A ROBUST SHIFT IN CHOICE FOR THE UNPAIRED FLAVOR. NOTABLY, RATS IN THE FLAVOR CHOICE PARADIGM EXHIBITED A STRONG AVOIDANCE OF THE STIMULATION-PAIRED FLAVOR THAT PERSISTED FOR WEEKS AFTER STIMULATION CEASED. TOGETHER, THESE DATA SUGGEST AN IMPORTANT ROLE FOR THE RMTG > VTA PATHWAY IN BOTH BEHAVIORAL INHIBITION AND CONDITIONED AVOIDANCE, WITH DIFFERING EFFECTS DEPENDING ON THE AVOIDANCE STRATEGY SUBJECTS EMPLOYED.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S22. WHO NEEDS FRIENDS? HYPOTHALAMIC-TO-VENTRAL TEGMENTAL AREA PROJECTIONS REGULATE MOTIVATION FOR FOOD BUT NOT SOCIAL REWARDS

JON CAVANAUGH*, MARCO LIERA, KYLE SMITH

THERE ARE NO PHARMACEUTICAL THERAPIES THAT SPECIFICALLY TARGET DEFICITS IN SOCIAL AND MOTIVATIONAL FUNCTIONING. TO THE EXTENT THAT MALADAPTIVE SOCIAL AND MOTIVATIONAL FUNCTIONING ARE CORE PHENOTYPES OF NEUROPSYCHIATRIC ILLNESS, IMPROVED KNOWLEDGE OF THE NEUROBIOLOGICAL PROCESSES THAT UNDERLY VARIATION IS VITAL TO ALLEVIATE THE BURDEN OF MENTAL ILLNESS AND SUBSTANCE USE. THIS PROJECT CHARACTERIZED THE FUNCTION OF NEURONAL PROJECTIONS FROM THE PARAVENTRICULAR NUCLEUS OF THE HYPOTHALAMUS (HT) TO THE PARABRACHIAL PIGMENTED NUCLEUS OF THE VENTRAL TEGMENTAL AREA (VTA) IN MOTIVATED BEHAVIORS UTILIZING CHEMOGENETIC MANIPULATION. TO THE EXTENT THAT HT PROMOTES PROSOCIAL BEHAVIORS AND CENTRAL OXYTOCIN INHIBITS FOOD-MOTIVATED BEHAVIOR VIA VTA, WE HYPOTHESIZED THAT THE HTVTA PATHWAY SITS AT THE INTERSECTION OF SOCIAL AND FOOD REWARD DECISIONS. 48F AND 48M WILD-TYPE RATS WERE TRAINED TO SELF-ADMINISTER GRAIN PELLETS AND SOCIAL INTERACTIONS WITH AGE- AND SEX-MATCHED PARTNER USING AN AUTOMATED OPERANT ASSAY. SUBJECTS THEN RECEIVED BILATERAL VIRAL DELIVERY OF ONE OF THREE DREADDS VIRUSES (CONTROL; INHIBITORY; EXCITATORY) INTO THE HT AND A CRE-DEPENDENT RETROGRADE VIRUS INTO THE VTA; MOTIVATED BEHAVIORS WERE MEASURED FOLLOWING IP ADMINISTRATION OF A DREADDS ACTUATOR OR PLACEBO. SELECTIVE EXCITATION OF HTVTA SIGNIFICANTLY ATTENUATED MOTIVATION FOR FOOD, AND EFFECTIVELY DIMINISHED THE INCENTIVE VALUE OF FOOD REWARDS; NEITHER SELECTIVE EXCITATION NOR INHIBITION IMPACTED SOCIAL MOTIVATION. HOWEVER, IN A CHOICE TASK WHERE BOTH REWARD TYPES WERE AVAILABLE, SELECTIVE EXCITATION OF HTVTA REDUCED THE FREQUENCY OF FOOD CHOICE IN FAVOR OF INCREASED SOCIAL REWARD CHOICE, REGARDLESS OF SOCIAL-PARTNER FAMILIARITY. THESE FINDINGS PROVIDE STRONG EVIDENCE FOR THE REGULATION OF FOOD MOTIVATION AND REWARD-RELATED DECISION-MAKING VIA THE HTVTA PATHWAY AND PROVIDE A SPRINGBOARD FOR THE GENERATION OF THERAPIES TO AMELIORATE DEFICITS IN SOCIAL AND MOTIVATIONAL FUNCTIONING ACROSS THE LIFESPAN.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S23. THE EFFECTS OF TRAUMATIC EXPERIENCES ON BRAIN AGING IN ADOLESCENTS: A PRELIMINARY NEUROIMAGING STUDY

SHRAVYA CHANAMOLU*, AHMAD ALMAAT, REEM TAMIMI, HILARY MARUSAK

EXPOSURE TO TRAUMATIC EVENTS DURING CHILDHOOD, SUCH AS VIOLENCE, INFLUENCES BRAIN AND BEHAVIORAL DEVELOPMENT, WHICH MAY INCREASE RISK OF NEUROPSYCHIATRIC DISORDERS. RESEARCH SHOWS THAT CHILDHOOD TRAUMA MAY ALTER THE PACE OF STRUCTURAL NEURODEVELOPMENT ACROSS ADOLESCENCE, A PERIOD OF DYNAMIC CHANGES IN NEURAL CIRCUITRY. THIS PRELIMINARY STUDY EXPLORES THE IMPACT OF CHILDHOOD TRAUMA EXPOSURE ON BRAINAGE — A NEUROIMAGING BIOMARKER OF BRAIN AGING — AND ITS DEVIATION FROM CHRONOLOGICAL AGE.

WE REPORT PRELIMINARY DATA FROM AN ONGOING NEUROIMAGING STUDY OF 12 ADOLESCENTS RECRUITED FROM AN URBAN AREA WITH HIGH RATES OF TRAUMA EXPOSURE (N=12; 75% MALE, M±SD AGE= 12.25±2.45 YEARS). ADOLESCENTS PROVIDED SELF-REPORTS ON NUMBER OF POTENTIALLY TRAUMATIC EVENTS EXPERIENCED. T1-WEIGHTED MAGNETIC RESONANCE IMAGES (MRI) DATA WAS ALSO ACQUIRED AND BRAINAGE WAS CALCULATED USING A MACHINE LEARNING ALGORITHM. WE EXPLORED ASSOCIATIONS BETWEEN NUMBER OF TRAUMAS AND BRAINAGE, AND THE DIFFERENCE BETWEEN BRAINAGE AND CHRONOLOGICAL AGE. THE YOUTH IN THIS SAMPLE REPORTED M±SD = 3.78±3.11 TRAUMATIC EVENTS, WITH 89% OF THEM REPORTING AT LEAST ONE TRAUMATIC EVENT. WE DID NOT OBSERVE A SIGNIFICANT ASSOCIATION BETWEEN TRAUMA EXPOSURE AND BRAINAGE, NOR THE DEVIATION OF BRAINAGE FROM CHRONOLOGICAL AGE (P'S > 0.05).

WE DID NOT FIND EVIDENCE THAT CHILDHOOD TRAUMA AFFECTS BRAINAGE NOR THE DIVERGENCE BETWEEN BRAINAGE AND CHRONOLOGICAL AGE IN THIS PRELIMINARY STUDY. HOWEVER, FUTURE ANALYSES IN LARGER STUDIES WILL SHED LIGHT ON WHETHER TRAUMA EXPOSURE EARLY IN LIFE MAY ACCELERATE, DELAY, OR CAUSE A DIVERGENCE IN STRUCTURAL NEURODEVELOPMENT.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S24. CORRELATION BETWEEN SUBCUTANEOUS ADIPOSE TISSUE OF THE HEAD AND BODY MASS INDEX IN CHILDREN AND YOUNG ADULTS AGED 8-19 YEARS: IMPLICATIONS FOR FUNCTIONAL NEUROIMAGING

STACEY GORNIAK*, HAO MENG, SABA YAZDEKHASTI, LUCA POLLONINI

HIGH BODY MASS INDEX (BMI) IS GENERALLY ASSUMED TO REPRESENT OVERALL AMOUNTS OF BODY ADIPOSE TISSUE (FAT). INCREASED ADIPOSE TISSUE AMOUNTS IN PERSONS WITH INCREASED BMI HAS BEEN CITED AS A BARRIER TO SOME NEUROIMAGING MODALITIES. SIGNIFICANT INCREASES IN THE AMOUNT OF ADIPOSE TISSUE BETWEEN THE DERMAL LAYER AND THE SKULL MAY RESULT IN HIGH ELECTRICAL IMPEDANCE AND INCREASED LIGHT DIFFUSION CAUSING A LOW SIGNAL TO NOISE RATIO DURING USE OF NEUROIMAGING TOOLS SUCH AS ELECTROENCEPHOLOGRAPHY (EEG), TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS), AND FUNCTIONAL NEAR INFRARED SPECTROSCOPY (FNIRS). INVESTIGATING HOW SUBCUTANEOUS ADIPOSE TISSUE IN THE HEAD REGION INCREASES WITH RESPECT TO TOTAL BODY FAT PERCENTAGE AND BMI IN SCHOOL-AGED CHILDREN AND ADOLESCENTS IS AN IMPORTANT STEP IN DETERMINING WHETHER MATHEMATICAL CORRECTIONS IN NEUROIMAGING MEASUREMENTS NEED TO BE IMPLEMENTED AS BMI INCREASES, AS REPORTED IN ADULTS AND OLDER ADULTS. WE HYPOTHESIZED THAT PERCENTAGE OF SUBCUTANEOUS ADIPOSE TISSUE IN THE HEAD REGION WOULD INCREASE WITH RESPECT TO BOTH TOTAL BODY FAT PERCENTAGE AND BMI. INDEED, A STATISTICALLY SIGNIFICANT INCREASE IN SUBCUTANEOUS HEAD FAT PERCENTAGE WAS ASSOCIATED WITH A POSITIVE LINEAR RELATIONSHIP WITH BMI AND A QUADRATIC RELATIONSHIP WITH TOTAL BODY FAT PERCENTAGE. THE DATA INVESTIGATED IN THIS STUDY STRONGLY INDICATE THAT PARTICIPANT AGE, SEX, AND ADIPOSITY MEASURES SHOULD ALL BE CONSIDERED IN MODEL CORRECTIONS DURING DATA SIGNAL PROCESSING AND NEUROIMAGING IN SCHOOL-AGED CHILDREN AND ADOLESCENTS. THE STRENGTH OF REGRESSION COEFFICIENTS IN THE GENERATED MODELS DIFFERED FROM WORK IN ADULTS AND OLDER ADULTS, INDICATING THAT AGE-SPECIFIC MODELS SHOULD BE UTILIZED.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S25. UNITARY STRIATOPALLIDAL CONNECTIONS IN THE MOUSE

JAMES JONES*, JACOB PEÑA, BRANDON GARCIA, CHARLES WILSON

DIRECT AND INDIRECT PATHWAY STRIATAL PROJECTION NEURONS (SPNS) ARBORIZE IN THE EXTERNAL GLOBUS PALLIDUS (GPE). SPN AXONS OVERLAP HEAVILY WITH THE DENDRITIC ARBORS OF BOTH PARVALBUMIN AND NPASI EXPRESSING NEURONS, THE TWO PREDOMINANT CELL CLASSES OF THE GPE. TO COMPARE THE STRENGTH OF SINGLE (UNITARY) CONNECTIONS BETWEEN BOTH TYPES OF SPNS AND GPE NEURONS, WE FIRST PRESERVED AND ISOLATED CONNECTIONS BETWEEN SPNS AND GPE NEURONS BY PREPARING MOUSE BRAIN SLICES IN A TILTED PARASAGITTAL PLANE. WE USED MALE AND FEMALE MICE WITH CHANNELRHODOPSIN EXPRESSED SELECTIVELY IN DIRECT OR INDIRECT PATHWAY SPNS. WE EVOKED UNITARY STRIATOPALLIDAL CONNECTIONS BY APPLYING SUSTAINED, LOW-POWER ILLUMINATION TO A SMALL AREA DEEP IN THE STRIATUM. THIS ILLUMINATION DROVE SPNS TO FIRE IN QUASI-UP STATES. WE PERFORMED WHOLE-CELL VOLTAGE CLAMP RECORDINGS OF GPE NEURONS TO MEASURE THE SYNAPTIC CURRENTS PRODUCED BY LIGHT-DRIVEN SPN FIRING. OUR FOCAL STIMULATION PRODUCED RATES OF INHIBITORY POSTSYNAPTIC CURRENTS (IPSCS) IN GPE NEURONS THAT MATCHED THE FIRING RATES OF SINGLE SPNS, INDICATING IT EVOKED SINGLE OR VERY FEW UNITARY STRIATOPALLIDAL CONNECTIONS. WE ISOLATED, ANALYZED, AND COMPARED THE PROPERTIES OF UNITARY IPSCS FROM DIRECT AND INDIRECT PATHWAY SPNS. BOTH SPN TYPES PRODUCED SURPRISINGLY LARGE IPSCS IN THE GPE, WITH KINETICS INDICATIVE OF DISTAL DENDRITIC SYNAPSES. TO DETERMINE THE EFFECT OF THESE INPUTS ON THE AUTONOMOUS FIRING OF PARVALBUMIN AND NPASI EXPRESSING GPE NEURONS, WE PERFORMED PERFORATED PATCH CURRENT CLAMP RECORDINGS OF GPE NEURONS WHILE ILLUMINATING SPNS DEEP IN THE STRIATUM. BEFORE ILLUMINATION, WE APPLIED A LONG HYPERPOLARIZING CURRENT STEP TO EACH GPE NEURON, WHICH WE HAVE PREVIOUSLY SHOWN IS HIGHLY PREDICTIVE OF ITS MOLECULAR CLASS. UNITARY CONNECTIONS FROM BOTH DIRECT AND INDIRECT PATHWAY SPNS PRODUCED POWERFUL INHIBITION OF THE TONIC FIRING OF BOTH TYPES OF GPE NEURON, AND WOULD IN SOME CASES COMPLETELY PAUSED FIRING FOR THE DURATION OF ILLUMINATION. OUR RESULTS INDICATE THAT UNITARY CONNECTIONS BETWEEN DIRECT AND INDIRECT PATHWAY SPNS AND PARVALBUMIN AND NPASI EXPRESSING GPE NEURONS ARE SIMILAR, SUGGESTING THAT DIFFERENCES BETWEEN THE TWO PATHWAYS IN THE GPE LIE IN THEIR CONVERGENCE PATTERNS.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S26. THE NANOSCALE ORGANIZATION OF DIVERSE GABAERGIC INHIBITORY SYNAPSES

KATHARINE SMITH*, SARA GOOKIN, AMBER STEWART, JOSHUA GARCIA, KEVIN CROSBY

INHIBITORY SYNAPTIC TRANSMISSION IS CRITICAL FOR MAINTAINING THE PROPER BALANCE OF NEURONAL CIRCUITS WHICH IS ESSENTIAL FOR LEARNING, MEMORY, COGNITION, AND BEHAVIOR. GABAERGIC SYNAPSES MEDIATE SYNAPTIC INHIBITION BY REGULATING NEURONAL EXCITABILITY, CELL FIRING, AND SYNAPTIC PLASTICITY. UNLIKE EXCITATORY SYNAPSES, INHIBITORY SYNAPSES ARE DISTRIBUTED THROUGHOUT THE SOMA AND DENDRITES AND ARE INNERVATED BY DISTINCT INTERNEURONS WHICH CONTRIBUTE TO THEIR DIVERSE FUNCTIONS. SOMATIC INHIBITORY SYNAPSES SYNCHRONIZE CIRCUITS THROUGH SCULPTING NEURONAL OUTPUT AND SPIKE TIMING, WHEREAS SYNAPSES FORMED ON THE DENDRITES CONTROL EXCITATORY ACTIVITY AND DENDRITIC INTEGRATION. WHILE WE UNDERSTAND HOW THESE PRESYNAPTIC DIFFERENCES MAY CONTRIBUTE TO INHIBITORY SYNAPSE DIVERSITY, LITTLE IS KNOWN ABOUT HOW THE POSTSYNAPTIC NANOSCALE ORGANIZATION MAY ALSO BE INVOLVED. OUR RECENT WORK HAS SHOWN THAT INHIBITORY SYNAPSES EXHIBIT A SIMILAR NANOSCALE ORGANIZATION TO THAT OF GLUTAMATERGIC SYNAPSES WHICH IS THOUGHT TO BE CRUCIAL FOR SYNAPSE FUNCTION AND PLASTICITY. FOR INHIBITORY SYNAPSES THIS ORGANIZATION MAY CONTRIBUTE TO THEIR UNIQUE AND STRIKING DIVERSITY OF FUNCTION. HERE WE INVESTIGATE THIS DIVERSITY USING SUPER-RESOLUTION MICROSCOPY TO INTERROGATE THE NANOSCALE ORGANIZATION OF DIFFERENT INHIBITORY SYNAPSE SUBTYPES. WE SHOW THAT THROUGHOUT THE SOMATO-DENDRITIC AXIS POSTSYNAPTIC GABAA RECEPTORS AND THE SCAFFOLD GEPHYRIN ARE DIFFERENTIALLY ORGANIZED. SOMATIC SYNAPSES APPEAR CONSISTENTLY LARGER THAN DENDRITIC, CONTAINING LARGER POSTSYNAPTIC DOMAINS, HIGHER NUMBERS OF GABAA RECEPTORS, AND LARGER ACTIVE ZONES. ADDITIONALLY SOMATIC SYNAPSES ARE STRUCTURALLY MORE COMPLEX COMPARED TO THEIR DENDRITIC COUNTERPARTS, EXHIBITING A MORE INTRICATE NANOSCALE ORGANIZATION OF GABAA RECEPTORS AND GEPHYRIN. TOGETHER OUR DATA SUGGEST THAT NANOSCALE ORGANIZATION OF INHIBITORY SYNAPSES COULD BE A KEY DRIVER UNDERLYING THE DIVERSITY OF SYNAPTIC INHIBITION.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S27. DECODING THE MOLECULAR COMPUTATION BY CAMKII HOLOENZYMES THAT DIRECTS SYNAPTIC PLASTICITY

CAROLYN BROWN*, KEVIN CROSBY, STEVEN COULTRAP, STEVE REICHOW, ULLI BAYER

LEARNING, COGNITION, AND MEMORY REQUIRE DYNAMIC REMODELING OF HIPPOCAMPAL SYNAPSES WHICH REQUIRES CA2+/CALMODULIN-DEPENDENT PROTEIN KINASE II (CAMKII). CAMKII DIRECTS TWO OPPOSING FORMS OF SYNAPTIC PLASTICITY, LONG TERM POTENTIATION (LTP) AND DEPRESSION (LTD), INDUCED BY DISTINCT CA2+ STIMULI. BOTH LOW AND HIGH [CA2+] INDUCE CAMKII AUTOPHOSPHORYLATION (P) AT T286, THAT IS REQUIRED FOR BOTH LTD AND LTP. LTP ADDITIONALLY REQUIRES CAMKII BINDING TO THE NMDA RECEPTOR (GLUN2B SUBUNIT); LTD INSTEAD REQUIRES ADDITIONAL CAMKII AUTOPHOSPHORYLATION AT T305/306. THESE THREE MECHANISMS UNDERGO CROSS-REGULATION BETWEEN THE I2 SUBUNITS WITHIN CAMKII HOLOENZYMES, FINE TUNING CA2+ DECODING BY THE PROTEIN. IT IS UNKNOWN HOW PT286, PT305/306, AND GLUN2B BINDING ARE ENCODED WITHIN HOLOENZYMES AND THUS HOW LTP VERSUS LTD CA2+ COMPUTATION IS ACCOMPLISHED BY CAMKII. FOR EXAMPLE, AUTOPHOSPHORYLATION OCCURS BETWEEN TWO NEIGHBORING KINASE DOMAINS WITHIN A HOLOENZYME. WHILE EACH HOLOENZYME KINASE DOMAIN HAS FIVE SPATIAL NEIGHBORS, IT IS UNCLEAR WHICH ARE FUNCTIONAL NEIGHBORS. ADDITIONALLY, IN VITRO BINDING STUDIES HAVE SUGGESTED THAT THE CAMKII-GLUN2B INTERACTION REQUIRES AVIDITY FROM MULTIPLE HOLOENZYME SUBUNITS. STILL, IT IS UNKNOWN WHAT IS THE REQUIRED STOICHIOMETRY AND SUBUNIT GEOMETRY REQUIRED FOR THIS BINDING. TO THIS END, WE HAVE DEVELOPED CAMKII HOLOENZYME FRAGMENTS WITH ALTERED SUBUNIT NUMBER AND QUATERNARY STRUCTURE. INITIAL BIOCHEMICAL EXPERIMENTS SUGGEST I) A DIRECTIONAL PREFERENCE FOR PT286 AND 2) A NOVEL REQUIREMENT FOR THE CAMKII ASSOCIATION DOMAIN IN GLUN2B BINDING. WE HYPOTHESIZE THAT LTP VERSUS LTD MECHANISMS ARE REGULATED BY STRUCTURALLY DISTINCT FEATURES WITHIN CAMKII HOLOENZYMES.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S28. REGULATION OF LUTEINIZING HORMONE TO PREVENT COGNITIVE DECLINE OF ALZHEIMER'S DISEASE

EMMA REDMON*, ARTHUR ZIMMERMAN, HENRY BAKER, BENSON AKINGBEMI, KENNY BROCK, DOUGLAS MARTIN, MIRANDA REED

ALZHEIMER'S DISEASE (AD) AFFECTS A LARGE PERCENTAGE OF OUR WORLD'S POPULATION, WITH WOMEN HAVING TWICE THE INCIDENCE OF THE DISEASE AS MEN. HORMONAL DIFFERENCES OBSERVED IN AGING MEN AND WOMEN ARE A LIKELY CULPRIT FOR THE DIFFERENCE IN THE PREVALENCE OF AD AMONG THE TWO GROUPS, AS DYSREGULATION OF GONADOTROPIC HORMONES DURING MENOPAUSE IS A RISK FACTOR FOR DEMENTIAS. FOR EXAMPLE, LUTEINIZING HORMONE (LH) LEVELS INCREASE 4-FOLD IN POSTMENOPAUSAL WOMEN, AND THE EFFECTS OF THIS SIGNIFICANT INCREASE ARE RELATIVELY UNDERSTUDIED COMPARED TO OTHER HORMONAL CHANGES, SUCH AS THE DECREASE IN ESTROGEN AFTER MENOPAUSE. HERE, WE TEST THE HYPOTHESIS THAT DOWNREGULATION OF LH CAN RESTORE THE MEMORY DEFICITS AND AD-RELATED PATHOLOGY OBSERVED IN THE TRANSGENIC APP/PSI MOUSE MODEL OF AD. LH LEVELS WERE DOWNREGULATED USING A NOVEL ADENO-ASSOCIATED VIRUS (AAV) VECTOR TO EXPRESS AN ANTI-LH ANTIBODY. WORKING AND SPATIAL REFERENCE MEMORY WERE ASSESSED USING THE Y-MAZE SPONTANEOUS ALTERNATION TEST AND MORRIS WATER MAZE. OTHER BEHAVIORAL MEASURES INCLUDED OPEN FIELD AND ELEVATED PLUS MAZE TO TEST FOR CHANGES IN MOVEMENT AND ANXIETY. WE ALSO DETERMINED WHETHER DOWNREGULATION OF LH COULD DECREASE BETAAMYLOID LEVELS AND TAU PHOSPHORYLATION USING WESTERN BLOT, IMMUNOHISTOCHEMISTRY, AND ELISA ASSAYS. THIS PROJECT WILL HELP ADDRESS THE GENDER DISPARITY OBSERVED IN AD AND HELP DETERMINE WHETHER RESTORATION OF REPRODUCTIVE HORMONE IMBALANCES CAN PREVENT DEMENTIA IN POST-MENOPAUSAL WOMEN.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S29. DISSOCIATION OF STRUCTURAL AND FUNCTIONAL CHANGES IN ALZHEIMER'S DISEASE AND MILD COGNITIVE IMPAIRMENT

ANNIE DANG*, DI WANG, MOHAMAD HABES, PETER FOX

THE AMYLOID-TAU-NEURODEGENERATION (ATN) BIOMARKER FRAMEWORK FOR ALZHEIMER'S DISEASE (AD) INDICATES BINARY (POSITIVE/NEGATIVE) DESIGNATIONS FOR EACH TYPE OF PATHOLOGY, WITHOUT REGARD FOR ANATOMICAL DISTRIBUTION. NEURODEGENERATION IS DESIGNATED AS POSITIVE IF ATROPHY OR HYPOMETABOLISM ARE FOUND ON IMAGING. HOWEVER, CLIFFORD JACK ET AL., 2016 NOTED THAT ATROPHY AND HYPOMETABOLISM WERE DIFFERENTLY DISTRIBUTED AND REFERENCED EACH TO DIFFERENT CO-LOCALIZED PATHOLOGIES. THUS, THERE EXISTS A NEED TO FURTHER CHARACTERIZE ATROPHY AND HYPOMETABOLIC CHANGES IN AD, WITH THE GOAL OF ADVANCING THE APPLICATION OF ANATOMICALLY-BASED BIOMARKERS IN THE ATN FRAMEWORK.

QUERY OF THE BRAINMAP DATABASES OF PUBLISHED, GROUP-WISE NEUROIMAGING, CASE-CONTROL CONTRASTS WAS USED TO IDENTIFY AD AND MILD COGNITIVE IMPAIRMENT (MCI) STUDIES FOR META-ANALYSIS. THE VOXEL-BASED MORPHOMETRY (VBM) AND VOXEL-BASED PHYSIOLOGY (VBP) DATABASES WERE USED TO IDENTIFY STUDIES INVOLVING ATROPHY AND HYPOMETABOLISM RESPECTIVELY. 157 VBM CONTRASTS (110 AD, 47 MCI) AND 146 VBP CONTRASTS (88 AD, 58 MCI) WERE IDENTIFIED. ACTIVATION LIKELIHOOD ESTIMATION COORDINATE-BASED META-ANALYSIS WAS PERFORMED SEPARATELY FOR VBM AND VBP, TO IDENTIFY CROSS-STUDY CONVERGENCE OF BRAIN ALTERATION PATTERNS. MANGO WAS THEN USED TO VISUALIZE RESULTS AND QUANTIFY SPATIAL OVERLAP BETWEEN VBM AND VBP.

STRUCTURAL AND FUNCTIONAL NEURODEGENERATIONS IN AD/MCI EXHIBIT MARKEDLY DIFFERENT NEUROANATOMICAL DISTRIBUTIONS. STRUCTURAL ABNORMALITIES CHIEFLY INVOLVE THE MEDIAL TEMPORAL LOBE AND INSULA; PHYSIOLOGICAL ABNORMALITIES CHIEFLY INVOLVE THE LATERAL PARIETAL LOBE AND POSTERIOR CINGULATE. THERE IS A SMALL OVERLAP (2184 MM3) BETWEEN VBM AND VBP, ACCOUNTING FOR 10.1% OF VBM AND 7.1% OF VBP.

VBM AND VBP PATTERNS OF ALTERATION APPEAR DISTINCT, ALIGNING WITH THE ANTERIOR AND POSTERIOR DEFAULT MODE NETWORK RESPECTIVELY. THIS DISSOCIATION MAY REFLECT DISTINCT UNDERLYING NEUROPATHOLOGIES. NETWORK MODELING OF VBM AND VBP DATA SEPARATELY IS CURRENTLY ONGOING.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S30. NEUROTOXIN MEDIATED NEURONAL DYSFUNCTION REGULATED BY LYSOSOMAL FUNCTION

JINHONG WIE*, WOONJOON KIM

NEUROTOXINS ENCOMPASS DIVERSE GROUPS OF DRUGS THAT HAVE DETRIMENTAL EFFECTS ON THE NEURONAL SYSTEM, LEADING TO COGNITIVE AND NEUROLOGICAL IMPAIRMENTS. THESE TOXINS CAN DISRUPT INTRACELLULAR SIGNALING AND HOMEOSTASIS. LYSOSOMES ARE CRUCIAL ORGANELLES RESPONSIBLE FOR WASTE DISPOSAL AND THE SUPPLY OF ESSENTIAL MATERIALS. THE CONNECTION BETWEEN LYSOSOMAL HOMEOSTASIS AND NEUROLOGICAL DYSFUNCTION REMAINS POORLY UNDERSTOOD. IN THIS STUDY, WE INVESTIGATED HOW TO ALLEVIATE NEURODEGENERATION THROUGH THE MANAGEMENT OF LYSOSOMAL FUNCTION. SOME NEUROTOXINS ARE KNOWN TO AFFECT LYSOSOMAL ION INFLUX OR EFFLUX. AFTER TREATING N2A CELLS WITH HYDROPEROXIDE, A KNOWN NEUROTOXIN, WE OBSERVED A DECREASE IN CELL PROLIFERATION. WHEN BLOCKING THE LYSOSOMAL ION EXCHANGE, IT PROTECTED N2A CELL VIABILITY AGAINST THE DAMAGING EFFECTS OF HYDROPEROXIDE. FOR INTRACELLULAR SIGNALING, HYDROPEROXIDE INCREASED AKT PHOSPHORYLATION, BUT THIS EFFECT WAS DIMINISHED AFTER REGULATING LYSOSOMAL ION EXCHANGE. HYDROPEROXIDE ALSO INCREASED THE LEVEL OF P-RAPTOR PROTEIN, A KEY COMPONENT OF MTORC1, WHICH PLAYS A FUNDAMENTAL ROLE IN LYSOSOMES. HOWEVER, THIS CHANGE DID NOT AFFECT THE TOTAL RAPTOR PROTEIN LEVEL. WHEN WE INDUCED STARVATION IN THE CELLS AND ADDED HYDROPEROXIDE, CELL VIABILITY DECREASED, AND THIS WAS ACCOMPANIED BY AN INCREASE IN AKT PHOSPHORYLATION AND P-RAPTOR LEVELS, BUT THOSE WERE ATTENUATED BY LYSOSOME REGULATION. LC3, A SPECIFIC MARKER FOR AUTOPHAGY, WAS ACCELERATED IN RESPONSE TO HYDROPEROXIDE TREATMENT BUT WAS ALSO DISRUPTED BY THE CONTROL OF LYSOSOMAL ION EXCHANGE. THUS, THE REGULATION OF LYSOSOMAL ACTIVITY CAN PREVENT NEURODEGENERATION AND IMPACT INTRACELLULAR SIGNALING PATHWAYS AFFECTED BY HYDROPEROXIDE.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S31. RESIDENT-PERIPHERAL IMMUNE INTERPLAY: THE POTENTIAL ROLE OF IL-IB IN DOPAMINERGIC NEURON VULNERABILITY AFTER INJURY

COLIN KELLY*, LAUREN FRITSCH, XIAORAN WEI, NICOLE DEFOOR, SAMANTHA BRINDLEY, CAROLINE DE JAGER, ALEXANDRA KALOSS, SWAGATIKA PAUL, HANNAH O'MALLEY, JING JU, MICHELLE OLSEN, MICHELLE THEUS, ALICIA PICKRELL

TRAUMATIC BRAIN INJURY (TBI) INCREASES THE RISK OF PARKINSON'S DISEASE (PD) DEVELOPMENT LATER IN LIFE, BUT MUCH REMAINS UNKNOWN REGARDING THE MECHANISMS DRIVING THIS RELATIONSHIP. INTERLEUKIN-1 BETA (IL-1B), A PROINFLAMMATORY CYTOKINE, IS PRODUCED IMMEDIATELY AFTER BRAIN INJURY AND HAS BEEN SHOWN TO BE A MEDIATOR OF CONTINUED MICROGLIAL ACTIVATION, WHICH WHEN DYSREGULATED CAN NEGATIVELY IMPACT TBI OUTCOME. ADDITIONALLY, IL-1B HAS BEEN SHOWN TO BE ELEVATED IN THE SERUM OF PARKINSON'S DISEASE PATIENTS. A DRIVER OF IL-1B CYTOKINE EXPRESSION IS STING, A KEY INNATE IMMUNE REGULATOR. OUR DATA IN A MURINE MODEL EVALUATING THE ROLE OF INNATE IMMUNE STING SIGNALING FOUND THAT IL-1B SIGNALING ORIGINATES FROM MICROGLIA AT ACUTE TIMEPOINTS POST-INJURY IN A CORTICAL CONTUSION INJURY PARADIGM. CONDITIONAL KNOCKOUT MICE (CKO), WHICH HAVE LOSS OF STING SIGNALING IN MICROGLIA, SHOWED NO UPREGULATION OF IL-1B AT THE TRANSCRIPTIONAL LEVEL AS COMPARED TO CONTROLS 2 HOURS POST-INJURY AND, COMPARATIVELY, SHOWED NEUROPROTECTIVE OUTCOMES. IN A MILDER CONCUSSIVE INJURY MODEL, WE DEMONSTRATE THAT DA NEURONS SHOW DYSREGULATION OF GENES KNOWN TO PLAY A ROLE IN PD PATHOGENESIS AT CHRONIC TIME POINTS POST-INJURY, IN ADDITION TO AN UPREGULATION OF GENES ASSOCIATED WITH NEUROINFLAMMATION AND PERIPHERAL IMMUNE SIGNALING. QUANTIFICATION OF DA NEURONS IN THE SUBSTANTIA NIGRA SHOWS SIGNIFICANT CELL DEATH AT 90 DAYS POST-INJURY COMPARED TO SHAM CONTROLS. THESE FINDINGS INDICATE THE POSSIBILITY OF SUSTAINED PERIPHERAL IMMUNE CELL INFILTRATION AND SIGNALING AND SUPPORT A COMPLEX AND PERSISTENT CROSSTALK BETWEEN BOTH RESIDENT AND PERIPHERAL IMMUNE CELLS AND DA NEURONS THAT IS ULTIMATELY DETRIMENTAL. FUTURE DIRECTIONS OF THIS STUDY WILL DETERMINE THE POSSIBLE ROLE OF RESIDENT-PERIPHERAL IMMUNE INTERPLAY AND IL-1B SIGNALING IN INCREASING THE SENSITIVITY OF DA NEURONS AFTER INJURY, AND WHETHER MILD TBI ACCELERATES PD-LIKE PATHOLOGIES, INCLUDING DA CELL DEATH, WHEN COMBINED WITH A PRECLINICAL MODEL OF MURINE PD.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S32. SUCROSE OVERCONSUMPTION IMPAIRS FEEDING CIRCUIT DYNAMICS AND PROMOTES PALATABLE FOOD INTAKE

CAROLYN LORCH*

RAPID GUT-BRAIN COMMUNICATION IS CRITICAL TO MAINTAIN ENERGY BALANCE AND IS DISRUPTED IN DIET-INDUCED OBESITY THROUGH MECHANISMS THAT REMAIN OBSCURE. SPECIFICALLY, THE ROLE OF CARBOHYDRATE OVERCONSUMPTION IN THE REGULATION OF INTEROCEPTIVE CIRCUITS HAS BEEN MINIMALLY EXAMINED IN VIVO. HERE WE REPORT THAT AN OBESOGENIC HIGH-SUCROSE DIET (HSD) SELECTIVELY BLUNTS POST-INGESTIVE SILENCING OF HUNGER-PROMOTING AGRP NEURONS IN RESPONSE TO GLUCOSE, WHEREAS WE PREVIOUSLY SHOWED THAT OVERCONSUMPTION OF A HIGH-FAT DIET (HFD) SELECTIVELY ATTENUATES LIPID-INDUCED AGRP NEURON SILENCING. BY CONTRAST, BOTH HSD AND HFD DAMPEN RAPID AGRP NEURON RESPONSE TO CHOW PRESENTATION AND PROMOTE PREFERENTIAL INTAKE OF MORE PALATABLE FOODS. OUR FINDINGS REVEAL THAT SUGAR AND FAT OVER-CONSUMPTION PATHOLOGICALLY MODULATE FEEDING CIRCUIT ACTIVITY IN BOTH MACRONUTRIENT-DEPENDENT AND -INDEPENDENT WAYS THAT MAY ADDITIVELY EXACERBATE OBESITY.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S33. THE ROLE OF PHASIC INHIBITION ONTO BDNF+ NEURONS IN THE VENTROMEDIAL HYPOTHALAMUS REGULATING METABOLIC FUNCTION

THERESA HARVEY*, YASEMIN ONDER, MADISION LEIMER, ALICE MENG, MARIBEL RIOS

NEURONS IN THE VENTROMEDIAL HYPOTHALAMUS (VMH) ARE PRIMARILY GLUTAMATERGIC AND PLAY KEY ROLES SUPPRESSING FEEDING, INCREASING ENERGY EXPENDITURE, AND FACILITATING GLYCEMIC CONTROL. INTACT BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF) SIGNALING IN THIS REGION IS REQUIRED FOR THESE ACTIONS. ACCORDINGLY, MICE WITH CENTRAL OR VMH-SPECIFIC BDNF DEPLETION EXHIBIT HYPERPHAGIA, OBESITY, HYPERGLYCEMIA, AND INSULIN RESISTANCE. CLINICALLY, IMPAIRED BDNF SIGNALING RESULTS IN OBESITY SUSCEPTIBILITY IN HUMANS, UNDERSCORING KEY ROLES OF BDNF MEDIATING METABOLIC HEALTH.

WE SHOWED PREVIOUSLY THAT EXCITATORY DRIVE AND ANOREXIGENIC NEURONAL ACTIVITY IN THE VMH IS PLASTIC AND ELEVATED IN THE FED STATE IN A BDNF-DEPENDENT MANNER. IT REMAINED UNCLEAR WHETHER SYNAPTIC INHIBITORY TRANSMISSION IN THE VMH IS ALSO REGULATED BY ENERGY STATE. WE OBSERVED INCREASED DENSITY OF INHIBITORY SYNAPSES AND HEIGHTENED INHIBITORY POST SYNAPTIC CURRENTS IN ANOREXIGENIC BDNF+ NEURONS IN THE VMH IN FED COMPARED TO FASTED WT MICE. THESE FINDINGS INDICATE THAT BOTH INHIBITORY AND EXCITATORY TONE ONTO VMH NEURONS IS INCREASED IN THE FED STATE WITH A NET INCREASE IN THE FIRING RATE OF THESE CELLS, INCREASING THE ANOREXIGENIC TONE. THE INCREASED INHIBITION OF BDNF NEURONS IN THE FED STATE MAY SERVE AS HOMEOSTATIC MECHANISM PREVENTING PROLONGED ANOREXIGENIC RESPONSES AND GLUCOSE UTILIZATION. TO TEST THIS, GABAAR GAMMA2 SUBUNITS WERE SELECTIVELY DEPLETED FROM VMH BDNF+ NEURONS TO INVESTIGATE THE METABOLIC EFFECTS OF DIMINISHED INHIBITORY SYNAPTIC TRANSMISSION ONTO THESE CELLS. ELUCIDATING THE ROLE OF PHASIC INHIBITION ONTO BDNF+ NEURONS IN THE VMH WILL EXPAND OUR UNDERSTANDING OF THE CALORIC DEPENDENT REGULATION OF THESE ANOREXIGENIC CELLS AND THE CONSEQUENCES OF DISRUPTING THIS HOMEOSTATIC MODULATION.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S34. LOCALIZATION AND CHARACTERIZATION OF TRANSPLANTED NEURAL STEM CELL POPULATIONS FOLLOWING CENTRAL NERVOUS SYSTEM INJURY

JEFFERY PLUNKETT*, ANDREW PARDO, BRIAN AVERA, LAUREN ALCINDOR, ALEXANDRA SANTIAGO

NEURAL STEM CELL (NSC) TRANSPLANTATION INTO THE CENTRAL NERVOUS SYSTEM (CNS) HAS BEEN STUDIED IN MULTIPLE MODEL SYSTEMS AS A POTENTIAL THERAPEUTIC APPROACH IN RESPONSE TO CNS TRAUMA. IN ADDITION TO CELL REPLACEMENT, THE BENEFITS OF NSC TRANSPLANTATION INTO THE CNS APPEAR TO INVOLVE AN INCREASED AVAILABILITY OF NEUROTROPHIC FACTORS AND INCREASES IN NEURONAL PLASTICITY COMBINED WITH A REDUCTION IN NEURODEGENERATION AND NEUROINFLAMMATION. TO UNDERSTAND NSCS' POTENTIAL, SOME OF THEIR ESSENTIAL BIOLOGICAL CHARACTERISTICS MUST BE THOROUGHLY INVESTIGATED, INCLUDING THE SPECIFIC MARKERS FOR NSC SUBPOPULATIONS, TO ALLOW PROFILING AND IDENTIFICATION PRIOR TO AND AFTER TRANSPLANTATION. WE ARE CURRENTLY INVESTIGATING THIS TRANSPLANTATION MODEL IN THE ZEBRAFISH (DANIO RERIO) CNS FOLLOWING TRAUMATIC BRAIN INJURY (TBI). IT IS WELL ESTABLISHED THAT UNLIKE THE MAMMALIAN BRAIN, ZEBRAFISH RETAIN MULTIPLE PROLIFERATIVE NEUROGENIC AND STEM CELL NICHES THROUGHOUT ADULT LIFE. CURRENTLY, WE HAVE DEVELOPED A STEM CELL CULTURE METHODOLOGY USING A ROTATING CULTURE TECHNIQUE THAT DEVELOPS AGGREGATES OF UNDIFFERENTIATED STEM CELLS AFTER 2-3 DAYS. THE AGGREGATE CULTURES THEN DIFFERENTIATE INTO NSC AGGREGATES BETWEEN DAYS 4 AND 7 IN CULTURE. FOLLOWING DIFFERENTIATION, THE NSC AGGREGATES ARE THEN TRANSPLANTED INTO THE ADULT ZEBRAFISH CNS FOLLOWING TBI STAB WOUND INJURY. WE ARE CURRENTLY ANALYZING THE EFFICACY OF INTEGRATION OF TRANSPLANTED NSC AGGREGATES INTO INJURY ZONE TISSUES.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S35. GLOBAL CEREBRAL ISCHEMIA DECREASES DENDRITIC SPINE DENSITY, ENHANCES MICROGLIAL REACTIVITY, AND INCREASES MICROGLIAL/SYNAPSE CO-LOCALIZATION IN A MOUSE MODEL OF CARDIAC ARREST

MACY FALK, ANNABELLE MOORE, ERIKA TIEMEIER, NIDIA QUILLINAN, JACOB BASAK*

LONG-TERM COGNITIVE DYSFUNCTION REMAINS COMMON IN SURVIVORS OF CARDIAC ARREST. THE MECHANISM OF ONGOING SYNAPTIC DYSFUNCTION FOLLOWING GLOBAL CEREBRAL ISCHEMIA IS NOT WELL UNDERSTOOD, BUT ALTERATIONS IN SYNAPTIC STRUCTURAL INTEGRITY MAY PLAY A ROLE. THE PRIMARY GOAL OF THIS STUDY IS TO ELUCIDATE CHANGES IN HIPPOCAMPAL DENDRITIC SPINE NUMBERS AND STRUCTURE AFTER A CARDIAC ARREST AT BOTH AN ACUTE AND SUBACUTE TIME POINT AFTER THE INJURY. INCREASING EVIDENCE ALSO SUGGESTS THAT REACTIVE MICROGLIA PLAY AN IMPORTANT ROLE IN MODULATING SYNAPTIC STRUCTURES IN THE SETTING OF BRAIN INJURY THROUGH PHAGOCYTOSIS OF SYNAPTIC MATERIAL. THEREFORE, WE ALSO EVALUATED THE EXTENT OF MICROGLIA ACTIVATION AFTER A CARDIAC ARREST INJURY AND ASSESSED FOR CHANGES IN BOTH MICROGLIAL/DENDRITIC SPINE INTERACTION AND MICROGLIAL PHAGOCYTIC CAPABILITY. USING A MURINE CARDIAC ARREST WITH CARDIOPULMONARY RESUSCITATION (CA/CPR) MODEL, WE OBSERVED A SIGNIFICANT DECREASE IN SECONDARY DENDRITIC SPINE DENSITY 72 HOURS POST INJURY IN THE HIPPOCAMPUS (1.7 VERSUS 2.5 SPINES/MM, P=0.016). MICROGLIA CELLS SHOW PERSISTENT ACTIVATION IN CARDIAC ARREST ANIMALS 72 HOURS POST INJURY COMPARED WITH SHAM ANIMALS. ADDITIONALLY, MICROGLIA-SPINE INTERACTIONS ARE INCREASED IN CA/CPR ANIMALS WITH SIGNIFICANTLY HIGHER LEVELS OF SPINES SHOWING > 70% ENGULFMENT (6.6% VERSUS 2.9%, P=0.0013). CD68 EXPRESSION, A MARKER OF CELLULAR PHAGOCYTOSIS, IS ALSO SIGNIFICANTLY INCREASED IN THE MICROGLIA OF CA/CPR ANIMALS AT 72 HOURS (13.6% VERSUS 2.9% OF MICROGLIA SURFACE, P < 0.0001), WITH A HIGHER PERCENTAGE OF SPINES ENGULFED BY MICROGLIA CO-LOCALIZED WITH CD68. THEREFORE, OUR RESULTS DEMONSTRATE AN EFFECT OF GLOBAL CEREBRAL ISCHEMIA ON DECREASING SYNAPTIC SPINE DENSITY, WITH THIS REDUCTION POSSIBLY IMPACTED BY PERSISTENT MICROGLIA ACTIVATION AND PHAGOCYTOSIS OF DENDRITIC SPINES FOR SEVERAL DAYS FOLLOWING THE INITIAL INJURY.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S36. IMPROVING THE REGIONAL SPECIFICITY OF GLUTAMATE RECEPTOR MODULATION BY TARGETING ACCESSORY PROTEINS

MICHAEL MAHER*

THE UBIQUITOUS EXPRESSION OF THE PRIMARY SUBUNITS OF AMPA RECEPTORS (AMPARS), AND THE LACK OF PHARMACOLOGICAL SELECTIVITY AMONGST THEM, PRECLUDE REGIONAL OR NEURONAL SUBTYPE SPECIFICITY. IN VIVO, AMPARS COMPRISE A VARIETY OF ACCESSORY PROTEINS. OF PARTICULAR INTEREST, TARP-GAMMA8 IS HIGHLY EXPRESSED IN THE HIPPOCAMPUS, PART OF THE LIMBIC CIRCUITRY THAT IS FREQUENTLY THE LOCUS OF TEMPORAL LOBE EPILEPSY. WE USED HIGH-THROUGHPUT SCREENING TO DISCOVER COMPOUNDS THAT SELECTIVELY MODULATE AMPARS CONTAINING TARP-GAMMA8. SUBSEQUENT MEDICINAL CHEMISTRY EFFORTS WERE USED TO IMPROVE POTENCY AND PHARMACOKINETICS OF THE HITS. LEAD MOLECULES WITH ORAL BIOAVAILABILITY AND HIGH BRAIN PENETRATION ALLOWED DEMONSTRATION OF A STRONG RELATIONSHIP BETWEEN PHARMACOKINETICS AND PHARMACODYNAMICS. THE COMPOUNDS SHOW ANTICONVULSANT AND ANXIOLYTIC PROFILES IN RODENT. MOLECULES IN THIS CLASS PROVIDE LARGE SAFETY MARGINS RELATIVE TO NON-SPECIFIC AMPAR INHIBITORS DUE TO THE IMPROVED REGIONAL SPECIFICITY OF TARP-GAMMA8 MODULATORS. AMPAR MODULATORS SELECTIVE FOR TARP-GAMMA8 HAVE THE POTENTIAL TO BE NOVEL TREATMENTS FOR TEMPORAL LOBE EPILEPSY, ANXIETY/DEPRESSION, BIPOLAR DISORDER, AND/OR PRODROMAL SCHIZOPHRENIA. THIS PROJECT ALSO REPRESENTS PROOF-OF-PRINCIPLE FOR PHARMACOLOGICAL TARGETING OF ACCESSORY PROTEINS AND SMALL-MOLECULE MODULATION OF PROTEIN-PROTEIN INTERACTIONS.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S37. TOWARD META-CONNECTOMIC ERGODICITY IN NEUROIMAGING: GRAPH THEORY MODELING EVIDENCE IN TEMPORAL LOBE EPILEPSY

JONATHAN TOWNE*, VICTOR LAMI, HEATH PARDOE, JOSE CAVAZOS, PETER FOX

ERGODICITY IN A DYNAMICAL SYSTEM ASSERTS THAT GROUP OBSERVATIONS AT A SINGLE TIME POINT ARE EQUIVALENT TO A SINGLE-INDIVIDUAL OBSERVATION OVER TIME. IN THE BRAIN, THIS WOULD MANDATE THAT NETWORK PROPERTIES DERIVED FROM CROSS-SECTIONAL DATA WILL BE OBSERVED LONGITUDINALLY IN INDIVIDUALS. THE IMPLICATION FOR NEUROIMAGING, IF ERGODICITY HOLDS, IS THAT META-ANALYTIC SAMPLING CAN ACCESS NETWORK ARCHITECTURE (DATA STRUCTURES) USEFUL FOR DETECTING NETWORKS PER-SUBJECT. ERGODICITY HAS BEEN IMPLICITLY SHOWN IN HEALTHY SUBJECTS BY GRAPH THEORY (CROSSLEY ET AL 2013) AND OTHER ANALYTICS (SMITH ET AL 2009). EQUIVALENT FUNCTIONAL ARCHITECTURE WAS IDENTIFIED BY CONNECTOMIC META-ANALYSIS OF TASK-BASED STUDIES AND CONNECTOMIC ANALYSIS OF TEMPORALLY CONCATENATED RS-FMRI. DISEASES FOLLOW COLLECTIVELY SIMILAR YET INDIVIDUALLY DISTINCT PATTERNS (VANASSE ET AL 2021), MOTIVATING ERGODIC HYPOTHESES. WE PRESENT EVIDENCE OF ERGODICITY IN A TEMPORAL LOBE EPILEPSY (TLE) COHORT.

META-CONNECTOMIC AND CONNECTOMIC MODELS WERE DERIVED FROM PUBLISHED COORDINATE DATA FROM CASE-CONTROL CONTRASTS (N=74 TLE EXPERIMENTS) AND FROM PRIMARY (PER-SUBJECT) RS-FMRI (N=37 TLE/19 CONTROLS), RESPECTIVELY. MODELS WERE COMPARED BY MODULARITY ANALYSIS AND NODE TOPOLOGY METRICS (E.G. CENTRALITY). TLE NETWORKS IDENTIFIED CROSS-SECTIONALLY (CASE-CONTROL CONTRASTS) WERE OBSERVED LONGITUDINALLY IN TLE, NOT CONTROLS. TWO TLE MODULES WERE FOUND META-ANALYTICALLY (LIMBIC AND LANGUAGE NETWORKS) AND PRESENT INDIVIDUALLY. THE MEDIAL DORSAL NUCLEUS WAS THE MOST TOPOLOGICALLY INFLUENTIAL NODE; OTHER COMMON HUBS INCLUDE HIPPOCAMPUS, CAUDATE BODY, SUP TEMPORAL GYRUS, AND INF PARIETAL LOBULE.

ERGODICITY WAS DEMONSTRATED IN TLE. CRITICS PURPORT ERGODICITY TO IMPLY INDIVIDUALS ARE IDENTICAL. WE SUGGEST NETWORK STRUCTURE IS SIMILAR CROSS-SECTIONALLY (MEAN COHERENT STRUCTURE) BUT EXHIBITED ERGODICALLY OVER TIME. THESE RESULTS MOTIVATE THE APPLICATION OF META-ANALYTIC FUNCTIONAL NETWORK MODELS IN PRIMARY DATA, TO DEVELOP PER-SUBJECT BIOMARKERS.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S38. PRENATAL CANNABINOID EXPOSURE AFFECTS MEMORY THROUGH ALTERATIONS IN GLUTAMATERGIC RECEPTOR EXPRESSION

KATIE MOERSCHEL*, KAWSAR CHOWDHURY, VISHNU SUPPIRAMANIAM

AS THE LEGALIZATION OF CANNABIS HAS INCREASED, PRENATAL EXPOSURE TO CANNABIS HAS ALSO INCREASED SIGNIFICANTLY AND IS EXPECTED TO CONTINUE RISING. CURRENTLY, NO THERAPY IS AVAILABLE FOR COGNITIVE DEFICITS ASSOCIATED WITH PRENATAL CANNABINOID EXPOSURE (PCE). COGNITION CAN BE RESEARCHED THROUGH LEARNING AND MEMORY WHICH OCCURS IN THE HIPPOCAMPUS OF THE BRAIN THROUGH THE NEUROTRANSMITTER, GLUTAMATE. THE TWO MAJOR GLUTAMATE RECEPTORS IN THE HIPPOCAMPUS, N-METHYL D-ASPARTATE RECEPTOR (NMDAR) AND ALPHA-AMINO-3-HYDROXY-5-METHYL-4-ISOXAZOLE PROPIONIC ACID RECEPTOR (AMPAR) ARE REQUIRED FOR LEARNING AND MEMORY FORMATION. THIS PROJECT HYPOTHESIZES THAT BEHAVIORAL DEFICITS OBSERVED IN BEHAVIORAL EXPERIMENTS ARE DUE TO PCE WHICH UPREGULATES AMPAR AND NMDAR. TO TEST OUR HYPOTHESIS, PREGNANT SPRAGUE DAWLEY RATS WERE ORALLY GAVAGED WITH 5 MG/KG OF PURE D9-TETRAHYDROCANNABINOL (THC) FROM GESTATIONAL DAY FIVE TO POST-NATAL DAY NINE AND EXAMINED BETWEEN PND 40-50. TO EVALUATE THE LEARNING CAPACITY AND MEMORY RETENTION BEHAVIORAL EXPERIMENTS WERE PERFORMED SUCH AS ELEVATED PLUS MAZE (EPM), TRACE FEAR CONDITIONING (TFC), AND CONTEXTUAL FEAR CONDITIONING (CFC). IMMUNOBLOTTING OF HIPPOCAMPAL PROTEINS REVEALED THAT PCE SIGNIFICANTLY INCREASED THE EXPRESSION OF GLUA2, A SUBUNIT OF AMPA RECEPTORS. GLUN2A, A SUBUNIT OF NMDA RECEPTORS ALSO SHOWED INCREASED EXPRESSION DUE TO PCE. IN BRIEF, OUR STUDIES DEMONSTRATE, AT LEAST IN PART, THE MOLECULAR MECHANISMS OF HIPPOCAMPAL-DEPENDENT MEMORY DEFICITS ASSOCIATED WITH PCE.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S39. SYMPTOM-NETWORK DISRUPTION: A MECHANISM OF ACTION FOR INTENSIVE PSYCHIATRIC POLYTHERAPY

PETER FOX*, LARRY PRICE, FELIPE SALINAS, FREDERICK GOODSON-GREGG

NETWORK THEORY OF MENTAL DISORDERS (NTMD) MODELS MENTAL DISORDERS AS NETWORKS IN WHICH SYMPTOMS ARE NODES AND SYMPTOM CO-OCCURRENCE PROBABILITIES ARE EDGES. SYMPTOM PRECIPITATION BY EXTERNAL EVENTS (E.G., TRAUMA EXPOSURE) INDUCES NETWORK ACTIVATION, FORMING A SYMPTOM COMPLEX (AKA, SUBNET, CLIQUE OR CLUSTER). MUTUAL ACTIVATION OF ADJACENT NODES LEADS TO A SELF-SUSTAINING, ACTIVATED-STATE THAT PERSISTS BEYOND THE INCITING EVENTS AS A MENTAL DISORDER. THE CONVERSION FROM EXPOSURE-INDUCED SYMPTOMS TO A SELF-SUSTAINING DISORDER IS TERMED HYSTERESIS. A COROLLARY OF THE NTMD CONSTRUCT IS THAT TREATING ANY SYMPTOM WILL REDUCE STRENGTH OF BOTH THE TREATED SYMPTOM AND ADJACENT (CONNECTED) SYMPTOMS IN PROPORTION TO THEIR CONNECTEDNESS.
NTMD, THEREFORE, IMPLICITLY ENCOURAGES INTENSIVE POLYTHERAPY. USING POSTTRAUMATIC STRESS DISORDER AS THE EXAMPLE: PROLONGED EXPOSURE (PE) WILL DECREASE TRIGGERING AND AVOIDANCE; BENZODIAZEPINES WILL DECREASE ANXIETY; AND TRANSCRANIAL MAGNETIC STIMULATION (TMS) WILL DISRUPT CONNECTIVITY THROUGHOUT THE NETWORK. MORE FREQUENT TREATMENTS WILL YIELD MORE RAPID REMISSION.
TWO RECENT RANDOMIZED CLINICAL TRIALS OF INTENSIVE POLYTHERAPY FOR POSTTRAUMATIC STRESS DISORDER (PTSD) WERE ANALYZED NETWORK MODELING. EACH TRIAL COMPARED A LESS-INTENSE ARM (ARM 1) TO A MORE-INTENSE ARM (ARM 2). TRIAL A COMPARED: 1) DAILY PE (DPE) ALONE; AND 2) DPE + DAILY, DAY-LONG COGNITIVE BEHAVIORAL THERAPY (DCBT). TRIAL B COMPARED: 1) DMPE + DCBT + SHAM TMS; AND 2) DMPE + DCBT + ACTIVE TMS. ALL FOUR TREATMENT ARMS EXHIBITED, HIGHLY SIGNIFICANT DECREASE OF SYMPTOMS, WITH MARKED DISRUPTION OF SYMPTOM NETWORKS. IN BOTH TRIALS MORE INTENSIVE TREATMENT GAVE BETTER OUTCOMES. CONCLUSION: NTMD PREDICTIONS ARE CONFIRMED.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S40. LATERAL VENTRICLES OF THE BRAIN: ANATOMIC VARIABILITY DEPENDING ON THE AGE

IULIIA ZHURAVLOVA*, ANNE MONTGOMERY

THE EVALUATION OF THE PARAMETERS OF THE BRAIN VENTRICLES AND MONITORING THE CHANGES OF THESE PARAMETERS IS USED IN THE DIAGNOSTICS OF THE DEGENERATIVE DISEASES OF THE CNS AND IN CERTAIN PSYCHIATRIC DISORDERS. THE PURPOSE OF OUR STUDY WAS TO OBTAIN DATA ABOUT THE NORMAL MORPHOLOGIC PARAMETERS OF THE LATERAL VENTRICLES OF THE BRAIN AND THEIR RELATION TO AGE.
THIS STUDY IS BASED ON THE ANALYSIS OF THE CT STUDIES OF HEALTHY SUBJECTS AGED 17-86 YEARS. THE WIDTH OF THE ANTERIOR, TEMPORAL, OCCIPITAL HORNS, AND BODY OF THE LATERAL VENTRICLE WAS MEASURED. IN STATISTICAL ANALYSIS FOR CONTINUOUS DATA ACROSS CATEGORIES, AN INDEPENDENT T-TEST WAS USED; FOR CATEGORICAL DATA, PEARSON'S R WAS APPLIED.
THE WIDTH OF THE ANTERIOR HORNS (R RIGHT 0.502, LEFT 0.549) AND OCCIPITAL HORNS (R RIGHT 0.401, LEFT 0.451) AND THE WIDTH OF THE ANTERIOR THIRD (R 0.384), MIDDLE THIRD (R 0.488) OF THE BODY, AND THE ATRIUM (R 0.401) OF THE LEFT VENTRICLE HAS MODERATE POSITIVE CORRELATION WITH AGE ($P < 0.001$). THE WIDTH OF THE ANTERIOR (R 0.384; $P < 0.001$) AND MIDDLE (R 0.331; $P < 0.001$) THIRDS, AND ATRIUM (R 0.277; $P < 0.004$) OF THE RIGHT VENTRICLE, AS WELL AS THE WIDTH OF THE TEMPORAL HORNS (R RIGHT 0.155, $P < 0.113$; LEFT 0.194, $P < 0.046$) OF BOTH RIGHT AND LEFT VENTRICLES HAS A WEAK POSITIVE CORRELATION WITH AGE. ONLY THE FRONTAL (RIGHT 0.5±0.22 CM; LEFT 0.41±0.19 CM) AND TEMPORAL (RIGHT 0.61±0.27 CM; LEFT 0.66±0.29 CM) HORNS, AND ANTERIOR THIRD OF THE BODY (RIGHT 0.77±0.24 CM; LEFT 0.74±0.18 CM), HAVE SHOWN STATISTICALLY SIGNIFICANT DIFFERENCES ($P < 0.001$) BETWEEN RIGHT AND LEFT SIDES.
THE ASSESSMENT OF THE ASSOCIATION OF THE WIDTH WITH THE AGE, FOR ALL THE MEASURED PORTIONS OF THE LATERAL VENTRICLES HAVE SHOWN THAT WIDTH INCREASES WITH ADVANCING AGE. SIGNIFICANT DIFFERENCES WERE FOUND BETWEEN THE WIDTHS OF THE FRONTAL AND TEMPORAL HORNS, AND ANTERIOR THIRD OF THE BODY OF THE RIGHT AND LEFT VENTRICLES.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S41. MECHANISTIC INSIGHTS INTO NMDA RECEPTOR POSITIVE ALLOSTERIC MODULATORS THAT ALTER EFFICACY, POTENCY, AND PERMEATION PROPERTIES

ELIJAH ULLMAN*, RILEY PERSZYK, RUSSELL FRITZEMEIER, NICHOLAS AKINS, SRINU PALADUGU, DENNIS LIOTTA, STEPHEN TRAYNELIS

OUR GROUP DISCOVERED A CLASS OF THERAPEUTICALLY RELEVANT NMDA RECEPTOR POSITIVE ALLOSTERIC MODULATORS THAT CAN ENHANCE THE RESPONSE TO MAXIMALLY EFFECTIVE CONCENTRATIONS OF AGONIST, CAN INCREASE AGONIST POTENCY, AND SURPRISINGLY REDUCE SINGLE CHANNEL CONDUCTANCE AND REDUCE CALCIUM PERMEABILITY OVER SODIUM. EU1622-A IS OUR PROTOTYPICAL COMPOUND THAT IS POTENT AND EFFICACIOUS. IT ACTS ON ALL COMBINATIONS OF NMDARS BUT WITH DIFFERENT RELATIVE ACTIONS FOR NDMARS WITH DIFFERENT SUBUNIT COMBINATIONS IN TERMS OF CHANGING MODALITIES. THIS SUBUNIT SPECIFICITY MAY PROVIDE UNIQUE THERAPEUTIC ADVANTAGES. HERE WE EVALUATE AT THE SINGLE-CHANNEL AND MACROSCOPIC LEVEL THE MECHANISM OF ACTIONS OF THIS NEW CLASS OF ALLOSTERIC MODULATOR. WE UTILIZED MULTIPLE PREPARATIONS (X. LAEVIS OOCYTES, HEK293 CELLS, CULTURED NEURONS) TO EXPLORE THE ACTIONS OF THIS CLASS OF POSITIVE ALLOSTERIC MODULATOR. ONGOING WORK IS FOCUSED ON HOW CHANGES IN CALCIUM PERMEABILITY AFFECT SYNAPTIC PLASTICITY IN RODENT BRAIN SLICES, AS WELL AS MORE DETAILED STUDIES OF IT EFFECTS ON PERMEATION AND GATING.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S42. THERMOREGULATORY ROLES OF PREOPTIC AREA HISTAMINE RECEPTOR H1 NEURONS

ARIANNA VALERI*, RAMÓN PIÑOL, OKSANA GAVRILOVA, CUIYING XIAO, MARC REITMAN

THE PREOPTIC AREA PLAYS AN IMPORTANT ROLE IN THE REGULATION OF BODY TEMPERATURE, CONTRIBUTING TO BEHAVIORAL AND PHYSIOLOGICAL THERMOREGULATORY FUNCTIONS, INCLUDING TORPOR, FEVER, AND DEFENSE FROM COLD AND HEAT. ACTIVATION OF MOST PREOPTIC AREA NEURONAL POPULATIONS DECREASES BODY TEMPERATURE, BUT TO DATE ONLY THREE POPULATIONS HAVE BEEN DESCRIBED TO INCREASE BODY TEMPERATURE WHEN ACTIVATED: TWO CONTRIBUTING TO FEVER AND ONE TO COLD DEFENSE. HISTAMINE RECEPTOR H1 IS EXPRESSED IN APPROXIMATELY 5% OF PREOPTIC NEURONS. NANOINJECTION OF HISTAMINE IN THE PREOPTIC AREA CAN INCREASE BODY TEMPERATURE AND PREOPTIC HISTAMINE LEVELS ARE CORRELATED WITH WAKEFULNESS. WE DEVELOPED A HRH1-CRE MOUSE TO TEST THE ROLE OF PREOPTIC HRH1 NEURONS IN THERMOREGULATION. OPTOGENETIC AND CHEMOGENETIC ACTIVATION OF PREOPTIC HRH1 NEURONS INCREASED BODY TEMPERATURE AND PHYSICAL ACTIVITY. CHEMOGENETIC INHIBITION ATTENUATED THE CIRCADIAN INCREASE IN BODY TEMPERATURE AT THE ONSET OF THE DARK CYCLE WITHOUT CHANGING PHYSICAL ACTIVITY. DURING THE LIGHT PHASE, HOWEVER, INHIBITION HAD NO EFFECT ON BODY TEMPERATURE OR PHYSICAL ACTIVITY. IN ADDITION, INHIBITION OF PREOPTIC AREA HRH1 NEURONS REDUCED COLD-ASSOCIATED NEST BUILDING IN BOTH SEXES. PREOPTIC AREA HRH1 NEURONS PROJECT WIDELY TO OTHER HYPOTHALAMIC AND BRAINSTEM STRUCTURES, INCLUDING TO HISTAMINE-PRODUCING NUCLEI. OPTOGENETIC STIMULATION OF PREOPTIC HRH1 NEURON TERMINALS IN THE ARCUATE, DORSOMEDIAL HYPOTHALAMIC AND VENTRAL TUBEROMAMMILLARY NUCLEI INCREASED BODY TEMPERATURE AND PHYSICAL ACTIVITY. IN CONCLUSION, PREOPTIC HRH1 NEURONS PARTICIPATE IN SEVERAL THERMOREGULATORY FUNCTIONS, INCLUDING BODY TEMPERATURE REGULATION, PHYSICAL ACTIVITY, AND NESTING. THESE NEURONS POSSIBLY CONTRIBUTE TO CIRCADIAN HISTAMINE-ASSOCIATED BODY TEMPERATURE CHANGES AND COLD-INDUCED NESTING BEHAVIOR.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S43. ALTERATIONS IN INTRINSIC PROPERTIES OF CORTICAL PARVALBUMIN CELLS FOLLOWING CHRONIC MORPHINE, INFLAMMATORY PAIN AND DOR AGONIST TREATMENT

MARIE WALICKI*, WILLIAM BIRDSONG

THE ANTERIOR CINGULATE CORTEX (ACC) IS A CORTICAL REGION INVOLVED IN PAIN PROCESSING AND ITS OUTPUT INFLUENCES DOWNSTREAM NEURAL CIRCUITS. ACC HYPEREXCITABILITY IS SHOWN IN CHRONIC PAIN CONDITIONS, AND DIRECT INHIBITION OF ACC ACTIVITY PROVIDES RELIEF FROM PAIN. ACC ACTIVITY IS REGULATED BY ENDOGENOUS OPIOIDS LIKE ENKEPHALINS, WHICH CAN ACT AT BOTH MU AND DELTA OPIOID RECEPTORS TO ALTER CORTICAL FUNCTION. THE DELTA OPIOID RECEPTOR (DOR) IS EXPRESSED IN A MAJORITY OF PARVALBUMIN (PV) INTERNEURONS WITHIN THE ACC AND DOR ACTIVATION ON THESE INTERNEURONS INHIBITS GABA RELEASE, DISINHIBITING NEARBY PYRAMIDAL CELLS. WHILE PV CELLS REGULATE INHIBITORY SIGNALING IN THE ACC, IT IS UNKNOWN HOW PV CELL NEUROTRANSMISSION ADAPTS FOLLOWING DRUG EXPOSURE OR IN PAIN STATES. TO ADDRESS THESE UNKNOWNS, WE USED PATCH CLAMP ELECTROPHYSIOLOGY, OPTOGENETICS AND PHARMACOLOGY IN BRAIN SLICES TO MEASURE INTRINSIC PROPERTIES OF ACC PV CELLS FROM MICE TREATED WITH OPIOID RECEPTOR AGONISTS OR PAIN. ANIMALS IN THESE STUDIES WERE TREATED WITH CHRONIC MORPHINE VIA AN OSMOTIC MINIPUMP, INFLAMMATORY PAIN VIA A HIND PAW INJECTION OF COMPLETE FREUND'S ADJUVANT (CFA) OR SNC-80 A SELECTIVE DOR AGONIST. WE FOUND THAT TREATMENT WITH CFA AND MORPHINE DOES NOT CHANGE DOR SIGNALING ON PV INTERNEURONS, BUT THERE ARE CHANGES IN PV CELL INTRINSIC PROPERTIES IN A TREATMENT-DEPENDENT AND SEX-SPECIFIC MANNER. PV CELLS FROM CFA-TREATED MALE ANIMALS ARE DEPOLARIZED, HAVE A LOWER RHEOBASE AND HIGHER INPUT RESISTANCES COMPARED TO CELLS FROM CFA-TREATED FEMALES AND NAÏVE GROUPS. THESE ALTERATIONS ARE REVERSED FOLLOWING PRETREATMENT WITH MORPHINE, WHICH SUGGESTS THAT CFA AND MORPHINE DISRUPT ENDOGENOUS OPIOID SIGNALING IN THE ACC. OVERALL, THESE DATA SUGGEST THAT PV CELL FUNCTION IS ALTERED IN PAIN AND DRUG STATES, WHICH MAY GIVE RISE TO CHANGES IN ACC OUTPUT.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S44. NEURONAL ACTIVITY REVEALS PARADOXICAL CORTICAL STATE DURING DESFLURANE ANESTHESIA

ANTHONY HUDETZ*, DUAN LI

DYNAMIC CHANGES IN NATURAL SLEEP STATES ARE WELL KNOWN, BUT THEY HAVE BEEN THOUGHT TO BE ABSENT DURING ANESTHESIA AT CONSTANT AGENT CONCENTRATION WITHOUT EXOGENOUS STIMULATION. RECENT STUDIES FOUND THAT ELECTROENCEPHALOGRAPHIC MARKERS MAY SPONTANEOUSLY CHANGE AT FIXED ANESTHETIC CONCENTRATION. HERE WE AIMED TO EXAMINE HOW LOCAL CORTICAL NEURON FIRINGS MAY PARTICIPATE IN SPONTANEOUS STATE TRANSITIONS DURING ANESTHESIA. EXTRACELLULAR UNIT ACTIVITY WAS MEASURED WITH CHRONICALLY IMPLANTED 64-SITE MICROELECTRODE ARRAYS IN CORTICAL LAYERS 5/6 OF PRIMARY VISUAL CORTEX OF SIX FREELY MOVING MALE RATS DURING STEPWISE DECREASE OF DESFLURANE CONCENTRATION AT 6, 4, 2, AND 0%. DISTINCT STATES OF NEURON POPULATION ACTIVITY ACROSS ALL ANESTHETIC LEVELS WERE IDENTIFIED BY PRINCIPAL COMPONENTS ANALYSIS. THE FIRST TWO PRINCIPAL COMPONENTS OF NEURON POPULATION SPIKING DISTINGUISHED FIVE POPULATION STATES. FOUR OF THE STATES REFLECTED THE CONCENTRATION-DEPENDENT EFFECT OF DESFLURANE, WHEREAS STATE 5 REPRESENTED A PARADOXICAL STATE WITH INCREASED AVERAGE FIRING RATE AND PERMUTATION ENTROPY – A MEASURE OF NEURONAL COMPLEXITY. THE LATTER WAS SIGNIFICANTLY HIGHER THAN IN STATES 4 AND 3, BUT COMPARABLE TO STATES 2 AND 1. THE PARADOXICAL STATE LASTED FOR SEVERAL MINUTES AND WAS PRESENT AT 4% AND 6% DESFLURANE IN ALL RATS. INDIVIDUAL NEURON FIRINGS SHOWED ADDITIONAL DYNAMIC FLUCTUATIONS WITHIN EACH POPULATION STATE. SINGLE NEURON STATES LASTED 10-30 SEC WITH 2-5 TIMES OF STATE TRANSITIONS PER MINUTE. THE RESULTS SUGGEST THAT THE ANESTHETIC STATE IS HIGHLY DYNAMIC, FEATURING PARADOXICAL INCREASES OF THE COMPLEXITY OF VISUAL CORTICAL NEURONAL ACTIVITY DURING RELATIVELY DEEP ANESTHESIA CONSISTENT WITH UNCONSCIOUSNESS. THESE FINDINGS MAY HAVE TRANSLATIONAL IMPLICATIONS FOR THE RESTORATIVE POTENTIAL OF ANESTHESIA AND ON POSTOPERATIVE SLEEP CHANGES. SUPPORTED BY NIGMS R01-GM056398 AND THE DEPARTMENT OF ANESTHESIOLOGY, UNIVERSITY OF MICHIGAN.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S45. ANALGESIC EFFICACY OF ALCOHOL IN THE CONTEXT OF HIV-ASSOCIATED PAIN

TAYLOR FITZPATRICK-SCHMIDT*, JESSICA CUCINELLO-RAGLAND, SOPHIA MARATHONITIS, KIMBERLY EDWARDS, DAVID WELSH, PATRICIA MOLINA, SCOTT EDWARDS

HIV-ASSOCIATED NEUROPATHY (HIV-N) IS ONE OF THE MOST COMMON NEUROLOGICAL COMORBIDITIES AMONG PEOPLE WITH HIV (PWH) AND AFFECTS UP TO 69% OF HIV+ PATIENTS. ALCOHOL USE DISORDER (AUD), A CHRONIC DISEASE CHARACTERIZED BY EXCESSIVE DRINKING, IS ALSO FREQUENTLY COMORBID IN PWH AND EXACERBATES HIV-N. IMPORTANTLY, THE RATIONALE FOR DRINKING IN PWH MAY STEM FROM A DESIRE FOR SELF-MEDICATION OF PAIN DUE TO THE ANALGESIC PROPERTIES OF ALCOHOL. TO STUDY THE CONTRIBUTIONS OF ALCOHOL AND HIV TO HIV-N, WE ARE USING AN ESTABLISHED PRECLINICAL RODENT MODEL THAT INVOLVES PERINEURAL EXPOSURE TO THE HIV ENVELOPE PROTEIN GLYCOPROTEIN 120 (GP120), ALONGSIDE DATA ANALYSIS FROM A CLINICAL COHORT OF PWH. WE HYPOTHESIZED THAT: 1) IN OUR PRECLINICAL MODEL, ACUTE ALCOHOL ALLEVIATES GP120-INDUCED MECHANICAL HYPERALGESIA, QUANTIFIED VIA ELECTRONIC VON FREY, AND 2) IN OUR CLINICAL COHORT, RECENT ALCOHOL USE, ASSESSED USING THE BLOOD BIOMARKER PHOSPHATIDYLETHANOL (PETH), IS ASSOCIATED WITH A REDUCTION IN PAIN INTENSITY AND INTERFERENCE, AS EVALUATED BY THE 36-ITEM SHORT FORM SURVEY (SF-36). IN OUR RODENT MODEL, ALCOHOL WAS ADMINISTERED AT THREE DOSES (0, 0.5, 1.0 G/KG) VIA INTRAPERITONEAL INJECTION FIVE MINUTES PRIOR TO BEHAVIORAL TESTING. OUR RESULTS INDICATE PERINEURAL HIV GP120 EXPOSURE IN MALE AND FEMALE RATS PRODUCES A SUSTAINED HYPERALGESIA THAT LASTS UP TO FOUR WEEKS. ADDITIONALLY, THIS HYPERALGESIA IS ATTENUATED BY MODERATE AND BINGE DOSES OF ALCOHOL IN BOTH SEXES. IN OUR CLINICAL COHORT, WE FOUND THAT RECENT ALCOHOL USE IS ASSOCIATED WITH DECREASED PAIN INTENSITY AND INTERFERENCE SYMPTOMS IN PWH IN ASSOCIATION WITH OTHER NEGATIVE AFFECTIVE SYMPTOMS. OUR ONGOING TRANSLATIONAL RESEARCH AIMS TO CHARACTERIZE THE MECHANISMS UNDERLYING HIV GP120-INDUCED HYPERALGESIA AND THE IMPLICATED PATHWAYS IN ALCOHOL-INDUCED ALLEVIATION OF THE PAIN TO INFORM THE DEVELOPMENT OF NOVEL THERAPEUTICS.
THIS RESEARCH WAS SUPPORTED BY NIAAA GRANTS F30AA030941, R01AA025996, T32AA007577, AND P60AA009803.

SUNDAY, JANUARY 28TH

POSTER SESSION I
3:30 P.M. - 4:30 P.M.
PEAK 4-5

S46. INFLAMMATORY STATUS SCHIZOPHRENIC PATIENTS AND CLASSIFICATION BASED ON BRAIN TRANSCRIPTOMICS IDENTIFY THE SAME GROUPS OF PATIENTS

C. HARKER RHODES*, CYNDI SHANNON WEICKERT

WHILE IT HAS LONG BEEN APPRECIATED THAT SCHIZOPHRENIA IS A CLINICAL SYNDROME, NOT A SINGLE DISEASE, A CLEAR AND CONSISTENT WAY TO STRATIFY INDIVIDUALS INTO DIFFERENT SUBTYPES IS NEEDED. WEICKERT ET AL. IDENTIFIED "HIGH" AND "LOW" INFLAMMATORY SUBGROUPS, WHILE RHODES ET AL. DIVIDED SCHIZOPHRENIC PATIENTS INTO THOSE WITH A RELATIVELY NORMAL DLPFC TRANSCRIPTOME ("TYPE 1") AND THOSE WITH THOUSANDS OF GENES DIFFERENTIALLY EXPRESSED IN THE DLPFC ("TYPE 2"). A SUBSEQUENT ANALYSIS REPORTED THE INCREASED EXPRESSION OF INFLAMMATORY PATHWAY GENES IN THE TYPE 2 BUT NOT TYPE 1 PATIENTS. THIS CURRENT ANALYSIS TESTED THE HYPOTHESIS THAT WHEN THE TRANSCRIPT-BASED SUBGROUPS ARE COMPARED TO THOSE IDENTIFIED BASED ON PROTEIN-BASED SUBGROUPS ONE THE SAME GROUP OF PATIENTS, THEY WILL IDENTIFY SUBSTANTIALLY OVERLAPPING SUBGROUPS.

AUTOPSY TISSUE FROM PEOPLE WITH CHRONIC SCHIZOPHRENIA COLLECTED BY THE NIMH HUMAN BRAIN COLLECTION CORE (HBCC) WAS USED. THE WGTA STUDY WAS BASED ON RNASEQ DATA MADE PUBLICLY AVAILABLE BY THE LIEBER INSTITUTE (CITE PAPER AS IT IS PUBLISHED). SUBGROUPS WERE IDENTIFIED WITH WEIGHTED GENE CO-EXPRESSION NETWORK ANALYSIS (WGCNA) USING R AND 52% WERE DEFINED AS TYPE 2 OR HIGH INFLAMMATION SUBGROUP. PROTEINS OF THE INFLAMMATORY MARKERS (ILI-BETA, IL6, IL8 ILI8, TNF AND CDI63) EXTRACTED FROM FROZEN DLPFC (N=32 SCHIZOPHRENIC PATIENTS) WERE MEASURED BY CYTOKINE PANELS (BIO-RAD) AND ELISAS. SUBGROUPS WERE IDENTIFIED USING TWO-STEP RECURSIVE CLUSTERING (SPSS) AND 56% WERE IDENTIFIED AS HIGH INFLAMMATION. WE FOUND THAT WHEN THE CLUSTERING RESULTS OF THOSE TWO STUDIES WERE COMPARED, THERE WERE 26 PATIENTS IN COMMON TO BOTH STUDIES AND OF THOSE 21/26 WERE ASSIGNED TO THE SAME SUBGROUP IN THE TWO STUDIES (CHI SQUARED P-VALUE < 0.002). THESE TWO STUDIES WERE DONE INDEPENDENTLY IN TWO DIFFERENT LABS, USING TWO COMPLETELY DIFFERENT TECHNOLOGIES, AND TWO MATHEMATICALLY DIFFERENT METHODS TO CLUSTER PATIENTS WITH SCHIZOPHRENIA.

THEIR CONCORDANCE SUGGESTS THAT THIS MOLECULARLY-BASED CLASSIFICATION OF SCHIZOPHRENIC PATIENTS WILL BE IMPORTANT IN FUTURE MOLECULAR AND CELLULAR STUDIES OF THE DISEASE AND SHOULD BE TAKEN INTO ACCOUNT IN THE DESIGN AND DATA ANALYSIS OF DRUG THERAPY TRIALS.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

MI. MODULATING LEVELS OF ΔFOSB ALTERS NUCLEUS ACCUMBENS MEDIUM SPINY NEURONS ACTIVITY TO SALIENT STIMULI

TAMARA MARKOVIC*, ARTHUR GODINO, LEANNE HOLT, ANGÉLICA MINIER-TORIBIO, TREVONN GYLES, RITHAKA LINGALA, KANZA CHOUDHRY, ERIC PARISE, FREDDYSON MARTINEZ-RIVERA, ERIC J. NESTLER

ΔFOSB IS A KEY TRANSCRIPTION FACTOR THAT MEDIATES GENE EXPRESSION CHANGES IN THE NUCLEUS ACCUMBENS (NAC) IN RESPONSE TO CHRONIC STIMULI. THE NAC IS COMPOSED OF GABAERGIC MEDIUM SPINY NEURONS (MSNS) THAT EXPRESS EITHER DOPAMINE RECEPTOR I (DI) OR DOPAMINE RECEPTOR 2 (D2). PREVIOUS WORK IN RODENTS SHOWED THAT COCAINE INDUCES ΔFOSB IN DI MSNS, CHRONIC STRESS INDUCES THE PROTEIN IN D2 MSNS IN STRESS-SUSCEPTIBLE BUT IN DI MSNS IN STRESS-RESILIENT ANIMALS, WHILE NATURAL REWARDS INDUCE ΔFOSB IN BOTH. THIS CELL-TYPE-SPECIFIC REGULATION OF ΔFOSB EXPRESSION IN THE NAC CORRELATES WITH DIFFERENTIAL EFFECTS OF THE PROTEIN ON SYNAPTIC PROPERTIES OF MSNS: ΔFOSB DECREASES EXCITATORY SYNAPTIC STRENGTH AND INCREASES SILENT SYNAPSES ONTO DI MSNS, WITH OPPOSITE EFFECTS SEEN FOR D2 MSNS. HOWEVER, NO STUDIES HAVE INVESTIGATED HOW CHANGES IN ΔFOSB EXPRESSION LEVELS IN THE NAC ALTER THE IN VIVO ACTIVITY OF MSNS. TO ADDRESS THIS, WE INJECTED DI-CRE AND D2-CRE MICE WITH CRE-DEPENDENT AAVS THAT EXPRESS A CALCIUM SENSOR AND EPIGENOME-EDITING TOOLS TO EITHER INDUCE OR REPRESS ENDOGENOUS ΔFOSB IN THE NAC. WE RECORDED IN VIVO ACTIVITY OF DI AND D2 MSNS USING FIBER PHOTOMETRY IN RESPONSE TO SOCIAL REWARD, SACCHARIN REWARD, FOOT SHOCK, AND DRUG REWARDS. WE FOUND THAT MANIPULATION OF ΔFOSB PRIMARILY ALTERED MSNS RESPONSES TO SALIENT STIMULI SUCH AS FOOT SHOCK AND COCAINE CONDITIONED PLACE PREFERENCE (CPP). IN FACT, DECREASING ΔFOSB IN DI MSNS ATTENUATED FOOT SHOCK-INDUCED CALCIUM TRANSIENTS, WHILE DECREASING ΔFOSB IN D2 MSNS ENHANCED THEM. SIMILARLY IN A CELL SPECIFIC MANNER, DECREASING ΔFOSB IN DI MSNS AND INCREASING ΔFOSB IN D2 MSNS DECREASES SOCIAL INTERACTION. IN ADDITION, DECREASING ΔFOSB IN DI MSNS ONLY BLOCKS COCAINE CPP AND ATTENUATES NEURONAL ACTIVITY ALIGNED WITH ENTRANCE TO COCAINE PAIRED SIDE. THESE FINDINGS OF OPPOSITE IN VIVO MODULATION OF DI VS. D2 MSN ACTIVITY BY ΔFOSB DEMONSTRATE HOW ΔFOSB INFLUENCES CIRCUIT ACTIVITY AND SHED LIGHT ON CELL-AUTONOMOUS MECHANISMS CONTROLLING BEHAVIORAL RESPONSES.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M2. VTA GLUTAMATERGIC AND GABAERGIC INPUTS FROM THE PEDUNCULOPONTINE TEGMENTAL NUCLEUS AND THEIR ROLE IN MOTIVATED BEHAVIOR AND ON COCAINE-INDUCED CPP BEHAVIOR

HUILING WANG*, RUCHA KULKARNI, QIANWEI SHEN, LIU BING, MARISELA MORALES

PEDUNCULOPONTINE TEGMENTAL NUCLEUS (PPTG) IS COMPOSED OF CHOLINERGIC, GABAERGIC, AND GLUTAMATERGIC NEURONS, WHICH PROVIDE INPUTS TO VENTRAL TEGMENTAL AREA (VTA). HERE, WE DETERMINED THE EXTENT TO WHICH PPTG GLUTAMATERGIC OR GABAERGIC NEURONS INNERVATE THE VTA. BY VTA INJECTION OF RETROGRADE TRACK TRACER FLUOROGOLD (FG) AND PHENOTYPING OF PPTGFG NEURONS, WE FOUND THAT WITHIN THE TOTAL POPULATION OF PPTGFG NEURONS, ~65% EXPRESSED THE VESICULAR GLUTAMATE TRANSPORTER 2 (VGLUT2), ~36% EXPRESSED GLUTAMIC ACID DECARBOXYLASE (GADS) AND ~5% EXPRESSED CHOLINE ACETYLTRANSFERASE (CHAT). WE NEXT ASSESS THE BEHAVIORAL CONSEQUENCE OF VTA PHOTOACTIVATION OF PPTGVGLUT2 OR PPTGVGAT FIBERS. WE EXPRESSED CHANNELRHODOPSINE (CHR2) IN PPTGVGLUT2 NEURONS BY PPTG INJECTION OF AAV2-DIO-CHR2-EYFP IN VGLUT2::CRE MICE OR EXPRESSED CHR2 IN PPTGVGAT NEURONS BY PPTG INJECTION IN VGAT::CRE MICE. WE IMPLANTED OPTICAL PROBE IN VTA TO PHOTOACTIVATE PPTGVGLUT2 OR PPTG VGAT FIBERS IN BEHAVING MICE. CHR2-EYFP MICE WERE TESTED IN A THREE-CHAMBER APPARATUS WHERE THEY RECEIVED OPTICAL STIMULATION WHEN THEY ENTERED THE LASER-PAIRED CHAMBER. WE FOUND THAT PHOTOACTIVATION OF PPTGVGLUT2- > VTA PATHWAY DROVE CONDITIONED PLACE AVERSION, PHOTOACTIVATION OF PPTG VGAT- > VTA PATHWAY DROVE CONDITIONED PLACE PREFERENCE. THESE DATA INDICATE THAT WHILE VTA RELEASE OF GLUTAMATE FROM PPTGVGLUT2 NEURONS PLAYS A ROLE IN AVERSION, THE VTA RELEASE OF GABA FROM PPTG VGAT NEURONS PLAYS A ROLE IN REWARD. GIVEN THAT PPTG HAS BEEN IMPLICATED IN COCAINE REWARD. NEXT, WE DETERMINED THE EXTENT TO WHICH PHOTOACTIVATION OF PPTGVGLUT2- > VTA OR PPTG VGAT- > VTA PATHWAY MODULATES COCAINE SEEKING BEHAVIOR. WE USED CONDITIONED PLACE PREFERENCE (CPP) PROCEDURE, AND OPTICALLY INDUCED VTA RELEASE OF GLUTAMATE OR GABA FROM PPTG INPUTS DURING ACQUISITION, EXPRESSION OR REINSTATEMENT PHASES OF COCAINE-INDUCED CPP. WE FOUND THAT ACTIVATION OF PPTG VGLUT2- > VTA PATHWAY DID NOT AFFECT ACQUISITION OF COCAINE-INDUCED CPP BUT INHIBITED EXPRESSION AND PRIMING-INDUCED REINSTATEMENT OF COCAINE BEHAVIOR. VTA RELEASE OF GABA FROM PPTG VGAT FIBERS DID NOT CHANGE ACQUISITION OF COCAINE-INDUCED CPP BUT REINSTATED COCAINE-INDUCED CPP. WE CONCLUDED THAT VTA GLUTAMATERGIC AND GABAERGIC INPUTS FROM PPTG PLAY A ROLE IN COCAINE-SEEKING BEHAVIOR.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M3. GLUTAMATERGIC AND GABAERGIC M-OPIOID RECEPTOR VTA NEURONS DIFFERENTIALLY MODULATE MOTIVATIONAL AND PHYSIOLOGICAL CONSEQUENCES OF FENTANYL USE

EMILY PREVOST*, DYLAN CAPES, LUCY WARD, MEGAN HEILBRON, DILLON MCGOVERN, DAVID ROOT

THE VENTRAL TEGMENTAL AREA (VTA) IS A MAJOR SITE OF OPIOID REWARD PROCESSING. CANONICALLY, M-OPIOID RECEPTOR (MOR) ACTIVATION INHIBITS GABAERGIC VTA INTERNEURONS, THEREBY DISINHIBITING DOPAMINE RELEASE FROM VTA NEURONS PROJECTING TO THE NUCLEUS ACCUMBENS (NAC). HOWEVER, RECENT STUDIES HAVE IDENTIFIED A POPULATION OF GLUTAMATERGIC MOR-EXPRESSING VTA NEURONS THAT ALSO MODULATE DOPAMINE RELEASE FROM NAC-PROJECTING VTA NEURONS. IN OPPOSITION TO THE CANONICAL MODEL OF GABA-MOR-GATED DISINHIBITION OF DOPAMINE RELEASE, THE VTA GLUTAMATE-MOR CIRCUIT DECREASES NAC DOPAMINE RELEASE THROUGH MOR-GATED REDUCTION IN EXCITATORY DRIVE TO DOPAMINERGIC VTA NEURONS. HERE, WE INVESTIGATED THE ROLE OF VTA GABA-MOR AND GLUTAMATE-MOR SUBPOPULATIONS IN THE REWARDING, AVERSIVE, AND PHYSIOLOGICAL CONSEQUENCES OF OPIOID USE. OPRM1::CRE MICE RECEIVED VTA INFUSIONS OF A CRE-DEPENDENT VECTOR ENCODING SHORT HAIRPIN RNA TO SILENCE GLUTAMATE TRANSMISSION (VIA THE VESICULAR GLUTAMATE TRANSPORTER TYPE 2), GABA TRANSMISSION (VIA THE VESICULAR GABA TRANSPORTER), OR A CONTROL (SCRAMBLED RNA SEQUENCE). MICE WERE THEN TESTED ON FENTANYL-CONDITIONED PLACE PREFERENCE, PRECIPITATED WITHDRAWAL-CONDITIONED PLACE AVERSION, FENTANYL-INDUCED HYPERLOCOMOTION, AND PRECIPITATED WITHDRAWAL SYMPTOM QUANTIFICATION. PRELIMINARY DATA SUGGEST THAT SILENCING GABA TRANSMISSION FROM VTA MOR NEURONS RESULTS IN REDUCED FENTANYL PLACE PREFERENCE AND INCREASED FENTANYL-INDUCED HYPERLOCOMOTION COMPARED TO GLUTAMATE SILENCING AND CONTROL GROUPS. FURTHER RESULTS WILL BE DISCUSSED AT THE MEETING.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M4. INVESTIGATION OF WITHIN-SESSION COCAINE VS. SUCROSE CHOICE BEHAVIOR USING A DRUG-BIASED PROGRESSIVE EFFORT PARADIGM IN RATS

DAVID NOWAK*, MARY ESTES, BAILEY SCHULTZ, JOHN MANTSCH

ALTERED REWARD VALUATION IS A SYMPTOM OF SUBSTANCE USE DISORDER (SUD) THAT COMPROMISES ADAPTIVE DECISION MAKING AND PERPETUATES DRUG MISUSE. GIVEN THE LIMITED TRANSLATIONAL SUCCESS OF THERAPEUTICS IDENTIFIED VIA DRUG-ONLY PARADIGMS, WE HAVE DEVELOPED A NOVEL, PROGRESSIVE EFFORT-BASED METHOD OF INTERROGATING COCAINE VS. SUCROSE CHOICE IN A WITHIN-SESSION, DISCRETE TRIAL FORMAT. RATS GENERALLY PREFER NON-DRUG REWARDS SUCH AS SUCROSE OR SOCIAL INTERACTION OVER DRUG REWARDS SUCH AS COCAINE WHEN OFFERED AT A SIMILAR EFFORT COST. WE TRAINED MALE AND FEMALE RATS TO CHOOSE BETWEEN SUCROSE PELLETS ON A PROGRESSIVE RATIO (PR) SCHEDULE AND COCAINE ON A LOW, FIXED RATIO (FR) SCHEDULE. AFTER TRAINING RATS TO OPERATE IN THIS MARKET, WE OBSERVED A "SWITCH POINT" IN MOST ANIMALS AS THEY TRANSITION FROM EARLY SUCROSE (LOW-EFFORT SUCROSE) TO LATE COCAINE CHOICE (HIGH-EFFORT SUCROSE). FOLLOWING INITIAL SUCROSE TRAINING AND A TWO-WEEK PERIOD OF DAILY COCAINE ACCESS (2HR), 8 DAILY CHOICE SESSIONS WERE ADMINISTERED. EACH CHOICE SESSION CONSISTED OF 21-DISCRETE TRIALS IN WHICH A DECISION AT EITHER LEVER COULD OCCUR. ONCE A REQUIREMENT WAS ACHIEVED, THE REWARD WAS ADMINISTERED AND A TIMEOUT OCCURRED BEFORE THE NEXT TRIAL, IN WHICH THE COST OF SUCROSE INCREASED. PRELIMINARY RESULTS INDICATE THAT FEMALE RATS SWITCH FROM SUCROSE TO COCAINE IN FEWER TRIALS THAN MALES AT A MODERATE COCAINE DOSE OF 0.5 MG/KG/INFUSION. AT A HIGHER DOSE (0.8 MG/KG/INF) THERE IS NO DIFFERENCE IN SWITCH POINT BETWEEN MALE AND FEMALE RATS. THERE IS A DOSE DEPENDENT RELATIONSHIP BETWEEN COCAINE PREFERENCE AND COCAINE DOSE IN MALE, BUT NOT FEMALE RATS. ONGOING STUDIES ARE EXAMINING CHOICE BEHAVIOR AT A LOW COCAINE DOSE (0.2 MG/KG/INF). WHEN COCAINE IS REPLACED WITH SALINE, MALE AND FEMALE RATS TRANSITION TO GREATER SUCROSE PREFERENCE. FUTURE STUDIES WILL PROBE THE EFFECTS OF PHARMACOLOGICAL AND ENVIRONMENTAL MANIPULATIONS (E.G., STRESS) ON DRUG CHOICE BEHAVIOR.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M5. PRESYNAPTIC KAPPA OPIOID CONTROL OF A GABAERGIC STRESS-SENSITIVE CIRCUIT INVOLVED IN REINSTATEMENT

VALENTINA MARTINEZ DAMONTE*, LYDIA G. BAYLEY, TRAVIS BROWN, JULIE A. KAUER

GABAERGIC SYNAPSES IN THE VENTRAL TEGMENTAL AREA (VTA) PLAY A PIVOTAL ROLE IN REGULATING THE EXCITABILITY OF DOPAMINE NEURONS. BOTH DRUGS OF ABUSE AND ACUTE STRESS BLOCK PLASTICITY AT THESE SYNAPSES. WE HAVE PREVIOUSLY SHOWN THAT A SINGLE ACUTE EXPOSURE TO COLD-WATER SWIM STRESS INDUCES REINSTATEMENT OF COCAINE SEEKING VIA KAPPA OPIOID RECEPTOR (KOR) ACTIVATION. THIS STRESSOR ALSO BLOCKS A NITRIC OXIDE-INDUCED POTENTIATION OF INHIBITORY POSTSYNAPTIC CURRENTS (LTPGABA) ONTO VTA DOPAMINE CELLS IN BRAIN SLICES.

HERE WE IDENTIFIED THE KOR AND DYNORPHIN CIRCUIT ELEMENTS INVOLVED IN STRESS-INDUCED BLOCK OF LTPGABA. WE ALSO CONFIRMED THE ABILITY OF FOOT SHOCK, A STRESSOR THAT PROMOTES REINSTATEMENT IN A MORE ROBUST MANNER THAN SWIM STRESS, TO BLOCK LTPGABA AND TESTED THE EFFECT OF LOCAL KOR ACTIVATION ON COCAINE-INDUCED PLACE PREFERENCE (CPP).

KOR ACTIVATION IS SUFFICIENT FOR STRESS TO BLOCK LTPGABA AND HENCE DELETING KORS FROM THE RELEVANT CELL TYPE SHOULD PREVENT THIS. FIRST, WE USED A GLOBAL KOR KNOCKOUT AND FOUND THAT AS EXPECTED IN THIS GENETICALLY MODIFIED MOUSE STRESS NO LONGER BLOCKS LTPGABA. TO IDENTIFY THE LOCATION OF THE RELEVANT KORS, USING A CONDITIONAL KNOCKOUT APPROACH WE SELECTIVELY DELETED KORS FROM POSTSYNAPTIC DOPAMINE NEURONS. THIS DELETION DOES NOT PREVENT STRESS-INDUCED LOSS OF LTPGABA. CONVERSELY, WHEN WE SELECTIVELY RECRUITED NUCLEUS ACCUMBENS (NAC) GABAERGIC TERMINALS (WHICH EXHIBIT LTPGABA) IN WHICH WE HAD DELETED KORS, WE FOUND THAT THIS REMOVAL PREVENTS STRESS-INDUCED BLOCK OF LTPGABA.

IN ADDITION TO SENDING GABAERGIC PROJECTIONS TO THE VTA, THE NAC IS ONE OF THE MAJOR DYNORPHINERGIC INPUTS TO THIS REGION. USING CHEMOGENETICS IN PDYNCRE MICE, WE ACTIVATED DYNORPHIN-CONTAINING NEURONS IN THE NAC AND TESTED WHETHER THIS ALONE COULD BLOCK LTPGABA. WE ARE CURRENTLY EXPLORING WHETHER ACTIVATION OF ANOTHER RELEVANT DYNORPHIN INPUT FROM THE LATERAL HYPOTHALAMUS BLOCKS LTPGABA.

FINALLY, WE CONDUCTED EXPERIMENTS TO ASSESS WHETHER THE KOR AGONIST U50,488 MICROINJECTED INTO THE VTA ALTERS COCAINE CPP. IN FUTURE STUDIES WE WILL TEST IF THIS MANEUVER MIMICS STRESS-INDUCED COCAINE REINSTATEMENT IN SELF-ADMINISTRATION ASSAYS.

OUR FINDINGS ESTABLISH KORS IN GABAERGIC PROJECTIONS TO THE VTA AS A PROMISING TARGET FOR THERAPEUTIC INTERVENTIONS AIMED AT MITIGATING STRESS-TRIGGERED REINSTATEMENT.

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M6. SCREENING FOR NOVEL ALLOSTERIC MODULATORS OF THE HUMAN DOPAMINE TRANSPORTER

FUYU YANG*, YIBIN XU, SAMANTHA ITA, OLE MORTENSEN

APPROXIMATELY 1.3 MILLION INDIVIDUALS IN THE POPULATION GRAPPLE WITH COCAINE USE DISORDER, AND THERE ARE AN ESTIMATED 16,000 ANNUAL OVERDOSE FATALITIES ATTRIBUTED TO COCAINE ABUSE. DESPITE THESE SIGNIFICANT ISSUES, THE COMPLEXITY OF COCAINE WITHDRAWAL PROFILES HAS HINDERED THE DEVELOPMENT OF EFFECTIVE TREATMENTS FOR THIS DISORDER.
COCAINE IS A POTENT CENTRAL NERVOUS SYSTEM STIMULANT THAT EXERTS ITS EFFECTS BY INTERACTING WITH THE DOPAMINE TRANSPORTER (DAT) AT THE ORTHOSTERIC BINDING SITE, PREVENTING THE REUPTAKE OF DOPAMINE FROM THE SYNAPTIC CLEFT. THIS MECHANISM RESULTS IN AN EXCESSIVE ACCUMULATION OF DOPAMINE IN THE SYNAPSE, LEADING TO THE OVERSTIMULATION OF POSTSYNAPTIC NEURONS. RECENTLY, OUR LABORATORY HAS FOUND KM822, AN ALLOSTERIC MODULATOR TO DAT, THAT EFFECTIVELY OBSTRUCTS COCAINE FROM BINDING TO DAT WHILE STILL PERMITTING PARTIAL DOPAMINE REUPTAKE. THE AIM OF THIS STUDY IS TO CHARACTERIZE A PANEL OF KM822 ANALOGS AND THEIR EFFECTS ON DAT FUNCTION. BY UTILIZING MUTATIONS OF SPECIFIC RESIDUES ON DAT, WE CAN PERFORM STRUCTURAL AND FUNCTIONAL STUDIES, AND IDENTIFY CRITICAL STRUCTURAL DETERMINANTS OF THE ALLOSTERIC EFFECTS OF THESE COMPOUNDS. THROUGH THIS STUDY, WE HOPE TO IDENTIFY POTENTIAL TREATMENT CANDIDATES FOR COCAINE USE DISORDER.
RVENTIONS AIMED AT MITIGATING STRESS-TRIGGERED REINSTATEMENT.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M7. A RANDOMIZED TRIAL OF THE EFFECTS OF COMT INHIBITION ON SUBJECTIVE RESPONSE TO ALCOHOL: MODERATION BY BASELINE COMT ACTIVITY AND MEDIATION OF ALCOHOL SELF-ADMINISTRATION

JOSEPH SCHACHT*, MATTHEW KUBICKI, RAYMOND ANTON

POOR INHIBITORY CONTROL AND ENHANCED SUBJECTIVE RESPONSE TO ALCOHOL ARE INTERRELATED RISK FACTORS FOR ALCOHOL USE DISORDER (AUD) THAT SHARE UNDERLYING NEURAL SUBSTRATES, INCLUDING DOPAMINE SIGNALING IN THE RIGHT PREFRONTAL CORTEX, A POTENTIAL TARGET FOR PHARMACOLOGICAL INTERVENTION. CORTICAL DOPAMINE INACTIVATION IS PRIMARILY REGULATED BY CATECHOL-O-METHYLTRANSFERASE (COMT), AN ENZYME WITH LARGE VARIATIONS IN ACTIVITY AS A FUNCTION OF VARIATION AT THE COMT RS4680 (VAL158MET) SINGLE NUCLEOTIDE POLYMORPHISM. IN A PREVIOUS RANDOMIZED, PLACEBO-CONTROLLED TRIAL OF THE COMT INHIBITOR TOLCAPONE (200 MG TID) IN NON-TREATMENT-SEEKING PARTICIPANTS WITH AUD, WE REPORTED THAT TOLCAPONE, RELATIVE TO PLACEBO, REDUCED ALCOHOL SELF-ADMINISTRATION ONLY AMONG RS4680 VAL-ALLELE HOMOZYGOTES, WHOSE COMT ACTIVITY IS HIGH RELATIVE TO MET-ALLELE CARRIERS.

HERE, WE CONDUCTED SECONDARY ANALYSES OF THE EFFECTS OF TOLCAPONE AND BASELINE COMT ACTIVITY, AS INDEXED BY BOTH RS4680 GENOTYPE AND AN ENZYMATIC ACTIVITY ASSAY, ON SUBJECTIVE RESPONSE TO ALCOHOL IN A BAR-LABORATORY PARADIGM AMONG PARTICIPANTS IN THE PREVIOUS TRIAL (N=60).

TOLCAPONE, RELATIVE TO PLACEBO, DID NOT AFFECT ALCOHOL-INDUCED STIMULATION OR SEDATION. HOWEVER, BASELINE COMT ACTIVITY MODERATED ITS EFFECTS ON BOTH OUTCOMES, SUCH THAT TOLCAPONE-TREATED PARTICIPANTS WITH HIGHER BASELINE COMT ACTIVITY HAD LESS STIMULATION (P=0.008) AND SEDATION (P=0.053) RELATIVE TO PARTICIPANTS WITH LOWER BASELINE COMT ACTIVITY AND TO PLACEBO. ADDITIONALLY, ALCOHOL-INDUCED STIMULATION SIGNIFICANTLY MEDIATED THE INTERACTING EFFECTS OF BASELINE COMT ACTIVITY AND TOLCAPONE ON BAR-LABORATORY SELF-ADMINISTRATION.

THESE DATA SUGGEST THAT TOLCAPONE MAY MORE EFFECTIVELY REDUCE SUBJECTIVE RESPONSE TO ALCOHOL AMONG INDIVIDUALS WITH PRE-EXISTING HIGH COMT ACTIVITY AND THAT THIS EFFECT MAY ACCOUNT FOR ITS REDUCTION OF ALCOHOL CONSUMPTION AMONG THESE INDIVIDUALS.

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MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M8. GENDER DIFFERENCES IN ACUTE COCAINE RESPONSE: EXPLORING DAT REGULATION THROUGH MKP3 OVEREXPRESSION IN RATS

RASHMI TANTRI*, STACIA LEWANDOWSKI, OLE MORETENSEN

COCAINE HAS A HIGH POTENTIAL OF BEING MISUSED, LEADING TO COCAINE USE DISORDER. DEPENDENCE ON COCAINE RESULTS IN COMPULSIVE DRUG SEEKING BEHAVIOR. ALTHOUGH THIS DISORDER AFFECTS ABOUT 2 MILLION PEOPLE, THERE IS NO APPROVED MEDICATION TO TREAT THIS HEALTH ISSUE. COCAINE ACTS ON THE REWARD REGION LOCATED IN THE BRAIN'S LIMBIC SYSTEM. DOPAMINE, THE KEY NEUROTRANSMITTER IN THIS REGION IS CENTRAL TO MEDIATING BEHAVIORS INVOLVED IN MOTIVATION, PLEASURE, AND LEARNING. FOLLOWING ITS RELEASE INTO THE SYNAPSE OF NEURONS, DOPAMINE IS REMOVED BY THE DOPAMINE TRANSPORTERS (DAT). COCAINE PRODUCES ITS EFFECTS BY BINDING TO DAT ON THE PRE-SYNAPTIC NEURONAL CELL SURFACE AND INHIBITING THE REUPTAKE OF DOPAMINE FROM THE SYNAPSE. THIS LEADS TO ACCUMULATION OF EXCESS DOPAMINE IN THE SYNAPTIC CLEFT, CAUSING EUPHORIA IN THE SUBJECTS. WE PREVIOUSLY FOUND A MAPK PHOSPHATASE (MKP3) THAT ATTENUATES SOME EFFECTS OF COCAINE IN RAT BEHAVIOR AND ENHANCES THE ACTIVITY OF DAT ON THE CELL SURFACE BY REGULATING DYNAMIN-DEPENDENT ENDOCYTOSIS. MOREOVER, WHEN RATS ARE GIVEN COCAINE, THERE ARE 2 TYPES OF LOCOMOTOR RESPONSES: HIGH AND LOW RESPONSE. WE FOUND THAT THE OVEREXPRESSION OF MKP3 IN MALE RATS PRIMARILY AFFECTS THE HIGH RESPONDING RATS. HERE, WE STUDIED THE ACUTE COCAINE EXPOSURE IN NAÏVE MALE AND FEMALE RATS AND CONFIRMED PREVIOUS FINDINGS THAT MKP3 INCREASES DAT SURFACE LEVELS. HOWEVER, WE FOUND THAT THERE IS A SIGNIFICANT DIFFERENCE IN HOW MALE AND FEMALE RATS RESPOND TO COCAINE AS WE FOUND A SIGNIFICANT DIFFERENCE IN DAT LEVELS BETWEEN MALE AND FEMALE RATS, WITH MALES HAVING MORE DAT SURFACE LEVELS AT 30 MINS TIME POINT COMPARED TO FEMALES. TO FURTHER STUDY THIS DIFFERENCE, WE PLAN TO STUDY ACUTE COCAINE EXPOSURE IN MKP3 OVEREXPRESSING FEMALE RATS USING THE LOCOMOTOR TEST AND STUDYING DAT SURFACE EXPRESSION AND UPTAKES AND CORRELATE THESE WITH HIGH VERSUS LOW RESPONDERS IN THE LOCOMOTION ASSAY. HOPEFULLY, OUR RESULTS WILL PROVIDE A BETTER UNDERSTANDING OF PROCESSES INVOLVED IN DAT REGULATION.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M9. DEVELOPMENT OF WIRELESS EQUIPMENT FOR AUTONOMOUS RODENT INFUSION TASKS

EUNYOUNG JEONG, FLORA D'OLIVEIRA DA SILVA, ANISHA REIMERT, KYLE PARKER, JAE-WOONG JEONG, JORDAN MCCALL, NICOLAS MASSALY*

DESPITE MAJOR ADVANCES IN BOTH THE PRECLINICAL AND CLINICAL ADDICTION FIELDS, THE NUMBER OF US CITIZENS AFFLICTED BY SUBSTANCE USE DISORDERS (SUDS) AND THE LETHAL OVERDOSE OUTCOMES HAS CONTINUOUSLY INCREASED OVER THE PAST TWO DECADES. TO TACKLE THIS ALARMING HEALTH ISSUE, INTRAVENOUS SELF-ADMINISTRATION PROCEDURES HAS BEEN USED THE GOLD STANDARD FOR TRANSLATIONAL RODENT SUD MODELS. HOWEVER, DESPITE BEING ONE OF THE MOST RELIABLE PROCEDURES, WITH CLEAR FACE VALIDITY, THIS PROCEDURE IS STILL LIMITED BY ITS TETHERED NATURE, CONSTRAINING ITS USE TO RESTRICTED SPACES IN WHICH RODENTS ARE EXPOSED TO UNENRICHED ENVIRONMENTS WITH LIMITED OR NO ACCESS FOOD, WATER, OR SOCIAL INTERACTION. AVAILABILITY FOR VOLITIONAL SOCIAL INTERACTION AND NON-SOCIAL REWARDS SUCH AS WHEEL RUNNING, AND OPERANT-DELIVERED PALATABLE FOODS CAN DECREASE THE CONSUMPTION, THE ESCALATION, AND THE REINSTATEMENT IN DRUG SELF-ADMINISTRATION. TO TACKLE THOSE LIMITATIONS, WE ARE DEVELOPING A WIRELESS-CONTROLLED WEARABLE DRUG RESERVOIR CONNECTED TO INTRAVENOUS INDWELLING CATHETER AND USE BLUETOOTH MESH TECHNOLOGY TO ENABLE HOMECAGE-BASED INTRAVENOUS SELF-ADMINISTRATION PROCEDURES. USING A COMBINATION OF 3D PRINTED ENCAPSULATION AND COMMERCIALLY AVAILABLE REPROGRAMMED MICRO-PUMPS TOGETHER WITH OPULSE OXIMETER, WE DEMONSTRATE THAT WIRELESS INFUSION OF FENTANYL (50UG.KG-1) IS SUFFICIENT TO PRODUCE RESPIRATORY DEPRESSION IN RATS. FURTHER, WE DEMONSTRATE THAT OUR WEARABLE DEVICES DO NOT IMPAIR HORIZONTAL LOCOMOTION AND PERFORMANCES IN OPERANT SELF-ADMINISTRATION IN ADULT MALE AND FEMALE RATS. TOGETHER, THOSE NEWLY DEVELOPED WEARABLE DEVICES SEEM TO BE ADAPTED TO 1) PERFORM HOME CAGE DRUG SELF-ADMINISTRATION AND 2) BE COMBINED WITH OTHER TETHERED APPROACHES TO INVESTIGATE NEURONAL CIRCUITS AND ENSEMBLE RESPONSIBLE FOR CONSUMPTION, ESCALATION, AND REINSTATEMENT OF DRUG USE.
OVERALL, WE ENVISION THAT THESE NEW OPEN-SOURCE APPROACHES WILL BROADEN THE TRANSLATIONAL VALUE OF PRE-CLINICAL SUD MODELS BY ENABLING NEW EXPERIMENTAL DESIGNS TO IMPROVE CURRENT STRATEGIES AIMING AT DEVELOPING SUBSTANCE USE DISORDERS TREATMENTS.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M10. CHRONIC ALCOHOL ALTERS ENDOCANNABINOID MODULATION OF ORBITOSTRIATAL ACTIVITY DURING GOAL-DIRECTED BEHAVIOR

NATALIE PAREDES*, JIALIN HE, BRETT JOHNSON, CHRISTINA GREMEL

CHRONIC ALCOHOL EXPOSURE PRODUCES LONG-LASTING DISRUPTIONS TO ACTION CONTROL PROCESSES, INCLUDING GOAL-DIRECTED CONTROL. ALCOHOL-INDUCED LOSS OF GOAL-DIRECTED CONTROL IS DUE TO REDUCED GLUTAMATERGIC TRANSMISSION FROM ORBITAL FRONTAL CORTEX (OFC) PROJECTIONS ONTO DORSAL STRIATUM (DS) SPINY NEURONS EXPRESSING THE DOPAMINE TYPE-1 RECEPTOR. LIKEWISE, IN VIVO MONITORING OF OFC-DS TERMINAL CALCIUM ACTIVITY DURING ACTION CONTROL FOUND INCREASED CALCIUM (CA2+) MODULATION DURING ACTIONS BUT REDUCED CA2+ MODULATION DURING REWARD-RELATED EPOCHS IN ALCOHOL-EXPOSED MICE. EX VIVO WORK FOUND THE REDUCED GLUTAMATERGIC TRANSMISSION AND CA2+ MODULATION AT OFC-DS TERMINALS WERE DUE TO INCREASED RETROGRADE ENDOCANNABINOID (ECB) SIGNALING. HOWEVER, IT IS UNCLEAR WHETHER CHRONIC ALCOHOL ALTERS THE RECRUITMENT AND TEMPORAL DYNAMICS OF ECB SIGNALING AT OFC-DS TERMINALS DURING ONGOING BEHAVIOR. WE USED NOVEL STATE-OF-THE-ART GENETICALLY-TARGETED FLUORESCENT SENSORS (GRABECB2.0) TO MONITOR ECB ACTIVITY DURING ACTION CONTROL. WE USED VIRAL APPROACHES TO TARGET THESE CONSTRUCTS TO OFC-DS PROJECTION NEURONS WITH OPTIC FERRULES POSITIONED ABOVE OFC-DS TERMINALS. MICE THEN UNDERWENT CHRONIC INTERMITTENT AIR OR ETHANOL VAPOR EXPOSURE (CIE) PROCEDURES FOR FOUR WEEKS. POST ACUTE WITHDRAWAL, MICE WERE FOOD-RESTRICTED AND TRAINED TO PRESS AN OPERANT LEVER FOR FOOD REWARD UNDER A SCHEDULE THAT BIASES GOAL-DIRECTED CONTROL OVER BEHAVIOR. FIBER PHOTOMETRY WAS USED TO EXAMINE THE TEMPORAL DYNAMICS OF ECB SIGNALING AT OFC-DS TERMINALS DURING ACTION CONTROL. WE FOUND ECB MODULATION OF OFC TERMINALS DURING DIFFERENT EPOCHS OF ACTION CONTROL. IN CIE MICE WE SAW A DECREASE IN ECB SIGNALING DURING ACTION-RELATED EPOCHS AND LARGE INCREASE IN ECB SIGNALING DURING REWARD-RELATED EPOCHS. WE ARE TAKING A PHARMACOLOGICAL APPROACH TO PROBE THE CONTRIBUTION OF SPECIFIC ECBS TO THE OBSERVED DYNAMICS. THESE DATA SHED LIGHT ON HOW CHRONIC ALCOHOL DEPENDENCE ABERRANTLY ALTERS NEURAL MECHANISMS SUPPORTING ACTION CONTROL.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

MII. RIBOSOMAL HETEROGENEITY AND SYNAPTIC DYSREGULATION: NEW INSIGHTS INTO MOOD DISORDER MECHANISMS AND TREATMENT

RAMMOHAN SHUKLA*, XIAOLU ZHANG, MAHMOOD ELADAWI, STEPHEN PREVOZNIK, WILLIAM RYAN, TRUPTI DEVALE, BARKHA RAMNANI, KRISHNAMURTHY MALATHI, ETIENNE SIBILLE, ROBERT MCCULLUMSMITH, TOSHIFUMI TOMODA

MOOD DISORDERS SPAN A CONTINUUM AND OFTEN PRESENT WITH AMBIGUOUS BOUNDARIES. FOR EFFECTIVE TREATMENTS, IT'S CRUCIAL TO UNDERSTAND THE UNDERLYING MECHANISMS DRIVING THESE DISORDERS. EXISTING TREATMENTS PRIMARILY FOCUS ON NEUROTRANSMISSION AND RECEPTOR-BASED MODELS. HOWEVER, DUE TO NOTABLE TREATMENT RESISTANCE, THESE FAIL TO FULLY ENCOMPASS MOOD DISORDER COMPLEXITIES. THE AUTHORS HYPOTHESIZED THAT COMPARING MOLECULAR DATA FROM CHRONIC STRESS AND MAJOR DEPRESSIVE DISORDER (MDD) EXPERIMENTAL SYSTEMS MIGHT PROVIDE DEEPER INSIGHT. THEY ANALYZED TRANSCRIPTOMIC PROFILES FROM POSTMORTEM MDD BRAIN TISSUES AND MICE SUBJECTED TO CHRONIC VARIABLE STRESS (CVS), IDENTIFYING A DOWNREGULATION IN RIBOSOMAL PROTEIN GENES (RPGS) AND AN UPREGULATION IN ASSOCIATED RP-PSEUDOGENES IN BOTH CONDITIONS. GENE CO-EXPRESSION ANALYSIS USING ALTERED RPGS COMMON BETWEEN THE MDD AND CVS GROUPS AS SEEDS, REVEALED THAT THESE ALTERED RPGS REGULATED SYNAPTIC CHANGES ACROSS BOTH GROUPS VIA A RP-PSEUDOGENE DRIVEN MECHANISM. IN-VITRO STUDIES HIGHLIGHTED THIS DYSREGULATION AS A GLUCOCORTICOID-INDUCED STRESS RESPONSE. ADDITIONAL, IN-SILICO FINDINGS SHOWED THAT THE RPG-DYSREGULATION REVERSED DURING MDD REMISSION. THEIR FINDINGS SUPPORT THE HYPOTHESIS THAT STRESS-INDUCED RPG CHANGES MODIFY RIBOSOMAL STOICHIOMETRY, WHICH IN SYNAPSES CAN DYSREGULATE HOMEOSTATIC PLASTICITY IN MDD AND CHRONIC STRESS-RELATED MOOD DISORDERS. THEY PROPOSE A MODEL ELUCIDATING RIBOSOMAL HETEROGENEITY'S ROLE IN THE DIVERSE MANIFESTATIONS OF DEPRESSION AND OTHER MOOD DISORDERS.

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

MI2. SUBJECTIVE AND PHARMACODYNAMIC EFFECTS OF THE NOVEL 5-HT2A RECEPTOR AGONIST GM-2505 IN HEALTHY VOLUNTEERS SHOW HIGH TRANSLATABILITY FROM RODENT DATA AND HOLD PROMISE FOR FUTURE DEVELOPMENT IN PATIENTS WITH DEPRESSION

ZOË HUGHES*, EDWARD CHRISTIAN, DINO DVORAK, LASZLO KISS, ADAM KLEIN, SHANE RAINES, JONATHAN SPORN, DANIEL UMBRICHT, JASON WINTERS, ANDREW KRUEGEL, GERARD MAREK

GM-2505 IS A NOVEL 5-HT2A AGONIST/5-HT RELEASER DESIGNED TO HAVE A HALF-LIFE INTERMEDIATE BETWEEN DMT AND PSILOCYBIN. HERE WE COMPARE THE PK/PD RELATIONSHIP FOR GM-2505 GENERATED IN HEALTHY VOLUNTEERS TO RODENT DATA.

THE PHI STUDY EVALUATED THE SAFETY, PK AND PD EFFECTS OF SINGLE ASCENDING DOSES OF GM-2505 (0.34-20MG). GM-2505 WAS SAFE AND WELL TOLERATED AT THE DOSES TESTED AND ACHIEVED DOSE PROPORTIONAL INCREASES IN EXPOSURE WITH A MEDIAN T½ OF 45 MIN. GM-2505 CAUSED TEAES CONSISTENT WITH A PSYCHEDELIC INCLUDING ALTERED STATES OF CONSCIOUSNESS AND PERCEPTION. TRANSIENT INCREASES IN BLOOD PRESSURE WERE OBSERVED WITH DOSES ≥10 MG. GM-2505 PRODUCED DOSE-DEPENDENT SUBJECTIVE EFFECTS ON 5D-ASC AND MEQ-30 AS WELL AS REDUCING LOW-FREQUENCY EEG POWER (ESPECIALLY ALPHA 8-13HZ) AT LOWER DOSES AND ALSO INCREASING GAMMA POWER AT HIGHER DOSES.

IN RATS, GM-2505 (0.03-10MG/KG) PRODUCED A DOSE-DEPENDENT INCREASE IN HEAD TWITCHES AND WET DOG SHAKES (PEAK @ 1MG/KG). GM-2505 (0.3-3MG/KG) PRODUCED CLEAR EFFECTS ON EEG POWER MEASURED IN TELEMETERED RATS WITH SKULL SCREW ELECTRODES. AT 1-3MG/KG LOW FREQUENCY EEG POWER WAS DECREASED, AND 3MG/KG CAUSED AN INCREASE IN GAMMA POWER. ANTIDEPRESSANT EFFICACY OF GM-2505 (0.3 AND 1MG/KG) WAS SEEN IN THE CHRONIC MILD STRESS PARADIGM (CMS) IN WKY RATS. GM-2505 (1-10MG/KG) DISPLACED [3H]CIMBI-36 IN VIVO BINDING WITH AN ED50 OF 0.32 MG/KG.

THE PK AND PD EFFECTS OF GM-2505 WERE CONSISTENT WITH AN INTERMEDIATE DURATION 5-HT2A AGONIST. THERE WAS A STRONG RELATIONSHIP BETWEEN PLASMA EXPOSURE, SUBJECTIVE EFFECTS AND EEG. CLINICAL PLASMA EXPOSURES ASSOCIATED WITH ROBUST PD EFFECTS WERE WELL ALIGNED WITH EXPOSURE CAUSING PEAK HEAD TWITCH IN RATS. DOSES OF GM-2505 WITH EFFICACY IN CMS ACHIEVED 25-50% 5-HT2A RECEPTOR OCCUPANCY CONSISTENT WITH THE CLINICAL REPORT ON PSILOCYBIN. SEEING STRONG TRANSLATABILITY OF PRECLINICAL PD EFFECTS PROVIDES CONFIDENCE IN THE PROSPECTIVE TRANSLATION OF GM-2505'S PRECLINICAL ANTIDEPRESSANT EFFECTS TO HUMAN SUBJECTS.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

MI3. A SUBSTANTIA NIGRA TO DORSOLATERAL STRIATUM PATHWAY MEDIATES THE EFFECTS OF FEMALE ESTROUS CYCLE ON FEAR EXTINCTION AND IS A NOVEL TARGET FOR THE PREVENTION OF RELAPSE

ALYSSA HOHORST*, MARGARET TANNER, LAREINA ALVAREZ, REMLA ABDUL, REBECCA HAN, JESSICA WESTERMAN, ESTEBAN LOETZ, ERIK OLESON, BENJAMIN GREENWOOD

THE IMPAIRED INHIBITION OF LEARNED FEAR IS A FEATURE OF STRESS-RELATED PSYCHIATRIC DISORDERS SUCH AS GENERALIZED ANXIETY DISORDER AND POST-TRAUMATIC STRESS DISORDER. EXTINCTION-BASED EXPOSURE THERAPY CAN SUCCESSFULLY TREAT THESE DISORDERS; HOWEVER, EFFICACY IS LIMITED, AND FEAR MEMORIES REMAIN VULNERABLE TO RELAPSE. ALTHOUGH WOMEN ARE MORE LIKELY TO EXPERIENCE STRESS-RELATED DISORDERS THAN MEN, SEX DIFFERENCES IN EXTINCTION AND RELAPSE REMAIN UNDERSTUDIED. EXTINCTION MEMORY RETENTION IN FEMALE RATS IS DEPENDENT ON ESTROUS PHASE DURING EXTINCTION. HOWEVER, HOW ESTROUS PHASE DURING EXTINCTION IMPACTS RELAPSE, HOW RELAPSE COMPARES BETWEEN SEXES, AND MECHANISMS UNDERLYING ESTROUS CYCLE-MODULATION OF EXTINCTION AND RELAPSE ARE UNKNOWN. WE OBSERVED THAT ADULT, FEMALE LONG EVANS RATS EXPOSED TO CUED FEAR EXTINCTION DURING PHASES WITH HIGH OVARIAN HORMONES (PROESTRUS AND ESTRUS; PRO/EST) HAVE REDUCED RELAPSE COMPARED TO MALES AND FEMALES EXPOSED TO EXTINCTION DURING PHASES WITH LOW OVARIAN HORMONES (METESTRUS AND DIESTRUS; MET/DI). USING FAST-SCAN CYCLIC VOLTAMMETRY, WE OBSERVED THAT FEMALES IN PRO/EST HAVE HIGHER STIMULUS-EVOKED STRIATAL DA THAN MALES AND FEMALES IN MET/DI. THIS IS IMPORTANT, SINCE DA NEURONS ORIGINATING IN THE SUBSTANTIA NIGRA PROJECTING TO THE DORSOLATERAL STRIATUM (DLS;SN-DLS) CONTRIBUTE TO STIMULUS-RESPONSE LEARNING, WHICH CAN BE RESISTANT TO MEMORY-DISRUPTING PHENOMENA THOUGHT TO CONTRIBUTE TO RELAPSE. WE OBSERVED THAT CHEMOGENETIC INHIBITION OF THE SN-DLS PATHWAY DURING EXTINCTION RESTORES RELAPSE IN FEMALES EXPOSED TO EXTINCTION DURING PRO/EST. FURTHERMORE, WE FOUND THAT CHEMOGENETIC ACTIVATION OF THE SN-DLS PATHWAY DURING EXTINCTION IS SUFFICIENT TO REDUCE RELAPSE IN MALES. THE EFFECTIVENESS AND REGIONAL SPECIFICITY OF THE INTERSECTIONAL CHEMOGENETIC APPROACHES WAS VERIFIED WITH VOLTAMMETRY. THESE DATA SUGGEST THAT A SN-DLS DA PATHWAY MEDIATES THE EFFECTS OF FEMALE OVARIAN HORMONES DURING FEAR EXTINCTION ON LATER RELAPSE AND IS A NOVEL TARGET FOR THE REDUCTION OF RELAPSE FOLLOWING FEAR EXTINCTION. RESULTS HAVE CLINICAL IMPLICATIONS FOR EXTINCTION-BASED THERAPIES IN BOTH SEXES.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

MI4. MECHANISMS BEHIND WORRY AND THEIR ROLE IN ANXIETY

AN YEE LOW*, KARL FRISTON, MICHAEL MOUTOUSSIS

ANXIETY DISORDERS SIGNIFICANTLY BURDEN THE INDIVIDUAL AND SOCIETY. CENTRAL TO ANXIETY IS WORRY, WHICH DIRECTLY CAUSES ANXIETY'S DISTRESSING NATURE. HOWEVER, WORRY CAN ALSO BE MAINTAINED BY BELIEFS THAT IT IS HELPFUL, AND LITERATURE INDICATES IT IMPROVES PROBLEM-SOLVING AND PERCEIVED CONTROL. THIS SUGGESTS THAT ADAPTIVE WORRY IS PART OF SEARCHING FOR SOLUTIONS TO AVERT THREATS, BUT MALADAPTIVE WORRIERS ARE UNABLE TO STOP THIS STRATEGY IF IT PROVES TO BE INEFFECTIVE.

MATHEMATICAL MODELLING PROVIDES AN AVENUE TO TEST THIS HYPOTHESIS. TAKING INTO ACCOUNT ESTABLISHED AND CONTEMPORARY MODELS OF WORRY, WE PRESENT AN EVIDENCE ACCUMULATION MODEL IN THE REINFORCEMENT LEARNING FRAMEWORK, WHICH AIMS TO MAKE EXTERNAL THE INTERNAL PROCESSES OF WORRY BY OPERATIONALISING WORRY AS PUNISHMENT-AVOIDING INFORMATION SEEKING. THE EXTENT OF REPETITIVENESS IN INFORMATION SEARCH – DISPROPORTIONATE TO ITS UTILITY – IS PROPOSED TO DETERMINE THE DIFFERENCE BETWEEN MALADAPTIVE AND ADAPTIVE THOUGHT PATTERNS.

EXPERIMENTALLY, TO PROVIDE AN EMPIRICAL BASIS FOR MODELLING, AN ECOLOGICALLY VALID PARADIGM HAS BEEN DEVELOPED, SIMILARLY RENDERING EXPLICIT AND MEASURABLE THE SEARCH OF INFORMATION DURING WORRY TO AVOID AN AVERSIVE OUTCOME. TESTING IS CURRENTLY UNDERGOING FOR THIS STUDY (APPROX. N = 500), BUT PRELIMINARY RESULTS HAVE BEEN OBTAINED. A KEY FINDING IS THAT A LOW OBSERVED PROBABILITY OF SUCCESS INCREASES SEARCH ATTEMPTS – SUGGESTING A COMPENSATORY, OR ADAPTIVE, MECHANISM, WHICH MAY DRIVE WORRY. INTRIGUINGLY, THIS OCCURRED IN SOME PARTICIPANTS BUT NOT OTHERS, SUGGESTING A DIFFERENTIATING FACTOR WHICH MAY IN FACT PREDISPOSE THEM TO WORRY.

TIED TOGETHER, THIS SET OF STUDIES WILL PROVIDE CRUCIAL INSIGHTS INTO WHAT CAUSES AND MAINTAINS WORRY ON BOTH A COMPUTATIONAL AND BEHAVIOURAL LEVEL OF ANALYSIS. THIS IS KEY, POTENTIALLY, TO THE TRANS-DIAGNOSTIC UNDERSTANDING OF ANXIETY AND RELATED DISORDERS, AND IN THE DEVELOPMENT OF INTERVENTIONS SUCH AS PERSONALISED PSYCHOTHERAPIES.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

MI5. POST-TRAUMATIC STRESS DISORDER AND MAJOR DEPRESSIVE DISORDER SHOW SIGNIFICANT NEUROBIOLOGICAL OVERLAP

ANNIE DANG*, PETER FOX

MENTAL HEALTH DISORDERS AFFECT ONE IN EVERY EIGHT PEOPLE WORLDWIDE. POST-TRAUMATIC STRESS DISORDER (PTSD) AND MAJOR DEPRESSIVE DISORDER (MDD) ARE TWO PREVALENT AND HIGHLY COMORBID DISORDERS, WITH A CORRELATION OF 0.50 FOR LIFETIME PREVALENCE. THUS, THERE IS A NEED TO UNDERSTAND AND COMPARE UNDERLYING NEUROBIOLOGY BETWEEN PTSD AND MDD. QUERY OF THE BRAINMAP DATABASES (PORTAL.BRAINMAP.ORG) OF PUBLISHED, GROUP-WISE NEUROIMAGING, CASE-CONTROL CONTRASTS IDENTIFIED 152 CONTRASTS FOR PTSD PATIENTS AND 478 FOR MDD PATIENTS. ACTIVATION LIKELIHOOD ESTIMATION (ALE) COORDINATE-BASED META-ANALYSIS WAS PERFORMED SEPARATELY FOR PTSD AND MDD, TO IDENTIFY CROSS-STUDY CONVERGENCE OF BRAIN ALTERATION PATTERNS. MANGO WAS THEN USED TO VISUALIZE RESULTS AND QUANTIFY SPATIAL OVERLAP BETWEEN PTSD AND MDD. RESULTS SHOWED SUBSTANTIAL NEUROBIOLOGICAL OVERLAP (17395 MM3) BETWEEN PTSD AND MDD, ACCOUNTING FOR 51.2% OF PTSD AND 21.7% OF MDD. OVERLAPPING REGIONS INCLUDED THE MEDIAL FRONTAL GYRUS, ANTERIOR CINGULATE, POSTERIOR CINGULATE, AND RIGHT AND LEFT PARAHIPPOCAMPUS. PTSD SHOWED ADDITIONAL ALTERATIONS IN THE CLAUSTRUM, LINGUAL GYRUS, LENTIFORM NUCLEUS, AND PRECUNEUS. MDD SHOWED ADDITIONAL ALTERATIONS IN THE RIGHT CAUDATE, PRECUNEUS, LEFT LENTIFORM NUCLEUS, LINGUAL GYRUS, SUPERIOR TEMPORAL GYRUS, INSULA, CLAUSTRUM, AND LEFT FRONTAL GYRUS. UNDERSTANDING THE INDIVIDUAL AND SHARED NEUROBIOLOGY OF PTSD AND MDD CONTRIBUTES TO A FRAMEWORK FOR DISEASE CLASSIFICATION, BIOMARKER DEVELOPMENT, AND DEVELOPMENT OF TARGETED THERAPEUTICS. NETWORK ANALYSIS OF THESE DATASETS IS IN PROGRESS.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

MI6. SHORT AND LONG-TERM BEHAVIORAL AND DOPAMINE CIRCUIT ADAPTATIONS TO CHRONIC STRESS

CAROLE MOREL*, EMILY TEICHMAN, ANTHONY BLANDO, SARAH MONTGOMERY, HSIAO-YUN LIN, LYONNA PARISE, LONG LI, NIKOLAOS TZAVARAS, ALLYSON FRIEDMAN, SCOTT RUSSO, JUN WANG

ANXIETY, ANHEDONIA, AND APATHY ARE WIDESPREAD COMORBID SYMPTOMS IN HUMAN NEUROPSYCHIATRIC PROFILES. THIS CO-OCCURRENCE IS ASSOCIATED WITH COMPLEX SYMPTOMATOLOGY, GREATER TREATMENT RESISTANCE, CHRONICITY, AND PROFOUND IMPACT IN AGING PATIENTS. WHILE NUMEROUS GENETIC AND ENVIRONMENTAL FACTORS HAVE BEEN IDENTIFIED IN DEVELOPING PSYCHIATRIC COMORBIDITY, THE BRAIN MECHANISMS AND THEIR TEMPORALITY REMAIN LARGELY UNKNOWN. STRESSFUL AND TRAUMATIC SOCIAL EXPERIENCES IN HUMANS ARE CRITICAL ENVIRONMENTAL FACTORS TRIGGERING NEUROPSYCHIATRIC PROFILES ACROSS THE LIFESPAN. BEYOND SOCIAL DOMAINS, SOCIAL STRESS CAN SEVERELY IMPAIR BIOLOGICAL RHYTHMS, MOTIVATION, AND COGNITIVE AND EXECUTIVE FUNCTIONS. SIMILARLY, REPEATED SOCIAL STRESS (RSS) IN MICE DISRUPTS SOCIAL BEHAVIORS, EXPLORATION, AND REWARD/PUNISHMENT PROCESSING. MIDBRAIN DOPAMINE PROJECTIONS TO THE CORTEX, THE NUCLEUS ACCUMBENS (NAC), AND THE AMYGDALA (AMG) ARE ESSENTIAL TO INTEGRATE POSITIVE AND ADVERSE LIFE EVENTS AND ENCODE ADAPTED BEHAVIORS. HERE, WE AIM TO DEFINE HOW PARALLEL DOPAMINE CIRCUITS COORDINATE BEHAVIORAL ADAPTATIONS TO RSS. WE ASSESS RSS'S SHORT- AND LONG-TERM IMPACT ON SOCIAL, APPROACH/AVOIDANCE, AND FLEXIBLE BEHAVIORS IN MALE AND FEMALE MICE. USING CIRCUIT-PROBING TECHNIQUES, OPTOGENETICS, ELECTROPHYSIOLOGICAL, MULTI-CIRCUIT FIBER PHOTOMETRY, AND OPERANT BEHAVIORAL METHODS, WE INVESTIGATE THE DOPAMINE ACTIVITY CIRCUIT DYNAMICS ASSOCIATED WITH STRESS-INDUCED BEHAVIORAL OUTCOMES. WE ESTABLISH THAT RSS 1-DISRUPTS THE COORDINATED DOPAMINE ACTIVITY BETWEEN CORTEX, AMG, AND NAC, RESULTING IN REWARD/PUNISHMENT PROCESSING DEFICITS AND COGNITIVE INFLEXIBILITY; 2-INDUCES VTA-AMG HYPOACTIVITY, REDUCING EXPLORATORY BEHAVIORS, AND 3-INCREASES VTA-NAC ACTIVITY RESULTING IN ANHEDONIA AND SOCIAL AVOIDANCE BEHAVIORS. OVERALL, THESE DATA ESTABLISH RSS-INDUCED PARALLEL AND OPPOSITE ALTERATIONS OF MIDBRAIN PROJECTIONS THAT CONTRIBUTE TO DISTINCT BEHAVIORAL FEATURES OF ANXIETY, ANHEDONIA, AND APATHY.
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MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

MI7. DISCOVERY AND CHARACTERIZATION OF A SPECIFIC INHIBITOR OF SERINE-THREONINE KINASE CYCLIN DEPENDENT KINASE-LIKE 5 (CDKL5) DEMONSTRATES ROLE IN HIPPOCAMPAL CAI PHYSIOLOGY

A. CASTANO, M. SILVERSTRE, CI WELLS, JL SANDERSON, W. RICHARDSON, JA SILVAROLI, NS PABLA, TIM BENKE*, SK ULTANIR, AD AXTMAN

PATHOLOGICAL LOSS-OF-FUNCTION MUTATIONS IN CYCLIN-DEPENDENT KINASE-LIKE 5 (CDKL5) CAUSE CDKL5 DEFICIENCY DISORDER (CDD), A RARE AND SEVERE NEURODEVELOPMENTAL DISORDER ASSOCIATED WITH SEVERE AND MEDICALLY REFRACTORY EARLY-LIFE EPILEPSY, MOTOR, COGNITIVE, VISUAL AND AUTONOMIC DISTURBANCES IN THE ABSENCE OF ANY STRUCTURAL BRAIN PATHOLOGY. ANALYSIS OF GENETIC VARIANTS IN CDD HAVE INDICATED THAT CDKL5 KINASE FUNCTION IS CENTRAL TO DISEASE PATHOLOGY. CDKL5 ENCODES A SERINE-THREONINE KINASE WITH SIGNIFICANT HOMOLOGY TO GSK3, WHICH HAS ALSO BEEN LINKED TO SYNAPTIC FUNCTION. FURTHER, CDKL5 KNOCK-OUT RODENTS HAVE INCREASED GSK3 ACTIVITY AND OFTEN INCREASED LONG-TERM POTENTIATION (LTP). THUS, DEVELOPMENT OF A SPECIFIC CDKL5 INHIBITOR MUST BE CAREFUL TO EXCLUDE CROSS-TALK WITH GSK3 ACTIVITY. WE SYNTHESIZED AND CHARACTERIZED SPECIFIC, HIGH-AFFINITY INHIBITORS OF CDKL5 THAT DO NOT HAVE DETECTABLE ACTIVITY FOR GSK3. THESE COMPOUNDS ARE VERY SOLUBLE IN WATER BUT BLOOD-BRAIN BARRIER PENETRATION IS LOW. ACUTE INHIBITION OF CDKL5 REDUCES PHOSPHORYLATION OF EB2 IN RODENT HIPPOCAMPAL CULTURES AND BRAIN SLICES. IN RAT HIPPOCAMPAL BRAIN SLICES, ACUTE INHIBITION OF CDKL5 REDUCES POST-SYNAPTIC FUNCTION OF AMPA-TYPE GLUTAMATE RECEPTORS IN A DOSE-DEPENDENT MANNER. ACUTE INHIBITION OF CDKL5 REDUCES HIPPOCAMPAL LTP IN A DEVELOPMENTALLY DEPENDENT MANNER. THESE STUDIES PROVIDE NEW TOOLS AND INSIGHTS INTO THE ROLE OF CDKL5 AS A NEWLY APPRECIATED, KEY KINASE NECESSARY FOR SYNAPTIC PLASTICITY. COMPARISONS TO RODENT KNOCK-OUT STUDIES SUGGEST THAT COMPENSATORY CHANGES HAVE LIMITED THE UNDERSTANDING OF THE ROLES OF CDKL5 IN SYNAPTIC PHYSIOLOGY, PLASTICITY AND HUMAN NEUROPATHOLOGY.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

MI8. CORTICAL TASTE PROCESSING CHANGES WITH TASTE EXPERIENCE ACROSS TRIALS AND DAYS

DANIEL SVEDBERG*, AVI PATEL, DONALD KATZ

TITLE: CORTICAL TASTE PROCESSING CHANGES WITH TASTE EXPERIENCE ACROSS TRIALS AND DAYS
LABORATORY RODENTS ARE TYPICALLY RAISED IN HIGHLY TASTE-IMPOVERISHED ENVIRONMENTS, WHICH MEANS THAT THESE RODENTS ENTER INTO EXPERIMENTS REMARKABLY "TASTE NAÏVE." UNDER THE STANDARD ASSUMPTION THAT FUNDAMENTAL TASTE PERCEPTION IS INNATE AND STABLE, THIS FACT SHOULD BE OF LITTLE IMPORT—THE FIRST EXPOSURE TO A TASTE SHOULD BE PROCESSED "NORMALLY." RECENT BEHAVIORAL AND ELECTROPHYSIOLOGICAL EVIDENCE, HOWEVER, SUGGEST THAT TASTE PERCEPTION CHANGES AS ANIMALS GROW FAMILIAR TO TASTE STIMULI, AT LEAST ON THE TIME SCALE OF HOURS TO DAYS. HERE, WE LEVERAGED OUR DEEP UNDERSTANDING OF GUSTATORY CORTICAL (GC) TASTE RESPONSES—NOT JUST WHICH NEURONS RESPOND, BUT THE PRECISE DYNAMICS OF ENSEMBLE RESPONSES IN SINGLE TRIALS—TO INVESTIGATE WHETHER TASTE PROCESSING CHANGES WITH EXPOSURE TO NOVEL TASTES ON AN EVEN SHORTER TIME SCALE, AND WHETHER ANY SUCH CHANGES DEPEND ON FAMILIARIZATION AT LONGER TIME SCALES. WE OBSERVED THAT THESE RESPONSES ARE IN FACT NOT INNATE: ACROSS INITIAL EXPOSURES TO NOVEL BATTERY OF 4 (SWEET, SALTY, SOUR, AND BITTER) TASTES, THEY BECAME MORE TASTE-SPECIFIC, AND THEIR TEMPORAL DYNAMICS CAME TO UNFOLD MORE QUICKLY; FURTHER EXPERIMENTATION REVEALS THAT HOME-CAGE PRE-EXPOSURE TO ONE TASTE DAMPENS THIS QUICK RESPONSE-EVOLUTION TO JUST THAT TASTE, BUT NOT TO NAIVE TASTES, SUGGESTING THAT TASTE-NOVELTY RELATED CHANGES IN PROCESSING ARE TASTE-SPECIFIC. LASTLY, WE EXAMINE CHANGES IN TASTE-LICKING BEHAVIOR ACROSS FAMILIARIZATION TO THE SAME BATTERY OF TASTANTS, AND DEMONSTRATE THAT TASTE-FAMILIARIZATION IMPACTS CONSUMPTION BEHAVIOR ON A SIMILAR TIMESCALE AS SEEN IN ELECTROPHYSIOLOGY. THESE EXPERIMENTS ADD TO A GROWING LITERATURE INDICATING THAT EXPOSURE TO EVEN SIMPLE SENSORY STIMULI IS A "LEARNING" EXPERIENCE AND DEMONSTRATE THAT THIS LEARNING PROCESS OCCURS ACROSS MULTIPLE TIME SCALES. AS SUCH, THEY REVEAL THE DANGER OF STARTING AN EXPERIMENT WITH A TRULY 'TASTE-NAÏVE' SUBJECT.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

MI9. NEUROPEPTIDES IN THE PARABRACHIAL NUCLEUS OF PRIMATES

SONSOLES DE LACALLE*, NICHOLAS BURDICK

THE PARABRACHIAL NUCLEUS (PBN) IS LOCATED IN THE PONS, SURROUNDING THE SUPERIOR CEREBELLAR PEDUNCLE (SCP). IT PLAYS AN INTEGRAL ROLE IN VARIOUS PHYSIOLOGICAL FUNCTIONS, INCLUDING SLEEP AND WAKEFULNESS, TASTE, APPETITE, VISCERAL SENSATION, NOCICEPTION, TEMPERATURE REGULATION, ITCH, AND CHEMOSENSATION. THE PRESENT WORK AIMS TO IDENTIFY WHETHER THE PRIMATE PBN CONTAINS THE DIVERSITY OF NEUROPEPTIDES THAT HAS BEEN DESCRIBED IN THE RODENT. WE MAPPED THE DISTRIBUTION OF CALBINDIN (CAL), CHOLECYSTOKININ (CCK), DYNORPHIN (DYN), GALANIN (GAL), NEUROTENSIN (NT), SOMATOSTATIN (SOM), AND SUBSTANCE P (SP) APPLYING IMMUNOHISTOCHEMICAL TECHNIQUES ON HORIZONTAL BRAINSTEM CROSS-SECTIONS OBTAINED FROM FOUR NEUROLOGICALLY NORMAL HUMAN SUBJECTS AND FIVE MALE CEBUS MONKEYS. WE USED THE SCP AS A MARKER TO COMPARE ACROSS SUBJECTS. OVERALL, CELL BODY MORPHOLOGY AND FIBER DISTRIBUTION IN THE EXTERNAL LATERAL AND EXTERNAL MEDIAL SUBNUCLEI WERE SIMILAR ACROSS SPECIES, BUT THERE WERE CLEAR DIFFERENCES IN PEPTIDE DISTRIBUTION. BOTH THE EXTERNAL LATERAL AND EXTERNAL MEDIAL SUBNUCLEI CONTAINED CAL, CCK, NT, SOM, AND SP IMMUNOREACTIVITY. DYN WAS OBSERVED IN THE EXTERNAL LATERAL PBN, AND GAL WAS PRESENT IN THE CENTRAL LATERAL AND DORSAL MEDIAL PBN. THE EXTERNAL LATERAL SUBNUCLEUS EXHIBITED A DISTINCT TOPOGRAPHICAL DISTRIBUTION OF GAL, CAL, CCK DYN AND SOM, WITH DYN AND SOM OVERLAPPING IN THE VENTRAL CORNER OF THE SUBNUCLEUS. THESE RESULTS SUGGEST THAT THE NEUROPEPTIDE DISTRIBUTION IN THE PRIMATE PBN IS SIMILAR TO THE ONE DESCRIBED IN THE RAT, ALLOWING TO INFER PHYSIOLOGICAL PARALLELS THAT MAY BE USEFUL IN THE UNDERSTANDING OF HUMAN DISEASE.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M20. HOW DO INTERAURAL TIME AND INTERAURAL LEVEL DIFFERENCES INTERACT IN SPATIAL HEARING WITH COCHLEAR IMPLANTS?

JAN SCHNUPP*, NICOLE ROSSKOTHEN-KUHL, SARAH BUCHHOLZ, THERESA PREYER, MOHAMMED ZEESHAN

NORMAL SPATIAL HEARING RELIES ON INTERAURAL TIME DIFFERENCES (ITDS) AND INTERARUAL LEVEL DIFFERENCES (ILDS). NEONATALLY DEAF (ND) BINAURAL COCHLEAR IMPLANT (BICI) PATIENTS ARE OFTEN INSENSITIVE TO ITD, BUT ADULT ND-RATS HAVE EXCELLENT ITD SENSITIVITY. THIS SUGGESTS THAT PATIENTS FITTED WITH CONVENTIONAL CLINICAL CIS MAY BECOME DESENSITIZED TO ITD, GIVEN THAT CLINICAL DEVICES PROVIDE NO USEFUL PULSE TIMING ITDS ("MALADAPTIVE PLASTICITY HYPOTHESIS").
TO INVESTIGATE THIS, IT IS USEFUL TO QUANTIFY RELATIVE ITD/ILD SENSITIVITY (TIME-INTENSITY TRADING RATIOS, OR TITRS) IN BI-CI EXPERIMENTAL ANIMALS. WISTAR RATS WERE DEAFENED BY P10-P20 KANAMYCIN, ALLOWED TO MATURE (> P60), AND THEN IMPLANTED WITH BICIS. SOME ANIMALS WERE TESTED BEHAVIORALLY, ON OTHERS WE PERFORMED RECORDINGS IN THE INFERIOR COLLICULUS (IC).
BEHAVIORAL RATS WERE TRAINED IN A LATERALIZATION TASKS. RATS INITIATE A TRIAL BY LICKING A CENTER SPOUT. THIS TRIGGERS 0.1 S LONG, 900 PPS BIPHASIC ELECTRIC PULSE TRAINS, WITH ITDS CHOSEN FROM THE SET +/-{0, 60, 80} MS, AND ILDS FROM +/-{0, 1, 4} DB. THE ANIMALS THEN CHOSE A ONE OF TWO RESPONSE SPOUTS, TO INDICATE THE SIDE ON WHICH THEY HEARD THE STIMULUS. CORRECT CHOICES WERE REWARDED. THE PROPORTION OF "RIGHT" RESPONSES WAS MODELLED WITH A 2D PSYCHOMETRIC FUNCTION TO COMPUTE TITRS. OBSERVED TITRS WERE ALL IN THE RANGE OF 15-21 MS/DB.
RECORDINGS OF JOINT ITD / ILD TUNING CURVES IN COMPLETELY NAIVE ND CI RATS FURTHERMORE INDICATED THAT THE LARGE MAJORITY OF IC NEURONS EXHIBIT A HIGHLY SENSITIVITY TO BOTH ITD AND ILD, WITH ITDS OVER THE SMALL RANGE OF +/- 80 MS EXPLAINING AS MUCH AS 80% OF THE OBSERVED VARIANCE IN NEURAL FIRING.

IN THE NATURAL STATE, ITDS ARE THEREFORE WEIGHTED VERY HIGHLY, AND IT IS INEVITABLE THAT CLINICAL PROCESSORS WHICH SUBJECT PATIENTS TO RANDOM PULSE TIMING ITDS IN THE RANGE [-500, 500] MS WILL CAUSE A GREAT DEAL OF CONFUSION UNLESS THEIR AUDITORY PATHWAY DESENSITIZES TO ITDS.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M21. ROLE OF NUCLEUS ACCUMBENS DOPAMINE RECEPTORS SIGNALING IN PUNISHED REWARD SEEKING

ANNA TOBUREN*, GRACE JOYNER, SERENA PARMAR, JACOB WATSON, PETER VENTO

ADDICTION IS CHARACTERIZED BY PERSISTENT REWARD-SEEKING DESPITE NEGATIVE CONSEQUENCES. THE NUCLEUS ACCUMBENS (NAC) CORE REGION IS KNOWN TO PLAY AN IMPORTANT ROLE IN MOTIVATION AND COST-BENEFIT DECISION-MAKING. WITHIN THE NAC ACTIVITY IN SUBPOPULATIONS OF DOPAMINE (DA)-RESPONSE NEURONS, CHARACTERIZED BY THE PRESENCE OF DI OR D2 RECEPTORS, IS CRITICAL FOR THE ENCODING AND EXPRESSION OF MOTIVATED BEHAVIOR. STILL, THE RELATIVE CONTRIBUTION OF THESE NEURAL RECEPTORS IN THE NAC CORE CONTRIBUTES TO PERSISTENT REWARD SEEKING UNDER PUNISHMENT. TO BETTER UNDERSTAND THE ROLE OF DA RECEPTOR SIGNALING WITHIN THE NAC, WE INCORPORATED A NOVEL TWO CHOICE PUNISHED FOOD-SEEKING TASK AND TESTED THE EFFECTS OF THE DI AGONIST SKF-81297 OR THE D2 AGONIST QUINPIROLE ON PUNISHED REWARD SEEKING. IN THIS TWO-LEVER SHOCK TASK RATS ARE PRESENTED WITH ONE LEVER THAT YIELDS A SMALL (1 PELLET) REWARD AND A SEPARATE LEVER YIELDING A LARGE (3 LARGE) REWARD. UPON TESTING, RESPONDING FOR THE LARGE REWARD IS IMMEDIATELY FOLLOWED BY FOOT SHOCK THAT PROGRESSIVELY INCREASES IN INTENSITY WITH REPEATED CHOICES ON THERE LARGE REWARD LEVER, WHILE RESPONDING FOR THE SMALL REWARD IS NEVER ACCOMPLISHED BY PUNISHMENT. RESULTS SUGGEST THAT NAC CORE MICRO INFUSION OF THE D2 AGONIST QUINPIROLE CAUSES AN INCREASE IN MAXIMUM SHOCK INTENSITY RATS ARE WILLING TO ENDURE TO RECEIVE THE LARGE REWARD. ONGOING TESTING WILL DETERMINE WHETHER EFFECTS OF QUINPIROLE ARE REPLICATED BY DI AGONIST SKF-81297, OR FURTHER ENHANCED BY CO-ADMINISTRATION OF THE TWO COMPOUNDS.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M22. PRENATAL CANNABINOID EXPOSURE LEADS TO ENHANCED GABAERGIC SIGNALING RESULTING IN LEARNING AND MEMORY DEFICITS IN ADOLESCENT RAT OFFSPRING

MILES WILEY*, KAWSAR CHOWDHURY, ADRIAN COURVILLE, EMMA REDMON, TIA DANIELS, VISHNU SUPPIRAMANIAM, MIRANDA REED

CANNABIS IS THE MOST ABUSED DRUG BY PREGNANT WOMEN. ITS USE IS EXPECTED TO INCREASE, WITH 39 STATES HAVING MEDICAL MARIJUANA LAWS AND 19 HAVING RECREATIONAL MARIJUANA LAWS. ALSO TROUBLING, THE CONCENTRATIONS OF TETRAHYDROCANNABINOL (THC) IN CANNABIS HAVE DOUBLED WORLDWIDE OVER 40 YEARS, AND HIGHER CONCENTRATIONS ARE LIKELY TO INCREASE ASSOCIATED PROBLEMS. CLINICAL DATA SHOWED THAT WHEN PREGNANT WOMEN USE CANNABIS, THEIR OFFSPRING HAVE LEARNING AND MEMORY DEFICITS. WE HYPOTHESIZE THAT PCE INCREASES GABAERGIC SIGNALING, RESULTING IN SYNAPTIC PLASTICITY AND MEMORY DEFICITS. IN THE CURRENT STUDY, PREGNANT DAMS WERE EXPOSED TO A VAPORIZED DRUG SOLUTION OF Δ9-THC 100MG/ML IN PEG400 VIA PASSIVE INHALATION PRENATALLY FROM GESTATIONAL DAY 5 TO 21/22. PK STUDIES REVEALED THE THC DETECTED IN DAMS TO BE CONSISTENT WITH A MODERATE DOSE OF THC IN HUMANS, AND THC WAS PRESENT IN THE BRAIN AND PLASMA OF PUPS IMMEDIATELY AFTER BIRTH. IN ADDITION, PREGNANT DAMS EXPOSED TO THC GAINED SIGNIFICANTLY MORE WEIGHT AND ATE MORE FOOD DURING TREATMENT THAN VEHICLE-EXPOSED PREGNANT DAMS. THC-EXPOSED OFFSPRING WEIGHED SIGNIFICANTLY LESS FROM POSTNATAL DAY 1 TO 40. THC EXPOSURE ALSO RESULTED IN DEFICITS IN THE NOVEL OBJECT RECOGNITION PARADIGM, INDICATING IMPAIRMENTS IN LONG-TERM MEMORY. THC OFFSPRING ALSO EXHIBITED INCREASED ANXIETY LEVELS IN THE ELEVATED PLUS MAZE TASK. THESE DEFICITS WERE ASSOCIATED WITH ALTERATIONS IN GABAERGIC PROTEINS IN THE HIPPOCAMPUS AND MEDIAL PREFRONTAL CORTEX. THESE EXPERIMENTS HELP ELUCIDATE HOW GABAERGIC DYSFUNCTION MAY LEAD TO BEHAVIORAL ALTERATIONS IN PCE OFFSPRING.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M23. MESOSCOPIC DYNAMICS IN LARGE NEURONAL POPULATIONS: INSIGHTS FROM SIMULATIONS AND STATISTICAL PHYSICS

ALEX SHEREMET*, YU QIN

THIS STUDY INVESTIGATES THE COLLECTIVE DYNAMICS OF LARGE POPULATIONS OF HODGKIN-HUXLEY NEURONS, EMPLOYING LARGE-SCALE SIMULATIONS TO GAIN AN UNDERSTANDING OF MESOSCOPIC COLLECTIVE DYNAMICS IN THE CORTEX. THE PRIMARY FOCUS IS ON UNCOVERING THE INTRICATE MESOSCOPIC OSCILLATORY PATTERNS THAT MANIFEST AS A MACROSCOPIC REPRESENTATION OF NEURAL ACTIVITY IN THESE POPULATIONS. OUR APPROACH INTEGRATES COMPUTATIONAL SIMULATIONS WITH A STATISTICAL PHYSICS-BASED POPULATION MODEL, PROVIDING A VALUABLE FRAMEWORK FOR EXPLORING MESOSCOPIC DYNAMICS COMPREHENSIVELY. THIS INTEGRATION ACTS AS A VITAL LINK BETWEEN INDIVIDUAL NEURONAL BEHAVIORS AND COLLECTIVE NEURAL ACTIVITY. THE STUDY PLACES SIGNIFICANT EMPHASIS ON UNRAVELING THE COMPLEXITIES OF COLLECTIVE DYNAMICS, INCLUDING THE EMERGENCE OF OSCILLATIONS AND NON-LINEAR PHENOMENA LIKE CROSS-FREQUENCY COUPLING. THESE INSIGHTS NOT ONLY YIELD A COMPREHENSIVE UNDERSTANDING OF THE COLLECTIVE BEHAVIOR OF LARGE NEURONAL POPULATIONS BUT ALSO ENHANCE OUR KNOWLEDGE OF LARGE-SCALE NEURAL POPULATIONS IN THE BRAIN. THE FINDINGS OF THIS STUDY PRESENT NOVEL INSIGHTS INTO MESOSCOPIC NEURAL DYNAMICS AND UNDERSCORE THE IMPORTANCE OF FURTHER VALIDATION AND ONGOING RESEARCH. MOREOVER, THEY HAVE THE POTENTIAL TO INFORM INNOVATIVE THERAPEUTIC STRATEGIES FOR NEUROLOGICAL DISORDERS. THIS WORK REINFORCES OUR UNDERSTANDING OF COLLECTIVE NEURAL ACTIVITY AT THE MESOSCOPIC LEVEL, EMPHASIZING THE NECESSITY OF CONTINUOUS VALIDATION AND EXPLORATION OF THESE INTRICATE DYNAMICS.
SFUNCTION MAY LEAD TO BEHAVIORAL ALTERATIONS IN PCE OFFSPRING.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M24. SUBREGION ENCODING OF DECISION VARIABLES AND UNDERLYING COMMUNICATION WITHIN MACAQUE VENTRAL FRONTAL CORTEX

FREDERIC STOLL*, PETER RUDEBECK

THE VENTRAL FRONTAL CORTEX (VFC) IN MACAQUES IS INVOLVED IN NUMEROUS AFFECTIVE AND COGNITIVE PROCESSES, FROM MULTIMODAL SENSORY INTEGRATION TO THE SELECTION AND USE OF INTERNAL AND EXTERNAL FEATURES TO FLEXIBLY GUIDE DECISION-MAKING. VFC IS COMPOSED OF A HETEROGENEOUS SET OF SUBREGIONS, ENCOMPASSING MANY SUBDIVISIONS WITHIN THE ORBITOFRONTAL CORTEX, VENTROLATERAL CORTEX, AND ANTERIOR INSULA. BASED ON THE INTERCONNECTIONS BETWEEN THESE SUBREGIONS, PRIOR ANATOMICAL WORK REVEALED THE EXISTENCE OF MULTIPLE NETWORKS WITHIN VFC. IT IS UNCLEAR, HOWEVER, WHETHER SPECIFIC FUNCTIONS MAP ONTO THESE KNOWN ANATOMICAL SUBREGIONS, IN PART, BECAUSE PRIOR STUDIES HAVE LACKED THE RESOLUTION TO TEST FOR DIFFERENCE. HERE WE RECORDED THE ACTIVITY OF THOUSANDS OF NEURONS ACROSS LARGE PORTIONS OF VFC IN MONKEYS PERFORMING A TWO-CHOICE PROBABILISTIC TASK FOR DIFFERENT FRUIT JUICES OUTCOMES. WE THEN COMPARED ENCODING TO PRECISE POST-MORTEM NEUROANATOMICAL PARCELLATIONS TO INVESTIGATE THE DIFFERENCES IN NEURAL ENCODING AND COMMUNICATION BETWEEN 8 DISTINCT CYTOARCHITECTONIC AREAS IN VFC. WE FOUND THAT THE VENTROLATERAL AREA 12L, NOT 12O, REPRESENTED MULTIPLE CHOICE ATTRIBUTES WHEN MONKEYS EVALUATED THE OPTIONS PRESENTED TO THEM, WHILE ORBITOFRONTAL AREA 11M/L CONTAINED MORE SPECIFIC REPRESENTATIONS OF THE QUALITY OF THE OUTCOME THAT COULD BE EARNED. WE ALSO FOUND A HIGHLY DISTRIBUTED REWARD DELIVERY ENCODING ACROSS ALL VFC SUBREGIONS, WHILE THE REWARD PROPERTIES WERE MORE SPECIFICALLY OBSERVED IN AREAS RECEIVING GUSTATORY INPUTS, NOTABLY 11M/L AND 13M. FURTHER, THE ONSET OF STIMULI AND REWARD GLOBALLY INCREASED COMMUNICATION WITHIN ALL VENTRAL FRONTAL CORTEX, WITH AREA 12L/O SHOWING THE HIGHEST CONNECTIVITY WITH OTHER AREAS. RESPONSES IN 12L/O WERE OFTEN PRECEDED BY RESPONSES IN OTHER SUBREGIONS, SUGGESTING A CRITICAL INTEGRATIVE ROLE FOR THIS AREA IN DECISION-MAKING. TAKEN TOGETHER, OUR WORK HIGHLIGHTS THE DIVERSITY OF ENCODING AND COMMUNICATION WITHIN THE VARIOUS SUBREGIONS OF VFC.
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MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M25. TARGETING DOPAMINERGIC NEURONS IN RHESUS MONKEY: A COMPARISON OF RETROGRADE VIRAL VECTORS

ANNA PLOTNIKOVA*, WALTER LERCHNER, ALEXANDER CUMMINS, LEONARDO SALHANI, BARRY RICHMOND, ZAYD KHALIQ, MARK ELDRIDGE

ENGINEERED VIRAL VECTORS HAVE BEEN USED TO TARGET THE NEUROMODULATORY SYSTEMS OF THE BRAIN, BUT A CONSPICUOUS OBSTACLE IS THE INABILITY OF MANY RETROGRADELY INFECTING VIRUSES TO TRANSDUCE DOPAMINERGIC (DA) CELLS (CUSHNIE, 2020; TERVO ET AL., 2016). IN A COMPARATIVE ANALYSIS, WE ASSESS FOUR VIRAL VECTORS IN THEIR ABILITY TO DRIVE EXPRESSION IN THE SOMATA OF DA NEURONS OF NONHUMAN PRIMATES (NHP) AFTER INJECTION INTO STRIATUM. AAV2-RETRO AND LENTIVIRAL VECTORS PSEUDOTYPED WITH RABIES FUSION GLYCOPROTEIN B, C, AND E (FUG-B2, FUG-C, AND FUG-E) ARE VIRUSES THAT HAVE BEEN ENGINEERED TO CONFER RETROGRADE TRANSDUCTION PROPERTIES. A VARIANT OF AAV2, RAAV2-RETRO, IS ENDOWED WITH THE ABILITY TO BE INTERNALIZED BY AXONS, ENHANCING RETROGRADE TRANSDUCTION (TERVO ET AL., 2016). FUG-B2 ('HIRET') TRANSDUCES ALL BRAIN CELL TYPES (GLIA AND NEURONS), WHILE FUG-C AND FUG-E ('NEURET') ARE NEURON SPECIFIC (KATO ET AL., 2020). TO EVALUATE RETROGRADE TRANSDUCTION OF DOPAMINERGIC CELLS IN THE RHESUS MACAQUE, VIRUS WAS TARGETED TO STRIATUM IN STEREOTAXIC SURGERIES. WE INJECTED BETWEEN 70 AND 150 ML (10 ML/SITE AT A RATE OF 0.5 ML/MIN TO 1.0 ML/MIN) UNILATERALLY ACROSS THREE ANTERIOR-POSTERIOR LEVELS OF EACH NHP. POST-MORTEM IMMUNOHISTOCHEMISTRY WAS VISUALIZED WITH FLUORESCENCE AND BRIGHTFIELD MICROSCOPY, AND THE TRANSDUCTION EFFICIENCY OF THE VIRAL VECTORS IN DOPAMINERGIC CELLS WAS QUANTIFIED. QUALITATIVE AND QUANTITATIVE ANALYSIS OF THE DATA REVEALED LENTIVIRUS-BASED VECTOR, FUG-B2, PRODUCED ROBUST RETROGRADE TRANSDUCTION OF DA CELLS, AS EVIDENCED BY THE NEURONAL CO-EXPRESSION OF FLUORESCENT REPORTER PROTEIN AND TYROSINE-HYDROXYLASE (TH) ANTIBODY IN SUBSTANTIA NIGRA. THIS FINDING IS CONTRASTED WITH THE OTHER THREE VIRAL VECTORS, WHICH DO NOT TRANSDUCE DOPAMINERGIC CELLS AS EFFICIENTLY. FUG-C EXPRESSION WAS APPROXIMATELY THREE TIMES LOWER THAN THAT OF FUG-B2. FUG-E SHOWED MINIMAL EXPRESSION, WHILE AAV2-RETRO PRODUCED ALMOST ZERO EXPRESSION.
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MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M26. PERIPUBERTAL SOCIAL DISRUPTION PERSISTENTLY ALTERS MOTIVATED BEHAVIORS IN ADULTHOOD

STUTI AGRAWAL*, JON CAVANAUGH, KYLE SMITH

SOCIAL CONNECTION PROFOUNDLY SHAPES OUR MENTAL, PHYSICAL, AND BEHAVIORAL WELL-BEING ACROSS THE LIFESPAN, AND BOLSTERS RESILIENCE AGAINST STRESS, ANXIETY, OR DEPRESSION. HOWEVER, LIMITED SOCIAL INTERACTIONS DURING FORMATIVE YEARS CAN IMPEDE COGNITIVE AND INTERPERSONAL DEVELOPMENT, WITH EARLY LIFE ADVERSITY RAISING THE RISK OF SUBSTANCE USE. WHILE IT IS EVIDENT THAT QUALITY SOCIAL ENGAGEMENTS PLAY A SIGNIFICANT ROLE IN BRAIN MATURATION, A DEEPER UNDERSTANDING IS STILL NEEDED REGARDING THE LONG-TERM EFFECTS OF DEVELOPMENTAL SOCIAL DEPRIVATION ON LIFETIME BEHAVIOR. THIS PROJECT IDENTIFIED THE LASTING IMPACT OF PUBERTAL ISOLATION ON MOTIVATED BEHAVIORS IN ADULTHOOD. 72 FEMALE AND 72 MALE WILD-TYPE RATS WERE ASSIGNED TO ONE OF THREE PUBERTAL ISOLATION CONDITIONS [CHRONIC ISOLATION (CI), RECURRENT SOCIAL DISRUPTION (RSD), OR PAIR HOUSING (PH)] AND WERE TRAINED TO SELF-ADMINISTER SOCIAL AND FOOD REWARDS IN AN AUTOMATED OPERANT ASSAY. FOLLOWING PUBERTY, INCENTIVE VALUES AND REWARD PREFERENCES WERE ASSESSED AT MULTIPLE TIME POINTS IN EARLY ADULTHOOD. THE DATA INDICATES THAT THE DEGREE OF PUBERTAL ISOLATION HAD LASTING EFFECTS ON MOTIVATED BEHAVIORS IN ADULTHOOD. IN A DIRECT CHOICE TASK WHERE ADULTS WERE GIVEN THE OPTION TO SELF-ADMINISTER FOOD REWARDS, SOCIAL REWARDS, OR NO REWARDS OVER 20 TRIALS, ADULTS WHO EXPERIENCED PUBERTAL RSD MADE SIGNIFICANTLY MORE CHOICES FOR SOCIAL REWARDS RELATIVE TO ADULTS WHO EXPERIENCED PUBERTAL CI OR PH. HOWEVER, ADULTS WHO EXPERIENCED PUBERTAL RSD, BUT NOT CI, DISPLAYED SUBSTANTIALLY REDUCED INCENTIVE VALUES FOR BOTH REWARDS, SUGGESTING THAT PUBERTAL SOCIAL DISRUPTION MALADAPTIVELY ALTERS IMPORTANT MOTIVATION FEATURES ACROSS REWARD MODALITIES. INTRIGUINGLY, SUBJECTS WHO EXPERIENCED ISOLATION DURING THE ENTIRETY OF PUBERTY DID NOT DISPLAY ALTERED MOTIVATED BEHAVIOR IN ADULTHOOD, SUGGESTING THAT THE LASTING IMPACT OF CI IS MORE BENIGN THAN ORIGINALLY THOUGHT. THESE FINDINGS DEMONSTRATE THE ENDURING IMPACT OF PERIPUBERTAL SOCIAL DISRUPTION ON REWARD PREFERENCES AND INCENTIVE VALUES IN ADULTHOOD WITH IMPLICATIONS FOR ALTERED DEVELOPMENT OF THE SOCIAL DECISION-MAKING NETWORK WHILE ILLUMINATING THE PERSISTENTLY PERNICIOUS EFFECTS OF PERIPUBERTAL SOCIAL DEPRIVATION ON THE DEVELOPMENT OF ADAPTIVE-MOTIVATED BEHAVIOR.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M27. DOXORUBICIN-INDUCED COGNITIVE IMPAIRMENT AND SYNAPTIC PLASTICITY

IVA DURDANOVIC*, KAWSAR CHOWDHURY, MILES WILEY, ADRIAN COURVILLE, EMMA REDMON, VISHNU SUPPIRAMANIAM, MIRANDA REED

DOXORUBICIN IS ONE OF THE LEADING DRUGS THAT CAUSE LONG-TERM COGNITIVE DEFICITS, OFTEN CALLED CHEMOBRAIN. AS OBSERVED IN OVER A THIRD OF BREAST CANCER PATIENTS PRESCRIBED DOXORUBICIN, COGNITIVE SYMPTOMS POST-TREATMENT PERSIST DUE TO THE DRUG'S ABILITY TO INDUCE NEUROTOXICITY DESPITE NEGLIGIBLE AMOUNTS BREACHING THE BLOOD-BRAIN BARRIER. EXTENSIVE CLINICAL EFFORTS TO IMPROVE CHEMOBRAIN SYMPTOMS HAVE MADE MINIMAL PROGRESS, POSSIBLY DUE TO THE UNDERLYING MECHANISM OF DOXORUBICIN-INDUCED CHEMOBRAIN BEING UNKNOWN. IN THIS STUDY, WE TEST THE HYPOTHESIS THAT DOXORUBICIN-INDUCED CHEMOBRAIN DYSREGULATES GLUTAMATE LEVELS, RESULTING IN EXCITOTOXICITY AND IMPAIRED SYNAPTIC PLASTICITY IN AN ANIMAL MODEL OF CHEMOBRAIN. WE AIM TO INVESTIGATE THE EFFECTS OF DOXORUBICIN ON THE EXPRESSION AND QUANTIFICATION OF SYNAPTIC PROTEINS (I.E., NMDA RECEPTORS) AND DOWNSTREAM SIGNALING PIVOTAL TO LEARNING AND MEMORY FORMATION THROUGH A SERIES OF TECHNIQUES INCLUDING ELECTROPHYSIOLOGY AND IMMUNOBLOTTING. OUR FINDINGS ARE ANTICIPATED TO ESTABLISH MECHANISTIC INTERPLAY THROUGH WHICH DOXORUBICIN DISRUPTS SYNAPTIC PLASTICITY, POTENTIALLY ELUCIDATING THE MULTIFACETED DYSREGULATION OF COGNITIVE PROCESSES SURROUNDING GLUTAMATE SIGNALING AND NEUROTRANSMISSION. BY BRIDGING THE GAP BETWEEN DOXORUBICIN TREATMENT AND GLUTAMATE EXCITOTOXICITY, THIS RESEARCH NOT ONLY ADVANCES THE FUNDAMENTAL KNOWLEDGE OF CHEMOTHERAPY-INDUCED COGNITIVE DEFICITS BUT ALSO CLINICALLY RELEVANT GLUTAMATE-MODULATING TARGETS DIRECTED TO MITIGATE THE COGNITIVE SYMPTOMS, THUS ENHANCING PATIENTS' OVERALL QUALITY OF LIFE DURING AND AFTER CHEMOTHERAPY. THE COMPREHENSIVE NATURE OF THIS WORK AND FUTURE OUTCOMES WILL SIGNIFICANTLY CONTRIBUTE TO BOTH THE ONCOLOGY AND NEUROSCIENCE FIELDS.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M28. LATERAL HABENULA CO-RELEASE OF GLUTAMATE AND GABA FROM THE VENTRAL TEGMENTAL AREA OR ENTOPEDUNCULAR NUCLEUS NEURONS: SYNAPTIC PROPERTIES AND THEIR ROLE IN BEHAVIOR

SUYUN HAHN*, HUILING WANG, RAUL GARCIA, SHILIANG ZHANG, LIU BING, MARISELA MORALES

WE HAVE PREVIOUSLY DEMONSTRATED THAT NEURONS CO-EXPRESSING VESICULAR GLUTAMATE TRANSPORTERS 2 (VGLUT2) AND VESICULAR GABA TRANSPORTER (VGAT) ARE PRESENT IN THE VENTRAL TEGMENTAL AREA (VTA) AND ENTOPEDUNCULAR NUCLEUS (EPN) AND SHOWN THAT SINGLE AXON TERMINALS FROM THE DUAL NEURONS CO-RELEASE GLUTAMATE AND GABA IN THE LATERAL HABENULA (LHB). HERE, WE EXAMINED THE LHB SYNAPTIC PROPERTIES ESTABLISHED BY AXONS FROM GLUTAMATE-GABA NEURONS OF THE VTA AND EPN. WE EXPRESSED CHANNELRHODOPSIN 2 IN DUAL GLUTAMATE-GABA NEURONS OF THE VTA OR EPN BY USING DUAL RECOMBINASE VGLUT2-CRE/VGAT-FLP MICE. BY EX VIVO ELECTROPHYSIOLOGY, WE FOUND THAT LHB-PHOTOSTIMULATION OF VTA VGLUT2-VGAT TERMINALS EVOKED LOCAL INHIBITORY POSTSYNAPTIC CURRENTS (IPSCS) AND EXCITATORY POSTSYNAPTIC CURRENTS (EPSCS). WE DETECTED THREE PATTERNS OF POSTSYNAPTIC CURRENTS, IN WHICH THE AVERAGE AMPLITUDE WAS LARGER FOR IPSCS THAN FOR EPSCS. IN CONTRAST, LHB-PHOTOSTIMULATION OF EPN DUAL TERMINALS EVOKED LARGER EPSCS THAN IPSCS. NEXT, BY APPLYING DIFFERENT LHB-PHOTOSTIMULATION FREQUENCIES IN VTA DUAL TERMINALS, WE FOUND THAT THE IPSC AMPLITUDES WERE LARGER THAN EPSC AMPLITUDES AT ALL TESTED FREQUENCIES. IN CONTRAST, THE AMPLITUDES OF EPSCS OR IPSCS EVOKED BY LHB-PHOTOSTIMULATION OF EPN TERMINALS WERE DIFFERENTIALLY AFFECTED BY FREQUENCY STIMULATIONS, INDICATING DIFFERENT RELEASE PROBABILITIES OF GLUTAMATE AND GABA FROM DISTINCT SYNAPTIC VESICLES. WE FURTHER DETERMINED THAT LHB-PHOTOSTIMULATION OF VTA DUAL TERMINALS HYPERPOLARIZED MEMBRANE POTENTIALS AND INHIBITED FIRING ACTIVITY IN LHB NEURONS, BUT LHB-PHOTOSTIMULATION OF EPN DUAL TERMINALS EVOKED ACTION POTENTIALS. BY BEHAVIORAL TESTING, WE FOUND THAT LHB-PHOTOSTIMULATION OF VTA OR EPN DUAL TERMINALS DID NOT INDUCE PLACE PREFERENCE OR PLACE AVERSION. COLLECTIVELY, THESE RESULTS INDICATE THAT GLUTAMATE AND GABA CO-RELEASE FROM GLUTAMATE-GABA NEURONS OF VTA OR EPN DIFFERENTIALLY EXCITES OR INHIBITS LHB NEURONS, AND DO NOT SEEM TO PLAY A ROLE IN REWARD OR AVERSION.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M29. ROLE OF INTRACELLULAR TRAFFICKING OF AMPAR DURING LTP

FRANÇOISE COUSSEN-CHOQUET*, CAROLINE BONNET, JUSTINE CHARPENTIER, DANIEL CHOQUET

ABUNDANCE OF AMPA RECEPTORS (AMPAR) AT SYNAPSE IS ESSENTIAL FOR THE ESTABLISHMENT AND MAINTENANCE OF SYNAPTIC FUNCTION. THEIR SYNAPTIC LOCALIZATION IS DEPENDENT ON A HIGHLY DYNAMIC EXOCYTOSIS, ENDOCYTOSIS AND PLASMA MEMBRANE MOBILITY EVENTS. USING OUR BIOCHEMICAL TOOL COMBINED WITH PHOTONIC LIVE IMAGING, WE CONTROLLED AND FOLLOWED THE INTRACELLULAR TRANSPORT OF TAGGED GLUAI CONTAINING RECEPTORS IN CULTURED RAT HIPPOCAMPAL NEURONS. ANALYZES ARE PERFORMED FOR GLUAI WT AND MUTANTS OF GLUAI C-TERMINUS DOMAIN IN BASAL CONDITION AND DURING LTP. IN ORGANOTYPIC HIPPOCAMPAL SLICES WE COMBINE IMAGING AND ELECTROPHYSIOLOGY EXPERIMENTS TO ANALYZE THE IMPACT OF INTRACELLULAR TRANSPORT OF AMPAR ON LTP. LOCALIZATION OF AMPAR IS REGULATED BY THEIR INTRACELLULAR TRAFFICKING THRU INTERACTION OF THEIR C-TERMINUS DOMAINS WITH DIFFERENT INTRACELLULAR PARTNERS. THESE INTERACTIONS PLAY A MAJOR RULE IN THE EXOCYTOSIS AND LOCALIZATION OF THE RECEPTOR AT THE PLASMA MEMBRANE BOTH IN BASAL CONDITION OF DURING CLTP. IN HIPPOCAMPAL SLICE INTRACELLULAR TRANSPORT OF AMPAR PLAYS A MAJOR ROLE DURING LTP.

M30. LTP INDUCTION BY STRUCTURAL RATHER THAN ENZYMATIC FUNCTIONS OF CAMKII

JONATHAN TULLIS, MATTHEW LARSEN, NICOLE RUMIAN, RONALD FREUND, EMMA BOXER, CAROLYN BROWN, STEVEN COULTRAP, HOWARD SCHULMAN, JASON AOTO, MARK DELL'ACQUA, ULLI BAYER*

LEARNING AND MEMORY ARE THOUGHT TO REQUIRE HIPPOCAMPAL LONG-TERM POTENTIATION (LTP), AND ONE OF THE FEW CENTRAL DOGMAS OF MOLECULAR NEUROSCIENCE THAT HAS STOOD UNDISPUTED FOR MORE THAN THREE DECADES IS THAT LTP INDUCTION REQUIRES ENZYMATIC ACTIVITY OF THE CA2+/CALMODULIN-DEPENDENT PROTEIN KINASE II (CAMKII). HOWEVER, AS WE DELINEATE HERE, THE EXPERIMENTAL EVIDENCE IS SURPRISINGLY FAR FROM CONCLUSIVE: ALL PREVIOUS INTERVENTIONS INHIBITING ENZYMATIC CAMKII ACTIVITY AND LTP ALSO INTERFERE WITH STRUCTURAL CAMKII ROLES, IN PARTICULAR BINDING TO THE NMDA-TYPE GLUTAMATE RECEPTOR (NMDAR) SUBUNIT GLUN2B. THUS, WE HERE CHARACTERIZED AND UTILIZED COMPLEMENTARY SETS OF NEW OPTO/PHARMACO-GENETIC TOOLS TO DISTINGUISH BETWEEN ENZYMATIC AND STRUCTURAL CAMKII FUNCTIONS. SEVERAL INDEPENDENT LINES OF EVIDENCE DEMONSTRATED LTP INDUCTION BY A STRUCTURAL FUNCTION OF CAMKII RATHER THAN BY ITS ENZYMATIC ACTIVITY. THE SOLE CONTRIBUTION OF KINASE ACTIVITY WAS AUTOREGULATION OF THIS STRUCTURAL ROLE VIA T286 AUTOPHOSPHORYLATION, WHICH EXPLAINS WHY THIS DISTINCTION HAS BEEN ELUSIVE FOR DECADES. DIRECTLY INITIATING THE STRUCTURAL FUNCTION IN A MANNER THAT CIRCUMVENTED THIS T286 ROLE WAS SUFFICIENT TO ELICIT ROBUST LTP, EVEN WHEN ENZYMATIC CAMKII ACTIVITY WAS BLOCKED.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M31. UNVEILING SYNAPTIC DYNAMICS: SYNAPTOJANINEI REGULATION OF DOPAMINE D2 RECEPTOR SHORT ISOFORM MEMBRANE AVAILABILITY REVEALED BY A NOVEL PH-SENSITIVE OPTICAL REPORTER

ELNAZ KHEZERLOU*, JASDEEP KAUR, SMIT PATEL, PRANITA SANNIDHI, PING-YUE PAN

DOPAMINE D2 RECEPTORS (DRD2) ARE ESSENTIAL FOR PROPER FUNCTIONING OF THE BASAL GANGLIA, WHOSE DYSFUNCTION RESULT IN A WIDE RANGE OF NEUROLOGICAL DISORDERS, SUCH AS PARKINSON'S DISEASE, SUBSTANCE ABUSE, AND ETC. UNDERSTANDING THE MOLECULAR REGULATION OF D2 RECEPTOR MEMBRANE AVAILABILITY IS OF PARAMOUNT IMPORTANCE FOR GAINING INSIGHTS INTO FUNDAMENTAL BEHAVIORS. IN THIS STUDY, WE GENERATED A NOVEL GENETICALLY-ENCODED OPTICAL SENSOR FOR THE D2 RECEPTOR SHORT ISOFORM (D2S), A PRESYNAPTIC AUTORECEPTOR THAT ACTS TO INHIBIT DOPAMINE (DA) RELEASE. BY TAGGING A PH-SENSITIVE RED FLUORESCENT PROTEIN, "PHMSCARLET/PHMS", TO THE EXTRACELLULAR N-TERMINUS OF HUMAN D2S CDNA, WE ARE ABLE TO TRACK THE MEMBRANE AVAILABILITY OF D2 IN THE AXONS OF CULTURED MIDBRAIN NEURONS WITH UNPRECEDENTED SPATIAL AND TEMPORAL RESOLUTION. THE PHMS-D2S SENSOR EXHIBITS PKA OF 7.5. WHEN EXPRESSED IN MIDBRAIN NEURONS, 75% OF THE SENSORS DISTRIBUTE EVENLY ACROSS SYNAPTIC AND NON-SYNAPTIC REGIONS OF THE AXON, WHILE THE REMAINING ARE INTRACELLULAR. PHMS-D2S INTERNALIZES UPON DA TREATMENT AND EXHIBITS DA-INDUCED INHIBITION OF PRESYNAPTIC CALCIUM SIMILAR TO THE FLAG-D2S. OUR RESULTS FURTHER SHOWED THAT SYNAPTOJANINI (SYNJI), A MOLECULE INVOLVED IN SYNAPTIC VESICLE ENDOCYTOSIS, IS ALSO IMPORTANT FOR MAINTAINING D2S AT THE SYNAPSE. WHILE THERE WAS LACK A DIFFERENCE BETWEEN THE WILDTYPE AND SYNJI-HAPLOINSUFFICIENT (+/-) NEURONS AT BASELINE, REPEATED EXPOSURE TO DA RESULTED IN A SIGNIFICANTLY GREATER LOSS OF PHMS-D2S AT THE SYNAPTIC SURFACE OF SYNJI+/- NEURONS. CONSISTENTLY, SYNJI+/- MALE MICE DISPLAYED BLUNTED QUINPIROLE-INDUCED LOCOMOTOR INHIBITION IN THE OPEN FIELD TEST. INTERESTINGLY, PHMS-D2S AT NON-SYNAPTIC SURFACE OF THE AXONS WAS NOT AFFECTED BY SYNJI DEFICIENCY, SUGGESTING DISTINCT MOLECULAR REGULATION FOR SYNAPTIC AND NON-SYNAPTIC D2S. TAKEN TOGETHER, OUR WORK EMPLOYING A NOVEL D2 SENSOR DEMONSTRATES A NOVEL ROLE OF SYNJI IN MAINTAINING SYNAPTIC D2 AVAILABILITY.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M32. GENOME-WIDE ASSOCIATION STUDY IDENTIFIES APOE AND ZMIZI VARIANTS AS MITOPHAGY MODIFIERS IN LEWY BODY DISEASE

XU HOU, MICHAEL HECKMAN, FABIENNE FIESEL, SHUNSUKE KOGA, ALEXANDRA SOTO-BEASLEY, JENS WATZLAWIK, JING ZHAO, PATRICK JOHNSON, LAUNIA WHITE, JOSE BRAS, RITA GUERREIRO, NA ZHAO, GUOJUN REDDY, DENNIS DICKSON, OWEN ROSS, WOLFDIETER SPRINGER*

THE PINKI-PRKN PATHWAY MEDIATES A CRITICAL QUALITY CONTROL TO MAINTAIN MITOCHONDRIAL HEALTH AND FUNCTION. TOGETHER THE KINASE-LIGASE PAIR IDENTIFIES AND DECORATE DAMAGED MITOCHONDRIA WITH PHOSPHORYLATED UBIQUITIN (P-S65-UB). THIS SELECTIVE LABEL SERVES AS THE MITOPHAGY TAG AND FACILITATES THEIR DEGRADATION VIA AUTOPHAGY-LYSOSOME SYSTEM. WHILE COMPLETE LOSS OF PINKI OR PRKN FUNCTION CAUSES EARLY-ONSET PARKINSON DISEASE, MUCH BROADER MITOPHAGY IMPAIRMENTS ARE EMERGING ACROSS NEURODEGENERATIVE DISORDERS. WE PREVIOUSLY FOUND AGE- AND DISEASE-DEPENDENT ACCUMULATION OF P-S65-UB SIGNAL IN THE HIPPOCAMPUS OF AUTOPSY BRAINS WITH LEWY BODY DISEASE (LBD). HOWEVER, THE CONTRIBUTION OF GENETIC VARIATION TO MITOCHONDRIAL DAMAGE AND P-S65-UB LEVELS REMAINS UNKNOWN IN LBD CASES. TO IDENTIFY NOVEL REGULATORS OF PINKI-PRKN MITOPHAGY IN LBD, WE PERFORMED AN UNBIASED GENOME-WIDE ASSOCIATION STUDY OF HIPPOCAMPAL P-S65-UB LEVEL WITH 1,012 AUTOPSY CONFIRMED LBD SAMPLES. USING AN ESTABLISHED, MOSTLY AUTOMATED WORKFLOW, HIPPOCAMPAL SECTIONS WERE IMMUNOSTAINED FOR P-S65-UB, SCANNED, AND QUANTIFIED WITH UNBIASED ALGORITHMS. FUNCTIONAL VALIDATION OF THE SIGNIFICANT HIT WAS PERFORMED IN ANIMAL MODEL AND HUMAN INDUCED PLURIPOTENT STEM CELLS (HIPSCS).
WE IDENTIFIED A STRONG ASSOCIATION WITH P-S65-UB FOR APOE4 (RS429358; B: 0.50, 95% CI: 0.41 TO 0.69; P=8.67X10-25) AND A GENOME-WIDE SIGNIFICANT ASSOCIATION FOR ZMIZI (RS6480922; B: -0.33, 95% CI: -0.45 TO -0.22; P=1.42X10-8). THE INCREASED P-S65-UB LEVELS IN APOE4-CARRIER MAY BE MEDIATED BY BOTH CO-PATHOLOGY-DEPENDENT AND -INDEPENDENT MECHANISMS, WHICH WAS CONFIRMED IN APOE-TARGETED REPLACEMENT MICE AND HIPSC-DERIVED ASTROCYTES. INTRIGUINGLY, ZMIZI RS6480922 ALSO SIGNIFICANTLY ASSOCIATED WITH INCREASED BRAIN WEIGHT AND REDUCED NEUROPATHOLOGICAL BURDEN INDICATING A POTENTIAL ROLE AS A RESILIENCE FACTOR. OUR FINDINGS NOMINATE NOVEL MITOPHAGY REGULATORS IN LBD BRAIN (ZMIZI LOCUS) AND HIGHLIGHT A STRONG ASSOCIATION OF APOE4 WITH MITOPHAGY ALTERATION. WITH APOE4 BEING THE STRONGEST KNOWN RISK FACTOR FOR CLINICAL ALZHEIMER'S DISEASE AND DEMENTIA WITH LEWY BODIES, OUR FINDINGS SUGGEST A COMMON MECHANISTIC LINK UNDERSCORING THE IMPORTANCE OF MITOCHONDRIAL QUALITY CONTROL.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M33. BEHAVIORAL AND NEURONAL CHARACTERIZATION, ACROSS AGES, OF THE TGSWDI MOUSE MODEL OF ALZHEIMER'S DISEASE

NATALIE TAN*, ANGELICA ALVARADO, H CRAIG HELLER, ELSA PITTARAS

ALZHEIMER'S DISEASE (AD) IS A NEURODEGENERATIVE DISORDER THAT RESULTS IN LOSS OF MEMORY AND COGNITIVE ABILITIES. AD CURRENTLY AFFECTS MORE THAN 6 MILLION AMERICANS OVER THE AGE OF 65. IT IS NEUROCHEMICALLY CHARACTERIZED BY THE AGGREGATION OF B-AMYLOID PLAQUES AND TAU NEUROFIBRILLARY TANGLES WHICH RESULTS IN NEURONAL DYSFUNCTION AND DEATH. NEURONAL DYSFUNCTION AND DEATH CAN LEAD TO COGNITIVE DECLINE AND A PROGRESSIVE LOSS OF BRAIN FUNCTION. TGSWDI IS A VERY WELL-STUDIED TRANSGENIC MOUSE MODEL OF AD BUT NO LONGITUDINAL STUDIES HAVE BEEN DONE TO CHARACTERIZE COGNITIVE DEFICITS OR B-AMYLOID PLAQUE ACCUMULATION IN THIS MOUSE MODEL OVER TIME FOR USE AS A BASELINE REFERENCE FOR THE MODEL IN FUTURE RESEARCH. THUS, WE HAVE USED BEHAVIORAL TESTS TO STUDY THE WORKING, RECOGNITION, AND SPATIAL MEMORY OF THE MICE, AND IMMUNOHISTOCHEMISTRY (IHC) TO STUDY THE BRAINS OF THE MICE AT 3, 5, 8, 12, AND 15 MONTHS. AN IMMUNOSTAINING PROTOCOL WAS USED TO STUDY THE LEVELS OF B-AMYLOID PLAQUE DEPOSITS IN HIPPOCAMPAL AND CORTICAL BRAIN SLICES IN TGSWDI MICE AND WILD TYPE (WT) MICE. BRAIN SLICE IMAGES WERE OBTAINED POST-IHC VIA MICROSCOPE AND QCAPTURE SOFTWARE, AND B-AMYLOID PLAQUE SURFACE AREAS WERE MEASURED USING IMAGEJ SOFTWARE. T-MAZE, NOVEL OBJECT RECOGNITION, NOVEL OBJECT LOCATION TESTS WERE USED TO STUDY WORKING MEMORY AND LONG TERM MEMORY. IMMUNOHISTOCHEMISTRY SHOWED AN EXPONENTIAL INCREASE IN B-AMYLOID PLAQUE IN BOTH THE HIPPOCAMPUS AND THE CORTEX IN TGSWDI MICE AS AGE INCREASED, WHEREAS NO SIGNIFICANT ACCUMULATION OF PLAQUE IN WT MICE WAS SEEN AT ANY AGE. BEHAVIORAL RESULTS SHOWED THAT TGSWDI MICE EXPERIENCE DEFICITS IN LONG-TERM RECOGNITION MEMORY STARTING AT 8 MONTHS AND IN LONG-TERM SPATIAL MEMORY AT ALL AGES. TGSWDI MICE EXPERIENCED NO DEFICITS IN WORKING MEMORY. THIS MOUSE IS WIDELY USED AS A MODEL FOR AD AND CEREBRAL AMYLOID ANGIOPATHY AND OUR DATA SHOWS BOTH THAT IT DIFFERS FROM WT MICE AND EXPERIENCE SEVERAL COGNITIVE DEFICITS AND NEUROCHEMICAL MARKERS CONSISTENT WITH AD, AS WELL AS ITS BASELINE LEVELS OF COGNITIVE FUNCTION AND B-AMYLOID PLAQUE LOAD THROUGHOUT ITS LIFE COURSE FOR FUTURE RESEARCH.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M34. MECHANISMS OF EAAT2 REGULATION FOLLOWING ISCHEMIC INSULT

SIMRAN GILL*, KATELYN REEB, ANDREIA MORTENSEN

ISCHEMIC STROKE IS ONE OF THE LEADING CAUSES OF DEATH IN THE UNITED STATES, HOWEVER ADEQUATE TREATMENT IS STILL LACKING, HIGHLIGHTING THE NEED FOR NOVEL THERAPIES. IN THIS WORK, WE EMPLOYED THE OXYGEN GLUCOSE DEPRIVATION (OGD) IN VITRO MODEL OF ISCHEMIC STROKE, WITH THE AIM OF STUDYING THE REGULATION OF EXCITATORY AMINO ACID TRANSPORTERS (EAATS), KEY PROTEINS IN THE BRAIN THAT CONTROL EXTRACELLULAR CONCENTRATIONS OF GLUTAMATE. DYSREGULATION OF GLUTAMATE LEVELS, SUCH AS FOLLOWING STROKE, CAN LEAD TO A NEURONAL DEATH THROUGH EXCITOTOXICITY. EAATS THEREFORE PLAY A CRUCIAL ROLE IN EXCITOTOXIC OUTCOMES BY KEEPING LOW LEVELS OF SYNAPTIC GLUTAMATE.

OUR STUDY DEMONSTRATED THAT INCREASING SEVERITIES OF ISCHEMIC INSULT RESULTED IN DECREASED GLUTAMATE TRANSPORT, SUGGESTING AN INABILITY OF THESE TRANSPORTERS TO EFFECTIVELY CLEAR EXCESS GLUTAMATE. WE ALSO FOUND THAT THE SURFACE EXPRESSION LEVELS OF ASTROCYTIC TRANSPORTERS EAATI AND EAAT2 ARE DIFFERENTIALLY REGULATED: EAATI EXPRESSION WAS NOT AFFECTED, WHEREAS EAAT2 SURFACE EXPRESSION DECREASED PROPORTIONAL TO THE SEVERITY OF ISCHEMIC INSULT. FURTHERMORE, QPCR ANALYSIS SHOWS NO CHANGE IN EAAT2 MRNA LEVELS FOLLOWING ISCHEMIA, SUGGESTING THAT THE ALTERATIONS IN CELL SURFACE EXPRESSION IS DUE TO ABERRATIONS IN EAAT2 TRAFFICKING. THEREFORE, WE NEXT BEGAN TO INVESTIGATE THE MECHANISMS OF EAAT2 DOWNREGULATION. WITH A FOCUS ON POST-TRANSLATIONAL MODIFICATIONS, WE FOUND THAT SUMOYLATION OF EAAT2 MAY BE A PRIMARY MECHANISM THAT DICTATES ITS INTERNALIZATION FOLLOWING STROKE. SUMOYLATION INVOLVES THE COVALENT ATTACHMENT OF A SUMO TAG TO THE TARGET PROTEIN, WHICH CAN MARK IT FOR ITS INTRACELLULAR COMPARTMENTALIZATION. BY USING CO-IMMUNOPRECIPITATION, WE FOUND THAT EAAT2 WAS SUMOYLATED FOLLOWING ISCHEMIA, WITH THE GREATEST INTERACTION WITH SUMO-I AFTER SEVERE INSULT. FUTURE STUDIES WILL DETERMINE IF INHIBITING SUMOYLATION OF EAAT2 CAN RESTORE SURFACE EXPRESSION AFTER ISCHEMIC INSULT TO PROVIDE NEUROPROTECTION.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M35. RESOLUTION OF HYPERGLYCEMIA AND DISEASE-RELATED CENTRAL AUTONOMIC NEUROPLASTICITY BY VERTICAL SLEEVE GASTRECTOMY IN A MURINE MODEL OF TYPE I DIABETES

KATALIN SMITH*, CARIE BOYCHUK, J. ANNA JURAS, SOLEDAD PITRA, JORDAN WEAN, JEFFERY BOYCHUK, CORWIN BUTLER, BRET SMITH

A PROPOSED BRAIN-CENTERED GLUCOREGULATORY VISCERAL CONTROL CIRCUIT CONTRIBUTES TO THE MAINTENANCE OF HYPERGLYCEMIA IN DIABETES. NEURAL CIRCUITRY IN THE DORSAL VAGAL COMPLEX TRANSMITS MOTOR CONTROL TO VISCERA THAT MAINTAIN GLUCOSE HOMEOSTASIS AND UNDERGOES SIGNIFICANT CHANGES AFTER SUSTAINED SYSTEMIC HYPERGLYCEMIA. BARIATRIC SURGERY CAN RAPIDLY NORMALIZE SYSTEMIC GLUCOSE CONTROL IN DIABETES, BUT CENTRAL CIRCUIT MECHANISMS CONTRIBUTING TO THIS EFFECT ARE UNKNOWN. WE TESTED THE HYPOTHESIS THAT VERTICAL SLEEVE GASTRECTOMY (VSG) IMPROVES SYSTEMIC GLUCOSE METABOLISM AND REINSTATES DIABETES-RELATED BRAINSTEM CIRCUIT MODIFICATIONS ASSOCIATED WITH HYPERGLYCEMIA IN A MOUSE MODEL OF TYPE I DIABETES. VSG RESTORED NORMOGLYCEMIA IN ~63% OF MICE WITH STREPTOZOTOCIN (STZ)-INDUCED, SUSTAINED HYPERGLYCEMIA, INDEPENDENT OF CALORIC INTAKE; NORMOGLYCEMIA WAS EVIDENT WITHIN 48 HRS OF SURGERY AND COULD BE MAINTAINED FOR THE 28-DAY STUDY DURATION. BLOOD INSULIN LEVELS WERE SIGNIFICANTLY REDUCED AFTER STZ TREATMENT AND WERE NOT RESTORED BY VSG AT 14 AND 28 DAYS POST-SURGERY. GLUCOSE TOLERANCE TESTS INDICATED THAT GLUCOSE UTILIZATION SIGNIFICANTLY IMPROVED AFTER VSG SURGERY IN STZ-TREATED MICE, EVEN THOUGH BLOOD INSULIN CONCENTRATION REMAINED LOW. SYNAPTIC EXCITATION OF GABAERGIC NEURONS IN THE NUCLEUS TRACTUS SOLITARIUS (NTS) SIGNIFICANTLY INCREASED IN STZ-TREATED MICE AND NORMALIZED SHORTLY AFTER VSG. CHEMOGENETIC INHIBITION OF GABAERGIC NTS NEURONS LOWERED SYSTEMIC GLUCOSE CONCENTRATION IN DIABETIC, BUT NOT CONTROL MICE. THESE RESULTS PROVIDE EVIDENCE THAT BARIATRIC SURGERY RAPIDLY RESOLVES HYPERGLYCEMIA AND RESTORES CENTRAL VAGAL CIRCUIT FUNCTION IN AN INSULIN-INDEPENDENT FASHION IN A MODEL OF TYPE I DIABETES, AND THAT SELECTIVELY DECREASING EXCITABILITY OF NTS GABAERGIC NEURONS IS ALSO SUFFICIENT TO REDUCE DIABETIC HYPERGLYCEMIA, SUPPORTING THE INVOLVEMENT OF A HINDBRAIN PREAUTONOMIC CIRCUIT IN MAINTAINING GLUCOSE HOMEOSTASIS.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M36. OPEN BOARD

M37. EAATS FOR STROKE: TO MODULATE OR NOT TO MODULATE

KATELYN REEB*, ANDREIA MORTENSEN

EXCITATORY AMINO ACID TRANSPORTERS (EAATS) ARE CRITICAL PROTEINS IN THE CNS THAT REGULATE SYNAPTIC GLUTAMATE LEVELS, CRUCIALLY PREVENTING EXCITOTOXICITY. THE ASTROCYTIC TRANSPORTER EAAT2 IS RESPONSIBLE FOR THE MAJORITY OF GLUTAMATE CLEARANCE IN THE CNS. ABERRANT EAAT2 ACTIVITY AND GLUTAMATERGIC SIGNALING OCCURS IN MANY NEUROPSYCHIATRIC DISORDERS. OUR WORK FOCUSED ON ISCHEMIC STROKE, A CONDITION THAT URGENTLY NEEDS NEW TREATMENTS. IN ISCHEMIC STROKE, EXCESSIVE LEVELS OF RELEASED GLUTAMATE CAUSE EXCITOTOXICITY, LEADING TO SECONDARY DAMAGE WHICH ULTIMATELY RESULTS IN COGNITIVE DEFICITS. WE HAVE DEVELOPED NOVEL ALLOSTERIC MODULATORS (AMS) OF EAATS, INCLUDING SELECTIVE-EAAT2 POSITIVE ALLOSTERIC MODULATORS (PAMS), AND NON-SPECIFIC AND BROAD-ACTING ANALOG AMS. WE HYPOTHESIZE THE PHARMACOLOGICAL ACTIVITY OF AMS IS DETERMINED BY DIFFERENTIAL INTERACTIONS WITH CRITICAL AMINO ACID RESIDUES LOCATED BETWEEN THE TRANSPORTER'S SCAFFOLD AND TRANSPORT DOMAINS. WE HAVE TWO MAIN GOALS: TO FURTHER UNDERSTAND THE MECHANISM OF THESE AMS, AND TO STUDY THEIR EFFECTS IN AN IN VITRO STROKE MODEL. COMPUTATIONAL MODELING PREDICTIONS SUGGEST SOME AMINO ACID RESIDUES ON EAAT2 THAT ARE CRITICAL TO MEDIATING THE ACTION OF NA-014, AN EAAT2-SPECIFIC PAM. DOSE-RESPONSE ASSAYS EVALUATING THE EFFECT OF NA-014 AND OTHER AMS OFFERED FURTHER INSIGHTS ON WHICH RESIDUES ARE IMPORTANT FOR THEIR ACTION, AND WHAT CHEMICAL MOIETIES CONFER EAAT SUBTYPE SELECTIVITY AND PHARMACOLOGICAL ACTION. ADDITIONALLY, WE EVALUATED POTENTIAL TRANSLATABILITY OF EAATS PAMS IN A MODEL OF ISCHEMIC STROKE. WE HYPOTHESIZE THAT THESE COMPOUNDS CAN RESTORE GLUTAMATERGIC HOMEOSTASIS BY AUGMENTING GLUTAMATE CLEARANCE. WE EVALUATED NA-014 IN AN IN VITRO MODEL OF ISCHEMIC STROKE, OXYGEN GLUCOSE DEPRIVATION, IN PRIMARY NEURON-GLIA CULTURES, AND FOUND THAT IT DEMONSTRATED NEUROPROTECTIVE PROPERTIES. COLLECTIVELY, THESE STUDIES EXPAND OUR MECHANISTIC UNDERSTANDING OF THE EAAT AMS AND DEMONSTRATE THEIR CLINICAL UTILITY FOR ISCHEMIC STROKE.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M38. TRPM2-CAMKII SIGNALING DRIVE EXCESSIVE GABAERGIC SYNAPTIC INHIBITION AFTER ISCHEMIA

AMELIA BURCH*, JOSHUA GARCIA, HEATHER O'LEARY, AMI HAAS, JAMES ORFILA, ERIKA TIEMEIER, NICHOLAS CHALMERS, KATHARINE SMITH, NIDIA QUILLINAN, PACO HERSON

EXCITOTOXICITY AND THE CONCURRENT LOSS OF INHIBITION ARE WELL-DEFINED MECHANISMS DRIVING ACUTE ELEVATION IN EXCITATORY/ INHIBITORY (E/I) BALANCE AND NEURONAL CELL DEATH FOLLOWING AN ISCHEMIC INSULT TO THE BRAIN. DESPITE THE HIGH PREVALENCE OF LONG-TERM DISABILITY IN SURVIVORS OF GLOBAL CEREBRAL ISCHEMIA (GCI) AS A CONSEQUENCE OF CARDIAC ARREST, IT REMAINS UNCLEAR WHETHER E/I IMBALANCE PERSISTS BEYOND THE ACUTE PHASE AND NEGATIVELY AFFECTS FUNCTIONAL RECOVERY. WE PREVIOUSLY DEMONSTRATED SUSTAINED IMPAIRMENT OF LONG-TERM POTENTIATION (LTP) IN HIPPOCAMPAL CA1 NEURONS CORRELATING WITH DEFICITS IN LEARNING AND MEMORY TASKS IN A MURINE MODEL OF CARDIAC ARREST/ CARDIOPULMONARY RESUSCITATION (CA/CPR). HERE, WE USE CA/CPR AND AN IN VITRO ISCHEMIA MODEL TO ELUCIDATE MECHANISMS BY WHICH E/I IMBALANCE CONTRIBUTES TO ONGOING HIPPOCAMPAL DYSFUNCTION. WE REVEAL INCREASED POSTSYNAPTIC GABAA RECEPTOR (GABAAR) CLUSTERING AND FUNCTION IN THE CA1 REGION OF THE HIPPOCAMPUS THAT REDUCES E/I RATIO. IMPORTANTLY, REDUCED GABAAR CLUSTERING OBSERVED IN THE FIRST 24 HOURS REBOUNDS TO AN ELEVATION OF GABAERGIC CLUSTERING BY 3 DAYS POST-ISCHEMIA. THIS INCREASE IN GABAERGIC INHIBITION REQUIRED ACTIVATION OF THE CA2+-PERMEABLE ION CHANNEL TRANSIENT RECEPTOR POTENTIAL MELASTATIN-2 (TRPM2), PREVIOUSLY IMPLICATED IN PERSISTENT LTP AND MEMORY DEFICITS FOLLOWING CA/CPR. FURTHERMORE, WE FIND CA2+-SIGNALING DOWNSTREAM OF TRPM2 ACTIVATION UPREGULATES CA2+/CALMODULIN-DEPENDENT PROTEIN KINASE II (CAMKII) ACTIVITY, THEREBY DRIVING THE ELEVATION OF POSTSYNAPTIC INHIBITORY FUNCTION. THUS, WE PROPOSE A NOVEL MECHANISM BY WHICH INHIBITORY SYNAPTIC STRENGTH IS UPREGULATED IN THE CONTEXT OF ISCHEMIA AND IDENTIFY A TRPM2-CAMKII PATHWAY AS A POTENTIAL PHARMACOLOGICAL TARGET TO RESTORE PERTURBED SYNAPTIC PLASTICITY AND AMELIORATE COGNITIVE FUNCTION.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M39. ALCOHOL AFTER INJURY: UNCOVERING THE SYNERGISTIC EFFECTS OF CHRONIC ALCOHOL USE AFTER BLAST-INDUCED MTBI

MAKENZIE PATARINO*, MATHEW SEVAO, TAMI WOLDEN-HANSON, GARTH TERRY, BRYAN SCHUESSLER, ALEXANDRIA MURRY, SAM GOLDEN, JEFFREY ILIFF, ABIGAIL SCHINDLER

MILD TRAUMATIC BRAIN INJURY (MTBI), COMMONLY CALLED THE "HALLMARK INJURY" OF THE IRAQ/AFGHANISTAN WARS, IS AN ESTABLISHED RISK FACTOR FOR ALZHEIMER'S DISEASE AND RELATED DEMENTIAS (ADRD). ALCOHOL USE DISORDER (AUD) CAN ALSO INCREASE THE RISK OF ADRD, AND IS OFTEN COMORBID WITH MTBI. HOWEVER, THE INTERACTION OF MTBI AND AUD IN CONTRIBUTING TO ADRD REMAINS UNDERSTUDIED. THE CURRENT STUDY INVESTIGATES HOW CHRONIC ALCOHOL AFTER BLAST-INDUCED MTBI AFFECTS DEVELOPMENT OF ADRD AND AGING RELATED BEHAVIORS AND BIOMARKERS. MALE MICE WERE EXPOSED TO REPETITIVE (3X) BLAST OR SHAM USING A TRANSLATIONALLY RELEVANT SHOCK TUBE. FOLLOWING RECOVERY FROM BLAST, GROUP-HOUSED MICE WERE ALLOWED INTERMITTENT ACCESS TO MULTIPLE DOSES OF ALCOHOL (2-20%) IN OUR NOVEL SOCIALLY INTEGRATED POLYSUBSTANCE CAGES FOR THREE SEPARATE FOUR WEEK PERIODS. BEHAVIORAL OUTCOMES (SPATIAL WORKING MEMORY, THERMAL SENSITIVITY, BLAST-CONDITIONED AVERSION, HYPERREACTIVITY) WERE ASSESSED PRIOR TO ALCOHOL EXPOSURE AND AGAIN THREE DAYS AFTER EACH ACCESS PERIOD. FLUID AND IMAGING-BASED BIOMARKERS WERE ALSO ASSESSED, INCLUDING BRAIN GLUCOSE METABOLISM (FDG-PET), PERIPHERAL CYTOKINES, GUT MICROBIOME, LIVER HEALTH, AND GLYMPHATIC FUNCTION (3D HISTOLOGY). INITIAL BEHAVIORAL RESULTS SHOW ESCALATION OF ALCOHOL INTAKE BETWEEN EXPOSURES, A POTENTIAL NEGATIVE EFFECT OF ALCOHOL ON SPATIAL WORKING MEMORY, HIGHER ALCOHOL INTAKE FOR BLAST-EXPOSED MICE, AND A COMBINED EFFECT OF BLAST-EXPOSURE AND ALCOHOL ON HYPERREACTIVITY. EARLY BIOMARKER ANALYSES SUGGEST HIGH ALCOHOL INTAKE IMPAIRS BRAIN GLUCOSE METABOLISM AND GLYMPHATIC CLEARANCE IN BOTH SHAM AND BLAST-EXPOSED MICE, WHILE ONLY BLAST-EXPOSED MICE SHOW IMPAIRMENTS AFTER LOW AMOUNTS OF CHRONIC ALCOHOL. THESE RESULTS PROVIDE A HOLISTIC CHARACTERIZATION OF HOW AGING IS AFFECTED BY TRAUMA AND ALCOHOL OVER THE LIFESPAN, HIGHLIGHT NEW BIOMARKERS TO PREDICT ADVERSE OUTCOMES, AND ULTIMATELY PROVIDE POTENTIAL CLINICAL TARGETS TO COMBAT ADVERSE COMORBID OUTCOMES IN THE AGING POPULATION.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M40. REFINED GENE ANNOTATIONS INCREASE THE ACCURACY OF QUANTIFYING MU OPIOID RECEPTOR RNAS AND OTHER NEURONAL GENES IN SINGLE-CELL RNA-SEQUENCING DATA

JESSE NIEHAUS*, HANNAH NOURIE, HONGKUI ZENG, GREG SCHERRER

OPIOIDS ARE INDISPENSABLE PAIN-RELIEVERS BUT PRODUCE DANGEROUS SIDE EFFECTS LIKE EUPHORIA AND RESPIRATORY DEPRESSION. OPIOIDS INDUCE THESE DIVERSE EFFECTS BY BINDING THE MU OPIOID RECEPTOR (MOR; ENCODED BY OPRM1) IN DIFFERENT REGIONS THROUGHOUT THE NERVOUS SYSTEM. ACTIVATING OR INHIBITING SPECIFIC OPIOID-SENSITIVE CIRCUITS MAY LEAD TO MORE EFFECTIVE ANALGESICS OR ADDICTION TREATMENTS, BUT THE IDENTITIES AND MOLECULAR CHARACTERISTICS OF OPRM1-EXPRESSING CELLS ARE STILL UNCLEAR. WE SOUGHT TO USE SINGLE-CELL RNA-SEQUENCING (SCRNA-SEQ) TO IDENTIFY AND ESTABLISH MOLECULAR PROFILES FOR OPRM1+ CELL TYPES THROUGHOUT THE BRAIN. QUANTIFYING OPRM1+ CELLS IN SCRNA-SEQ DATA HINGES ON PROPERLY ALIGNING CDNA READS TO A REFERENCE GENOME. HERE, WE IDENTIFIED INCONSISTENCIES IN OPRM1+ CELL PROPORTIONS BETWEEN TRANSCRIPTOMIC AND HISTOLOGICAL DATASETS USING MULTIPLE SCRNA-SEQ MODALITIES. WE DETERMINED THESE INCONSISTENCIES AROSE FROM INACCURATE READ ALIGNMENT CAUSED BY GENOMIC MONOMERIC REPEATS AND INCOMPLETE GENE ANNOTATIONS, WHICH GENERATED FALSE POSITIVE AND FALSE NEGATIVE OPRM1 READ ASSIGNMENTS. BY UTILIZING A CUSTOM REFINED GENE ANNOTATION, WE INCREASED READ ASSIGNMENT ACCURACY AND THE CONSISTENCY OF OPRM1+ CELL POPULATIONS BETWEEN TRANSCRIPTOMIC AND HISTOLOGICAL DATASETS. REFINED GENE ANNOTATIONS ALSO INCREASED THE ACCURACY OF OPRM1 ISOFORM DETECTION BASED ON CONSISTENCY WITH COMPLEMENTARY SPLICE-AWARE IN SITU HYBRIDIZATION. BEYOND OPRM1, MONOMERIC REPEATS ARE HIGHLY PREVALENT THROUGHOUT THE GENOME AND ARE PREFERENTIALLY ENRICHED IN NEURONAL GENES. IN ONGOING WORK, WE ARE EXTRAPOLATING OUR REFINEMENT METHOD TO ALL GENES AFFECTED BY MONOMERIC REPEATS AND AIM TO PROVIDE A TOOL TO OPTIMIZE USER-PROVIDED ANNOTATIONS FOR SCRNA-SEQ TECHNOLOGIES.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M41. THE HISTORY OF DANISH NEUROSCIENCE

OLAF PAULSON*, ARNE SCHOUSBOE, HANS HULTBORN

THE HISTORY OF DANISH NEUROSCIENCE STARTS WITH AN ACCOUNT OF IMPRESSIVE CONTRIBUTIONS MADE AT THE 17TH CENTURY. THOMAS BARTHOLIN WAS THE FIRST DANISH NEUROSCIENTIST AND HIS DISCIPLE NICOLAUS STENO BECAME INTERNATIONALLY ONE OF THE MOST PROMINENT NEUROSCIENTISTS IN THIS PERIOD. FROM THE START, DANISH NEUROSCIENCE WAS LINKED TO CLINICAL DISCIPLINES. THIS CONTINUED IN THE 19TH AND FIRST HALF OF THE 20TH CENTURY WITH NEW INITIATIVES LINKING BASIC NEUROSCIENCE TO CLINICAL NEUROLOGY AND PSYCHIATRY IN THE SAME SCIENTIFIC ENVIRONMENT. SUBSEQUENTLY, FROM THE MIDDLE OF THE 20TH CENTURY, BASIC NEUROSCIENCE WAS DEVELOPING RAPIDLY WITHIN THE PRECLINICAL UNIVERSITY SECTORS. CLINICAL NEUROSCIENCE CONTINUED AND WAS EVEN REINFORCED DURING THIS PERIOD WITH IMPORTANT TRANSLATIONAL RESEARCH AND A CLOSE CO-OPERATION BETWEEN BASIC AND CLINICAL NEUROSCIENCE. THIS LONG HISTORY WAS RECENTLY REVIEWED IN AN EDITORIAL IN THE EUROPEAN JOURNAL OF NEUROSCIENCE (1). THE PRESENT PRESENTATION ILLUSTRATES HIGHLIGHTS OF THE 400 YEARS LONG HISTORY OF DANISH NEUROSCIENCE. STENO (1638-1686) WAS ACTIVE IN MANY SCIENTIFIC FIELDS. ONE OF HIS MAIN CONTRIBUTIONS TO NEUROSCIENCE WAS RELATED TO THE INVESTIGATION OF THE ANATOMY OF THE PINEAL GLAND. RENÉ DESCARTES HAD PROPOSED HOW THE PINEAL GLAND WAS THE SEAT OF THE SOUL, ACTING BY ROTATION TO DISTRIBUTE ANIMAL SPIRITS. STENO DEMONSTRATED THAT THE PINEAL GLAND WAS MERELY GREY MATTER WITH BLACK SPOTS. IN THE 19TH CENTURY CARL LANGE (1834-1900) HAD MAIN CONTRIBUTIONS IN NEUROLOGY AND PSYCHIATRY. HE WAS THE FIRST TO USE LITHIUM IN THE TREATMENT OF DEPRESSION. HE RODE A BOOK IN DANISH, "ON EMOTIONS - PSYCHO-PHYSIOLOGICAL STUDY" IN 1885, TRANSLATED TO GERMAN, FRENCH AND ENGLISH, E.G., PUBLISHED IN ENGLISH IN 1967. FRITZ BUCHTHAL (1907-2003) HAD A MAIN ROLE IN THE DANISH AND INTERNATIONAL DEVELOPMENT OF CLINICAL NEUROPHYSIOLOGY AND ESPECIALLY ELECTROMYOGRAPHY. NIELS A. LASSEN (1926-1997) MAIN RESEARCH FIELD WAS THE CEREBRAL CIRCULATION. HE, HIS GROUP AND COLLABORATORS WERE THE FIRST TO DEMONSTRATE THAT ACTIVATION LED TO BLOOD FLOW INCREASE, FUNCTIONAL ACTIVATION. FINALLY, JENS CHRISTIAN SKOU (1918-2018) RECEIVED THE NOBEL PRIZE IN 1997 FOR THE DISCOVERY OF THE SODIUM-POTASSIUM PUMP.

REFERENCE: PAULSON OB, SCHOUSBOE A, HULTBORN H. THE HISTORY OF DANISH NEUROSCIENCE. EUR J NEUROSCI. 2023;58:2893-2960.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M42. BIDIRECTIONAL ERK1/2 MODULATION IN DOPAMINERGIC NEURONS REGULATES DAT TRAFFICKING AND FUNCTION

CHRISTINA BESADA*, STACIA LEWANDOWSKI, OLE MORTENSEN

DOPAMINE (DA) IS A NEUROTRANSMITTER THAT PLAYS A CRITICAL ROLE IN MOTIVATION AND REWARD, AND ABERRANT DA SIGNALING IS ASSOCIATED WITH NEUROPSYCHIATRIC DISORDERS SUCH AS SUBSTANCE USE DISORDER. DA TRANSMISSION IS REGULATED BY THE DOPAMINE TRANSPORTER (DAT), WHICH TRANSLOCATES DA FROM THE EXTRACELLULAR SPACE. DAT FUNCTION IS REGULATED BY TRAFFICKING TO AND FROM THE PLASMA MEMBRANE. DAT TRAFFICKING IS CONTROLLED BY SEVERAL SIGNALING PATHWAYS, INCLUDING PKC AND MAP KINASES. OUR IN VIVO DATA SHOWS THAT OVEREXPRESSION OF MAP KINASE PHOSPHATASE 3 (MKP3) IN DA NEURONS PREVENTS PKC-MEDIATED DAT INTERNALIZATION, THUS INCREASING DAT SURFACE-EXPRESSION. FURTHERMORE, MKP3 DECREASES PHOSPHORYLATION AT THR53, WHICH IS THOUGHT TO PLAY A ROLE IN DAT TRAFFICKING. BECAUSE ERK1/2 IS THE SOLE SUBSTRATE FOR MKP3, THESE FINDINGS SUGGEST THAT ERK1/2 MAY HAVE A SIGNIFICANT ROLE IN DAT TRAFFICKING. ADDITIONALLY, DAT IS REGULATED BY RECEPTOR SIGNALING, NOTABLY BY THE GI-COUPLED DOPAMINE RECEPTOR 2 (DRD2), AND THE GQ-COUPLED GLUTAMATE RECEPTOR 5 (MGLU5). DRD2 ANTAGONISM HAS BEEN SHOWN TO INCREASE DAT SURFACE EXPRESSION. SIMILARLY, MGLU5 SILENCING INCREASES DAT SURFACE-EXPRESSION. HOWEVER, WE STILL DO NOT HAVE A COMPLETE UNDERSTANDING OF THE CONTRIBUTION OF INTRACELLULAR FACTORS THAT GOVERN THESE CHANGES IN DAT SURFACE-EXPRESSION, BUT ERK1/2 IS LIKELY PLAYING A ROLE. TO FURTHER CHARACTERIZE THE CONTRIBUTIONS OF ERK1/2 TO DAT EXPRESSION AND FUNCTION, WE WILL USE TWO VIRAL CONSTRUCTS WHICH ENABLE CRE RECOMBINASE-DEPENDENT EXPRESSION IN DA NEURONS, ALLOWING FOR SPATIOTEMPORAL INACTIVATION OR ACTIVATION OF ERK1/2: (1) MKP3 AND (2) OPTOSOS, AN OPTOGENETIC TOOL THAT ENABLES BLUE-LIGHT ACTIVATION OF ERK1/2. THESE TOOLS WILL BE COMBINED WITH PHARMACOLOGICAL INHIBITORS TO INVESTIGATE THE ROLE OF ERK1/2 IN DAT SURFACE-EXPRESSION AND RECEPTOR-MEDIATED DAT TRAFFICKING. THESE STUDIES WILL HELP US TO BETTER PARSE OUT THE ROLE OF ERK1/2 SIGNALING IN THE REGULATION OF DAT.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M43. PRENATAL CANNABINOID EXPOSURE ALTERS MEMORY BY MODULATING GLUTAMATERGIC NEUROTRANSMISSION

KAWSAR CHOWDHURY*, MILES WILEY, ADRIAN COURVILLE, EMMA REDMON, WARREN SMITH, MIRANDA REED, VISHNU SUPPIRAMANIAM

WITH THE INCREASED LEGALIZATION OF CANNABIS, PRENATAL EXPOSURE TO CANNABINOIDS (PCE) HAS INCREASED SIGNIFICANTLY AND IS EXPECTED TO CONTINUE RISING. CURRENTLY, THERE IS NO THERAPY AVAILABLE FOR COGNITIVE DEFICITS ASSOCIATED WITH PRENATAL CANNABINOID EXPOSURE (PCE). OUR PROJECT HYPOTHESIZES THAT PCE CAUSES ALTERED EXPRESSION AND FUNCTION OF GLUTAMATERGIC RECEPTORS, NAMELY THE NMDAR (N-METHYL D-ASPARTATE RECEPTOR) AND AMPAR (A-AMINO-3-HYDROXY-5-METHYL-4-ISOXAZOLE PROPIONIC ACID RECEPTORS) LEADING TO COGNITIVE AND MEMORY DEFICITS. PREGNANT SPRAGUE DAWLEY RATS WERE EXPOSED TO A VAPORIZED SOLUTION OF EITHER PEG400 ONLY OR PURE D9-TETRAHYDROCANNABINOL (THC) MIXED IN PEG400 FROM GESTATIONAL DAY FIVE TO POST-NATAL DAY NINE AND WERE EXAMINED BETWEEN PND 40-50. IMMUNOBLOTTING OF HIPPOCAMPAL SYNAPTOSOMAL PROTEINS REVEALED THAT PCE ALTERED GLUTAMATE RECEPTOR LEVELS. TO FURTHER EVALUATE IF THESE RECEPTOR-LEVEL CHANGES TRANSLATED INTO FUNCTIONAL CHANGES AT THE CELLULAR LEVEL, WE PERFORMED WHOLE-CELL ELECTRICAL MEASUREMENTS FROM HIPPOCAMPAL PYRAMIDAL CELLS AND FIELD ACTIVITY FROM HIPPOCAMPAL CA3-CA1 SCHAFFER COLLATERALS OF PCE OFFSPRING. SPONTANEOUS EXCITATORY POSTSYNAPTIC CURRENTS DRIVEN BY AMPA AND NMDA RECEPTORS SHOWED ALTERATIONS IN FREQUENCY AND AMPLITUDE BETWEEN PCE AND CONTROL ANIMALS. LONG-TERM POTENTIATION (LTP), A CELLULAR CORRELATE OF LEARNING AND MEMORY WITHIN THE CA3-CA1 NEURONAL PATHWAY, ALSO SHOWED DEFICITS IN PCE OFFSPRING. WE EVALUATED THE COGNITIVE IMPAIRMENTS THROUGH TRACE FEAR CONDITIONING (TFC) EXPERIMENTS. IN BRIEF, OUR STUDY ELUCIDATES THE MOLECULAR MECHANISMS OF HIPPOCAMPAL-DEPENDENT MEMORY DEFICITS ASSOCIATED WITH PCE.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M44. ASSESSING THE FUNCTIONAL PROFILE AND CONTRIBUTION OF SENESCENT DRG NEURONS TO OSTEOARTHRITIS PAIN

CHELSIE BREWER*, LAUREN DONOVAN, VIVIANNE TAWFIK, JULIE KAUER

ADVANCED AGE IS A MAJOR RISK FACTOR FOR CHRONIC PAIN, WITH HALF OF PEOPLE OVER 65 AFFLICTED WITH A CHRONIC PAIN DISORDER. DESPITE THIS OVERWHELMING PREVALENCE, THERE IS A LACK OF INSIGHT INTO THE SPECIFIC MECHANISMS PREDISPOSING OR GENERATING DISORDERED PAIN IN THE ELDERLY. OSTEOARTHRITIS (OA) IS A PROGRESSIVE JOINT DISEASE CHARACTERIZED BY STIFFNESS AND PAIN THAT LIMITS MOBILITY AND LOWERS QUALITY OF LIFE, AND AGING IS MAJOR RISK FACTOR FOR DEVELOPMENT OF OA. WE ARE ACTIVELY RESEARCHING WAYS TO TARGET KNEE JOINT-INNERVATING DRG NEURONS, THE INITIAL DRIVER OF PERIPHERAL PAIN, DRIVING OSTEOARTHRITIS PAIN, BY LABELING NERVES IN THE MOUSE JOINT AND ELECTROPHYSIOLOGICALLY RECORDING FROM THESE NERVES IN AN INTACT DORSAL ROOT GANGLION (DRG) PREPARATION. ADDITIONALLY, SENESCENCE, A CELLULAR PHENOTYPE CHARACTERIZED BY RESISTANCE TO APOPTOSIS AND THE NASCENT SECRETION OF INFLAMMATORY MEDIATORS, INCREASES WITH AGE. INTERESTINGLY, WE HAVE SHOWN THAT IN AGED OR NERVE INJURY CONDITIONS, SENESCENT CELL LOAD INCREASES IN DRG NEURONS. INTRIGUINGLY, WE ALSO FOUND THAT ABLATION OF SENESCENT DRG NEURONS REDUCES NEUROPATHIC PAIN IN MICE. WE ARE CURRENTLY USING ELECTROPHYSIOLOGY IN EX VIVO INTACT DRG FOLLOWED BY SINGLE-CELL QPCR TO FUNCTIONALLY CHARACTERIZE AND PHENOTYPE SENESCENT DRG NEURONS IN YOUNG AND AGED MICE IN THE CONTEXT OF SPARED NERVE INJURY, A MOUSE MODEL OF NEUROPATHIC PAIN. WE ARE SYNERGISTICALLY ANALYZING MULTIPLE ASPECTS OF INTRINSIC EXCITABILITY (E.G. ACTION POTENTIAL PROPERTIES, SPONTANEOUS ACTIVITY, ETC.) IN COMBINATION WITH GENE EXPRESSION OF MARKERS OF SENESCENCE (E.G. P21 AND P16), NERVE INJURY (E.G. ATF3), CYTOKINE PRODUCTION (E.G. IL6), NEUROPEPTIDES (E.G. CGRP), AND MECHANO- AND THERMOTRANSDUCER CHANNELS (E.G. TRPV1, PIEZO2) TO CONNECT SPECIFIC DRG POPULATIONS TO PAIN GENERATION. NOTABLY, EVIDENCE SUGGESTS THAT SENESCENT CELLS PLAY A ROLE IN OSTEOARTHRITIS PAIN, EVIDENCED BY THE ANALGESIC EFFECTS OF SENOLYTIC ABLATION OF THESE CELLS IN THE KNEE JOINT. HOWEVER, THESE STUDIES FOCUSED ON SENESCENT ARTICULAR AND SYNOVIAL CELLS, AND YET SENESCENCE IN DRG NEURONS COULD BE A POTENTIAL MECHANISM UNDERLYING OSTEOARTHRITIS PAIN. WE HAVE EVIDENCE THAT KNEE-INNERVATING DRG EXPRESS SENESCENT MARKERS IN AGED MICE. NEXT, WE WILL INVESTIGATE HOW MODELS OF KNEE OSTEOARTHRITIS AFFECT THE SENESCENT DRG LANDSCAPE.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M45. HOW THE CLAUSTRUM INSTANTIATES COGNITIVE NETWORK ACTIVITY IN ACUTE AND CHRONIC PAIN

BRENT STEWART, MICHAEL KEASER, HWIYOUNG LEE, SARAH MARGERISON, MARTIN LINDQUIST, SHUO CHEN, BRIAN MATHUR, DAVID SEMINOWICZ*

ABERRANT COGNITIVE NETWORK ACTIVITY AND COGNITIVE DEFICITS ARE ESTABLISHED FEATURES OF CHRONIC PAIN. HOWEVER, THE NATURE OF COGNITIVE NETWORK ALTERATIONS ASSOCIATED WITH CHRONIC PAIN AND THEIR UNDERLYING MECHANISMS REQUIRE ELUCIDATION. WE ANALYZED TWO DATASETS: ONE CONSISTING OF 3T FMRI SCANS IN 39 HEALTHY PARTICIPANTS WHILE EXPERIENCING PAIN, AND A SECOND CONSISTING OF 35 HEALTHY PARTICIPANTS AND 112 MIGRAINE PATIENTS WHO EXPERIENCED PAIN AND ALSO PERFORMED A COGNITIVE TASK IN SEPARATE RUNS. WE FOUND THE FOLLOWING: 1) THE CLAUSTRUM BOLD SIGNAL INCREASED IN RESPONSE TO EXPERIMENTAL HEAT PAIN; 2) CLAUSTRUM BOLD SIGNAL WAS DISTINGUISHABLE FROM NEIGHBORING REGIONS; 3) CLAUSTRUM ACTIVITY INCREASED IN RESPONSE TO A PAIN-PREDICTIVE CUE; 4) MIGRAINE PATIENTS EXHIBITED GREATER COGNITIVE TASK ASSOCIATED NETWORK ACTIVITY THAN CONTROLS; 5) MIGRAINE PATIENTS ENGAGED A PAIN-RESPONSIVE PREFRONTAL CORTEX REGION – LATDLPFC – DURING PAIN-FREE COGNITIVE TASK PROCESSING. DYNAMIC CAUSAL MODELING SUGGESTED A DIRECTIONAL INFLUENCE OF THE CLAUSTRUM ON ACTIVITY IN THIS LATDLPFC REGION. ALTOGETHER, OUR STUDY REVEALED A RELATIONSHIP BETWEEN CLAUSTRUM AND COGNITIVE CONTROL NETWORK ACTIVITY DURING ACUTE PAIN AND UNCOVERED EVIDENCE OF A CLAUSTRUM-DLPFC CIRCUIT UNDERLYING COGNITIVE NETWORK DYSFUNCTION IN CHRONIC PAIN. THESE FINDINGS REPRESENT EMPIRICAL SUPPORT FOR OUR PREVIOUSLY DESCRIBED NETWORK INSTANTIATION IN COGNITIVE CONTROL MODEL OF CLAUSTRUM FUNCTION AND RAISE THE POSSIBILITY OF THE CLAUSTRUM AS A FUTURE THERAPEUTIC TARGET FOR CHRONIC PAIN CONDITIONS, WITH POTENTIAL IMPLICATIONS FOR OTHER NEUROPSYCHIATRIC DISORDERS CHARACTERIZED BY COGNITIVE IMPAIRMENT AND CORTICAL NETWORK ABNORMALITIES.

MONDAY, JANUARY 29TH

POSTER SESSION II
3:30 P.M. - 4:30 P.M.
PEAK 4-5

M46. THE SUICIDAL BRAIN: BIOLOGICAL INSIGHT FROM POSTMORTEM HUMAN TISSUE

GIOVANNA PUNZI*

DEATH BY SUICIDE IN THE ABSENCE OF IDENTIFIABLE PSYCHIATRIC DISORDERS IS NOT RARE, AND MOST PATIENTS WITH PSYCHIATRIC CONDITIONS RAISING RISK OF SUICIDE DO NOT KILL THEMSELVES. SUICIDAL BEHAVIOR HAS BEEN ASSOCIATED WITH TRANSDIAGNOSTIC BIOLOGICAL FEATURES AND RISK FACTORS, SUCH AS SEVERE ANXIETY/AGITATION AND POOR IMPULSE CONTROL. TRANSCRIPTOMIC AND GENOMIC FEATURES OF SUICIDE MAY BE MORE CLEARLY DETERMINABLE IN THE CONTEXT OF COMPLETED BEHAVIOR THAN IN IDEATION OR ATTEMPT, PARTICULARLY WHEN VIOLENT AND MORE LETHAL METHODS ARE EMPLOYED, IMPLICATING A HIGH LEVEL OF AGGRESSION. PARSING THE METHOD CHOSEN MIGHT CAPTURE THE MOLECULAR CORRELATES OF THE DISTINCTIVE FRAME OF MIND OF INDIVIDUALS WHO DIED BY SUICIDE, WHILE REDUCING PHENOTYPICAL HETEROGENEITY.

WE PRESENT GENE EXPRESSION (RNA-SEQ) DATA FROM POSTMORTEM DORSOLATERAL PREFRONTAL CORTEX OF PATIENTS (N=329) WHO DIED BY SUICIDE WITH VIOLENT VERSUS NON-VIOLENT MEANS, OF NON-SUICIDE PATIENTS WITH THE SAME PSYCHIATRIC DISORDERS, AND OF NEUROTYPICALS. WE ALSO PRESENT GENOMIC RISK-SCORES (GRS, N=888) FOR EACH DISORDER, GRS FOR COGNITION (IQ) AND GRS FOR SUICIDE ATTEMPT, ANALYZING HOW THEY PREDICT THE RESPECTIVE DIAGNOSIS OR TRAITS. QPCR PROVIDES TECHNICAL VALIDATION OF TOP-LIST DEGS. ADDITIONAL SENSITIVITY ANALYSES ACCOUNT FOR RNA QUALITY, POSTMORTEM PARAMETERS, DIAGNOSIS, BRAIN TRAUMA, TOXICS EXPOSURE, AGE, SEX BIAS, CELL TYPE, AGONAL STATE, AND MORE.

SUICIDES BY VIOLENT MEANS MAY BE IN PART BIOLOGICALLY SEPARABLE FROM OTHER PATIENTS WITH THE SAME DIAGNOSES, AND THEIR BEHAVIORAL OUTCOME MAY BE LESS DEPENDENT ON GENETIC RISK FOR CONVENTIONAL PSYCHIATRIC DISORDERS, WHILE ASSOCIATED WITH ALTERED CELL-TO-CELL COMMUNICATION.

WE ALSO PRESENT SINGLE-NUCLEI LEVEL DATA (N=27) THAT MIGHT PROVIDE FURTHER INSIGHT INTO THESE FINDINGS.

THIS IS A WELL POWERED INVESTIGATION OF A PHENOTYPE DIFFICULT TO ACCESS (COMPLETED SUICIDE). DIFFERENTLY FROM A NATURAL OR ACCIDENTAL DEATH, SUICIDE CORRESPONDS TO THE FINAL BEHAVIOR THAT THE BRAIN HAS PRODUCED, SO THAT THE BIOLOGY UNDERNEATH THAT VERY BEHAVIOR CAN BE STUDIED IN THE TISSUE, POSTMORTEM, AS REFLECTED IN GENE EXPRESSION. ADDRESSING SUICIDE BY VIOLENT MEANS AS A DISTINCT CONDITION MAY BE DECISIVE TO UNDERSTAND ITS BIOLOGICAL AND GENETIC BASES AND INFORM PREVENTION.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

TI. RESPONSES OF DOPAMINE NEURONS TO DISCRIMINATIVE AND PAVLOVIAN-CONDITIONED CUES ASSOCIATED WITH OPIOID VS. NATURAL REWARDS

NORA MILLER*, COLLIN LEHMANN, VARUN NAIR, GEOFFREY SCHOENBAUM, KHALED MOUSSAWI

DRUG-ASSOCIATED CUES ACQUIRE HEIGHTENED AND ENDURING SALIENCE THAT IS CAUSALLY LINKED TO CRAVING AND RELAPSE. HOWEVER, THE UNDERLYING MECHANISM OF DRUG-CUE REACTIVITY IS NOT FULLY ELUCIDATED. IT HAS BEEN PROPOSED THAT THE PHARMACOLOGICAL EFFECT OF DRUGS OF ABUSE INCLUDING OPIOIDS ON MIDBRAIN DOPAMINE NEURONS MIMICS PERSISTENT POSITIVE PREDICTION ERRORS, LEADING TO OVERVALUATION OF DRUG-ASSOCIATED CUES. THIS STUDY AIMS TO DIRECTLY TEST THIS MODEL BY MEASURING DOPAMINERGIC RESPONSES TO CUES ASSOCIATED WITH DRUG VS. NATURAL REWARDS USING SINGLE-UNIT RECORDINGS. LONG-EVANS RATS WERE IMPLANTED WITH MICROELECTRODE BUNDLES IN THE VENTRAL TEGMENTAL AREA AND JUGULAR IV CATHETERS FOR DELIVERY OF REMIFENTANIL (RMF). RATS WERE WATER-RESTRICTED AND TRAINED IN AN OPERANT TASK TO ASSOCIATE SPECIFIC DISCRIMINATIVE AND PAVLOVIAN CUES WITH DRUG VS. NON-DRUG REWARDS. DURING THE TASK, A LEVER PRESS RESULTED IN PSEUDO-RANDOMIZED AUDITORY CUES THAT SIGNALED AVAILABILITY OF RMF (4 MG/KG, IV), NON-DRUG REWARD (WATER DELIVERY INTO A DIPPER), OR NO CONSEQUENCE. RMF AND WATER REWARDS WERE DELIVERED AFTER CORRECT ENTRY INTO DESIGNATED FEEDER PORTS, WHICH WAS SIGNALED BY A LIGHT CUE PRESENTATION WITHIN THE FEEDER PRIOR TO REWARD DELIVERY. IN A DRUG-NAÏVE COMPARISON GROUP, IV SALINE WAS SUBSTITUTED FOR RMF. SINGLE-UNIT RECORDINGS WERE COLLECTED DURING THE OPERANT TASK UNDER EXTINCTION CONDITION TO AVOID PHARMACOLOGICAL DRUG EFFECTS ON NEURONAL FIRING. PUTATIVE DOPAMINE UNITS WERE IDENTIFIED BASED ON PHASIC RESPONSES TO CUES/REWARDS AND PHYSIOLOGIC PROPERTIES. IN THE RMF GROUP, WE DID NOT OBSERVE WITHIN-NEURON DIFFERENCES IN PHASIC RESPONSES BETWEEN DRUG VS. NON-DRUG CUES. HOWEVER, CUE RESPONSES WERE GREATER IN THE RMF GROUP COMPARED TO SALINE CONTROLS. THESE RESULTS DO NOT SUPPORT THE REWARD PREDICTION ERROR HYPOTHESIS OF CUE REACTIVITY AND SUGGEST THAT OPIOID EXPOSURE MAY LEAD TO ENHANCED SALIENCE OF ALL CUES LEARNED IN THE DRUG CONTEXT.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T2. METHAMPHETAMINE-INDUCED NEUROINFLAMMATION IN THE PREFRONTAL CORTEX CORRESPONDS WITH COGNITIVE FLEXIBILITY DEFICITS THAT ARE ATTENUATED BY COX-2 INHIBITION

AMANDA ACUNA*, ERIN NAGY, PAULA OVERBY, SKYLAR BICKLEY, ANNABEL CARLSON, LORI FRANCIS, GAIL HUTCHINGS, EMMA PEACOCK, SERENA RODARTE, M. FOSTER OLIVE

METHAMPHETAMINE (METH) USE DISORDER (MUD) AND METH-RELATED OVERDOSE DEATHS CONTINUE TO RISE IN THE UNITED STATES. UNFORTUNATELY, ABOUT 60% OF THOSE SEEKING TREATMENT FOR MUD RELAPSE WITHIN ONE YEAR OF ATTEMPTING TO ABSTAIN. RECENT WORK HAS REVEALED NEUROINFLAMMATORY RESPONSES TO METH THAT CORRESPOND WITH IMPAIRED EXECUTIVE FUNCTIONING, WHICH COULD CONVEY A VULNERABILITY TO ADDICTIVE BEHAVIORS AND RELAPSE IN PATIENTS WITH MUD. THE CURRENT STUDY SOUGHT TO INVESTIGATE THE ABILITY OF METH TO INDUCE INFLAMMATION AND SUBSEQUENT COGNITIVE DEFICITS IN ABSTINENCE. MALE AND FEMALE RATS WERE GIVEN BINGE-LIKE ACCESS (96 HRS/WEEK FOR 3 WEEKS) TO METH VIA INTRAVENOUS SELF-ADMINISTRATION (IVSA) AT 0.05 MG/KG/INFUSION, OR SALINE AS A CONTROL. NEUROIMMUNE MARKERS IN THE PREFRONTAL CORTEX (PFC) WERE ASSESSED VIA MULTIPLEX LASER BEAD ARRAY AFTER 3 WEEKS OF ABSTINENCE IN A SET OF RATS. PRIOR TO AND AFTER DRUG ACCESS, COGNITIVE FLEXIBILITY WAS ASSESSED USING THE ATTENTIONAL SET SHIFTING TASK (ASST) IN SEPARATE RATS. THE EFFECTS OF THE COX-2 INHIBITOR, PARECOXIB, ON POST-DRUG ASST PERFORMANCE WAS ALSO OBSERVED. WE FOUND THAT RATS WHO SELF-ADMINISTERED METH SHOWED AN ELEVATION IN IL-6, IL-18, CX3CL1, INF-GAMMA, CCL2, AND LEPTIN IN THE PFC COMPARED TO SALINE CONTROLS (N=4-6/GROUP). AFTER IVSA, RATS WHO SELF-ADMINISTERED METH (N=22) REQUIRED MORE TRIALS TO REACH CRITERION IN THE EXTRADIMENSIONAL SHIFT PART OF THE ASST THAN THEY DID PRIOR TO METH, WHEREAS BOTH SALINE-ADMINISTERING CONTROLS (N=21) AND SALINE-ADMINISTERING RATS TREATED WITH PARECOXIB (N=21) REQUIRED FEWER TRIALS AFTER IVSA. STRIKINGLY, RATS TREATED WITH PARECOXIB (N=28) FOLLOWING METH IVSA PERFORMED SIMILARLY TO SALINE-ADMINISTERING RATS, SUGGESTING AN ATTENUATION OF COGNITIVE DEFICITS INDUCED BY METH. THESE RESULTS, ALONG WITH THE FINDING THAT NEUROINFLAMMATION APPEARS TO PERSIST INTO ABSTINENCE FROM METH, REINFORCE THE ARGUMENT THAT PHARMACOLOGICALLY TARGETING THE NEUROIMMUNE RESPONSE TO METH MAY FACILITATE RECOVERY FROM MUD.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T3. ALLOSTERIC DOPAMINE TRANSPORTER MODULATOR INHIBITS COCAINE-INDUCED BEHAVIORS

YIBIN XU*, STACIA LEWANDOWSKI, CHRISTINA BESADA, OLE MORTENSEN

DOPAMINE (DA) IS INVOLVED IN MOTIVATION AND REWARD. DA IS TRANSPORTED INTO THE PRESYNAPTIC NEURONS BY DOPAMINE TRANSPORTER (DAT). THE PSYCHOSTIMULANT COCAINE IS AN INHIBITOR OF DAT, IT INHIBITS DAT, HENCE INCREASING DA IN THE SYNAPTIC CLEFT AND AMPLIFYING DOPAMINERGIC TRANSMISSION IN THE MESOLIMBIC AREA. THIS INCREASE IN DA SIGNALING IS RESPONSIBLE FOR THE ADDICTIVE PROPERTIES OF COCAINE. AS DAT IS THE PRIMARY TARGET OF COCAINE, NOVEL DAT-TARGETING COMPOUNDS COULD POTENTIALLY TREAT COCAINE DEPENDENCE. WE PREVIOUSLY FOUND A NOVEL COMPOUND—KM822 AND CHARACTERIZED IT AS AN ALLOSTERIC MODULATOR OF DAT. KM822 SIGNIFICANTLY DECREASES COCAINE-INDUCED LOCOMOTIVE RESPONSE IN PLANARIANS. TO TEST THE EFFECT OF KM822 IN MAMMALS, WE INFUSED KM822 AND COCAINE INTRACRANIALLY INTO THE NUCLEUS ACCUMBENS (NAC) OF LONG EVANS RATS AND MEASURED CHANGES IN LOCOMOTION. WE TARGETED THE NAC FOR ITS CRUCIAL ROLE IN THE MESOLIMBIC DOPAMINERGIC PATHWAY AND HIGH DENSITY OF DAT. RESULTS SHOWED THAT KM822 SIGNIFICANTLY DECREASED HYPERLOCOMOTION INDUCED BY COCAINE AND DID NOT CAUSE ANY CHANGES IN LOCOMOTION BY ITSELF. KM822'S ABILITY TO INTERFERE WITH COCAINE'S REWARDING EFFECT IS ALSO DEMONSTRATED USING THE CONDITIONED PLACE PREFERENCE (CPP) ASSAY. CPP CLOSELY MODELS BEHAVIORS RELEVANT TO COCAINE DEPENDENCE, THEREFORE HAS HIGHER TRANSLATIONAL VALUE. THE EXPRESSION OF THE IMMEDIATE EARLY GENE C-FOS IS FREQUENTLY UTILIZED AS A FUNCTIONAL MARKER TO INVESTIGATE NEURONAL RESPONSE TO STIMULI. TO EXAMINE HOW KM822 AFFECTS NEURONAL ACTIVITY IN THE NAC, C-FOS STAINING WAS CONDUCTED, AND THE EXPRESSION OF C-FOS WAS COMPARED BETWEEN RATS IN KM822 AND VEHICLE GROUP. IN THE FUTURE, WE PLAN TO FURTHER ASSESS THE IMPACT OF KM822 IN COCAINE EXTINCTION AND RELAPSE UTILIZING CPP. OVERALL, THESE STUDIES DEMONSTRATE THE ABILITY OF KM822 TO BLOCK DAT INHIBITOR-INDUCED BEHAVIORS IN RATS AND PROVIDED STRONG EVIDENCE OF NOVEL ALLOSTERIC DAT MODULATOR KM822 IN TREATING COCAINE USE DISORDERS.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T4. ADOLESCENT BINGE DRINKING CAUSES FOREBRAIN CHOLINERGIC NEURON GENE SILENCING THROUGH HMGBI-TLR AND REST-G9A SIGNALING, IMPACTING REVERSAL LEARNING

FULTON CREWS*, RYAN VETRENO

NEUROIMMUNE SIGNALING CONTRIBUTES TO MULTIPLE BRAIN DISEASES. STUDIES OF HUMAN POST-MORTEM ALCOHOL USE DISORDER (AUD) AND MODELS OF RAT ADOLESCENT INTERMITTENT BINGE-ETHANOL DRINKING (AIE) FIND INCREASED EXPRESSION OF MULTIPLE TOLL-LIKE RECEPTORS (TLRS) AND THE TLR AGONIST HMGBI. HMGBI IS A RELEASED NUCLEAR PROTEIN THAT ACTIVATES MULTIPLE TLRS SPREADING PROINFLAMMATORY SIGNALING. IN VIVO, WE FIND AIE CAUSES LONG-LASTING PERSEVERATION-BEHAVIORAL FLEXIBILITY DEFICITS THAT PARALLELS PERSISTENT REDUCTIONS OF FOREBRAIN CHAT+ CHOLINERGIC NEURONS IN THE ABSENCE OF CELL DEATH. WHILE LOSS OF CHAT+ NEURONS IS GENERALLY INTERPRETED AS NEURODEGENERATION, POST-AIE ANTI-INFLAMMATORY TREATMENTS REVERSE ADULT BEHAVIORAL FLEXIBILITY DEFICITS, LOSS OF CHAT+ NEURONS, AND HMGBI-TLR SIGNALING. USING AN EX VIVO FOREBRAIN CULTURE MODEL, WE DISCOVERED TREATMENT WITH ETHANOL AND LPS (TLR4 LIGAND) CAUSES HMGBI RELEASE, INDUCTION OF PROINFLAMMATORY HMGBI-TLR SIGNALING, AND A LOSS OF CHAT+ NEURONS AND CHOLINERGIC NEURON PHENOTYPE GENES, EFFECTS THAT ARE MIMICKED BY APPLICATION OF HMGBI. CONSISTENT WITH REVERSIBILITY OF CHOLINERGIC PHENOTYPE, EX VIVO TREATMENT WITH ETHANOL OR LPS INCREASE OCCUPANCY OF THE EPIGENETIC REPRESSIVE MARKERS RE-I SILENCING TRANSCRIPTION FACTOR (REST) AND H3K9ME2 ON CHOLINERGIC GENE PROMOTERS. TREATMENT WITH THE HMGBI ANTAGONIST GLYCYRRHIZIN AND OTHER ANTI-INFLAMMATORY DRUGS AS WELL AS INHIBITORS OF REST AND THE H3K9ME2 METHYLTRANSFERASE G9A REVERSE EPIGENETIC SILENCING OF THE CHOLINERGIC NEURON PHENOTYPE. HMGBI-TLR SIGNALING INDUCES REST AND G9A CHOLINERGIC PHENOTYPE SILENCING CONSISTENT WITH PROINFLAMMATORY SIGNALING ALTERING TRANSCRIPTION, INDEPENDENT OF CELL DEATH THAT IS REVERSIBLE. (FUNDED BY NIH-NIAAA).

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T5. EVALUATING THE EFFECTS OF PSYCHEDELIC DOI TREATMENT ON COGNITIVE FLEXIBILITY AFTER PROLONGED COCAINE EXPOSURE

ARTIN ASADIPOOYA*, TANNER ANDERSON, PAVEL ORTINSKI

COCAINE WITHDRAWAL IMPAIRS COGNITIVE FLEXIBILITY, THE ABILITY TO ADAPT BEHAVIOR IN RESPONSE TO CONTEXTUAL CHANGES, THEREBY INCREASING THE ODDS OF RELAPSE. WHILE THE UNDERLYING NEURONAL MECHANISMS OF COCAINE-INDUCED COGNITIVE INFLEXIBILITY REMAIN RELATIVELY UNKNOWN, IT HAS BEEN DEMONSTRATED THAT PSYCHEDELIC 5-HT2AR AGONISTS, SUCH AS PSILOCYBIN, NOT ONLY ENHANCE COGNITIVE FLEXIBILITY BUT ALSO EXHIBIT THERAPEUTIC POTENTIAL FOR VARIOUS PSYCHIATRIC DISORDERS, INCLUDING SUBSTANCE USE DISORDERS. WE SPECULATE THAT PSYCHEDELICS CAN BE THERAPEUTIC FOR COCAINE USE DISORDER BY ALLEVIATING COCAINE-INDUCED COGNITIVE FLEXIBILITY DEFICITS. IN OUR COHORT OF 12 MALE AND 12 FEMALE SPRAGUE-DAWLEY RATS, 6 MALES AND 6 FEMALES RECEIVED 14 ONCE-DAILY IP INJECTIONS OF 30 MG/KG COCAINE-HCL, WHILE THE REMAINDER RECEIVED AN EQUIVALENT DOSE OF SALINE. WE USED A STRATEGY SET-SHIFTING TASK TO ASSESS THE COGNITIVE FLEXIBILITY OF EACH SUBJECT WITHIN 24 HOURS OF WITHDRAWAL FROM THEIR LAST INJECTION. FOLLOWING THIS EVALUATION, WITHIN EACH GROUP, 3 MALES AND 3 FEMALES RECEIVED A SINGLE IP INJECTION OF 1 MG/KG DOI, A PSYCHEDELIC 5-HT2AR AGONIST, WHILE THE REMAINDER RECEIVED A VEHICLE TREATMENT. WE SUBSEQUENTLY MEASURED THE HEAD-TWITCH RESPONSE (HTR) OF EACH DOI SUBJECT, IN ADDITION TO REASSESSING THE COGNITIVE FLEXIBILITY OF EACH SUBJECT WITHIN 48 HOURS OF DOI OR VEHICLE TREATMENT. WE FOUND NO SIGNIFICANT DIFFERENCES IN COGNITIVE FLEXIBILITY BETWEEN COCAINE AND SALINE GROUPS. HOWEVER, 48 HOURS POST-DOI INJECTION, DOI TREATMENT SIGNIFICANTLY IMPAIRED THE COGNITIVE FLEXIBILITY OF MALE RATS, RELATIVE TO FEMALES. ADDITIONALLY, FEMALE RATS EXHIBITED A HIGHER-FREQUENCY HTR AFTER DOI ADMINISTRATION COMPARED TO THEIR MALE COUNTERPARTS. THE SEX DIFFERENCES OBSERVED IN THIS EXPERIMENT, ALONG WITH THE INFLUENCE OF COCAINE SELF-ADMINISTRATION (AS OPPOSED TO NONCONTINGENT ADMINISTRATION) ON COGNITIVE FLEXIBILITY AND PSYCHEDELIC TREATMENT OUTCOMES, WILL BE FURTHER EXPLORED IN FUTURE STUDIES.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T6. ELEVATED DNA DAMAGE AND NEUROINFLAMMATORY MARKERS IN SPECIFIC STRIATAL CELL TYPES ASSOCIATED WITH OPIOID USE DISORDER USING SINGLE NUCLEI RNASEQ OF HUMAN POSTMORTEM BRAIN

BADOI PHAN, MADELYN RAY, XIANGNING XUE, CHEN FU, ROBERT FENSTER, STEPHEN KOHUT, JACK BERGMAN, MADELINE FISH, JILL GLAUSIER, QIAO SU, ALLISON TIPTON, DAVID LEWIS, MARIANNE SENEY, ANDREAS PFENNING, RYAN LOGAN*

TO DATE, WE HAVE A LIMITED UNDERSTANDING OF THE CELLULAR AND MOLECULAR CHANGES IN BRAINS OF PEOPLE WITH OPIOID USE DISORDER (OUD). THE DORSAL STRIATUM IS IMPLICATED IN OPIOID CRAVING AND RELAPSE IN OUD. TO ADDRESS THIS LIMITATION, THE CURRENT STUDY USED SINGLE NUCLEUS RNA-SEQUENCING IN DORSAL STRIATUM FROM POSTMORTEM BRAINS OF SUBJECTS WITH OUD. NUCLEI EXTRACTED FROM POSTMORTEM DORSAL STRIATUM (N=12 SUBJECTS; 3 PER SEX PER UNAFFECTED AND OUD; 7,500 NUCLEI PER SAMPLE) WERE PROCESSED FOR RNA-SEQUENCING USING 10X GENOMICS AND ILLUMINA PLATFORMS. SEQUENCING DATA WAS ALIGNED (STARSOLO) AND PROCESSED FOR QC (AMBIENT MRNA DETECTION AND CORRECTION; EMPTY DROPLET AND DOUBLET FILTERING). DORSAL STRIATUM NON-HUMAN PRIMATE SINGLE CELL DATASETS WERE USED FOR CELL ANNOTATION TRANSFERS TO IDENTIFY CLUSTER CELL TYPES. MODIFIED LIMMA MODELS WERE USED TO IDENTIFY DIFFERENTIALLY EXPRESSED GENES (DEGS; FDR < 0.05) AND OTHER ANALYSES INCLUDED AREA UNDER-THE-CURVE (AUC) MARKER ENRICHMENTS TO CHARACTERIZE DNA DAMAGE SIGNATURES BY CELL TYPE. SIGNIFICANT DEGS WERE IDENTIFIED FOR EACH OF THE MAJOR CELL TYPES, INCLUDING ASTROCYTES, MICROGLIA, ENDOTHELIAL CELLS, OLIGODENDROCYTES, AND SPECIFIC NEURONAL SUBTYPES, SUCH AS DRD1, DRD2, AND INTERNEURON SUBCLASSES. SEX-SPECIFIC DEGS IDENTIFIED KEY GENES RELATED TO OUD. ENRICHMENT ANALYSES HIGHLIGHTED PATHWAYS RELATED TO NEURONINFLAMMATION, AGING, AND CELLULAR STRESS. HIGHER PROPORTIONS OF DNA DAMAGE MARKERS WERE FOUND IN OUD SUBJECTS COMPARED TO UNAFFECTED SUBJECTS. DNA DAMAGE SCORES WERE PRIMARILY ELEVATED IN GLIAL SUBTYPES AND INTERNEURONS. OVERALL, OUR RESULTS ARE THE FIRST TO IDENTIFY SIGNIFICANT TRANSCRIPTIONAL ALTERATIONS ACROSS SPECIFIC CELL TYPES IN HUMAN STRIATUM ASSOCIATED WITH OUD RELATED TO NEUROINFLAMMATION AND DNA DAMAGE.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T7. FURANYLFENTANYL DECREASES RESPIRATION BUT NOT OXYGEN SATURATION IN MICE

CATHERINE DEMERY-POULOS*, SIERRA C. MOORE, KELSEY E. KOCHAN, JESSICA R. WHITAKER-FORNEK, THOMAS D. PRINCE, BENJAMIN M. CLEMENTS, ERICA S. LEVITT, JESSICA P. ANAND, JOHN R. TRAYNOR

FATAL OPIOID OVERDOSES IN THE U.S. HAVE NEARLY TRIPLED SINCE 2015, SURPASSING 80,000 IN 2022. THIS UNPRECEDENTED MORTALITY IS DRIVEN BY SYNTHETIC OPIOIDS SUCH AS FENTANYL AND ITS ANALOGS. FURANYLFENTANYL IS AMONG THE MOST CONSISTENTLY DETECTED FENTANYL ANALOGS IN OVERDOSES IN THE U.S., BUT ITS EFFECTS ARE NOT WELL-CHARACTERIZED. ALL OPIOIDS EXERT THEIR ACTIONS – INCLUDING PAIN RELIEF, REWARD, AND RESPIRATORY DEPRESSION – THROUGH THE MU-OPIOID RECEPTOR (MOR). IN VITRO, FURANYLFENTANYL AND FENTANYL HAD SIMILAR AFFINITY AND POTENCY AT MOR, BUT FURANYLFENTANYL HAD LOWER EFFICACY IN G-PROTEIN ACTIVATION AND BETA-ARRESTIN RECRUITMENT ASSAYS. DESPITE THIS, IN MALE AND FEMALE CD-1 MICE, FURANYLFENTANYL AND FENTANYL INDUCED AN EQUAL DEGREE OF ANTINOCICEPTION AGAINST A THERMAL STIMULUS. MOREOVER, WHEN EVALUATING RESPIRATORY DEPRESSION USING WHOLE-BODY PLETHYSMOGRAPHY IN AIR, FENTANYL (0.32-10 MG/KG) AND FURANYLFENTANYL (0.32-32 MG/KG) HAD SIMILAR EFFECTS ON BREATHING PARAMETERS, ALTHOUGH FENTANYL WAS THREE-FOLD MORE POTENT. BOTH DRUGS REDUCED BREATHING RATE TO A SIMILAR EXTENT RELATIVE TO SALINE, EXCEPT FOR 32 MG/KG FURANYLFENTANYL, WHICH DEPRESSED BREATHING RATE FURTHER. BOTH DRUGS DOSE-DEPENDENTLY INCREASED INSPIRATION TIME AND DECREASED PEAK INSPIRATORY FLOW. NALOXONE ADMINISTRATION ADEQUATELY RESCUED THE RESPIRATORY CHANGES INDUCED BY BOTH DRUGS. SURPRISINGLY, FENTANYL REDUCED OXYGEN SATURATION TO A MUCH GREATER EXTENT THAN FURANYLFENTANYL, EVEN AT DOSES THAT SHOWED EQUIVALENT EFFECTS IN PLETHYSMOGRAPHY. THE APPARENT DISCREPANCY BETWEEN THE EFFECTS ON BREATHING PARAMETERS AND OXYGEN SATURATION MAY REFLECT THE DIFFERENCES IN EFFICACY OBSERVED IN VITRO. THIS WORK WAS SUPPORTED BY NIDA R21 DA051723 AND UG3 DA056884.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T8. DEVELOPING TOOLS FOR STUDYING NEURONAL ENSEMBLES THAT ENCODE VOLITIONAL SOCIAL REWARD IN MICE

SAMANTHA LEE*, MARCO VENNIRO, YAVIN SHAHAM, BRUCE HOPE, LESLIE RAMSEY

WE RECENTLY DEVELOPED A MOUSE MODEL OF OPERANT SOCIAL SELF-ADMINISTRATION AND CHOICE. USING THIS MODEL, WE FOUND THAT OUTBRED FEMALE CDI MICE, BUT NOT C57BL/6J FEMALE MICE, SHOWED RELIABLE SOCIAL INTERACTION SELF-ADMINISTRATION, STRONG SOCIAL-SEEKING BEHAVIOR DURING ISOLATION, AND PREFERENCE FOR SOCIAL INTERACTION OVER FOOD. CURRENT NEUROBIOLOGICAL INVESTIGATIONS OF SOCIAL BEHAVIOR ARE PRIMARILY PERFORMED IN C57BL/6J MICE, THE MOST COMMON BACKGROUND STRAIN OF TRANSGENIC MICE. GIVEN THAT FEMALE C57BL/6J MICE ARE NOT SUITABLE FOR STUDYING OPERANT SOCIAL REWARD, WE CREATED NEW TRANSGENIC LINES TO STUDY ACTIVITY-DEPENDENT NEURONAL ENSEMBLES THAT ENCODE SOCIAL SELF-ADMINISTRATION AND SOCIAL SEEKING BEHAVIOR. WE TESTED WHETHER BREEDING OUTBRED FEMALE CDI MICE WITH FOSGFP, FOSTRAP2, AND FOSTRAP2 X AI14 TRANSGENIC C57BL/6J MALE MICE WILL MAINTAIN THE SOCIAL PHENOTYPE IN THE HYBRID F1 OFFSPRING. WE TRAINED THE F1 GENERATION TO LEVER-PRESS FOR PALATABLE FOOD PELLETS AND THEN TO LEVER-PRESS FOR ACCESS TO A SAME-SEX SOCIAL PARTNER. NEXT, WE TESTED THEIR MOTIVATION TO SEEK SOCIAL INTERACTION AFTER 15 DAYS OF SOCIAL ISOLATION. MALE AND FEMALE MICE FROM THE HYBRID TRANSGENIC MOUSE LINES SHOWED RELIABLE SOCIAL SELF-ADMINISTRATION AND SOCIAL SEEKING AFTER ISOLATION, SIMILAR TO WILD-TYPE CDI MICE. WE THEN OPTIMIZED THE TIME COURSE FOR 4-OHT ADMINISTRATION USING FOSTRAP2 X AI14 CDI F1 HYBRID MICE BY INJECTING 4-OHT AT 1, 2, OR 3 HOURS AFTER SOCIAL SEEKING CONTEXT EXPOSURE. WE FOUND THAT INJECTING 4-OHT 3 HOURS AFTER TESTING PRODUCES THE HIGHEST NUMBER OF TRAPED NEURONS. WE ALSO TESTED ACTIVITY-DEPENDENCE OF TRAPING USING THE FOSTRAP2 CDI MICE INJECTED WITH DIO-HM4DI OR DIO-MCHERRY VIRUSES. OUR DATA INDICATE THAT THE SOCIAL PHENOTYPE IS MAINTAINED IN THE F1 GENERATION IN ALL THREE STRAINS TESTED USING THE HYBRID BREEDING SCHEME. THIS WILL ENABLE US AND OTHER RESEARCHERS TO IDENTIFY, CHARACTERIZE, AND MANIPULATE ACTIVITY-DEPENDENT NEURONAL ENSEMBLES INVOLVED IN OPERANT SOCIAL REWARD.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T9. MODULATION OF PRELIMBIC CORTEX TO ROSTROMEDIAL TEGMENTAL NUCLEUS PATHWAY ELICITS DIFFERENTIAL RESPONDING IN CONDITIONED SUPPRESSION

EMMA CARLSON*, ANNA TOBUREN, SERENA PARMAR, RACHEL KISER, PETER VENTO

RELAPSE IS A MAJOR OBSTACLE IN THE PATH TO SOBRIETY FOR INDIVIDUALS WITH SUBSTANCE USE DISORDER, WITH A LEADING CONTRIBUTOR BEING ENVIRONMENTAL CUES FORMERLY ASSOCIATED WITH DRUG USE. PREVIOUS WORK FROM OUR LAB AND OTHERS SUGGESTS THE ROSTROMEDIAL TEGMENTAL NUCLEUS (RMTG), A GABAERGIC MIDBRAIN REGION WITH DENSE INHIBITORY PROJECTIONS TO MIDBRAIN DOPAMINE NEURONS, MODULATES BOTH CUE- AND DRUG-PRIMED REINSTATEMENT OF COCAINE SEEKING. WHILE A LARGE BODY OF RESEARCH HAS DEMONSTRATED THE PREFRONTAL CORTEX TO ALSO BE CRITICAL FOR REINSTATEMENT AND CUE ASSOCIATIONS, LESS IS KNOWN REGARDING HOW THESE MIDBRAIN AND CORTICAL REGIONS INTERACT TO INFLUENCE DRUG SEEKING. NOTABLY, THE PRELIMBIC (PL) PREFRONTAL CORTEX SENDS AN EXCITATORY PROJECTION TO THE RMTG, AND EMERGING FINDINGS DEMONSTRATE STIMULATION OF THIS PATHWAY PROMOTES AVOIDANCE, WHILE PHARMACOLOGICAL INACTIVATION OF THE PATHWAY INCREASES CUE-INDUCED REINSTATEMENT OF COCAINE SEEKING. HERE, WE DEMONSTRATE THAT CHEMOGENETIC PL- > RMTG STIMULATION ROBUSTLY SUPPRESSES CUE-INDUCED REINSTATEMENT OF COCAINE SEEKING. TO BETTER UNDERSTAND ENCODING OF MOTIVATIONALLY-SALIENT STIMULI BY THE PL- > RMTG PATHWAY, WE USED A CHEMOGENETIC APPROACH TO BIDIRECTIONALLY MODULATE THIS CIRCUIT DURING A CUE DISCRIMINATION TASK. SPECIFICALLY, RATS WERE TRAINED TO LEVER PRESS FOR SUCROSE IN THE PRESENCE OF A REWARD-ASSOCIATED CUE (LIGHT), A NEUTRAL CUE (WHITE NOISE) PAIRED WITH NO OUTCOME, OR AN AVERSIVE CUE (2KHZ TONE) FOLLOWED BY MILD FOOT SHOCK. RESULTS SUGGEST THE PL- > RMTG PATHWAY IS IMPORTANT FOR MODULATING REWARD SEEKING IN THE PRESENCE OF ENVIRONMENTAL CUES SIGNALING AVERSIVE OUTCOMES. NEURONAL ENSEMBLES INVOLVED IN OPERANT SOCIAL REWARD.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T10. N-ACETYLCYSTEINE EFFECTS ON NEUROMETABOLITES, FUNCTIONAL CONNECTIVITY AND CUE REACTIVITY: A NEUROIMAGING STUDY OF TREATMENT-SEEKING INDIVIDUALS WITH ALCOHOL USE DISORDER

KIRSTEN MORLEY*, WARREN LOGGE, MARILENA DEMAYO, KRISTIANE YACOU DUNBAR, TRISTAN HURZELER, GEZELLE DALI, ELLEN TOWERS, PAUL HABER

N-ACETYL CYSTEINE (NAC) IS A POTENTIAL PHARMACOTHERAPY FOR ALCOHOL USE DISORDER (AUD), BUT IT IS NOT KNOWN WHETHER IT MODULATES NEUROMETABOLITES, NEURAL ACTIVATION TO ALCOHOL CUES, INTRINSIC FUNCTIONAL CONNECTIVITY OR COGNITIVE FUNCTIONING. THIS STUDY INVESTIGATED WHETHER N-ACETYL CYSTEINE EFFECTS I) NEUROMETABOLITES GLUTAMATE AND GLUTATHIONE; I) ALCOHOL CUE-ELICITED ACTIVATION, AND II) INTRINSIC FUNCTIONAL CONNECTIVITY COMPARED TO PLACEBO IN PATIENTS WITH AUD.

PARTICIPANTS INCLUDED 23 INDIVIDUALS WITH MODERATE TO SEVERE AUD WHO HAD RECEIVED DAILY NAC (2400 MG/DAY, N = 9), OR A PLACEBO (N = 14) FOR AT LEAST 2 WEEKS. PARTICIPANTS COMPLETED A PRE-TREATMENT MAGNETIC RESONANCE SPECTROSCOPY (MRS) AND A FUNCTIONAL MAGNETIC RESONANCE IMAGING (FMRI) SESSION (T0) AND A POST-TREATMENT SESSION (T1, MEAN TRIAL DAY = 21) COMPRISING A RESTING-STATE AND VISUAL ALCOHOL CUE REACTIVITY TASK ACQUISITIONS PLUS THE STROOP TEST FOR EXECUTIVE FUNCTIONING. BRAIN ACTIVATION DIFFERENCES BETWEEN SESSIONS (T0, T1), TREATMENT (NAC, PLACEBO), AND TWO-WAY SESSION*TREATMENT INTERACTION WERE ASSESSED. FIVE BRAIN REGIONS OF INTEREST (ROIS) (VENTROMEDIAL PREFRONTAL CORTEX, LEFT/RIGHT CAUDATE, LEFT /RIGHT DORSOLATERAL PREFRONTAL CORTEX) WERE DEFINED FOR ALCOHOL CUE REACTIVITY. RESTING-STATE FUNCTIONAL CONNECTIVITY EXAMINED USING 376 NODE ROI-TO-ROIS EVALUATED WHETHER NAC REDUCED INTRINSIC FUNCTIONAL CONNECTIVITY AFTER TREATMENT COMPARED TO PLACEBO.

THERE WERE NO DIFFERENCES IN GLUTAMATE, GLUTATHIONE OR ALCOHOL CUE REACTIVITY FOR BRAIN ACTIVATION BETWEEN NAC AND PLACEBO DURING TREATMENT OR ACROSS SESSIONS (T0 VERSUS T1), OR SIGNIFICANT INTERACTION. THERE WAS A SIGNIFICANT TREATMENT-BY-TIME INTERACTION, WITH REDUCED INTRINSIC CONNECTIVITY OBSERVED AFTER TREATMENT (T1) FOR NAC-TREATED COMPARED TO PLACEBO-TREATED PATIENTS, SEEN IN THE POSTERIOR CINGULATE NODE (9, LEFT HEMISPHERE) OF THE DORSAL ATTENTIONAL NETWORK AND CONNECTIONS TO SALIENCE VENTRAL ATTENTIONAL, SOMATOSENSORY, AND VISUAL-PERIPHERAL NETWORKS IMPLICATED IN AUD (PFDR=0.011).

NAC REDUCED INTRINSIC FUNCTIONAL CONNECTIVITY IN PATIENTS WITH MODERATE-SEVERE AUD AFTER TREATMENT COMPARED TO PLACEBO, BUT DID NOT ATTENUATE ALCOHOL CUE-ELICITED ACTIVATION OR MODULATE NEUROMETABOLITE LEVELS.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

TII. DOPAMINE RELEASE IN RESPONSE TO CUES PREDICTING AVOIDABLE AVERSIVE STIMULI DIFFERENTIATES BEHAVIORAL RESPONSES: ESCAPE VERSUS HELPLESSNESS

STEPHANIE CAJIGAS*, MAXIME CHEVEE, JAELA MELTON, KRISTINE YOON, MICHAEL LEONARD, ERIN CALIPARI

THE EXECUTION OF ADAPTIVE BEHAVIOR DEPENDS ON THE ABILITY OF ORGANISMS TO PREDICT POTENTIAL THREATS IN THEIR ENVIRONMENT; ANIMALS LEARN TO PREDICT WHEN AVERSIVE STIMULI WILL OCCUR AND LEARN WHAT ACTIONS ARE NECESSARY TO AVOID CONTEXTS WITH POTENTIAL NEGATIVE OUTCOMES. IN SOME SITUATIONS, NEGATIVE OUTCOMES ARE AVOIDABLE WHILE OTHERS ARE NOT. THE INABILITY TO EFFECTIVELY DISCRIMINATE BETWEEN THESE SITUATIONS AND UPDATE INFORMATION ABOUT THESE RELATIONSHIPS IS A HALLMARK OF PATHOLOGICAL DISEASE STATES (I.E., PTSD AND ANXIETY DISORDERS). HERE WE UTILIZED A SHOCK-BASED NEGATIVE REINFORCEMENT PARADIGM TO INVESTIGATE DOPAMINE RELEASE PATTERNS OVER LEARNING AND DETERMINE HOW NEURAL SIGNALS CAN DIFFERENTIATE ANIMALS THAT LEARN TO AVOID FOOTSHOCKS VERSUS THOSE THAT DO NOT. MICE THEN WENT THROUGH AN FRI POSITIVE REINFORCEMENT SCHEDULE WITH SUCROSE PRESENTATION. AFTER COMPLETING THIS INSTRUMENTAL LEARNING PHASE, MICE RETURNED TO THE INITIAL NEGATIVE REINFORCEMENT PARADIGM WITH A WHITE NOISE DISCRIMINATIVE CUE INSTEAD OF A TONE. THE OPTICAL DOPAMINE SENSOR DLIGHT WITH IN-VIVO FIBER PHOTOMETRY WAS USED TO MONITOR DOPAMINE RESPONSES IN THE NUCLEUS ACCUMBENS CORE. DESPITE THE ESCAPABLE NATURE OF THESE SHOCKS, MANY MICE DEVELOPED A FREEZING RESPONSE TO THE CUE, RATHER THAN LEARNING TO AVOID THEM. THE MICE THAT DID NOT LEARN TO AVOID HAD FUTURE DEFICITS IN NEGATIVE REINFORCEMENT LEARNING AS WELL, DESPITE SUCCESSFUL INSTRUMENTAL LEARNING, SUGGESTING THAT THIS LEARNED EXPERIENCE ULTIMATELY INFLUENCED BEHAVIOR IN OTHER CONTEXTS. INTERESTINGLY, THERE WERE STILL CHANGES IN DOPAMINE RELEASE THROUGHOUT TRAINING IN NON-LEARNERS, SUCH AS IN THE NEURAL RESPONSES TO THE CUE AND SHOCK ITSELF. THESE DATA DEMONSTRATE BEHAVIORAL CHANGES DEPENDENT ON LEARNING ABILITY AND CHANGES IN DOPAMINE SIGNALING OVER TIME MAY UNDERLY HOW A SUBJECT NAVIGATES THEIR ENVIRONMENT AND PERCEIVES THE AVAILABILITY OF BEHAVIORAL OUTCOMES (ABILITY TO ESCAPE SHOCKS VS. PERCEIVED INESCAPABILITY).

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

TI2. DISCOVERY AND CHARACTERIZATION OF ITI-1549, A NOVEL NON-HALLUCINOGENIC PSYCHEDELIC FOR THE TREATMENT OF NEUROPSYCHIATRIC DISORDERS

GRETCHEN SNYDER*, SOPHIE DUTHEIL, LEI ZHANG, EMMA LEHMANN, NORA AWADALLAH, WEI YAO, ROBERT DAVIS, PENG LI

SEROTONERGIC HALLUCINOGENS (PSYCHEDELICS) ARE POWERFUL PSYCHOACTIVE SUBSTANCES THAT ALTER PERCEPTION, MOOD AND COGNITION AS AGONISTS AT BRAIN SEROTONIN 5-HYDROXYTRYPTAMINE 2A (5-HT2A) RECEPTORS. ADVERSE EFFECTS OF PSYCHEDELIC HALLUCINOGENS HAVE RAISED SAFETY ISSUES (I.E., ABUSE LIABILITY, PERSISTENCE OF PERCEPTUAL DISORDERS RELATED TO 5-HT2A AGONISM) LIMITING THEIR BROAD USE. WE USED STRUCTURE- AND LIGAND-BASED DRUG DESIGN TO DISCOVER NOVEL CLASSES OF PSYCHEDELIC COMPOUNDS, CHEMICALLY UNRELATED TO PLANT-DERIVED AND OTHER SYNTHETIC PSYCHEDELICS. WE REPORT HERE ON ITI-1549, A NOVEL NON-HALLUCINOGENIC PSYCHEDELIC BEING DEVELOPED FOR TREATMENT OF MOOD, ANXIETY AND OTHER NEUROPSYCHIATRIC DISORDERS.

ITI-1549 BINDS WITH HIGH AFFINITY (LOW NM) TO 5-HT2A RECEPTORS. UNLIKE PSYCHEDELIC HALLUCINOGENS, WHICH ARE FULL AGONISTS AT BOTH B-ARRESTIN AND GQ SIGNALING PATHWAYS LINKED TO THE 5-HT2A RECEPTOR, ITI-1549 ACTS AS A BIASED PARTIAL AGONIST WITHIN THE B-ARRESTIN PATHWAY (INTRINSIC EFFICACY OF 72% RELATIVE TO THE POSITIVE CONTROL -METHYLSEROTONIN). ITI-1549 DOES NOT ACTIVATE 5-HT2A COUPLED GQ SIGNALING NOR DOES NOT ELICIT HEAD TWITCH BEHAVIORS IN MICE LINKED TO 5-HT2A AGONIST (GQ) ACTIVITY. THUS, ITI-1549 IS CLASSIFIED AS NON-HALLUCINOGENIC. FURTHER, ITI-1549 REDUCES ANXIETY IN MICE IN OPEN FIELD TEST AND PROMOTES PROSOCIAL BEHAVIOR (SOCIAL INTERACTION) OF RATS (DOSES OF < 1.0 MG/KG IN BOTH TESTS). ITI-1549 ALSO LACKS FUNCTIONAL AGONIST ACTIVITY AT 5-HT2B RECEPTORS, A RECEPTOR RESPONSIBLE FOR HEART VALVE PATHOLOGIES ASSOCIATED WITH MOST PSYCHEDELIC HALLUCINOGENS. THE DATA SHOW THAT ITI-1549 IS A BIASED (TOWARDS B -ARRESTIN SIGNALING) NON-HALLUCINOGENIC 5-HT2A RECEPTOR PARTIAL AGONIST WITHOUT 5-HT2B AGONISTIC ACTIVITY. THIS PROFILE PREDICTS THAT ITI-1549 MAY BE A SAFE, NON-HALLUCINOGENIC PSYCHEDELIC LACKING THE POTENTIAL TO INDUCE HALLUCINATIONS AND CARDIAC PATHOLOGIES, BUT WITH POTENTIAL TO TREAT MOOD, ANXIETY, AND OTHER NEUROPSYCHIATRIC DISORDERS.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

TI3. VALIDATION OF INTERSECTIONAL CHEMOGENETIC APPROACHES FOR IN-VIVO MANIPULATION OF PROJECTION-DEFINED SUBSTANTIA NIGRA CIRCUITS

MARGARET TANNER*, ERIK OLESON, BENJAMIN GREENWOOD

RECENT EVIDENCE SUGGESTS THAT MIDBRAIN DOPAMINE (DA) NEURONS ARE ORGANIZED INTO FUNCTIONAL SUBSETS DEFINED BY THEIR PROJECTIONS. DUE TO THE BROAD ROLE OF DA IN MOTIVATED BEHAVIOR, APPROACHES TO MANIPULATE DA RELEASE IN BEHAVING ANIMALS IS OF HIGH IMPORTANCE. RECENT ADVANCES IN INTERSECTIONAL CHEMOGENETIC TECHNOLOGIES ALLOW FOR MANIPULATION OF DISTINCT MIDBRAIN DA PATHWAYS DURING BEHAVIOR. HOWEVER, BECAUSE OF THE CHALLENGE IN MEASURING DA RELEASE, THE EFFECTIVENESS OF THESE APPROACHES AT ALTERING DA RELEASE DYNAMICS IS UNCLEAR. THUS, THE GOAL OF THIS STUDY IS TO USE FAST SCAN CYCLIC VOLTAMMETRY (FSCV) TO DETERMINE THE EFFECTIVENESS AND SPECIFICITY OF AN INTERSECTIONAL CHEMOGENETIC APPROACH TO STIMULATE OR INHIBIT MIDBRAIN DA NEURONS PROJECTING TO THE DORSOLATERAL STRIATUM (DLS). FSCV ALLOWS FOR THE MEASUREMENT OF DA RELEASE WITH HIGH SPATIOTEMPORAL RESOLUTION AND CAN REVEAL THE EFFECTS OF CHEMOGENETIC MANIPULATIONS ON PHASIC DA RELEASE IN DISCRETE BRAIN REGIONS. ADULT, MALE AND FEMALE, LONG-EVANS RATS WERE INJECTED BILATERALLY WITH EITHER AAV-DIO-HM4DI-MCHERRY (GI-DREADD), AAV-DIO-HM3DQ-MCHERRY (GQ-DREADD), OR AAV-DIO-MCHERRY (CONTROL) INTO THE SUBSTANTIA NIGRA (SN). ALL RATS WERE BILATERALLY INJECTED IN THE DLS WITH AAV2/RETRO-ESYN-EGFP-T2A-ICRE-WPRE TO DRIVE THE EXPRESSION OF CRE-RECOMBINASE IN DLS-PROJECTING SN NEURONS. FOUR WEEKS AFTER SURGERY, UNDER URETHANE ANESTHESIA, A CARBON FIBER MICROELECTRODE WAS IMPLANTED INTO THE DLS AND A BIPOLAR STIMULATING ELECTRODE WAS PLACED IN THE SN. DA RELEASE WAS EVOKED USING ELECTRICAL STIMULATIONS CONSISTING OF 24 BIPHASIC RECTANGULAR PULSES DELIVERED AT 60 HZ (300 MA, 2 MS/PHASE). RECORDINGS WERE TAKEN FROM THE DLS AFTER INTRAPERITONEAL (I.P.) INJECTION OF SALINE TO ESTABLISH BASELINE EVOKED DA RELEASE. RECORDINGS WERE ALSO TAKEN 30 MIN AFTER I.P. INJECTION OF THE DREADD LIGAND JHU37160-DIHYDROCHLORIDE (J60; 0.1 MG/ML). J60 REDUCED EVOKED DLS DA RELEASE IN GI-DREADD RATS BY 60% AND HAD NO EFFECT ON DLS DA RELEASE IN GQ-DREADD RATS. THE ANATOMICAL SELECTIVITY OF THIS APPROACH WAS ASSESSED BY MEASURING EVOKED DA RELEASE IN THE DORSOMEDIAL STRIATUM (DMS) OF GI-DREADD RATS, WHICH REVEALED A 30% SUPPRESSION. THESE FINDINGS VERIFY THAT THIS INTERSECTIONAL CHEMOGENETIC APPROACH SUCCESSFULLY INHIBITS DA RELEASE DYNAMICS IN THE NIGROSTRIATAL DA PATHWAY.

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

TI4. DOPAMINE PATHWAYS MEDIATING AFFECTIVE STATE TRANSITIONS AFTER SLEEP LOSS

MINGZHENG WU*, YEVGENIA KOZOROVITSKIY

PATHOPHYSIOLOGY OF AFFECTIVE DISORDERS—PARTICULARLY CIRCUIT-LEVEL MECHANISMS UNDERLYING BIDIRECTIONAL, PERIODIC AFFECTIVE STATE TRANSITIONS—REMAINS POORLY UNDERSTOOD. IN PATIENTS, DISRUPTIONS OF SLEEP AND CIRCADIAN RHYTHM CAN TRIGGER TRANSITIONS TO MANIC EPISODES, WHILE DEPRESSIVE STATES ARE REVERSED. HERE, WE INTRODUCE A HYBRID AUTOMATED SLEEP DEPRIVATION PLATFORM TO INDUCE TRANSITIONS OF AFFECTIVE STATES IN MICE. ACUTE SLEEP LOSS CAUSES MIXED BEHAVIORAL STATES FEATURING HYPERACTIVITY, ELEVATED SOCIAL AND SEXUAL BEHAVIORS, AND DIMINISHED DEPRESSIVE-LIKE BEHAVIORS, WHERE TRANSITIONS DEPEND ON DOPAMINE. USING DOPAMINE SENSOR PHOTOMETRY AND PROJECTION-TARGETED CHEMOGENETICS, WE REVEAL THAT ELEVATED DOPAMINE RELEASE IN SPECIFIC BRAIN REGIONS MEDIATES DISTINCT BEHAVIORAL CHANGES IN AFFECTIVE STATE TRANSITIONS. ACUTE SLEEP LOSS INDUCES DOPAMINE-DEPENDENT ENHANCEMENT IN DENDRITIC SPINE DENSITY AND UNCAGING-EVOKED DENDRITIC SPINOGENESIS IN THE MEDIAL PREFRONTAL CORTEX, WHEREAS OPTICALLY MEDIATED DISASSEMBLY OF ENHANCED PLASTICITY REVERSES THE ANTIDEPRESSANT EFFECTS OF SLEEP DEPRIVATION ON LEARNED HELPLESSNESS. THESE FINDINGS DEMONSTRATE THAT BRAIN-WIDE DOPAMINERGIC PATHWAYS CONTROL SLEEP LOSS-INDUCED POLYMODAL AFFECTIVE STATE TRANSITIONS.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

TI5. COMPARING PLASTICITY EFFECTS OF ITBS AND 10-HZ RTMS WITH NMDA AND GABA RECEPTOR MODULATION

JOSHUA BROWN*

LITTLE IS KNOWN ABOUT THE COMPARATIVE NEURONAL MECHANISMS OF INTERMITTENT THETA-BURST STIMULATION (ITBS) AND 10-HZ REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION (RTMS). WE HYPOTHESIZED THAT ITBS WORKS PRIMARILY THROUGH NMDA RECEPTOR-DEPENDENT MECHANISMS (I.E., LONG-TERM POTENTIATION (LTP)), WHILE 10-HZ RTMS MAY WORK THROUGH A COMBINATION OF LTP AND GABAR REDUCTION. WE CONDUCTED A DOUBLE-BLIND, PLACEBO-CONTROLLED, 8-ARM CROSSOVER STUDY WITH HEALTHY ADULT SUBJECTS IN TWO PHASES, ITBS (N=13), THEN 10HZ (N=6), WITH AT LEAST 1-WEEK BETWEEN EACH SESSION. EACH ARM CONSISTED OF ITBS OR 10-HZ RTMS OVER THE LEFT MOTOR CORTEX (BOTH FOLLOWING STANDARD CLINICAL PARAMETERS WITH EXCEPTION OF 80% RESTING MOTOR THRESHOLD FOR SAFETY PURPOSES), ALONG WITH A SINGLE DOSE OF PLACEBO, 100MG D-CYCLOSERINE, 2.5MG LORAZEPAM, OR 150MG DEXTROMETHORPHAN + 100MGD-CYCLOSERINE. MOTOR-EVOKED POTENTIALS (MEPS) WERE RECORDED AFTER DRUG, BEFORE AND AFTER RTMS, AND NORMALIZED TO BASELINE. REPEATED-MEASURES ANOVA AND POST-HOC T-TESTS ANALYZED DIFFERENCES ACROSS ALL GROUPS, AND BETWEEN INDIVIDUAL CONDITIONS, RESPECTIVELY. BASELINE MEP AMPLITUDES WERE SIMILAR ACROSS ALL CONDITIONS. OUR STUDY WAS TERMINATED PREMATURELY DUE TO CHANGE OF INSTITUTIONS. AS SUCH, NO COMPARISONS WERE STATISTICALLY DIFFERENT, THOUGH TRENDS IN NORMALIZED MEP AMPLITUDES WERE OBSERVED AS FOLLOWS: ITBS [PLACEBO:1.14 (0.48), DCS:1.51 (0.84), LZP:1.21 (0.61), DMO/DCS:1.32 (0.66)] AND 10-HZ: [PLACEBO:1.04 (0.24), DCS:1.40 (0.67), LZP:0.74 (0.23), DMO/DCS:1.34 (0.55)].

LIMITATIONS TO THIS STUDY INCLUDE AN ORDER EFFECT OF ITBS PRECEDING 10HZ, AND AN UNDERPOWERED SAMPLE. NEVERTHELESS, AS A PILOT STUDY, THESE PRELIMINARY DATA ARE THE FIRST TO DIRECTLY COMPARE ITBS AND 10-HZ MECHANISMS OF ACTION WITHIN SUBJECTS, THE FIRST TO TEST MOTOR PHYSIOLOGY WITH THE PULSE NUMBER, TRAIN DURATION AND INTERTRAIN INTERVAL USED IN CONVENTIONAL 10-HZ CLINICAL PROTOCOLS, AND THE FIRST TO COMPARE NMDA AND GABA RECEPTOR EFFECTS OF RTMS.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

TI6. LATERAL HYPOTHALAMIC GLUTAMATERGIC INPUTS TO VTA GLUTAMATERGIC NEURONS MEDIATE PRIORITIZATION OF INNATE DEFENSIVE BEHAVIOR OVER FEEDING

FLAVIA BARBANO*, SHILIANG ZHANG, EMMA CHEN, ORLANDO ESPINOZA, UZMA MOHAMMAD, YOCASTA ALVAREZ-BAGNAROL, BING LIU, MARISELA MORALES

THE LATERAL HYPOTHALAMUS (LH) HAS LONG BEEN IMPLICATED IN FEEDING BEHAVIOR AND DEFENSE RESPONSES BY ITS INTERACTIONS WITH DISTINCT BRAIN STRUCTURES, INCLUDING THE VENTRAL TEGMENTAL AREA (VTA). WE HAVE PREVIOUSLY DEMONSTRATED THAT LH-GLUTAMATERGIC NEURONS INFREQUENTLY SYNAPSE ON VTA-DOPAMINE NEURONS, BUT ESTABLISH MULTIPLE SYNAPSES ON VTA-GLUTAMATERGIC NEURONS, MEDIATING INNATE DEFENSIVE BEHAVIOR (BARBANO ET AL., 2020, NEURON). HERE, WE INVESTIGATE WHETHER LH-GLUTAMATERGIC INPUTS TO VTA-GLUTAMATERGIC NEURONS PLAY A ROLE IN DIFFERENT TYPES OF INNATE BEHAVIOR. WE FOUND THAT ACTIVATION OF LH-GLUTAMATERGIC NEURONS INNERVATING THE VTA PROMOTED ACTIVE AVOIDANCE, LONG-TERM AVERSION, AND ESCAPE ATTEMPTS. IN ADDITION, ACTIVATION OF THIS LH-GLUTAMATERGIC PATHWAY TO VTA DECREASED FEEDING BEHAVIOR IN BOTH SATED AND FOOD RESTRICTED MICE. BY TESTING FEEDING BEHAVIOR IN THE PRESENCE OF A PREDATOR, WE OBSERVED THAT VTA PHOTOINHIBITION OF GLUTAMATE RELEASE FROM LH-GLUTAMATERGIC FIBERS INTERRUPTED ONGOING FEEDING BEHAVIOR IN FOOD RESTRICTED MICE AND ABOLISHED THE PREDATOR-INDUCED DECREASE IN FEEDING BEHAVIOR. BY VTA SPECIFIC NEURONAL GENETIC ABLATION, WE ESTABLISHED THAT PREDATOR-INDUCED DECREASES IN FEEDING BEHAVIOR WERE MEDIATED BY VTA-GLUTAMATERGIC NEURONS BUT NOT BY NEIGHBORING DOPAMINE OR GABA NEURONS. THUS, WE UNCOVERED AN UNANTICIPATED NEURONAL CIRCUITRY BETWEEN LH-GLUTAMATERGIC INPUTS TO VTA-GLUTAMATERGIC NEURONS THAT PLAY A ROLE IN (1) PRIORITIZING ESCAPE INSTEAD OF OTHER DEFENSIVE RESPONSES, AND (2) THE SWITCH FROM FEEDING TO ESCAPE.
THIS STUDY WAS SUPPORTED BY THE INTRAMURAL RESEARCH PROGRAM OF THE NATIONAL INSTITUTE ON DRUG ABUSE

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

TI7. CHARACTERIZING THE KINEMATICS OF SKILLED ACTION IN A MOUSE MODEL OF DYTI DYSTONIA

TIFFANY LIN*, ALEXANDER T. HODGE, CHRISTIAN R. BURGESS, DANIEL K. LEVENTHAL

DYSTONIAS ARE A GROUP OF DISORDERS CHARACTERIZED BY ABNORMAL TWISTING MOVEMENTS DUE TO INVOLUNTARY CO-CONTRACTIONS OF OPPOSING MUSCLES. CONTRACTIONS IN TASK-SPECIFIC DYSTONIA, A PRIMARY FOCAL DYSTONIA, HAPPENS DURING SPECIFIC ACTIVITIES THAT USUALLY INVOLVE HIGHLY SKILLED AND REPETITIVE MOVEMENTS. EMERGING EVIDENCE SHOWS THAT THESE MOVEMENTS MAY BE REGULATED BY ABNORMAL NEUROPLASTIC MECHANISMS. HOWEVER, PRIMARY DYSTONIA HAS BEEN DIFFICULT TO STUDY IN RODENT MODELS AS KNOCK-IN MICE WITH THE HUMAN MUTANT TORIA GENE (DYTI-KI MICE) DO NOT EXHIBIT A CLEAR PHENOTYPE WHEN TESTED ON CLASSIC BEHAVIORAL TESTS LIKE THE ROTAROD AND SIMPLE LEVER PRESSING. ONE EXPLANATION IS THAT THESE BEHAVIORAL TESTS CAN BE COMPLETED BY MICE WITHOUT UTILIZING CORTICOSTRIATAL OR CEREBELLOTHALAMOCORTICAL CIRCUITS. REDUCED CONNECTIVITY BETWEEN THESE BRAIN REGIONS HAS BEEN SHOWN BY IMAGING STUDIES TO CORRELATE WITH DYSTONIC MOTOR SYMPTOMS. SKILLED REACHING IS A BEHAVIOR THAT INVOLVES THE CORTICOSTRIATAL AND CEREBELLOTHALAMOCORTICAL CIRCUITS. WE THEREFORE HYPOTHESIZED THAT TASK-SPECIFIC DYSTONIC BEHAVIORS WOULD BE REVEALED IN DYTI-KI MICE AFTER EXTENSIVE TRAINING IN SKILLED REACHING. HERE WE SHOW THAT DYTI-KI MICE CONSISTENTLY HAD MORE "FUMBLES," WHERE THE PELLET WAS LOST MID-RETRIEVAL. AND, WHILE OVERT DYSTONIC BEHAVIORS WERE NOT DETECTED, 30% OF DYTI MICE DISPLAYED ABNORMAL MOVEMENTS. THIS IS CONSISTENT WITH THE PENETRANCE OF DYTI-DYSTONIA IN HUMANS. THESE RESULTS INDICATE THAT THE HUMAN TORIA MUTATION IS SUFFICIENT TO GENERATE MOTOR DEFICITS IN SKILLED BEHAVIORS. FURTHER, DYTI-KI MICE PROVIDE AN INVALUABLE MODEL TO DETERMINE THE CIRCUIT MECHANISMS THAT FACTOR INTO THE PATHOGENESIS OF DYSTONIA.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

TI8. NUCLEUS ACCUMBENS DOPAMINE DYNAMICS UNDERLYING FLEXIBLE SIGN-TRACKING DURING A REWARD CONTINGENCY CHANGE

ERICA TOWNSEND*, KYLE SMITH

ANIMALS CAN ATTRIBUTE INCENTIVE SALIENCE, OR MOTIVATIONAL VALUE, TO REWARD-PREDICTIVE CUES. THIS ATTRIBUTION MANIFESTS AS A CUE-APPROACH RESPONSE, KNOWN AS SIGN-TRACKING, IN WHICH ANIMALS PHYSICALLY ENGAGE WITH THE CUE AS IF IT WERE THE REWARD ITSELF. WHILE SIGN-TRACKING IS NOTORIOUSLY PERSISTENT, IT IS NOT HABITUAL; RECENT STUDIES HAVE SHOWN THAT IT IS SENSITIVE TO CHANGES IN OUTCOME VALUE AND CUE-REWARD CONTINGENCIES. ONE EXAMPLE IS IN THE FORM OF AN OMISSION SCHEDULE, IN WHICH SIGN-TRACKING THAT RESULTS IN LEVER-CUE DEFLECTIONS IS PUNISHED BY REWARD CANCELLATION. IN THIS SCHEDULE, ANIMALS WILL CONTINUE TO SIGN-TRACK BUT WILL ADJUST THEIR RESPONSES TO AVOID REWARD CANCELLATION. THIS KIND OF FLEXIBILITY UNCOVERS NEW PERSPECTIVES ON A WELL-DOCUMENTED BEHAVIOR, IN WHICH PRECISE BEHAVIORAL DETAILS—RATHER THAN ONLY LEVER DEFLECTIONS—CAN REVEAL MORE ABOUT THE NEURAL UNDERPINNINGS OF MOTIVATION AND LEARNING. THERE ARE KNOWN NUCLEUS ACCUMBENS DOPAMINE SIGNALS THAT ARE REQUIRED FOR THE ACQUISITION OF SIGN-TRACKING, AND OTHERS THAT ARE REQUIRED FOR PREDICTIVE LEARNING. OMISSION LEARNING, IN WHICH ANIMALS CHANGE THEIR BEHAVIOR BUT PERSIST IN SIGN-TRACKING, OFFERS AN OPPORTUNITY TO ASSESS INCENTIVE AND PREDICTIVE ASPECTS OF THE DOPAMINE SIGNAL. TO ADDRESS THIS, WE USED FIBER PHOTOMETRY IN SIGN-TRACKING ANIMALS TO RECORD THE FLUORESCENCE LEVEL OF GRABDA2M SENSORS DURING THE OMISSION SCHEDULE IN THE NUCLEUS ACCUMBENS. WE SHOW EVENT RELATED DOPAMINERGIC DYNAMICS THAT UNDERLY OMISSION LEARNING AND THEIR RESULTING FLEXIBLE SIGN-TRACKING STRUCTURES. WE EXPECT THAT THIS WILL REVEAL MULTIPLE MECHANISMS FOR DOPAMINE DURING THIS SINGLE BEHAVIORAL RESPONSE.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

TI9. IDENTIFYING A DOWNSTREAM TARGET OF TBX1, A GENE ENCODED IN THE 22Q11.2 LOCUS, FOR OLIGODENDROGENESIS AND COGNITIVE FUNCTION

ANNE WELLS*, TAKESHI HIRAMOTO, TAKAHIRA YAMAUCHI, SHUKEN BOKU, GINA KANG, NOBORU HIROI

COGNITIVE DEFICITS ARE DEBILITATING IMPAIRMENTS SEEN ACROSS NEUROPSYCHIATRIC DISORDERS, SOME OF WHICH ARE THOUGHT TO ARISE FROM ABERRANT STRUCTURAL DEVELOPMENT. COPY NUMBER VARIATIONS (CNVS) ARE RELATIVELY LARGE GENETIC DELETIONS OR DUPLICATIONS THAT RESULT IN A WIDE SPECTRUM OF NEUROPSYCHIATRIC SYMPTOMS IN HUMANS. CARRIERS OF 22Q11.2 HEMIZYGOUS DELETIONS EXHIBIT VARIOUS COGNITIVE DEFICITS. HETEROZYGOUS DELETION OF TBX1, A TRANSCRIPTION FACTOR GENE ENCODED WITHIN THE 22Q11.2 LOCUS, RESULTS IN COGNITIVE SPEED DEFICITS AND MYELIN DEFICITS IN THE FIMBRIA OF ADULT MICE (HIRAMOTO ET AL., 2022; MOL PSYCH). MOREOVER, WHEN TBX1+/- WAS INITIATED IN POST-EMBRYONIC STEM CELLS BY TAMOXIFEN IN NEONATAL MICE (P1-5) IN NESTINCREERTM;TBX1FLOX/+ MICE, MICE EXHIBITED SLOW SPEED TO COMPLETE SPONTANEOUS ALTERNATION IN A T-MAZE WITHOUT SLOW MOTOR MOVEMENT; WHEN TBX1+/- WAS INITIATED IN ADOLESCENT MICE (P21-25), THERE WAS NO COGNITIVE DEFICIT. AS TBX1 IS ENRICHED IN POST-EMBRYONIC STEM CELLS AND IN ZONES OF POSTNATAL NEUROGENESIS (E.G., SUBVENTRICULAR ZONE [SVZ]), WE HYPOTHESIZE THAT TBX1 MAY PLAY CRITICAL ROLE IN THE PROLIFERATION AND MAINTENANCE OF STEM CELLS IN THE SVZ VIA AN OLIGODENDROCYTE-SPECIFIC DOWNSTREAM TARGET, WHICH MAY BE CRITICAL TO THE MYELINATION OF THE FIMBRIA (HIRAMOTO ET AL., 2011; HUMAN MOL GENET.). OUR CHIP-SEQ ANALYSIS SHOWED THAT TBX1 BINDS TO A LOCUS NEAR FOXG1, A GENE IMPLICATED IN ADULT NEUROGENESIS, CEREBRAL DYSMYELINATION, AND NEURODEVELOPMENTAL DISORDERS. IN NEONATAL MICE, WE DEMONSTRATE DIFFERENTIAL COLOCALIZATION OF FOXG1 AND TBX1, AS WELL AS MARKERS FOR SUBPOPULATIONS OF STEM CELLS, IMMATURE NEURONS, AND OLIGODENDROCYTE PRECURSOR CELLS (OPCS) IN THE SVZ PROPER AND THE FIMBRIA. WE ALSO DEMONSTRATE THAT FOXG1 ALSO COLOCALIZES WITH TBX1 IN PROLIFERATING STEM CELLS HARVESTED FROM THE SVZ IN VITRO. EXPERIMENTS ARE IN PROGRESS TO DEMONSTRATE SUCCESSFUL SIRNA SILENCING OF TBX1 AND ITS EFFECT ON FUNCTIONAL FOXG1 EXPRESSION.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T20. SUFFERING IN SILENCE OR SATISFIED IN SOLITUDE? PERIPUBERTAL SOCIAL DISRUPTION DIFFERENTIALLY ALTERS MOTIVATED BEHAVIORS IN JUVENILES

CATHERINE NEMESKAL*, JON CAVANAUGH, KYLE SMITH

WHILE POSITIVE SOCIAL CONNECTIONS ENHANCE OUR LIVES AND PROTECT AGAINST STRESS AND DISEASE, DISRUPTED RELATIONSHIPS INCREASE VULNERABILITY TO ADDICTION, MORBIDITY, AND MORTALITY. IN PARTICULAR, THE QUANTITY AND QUALITY OF SOCIAL INTERACTIONS DURING CRITICAL PERIODS HAS BEEN SHOWN TO PLAY A VITAL ROLE IN BRAIN DEVELOPMENT AND LIFE-LONG SOCIAL FUNCTIONING. WHILE THERE IS STRONG EVIDENCE THAT SOCIAL DISRUPTION DURING CRITICAL PERIODS PRODUCES DEVELOPMENTAL DELAYS, A GAP REMAINS IN UNDERSTANDING THE IMPACT OF SOCIAL DISRUPTION ON MOTIVATED BEHAVIORS ACROSS THE LIFESPAN. THIS PROJECT MEASURED THE IMPACT OF DEGREES OF PERIPUBERTAL ISOLATION [CHRONIC ISOLATION (CI), RECURRENT SOCIAL DISRUPTION (RSD), PAIR-HOUSING (PH)] ON MOTIVATED BEHAVIORS IN JUVENILE RATS. THE DATA INDICATE THAT VARYING DEGREES OF PERIPUBERTAL ISOLATION AFFECT MOTIVATION FOR SOCIAL AND FOOD REWARDS DIFFERENTLY IN FEMALES AND MALES. CI SUBSTANTIALLY ENHANCED, WHILE RSD DIMINISHED, SELF-ADMINISTRATION OF SOCIAL REWARDS IN BOTH SEXES. CI ALSO ENHANCED SELF-ADMINISTRATION OF FOOD REWARDS IN MALES, WHILE RSD REDUCED SELF-ADMINISTRATION OF FOOD REWARDS IN FEMALES. SEX DIFFERENCES PREVAILED IN THE EFFECTS OF PERIPUBERTAL ISOLATION ON SOMATIC GROWTH RATES. WHILE CI INCREASED PREFERENCE FOR SOCIAL REWARDS, RSD PROMOTED SELECTION OF NO REWARD CHOICE OVER SOCIAL REWARDS. FINALLY, CI AND RSD INTERACTED DIFFERENTIALLY WITH SOCIAL NOVELTY TO ALTER THE INCENTIVE VALUE OF SOCIAL REWARDS DURING PUBERTY. THESE DATA SUGGEST THAT VARYING DEGREES OF PERIPUBERTAL ISOLATION DIFFERENTIALLY IMPACT LEARNING, REWARD PREFERENCES, INCENTIVE VALUES, AND SOMATIC GROWTH, IN A SEX DEPENDENT MANNER DURING PUBERTY. THESE FINDINGS ILLUMINATE THE IMPORTANT IMPACT OF PERIPUBERTAL SOCIAL DISRUPTION ON MOTIVATED BEHAVIORS, IMPLICATING ALTERED DEVELOPMENT OF THE SOCIAL DECISION-MAKING NETWORK. ULTIMATELY, THESE DATA PROVIDE A FRAMEWORK FOR THE DEVELOPMENT OF TARGETED THERAPEUTICS TO AMELIORATE SOCIAL AND MOTIVATIONAL DYSFUNCTION IN HUMANS.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T21. TRAINING, CAREER DEVELOPMENT AND FUNDING OPPORTUNITIES VIA THE NATIONAL INSTITUTE ON AGING

DANA PLUDE*

NIA SUPPORTS TRAINING, CAREER DEVELOPMENT, BASIC RESEARCH AND SMALL BUSINESS FUNDING FOR RESEARCH AND DEVELOPMENT ACTIVITIES ACROSS THE ADULT LIFESPAN. THE FOUR EXTRAMURAL DIVISIONS OF NIA (AGING AND BIOLOGY, BEHAVIORAL AND SOCIAL SCIENCE, NEUROSCIENCE AND GERIATRICS AND CLINICAL GERONTOLOGY) OFFER A RANGE OF FUNDING ACTIVITIES TO SUPPORT BASIC, APPLIED AND TRANSLATIONAL RESEARCH AND DEVELOPMENT ACTIVITIES. OTHER RESOURCES SUCH AS CENTER AND NETWORK PROGRAMS ARE SUPPORTED AS WELL. THIS PRESENTATION OFFERS AN OVERVIEW OF THESE OPPORTUNITIES AND THE NIA POINTS OF CONTACT FOR ADDITIONAL INFORMATION.

T22. TRANSIENT CAMP PRODUCTION DRIVES RAPID AND SUSTAINED SPIKING IN BRAINSTEM PARABRACHIAL NEURONS TO SUPPRESS FEEDING

JONNATHAN SINGH ALVARADO, ANDREW LUTAS, JOSEPH MADARA, JEREMIAH ISAAC*, CAROLINE LOMMER, MARK ANDERMANN

BRIEF STIMULI CAN TRIGGER LONGER LASTING BRAIN STATES. G PROTEIN-COUPLED RECEPTORS (GPCRS) COULD HELP SUSTAIN SUCH STATES BY COUPLING SLOW-TIMESCALE MOLECULAR SIGNALS TO NEURONAL EXCITABILITY. BRAINSTEM PARABRACHIAL NUCLEUS GLUTAMATERGIC NEURONS (PBNGLUT) REGULATE SUSTAINED BRAIN STATES SUCH AS PAIN, AND EXPRESS GS-COUPLED GPCRS THAT INCREASE CAMP SIGNALING. WE ASKED WHETHER CAMP DIRECTLY INFLUENCES PBNGLUT EXCITABILITY AND BEHAVIOR. BOTH BRIEF TAIL SHOCKS AND BRIEF OPTOGENETIC STIMULATION OF CAMP PRODUCTION IN PBNGLUT NEURONS DROVE MINUTES-LONG SUPPRESSION OF FEEDING. THIS SUPPRESSION MATCHED THE DURATION OF PROLONGED ELEVATIONS IN CAMP, PROTEIN KINASE A (PKA), AND CALCIUM ACTIVITY IN VIVO AND IN VITRO. SHORTENING THIS ELEVATION IN CAMP REDUCED THE DURATION OF FEEDING SUPPRESSION FOLLOWING TAIL SHOCKS. CAMP ELEVATIONS IN PBNGLUT NEURONS RAPIDLY LEAD TO SUSTAINED INCREASES IN ACTION POTENTIAL FIRING VIA PKA-DEPENDENT MECHANISMS. THUS, MOLECULAR SIGNALING IN PBNGLUT NEURONS HELPS PROLONG NEURAL ACTIVITY AND BEHAVIORAL STATES EVOKED BY BRIEF, SALIENT BODILY STIMULI.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T23. AKAP-SCAFFOLDING OF CALCINEURIN IN AMYLOID B-MEDIATED SYNAPTIC DYSFUNCTION

MARK DELL'ACQUA*, TYLER MARTINEZ, OLGA PRIKHODKO, RONALD FREUND

REGULATION OF SYNAPTIC INSERTION AND REMOVAL OF AMPA-TYPE GLUTAMATE RECEPTORS (AMPARS) IN COORDINATION WITH CHANGES IN DENDRITIC SPINE STRUCTURE MEDIATE NMDA-TYPE GLUTAMATE RECEPTOR (NMDAR)-DEPENDENT LONG-TERM POTENTIATION (LTP) AND DEPRESSION (LTD) PLASTICITY OF SYNAPTIC STRENGTH THAT UNDERLIES LEARNING AND MEMORY. IN ALZHEIMER'S DISEASE (AD) AMYLOID-B (AB) MAY IMPAIR LEARNING AND MEMORY THROUGH HIJACKING NMDAR-DEPENDENT CA2+ SIGNALING PATHWAYS TO BIAS THEM TOWARD LTD AND SYNAPSE WEAKENING AND SPINE ELIMINATION OVER LTP AND SYNAPSE STRENGTHENING AND SPINE MAINTENANCE. BY EMPLOYING AKAP150ΔPIX KNOCK-IN MICE WITH A MUTATION THAT DISRUPTS ANCHORING OF THE CA2+-DEPENDENT PROTEIN PHOSPHATASE CALCINEURIN (CAN) TO THE SCAFFOLD PROTEIN A-KINASE ANCHORING PROTEIN (AKAP)150, WE REVEALED THAT LOCAL, POSTSYNAPTIC AKAP-CAN-LTD SIGNALING WAS REQUIRED FOR ACUTE AB-MEDIATED IMPAIRMENT OF SYNAPTIC CA2+ INFLUX THROUGH NMDARS IN NEURONAL CULTURES AND INHIBITION OF LTP IN EX VIVO BRAIN SLICES. FURTHERMORE, WE FOUND THAT AKAP-CAN SIGNALING WAS ALSO REQUIRED FOR AB-MEDIATED DENDRITIC SPINE/SYNAPSE LOSS THAT OCCURS OVER SEVERAL DAYS IN NEURONAL CULTURES. IN PARTICULAR, WE FOUND THAT AB ACUTELY ENGAGES AKAP-CAN SIGNALING TO DEPHOSPHORYLATE BOTH NMDAR-GLUN2B SUBUNITS TO DECREASE NMDAR CA2+ INFLUX AND THE F-ACTIN SEVERING PROTEIN ADF-COFILIN TO DESTABILIZE THE DENDRITIC SPINE CYTOSKELETON. BY EMPLOYING SHRNAI TO KNOCKDOWN EXPRESSION OF THE CAN-REGULATED NFAT TRANSCRIPTION FACTORS, WE FURTHER DEMONSTRATED THAT DOWNSTREAM CAN-NFAT SIGNALING TO NUCLEUS WAS REQUIRED FOR SUSTAINING AB-MEDIATED SPINE LOSS. FINALLY, WE IDENTIFIED THE E3-UBIQUITIN LIGASE MDM2, WHICH WAS PREVIOUSLY LINKED TO LTD AND DEVELOPMENTAL SYNAPSE ELIMINATION, AS A DOWNSTREAM NFAT TARGET GENE THAT IS TRANSCRIPTIONALLY UPREGULATED BY AB AND WHOSE ENZYMATIC ACTIVITY IS REQUIRED FOR AB-MEDIATED SPINE LOSS. THESE FINDINGS IDENTIFY MDM2 AS A POTENTIALLY NOVEL THERAPEUTIC TARGET IN AD.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T24. BRAIN-WIDE IN VIVO DOPAMINE DYNAMICS REVEALED WITH THE NEXT GENERATION OF DLIGHT SENSORS

JACOB ROSHGADOL*, TIM HANKS, LIN TIAN

DOPAMINE PLAYS A KEY ROLE IN FACILITATING COGNITIVE PROCESSES, AND ALTERED DOPAMINE SIGNALING IS CENTRAL TO MANY NEUROLOGICAL AND NEUROPSYCHIATRIC DISORDERS SUCH AS SCHIZOPHRENIA AND PARKINSON'S DISEASE. YET WE LACK EFFECTIVE TREATMENTS FOR THESE DISORDERS, HIGHLIGHTING THE NEED FOR A MECHANISTIC UNDERSTANDING OF DOPAMINE BIOLOGY TO DEVELOP MORE EFFICACIOUS TREATMENTS. TO UNDERSTAND HOW DOPAMINE NEUROMODULATORY SIGNALING SHAPES NEURAL ACTIVITY, WE MUST BE ABLE TO PRECISELY RECORD THE TIMING AND LOCATION OF DOPAMINE RELEASE. THE TIAN LAB PIONEERED THE DEVELOPMENT OF THE FIRST GENERATION OF GENETICALLY ENCODED DOPAMINE SENSORS, DLIGHTS, WHICH ALLOWS DIRECT RECORDING OF DOPAMINE SIGNALING. THE ORIGINAL DLIGHT VARIANT, DLIGHT1.3B, ENABLED RESEARCHERS TO MEASURE SUB-SECOND DA DYNAMICS IN BEHAVING ANIMALS. THE LAB HAS OPTIMIZED DLIGHT1.3B FURTHER TO CREATE TWO NEW SENSOR VARIANTS, DLIGHT3.6 AND DLIGHT3.8, WITH IMPROVED SENSITIVITY AND APPARENT DYNAMIC RANGE. THE ENHANCED PROPERTIES OF THE NEW VARIANTS PERMIT THE RECORDING OF DOPAMINE DYNAMICS IN A RANGE OF PHYSIOLOGICAL CONTEXTS. USING FIBER PHOTOMETRY RECORDING METHODS DURING OPTOGENETIC STIMULATION OF DOPAMINE NEURONS AND FREELY MOVING BEHAVIORS IN MICE, I HAVE DETERMINED IN VIVO SENSOR PERFORMANCE METRICS OF DLIGHT3.6 AND 3.8 IN REGIONS RECEIVING VARYING LEVELS OF DOPAMINE INPUT INCLUDING STRIATUM, PREFRONTAL CORTEX, AMYGDALA, AND HIPPOCAMPUS. FURTHERMORE, I HAVE DEVELOPED AN ONLINE RESOURCE FOR DLIGHT RECORDING AND DATA ANALYSIS MODELED AFTER THE ALLEN BRAIN PROJECTION ATLAS, WHICH INCLUDES A DATABASE OF METADATA, EXPERIMENTAL RESULTS, AND VISUALIZATIONS. PRESENTING THIS WORK AT WCBR WILL PROVIDE ME WITH A UNIQUE OPPORTUNITY TO DISSEMINATE THE DATABASE TO A BROAD NEUROSCIENCE RESEARCH COMMUNITY, ACCELERATING THE ADOPTION OF THESE NOVEL TOOLS BY ALLOWING RESEARCHERS TO MAKE PREVIOUSLY INACCESSIBLE MEASUREMENTS ABOUT DOPAMINE BIOLOGY.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T25. RIT2 REGULATES INDUCTION OF THE AUTOPHAGY LYSOSOMAL PATHWAY AND PROTECTS AGAINST A-SYNUCLEIN PATHOLOGY IN A CELLULAR MODEL OF PARKINSON'S DISEASE

ANDY GAO, DAN MONTAGNA, WARREN HIRST*, PAUL TEMKIN

SIGNIFICANT EFFORTS HAVE BEEN DEDICATED TO UNDERSTANDING THE DIVERSE GENETIC INFLUENCES CONTRIBUTING TO THE DEVELOPMENT OF PARKINSON'S DISEASE (PD) AND THE CELLULAR ROLES OF THESE PROTEINS IN DISEASE PATHOLOGY. ONE SUCH GENETIC RISK FACTOR IS THE RIT2 GENE, WHICH ENCODES THE NOVEL SMALL GTPASE RAS-LIKE WITHOUT CAAX 2 (RIT2), A MEMBER OF THE RAS SUPERFAMILY OF SMALL GTPASES. A SINGLE NUCLEOTIDE POLYMORPHISM IN THE RIT2 LOCUS, RSI2456492, HAS BEEN ASSOCIATED WITH A HIGHER RISK OF PD ACROSS MULTIPLE ETHNICITIES. WHILE ITS PRECISE PHYSIOLOGICAL FUNCTION IS MECHANISTICALLY UNCLEAR, RIT2 HAS BEEN SHOWN TO INFLUENCE SIGNALING PATHWAYS, DOPAMINE TRANSPORTER TRAFFICKING AND LRRK2 ACTIVITY. IN THE CURRENT STUDY, WE HAVE ESTABLISHED AN UPSTREAM REGULATORY ROLE FOR RIT2 WHEREBY IT CAN INFLUENCE DIVERSE PROCESSES ASSOCIATED WITH PD. USING CELLULAR MODELS, WE HAVE SHOWN THAT RIT2 IS NECESSARY FOR ACTIVITY-DEPENDENT CHANGES IN GENE TRANSCRIPTION RELATED TO THE AUTOPHAGY-LYSOSOMAL PATHWAY (ALP) BY CONTROLLING THE NUCLEAR TRANSLOCATION OF ALP-REGULATING TRANSCRIPTION FACTORS. MOREOVER, RIT2 IS ASSOCIATED WITH LYSOSOMES AND REGULATES AUTOPHAGIC FLUX AND AGGREGATED PROTEIN CLEARANCE BY MODULATING HYDROLASE ACTIVITY. OVEREXPRESSION OF ACTIVE RIT2 IN NEURONS ALSO ENHANCES ENDOLYSOSOMAL PROCESSING AND IS PROTECTIVE AGAINST A-SYNUCLEIN AGGREGATION. THE PRESENT STUDY CONFIRMS THAT THE LOSS OF RIT2 IS UPSTREAM OF VARIOUS DEFICITS THAT PERPETUATE PD PROGRESSION AND SUGGESTS THAT ENHANCING ITS FUNCTION COULD HAVE THERAPEUTIC BENEFIT.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T26. OPEN BOARD

T27. THE UFMI PATHWAY IS DYSREGULATED IN ALZHEIMER'S DISEASE

FABIENNE FIESEL*, TINGXIANG YAN, MICHAEL HECKMAN, MELISSA MURRAY, DENNIS DICKSON, WOLFDIETER SPRINGER

NEUROPATHOLOGICALLY, ALZHEIMER'S DISEASE (AD) IS CHARACTERIZED BY THE PRESENCE OF SENILE PLAQUES COMPOSED OF BETA-AMYLOID (AB) AND NEUROFIBRILLARY TANGLES MADE OF HYPERPHOSPHORYLATED TAU (P-TAU). AB AND P-TAU HAVE BEEN SHOWN TO IMPACT ENDOPLASMIC RETICULUM HOMEOSTASIS, THE DNA DAMAGE RESPONSE AS WELL AS AUTOPHAGIC FUNCTIONS. ALTERATIONS IN THESE SYSTEMS HAVE ALSO BEEN CONNECTED TO UFMI, A UBIQUITIN-LIKE MODIFIER PROTEIN. ANALOGOUS TO UBIQUITIN, UFMI IS CONJUGATED TO SUBSTRATES VIA A CATALYTIC CASCADE INVOLVING A SPECIFIC SET OF EI (UBA5), E2 (UFCI), AND A COMPLEX THAT CONSISTS OF E3 LIGASE (UFLI), DDRGKI AND CDK5RAP3. THE CONJUGATION OF UFMI TO SUBSTRATES (UFMYLATION) IS REVERSIBLE, AND THIS IS MEDIATED BY UFSP2. THE UFMYLATION PATHWAY IS ESSENTIAL FOR BRAIN DEVELOPMENT AS COMPLETE LOSS OF FUNCTION OF ANY OF ITS COMPONENTS RESULT IN SEVERE NEURODEVELOPMENTAL DISORDERS. HOWEVER, THE ROLE AND SIGNIFICANCE OF UFMI FOR AGE-RELATED AD REMAINS UNKNOWN.

WE USED WESTERN BLOT AND MESO SCALE DISCOVERY ELISA TO ANALYZE UFMI, UFSP2 AND OTHER UFMYLATION PROTEINS AS WELL AS TAU AND P-TAU IN THE FRONTAL CORTEX OF CONTROLS (N=41) AND AD (N=72). WE FURTHER GENE-EDITED NEURONAL PRECURSOR CELLS WITH CRISPR/CAS9 TO INVESTIGATE THE RELATIONSHIP OF UFMI AND UFSP2 IN NEURONS.

WE FOUND A SIGNIFICANT INCREASE OF UFMI AS WELL AS A SIGNIFICANT REDUCTION OF SOLUBLE UFSP2 PROTEIN IN AD COMPARED TO CONTROLS. INTERESTINGLY, PROTEIN LEVELS OF UFMI STRONGLY CORRELATED WITH P-TAU, INDICATING THAT INCREASED UFMI LEVELS MIGHT BE LINKED TO DISEASE PATHOGENESIS. THERE WAS FURTHER A STRONG NEGATIVE CORRELATION BETWEEN UFMI AND UFSP2 LEVELS IN BRAIN. IN CELL CULTURE EXPERIMENTS, WE FOUND THAT THE ABSENCE OF UFSP2 IN KO CELLS INCREASED UFMI LEVELS BY INCREASING THE AMOUNT OF CONJUGATED UFMI.

WE CONCLUDE THAT UFMI PATHWAY IS DYSREGULATED IN ALZHEIMER'S DISEASE. THE OBSERVED INCREASE OF UFMI PROTEIN MIGHT REFLECT ABNORMAL UFMYLATION AND IS LIKELY LINKED TO THE DECREASE OF SOLUBLE UFSP2 PROTEIN. WHILE THE CONSEQUENCES OF ABNORMAL UFMYLATION REMAIN UNKNOWN, SEVERAL UFMI-REGULATED PATHWAYS ARE KNOWN TO BE AFFECTED IN AND CONTRIBUTE TO AD. FUTURE STUDIES THAT ADDRESS THE MOLECULAR MECHANISMS AND THE CONSEQUENCES OF DYSREGULATED UFMI ARE NEEDED TO DETERMINE WHETHER UFMI COULD BE A THERAPEUTIC TARGET FOR AD.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T28. DISSECTING INCRETIN-MEDIATED MODULATION OF HYPOTHALAMIC FEEDING CIRCUIT

HAYLEY MCMORROW*, CAROLYN LORCH, NIKOLAS HAYES, HALEY PROVINCE, JOSH FRYDMAN, JESSICA XIA, LISA BEUTLER

ANALOGS OF THE INCRETIN HORMONES GLPI AND GIP HAVE RAPIDLY BECOME MAINSTAYS OF OBESITY AND DIABETES MANAGEMENT. HOWEVER, BOTH THE PHYSIOLOGIC ROLE OF INCRETIN HORMONES IN APPETITE REGULATION AND THE PHARMACOLOGIC MECHANISMS BY WHICH INCRETIN MIMETIC DRUGS SUPPRESS APPETITE REMAIN INCOMPLETELY UNDERSTOOD. HUNGER-PROMOTING AGRP-EXPRESSING NEURONS ARE AN IMPORTANT HYPOTHALAMIC TARGET OF GUT-BRAIN COMMUNICATION THAT REGULATES FOOD INTAKE. USING FIBER PHOTOMETRY, WE HAVE NOW SHOWN THAT THESE NEURONS ARE AN IMPORTANT IN VIVO TARGET OF PHARMACOLOGIC DOSES OF INCRETIN ANALOGS. SPECIFICALLY, INCRETIN ANALOGS ACUTELY INHIBIT AGRP NEURON ACTIVITY IN FASTED MICE AND REDUCE BOTH THE RESPONSE OF AGRP NEURONS TO FOOD PRESENTATION AND SUBSEQUENT FOOD INTAKE. MOREOVER, THIS FEEDING SUPPRESSION CAN BE PARTIALLY OVERCOME WITH AGRP NEURON STIMULATION, SUGGESTING THAT INCRETIN-INDUCED AGRP NEURON INHIBITION PARTIALLY MEDIATES THE APPETITE-SUPPRESSING EFFECTS OF INCRETIN ANALOGS. TAKEN TOGETHER, WE HAVE CLARIFIED MECHANISMS UNDERLYING THE EFFICACY OF INCRETIN-BASED ANTI-OBESITY THERAPIES PAVING THE WAY FOR NOVEL TREATMENT APPROACHES THAT MAY AVOID SOME OF THE ADVERSE EFFECTS OF THESE DRUGS.TO DETERMINE WHETHER UFMI COULD BE A THERAPEUTIC TARGET FOR AD.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T29. OXYTOCIN RECEPTOR CO-LOCALIZATION IN BRAINSTEM PARASYMPATHETIC NEURONS

DAVID MENDELOWITZ*, JOAN ESCOBAR, BRIDGET ALBER, XIN WANG

SURPRISINGLY LITTLE IS KNOWN ABOUT THE EXPRESSION OF OXYTOCIN (OXT) RECEPTORS IN THE NUCLEUS AMBIGUUS (NA) AND DORSAL MOTOR NUCLEUS OF THE VAGUS (DMNX), AND IN PARTICULAR WHETHER SOME, ALL, OR NONE OF THE PARASYMPATHETIC CARDIAC VAGAL NEURONS (CVNS) WITHIN THESE DIFFERENT NUCLEI EXPRESS OXT RECEPTORS. IN THIS STUDY WE CHARACTERIZED THE CO-LOCALIZATION OF OXT RECEPTORS IN CVNS, AND NON-CVN CHOLINERGIC NEURONS LOCATED IN THE NA AND DMNX NUCLEI. THE TRANSGENIC OXYTOCIN RECEPTOR (OXTR)-CRE MOUSE JAX #031303 AND THE CRE DEPENDENT FLOXED CHR2-EYFP MOUSE JAX #012569 WERE CROSSBRED FOR THIS STUDY. ALEXA FLUOR 555 CONJUGATES OF CHOLERA TOXIN SUBUNIT B WAS INJECTED INTO THE PERICARDIAL SAC TO RETROGRADELY LABEL CVNS. COLOCALIZATION ANALYSIS WAS PERFORMED USING AN IMARIS ALGORITHM FOR CO-EXPRESSION OVERLAPPED CELLS AND THE PERCENTAGE OF COLOCALIZATION WAS CALCULATED FOR EACH CELL POPULATION. WE FOUND THAT OVER HALF OF THE CVNS IN THE DMNX CO-LOCALIZE WITH OXT RECEPTOR POSITIVE NEURONS. SURPRISINGLY, CVNS IN THE NA, AS WELL AS THE OTHER CHAT NEURONS IN THE NA, HAVE SPARSE CO-LOCALIZATION WITH OXT RECEPTOR POSITIVE NEURONS. FUTURE WORK IS NEEDED TO TEST IF SELECTIVE ACTIVATION OF OXT RECEPTOR POSITIVE CVNS IN THE DMNX PREFERENTIALLY ALTERS HEART RATE AND/OR CONTRACTILITY, AND MORE IMPORTANTLY, WHETHER ACTIVATION OF OXT RECEPTOR POSITIVE CVNS PREVENTS OR REVERSES CARDIOVASCULAR DYSFUNCTION IN CARDIORESPIRATORY DISEASES.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T30. STROKE-RELATED BLOOD-BRAIN BARRIER DISRUPTION IS HIGHER IN POSTERIOR CEREBRAL ARTERY INFARCTS WHEN COMPARED WITH OTHER VASCULAR TERRITORIES

RICHARD LEIGH*, ANDREIA FARIA

WE INVESTIGATED THE IMPACT OF STROKE LOCATION ON THE AMOUNT OF BLOOD-BRAIN BARRIER (BBB) DISRUPTION DETECTED WITHIN THE CORRESPONDING ISCHEMIC LESION.
THIS WAS A RETROSPECTIVE ANALYSIS OF A DE-IDENTIFIED DATASET OF STROKE PATIENTS ADMITTED TO A SINGLE CENTER OVER 10 YEARS. PATIENTS WERE INCLUDED IF THEY HAD AN MRI WITH PERFUSION WEIGHTED IMAGING (PWI) DEMONSTRATING AN AREA OF HYPOPERFUSION AND A CORRESPONDING INFARCT THAT AFFECTED A SINGLE VASCULAR TERRITORY. BBB DISRUPTION WAS MEASURED FROM THE PWI SOURCE IMAGES, DETECTED AS GADOLINIUM LEAKAGE, AND AVERAGED WITHIN THE PERFUSION DEFICIT. LOGISTIC REGRESSION WAS USED TO COMPARE BETWEEN DIFFERENT VASCULAR TERRITORIES.
THERE WERE 149 PATIENTS INCLUDED IN THE STUDY: 116 MIDDLE CEREBRAL ARTERY (MCA), 15 POSTERIOR CEREBRAL ARTERY (PCA), 4 ANTERIOR CEREBRAL ARTERY (ACA), AND 14 INFRATENTORIAL. FIGURE SHOWS THE BBB DISTRIBUTION FOR EACH VASCULAR TERRITORY. THE PCA TERRITORY APPEARED HIGHER THAN ALL OTHER TERRITORIES; WE SUBSEQUENTLY COMPARED BBB DISRUPTION FOR THE PCA TERRITORY WITH EACH OF THE OTHER TERRITORIES COMBINED AND INDIVIDUALLY. COMPARED WITH ALL OTHER TERRITORIES, BBB DISRUPTION WAS SIGNIFICANTLY HIGHER IN THE PCA TERRITORY (OR 1.34; CI 1.10:1.64; P=0.003). BBB DISRUPTION WAS ALSO HIGHER WHEN COMPARED WITH THE MCA TERRITORY (OR 1.37; CI 1.07:1.60; P=0.007) AND INFRATENTORIAL (OR 1.68; CI 1.004:2.81; P=0.048) BUT DID NOT REACH SIGNIFICANCE FOR THE ACA TERRITORY (OR 2.10; CI 0.81:5.40; P=0.125).
WE FOUND THAT STROKES IN THE PCA VASCULAR DISTRIBUTION HAD MORE DISRUPTION OF THE BBB WHEN COMPARED WITH OTHER TERRITORIES. THESE FINDINGS MAY HAVE IMPLICATIONS FOR RISK OF HEMORRHAGIC COMPLICATIONS AND RECOVERY AFTER STROKE.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T31. METAGENOMIC SEQUENCING TO BETTER UNDERSTAND GUT MICROBIOME CONTRIBUTIONS TO TBI

KRIS MARTENS*, CARISSA GRATZOL, NOAH BRESSLER, MICHAEL BAILEY, COLE VONDER HAAR

TRAUMATIC BRAIN INJURY (TBI) CAUSES COGNITIVE IMPAIRMENT, INCREASES RISK FOR PSYCHIATRIC DISEASE, AND EXACERBATES RELATED SYMPTOMS SUCH AS RISKY DECISION-MAKING AND IMPULSIVITY. IMPAIRED MONOAMINE NEUROTRANSMISSION IS A LIKELY CONTRIBUTOR TO SUCH SYMPTOMS, WITH SEROTONIN SIGNALING CONTRIBUTING TO ANXIETY AND MOOD-RELATED DISORDERS, IMPULSIVE DYSFUNCTION, AND IMPAIRED DECISION-MAKING. DESPITE THIS KNOWLEDGE, PRECISELY WHY THESE SYSTEMS ARE VULNERABLE TO TBI IS UNKNOWN. HOWEVER, EMERGING DATA INDICATE A ROLE FOR THE GUT MICROBIOME. GUT DYSBIOSIS, OR AN IMBALANCE IN MICROBIAL POPULATIONS, OCCURS RAPIDLY AFTER TBI AND MAY PERSIST FOR YEARS IN PATIENTS. IN A PREVIOUS STUDY, OUR LAB MANIPULATED THE MICROBIOME OF RODENTS USING ANTIBIOTIC DYSBIOSIS. WE THEN ASSESSED FUNCTION ON THE RODENT GAMBLING TASK, A CLINICALLY RELEVANT ASSESSMENT OF IMPULSIVITY AND DECISION-MAKING. THE FINDINGS FROM THE STUDY SHOWED A DELAY IN THE ONSET OF TBI SYMPTOMS IN THE ANTIBIOTIC COCKTAIL GROUP POINTING TO A POTENTIAL CAUSAL ROLE FOR THE GUT MICROBIOME IN PSYCHIATRIC DISEASE FOLLOWING TBI. THE MOST COMMON SEQUENCING METHOD OF GUT MICROBIOME, 16S AMPLICON-BASED SEQUENCING, IDENTIFIED BROAD CHANGES IN THE MICROBIOME, BUT COULD NOT IDENTIFY SPECIES-LEVEL INFORMATION. TO BETTER UNDERSTAND THE MECHANISMS AT PLAY, WE PERFORMED METAGENOMIC SHOTGUN SEQUENCING WHICH RECONSTRUCTS INDIVIDUAL GENES, AND THEN SPECIES. FROM THESE DATA, WE WERE ABLE TO CONSTRUCT BACTERIAL METAGENOME-ASSEMBLED GENOMES (MAGS) TO DETERMINE CHANGES OCCURRING AT KEY TIME POINTS POST INJURY AND AT THE SPECIES LEVEL. ONGOING ANALYSES WILL DETERMINE WHICH INDIVIDUAL SPECIES ARE CHANGED DUE TO TBI, ANTIBIOTICS, AND DURING THE POST-INJURY RECOVERY PERIOD AS WELL AS SPECIFIC METABOLIC GENES INVOLVED IN REGULATING SEROTONIN AND OTHER IMPORTANT GUT SIGNALING TRANSMITTERS.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T32. NOVEL A3 ADENOSINE RECEPTOR AGONIST MRS5980 PREVENTS TRAUMATIC BRAIN INJURY INDUCED COGNITIVE IMPAIRMENT

SUSAN FARR*, MONICA GOODLAND, DANIELA SALVEMINI

TRAUMATIC BRAIN INJURY (TBI) SURVIVORS REPORT LONG LASTING COGNITIVE DYSFUNCTIONS THAT DEEPLY IMPAIR THEIR QUALITY OF LIFE. POST-TBI COGNITIVE CHANGES INCLUDE IMPAIRED CONCENTRATION, THINKING, MEMORY, AND LEARNING. LONG-TERM COGNITIVE IMPAIRMENT (CI) RESULTING FROM MILD TBI (MTBI) HAS NO FDA-APPROVED TREATMENT AND IS A KNOWN RISK FACTOR FOR DEPRESSION AND AGE-RELATED DEMENTIA, REPRESENTING A GROWING PUBLIC HEALTH CONCERN. PREVIOUSLY, WE DEMONSTRATED THAT INTRAPERITONEAL ADMINISTRATION OF MRS5980, A HIGHLY SELECTIVE A3 ADENOSINE RECEPTOR (A3AR) AGONIST, IH AFTER TBI PREVENTED THE DEVELOPMENT OF CI IN MICE UP TO 4 WEEKS POST-INJURY. PRESERVED COGNITIVE PERFORMANCE CORRESPONDED WITH REDUCED MARKERS OF NEUROINFLAMMATION. IT HAS BEEN SHOWN THAT GLYCOGEN SYNTHASE KINASE-3 (GSK-3B) INHIBITION FOLLOWING TBI PREVENTS CI IMPAIRMENT AND A3AR AGONISTS ARE KNOWN MODULATORS OF THE GSK PATHWAY. WE ALSO INVESTIGATED HOW LONG THE TREATMENT WITH MRS5980 COULD BE DELAYED AFTER INJURY TO STILL RETAIN COGNITIVE BENEFITS. THIS INFORMATION IS CLINICALLY RELEVANT AS MANY MTBI SURVIVORS ARE NOT GIVEN IMMEDIATE MEDICAL ATTENTION POST-TRAUMA. MICE WERE SUBJECTED TO EITHER A SHAM PROCEDURE OR A CLOSED-HEAD WEIGHT-DROP TBI AND MRS5980 WAS ADMINISTERED AT IH, 24H, OR 72H POST-INJURY. DOSING CONTINUED EVERY OTHER DAY FOR THE DURATION OF THE STUDY. FOUR WEEKS LATER, MOTOR ACTIVITY, ANXIETY, LEARNING, MEMORY, AND DEPRESSION WERE ASSESSED VIA EXTENSIVE BEHAVIORAL TESTING. NO DIFFERENCES IN ACTIVITY, ANXIETY, OR DEPRESSIVE BEHAVIOR WERE DETECTED BETWEEN GROUPS. NOVEL OBJECT RECOGNITION AND T-MAZE TESTING REVEALED THAT MICE RECEIVING MRS5980 IH AND 24H POST INJURY HAD CONSERVED LEARNING AND MEMORY COMPARED TO VEHICLE-TREATED MICE, WHICH CORRELATED WITH INCREASED PHOSPHORYLATED GSK-3SER9 AND DECREASED HYPERPHOSPHORYLATED TAU. INCREASES IN GSK-3BSER9 RESULT IN THE RELEASE OF THE ANTI-INFLAMMATORY CYTOKINE IL-10 WHICH IS POTENTIALLY AN IMPORTANT MECHANISM OF ACTION FOR MRS5980. HIGHLY SELECTIVE A3AR AGONISTS SIMILAR TO MRS5980 ARE CURRENTLY IN ADVANCED CLINICAL TRIALS FOR PAIN AND NEUROINFLAMMATORY CONDITIONS WITH EXCELLENT SAFETY AND EFFICACY PROFILES. OUR DATA SUPPORT MRS5980 AS A CANDIDATE THERAPEUTIC FOR NEUROPROTECTION AGAINST TBI-INDUCED COGNITIVE IMPAIRMENT.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T33. SEIZURE AVALANCHE AFTER SUPPRESSION WITH MTOR INHIBITION IN A MOUSE MODEL OF TSC

LUIS MARTINEZ, QIANQIAN MA, WAI LING LEE, XIAOLONG JIANG, ANNE ANDERSON*

TUBEROUS SCLEROSIS COMPLEX (TSC) IS A DISORDER CAUSED BY MUTATIONS IN TSC1 OR TSC2 AND IS CHARACTERIZED BY BRAIN MALFORMATIONS AND SEVERE EPILEPSY IN UP TO 90% OF PATIENTS. MTOR INHIBITORS CAN REDUCE SEIZURES IN HUMANS WITH TSC BUT MAY NOT HAVE A DISEASE MODIFYING EFFECT. USING A GENETIC MOUSE MODEL OF TSC2 WITH EPILEPSY, WE EVALUATED CELLULAR EXCITABILITY IN CORTICAL NEURONS IN MULTIPLE LAYERS. IN WHOLE ANIMAL STUDIES, WE EVALUATED THE EFFECTS OF A SEIZURE MEDICATION [(PHENOBARBITAL (PHB)] COMPARED TO THE MTOR INHIBITOR RAD001. MOUSE PUPS WITH CONDITIONAL FOREBRAIN DELETION OF THE TSC2 GENE IN EXCITATORY NEURONS WERE TREATED WITH VEHICLE (VEH), PHB (25MG/KG ONCE DAILY), OR RAD001 (6MG/KG EVERY OTHER DAY) BY INTRAPERITONEAL ROUTE STARTING ON POSTNATAL DAY 8 (P8). VEEG ACTIVITY WAS RECORDED AND ANALYSIS OF EPILEPTIFORM AND SEIZURE ACTIVITY WAS PERFORMED. MTOR SIGNALING WAS ASSESSED USING WESTERN BLOTTING OF CORTICAL TISSUE AT VARIOUS TIME POINTS. CORTICAL SLICES WERE PREPARED FOR WHOLE CELL PATCH RECORDINGS OF EXCITATORY AND INHIBITORY POSTSYNAPTIC POTENTIALS ACQUIRED BY QUADRO EPC 10 AMPLIFIERS, PATCHMASTER SOFTWARE (HEKA), AND CUSTOM-WRITTEN MATLAB-BASED PROGRAMS. TREATMENT WITH PHB HAD NO EFFECT ON SEIZURE ACTIVITY OR SURVIVAL OF TSC2 KO MICE, WHEREAS TREATMENT WITH THE MTOR INHIBITOR RAD001 TRANSIENTLY NORMALIZED PS6 LEVELS, ABOLISHED SEIZURE ACTIVITY, AND PROLONGED THE LIFESPAN OF NEX-TSC2 MICE ($P < 0.001$). RAD001 SIGNIFICANT DELAYED THE DEVELOPMENT OF SEIZURES FROM P12 TO APPROXIMATELY P50. PS6 LEVELS WERE REDUCED AND COMPARABLE TO WT VEH ($P > 0.05$) STARTING AFTER THE FIRST DOSE OF RAD001 TO P35 BUT INCREASED AT P45 ($P < 0.05$). IN WHOLE CELL PATCH RECORDINGS FROM TSC2 KO SLICES, LAYER 6 EXCITATORY AND INHIBITORY NEURONS EXHIBITED INCREASED FIRING FREQUENCIES COMPARED TO WT SLICES ($P < 0.05$). OUR RESULTS IN NEX-TSC2 KO MICE SUGGEST THAT MTOR INHIBITION SUPPRESSES EPILEPTIFORM ACTIVITY BUT DOES NOT RENDER SUSTAINED DISEASE MODIFICATION. CORTICAL EXCITATORY NEURONS WITH LOSS OF TSC2 IN LAYER 6 EXHIBIT INCREASED FIRING FREQUENCY WHICH MAY INDUCE NON-CELL AUTONOMOUS HYPEREXCITABILITY ON INHIBITORY INTERNEURONS. ADDITIONAL MOLECULAR STUDIES AND CIRCUIT ANALYSIS MAY HELP REVEAL MECHANISMS OF DRUG RESISTANCE AND SEIZURE RECURRENCE IN THIS MODEL WITH POTENTIAL TRANSLATIONAL RELEVANCE.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T34. COMPARISON OF FIVE SECOND-LINE DRUGS IN THE TREATMENT OF EXPERIMENTAL STATUS EPILEPTICUS

CLAUDE WASTERLAIN*, JEROME NIQUET

STATUS EPILEPTICUS (SE) REMAINS A THERAPEUTIC CHALLENGE, AND BETTER TREATMENTS ARE URGENTLY NEEDED. THE POTENT AMPA RECEPTOR ANTAGONIST PERAMPANEL MAY BLOCK THE PHYSIOLOGICAL CONSEQUENCES OF SE-INDUCED INCREASE IN SYNAPTIC AMPA RECEPTORS. WE COMPARED PERAMPANEL TO THE DRUGS MOST FREQUENTLY USED AS SECOND-LINE AGENTS IN THE TREATMENT OF SE (LEVETIRACETAM, VALPROATE, FOSPHENYTOIN AND LACOSAMIDE) IN A RODENT MODEL OF BENZODIAZEPINE-REFRACTORY SE.

SE WAS INDUCED IN ADULT MALE SPRAGUE-DAWLEY RATS BY HIGH-DOSE LITHIUM (5 MEQ/KG)/PILOCARPINE (320 MG/KG). MIDAZOLAM (1 MG/KG; IP) WAS INJECTED I.P. 40 MIN AFTER SE ONSET. IF SE CONTINUED, PERAMPANEL (2-4 MG/KG), VALPROATE (270 MG/KG), LEVETIRACETAM (240 MG/KG), FOSPHENYTOIN (120 MG/KG PE) OR LACOSAMIDE (24 MG/KG) WERE INJECTED I.P. 20 MIN AFTER MIDAZOLAM. NEUROPATHOLOGY WAS STUDIED AT 48 HRS.

SEIZURE CONTROL: PERAMPANEL REDUCED EEG POWER INTEGRAL RATIO (EEGPI) DURING THE FIRST HOUR AFTER TREATMENT TO BELOW THE PRE-SEIZURE BASELINE, DEMONSTRATING SEIZURE TERMINATION ($P < 0.0001$) AND KEPT IT BELOW THERE FOR 6 HOURS. VALPROATE, LEVETIRACETAM OR LACOSAMIDE (VLELA) DID NOT REDUCE EEGPI. FOSPHENYTOIN REDUCED IT MILDLY (238 ±139, $P < 0.01$) BUT IT REMAINED ABOVE BASELINE 6 HOURS.

NEURONAL INJURY: PERAMPANEL REDUCED NEURONAL INJURY IN CA1 FROM 4+ TO 0 ($P < 0.0001$) AND REDUCED IT IN CA3, THALAMUS, PARIETAL, PIRIFORM AND ENTORHINAL CORTEX, AND AMYGDALA. FOSPHENYTOIN REDUCED IT LESS THAN PERAMPANEL IN 4 REGIONS. OTHER DRUGS FAILED.

CELL-MEDIATED INFLAMMATION: PERAMPANEL ELIMINATED IT IN CA1 AND REDUCED IT IN OTHER REGIONS. FOSPHENYTOIN REDUCED IT IN CA1 ONLY, OTHER DRUGS FAILED.

BLOOD-BRAIN BARRIER BREAKDOWN: PERAMPANEL COMPLETELY BLOCKED IGG LEAKAGE. FOSPHENYTOIN BLOCKED IT IN CA1 AND THALAMUS. OTHER DRUGS FAILED.

BY TWO-WAY ANOVA, PERAMPANEL IS SUPERIOR TO FOSPHENYTOIN, VALPROATE, LEVETIRACETAM AND LACOSAMIDE IN STOPPING RSE AND REDUCING NEURONAL INJURY AND CELL-MEDIATED INFLAMMATION.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T35. DIHEXA RESCUES COGNITIVE IMPAIRMENTS FOLLOWING REPEATED MILD TRAUMATIC BRAIN INJURY

KATELYN MARTINO, LAURA MILOVIC, JOSEPH KALISH, MAURICE LINDNER-JACKSON, DAVID DEVILBISS*

MILD TRAUMATIC BRAIN INJURY (MTBI), OR CONCUSSION, IS A CRITICAL HEALTH AND ECONOMIC ISSUE AFFECTING APPROXIMATELY 3 MILLION AMERICANS EACH YEAR. MILD TBI IS A COMPLEX PATHOPHYSIOLOGICAL PROCESS RESULTING IN BEHAVIORAL AND COGNITIVE DEFICITS INCLUDING IMPAIRED AROUSAL, ATTENTION, DECISION-MAKING, AND OTHER EXECUTIVE FUNCTIONS. REPEATED MTBI CAN PRODUCE MORE SEVERE, LONGER-LASTING COGNITIVE IMPAIRMENTS AND BRAIN DAMAGE THAN SINGLE INJURIES AND CAN RESULT IN OUTCOMES SIMILAR TO SEVERE TBI. ALTHOUGH SYMPTOMS CAN RESOLVE WITHIN A WEEK, EVIDENCE INDICATES THAT SYMPTOMS CAN PERSIST FOR 3 MONTHS OR MORE. MOREOVER, CHRONIC IMPAIRMENT OF THESE HIGHER COGNITIVE PROCESSES ARE CENTRAL TO PATIENT DIFFICULTIES RETURNING TO WORK AND ACTIVITIES AFFECTING QUALITY-OF-LIFE.

DIHEXA IS AN ANGIOTENSIN IV-DERIVED PEPTIDE THAT ACTS AS A POSITIVE MODULATOR OF THE HEPATOCYTE GROWTH FACTOR/C-MET (HGF/C-MET) RECEPTOR SYSTEM. DIHEXA HAS PREVIOUSLY BEEN SHOWN TO STIMULATE NEUROGENESIS, BE NEUROPROTECTIVE, AND ENHANCE COGNITIVE FUNCTION IN RODENT MODELS OF NEURODEGENERATIVE DISEASE. WE HYPOTHESIZE THAT FOLLOWING MTBI, ENHANCING C-MET SIGNALING CAN IMPROVE COGNITIVE IMPAIRMENT, AMELIORATE ELECTROENCEPHALOGRAPHIC (EEG) MEASURES OF CORTICAL ACTIVITY, AND ACT AS A NEUROPROTECTANT. WE FOUND PROCOGNITIVE EFFECTS OF DIHEXA ON PERFORMANCE IN THE T-MAZE TEST OF WORKING MEMORY AND EEG SIGNATURES OF COGNITIVE ENHANCEMENT AFTER EXPOSING RATS TO REPEATED MTBI. WE ALSO OBSERVED CHANGES IN MARKERS OF AXONAL INTEGRITY FOLLOWING DIHEXA TREATMENT. TOGETHER THESE DATA SUPPORT THE HYPOTHESIS THAT DIHEXA CAN IMPROVE COGNITIVE IMPAIRMENTS AFTER MTBI. THESE FINDINGS PROVIDE CRITICAL INSIGHT INTO A NEW THERAPEUTIC STRATEGY FOR REPEATED MILD TBI AND SUPPORT FOR THE ROLE OF THE HGF/C-MET SYSTEM IN RESCUING THE COGNITIVE DEFICITS RESULTING FROM REPEATED INJURY.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T36. EFFECTS OF COMPLEX I DEFICIENCY AND PINK1/ PARKIN MEDIATED MITOPHAGY ON NEUROGENESIS OF THE SUBVENTRICULAR ZONE IN NDUFS4 KO MOUSE MODEL OF LEIGH SYNDROME

SAHITYA RANJAN BISWAS*, SAMANTHA BRINDLEY, NICOLE DEFOOR, SARA HENRY, YAIRIS SOTO, COLIN KELLY, ALICIA PICKRELL

LEIGH SYNDROME IS ONE OF THE MOST COMMON FORMS OF HERITABLE MITOCHONDRIAL DISEASE WITH PEDIATRIC PRESENTATION. MOST RESEARCH ON LEIGH SYNDROME IS FOCUSED ON UNDERSTANDING THE PATHOGENESIS OF CHARACTERISTIC BRAIN LESIONS, WHILE VERY LITTLE IS KNOWN ABOUT THE EFFECTS OF CHRONICALLY DISRUPTED MITOCHONDRIA ON NEUROGENESIS WHICH MAY CONTRIBUTE TO THE OBSERVED PSYCHOMOTOR REGRESSION. TO ADDRESS THIS, WE HAVE USED A WELL-ESTABLISHED MOUSE MODEL OF LEIGH SYNDROME LACKING THE NDUFS4 GENE (NDUFS4KO) WHICH IS ESSENTIAL FOR COMPLEX I ASSEMBLY. WE CROSSED THESE MICE WITH THOSE LACKING PINK1 AND PARKIN, TO FURTHER INVESTIGATE WHETHER THESE MITOPHAGY GENES INFLUENCE NEURAL STEM CELL (NSC) FUNCTIONING DURING MITOCHONDRIAL DAMAGE. WE PERFORMED IMMUNOHISTOCHEMISTRY (IHC) ON P24 BRAIN SECTIONS TO LABEL SOX2 (UNCOMMITTED PROGENITORS) AND DCX (NEUROBLASTS) CELLS IN THE SUBVENTRICULAR ZONE (SVZ). ALTHOUGH NDUFS4KO AND PINK1 NDUFS4 DKO MICE HAD SIGNIFICANTLY DECREASED BRAIN WEIGHT AND SVZ VOLUME AS COMPARED TO WT, WE DID NOT OBSERVE ANY SIGNIFICANT DIFFERENCES IN SOX2+, DCX+ AND DOUBLE POSITIVE CELL DENSITY AMONG THE GROUPS. HOWEVER, NDUFS4KO AND PINK1 NDUFS4 DKO MICE HAD SIGNIFICANTLY REDUCED COMMITTED NEUROBLASTS IN THEIR NSC POOL, INDICATING MITOCHONDRIAL DAMAGE MAY NEGATIVELY AFFECT NSC DIFFERENTIATION. INTERESTINGLY, PINK1 KO MICE HAD A SIGNIFICANTLY HIGHER DOUBLE +/SOX2+ CELL RATIO AS COMPARED TO WT. WE ALSO PERFORMED IHC ON PARKIN NDUFS4 DKO MICE. ALTHOUGH PARKIN OPERATES AT THE SAME PATHWAY AS PINK1, MICE PARKIN NDUFS4 DKO MICE HAD SIMILAR SVZ VOLUME, BRAIN WEIGHT, AND NO DISCERNABLE DIFFERENCES IN CELL DENSITY OR DOUBLE +/SOX2+ CELLS COMPARED TO WT AT P30. IN CONCLUSION, COMPLEX I DEFICIENCY NEGATIVELY IMPACTS SVZ NEURODEVELOPMENT IN YOUNG ADOLESCENT RODENTS. FUTURE WORK WILL ESTABLISH IF THIS REDUCTION IN NEUROBLASTS IS TRULY DUE TO A DIFFERENTIATION DEFECT, ESTABLISH A TIMELINE FOR THESE DEFICITS, AND UNDERSTAND IF PINK1 FUNCTIONS OUTSIDE OF THE PARKIN PATHWAY IN VIVO.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T37. TRANSCRIPTIONAL AND TOPOGRAPHICAL CHARACTERIZATION AND COMPARISON OF ROSTRAL MEDIAL TEGMENTAL NUCLEUS AND VENTRAL TEGMENTAL AREA GABA NEURONS AND ASSOCIATED SUBTYPES

ZACHARY HOUGH*, BRANDON HUGHES, CHRISTOPHER COWAN, THOMAS JHOU

MOUNTING EVIDENCE POINTS TO SUBSTANTIAL HETEROGENEITY IN BOTH THE FUNCTION AND GENE EXPRESSION PROFILES OF GABA NEURONS IN THE VENTRAL MIDBRAIN, CRUCIAL FOR REGULATING MOTIVATED BEHAVIOR. THEREFORE, IT IS ESSENTIAL TO FURTHER CLARIFY THE MOLECULAR DISTINCTIONS AMONG DISTINCT GABAERGIC SUBPOPULATIONS AND THEIR SPATIAL DISTRIBUTION. THIS STUDY PREDOMINANTLY FOCUSED ON TWO SPECIFIC MIDBRAIN REGIONS, THE VENTRAL TEGMENTAL AREA (VTA) AND THE ROSTROMEDIAL TEGMENTAL NUCLEUS (RMTG, ALSO KNOWN AS THE TAIL OF THE VTA), RECOGNIZED FOR THEIR ROLES IN MOTIVATED BEHAVIOR REGULATION. NOTABLY, NEARLY ONE THIRD OF THE VTA IS COMPOSED OF GABA NEURONS, INCREASINGLY ACKNOWLEDGED FOR THEIR HETEROGENEITY. INTRIGUINGLY, IN SITU HYBRIDIZATION (ISH) REVEALED A DENSELY CLUSTERED COHORT OF NEURONS CO-EXPRESSING TH, VGAT, AND GAD2, BUT NOT GADI. IMPORTANTLY, TH LEVELS IN THIS SUBPOPULATION WERE NOTABLY LOWER COMPARED TO TH+ CELLS LACKING VGAT OR GAD2. IN CONTRAST TO THE VTA, RMTG NEURONS ARE PREDOMINANTLY GABAERGIC, YET THEIR POTENTIAL HETEROGENEITY AND OVERLAP WITH SPECIFIC VTA GABAERGIC SUBPOPULATIONS REMAIN LESS EXPLORED. THEREFORE, SINGLE NUCLEI RNA SEQUENCING WAS CONDUCTED ON VTA AND RMTG TISSUE POOLED FROM FOUR APPROXIMATELY 12-WEEK-OLD MALE SPRAGUE DAWLEY RAT BRAINS, ALLOWING FOR A COMPARATIVE ASSESSMENT OF GENE EXPRESSION PROFILES BETWEEN BOTH REGIONS, AS WELL AS ASSOCIATED GABA NEURONS. PRELIMINARY ANALYSIS OF THESE DATASETS ALIGNS WITH PRIOR FINDINGS, CONFIRMING THE HETEROGENEOUS NATURE OF VTA GABA NEURONS, INCLUDING THE PRESENCE OF A DISTINCT SUBSET CONTAINING TH TRANSCRIPTS. FURTHERMORE, EMPLOYING A COMBINATION OF ISH, IHC, AND SNRNA-SEQ, WE OBSERVED THAT RMTG GABA NEURONS, UNLIKE THOSE IN THE VTA, EXHIBIT A REMARKABLE DEGREE OF UNIFORMITY, COUPLED WITH HEIGHTENED EXPRESSION OF FOXPI, OPRMI, AND HT2CR RELATIVE TO GABA NEURONS IN ADJACENT BRAIN REGIONS AND THE VTA. THE ONGOING ANALYSIS, IN CONJUNCTION WITH TOPOGRAPHICAL CHARACTERIZATION, IS POISED TO YIELD FURTHER INSIGHTS INTO DISTINCT SUBTYPES AND UNIQUE ATTRIBUTES WITHIN THESE NEURAL ENCLAVES. IN CONCLUSION, OUR FINDINGS INDICATE THAT RMTG GABA NEURONS ARE TRANSCRIPTIONALLY DISTINGUISHABLE FROM THEIR VTA COUNTERPARTS AND REAFFIRM THE HETEROGENEOUS NATURE OF VTA GABA NEURONS, UNDERSCORING THE NEED FOR DEEPER EXPLORATION OF THEIR FUNCTIONAL IMPLICATIONS.

TUESDAY JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T38. ASSESSMENT OF FUNCTIONAL AND CLINICAL CHARACTERISTICS OF GRIN VARIANTS IN A PUBLIC DATABASE: THE GRIN PORTAL

TIM BENKE, ILONA KREY, DENNIS LAL, JENNIFER BAIN, JOHANNES LEMKE, SCOTT MYERS, HONGJIE YUAN, STEPHEN TRAYNELIS*

NMDA RECEPTORS MEDIATE A SLOW, CA2+-PERMEABLE COMPONENT OF EXCITATORY SYNAPTIC TRANSMISSION IN THE CENTRAL NERVOUS, AND ARE ENCODED BY 7 GENES (GRIN1, GRIN2A-D, GRIN3A-B). THESE RECEPTORS ARE INVOLVED IN NUMEROUS BRAIN FUNCTIONS SUCH AS LEARNING AND MEMORY, DEVELOPMENT, COGNITION, AND MOTOR FUNCTION. IN ADDITION, NMDA RECEPTORS HAVE BEEN IMPLICATED IN MULTIPLE NEUROLOGICAL CONDITIONS AND THUS ARE IMPORTANT DRUG TARGETS. THIS GENE FAMILY IS LARGELY INTOLERANT TO GENETIC VARIATION, AND THUS A SIGNIFICANT NUMBER OF PATIENTS HARBOR RARE GENETIC VARIANTS WITHIN THESE GENES. WE HAVE COLLECTED CLINICAL LONGITUDINAL DATA FOR MORE THAN 300 PATIENTS HARBORING VARIANTS IN GRIN1, GRIN2A, GRIN2B, AND GRIN2D GENES. WE HAVE ALSO DEVELOPED A SUITE OF IN VITRO ASSAYS IN HETEROLOGOUS EXPRESSION SYSTEMS THAT ASSESS 6 FEATURES THAT ARE KEY DETERMINANTS OF NMDA RECEPTOR FUNCTION. WE HAVE APPLIED THIS TO HUNDREDS OF MISSENSE VARIANTS, AND DEVELOPED A LOGICAL CRITERIA WITH WHICH TO CATEGORIZE THE NET FUNCTIONAL OUTCOME FOR THE NMDA RECEPTOR AS GAIN- OR LOSS-OF-FUNCTION, WHICH IS A NECESSARY STEP FOR EVENTUAL DEVELOPMENT OF CLINICAL TRIALS. THESE RESULTS HAVE REVEALED A WEALTH OF INFORMATION ABOUT THE GRIN DISORDERS, ABOUT PATIENT CHARACTERISTICS AND PROGNOSIS, ABOUT POTENTIAL TREATMENT STRATEGIES, AND ABOUT NMDA RECEPTOR FUNCTION IN GENERAL. THIS RICH DATA SET HAS BEEN CAPTURED BY A FLEXIBLE AND DETAILED WEBSITE (THE GRIN PORTAL) THAT ALLOWS EXPLORATION OF ALL THAT IS KNOWN ABOUT VARIANTS, AND ALLOWS EVALUATION OF CLINICAL-FUNCTIONAL CORRELATIONS. WE HAVE ALSO BEGUN EXPLORATORY WORK ON HOW TO USE THIS INFORMATION FOR PREDICTIVE PURPOSES AS WELL AS RECLASSIFICATION OF VARIANTS.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T39. THE EFFECTS OF NEURAL ACTIVITY AND INCREASED CAMP LEVELS IN PERIFORNICAL NUCLEUS OF HYPOTHALAMUS ON FOOD INTAKE

AMIN ATTARI*, ANDREW LUTAS

THE HYPOTHALAMUS CONTAINS SEVERAL REGIONS THAT CONTRIBUTE TO THE REGULATION OF FOOD INTAKE AND ENERGY HOMEOSTASIS. THE PERIFORNICAL NUCLEUS OF HYPOTHALAMUS (PFH) IS AMONG THE NUCLEI INVOLVED IN EATING BEHAVIOR. PRIOR STUDIES SHOWED THAT DIRECT INFUSIONS OF CAMP INTO THE PFH AFFECTED FOOD INTAKE. HOWEVER, THE FINDINGS OF PREVIOUS PUBLICATIONS STAND IN CONTRADICTION OF EACH OTHER WITH HIGH CAMP LEVELS SHOWN TO CORRELATE WITH BOTH REDUCED AND ELEVATED FOOD INTAKE. IN ADDITION, THE SPECIFIC CELL TYPES INVOLVED ARE UNKNOWN AS PREVIOUS STUDIES HAVE NOT INVESTIGATED DISTINCT NEURONAL AND NON-NEURONAL CELL POPULATIONS. USING GENETICALLY ENCODED TOOLS, WE HAVE SELECTIVELY MANIPULATED CAMP LEVELS IN ALL PFH NEURONS. MOREOVER, WE HAVE SEPARATELY STIMULATED NEURAL ACTIVITY IN EITHER ALL PFH NEURONS OR JUST GABAERGIC NEURONS. OUR PRELIMINARY RESULTS SHOW THAT INCREASED PRODUCTION OF CAMP, USING LIGHT-ACTIVATED ADENYLYL CYCLASE (BIPAC), WITHIN ALL PFH NEURONS CAUSES AN INCREASE IN TOTAL FOOD INTAKE. HOWEVER, STIMULATING NEURAL ACTIVITY IN ALL PFH NEURONS, USING LIGHT-ACTIVATED CHANNELRHODOPSIN, CAUSES A SIGNIFICANT REDUCTION OF FOOD INTAKE IN FOOD-RESTRICTED MICE. THE ACTIVATION OF GABAERGIC NEURONS OF THE PFH ALSO CAUSED A SIMILAR REDUCTION IN FOOD INTAKE, THOUGH LIKELY THROUGH DIFFERENT BEHAVIORAL MECHANISMS. OUR FINDINGS SUGGEST THAT THE ROLE OF CAMP IS LIKELY SPECIALIZED WITHIN A SUBSET OF PFH NEURONS. TO FURTHER INVESTIGATE THIS HYPOTHESIS, WE AIM TO INCREASE CAMP IN DISTINCT NEURONAL POPULATIONS OF PFH USING GENETICALLY ENCODED TOOLS AND COMPARE ITS EFFECTS TO THE STIMULATION OF DISTINCT NEURAL POPULATIONS OF PFH. TOGETHER WITH FUTURE BRAIN IMAGING STUDIES, WE AIM TO DISCOVER THE NEURAL MECHANISM BY WHICH CAMP SIGNALING WITHIN THE PFH INFLUENCES FOOD INTAKE.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T40. INVESTIGATING THE ROLE OF SOMATOSTATIN INTERNEURONS IN ENDOGENOUS OPIOID SIGNALING WITHIN THE ANTERIOR CINGULATE CORTEX

JACOB REEVES*, WILLIAM BIRDSONG

THE ANTERIOR CINGULATE CORTEX (ACC) PLAYS A ROLE IN PAIN PROCESSING. THIS PAIN PROCESSING IS CARRIED OUT BY AN INTERACTION BETWEEN EXCITATORY PRINCIPAL NEURONS AND INHIBITORY INTERNEURONS, BOTH OF WHICH RECEIVE AFFERENT INPUTS FROM CORTICAL AND THALAMIC REGIONS. THE ENDOGENOUS OPIOID SYSTEM MODULATES PAIN PROCESSING BY ACTIVATION OF OPIOID RECEPTORS ON BOTH AFFERENT INPUTS AND INHIBITORY INTERNEURONS IN ACC CIRCUITS. ACTIVATION OF OPIOID RECEPTORS DECREASES NEURONAL FIRING AND NEUROTRANSMITTER RELEASE, RESULTING IN EXCITATORY:INHIBITORY CIRCUIT CHANGES. MOREOVER, ACTIVATION OF OPIOID RECEPTORS ON INHIBITORY INTERNEURONS RESULTS IN DISINHIBITION OF NEARBY PYRAMIDAL CELLS. IN THE ACC, THERE ARE SEVERAL SUBTYPES OF INHIBITORY INTERNEURONS: INCLUDING PARVALBUMIN (PV) AND SOMATOSTATIN (SST) -EXPRESSING INTERNEURONS. WE HAVE PREVIOUSLY FOUND THAT PV INTERNEURONS EXPRESS THE DELTA OPIOID RECEPTOR (DOR) BUT NOT THE MU OPIOID RECEPTOR (MOR) OR KAPPA OPIOID RECEPTOR (KOR). WHILE MUCH IS KNOWN ABOUT THE ROLE ACC PV INTERNEURONS PLAY IN THE ENDOGENOUS OPIOID SYSTEM, LITTLE IS UNDERSTOOD ABOUT SST NEURONS AND THEIR ROLE IN THE ACC ENDOGENOUS OPIOID CIRCUITS. THE AIM OF THIS STUDY IS TO UNDERSTAND THE EXPRESSION OF OPIOID RECEPTOR SUBTYPES ON SOMATOSTATIN NEURONS IN THE ACC AND HOW THEY REGULATE THE PHYSIOLOGY OF LOCAL CIRCUITS. WE USED A COMBINATION OF OPTOGENETICS, BRAIN SLICE ELECTROPHYSIOLOGY, AND PHARMACOLOGY IN MICE TO CHARACTERIZE THE EFFECTS OF OPIOID RECEPTOR AGONISTS ON SOMATOSTATIN INTERNEURON SIGNALING. WE FOUND THAT THE ENDOGENOUS OPIOID PEPTIDE MET-ENKEPHALIN ACTIVATED A GIRK-MEDIATED CONDUCTANCE ON SST INTERNEURONS. MOR-SELECTIVE AND DOR-SELECTIVE AGONISTS, BUT NOT KOR-SELECTIVE AGONISTS ACTIVATED A GIRK-MEDIATED CONDUCTANCE, INDICATING THESE NEURONS EXPRESS MOR, BUT LACK DOR AND KOR. OVERALL, THIS WORK SUGGESTS A ROLE OF ENDOGENOUS OPIOID SIGNALING IN REGULATING SST NEURONS IN CORTICAL CIRCUITS.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T41. ADAPTATIONS OF THE ENDOCANNABINOID SYSTEM DURING PERSISTENT INFLAMMATION ARE DRIVEN BY CORTICOSTERONE WITHIN THE VLPAG

BASILE COUTENS*, COURTNEY BOUCHET, KYLIE MCPHERSON, BETHANY BOSTON, SUSAN INGRAM

CHRONIC PAIN POSES A SIGNIFICANT PERSONAL AND ECONOMIC BURDEN, IMPACTING OVER 30% OF THE GLOBAL POPULATION. EFFECTIVELY ADDRESSING THIS ISSUE IN CLINICAL SETTINGS REMAINS A FORMIDABLE CHALLENGE. THE VENTROLATERAL PERIAQUEDUCTAL GRAY (VLPAG) PLAYS A PIVOTAL ROLE IN PAIN MODULATION, INTEGRATING SIGNALS FROM VARIOUS BRAIN REGIONS ASSOCIATED WITH NOCICEPTIVE, COGNITIVE, AND AFFECTIVE ASPECTS OF CHRONIC PAIN. IT STANDS AS A CRUCIAL HUB FOR THE MODULATION OF PAIN BY OPIOIDS AND ENDOCANNABINOIDS (ECBS). BOTH OPIOIDS AND ECBS SHARE A COMMON MECHANISM REDUCING GABA RELEASE VIA THEIR PRESYNAPTIC RECEPTORS (MORS AND CBIRS, RESPECTIVELY). CHRONIC INFLAMMATION, INDUCED BY COMPLETE FREUD'S ADJUVANT (CFA) INJECTIONS INTO A HINDPAW, LEADS TO DESENSITIZATION OF CBIRS AND SENSITIZATION OF MOR RESPONSES. INTRIGUINGLY, CBIR DESENSITIZATION PROGRESSES MORE RAPIDLY IN FEMALES THAN IN MALES, INDICATING A SEX-SPECIFIC REGULATION OF THE ECB SYSTEM.
OUR CURRENT STUDIES AIM TO TEST THE HYPOTHESIS THAT CFA-INDUCED INFLAMMATION ELEVATES CORTICOSTERONE LEVELS, THEREBY MEDIATING THE OBSERVED ADAPTATIONS IN CBIRS IN THE VLPAG OF BOTH MALE AND FEMALE RATS. USING WHOLE-CELL PATCH-CLAMP RECORDINGS FROM NEURONS IN EX VIVO SLICES CONTAINING THE VLPAG FROM SPRAGUE-DAWLEY MALE AND FEMALE RATS, WE INITIALLY OBSERVED THAT CORTICOSTERONE, UPON ACTIVATING THE GLUCOCORTICOID RECEPTOR (GR), PROMPTLY ENHANCES AND PROLONGS ECB TONE. THIS RESULTS IN THE INHIBITION OF PRESYNAPTIC GABA RELEASE VIA THE ACTIVATION OF CBIRS. NOTABLY, THESE EFFECTS ARE ABSENT WITH INHIBITION OF 2-ARACHIDONOYLGLYCEROL (2-AG) SYNTHESIS. THE RAPID EFFECTS SUGGEST THAT CORTICOSTERONE ACTS VIA MEMBRANE GRS. IMPORTANTLY, THESE EFFECTS ARE INDEPENDENT OF MORS. IN CFA-TREATED RATS, DESPITE CBIR DESENSITIZATION, DEPOLARIZATION-INDUCED SUPPRESSION OF INHIBITION (DSI)-INDUCED ECB RELEASE PERSISTS AND RELIES ON MONOACYLGLYCEROL LIPASE (MAGL) ACTIVITY. THIS EFFECT IS ALSO DEPENDENT ON GRS. IN SUMMARY, OUR RESULTS INDICATE THAT THE ECB SYSTEM IS INTRICATELY REGULATED BY CORTICOSTERONE, ACTING THROUGH MEMBRANE GRS.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T42. COMPARISON OF SPECTRAL ANALYSIS, MULTIFRACTAL DETRENDED FLUCTUATION ANALYSIS, AND INFORMATION TRANSFER MODELING APPLIED TO EEG IN SCHIZOPHRENIA

TODD ZORICK*, MARK MANDELKERN, JASON SMITH, MICHAEL GREENBERG

DESPITE THE PROFOUND EFFECT OF THE DIAGNOSIS OF SCHIZOPHRENIA ON AFFECTED INDIVIDUALS' BEHAVIOR, COGNITION, AND FUNCTIONALITY, THERE ARE NO GOOD SPECIFIC BIOMARKERS TO AID IN DIAGNOSIS AND TREATMENT. WHILE ELECTROENCEPHALOGRAPHY (EEG) HAS LONG BEEN STUDIED AS A NON-INVASIVE, RAPID, OFFICE-BASED TOOL, THERE IS LITTLE SUPPORT FOR ITS ROUTINE USE IN THE DIAGNOSIS OR TREATMENT OF SCHIZOPHRENIA USING TRADITIONAL METHODS OF ANALYSIS. RECENT ADVANCES IN THE NEUROSCIENCE OF CORTICAL CONNECTIVITY HAVE SUGGESTED TO MANY INVESTIGATORS THAT NOVEL TECHNIQUES DERIVED FROM STATISTICAL PHYSICS MAY HAVE UTILITY IN EEG ANALYSIS. UTILIZING A DATABASE OF RESTING STATE EEG (3 MIN EACH EYES CLOSED), PSYCHIATRIC SYMPTOMS, AND COGNITIVE ASSESSMENTS FROM N=27 PATIENTS WITH SCHIZOPHRENIA, AND A MATCHED GROUP OF N=18 HEALTHY CONTROLS, WE EMPLOYED SPECTRAL ANALYSIS (FOURIER TRANSFORM; FT), MULTIFRACTAL DETRENDED FLUCTUATION ANALYSIS (MF-DFA), AND INFORMATION TRANSFER MODELING (ITM). USING A STANDARD MACHINE LEARNING PARADIGM, WE USED SEPARATE TRAINING AND TEST EEG DATASETS FROM THE PARTICIPANTS TO TRAIN AND TEST PREDICTIVE MODELS FOR DIAGNOSIS, PSYCHIATRIC SYMPTOMATOLOGY, AND COGNITION.

EEG-BASED ITM PROVIDED THE BEST ABILITY TO CORRELATE MACHINE-LEARNED MODELS WITH OUT-OF-SAMPLE DATA FOR COGNITION, WITH MF-DFA SECOND BEST, AND FT THIRD BEST. THE SAME OVERALL PATTERN WAS TRUE FOR MACHINE-LEARNED MODELS WITH OUT-OF-SAMPLE DATA FOR PSYCHIATRIC SYMPTOMATOLOGY AND SCHIZOPHRENIA GROUP CLASSIFICATION: ITM SUPERIOR TO MF-DFA, WHICH WAS SLIGHTLY BETTER THAN FT.

EEG-BASED ITM SHOWED THE BEST OVERALL CAPACITY TO ASSESS FOR COGNITION AND PSYCHIATRIC SYMPTOMATOLOGY. NOTABLY, SOME SYMPTOMS AND COGNITIVE DOMAINS WERE ALSO WELL-PREDICTED VIA MF-DFA AND SPECTRAL ANALYSIS. A COMBINATION OF ANALYTIC TECHNIQUES FOR EEG MAY PROVE EFFECTIVE IN EEG-BASED AUTOMATIC ASSESSMENT AND DIAGNOSIS OF MENTAL ILLNESS.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T43. REGIONAL- AND CELL TYPE-SPECIFIC ALTERATIONS IN A UNIQUE SUBTYPE OF SOMATOSTATIN-EXPRESSING NEURONS IN SCHIZOPHRENIA

KENNETH FISH*, JULIA VESPOLI, SAMUEL DIENEL, DAVID LEWIS

IN SCHIZOPHRENIA, GABA NEURONS EXPRESSING THE NEUROPEPTIDE SOMATOSTATIN (SST) ARE MARKEDLY AFFECTED IN THE DORSOLATERAL PREFRONTAL CORTEX (DLPFC). CORTICAL SST NEURONS COMPRISE A HETEROGENOUS GROUP OF NEURONS, AND THE SUBTYPE(S) THAT ARE AFFECTED IN SCHIZOPHRENIA ARE UNKNOWN. ONE SST SUBTYPE, DISTINGUISHED BY THE EXPRESSION OF CHONDROLECTIN (CHODL), RESIDES PRIMARILY IN THE SUBCORTICAL WHITE MATTER (SWM), CONTAINS HIGH LEVELS OF NEUROPEPTIDE Y (NPY) AND NITRIC OXIDE SYNTHASE I (NOSI) AND REGULATES NEUROVASCULAR COUPLING (NVC). IN ADDITION, CHODL-SST NEURONS ARE THE NEAR-EXCLUSIVE SUBTYPE OF SST NEURON FOUND IN THE STRIATUM. HERE, WE INVESTIGATED THIS SST NEURON SUBTYPE IN THESE TWO BRAIN REGIONS IN SCHIZOPHRENIA.
MULTIPLEX FLUORESCENT IN SITU HYBRIDIZATION WAS USED TO LABEL SST, CHODL, NPY, AND NOSI MRNAS IN POSTMORTEM DLPFC AND DORSAL CAUDATE SECTIONS FROM 18 MATCHED PAIRS OF SCHIZOPHRENIA AND UNAFFECTED COMPARISON SUBJECTS. TRANSCRIPT LEVELS WERE QUANTIFIED IN CHODL-SST NEURONS.
IN SCHIZOPHRENIA, CHODL-SST NEURONS IN THE SWM OF THE DLPFC EXHIBITED DEFICITS IN NOSI (EFFECT SIZE (ES)=−0.86, P=0.015) AND NPY (ES=−0.55, P=0.18) MRNAS, BUT NORMAL LEVELS OF SST (ES=−0.33, P=0.62). IN CONTRAST, CHODL-SST NEURONS IN THE CAUDATE EXHIBITED NORMAL LEVELS OF SST, NPY, AND NOSI MRNAS (ALL P > 0.85) IN SCHIZOPHRENIA.
THE FINDINGS HERE SHOW THAT CHODL-SST NEURONS ARE DIFFERENTIALLY AFFECTED IN SCHIZOPHRENIA AT BOTH THE TRANSCRIPT AND REGION LEVEL. THROUGH RELEASE OF NOSI AND NPY, CHODL-SST NEURONS PLAY A CRITICAL ROLE IN NVC. LOWER EXPRESSION OF THESE TRANSCRIPTS IN CHODL-SST NEURONS MIGHT CONTRIBUTE TO ALTERED TASK-RELATED BOLD SIGNAL OBSERVED IN THE DLPFC OF SUBJECTS WITH SCHIZOPHRENIA.

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T44. CHANGES IN NEUROPEPTIDE LARGE DENSE CORE VESICLE TRAFFICKING DYNAMICS CONTRIBUTE TO ADAPTIVE RESPONSES TO A SYSTEMIC HOMEOSTATIC CHALLENGE

JAVIER STERN*, MATTHEW KIRCHNER

NEUROPEPTIDES ARE PACKED INTO LARGE DENSE CORE VESICLES (LDCVS) THAT ARE TRANSPORTED FROM THE SOMA OUT INTO THEIR PROCESSES. LIMITED INFORMATION EXISTS REGARDING MECHANISMS REGULATING LDCV TRAFFICKING, PARTICULARLY DURING CHALLENGES TO BODILY HOMEOSTASIS. ADDRESSING THIS GAP, WE USED 2-PHOTON IMAGING IN AN EX-VIVO PREPARATION TO STUDY LDCVS TRAFFICKING DYNAMICS IN VASOPRESSIN (VP) NEURONS, WHICH TRAFFIC AND RELEASE NEUROPEPTIDE FROM THEIR DENDRITES AND AXONS. WE REPORT A DYNAMIC BIDIRECTIONAL TRAFFICKING OF VP-LDCVS WITH IMPORTANT DIFFERENCES IN SPEED AND DIRECTIONALITY BETWEEN AXONS AND DENDRITES. ACUTE, SHORT-LASTING STIMULI KNOWN TO ALTER VP FIRING ACTIVITY AND AXONAL/DENDRITIC RELEASE CAUSED MODEST CHANGES IN VP-LDCVS TRAFFICKING DYNAMICS. CONVERSELY, CHRONIC/SUSTAINED SYSTEMIC OSMOTIC CHALLENGES UPREGULATED VP-LDCVS TRAFFICKING DYNAMIC, WITH A LARGER EFFECT IN DENDRITES. THESE RESULTS SUPPORT DIFFERENTIAL REGULATION OF DENDRITIC AND AXONAL LDCV TRAFFICKING, AND THAT CHANGES IN TRAFFICKING DYNAMICS CONSTITUTE A NOVEL MECHANISM BY WHICH PEPTIDERGIC NEURONS CAN EFFICIENTLY ADAPT TO CONDITIONS OF INCREASED HORMONAL DEMAND.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T45. EXPLORING COLLECTIVE NEURAL ACTIVITY: MESOSCOPIC DYNAMICS AND IMPLICATIONS FOR NEUROLOGICAL PHENOMENA

YU QIN*, ALEX SHEREMET

THIS STUDY PROVIDES A THEORETICAL AND NUMERICAL EXAMINATION OF MESOSCOPIC COLLECTIVE NEURAL ACTIVITY, SPECIFICALLY THE SPATIOTEMPORAL OSCILLATORY PATTERNS WITHIN THE CORTEX. WE PRESENT A NOVEL STATISTICAL MODEL USING THE PRINCIPLES OF STATISTICAL PHYSICS, WHERE WE CONSIDER INDIVIDUAL HODGKIN-HUXLEY NEURONS AS DISCRETE PARTICLES. BY INTEGRATING THE MICROSCOPIC DESCRIPTIONS OF CELL DYNAMICS DETAILED BY THE HODGKIN-HUXLEY EQUATIONS WITH STATISTICAL PHYSICS, WE DERIVE GOVERNING EQUATIONS FOR COLLECTIVE ACTIVITY. OUR STUDY SHOWS THAT COLLECTIVE ACTIVITY EMERGES AS A MACROSCOPIC EXPRESSION OF NEURAL ACTIVITY.
OUR FINDINGS REVEAL INTRICATE CHARACTERISTICS OF MESOSCOPIC DYNAMICS, INCLUDING OSCILLATIONS AND WAVE PROPAGATION, CROSS-FREQUENCY COUPLING DUE TO NONLINEARITY, AND THE POTENTIAL FOR TURNING PATTERNS BASED ON WAVE DISPERSION/DISSIPATION ANALYSIS. ALTHOUGH FURTHER VALIDATION OF THE PROPOSED MODEL IS REQUIRED, THE RESULTS ARE IN LINE WITH KNOWN FEATURES OF BRAIN ACTIVITY.
IN ADDITION, OUR WORK PROVIDES FRESH INSIGHTS INTO COMPLEX NEUROLOGICAL PHENOMENA, SUCH AS THE ROLE OF NONLINEARITY IN BRAIN RHYTHM MODULATION, THE INTERACTIVE DYNAMICS BETWEEN CALCIUM AND SODIUM CHANNELS IN WORKING MEMORY, AND MEMORY FORMATION THROUGH THE REINFORCEMENT OF INHOMOGENEITY VIA TURING INSTABILITY. THESE INSIGHTS MAY LAY THE FOUNDATION FOR NOVEL THERAPEUTIC STRATEGIES FOR RELATED NEUROLOGICAL DISORDERS.

TUESDAY, JANUARY 30TH

POSTER SESSION III
3:30 P.M. - 4:30 P.M.
PEAK 4-5

T46. ISOLATING THE ROLE OF LC-NORADRENERGIC DOPAMINE RELEASE DURING AVERSIVE AND APPETITIVE BEHAVIORS

AVI MATARASSO*, ELENA SEAHOLM, ITZEL RODRIGUEZ-REYES, SEAN PIANTADOSI, LI LI, MICHAEL BRUCHAS

THE LOCUS COERULEUS (LC) IS A MAJOR SOURCE OF NOREPINEPHRINE (NE) THAT PROJECTS TO DISTINCT, FUNCTIONAL TARGETS. THE LC MODULARLY INFLUENCES AROUSAL, ANXIETY, AND LEARNING. RECENT PHARMACOLOGICAL DATA SUGGEST DOPAMINE (DA) IS ALSO RELEASED FROM THE LC, YET DEFINITIVE MEASURES OF RELEASE ACROSS REGIONS, PARADIGMS, AND BEHAVIORS TYPICALLY ASSOCIATED WITH LC HAVE NOT BEEN CHARACTERIZED, DUE TO DIFFICULTY IN SEPARATING DA FROM NE USING TRADITIONAL SENSING METHODS.HERE, WE USED FLUORESCENT BIOSENSORS TO ISOLATE MONOAMINE RELEASE FOLLOWING SELECTIVE PHOTO-STIMULATION OF LC TERMINALS IN DORSAL CAI, VENTRAL CAI, AND BLA. WE ALSO INVESTIGATED THE ENDOGENOUS DYNAMICS OF NE AND DA RELEASE IN HIPPOCAMPUS IN RESPONSE TO APPETITIVE AND AVERSIVE STIMULI WITH AND WITHOUT GI-DREADD INHIBITION OF LC AND VTA TO ISOLATE LC AND VTA CONTRIBUTIONS TO DOPAMINE RELEASE. WE ALSO STIMULATED CHRIMSONR-EXPRESSING LC TERMINALS AT SEVERAL FREQUENCIES (FOR 3S BETWEEN 1-20HZ) TO MIMIC PHYSIOLOGICAL ACTIVITY, REVEALING NE AND DA RELEASE INCREASE NONLINEARLY WITH STIMULATION FREQUENCY. EX VIVO 2-PHOTON IMAGING REVEALED OPTOGENETIC STIMULATION EVOKED DA RELEASE FROM LC. IN EXPERIMENTS MEASURING ENDOGENOUS RELEASE, WE FOUND INCREASED NE RELEASE IN RESPONSE TO SALIENT ANXIOGENIC STIMULI, SUCH AS SHOCK AND LOOMING STIMULI. MORE NE THAN DA WAS RELEASED IN CAI DURING LOOMING, AND THERE WAS A STRONGER DA RESPONSE THAN NE IN BLA. SHOCK EVOKED RELEASE OF NE AND DA ACROSS THE BRAIN. IN RESPONSE TO REWARD GIVEN AD LIBITUM, WE FOUND CAI DA WAS NOT STRONGLY RELEASED TO APPETITIVE STIMULI, AND NE SIGNAL HAD A SMALL DECREASE AFTER MICE RETRIEVED THE PELLET. INHIBITING VTA ALSO REVERSED AN INHIBITION IN NE RELEASE, INCREASING NE RELEASE IN CAI. INHIBITING LC LED TO A DECREASE IN DA RELEASED DURING FREE REWARD IN BLA. THIS WORK SUGGESTS THAT LC RELEASES DOPAMINE ACROSS STIMULATION FREQUENCIES, AND THE LC IS NECESSARY TO RELEASE DA DURING APPETITIVE CONDITIONS.

(FUNDED BY ROIMHII2355, F3IDA056148)

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

WI. KAPPA OPIOID RECEPTOR SYSTEM IN THE NUCLEUS ACCUMBENS MEDIATES ESCALATION OF COCAINE CONSUMPTION

LYDIA GORDON-FENNELL*, RYAN FARERO, LAUREN BURGENO, NICOLE MURRAY, CHARLES CHAVKIN, LARRY ZWEIFEL, PAUL PHILLIPS

THE NEURAL PROCESSES UNDERLYING THE PROGRESSION OF SUBSTANCE USE DISORDER (SUD) REMAIN POORLY UNDERSTOOD – LIMITING CURRENT TREATMENT OPTIONS. DOPAMINE HAS HISTORICALLY BEEN IMPLICATED IN SUD, SPECIFICALLY DOPAMINE RELEASE IN THE NUCLEUS ACCUMBENS (NAC), BUT OTHER NEUROMODULATOR SYSTEMS MAY ALSO BE CRITICAL TO SUD AND REPRESENT A BETTER TREATMENT TARGET. THE KAPPA OPIOID SYSTEM IS KNOWN TO BE ACTIVATED BY DRUG CONSUMPTION, HAS BEEN IMPLICATED IN GENERAL NEGATIVE AFFECT, AND INTERACTS WITH THE DOPAMINE SYSTEM IN THE NAC, MAKING IT A PROMISING CANDIDATE IN THE DEVELOPMENT OF SUD. TO INVESTIGATE THE NECESSITY OF THE KOR SYSTEM IN THE NAC DURING ESCALATION (AN SUD-LIKE PHENOTYPE), WE UTILIZED TWO APPROACHES: PHARMACOLOGY AND CRISPR TECHNOLOGY. AFTER BEING TRAINED ON DRUG SELF-ADMINISTRATION, RATS WERE MICRO-INJECTED IN THE NAC WITH A LONG-LASTING KOR ANTAGONIST (NOR-BNI) AND THEN CONTINUED WITH LONG-ACCESS SELF-ADMINISTRATION. CONTROL RATS INCREASED IN THEIR DRUG CONSUMPTION ACROSS THE TWO WEEKS OF LONG-ACCESS, DEMONSTRATING ESCALATION OF DRUG INTAKE, WHEREAS RATS INJECTED WITH NOR-BNI DID NOT, PROVIDING EVIDENCE THAT ACTIVATION OF THE NAC KOR SYSTEM IS NECESSARY FOR ESCALATION. TO DELINEATE WHICH ANTAGONIZED KOR SUBPOPULATION PRODUCED THIS BEHAVIORAL EFFECT, WE UTILIZED CRISPR TECHNOLOGY TO KNOCK-OUT OPRKI IN TWO POPULATIONS SEPARATELY: NAC AND VENTRAL TEGMENTAL AREA (VTA). OPRKI NAC KO AND CONTROL RATS INCREASED IN THEIR DRUG INTAKE ACROSS LONG-ACCESS SESSIONS (ESCALATION) WHEREAS OPRKI VTA KO RATS DID NOT ESCALATE IN THEIR DRUG INTAKE. THESE DATA SUPPORT THE HYPOTHESIS THAT ACTIVATION OF KOR ON VTA NEURONS, SPECIFICALLY VTA TERMINALS IN THE NAC, DURING DRUG CONSUMPTION IS NECESSARY FOR THE DEVELOPMENT OF A SUD-LIKE PHENOTYPE, POTENTIALLY THROUGH SUPPRESSING CUE-CONTINGENT PHASIC DOPAMINE RELEASE. UNDERSTANDING THE CHANGES IN NEURAL SYSTEMS THROUGHOUT THE DEVELOPMENT OF SUD WILL INFORM FUTURE THERAPEUTIC APPROACHES TO SUD AND THE ONGOING DRUG EPIDEMICS.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W2. ROLE OF DORSAL RAPHE GLUTAMATERGIC NEURONS IN COCAINE PREFERENCE

ORLANDO ESPINOZA*, UZMA MOHAMMAD, FLAVIA BARBANO, MARISELA MORALES

THE DORSAL RAPHE NUCLEUS (DR) IS BEST KNOWN FOR CONTAINING SEROTONERGIC NEURONS THAT MODULATE DIFFERENT FUNCTIONS SUCH AS WAKEFULNESS AND MOOD REGULATION. HOWEVER, THE DR ALSO CONTAINS OTHER TYPES OF NEURONS, INCLUDING GLUTAMATERGIC NEURONS THAT EXPRESS THE VESICULAR GLUTAMATE TRANSPORTER TYPE 3 (VGLUT3). WE HAVE PREVIOUSLY DEMONSTRATED THAT DR-VGLUT3 NEURONS ESTABLISH EXCITATORY MONOSYNAPTIC CONNECTIONS WITH A SUBSET OF VENTRAL TEGMENTAL AREA (VTA) DOPAMINERGIC NEURONS THAT PROJECT TO THE NUCLEUS ACCUMBENS. WE FURTHER DEMONSTRATED THAT VTA RELEASE OF GLUTAMATE FROM DR-VGLUT3 FIBERS INDUCES RELEASE OF DOPAMINE IN THE NUCLEUS ACCUMBENS AND IS REWARDING. HERE, BY A COMBINATION OF OPTOGENETICS AND A CONDITIONED PLACE PREFERENCE (CPP) PROCEDURE, WE INVESTIGATED THE EXTENT TO WHICH DR-VGLUT3 INPUTS TO THE VTA PLAY A ROLE IN COCAINE PREFERENCE. INTO THE VTA OF DIFFERENT COHORTS OF VGLUT3-CRE MICE, WE INJECTED VIRAL VECTORS ENCODING CHANNELRHODOPSIN-2 (CHR2), HALORHODOPSIN (HALO), OR EYFP. AFTER CPP TRAINING, WE FOUND THAT VTA OPTOGENETIC RELEASE OF GLUTAMATE FROM DR-VGLUT3 FIBERS IN CHR2-MICE INDUCED REINSTATEMENT OF COCAINE-INDUCED CPP. IN CONTRAST, WE FOUND THAT VTA OPTOGENETIC INHIBITION OF GLUTAMATE RELEASE FROM DR-VGLUT3 FIBERS IN HALO-MICE PREVENTED STRESS- AND PRIMING-INDUCED REINSTATEMENT OF COCAINE-INDUCED CPP. WE CONCLUDE THAT VTA RELEASE OF GLUTAMATE FROM DR GLUTAMATERGIC FIBERS PLAYS A CRITICAL ROLE IN THE REINSTATEMENT OF COCAINE-INDUCED CPP.
THIS WORK WAS SUPPORTED BY THE INTRAMURAL RESEARCH PROGRAM OF NIDA (NIH).

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W3. LATERAL HABENULA INHIBITION SUPPRESSES FUTURE FENTANYL SEEKING

CHRISTOPHER O'BRIEN*, DHRUVI DESAI, HAYDEN KENNY, ROSHNI VEMIREDDY, JESSICA OPHER, DAVID BARKER

OPIOID USE DISORDER (OUD) AND OPIOID RELATED DEATHS HAVE INCREASED DRAMATICALLY FROM 2019-2021. HOWEVER, ONLY A SUBSET OF INDIVIDUALS TRANSITION TO ABUSE WHILE OTHERS REMAIN RESILIENT. PREVIOUS RESEARCH HAS SHOWN THAT INDIVIDUAL SUSCEPTIBILITY TO OUD IN MICE CAN DEPEND ON A HISTORY OF STRESS. FOLLOWING STRESS, REWARD-SEEKING AND HEIGHTENED MECHANICAL SENSITIVITY IS PREDICTIVE OF FUTURE FENTANYL SEEKING, WHILE NEGATIVE AFFECTIVE STATES ARE MORE PREDICTIVE IN CONTROL MICE. THE LATERAL HABENULA (LHB) IS AN EVOLUTIONARILY CONSERVED STRUCTURE IMPORTANT FOR PROCESSING AVERSIVE STIMULI AND MODULATING RESPONSES TO REWARD. THE LHB ALSO HAS KNOWN ROLES IN CHRONIC PAIN AND DEPRESSION. WE HYPOTHESIZED THAT INHIBITION OF THE LATERAL HABENULA DURING STRESSFUL EVENTS WILL ALTER THE SUSCEPTIBILITY PROFILE FOR FUTURE OPIOID SEEKING. USING INHIBITORY HM4D(GI)-DREADDS ALONG WITH THE DESIGNER DRUG J60 WE HAVE MODULATED THE ACTIVATION OF THE HABENULA DURING A FOOT SHOCK STRESS PARADIGM. ANIMALS WERE THEN PUT THROUGH A BEHAVIOR BATTERY ASSESSING NEGATIVE VALENCE, THRESHOLDS, AND ORAL FENTANYL CONSUMPTION AND PREFERENCE. OUR RESULTS SHOW THAT INHIBITION OF THE LHB CAN BLOCK THE INDUCTION OF MECHANICAL HYPERSENSITIVITY FOLLOWING STRESS AND THAT INHIBITION CAN BLOCK FUTURE FENTANYL CONSUMPTION AND PREFERENCE. WHILE STRESS MAY ACT TO TRIGGER INDIVIDUAL DIFFERENCES THAT CAN HELP DETERMINE THE RISK FOR DEVELOPING A SUBSTANCE USE DISORDER, WE SHOW THAT THE MODULATION OF LHB ACTIVITY HAS BROAD AND LONG-LASTING BEHAVIORAL EFFECTS ON OPIOID SEEKING.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W4. NUCLEUS ACCUMBENS NITRERGIC INTERNEURONS ARE REQUIRED FOR THE CELL TYPE-SPECIFIC PLASTICITY IN MEDIUM SPINY NEURONS UNDERLYING CUED COCAINE SEEKING

ADAM DENTON*, RACHEL CLARKE, JAYDA CARROLL-DEATON, ANNAKA WESTPHAL, LISA GREEN, ELIZABETH HOCHBURG, JAMES OTIS, MICHAEL SCOFIELD

RELAPSE TO COCAINE USE FOLLOWING ABSTINENCE REPRESENTS THE MOST SIGNIFICANT IMPEDIMENT TO SUCCESSFUL TREATMENT OF COCAINE USE DISORDER AND IS OFTEN TRIGGERED BY DRUG CRAVING FOLLOWING EXPOSURE TO DRUG-ASSOCIATED ENVIRONMENTAL CUES. STUDIES FROM RODENT MODELS DEMONSTRATE THAT COCAINE SELF-ADMINISTRATION AND EXTINCTION ENGAGE MALADAPTIVE PLASTICITY IN THE NUCLEUS ACCUMBENS CORE (NAC). THIS PLASTICITY CAUSES RE-EXPOSURE TO DRUG-PREDICTIVE CUES TO ENGAGE GLUTAMATE RELEASE IN THE NAC, WHICH IS REQUIRED TO DRIVE STRUCTURAL AND FUNCTIONAL ADAPTATIONS TO MEDIUM SPINY NEURONS (MSNS) MECHANISTICALLY LINKED TO CUED DRUG SEEKING. RECENTLY, IT HAS BEEN ESTABLISHED THAT COCAINE-CUE INDUCED PLASTICITY OCCURS SELECTIVELY IN DOPAMINE RECEPTOR DI EXPRESSING MEDIUM SPINY NEURONS (DI MSNS), YET THE LINK BETWEEN CUE-INDUCED GLUTAMATE RELEASE AND THIS PLASTICITY HAD YET TO BE ELUCIDATED. WE SHOW HERE THAT A SMALL POPULATION OF NITRIC OXIDE (NO) RELEASING INTERNEURONS IN THE NAC FUNCTIONALLY LINK CUED GLUTAMATE RELEASE TO THE DI MSN PLASTICITY REQUIRED FOR CUED COCAINE SEEKING. USING IN-VIVO CALCIUM (CA2+) IMAGING OF NO INTERNEURONS, WE SHOW THAT COCAINE ACTIVATES NAC NO INTERNEURONS, ENHANCING NUMBERS OF CA2+ EVENTS PER MINUTE THAT PERSIST DURING REPEATED ADMINISTRATIONS OF COCAINE. FURTHER, WE DEMONSTRATE THAT KNOCKDOWN OF METABOTROPIC GLUTAMATE RECEPTOR 5 (MGLUR5), SELECTIVELY ON NAC NO INTERNEURONS, IS SUFFICIENT TO BLOCK BOTH CONDITIONED PLACE PREFERENCE AND CUE-INDUCED REINSTATEMENT TO COCAINE. FINALLY, KNOCKDOWN OF THE ENZYME REQUIRED FOR PRODUCTION OF NO, NEURONAL NITRIC OXIDE SYNTHASE (NNOS), BLOCKS CUED COCAINE SEEKING AND PREVENTS COCAINE CUE-MEDIATED ADAPTATIONS TO DI, BUT NOT D2 MSNS. OUR FINDINGS DEMONSTRATE THAT NNOS/NO IN THE NAC IS REQUIRED FOR CELL-TYPE SPECIFIC ADAPTATIONS DRIVING CUED COCAINE SEEKING AND DEMONSTRATE THAT NO INTERNEURON ACTIVATION REPRESENTS A CRITICAL BOTTLENECK IN THE BIOCHEMICAL CASCADE THAT PRECIPITATES MOTIVATED COCAINE SEEKING BEHAVIOR.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W5. VTA GLUTAMATERGIC INPUTS FROM THE PARABRACHIAL NUCLEUS REGULATE LONG-LASTING FEAR MEMORY

RODRIGO OSNAYA*, HUILING WANG, JESSE TORIJA MAXIMO, SHILIANG ZHANG, LIU BING, MARISELA MORALES

THE VENTRAL TEGMENTAL AREA (VTA) IS A MIDBRAIN STRUCTURE THAT PLAYS A ROLE IN REWARD PROCESSING. THE VTA CONTAINS DOPAMINE NEURONS INTERMINGLED WITH GLUTAMATE AND GABA NEURONS THAT RESPOND TO REWARD AND AVERSION. THE VTA NEURONS ESTABLISH SYNAPSES WITH INPUTS FROM SEVERAL BRAIN AREAS, INCLUDING THE PARABRACHIAL NUCLEUS (PBN), WHICH PLAYS A ROLE IN BOTH PAIN AND AVERSION. HERE, BY A MULTIDISCIPLINARY APPROACH, WE DETERMINED THE EXTENT TO WHICH PBN INPUTS TO SPECIFIC SUBCLASSES OF VTA NEURONS PLAY A ROLE IN AVERSION. BY VTA INJECTION OF THE RETROGRADE TRACK TRACER FLUOROGOLD (FG), WE OBSERVED FG-NEURONS IN THE LATERAL PBN. BY PHENOTYPING OF PBN FG NEURONS, WE DEMONSTRATED THAT WITHIN THE TOTAL POPULATION OF FG NEURONS, ~94% CO-EXPRESSED GLUTAMATE TRANSPORTER 2 (VGLUT2) INDICATING THAT PBNVGLUT2 NEURONS PROVIDE A MAJOR INPUT TO VTA. WE NEXT INJECTED AAV5-DIO-CHR2-EYFP VIRUS INTO THE PBN OF VGLUT2::CRE MICE AND IMPLANTED AN OPTICAL FIBER ON THE VTA OF CHR2-EYFP MICE TO INDUCE LOCAL RELEASE OF GLUTAMATE. CHR2-EYFP MICE WERE TESTED IN A THREE-CHAMBER APPARATUS IN WHICH THEY RECEIVED OPTICAL STIMULATION WHEN THEY ENTERED THE LASER-PAIRED CHAMBER. WE FOUND THAT CHR2-EYFP MICE AVOIDED THE LASER-PAIRED CHAMBER DURING 4 DAYS OF OPTICAL STIMULATION SESSIONS, AS WELL AS IN SUBSEQUENT DAYS WHEN MICE WERE TESTED IN THE ABSENCE OF OPTICAL STIMULATION (UP TO 7 WEEKS). NEXT, WE INJECTED THE RETROGRADE HSV-LSIL-GCAMP6S VIRAL VECTOR IN THE VTA OF VGLUT2::CRE MICE TO EXPRESS GCAMP6S IN PBNVGLUT2 NEURONS INNERVATING THE VTA AND BY FIBER PHOTOMETRY WE RECORDED CALCIUM TRANSIENTS IN RESPONSE TO INNATE AND LEARNED THREATS. WE OBSERVED INCREASES IN CALCIUM SIGNALS PBNVGLUT2-VTA NEURONS IN RESPONSE TO THE PRESENCE OF A PREDATOR (RAT) AND A PREDATOR ODOR (TRIMETHYLTHIAZOLINE, TMT). ADDITIONALLY, WE RECORDED THE ACTIVITY OF PBNVGLUT2-VTA NEURONS WHEN MICE WERE EXPOSED TO A CUE PREDICTING A SHOCK, WE FOUND THAT PBNVGLUT2-VTA NEURONS RESPOND TO THE CUE PREDICTING A SHOCK UP TO 4 WEEKS AFTER THE LAST TRAINING SESSION. THESE FINDINGS INDICATE THAT THE PBNVGLUT2-VTA PATHWAY IS INVOLVED IN THE RESPONSE TO INNATE AVERSIVE STIMULI AND LONG-LASTING FEAR MEMORY.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W6. SEROTONIN, PSYCHEDELICS, AND CLAUSTRUM SIGNALING TO THE ANTERIOR CINGULATE CORTEX

TANNER ANDERSON*, JACK KEADY, JUDY SONGRADY, JILL TURNER, PAVEL ORTINSKI

THE CLAUSTRUM (CLA), A SUBCORTICAL NUCLEUS, HAS THE HIGHEST DENSITY OF THE SEROTONIN 2A RECEPTOR (5HT2AR) IN THE BRAIN WITH EXTENSIVE CONNECTIONS TO OTHER BRAIN AREAS, MOST PROMINENTLY THE ANTERIOR CINGULATE CORTEX (ACC) THAT IS INVOLVED IN BOTH COGNITIVE FLEXIBILITY AND DRUG-SEEKING BEHAVIORS. THOUGH THE CLA IS GAINING INCREASING ATTENTION FOR ITS' POTENTIAL IMPORTANCE IN REGULATING SEVERAL ASPECTS OF COGNITION, ALMOST NOTHING IS KNOWN ABOUT THE ROLE OF ITS' ROBUST SEROTONERGIC INNERVATION. HERE, WE TARGET SEVERAL 5-HTRS IN THE CLA WITH RT-QPCR, RNASCOPE, AND WHOLE CELL PATCH CLAMP ELECTROPHYSIOLOGY TO CHARACTERIZE THE FUNCTION OF 5-HTRS IN CLA-ACC SIGNALING WITH AND WITHOUT COCAINE SELF-ADMINISTRATION.

5-HT CAUSED DRAMATIC INHIBITION IN CLA-ACC NEURONS. SIGNIFICANT DECREASES IN SEPSC FREQUENCY AND AMPLITUDE WERE OBSERVED, AS WELL AS DECREASES IN ACTION POTENTIAL FIRING RATE AND HYPERPOLARIZATION OF THE RESTING MEMBRANE POTENTIAL. NEXT, WE USED QPCR TO OBSERVE THE RELATIVE ABUNDANCE OF 13 DIFFERENT 5-HT RECEPTOR SUBTYPES WITHIN THE CLA, FINDING ELEVATED LEVELS OF 5-HTIA, 2A, 2B, AND 2C RECEPTORS. CLA-ACC NEURONS WERE THEN RECORDED IN THE PRESENCE OF 5-HT AND ANTAGONISTS OF EACH OF THESE RECEPTORS TO OBSERVE THEIR CONTRIBUTIONS TO THE 5-HT EFFECTS IN BOTH COCAINE AND SALINE-YOKED, AND NAIVE ANIMALS. RECORDINGS PERFORMED IN THE PRESENCE OF THE PSYCHEDELIC 5-HT2AR AGONIST, DOI, CAUSED INCREASES IN SEPSC FREQUENCY AND AMPLITUDE. ANTAGONISM OF THE 5-HTIA RECEPTOR ALSO ATTENUATED THE 5-HT EFFECTS ON RMP IN SALINE RATS, AN EFFECT THAT WAS ABSENT IN COCAINE RATS. NEXT, WE OBSERVED SPIKE-TIMING DEPENDENT PLASTICITY (STDP) IN CLA-ACC NEURONS, REVEALING ANTI-HEBBIAN LONG-TERM DEPRESSION. DOI REVERSED THIS LTD INTO A ROBUST LONG-TERM POTENTIATION. FINALLY, RNA SCOPE COMBINED WITH CONFOCAL IMAGING WAS PERFORMED TO INTERROGATE THE COLOCALIZATION OF EACH OF THE 5-HT RECEPTOR SUBTYPES IN THE CLAUSTRUM.
THESE FINDINGS PROVIDE THE FIRST EVIDENCE THAT THE LARGE POPULATION OF CLA-ACC NEURONS ARE UNDER INHIBITORY CONTROL FROM 5-HT, AND SUGGEST THAT 5-HTI AND 5-HT2 RECEPTORS ARE SEPARATELY INVOLVED IN SEROTONIN REGULATION OF INTRINSIC MEMBRANE PROPERTIES AND EXCITATORY SYNAPTIC PLASTICITY, RESPECTIVELY.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W7. EXPLORING THE ASSOCIATION BETWEEN SEX STEROIDS AND NICOTINIC ACETYLCHOLINE RECEPTORS IN HETEROGENEOUS STOCK (HS) RATS THAT ARE RESISTANT OR SUSCEPTIBLE TO COCAINE ADDICTION-LIKE BEHAVIORS

ELIZABETH SNEDDON*, KOKILA SHANKAR, SUPAKORN CHONWATTANAGUL, MICHAELA CULLUM-DOYLE, BENJAMIN SICHEL, DYAR OTHMAN, NARAYAN POKHREL, MOLLY BRENNAN, LISA MATURIN, LIESELOT CARRETTE, FRANCESCA TELESE, ABRAHAM PALMER, OLIVIER GEORGE

OVER THE PAST DECADE, COCAINE USE AMONG WOMEN IN THE UNITED STATES HAS INCREASED. SEX STEROIDS INFLUENCE COCAINE-RELATED BEHAVIORS. PROGESTERONE REDUCES COCAINE SELF-ADMINISTRATION AND IS ELEVATED IN THE HIPPOCAMPUS AFTER COCAINE EXPOSURE. NICOTINIC ACETYLCHOLINE RECEPTORS (NACHRS), PARTICULARLY NACHR A5, IS IDENTIFIED AS A RISK FACTOR FOR COCAINE USE IN HUMANS. PROGESTERONE APPLICATION IN CULTURED TISSUE UPREGULATES NACHR A5 PROTEIN EXPRESSION. WE HYPOTHESIZED THAT PROGESTERONE AND NACHR A5 RECEPTORS WOULD BE DOWNREGULATED IN THE HIPPOCAMPUS OF SEVERELY DEPENDENT FEMALE RATS.

HETEROGENEOUS STOCK RATS (N=57) UNDERWENT INTRAJUGULAR CATHETERIZATION SURGERIES AND THEN VARIOUS OPERANT TASKS (SHORT- AND LONG-ACCESS SELF-ADMINISTRATION, PROGRESSIVE RATIO, AND AVERSION-RESISTANT RESPONDING). RATS WERE GROUPED INTO NAÏVE, RESISTANT, AND SEVERE ADDICTION-LIKE BEHAVIOR GROUPS BASED ON AN ADDICTION INDEX DETERMINED BY BEHAVIORAL MEASURES. BRAIN SAMPLES WERE COLLECTED, AND PUNCHES OF THE HIPPOCAMPUS, PRELIMBIC AND INFRALIMBIC CORTICES, AND VENTRAL MIDBRAIN WERE TAKEN FOR RT-QPCR. GENES OF INTEREST INCLUDED, ESR1, ESR2, AR, PGR, CHRNA3, CHRB4, CHRNA5, AND CHRNA7.

PRELIMINARY DATA SHOWS ESR1 MRNA IS UPREGULATED IN THE HIPPOCAMPUS IN FEMALES IN THE SEVERE GROUP VS. NAIVE. AR AND ESR1 MRNA IN THE HIPPOCAMPUS ARE UPREGULATED IN FEMALES IN THE SEVERE GROUP VS. MALES. PGR MRNA IS UPREGULATED IN THE PRELIMBIC AND INFRALIMBIC CORTICES IN FEMALES IN THE SEVERE GROUP VS. NAIVE. IN THE PRELIMBIC AND INFRALIMBIC CORTICES, CHRNA3 AND CHRNB4 MRNA ARE UPREGULATED IN FEMALES IN THE RESISTANT AND SEVERE GROUPS, RESPECTIVELY, VS. MALES.

THESE DATA SHOW SEX DIFFERENCES IN SEX STEROID AND NACHR EXPRESSION FOLLOWING THE DEVELOPMENT OF COCAINE ADDICTION-LIKE BEHAVIOR. RESEARCH IS UNDERWAY TO CONFIRM THESE DATA AND TO EXPLORE THE CAUSAL LINK BETWEEN THESE SYSTEMS AND COCAINE-RELATED BEHAVIORS. THIS STUDY HIGHLIGHTS POTENTIAL MECHANISMS DRIVING SEX-SPECIFIC DIFFERENCES IN COCAINE USE DISORDER.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W8. DEVELOPMENT OF MULTIPLEXED POPULATION SELECTION AND ENRICHMENT SINGLE NUCLEI RNA SEQUENCING TO CHARACTERIZE NEURONAL ENSEMBLES IN COCAINE RELAPSE

KAREEM WOODS*, KATHERINE SAVELL, RAJTARUN MADANGOPAL, RYAN PALAGANAS, OLIVIA DRAKE, DRAKE THOMPSON, PADMASHRI SARAVANAN, MEGAN BRENNER, TONI MARTIN, MIA STEINBERG, JODY MARTIN, JAE CHOI, SOPHIA WEBER, ELISE VAN LEER, BRUCE HOPE

RELAPSE IS AN ONGOING CLINICAL PROBLEM, AND THERE ARE CURRENTLY NO EFFECTIVE TREATMENTS TO REDUCE THE RISK OF RELAPSE TO PSYCHOSTIMULANTS LIKE COCAINE. ENVIRONMENTAL STIMULI PREVIOUSLY ASSOCIATED WITH DRUG-TAKING CAN PRECIPITATE RELAPSE LONG AFTER CESSATION OF DRUG USE. THESE MALADAPTIVE CUE-DRUG ASSOCIATIONS ARE HYPOTHESIZED TO BE ENCODED WITHIN SPECIFIC PATTERNS OF STRONGLY ACTIVATED NEURONS (NEURONAL ENSEMBLES) THAT CAN BE IDENTIFIED BY FOS. OUR LAB AND OTHERS HAVE SHOWN CAUSAL ROLES FOR FOS-EXPRESSING NEURONAL ENSEMBLES IN REWARD-SEEKING BEHAVIORS AND IDENTIFIED UNIQUE MOLECULAR AND FUNCTIONAL ALTERATIONS WITHIN THEM. HOWEVER, DUE TO METHODOLOGICAL LIMITATIONS, PREVIOUS STUDIES POOLED SAMPLES OF FOS-NEGATIVE AND FOS-POSITIVE NEURON FROM DIFFERENT ANIMALS, COULD NOT CHARACTERIZE CELL-TYPE DIVERSITY OF ENSEMBLES OR IDENTIFY MOLECULAR ALTERATIONS WITHIN SPECIFIC ENSEMBLE CELL-TYPES. TO ADDRESS THIS GAP, WE DEVELOPED A NEW MULTIPLEXED POPULATION SELECTION AND ENRICHMENT SINGLE NUCLEI RNA-SEQUENCING (XPOSE-SEQ) PIPELINE TO DETERMINE CELL-TYPE COMPOSITION OF RARE ENSEMBLE POPULATIONS (< 10% OF NEURONS IN A REGION) AND DEFINE THEIR TRANSCRIPTIONAL PROFILES FOLLOWING LEARNED BEHAVIORS.
WE USED XPOSE-SEQ TO CREATE A NEURONAL CELL-TYPE ATLAS OF RAT MEDIAL PREFRONTAL CORTEX (MPFC), EXAMINED WHICH MPFC CELL-TYPES ARE ACTIVATED IN FOS-BASED TRANSGENIC MALE AND FEMALE RATS DURING NOVEL CONTEXT EXPLORATION, AND CHARACTERIZED CELL-TYPE SPECIFIC TRANSCRIPTIONAL RESPONSES WITHIN THESE ENSEMBLES. OUR ANALYSIS SHOWED DISTINCT CLUSTERS CORRESPONDING TO KNOWN EXCITATORY AND INHIBITORY CELL TYPES IN THE MPFC THAT FURTHER SUBCLUSTER INTO EXPECTED LAYER AND INTERNEURON SUB-TYPES. ADDITIONALLY, WE FOUND THAT THESE SUB-TYPES HAVE DISTINCT TRANSCRIPTIONAL SIGNATURES AFTER NOVEL CONTEXT EXPLORATION. USING THE XPOSE-SEQ PIPELINE, ONGOING ANALYSIS IS AIMED AT CHARACTERIZING CELL-TYPE AND ENSEMBLE-SPECIFIC TRANSCRIPTIONAL SIGNATURES INVOLVED IN COCAINE-RELAPSE ENSEMBLES. IN FUTURE STUDIES, WE WILL EMPLOY CRISPR-BASED TRANSCRIPTIONAL MODULATORS TO ASSESS CAUSAL ROLES FOR IDENTIFIED COCAINE MEMORY-SPECIFIC TRANSCRIPTIONAL FINGERPRINTS IN PERSISTENT COCAINE RELAPSE DURING ABSTINENCE.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W9. SEX DIFFERENCES IN THE NEURAL CIRCUITS THAT PREDICT ALCOHOL DEPENDENCE DEVELOPMENT

KELLY HEWITT*, SKYLAR NICHOLSON, ANGELA HENRICKS

ALTHOUGH NEUROBIOLOGICAL MECHANISMS UNDERLYING ALCOHOL USE AND DEPENDENCE HAVE BEEN EXTENSIVELY RESEARCHED, MECHANISMS EXPLAINING OBSERVED SEX DIFFERENCES IN ALCOHOL DRINKING ARE POORLY UNDERSTOOD. THE CORTICAL-STRIATAL CIRCUIT PLAYS A KEY ROLE IN THE DEVELOPMENT OF ALCOHOL DEPENDENCE, AND WE HAVE PREVIOUSLY SHOWN THAT OSCILLATIONS FROM THESE REGIONS PREDICT DRINKING IN NON-DEPENDENT MALE RATS, BUT NOT IN FEMALE RATS. SINCE WOMEN ARE MORE LIKELY TO REPORT USING ALCOHOL FOR NEGATIVE REINFORCEMENT REASONS AND BEING MORE SENSITIVE TO STRESS-INDUCED RELAPSE, WE HYPOTHESIZED THAT STRESS-RELATED NEURAL CIRCUITS MAY CONTAIN MORE INFORMATION PREDICTIVE OF FEMALE DRINKING. TO TEST THIS, WE DETERMINED WHETHER CORTICAL, STRIATAL, AND/OR LIMBIC OSCILLATIONS DURING ALCOHOL SELF-ADMINISTRATION WOULD DISTINGUISH BETWEEN DEPENDENT AND NON-DEPENDENT RATS IN A SEX-SPECIFIC MANNER. SPRAGUE-DAWLEY RATS WERE TRAINED TO SELF-ADMINISTER 10% ALCOHOL BEFORE IMPLANTING BILATERAL ELECTRODES TARGETING THE MEDIAL PREFRONTAL CORTEX (MPFC), NUCLEUS ACCUMBENS SHELL (NACSH), AND CENTRAL NUCLEUS OF THE AMYGDALA (CEA). THEN, HALF OF THE RATS WERE EXPOSED TO FOUR WEEKS OF CHRONIC INTERMITTENT ALCOHOL (CIA) VAPOR EXPOSURE TO INDUCE DEPENDENCE. DURING ACUTE WITHDRAWAL, LOCAL FIELD POTENTIALS (LFPS) WERE RECORDED DURING ANOTHER ROUND OF SELF-ADMINISTRATION SESSIONS. OVERALL, FEMALE RATS SELF-ADMINISTERED MORE ALCOHOL THAN MALES. CIA EXPOSURE INCREASED ALCOHOL SELF-ADMINISTRATION IN BOTH SEXES, BUT TO A LARGER EXTENT IN MALES. PRELIMINARY ANALYSIS REVEALED THAT NACSH AND MPFC LFPS BEST PREDICT CIA EXPOSURE IN MALES, WHILE CEA OSCILLATIONS BEST PREDICT CIA EXPOSURE IN FEMALES. THESE DATA PROVIDE SUPPORT FOR SEX-SPECIFIC NEUROBIOLOGICAL CORRELATES OF DEPENDENCY, WHICH COULD CONTRIBUTE TO THE DEVELOPMENT OF MORE EFFECTIVE THERAPIES FOR ALCOHOL DEPENDENCE IN MEN AND WOMEN.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

WI0. OPTOGENETIC MANIPULATION OF PRELIMBIC CORTICAL ENSEMBLES DISRUPTS CUED REWARD SEEKING

ROGER GRANT*, RACHEL CLARKE, JACQUELINE PANICCIA, ELIZABETH DONCHECK, KELSEY VOLLMER, KION WINSTON, SOPHIE BUCHMAIER, JAMES OTIS

THE PRELIMBIC SUBREGION OF THE DORSOMEDIAL PREFRONTAL CORTEX COORDINATES LEARNED CUED REWARD-SEEKING BEHAVIOR IN MICE. HOWEVER, AT THE SINGLE CELL AND POPULATION LEVEL, THE PRELIMBIC CORTEX EXHIBITS HETEROGENEOUS ACTIVITY DURING REWARD SEEKING. RECENTLY, WE CHARACTERIZED FIVE FUNCTIONAL NEURONAL ENSEMBLES IN THE PRELIMBIC CORTEX BASED ON THEIR COORDINATED ACTIVITY DURING A PAVLOVIAN SUCROSE SEEKING TASK. FURTHERMORE, WE SHOWED THAT THE ACTIVITY OF THESE ENSEMBLES IS STABLE ACROSS DAYS AND DIFFERENTIALLY ENCODES SPECIALIZED INFORMATION RELATED TO THE TASK. GIVEN THE ROBUST INFORMATION ENCODING BY THESE ENSEMBLES, WE HYPOTHESIZED THAT BY MANIPULATING THEIR ACTIVITY, WE COULD UNCOVER THE INFLUENCE OF EACH ENSEMBLE ON NATURAL REWARD-SEEKING BEHAVIOR. USING MICE WHICH CO-EXPRESS A CALCIUM INDICATOR (AAVDJ-CAMKIIA-GCAMP6S) AND RED-SHIFTED EXCITATORY OPSIN (AAVDJ-CAMKIIA-CHRMINE) IN PUTATIVE PRELIMBIC EXCITATORY OUTPUT NEURONS, WE PERFORMED CONCURRENT IN VIVO TWO-PHOTON CALCIUM IMAGING AND SINGLE-CELL OPTOGENETICS WHILE MICE ENGAGED IN A PAVLOVIAN SUCROSE SEEKING TASK. USING THIS APPROACH, WE WERE ABLE TO SIMULTANEOUSLY STIMULATE MULTIPLE CELLS FROM THE SAME ENSEMBLE WITH PRECISE SPATIOTEMPORAL RESOLUTION WHILE MONITORING POPULATION CALCIUM DYNAMICS. OUR PRELIMINARY RESULTS INDICATE THAT ACTIVATION OF AN ENSEMBLE THAT ENCODES LICKING IS SUFFICIENT TO INFLUENCE CONDITIONED LICKING BEHAVIOR. IN ONGOING EXPERIMENTS, WE ARE TARGETING OTHER ENSEMBLES, INCLUDING THOSE THAT ENCODE CUE DISCRIMINATION, AND REWARD AVAILABILITY TO DETERMINE THEIR INFLUENCE ON REWARD SEEKING IN OUR PARADIGM.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

WII. TRANSCRIPTOME-GUIDED DIAGNOSIS AND DRUG REPURPOSING FOR ALCOHOL USE DISORDER: A TALE OF MICE AND HUMANS

LAURA FERGUSON*, R. DAYNE MAYFIELD, AMANDA ROBERTS, VATSALYA VALTSALYA, VIJAY RAMCHANDANI, ROBERT MESSING

BRAIN GENE EXPRESSION PATTERNS CAN CLASSIFY SUBJECTS AS AUD OR NON-AUD AND PREDICT TREATMENTS THAT REDUCE DRINKING IN RODENTS. IT IS NOT POSSIBLE TO ACCESS THE BRAIN IN PATIENTS, SO A MORE ACCESSIBLE TISSUE IS REQUIRED FOR CLINICAL USE. HERE WE PRESENT FINDINGS REGARDING WHOLE BLOOD TRANSCRIPTIONAL SIGNATURES OF ALCOHOL EXPOSURE IN MICE AND HUMANS.

WE ANALYZED WHOLE BLOOD TRANSCRIPTOME PROFILES FROM C57BL/6J MICE EXPOSED TO CHRONIC INTERMITTENT ETHANOL VAPOR (CIE) OR AIR. MACHINE LEARNING MODELS CLASSIFIED SUBJECTS AS CIE OR AIR-EXPOSED WITH A HIGH DEGREE OF ACCURACY BASED ON BLOOD RNA PREDICTORS (MAXIMUM AUC OF 90.4% FOR THE REGULARIZED LOGISTIC REGRESSION MODEL). WE COMPARED THE BLOOD CIE SIGNATURE TO THOSE OF PHARMACEUTICALS IN THE NIH CONNECTIVITY MAP DATABASE TO IDENTIFY COMPOUNDS THAT HAVE THE OPPOSITE EFFECT ON GENE EXPRESSION AS CIE ("REVERSERS"). AS PREDICTED, THE TOP DRUG CANDIDATE REDUCED VOLUNTARY ALCOHOL CONSUMPTION IN CIE-EXPOSED C57BL/6J MICE TO CONTROL LEVELS. WE ALSO ANALYZED WHOLE BLOOD TRANSCRIPTOME PROFILES FROM HEALTHY HUMAN SUBJECTS WITH AND WITHOUT A FAMILY HISTORY OF AUD BEFORE AND DURING IV ETHANOL INFUSIONS. THERE WAS A LARGER BLOOD TRANSCRIPTIONAL RESPONSE TO ACUTE ETHANOL IN FAMILY HISTORY POSITIVE (FHP) PARTICIPANTS THAN IN FAMILY HISTORY NEGATIVE (FHN). THERE WERE ALSO BASELINE GENE EXPRESSION DIFFERENCES BETWEEN FHP AND FHN INDIVIDUALS THAT REMAINED STABLE THROUGHOUT ALCOHOL EXPOSURE. THIS REPRESENTS TWO CATEGORIES OF RISK BIOMARKERS: RNAS THAT CAPTURE STABLE DIFFERENCES BETWEEN FHP AND FHN INDIVIDUALS (APPARENT AT BASELINE), AND RNAS THAT HAVE DIFFERENT RESPONSES TO ACUTE ALCOHOL (APPARENT ONLY AFTER ALCOHOL CHALLENGE).

WE CONCLUDE THAT THERE IS A TRANSCRIPTIONAL SIGNATURE OF ETHANOL EXPOSURE IN BLOOD IN MICE AND HUMANS. THESE FINDINGS SUPPORT THE UTILITY OF BLOOD AS AN ACCESSIBLE TISSUE THAT CAN BE USED FOR TRANSCRIPTOME-BASED DRUG REPURPOSING TO IDENTIFY THERAPEUTICS FOR AUD AND POTENTIALLY PERSONALIZE AUD TREATMENT.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

WI2. HEROIN-MEDIATED DISRUPTION OF THALAMO-ACCUMBAL BEHAVIORAL SUPPRESSION IS REQUIRED FOR REINSTATEMENT OF HEROIN SEEKING

JACQUELINE PANICCIA*, KELSEY VOLLMER, LISA GREEN, ROGER GRANT, KION WINSTON, SOPHIE BUCHMAIER, ANNAKA WESTPHAL, RACHEL CLARKE, ELIZABETH DONCHECK, BOGDAN BORDIEANU, LOGAN MANUSKY, MICHAEL MARTINO, AMY WARD, MICHAEL SCOFIELD, JAMES OTIS

LACK OF BEHAVIORAL SUPPRESSION TYPIFIES SUBSTANCE USE DISORDER, YET A MECHANISTIC UNDERSTANDING OF THE CIRCUIT- AND CELL TYPE-SPECIFIC CHARACTERISTICS OF DRUG-INDUCED BEHAVIORAL DISINHIBITION REMAINS ELUSIVE. WE HAVE ESTABLISHED A PARAVENTRICULAR THALAMO-ACCUMBAL SYSTEM GOVERNS THE SUPPRESSION OF REWARD-SEEKING BEHAVIORS. SPECIFICALLY, WE HAVE SHOWN THAT PARAVENTRICULAR THALAMUS INNERVATION OF PARVALBUMIN INTERNEURONS IN THE NUCLEUS ACCUMBENS (PVT-NACPV-IN), DRIVES SUPPRESSION OF SUCROSE SEEKING IN DRUG-NAÏVE MICE. CRITICALLY, WE HAVE SHOWN THAT OPIOID EXPOSURE RAPIDLY DISENGAGES THE PVT-NACPV-IN CIRCUIT THROUGH ACTION AT THALAMIC M-OPIOID RECEPTORS (ORS) AND UNLEASHES REWARD SEEKING, EFFECTIVELY REMOVING A PHYSIOLOGICAL "BRAKE" ON BEHAVIOR. HERE, WE IDENTIFY ADAPTATIONS IN THE PVT-NACPV-IN CIRCUIT THAT ARISE DURING HEROIN SELF-ADMINISTRATION (SA) WHICH ARE REQUIRED TO DRIVE RELAPSE TO HEROIN SEEKING. USING A HEAD-FIXED MODEL OF HEROIN SA, EXTINCTION, AND REINSTATEMENT IN COMBINATION WITH IN VIVO TWO-PHOTON CALCIUM IMAGING AND PATCH-CLAMP ELECTROPHYSIOLOGY, WE OBSERVED PROFOUND HYPOACTIVITY IN SELECT PVT-NAC PROJECTION NEURONS AND DECREASED EFFICACY AT PVT-NACPV-IN SYNAPSES FOLLOWING HEROIN SA AND EXTINCTION TRAINING. FURTHER, WE FIND DUE TO HEROIN EXPOSURE, OPTOGENETIC ACTIVATION OF THE PVT-NAC CIRCUIT WAS UNABLE TO PREVENT REINSTATEMENT OF HEROIN SEEKING. TO GAIN MECHANISTIC INSIGHT INTO HEROIN-INDUCED BEHAVIORAL DISINHIBITION, WE USED OPRMIFL/FL MICE AND GENETICALLY DELETED M-ORS IN THE PVT PRIOR TO HEROIN SA AND EXTINCTION. USING THIS GENETIC MANIPULATION, WE FIND THAT KNOCKDOWN OF THALAMIC M-ORS RESTORED SYNAPTIC EFFICACY AT PVT-NACPV-IN SYNAPSES AND ENABLED PVT-NAC PHOTOSTIMULATION TO SUPPRESS HEROIN SEEKING. COLLECTIVELY, OUR RESULTS IDENTIFY THE CIRCUIT- AND CELL TYPE-SPECIFIC CHARACTERISTICS OF HEROIN-MEDIATED BEHAVIORAL DISINHIBITION WITHIN THE THALAMO-ACCUMBAL NETWORK AND ESTABLISH THAT THESE ADAPTATIONS ARE A CENTRAL COMPONENT OF RELAPSE VULNERABILITY.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

WI3. CORTICOSTRIATAL NEURONAL ENSEMBLES REGULATE CUE-INDUCED HEROIN SEEKING

RACHEL CLARKE*, BOGDAN BORDIEANU, SOPHIE BUCHMAIER, SHANNON WOODS, ROGER GRANT, ANNAKA WESTPHAL, JAYDA CARROLL-DEATON, KELSEY VOLLMER, JACQUELINE PANICCIA, ELIZABETH DONCHECK, AMY WARD, MICHAEL MARTINO, MICHAEL SCOFIELD, JACQUELINE MCGINTY, JAMES OTIS

PRELIMBIC CORTEX (PRL) GLUTAMATERGIC INPUTS TO THE NUCLEUS ACCUMBENS CORE (PRLNACC) ARE CRITICALLY INVOLVED IN CUED HEROIN SEEKING. WHILE THE IMPORTANCE OF THE PRLNACC CIRCUIT HAS BEEN ESTABLISHED, VERY LITTLE IS KNOWN ABOUT THE IN VIVO ACTIVITY DYNAMICS OF PRLNACC NEURONS DURING CUED HEROIN SEEKING. OUR PRELIMINARY DATA SUGGEST THAT DURING CUE-INDUCED HEROIN SEEKING, FOUR NEURONAL ENSEMBLES WITHIN THE PRLNACC CIRCUIT EMERGE, EACH WITH A UNIQUE ACTIVITY PATTERN DURING ACTIVE LEVER PRESSING, WITH BOTH EXCITED AND INHIBITED ENSEMBLES OBSERVED. HOWEVER, WHETHER THESE ACTIVITY PATTERNS REFLECT DIFFERENCES IN CELL-TYPE, OR OTHER FACTORS IS UNCLEAR. WITHIN THE POPULATION OF PRLNACC NEURONS, TWO NON-OVERLAPPING CELL-TYPES HAVE BEEN IDENTIFIED BY VIRTUE OF EITHER DOPAMINE RECEPTOR 1 (D1) OR DOPAMINE RECEPTOR 2 (D2) EXPRESSION. RECENT STUDIES DEMONSTRATE THAT D1 AND D2 EXPRESSING PRLNACC NEURONS UNDERGO DIFFERENTIAL PHYSIOLOGICAL ADAPTATIONS FOLLOWING HEROIN SELF-ADMINISTRATION BUT WHETHER THESE DISTINCT SUBPOPULATIONS OF PRLNACC NEURONS FUNCTIONALLY REGULATE HEROIN SEEKING REMAINS UNKNOWN. USING CIRCUIT-SPECIFIC OPTOGENETICS, WE INHIBITED EITHER D1+ OR D2+ PRL TERMINALS IN THE NACC AND FOUND THAT PRLD1NACC, BUT NOT PRLD2NACC, NEURONS ARE NECESSARY FOR CUED HEROIN SEEKING. NEXT, WE USED AN INTERSECTIONAL VIRAL STRATEGY TO RESTRICT A GENETICALLY ENCODED CALCIUM INDICATOR (GCAMP6M) TO PRLD1NACC NEURONS AND USED TWO-PHOTON CALCIUM IMAGING TO RECORD ACTIVITY DURING CUE-INDUCED HEROIN SEEKING. AGAIN, WE FOUND THERE ARE DISTINCT ENSEMBLES OF PRLD1NACC NEURONS DEFINED BY ACTIVITY PATTERN THAT EMERGED DURING CUED HEROIN SEEKING. OUR ONGOING EFFORTS AIM TO UTILIZE SINGLE-CELL OPTOGENETICS TO MANIPULATE EACH ENSEMBLE IN THE PRESENCE OR ABSENCE OF CUES TO DETERMINE HOW EACH PRLD1NACC NEURONAL ENSEMBLE FUNCTIONALLY CONTRIBUTES TO HEROIN SEEKING.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

WI4. XYLAZINE ACTS ON THE KAPPA OPIOID RECEPTOR AND WORSENS OPIOID WITHDRAWAL IN FEMALE BUT NOT MALE MICE

MADIGAN BEDARD*, JACKSON MURRAY, ALEXANDRA NOWLAN, XI-PING HUANG, BRYAN ROTH, ZOE MCELLIGOTT

THE OPIOID CRISIS IS AN EVER-CHANGING AND GROWING PROBLEM ACROSS THE UNITED STATES WITH MORE THAN 130 PEOPLE DYING DAILY FROM OVERDOSES. RECENTLY, THIS PROBLEM HAS BEEN FURTHER COMPLICATED BY THE ADDITION OF XYLAZINE TO THE UNREGULATED DRUG SUPPLY. XYLAZINE IS CANONICALLY KNOWN AS AN ADRENERGIC AGONIST AND VETERINARY SEDATIVE THAT IS THOUGHT TO WORSEN FENTANYL OVERDOSES AND BELIEVED TO BE UNAFFECTED BY THE OPIOID ANTAGONIST, NALOXONE. ANECDOTAL REPORTS DESCRIBE A WIDE ARRAY OF RESPONSES TO FENTANYL AND XYLAZINE IN PEOPLE AND ACROSS SEXES. HERE, WE SHOW THAT XYLAZINE/FENTANYL RESULTS IN WORSENED WITHDRAWAL SYMPTOMS IN A NALOXONE-PRECIPITATED WITHDRAWAL PARADIGM IN FEMALE BUT NOT MALE MICE COMPARED TO FENTANYL ALONE. ADDITIONALLY, WE SHOW THAT MICE WHO RECEIVED XYLAZINE AND THEN NALOXONE STILL EXHIBITED WITHDRAWAL SYMPTOMS DESPITE THEIR PUTATIVE EFFECTS ON SEPARATE SYSTEMS. C-FOS IMMUNOHISTOCHEMISTRY FOLLOWING PRECIPITATED WITHDRAWAL SHOWED ALTERED ACTIVITY IN SEVERAL KEY BRAIN REGIONS (LC, CEA, DBNST, ETC.) WITH SEX DIFFERENCES DRIVING MODULATION IN DIFFERENT DIRECTIONS. FURTHER, WE ARE THE FIRST TO REPORT THAT XYLAZINE HAS ACTIVITY AT THE KAPPA OPIOID RECEPTOR, DOPAMINE D2 RECEPTOR, SIGMA 1 AND 2 RECEPTORS AS WELL AS THREE ALPHA ADRENERGIC RECEPTORS. WHILE MORE STUDIES ARE NEEDED TO PINPOINT THE MECHANISTIC ROOT OF THE BEHAVIORAL DIFFERENCES, THE BINDING DATA PROVIDE US WITH NEW TARGETS FOR INVESTIGATION. ADDITIONALLY, WE SHOW THAT FEMALES FIND A LOW DOSE OF XYLAZINE REWARDING IN A CPP, WHILE MALES DID NOT. TOGETHER, THESE FINDINGS FURTHER OUR UNDERSTANDING OF THE INTERPLAY BETWEEN THE ADRENERGIC AND OPIOID SYSTEMS AND WILL BE CRUCIAL IN INFORMING MEDICAL TREATMENT OF OVERDOSE AND RECOVERY.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

WI5. NICOTINE AND THE NODOSE GANGLIA: EVIDENCE FOR BRAIN-BODY INTERACTIONS IN SUBSTANCE USE DISORDERS

KEVIN BRAUNSCHEIDEL*, ROHAN GHOSHAL, MOHAMMAD ISHMAM, MASAGO ISHIKAWA, LAUREN WILLS, PAUL KENNY

NICOTINE ADDICTION IN THE FORM OF HABITUAL TOBACCO USE IS A LEADING CAUSE OF PREMATURE DEATH IN THE UNITED STATES. RECENT EVIDENCE FROM OUR LAB IMPLICATES PERIPHERAL SYSTEMS IN NICOTINE ADDICTION. FOR INSTANCE, NICOTINE DRASTICALLY ALTERS THE TRANSCRIPTOME OF THE NODOSE GANGLIA (NG) AND ELEVATES POSTPRANDIAL CHOLECYSTOKININ (CCK) LEVELS IN MICE, SIMILAR TO SMOKERS. HERE, WE TEST THE HYPOTHESIS THAT CCK RECEPTORS (CCKRS) IN GUT-INNERVATING NG (VAGAL) SENSORY NEURONS POTENTIATES NICOTINE SIGNAL TRANSMITTANCE SIMILAR TO CCK'S REGULATION OF APPETITE.
CONDITIONED PLACE AVERSION (CPA) TO AN AVERSIVE DOSE OF NICOTINE AND A PERIPHERY-RESTRICTED NICOTINE RECEPTOR AGONIST, METHYLNICOTINIUM WAS PERFORMED. NEXT, PHP.S-DIO-HM4DI WAS INJECTED INTO TRAP2 ANIMALS THAT EXPRESS CRE IN AN ACTIVITY-DEPENDENT, TEMPORALLY-RESTRICTED MANNER YIELDING INHIBITORY CHEMOGENETIC ACCESS TO METHYLNICOTINIUM-RESPONSIVE PERIPHERAL NERVOUS TISSUE PRIOR TO NICOTINE CPA. WE THEN RECORDED GCAMP ACTIVITY EX VIVO IN CCKR+ NG IN RESPONSE TO NICOTINE IN CCKR-AI96 MICE. NEXT, WE MEASURED NICOTINE SELF-ADMINISTRATION FOLLOWING STIMULATION OF PERIPHERAL CCKRS WITH CCK-8 OR INHIBITION WITH DEXAMETHONIUN. IN SEPARATE COHORT, CCKR+ NG WERE ABLATED USING CCK-SAPORIN PRIOR TO NICOTINE SELF-ADMINISTRATION METHYLNICOTINIUM INDUCED CONDITIONED PLACE AVERSION IN EXCESS OF AN EQUIMOLAR, AVERSIVE DOSE OF NICOTINE. NICOTINE STRONGLY ACTIVATED CCKR+ NG NEURONS AND STIMULATING PERIPHERAL CCKRS DECREASED NICOTINE INTAKE. INHIBITION OF METHYLNICOTINIUM-RESPONSIVE PERIPHERAL NERVOUS TISSUE DID NOT IMPACT NICOTINE CPA, BUT BOTH A SYSTEMIC CCKR BLOCKADE AND SELECTIVE CCKR+ NG LESION INCREASED NICOTINE INTAKE.

PERIPHERAL CCKRS REGULATE NICOTINE INTAKE DUE IN PART TO ACTIONS ON VAGAL SENSORY AFFERENTS. THE EXISTENCE OF THIS NOVEL "BOTTOM-UP" REGULATION OF NICOTINE INTAKE BY THE NG MAY PROVE USEFUL FOR THE DEVELOPMENT OF NOVEL ADDICTION THERAPIES.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

WI6. ELUCIDATING THE ROLE OF MEDIAL SEPTUM GLUTAMATE NEURONS IN REWARD SEEKING BEHAVIORS

ANDREW KESNER*, STEPHANIE RAMOS-MACIEL, NINA WESTCOTT

THE SEPTUM WAS FIRST REGION DISCOVERED BY OLDS AND COLLEAGUES TO SUPPORT ELECTRICAL INTRACRANIAL SELF-STIMULATION IN THE RAT. FURTHER STUDIES BY HEATH IN THE 1970S SHOWED HUMANS WILL SIMILARLY PRESS A BUTTON TO EARN INTRA-SEPTAL ELECTRICAL STIMULATION. DESPITE THESE LANDMARK STUDIES, FURTHER INTEREST IN THE SEPTUM, IN PARTICULAR THE MEDIAL SEPTUM (MS), AS A LOCUS FOR REWARD RELATED BEHAVIORS REMAINED LIMITED. WE PREVIOUSLY FOUND THAT MICE WILL LEVER PRESS TO EARN OPTOGENETIC STIMULATION OF THE MS, AND IN PARTICULAR MS GLUTAMATE NEURONS (MS-GLUN), AND MS-GLUN IN TURN PROJECT TO THE VTA TO INFLUENCE DOPAMINE (DA) RELEASE IN THE NUCLEUS ACCUMBENS (NAC) (KESNER ET AL., 2021). LITTLE ELSE IS KNOWN ABOUT THE ROLE OF MS-GLU NEURONS DURING NATURAL REWARD-SEEKING BEHAVIORS. TO ADDRESS THIS KNOWLEDGE GAP, WE RECORDED MS-GLUN POPULATION ACTIVITY USING GCAMP7F AND FIBER PHOTOMETRY TECHNIQUES WHILE MICE PERFORMED VARIOUS OPERANT AND PAVLOVIAN REWARD-SEEKING BEHAVIORS. WE FOUND THAT MS-GLUN INDEED RESPOND DIFFERENTIALLY TO REWARD-RELATED STIMULI (E.G., ACTIVE VS INACTIVE LEVER PRESSES, REWARD CONSUMPTION, AND REWARD PREDICTIVE CUES). WE NEXT MODULATED MS-GLUN ACTIVITY USING A CHEMOGENETIC APPROACH (GI AND GQ DREADDS, OR MCHERRY CONTROL), AND FOUND THAT ENHANCING MS-GLUN EXCITABILITY INCREASED THE RATE THAT MICE INCORPORATED NEW INFORMATION TO OBTAIN GOALS, I.E., STRATEGY SWITCHING. SINCE WE PREVIOUSLY FOUND OPTOGENETIC STIMULATION OF MS-GLUN CAN INCREASE NAC-DA, WE NEXT HYPOTHESIZED THAT THE EFFECT ON STRATEGY SWITCHING BEHAVIOR FROM CHEMOGENETIC MODULATION OF MS-GLUN MAY BE DRIVEN BY RESULTANT CHANGES IN NAC-DA DURING THESE TASKS. WE RECORDED NAC-DA VIA FIBER PHOTOMETRY OF DLIGHT1.3B DURING THE SAME OPERANT AND PAVLOVIAN STRATEGY SWITCHING BEHAVIORS WHILE MS-GLUN WERE CHEMOGENETICALLY MANIPULATED. WE OBSERVED DIFFERENCES IN NAC-DA DURING THESE TASKS THAT WERE DEPENDENT ON CHEMOGENETIC MODULATION OF MS-GLUN THAT APPEARS TO CORRESPOND TO NAC-DA RESPONSES TO NEW REWARD RELATED CUES/STIMULI. THESE FINDINGS ARE AN IMPORTANT STEP IN UNDERSTANDING THE ROLE OF THIS UNDERSTUDIED POPULATION OF NEURONS IN AN UNDERSTUDIED BRAIN REGION RELATED TO REWARD AND MOTIVATIONAL PROCESSES, AND COULD LEAD TO NOVEL THERAPEUTIC INTERVENTIONS FOR TREATING PSYCHIATRIC DISORDERS RELATED TO MALADAPTATION IN MOTIVATED BEHAVIORS.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

WI7. RESILIENT SPECIFIC SEX-CONSERVED TRANSCRIPTOMIC CHANGES IN THE NUCLEUS ACCUMBENS FOLLOWING CHRONIC SOCIAL DEFEAT STRESS IN MICE

TREVONN GYLES*, ERIC PARISE, LEANNE HOLT, ANGELICA MINIER TORIBIO, TAMARA MARKOVIC, LYONNA PARISE, ROMAIN DURAND-DE CUTTOLI, LONG LI, YUN YOUNG YIM, CALEB BROWNE, ARTHUR GODINO, ASTRID CARDONA-ACOSTA, CARLOS BOLAÑOS, SCOTT RUSSO, ERIC J. NESTLER

CHRONIC STRESS IS A PRIMARY RISK FACTOR FOR MAJOR DEPRESSIVE DISORDER MDD AND IS MODELED IN RODENTS USING THE CHRONIC SOCIAL DEFEAT STRESS (CSDS) PARADIGM. IMPORTANTLY, THIS PARADIGM ALLOWS FOR THE IDENTIFICATION OF ANIMALS ACROSS A CONTINUUM OF RESPONSES. THOSE THAT DEVELOP DEPRESSION-LIKE BEHAVIORAL ABNORMALITIES ARE TERMED SUSCEPTIBLE, AND THOSE THAT MAINTAIN MOSTLY NORMAL BEHAVIORAL FUNCTION ARE TERMED RESILIENT. THIS APPROACH HAS PROVEN TO BE HIGHLY USEFUL BUT HAS BEEN MOSTLY EXAMINED IN MALE MICE, LEAVING THE EXAMINATION OF FEMALE MICE UNDERSTUDIED. GIVEN THAT DEPRESSION IS MORE PREVALENT IN WOMEN, IT IS CRUCIAL TO INVESTIGATE POTENTIAL SEX-SPECIFIC MOLECULAR MECHANISMS UNDERLYING SUSCEPTIBILITY VS. RESILIENCE. THUS, WE CONDUCTED RNA-SEQUENCING ON FEMALE MICE SUBJECTED TO AN ADAPTED MODEL OF CSDS AND IDENTIFIED TRANSCRIPTIONAL CHANGES ASSOCIATED WITH THE SUSCEPTIBILITY-RESILIENCE SPECTRUM ACROSS MULTIPLE BRAIN REGIONS. INITIAL COMPARISON OF THIS NEW DATASET WITH PUBLISHED FINDINGS ON MALE MICE REPLICATED EARLIER FINDINGS OF STRIKING SEXUAL DIMORPHISM IN ADAPTATIONS ASSOCIATED WITH SUSCEPTIBILITY OR WITH RESILIENCE IN FEMALE VS. MALE MICE IN THE BRAIN REGIONS STUDIED. DESPITE THIS DIMORPHISM, WE IDENTIFIED A CLUSTER OF GENES UNIQUELY UPREGULATED IN THE NAC OF RESILIENT FEMALE MICE THAT OVERLAPPED ~50% WITH A PREVIOUSLY IDENTIFIED RESILIENT-SPECIFIC GENE NETWORK IN NAC OF MALE MICE. WITHIN THIS GENE NETWORK, TWO KEY DRIVER GENES, GPRINI AND STXIA, WERE PREDICTED TO REGULATE OTHER GENES IN THE NETWORK. TO ELUCIDATE THE ROLE OF THESE KEY DRIVER GENES, WE ARE CURRENTLY INVESTIGATING THE CONSEQUENCES OF VIRAL MANIPULATION WITHIN MEDIUM SPINY NEURON SUBTYPES OF THE NAC IN BOTH MALE AND FEMALE MICE PRIOR TO CSDS. BILATERAL OVEREXPRESSION OF GPRINI OR STXIA IN ALL NAC NEURONS OF MALE MICE INDUCES A PRO-RESILIENT EFFECT. ONGOING RESEARCH AIMS TO CHARACTERIZE THE EFFECTS OF CELL-TYPE-SPECIFIC MANIPULATION IN BOTH SEXES AND TO EXAMINE CHANGES IN NEURONAL AND CIRCUIT FUNCTION THAT UNDERLIE THE PROMOTION OF BEHAVIORAL RESILIENCE. OUR FINDINGS HIGHLIGHT THE IMPORTANCE OF CONSIDERING SEX-SPECIFIC FACTORS IN UNDERSTANDING DEPRESSION AND DEVELOPING TARGETED INTERVENTIONS.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

WI8. STRESS-INDUCED NEUROIMMUNE MECHANISMS UNDERLYING REWARD DEFICITS

RACHEL FISHER-FOYE*, ROMAIN DURAND-DE CUTTOLI, FLURIN CATHOMAS, ANTONIO AUBRY, LONG LI, LYONNA PARISE, SARA COSTI, ERIC J. NESTLER, JAMES W. MURROUGH, SCOTT J. RUSSO

MAJOR DEPRESSIVE DISORDER (MDD) IS A LEADING CAUSE OF DISABILITY WORLDWIDE, CREATING AN IMMENSE BURDEN ON COUNTLESS INDIVIDUALS AND THE GREATER GLOBAL POPULATION. A PROMINENT SYMPTOM ASSOCIATED WITH MDD, IS ANHEDONIA: THE LOSS OF INTEREST FOR HEDONIC STIMULI. IN PARALLEL, SEVERAL CLINICAL AND PRE-CLINICAL STUDIES HAVE LINKED EXPOSURE TO STRESS AND MDD WITH PERIPHERAL IMMUNE SYSTEM ALTERATIONS. HOWEVER, THE NEUROIMMUNE MECHANISMS THAT LEAD TO BRAIN CIRCUIT AND BEHAVIORAL ALTERATIONS ARE NOT WELL UNDERSTOOD. WE INVESTIGATE THE IMPACT OF STRESS ON BLOOD-BRAIN BARRIER (BBB) INTEGRITY, PERIPHERAL IMMUNE MARKER BRAIN INFILTRATION, AND EFFECTS IN BRAIN REWARD CENTERS. WE ASSESS REWARD DEFICITS IN A MOUSE VERSION OF THE PROBABILISTIC REWARD TASK (PRT) AFTER CHRONIC EXPOSURE TO SOCIAL DEFEAT STRESS(CSDS) AND MANIPULATIONS OF BBB INTEGRITY OR PERIPHERAL IMMUNITY. OUR GROUP HAS SHOWN IN MICE EXPOSED TO CSDS, BBB ALTERATIONS LEAD TO INFILTRATION OF PERIPHERAL MONOCYTES INTO THE VENTRAL STRIATUM. A CONSEQUENCE OF THIS INFILTRATION IS A PERTURBATION OF THE NEURONAL FUNCTION IN THE NUCLEUS ACCUMBENS AND REWARD SENSITIVITY DEFICITS IN THE PRT. FOLLOWING CSDS, ONLY SUSCEPTIBLE MICE SHOWED A BLUNTED RESPONSE BIAS. NEXT, WE FOUND THAT ARTIFICIALLY OPENING THE BBB USING A VIRAL KNOCK-DOWN OF THE CLAUDIN-5 TIGHT JUNCTION PROTEIN LED TO AN EXAGGERATED IMPACT OF A SUB-THRESHOLD STRESSOR ON REWARD SENSITIVITY IN THE PRT. OUR RESULTS INDICATE THAT CSDS CAUSES SYSTEMIC INFLAMMATION AND BBB ALTERATIONS LEAD TO AN INFILTRATION OF IMMUNITY MARKERS CAUSING REWARD DEFICITS. WE ALSO WORK WITH THE DEPRESSION AND ANXIETY CENTER AT MOUNT SINAI ON USING HUMAN PRT DATASETS AND BLOOD SAMPLES TO INFORM OUR PRECLINICAL FINDINGS THROUGH AN EXISTING LIQUID BIOMARKER PIPELINE ESTABLISHED BY OUR GROUPS. THIS STUDY PROVIDES A BETTER UNDERSTANDING OF THE NEUROIMMUNE INFLUENCE ON REWARD DEFICITS IN MDD AND OFFERS NEW PERSPECTIVES IN THE DEVELOPMENT OF NEW PERSONALIZED IMMUNE-BASED THERAPEUTICS TO TREAT DEPRESSION.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

WI9. DOES ACUTE PSYCHEDELIC "THERAPY" IN RATS PERSISTENTLY REVERSE STRESS-INDUCED BEHAVIORAL ABNORMALITIES?

KATE LAWSON*, CHRISTINA RUIZ, STEPHEN MAHLER

DEPRESSION, PTSD, AND ADDICTION ARE COMMON MENTAL HEALTH DISORDERS THAT AFFECT MILLIONS OF PEOPLE WORLDWIDE. RISK OF DEVELOPING THESE DISORDERS IS INCREASED IN THOSE WITH A HISTORY OF STRESS DURING CHILDHOOD, OR TRAUMA AS AN ADULT. IN OUR WELL VALIDATED MODEL OF EARLY-LIFE ADVERSITY (ELA) IN RATS, WE FOUND THAT ELA CAUSES PROFOUND SEX-DEPENDENT CHANGES IN REWARD AND STRESS CIRCUITS, LEADING FEMALES TO SEEK DRUGS AND PALATABLE FOOD REWARDS EXCESSIVELY, WHILE ELA MALES INSTEAD APPEAR BROADLY ANHEDONIC FOR NATURAL AND DRUG REWARDS. USING A STRESS-INDUCED ENHANCED FEAR LEARNING MODEL AS A FORM OF ADULTHOOD STRESS TO MODEL PTSD, WE ALSO SEE EXCESSIVE AND MALADAPTIVE FEAR RESPONSES TO SUBSEQUENT MILD STRESS IN BOTH SEXES. WE THEREFORE HAVE ESTABLISHED BEHAVIORAL MODELS OF BOTH EARLY-LIFE AND ADULTHOOD ADVERSITIES THAT ARE RELEVANT TO HUMAN PSYCHIATRIC DISORDERS, WHICH WILL BE USEFUL IN OUR UPCOMING EXPERIMENTS TESTING PRECLINICALLY POTENTIAL NEW THERAPEUTIC STRATEGIES.
IN THE LAST FEW YEARS, PSYCHEDELIC DRUGS LIKE LSD, PSILOCYBIN, AND DMT HAVE RE-EMERGED IN PSYCHIATRY, WITH APPARENT POTENTIAL FOR TREATING DEPRESSION, ADDICTION, AND OTHER PSYCHIATRIC DISORDERS. THESE PROMISING INITIAL CLINICAL FINDINGS INSPIRED US TO DEVELOP A NEW RAT MODEL OF “PSYCHEDELIC THERAPY”, ALLOWING MECHANISTIC INVESTIGATIONS INTO THEIR THERAPEUTIC ACTIONS IN THE BRAIN. OUR PRELIMINARY DATA PROVIDES EVIDENCE THAT A SINGLE DOSE OF THE PSYCHEDELIC SEROTONIN 2A (5-HT2A) RECEPTOR AGONIST 2,5-DIMETHOXY-4-IODOAMPHETAMINE (DOI) MAY REVERSE ELA-INDUCED ANHEDONIA IN MALE RATS. WE ALSO TEST EFFICACY OF DOI FOR REVERSING DEFICITS RESULTING FROM TRAUMATIC ADULTHOOD EXPERIENCES, EMPLOYING A STRESS-ENHANCED FEAR LEARNING MODEL OF TRAUMATIC STRESS. RESULTS WILL CONTRIBUTE TO THE SORELY NEEDED BODY OF BASIC RESEARCH ON PSYCHEDELIC DRUG EFFECTS IN THE BRAIN, AND PROVIDE NEW INSIGHTS THAT COULD BE CAPITALIZED UPON WHEN DEVELOPING MAXIMALLY EFFECTIVE, BUT MINIMALLY DISRUPTIVE THERAPEUTIC STRATEGIES IN HUMANS.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W20. EXPLORING THE SNOWBALL EFFECTS OF POSTTRAUMATIC STRESS SYMPTOMS ON ATTENTION-RELATED BRAIN AND BEHAVIORAL RESPONSES IN ADOLESCENTS

SAMANTHA ELY*, CLARA ZUNDEL, LEAH GOWATCH, AMANPREET BHOGAL, CARMEN CARPENTER, MACKENNA SHAMPINE, SHRAVYA CHANAMOLU, JOVAN JANDE, EMILIE O'MARA, HILARY MARUSAK

BACKGROUND: EMERGING LITERATURE SHOWS THAT ADULTS WITH POSTTRAUMATIC STRESS DISORDER CAN EXPERIENCE ALTERED ATTENTION-RELATED BEHAVIOR AND BRAIN FUNCTIONING, EVEN OUTSIDE OF EMOTIONAL CONTEXTS (E.G., THREAT). HOWEVER, THE ASSOCIATION BETWEEN POSTTRAUMATIC STRESS SYMPTOMS (PTSS) AND ATTENTION DURING ADOLESCENCE, A PERIOD OF RAPID NEURODEVELOPMENT AND A HIGH INCIDENCE OF TRAUMA EXPOSURE, REMAINS UNDER-EXPLORED. THIS PRELIMINARY STUDY EXPLORES THIS RELATIONSHIP AMONG ADOLESCENTS.
METHOD: PARTICIPANTS INCLUDED 46 DETROIT-AREA ADOLESCENTS (60% MALE, M±SD=13.6±2.3 YEARS) WITH A HIGH INCIDENCE OF TRAUMA (93%) AND VARIABLE PTSS (M±SD=18.0±15.2), AS REPORTED THROUGH THE UCLA PTSD REACTIVITY INDEX FOR DSM-5. DURING FUNCTIONAL NEUROIMAGING, YOUTH COMPLETED THE ATTENTION NETWORK TEST TO ASSESS THREE TYPES OF ATTENTION WITH NON-EMOTIONAL STIMULI: ORIENTING (SPATIAL ORIENTATION), ALERTING (TEMPORAL AWARENESS), AND EXECUTIVE (CONFLICT RESOLUTION). PTSS SERVED AS A CONTINUOUS PREDICTOR FOR ATTENTION-RELATED BEHAVIOR (I.E., REACTION TIME, ACCURACY) AND WHOLE-BRAIN ACTIVATION.
RESULTS: BEHAVIORALLY, MORE SEVERE PTSS WERE CORRELATED WITH SLOWER ORIENTING ATTENTION (R=-0.453, P=0.003); HOWEVER, PTSS WERE NOT RELATED TO ALERTING OR EXECUTIVE REACTION TIME, NOR TRIAL ACCURACY. IN THE BRAIN, MORE SEVERE PTSS WERE ASSOCIATED WITH GREATER ACTIVATION RELATED TO ORIENTING ATTENTION IN THE LEFT FUSIFORM AND POSTCENTRAL GYRI, AND LOWER ACTIVITY IN THE LEFT PREGENUAL ANTERIOR CINGULATE CORTEX. PTSS WERE ALSO ASSOCIATED WITH HIGHER ACTIVATION RELATED TO ALERTING AND EXECUTIVE ATTENTION IN AREAS THROUGHOUT THE PARIETAL, FRONTAL, AND LIMBIC LOBES (E.G., PRECUNEUS, PRECENTRAL GYRUS, CINGULATE GYRUS).
CONCLUSION: LIKE IN ADULTHOOD, PTSS MAY AFFECT BOTH ATTENTION-RELATED BEHAVIORAL AND BRAIN FUNCTIONING DURING ADOLESCENCE. GIVEN THE SUBSTANTIAL NEURODEVELOPMENT IN ADOLESCENCE, FUTURE WORK EXPLORING THE IMPACT OF PTSS ON ATTENTION-RELATED PROCESSES AND THEIR DEVELOPMENT IS NEEDED.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W21. CELL TYPE-SPECIFIC ROLES OF H3 SEROTONYLATION IN NORMAL AND DISRUPTED POSTNATAL BRAIN DEVELOPMENT

ASHLEY CUNNINGHAM*, JENNIFER CHAN, ELIZABETH BRINDLEY, MOLLY ESTILL, ERIC NESTLER, IAN MAZE

THE SEROTONERGIC (5HTERGIC) SYSTEM IS IMPLICATED IN A WIDE RANGE OF NEURODEVELOPMENTAL AND NEUROPSYCHIATRIC PHENOMENA. WHILE 5HT ACTIONS HAVE BEEN ASSUMED TO WORK EXCLUSIVELY THROUGH 5HT RECEPTORS AND THEIR SYNAPTIC EFFECTS, RECENT STUDIES ESTABLISHED THAT 5HT FORMS COVALENT BONDS WITH HISTONE H3 GLUTAMINE 5 (H3 SEROTONYLATION). H3 SEROTONYLATION REGULATES NORMAL PATTERNS OF NEUROPLASTICITY. HOWEVER, FUNCTIONAL ROLES FOR H3 SEROTONYLATION DURING POST-NATAL NEURODEVELOPMENT, A CRITICAL PERIOD OF NEUROPLASTICITY, HAVE LARGELY BEEN UNEXPLORED, AND THE IMPACT OF ENVIRONMENTAL STIMULI (ABERRANT OR OTHERWISE) ON THIS MODIFICATION DURING EARLY LIFE REMAINS UNKNOWN. INTERESTINGLY, WE IDENTIFIED REGION- AND DEVELOPMENTAL-DEPENDENT ABUNDANCE OF H3 SEROTONYLATION. WE USED FANS-COUPLED CUT AND RUN TO PROFILE THE CELL TYPE-SPECIFIC DEVELOPMENTAL LANDSCAPE OF THE MOUSE PREFRONTAL CORTEX (PFC) A BRAIN REGION THAT RECEIVES RECIPROCAL PROJECTIONS FROM THE DORSAL RAPHE NUCLEUS (DRN), WHICH INFLUENCES CORTICAL 5HT RELEASE. WE FOUND THAT AT POSTNATAL DAYS 10, 21, AND 70, THERE WAS CELL-TYPE SPECIFIC GENOMIC DISTRIBUTION OF H3 SEROTONYLATION IN THE MALE AND FEMALE PFC. IMPORTANTLY, WE FIND THAT EXPOSURE TO EARLY LIFE STRESS PERTURBS NORMAL GENOMIC ENRICHMENT OF H3 SEROTONYLATION IN A TEMPORAL- AND CELL TYPE-SPECIFIC MANNER. WE USED FANS-COUPLED RNA SEQUENCING AND MULTI-OMIC INTEGRATION TO ELUCIDATE THE CAUSAL RELATIONSHIP OF THIS NOVEL HISTONE MODIFICATION ON GENE EXPRESSION REGULATION. OVERALL, WE PROVIDE NOVEL INSIGHT INTO HOW H3 SEROTONYLATION REGULATES NEURODEVELOPMENT AND THE MECHANISMS BY WHICH DISRUPTIONS TO THIS POSTTRANSLATIONAL MODIFICATION CAUSE ABERRANT PATHOPHYSIOLOGICAL STATES.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W22. SEX-SPECIFIC EFFECTS OF PSYCHEDELIC DRUG ADMINISTRATION ON THREAT RESPONDING AND REACTIVITY WITHIN THE PARAVENTRICULAR NUCLEUS OF THE HYPOTHALAMUS

DEVIN EFFINGER*, JESSICA HOFFMAN, SARAH MOTT, SEMA QAUDIR, CHRISTIAN ROLLISON, DANIEL TOEDT, MARGARET HIGH, CLYDE HODGE, MELISSA HERMAN

PSYCHEDELICS HAVE EXPERIENCED RENEWED INTEREST FOLLOWING STUDIES SUGGESTING RAPID-ACTING AND LONG-LASTING THERAPEUTIC EFFECTS IN PATIENTS WITH AFFECTIVE PSYCHIATRIC DISORDERS. WHILE CLINICAL RESULTS LOOK PROMISING, THE CIRCUIT-LEVEL NEUROBIOLOGICAL MECHANISMS UNDERLYING ACUTE AND PROLONGED EFFECTS REMAIN UNCLEAR. MANY PSYCHIATRIC DISORDERS INVOLVE DYSFUNCTION OF THE HYPOTHALAMIC-PITUITARY-ADRENAL (HPA) AXIS. THE PARAVENTRICULAR NUCLEUS OF THE HYPOTHALAMUS (PVN) IS A KEY REGION WITHIN THE HPA AXIS ORCHESTRATING THE NEURAL AND ENDOCRINE STRESS RESPONSE. HERE, WE AIMED TO TEST HOW A SINGLE ADMINISTRATION OF PSILOCIN, THE PSYCHOACTIVE METABOLITE OF PSILOCYBIN, ALTERS REACTIVITY OF THE PVN IN SPRAGUE DAWLEY RATS. FIRST, TO TEST HOW PSILOCIN (2 MG/KG, S.C.) ALTERS BASAL ACTIVITY IN THE PVN, C-FOS EXPRESSION WAS MEASURED. PSILOCIN INCREASED C-FOS EXPRESSION AS COMPARED TO VEHICLE CONTROL IN MALES ($T(8)=2.603$, $P=0.03$) AND FEMALES ($T(8)=2.324$, $P=0.04$). NEXT, UTILIZING FIBER PHOTOMETRY WITH AN AVERSIVE AIR PUFF STIMULUS, WE FOUND THAT PSILOCIN (2 MG/KG, S.C.) PRODUCED AN INCREASE IN PVN REACTIVITY ($\Delta F/F$) FOLLOWING AIR PUFF COMPARED TO VEHICLE CONTROL IN MALES ($T(11)=2.31$, $P=0.04$) BUT NOT FEMALES. PVN REACTIVITY WAS RESTORED AT 2- AND 7-DAYS POST-INJECTION WITH NO DIFFERENCES BETWEEN GROUPS. FURTHER ANALYSIS FOUND THAT PSILOCIN INDUCED INCREASES IN MALES WERE DRIVEN BY ANIMALS EMPLOYING AN ACTIVE THREAT RESPONDING STRATEGY TO THE AIR-PUFF AT BASELINE. DARTING BEHAVIOR WAS ANALYZED, ASSESSING VELOCITY FOLLOWING AIR-PUFF. AT BASELINE, NO DIFFERENCES WERE SEEN BETWEEN GROUPS, HOWEVER FOLLOWING INJECTION PSILOCIN TREATED MALES SHOWED A SIGNIFICANT REDUCTION IN SPEED (2-WAY ANOVA: $F_{TREATMENT}(1,16)=10.05$, $P=0.005$) COMPARED TO VEHICLE CONTROL. OVERALL, THESE DATA PROVIDE NEW INFORMATION ON SEX-SPECIFIC EFFECTS OF PSILOCIN ON PVN REACTIVITY AND THREAT RESPONDING.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W23. NEURAL MECHANISMS OF AFFECTIVE STATES IN THE PRIMATE BRAIN

DAVIDE FOLLONI*, FREDERIC STOLL, PETER RUDEBECK

DETERMINING HOW FLUCTUATIONS IN CONTEXT CONTINGENCIES REGULATE OUR AFFECTIVE STATES IS KEY TO UNDERSTAND THE ROLE OF THE ENVIRONMENT ON THE ETIOLOGY AND PREVENTION OF MOOD DISORDERS LIKE MAJOR DEPRESSIVE DISORDER (MDD). THE NEURAL MECHANISMS OF MDD ARE, HOWEVER, STILL POORLY UNDERSTOOD. DEPRESSED PATIENTS QUICKLY RECOVER AFTER DEEP BRAIN STIMULATION IN THE SUBGENUAL ANTERIOR CINGULATE CORTEX (SACC) BUT IT IS STILL UNCLEAR WHY THIS THERAPEUTIC EFFECT HAPPENS AND, CRUCIALLY, WHAT IS THE ROLE OF SACC CIRCUITS. HERE WE INVESTIGATED HOW SACC AND A SET OF INTERCONNECTED AREAS REPRESENT CHOICES AND OUTCOMES IN A REWARD-GUIDED LEARNING WITH CONTEXT MANIPULATION.
MACAQUE MONKEYS PERFORMED A THREE-ARMED BANDIT TASK WITH TRANSITIONS ACROSS MULTIPLE VALUE CONTEXTS FOR FLUID REWARD WHILE NEURAL ACTIVITY WAS RECORDED FROM SACC, AMYGDALA, STRIATUM, INSULA AND VENTROLATERAL PREFRONTAL CORTEX (VLPFC). SIMULTANEOUS AUTONOMIC ACTIVITY WAS ALSO RECORDED. MONKEYS LEARNED CHOICE-OUTCOME CONTINGENCIES IN ONE CONTEXT AND THEN USED THEM TO GUIDE THEIR BEHAVIOR AS THEY TRANSITIONED AMONG OTHER VALUE CONTEXTS.
CONTEXT TRANSITION AND THEIR SPECIFIC ORDER AFFECTED ANIMALS'. NEURONS IN SACC SHOWED SEPARATE ENCODING SIGNALS ASSOCIATED WITH THE TIMING OF CHOICE AND WITH REWARD ONSET. SIMILAR SIGNALS WERE ENCODED ALSO IN AREAS WITHIN THE PROXIMAL SACC: AMYGDALA, STRIATUM, INSULA AND VLPFC. CONCOMITANT HEART RATE SIMILARLY CHANGED ACROSS THE DIFFERENT VALUE CONTEXTS AND WAS MODULATED BY THEIR TRANSITION ORDERS.
CONTEXT CONTINGENCIES HAVE A CRUCIAL IMPACT ON OUR MOOD AND SACC REPRESENT A KEY HUB FOR TREATMENT OF MOOD-RELATED DISORDERS. HERE WE SHOW THAT DIFFERENT VALUE CONTEXTS AFFECT MONKEYS' BEHAVIOR AND THEIR AUTONOMIC STATES DIFFERENTLY. WE ALSO SHOW THAT ACTIVITY IN SACC AND WITHIN INTERCONNECTED AREAS IN LIMBIC AND PREFRONTAL CORTEX ENCODE BOTH CHOICES AND THE OUTCOME RESULTING FROM THESE DECISIONS.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W24. INTERPEDUNCULAR NUCLEUS CIRCUITRY IN INNATE AND ADAPTIVE DEFENSIVE LEARNING

ELORA WILLIAMS*, BEN O'MEARA, HANNAH JACOBS, MIRANDA KOLB, ANDREW TAPPER, SUSANNA MOLAS

A CORE ASPECT AMONG THE CLINICAL HETEROGENEITY OF ANXIETY DISORDERS IS THE ABNORMAL PROCESSING OF THREAT-RELATED INFORMATION AND THE IMPAIRMENT IN MODIFYING THE DEFENSIVE RESPONSE IN THE ABSENCE OF REAL THREAT. UNDERSTANDING THE NEURONAL UNDERPINNINGS OF THESE INNATE DEFENSIVE RESPONSES TO POTENTIAL THREATS AND HOW THEY ARE DYSREGULATED IN ANXIETY DISORDERS IS FUNDAMENTAL FOR IMPROVING THERAPEUTIC STRATEGIES. EXPOSURE TO AN OVERHEAD DARK VISUAL LOOMING STIMULUS (VLS) ELICITS INNATE DEFENSE RESPONSES ACROSS MULTIPLE SPECIES. REPEATED EXPOSURES TO THESE STIMULI, WITHOUT EXPERIENCING A NEGATIVE OUTCOME, RESULT IN LEARNING TO ALTER THESE DEFENSIVE BEHAVIORS. THE INTERPEDUNCULAR NUCLEUS (IPN), AN INHIBITORY REGION THAT IS HIGHLY ENRICHED WITH GABAERGIC NEURONS, HAS BEEN IMPLICATED IN FEAR-RELATED BEHAVIORS. THE IPN RECEIVES INFORMATION FROM THE MEDIAL HABENULA AND SENDS PROJECTIONS TO REGIONS INVOLVED IN AFFECTIVE BEHAVIORS INCLUDING THE THE LATERODORSAL TEGMENTAL NUCLEUS (LDTG), RAPHE NUCLEUS AND THE LOCUS COERULEUS (LC). HOWEVER, THE CELLULAR AND CIRCUIT MECHANISMS WITHIN THE IPN-CONNECTED NETWORKS REGULATING ANXIETY AND INNATE DEFENSIVE RESPONSES ARE STILL LARGELY UNKNOWN.

WE USED THE VLS PARADIGM TO ASSESS BEHAVIOR AND NEURONAL MECHANISMS UNDERLYING THREAT PROCESSING AND HABITUATION IN MICE. WE FIRST ASSESSED BEHAVIOR DURING SESSIONS WHERE 3-7 LOOMS WERE DISPLAYED WHILE THE ANIMAL WAS EXPLORING THE ARENA, WITH A MINIMUM INTER-LOOM-INTERVAL OF 60S. THESE VLS SESSIONS WERE REPEATED FOR 3 CONSECUTIVE DAYS. WE THEN MEASURED IPN GABAERGIC NEURONAL RESPONSES TO THE VLS USING IN VIVO FIBER PHOTOMETRY. FINALLY, TO FUNCTIONALLY ASSESS THE ROLE OF THESE NEURONS IN DEFENSIVE BEHAVIORS, WE UTILIZED OPTOGENETIC METHODS DURING VLS SESSIONS. WE FOUND THAT MICE LEARN TO ADJUST THEIR BEHAVIORS AFTER MULTIPLE EXPOSURES TO VLS, MANIFESTED BY A DECREASE IN TIME SPENT INSIDE THE NEST AND CHANGE IN SPEED GIVEN THE LOOM. THIS ADAPTIVE PROCESS IS ALSO ASSOCIATED WITH PROGRESSIVE REDUCTIONS IN VLS-EVOKED ACTIVATION OF GABAERGIC NEURONAL ACTIVITY. THE OPTOGENETIC SILENCING OF THE GABAERGIC NEURONS DURING VLS PRESENTATION LED TO REDUCED TIME SPENT IN NEST, WHEREAS OPTOGENTIC ACTIVATION RESULTED IN INCREASED FREEZING, INDICATING THAT THESE NEURONS ARE NECESSARY FOR THREAT PROCESSING AND ADAPTIVE DEFENSIVE LEARNING.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W25. PERIRHINAL CORTEX HYPOACTIVITY UNDERLIES SPATIAL LEARNING DEFICITS IN THE SCN2A AUTISM MOUSE MODEL

RACHEL KEITH*, JORDAN MEZA, YIMING SHEN, PRISCILA CORREA ANTONELLO, AYSHA HAMEED, MICHELLE ANTOINE

AUTISM SPECTRUM DISORDER (ASD) IS A NEURODEVELOPMENTAL DISORDER WHICH OFTEN RESULTS IN COGNITIVE DEFICITS. ONE ASPECT OF COGNITION THAT IS COMMONLY IMPAIRED IN ASD IS SPATIAL LEARNING AND MEMORY, WHICH RESULTS IN STRUGGLES WITH DAILY NAVIGATION AND OBJECT PLACEMENT RECALL. MOUSE MODELS OF ASD OFTEN RECAPITULATE SPATIAL LEARNING AND MEMORY DEFICITS, PERMITTING AN ASSESSMENT OF THE NEUROBIOLOGICAL UNDERPINNING OF THESE IMPAIRMENTS. SCN2A, FMRI, OR CDKL5 GENE MUTATIONS ARE ALL ASSOCIATED WITH ASD, AND MOUSE MODELS OF THESE MUTATIONS DISPLAY SPATIAL LEARNING DEFICITS. WHILE THE HIPPOCAMPUS IS THE REGION TRADITIONALLY ASSOCIATED WITH SPATIAL NAVIGATION, SURPRISINGLY, WE FOUND THE PERIRHINAL CORTEX, NOT THE HIPPOCAMPUS AS EXPECTED, MAY BE A CENTRAL SITE OF DYSFUNCTION.

USING THE BARNES MAZE, WE CONFIRMED IMPAIRED SPATIAL LEARNING IN SCN2A+/-, FMRI KNOCKOUT, AND CDKL5 KNOCKOUT MICE. WHOLE-BRAIN IMAGING IN SCN2A+/-;FOS-EGFP MICE REVEALED REDUCED NEURAL ACTIVITY IN SEVERAL CORTICAL AREAS BUT, CRUCIALLY, NOT THE HIPPOCAMPUS. CONDITIONAL GENETIC REDUCTION OF SCN2A IN THE HIPPOCAMPUS DID NOT IMPACT SPATIAL LEARNING OR LONG-TERM POTENTIATION (LTP), A CELLULAR CORRELATE FOR MEMORY ENCODING. BY CONTRAST, MICE WITH SCN2A REDUCTIONS IN THE CORTEX MIRRORED THE NEURAL HYPOACTIVITY SEEN IN SCN2A+/- MICE, RESULTING IN DEFICITS IN SPATIAL LEARNING AND LTP. FOCUSING ON SCN2A REDUCTION IN THE PERIRHINAL CORTEX, WE FOUND THIS REGION CRUCIAL FOR SPATIAL LEARNING DEFICITS. VIRAL-MEDIATED CRE KNOCKDOWN OF SCN2A IN THE PERIRHINAL CORTEX IMPAIRED SPATIAL LEARNING, WHILE CHEMOGENETIC PYRAMIDAL NEURON ACTIVATION RESCUED LEARNING. ADDITIONALLY, WE LINKED PERIRHINAL HYPOACTIVITY TO SPATIAL DEFICITS IN THE FMRI AND CDKL5 KNOCKOUT ASD MOUSE MODELS. THIS STUDY UNDERSCORES THE CRITICAL ROLE OF THE PERIRHINAL CORTEX IN ASD-RELATED SPATIAL LEARNING DEFICITS.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W26. VALENCE-SPECIFIC GATING OF BEHAVIORAL FLEXIBILITY BY MEDIAL PREFRONTAL CORTEX PROJECTIONS TO THE VENTRAL TEGMENTAL AREA

MERRIDEE LEFNER*, BITA MOGHADDAM

IN ORDER TO EFFICIENTLY TRAVERSE AN ENVIRONMENT, ONE MUST LEARN TO DISTINGUISH BETWEEN CUES THAT PREDICT DIFFERENT OUTCOMES. IN A DYNAMIC ENVIRONMENT WHERE CUES PREDICTING REWARDING OR AVERSIVE CONSEQUENCES UNEXPECTEDLY CHANGE, IT IS ADAPTIVE TO FLEXIBLY UPDATE BEHAVIOR. IMPAIRMENTS IN THE ABILITY TO APPROPRIATELY RESPOND TO CUES ACCORDING TO THE OUTCOME ARE EVIDENT IN A NUMBER OF PSYCHIATRIC DISORDERS. BOTH DOPAMINE AND Γ-AMINOBUTYRIC ACID (GABA) NEURONS IN THE VENTRAL TEGMENTAL AREA (VTA) ARE INVOLVED IN ASSOCIATIVE LEARNING, AND THE MEDIAL PREFRONTAL CORTEX (MPFC) IS NECESSARY FOR BEHAVIORAL FLEXIBILITY. WE HYPOTHESIZE THAT RESPONDING TO CHANGES IN LEARNED ASSOCIATIONS IS VALENCE-SPECIFIC, AND IS MODULATED BY MPFC PROJECTIONS TO THE VTA. MALE AND FEMALE RATS WERE TRAINED ON A FLEXIBLE CONTINGENCY LEARNING (FCL) TASK IN WHICH THREE DISTINCT AUDITORY CUES ARE PAIRED WITH EITHER AN APPETITIVE OUTCOME (SUGAR PELLET REWARD), AN AVERSIVE OUTCOME (MILD FOOT SHOCK), OR NO OUTCOME. AFTER INITIAL LEARNING, THE APPETITIVE AND AVERSIVE OUTCOMES REVERSE SUCH THAT THE CUE PREVIOUSLY PAIRED WITH A SHOCK WILL INSTEAD PRECEDE REWARD DELIVERY AND VICE VERSA. FIBER PHOTOMETRY RECORDINGS WERE PERFORMED TO MEASURE CHANGES IN CALCIUM ACTIVITY OF VTA DOPAMINE AND GABA NEURONS THROUGHOUT FCL. OUR FINDINGS INDICATE A DISSOCIATION BETWEEN VTA CELL GROUPS: THE DOPAMINE POPULATION INCREASES CALCIUM ACTIVITY IN RESPONSE TO INITIAL LEARNING AND REVERSAL OF REWARD ASSOCIATIONS, WHEREAS THE GABA POPULATION ENCODES INITIAL LEARNING AND REVERSAL OF BOTH APPETITIVE AND AVERSIVE ASSOCIATIONS. WE USED PATHWAY-SPECIFIC CHEMOGENETIC INHIBITION TO PROBE WHETHER MPFC-VTA PROJECTIONS MODULATED FLEXIBLE RESPONDING TO THE REVERSAL OF CONTINGENCIES IN FCL. INHIBITING THE MPFC-VTA PATHWAY ENHANCED CONDITIONED RESPONDING SELECTIVELY TO THE APPETITIVE-PAIRED CUE THAT WAS PREVIOUSLY ASSOCIATED WITH THE AVERSIVE OUTCOME. TAKEN TOGETHER, OUR DATA HIGHLIGHTS A ROLE FOR TOP-DOWN REGULATION OF FLEXIBLE LEARNING.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W27. THALAMIC INTERACTION OF BASAL GANGLIA AND CEREBELLAR CIRCUITS DURING MOTOR LEARNING

RICHARD ROTH*, FUU-JIUN HWANG, MICHAEL MUNIAK, CHARLES HUANG, YUE SUN, TIANYI MAO, JUN DING

THE ABILITY TO CONTROL MOVEMENT AND TO REFINE AND LEARN NEW MOTOR SKILLS IS ONE OF THE FUNDAMENTAL FUNCTIONS OF THE BRAIN. THE BASAL GANGLIA (BG) AND THE CEREBELLUM (CB) ARE TWO KEY BRAIN REGIONS INVOLVED IN CONTROLLING MOVEMENT, AND NEURONAL PLASTICITY WITHIN THESE TWO REGIONS UNDERLIES THE ACQUISITION OF NEW MOTOR SKILLS. HOWEVER, HOW THESE TWO CRITICAL MOTOR REGIONS INTERACT AND ORCHESTRATE TOGETHER TO PRODUCE A COHESIVE MOTOR OUTPUT REMAINS POORLY UNDERSTOOD. HERE, WE USED AN INTERSECTIONAL VIRAL TRACING APPROACH TO IDENTIFY NEURONS IN THE MOTOR THALAMUS THAT RECEIVE INPUTS FROM BG AND CB AND FOUND THAT A SUBSET OF NEURONS IN VM AND VAL RECEIVE CONVERGING BG AND CB INPUTS. USING SLICE ELECTROPHYSIOLOGY IN COMBINATION WITH OPTOGENETIC ACTIVATION OF BG AND CB PROJECTIONS WE SHOW THAT THESE THALAMIC NEURONS RECEIVE FUNCTIONAL INHIBITORY INPUTS FROM THE BG AND EXCITATORY INPUTS FROM THE CB. MOREOVER, USING CHEMO- AND OPTOGENETIC SILENCING, WE DEMONSTRATE THE ROLE OF THESE THALAMIC NEURONS AND THEIR INPUTS IN MOTOR LEARNING. LASTLY, USING IN VIVO TWO-PHOTON CALCIUM IMAGING THROUGH AN IMPLANTED GRIN LENS IN THE MOTOR THALAMUS, WE MEASURED NEURONAL ACTIVITY IN MICE OVER THE COURSE OF MOTOR LEARNING AND FOUND THAT NEURONS IN VM SHOW DISTINCT MOVEMENT RELATED ACTIVITY PATTERNS. THESE RESULTS INDICATE THAT NEURONS IN THE MOTOR THALAMUS RECEIVE CONVERGING INPUT FROM BG AND CB AND MAY PLAY AN IMPORTANT ROLE IN INTEGRATING MOVEMENT SIGNALS DURING MOTOR LEARNING.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W28. CORTICOFUGAL CONTROL OVER REFLEXIVE VISUOMOTOR BEHAVIOR IN MICE

GAL ATLAN*, MASSIMO SCANZIANI

MANY EVOLUTIONARY-CONSERVED INNATE BEHAVIORS ARE GATED BY SUBCORTICAL STRUCTURES VIA DIRECT INPUT FROM THE SENSORY ORGANS. THE MAMMALIAN NEOCORTEX, WIDELY CONSIDERED A PINNACLE OF BRAIN EVOLUTION, PROVIDES AN ADDITIONAL STREAM OF INFORMATION TO THESE ANCESTRAL SUBCORTICAL CENTERS VIA CORTICOFUGAL PROJECTIONS. HOWEVER, MANY BEHAVIORS DO NOT DEPEND ON NEOCORTEX, AND NUMEROUS EVOLUTIONARY-SUCCESSFUL SPECIES LACK CORTEX ALTOGETHER. THUS, THE ADVANTAGE CONFERRED BY CORTICOFUGAL PATHWAYS REMAINS UNCLEAR.

EVOLUTIONARY-CONSERVED VISUOMOTOR TRANSFORMATIONS UNDERLIE CRUCIAL INNATE CAPABILITIES SUCH AS MAINTAINING HEADING, HUNTING, AND ESCAPE. THE OPTOLOCOMOTOR REFLEX (OLR) IS A FUNDAMENTAL INNATE RESPONSE THAT MAINTAINS HEADING DURING LOCOMOTION, BASED ON CHANGES IN THE VISUAL ENVIRONMENT. ORIENTING REFLEXES LIKE OLR HAVE BEEN STUDIED IN A WIDE RANGE OF SPECIES, INCLUDING FLIES AND VERTEBRATES THAT DO NOT HAVE A NEOCORTEX. THIS SUGGESTS THAT OLR RELIES ON EVOLUTIONARY-CONSERVED NEURAL MECHANISMS AND THAT THE CONTRIBUTION OF NEOCORTEX TO OLR MAY BE LIMITED, AS IS THE CASE FOR MANY OTHER INNATE BEHAVIORS.

WE SHOW THAT THE OLR CAN BE EVOKED IN FREELY MOVING MICE THROUGH A FULL-FIELD HORIZONTAL ROTATION OF THEIR VISUAL ENVIRONMENT. THIS IS ACHIEVED IN A CLOSED-LOOP MANNER, TRIGGERED BY THE RUNNING OF THE ANIMAL. TO MAINTAIN HEADING, THE MICE PERFORM CORRECTIVE TURNS IN THE DIRECTION OF THE MOTION OF THE VISUAL STIMULUS. SIMILARLY, THE OLR CAN BE TRIGGERED IN HEAD-FIXED MICE RUNNING ON A BALL. SURPRISINGLY, LESIONS AS WELL AS ACUTE SILENCING OF VISUAL CORTEX GREATLY REDUCE THE GAIN OF THE OLR IN A LATERALIZED MANNER. DRIVEN BY THIS FINDING, WE UTILIZE IN-VIVO MULTIUNIT RECORDINGS IN VISUAL CORTEX AND ITS DOWNSTREAM TARGETS TO IDENTIFY AND CHARACTERIZE THE CORTICOFUGAL CIRCUIT OVERSEEING OLR.

THE ABILITY TO INTEGRATE ENVIRONMENTAL CUES AND ACT UPON THEM IS A FUNDAMENTAL ASPECT OF ADAPTIVE BEHAVIOR. HERE, WE FIND THAT VISUAL CORTEX, VIA CORTICOFUGAL PROJECTIONS, PLAYS AN INSTRUCTIVE ROLE IN CONTROLLING A BASIC, EVOLUTIONARY-CONSERVED INNATE BEHAVIOR.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W29. CHOLINERGIC VENTRAL PALLIDUM CELLS AND THEIR ROLE IN CUE- AND REWARD- RELATED MOTIVATION

ELIZABETH BIEN*, ALYSSA DILEO, SILVIA NAVARRO, CONSTANCE TAZELAAR, KYLE SMITH

THE VENTRAL PALLIDUM (VP), A BASAL FOREBRAIN REGION, HAS BEEN IMPLICATED IN MOTIVATION AND HEDONICS FOR REWARDS. FOR EXAMPLE, INHIBITION OF THE VP WAS FOUND TO DISRUPT THE ACQUISITION OF INCENTIVE SALIENCE TO CUES THAT PREDICT FOOD REWARDS, SPECIFICALLY WITH RESPECT TO SIGN-TRACKING BEHAVIOR IN WHICH CUES ARE MOTIVATIONALLY PURSUED. ALSO, DAMAGE TO THE VP HAS BEEN FOUND TO IMPAIR MOTIVATION TO CONSUME FOOD REWARDS. THE VP IS A HETEROGENOUS COLLECTION OF DIFFERENT CELL TYPES, AND IT NEEDS TO BE DETERMINED WHICH CELL TYPE WITHIN THIS COLLECTION IS RESPONSIBLE FOR THESE REWARD FUNCTIONS. GIVEN THE ROLE OF BASAL FOREBRAIN ACETYLCHOLINE CELLS IN ATTENTION AND THE PRESENCE OF CHOLINERGIC CELLS IN THE VP, WE SOUGHT TO TEST THEIR INVOLVEMENT. WE USED CHEMOGENETICS AND TRANSGENIC CHAT-CRE RATS TO INHIBIT CHOLINERGIC VP CELLS DURING SIGN-TRACKING ACQUISITION AND REWARD APPROACH. WE DID NOT FIND SIGNIFICANT DIFFERENCES IN TRADITIONAL SIGN-TRACKING MEASUREMENTS WHEN WE COMPARED THE DREADD GROUP TO THE CONTROL GROUP, BUT WE DID FIND GROUP DIFFERENCES IN THAT THE DREADD GROUP TOOK SIGNIFICANTLY LONGER TO REACH SIGN-TRACKING STATUS WHEN COMPARED TO THE CONTROL GROUP. WE ALSO FOUND REWARD-RELATED GROUP DIFFERENCES IN THAT THE DREADD GROUP ENTERED THE MAGAZINE SIGNIFICANTLY LESS THAN THE CONTROL GROUP DURING THE REWARD PERIOD. TOGETHER, THIS EXPERIMENT SHOWS THAT CHOLINERGIC VP CELLS CONTRIBUTE TO CUE- AND REWARD- RELATED ASPECTS OF FOOD MOTIVATION. THIS FINDING SUPPORTS PRIOR WORK ON THE BASAL FOREBRAIN CHOLINERGIC SYSTEM IN MOTIVATION AND SHOWS THAT CHOLINERGIC CELLS IN THE VP MAY BE KEY TO THE OVERALL FUNCTION OF THE VP.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W30. VTA GABA NEURON ACTIVITY ENCODES SALIENCE, REINFORCES ACTIONS, AND SHAPES STRIATAL DOPAMINE SIGNALING

MARGARET STELZNER*, AMY WOLFF, BENJAMIN SAUNDERS

THE VENTRAL TEGMENTAL AREA (VTA), PLAYS A CENTRAL ROLE IN CUE-DRIVEN BEHAVIOR VIA ITS TWO MAIN NEURONAL SUBTYPES: DOPAMINE (DA) AND GABA. GABA NEURONS SYNAPSE DIRECTLY ONTO LOCAL DA NEURONS AND MODULATE DA TRANSMISSION. VTA DA NEURONS ARE WIDELY THOUGHT TO ENCODE REWARD-RELATED LEARNING AND PREDICTION ERRORS. THE IN VIVO ACTIVITY PROFILE OF VTA GABA NEURONS HOWEVER, IS NOT WELL UNDERSTOOD. TO INVESTIGATE THIS, WE VIRALLY TARGETED VTA GABA NEURONS IN WILDTYPE RATS BY DELIVERING AN ADENO-ASSOCIATED VIRUS WITH CRE EXPRESSED UNDER THE GADI PROMOTER. A CRE-DEPENDENT FLUORESCENT CA2+ REPORTER (GCAMP8F) WAS THEN EXPRESSED IN GADI+ NEURONS, TO RECORD GABAERGIC ACTIVITY. IN A SEPARATE GROUP OF ANIMALS WE TARGETED VTA DA NEURONS WITH CRE-DEPENDENT GCAMP8F IN TH-CRE RATS. WE THEN PAIRED DISTINCT AUDITORY CUES WITH EITHER REWARD OR A FOOT SHOCK WHILE RECORDING IN THE VTA. OUR RESULTS SHOW THAT VTA GABA NEURONS ARE ACTIVATED BY BOTH POSITIVELY AND NEGATIVELY VALENCED ASSOCIATIONS (REPRESENTING SALIENCE) WHILE DA NEURONS ARE ACTIVATED BY POSITIVE VALENCE AND INHIBITED BY NEGATIVE VALENCE (REPRESENTING VALUE). THIS SUGGESTS THAT, RATHER THAN OPPOSING VTA DA NEURONS IN FUNCTION, VTA GABA NEURONS CONTRIBUTE A UNIQUE SIGNAL THAT MAY INTEGRATE DIFFERENT MOTIVATIONAL PROCESSES DURING LEARNING. LOCAL SYNAPSES ONTO DA NEURONS DO NOT FULLY EXPLAIN THIS PHENOMENON. THUS, IT IS LIKELY THAT DISTAL PROJECTIONS ADD COMPLEXITY TO THE ROLE OF VTA GABA NEURONS. IN ONGOING EXPERIMENTS, WE ARE USING A DUAL OPTOGENETIC AND FIBER PHOTOMETRY PREPARATION TO SIMULTANEOUSLY STIMULATE OR INHIBIT VTA GABA NEURONS WHILE RECORDING DOWNSTREAM DA WITH FLUORESCENT DA REPORTER, DLIGHT. INTRIGUINGLY WE FIND THAT RATS WILL WORK FOR OPTOGENETIC INHIBITION OR EXCITATION OF VTA GABA NEURONS, WHICH RESULT IN OPPOSITE FLUCTUATIONS IN STRIATAL DA LEVELS. TOGETHER, OUR RESULTS HIGHLIGHT THE COMPLEX ROLE OF VTA GABA NEURONS IN MOTIVATED BEHAVIOR AND EMPHASIZE THE ROLE THEY PLAY IN REINFORCEMENT VIA VTA MICROCIRCUITRY.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W31. SCHEMA CELL FORMATION IN ORBITOFRONTAL CORTEX IS SUPPRESSED BY HIPPOCAMPAL OUTPUT

WENHUI ZONG*, JINGFENG ZHOU, MATTHEW GARDNER, ZHEWEI ZHANG, KAUÊ COSTA, GEOFFREY SCHOENBAUM

BOTH ORBITOFRONTAL CORTEX (OFC) AND HIPPOCAMPUS (HC) ARE IMPLICATED IN THE FORMATION OF COGNITIVE MAPS AND THEIR GENERALIZATION INTO SCHEMAS. HOWEVER HOW THESE AREAS INTERACT IN SUPPORTING THIS FUNCTION REMAINS AN OPEN QUESTION, WITH SOME PROPOSALS SUPPORTING A SERIAL MODEL IN WHICH OFC DRAWS UPON TASK REPRESENTATIONS CREATED BY HC TO EXTRACT KEY BEHAVIORAL FEATURES AND OTHERS PROPOSING A PARALLEL MODEL IN WHICH BOTH REGIONS CONSTRUCT REPRESENTATIONS THAT HIGHLIGHT DIFFERENT TYPES OF INFORMATION. HERE WE TESTED BETWEEN THESE TWO MODELS BY ASKING HOW SCHEMA CORRELATES IN OFC WOULD BE AFFECTED BY INACTIVATION OF HC OUTPUT, AFTER LEARNING AND DURING TRANSFER ACROSS PROBLEMS. WE FOUND THE PREVALENCE AND CONTENT OF SCHEMA CORRELATES WERE UNAFFECTED BY INACTIVATION AFTER LEARNING, WHILE INACTIVATION DURING LEARNING ACCELERATED THEIR FORMATION. THESE RESULTS CONTRADICT A SERIAL MODEL AND FAVOR THE PROPOSAL THAT OFC AND HC OPERATE IN PARALLEL TO EXTRACT DIFFERENT FEATURES DEFINING COGNITIVE MAPS AND SCHEMAS.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W32. A SPECIAL ROLE FOR ANTERIOR CINGULATE CORTEX, BUT NOT ORBITOFRONTAL CORTEX OR BASOLATERAL AMYGDALA, IN CHOICES INVOLVING INFORMATION

VALERIA GONZALEZ*, SONYA A. ASHIKYAN, YIFAN ZHANG, ANNE RICKARD, JUAN LUIS ROMERO-SOSA, AARON BLAISDELL, ALICIA IZQUIERDO

HUMANS AND OTHER ANIMALS MAKE DECISIONS UNDER UNCERTAINTY. CHOOSING AN OPTION THAT PROVIDES INFORMATION CAN IMPROVE DECISION MAKING. HOWEVER, SUBJECTS OFTEN CHOOSE INFORMATION THAT DOES NOT INCREASE THE CHANCES OF OBTAINING REWARD. IN A PROCEDURE THAT PROMOTES SUCH PARADOXICAL CHOICE, ANIMALS CHOOSE BETWEEN TWO ALTERNATIVES: THE RICHER OPTION IS FOLLOWED BY A CUE THAT IS REWARDED 50% OF THE TIME (NO-INFO OPTION) AND THE LEANER OPTION IS FOLLOWED BY ONE OF TWO CUES, ONE ALWAYS REWARDED (100%), AND THE OTHER NEVER REWARDED, 0% (INFO OPTION). SINCE DECISIONS INVOLVE COMPARING THE SUBJECTIVE VALUE OF OPTIONS AFTER INTEGRATING ALL THEIR FEATURES PERHAPS INCLUDING INFORMATION VALUE, PREFERENCE FOR INFORMATION MAY RELY ON CORTICO-AMYGDALAR CIRCUITRY. TO TEST THIS, MALE AND FEMALE LONG-EVANS RATS WERE PREPARED WITH BILATERAL INHIBITORY DREADDS IN THE ANTERIOR CINGULATE CORTEX (ACC), ORBITOFRONTAL CORTEX (OFC), BASOLATERAL AMYGDALA (BLA), OR NULL VIRUS INFUSIONS AS A CONTROL. USING A COUNTERBALANCED DESIGN, WE INHIBITED THESE REGIONS AFTER STABLE PREFERENCE WAS ACQUIRED AND DURING LEARNING OF NEW INFO AND NO-INFO CUES. WE FOUND THAT INHIBITION OF ACC, BUT NOT OFC OR BLA, SELECTIVELY DESTABILIZED CHOICE PREFERENCE IN FEMALE RATS WITHOUT AFFECTING LATENCY TO CHOOSE OR THE RESPONSE RATE TO CUES. A LOGISTIC REGRESSION FIT REVEALED THAT THE PREVIOUS CHOICE STRONGLY PREDICTED PREFERENCE IN CONTROL ANIMALS, BUT NOT IN FEMALE RATS FOLLOWING ACC INHIBITION. BLA INHIBITION TENDED TO DECREASE THE LEARNING OF NEW CUES THAT SIGNALED THE INFO OPTION, BUT HAD NO EFFECT ON PREFERENCE. THE RESULTS REVEAL A CAUSAL, SEX-DEPENDENT ROLE FOR ACC IN DECISIONS INVOLVING INFORMATION.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W33. ROLE OF MEDIODORSAL THALAMIC INPUT TO DORSAL STRIATUM IN ACTION CONTROL

EMILY BALTZ*, CHRISTINA GREMEL

IT IS WELL-KNOWN THAT DORSAL MEDIAL STRIATUM (DMS) CONTRIBUTES TO GOAL-DIRECTED ACTION CONTROL. THE DORSAL STRIATUM RECEIVES INPUT FROM THE CORTEX AND THE THALAMUS. WHILE CORTICAL CONTRIBUTIONS TO ACTION CONTROL HAVE BEEN WELL-INVESTIGATED, THALAMIC INPUTS HAVE BEEN RELATIVELY LESS EXAMINED. ONE THALAMIC NUCLEUS THAT PROVIDES GLUTAMATERGIC INPUTS TO DMS, THE MEDIODORSAL THALAMUS (MD), HAS BEEN SHOWN TO BE IMPORTANT FOR OUTCOME DEVALUATION AND UNDERSTANDING ACTION-OUTCOME CONTINGENCIES. THIS SUGGESTS MD IS IMPORTANT FOR GOAL-DIRECTED BEHAVIOR THAT NECESSITATES USE OF RECENT EXPERIENCE TO MODIFY BEHAVIOR. IN ORDER TO INVESTIGATE THE ROLE OF MD-DMS PROJECTIONS IN CONTROLLING ACTIONS, WE FIRST PERFORMED FIBER PHOTOMETRY OF MD TERMINAL CALCIUM ACTIVITY IN STRIATUM. MICE LEARNED AN ACTION TASK WHERE THEY HAD TO HOLD A LEVER FOR A GIVEN DURATION CRITERIA OR LONGER IN ORDER TO RECEIVE A REWARD. WE INVESTIGATED PERI-EVENT CHANGES IN CALCIUM AND SAW PREDICTIVE MODULATION DEPENDING ON WHETHER OR NOT THE LEVER PRESS WAS GOING TO BE REWARDED. MODULATION WAS ESPECIALLY STRONG AT REWARD-RELATED EPOCHS WHERE ANIMALS MAY BE EVALUATING ACTION SUCCESS. TO INVESTIGATE WHETHER ACTION (LEVER PRESS DURATION) AND REWARD RELATED INFORMATION WAS INFLUENCING MD TERMINAL ACTIVITY, WE APPLIED A LINEAR MIXED EFFECT MODEL EXAMINING THE RELATIVE CONTRIBUTION OF ACTION AND REWARD TO THE CALCIUM ACTIVITY OBSERVED. WE FOUND THAT IN EARLY DAYS OF TRAINING, MD ACTIVITY REFLECTED PRIOR AND CURRENT LEVER PRESS DURATION INFORMATION. BECAUSE MD REPRESENTED ACTION-RELATED INFORMATION, WE HYPOTHESIZED THAT INHIBITING MD-DMS PROJECTIONS WOULD DISRUPT USE OF ACTION EXPERIENCE TO GUIDE ONGOING BEHAVIOR. WE USED A DUAL VIRAL STRATEGY TO TARGET CHEMOGENETIC INHIBITORY VIRUS TO MD NEURONS PROJECTING TO DMS. INHIBITION OF MD-DMS DID NOT LEAD TO CHANGES IN THE TOTAL LEVER PRESSES OR SUCCESSFUL LEVER PRESSES, BUT DID PRODUCE CHANGES IN THE USE OF THE LAST LEVER PRESS DURATION TO GUIDE THE SUBSEQUENT PRESS. A LINEAR MIXED EFFECT MODEL ANALYSIS SHOWED ANIMALS WITH ATTENUATED MD-DMS ACTIVITY RELIED ON REPETITIVE BEHAVIOR DURING EARLY LEARNING. THIS SUGGESTS MD-DMS FUNCTIONS TO SUPPORT EARLY GOAL-DIRECTED ACTION LEARNING. OVERALL, THIS WORK PROVIDES INITIAL EVIDENCE FOR THE IMPORTANCE OF THE MD-DMS PATHWAY IN GOAL-DIRECTED ACTION CONTROL.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W34. ORBITOFRONTAL ENSEMBLES INTEGRATE TASTE, MOVEMENT, AND REWARD PREDICTIONS DURING LEARNING

EVAN HART*, LISETTE BAHENA, GEOFFREY SCHOENBAUM

LEARNING THE MEANING OF CUES IS NECESSARY FOR SURVIVAL. HUMANS AND OTHER ANIMALS LEARN WHERE AND HOW TO ACQUIRE FOOD, FIND MATES, OR AVOID PREDATORS. CUES SIGNAL MANY ASPECTS OF SURVIVAL BEHAVIOR. ROAD SIGNS TELL US WHERE TO TURN TO ACQUIRE FOOD (MOVEMENT DIRECTION), WHICH SPECIFIC FOOD IS OFFERED (E.G., ICE CREAM VS FROZEN YOGURT), AS WELL AS WHETHER FOOD IS OFFERED AT ALL (REWARD PREDICTION/VALUE). WE ALSO DISCRIMINATE CUES WHICH SHARE THE SAME MEANING (SENSORY CUE IDENTITY - E.G., A RED OCTAGON AND A RED LIGHT BOTH MEAN STOP). THE INTEGRATED REPRESENTATION OF THESE FEATURES OF THE BEHAVIORAL LANDSCAPE HAS BEEN CALLED A "COGNITIVE MAP", THE CONSTRUCTION AND USE OF WHICH CONFER THE ABILITY TO MAKE PREDICTIONS BASED ON DIRECT EXPERIENCE AND TO MAKE INFERENCES IN NOVEL SITUATIONS. BUT HOW IS THIS KIND OF INFORMATION ACQUIRED, INTEGRATED, AND USED - WHAT NEURAL CIRCUITS UNDERLY COGNITIVE MAP FORMATION? THE ORBITOFRONTAL CORTEX (OFC) IS THOUGHT TO BE IMPORTANT FOR COGNITIVE MAP FORMATION, PARTICULARLY GENERATING REWARD PREDICTIONS. GENERALLY THESE STUDIES WERE PERFORMED IN HIGHLY TRAINED SUBJECTS AND NOT DURING LEARNING, WHEN MAPS ARE FORMED, LEAVING UNANSWERED QUESTIONS ABOUT HOW THE OFC FORMS INTEGRATED REPRESENTATIONS AND HOW THEIR ACTIVITY EVOLVES TO HIGHLIGHT INFORMATION OF BIOLOGICAL RELEVANCE. I RECORDED OFC ENSEMBLE SPIKING ACTIVITY IN RATS DURING THE LEARNING OF A TASK THAT ALLOWED ME TO DISSOCIATE SENSORY FROM MOTOR, TASTE, AND REWARD ENCODING. DURING LEARNING, OFC ENSEMBLE ACTIVITY EVOLVED TOWARD SIMPLER REPRESENTATIONS OF REWARD AND MOVEMENT PREDICTION. ONCE LEARNING HAD OCCURRED, INFORMATION ABOUT SPECIFIC TASTE OUTCOMES ACCOUNTED FOR LITTLE VARIANCE IN OFC ACTIVITY. HOWEVER, DEVALUATION OF ONE TASTE PRIOR TO TESTING REVEALED LATENT TASTE-PREDICTIVE INFORMATION IN OFC ENSEMBLES. THESE DATA SUGGEST THAT COGNITIVE MAP FORMATION IN THE OFC INVOLVES SIMPLIFYING TASK DEMANDS INTO WHICHEVER INFORMATION IS MOST DIRECTLY RELEVANT TO SOLVING THE PROBLEM, WHILE INFORMATION WHICH IS NOT DIRECTLY USED FOR MAKING CORRECT DECISIONS REMAINS LATENT IN THE OFC. OUR FINDINGS HAVE IMPORTANT IMPLICATIONS FOR UNDERSTANDING THE ROLE OF THE OFC IN LEARNING AND USING PREDICTIVE INFORMATION CARRIED BY CUES TO MAKE CORRECT DECISIONS, PSYCHOLOGICAL PROCESSES AFFECTED IN MYRIAD NEUROLOGICAL AND PSYCHIATRIC CONDITIONS.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W35. MESOCORTICAL DOPAMINE ACTIVITY ENCODES TIMING-RELATED COGNITIVE PROCESSING

MACKENZIE (SPICER) RYSTED*, MATTHEW WEBER, ALEXANDRA BOVA, KARTIK SIVAKUMAR, NANDAKUMAR NARAYANAN

PARKINSON'S DISEASE (PD) IS A NEURODEGENERATIVE DISORDER RESULTING IN DEVASTATING COGNITIVE SYMPTOMS, INCLUDING IMPAIRED WORKING MEMORY, ATTENTION, AND TIMING. INTERVAL TIMING IS THE ABILITY TO ESTIMATE INTERVALS OF SEVERAL SECONDS AND IS LINKED TO COGNITIVE DYSFUNCTION IN PD. MOREOVER, TIMING IS DEPENDENT ON DOPAMINE AND IMPAIRED IN PD PATIENTS. PRIOR WORK FROM OUR LAB AND OTHERS HAVE RELIABLY SHOWN THAT DISRUPTING EITHER VENTRAL TEGMENTAL AREA (VTA) OR PREFRONTAL (PFC) DOPAMINE SIGNIFICANTLY IMPAIRS INTERVAL TIMING BEHAVIOR. OUR LAB ALSO FOUND THAT TIMING-RELATED RAMPING ACTIVITY OF PFC NEURONS, OR MONOTONIC CHANGES IN FIRING RATE OVER AN INTERVAL, IS DEPENDENT ON VTA DOPAMINE. HERE, WE INVESTIGATED INTERVAL TIMING-RELATED DYNAMICS OF VTA DOPAMINE NEURONS AND HOW THESE DYNAMICS RELATED TO PREFRONTAL ACTIVITY. WE INJECTED CRE-DEPENDENT GCAMP6S INTO THE VTA OF DATIRES-CRE MICE AND IMPLANTED A FIBER OPTIC TO MEASURE CALCIUM DYNAMICS WHILE MICE PERFORM AN INTERVAL TIMING TASK. WE FOUND THAT CALCIUM DYNAMICS (ΔF/F0), FROM VTA DOPAMINE NEURONS RAPIDLY INCREASES AT TRIAL START AND STAYS ELEVATED THROUGH THE TRIAL. INTERESTINGLY, THE GREATER ΔF/F0 EARLY IN THE TRIAL, THE MORE PRECISELY AN ANIMAL CONTROLS ITS ACTIONS IN TIME, SUGGESTING THIS ACTIVITY IS IMPERATIVE FOR OPTIMAL COGNITIVE PROCESSING. IN WILD-TYPE MICE, WE INJECTED DLIGHT3.0 INTO THE PFC AND IMPLANTED A FIBER OPTIC TO MEASURE DOPAMINE DYNAMICS DURING THE SAME INTERVAL TIMING TASK. OUR PRELIMINARY DATA SUGGEST THAT PFC DOPAMINE INCREASES IMMEDIATELY BEFORE TRIAL START, SUGGESTING ANTICIPATORY ACTIVITY. FURTHER, PFC DOPAMINE ACTIVITY REMAINS ELEVATED THROUGHOUT THE TRIAL, SIMILAR TO VTA CALCIUM DYNAMICS. TOGETHER, THESE DATA SUGGEST THAT MESOCORTICAL DOPAMINE PLAYS AN INTEGRAL ROLE DURING INTERVAL TIMING AND ONGOING EXPERIMENTS SEEK TO STUDY HOW PFC DOPAMINE ACTIVITY RELATES TO PFC NEURONAL ENSEMBLES.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W36. THE COMPARATIVE ORGANIZATION OF SINGLE AMYGDALA NEURON PROJECTION PATTERNS TO FRONTAL CORTEX AND STRIATUM IN MACAQUES AND MICE

ZACHARY ZEISLER*, KELSEY HESLIN, ROGER CLEM, PETER RUDEBECK

BASOLATERAL AMYGDALA (BLA) IS INVOLVED IN A WIDE RANGE OF COGNITIVE PROCESSES, FROM DEFENSIVE THREAT RESPONDING, TO APPETITIVE DECISION-MAKING, TO ATTENTION. SUCH A DIVERSE SET OF FUNCTIONS IS LIKELY DUE TO THE WIDE-RANGING PROJECTIONS OF BLA ACROSS FRONTAL CORTEX. YET, LITTLE IS KNOWN ABOUT THE PROJECTION PATTERNS OF SINGLE BLA NEURONS TO THIS AREA. SPECIFICALLY, THE EXTENT TO WHICH SINGLE BLA NEURONS BRANCH AND PROJECT TO MULTIPLE LOCATIONS IN FRONTAL CORTEX IS UNCLEAR, AND EVEN LESS IS KNOWN ABOUT HOW SUCH BRANCHING MIGHT VARY ACROSS SPECIES. HERE, WE USED MULTIPLEXED ANALYSIS OF PROJECTIONS BY SEQUENCING (MAPSEQ), A BARCODED VIRUS APPROACH TO ESTABLISH THE CONNECTIVITY OF INDIVIDUAL BLA NEURONS IN MACAQUES AND MICE. WE WERE ABLE TO PROFILE THE CONNECTIVITY OF OVER 3,000 MACAQUE AND OVER 1,600 MOUSE BLA NEURONS TO FRONTAL CORTEX AND OTHER SUBCORTICAL STRUCTURES. AS A FIRST STEP, WE THEN COMPARED THE NUMBER OF AREAS THAT EACH SINGLE BLA NEURON PROJECTED TO IN MACAQUES AND MICE. HERE WE FOUND THAT A LARGER PROPORTION OF MOUSE BLA NEURONS BRANCHED TO TWO OR MORE AREAS IN FRONTAL CORTEX COMPARED TO MACAQUE BLA NEURONS.

NEXT, WE INVESTIGATED THE NETWORK-LEVEL FEATURES OF SINGLE BLA NEURONS BY COMPARING THE PROJECTIONS TO ANALOGOUS PARTS OF MEDIAL AND VENTRAL FRONTAL CORTEX. IN MONKEYS, BLA NEURONS THAT PROJECT TO DORSAL ANTERIOR CINGULATE CORTEX (DACC) WERE HIGHLY LIKELY TO ALSO BRANCH TO THE VENTRAL FRONTAL CORTEX, CONSISTENT WITH THESE AREAS' SHARED ROLES IN VALUE-BASED DECISION-MAKING. IN MICE, BY CONTRAST, BLA NEURONS THAT PROJECT TO THE EQUIVALENT OF DACC (CG1/CG2) ARE LESS LIKELY TO ALSO PROJECT TO VENTRAL AREAS COMPARED TO NEURONS THAT PROJECT TO PRELIMBIC OR INFRALIMBIC CORTEX. WE ALSO IDENTIFIED A HIGHLY SPECIFIC GRADIENT OF BLA CONNECTIVITY WITH NUCLEUS ACCUMBENS (NACC) ACROSS FRONTAL CORTEX IN MACAQUES THAT WAS LARGELY ABSENT IN MICE. SPECIFICALLY, MOUSE BLA NEURONS PROJECTING TO FRONTAL CORTEX WERE UNIFORMLY AND HIGHLY LIKELY TO CONNECT TO NACC.

OVERALL, OUR DATA SHOW THAT MOUSE BLA NEURONS ARE MORE LIKELY TO PROJECT TO MULTIPLE PARTS OF FRONTAL CORTEX AND THUS LIKELY BROADCAST INFORMATION OVER A WIDE SWATHE OF CORTEX. BY CONTRAST, INDIVIDUAL MACAQUE BLA NEURONS PROJECT TO RELATIVELY FEWER LOCATIONS IN FRONTAL CORTEX AND THUS TEND TO FORM MORE SEGREGATED NETWORKS.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W37. DYNAMIC NEUROMODULATION BY THE ENDOGENOUS OPIOID DYNORPHIN PROMOTES REWARD-WEEKING

RAAJARAM GOWRISHANKAR*, MADELYN HJORT, ABIGAIL ELERDING, SOFIA SHIRLEY, JOSIE VAN TILBURG, KHALID ABRERA, DAVID MARCUS, KAT MOTOVILOV, SEAN PIANTADOSI, ADAM GORDON-FENNELL, CHARLES ZHOU, CHUNYANG DONG, LIN TIAN, GARRET STUBER, MICHAEL BRUCHAS

ENDOGENOUS OPIOIDS AND THEIR COGNATE GPCRS ARE UNIQUELY POISED TO AFFORD MODULATORY CONTROL OF NEURONAL ACTIVITY. HOWEVER, THEY HAVE LARGELY ONLY BEEN USED AS ANATOMICAL MARKERS, WITH STUDIES USING EXOGENOUS LIGANDS TO ASCRIBE BEHAVIORAL FUNCTIONS TO THEM. FOR EXAMPLE, THE ENDOGENOUS OPIOID DYNORPHIN (DYN), SIGNALING THROUGH THE KAPPA OPIOID RECEPTOR (KOR), IS SUGGESTED TO BE INVOLVED IN THE ESCALATION OF DRUG SEEKING BASED ON THE USE OF KOR ANTAGONISTS. HOWEVER, ENDOGENOUS DYN'S LOCUS OF ACTION, AND ITS ROLE IN NATURAL OR DRUG REWARD-SEEKING IS UNKNOWN. THE DORSOMEDIAL STRIATUM (DMS) IS ESSENTIAL FOR REWARD-SEEKING AND ~43% OF DMS NEURONS EXPRESS DYN, ALTHOUGH THE NEUROMODULATORY MECHANISMS THAT REFINE STRIATAL ACTIVITY ARE UNCLEAR. USING IN VIVO 2-PHOTON MICROSCOPY AS ANIMALS SEEK REWARDS, WE FIND THAT DYN NEURONS CHANGE THEIR ACTIVITY DURING ACTION, OR ANTICIPATION OF REWARD. USING A NOVEL DYN BIOSENSOR IN VIVO VIA FIBER PHOTOMETRY, WE OBSERVE THAT DYN IS RELEASED SPECIIFICALLY IN ANTICIPATION OF THE REWARD. TO ASCERTAIN THE SOURCE OF DYN ACTIVATION, WE MULTIPLEXED OPTOGENETICS WITH DYN BIOSENSOR PHOTOMETRY IN VIVO, AND FIND THAT STIMULATING KOR-EXPRESSING BASOLATERAL AMYGDALA (BLA) TERMINALS IN THE DMS ELICITS DYN RELEASE. SINCE DMS-PROJECTING BLA NEURONS ARE INVOLVED IN REWARD-SEEKING, WE MEASURED THE ACTIVITY OF BLA-DMS TERMINALS USING IN VIVO FIBER PHOTOMETRY, MULTIPLEXED WITH CONDITIONAL DMS DYN, OR BLA KOR DELETION. IN CONTROLS, BLA-DMS ACTIVITY IS INCREASED DURING ACTION, AND INHIBITED DURING OUTCOME, WHEREAS CONDITIONAL DMS DYN, OR BLA KOR DELETION, SIGNIFICANTLY DIMINISHES BLA-DMS ACTIVITY AND NEGATIVELY IMPACTS REWARD-SEEKING. CONVERSELY, OPTOGENETIC STIMULATION OF DMS DYN DURING ANTICIPATION ENHANCES BLA-DMS ACTIVITY AND REWARD-SEEKING. ALTOGETHER, WE REVEAL THAT RETROGRADE DYN TRANSMISSION FROM THE DMS ONTO KOR AT BLA TERMINALS DYNAMICALLY REGULATES BLA-DMS ACTIVITY AND PROMOTES REWARD-SEEKING.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W38. OLIGODENDROCYTES AND MYELIN RESTRICT CORTICAL EXPERIENCE-DEPENDENT NEURONAL PLASTICITY

WENDY XIN*, MEGUMI KANEKO, RICHARD ROTH, ALBERT ZHANG, SONIA NOCERA, JUN DING, MICHAEL STRYKER, JONAH CHAN

DEVELOPMENTAL MYELINATION IS A PROTRACTED PROCESS IN THE MAMMALIAN BRAIN. ONE THEORY FOR WHY OLIGODENDROCYTES MATURE SO SLOWLY POSITS THAT MYELINATION MAY STABILIZE NEURONAL CIRCUITS AND TEMPER NEURONAL PLASTICITY AS ANIMALS AGE. WE TESTED THIS HYPOTHESIS IN THE VISUAL CORTEX, WHICH HAS A WELL-DEFINED CRITICAL PERIOD FOR EXPERIENCE-DEPENDENT NEURONAL PLASTICITY. TO PREVENT MYELIN PROGRESSION, WE CONDITIONALLY DELETED MYRF, A TRANSCRIPTION FACTOR NECESSARY FOR OLIGODENDROCYTE MATURATION, FROM OLIGODENDROCYTE PRECURSOR CELLS (MYRF CKO) IN ADOLESCENT MICE. THE DENSITY OF MATURE OLIGODENDROCYTES AND MYELIN SHEATHS PROGRESSIVELY INCREASED FROM 4 TO 8 WEEKS POSTNATALLY IN CONTROL MICE BUT PLATEAUED BY 4 WEEKS IN MYRF CKO MICE. TO INDUCE EXPERIENCE-DEPENDENT PLASTICITY, ADULT CONTROL AND MYRF CKO MICE WERE MONOCULARLY DEPRIVED BY EYELID SUTURE. FUNCTIONAL AND STRUCTURAL NEURONAL PLASTICITY IN THE VISUAL CORTEX WERE ASSESSED BY INTRINSIC SIGNAL IMAGING AND IN VIVO LONGITUDINAL TWO PHOTON IMAGING OF DENDRITIC SPINES, RESPECTIVELY. FOLLOWING MONOCULAR DEPRIVATION, VISUAL CORTEX ACTIVITY IN RESPONSE TO VISUAL STIMULATION OF THE DEPRIVED EYE REMAINED STABLE IN ADULT CONTROL MICE, AS IS TYPICAL FOR POST-CRITICAL PERIOD ANIMALS. BY CONTRAST, VISUAL CORTEX RESPONSES TO THE DEPRIVED EYE DECREASED SIGNIFICANTLY FOLLOWING MONOCULAR DEPRIVATION IN ADULT MYRF CKO MICE, REMINISCENT OF THE PLASTICITY OBSERVED IN ADOLESCENT MICE. FURTHERMORE, MONOCULAR DEPRIVATION INDUCED SPATIALLY COORDINATED DECREASES IN SPINE SIZE IN ADULT MYRF CKO, BUT NOT CONTROL, MICE. THESE RESULTS SUPPORT THE CONCEPT OF MYELIN SERVING AS A BRAKE ON NEURONAL PLASTICITY AND DEMONSTRATE THAT OLIGODENDROCYTES AND MYELINATION PLAY A CRITICAL ROLE IN SHAPING THE MATURATION AND STABILIZATION OF CORTICAL CIRCUITS.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W39. MICE WITH SYNAPTOJANINI DELETION IN DOPAMINERGIC NEURONS EXHIBIT SEX AND AGE DEPENDENT MOTOR FUNCTION ABNORMALITY

JACQUELINE SAENZ*, SANJANA SURYA-PRAKASH, JESSICA LEE, PINGYUE PAN

PARKINSON'S DISEASE (PD) IS A COMMON NEURODEGENERATIVE DISORDER AND IS CHARACTERIZED BY DYSFUNCTIONAL DOPAMINERGIC SIGNALING IN THE EARLY STAGE. STUDIES HAVE SHOWN THAT MISSENSE MUTATIONS IN SYNJI (SYNAPTOJANINI/SYNJI) OR LOSS OF SYNJI TRANSCRIPTS ARE ASSOCIATED WITH PD OR CLINICAL PARKINSONISM, SUGGESTING AN ESSENTIAL ROLE OF SYNJI IN THE FUNCTION AND INTEGRITY OF THE DOPAMINERGIC SYSTEM. WE AND OTHERS HAVE REPORTED THAT GLOBAL SYNJI LOSS-OF-FUNCTION IN MICE RESULTS IN SYNAPTIC ABNORMALITIES INCLUDING IMPAIRED SYNAPTIC VESICLE ENDOCYTOSIS AND ABERRANT DOPAMINE TRANSPORTER (DAT) CLUSTERS. TO FURTHER UNDERSTAND THE ROLE OF SYNJI IN DOPAMINE (DA) NEURONS, WE RECENTLY GENERATED A MOUSE WITH CONDITIONAL DELETION OF SYNJI (CKO) IN DA NEURONS BY CROSSING DAT-CRE MICE TO THE SYNJIFLOX/FLOX (F/F) MICE. THE CONDITIONAL DELETION OF SYNJI DOES NOT SIGNIFICANTLY AFFECT THE OVERALL HEALTH OF THE MICE ASSESSED BY LIFE SPAN, WEIGHT GAIN AND FERTILITY. TO ANALYZE THE EFFECTS OF SYNJI LOSS IN THE MIDBRAIN DA SYSTEM, WE PERFORMED A BATTERY OF LOCOMOTOR BEHAVIORAL STUDIES AT MULTIPLE AGE POINTS FROM 3 MONTHS TO 12 MONTHS FOR A MALE AND FEMALE COHORT OF LITTERMATE CKO AND F/F MICE. MEASURES OF MOTOR COORDINATION AND BALANCE USING THE ACCELERATED ROTAROD SHOWED A SIGNIFICANT IMPAIRMENT IN FEMALE CKO MICE COMPARED TO THEIR LITTERMATE AT 3, 6, 9 AND 12 MONTHS. NEUROMUSCULAR ABNORMALITIES WERE EVALUATED BY THE WIRE-HANG TEST, AND SIMILARLY, WE FOUND A ROBUST DEFECT IN FEMALE CKO MICE COMPARED TO THEIR LITTERMATE MICE AT ALL AGES, WHILE THE DIFFERENCE IN MALE CKO WAS ONLY NOTED AT 3 MONTHS. IN THE BALANCE BEAM TRAVERSAL TEST FOR SENSORY MOTOR FUNCTION, THE FEMALE CKO MICE EXHIBITED SIGNIFICANTLY HIGHER NUMBER OF MISSTEPS AT 12 MONTHS, HOWEVER, THIS CHANGE WAS NOT OBSERVED IN THE MALE CKO MICE AT ALL AGES. TAKEN TOGETHER, OUR PRELIMINARY STUDY OF THE SYNJI CKO MICE SUGGESTED COMPLEX MOTOR FUNCTION ABNORMALITY THAT IS SEX AND AGE DEPENDENT.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W40. CHARACTERIZING THE ROLE OF MS4AS IN ALZHEIMER'S DISEASE

THUYVAN LUU*, I-HAO WANG, ABIGAIL HILLER, PAUL GREER

ALZHEIMER'S DISEASE (AD) IS THE MOST COMMON NEURODEGENERATIVE DISEASE AND FORM OF DEMENTIA, AFFECTING APPROXIMATELY 55 MILLION PEOPLE WORLDWIDE. DESPITE THE GROWING PREVALENCE AND ECONOMIC BURDEN OF AD, CURRENT AD THERAPIES ARE LIMITED IN NUMBER AND EFFICACY, DEMONSTRATING THE NEED FOR NEW THERAPEUTIC APPROACHES. HOPE FOR NEW THERAPEUTIC STRATEGIES HAS EMERGED FROM RECENT GENOME WIDE ASSOCIATION STUDIES (GWAS), WHICH HAVE IDENTIFIED GENES WHOSE POLYMORPHISM IS LINKED TO ALTERED AD SUSCEPTIBILITY. SOME OF THE MOST STRONGLY ASSOCIATED AND REPRODUCIBLE GENETIC ASSOCIATIONS WITH ALTERED AD RISK ARE POLYMORPHISMS IN THE MEMBRANE-SPANNING 4-DOMAINS, SUBFAMILY A (MS4A) GENE FAMILY. ESTIMATES FROM CURRENT GENETIC DATA SUGGEST THAT MS4A POLYMORPHISMS ACCOUNT FOR APPROXIMATELY 5-10% OF ALL LATE-ONSET AD CASES, SUGGESTING THAT THEY REPRESENT ATTRACTIVE NEW THERAPEUTIC TARGETS FOR TREATING OR PREVENTING AD. HOWEVER, LIMITED UNDERSTANDING OF MS4A FUNCTION IN AD PATHOGENESIS HAS HINDERED THE DEVELOPMENT OF THERAPIES TARGETING THESE PROTEINS. THEREFORE, WE AIMED TO ELUCIDATE THE ROLE OF MS4AS DURING AD PATHOGENESIS. USING MICE IN WHICH MS4A6C (A HOMOLOG OF THE HUMAN MS4A6A RISK GENE) IS HOMOZYGOUSLY DELETED CROSSED TO THE P301S TAUOPATHY MODEL, WE FIND THAT LOSS OF MS4A6C AMELIORATES COGNITIVE DEFICITS AND NEURONAL LOSS. ADDITIONALLY, THROUGH SINGLE-CELL RNA TRANSCRIPTIONAL PROFILING OF ADULT MOUSE BRAIN, WE FIND THAT HOMOLOGUES OF THE 5 MS4A FAMILY MEMBERS WHOSE MUTATION IS ASSOCIATED WITH AD ARE EXPRESSED SPECIFICALLY IN MICROGLIA. MICROGLIA PLAY A CRUCIAL ROLE IN AD PATHOGENESIS, SUGGESTING THAT MICROGLIAL EXPRESSION OF MS4AS MAY BE CRITICAL FOR REGULATING AD PATHOLOGY. WE FIND THAT MS4A6C REGULATES MICROGLIAL ACTIVATION IN RESPONSE TO TAU, MICROGLIAL SYNAPSE ENGULFMENT, AND IMMUNE RESPONSES. THIS WORK WILL HELP TO UNDERSTAND HOW MS4A GENES AFFECT MICROGLIAL FUNCTION AND AD PATHOGENESIS WITH THE ULTIMATE GOAL OF EVENTUALLY DEVELOPING THERAPIES TARGETING THESE MS4A RECEPTORS.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W41. IMPACT OF TAU EXPRESSION ON THE DEVELOPMENT OF ACQUIRED TEMPORAL LOBE EPILEPSY

MADELEINE MOSELEY*, RYAN A. CLOYD, YOUNG-JIN KANG, SANGHUN LEE, BRET N. SMITH

TEMPORAL LOBE EPILEPSY (TLE) IS THE MOST COMMON FOCAL EPILEPSY IN ADULTS AND IS OFTEN RESISTANT TO ANTI-EPILEPTIC DRUGS. UNDERSTANDING THE MECHANISMS THAT DRIVE THE DEVELOPMENT OF TLE IS CRUCIAL TO DEVELOPING NEW SPECIFIC THERAPIES. A POTENTIAL TARGET FOR TREATMENT AND/OR PREVENTION OF EPILEPSY IS MICROTUBULE-ASSOCIATED TAU PROTEIN. FOR EXAMPLE, GENETIC DELETION OR SUPPRESSION OF TAU EXPRESSION IMPROVES SEIZURE OUTCOMES IN CHANNELOPATHY MODELS OF GENETIC EPILEPSIES. TAU EXPRESSION MAY ALTER SYNAPTIC FUNCTION AND NEURONAL EXCITABILITY, BUT THE MECHANISM(S) BY WHICH LACK OF TAU EXPRESSION INFLUENCES SEIZURE SUSCEPTIBILITY OR TLE DEVELOPMENT IS UNCLEAR. TO DETERMINE THE IMPACT OF TAU EXPRESSION ON EPILEPTOGENESIS OF ACQUIRED TLE, WE TREATED TAU-/- AND C57BL/6 MICE WITH AN INTRAHIPPOCAMPAL INJECTION OF KAINATE (IHK). THE IHK MODEL INDUCES STATUS EPILEPTICUS (I.E., SE) IN RODENTS AND, AFTER A DELAY, THE DEVELOPMENT OF TLE WITH SPONTANEOUS RECURRENT SEIZURES (SRS; I.E., EPILEPTOGENESIS). IN THIS STUDY WE USED MICE THAT LACK NATIVE MURINE TAU (I.E., TAU-/-) AND C57BL/6J MICE. WE ASSESSED THE SEVERITY OF SE, EPILEPTIFORM ACTIVITY, AND THE DEVELOPMENT OF SRS USING VIDEO ELECTROENCEPHALOGRAPHY (V-EEG). WE FURTHER MEASURED THE IMPACT OF SRS ON CELLULAR EXCITABILITY OF DENTATE GRANULE CELLS (DGCS) USING IN VITRO WHOLE-CELL PATCH-CLAMP ELECTROPHYSIOLOGY. WE FOUND THAT LACK OF TAU EXPRESSION IS ASSOCIATED WITH RESISTANCE - BUT NOT ELIMINATION -- OF SE INDUCTION AND EPILEPTOGENESIS. STRIKINGLY, DEVELOPMENT OF SRS IN MICE THAT LACK TAU EXPRESSION RESULTED IN GREATER SYNAPTIC DYSFUNCTION AND CELLULAR EXCITABILITY COMPARED TO IHK-TREATED C57BL/6 MICE. RESULTS FROM THIS STUDY HIGHLIGHT THE ROLE OF TAU IN THE DEVELOPMENT OF ACQUIRED TLE. SUBSEQUENT STUDIES WILL FURTHER INVESTIGATE HOW TAU ALTERS DGC NEUROTRANSMISSION.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W42. ENLARGED PERIVASCULAR SPACES CHARACTERIZE SEIZURE OUTCOME AFTER TRAUMATIC BRAIN INJURY

CELINA ALBA*, GIUSEPPE BARISANO, ALEXIS BENNETT, AKUL SHARMA, ANNIE ADHIKARY, PAUL VESPA, DOMINIQUE DUNCAN

ALTHOUGH POST-TRAUMATIC EPILEPSY (PTE) REMAINS ONE OF THE MOST DEBILITATING OUTCOMES OF TRAUMATIC BRAIN INJURY (TBI), THERE ARE NO PREVENTATIVE TREATMENTS.1 THE EPILEPSY BIOINFORMATICS STUDY FOR ANTIEPILEPTOGENIC THERAPY (EPIBIOS4RX) IS AN INTERNATIONAL PROJECT DESIGNED TO IDENTIFY MULTIMODAL BIOMARKERS OF PTE.2 PRIOR RESEARCH SUGGESTS THAT PERIVASCULAR SPACES (PVS), A LOCATION IN THE GLYMPHATIC SYSTEM FOR CLEARANCE OF NEUROTOXINS, ARE A PROMISING BIOMARKER.3-5 WHILE PAST STUDIES HAVE FOCUSED ON PVS COUNT, WE EVALUATE A MORE REPRESENTATIVE METRIC: VOLUME FRACTION (VF), THE VOLUME OF PVS RELATIVE TO TOTAL BRAIN VOLUME.6 THIS STUDY INVESTIGATES THE ASSOCIATION BETWEEN PVS VF AND POST-TRAUMATIC SEIZURE (PTS) OCCURRENCE, THE MOST PROMINENT CHARACTERISTIC OF PTE. A SUBSET OF 62 SUBJECTS (49 MALE; 13 FEMALE, AGE=40.3+/-17.3, GLASGOW COMA SCALE=8.7+/-4.3) FROM EPIBIOS4RX WAS CHOSEN BASED ON THEIR SUFFICIENT ACQUISITION OF T1- AND T2-WEIGHTED IMAGES AND COMPLETION OF THE OTTMAN QUESTIONNAIRE TWO-YEAR FOLLOW-UP.7 THE SEIZURE-POSITIVE GROUP INCLUDES 22 SUBJECTS WITH AT LEAST ONE LATE PTS, SEIZURES THAT OCCUR AT LEAST 7 DAYS POST-INJURY, AND THE SEIZURE-NEGATIVE GROUP INCLUDES 40 SUBJECTS WITH NO LATE PTS. MR IMAGES WERE PROCESSED THROUGH THE HUMAN CONNECTOME PROJECT'S STRUCTURAL PROCESSING PIPELINE.8 A SECOND PROCESSING PIPELINE WAS USED TO CREATE ENHANCED PVS CONTRAST IMAGES, SEGMENT PVS, AND EXTRACT FEATURES.9 A GENERAL LINEAR MODEL WAS RUN WITH AGE AS A COVARIATE10; A SIGNIFICANT DIFFERENCE ($P < 0.05$) WAS FOUND BETWEEN THE SEIZURE-POSITIVE GROUP (MEAN=0.0180VOXELS+/-0.0051) AND SEIZURE-NEGATIVE GROUP (MEAN=0.0157VOXELS+/-0.0018). OUR RESULTS INDICATE THAT ENLARGED PVS VF IS ASSOCIATED WITH LATE PTS WHEN CONTROLLING FOR AGE. THESE FINDINGS SUGGEST THAT CHANGES IN PVS STRUCTURE MAY PLAY A ROLE IN THE MOLECULAR MECHANISMS OF PTE. FUTURE STUDIES WITH LARGER COHORTS WILL EXPLORE MORE COMPLEX PVS METRICS TO BE USED TO TRAIN MACHINE LEARNING MODELS TO PREDICT SEIZURE SUSCEPTIBILITY AFTER TBI.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W43. SEX AND CIRCUIT SPECIFIC AMYGDALA DYSFUNCTION AFTER GLOBAL CEREBRAL ISCHEMIA

JOSE VIGIL*, PACO HERSON, ERIKA TIEMEIER, NICHOLAS CHALMERS, NIDIA QUILLINAN

MODERN MEDICAL ADVANCES HAVE INCREASED THE ODDS OF SURVIVING AN ISCHEMIC EVENT SUCH AS CARDIAC ARREST OR STROKE. WITH MORE PEOPLE SURVIVING AND RECOVERING FROM THESE ISCHEMIC INSULTS, IT IS APPARENT THAT SURVIVORS EXPERIENCE LONG-TERM EFFECTS ON BRAIN FUNCTION. HOWEVER, NO STUDY HAS ATTEMPTED TO IDENTIFY AMYGDALA DYSFUNCTION AFTER GLOBAL CEREBRAL ISCHEMIA (GCI), DESPITE CLINICAL EVIDENCE OF EMOTIONAL DYSFUNCTION. THEREFORE, IT IS IMPORTANT TO IDENTIFY THE EFFECT THAT GCI HAS ON THE AMYGDALA, THE EMOTIONAL CENTER OF THE BRAIN. I HYPOTHESIZE GCI INDUCES DYSFUNCTION OF L-TYPE CALCIUM CHANNELS (LTCCS) WITHIN THE BASOLATERAL AMYGDALA (BLA) THEREBY CONTRIBUTING TO DEFICITS IN AMYGDALA-DEPENDENT BEHAVIOR AND LTP IN MALE MICE.
GCI WAS INDUCED IN ADULT MICE VIA CARDIAC ARREST AND SUBSEQUENT CARDIOPULMONARY RESUSCITATION (CA/CPR) FOR 8-MINUTES BEFORE RESUSCITATION BY EPINEPHRINE INJECTION, VENTILATION, AND MILD CHEST COMPRESSIONS. DELAY FEAR CONDITIONING WAS USED TO ASSESS AMYGDALA-DEPENDENT LEARNING AND MEMORY, SYNAPTIC PLASTICITY WAS EVALUATED BY PERFORMING LTP RECORDINGS IN THE BLA, LTCC FUNCTION WAS ASSESSED USING WHOLE-CELL VOLTAGE CLAMP RECORDINGS, AND NEURONAL INJURY WAS EVALUATED BY FLUOROJADE STAINING.
BEHAVIORAL TESTING REVEALED THAT ONLY MALE MICE ARE DIMINISHED IN THEIR ABILITY TO FORM ASSOCIATIVE MEMORIES. SIMILARLY, PLASTICITY OF THE CORTICAL INPUTS TO THE BLA ARE IMPAIRED ONLY IN MALES, HOWEVER, INTRA-AMYGDALA RECORDINGS REVEALED NO DISRUPTION OF LTP, WHOLE-CELL LTCC MEDIATED CURRENTS WERE MINIMALLY AFFECTED BY GCI, AND THERE IS NO CELL DEATH WITHIN THE BLA OF EITHER SEX. ADDITIONAL 2-PHOTON CALCIUM IMAGING EXPERIMENTS WILL EVALUATE LTCC FUNCTION AT MORE DISTAL SYNAPSES AFTER GCI. THESE RESULTS SUPPORT THE ROLE OF THE AMYGDALA IN COGNITIVE-AFFECTIVE IMPAIRMENTS AFTER CA. WE HAVE REVEALED A SEX AND CIRCUIT SPECIFIC DEFICIT IN AMYGDALA FUNCTION THAT PROVIDES NEW INSIGHTS INTO THE ROLE THAT BIOLOGICAL SEX PLAYS IN MEDIATING BRAIN DYSFUNCTION FOLLOWING CA.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W44. THE TANDEM ROLE OF LATERAL HYPOTHALAMIC GABA AND GLUTAMATE NEURONS IN REGULATING STRIATAL DOPAMINE RELEASE AND MOTIVATED BEHAVIOR

ADAM GORDON-FENNELL*, JOUMANA BARBAKH, BARBARA BENOWITZ, GARRET STUBER

THE LATERAL HYPOTHALAMUS (LHA) CONSISTS OF DIVERSE POPULATIONS OF NEURONS WITH DISTINCT GENETIC IDENTITIES THAT CONTRIBUTE TO MOTIVATED BEHAVIORS. LHA GABA AND GLUTAMATE (GLUT) NEURONS HAVE OPPOSING EFFECTS ON CONSUMPTION. HOWEVER, BOTH POPULATIONS SHOW AN INCREASE IN ACTIVITY DURING SUCROSE CONSUMPTION, RAISING QUESTIONS ABOUT THEIR COLLABORATIVE. LHA GABA AND GLUT POPULATIONS SEND DIRECT PROJECTIONS TO THE VTA AS WELL AS PROJECTIONS TO STRUCTURES KNOWN TO REGULATE THE VTA. LHA GABA AND GLUT NEURONS DRIVE OPPOSING EFFECTS ON DOPAMINE RELEASE IN THE NUCLEUS ACCUMBENS CORE IMPLYING THAT THE LHA GABA AND GLUT COULD MEDIATE MOTIVATIONAL EFFECTS THROUGH BALLANCED REGULATION OF THE DOPAMINE SYSTEM. HOWEVER, THE IN VIVO SIGNALING PATTERNS OF LHA GABA AND GLUT NEURONS AND DOPAMINE RELEASE THROUGHOUT THE STRIATUM DURING CONSUMPTION REMAINS POORLY UNDERSTOOD. WE RECORDED LHA GABA AND GLUT NEURONS SIMULTANEOUSLY USING DUAL-COLOR FIBER PHOTOMETRY, AND RECORDED DOPAMINE RELEASE ACROSS THE STRIATUM USING MULTI-SITE FIBER-PHOTOMETRY. TO DETERMINE THE ACTIVITY DYNAMICS OF THE HYPOTHALAMIC AND MESOLIMBIC SYSTEM DURING CONSUMPTION BEHAVIOR, WE TRAINED HEAD-FIXED MICE IN A BRIEF-ACCESS TASTE TASK USING OHRBETS WITH A SET OF POSITIVELY VALANCED SOLUTIONS (0-30% SUCROSE) OR NEGATIVELY VALANCED SOLUTIONS (0-1.5M NACL). IN THE LHA WE FOUND THAT LHA GABA NEURON ACTIVITY SCALES WITH CONSUMPTION AND SOLUTION VALUE REGARDLESS OF THE VALANCE OF THE SOLUTION SET WHILE LHA GLUT NEURONS ONLY SCALE DURING CONSUMPTION OF A RANGE OF AVERSIVE SOLUTIONS, AND THE TANDEM SIGNALING IN LHA GABA AND GLUT IS TIGHTLY CORRELATED WITH DOPAMINE RELEASE ACROSS THE VENTRAL STRIATUM. THESE FINDINGS SUGGEST THAT LHA GABA AND LHA GLUT NEURONS WORK IN TANDEM TO REGULATE CONSUMPTION OF REWARDING AND AVERSIVE TASTANTS.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W45. DISSECTING THE ACCUMBAL DYNORPHINERGIC OUTPUTS UNDERLYING AFFECTIVE PAIN

FLORA D'OLIVEIRA DA SILVA*, KRISTINE YOON, ROSSANA SANDOVAL, CATHERINE CAHILL, MARCO PIGNATELLI, JOSE MORON-CONCEPCION, NICOLAS MASSALY

PAIN REPRESENTS A GROWING EPIDEMIC IN THE U.S., AFFLICTING MORE THAN 30% OF THE POPULATION. DESPITE THE AVAILABILITY OF EFFECTIVE TREATMENTS FOR ACUTE NOCICEPTIVE PAIN CONDITIONS, NEGATIVE AFFECTIVE STATES INDUCED BY PERSISTENT OR CHRONIC PAIN REMAIN UNDER- OR UNTREATED. THE NUCLEUS ACCUMBENS (NAC) IS A CRITICAL COMPONENT OF THE MESOLIMBIC SYSTEM AND IS INVOLVED IN INTEGRATING BOTH REINFORCING AND AVERSIVE PROPERTIES OF EXTERNAL STIMULI. ACTIVATION OF KAPPA OPIOID RECEPTORS (KORS) THROUGH EXOGENOUS OR ENDOGENOUS AGONIST, DYNORPHIN, PRODUCES DYSPHORIC EFFECTS AND IMPAIRS ACTIVE COPING STRATEGIES IN PRECLINICAL MODELS OF PAIN. USING CHEMOGENETIC APPROACHES AND MICROPET IMAGING, WE RECENTLY DEMONSTRATED THAT 1) DYNORPHIN-CONTAINING (DYN+) NEURONS IN THE NAC ARE NECESSARY TO DRIVE PAIN-INDUCED NEGATIVE AFFECT AND 2) INFLAMMATORY PAIN INCREASES OVERALL CENTRAL KORS OCCUPANCY. HOWEVER, THE NATURE OF THE DOWNSTREAM STRUCTURES THROUGH WHICH DYN+ NEURONS MEDIATE BEHAVIORAL ADAPTATIONS TO PAIN REMAIN TO BE DETERMINED. INDEED, NAC DYN+ NEURONS PROJECT TO MANY STRUCTURES INVOLVED IN MOTIVATION INCLUDING THE VENTRAL PALLIDUM, THE VENTRAL TEGMENTAL AREA (VTA) AND THE LATERAL HYPOTHALAMUS (LH). RECENT EVIDENCE HAS UNCOVERED THAT DYN+ NEURONS PROJECTING FROM THE NAC TO THE LH (DYNNACLH) ARE NECESSARY TO DRIVE STRESS-INDUCED ANHEDONIA. IN THIS LINE OF THOUGHTS, USING BOTH MALES AND FEMALES ADULT MICE WE EMPLOYED A COMBINATION OF EX VIVO PHYSIOLOGY, IMAGING AND BEHAVIORAL PHARMACOLOGY AND DETERMINED THAT PAIN 1) INCREASES THE EXCITABILITY OF DYNNACLH PROJECTIONS, 2) INCREASES KOR FUNCTION IN THE LH AND 3) ENGAGES LH KOR SIGNALING TO DECREASE REWARD-DRIVEN MOTIVATION (N=8, P < 0.0001). OUR RESULTS PARTICIPATE IN FURTHER UNDERSTANDING THE ALLOSTATIC CHANGES IN DYN+ NAC SYNAPTIC EFFERENTS IN PAIN AND THEIR IMPACT ON NEGATIVE AFFECTIVE STATES.

SUPPORT: MCDONNELL FOUNDATION SMALL GRANT (NM), R21DA055047 (NM)

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W46. NEUROPATHIC PAIN INCREASES BASOLATERAL AMYGDALA KAPPA OPIOID RECEPTOR EXPRESSION AND FUNCTION IN MALE BUT NOT FEMALE MICE

JAMIE MONDELLO*, SHIWEI STEVE LIU, CATHERINE CAHILL

PAIN IS A MULTIDIMENSIONAL CONDITION, COMPRISING BOTH A SENSORY AND AN AFFECTIVE COMPONENT. NEGATIVE AFFECT IN CHRONIC PAIN PATIENTS IS NOT ONLY ASSOCIATED WITH WORSE PAIN SYMPTOMS BUT ALSO INCREASED RISK FOR OPIOID MISUSE. AN EMERGING TARGET FOR TREATING THE EMOTIONAL COMPONENT OF PAIN IS THE KAPPA OPIOID SYSTEM, WHICH IS INVOLVED IN INDUCING DYSPHORIA, ANXIETY-LIKE BEHAVIORS, AND REINSTATEMENT OF DRUG SEEKING. RECENT WORK FROM OUR LAB FOUND THAT CHRONIC PAIN CAUSES A FUNCTIONAL UPREGULATION OF THE DYNORPHIN/KOR SYSTEM IN THE NUCLEUS ACCUMBENS AND VENTRAL TEGMENTAL AREA IN A SEX-SPECIFIC MANNER. IN CONTINUATION OF THIS WORK, THE PRESENT SET OF STUDIES SOUGHT TO DETERMINE WHETHER KOR EXPRESSION AND FUNCTION WERE SIMILARLY INCREASED IN THE BASOLATERAL AMYGDALA (BLA), A KEY REGION IN PROCESSING STRESS, REWARD, AND LEARNING. ALL STUDIES USED A PERIPHERAL NERVE INJURY NEUROPATHIC PAIN MODEL IN C57BL/6J ADULT MALE AND FEMALE MICE. WE FIRST FOUND THAT AMYGDALAR KOR MRNA EXPRESSION MEASURED WITH QUANTITATIVE REAL-TIME PCR 8 WEEKS POST-INJURY WAS HIGHER IN PAIN MALE MICE BUT NOT FEMALE PAIN MICE, AS COMPARED TO SHAM AND NAÏVE CONTROL GROUPS. LIKEWISE, WE FOUND INCREASED KOR EXPRESSION IN MALE PAIN MICE 2 WEEKS POST-INJURY USING FLUORESCENCE IN SITU HYBRIDIZATION. ACTIVATION OF BLA KOR MEASURED VIA GTPGS AUTORADIOGRAPHY WAS HIGHER IN MALE PAIN MICE BUT NOT FEMALE PAIN MICE 2 WEEKS POST-INJURY. USING A CONDITIONED PLACE PREFERENCE (CPP) ASSAY, OUR PRELIMINARY DATA SUGGEST THE KOR AGONIST U50488H (5 MG/KG, I.P.) INDUCED REINSTATEMENT OF OXYCODONE CPP IN CHRONIC PAIN MALE BUT NOT FEMALE MICE. REINSTATEMENT OF OXYCODONE CPP WAS NOT EVIDENT IN THE SHAM MICE OF EITHER SEX. TAKEN TOGETHER, THESE FINDINGS SUPPORT OUR PREVIOUS WORK THAT MALES ARE MORE SENSITIVE TO KAPPA OPIOID SYSTEM-INDUCED CHANGES AS A RESULT OF CHRONIC PAIN. AS SUCH, THIS WORK HAS IMPORTANT IMPLICATIONS FOR DIFFERENTIAL REGULATION OF NEGATIVE AFFECT IN CHRONIC PAIN BETWEEN MALES AND FEMALES.

WEDNESDAY, JANUARY 31ST

POSTER SESSION IV
3:30 P.M. - 4:30 P.M.
PEAK 4-5

W47. THE ROLE OF NIGROSTRIATAL AND STRIATAL CELL SUBTYPE SIGNALING IN BEHAVIORAL IMPAIRMENTS RELATED TO SCHIZOPHRENIA

NICOLETTE MOYA*, ALLISON KANE, STEFAN FLEPS, SEONGSIK YUN, JONES PARKER

EXCESS NIGROSTRIATAL (NS) DOPAMINE SIGNALING IS LINKED TO THE POSITIVE SYMPTOMS OF SCHIZOPHRENIA, WHICH ARE MAINLY RESPONSIVE TO ANTIPSYCHOTIC DRUGS THAT BLOCK D2 DOPAMINE RECEPTORS (D2RS). BY CONTRAST, COGNITIVE SYMPTOMS ARE LARGELY RESISTANT TO THESE SAME TREATMENTS. THIS OBSERVATION FUELED THE DOGMA THAT EXCESS STRIATAL DOPAMINE IS NOT INVOLVED IN COGNITIVE SYMPTOMS. HOWEVER, THE STRIATUM ALSO EXPRESSES DI DOPAMINE RECEPTORS (DIRS), WHICH ARE NOT TARGETED BY CURRENT ANTIPSYCHOTICS. THEREFORE, INCREASED NS DOPAMINE TRANSMISSION MAY CONTRIBUTE TO COGNITIVE SYMPTOMS THROUGH ITS ACTIONS ON STRIATAL DIR SIGNALING, AN IDEA THAT HAS NEVER BEEN DIRECTLY TESTED. WE ASKED WHETHER STRIATAL DIR- AND D2R-EXPRESSING SPINY PROJECTION NEURONS (SPNS) DIFFERENTIALLY CONTRIBUTE TO DOPAMINE-DRIVEN DEFICITS IN COGNITIVE FUNCTION. TO DO THIS, WE DEVELOPED AN APPROACH TO MIMIC THE PATHWAY-SPECIFIC EXCESS IN DOPAMINE OBSERVED IN SCHIZOPHRENIA BY SELECTIVELY EXPRESSING THE EXCITATORY CATION CHANNEL TRPVI IN SNC DOPAMINE NEURONS OF TRPVI KNOCKOUT MICE. SYSTEMICALLY TREATING THESE MICE WITH THE TRPVI AGONIST CAPSAICIN INCREASED DOPAMINE RELEASE IN THE STRIATUM AND INDUCED HYPERLOCOMOTION, BUT ALSO DISRUPTED WORKING MEMORY, A BEHAVIORAL PROXY FOR COGNITIVE SYMPTOMS (MOYA ET AL., 2022). WE ARE CURRENTLY USING THIS TRPVI-BASED APPROACH WITH MINIATURE MICROSCOPES TO IMAGE CA2+ ACTIVITY IN DI- OR D2-SPNS UNDER NORMAL AND HYPERDOPAMINERGIC CONDITIONS TO DETERMINE HOW ALTERED ACTIVITY IN EACH SPN TYPE MAY DIFFERENTIALLY CONTRIBUTE TO COGNITIVE DEFICITS. WE FOUND THAT DRIVING NS DOPAMINE TRANSMISSION WITH CAPSAICIN DECREASED D2-SPN CA2+ ACTIVITY, AND MAY INCREASE DI-SPN CA2+ ACTIVITY. DURING WORKING MEMORY MAINTENANCE, D2-SPNS EXHIBIT A SEQUENTIAL ACTIVITY PATTERN THAT MAY ENCODE SUBSEQUENT CHOICE. WE ARE CURRENTLY IMAGING DI-SPN DYNAMICS TO DETERMINE THEIR ROLE IN COGNITIVE FUNCTION. BY DEFINING THE ROLES OF STRIATAL DI- AND D2-SPNS IN DOPAMINE-DRIVEN CHANGES IN BEHAVIORAL CONSTRUCTS RELATED TO SCHIZOPHRENIA, THESE EXPERIMENTS HAVE THE POTENTIAL TO IDENTIFY NOVEL THERAPEUTIC STRATEGIES FOR PSYCHOSIS THAT MORE COMPREHENSIVELY ADDRESS ITS SYMPTOMS.

SUNDAY, JANUARY 28TH

OPENING PLENARY
8:00 A.M. - 9:30 A.M.
COLORADO BALLROOM

2024 PLENARY: SLEEP TO CHANGE YOUR MIND
PRESENTER: GINA POE

THIS PRESENTATION WILL EXPLORE THE CONDITIONS OF SLEEP-DEPENDENT NEURAL PLASTICITY NECESSARY TO UPDATE ONE'S COGNITIVE SCHEMA. UPDATES ARE NECESSARY DURING LEARNING, WHEN RECOVERING FROM ADDICTION OR POST-TRAUMATIC STRESS DISORDER, OR ANY OTHER CONDITION WHEN ONE CHANGES ONE'S MIND.

PIONEER SESSION
9:45 A.M. - 11:15 A.M.
PEAK 11-12, FLOOR 2

PIONEER SESSION: DISSECTING THE HETEROGENEITY OF PSYCHOTROPIC TREATMENT RESPONSE
PIONEER: ANIL MALHOTRA
CHAIR: KATHERINE BURDICK
INVESTIGATORS: MIKLOS ARGYELAN, CAITLIN MILLETT

DR. KATHERINE BURDICK (HARVARD) WILL OPEN THE SESSION WITH BRIEF REMARKS INTRODUCING DR. MALHOTRA (FEINSTEIN INSTITUTE FOR MEDICAL RESEARCH; FIMR). DR. MALHOTRA WILL PROVIDE AN OVERVIEW OF HIS GROUP'S PAST STUDIES FOCUSED ON THE IDENTIFICATION OF BIOMARKERS FOR ANTIPSYCHOTIC TREATMENT RESPONSE. THESE WILL INCLUDE EARLY CANDIDATE GENE STUDIES FOCUSED ON CLOZAPINE RESPONSE, GENOME-WIDE ASSOCIATION STUDIES ON KEY SIDE EFFECTS OF TREATMENT SUCH AS WEIGHT GAIN AND AGRANULOCYTOSIS, AND MORE RECENT NEUROIMAGING STUDIES DETECTING RELATIONSHIPS BETWEEN CORTICO-STRIATAL CONNECTIVITY AND RESPONSE TO SECOND-GENERATION ANTIPSYCHOTICS. THESE DATA MAY LAY THE GROUNDWORK FOR A NOVEL STUDY ASSESSING THE CLINICAL EFFICACY OF USING BIOMARKERS TO IDENTIFY PATIENTS WITH SCHIZOPHRENIA FOR CLOZAPINE TREATMENT EARLY IN THE COURSE OF ILLNESS. TWO MEMBERS OF HIS CURRENT RESEARCH TEAM WILL FOLLOW. DR. MIKLOS ARGYELAN (FIMR) WILL PRESENT DATA ON BIOMARKER WORK WITH ELECTROCONVULSIVE THERAPY (ECT). RECENT ADVANCES IN ELECTRIC FIELD MODELING HAVE ALLOWED FOR THE SEPARATION OF THE DIRECT ELECTRIC IMPACT OF STIMULATION FROM THE EFFECT OF INDUCED SEIZURES IN ECT. HE WILL PRESENT RESULTS FROM A COMPREHENSIVE STUDY ESTABLISHING THE CONNECTION BETWEEN THE ECT-INDUCED ELECTRIC FIELD AND RESULTING BRAIN VOLUME CHANGES. ADDITIONALLY, HE WILL HIGHLIGHT THE LATEST ADVANCES IN CORRELATING THESE CHANGES WITH CLINICAL OUTCOMES AND POTENTIAL SIDE EFFECTS. DR. CAITLIN MILLETT (FIMR) WILL NEXT PRESENT HER WORK ON THE IDENTIFICATION OF BIOMARKERS FOR ECT-INDUCED COGNITIVE SIDE EFFECTS IN PATIENTS WITH BIPOLAR DISORDER BEING TREATED FOR A DEPRESSIVE EPISODE. SHE HAS MEASURED WHITE MATTER INTEGRITY WITH FRACTIONAL ANISOTROPY (FA), FREE-WATER (FW; A PUTATIVE MEASURE OF NEUROINFLAMMATION), AND FW-CORRECTED FA (FA-T) AT BASELINE AND AFTER A COURSE OF ECT TREATMENT IN PATIENTS WITH BIPOLAR DISORDER. SHE WILL REPORT ON THE RELATIONSHIPS OBSERVED BETWEEN THESE NEUROIMAGING METRICS AND COGNITIVE PERFORMANCE DURING ECT.

SUNDAY, JANUARY 28TH

PROFESSIONAL DEVELOPMENT SESSION #1
2:00 P.M. - 3:30 P.M.
PEAK 6-8, FLOOR 2

NON-ACADEMIC PATHWAYS IN NEUROSCIENCE AFTER PHD

CHAIR: ELORA WILLIAMS
PRESENTERS: ERIK CARLSON, RACHEL HERDER, PATRICIO O'DONNELL, GRETCHEN SNYDER, LYRIC JORGENSON

ACKNOWLEDGING OCCUPATIONAL OPTIONS POST-PHD IS IMPERATIVE FOR THE CONTINUATION OF CONTRIBUTIONS TO SCIENCE AND INNOVATION. HERE, EACH PANELIST WILL DISCUSS THEIR OWN PATHWAY THROUGH SCIENCE AND PROVIDE INSIGHT ON HOW TO BEST PREPARE FOR THE DIVERSE CHOICES AVAILABLE. RACHEL HERDER RECEIVED HER PHD IN MOLECULAR, CELLULAR, DEVELOPMENTAL BIOLOGY AND GENETICS AS WELL AS EARNING A JD WITH A FOCUS IN HEALTH LAW AND BIOETHICS FROM THE UNIVERSITY OF MINNESOTA. SHE UTILIZES BOTH DEGREES AS THE VICE PRESIDENT OF INTELLECTUAL PROPERTY AND ASSOCIATE GENERAL COUNSEL FOR MAMMOTH BIOSCIENCES, WHICH LEVERAGES THE CRISPR-CAS SYSTEM FOR DETECTION AND TREATMENT OF DISEASE. PATRICIO O'DONNELL EARNED HIS PHD AND MD FROM THE UNIVERSITY OF BUENOS AIRES WHERE HE WENT ON TO HAVE QUITE THE DIVERSE CAREER PATH AS HE HAS EXPERIENCE AS A PHYSICIAN, POST-DOCTORATE, AND PROFESSOR AS WELL AS MULTIPLE LEADERSHIP ROLES WITHIN THE BIOMEDICAL FIELD. HE IS CURRENTLY THE VICE PRESIDENT AND HEAD OF TRANSLATIONAL MEDICINE AT SAGE THERAPEUTICS. GRETCHEN SNYDER OBTAINED HER DOCTORATE IN BEHAVIORAL NEUROSCIENCE FROM THE UNIVERSITY OF PITTSBURGH AND WENT DOWN THE ACADEMIC PATH TO ASSOCIATE PROFESSOR BUT UNDERWENT CAREER CHANGES AND IS NOW THE VICE PRESIDENT OF BIOLOGY AT INTRA-CELLULAR THERAPIES INC. LYRIC JORGENSON EARNED HER PHD IN NEUROSCIENCE AT THE UNIVERSITY OF MINNESOTA-TWIN CITIES AND HAS EXPERIENCE WORKING WITHIN GOVERNMENTAL INITIATIVES SUCH AS THE BRAIN RESEARCH THROUGH ADVANCING INNOVATIVE NEUROTECHNOLOGIES (BRAIN) INITIATIVE AND NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES (NCATS). THIS WORK HAS LED HER TO CURRENTLY BE THE ACTING NIH ASSOCIATE DIRECTOR FOR SCIENCE POLICY AND THE ACTING DIRECTOR OF THE OFFICE OF SCIENCE POLICY AT THE NIH. ELORA WILLIAMS, PHD CANDIDATE, AND ERIK CARLSON, PHD, WILL PROVIDE THE INTRODUCTORY COMMENTS AND CHAIR THE DISCUSSION.

SUNDAY, JANUARY 28TH

PANEL
4:30 P.M. - 6:30 P.M.
IMPERIAL BALLROOM, FLOOR 4

ADVANCED SENSING STRATEGIES TO TAKE ON THE DOUBLE DIAMONDS OF BRAIN DYNAMICS

CHAIRS: TOD KIPPIN, YEN-YU IAN SHIH, NICOLE EMMONS
PRESENTERS: JULIAN GERSON, TATIANA SHNITKO, ARNAB MUKHERJEE, HOJIN SHIN

BRAIN FUNCTION ULTIMATELY ARISES FROM THE COMPLEX CHEMICAL DYNAMICS THAT IMPACT THE ACTIVITY BOTH BETWEEN AND WITHIN NEURONS. MUCH OF OUR UNDERSTANDING OF THESE SIGNALS IS DERIVED FROM EITHER POST-MORTEM ANALYSES OR FROM MICRODIALYSIS AND ELECTROCHEMISTRY WHICH, WHILE PROVIDE CRITICAL INFORMATION, ALSO PRESENT LIMITATIONS IN TERMS OF MEASURING THE VAST VARIETY OF RELEVANT MOLECULES AT THE APPROPRIATE TEMPORAL AND SPATIAL RESOLUTION. THE PANEL WILL DISCUSS EMERGING SENSING STRATEGIES AIMED AT MONITORING MOLECULAR TARGETS REGARDLESS OF CHEMICAL CLASS, IN MULTIPLEXED FASHION, AS WELL AS ACROSS TIME- AND SPATIAL SCALES CRITICAL FOR ELUCIDATING THE NEUROBIOLOGY OF ADDICTION. FIRST, YOONBAE OH (MAYO CLINIC) WILL DISCUSS NEW ADVANCES IN VOLTAMMETRY ALLOWING MEASUREMENT OF TONIC AND PHASIC CHANGES IN AS WELL AS ROUTES TO DISSECT OUT CONTRIBUTIONS OF DIFFERENT NEUROTRANSMITTERS. JULIAN GERSON (NUTROMICS) WILL DISCUSS THE APPLICATION OF ELECTROCHEMICAL APTAMER-BASED BIOSENSORS TO THE STUDY OF BRAIN NEUROPHARMACOLOGY WHICH PROVIDE UNIQUE INSIGHTS INTO SUBJECT-SPECIFIC PHARMACOKINETICS AND PERMIT THE ANALYSES OF DRUG ACTION IN TERMS OF IN-BRAIN CONCENTRATIONS, RATHER THAN TRADITIONAL DOSING. YEN-YU (IAN) SHIH (UNC) WILL DISCUSS THE DEVELOPMENT AND APPLICATION OF SPECTRAL FIBER PHOTOMETRY TO STUDY NEUROTRANSMISSION AS WELL AS ITS INCORPORATION INTO MRI BASED MEASUREMENTS OF BRAIN ACTIVITY. HIS WORK DEMONSTRATES THAT ABILITY TO PERFORM HIGH TEMPORAL RESOLUTION MEASUREMENTS IN A MULTIPLEXED FASHION INFORMING THE TIMING OF A VARIETY OF MOLECULAR EVENTS CRITICAL TO NEURONAL COMMUNICATION. LASTLY, ARNAB MUKHERJEE (UCSB) WILL DESCRIBE HIS ON THE DEVELOPMENT OF GENETICALLY-ENCODED SENSORS FOR MRI BASED MEASUREMENTS EMPLOYING AQUAPORINS AS REPORTERS. HIS WORK CAN BE GENETICALLY COUPLED TO MONITOR NEURONAL EVENTS EXTENDING FROM CALCIUM SIGNALING TO GENE EXPRESSION AND ENABLE MEASUREMENTS OF ON-GOING BRAIN ACTIVATION ACROSS TIMESCALES OF MINUTES TO MONTHS.

SUNDAY, JANUARY 28TH

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 1-3, FLOOR 3

ION CHANNEL MECHANISMS OF A FUNCTIONAL AND DYSFUNCTIONAL MESOLIMBIC SYSTEM

CHAIRS: EMILY TEICHMAN, ELYSSA MARGOLIS
PRESENTERS: ELYSSA MARGOLIS, EMILY JORGENSEN, ALLYSON FRIEDMAN, EMILY TEICHMAN

ION CHANNELS ARE CRITICAL REGULATORS OF NEURONAL ACTIVITY THROUGHOUT THE BRAIN. THEY FACILITATE AND MANIPULATE ACTION POTENTIAL FIRING, CONTRIBUTE TO CELL SIGNALING, MEDIATE EPIGENETIC CHANGES, AND ALSO PLAY KEY ROLES IN PLASTICITY AND MAINTAINING HOMEOSTASIS IN THE BRAIN. IN PARTICULAR, THE MESOLIMBIC PATHWAY HAS BEEN A HOTSPOT OF RESEARCH ON ION CHANNEL ACTIVITY, ESPECIALLY HCN CHANNELS AND VOLTAGE GATED POTASSIUM CHANNELS. ALTERATIONS OR IMPAIRMENTS IN ION CHANNEL ACTIVITY CAN HAVE DRASTIC EFFECTS ON BEHAVIOR. CONVERSELY, BEHAVIORAL CHALLENGES SUCH AS AVERSIVE STRESSORS CAN INDUCE CHANGES IN ION CHANNEL FUNCTION THAT CAN SUBSEQUENTLY CONTRIBUTE TO THE DEVELOPMENT OF CHRONIC DISORDERS INCLUDING PAIN, DEPRESSION, AND ADDICTION. UNDERSTANDING THE INTRICACIES OF THIS DYSFUNCTION CAN OPEN NEW THERAPEUTIC AVENUES FOR THESE DISORDERS. IN OUR PANEL WE WILL EXAMINE ION CHANNEL FUNCTION IN THE HEALTHY AND DYSFUNCTIONAL MESOLIMBIC SYSTEM. FIRST ELYSSA MARGOLIS FROM THE UNIVERSITY OF CALIFORNIA, SAN FRANCISCO WILL DESCRIBE UNPUBLISHED OBSERVATIONS SHOWING THAT AVERSIVE STRESS AND PAIN SWITCH ION CHANNEL COUPLING OF KAPPA OPIOID RECEPTORS IN VTA DOPAMINE NEURONS. NEXT, EMILY JORGENSEN FROM THE UNIVERSITY OF ALABAMA AT BIRMINGHAM WILL TALK ABOUT THE CONTRIBUTIONS OF KCNQ2 AND KCNQ3 CHANNELS TO MEDIUM SPINY NEURON EXCITABILITY. THEN, ALLYSON FRIEDMAN FROM HUNTER COLLEGE WILL SHARE RESULTS REGARDING ELECTROPHYSIOLOGICAL SIGNATURES OF STRESS ADAPTABILITY IN THE BNST-VTA CIRCUIT. FINALLY, EMILY TEICHMAN FROM THE ICAHN SCHOOL OF MEDICINE AT MOUNT SINAI WILL DESCRIBE HOW TARGETING ION CHANNELS SUCH AS THE HCN CHANNEL CAN PREVENT VTA DOPAMINE DYSFUNCTION INDUCED BY THE CHRONIC SOCIAL DEFEAT STRESS MODEL OF DEPRESSION IN MICE. TOGETHER THESE STUDIES HIGHLIGHT THE VARIETY OF WAYS THAT ION CHANNEL FUNCTION IS MODULATED BY BEHAVIOR AND VICE VERSA, AND THE THERAPEUTIC POTENTIAL OF TARGETING THESE PROTEINS.

SUNDAY, JANUARY 28TH

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 11-12, FLOOR 2

DELIRIUM: "THERE'S TOO MUCH CONFUSION"

CHAIR: ROBERT PEARCE
PRESENTERS: RICHARD LENNERTZ, NICCOLO TERRANDO, ROB SANDERS, CHRISTINA BONCYK

DELIRIUM IS A STATE OF CONFUSION THAT TYPICALLY AFFECTS OLDER INDIVIDUALS WHO INCUR A MEDICAL, SURGICAL OR PHARMACOLOGICAL STRESSOR. DELIRIUM IS ASSOCIATED WITH INCREASED RISK OF MORBIDITY, MORTALITY, INSTITUTIONALISATION AND DEMENTIA. IN THIS PANEL WE WILL EXPLORE THE PATHOPHYSIOLOGY OF DELIRIUM IN PRECLINICAL ANIMAL MODELS AND HUMAN TRANSLATIONAL WORK. WE WILL PROVIDE EVIDENCE LINKING CELLULAR RESPONSES, TO SYSTEMS LEVEL CHANGES IN NEURAL DYNAMICS AND DISCUSS HOW THESE CHANGES MAY LINK TO SUBSEQUENT DEMENTIA. THROUGH A CRITICAL LENS WE WILL HIGHLIGHT DEFICITS IN OUR KNOWLEDGE AND LOOK FORWARD TO INTERESTING DISCUSSION WITH THE AUDIENCE ABOUT FUTURE DIRECTIONS FOR THIS RELATIVELY NEW FIELD.
DR. LENNERTZ WILL DEFINE DELIRIUM AND GIVE AN OVERVIEW OF DELIRIUM PATHOPHYSIOLOGY BASED ON BIOMARKER STUDIES IN HUMANS. THIS WILL INCLUDE REVIEW OF CEREBROSPINAL FLUID AND PLASMA BIOMARKERS AND BASIC ELECTROPHYSIOLOGICAL OBSERVATIONS.
DR. TERRANDO WILL PROVIDE CRITICAL INSIGHTS FROM THE STUDY OF ANIMAL MODELS EXPLAINING HOW SURGICAL INFLAMMATION LEADS TO BREAKDOWN OF THE BLOOD BRAIN BARRIER, IMMUNE CELL ACTIVATION AND NEUROINFLAMMATION.
DR. SANDERS WILL BUILD ON THESE RESULTS AND EXPLAIN HOW HUMAN FLUID BIOMARKER AND ELECTROENCEPHALOGRAM STUDIES ARE BEING COMBINED WITH MODELLING APPROACHES TO PROVIDE INSIGHTS ABOUT DELIRIUM PATHOPHYSIOLOGY BASED ON TENETS FROM PREDICTIVE CODING.
DR. BONCYK WILL PROVIDE A CRITICAL REVIEW OF THE LINKS BETWEEN DELIRIUM AND LATER COGNITIVE DECLINE AND DEMENTIA BASED ON HER WORK ON BIOMARKERS AND COGNITIVE CHANGE.

SUNDAY, JANUARY 28TH

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 14, FLOOR 1

TRANSLATIONAL DEVELOPMENTS IN CANNABIS-BASED THERAPEUTICS

CHAIRS: RYAN VANDREY, MARCEL BONN-MILLER
PRESENTERS: ELISE WEERTS, PATRICK FINAN, ZIVA COOPER, BRIAN THOMAS

THIS PANEL PRESENTATION WILL PROVIDE A TRANSLATIONAL EVALUATION OF NEW RESEARCH FOCUSED ON THE EVALUATION OF CANNABINOIDS AS NOVEL THERAPEUTICS IN PAIN MANAGEMENT AND FRAGILE X SYNDROME. PAIN IS THE MOST COMMONLY REPORTED REASON FOR MEDICINAL CANNABIS USE GLOBALLY, BUT RESEARCH TO DATE HAS SHOWN MIXED EFFICACY AND OPIOID SPARING EFFECTS. MULTIPLE LINES OF EVIDENCE SUGGEST A CENTRAL ROLE FOR THE ENDOCANNABINOID SYSTEM IN NEURONAL DEVELOPMENT AND COGNITIVE FUNCTION AND IN THE PATHOGENESIS OF FRAGILE X SYNDROME (FXS). DR. WEERTS WILL PRESENT PRECLINICAL DATA EVALUATING THE INTERACTIONS OF DELTA-9-TETRAHYDROCANNABINOL (THC) AND CANNABIDIOL (CBD) AT VARIOUS DOSES AND RATIOS IN RODENT MODELS OF PAIN AND COGNITION, THE LATTER BEING IMPORTANT FOR PATIENT POPULATIONS WHO THAT SUFFER FROM INTELLECTUAL DISABILITY, SUCH AS FXS. DR. COOPER WILL PRESENT HUMAN LABORATORY RESEARCH IN WHICH THE ANALGESIC AND SUBJECTIVE EFFECTS OF ACUTE DOSES OF CANNABINOIDS AND TERPENES WERE EVALUATED IN EXPERIMENTAL PAIN MODELS. DR. FINAN WILL PRESENT "REAL WORLD" DATA COLLECTED IN REAL TIME USING MOBILE TECHNOLOGY RELATED TO THE ANALGESIC AND OPIOID-SPARING EFFECTS OF MEDICINAL CANNABIS USE OBTAINED FROM CANNABIS DISPENSARIES OR ALTERNATIVE RETAIL SOURCES. DR. BRIAN THOMAS WILL CONCLUDE THE SESSION WITH A SUMMARY OF DATA FROM CONTROLLED CLINICAL TRIALS SHOWING POSITIVE TREATMENT RESPONSES OF A NOVEL TRANSDERMAL CBD PRODUCT (ZYN002), COMPARED WITH PLACEBO, IN THE TREATMENT OF FXS. DRS. RYAN VANDREY AND MARCEL BONN-MILLER, INTERNATIONALLY RECOGNIZED EXPERTS IN CANNABINOID PHARMACOLOGY AND DRUG DEVELOPMENT RESPECTIVELY, WILL CO-CHAIR THE SESSION AND FACILITATE DISCUSSION AMONGST ATTENDEES. THE INTEGRATION OF PRE-CLINICAL, HUMAN LABORATORY, "REAL WORLD", AND CLINICAL RESEARCH ON PAIN AND FXS TREATMENT, PROMINENT AND PROMISING AREAS OF CANNABINOID TREATMENT APPLICATION, IS LIKELY TO HAVE BROAD APPEAL TO WINTER CONFERENCE ON BRAIN RESEARCH ATTENDEES.

SUNDAY, JANUARY 28TH

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 15-16, FLOOR 1

INTERPLAY BETWEEN TRAUMATIC BRAIN INJURY AND GUT MICROBIOME COMPOSITION: IMPLICATIONS FOR NEUROINFLAMMATION AND RECOVERY

CHAIR: DAVID DEVILBISS
PRESENTERS: COLE VONDER HAAR, ABIGAIL SCHINDLER, MASHKOOR CHOUDHRY, SUSANNAH NICHOLSON

TRAUMATIC BRAIN INJURY (TBI) AFFECTS APPROXIMATELY 1.7-3.8 MILLION AMERICANS EACH YEAR AND IS A COMPLEX PATHOPHYSIOLOGICAL PROCESS RESULTING IN A NUMBER OF COGNITIVE IMPAIRMENTS INCLUDING DEFICITS IN AROUSAL, ATTENTION, WORKING MEMORY, DECISION-MAKING, AND OTHER EXECUTIVE FUNCTIONS. THE GUT MICROBIOME, A COMPLEX ECOSYSTEM OF MICROORGANISMS RESIDING IN THE GASTROINTESTINAL TRACT, HAS EMERGED AS A POTENTIAL MODULATOR OF POST-TBI OUTCOMES. MOUNTING EVIDENCE SUGGESTS THAT DISRUPTIONS IN THE GUT MICROBIOTA COMPOSITION MAY INFLUENCE NEUROINFLAMMATORY RESPONSES, IMMUNE MODULATION, AND SUBSEQUENT NEURAL PROCESSES FOLLOWING TBI. BIDIRECTIONAL COMMUNICATION ALONG THE GUT-BRAIN AXIS IS HYPOTHESIZED TO UNDERLIE THESE EFFECTS, WITH MICROBIAL METABOLITES AND SIGNALING MOLECULES POTENTIALLY IMPACTING NEUROINFLAMMATORY CASCADES AND NEURAL PLASTICITY. WHILE THE PRECISE MECHANISMS REMAIN ENIGMATIC, INVESTIGATIONS INTO THE ROLE OF THE GUT MICROBIOME IN TBI HOLD SIGNIFICANT PROMISE FOR ADVANCING OUR UNDERSTANDING OF THE COMPLEX PATHOPHYSIOLOGY OF TBI AND IDENTIFYING NOVEL THERAPEUTIC AVENUES TO ENHANCE NEUROLOGICAL RECOVERY. DR. COLE VONDER HAAR WILL PRESENT RECENT FINDINGS ON MICROBIOME CHANGES AS PREDICTOR AND CAUSE OF NEUROCOGNITIVE IMPAIRMENTS AFTER TBI AND TREATMENT STRATEGIES TARGETING MODIFICATION OF THE MICROBIOME. DR. ABIGAIL SCHINDLER WILL PRESENT NEW WORK ON THE MICROBIOME, SYSTEMIC INFLAMMATION, AND OUTCOMES RELATED TO THE POLYTRAUMA CLINICAL TRIAD OF TBI. DR. MASHKOOR CHOUDHRY WILL PRESENT EMERGING FINDINGS ON THE INTERPLAY BETWEEN TBI OR POLYTRAUMA AND GUT DYSFUNCTION, SYSTEMIC INFLAMMATION, AND NEUROINFLAMMATION. DR. SUSANNAH NICHOLSON WILL PRECENT NOVEL DATA ON THE TIME COURSE OF GUT DYSBIOSIS CORRELATED WITH LESION VOLUME AND BEHAVIORAL DYSFUNCTION AFTER TBI AND SPINAL CORD INJURY.

SUNDAY, JANUARY 28TH

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 17, FLOOR 1

STRESS AND ADDICTION: NEW INSIGHTS FROM ANIMAL MODELS AND HUMAN STUDIES

CHAIR: YAVIN SHAHAM
PRESENTERS: JOHN MANTSCH, YAVIN SHAHAM, MARIE EIKEMO, RAJITA SINHA

DRUG USE AND RELAPSE ARE ASSOCIATED WITH STRESS AND TRAUMA. DECADES OF ANIMAL AND HUMAN RESEARCH HAS SHOWN THAT STRESS INCREASES CRAVING AND RELAPSE RISK. HOWEVER, MANY UNANSWERED QUESTIONS REMAIN ON BEHAVIORAL AND BRAIN MECHANISMS OF THE COMPLEX STRESS-ADDICTION INTERACTION. OUR PANEL WILL PRESENT NEW DATA FROM ANIMAL MODELS AND HUMAN STUDIES ON NOVEL BEHAVIORAL EFFECTS AND NEUROPHARMACOLOGICAL MECHANISMS OF THIS INTERACTION.
MANTSCH WILL INTRODUCE A RAT MODEL WHERE MILD STRESS (WHICH DOES NOT CAUSE RELAPSE ON ITS OWN) POTENTIATES RELAPSE INDUCED BY ACUTE REEXPOSURE TO THE SELF-ADMINISTERED DRUG (COCAINE). HE WILL DESCRIBE A NOVEL MECHANISM—ELEVATED CORTICOSTERONE AND ENDOCANNABINOID SIGNALING VIA CB1 RECEPTORS IN PRELIMBIC PREFRONTAL CORTEX—THAT MEDIATES THIS 'INDIRECT' MILD-STRESS EFFECT ON RELAPSE.
SHAHAM WILL INTRODUCE A NEW RAT MODEL WHERE INCUBATION OF OPIOID SEEKING IS POTENTIATED AFTER ABSTINENCE INDUCED BY EXPOSURE TO AN ELECTRIC-BARRIER STRESSOR. SHE WILL SHOW RESULTS FROM STUDIES USING MODERN NEUROSCIENCE METHODS ON THE IDENTIFICATION OF A NOVEL VENTRAL SUBICULUM-CLAUSTRUM CIRCUIT CRITICAL TO THE EFFECT OF THE STRESSOR ON INCUBATION.
EIKEMO WILL INTRODUCE A NEW METHOD TO MEASURE STRESS EFFECTS ON OXYCODONE INTAKE IN HEALTHY VOLUNTEERS. SHE WILL ALSO PRESENT DATA ON EFFECTS OF PRE-ANESTHESIA OPIOID INJECTIONS ON SUBJECTIVE MEASURES OF ANXIETY AND WELL-BEING IN SURGICAL (A STRESSFUL LIFE EVENT) PATIENTS. SHE WILL SHOW THAT (1) STRESS INCREASES OPIOID INTAKE IN MEN BUT NOT WOMEN, AND (2) PRE-ANESTHESIA OPIOID EXPOSURE HAS MINIMAL EFFECTS ON ANXIETY AND WELL-BEING MEASURES.
SINHA WILL INTRODUCE A NEW STRESS MANIPULATION THAT IDENTIFIES ADAPTATIONS SPECIFIC TO CHRONIC STRESS, DRUG USE, AND THEIR INTERACTIONS. SHE WILL SHOW HOW THESE INTERACTIONS MODULATE DRUG INTAKE AND CRAVING, AND THE RESCUE OF THESE PROCESSES WITH NEUROACTIVE STEROIDS. SHE WILL DISCUSS THE RELEVANCE OF THESE DATA TO PERSONALIZED MEDICINE APPROACHES TO TREAT ADDICTION.

SUNDAY, JANUARY 28TH

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 6-8, FLOOR 2

VISUAL PROCESSING AND BEHAVIOR IN THE MOUSE

CHAIR: CRISTOPHER NIELL
PRESENTERS: HUIZHONG TAO, JASON SAMONDS, CRISTOPHER NIELL, JENNIFER HOY

OVER THE PAST DECADE, THE MOUSE HAS EMERGED AS A POWERFUL GENETIC MODEL SYSTEM FOR STUDYING THE NEURAL CIRCUITS THAT MEDIATE VISION. WHILE PREVIOUS STUDIES OFTEN FOCUSED ON LOW-LEVEL FEATURES, SUCH AS ORIENTATION SELECTIVITY, MORE RECENT WORK HAS BEGUN TO EXAMINE HOW THE BRAIN EXTRACTS ETHOLOGICALLY RELEVANT INFORMATION FROM THE VISUAL SCENE AND USES THIS TO DRIVE BEHAVIOR. SPEAKERS IN THIS PANEL SPAN THE INTERACTION OF NEURAL CIRCUITS, VISUAL CODING, AND NATURAL BEHAVIOR. DR. HUIZHONG TAO (UNIVERSITY OF SOUTHERN CALIFORNIA) WILL DESCRIBE HOW AN INHIBITORY THALAMOCOLLICULAR PROJECTION SHAPES THE VISUOSPATIAL PROCESSING OF SUPERIOR COLLICULUS NEURONS AND ENHANCES VISUAL DETECTION OF SMALL OBJECTS. DR. JASON SAMONDS (UNIVERSITY OF TEXAS - AUSTIN) WILL EXPLAIN THE ROLE OF NEURONAL INTERACTIONS AND INHIBITORY INTERNEURON INTEGRATION IN DISPARITY TUNING AND SUPPRESSING RESPONSES TO ANTI-CORRELATED STEREOGRAMS, DEMONSTRATING THEIR IMPORTANCE IN SOLVING THE STEREO CORRESPONDENCE PROBLEM. DR. CRISTOPHER NIELL (UNIVERSITY OF OREGON) WILL PRESENT NEW APPROACHES FOR STUDYING VISUAL PROCESSING IN FREELY MOVING ANIMALS, WHICH REVEAL HOW VISUAL AND MOVEMENT SIGNALS ARE INTEGRATED UNDER NATURAL CONDITIONS. DR. JENNIFER HOY (UNIVERSITY OF NEVADA – RENO) WILL DESCRIBE A LEPTIN SIGNALING PATHWAY THAT DECREASES INSECT PREDATION, YET ENHANCES VISUAL-STIMULUS-EVOKED APPETITIVE ORIENTING RESPONSES, REVEALING A HORMONALLY-DRIVEN DISSOCIATION BETWEEN PREDATORY VERSUS VISUAL STIMULATION-BASED MOTIVATIONS.

SUNDAY, JANUARY 28TH

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 9-10, FLOOR 2

THE INFLUENCE OF SIGHTS, SMELLS, SOUNDS, AND REWARDS ON HIPPOCAMPAL DYNAMICS AND REPRESENTATIONS
CHAIR: KAMRAN DIBA

PRESENTERS: LARA RANGEL, GIDEON ROTHSCHILD, MARIELENA SOSA, SEBASTIEN ROYER

THE MAMMALIAN HIPPOCAMPUS IS ENDOWED WITH RICH DYNAMICS THAT GENERATE MULTI-SENSORY REPRESENTATIONS IN SUPPORT OF MEMORY. OUR PANEL PROVIDES A MULTI-FACETED INVESTIGATION OF THE FACTORS THAT DRIVE THESE ACTIVITIES.

STARTING WITH THE ROLE OF INHIBITION, LARA RANGEL WILL SHOW THAT CA1 INTERNEURONS CLUSTER BY THE TIMING OF THEIR ACTIVITY WITHIN HIPPOCAMPAL RHYTHMS, AND THAT TIMING IN ONE RHYTHM PREDICTS TIMING IN OTHER RHYTHMS. CHANGING SENSORY INPUTS DIFFERENTIALLY ENGAGE INTERNEURONS IN RHYTHMIC ACTIVITY, BUT DO NOT ALTER THEIR TIMING WITHIN RHYTHMS IF THEY ENGAGE. THIS SUGGESTS A STABLE TEMPORAL ORDER OF INTERNEURONAL ACTIVITY ACROSS MULTIPLE RHYTHMIC CIRCUITS.

GIDEON ROTHSCHILD'S STUDY COMBINES ELECTROPHYSIOLOGICAL RECORDINGS AND CLOSED-LOOP SOUND PRESENTATION IN RATS TO DEMONSTRATE THAT EXPOSURE TO SOUNDS DURING SLEEP INTERFERES WITH THE HIPPOCAMPAL SIGNATURES OF MEMORY CONSOLIDATION AND IMPAIRS SUBSEQUENT PERFORMANCE IN A MEMORY TASK.

MARIELENA SOSA INVESTIGATES HOW THE HIPPOCAMPAL REPRESENTATION OF REWARD FLEXIBLY UPDATES WITHIN AND ACROSS ENVIRONMENTS AND REPORTS A SUBPOPULATION OF CELLS THAT REMAP TO THE SAME RELATIVE POSITION WITH RESPECT TO REWARD WHEN REWARDS MOVES. THESE 'REWARD-RELATIVE' CELLS CONSTRUCT SEQUENCES SPANNING THE TASK THAT INCREASE IN DENSITY WITH EXTENDED TASK EXPERIENCE, SUGGESTING THAT THE HIPPOCAMPUS BUILDS A GENERALIZED REPRESENTATION OF THE TASK STRUCTURE ANCHORED TO REWARD IN PARALLEL TO A STABLE SPATIAL MAP.

FINALLY, THE HIPPOCAMPUS SUPPORTS EPISODIC MEMORY BY ALLOWING RAPID 'ONE-SHOT' ENCODING OF EVENTS. DR. SEBASTIEN ROYER WILL PRESENT AN EXAMINATION OF TRANSIENT/PERSISTENT PLACE CELL REMAPPING RESPONSES TO THE TRANSIENT ENCOUNTER OF A BUTTERFLY DUMMY BY MICE RUNNING ON A TREADMILL. THIS STUDY FINDS THAT A MODEL OF COMPETITIVE LEARNING LARGELY PREDICTS THE SPECTRUM OF CELL RESPONSES AND THE ONE-SHOT IMPRINTING OF ENGRAMS IN THE MATRIX OF SYNAPTIC WEIGHTS.

SUNDAY, JANUARY 28TH

SHORT COURSE
7:00 P.M. - 8:30 P.M.
IMPERIAL BALLROOM, FLOOR 4

CURRENT TRENDS IN CLINICAL PHYTOCANNABINOID MOLECULE DEVELOPMENT

CHAIR: THOMAS SWANSON
PRESENTERS: THOMAS SWANSON, CARL LUPICA, JACCI BAINBRIDGE, HUNTER LAND

MANY MOLECULES HAVE BEEN IDENTIFIED IN CANNABIS SATIVA, AND SEVERAL HAVE BOTH PRE-CLINICAL AND CLINICAL PROVEN EFFICACY IN A VARIETY OF CONDITIONS. HOWEVER, THE REAL-WORLD DELIVERY OF THESE THERAPIES TO PATIENTS REMAINS SEVERELY LIMITED. PHYSICIANS LACK INFORMATION ON WHICH MOLECULES AND DOSES TO USE, DRUG / DRUG INTERACTIONS, SIGNIFICANT ADVERSE EVENTS, AND POTENTIAL SIDE EFFECTS. CANNABIS DISPENSARIES SELL PREDOMINATELY THC PRODUCTS, AND THEIR STAFF HAVE LIMITED CLINICAL KNOWLEDGE. IT IS ALSO DIFFICULT TO FIND RELIABLE SOURCES OF NON-THC CANNABINOIDS, WITH CONSISTENT AMOUNTS OF THE MOLECULE, BATCH TO BATCH, VALIDATED BY ACCURATE ANALYTICAL TESTING. THIS COURSE WILL COVER THE SCIENCE BEHIND PHYTOCANNABINOID ACTIONS, EMERGING TRENDS IN CANNABINOID THERAPEUTIC USE, CLINICAL TRIAL DATA, AND COMMERCIAL / INDUSTRY CONSTRAINTS WHICH HAVE HAMPERED THE WIDE-SPREAD USE OF CANNABIS. TOM SWANSON WILL DISCUSS WHY CANNABINOIDS REPRESENT AN INCREASINGLY VIABLE THERAPY FOR MANY SYMPTOMS, PROBLEMS WITH CURRENT MOLECULE DEVELOPMENT STRATEGIES, AND FORWARD-LOOKING SOLUTIONS. CARL LUPICA WILL REVIEW THE ENDOCANNABINOID SYSTEM AND DISCUSS THE MECHANISMS BY WHICH THERAPEUTICALLY PROMISING PHYTOCANNABINOIDS ACT IN THE CENTRAL NERVOUS SYSTEM. JACCI BAINBRIDGE WILL DISCUSS CURRENT CANNABIS CLINICAL TRIALS IN A VARIETY OF NEUROLOGICAL CONDITIONS, INCLUDING PAIN AND OPIATE REDUCTION. HUNTER LAND WILL DISCUSS RATIONAL CANNABINOID POLYPHARMACY: "ENTOURAGE VS NON-TORAGE", AND THE DEVELOPMENT OF CANNABINOID MEDICINES ACCORDING TO THE FDA BOTANICAL DRUG DEVELOPMENT GUIDANCE FOR INDUSTRY.

SUNDAY, JANUARY 28TH

PANEL
7:00 P.M. - 8:30 P.M.
PEAK 1-3, FLOOR 3

ION CHANNELS AND EXCITABILITY: CULPRITS IMPAIRING NEURONAL ACTIVITY IN DISEASE?

CHAIR: JOSHUA GARCIA
PRESENTERS: JOSHUA GARCIA, DARRIN BRAGER, NIDIA QUILLINAN

THE OVERALL EXCITABILITY OF INDIVIDUAL NEURONS RESULTS FROM THE ACTIVATION OF SPECIFIC ION CHANNEL SUBTYPES INCLUDING BOTH VOLTAGE- AND LIGAND-GATED CHANNELS, WHICH MAINLY FUNCTION TO ENHANCE OR REDUCE CELLULAR ACTIVITY. FURTHER, THE COMPLEXITY OF ION CHANNEL EXPRESSION ACROSS DISTINCT NEURONAL POPULATIONS AND EVEN AT SPECIFIC LOCALITIES THROUGHOUT THE SOMATODENDRITIC ARBOR OR AXON DIRECTLY CONTROLS UNIQUE ELECTROPHYSIOLOGICAL PROPERTIES OF INDIVIDUAL CELLS. ION CHANNEL EXPRESSION IS HIGHLY DYNAMIC WITH CHANGES TO THEIR ACCUMULATION AT SPECIFIC LOCALITIES BEING OBSERVED BOTH THROUGH DEVELOPMENT AND IN RESPONSE TO ACTIVITY. DISRUPTING NORMAL PHYSIOLOGICAL ION CHANNEL FUNCTION CAN HAVE SEVERE DELETERIOUS DEFICITS TO SPECIFIC NEURONAL SUB-POPULATIONS, RESULTING IN ALTERED EXCITABILITY, AND THESE CHANGES ARE A HALLMARK CONTRIBUTING TO A HOST OF DISEASE STATES LIKE EPILEPSY, AUTISM, OR INTELLECTUAL DISABILITY.

IN THIS PANEL, WE AIM TO FOCUS ON THE CONTRIBUTIONS DIFFERENT ION CHANNELS HAVE ON INDIVIDUAL NEURONS, AND HOW THEIR DYSFUNCTION IMPACTS SPECIFIC PROPERTIES OF DISCRETE CELL-TYPES LIKE ALTERED CELLULAR EXCITABILITY THAT MAY EXACERBATE CIRCUIT DYSFUNCTION LEADING TO DISEASE ONSET OR PROGRESSION. JOSHUA GARCIA (UCSF) WILL PRESENT DATA DETAILING SPECIFIC CONTRIBUTIONS INDIVIDUAL SODIUM CHANNEL ISOFORMS HAVE AT SPECIFIC NEURONAL COMPARTMENTS OR ACROSS DIFFERENT CELL-TYPES AND EMPATHIZE HOW TARGETING DISTINCT CHANNELS IS NECESSARY TO ALLEVIATE ENHANCED NEURONAL ACTIVITY IN DISCRETE PATHOGENETIC CONDITIONS. DARRIN BRAGER (UNLV) WILL DISCUSS HOW CHANGES IN DIFFERENT TYPES OF VOLTAGE-GATED ION CHANNELS PRODUCE SIMILAR DENDRITIC EXCITABILITY CHANGES BETWEEN HIPPOCAMPAL AND PREFRONTAL NEURONS IN A MOUSE MODEL OF FRAGILE X SYNDROME. LASTLY, NIDIA QUILLINAN (COLORADO) WILL PRESENT DATA SHOWING HOW EXCITOTOXICITY ALTERS EXCITATORY AND INHIBITORY TONE MAINLY IN THE HIPPOCAMPUS USING MODELS OF CEREBRAL ISCHEMIA.

SUNDAY, JANUARY 28TH

PANEL
7:00 P.M. - 8:30 P.M.
PEAK 11-12, FLOOR 2

NEURAL CIRCUITS AND CORTICAL PLASTICITY FOR INNATE AND LEARNED AUDITORY BEHAVIORS

CHAIRS: LI ZHANG, ALFONSO JUNIOR APICELLA
PRESENTERS: MICHELE INSANALLY, DAVID SCHNEIDER, ROBERT FROEMKE, ROBERT LIU

THE PANEL WILL PROVIDE AN OPPORTUNITY FOR A BROAD DISCUSSION ON THE NEURAL CIRCUIT AND PLASTICITY MECHANISMS UNDERLYING VARIOUS AUDITORY BEHAVIORS. PARTICULARLY, THE PANEL WILL DISCUSS THE DIFFERENCES AND COMMONALITIES OF THE UNDERLYING CIRCUITS OF INNATE (LIKE REFLEXES) AND LEARNED BEHAVIORS (EXPERIENCES-DEPENDENT). DR. MICHELE INSANALLY FROM PITTSBURGH UNIVERSITY WILL PRESENT HER WORK ON HOW THE AUDITORY SYSTEM FLEXIBLY GATES SENSORY INFORMATION TO SELECT APPROPRIATE BEHAVIORAL STRATEGIES BASED ON SENSORY INPUT AND CONTEXT. SHE WILL DESCRIBE HOW DIVERSE CORTICAL RESPONSES EMERGE AND EVOLVE DURING FLEXIBLE BEHAVIOR AND HOW TOP-DOWN INPUTS SHAPE THESE RESPONSES DURING AUDITORY LEARNING. DR. DAVID SCHNEIDER FROM NYU WILL INTRODUCE HIS RECENT STUDY ON NEURAL CIRCUITS FOR DETECTING ERRORS AND IMPROVING PERFORMANCE FOLLOWING MISTAKES IN BEHAVIORAL PERFORMANCE. HE WILL FOCUS ON THE ROLE OF THE MOUSE AUDITORY CORTEX IN ENCODING ERROR- AND LEARNING-RELATED SIGNALS DURING A SKILLED SOUND-GENERATING BEHAVIOR. DR. ROBERT FROEMKE, NYU MEDICAL SCHOOL, WILL DISCUSS NEUROMODULATION AND PLASTICITY BY COCHLEAR IMPLANTS. HE WILL DESCRIBE NEW AND ONGOING STUDIES OF DEAFENED RATS USING COCHLEAR IMPLANTS TO PERFORM AN AUDITORY TASK. DR. ROBERT LIU FROM EMORY UNIVERSITY WILL PRESENT HIS WORK ON NEURAL CORRELATES OF LEARNING A NEW SOUND-CUED STRATEGY TO GUIDE AN INNATE SOCIAL BEHAVIOR. HE WILL DESCRIBE THEIR FINDINGS ON HOW THE AUDITORY AND MEDIAL PREFRONTAL CORTEX CHANGES IN SOUND-INITIATED PARENTAL BEHAVIORS. DRS. LI ZHANG (USC) AND ALFONSO APICELLA (UTSA) WILL PROVIDE INTRODUCTORY COMMENTS AND LEAD THE PRESENTATION'S DISCUSSION.

SUNDAY, JANUARY 28TH

PANEL
7:00 P.M. - 8:30 P.M.
PEAK 14, FLOOR 1

MOLECULAR MECHANISMS SUPPORTING ADDICTION DEVELOPMENT AND RELAPSE

CHAIRS: KATHERINE SAVELL, CALEB BROWNE
PRESENTERS: JENNIFER TUSCHER, BOWEN TAN, CALEB BROWNE, KATHERINE SAVELL

ILLICIT DRUG USE AND PRESCRIPTION DRUG MISUSE INDUCE LONG-TERM MOLECULAR REMODELING IN REWARD CIRCUITS THAT PLAY A CRITICAL ROLE IN DRUG-SEEKING AND RELAPSE DURING ABSTINENCE. UNDERSTANDING HOW THESE CHANGES OCCUR DURING DRUG USE AND PERSIST THROUGHOUT ABSTINENCE AT CELL-TYPE- AND CIRCUIT-SPECIFIC LEVELS IS CRUCIAL TO THE DEVELOPMENT OF NEW STRATEGIES FOR RELAPSE PREVENTION. THIS PANEL WILL PRESENT RESEARCH SPANNING MULTIPLE DRUG CLASSES AND BRAIN REGIONS WITHIN THE REWARD CIRCUIT, THAT SHOWS HOW DRUGS IMPACT MOTIVATION, PHYSIOLOGICAL STATES, MEMORY SYSTEMS, AND CREATE MOLECULAR IMPRINTS THAT HEIGHTEN CRAVING AND RELAPSE SUSCEPTIBILITY.
JENNIFER TUSCHER (UAB) WILL DESCRIBE SNRNASEQ TRANSCRIPTIONAL PROFILING IN THE RAT VENTRAL TEGMENTAL AREA TO OUTLINE CELL-TYPE-SPECIFIC MOLECULAR SIGNATURES OF OPIOID EXPERIENCE AND HOW THESE SIGNATURES ARE MODULATED BY A PRE-EXISTING PAIN STATE.
BOWEN TAN (ROCKEFELLER) WILL PRESENT ONGOING STUDIES USING WHOLE-BRAIN ACTIVITY MAPPING, SNRNA-SEQ, AND CRISPR-MODULATION IN MICE TO STUDY MOLECULAR AND CELLULAR DYNAMICS ACROSS NATURAL AND DRUG REWARDS WITHIN THE NUCLEUS ACCUMBENS AND WILL DISCUSS MECHANISMS THAT PERMIT DRUGS TO REMODEL HOMEOSTASIS IN REWARD CIRCUITS.
CALEB BROWNE (MOUNT SINAI) WILL OUTLINE STUDIES REVEALING A NOVEL GENE NETWORK ASSOCIATED WITH RELAPSE TO HEROIN-SEEKING WITHIN THE VENTRAL HIPPOCAMPUS OF MICE THAT IMPLICATES KEY EPIGENETIC REGULATORY FACTORS SUPPORTING LONG-TERM RELAPSE SUSCEPTIBILITY.
KATHERINE SAVELL (NIDA IRP) WILL SHOWCASE ONGOING STUDIES USING A NEWLY DEVELOPED SNRNA-SEQ PIPELINE TO UNCOVER THE MOLECULAR SIGNATURES OF COCAINE-MEMORY-SPECIFIC ACTIVE (ENSEMBLE) NEURONS IN RAT INFRALIMBIC CORTEX DURING COCAINE RELAPSE.
THIS PANEL WILL SHOW HOW INTEGRATION OF THESE MULTI-DIMENSIONAL APPROACHES CAN IMPROVE OUR UNDERSTANDING OF DRUG EXPERIENCE-INDUCED CELLULAR AND MOLECULAR ALTERATIONS, PAVING THE WAY TO NOVEL THERAPEUTIC INTERVENTIONS AIMED AT SUPPRESSING ADDICTION DEVELOPMENT AND PREVENTING RELAPSE.

SUNDAY, JANUARY 28TH

PANEL
7:00 P.M. - 8:30 P.M.
PEAK 15-16, FLOOR 1

SEX DIFFERENCES IN AVERSIVE PROCESSING

CHAIR: JULIA MITCHELL
PRESENTERS: JULIA MITCHELL, LAURA O'DELL, EDITA NAVRATILOVA, TIFFANY WILLS

WOMEN ARE TWICE AS LIKELY AS MEN TO DEVELOP POST TRAUMATIC STRESS DISORDER, ARE MORE LIKELY TO DEVELOP A CHRONIC PAIN CONDITION AND EXHIBIT GREATER VULNERABILITY TO THE DEVELOPMENT OF SUBSTANCE USE DISORDERS. UNFORTUNATELY, FEMALE ANIMALS HAVE HISTORICALLY BEEN EXCLUDED FROM RELEVANT PRECLINICAL RESEARCH, LEAVING A GAP IN OUR UNDERSTANDING ON THE INFLUENCES OF SEX ON THE UNDERLYING NEURAL MECHANISMS AND TREATMENT OF THESE DISORDERS. JULIA MITCHELL (PANEL CHAIR, PHD CANDIDATE, NORTHEASTERN UNIVERSITY) WILL PRESENT FINDINGS SHOWING THAT ACTIVATION OF THE IL AND PAG DURING PAVLOVIAN FEAR CONDITIONING IS SEX DEPENDENT, AND VIA A CHEMOGENETIC APPROACH, THAT MANIPULATION OF THE IL-PAG CIRCUIT LEADS TO SEX DEPENDENT CHANGES IN CONDITIONED AND UNCONDITIONED RESPONSES. LAURA O'DELL (PROFESSOR AND ASSOCIATE VICE PRESIDENT FOR RESEARCH, UNIVERSITY OF TEXAS EL PASO) WILL PRESENT WORK DEMONSTRATING SEX DIFFERENCES IN THE REWARDING EFFECTS OF NICOTINE AND NICOTINE WITHDRAWAL, AND DATA SHOWING THE ROLE OVARIAN HORMONES PLAY IN ENHANCING NICOTINE'S REWARDING EFFECTS AND IN PROMOTING THE STRESS RESPONSES FOLLOWING NICOTINE WITHDRAWAL. EDITA NAVRATILOVA (ASSOCIATE PROFESSOR, UNIVERSITY OF ARIZONA) WILL PRESENT RECENT FINDINGS ON THE ROLE OF PROLACTIN IN SELECTIVE SENSITIZATION OF FEMALE NOCICEPTORS THAT MAY CONTRIBUTE TO THE HIGHER PREVALENCE OF CHRONIC PAIN CONDITIONS OBSERVED IN WOMEN. TIFFANY WILLS (ASSOCIATE PROFESSOR, LOUISIANA STATE UNIVERSITY HEALTH SCIENCES CENTER NEW ORLEANS) WILL PRESENT HER WORK SHOWING THAT CHRONIC ADOLESCENT ALCOHOL EXPOSURE PRODUCED LONG-TERM CHANGES IN HYPERALGESIA IN A SEX- AND SPECIES-SPECIFIC MANNER, WHICH IS ASSOCIATED WITH CHANGES IN THE CENTRAL AMYGDALA TO PAG CIRCUIT. THIS PANEL BRINGS TOGETHER A COMPREHENSIVE AND DIVERSE GROUP OF RESEARCHERS WHO WILL HIGHLIGHT THE IMPORTANCE OF CONDUCTING RIGOROUS SABV WORK ACROSS VARIED AVERSIVE PARADIGMS.

SUNDAY, JANUARY 28TH

SHORT COURSE
7:00 P.M. - 8:30 P.M.
PEAK 17, FLOOR 1

TRANSCRIPTOMIC STUDIES IN NEUROSCIENCE RESEARCH

CHAIR: LAURA FERGUSON
PRESENTERS: LAURA FERGUSON, LAURA SABA, R. DAYNE MAYFIELD

CELL FUNCTION IS DICTATED BY GENE EXPRESSION, AND DISRUPTED GENE EXPRESSION IS ASSOCIATED WITH ADVERSE OUTCOMES. MICROARRAY AND RNA SEQ TECHNOLOGIES PERMIT THE MEASUREMENT OF THE EXPRESSION LEVEL FOR EVERY TRANSCRIPT SIMULTANEOUSLY WHICH ENABLES UNBIASED, SYSTEMS-LEVEL APPROACHES TO ADDRESS IMPORTANT QUESTIONS IN NEUROSCIENCE RESEARCH. BECAUSE OF THE IMPORTANCE OF GENE EXPRESSION IN DICTATING CELL FUNCTION (WHICH THEN AFFECTS CIRCUIT FUNCTION, AND ULTIMATELY BEHAVIOR), AND THE INCREASING ACCESSIBILITY AND AFFORDABILITY OF MICROARRAY AND RNA SEQ TECHNOLOGY, TRANSCRIPTOME STUDIES ARE BECOMING MORE COMMON IN NEUROSCIENCE RESEARCH. GENE EXPRESSION STUDIES CAN BE USED TO MOLECULARLY DEFINE SPECIFIC CELL TYPES, AND MARKERS IDENTIFIED FROM THESE STUDIES CAN BE USED IN COMBINATION WITH OTHER TOOLS (E.G., CHEMOGENETIC AND OPTOGENETIC APPROACHES) TO MOLECULARLY TARGET SPECIFIC CELL TYPES OF INTEREST. GENE EXPRESSION STUDIES CAN ALSO ENABLE RESEARCHERS TO FORMULATE HYPOTHESES ABOUT WHAT IS UNDERLYING COMPLEX CONDITIONS AT A SYSTEMS-LEVEL IN AN UNBIASED MANNER. IN THIS SHORT COURSE YOU CAN LEARN (1) IMPORTANT CONSIDERATIONS IN TRANSCRIPTOME STUDIES (E.G., SAMPLE SIZE, NECESSARY CONTROLS, UNDERLYING ASSUMPTIONS, QUALITY CONTROL STEPS), (2) HOW GENE EXPRESSION DATA CAN BE USED IN YOUR RESEARCH, AND (3) COMMON ANALYSES AND GRAPHS THAT ARE ENCOUNTERED FROM THESE STUDIES AND THEIR INTERPRETATION FOR BULK SEQUENCING AND SINGLE-CELL / SINGLE-NUCLEI SEQUENCING EXPERIMENTS. THE MAIN GOAL OF THIS SHORT COURSE IS TO ENABLE RESEARCHERS WITH NO BACKGROUND IN TRANSCRIPTOMICS TO BE ABLE TO CRITICALLY EVALUATE THE RESULTS AND GRAPHS PRODUCED FROM GENE EXPRESSION STUDIES THAT ARE COMMONLY ENCOUNTERED IN THE LITERATURE. ADDITIONAL GOALS INCLUDE FOSTERING COLLABORATIONS AND PROMOTING SYSTEMS-LEVEL RESEARCH APPROACHES USING TRANSCRIPTOMICS.

SUNDAY, JANUARY 28TH

PANEL
7:00 P.M. - 8:30 P.M.
PEAK 6-8, FLOOR 2

NEUROMODULATORY SYSTEMS IN THE CONTROL OF BREATHING

CHAIRS: ADRIENN VARGA, ERICA LEVITT
PRESENTERS: GASPARD MONTANDON, JESSICA WHITAKER-FORNEK, ADRIENN VARGA, NATALIE JOHNSON

BREATHING IS A SEEMINGLY AUTOMATED BEHAVIOR, THAT IS CONSTANTLY ADJUSTED BY NEUROTRANSMITTER AND NEUROMODULATOR SYSTEMS TO ACCOMMODATE METABOLIC AND SYSTEMIC DEMANDS. THE GOAL OF THIS SESSION IS TO DESCRIBE THE EMERGING UNDERSTANDING OF THE MECHANISMS THAT CONTRIBUTE TO THE APPROPRIATE SHAPING OF THE BREATH. ADRIENN VARGA AND ERICA LEVITT WILL CHAIR AND CO-CHAIR THE PANEL, AND PROVIDE INTRODUCTORY COMMENTS. GASPARD MONTANDON (UNIVERSITY OF TORONTO) WILL DESCRIBE HOW MEDULLARY BREATHING RHYTHM GENERATION IS IMPACTED BY NEUROMODULATION FROM MULTIPLE SOURCES, INCLUDING GLUTAMATE, TACHYKININ, GABA, AND OPIOIDS. JESSICA WHITAKER-FORNEK (UNIVERSITY OF MICHIGAN) WILL DISCUSS HOW SEROTONERGIC NEURONS IMPACT OPIOID EFFECTS ON BREATHING IN THE PONTINE RESPIRATORY NUCLEI. ADRIENN VARGA (UNIVERSITY OF FLORIDA) WILL TALK ABOUT NORADRENERGIC AND GLUTAMATERGIC INFLUENCES ON THE ACTIVITY OF RESPIRATORY NEURONS IN A LOCUS COERULEUS AROUSAL-BREATHING CIRCUIT. NATALIE JOHNSON (UNIVERSITY OF FLORIDA) WILL DISCUSS THE ROLE OF BASAL GANGLIA DOPAMINERGIC NEURONS IN CONTROLLING BREATHING FREQUENCY TO PRODUCE SNIFFING.

SUNDAY, JANUARY 28TH

PANEL
7:00 P.M. - 8:30 P.M.
PEAK 9-10, FLOOR 2

EMERGING ROUTES TO MODIFY EPILEPTOGENESIS AND NEUROPATHOLOGY AFTER TRAUMATIC BRAIN INJURY

CHAIR: BRET SMITH
PRESENTERS: BRET SMITH, MARK SHAPIRO, NAOMI SAYRE

OVER ONE MILLION PEOPLE PRESENT FOR MEDICAL CARE AFTER A TRAUMATIC BRAIN INJURY (TBI) EACH YEAR IN THE UNITED STATES. BESIDES ACUTE SEQUELAE, SUCH AS POST-TRAUMATIC SEIZURES (PTS), THESE INDIVIDUALS OFTEN DEVELOP POST-TRAUMATIC EPILEPSY (PTE) OR OTHER COGNITIVE PATHOLOGIES AFTER A VARIABLE AND OFTEN LONG DELAY, FOR WHICH THERE ARE FEW EFFECTIVE THERAPIES. THE MECHANISMS UNDERLYING DEVELOPMENT OF THESE LONG-TERM SEQUELAE ARE POORLY UNDERSTOOD. THUS, THERE ARE PRESENTLY NO APPROVED TREATMENTS THAT ABROGATE POST-TBI NEUROPATHOLOGY, SUCH AS DEVELOPMENT OF PTE. WHEREAS MOTOR VEHICLE ACCIDENTS, WARTIME INJURY, VIOLENCE AGAINST WOMEN, AND INJURIES SUFFERED IN CONTACT SPORTS ACCOUNT FOR MOST SERIOUS BRAIN TRAUMA, TBI IS ALSO RELEVANT TO ALPINE SKIING AND SNOWBOARDING, SINCE TBIS ACCOUNT FOR UP TO 20% OF INJURIES SUFFERED ON THE SLOPES. ALTHOUGH USE OF SKI HELMETS REACHED 90% IN THE 2021/2022 SKI SEASON AND SIGNIFICANTLY REDUCED THE INCIDENCE OF SEVERE TBI, HELMETS DO NOT ELIMINATE THE RISK OF TBI, ESPECIALLY FOR ACCIDENTS THAT OCCUR AT SPEEDS GREATER THAN 25 KPH. THIS PANEL WILL DISCUSS EMERGING HYPOTHESES GUIDING RESEARCH INTO THE MECHANISMS UNDERLYING PTE DEVELOPMENT AND COGNITIVE DECLINE AFTER TBI. FOLLOWING A BRIEF INTRODUCTION TO THE EPIDEMIOLOGY OF TBI, BRET SMITH (COLORADO STATE UNIVERSITY) WILL PRESENT STUDIES ON THE PATHOPHYSIOLOGY OF PTE DEVELOPMENT IN MICE AFTER FOCAL BRAIN INJURY, HIGHLIGHTING SYNAPTIC REORGANIZATION OF INHIBITORY NEURAL CIRCUITS IN DENTATE GYRUS POST-TBI. MARK SHAPIRO (UTHSCSA) WILL THEN DISCUSS HIS RECENT WORK ON DEVELOPING NEW PHARMACOLOGICAL TOOLS TO PREVENT PTS, PTE AND CTE IN MULTIPLE MOUSE MODELS OF TBI. FINALLY, NAOMI SAYRE (S TEXAS VETERANS HEALTH CARE SYSTEM) WILL DISCUSS THE MULTIPLE ROLES OF ASTROCYTES IN SUPPORTING NEURONAL HEALTH AND RESPONDING TO DAMAGE AFTER TBI, WITH A FOCUS ON NEUROTOXIC RESPONSES OF ASTROCYTES THAT MAY BE TARGETS FOR DEVELOPING NOVEL TREATMENTS FOR AGE-ASSOCIATED PATHOLOGY IN PATIENTS WITH A TBI MUCH EARLIER IN LIFE.

MONDAY, JANUARY 29TH

PANEL
7:30 A.M. - 9:30 A.M.
IMPERIAL BALLROOM, FLOOR 4

UNLOCKING THE BRAIN'S REWARD SYSTEM: INSIGHTS INTO THE STRIATAL AND DOPAMINERGIC MECHANISMS OF LEARNING AND DECISION MAKING

CHAIRS: ROBIN MAGNARD, SHARLEN MOORE
PRESENTERS: MAI-ANH VU, ALEX LEGARIA, SHARLEN MOORE, ROBIN MAGNARD

REWARD-SEEKING BEHAVIORS ARE ESSENTIAL FOR OUR SURVIVAL, INFLUENCING OUR DAILY ACTIONS AND DECISION-MAKING PROCESSES THROUGH THE COMPLEX NEURAL NETWORK OF THE BRAIN'S REWARD SYSTEM. THE STRIATUM PLAYS A CENTRAL ROLE IN COMPUTING THESE BEHAVIORS, NOTABLY THROUGH ITS DOPAMINERGIC INPUTS. WHILE SIGNIFICANT EFFORTS HAVE BEEN DEDICATED TO UNDERSTANDING THE INTRICACIES OF REWARD-SEEKING BEHAVIORS, NUMEROUS UNRESOLVED QUESTIONS REMAIN REGARDING ITS FUNDAMENTAL MECHANISMS AND NEURAL CIRCUITRY. IN THIS PANEL, WE AIM TO PRESENT CUTTING-EDGE ADVANCEMENTS IN THE STUDY OF DOPAMINE AND ITS STRIATAL TARGET ACROSS REWARD-GUIDED LEARNING. OUR SCOPE COVERS VARIOUS FACETS OF THIS SUBJECT, SPANNING FROM THE DEVELOPMENT OF HIGH-RESOLUTION RECORDING STRATEGIES TO REVEAL THE DISTRIBUTION OF DOPAMINE SIGNALS WITHIN THE STRIATUM DURING REWARD-SEEKING BEHAVIOR (MAI-ANH VU, SPEAKER, BOSTON UNIVERSITY) TO THE SYNERGISTIC ROLE OF STRIATAL CALCIUM AND DOPAMINE FOR CREDIT ASSIGNMENT DURING LEARNING (ALEX LEGARIA, SPEAKER, WASHINGTON UNIVERSITY). WE INTRODUCE INNOVATIVE BEHAVIORAL APPROACHES DESIGNED TO PRECISELY PINPOINT THE TRANSITION FROM GOAL-DIRECTED TO HABITUAL BEHAVIORS OVER TIME (SHARLEN MOORE, SPEAKER/ CO-CHAIR, JOHNS HOPKINS UNIVERSITY). LASTLY, WE EMPHASIZE THE SIGNIFICANCE OF REWARD-PREDICTING CUES IN SHAPING AUTOMATICITY AND BEHAVIORAL CHUNKING STRATEGIES, WITH A SPECIFIC FOCUS ON THE MESOLIMBIC DOPAMINE SIGNALING (ROBIN MAGNARD, SPEAKER/ CHAIR, JOHNS HOPKINS UNIVERSITY). OVERALL, THIS PANEL AIMS TO INVESTIGATE THE NEURAL UNDERPINNINGS OF REWARD-SEEKING BEHAVIORS, WITH A FOCUS ON THE STRIATUM AND ITS DOPAMINE INPUTS, WHILE ALSO PRESENTING TECHNIQUES AND INNOVATIVE APPROACHES TO BETTER COMPREHEND THE COMPLEXITY OF DECISION-MAKING AND REWARD SEEKING.

MONDAY, JANUARY 29TH

PANEL
7:30 A.M. - 9:30 A.M.
PEAK 1-3, FLOOR 3

NOVEL THERAPEUTICS FOR TREATING SUBSTANCE USE DISORDERS

CHAIR: ALAN BUDNEY
PRESENTERS: ARON LICHTMAN, MARGARET HANEY, STERLING MCPHERSON, CRYSTAL SMITH

ALTERNATIVE, ACCESSIBLE, AND MORE EFFECTIVE INTERVENTIONS ARE NEEDED TO REDUCE THE UBIQUITOUS HEALTH AND ECONOMIC CONSEQUENCES OF SUBSTANCE USE DISORDERS. THIS TRANSLATIONAL PANEL SHOWCASES NOVEL LINES OF RESEARCH RANGING FROM PRECLINICAL TO HEALTH SERVICES. DR. BUDNEY WILL PROVIDE INTRODUCTORY REMARKS AND LEAD DISCUSSION OF THE PRESENTATIONS. DR. LICHTMAN WILL BEGIN THE SESSION WITH AN OVERVIEW OF NOVEL PRECLINICAL DATA THAT PROVIDE PROOF OF PRINCIPLE THAT CBIR ALLOSTERIC MODULATORS REPRESENT A VIABLE STRATEGY TO TREAT SELECTIVE AND SEVERE OPIOID WITHDRAWAL EFFECTS. IN PARTICULAR, ZCZ011, A CBIR POSITIVE ALLOSTERIC MODULATOR, ATTENUATES NALOXONE-PRECIPITATED WITHDRAWAL SIGNS IN OXYCODONE-DEPENDENT MICE WITH PROFOUND ANTI-DIARRHEAL AND ANTI-TRANSIT EFFECTS. DR. HANEY WILL PRESENT FINDINGS FROM PHASE 1-PHASE 2A CLINICAL STUDIES TESTING A NOVEL CBI INHIBITOR, THE PREGNENOLONE ANALOGUE, AEF0117. RESULTS INDICATE THAT AEF0117 IS SAFE AND WELL TOLERATED, HAS NO DISCERNIBLE EFFECTS ON BEHAVIOR, HAS FAVORABLE PHARMACOKINETIC CHARACTERISTICS, AND DECREASES CANNABIS SELF-ADMINISTRATION IN DAILY CANNABIS SMOKERS WITHOUT PRODUCING PHYSICAL DISCOMFORT, DISRUPTING MOOD OR SLEEP. DR. MCPHERSON WILL DESCRIBE TWO EXPERIMENTS THAT HIGHLIGHT EFFICACIOUS REMOTE BIOMARKER MONITORING TECHNOLOGIES FOR THE TREATMENT OF ALCOHOL USE DISORDER WITH CONTINGENCY MANAGEMENT. THE FIRST EXPERIMENT USED PHOSPHATIDYLETHANOL AND A BLOOD SPOT COLLECTION DEVICE AS A LONG-TERM, 30-DAY BIOMARKER, AND THE SECOND USED A MOBILE-BASED APP WITH BREATHALYZER AND FACIAL RECOGNITION TECHNOLOGY DEVELOPED IN PARTNERSHIP WITH INDUSTRY. DR. SMITH WILL END THE SESSION WITH QUALITATIVE RESEARCH ON CURRENT UNDERGROUND PSYCHEDELIC ASSISTED PSYCHOTHERAPY, INCLUDING THEMES OF ALTRUISM, MEDICAL VS SPIRITUAL MECHANISMS OF ACTION, HEALING PAST TRAUMAS AND PROMOTING SELF-ACTUALIZATION, AND ANTITHETICAL OPINIONS ON LEGALIZATION. DISCUSSION WILL FOCUS ON THE PURPORTED MECHANISMS OF CHANGE AND VARIATION IN IMPLEMENTATION.

MONDAY, JANUARY 29TH

PANEL
7:30 A.M. - 9:30 A.M.
PEAK 11-12, FLOOR 2

CONNECTOMIC NEUROMODULATION IN PSYCHIATRY: PERSPECTIVES FROM MULTI-MODAL AND CROSS-SPECIES STUDIES

CHAIR: LUCAS TRAMBAIOLLI
PRESENTERS: SHAN SIDDIQI, DARIN DOUGHERTY, LUCAS TRAMBAIOLLI, MARINA CELESTINE

NEUROMODULATION OF STRUCTURES AFFECTED BY SPECIFIC SYMPTOMS AND DISORDERS HAS BEEN EXPLORED AS A TREATMENT FOR REFRACTORY PATIENTS. HOWEVER, INSTEAD OF FOCUSING ON THE LOCAL IMPACT AT THE STIMULATION SITE, NEW RESEARCH HAS BEEN CONSIDERING THE EFFECTS OF NEUROMODULATION ON BRAIN REGIONS CONNECTED TO THE STIMULATION SITE. THIS PANEL WILL DISCUSS HOW BRAIN CONNECTIVITY INFORMATION DERIVED FROM TRACT-TRACING DATA FROM NONHUMAN PRIMATES (NHP) AND MAGNETIC RESONANCE IMAGING (MRI) DATA FROM NHP AND HUMANS CAN IDENTIFY TARGETS OR DELINEATE THE EFFECTS OF DIFFERENT NEUROMODULATION TECHNIQUES.

DR. SHAN SIDDIQI (BRIGHAM AND WOMEN'S HOSPITAL) WILL DISCUSS HOW FUNCTIONAL MRI (FMRI) CONNECTIVITY DATA CAN PROVIDE PRECISE AND INDIVIDUALIZED CORTICAL TARGETS FOR TRANSCRANIAL MAGNETIC STIMULATION (TMS) IN PATIENTS WITH DEPRESSION AND POST-TRAUMATIC STRESS DISORDER (PTSD).
DR. DARIN DOUGHERTY (MASSACHUSETTS GENERAL HOSPITAL) WILL PRESENT NEW DATA ON NONINVASIVE LOW-INTENSITY FREQUENCY ULTRASOUND (LIFU) STIMULATION OF THE VENTRAL CAPSULE/VENTRAL STRIATUM IN PATIENTS WITH OCD AND HOW IT MODULATES THE FUNCTIONAL CONNECTIVITY OF THE CORTICO-STRIATO-THALAMO-CORTICAL CIRCUIT.
DR. LUCAS TRAMBAIOLLI (MCLEAN HOSPITAL) WILL USE TRACT-TRACING DATA IN NHP AND DIFFUSION MRI DATA IN NHP AND HUMANS TO DESCRIBE THE MONOSYNAPTIC CONNECTIONS MODULATED BY FUNCTIONAL MRI NEUROFEEDBACK TARGETING THE AMYGDALA IN PATIENTS WITH DEPRESSION AND PTSD.
DR. MARINA CELESTINE (UNIVERSITY OF ROCHESTER) WILL SHOW NEW DATA IDENTIFYING THE ORGANIZATION OF PATHWAYS FROM THE FRONTAL POLE, PREMOTOR, AND MOTOR REGIONS, AND HOW THEY CAN BE TARGETED TO MODULATE SUBCORTICAL STRUCTURES.
THESE DATA HIGHLIGHT THAT THE COMBINATION OF NEUROMODULATION AND BRAIN CONNECTIVITY PROVIDES NEW OPPORTUNITIES TO UNDERSTAND LARGE-SCALE EFFECTS BETTER, DELINEATE THE NEUROBIOLOGICAL BASIS OF TARGETED STIMULATION, AND IDENTIFY UNIQUE AND PERSONALIZED TARGETS FOR NEUROMODULATION THERAPY.

MONDAY, JANUARY 29TH

PANEL
7:30 A.M. - 9:30 A.M.
PEAK 14, FLOOR 1

METABOLIC SWITCHES REQUIRED FOR DEVELOPMENT OF NORMAL NEURONAL EXCITABILITY AND SYNAPTIC PLASTICITY

CHAIR: ELIZABETH JONAS
PRESENTERS: RYANN FAME, ELIZABETH JONAS, LEONARD KACZMAREK, GULCIN PEKKURNAZ

RECENT DISCOVERIES HAVE HIGHLIGHTED THE IMPORTANCE OF ENERGY METABOLISM IN THE NORMAL DEVELOPMENT AND FUNCTION OF THE BRAIN. ABNORMALITIES OF BRAIN FUNCTION ARE INCREASING ATTRIBUTED TO DISORDERS OF NEURONAL METABOLISM. THIS PANEL WILL FOCUS ON HOW SWITCHES IN METABOLIC PHENOTYPES PLAY A KEY ROLE BOTH IN NORMAL BRAIN DEVELOPMENT AND IN PROCESSES OF THE ADULT BRAIN SUCH AS LEARNING AND MEMORY. DR. FAME WILL DISCUSS HOW K+ IN THE EXTRACELLULAR BRAIN ENVIRONMENT (I.E., CEREBROSPINAL AND AMNIOTIC FLUID) SHIFTS DURING EARLY NEUROGENESIS AND GLIOGENESIS IN CONCERT WITH METABOLIC ACTIVITY IN THE CHOROID PLEXUS. THESE SHIFTS ARE POISED TO AFFECT EARLY NEURAL DIFFERENTIATION AND ACTIVITY, A ROLE THAT MAY BE DISRUPTED IN OPEN NEURAL TUBE DEFECTS OR HYDROCEPHALUS. DR. JONAS WILL DISCUSS HOW ATP SYNTHASE ASSEMBLY AND STOICHIOMETRY REGULATE A SWITCH FROM GLYCOLYTIC METABOLISM TO OXIDATIVE PHOSPHORYLATION DURING BRAIN DEVELOPMENT. PREVENTION OF THIS SWITCH INHIBITS THE ABILITY OF SYNAPSES TO UNDERGO LONG TERM POTENTIATION (LTP) AND PROMOTES ABERRANT NEURONAL EXCITABILITY. DR. KACZMAREK WILL DISCUSS THE MECHANISMS BY WHICH HUMAN MUTATIONS OF THE PLASMA MEMBRANE POTASSIUM CHANNEL SLACK (KCNTI) RESULT IN SEVERE CHILDHOOD DEVELOPMENTAL DISORDERS. THESE MUTATIONS AND GENE KO IN MICE ALSO CAUSE CHANGES IN LEVELS OF INNER MITOCHONDRIAL MEMBRANE PROTEINS, PARTICULARLY THOSE OF THE ATPASE. SUCH MUTATIONS ALSO ABOLISH SYNAPTIC PLASTICITY (LTP AND LTD), AS WELL AS ACTIVITY-DEPENDENT TRANSLATION OF SPECIFIC NEURONAL MRNAS. DR. PEKKURNAZ WILL DISCUSS THE DYNAMIC POST TRANSLATIONAL MODIFICATION OF O-GLCNACYLATION OF HEXOKINASE THAT PROMOTES THE ASSEMBLY OF THE GLYCOLYTIC METABOLON ON THE OUTER MITOCHONDRIAL MEMBRANE. THIS ASSEMBLY ORCHESTRATES A LINK BETWEEN GLYCOLYTIC AND MITOCHONDRIAL ATP PRODUCTION. MUTATIONS IN THIS PATHWAY ALTER NEURONAL METABOLISM, AFFECTING SYNAPTIC PLASTICITY.

MONDAY, JANUARY 29TH

PANEL
7:30 A.M. - 9:30 A.M.
PEAK 15-16, FLOOR 1

NEURON-GLIAL INTERACTIONS: MECHANISMS UNDERLYING DEVELOPMENT AND REPAIR OF PERIPHERAL NERVES

CHAIR: MONIQUE LILLIS
PRESENTERS: MATTHEW RASBAND, MONIQUE LILLIS, LYDIA DABOUSSI, YANNICK POITELON

PERIPHERAL NERVES ARE MADE UP OF NUMEROUS SCHWANN CELLS THAT CLOSELY ASSOCIATE WITH AXONS TO ENABLE SENSORIMOTOR FUNCTION, PROVIDE AXONAL SUPPORT, AND PROMOTE REPAIR IN INJURY AND DISEASE. DURING DEVELOPMENT SCHWANN CELLS PROLIFERATE RAPIDLY, SEPARATE AXONS BY SIZE, AND FORM 1:1 RELATIONSHIPS WITH LARGE-CALIBER AXONS THAT GO ON TO BE MYELINATED. THE FORMATION OF MYELIN ALONG THESE AXONS INDUCES NEURONAL CHANGES LEADING TO NODES OF RANVIER, WHICH ENABLE SALTATORY CONDUCTION AND A SIGNIFICANT INCREASE IN CONDUCTION VELOCITY IN SENSORIMOTOR NEURONS. THE SCHWANN CELLS ALSO IDENTIFY SMALL-CALIBER AXONS AND ENSHEATHE A NUMBER OF THEM IN A REMAK BUNDLE THAT PROMOTES AXONAL HEALTH. THESE SCHWANN CELL–AXON INTERACTIONS ARE CRITICAL FOR PROPER NERVE FUNCTION, AND AFTER INJURY SCHWANN CELLS WILL REVERT TO A TRANSCRIPTIONALLY SIMILAR IMMATURE STATES TO REPAIR DAMAGE AND PROMOTE REGENERATION.
IN THIS PANEL, MATTHEW RASBAND WILL ADDRESS HOW SCHWANN CELL MYELINATION LEADS TO CYTOSKELETAL CHANGES IN NEURONS TO FORM THE NODES OF RANVIER. MONIQUE LILLIS WILL THEN DISCUSS HOW SCHWANN CELL SECRETED BASEMENT MEMBRANE PROTEINS PROMOTE PROPER NERVE ORGANIZATION AND REMAK BUNDLE FORMATION. THE SECOND HALF OF THE PANEL WILL DISCUSS THE ROLE OF SCHWANN CELLS AFTER INJURY AND IN DISEASE WHEN THEY REVERT TO A REPAIR STATE, WHICH HAS NUMEROUS SIMILARITIES TO DEVELOPMENTAL SCHWANN CELLS. LYDIA DABOUSSI WILL DISCUSS THE WAYS SCHWANN CELLS MONITOR AXONAL HEALTH AND THE TRANSCRIPTIONAL CHANGES THEY UNDERGO TO REVERT INTO A 'REPAIR STATE.' YANNICK POITELON WILL THEN ADDRESS HOW TO PROLONG THE SCHWANN CELL REPAIR STATE USING LOW INTENSITY ULTRASOUND; THEREBY INCREASING THE THERAPEUTIC WINDOW OF REPAIR IN HUMANS.

MONDAY, JANUARY 29TH

PANEL
7:30 A.M. - 9:30 A.M.
PEAK 17, FLOOR 1

DISSECTION OF BRAIN CIRCUITRY DRIVING PAIN INDUCED NOCICEPTIVE BEHAVIOR AND DRUG SEEKING BEHAVIOR

CHAIR: JOSE MORON-CONCEPCION
PRESENTERS: REBECCA LORSUNG, JOSE MORON-CONCEPCION, CATHERINE CAHILL

PAIN IS A COMPLEX PHENOMENON COMPOSED OF SENSORY AND EMOTIONAL-AFFECTIVE COMPONENTS. AS PAIN PERSISTS, THE PRESENCE OF NEGATIVE AFFECTIVE STATES CAN LEAD TO THE DEVELOPMENT OF NEGATIVE EMOTIONAL STATES AND SUBSTANCE USE DISORDERS. IN THIS PANEL WE WILL DISCUSS RECENT FINDINGS INVESTIGATING PAIN-INDUCED ALTERATIONS IN NEUROCIRCUITS UNDERLYING ALLODYNIA/HYPERALGESIA, NEGATIVE AFFECTIVE STATES, AND DRUG AND SUBSTANCE SEEKING/CONSUMPTION. MS LORSUNG (UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE) INVESTIGATES WHETHER ENDOGENOUS RELEASE OF CGRP FROM PB TERMINALS POTENTIATES EXCITATORY CURRENTS AT THE PARABRACHIO-AMYGDALOID SYNAPSE.THEIR DATA SUGGESTS THAT WHILE FEMALE CENTRAL AMYGDALA (CEA) NEURONS ARE MORE SUSCEPTIBLE TO TRANSIENT INCREASES IN NEUROPEPTIDE RELEASE, MALE NEURONS REQUIRE SUSTAINED ELEVATED SIGNALING ON THE ORDER OF SEVERAL MINUTES BEFORE POTENTIATION CAN OCCUR. DR MORON-CONCEPCION'S (WASHINGTON UNIVERSITY) WILL SHOW DATA THAT DEMONSTRATES THAT INFLAMMATORY PAIN PROMOTES THE RECRUITMENT OF DYNORPHIN PROJECTIONS FROM THE CEA TO THE NUCLEUS ACCUMBENS (NAC) IN A SEX- AND TIME-DEPENDENT MANNER TO DRIVE THE EMERGENCE OF NEGATIVE AFFECTIVE STATES THAT MAY LEAD TO ALCOHOL DRINKING. FINALLY, DR CAHILL (UCLA) WILL PRESENT DATA SHOWING THAT DURING ACQUISITION OF OPIOID DRUG-TAKING, CHRONIC PAIN ANIMALS SHOW NO CHANGES IN TOTAL DRUG REINFORCERS BUT THAT THEY EXHIBIT ENHANCED DRUG TAKING WITHIN THE TIME FRAME FOR DRUG-TAKING COMPARED TO CONTROL ANIMALS. IN ADDITION, CHRONIC PAIN IMPACTS WORK EFFORT AND MOTIVATION FOR DRUG SEEKING BEHAVIOR USING BEHAVIORAL ECONOMICS AND PROGRESSIVE RATIO TASKS.

MONDAY, JANUARY 29TH

PANEL
7:30 A.M. - 9:30 A.M.
PEAK 6-8, FLOOR 2

DEVELOPMENT AND PLASTICITY OF THE VISUAL SYSTEM

CHAIR: SANDRA KUHLMAN
PRESENTERS: CHINFEI CHEN, AARON MCGEE, SANDRA KUHLMAN, JIANHUA CANG

IN THIS PANEL WE WILL EXPLORE THE SYNAPTIC AND CIRCUIT MECHANISMS THAT UNDERLIE PLASTICITY IN THE DEVELOPING VISUAL SYSTEM OF MAMMALS, IN HEALTH AND DISEASE. EARLY-LIFE PLASTICITY GIVES THE BRAIN THE ABILITY TO ADAPT TO NEW EXPERIENCES AND CHANGES IN THE ENVIRONMENT. THIS IS AN ESSENTIAL STEP IN DEVELOPMENT AND ENSURES THAT SENSORY CIRCUITS ARE APPROPRIATELY TUNED TO ENCODE INFORMATION AVAILABLE TO THE INDIVIDUAL, INFORMATION THAT THE INDIVIDUAL CAN THEN USE TO GUIDE GOAL-DIRECTED BEHAVIOR. A CURRENT CHALLENGE IN THE FIELD IS TO UNDERSTAND PRECISELY HOW THIS TUNING OCCURS, HOW PLASTICITY ACROSS SENSORY AREAS IS COORDINATED DURING THIS HEIGHTENED PERIOD OF ADAPTABILITY, AND THE EXTENT TO WHICH THIS HEIGHTENED PLASTICITY CAN BE RE-INSTATED TO RESCUE AND AUGMENT PLASTICITY AND LEARNING IN ADULTS. CHINFEI CHEN (HARVARD UNIVERSITY) WILL CONSIDER THE PRINCIPLES BY WHICH THALAMIC INPUTS TRANSFORM INCOMING SENSORY INFORMATION, AND PRESENT FINDINGS ON HOW THIS TRANSFORMATION CHANGES AS AN ANIMAL MATURES AND ACCUMULATES EXPERIENCES. AARON MCGEE (UNIVERSITY OF LOUISVILLE) WILL PRESENT DATA ON THE IMPACT OF MANIPULATING SPECIFIC GENES ASSOCIATED WITH NEURODEVELOPMENTAL DISORDERS ON VISUAL PROCESSING AND PERCEPTUAL LEARNING. SANDRA KUHLMAN'S (UNIVERSITY AT BUFFALO) RECENT RESEARCH EXAMINES A SPECIFIC CLASS OF INHIBITORY NEURON, THE SOMATOSTATIN NEURON. SHE WILL PRESENT EVIDENCE THAT THE PROTRACTED DEVELOPMENT OF THIS NEURONAL SUBTYPE MAY IMPROVE NATURAL SCENE PROCESSING IN THE BINOCULAR ZONE OF PRIMARY VISUAL CORTEX. JIANHUA CANG (UNIVERSITY OF VIRGINIA) WILL CONCLUDE THE SESSION WITH A PRESENTATION DESCRIBING THE MECHANISMS BY WHICH INPUT FROM THE TWO EYES IS INTEGRATED IN THE MOUSE AS WELL AS THE TREE SHREW, A SMALL MAMMAL THAT IS CLOSELY RELATED TO PRIMATES.

MONDAY, JANUARY 29TH

PANEL
7:30 A.M. - 9:30 A.M.
PEAK 9-10, FLOOR 2

DEFINING THE MOLECULAR AND ENVIRONMENTAL CONTEXT WHERE GENES FOR SCHIZOPHRENIA WORK

CHAIR: GIANLUCA URSINI
PRESENTERS: GIANLUCA URSINI, LAURA WORTINGER, BART RUTTEN, MARTIN BEAULIEU

GENES CRITICAL FOR BRAIN DEVELOPMENT EXERT THEIR EFFECTS DIFFERENTLY DEPENDING ON THE CONTEXT WHERE THEY ACT, IN TERMS OF ENVIRONMENTAL FACTORS AND MECHANISMS OF EPIGENETIC REGULATION AND GENETIC INTERACTIONS. CONSEQUENTLY, THE PATH THAT LEADS FROM GENETIC SUSCEPTIBILITY TO DISEASE IS NOT LINEAR, AND GENETIC DISCOVERIES ARE FAR TO BE TRANSLATED IN THERAPEUTIC AND PREVENTIVE INTERVENTIONS. IN THIS SYMPOSIUM, WE WILL PRESENT RESEARCH AIMED AT DEFINING THE ENVIRONMENTAL AND MOLECULAR CONTEXTS IN WHICH GENES ENHANCE SUSCEPTIBILITY TO SCHIZOPHRENIA (SZ).
DR. URSINI (LIBD) WILL SHOW HOW GENOMIC RISK FOR SZ INTERACTS WITH EARLY-LIFE COMPLICATIONS (ELCS) IN AFFECTING PLACENTA BIOLOGY AND NEURODEVELOPMENT, USING DATA FROM TRANSCRIPTOMIC STUDIES AND TROPHOBLASTS DERIVED FROM IPSCS OF PATIENTS AND CONTROLS.
DR. WORTINGER (U. OF OSLO) WILL SHOW FINDINGS FROM THE MOBA STUDY (N=70,000), SUPPORTING THE NEED OF CONSIDERING MULTIPLE DEVELOPMENTAL OUTCOMES IN GXE STUDIES. HER FINDINGS SUGGESTS THAT GENOMIC RISK FOR SZ MAY ACT IN EARLY LIFE, ALSO CONFERRING RESILIENCE TO THE EMBRYO/FETUS EXPOSED TO ELCS, SO THAT THE DEVELOPMENT OF SZ MAY BE THE EFFECT OF EPIGENETIC PROCESSES LINKED WITH ELCS, RATHER THAN OF GENOMIC RISK.
WE WILL THEN DISCUSS HOW OTHER COMPLEX EXPOSURES MAY CONTRIBUTE TO THE TRANSITION FROM SUSCEPTIBILITY TO ACTUAL DISEASE. IN THIS REGARD, DR. RUTTEN (MAASTRICHT U.) WILL PRESENT RESULTS OF HIS GENE-ENVIRONMENT INTERACTION STUDIES, USING NEWLY DEVELOPED EXPOSOME SCORES AS A CUMULATIVE MEASURE OF ENVIRONMENTAL LIABILITY TO SZ.
FINALLY, DR. BEAULIEU (U. OF TORONTO) WILL PRESENT HIS RESEARCH SHOWING THE GENOME-WIDE IMPACT, AT THE RNA LEVEL, OF THE SZ-ASSOCIATED PROTEIN FXR1 IN THE ADULT BRAIN. HIS RESULTS HIGHLIGHT A POSSIBLE MOLECULAR MECHANISM THROUGH WHICH THIS RNA-BINDING PROTEIN MAY AFFECT SLEEP, SYNAPTIC HOMEOSTASIS, AND RISK FOR SZ.
DEFINING THE CONTEXT IN WHICH GENES ENHANCE DISEASE SUSCEPTIBILITY CAN PROVIDE INSIGHT INTO THE PATHOGENESIS OF SZ.

MONDAY, JANUARY 29TH

PANEL
4:30 P.M. - 6:30 P.M.
IMPERIAL BALLROOM, FLOOR 4

CORTICAL DYSFUNCTION IN PARKINSON'S DISEASE

CHAIRS: HONG-YUAN CHU, ADRIANA GALVAN
PRESENTERS: COLUM MACKINNON, ADRIANA GALVAN, HONG-YUAN CHU, ROBERT CHEN

THE MOTOR CORTEX IS THOUGHT TO HAVE AN IMPORTANT ROLE IN THE PATHOPHYSIOLOGY OF PARKINSON'S DISEASE (PD) BASED ON THE CLASSICAL MODEL OF THE CORTICO-BASAL GANGLIA-THALAMOCORTICAL NETWORK. HOWEVER, MOST INVESTIGATIONS INTO THE PATHOPHYSIOLOGY OF PD HAVE FOCUSED INSTEAD ON CHANGES IN BASAL GANGLIA ACTIVITY TRIGGERED BY DOPAMINE LOSS IN THE STRIATUM. HOWEVER, IN THE LAST FEW YEARS, EVIDENCE FOR ANATOMICAL AND FUNCTIONAL ABNORMALITIES OF THE MOTOR CORTEX HAS BEEN ACCUMULATING RAPIDLY. THIS PANEL WILL PRESENT AND DISCUSS RECENT FINDINGS ON MOTOR CORTICAL DYSFUNCTION IN PEOPLE WITH PARKINSON'S DISEASE AND ANIMAL MODELS OF PARKINSONISM. DR. COLUM MACKINNON (UNIVERSITY OF MINNESOTA) WILL REVIEW KEY FINDINGS ON CORTICAL DYSFUNCTION FROM HUMAN FUNCTIONAL IMAGING STUDIES. DRS. ADRIANA GALVAN (EMORY UNIVERSITY) AND HONG-YUAN CHU (VAN ANDEL INSTITUTE) WILL DISCUSS ANATOMICAL AND PHYSIOLOGICAL STUDIES ON CORTICAL CHANGES FROM NONHUMAN PRIMATE AND RODENT MODELS OF PARKINSONISM, RESPECTIVELY. FINALLY, DR. ROBERT CHEN (UNIVERSITY OF TORONTO) WILL TALK ABOUT THE MOTOR CORTEX AS A POTENTIAL TARGET OF NEUROMODULATION TO TREAT PD. THIS PANEL WILL BE OF INTEREST TO A BROAD AUDIENCE OF RESEARCHERS IN THE FIELDS OF MOTOR SYSTEMS, MOVEMENT DISORDERS AND NEURODEGENERATIVE DISEASES.

MONDAY, JANUARY 29TH

PANEL
4:30 P.M. - 6:30 P.M.
PEAK I-3, FLOOR 3

RECENT ADVANCES IN UNDERSTANDING THE ORBITOFRONTAL CORTEX
CHAIR: IDO MAOR

PRESENTERS: PETER RUDEBECK, ALESSANDRO LIVI, JONI WALLIS, IDO MAOR

THE ORBITOFRONTAL CORTEX (OFC) HAS CAPTURED THE IMAGINATION OF NEUROSCIENTISTS EVER SINCE THE PIONEERING CASE OF PHINEAS GAGE, WHOSE DRASTIC PERSONALITY CHANGE FOLLOWING OFC DAMAGE OFFERED SEMINAL INSIGHTS INTO THE BRAIN'S ENIGMATIC WORKINGS. OVER NEARLY TWO CENTURIES, THE OFC HAS REMAINED A FOCAL POINT OF INVESTIGATION, YET ITS PRECISE FUNCTION CONTINUES TO PUZZLE US, GIVING RISE TO A DIVERSE ARRAY OF THEORIES. THIS PANEL WILL EXPLORE RECENT ADVANCES IN COMPREHENDING THE OFC'S MULTIFACETED ROLE IN COGNITION, RANGING FROM ITS INVOLVEMENT IN ECONOMIC VALUATION TO ITS POTENTIALLY BROADER ROLE IN REPRESENTING COGNITIVE MAPS THAT CAN BE USED TO GUIDE BEHAVIOR.

DR. RUDEBECK WILL DELVE INTO THE OFC'S CONTRIBUTIONS TO COMPUTING THE COSTS AND BENEFITS ASSOCIATED WITH DIFFERENT CHOICES. USING A COMBINATION OF FUNCTIONAL NEUROIMAGING, PATHWAY-SPECIFIC CHEMOGENETICS, AND NEURAL RECORDINGS IN MACAQUES, HE WILL DISCUSS HOW THE OFC, AND OTHER CONNECTED AREAS, CONTRIBUTE TO REWARD GUIDED DECISION-MAKING.

DR. LIVI WILL PROPOSE AN INTRIGUING DIVISION OF LABOR WITHIN THE OFC. HE WILL SHOW FUNCTIONAL IMAGING DATA FROM A MOUSE MODEL OF ECONOMIC CHOICE BEHAVIOR AND DEMONSTRATE HOW DIFFERENT NEURONS AND LAYERS WITHIN THE OFC CONTRIBUTE TO THE REPRESENTATION OF VARIOUS ASPECTS OF ECONOMIC DECISION-MAKING.

PROF. WALLIS WILL PRESENT A SERIES OF RECENT EXPERIMENTS THAT SEEK TO UNDERSTAND OFC-HIPPOCAMPAL INTERACTIONS AND THEIR CONTRIBUTION TO VALUE-BASED DECISION-MAKING. SHE WILL PRESENT A MODEL OF THIS PROCESS IN WHICH HIPPOCAMPUS REPRESENTS A STATE-TRANSITION GRAPH, AND OFC USES KNOWLEDGE OF THE REWARD'S LOCATION TO CALCULATE THE VALUE OF THE VERTICES IN THE GRAPH, THEREBY HELPING TO GUIDE THE OPTIMAL CHOICE AT EACH DECISION POINT.

DR. MAOR WILL FOCUS ON THE OFC'S ROLE IN SOLVING RULE-CONFLICTING PROBLEMS. USING NEURAL RECORDING IN RATS HE WILL DEMONSTRATE THE PRINCIPLE OF MULTIPLE COGNITIVE MAPS, MULTIPLEXED IN OFC ACTIVITY, AND PROPOSE ITS ROLE IN CONTINUOUS LEARNING.

MONDAY, JANUARY 29TH

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 11-12, FLOOR 2

SYNAPSE PLASTICITY IN HEALTH AND DISEASE

CHAIR: MATTHEW KENNEDY
PRESENTERS: STEPHEN SMITH, MATTHEW KENNEDY, GRAHAM DIERING, SERENA DUDEK

POINTS OF CONTACT BETWEEN NEURONS, OR SYNAPSES, ARE CONTINUOUSLY REMODELED AT THE MOLECULAR LEVEL TO DRIVE CELLULAR AND CIRCUIT-WIDE CHANGES IN NEURAL ACTIVITY. THIS PLASTICITY MANIFESTS IN RESPONSE TO DIVERSE EXPERIENCES AND CAN BE FURTHER MODIFIED DURING SUBSEQUENT BEHAVIORAL STATES SUCH AS SLEEP. MOREOVER, SYNAPTIC MOLECULES CENTRAL TO PLASTICITY ARE DISRUPTED IN DIVERSE BRAIN DISEASES AND DISORDERS. THE THEME OF THIS PANEL CENTERS ON THE MOLECULAR AND CELLULAR MECHANISMS RESPONSIBLE FOR DIVERSE FORMS OF PLASTICITY AND HOW SYNAPSE FUNCTION IS IMPACTED IN DISEASE STATES. WE WILL PRESENT WORK ACROSS SCALES, RANGING FROM HOW THE MOLECULAR ORGANIZATION AND SIGNALING OF SYNAPSES IS ALTERED IN FRAGILE X SYNDROME AND AUTISM (STEPHEN SMITH), NEW TOOLS AND APPROACHES FOR VISUALIZING AND MANIPULATING SYNAPTIC NEUROTRANSMITTER RECEPTORS (MATT KENNEDY), THE CONSEQUENCES OF SLEEP, AND SLEEP DEPRIVATION ON MOLECULAR AND BEHAVIORAL PLASTICITY (GRAHAM DIERING) AND HOW DISTINCT NEURAL SUBTYPES USE DIVERSE MOLECULAR EXPRESSION PROGRAMS TO DRIVE OR SUPPRESS PLASTICITY (SERENA DUDEK).

MONDAY, JANUARY 29TH

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 14, FLOOR 1

NEURAL REGULATION OF APPETITIVE AND AVERSIVE LEARNING
CHAIRS: MERRIDEE LEFNER, MATTHEW WANAT

PRESENTERS: ALEXEY OSTROUMOV, MORGAN JOHNSTON, STEPHANIE CAJIGAS, MERRIDEE LEFNER

LEARNING TO DISTINGUISH BETWEEN CUES THAT SIGNAL EITHER APPETITIVE OR AVERSIVE OUTCOMES IS CRITICAL FOR SURVIVAL. THE ABILITY TO RESPOND OPTIMALLY TO CUE-OUTCOME ASSOCIATIONS CAN DIFFER BY SEX, STRESSFUL EXPERIENCES, OR THE OCCURRENCE OF A NUMBER OF PSYCHIATRIC DISORDERS. BEHAVIORAL RESPONDING TOWARDS PREDICTIVE STIMULI ARISES FROM A COMPLEX INTERPLAY OF NEURAL REGIONS INCLUDING THE MEDIAL PREFRONTAL CORTEX, THE VENTRAL TEGMENTAL AREA, THE SUBSTANTIA NIGRA, AND THE VENTRAL STRIATUM. THIS PANEL WILL FEATURE RESEARCH EMPLOYING MALE AND FEMALE RODENTS, IN VIVO FIBER PHOTOMETRY, IN VIVO AND SLICE ELECTROPHYSIOLOGY, CHEMOGENETICS, OPTOGENETICS, PHARMACOLOGY, AND GENETIC LABELING TO ELUCIDATE THE VARIOUS NEURAL SYSTEMS THAT CONTRIBUTE TO APPETITIVE AND AVERSIVE LEARNING. ALEXEY OSTROUMOV (GEORGETOWN UNIVERSITY) WILL DISCUSS HOW EXPERIENCE-DEPENDENT PLASTICITY OF MIDBRAIN INHIBITORY CIRCUITS CONTRIBUTES TO REWARD-RELATED LEARNING. MORGAN P. JOHNSTON (UNIVERSITY OF TEXAS AT SAN ANTONIO) WILL DISCUSS SEX AND ESTROUS CYCLE DIFFERENCES IN THE EFFECTS OF STRESS ON PAVLOVIAN CONDITIONING AND REWARD-EVOKED DOPAMINE RELEASE IN THE VENTRAL LATERAL STRIATUM. STEPHANIE CAJIGAS (VANDERBILT UNIVERSITY SCHOOL OF MEDICINE) WILL DISCUSS HOW DOPAMINE RELEASE IN THE NUCLEUS ACCUMBENS CORE DIFFERS BASED ON THE PERCEIVED AVAILABILITY OF OUTCOMES (ABILITY TO ESCAPE SHOCKS VS. PERCEIVED INESCAPABILITY), WHICH MAY UNDERLY THE ABILITY TO LEARN DIFFICULT REINFORCEMENT TASKS. MERRIDEE LEFNER (OREGON HEALTH AND SCIENCE UNIVERSITY) WILL DISCUSS HOW THE MEDIAL PREFRONTAL CORTEX PROJECTION TO THE VENTRAL TEGMENTAL AREA GATES FLEXIBLE RESPONDING WHEN LEARNED APPETITIVE AND AVERSIVE ASSOCIATIONS UPDATE. TOGETHER, THIS PANEL WILL HIGHLIGHT THE DIVERSE NEURAL SYSTEMS THAT ARE RESPONSIBLE FOR BEHAVIORAL RESPONDING TOWARD APPETITIVE AND AVERSIVE EVENTS.

MONDAY, JANUARY 29TH

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 15-16, FLOOR 1

COMPUTATIONAL METHODS FOR INVESTIGATING THE COGNITIVE PROCESSES INVOLVED IN ADDICTIONS AND BRAIN INJURY

CHAIRS: CLAIRE HALES, PEYTON MUELLER
PRESENTERS: PEYTON MUELLER, CLAIRE HALES, STEPHANIE GROMAN, NICHOLAS HARP

WITHIN NEUROSCIENCE, COMPUTATIONAL APPROACHES ARE BECOMING MORE WIDELY USED AS A WAY TO GAIN ADDITIONAL INSIGHT INTO BEHAVIORAL DATA, IMPROVE EXPLANATORY POWER AND MAKE PREDICTIONS ABOUT SUSCEPTIBILITY AND THERAPEUTIC POTENTIAL FOR PSYCHIATRIC DISORDERS. IN THIS PANEL, WE WILL HIGHLIGHT FOUR DIFFERENT COMPUTATIONAL APPROACHES SPANNING PRECLINICAL, CLINICAL AND TRANSLATIONAL RESEARCH THAT ARE BEING USED TO PROBE COGNITIVE PROCESSES THAT ARE IMPORTANT IN ADDICTION AND BRAIN INJURY. DR. PEYTON MUELLER WILL PRESENT HER WORK ON IMPROVING STATISTICAL POWER USING BAYESIAN ANALYSES AND APPROPRIATELY DEFINED PRIORS FOR DIFFERENT TYPES OF BEHAVIORAL DATA IN RATS EXPOSED TO TRAUMATIC BRAIN INJURY. DR. CLAIRE HALES WILL EXPLORE USING A SEQUENTIAL SAMPLING MODEL OF TWO-CHOICE DECISION MAKING, THE DRIFT DIFFUSION MODEL, TO INVESTIGATE THE COGNITIVE PROCESSES UNDERLYING RISKY DECISION MAKING IN RATS ON A TRANSLATIONAL GAMBLING TASK. DR. STEPHANIE GROMAN WILL TALK ABOUT UTILIZING COMPUTATIONAL APPROACHES COMMON TO HUMAN STUDIES IN RATS TO UNDERSTAND THE BIOBEHAVIORAL MECHANISMS THAT REGULATE GOAL-DIRECTED BEHAVIORS IN NORMAL AND ADDICTED STATES. DR. NICHOLAS HARP WILL PRESENT RECENT WORK USING MACHINE LEARNING TO DEVELOP AND VALIDATE THE NEURAL CRAVING SIGNATURE (NCS), WHICH CAN DECODE SELF-REPORTED CRAVING FROM BRAIN ACTIVITY, AND BE USED TO CLASSIFY HUMAN DRUG USERS FROM NON-USERS. THESE FOUR TALKS WILL SHOWCASE JUST A FEW OF THE WAYS COMPUTATIONAL APPROACHES CAN BE COMBINED WITH COMPLEX DATA ANALYSES TO EXEMPLIFY THE BENEFITS OF MODELING TECHNIQUES. BY HIGHLIGHTING HOW THESE TOOLS CAN BE USED IN ADDICTION RESEARCH, WE HOPE TO DEMONSTRATE THAT SIMILAR APPROACHES CAN BE EXTENDED TO ANY AREA OF NEUROSCIENCE, AND ACROSS MULTIPLE LEVELS OF SCIENTIFIC ENDEAVOR.

MONDAY, JANUARY 29TH

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 17, FLOOR 1

STRIATAL CIRCUIT AND SYNAPTIC MECHANISMS OF COCAINE AND OPIATE ADDICTION

CHAIR: LAUREN DOBBS
PRESENTERS: DAVID BARKER, FLAVIA BARBANO, LAUREN DOBBS, EMILIA LEFEVRE

THE MECHANISMS MEDIATING COCAINE AND OPIATE ADDICTION ARE COMPLEX AND CAN OVERLAP. THIS PANEL WILL PRESENT DATA FROM ANIMAL MODELS USING IN VIVO AND EX VIVO APPROACHES THAT EXPLORES THE CONTRIBUTION OF THE AFFERENTS TO AND ACTIVITY AND SYNAPTIC PLASTICITY OF STRIATAL NEURONS IN REGULATING COCAINE AND OPIATE SEEKING, TAKING, AND AVERSION.
DR. BARKER WILL PRESENT LONGITUDINAL PHARMACOKINETICS DATA SHOWING THAT STRIATAL NEURON FIRING DURING EARLY COCAINE SELF-ADMINISTRATION PREDICTS FUTURE INTAKE. SPECIFICALLY, FIRING PATTERNS OF NUCLEUS ACCUMBENS NEURONS INCREASE SENSITIVITY TO COCAINE IN EARLY SELF-ADMINISTRATION AND THE EARLY SENSITIVITY OF ACCUMBENS SHELL NEURONS TO COCAINE IS CORRELATED WITH FUTURE INCREASES IN DRUG INTAKE.
DR. BARBANO WILL DISCUSS THE CONTRIBUTION OF VENTRAL TEGMENTAL GLUTAMATERGIC AFFERENTS TO THE NUCLEUS ACCUMBENS IN COCAINE REWARD. BY USING IN VIVO OPTOGENETICS, SHE WILL SHOW THAT THE MESOACCUMBAL GLUTAMATERGIC PATHWAY SUPPRESSES PSYCHOSTIMULANT SEEKING BEHAVIOR AND THUS PLAYS A ROLE IN PSYCHOSTIMULANT CONDITIONED PLACE PREFERENCE AND SELF-ADMINISTRATION IN MICE.
DR. DOBBS WILL DISCUSS HOW STRIATAL ENKEPHALIN IS NOT NECESSARY FOR COCAINE REWARD, BUT THE BALANCE BETWEEN STRIATAL PROENKEPHALIN AND PRODYNORPHIN IS IMPLICATED IN COCAINE AVERSION. GREATER STRIATAL PROENKEPHALIN TO PRODYNORPHIN MRNA IS ASSOCIATED WITH COCAINE AVERSION. CONVERSELY, LACK OF ENKEPHALIN FROM STRIATAL MEDIUM SPINY NEURONS DOES NOT AFFECT ACQUISITION, EXPRESSION, OR EXTINCTION OF COCAINE PLACE PREFERENCE.
DR. LEFEVRE WILL PRESENT DATA INVESTIGATING HOW CONTINUOUS AND INTERRUPTED MORPHINE ADMINISTRATION ALTERS SYNAPTIC PLASTICITY OF NUCLEUS ACCUMBENS MEDIUM SPINY NEURONS. MORPHINE-EVOKED ADAPTATIONS AT EXCITATORY SYNAPSES ARE CONSERVED BETWEEN PATTERNS OF ADMINISTRATION; HOWEVER, THERE ARE DIVERGENT EFFECTS ON INHIBITORY SYNAPSES AND THE SUBSEQUENT BALANCE BETWEEN EXCITATORY AND INHIBITORY SYNAPTIC INPUTS.

MONDAY, JANUARY 29TH

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 6-8, FLOOR 2

CELLULAR AND NETWORK DYNAMICS OF SOUND DRIVEN BEHAVIOR AND DYSFUNCTION

CHAIR: RAMNARAYAN RAMACHANDRAN, PATRICK KANOLD
PRESENTERS: MARIA GEFFEN, LIBERTY HAMILTON, SHAOWEN BAO, JUN HEE KIM

THIS PANEL WILL FOCUS ON HOW THE RESPONSES TO SOUND ARE TRANSFORMED ACROSS THE AUDITORY PATHWAY, IN A CELL-TYPE DEPENDENT MANNER TO GENERATE MEANINGFUL BEHAVIOR IN NORMAL HEARING AND HEARING DYSFUNCTION.
TO ACHIEVE THIS, THE PANEL WILL DISCUSS CELL TYPE SPECIFIC RESPONSES IN THE AUDITORY PROCESSING HIERARCHY, THE INTERACTION OF GLIA AND NEURONS, AS WELL AS THE MECHANISMS OF PATHOLOGY THAT LEAD TO HEARING DYSFUNCTION.
RAM RAMACHANDRAN AND PATRICK KANOLD WILL PROVIDE INTRODUCTORY COMMENTS AND SHOW SOME PRELIMINARY DATA ON CELL TYPE SPECIFIC RESPONSE DYNAMICS AND BEHAVIOR.
MARIA GEFFEN (UNIVERSITY OF PENNSYLVANIA) WILL DISCUSS BEHAVIOR- AND SOUND-RELATED DYNAMICS OF NEURONAL ASSEMBLIES IN THE AUDITORY SYSTEM.
LIBERTY HAMILTON (THE UNIVERSITY OF TEXAS, AUSTIN) WILL DISCUSS THE DYNAMICS OF BRAIN RESPONSES UNDERLYING NATURALISTIC SPEECH PROCESSING IN HUMAN SUBJECTS, BOTH PEDIATRIC AND ADULT.
SHAOWEN BAO (THE UNIVERSITY OF ARIZONA) WILL PRESENT EVIDENCE THAT NOISE TRAUMA LEADS TO DEATH AND DYSFUNCTION OF THE CORTICAL PARVALBUMIN (PV) NEURON, AND THE FATE OF PV NEURONS IS INFLUENCED BY ITS DIFFERENTIAL EXPRESSION AND THE SIGNALING OF TUMOR NECROSIS FACTOR (TNF) RECEPTORS TNFRI AND TNFR2.
JUN HEE KIM (THE UNIVERSITY OF MICHIGAN) WILL PRESENT NOVEL DATA ON HOW LOSS OF OLIGODENDROGLIAL SCN2A (A GENE ENCODING THE ALPHA SUBUNIT OF THE VOLTAGE-GATED NA+ CHANNEL 1.2, AND IS HIGHLY LINKED TO AUTISM SPECTRUM DISORDERS (ASD)) IMPACTS NEURON-GLIA INTERACTION, MYELINATION, AND NEURAL CONNECTIVITY IN THE AUDITORY SYSTEM, LEADING TO AUDITORY PROCESSING DISORDERS.

MONDAY, JANUARY 29TH

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 9-10, FLOOR 2

MULTI-CELLULAR INTERACTIONS IMPACTING REPAIR AND RECOVERY AFTER TRAUMATIC INJURY IN THE CENTRAL AND PERIPHERAL NERVOUS SYSTEM

CHAIR: YIMIN ZOU
PRESENTERS: YIMIN ZOU, MAYSSA MOKALLED, DARIO BONANOMI, PETER GALIE

TRAUMATIC INJURIES IN THE CNS AND PNS LEAD TO SEVERE IMPAIRMENTS OF NEUROLOGICAL FUNCTIONS. RESTORING FUNCTION IS CHALLENGING, ESPECIALLY IN THE MAMMALIAN CENTRAL NERVOUS SYSTEM. CELLULAR RESPONSES DURING WOUND HEALING VARY BETWEEN CENTRAL AND PERIPHERAL NERVOUS SYSTEMS AND AMONG DIFFERENT ANIMAL SPECIES BUT THE UNDERLYING PRINCIPLES AND MECHANISMS ARE POORLY UNDERSTOOD. THIS SYMPOSIUM WILL EXAMINE AND COMPARE DIFFERENT INJURY ENVIRONMENTS –THE MAMMALIAN SPINAL CORD, MAMMALIAN SCIATIC NERVE AND ZEBRAFISH SPINAL CORD– TO ILLUSTRATE THE KEY MOLECULAR SIGNALING MECHANISMS THAT IMPACT CELLULAR INTERACTIONS AND THE ABILITY OF NERVE REGENERATION AND FUNCTIONAL RECOVERY. THIS SYMPOSIUM WILL ALSO FEATURE CHEMICAL AND BIOENGINEERING APPROACHES TO MODIFY INJURY SITES IN THE MAMMALIAN SPINAL CORD. YIMIN ZOU WILL DISCUSS THE NEAR COMPLETE BLOCKADE OF AXON REGENERATION IMPOSED BY THE HIGHLY HOSTILE INJURY SITE AND SECONDARY INJURY IN MAMMALIAN SPINAL CORD. HE WILL REPORT A NEW APPROACH TO ACCELERATE WOUND HEALING BY TARGETING A SIGNALING NETWORK IN ASTROCYTES. MAYSSA MOKALLED WILL SHOW HOW GLIAL BRIDGES MEDIATE ROBUST AXON REGENERATION IN INJURED ZEBRAFISH SPINAL CORD. SHE WILL COMPARE ZEBRAFISH AND MOUSE SPINAL CORDS AND LOOK FOR ANSWERS THAT GIVE RISE TO THE STARK DIFFERENCES. DARIO BONANOMI WILL FOCUS ON THE SIGNALING MECHANISMS MEDIATING THE INTERACTIONS BETWEEN BLOOD VESSELS AND AXONS IN DEVELOPMENT AS WELL AS DURING REPAIR OF THE MOUSE PERIPHERAL NERVOUS SYSTEM. PETER GALIE WILL DESCRIBE SCAFFOLDS TO BE DELIVERED TO THE SITE OF CENTRAL NERVOUS SYSTEM INJURY TO MODIFY THE INJURY MICROENVIRONMENT TO FOSTER REGENERATION. HIS LABORATORY HAS DEVELOPED BIOMATERIALS-BASED APPROACHES TO TUNE SCAFFOLD MECHANICAL PROPERTIES, TOPOLOGY, AND CELL-MATRIX INTERACTIONS. THE GOAL OF THIS INTERDISCIPLINARY PANEL IS TO PROVIDE A FORUM TO BRAINSTORM INNOVATIVE STRATEGIES BY COMBINING NEW KNOWLEDGE, PARTICULARLY THE INTERCELLULAR SIGNALING MECHANISMS, AND TISSUE ENGINEERING APPROACHES.

TUESDAY, JANUARY 30TH

PANEL
7:30 A.M. - 9:30 A.M.
IMPERIAL BALLROOM, FLOOR 4

DELTA OPIOID RECEPTOR FUNCTION IN PAIN AND REWARD CIRCUITS

CHAIRS: WILLIAM BIRDSONG, MARIE WALICKI
PRESENTERS: LOUIS GENDRON, ELIZAVETA MANGUTOV, EMILY JUTKIEWICZ, MARIE WALICKI

THE OPIOID SYSTEM HAS BEEN MANIPULATED FOR THERAPEUTIC INTERVENTION FOR THOUSANDS OF YEARS. OPIOID RECEPTORS AND THEIR ENDOGENOUS PEPTIDES ARE CRUCIAL FOR THE MODULATION OF PAIN BEHAVIORS AND ARE HIGHLY EXPRESSED IN BRAIN REGIONS INVOLVED IN REWARD AND EMOTIONAL REGULATION. WHILE THE MU OPIOID RECEPTOR MEDIATES THE ANALGESIC AND REINFORCING EFFECTS OF TRADITIONAL OPIOIDS LIKE MORPHINE, THE DELTA OPIOID RECEPTOR (DOR) REPRESENTS A POTENTIAL THERAPEUTIC TARGET FOR ANALGESIA WITH REDUCED ADDICTION LIABILITY. IN THIS PANEL, WE WILL DISCUSS NOVEL STUDIES OF DELTA OPIOID RECEPTOR SIGNALING AND ITS REGULATION OF PAIN AND REWARD-RELATED BEHAVIORS AT CELLULAR, CIRCUIT AND BEHAVIORAL LEVELS. THE SPEAKERS IN THIS PANEL WILL PRESENT CONVERGING EVIDENCE FOR DOR AS A THERAPEUTIC TARGET AND HIGHLIGHT DOR SIGNALING AS A DYNAMIC REGULATOR OF AFFECTIVE STATES. DR. WILL BIRDSONG WILL PROVIDE INTRODUCTORY COMMENTS AND FACILITATE DISCUSSION. DR. LOUIS GENDRON WILL BEGIN THE PANEL BY DISCUSSING THE ROLE OF THE DELTA OPIOID RECEPTOR ON THE AFFECTIVE COMPONENT OF PAIN AND HOW THE ACTIVATION OF DOR PRODUCED A SEX-DEPENDENT PLACE PREFERENCE IN THE MOUSE CHRONIC CONSTRICTION NERVE INJURY MODEL. NEXT, ELIZAVETA MANGUTOV, OF DR. AMYNAH PRADHAN'S GROUP WILL SHARE HER WORK ON THE DELTA OPIOID RECEPTOR AS A PROMISING TARGET FOR HEADACHE DISORDERS. THE PITUITARY ADENYLATE CYCLASE ACTIVATING POLYPEPTIDE (PACAP) TRIGGERS MIGRAINE, AND MANGUTOV'S INVESTIGATION ADDRESSES THE MECHANISTIC RELATIONSHIP BETWEEN DOR, PACAP, AND ITS RECEPTOR PACI. DR. EMILY JUTKIEWICZ WILL THEN DISCUSS HER LAB'S WORK STUDYING THE BEHAVIORAL EFFECTS OF DOR AGONISTS AND HIGHLIGHT A ROLE OF DOR IN REWARD PROCESSING. FINALLY, MARIE WALICKI OF DR. BIRDSONG'S LAB WILL PRESENT HER WORK INVESTIGATING THE REGULATION OF DOR SIGNALING ON CORTICAL INTERNEURONS BY DOR AGONIST TREATMENT AND PAIN.

TUESDAY, JANUARY 30TH

PANEL
7:30 A.M. - 9:30 A.M.
PEAK I-3, FLOOR 3

MONITORING AND MANIPULATING THE CAMP SIGNALING PATHWAY

CHAIR: ANDREW LUTAS
PRESENTERS: YAO CHEN, ANDREW LUTAS, ALFRED KAYE, HAINING ZHONG

THIS PANEL FOCUSES ON ADVANCES IN THE USE OF BIOSENSORS AND ACTUATORS TO MONITOR AND MANIPULATE CAMP SIGNALING IN NEURAL CIRCUITS OF LIVE ANIMALS. NEUROPLASTICITY, NEUROMODULATION, BEHAVIORAL FLEXIBILITY, AND LEARNING ARE ALL CRITICAL PROCESSES THAT INVOLVE THE ACTIONS OF G PROTEIN-COUPLED RECEPTORS (GPCRS), SUCH AS THOSE ACTIVATED BY DOPAMINE OR NOREPINEPHRINE. THE FUNCTIONAL CONSEQUENCE OF ACTIVATION OF MANY GPCRS IS AN INCREASE OR DECREASE IN CAMP PRODUCTION AND PROTEIN KINASE A (PKA) SIGNALING. TO UNDERSTAND HOW THIS KEY SIGNALING PATHWAY IN THE BRAIN FUNCTIONS IN HEALTHY AND DISEASE CONDITIONS, WE NEED BETTER APPROACHES TO TRACK AND CASUALLY MANIPULATE THIS PATHWAY IN LIVE ANIMALS.

YAO CHEN, PH.D., ASSISTANT PROFESSOR OF NEUROSCIENCE AT WASHINGTON UNIVERSITY SCHOOL OF MEDICINE IN ST. LOUIS, WILL PRESENT FIRST ON APPROACHES HER LAB HAS BEEN DEVELOPING TO TRACK AND MANIPULATE NEUROMODULATORS AND PKA SIGNALING. THESE INCLUDE THE USE OF FLUORESCENCE LIFETIME IMAGING MICROSCOPY APPROACHES FOR MORE QUANTITATIVE COMPARISONS ACROSS ANIMALS AND STATES.

ANDREW LUTAS, PH.D., STADTMAN TENURE-TRACK INVESTIGATOR AT THE NATIONAL INSTITUTES OF HEALTH, WILL PRESENT ON THE USE OF GENETICALLY-ENCODED TOOLS FOR TRACKING AND MANIPULATING CAMP SIGNALING IN THE AMYGDALA DURING APPETITIVE AND AVERSIVE LEARNING IN MICE.

ALFRED KAYE, M.D., PH.D. ASSISTANT PROFESSOR OF PSYCHIATRY AT YALE SCHOOL OF MEDICINE WILL PRESENT ON THE USE OF SECOND MESSENGER FLUORESCENT REPORTERS IN FRONTAL CORTEX TO UNDERSTAND THE CELL-TYPE SPECIFIC BASIS OF EMOTIONAL STATE CHANGES WITH THE GOAL OF DEVELOPING NOVEL THERAPEUTIC APPROACHES TO PSYCHIATRIC DISORDERS.

HAINING ZHONG, PH.D. SENIOR SCIENTIST AT VOLLUM INSTITUTE, WILL DISCUSS NOVEL FLUORESCENT SENSORS FOR MONITORING CAMP AND PKA THAT UTILIZE THE FLUORESCENCE LIFETIME MODALITY AND THE IMPLEMENTATION OF THESE TOOLS TO UNDERSTAND SIGNALING IN STRIATUM DURING LOCOMOTION.

TUESDAY, JANUARY 30TH

PANEL
7:30 A.M. - 9:30 A.M.
PEAK 11-12, FLOOR 2

BEHAVIORAL AND MOLECULAR MECHANISMS UNDERLYING FENTANYL INTAKE

CHAIR: DAVID BARKER
PRESENTERS: RENATA MARCHETTE, EMILY PREVOST, DAVID BARKER, ANTHONY DOWNS

FENTANYL MISUSE POSES A CRITICAL PUBLIC HEALTH CHALLENGE DUE TO ITS EXTRAORDINARY POTENCY AND POTENTIAL FOR OVERDOSE. AS A SYNTHETIC OPIOID, EVEN MINUSCULE AMOUNTS CAN LEAD TO SEVERE RESPIRATORY DEPRESSION AND FATAL OUTCOMES. THE DRUG'S INCREASING PRESENCE IN ILLICIT DRUG MARKETS AND ITS ROLE IN A RISING NUMBER OF OVERDOSE DEATHS HAVE TRIGGERED WIDESPREAD CONCERNS, DEMANDING COMPREHENSIVE STRATEGIES FOR PREVENTION, TREATMENT, AND HARM REDUCTION TO MITIGATE ITS DEVASTATING IMPACT ON INDIVIDUALS AND COMMUNITIES. THIS PANEL WILL FOCUS ON PRECLINICAL MODELS OF FENTANYL MISUSE WITH THE GOAL OF SHARING NEW SELF-ADMINISTRATION MODELS, EXAMINING CRITICAL BIOMARKERS AND NEURAL SIGNALING MECHANISMS, AND EXPLORING CIRCUITS THAT PLAY CAUSAL ROLES IN FENTANYL MISUSE. DR. RENATA MARCHETTE (NIDA) WILL PRESENT AN IN-DEPTH BEHAVIORAL ANALYSIS OF MALE AND FEMALE MICE TESTED IN THE FENTANYL VAPOR SELF-ADMINISTRATION MODEL AND THE POTENTIAL BRAIN AND BLOOD BIOMARKERS ASSOCIATED WITH AN ADDICTION-LIKE PHENOTYPE. DR. DAVID BARKER (RUTGERS) WILL PRESENT DATA SHOWING HOW STRESS CAN SHAPE REWARD CONSUMPTION, PAIN RESPONSES, AND FENTANYL INTAKE. HE WILL FURTHER DISCUSS A ROLE FOR THE LATERAL HABENULA IN MITIGATING THE EFFECTS OF STRESS ON FENTANYL INTAKE. EMILY PREVOST (UNIVERSITY OF COLORADO BOULDER) WILL PRESENT INITIAL EVIDENCE THAT GABAERGIC AND GLUTAMATERGIC MU-OPIOID RECEPTOR VENTRAL TEGMENTAL AREA NEURONS CONTROL DIFFERENT ASPECTS OF FENTANYL USE AND WITHDRAWAL.
FINALLY, DR. ANTHONY DOWNS (UNC) WILL PRESENT A FENTANYL MODEL OF DRINKING IN THE DARK (DID). HE WILL PRESENT DATA SHOWING THAT FENTANYL DID ALTERS SLEEP BEHAVIOR, SUPPORTS WITHDRAWAL BEHAVIOR FOLLOWING A NALOXONE CHALLENGE, ALTERS FEAR EXTINCTION LEARNING, AND DISRUPTS EXCITATORY/INHIBITORY BALANCE AND NEURONAL EXCITABILITY OF PRINCIPAL CELLS IN THE BASOLATERAL AMYGDALA.

TUESDAY, JANUARY 30TH

PANEL
7:30 A.M. - 9:30 A.M.
PEAK 14, FLOOR 1

DISTRIBUTED AND LOCAL CIRCUITS FOR ENCODING AVERSIVE EMOTIONS

CHAIR: JOSHUA JOHANSEN
PRESENTERS: JAN GRUNDEMANN, JOSHUA JOHANSEN, SABINE KRABBE, HUGO TEJEDA,

INNATELY AVERSIVE EXPERIENCES PRODUCE EMOTIONAL STATES IN THE BRAIN, TRIGGER CONCERTED DEFENSIVE BEHAVIORS AND LONG-TERM MEMORY FORMATION. DECADES OF WORK HAS IMPLICATED FOREBRAIN REGIONS SUCH AS THE MEDIAL THALAMUS, AMYGDALA AND MEDIAL PREFRONTAL CORTEX IN ORCHESTRATING DEFENSIVE RESPONDING AND STORING EMOTIONAL MEMORIES. HOWEVER, THE NEURAL PATHWAYS WHICH ARE RECRUITED TO TRIGGER FOREBRAIN EMOTIONAL REPRESENTATIONS AND HOW AVERSIVE INFORMATION IS INTEGRATED IN THESE FOREBRAIN AREAS IS NOT WELL UNDERSTOOD. IN THIS SYMPOSIUM, SPEAKERS WILL FOCUS ON THE ROLE OF BRAINSTEM CIRCUITS FOR CONVEYING AVERSIVE SIGNALS TO THE FOREBRAIN AND LOCAL CIRCUIT MECHANISMS IN FOREBRAIN REGIONS WHICH INTEGRATE THESE SIGNALS AND HELP COORDINATE EMOTIONAL STATES. THE FIRST SPEAKER, JAN GRUNDEMANN, WILL DISCUSS HOW BRAINSTEM CHOLINERGIC INPUTS TO THE MEDIAL GENICULATE AUDITORY THALAMUS REGULATE SENSORY PROCESSING DURING AVERSIVE LEARNING. NEXT, JOSH JOHANSEN WILL DESCRIBE A BRAINSTEM CUNEIFORM NUCLEUS-TO-AMYGDALA CIRCUIT WHICH CONVEYS INFORMATION ABOUT BOTH THE EXTERNAL-SENSORY AND INTERNAL-MOTOR ASPECTS OF INNATELY AVERSIVE EXPERIENCES TO THE AMYGDALA TO TRIGGER AN AVERSIVE SENSORIMOTOR STATE UNDERLYING ASSOCIATIVE MEMORY FORMATION. SABINE KRABBE WILL THEN DISCUSS HOW AMYGDALA INTERNEURONS UNDERGO PLASTICITY DURING AVERSIVE LEARNING AND ENCODE EMOTIONAL STATES. FINALLY, HUGO TEJEDA WILL DISCUSS THE ROLE OF THE PREFRONTAL CORTICAL DYNORPHIN SYSTEM IN REGULATING DEFENSIVE BEHAVIORS IN RESPONSE TO THREATS DURING MOTIVATIONAL CONFLICT AND HOW STATE TRANSITIONS IN PREFRONTAL CORTICAL NETWORKS UNDERLIE THREAT PROCESSING. TOGETHER, THESE PRESENTATIONS WILL PROVIDE NEW INSIGHTS INTO HOW DISTRIBUTED BRAINSTEM-FOREBRAIN CIRCUITS AND LOCAL MECHANISMS WITHIN FOREBRAIN MICROCIRCUITS GIVE RISE TO EMOTIONAL STATES AND LEARNING WITH IMPLICATIONS FOR UNDERSTANDING AND TREATING PSYCHIATRIC CONDITIONS ASSOCIATED WITH ANXIETY AND TRAUMA.

TUESDAY, JANUARY 30TH

PANEL
7:30 A.M. - 9:30 A.M.
PEAK 15-16, FLOOR 1

ASTROCYTES: A FLURRY OF ROLES IN DEVELOPMENT AND DISEASE

CHAIRS: JUSTIN TROTTER, STACEY GLASGOW
PRESENTERS: JUSTIN TROTTER, STACEY GLASGOW, SARAH ACKERMAN, NICOLA ALLEN

ASTROCYTES CONTRIBUTE TO A FLURRY OF ESSENTIAL BRAIN FUNCTIONS, INCLUDING NEUROTRANSMITTER METABOLISM, NEUROVASCULAR COUPLING, SYNAPTOGENESIS, SYNAPTIC MATURATION, SYNAPTIC PRUNING, AND BASAL SYNAPTIC TRANSMISSION. THE MECHANISTIC UNDERPINNINGS THAT ALLOW ASTROCYTES TO EXECUTE DIVERSE FUNCTIONS IN THE HEALTHY BRAIN AND HOW THESE MECHANISMS GO AWRY AND CONTRIBUTE TO DISEASE REMAIN BURIED IN SNOW. THIS PANEL BRINGS TOGETHER FOUR LABS THAT EMPLOY DIVERSE APPROACHES AND PERSPECTIVES TO PLOW THROUGH THE WHITE, FLUFFY MYSTERIUM THAT STILL SURROUNDS ASTROCYTE BIOLOGY. THE SESSION WILL BE CO-CHAIRED BY DRS. JUSTIN TROTTER (INSTRUCTOR, STANFORD UNIVERSITY) AND STACEY GLASGOW (ASSISTANT PROFESSOR, UCSD). IN ADDITION, THE PANEL WILL INCLUDE TALKS BY DRS. NICOLA ALLEN (ASSOCIATE PROFESSOR, SALK INSTITUTE) AND SARAH ACKERMAN (ASSISTANT PROFESSOR, WASHINGTON UNIVERSITY). JUSTIN WILL PROVIDE A BRIEF OVERVIEW OF THE FIELD AND THEN PRESENT HIS RECENT AND UNPUBLISHED WORK ON THE JANUS-FACED NATURE OF A CLASSICAL PRESYNAPTIC ORGANIZER, NRXN1, IN ORGANIZING ASTROCYTE-SYNAPSE AND ASTROCYTE-VASCULAR INTERACTIONS. STACEY WILL PRESENT HER LAB'S RECENT EFFORTS ON TRANSCRIPTIONAL PARALLELS BETWEEN HOW GLIA ARE GENERATED IN THE HEALTHY BRAIN AND HOW CANCEROUS GLIOMAS EMERGE. THEREAFTER, SARAH WILL DESCRIBE HER LAB'S EFFORTS USING FRUIT FLIES TO UNCOVER HOW SYNAPTIC ACTIVITY REGULATES ASTROCYTE MITOCHONDRIA AND THEIR INTERACTIONS WITH SYNAPSES. FINALLY, NICOLA WILL CLOSE THE SESSION BY DISCUSSING RECENT EFFORTS BY HER LAB TO UNDERSTAND THE ROLE THAT ASTROCYTES PLAY IN PROMOTING SYNAPSE MATURATION. JUSTIN AND STACEY WILL BOTH LEAD DISCUSSIONS OF THE PRESENTATIONS.

TUESDAY, JANUARY 30TH

PANEL
7:30 A.M. - 9:30 A.M.
PEAK 17, FLOOR 1

STRIATAL MECHANISMS OF ADAPTIVE AND MALADAPTIVE BEHAVIORAL CONTROL STRATEGY

CHAIRS: KATE WASSUM, JACQUELINE GIOVANNIELLO
PRESENTERS: MELISSA MALVAEZ, KYLE SMITH, MARY TORREGROSSA, JACQUELINE GIOVANNIELLO

WHEN MAKING A DECISION WE OFTEN EVALUATE THE CONSEQUENCES OF OUR POTENTIAL ACTIONS AND CHOOSE THE ONE THAT IS MOST BENEFICIAL. CHOOSING TO SKI THE SLOPE YOU KNOW PROVIDES A DESIRABLE COMBINATION OF THRILL AND SAFETY, FOR EXAMPLE. THIS GOAL-DIRECTED STRATEGY IS ADAPTIVE, BUT COGNITIVELY TAXING. HABITS ENABLE ROUTINE BEHAVIORS TO BE EXECUTED MORE AUTOMATICALLY. FOR EXAMPLE, ALWAYS FOLLOWING YOUR SKI BUDDY DOWN THE SLOPE. THIS IS STRATEGY IS EFFICIENT, BUT INFLEXIBLE. YOU MIGHT FOLLOW YOUR PARTNER DOWN A SLOPE TOO CHALLENGING FOR YOU. TYPICALLY, THE BRAIN BALANCES GOAL-DIRECTED AND HABITUAL CONTROL TO ALLOW BEHAVIOR TO BE ADAPTIVE WHEN NEEDED, BUT EFFICIENT WHEN APPROPRIATE. OVERRELIANCE ON HABITS CAN BE CAUSED BY STRESS AND LEAD TO THE SUBOPTIMAL DECISION MAKING AND COMPULSIVITY THAT CAN CHARACTERIZE MENTAL ILLNESSES AND SUBSTANCE USE DISORDERS. WE WILL DISCUSS RECENT ADVANCES IN THE BRAIN SYSTEMS THAT SUPPORT GOAL-DIRECTED ACTIONS AND HABITS.
WE FOCUS ON THE STRIATUM, A KEY CORTICOLIMBIC-MOTOR INTERFACE. DRS. KYLE SMITH AND MELISSA MALVAEZ WILL PROVIDE CRITICAL NEW INSIGHTS INTO HOW STRIATAL NETWORKS COORDINATE GOAL-DIRECTED ACTIONS AND HABITS. DR. MALVAEZ WILL REVEAL HOW DORSOMEDIAL STRIATAL NEURONS ENCODE AND REGULATE THE LEARNING THAT SUPPORTS GOAL-DIRECTED ACTIONS AND HOW THIS SHIFTS AS HABITS FORM. DR. SMITH WILL REVEAL HOW THE DORSOLATERAL STRIATUM, A CANONICAL HABIT REGION, IS SURPRISINGLY NEEDED FOR PROSPECTIVE PLANNING OF ACTIONS RATHER THAN PREVIOUSLY LEARNED ACTION ROUTINES. DRS. MARY TORREGROSSA AND JACQUELINE GIOVANNIELLO WILL DISCUSS HOW DISRUPTION TO DORSAL STRIATAL NETWORKS CAN TIP THE BALANCE OF BEHAVIORAL CONTROL TOWARDS PATHOLOGICAL HABITS. DR. TORREGROSSA WILL SHOW HOW DORSOMEDIAL STRIATUM DOPAMINE RELEASE AND NEURONAL ACTIVITY BECOMES SUPPRESSED ONCE COCAINE SEEKING BECOMES PUTATIVELY HABITUAL. DR. GIOVANNIELLO WILL REVEAL HOW TWO OPPOSING AMYGDALA INPUTS TO THE DORSOMEDIAL STRIATUM ALLOW CHRONIC STRESS TO PROMOTE PREMATURE HABIT FORMATION.

TUESDAY, JANUARY 30TH

PANEL
7:30 A.M. - 9:30 A.M.
PEAK 6-8, FLOOR 2

CIRCUIT DISRUPTIONS AS A COMMON CONSEQUENCE OF HETEROGENEOUS TYPES OF TRAUMATIC BRAIN INJURY

CHAIR: OLGA KOKIKO-COCHRAN
PRESENTERS: CORINA BONDI, COLE VONDER HAAR, AKIVA COHEN, CORINA BONDI

TRAUMATIC BRAIN INJURY (TBI) IS A MAJOR HEALTH CONCERN, WITH MORE THAN 2.8 MILLION SURVIVORS PER YEAR IN THE US. DECADES OF RESEARCH REVEAL THE COMPLEX PATHOPHYSIOLOGY AND FUNCTIONAL CONSEQUENCES OF TBI EVOLVE OVER TIME. NONETHELESS, EFFECTIVE THERAPEUTICS ARE LIMITED. PATHOLOGIES ASSOCIATED WITH TBI RANGE FROM IMPAIRMENTS IN MEMORY AND COGNITION TO EMOTIONAL LIABILITY. THE PANEL WILL EXPLORE CIRCUIT DISRUPTION AS A COMMON PHENOMENON FOLLOWING TBI WHICH CONTRIBUTE TO THE ABOVE PATHOLOGIES. SPEAKERS WILL DETAIL HOW HETEROGENEOUS INSULTS FROM PRECLINICAL MODELS RESULT IN HOMOGENEOUS NEURAL CIRCUIT DISRUPTION, POTENTIALLY SERVING AS THE FOUNDATION THROUGH WHICH FUNCTIONAL DEFICITS PERSIST AND HIGHLIGHT POTENTIAL THERAPEUTIC TARGETS. CORINA BONDI (UNIVERSITY OF PITTSBURGH) WILL FOCUS ON COMPLEX COGNITIVE- AND ANXIETY-LIKE BEHAVIORAL ALTERATIONS, AS WELL AS MODULATORY NEUROTRANSMITTERS AND ASSESSING EFFECTIVE THERAPIES THROUGHOUT THE LIFE SPAN IN MALES AND FEMALES. COLE VONDER HAAR (OHIO STATE UNIVERSITY) WILL DISCUSS HOW FRONTAL CONTUSION DYSREGULATES DOWNSTREAM PROJECTIONS TO THE NUCLEUS ACCUMBENS, RESULTING IN SUBSTANTIAL DEFICITS RELATED TO PROCESSING OUTCOMES. AKIVA COHEN (UNIVERSITY OF PENNSYLVANIA) WILL DISCUSS MECHANISMS UNDERLYING EXCITATORY-INHIBITORY (E-I) IMBALANCES THAT BRING ABOUT AND CONTRIBUTE TO CIRCUIT DISRUPTIONS ASSOCIATED WITH MILD TBI IN BRAIN REGIONS IMPORTANT FOR MEMORY AND COGNITION. OLGA KOKIKO-COCHRAN (OHIO STATE UNIVERSITY) WILL SERVE AS THE CHAIR AND DISCUSS HOW ENVIRONMENTAL SLEEP FRAGMENTATION AFTER LATERAL FLUID PERCUSSION TBI INFLUENCES BRAIN REGIONS INVOLVED IN STRESS SIGNALING AND COGNITION. AT THE CONCLUSION, AUDIENCE MEMBERS WILL HAVE AN APPRECIATION FOR DOWNSTREAM CONSEQUENCES OF TBI AND NEURONAL CIRCUITS THAT ARE PARTICULARLY VULNERABLE TO DYSFUNCTION OVER TIME.

TUESDAY, JANUARY 30TH

PANEL
7:30 A.M. - 9:30 A.M.
PEAK 9-10, FLOOR 2

SKIING THROUGH THE MOLECULAR LANDSCAPE OF PSYCHIATRIC DISORDERS IN POSTMORTEM HUMAN BRAINS

CHAIR: RYAN LOGAN
PRESENTERS: KIRSTEN SCHOONOVER, MICHAEL TOTTY, SHELBY RUIZ, RYAN LOGAN

RESEARCH USING BRAIN TISSUES FROM DECEDENTS WITH BRAIN DISORDERS HAVE PROVED VALUABLE FOR DISCOVERING DISEASE-RELATED MECHANISMS AND PUTATIVE, NOVEL, TREATMENT TARGETS. THE ADVENT OF NEWER MULTI-OMICS APPROACHES APPLIED TO POSTMORTEM HUMAN BRAIN TISSUE ENABLES THE LARGE-SCALE CHARACTERIZATION OF THE MOLECULAR ALTERATIONS AT THE CELLULAR LEVEL ASSOCIATED WITH BRAIN DISORDERS. THE PANEL WILL HIGHLIGHT VARIOUS APPROACHES ACROSS MULTIPLE BRAIN DISORDERS FROM THE FOLLOWING: 1) DR. KIRSTEN SCHOONOVER (ASSISTANT PROFESSOR); 2) DR. MICHAEL TOTTY (POSTDOC); 3) SHELBY RUIZ (GRADUATE STUDENT); AND 4) DR. RYAN LOGAN (PROFESSOR). DR. SCHOONOVER WILL DISCUSS UNPUBLISHED FINDINGS WHERE SHE DEVELOPED AN UNBIASED METHODOLOGY TO IDENTIFY LAYER-SPECIFIC CORTICAL NEURONS IN HUMAN BRAIN. SHE WILL PRESENT MORPHOLOGICAL AND TRANSCRIPTIONAL ALTERATIONS IN CORTICAL LAYER 3 PARVALBUMIN NEURONS IN SUBJECTS WITH SCHIZOPHRENIA, HIGHLIGHTING THE RELATIONSHIPS BETWEEN LOWER ENERGY PRODUCTION AND LOWER EXCITATORY DRIVE IN THE ILLNESS. DR. TOTTY WILL DISCUSS UNPUBLISHED WORK ON CROSS-SPECIES INVESTIGATIONS OF THE AMYGDALA USING SINGLE NUCLEI RNA-SEQUENCING (SNRNA-SEQ) OF HUMAN AND NON-HUMAN PRIMATES, FINDING RELATIVELY STRONG CONSERVATION OF BOTH EXCITATORY AND INHIBITORY NEURONAL CELL-CLASSES THAT ARE ASSOCIATED WITH GENETIC RISK FOR SEVERAL PSYCHIATRIC DISORDERS. MRS. RUIZ WILL PRESENT UNPUBLISHED FINDINGS FROM POSTMORTEM PRIMARY VISUAL CORTEX OF ASD AND NEUROTYPICAL SUBJECTS (AGES 4-33), SHOWING ALTERATIONS IN ASD IN SYNAPTIC PROTEIN LOCALIZATION ACROSS DEVELOPMENT, WITH DIFFERENTIAL DEVELOPMENTAL TRAJECTORIES ENRICHED FOR ASD RISK GENES. DR. LOGAN WILL PRESENT NEW SNRNA-SEQ AND ATAC-SEQ FINDINGS FROM CORTICAL AND STRIATAL BRAIN REGIONS OF SUBJECTS WITH OUD AND MAJOR DEPRESSIVE DISORDER (MDD), INDICATING SEX-SPECIFIC MOLECULAR MECHANISMS IN NEURONAL AND GLIAL SUBTYPES ASSOCIATED WITH CO-OCCURRING DISORDERS. FEMALE-SPECIFIC CHANGES IN STRESS-RELATED SIGNALING IN GLIA.

TUESDAY, JANUARY 30TH

PIONEER SESSION
9:45 A.M. - 11:15 A.M.
PEAK 11-12, FLOOR 2

HOW TO STUDY THE HUMAN BRAIN: FROM AUTOPSY TO ASSAY – TRUTH IS STRANGER THAN FICTION

PIONEER: THOMAS HYDE
CHAIR: ELIZABETH TUNBRIDGE
INVESTIGATORS: ELIZABETH TUNBRIDGE, GREGORY CARR

THE STUDY OF NEUROLOGICAL AND PSYCHIATRIC DISORDERS IS OFTEN BEST SERVED THROUGH THE STUDY OF HUMAN BRAIN TISSUE. UNLIKE OTHER ORGAN SYSTEMS SUCH AS KIDNEY OR LIVER, ACQUISITION OF BRAIN TISSUE FROM LIVING DONORS IS ALMOST IMPOSSIBLE. ACCORDINGLY, POST-MORTEM HUMAN BRAIN TISSUE HAS TO SERVE AS A SUBSTITUTE. FOR NEARLY THIRTY-FIVE YEARS, FIRST AT THE NIMH AND MORE RECENTLY AT THE LIEBER INSTITUTE, DR. HYDE HAS SPEARHEADED BOTH THE COLLECTION, CHARACTERIZATION, AND CURATION OF POST-MORTEM HUMAN BRAIN, AS WELL THE STUDY OF THIS TISSUE IN NEUROPSYCHIATRIC DISORDERS. UNDER HIS LEADERSHIP, THE LIEBER INSTITUTE HAS DEVELOPED ONE OF THE LARGEST POST-MORTEM HUMAN BRAIN COLLECTIONS IN THE WORLD DEDICATED TO THE STUDY OF NEUROPSYCHIATRIC DISORDERS, WITH NEARLY 5000 SPECIMENS ON SITE. DR. HYDE WILL GIVE AN OVERVIEW OF THE PROCESS BY WHICH HUMAN BRAINS ARE COLLECTED, CHARACTERIZED, AND CURATED. HE THEN WILL SEGUE INTO A DISCUSSION OF THE USE OF THESE TISSUES IN HIGH THROUGHPUT ASSAYS INCLUDING RNASEQ, SINGLE CELL RNASEQ, LASER CAPTURE MICRODISSECTION, AND PROTEOMICS. THE FOCUS WILL BE ON THE USE OF THESE TISSUES IN COUPLING GENETIC FINDINGS FROM CLINICAL STUDIES WITH THE ELUCIDATION OF MECHANISMS OF GENETIC RISK. DR. ELIZABETH TUNBRIDGE, A FREQUENT COLLABORATOR WITH DR. HYDE, WILL DISCUSS THE USE OF POST-MORTEM HUMAN BRAIN TISSUE IN THE STUDY OF ION CHANNELS IN NEUROPSYCHIATRIC DISEASE. FINALLY, DR. GREG CARR, ANOTHER CLOSE SCIENTIFIC COLLEAGUE OF DR. HYDE, WILL PRESENT HIS STUDIES USING FINDINGS FROM HUMAN POST-MORTEM BRAIN TISSUE TO DEVELOP MORE FAITHFUL ANIMAL MODELS OF NEUROPSYCHIATRIC DISORDERS. DR. CARR WILL ALSO DISCUSS THE UTILITY OF THESE MODELS IN IDENTIFYING NOVEL TARGETS FOR DRUG DEVELOPMENT.

TUESDAY, JANUARY 30TH

SPECIAL SESSION
2:00 P.M. - 3:30 P.M.
PEAK 6-8, FLOOR 2

INSIDER TIPS FOR NIH GRANT SUCCESS

CHAIR: ERIK CARLSON
PRESENTERS: SUNILA NAIR, DEANNA ADKINS, KATHRYN REISSNER, ALISON HALL

THIS EDUCATION PANEL'S PRIMARY GOAL IS TO HAVE AN INTERACTIVE DISCUSSION BETWEEN PANELISTS AND ATTENDEES ABOUT SUBMITTING BETTER GRANTS. THIS PANEL WILL DEMYSTIFY THE EXPERIENCE OF THE GRANT REVIEW PROCESS WITH PANELISTS WHO PLAY SPECIFIC ROLES SUCH AS PROGRAM OFFICER, SCIENTIFIC REVIEW OFFICER, AND STUDY SECTION CHAIR. PROCESSES SUCH AS TRIAGE AND CALIBRATION, INTERACTING WITH PROGRAM OFFICERS, AS WELL AS A FRANK DISCUSSION OF COMMON WEAKNESSES IN SPECIFIC DOMAINS ASSESSED BY REVIEWERS SEEN IN GRANTS FROM TRAINEES AND INDEPENDENT INVESTIGATORS WILL BE ADDRESSED.

TUESDAY, JANUARY 30TH

PANEL
4:30 P.M. - 6:30 P.M.
IMPERIAL BALLROOM, FLOOR 4

TOOLS TO TRAVERSE THE SLOPES OF D2-LIKE RECEPTOR ACTIVATION IN HEALTH AND DISEASE

CHAIRS: KIM NEVE, AMY NEWMAN
PRESENTERS: AMY NEWMAN, JAVIER GARCIA-NAFRIA, VERONICA ALVAREZ, KIM NEVE

AGONISTS AND ANTAGONISTS OF THE DOPAMINE D2 AND D3 RECEPTORS ARE COMMONLY USED TO TREAT A VARIETY OF NEUROPSYCHIATRIC DISORDERS, BUT THEIR THERAPEUTIC UTILITY IS GENERALLY LIMITED BY THE DEVELOPMENT OF DRUG-INDUCED SIDE EFFECTS, INCLUDING MOTOR, METABOLIC, COGNITIVE, AND/OR PSYCHOLOGICAL DYSFUNCTION. NEW APPROACHES FOR MANIPULATING BRAIN CIRCUIT FUNCTION, THE INCREASING AVAILABILITY OF STRUCTURES OF DOPAMINE RECEPTORS IN A VARIETY OF FUNCTIONAL STATES, AND THE DISCOVERY OF HUMAN PATHOGENIC D2 RECEPTOR VARIANTS HAVE CREATED OPPORTUNITIES TO REFINE STRATEGIES FOR MEDICATION DEVELOPMENT AND DRUG SCREENING WITH THE GOAL OF AVOIDING SOME OF THOSE SIDE EFFECTS. IN THIS PANEL, AMY NEWMAN WILL DESCRIBE THE DISCOVERY OF NOVEL D3 RECEPTOR (D3R)-PREFERRING LIGANDS THAT VARY IN FUNCTIONAL EFFICACY AND SELECTIVITY AND THAT MAY BE USEFUL FOR THE TREATMENT OF SUBSTANCE USE DISORDERS THAT ARE OFTEN COMORBID WITH OTHER AFFECTIVE DISEASES. JAVIER GARCÍA-NAFRÍA WILL PRESENT THE CRYO-EM STRUCTURE OF A FULLY ACTIVATED D3R COUPLED TO GALPHA-O, WHICH PROVIDES A STRUCTURAL EXPLANATION FOR THE SELECTIVITY OF A BITOPIC LIGAND BASED ON EXPLOITATION OF A SECONDARY BINDING POCKET. VERONICA ALVAREZ WILL DISCUSS HOW LOW D2 RECEPTOR EXPRESSION IN DIFFERENT NEURONAL TYPES ALTERS MURINE RESPONSE TO DRUGS AND VULNERABILITY FOR SUBSTANCE USE DISORDERS. KIM NEVE WILL COMPARE AND CONTRAST THE EFFECTS OF TWO RECENTLY DISCOVERED D2 RECEPTOR PATHOGENIC MUTATIONS AND DISCUSS THE IMPLICATIONS FOR TREATMENT OF HYPERKINETIC MOVEMENT DISORDERS.

TUESDAY, JANUARY 30TH

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 1-3, FLOOR 3

RECONSIDERING PARKINSON'S DISEASE FROM A MULTI-SYSTEM PERSPECTIVE

CHAIRS: LOUIS-ERIC TRUDEAU, FREJA HERBORG
PRESENTERS: LOUIS-ERIC TRUDEAU, ULRIK GETHER, PER BORGHAMMER, MICHELA DELEIDI

PARKINSON'S DISEASE (PD), ONCE CONSIDERED A PURELY DOPAMINE NEURON PATHOLOGY, IS NOW INCREASINGLY CONSIDERED AS A SYSTEMIC DISEASE AFFECTING MULTIPLE CELL TYPES IN THE BRAIN AND PERIPHERY. ALTHOUGH NEURONAL DYSFUNCTION AND DEATH IS CENTRAL TO THE MAJOR MOTOR AND NON-MOTOR SYMPTOMS OF PD, AN INCREASING AMOUNT OF WORK SUGGESTS THAT NON-NEURONAL CELLS INCLUDING GLIAL CELLS AND IMMUNE CELLS ARE ALSO INVOLVED IN BOTH INITIATION AND PROGRESSION. RESEARCH ALSO SUGGESTS THAT MULTIPLE FORMS OF PD ARE LIKELY TO EXIST, AND THAT THE PATHOLOGY CAN BE INITIATED EITHER CENTRALLY, IN THE BRAIN, OR PERIPHERALLY, IN THE GUT OR OTHER ORGANS. BUT MUCH REMAINS TO BE WORKED OUT. NEW ANIMAL AND CELL MODELS ARE NEEDED TO BETTER REPRESENT THE VARIOUS FORMS OF THE DISEASE AND THE PROGRESSION OF PATHOLOGY. AND NEW DISCOVERIES ARE NEEDED IN HUMAN SUBJECTS TO GUIDE SUCH DISEASE MODELLING AND IDENTIFY NEW THERAPEUTIC LEADS. IN THIS PANEL, THE INITIATING FACTORS AND PATHOLOGICAL MECHANISMS OF PD PROGRESSION WILL BE EXAMINED FROM MULTIPLE ANGLES, FROM A MULTI-SYSTEM PERSPECTIVE. LOUIS-ERIC TRUDEAU FROM THE UNIVERSITÉ DE MONTRÉAL WILL SHARE SOME OF HIS RECENT WORK ON THE ORIGIN OF THE HIGH VULNERABILITY OF NEUROMODULATORY NEURONS IN PD AND THE HYPOTHESIS OF A CRITICAL IMPLICATION OF IMMUNE MECHANISMS IN DISEASE INITIATION. ULRIK GETHER, FROM THE UNIVERSITY OF COPENHAGEN WILL SHOW HOW LARGE-SCALE EXOME-SEQUENCING CAN HELP TO IDENTIFY NOVEL MUTATIONS THAT LEAD TO EARLY-ONSET NEURODEGENERATIVE PARKINSONISM. PER BORGHAMMER, FROM AARHUS UNIVERSITY WILL PRESENT WORK BOTH IN HUMAN SUBJECTS AND IN ANIMAL MODELS SUGGESTING THAT PD EXISTS IN MULTIPLE FORMS AND CAN BE INITIATED FROM THE PERIPHERY OR FROM THE BRAIN. FINALLY, MICHELA DILEIDI FROM THE IMAGINE INSTITUTE IN FRANCE WILL SHOW HOW ORGANOID PREPARATIONS CAN HELP TO SHED NEW INSIGHTS INTO THE CELLULAR MECHANISMS LEADING TO PARKINSON'S DISEASE. FREJA HERBORG FROM THE UNIVERSITY OF COPENHAGEN WILL ACT AS CO-CHAIR OF THIS SESSION.

TUESDAY, JANUARY 30TH

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 11-12, FLOOR 2

SYSTEMATIC INVESTIGATION INTO THE EFFECTS OF SUBSTANCE USE

CHAIRS: YIFENG CHENG, ROBIN MAGNARD
PRESENTERS: YVAN VACHEZ, YIFENG CHENG, MIGUEL LUJAN, QIAOWEI XIE

SUBSTANCE USE DISORDERS POSE A SIGNIFICANT PUBLIC HEALTH CHALLENGE, MAINLY DUE TO THE LOSS OF BEHAVIORAL CONTROL AND FLEXIBILITY, MANIFESTING AS COMPULSIVE AND IMPULSIVE BEHAVIORS. THESE COGNITIVE DYSFUNCTIONS ARE BELIEVED TO BE ASSOCIATED WITH ALTERATIONS IN THE MESOLIMBIC AND NIGROSTRIATAL PATHWAYS. YIFENG CHENG (JHU, CHAIR) WILL GIVE THE INTRODUCTORY COMMENTS. ROBIN MAGNARD (JHU, CO-CHAIR) WILL MODERATE THE FOLLOWING SPEAKERS' PRESENTATIONS. YVAN VACHEZ (INSERM) WILL PRESENT THE ETHANOL-INDUCED PLASTICITY ON THE VP- GREATER THAN STN SYNAPSES, AN ESSENTIAL PATHWAY FOR BEHAVIORAL INHIBITION PROCESSES. THEN, WITH IN VIVO EXTRACELLULAR RECORDING AND COMPUTATIONAL MODELING, YIFENG CHENG (JHU) WILL FURTHER DELVE INTO HOW CHRONIC ALCOHOL EXPOSURE IMPACTS NEUROCOMPUTATIONAL AND COGNITIVE PROCESSES IN DECISION-MAKING TASKS. STRIATAL ACTIVITY IS HIGHLY DEPENDENT ON THE HOMEOSTASIS OF LOCAL NEUROMODULATORS. THUS, MIGUEL A. LUJAN (UMB) WILL DISCUSS THE INTERACTION BETWEEN THE ENDOCANNABINOID AND DOPAMINE SYSTEMS IN THE VTA- GREATER THAN NAC PATHWAY WITH IN VIVO FIBER PHOTOMETRY RECORDING, PROVIDING INSIGHTS INTO PROACTIVE BEHAVIORAL CONTROL AND CONDITIONED REWARD-SEEKING BEHAVIORS. NOTABLY, AMONG INDIVIDUALS WITH SUBSTANCE USE DISORDER, THERE IS A SIGNIFICANT COMORBIDITY OF HIV. OUR LAST SPEAKER, QIAOWEI XIE (DREXEL UNIVERSITY), WILL ELUCIDATE THE ROLE OF NAC ASTROCYTES IN HIV-ENHANCED COCAINE SENSITIZATION, SHEDDING LIGHT ON A UNIQUE CELLULAR MECHANISM UNDERLYING THE COMORBIDITY OF HIV AND COCAINE USE DISORDERS. HER INSIGHTS OFFER A TRANSLATIONAL PERSPECTIVE TO OUR PANEL DISCUSSION. COLLECTIVELY, THIS PANEL PROVIDES A COMPREHENSIVE DISCUSSION OF THE NEUROBEHAVIORAL CONSEQUENCES AND MECHANISMS UNDERLYING SUBSTANCE USE, SPANNING FROM CELLULAR TO COGNITIVE LEVELS AND BRIDGING BASIC RESEARCH TO CLINICALLY RELEVANT TOPICS. OUR OBJECTIVE IS TO PROVIDE AN IN-DEPTH INSIGHT INTO ADDICTION NEUROSCIENCE AND TO ENCOURAGE INTERDISCIPLINARY COLLABORATION.

TUESDAY, JANUARY 30TH

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 14, FLOOR 1

AMPA RECEPTORS AND THEIR AUXILIARIES IN HEALTH, DISEASE AND SYNAPTIC PLASTICITY

CHAIRS: INGO GREGER
PRESENTERS: JOHANNES HELL, INGO GREGER, DAVID BREDT, ROGER NICOLL

AMPA-TYPE GLUTAMATE RECEPTORS (AMPARS) SERVE AS THE PRIMARY MEDIATORS OF SIGNAL TRANSMISSION AT EXCITATORY SYNAPSES. THEY PLAY A PIVOTAL ROLE IN SYNAPTIC PLASTICITY MECHANISMS UNDERLYING LEARNING AND MEMORY BUT ALSO CONTRIBUTE TO VARIOUS DISEASES, MAKING THEM POTENTIAL DRUG TARGETS. WHAT SETS THESE RECEPTORS APART IS THE INTRICATE NETWORK OF AUXILIARY PROTEINS THAT ASSOCIATE WITH THEM IN VARIOUS STOICHIOMETRIES. THESE PROTEINS PLAY A CRUCIAL ROLE IN ORCHESTRATING RECEPTOR BIOGENESIS, DETERMINING THE PRECISE SUBSYNAPTIC LOCATIONS TO ENSURE EFFICIENT TRANSMISSION, AND FINELY TUNING AMPAR SIGNALING IN DIVERSE CIRCUITRIES. THIS INTRICATE INTERPLAY OF AUXILIARY PROTEINS NOT ONLY DIVERSIFIES AMPAR FUNCTIONS BUT ALSO PAVES THE WAY FOR THE DEVELOPMENT OF SPECIALIZED MODULATORS TAILORED TO SPECIFIC BRAIN REGIONS.
OUR PANEL WILL COVER THE LATEST BREAKTHROUGHS IN UNRAVELING THE ORGANIZATION OF AMPAR SIGNALING COMPLEXES AND UNDERSTANDING HOW THEY ARE REGULATED IN VARIOUS SYNAPTIC PLASTICITY MECHANISMS, BOTH IN THE CONTEXT OF THE HEALTHY BRAIN AND WHEN IMPACTED BY DISEASES. THE TALKS WILL ENCOMPASS A BROAD RANGE OF EXPERIMENTAL APPROACHES, INCLUDING ELECTROPHYSIOLOGY, PHARMACOLOGY, CRYO-ELECTRON MICROSCOPY, AND SUPER-RESOLUTION LIGHT MICROSCOPY. DR. HELL WILL SPEAK ON THE REGULATION OF POSTSYNAPTIC AMPA RECEPTORS. DR. GREGER WILL DISCUSS SELECTIVE AMPAR THERAPEUTICS DERIVED FROM AMPAR AUXILIARIES. DR. BREDT WILL BRIDGE THE GAP BETWEEN BASIC SCIENCE AND INDUSTRY. DR. NICOLL WILL CLOSE WITH A DISCUSSION ON CAMKII-DEPENDENT SYNAPTIC MEMORY.

TUESDAY, JANUARY 30TH

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 15-16, FLOOR 1

SEX DIFFERENCES IN PAIN AND NEGATIVE AFFECT AND IMPLICATIONS FOR ALCOHOL AND OPIOID USE DISORDER RISK

CHAIRS: SCOTT EDWARDS, DAYNA AVERITT
PRESENTERS: SCOTT EDWARDS, DAYNA AVERITT, KHALIN NISBETT, AMANDA PAHNG

CHRONIC PAIN AND SUBSTANCE USE DISORDERS (SUDS) ARE DEVASTATING CONDITIONS THAT SHARE AN OVERLAPPING NEUROBIOLOGY, INTERSECTING CLINICAL FEATURES, AND FEW EFFECTIVE TREATMENTS. THE USE OF ALCOHOL OR OPIOIDS TO MANAGE PAIN OR COPE WITH ASSOCIATED NEGATIVE AFFECTIVE SYMPTOMS MAY DRIVE NEGATIVE REINFORCEMENT MECHANISMS THAT UNDERLIE THE PROGRESSIVE SEVERITY OF SUDS. THIS SYMPOSIUM FEATURES A DIVERSE SET OF SPEAKERS BALANCED BY SEX, RACE, CAREER STAGE, AND EXPERIMENTAL APPROACH AND WILL FOCUS ON RECENT INSIGHTS INTO SEX-SPECIFIC NEUROBIOLOGICAL MECHANISMS UNDERLYING PAIN, PAIN-RELATED NEGATIVE AFFECT, AND MOTIVATION FOR SUBSTANCE USE. DR. SCOTT EDWARDS (ASSOCIATE PROFESSOR, LSU HEALTH-NEW ORLEANS) WILL PROVIDE AN OVERVIEW OF THE NEUROBIOLOGY OF CHRONIC PAIN AND SUDS WITH A FOCUS ON INFORMING TRANSLATIONAL INSIGHTS INTO THESE CONDITIONS. HE WILL ALSO DESCRIBE PRECLINICAL AND CLINICAL RESEARCH IN HIS LAB EXAMINING SEX-SPECIFIC ENDOCANNABINOID MECHANISMS UNDERLYING THE ANALGESIC EFFICACY OF ALCOHOL AND ASSOCIATIONS WITH NEGATIVE AFFECT. DR. DAYNA L. AVERITT (ASSOCIATE PROFESSOR, TEXAS WOMEN'S UNIVERSITY) WILL DESCRIBE FUNCTIONAL SEX DIFFERENCES IN THE EFFECTS OF STRESS ON NOCICEPTIVE CIRCUITRY AND HORMONAL INFLUENCES ACROSS MULTIPLE PRECLINICAL PAIN MODELS. MS. KHALIN E. NISBETT (PREDOCTORAL VISITING FELLOW, NIDA) WILL DESCRIBE SEX AND ESTROUS CYCLE DIFFERENCES IN THE EFFECT OF OXYTOCIN ON ANXIETY-LIKE BEHAVIOR AND WILL DISCUSS RELEVANT MECHANISMS UNDERLYING THE OBSERVED SEX AND ESTROUS CYCLE DIFFERENCES. FINALLY, DR. AMANDA R. PAHNG (RESEARCH HEALTH SCIENTIST, SOUTHEAST LOUISIANA VETERANS HEALTH CARE SYSTEM) WILL DISCUSS SEX-SPECIFIC NEUROADAPTATIONS IN THE MESOLIMBIC DOPAMINE SYSTEM IN ASSOCIATION WITH DIFFERENTIAL FENTANYL REWARD AND REINFORCEMENT IN RODENTS. THESE DISCUSSIONS WILL SHAPE FUTURE TRANSLATIONAL INVESTIGATIONS TOWARD MORE NOVEL AND EFFECTIVE THERAPEUTIC AVENUES FOR TREATING PAIN AND NEGATIVE AFFECT IN INDIVIDUALS AT-RISK OR CURRENTLY SUFFERING FROM SUDS.

TUESDAY, JANUARY 30TH

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 17, FLOOR 1

CELL-TYPE SPECIFIC STRIATAL CONTROL OF MOTIVATION AND DECISION-MAKING IN HEALTH AND DISEASE

CHAIRS: MATTHEW HEARING, ERIN CALIPARI
PRESENTERS: MATTHEW HEARING, ERIN CALIPARI, BRAD GRUETER, CONSTANZA GARCIA KELLER

THE PREFRONTAL CORTEX-NUCLEUS ACCUMBENS (MPFC-NAC) IS AT THE HUB OF LEARNING, SELECTING, AND EXECUTING GOAL-ORIENTED BEHAVIORS ASSOCIATED WITH BOTH APPETITIVE AND AVERSIVE STIMULI THAT IS COMPOSED OF A HETEROGENEOUS POPULATION OF PYRAMIDAL AND MEDIUM SPINY NEURONS (MSNS) LARGELY CLASSIFIED BY EXPRESSION OF DI- OR D2-TYPE DOPAMINE RECEPTORS. MUCH OF OUR UNDERSTANDING OF THE ROLE THESE POPULATIONS PLAY IN BEHAVIORAL CONTROL HAS BEEN BASED ON THEIR ROLE IN REWARD-BASED BEHAVIORS AND IN RESPONSE TO DRUGS OF ABUSE, WHERE THE CELL-TYPE SPECIFIC MODULATION OF THESE POPULATIONS PLAYS A CRITICAL ROLE. THIS PANEL WILL DISCUSS THE ROLE OF THESE DEFINED CELL-TYPES IN BEHAVIORAL CONTROL AND OUTLINE HOW PRIOR EXPERIENCE ALTERS THEIR ABILITY TO CONTROL MOTIVE BEHAVIOR AND DECISION-MAKING, WITH AN ADDITIONAL FOCUS ON UNDERLYING EXPERIENCE-RELATED PLASTICITY IN THESE CIRCUITS. DR. HEARING WILL DISCUSS THE ROLE OF MPFC-NAC DI- VERSUS D2-EXPRESSING PYRAMIDAL AND MSN CIRCUITS IN THE REGULATION OF COGNITIVE FLEXIBILITY AND THEIR CONTRIBUTION TO STRESS-RELATED PATHOLOGY WITH A FOCUS ON HOW THESE CIRCUITS UNIQUELY CONTRIBUTE BASED ON BIOLOGICAL SEX. NEXT, DR. CALIPARI WILL CHALLENGE THE DOGMA THAT DI AND D2-TYPE MSNS HAVE OPPOSING ACTIONS AND HIGHLIGHT A SYNERGISTIC ROLE IN LEARNING THROUGH SIGNALING STIMULUS INTENSITY IN DI MSNS AND PREDICTION ERRORS IN D2 MSNS. DR. GRUETER WILL PRESENT DATA OUTLINING THE RECEPTOR-BASED MECHANISMS BY WHICH HUNGER ALTERS THE PHYSIOLOGICAL PROPERTIES OF DI AND D2-CONTAINING MSNS AND HOW THIS DRIVES FOOD SEEKING. FINALLY, DR. GARCIA KELLER WILL PRESENT DATA SHOWING HOW Δ9-TETRAHYDROCANNABINOL (THC) INDUCES CELL-TYPE SPECIFIC ADAPTATIONS IN DI- AND D2-MSNS SPINE MORPHOLOGY AND THE ASSOCIATED CHANGES IN CBIR REGULATION OF GLUTAMATE TRANSMISSION. THIS PANEL WILL HELP BROADEN OUR UNDERSTANDING OF THE NEURAL DYNAMICS UNDERLYING REWARD AND MOTIVATION AND REFINE OUR UNDERSTANDING OF THE ROLE OF THE VENTRAL STRIATUM IN ADAPTIVE AND MALADAPTIVE BEHAVIORS.

TUESDAY, JANUARY 30TH

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 6-8, FLOOR 2

INVESTIGATIONS INTO SLEEP CIRCUITRY AND PLASTICITY IN PHYSIOLOGICAL AND PATHOLOGICAL CONDITIONS

CHAIR: ADA EBAN-ROTHSCHILD
PRESENTERS: FRANZ WEBER, ASHLEY INGIOSI, SHINJAE CHUNG, ADA EBAN-ROTHSCHILD

SLEEP IS A MULTIFACETED BEHAVIORAL AND NEUROPHYSIOLOGICAL STATE THAT PLAYS A CRITICAL ROLE IN VARIOUS PHYSIOLOGICAL AND COGNITIVE FUNCTIONS. IN RECENT YEARS, SIGNIFICANT PROGRESS HAS BEEN ACHIEVED THROUGH THE APPLICATION OF STATE-OF-THE-ART TECHNIQUES IN SYSTEMS NEUROSCIENCE, UNVEILING SLEEP CIRCUITRY, FUNCTION AND PLASTICITY. OUR PANEL AIMS TO DELVE INTO THESE BREAKTHROUGHS, SHEDDING LIGHT ON THE DIVERSE FACETS OF SLEEP. DR. WEBER, FROM THE UNIVERSITY OF PENNSYLVANIA, WILL SPEAK ABOUT HIS LAB'S WORK ON THE BRAINSTEM DYNAMICS UNDERLYING THE REGULATION OF REM SLEEP. DR. INGIOSI, FROM OHIO STATE UNIVERSITY COLLEGE OF MEDICINE, WILL DISCUSS HER FINDINGS REGARDING THE MECHANISTIC AND REGION-SPECIFIC ROLES PLAYED BY ASTROCYTES IN SHAPING SLEEP-WAKE BEHAVIOR AND MAINTAINING SLEEP HOMEOSTASIS. DR. CHUNG, FROM THE UNIVERSITY OF PENNSYLVANIA, WILL DESCRIBE HER WORK ON THE INTRICATE NEURAL CIRCUITS INVOLVED IN STRESS-INDUCED SLEEP DISTURBANCES. LASTLY, DR. EBAN-ROTHSCHILD, FROM THE UNIVERSITY OF MICHIGAN, WILL DISCUSS HOW THE SOCIAL ENVIRONMENT INFLUENCES THE SYNCHRONIZATION OF BEHAVIOR AND NEUROPHYSIOLOGICAL OSCILLATORY ACTIVITY DURING SLEEP.

TUESDAY, JANUARY 30TH

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 9-10, FLOOR 2

FOSTERING SUCCESSFUL PARTNERSHIPS BETWEEN ACADEMIA AND INDUSTRY

CHAIR: ELIZABETH TUNBRIDGE
PRESENTERS: ELIZABETH TUNBRIDGE, THOMAS HYDE, WILFRIED HAERTY, GREGORY CARR

THE SUCCESSFUL TRANSLATION OF CUTTING-EDGE SCIENTIFIC ADVANCES INTO THERAPEUTIC BENEFITS, PARTICULARLY IN THE CHALLENGING AREA OF NEUROPSYCHIATRIC DISORDERS, REQUIRES EFFECTIVE COLLABORATIONS BETWEEN SCIENTISTS IN ACADEMIA AND INDUSTRY. THIS PANEL WILL FOCUS ON WHAT MAKES A SUCCESSFUL COLLABORATION AND WHAT ACADEMIA AND INDUSTRY CAN LEARN FROM ONE-ANOTHER. IT DRAWS ON THE EXPERIENCES OF RESEARCHERS INVOLVED IN SUCH COLLABORATIONS WITH DIFFERENT PERSPECTIVES. THE CHAIR, LIZ TUNBRIDGE (OXFORD, UK/BOEHRINGER INGELHEIM, GERMANY), WILL TALK BRIEFLY ABOUT HER EXPERIENCES WORKING WITH INDUSTRIAL PARTNERS AS AN ACADEMIC AND HER SUBSEQUENT TRANSITION INTO INDUSTRY. THOMAS HYDE (LIEBER INSTITUTE FOR BRAIN DEVELOPMENT, US) WILL DISCUSS HIS COLLABORATIONS WITH INDUSTRY WORKING ON SPECIFIC DRUG DEVELOPMENT PROJECTS. WILFRIED HAERTY (EARLHAM INSTITUTE, UK), WILL DESCRIBE HIS EXPERIENCE OF CO-DESIGNING AND CONDUCTING AN EARLY-STAGE TARGET IDENTIFICATION PROJECT WITH MULTIPLE PHARMACEUTICAL PARTNERS AS PART OF A PRECOMPETITIVE CONSORTIUM. FINALLY, GREGORY CARR (LIEBER INSTITUTE FOR BRAIN DEVELOPMENT, US) WILL PROVIDE INSIGHTS INTO WHAT INDUSTRY SEEKS TO LEARN FROM ACADEMIA, DRAWING ON HIS EXPERIENCE OF CONDUCTING NEUROSCIENCE RESEARCH WITHIN MULTIPLE PHARMACEUTICAL COMPANIES. TOGETHER, THESE PRESENTATIONS AND Q AND A SESSIONS AIM TO PROVIDE PRACTICAL INSIGHTS INTO HOW TO BUILD AND MAINTAIN PRODUCTIVE AND MUTUALLY-BENEFICIAL COLLABORATIONS TO ENSURE THAT THE FRUITS OF ACADEMIC NEUROSCIENCE RESEARCH CAN BE TURNED INTO NOVEL AND IMPROVED THERAPIES FOR CNS DISORDERS.
VIOR AND NEUROPHYSIOLOGICAL OSCILLATORY ACTIVITY DURING SLEEP.

TUESDAY, JANUARY 30TH

SHORT COURSE
7:00 P.M. - 8:30 P.M.
IMPERIAL BALLROOM, FLOOR 4

OPTIMIZING USE OF NEUROIMAGING TOOLS FOR EVALUATION AND MANAGEMENT OF COGNITIVE DECLINE

CHAIR: DANIEL SILVERMAN, CYRUS RAJI
PRESENTERS: CYRUS RAJI, JOHN SEIBYL, SARAH BANKS, DANIEL SILVERMAN

IN THE UNITED STATES ALONE, APPROXIMATELY 13 MILLION PEOPLE HAVE DEMENTIA OR MILD COGNITIVE IMPAIRMENT DUE TO ALZHEIMER'S DISEASE, INCURRING SOCIETAL COSTS COLLECTIVELY VALUED AT NEARLY $700 BILLION DOLLARS PER YEAR. PARKINSON'S DISEASE IS THE LEADING NEURODEGENERATIVE CAUSE OF CENTRAL MOTOR DISORDERS, AND AFFECTS ANOTHER APPROXIMATELY 1.2 MILLION PEOPLE AT A COST OF APPROXIMATELY $57 BILLION. FDA-APPROVED TREATMENT OPTIONS FOR THESE CONDITIONS HAVE RECENTLY EXPANDED, WITH A NUMBER OF OTHERS ADVANCING ALONG THE DEVELOPMENT PIPELINE, AND THEIR IMPLEMENTATION REQUIRES ADVANCED NEUROIMAGING TOOLS FOR THE MOST ACCURATE DIAGNOSES TO BE MADE AT THE EARLY STAGES OF DISEASE WHEN THE TREATMENTS CAN BE MOST EFFECTIVE. UNDERSTANDING WHICH IMAGING TOOLS TO UTILIZE, IN WHAT ORDER AND AT WHAT POINTS DURING THE TRAJECTORY OF DISEASE EVOLUTION HAS THUS BECOME INCREASINGLY CRITICAL FOR OPTIMAL EVALUATION AND MANAGEMENT OF THE UNDERLYING CONDITIONS IN SYMPTOMATICALLY AFFECTED PATIENTS.

TUESDAY, JANUARY 30TH

PANEL
7:00 P.M. - 8:30 P.M.
PEAK I-3, FLOOR 3

INTERNEURON CIRCUITRY AT THE INTERSECTION OF OPIOIDS AND REWARD

CHAIR: EMILIA LEFEVRE, CARLEE TODDES
PRESENTERS: ELYSIA GAUTHIER, JAMES OTIS, CARLEE TODDES

A KEY NEUROMODULATOR OF REWARD BEHAVIOR IS THE MU OPIOID RECEPTOR (MOR) ACTING WITHIN THE NUCLEUS ACCUMBENS. THIS SESSION WILL ENCOMPASS DATA FROM A SERIES OF YOUNG INVESTIGATORS HIGHLIGHTING THE INTERSECTIONAL ROLE OF NUCLEUS ACCUMBENS INTERNEURONS AND MORS IN BOTH NATURALISTIC AND OPIOID REWARD SEEKING BEHAVIORS. DR. LEFEVRE (SESSION CHAIR) WILL PROVIDE INTRODUCTORY COMMENTS AND LEAD DISCUSSION ON THE PRESENTATIONS.
ELYSIA GAUTHIER WILL PRESENT ELECTROPHYSIOLOGY DATA DEMONSTRATING THE OPIOID SENSITIVITY OF PARVALBUMIN INTERNEURONS IN THE NUCLEUS ACCUMBENS, AND THE RECIPROCAL ROLE OF PARVALBUMIN INTERNEURONS IN FENTANYL-EVOKED BEHAVIOR. SPECIFICALLY, HER DATA SHOWS THAT CHEMOGENETIC INHIBITION OF THE PARVALBUMIN INTERNEURONS BLUNTS FENTANYL EVOKED LOCOMOTOR SENSITIZATION, AS WELL AS CUE-INDUCED REINSTATEMENT FOLLOWING FENTANYL SELF-ADMINISTRATION.
DR. JIM OTIS WILL PRESENT RECENT WORK FROM HIS LAB THAT IDENTIFIED A PARAVENTRICULAR THALAMUS (PVT) TO NUCLEUS ACCUMBENS PARVALBUMIN INTERNEURON CIRCUIT THAT IS REQUIRED FOR BEHAVIORAL INHIBITION, WEAKENED BY OPIOID USE, AND PROFOUNDLY INHIBITED DURING OPIOID SEEKING. USING A MOUSE MODEL OF HEROIN SELF-ADMINISTRATION, HE DEMONSTRATED THAT THESE EFFECTS ARE REGULATED BY PVT MORS, SUCH THAT GENETIC KNOCKDOWN OF THESE RECEPTORS OR RESTORATION OF ACTIVITY AT PVT-ACCUMBAL SYNAPSES CAN ABOLISH HEROIN-INDUCED BEHAVIORAL DISINHIBITION AND HEROIN SEEKING.
DR. CARLEE TODDES WILL DISCUSS THE ROLE OF NUCLEUS ACCUMBENS MORS IN MEDIATING SOCIAL BEHAVIOR IN MICE. SHE WILL SHOW THAT CONCOMITANT DELETION OF THE MORS FROM THE NUCLEUS ACCUMBENS PARVALBUMIN AND SOMATOSTATIN INTERNEURONS, SIGNIFICANTLY ATTENUATED THE TIME EXPERIMENTAL MICE SPENT INTERACTING WITH A NOVEL SOCIAL PARTNER. THESE RESULTS INDICATE THAT INHIBITORY INTERNEURONS WITHIN THE NUCLEUS ACCUMBENS MAY BE A KEY TARGET FOR MU OPIOID RECEPTOR MODULATION OF SOCIAL INTERACTION IN MALE AND FEMALE MICE THROUGH PARALLEL FEED-FORWARD INHIBITION.

TUESDAY, JANUARY 30TH

PANEL
7:00 P.M. - 8:30 P.M.
PEAK 6-8, FLOOR 2

MOGULS, MODELS, AND MARKERS: TACKLING THE MOUNTAIN OF POST-TRAUMATIC EPILEPSY

CHAIR: DOMINIQUE DUNCAN
PRESENTERS: JOHN HUGUENARD, JOHN WOLF, DOMINIQUE DUNCAN

POST-TRAUMATIC EPILEPSY (PTE), DEFINED BY RECURRENT SEIZURES AFTER BRAIN TRAUMA, IS ONE OF THE MAJOR COMPLEX COMPLICATIONS ASSOCIATED WITH TRAUMATIC BRAIN INJURY (TBI). THE DEVELOPMENT OF EPILEPSY AFTER TBI IS A MULTIFACTORIAL PROCESS AND CROSSES MULTIPLE MODALITIES. WITHOUT A FULL UNDERSTANDING OF THE UNDERLYING BIOLOGICAL EFFECTS, THERE ARE CURRENTLY NO CURES FOR EPILEPSY. THERE IS A NEED FOR DEVELOPMENT OF TRANSLATIONAL AND EFFECTIVE ANIMAL MODELS OF PTE TO BETTER UNDERSTAND THE UNDERLYING PATHOPHYSIOLOGY AND PROVIDE TREATMENT.
DR. HUGUENARD WILL DISCUSS DETECTING PRESEIZURE STATES AND ITS USE IN POTENTIAL THERAPIES. HE WILL GIVE AN OVERVIEW OF INNOVATIVE THERAPEUTIC APPROACHES, INCLUDING REAL-TIME MONITORING SYSTEMS, TARGETED PHARMACOLOGICAL TREATMENTS, AND NEUROMODULATION TECHNIQUES.DR. GALANOPOULOU WILL GIVE AN OVERVIEW OF THE EPILEPSY BIOINFORMATICS STUDY FOR ANTIEPILEPTOGENIC THERAPY (EPIBIOS4RX). SHE WILL DISCUSS THE IMPORTANCE OF STUDYING ANIMAL MODELS OF PTE IN THE SEARCH FOR ANTIEPILEPTOGENIC TREATMENTS AND THERAPIES AND FOR BIOMARKER DISCOVERY AS WELL AS ISSUES POTENTIALLY AFFECTING TRANSLATION OF FINDINGS.
DR. WOLF WILL DESCRIBE HIS WORK ON MODELING PTE IN THE GYRENCEPHALIC PIG BRAIN. HIS WORK AIMS TO UNDERSTAND THE CONTRIBUTIONS OF VARIOUS INJURY COMPONENTS SUCH AS INERTIAL INJURY OR CONTUSION OF THE BRAIN TO THE DEVELOPMENT OF PTE. AFTER TBI, HIGH DENSITY ELECTRODES ARE IMPLANTED IN THE PIG BRAIN. EEG AND BLOOD BIOMARKERS ARE STUDIED AS POTENTIAL PROGNOSTIC MEASURES FOR THE DEVELOPMENT OF PTE.
DR. DUNCAN WILL PRESENT THE DATA ARCHIVE FOR THE BRAIN INITIATIVE (DABI), A CENTRALIZED ARCHIVE FOR NEUROPHYSIOLOGY, IMAGING, AND ASSOCIATED DATA. DABI ALLOWS RESEARCHERS TO ACCESS SHARED DATA AND USE A VARIETY OF ANALYTIC TOOLS TO IDENTIFY AND VALIDATE BIOMARKERS OF EPILEPTOGENESIS IN IMAGING AND ELECTROPHYSIOLOGY AS WELL AS IN MOLECULAR, SEROLOGICAL, AND TISSUE DATA.

TUESDAY, JANUARY 30TH

PANEL
7:00 P.M. - 8:30 P.M.
PEAK 9-10, FLOOR 2

IMMUNE-SYMPATHETIC EFFECTS OF SPINAL CORD INJURY

CHAIRS: PATRICIA WARD, DYLAN MCCREEDY
PRESENTERS: DYLAN MCCREEDY, VERONICA TOM, PATRICIA WARD, ANDREW GAUDET

NEUROTRAUMA CAN HAVE WIDESPREAD IMPACT THAT EXTENDS WELL BEYOND THE SITE OF INJURY. THERE IS A GROWING BODY OF EVIDENCE THAT SPINAL CORD INJURY (SCI) RESULTS IN SYSTEMIC RESPONSES THAT GREATLY INFLUENCE LONG-TERM TISSUE LOSS AND FUNCTIONAL OUTCOMES. THIS PANEL WILL PRESENT RECENT FINDINGS ON HOW SCI AFFECTS TWO HIGHLY CONNECTED SYSTEMS, THE IMMUNE SYSTEM AND SYMPATHETIC NERVOUS SYSTEM. DR. MCCREEDY WILL FIRST DISCUSS HOW SCI TRIGGERS RAPID AND SEX-DEPENDENT CHANGES IN CIRCULATING IMMUNE CELL POPULATIONS, AS WELL AS THE RESULTING IMPACT ON LOCAL INFLAMMATION AND LONG-TERM FUNCTIONAL RECOVERY. FOLLOWING THIS SESSION, DR. TOM WILL DISCUSS THE INFLUENCE OF SCI, INCLUDING INJURY-INDUCED NEUROINFLAMMATION, ON SYMPATHETIC FUNCTION AND DOWNSTREAM EFFECTS ON ORGAN SYSTEMS. DR. WARD WILL THEN FOLLOW-UP ON THIS SESSION TO DISCUSS HOW SCI CAUSES LONG-TERM CHANGES IN SYMPATHETIC-DEPENDENT FUNCTION OF SKELETAL MUSCLE. FINALLY, DR. GAUDET WILL REVEAL CIRCADIAN STRATEGIES THAT BOOST PROTECTIVE INFLAMMATORY RESPONSES TO ENHANCE RECOVERY AFTER SCI. COLLECTIVELY, THESE PRESENTATIONS WILL DEMONSTRATE THE SYSTEMIC IMPACT OF SCI AND HOW OTHER ORGAN SYSTEMS CONTRIBUTE TO TISSUE PATHOLOGY AND LONG-TERM FUNCTIONAL OUTCOMES.

TUESDAY, JANUARY 30TH

PANEL
7:00 P.M. - 8:30 P.M.
PEAK 11-12, FLOOR 2

CONSEQUENCES OF NEURODEVELOPMENTAL INSULTS AND DYSFUNCTION
CHAIR: MIRANDA REED

PRESENTERS: MIRANDA REED, NATHANIEL ROBINSON, ZIJUN WANG

PERINATAL AND ADOLESCENT BRAINS ARE CHARACTERIZED BY SENSITIVE PERIODS OF DEVELOPMENT IN WHICH BRAIN REGIONS ARE ALTERED IN SUCH A WAY THAT FUTURE MODIFICATIONS BECOME MORE DIFFICULT. THE DEVELOPMENTAL MECHANISMS THAT OPERATE DURING THESE PERIODS ARE HEAVILY INFLUENCED BY INTERACTIONS BETWEEN GENETIC AND ENVIRONMENTAL CONDITIONS, WHICH CAN PRODUCE LONG-LASTING MOLECULAR, PHYSIOLOGIC, AND BEHAVIORAL ADAPTATIONS. THUS, ALTERATIONS TO A DEVELOPING BRAIN CAN HAVE ENDURING CONSEQUENCES ACROSS THE LIFESPAN. THESE DEVELOPMENTAL INSULTS MAY HAVE IMMEDIATE AND OBVIOUS NEUROBEHAVIORAL EFFECTS, OR THEY MAY REMAIN LATENT UNTIL UNMASKED BY A LATER LIFE EVENT, SUCH AS AGING, STRESS, OR DRUG EXPOSURE. MIRANDA REED (CHAIR AND PANELIST) WILL OPEN WITH AN OVERVIEW AND DISCUSS THE CONSEQUENCES OF PRENATAL EXPOSURE TO CANNABINOIDS ON SYNAPTIC PLASTICITY AND MEMORY DURING ADOLESCENCE. NATHANIEL ROBINSON WILL DISCUSS HOW MASTER TRANSCRIPTIONAL FACTORS GOVERN IN UTERO AND EARLY POSTNATAL NEUROGENESIS IN THE BASAL GANGLIA. ZIJUN WANG WILL CLOSE THE SESSION WITH A DISCUSSION ON HOW ADOLESCENT SOCIAL ISOLATION LATER AFFECTS OPIOID ADDICTION VULNERABILITY, FOCUSING ON NEURONAL AND TRANSCRIPTIONAL MALADAPTATIONS IN PREFRONTAL PYRAMIDAL NEURONS.

TUESDAY, JANUARY 30TH

PANEL
7:00 P.M. - 8:30 P.M.
PEAK 14, FLOOR 1

BRAIN MECHANISMS OF SOCIAL INTERACTIONS TO MODULATE PAIN AND EMPATHY - NEW TOOLS AND METHODS

CHAIR: VITALY NAPADOW, MONIQUE SMITH
PRESENTERS: MONIQUE SMITH, WEIZHE HONG, FADEL ZEIDAN, VITALY NAPADOW

DURING NEGATIVE AFFECTIVE STATES, SUCH AS PAIN, THE PRESENCE OF A SUPPORTIVE OTHER CAN BE PIVOTAL. FOR INSTANCE, THE PRESENCE OF A FRIEND, ROMANTIC PARTNER, OR EVEN A SUPPORTIVE STRANGER CAN REDUCE PAIN INTENSITY. WHILE THE MECHANISMS SUPPORTING SUCH EFFECTS ARE NOT WELL UNDERSTOOD, A NUMBER OF RECENT PRECLINICAL AND HUMAN NEUROIMAGING STUDIES HAVE INVESTIGATED BRAIN PROCESSES SUPPORTING PSYCHOSOCIAL PAIN MODULATION AND VICARIOUS/EMPATHIC EXPERIENCE OF PAIN IN ANOTHER. SOCIAL MODULATION OF PAIN FROM THE FIRST-PERSON PERSPECTIVE (THE INDIVIDUAL THAT EXPERIENCES PAIN) AND VICARIOUS/EMPATHIC PAIN-RELATED PROCESSING FROM THE SECOND-PERSON PERSPECTIVE (THE INDIVIDUAL THAT INTERACTS WITH THE PERSON IN PAIN) ARE INTEGRATIVE PARTS OF A DYNAMIC SOCIAL INTERACTION. HOWEVER, NEW METHODS ARE NEEDED TO PROBE THIS INTER-INDIVIDUAL DYNAMIC, AND EXPLORE THE MECHANISMS BY WHICH SOCIAL INTERACTIONS MODULATE PAIN AND EMPATHY. THIS PANEL WILL OFFER INSIGHTS GLEANED FROM NOVEL APPROACHES COVERING BOTH PRECLINICAL AND HUMAN NEUROIMAGING APPROACHES USING TRANSLATIONAL, SYSTEMS LEVEL NEUROSCIENCE METHODS. OUR PRESENTERS WILL INCLUDE DR. MONIQUE SMITH FROM UCSD WHO WILL PRESENT HER LATEST RESEARCH ON MECHANISTIC INSIGHTS INTO THE NEUROBIOLOGICAL RELATIONSHIPS BETWEEN SOCIAL BEHAVIOR, PAIN, AND EMOTION IN RODENT MODELS. DR. WEIZHE HONG FROM UCLA WILL DEMONSTRATE HOW MICE DISPLAY DIFFERENT FORMS OF PROSOCIAL BEHAVIOR TO BENEFIT OTHERS EXPERIENCING STRESS OR PAIN, AND HOW THESE ARE REGULATED BY NEURAL CIRCUITS. DR. FADEL ZEIDAN FROM UCSD WILL DISCUSS THE DIFFERENTIAL HUMAN NEURAL EMPATHETIC RESPONSES ELICITED BY VIEWING A ROMANTIC PARTNER VERSUS A STRANGER IN PAIN, LEADING TO HIGHER EMPATHY RATINGS ASSOCIATED WITH GREATER BRAIN RESPONSE FOR THE FORMER. DR. VITALY NAPADOW FROM HARVARD MEDICAL SCHOOL WILL THEN REPORT ON NOVEL APPLICATION OF HUMAN HYPERSCAN NEUROIMAGING TO EVALUATE THE BRAIN CIRCUITS ASSOCIATED WITH EMPATHY AND THERAPEUTIC ALLIANCE IN INTERACTING PAIN PATIENT-CLINICIAN DYADS.

TUESDAY, JANUARY 30TH

PANEL
7:00 P.M. - 8:30 P.M.
PEAK 15-16, FLOOR 1

PROMOTING STUDENT ENGAGEMENT: A NEUROSCIENCE EDUCATION WORKSHOP

CHAIR: KIRSTEN PORTER-STRANSKY
PRESENTERS: KIRSTEN PORTER-STRANSKY, LLOYD FRICKER, SYBIL STACPOOLE, MICHAEL STEFANIK

EDUCATIONAL RESEARCH HAS SHOWN THAT STUDENTS LEARN BETTER WHEN THEY ARE ACTIVE PARTICIPANTS RATHER THAN PASSIVE OBSERVERS. THEREFORE, MANY INSTITUTIONS AND ACCREDITING BODIES ARE ENCOURAGING FACULTY TO USE ACTIVE LEARNING IN THEIR CLASSROOMS. EXPERIENTIAL ACTIVITIES CAN BE TAILORED TO ALL LEVELS OF NEUROSCIENCE TRAINING RANGING FROM CHILDREN THROUGH ADULT LEARNERS. A PANEL OF NEUROSCIENCE EDUCATORS WILL DESCRIBE WAYS IN WHICH THEY INCORPORATE ACTIVE LEARNING INTO THEIR COURSES TO IMPROVE STUDENTS' ENGAGEMENT WITH THE CONTENT. ATTENDEES WILL HAVE TIME TO SHARE EXAMPLES OF HOW THEY ENGAGE LEARNERS AS WELL AS BRAINSTORM ACTIVITIES TO INCORPORATE INTO THEIR FUTURE TEACHING. THE SESSION WILL BE MODERATED BY KIRSTEN PORTER-STRANSKY (UNIVERSITY OF SOUTH CAROLINA SCHOOL OF MEDICINE GREENVILLE), WHO WILL SHARE EXAMPLES OF HANDS-ON ACTIVITIES FOR MIDDLE SCHOOL NEUROSCIENCE OUTREACH AS WELL AS FOR MEDICAL STUDENTS LEARNING FUNCTIONAL NEUROANATOMY. LLOYD FRICKER (EINSTEIN COLLEGE OF MEDICINE) WILL SHARE STRATEGIES TO INCORPORATE ACTIVE LEARNING IN MEDICAL SCHOOL, BOTH FOR MD AND PHD STUDENTS, SUCH AS A ROLE-PLAYING EXERCISE IN WHICH STUDENTS PITCH AN IDEA FOR DRUG DEVELOPMENT TO THEIR PEERS AND FACULTY. SYBIL STACPOOLE (UNIVERSITY OF CAMBRIDGE) WILL DISCUSS USING SIMULATION TRAINING IN MEDICAL EDUCATION. MICHAEL STEFANIK (NORTH CENTRAL COLLEGE) WILL PRESENT ON AN UPPER-LEVEL UNDERGRADUATE COURSE DESIGNED TO PROVIDE "REAL WORLD" RESEARCH EXPERIENCE AND MAXIMIZE CONTRIBUTIONS TO THE INSTRUCTOR'S PERSONAL RESEARCH PROGRAM. COLLECTIVELY, THESE PRESENTATIONS WILL PROVIDE A RANGE OF STRATEGIES FOR STUDENTS AT DIFFERENT LEVELS. PRESENTATIONS WILL BE SHORT IN ORDER TO PROVIDE TIME FOR DISCUSSION AMONG ALL ATTENDEES.

TUESDAY, JANUARY 30TH

SHORT COURSE
7:00 P.M. - 8:30 P.M.
PEAK 17, FLOOR 1

MACHINE LEARNING METHODS TO STUDY ANIMAL BEHAVIOR

CHAIR: AMELIA GALLITANO
PRESENTERS: TALMO PEREIRA, JESSICA VERPEUT, ANN KENNEDY, CALEB WEINREB

MACHINE LEARNING HAS TRANSFORMED THE WAY BEHAVIOR IS MEASURED AND QUANTIFIED. PHENOTYPES
RANGING FROM FINE-SCALE KINEMATICS TO MULTI-INDIVIDUAL SOCIAL DYNAMICS CAN NOW BE RELIABLY CAPTURED AT UNPRECEDENTED DETAIL ACROSS THE DIVERSE RANGE OF EXPERIMENTAL SETTINGS EMPLOYED BY NEUROSCIENTISTS. THIS SHORT COURSE BRINGS TOGETHER LEADING TOOL DEVELOPERS AND EXPERT PRACTITIONERS TO PROVIDE A UNIQUE PERSPECTIVE ON HOW BEHAVIORAL QUANTIFICATION TECHNOLOGY CAN ENABLE THE NEXT GENERATION IN BEHAVIOR-DRIVEN NEUROSCIENCE.
THE GOAL OF THIS COURSE IS TO TEACH PARTICIPANTS ABOUT METHODS AND APPLICATIONS OF BEHAVIORAL QUANTIFICATION TECHNOLOGY. THIS COURSE WILL APPEAL TO ANY NEUROSCIENTIST SEEKING MORE SENSITIVE, REPRODUCIBLE, AND SCALABLE QUANTITATIVE MEASUREMENTS OF BEHAVIOR. IT BRINGS TOGETHER BOTH TOOLMAKERS AND PRACTITIONERS TO ENSURE THAT THE ENGINEERING EFFORTS REMAIN GROUNDED IN THE LARGER GOALS OF UNDERSTANDING THE BRAIN. DR. GALLITANO WILL LEAD DISCUSSION OF THE PRESENTATIONS. DR. PEREIRA WILL DISCUSS SOCIAL LEAP ESTIMATES ANIMAL POSE (SLEAP), A MACHINE LEARNING SYSTEM FOR MULTI-ANIMAL POSE TRACKING. DR. VERPEUT WILL PRESENT HER RESEARCH USING SLEAP TO ANSWER QUESTIONS ABOUT THE ROLE OF THE CEREBELLUM IN COGNITIVE AND SOCIAL BEHAVIOR. DR. KENNEDY WILL PRESENT HER WORK ON BENTO, A SOFTWARE TOOL FOR VISUALIZING AND ANNOTATING SIMULTANEOUS STREAMS OF BEHAVIOR AND NEUTRAL DATA TO FACILITATE SUPERVISED BEHAVIOR SEGMENTATION. DR. WEINREB WILL BE DEMONSTRATING KEYPOINT-MOSEQ, A NEW ALGORITHM FOR UNSUPERVISED BEHAVIOR SEGMENTATION THAT IS SPECIALLY DESIGNED FOR DETECTING "SYLLABLES" OF BODY LANGUAGE FROM POSE TRACKING DATA.
LEARNING OBJECTIVES: 1) GAIN INSIGHT INTO HOW TO SELECT THE APPROPRIATE METHOD FOR THE INTENDED RESEARCH QUESTION, 2) UNDERSTAND THE TECHNICAL DETAILS OF THE APPROACHES, THEIR LIMITATIONS AND HOW TO DEVELOP AND EXTEND THEM TO ANSWER THE SCIENTIFIC QUESTION, 3) DISCUSS THE IMPACT THAT THESE TOOLS HAVE HAD, AND WILL HAVE, ON THE FIELD OF NEUROSCIENCE.

PANEL
7:30 A.M. - 9:30 A.M.
IMPERIAL BALLROOM, FLOOR 4

USING PRECLINICAL MODELS TO STUDY THE NEUROBIOLOGICAL MECHANISMS OF PSYCHEDELICS IN ANXIETY AND DEPRESSIVE DISORDERS

CHAIR: KATHERINE NAUTIYAL, SIXTINE FLEURY
PRESENTERS: CHARLES NICHOLS, CODY WENTHUR, SIXTINE FLEURY, BORIS HEIFETS

RECENT STUDIES HAVE DEMONSTRATED THE POTENTIAL FOR PSYCHEDELIC THERAPIES IN THE TREATMENT OF PSYCHIATRIC DISORDERS INCLUDING MAJOR DEPRESSIVE DISORDER AND ANXIETY DISORDERS. WHILE MANY CLINICAL TRIALS ARE ONGOING, THE MECHANISMS OF THE PERSISTING BEHAVIORAL EFFECTS ARE STILL LARGELY UNKNOWN. THIS PANEL AIMS TO HIGHLIGHT COMPELLING PRECLINICAL MODELS TO STUDY THE MECHANISMS OF THE LONG TERM NEURAL AND BEHAVIORAL CHANGES FOLLOWING A SINGLE ADMINISTRATION OF A PSYCHEDELIC SUCH AS PSILOCYBIN OR LSD. KATE NAUTIYAL WILL MAKE BRIEF INTRODUCTORY COMMENTS. CHUCK NICHOLS (LSU) WILL PRESENT HIS WORK ON THE PERSISTENT AND SYNAPTIC EFFECTS OF PSYCHEDELICS IN RAT EXPERIMENTAL SYSTEMS RELEVANT TO DEPRESSION. CODY WENTHUR (UNIVERSITY OF WISCONSIN-MADISON) WILL DISCUSS THE IMPACT OF PSYCHEDELIC-INDUCED HPA AXIS ACTIVATION ON MODIFICATION OF THREAT-ASSOCIATED LEARNING IN MICE. SIXTINE FLEURY (DARTMOUTH) WILL PRESENT HER RESEARCH ON THE ROLE OF THE SEROTONIN IB RECEPTOR, A NON-HALLUCINATORY SEROTONIN RECEPTOR, IN THE NEURAL ACTIVATION AND LONG-TERM BEHAVIORAL EFFECTS OF PSILOCYBIN IN MICE. FINALLY BORIS HEIFETS (STANFORD) WILL PRESENT HIS WORK ON PSILOCIN ADMINISTERED UNDER GENERAL ANESTHESIA IN MICE AS A PRECURSOR FOR HUMAN TRIALS. OVERALL THE DISCUSSION OF OUR PRECLINICAL PROTOCOLS TO STUDY THE PERSISTING BEHAVIORAL AND NEURAL EFFECTS OF PSYCHEDELIC TREATMENTS IN PSYCHIATRY WILL HELP ADVANCE OUR STUDIES AND PROVIDE THE GROUNDWORK FOR FUTURE WORK. SOLID PRECLINICAL RESEARCH IS INTEGRAL TO UNDERSTANDING THE MECHANISMS OF THE PERSISTING EFFECTS OF PSYCHEDELICS IN ITS CLINICAL APPLICATIONS.

WEDNESDAY, JANUARY 31ST

PANEL
7:30 A.M. - 9:30 A.M.
PEAK I-3, FLOOR 3

INTERACTIONS BETWEEN IMMUNE SIGNALING, MESOLIMBIC CIRCUITRY AND BEHAVIOR

CHAIRS: JORDAN YORGASON, DREW KIRALY
PRESENTERS: ASHLEY ROSS, PHILIPP MEWS, JORDAN YORGASON, DREW KIRALY

MOST OF OUR UNDERSTANDING OF CIRCUITS UNDERLYING MOTIVATION FOR DRUG SEEKING HAS FOCUSED ON THE DIRECT EFFECTS OF THESE SUBSTANCES ON NEURONS OR THE CLEARANCE OF TRANSMITTERS INVOLVED (E.G. PSYCHOSTIMULANTS). RECENT WORK HAS HIGHLIGHTED THE NEED TO UNDERSTAND HOW PERIPHERAL IMMUNE CIRCUITS CAN GOVERN CENTRAL ACTIVITY TO FACILITATE DRUG SEEKING. THIS PANEL SEEKS TO PRESENT DATA THAT ENCOMPASSES NOVEL APPROACHES FOR MEASURING COMMUNICATION BETWEEN THE LEUKOCYTIC AND MESOLIMBIC CIRCUITS. FIRST, DR. ASHLEY ROSS (UNIVERSITY OF CINCINNATI) WILL OPEN OUR SYMPOSIUM WITH RECENT WORK ON MEASURING NEUROIMMUNE COMMUNICATION ALONG THE GUT-BRAIN ACCESS. SECOND, DR. PHILIPP MEWS (BOSTON UNIVERSITY MEDICAL CAMPUS) WILL TALK ABOUT THE EFFECTS OF COCAINE ON NEUROINFLAMMATORY SIGNALING IN THE STRIATUM. NEXT, DR. JORDAN YORGASON (BRIGHAM YOUNG UNIVERSITY, CHAIR) WILL SHOW FINDINGS ON INTERACTIONS BETWEEN MICROGLIA AND DOPAMINE TERMINAL ACTIVITY AND EFFECTS OF METHAMPHETAMINE. FINALLY, DR. DREW KIRALY (WAKE FOREST UNIVERSITY SCHOOL OF MEDICINE, CO-CHAIR) WILL CLOSE OUR SYMPOSIUM WITH EXPLORING THE NEUROIMMUNE REGULATION OF DOPAMINE RELEASE AND PSYCHOSTIMULANT SEEKING. TOGETHER, THESE DATA WILL HIGHLIGHT THE COMPLEX COMMUNICATION PATHWAYS USED BETWEEN IMMUNE CELLS AND NEURONAL PATHWAYS IMPLICATED IN MOTIVATION AND SUBSTANCE USE DISORDERS.

WEDNESDAY, JANUARY 31ST

PANEL
7:30 A.M. - 9:30 A.M.
PEAK 11-12, FLOOR 2

DISEASE-SPECIFIC RESPONSES OF REACTIVE ASTROGLIAL CELLS – CONCEPTS, MOLECULAR SIGNATURES AND OPPORTUNITIES FOR INTERVENTION

CHAIR: MILOS PEKNY
PRESENTERS: MILOS PEKNY, JAN MULDER, FLORENCE PERRIN, RACHEL KIM

REACTIVE GLIOSIS ACCOMPANIES A WHOLE RANGE OF NEUROLOGICAL DISEASES, FROM NEUROTRAUMA TO STROKE AND NEURODEGENERATIVE DISEASES. WHILE IN MANY DISEASE CONTEXTS, REACTIVE GLIOSIS IS A BENEFICIAL RESPONSE, IN SOME SITUATIONS, IT IS MALADAPTIVE, RESULTING EITHER IN THE EXACERBATION OF THE DISEASE PROCESS OR IN THE INHIBITION OF REPAIR RESPONSES. RECENT ANALYSES OF MOLECULAR SIGNATURES OF REACTIVE ASTROCYTES AND MICROGLIA HAVE IDENTIFIED DISTINCT SUBPOPULATIONS OF THESE CELLS AND DEMONSTRATED THAT REACTIVE GLIOSIS IS HIGHLY CONTEXT-SPECIFIC. THIS SYMPOSIUM WILL SHOW DETAILED MOLECULAR CLASSIFICATION OF ASTROCYTE AND MICROGLIAL SUBPOPULATIONS IN SEVERAL NEUROLOGICAL SITUATIONS, AND OFFER POSSIBLE INTERPRETATIONS OF THESE CONTEXT-DEPENDENT RESPONSES BY PRESENTING RESULTS FROM ANIMAL DISEASE MODELS AND MODELS OF MODULATED REACTIVE GLIOSIS. MILOS PEKNY WILL INTRODUCE THE CONCEPT AND WILL PRESENT NOVEL INSIGHTS INTO THE MECHANISMS THROUGH WHICH REACTIVE ASTROCYTES AFFECT PROGRESSION OF AMYOTROPHIC LATERAL SCLEROSIS AND STROKE OUTCOME. JAN MULDER WILL SHOW THE POWER OF SPATIAL TRANSCRIPTOMICS AND ANTIBODY-BASED METHODS FOR DETERMINING MOLECULAR SIGNATURE OF ASTROGLIAL CELL RESPONSES TO DISEASE CONDITIONS. FLORENCE PERRIN WILL DISCUSS THE ROLE OF REACTIVE GLIOSIS AND PROSPECTIVE TREATMENT TARGETS IN SPINAL CORD INJURY. RACHEL KIM WILL DEMONSTRATE HOW SPATIAL AND SINGLE NUCLEI TRANSCRIPTOMICS DATA SERVE AS THE BASIS FOR MOLECULAR CLASSIFICATION OF ASTROCYTES, AND FOR THE UNDERSTANDING OF THEIR CONTEXT-SPECIFIC ROLES IN THE POST-STROKE BRAIN.

WEDNESDAY, JANUARY 31ST

PANEL
7:30 A.M. - 9:30 A.M.
PEAK 14, FLOOR 1

SHIFTING MOGULS: LIVES OF DENDRITIC SPINES

CHAIR: YI ZUO
PRESENTERS: YI ZUO, KRISTEN HARRIS, KAREN ZITO, YOSHIYUKI KUBOTA

SYNAPSES ARE THE FUNDAMENTAL UNIT OF NEURONAL CONNECTION AND PLASTICITY. THEIR STRUCTURE AND FUNCTION ARE REGULATED BY EXPERIENCES THROUGH A COMPLEX NETWORK OF MOLECULAR SIGNALS. MOST OF EXCITATORY SYNAPSES IN THE MAMMALIAN CORTEX RESIDE ON DENDRITIC SPINES, TINY PROTRUSIONS FROM DENDRITIC PROCESSES. ABNORMAL SPINE DENSITY AND MORPHOLOGY HAVE BEEN LINKED TO SYNAPTIC DEFECTS AND ARE HALLMARKS OF MANY NEUROLOGICAL AND PSYCHIATRIC DISORDERS. IN THIS PANEL, DR. YI ZUO (UNIVERSITY OF CALIFORNIA SANTA CRUZ) WILL GIVE AN OVERVIEW OF SYNAPTIC PLASTICITY AND DENDRITIC SPINES AND PRESENT HER NEW WORK ON HOW BEHAVIORAL AND PHARMACOLOGICAL INTERVENTIONS AFFECT SPINE DYNAMICS AND LEARNING AND MEMORY CONSOLIDATION. DR. KRISTEN HARRIS (UNIVERSITY OF TEXAS AT AUSTIN) WILL DISCUSS CONTRASTING SPINE PLASTICITY IN THE DEVELOPING, MATURE, AND AGED BRAIN. DR. KAREN ZITO (UNIVERSITY OF CALIFORNIA DAVIS) WILL TALK ABOUT ONGOING WORK FROM HER LAB FOCUSED ON THE MOLECULAR MECHANISMS THAT REGULATE THE LONG-TERM GROWTH AND STABILIZATION OF INDIVIDUAL DENDRITIC SPINES DURING CIRCUIT PLASTICITY. DR. YOSHIYUKI KUBOTA (NATIONAL INSTITUTE FOR PHYSIOLOGICAL SCIENCES, JAPAN) WILL PRESENT HIS WORK ON CORTICO-CORTICAL AND THALAMO-CORTICAL SYNAPTIC NETWORK REMODELING IN PRIMARY MOTOR CORTEX DURING MOTOR SKILL ACQUISITION BY IN VIVO IMAGING USING 2-PHOTON AND CORRELATED LIGHT AND ELECTRON MICROSCOPY. THE PANEL WILL CONCLUDE WITH DISCUSSION AND QUESTIONS.

WEDNESDAY, JANUARY 31ST

PANEL
7:30 A.M. - 9:30 A.M.
PEAK 15-16, FLOOR 1

LIFELONG OLIGODENDROGLIAL DYNAMICS IN BRAIN HEALTH AND DISEASE

CHAIR: WENDY XIN
PRESENTERS: TSAI-YI LU, PABLO PAEZ, WENDY XIN, TOBIAS MERSON

OLIGODENDROCYTES ENSHEATH AXONS WITH MYELIN SHEATHS AND PLAY CRITICAL ROLES IN SUPPORTING NEURONAL HEALTH AND FUNCTION. THEY ARE GENERATED THROUGHOUT LIFE BY A GROUP OF LINEAGE-RESTRICTED OLIGODENDROCYTE PRECURSOR CELLS (OPCS). OPCS ARE THE SOLE GLIAL CELL TYPE TO DIRECTLY RECEIVE SYNAPSES FROM AXONS AND ALSO EXPRESS NUMEROUS NEUROTRANSMITTER RECEPTORS AND ION CHANNELS, MAKING THEM HIGHLY SENSITIVE TO NEURONAL ACTIVITY. THIS PANEL WILL HIGHLIGHT NEW INSIGHTS INTO THE REGULATION OF OLIGODENDROCYTE LINEAGE CELLS BY SENSORY EXPERIENCE AND NEURONAL ACTIVITY, AS WELL AS THE DYNAMICS OF OPC AND OLIGODENDROCYTE REGENERATION IN INJURY. DR. TSAI-YI LU WILL PRESENT THEIR RECENT WORK SHOWING THAT THE POPULATION HOMEOSTASIS OF CORTICAL OPCS IS DIRECTLY MODULATED BY NORADRENERGIC SIGNALING. NOREPINEPHRINE RELEASED DURING AROUSAL ENHANCES OPC CALCIUM DYNAMICS VIA ALPHAIA ADRENERGIC RECEPTORS. THE ACTIVATION OF ALPHAIA ADRENERGIC RECEPTORS IS REQUIRED FOR THE MAINTENANCE OF THE OPC POPULATION. DR. PABLO PAEZ WILL PRESENT RECENT FINDINGS SHOWING THE EFFECT OF EXCLUSIVELY ACTIVATED BY DESIGNER DRUGS (DREADD)-BASED RECEPTORS IN OPC DEVELOPMENT AND FUNCTION. ADDITIONALLY, HE WILL DISCUSS HOW THESE MOLECULES INFLUENCE THE ELECTRICAL PROPERTIES OF OPCS AND THE ESTABLISHMENT OF SYNAPSES BETWEEN THESE CELLS AND NEURONS. DR. WENDY XIN WILL PRESENT EVIDENCE THAT VISUAL EXPERIENCE MODULATES THE DYNAMICS OF OLIGODENDROCYTE GENERATION IN THE ADOLESCENT VISUAL CORTEX, AND THAT ADOLESCENT OLIGODENDROGENESIS AND MYELINATION RESTRICT BOTH STRUCTURAL AND FUNCTIONAL NEURONAL PLASTICITY IN ADULT VISUAL CORTEX. DR. TOBY MERSON WILL DISCUSS HOW DISTINCT PROGENITOR CELL TYPES IN THE CENTRAL NERVOUS SYSTEM PARTICIPATE IN THE REGENERATION OF OLIGODENDROCYTES AND MYELIN FOLLOWING A DEMYELINATING INSULT. A NOVEL PHARMACOGENETIC APPROACH TO ABLATE OPCS WILL BE DESCRIBED THAT HAS UNCOVERED A MAJOR ROLE FOR VENTRICULAR-SUBVENTRICULAR ZONE NEURAL PRECURSOR CELLS IN OPC REGENERATION.

WEDNESDAY, JANUARY 31ST

PANEL
7:30 A.M. - 9:30 A.M.
PEAK 17, FLOOR 1

DOUBLE DIAMOND: THE PURSUIT OF REWARD DESPITE CONSEQUENCE

CHAIR: DONNA CALU
PRESENTERS: LAURA CORBIT, RACHEL SMITH, DONNA CALU, SEAN OSTLUND

A BEHAVIORAL HALLMARK OF SUBSTANCE USE DISORDER IS THE PURSUIT OF DRUG REWARDS DESPITE UNSUCCESSFUL ATTEMPTS TO PROCURE THE DRUG AND/OR POTENTIAL NEGATIVE CONSEQUENCES. SEVERAL LEARNING PROCEDURES SUCCESSFULLY REDUCE SUCH MALADAPTIVE REWARD PURSUIT, INCLUDING PUNISHED REWARD SEEKING AND REWARD DEVALUATION. HOWEVER, THERE IS CONSIDERABLE VARIABILITY IN THE SENSITIVITY TO THESE PROCEDURES BETWEEN INDIVIDUALS. FURTHER, DRUGS OF ABUSE INCLUDING ALCOHOL, PSYCHOSTIMULANTS AND OPIOIDS DIMINISH THE SENSITIVITY OF REWARD SEEKING TO UNDESIRABLE OUTCOMES (E.G., PUNISHMENT OR DEVALUED REWARDS). ANOTHER STRATEGY FOR REDUCING UNWANTED BEHAVIORS IS EXTINCTION; ESTABLISHED BEHAVIORS THAT DECLINE WHEN REWARD IS WITHHELD- HOWEVER, EXTINGUISHED REWARD SEEKING IS NOT ALWAYS PERMANENT. DR. LAURA CORBIT WILL DESCRIBE AN EXPERIMENT DESIGNED TO ENHANCE INHIBITORY LEARNING DURING EXTINCTION AS A STRATEGY FOR PRODUCING A MORE PERMANENT REDUCTION OF ALCOHOL SEEKING. DR. RACHEL SMITH WILL PRESENT WORK USING A MODEL OF COCAINE SELF-ADMINISTRATION DESPITE FOOTSHOCK PUNISHMENT. LESIONS OF DORSOLATERAL STRIATUM, BUT NOT DORSOMEDIAL STRIATUM, INCREASE SENSITIVITY TO PUNISHMENT OF COCAINE SEEKING. DR. DONNA CALU WILL DESCRIBE THE BRAIN BASIS OF INDIVIDUAL AND SEX DIFFERENCES IN BEHAVIORAL FLEXIBILITY THAT ARE NO LONGER EVIDENT AFTER OPIOID EXPERIENCE, WHICH PROMOTES HIGH LEVELS OF OPIOID RELAPSE THAT PERSISTS DESPITE NEGATIVE CONSEQUENCES. DR. SEAN OSTLUND WILL PRESENT RESEARCH EXAMINING THE EFFECTS OF CHRONIC MORPHINE EXPOSURE AND WITHDRAWAL ON EMOTIONAL, MOTIVATIONAL, AND COGNITIVE PROCESSES CONTROLLING THE PURSUIT AND CONSUMPTION OF NATURAL FOOD REWARDS. DURING EARLY WITHDRAWAL, RATS SHOW DEFICITS IN MOTIVATION AND GOAL-DIRECTED ACTION SELECTION THAT DIMINISH WITH PROTRACTED WITHDRAWAL, BUT ARE REINSTATED BY BRIEF MORPHINE PRE-EXPOSURE. TOGETHER, THE PANELISTS PRESENT NEW FINDINGS ON ADAPTIVE AND DYSREGULATED REWARD SEEKING USING A VARIETY OF LEARNING PARADIGMS AND REWARDS.

WEDNESDAY, JANUARY 31ST

PANEL
7:30 A.M. - 9:30 A.M.
PEAK 6-8, FLOOR 2

PROGRESSING FROM GREEN TO BLUE TO BLACK: EXPERIENCE, CHOICE, AND SEX DIFFERENCES ACROSS THE LIFESPAN INFLUENCE DRUG USE AND BEHAVIOR

CHAIRS: DEVIN MUELLER, TOD KIPPIN
PRESENTERS: TOD KIPPIN, MATTHEW HEARING, ZIJUN WANG, DEVIN MUELLER

SEX DIFFERENCES IN DRUG TAKING AND SEEKING EMERGE AS THE RESULT OF THE INTERACTION OF HORMONES AND EXPERIENCE ACROSS THE LIFESPAN. IN THIS SYMPOSIUM, WE WILL PROVIDE RECENT FINDINGS ON THE EMERGENCE OF NEURAL AND BEHAVIORAL SEX DIFFERENCES IN DEVELOPMENT AND ADULTHOOD AND HOW THEY INFLUENCE DRUG CHOICE AND SENSITIVITY TO DRUGS OF ABUSE. TOD KIPPIN WILL DISCUSS SEX DIFFERENCES IN THE PROPENSITY TO OBTAIN DRUG REINFORCEMENT AT THE EXPENSE OF A NATURAL (FOOD) REINFORCEMENT, INCLUDING IMPACTS OF RELATIVE COST AND TEMPORAL AVAILABILITY OF THE REINFORCERS. NEXT, HE WILL DESCRIBE THE IMPACT OF GONADAL HORMONE MANIPULATIONS ON DRUG CHOICE IN MALE AND FEMALE RATS. MATTHEW HEARING WILL DISCUSS HOW CORTICO-STRIATAL REGULATION OF OPIOID TAKING AND DECISION-MAKING IS ALTERED BASED ON DURATION OF EXPOSURE, BIOLOGICAL SEX, AND AGE OF EXPOSURE AS WELL AS THE UNDERLYING PLASTICITY WITHIN THESE CIRCUITS. ZIJUN WANG WILL HIGHLIGHT THE CIRCUIT AND MOLECULAR MECHANISMS UNDER EARLY SOCIAL ISOLATION STRESS-INDUCED SEX-SPECIFIC BEHAVIORAL ABNORMALITIES. SHE WILL FOCUS ON PREFRONTAL PROJECTIONS TO DOWNSTREAM TARGETS SUCH AS THE BASOLATERAL AMYGDALA AND VENTRAL TEGMENTAL AREA. NEXT, SHE WILL EXPAND ON HOW EARLY SOCIAL ISOLATION STRESS AFFECTS HEROIN ADDICTION VULNERABILITY AND CHANGES THE NEURONAL ACTIVITIES IN THE MESOCORTICOLIMBIC SYSTEM IN MALE AND FEMALE MICE. DEVIN MUELLER WILL DISCUSS THE EFFECTS OF EARLY LIFE ADVERSITY ON SENSITIVITY TO DRUGS OF ABUSE, INCLUDING COCAINE AND FENTANYL, IN ADOLESCENCE AND ADULTHOOD ACROSS SEXES. UNDERSTANDING THE IMPACT OF HORMONAL STATUS AND EXPERIENCE DURING DEVELOPMENT ON SEX-DEPENDENT DRUG SEEKING IS NECESSARY FOR THE DEVELOPMENT OF TARGETED AND INDIVIDUALIZED TREATMENTS TO PREVENT OR DISRUPT SUBSTANCE USE.

WEDNESDAY, JANUARY 31ST

PANEL
7:30 A.M. - 9:30 A.M.
PEAK 9-10, FLOOR 2

APPLYING VISUAL ETHOLOGY AND VIRTUAL REALITY IN EMOTION AND COGNITIVE CIRCUITS

CHAIR: ALFRED KAYE
PRESENTERS: MATTHEW ISAACSON, STEPHANIE STASZKO, YUTA SENZAI, CRISTOPHER NIELL

INFERENCE INTO THE CELLULAR BASIS OF COGNITION AND EMOTION HAS HISTORICALLY RELIED ON STRUCTURED LABORATORY TASKS. VIRTUAL REALITY AND COMPUTATIONAL TRACKING IN NATURALISTIC ENVIRONMENTS PERMIT INTERROGATION OF THE INTERPLAY BETWEEN VISION AND EMOTION DURING CIRCUIT INTERROGATION. THESE APPROACHES HAVE REVOLUTIONIZED HUMAN COGNITIVE NEUROSCIENCE AND ARE NOW BEING APPLIED TO RODENT CIRCUIT NEUROSCIENCE. THIS PANEL INCLUDES A PRESENTATION ON A NEWLY DEVELOPED MOUSE VIRTUAL REALITY GOGGLE APPROACH TO CREATE IMMERSIVE VIRTUAL ENVIRONMENTS AND APPLICATION TO EMOTIONAL LEARNING TASKS (MATTHEW ISAACSON). ANOTHER PRESENTATION PRESENTS THE DEVELOPMENT OF A FREELY BEHAVING VIRTUAL FEAR OF HEIGHTS PARADIGM AND ITS REPRESENTATION IN LOCUS COERULEUS AND PREFRONTAL CORTEX, WHICH MAY FACILITATE FURTHER TRANSLATIONAL STUDIES OF INNATE FEAR (STEPHANIE STASZKO). DURING SLEEP, NEURAL REPRESENTATIONS OF HEAD DIRECTION CAN BE INFERRED FROM EYE MOVEMENTS, YIELDING INSIGHT INTO THE NATURE OF INTERNAL EXPLORATION IN REM SLEEP (YUTA SENZAI). FINALLY, CIRCUIT APPROACHES TO ETHOLOGICALLY DRIVEN VISUAL BEHAVIORS HAVE YIELDED FUNDAMENTAL INSIGHTS INTO PRINCIPLES OF NATURAL BEHAVIOR (CRIS NIELL). ALFRED KAYE, A SYSTEMS NEUROSCIENTIST AND PSYCHIATRIST, WILL PROVIDE INTRODUCTORY COMMENTS AND LEAD DISCUSSION OF THESE INNOVATIVE TRANSLATIONAL APPROACHES TO VISUAL ETHOLOGY IN CONNECTION WITH EMOTIONAL BEHAVIOR.

WEDNESDAY, JANUARY 31ST

PANEL
4:30 P.M. - 6:30 P.M.
IMPERIAL BALLROOM, FLOOR 4

SHREDDING SEX DIFFERENCES IN OPIOID REWARD SYSTEMS FROM TRANSCRIPT TO CIRCUIT

CHAIRS: ELIZABETH DONCHECK, JESSICA HIGGINBOTHAM
PRESENTERS: JESSE NIEHAUS, YANAIRA ALONSO-CARABALLO, ELIZABETH DONCHECK, JESSICA HIGGINBOTHAM

THE FAILURE OF THERAPIES TO TRANSLATE FOR TREATMENT OF OPIOID USE DISORDER MAY BE DUE IN PART TO INSUFFICIENT CONSIDERATION OF SEX DIFFERENCES IN THE UNDERLYING NEUROBIOLOGICAL MECHANISMS. THIS PANEL USES INNOVATIVE MULTIDISCIPLINARY TECHNIQUES AND CONCEPTUAL PERSPECTIVES TO DISSECT THE ROLE OF BIOLOGICAL SEX IN NEUROADAPTIVE PROCESSES MEDIATING OPIOID REWARD AND MISUSE LIABILITY. JESSE NIEHAUS (UNC) WILL USE SINGLE-CELL TRANSCRIPTOMICS TO MAP SEX DIFFERENCES AND OPIOID EXPOSURE-INDUCED CHANGES IN THE CELLULAR AND MOLECULAR ARCHITECTURE OF THE ENDOGENOUS OPIOID SYSTEM THROUGHOUT THE REWARD CIRCUITRY. YANAIRA ALONSO-CARABALLO (UMN) WILL HIGHLIGHT SEX DIFFERENCES IN THE SYNAPTIC PHYSIOLOGY OF THE PARAVENTRICULAR THALAMO-ACCUMBAL PATHWAY UNDERLYING OXYCODONE SEEKING USING IN VIVO AND EX VIVO ELECTROPHYSIOLOGY. ELIZABETH DONCHECK (MUSC) WILL USE IN VIVO TWO-PHOTON CALCIUM IMAGING TO DISSECT SEX DIFFERENCES IN THE PRELIMBIC CORTICAL ACTIVITY DYNAMICS THAT EMERGE WITH HEROIN SELF-ADMINISTRATION AND REINSTATEMENT. JESSICA HIGGINBOTHAM (WUSTL) WILL USE WIRELESS IN VIVO FIBER PHOTOMETRY TO EXAMINE SEX DIFFERENCES IN PAIN-INDUCED DOPAMINE NEUROADAPTATIONS IN THE VENTRAL TEGMENTAL AREA THAT MEDIATE FENTANYL SELF-ADMINISTRATION. WE AIM TO CLOSE WITH RECOMMENDATIONS FOR FUTURE RESEARCH WHEREIN BIOLOGICAL SEX IS CONSIDERED, FROM MULTIPLE LEVELS OF ANALYSIS, AS A VARIABLE IN TREATMENT IDENTIFICATION FOR OPIOID USE DISORDER.

WEDNESDAY, JANUARY 31ST

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 1-3, FLOOR 3

IMPACT OF STRESS AND SOCIAL ISOLATION ON BEHAVIORS CRITICAL FOR SURVIVAL

CHAIR: TARA RAAM
PRESENTERS: REESHA PATEL, HOLLY HUNSBERGER, ASHA CASLIN, TARA RAAM

SOCIAL BEHAVIORS ARE CRITICAL TO THE HEALTH AND WELLBEING OF A WIDE VARIETY OF SPECIES, INCLUDING HUMANS. DISRUPTIONS TO SOCIAL INTERACTIONS BY NEUROPSYCHIATRIC DISORDERS OR SOCIAL ISOLATION CAN SIGNIFICANTLY PERTURB ONE'S PHYSICAL AND MENTAL HEALTH. NOTABLY, SOCIAL BEHAVIORS HAVE A DYNAMIC AND RECIPROCAL RELATIONSHIP TO STRESS. ON THE ONE HAND, NEGATIVE SOCIAL INTERACTIONS SUCH AS AGGRESSION OR VIOLENCE CAN INDUCE STRESS. ON THE OTHER HAND, POSITIVE SOCIAL INTERACTIONS CAN BUFFER THE EFFECTS OF STRESS AND PROTECT FROM INDIVIDUAL VULNERABILITY. WHILE BEHAVIORAL NEUROSCIENCE HAS MADE GREAT STRIDES IN UNDERSTANDING THE CIRCUIT BASIS FOR SOCIAL INTERACTIONS, WE HAVE A POOR UNDERSTANDING OF HOW SOCIAL BEHAVIORS ADAPT TO AND ARE IMPACTED BY STRESS. HERE, WE AIM TO ADDRESS THIS GAP BY EXAMINING HOW STRESSORS SUCH AS SOCIAL ISOLATION, SICKNESS, AND THERMAL CHALLENGE DRIVE ADAPTIVE AND MALADAPTIVE BEHAVIORS IN THE CONTEXT OF SOCIAL HIERARCHIES, AGING, PARENTING, AND MULTI-ANIMAL SOCIAL GROUPS. THE PANEL GATHERS EXPERTISE FROM NEW INVESTIGATORS IN THE FIELD OF SOCIAL BEHAVIOR RESEARCH SPANNING CELLULAR, CIRCUIT AND BEHAVIORAL ANALYSIS.
REESHA PATEL WILL EXPLAIN HOW SOCIAL ISOLATION STRESS LEADS TO ESCALATED ALCOHOL CONSUMPTION IN A RANK-DEPENDENT MANNER, AND HOW THE BASOLATERAL AMYGDALA-PREFRONTAL CORTEX CIRCUIT IS A KEY NEURAL SUBSTRATE MEDIATING THIS LINK, USING SLICE ELECTROPHYSIOLOGY, OPTOGENETICS AND MINISCOPES. HOLLY HUNSBERGER WILL NEXT EXAMINE THE SHORT AND LONG-TERM IMPACTS OF SOCIAL ISOLATION ON FEAR MEMORY AND HIPPOCAMPAL-AMYGDALA CIRCUITRY IN BOTH AGING AND ALZHEIMER'S DISEASE. ASHA CASLIN WILL DISCUSS HOW HYPOTHALAMIC OXYTOCIN NEURONS ENABLE MOTHERS TO ADAPT THEIR BEHAVIORS TO TAKE CARE OF SICK PUPS USING ELECTROPHYSIOLOGY AND LONGITUDINAL BEHAVIOR TRACKING. TARA RAAM WILL DEMONSTRATE HOW PREFRONTAL CIRCUITS ENABLE SOCIAL GROUPS RESPOND TO THERMAL STRESSORS BY ORGANIZING INTO HUDDLES USING CHEMOGENETICS, MINISCOPE IMAGING, AND BEHAVIOR TRACKING.

WEDNESDAY, JANUARY 31ST

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 11-12, FLOOR 2

SYNAPTIC AND ELECTROPHYSIOLOGICAL CORRELATES OF DIFFERENT FORMS OF ASSOCIATIVE LEARNING

CHAIR: JONATHAN MORROW
PRESENTERS: ANKIT SOOD, SARA MORRISON, JONATHAN MORROW, BRYAN SINGER

MANY NEUROPSYCHIATRIC DISORDERS, SUCH AS SCHIZOPHRENIA, POST-TRAUMATIC STRESS DISORDER, AND ADDICTIVE DISORDERS, ARE ASSOCIATED WITH DISRUPTIONS IN ASSOCIATIVE LEARNING PROCESSES. UNDERSTANDING THE PHYSICAL BASIS OF THESE PROCESSES MAY ALLOW RESEARCHERS AND CLINICIANS TO MODIFY AND RESHAPE MALADAPTIVE BEHAVIORAL PATTERNS, BOTH IN CLINICAL SETTINGS (E.G., ADDICTION TREATMENT) AND EVERYDAY LIFE (E.G., HABIT FORMATION AND BREAKING). THIS PANEL WILL PRESENT EMERGING DATA THAT LINKS DIFFERENT TYPES OF ASSOCIATIVE LEARNING TO SPECIFIC VARIATIONS IN NEURONAL ACTIVITY AND SYNAPTIC TRANSMISSION. FIRST, ANKIT SOOD WILL PRESENT IN-VIVO ELECTROPHYSIOLOGY DATA COLLECTED FROM JOCELYN RICHARD'S LAB DETAILING NEURONAL ACTIVITY OF VENTRAL PALLIDUM NEURONS IN RATS RESPONDING TO PAVLOVIAN CUES BEFORE AND AFTER SPECIFIC SATIETY OUTCOME DEVALUATION. NEXT, SARA MORRISON WILL PRESENT IN-VIVO ELECTROPHYSIOLOGICAL DATA FROM HER LAB COMPARING CUE-EVOKED NEURONAL ACTIVITY IN THE NUCLEUS ACCUMBENS OF SIGN- AND GOAL-TRACKING RATS, AS WELL AS THE EFFECTS OF OUTCOME DEVALUATION AND EXTINCTION ON THIS ACTIVITY. JONATHAN MORROW WILL THEN PRESENT DATA FROM HIS LAB RELATING INDIVIDUAL DIFFERENCES IN PAVLOVIAN CONDITIONING TO NEURONAL EXCITABILITY, SYNAPTIC EFFICACY, AND PATHWAY-SPECIFIC ACTIVITY IN THE PROJECTION FROM VENTRAL HIPPOCAMPUS TO NUCLEUS ACCUMBENS. FINALLY, BRYAN SINGER WILL PRESENT DATA FROM HIS LAB CHARACTERIZING CUE-EVOKED CHANGES IN NEUROTRANSMITTER RELEASE AND DENDRITIC STRUCTURE THAT MAY CONTRIBUTE TO INDIVIDUAL VARIATION ACROSS ANIMALS AND SEXES. BOTH DR. MORROW AND DR. SINGER WILL PRESENT SOME TRANSLATIONAL DATA THAT RELATES THEIR FINDINGS IN ANIMALS TO PARALLEL FINDINGS IN HUMAN SUBJECTS. TOGETHER, THESE PRESENTATIONS WILL DEMONSTRATE HOW PROCESSES RANGING FROM INTRINSIC NEURONAL EXCITABILITY TO SYNAPTIC CONNECTIVITY MAY INFLUENCE ASSOCIATIVE LEARNING PROCESSES AND CONTRIBUTE TO NEUROPSYCHIATRIC DISORDERS.

WEDNESDAY, JANUARY 31ST

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 14, FLOOR 1

DOPAMINE NEUROMODULATION IN HIPPOCAMPUS AND AMYGDALA
CHAIR: ARTHUR GODINO, ANDREW LUTAS

PRESENTERS: AVI MATARASSO, HYE SUN (SUNNY) CHOI, ARTHUR GODINO, DAMIEN KERSPERN

DOPAMINE CIRCUITS BROADCAST INFORMATION THROUGHOUT THE BRAIN IN BOTH HEALTHY AND PATHOLOGICAL CONDITIONS. HOWEVER, THE MAJORITY OF THE WORK ON DOPAMINE SYSTEMS HAS REMAINED CENTERED ON MIDBRAIN DOPAMINE CELLS THEMSELVES OR THEIR OUTPUT TO THE STRIATUM – WHILE LARGELY OVERLOOKING DOPAMINERGIC TRANSMISSION ELSEWHERE. THIS PANEL WILL THUS REVIEW NOVEL, UNPUBLISHED, DATA ON DOPAMINE NEUROMODULATION IN THE HIPPOCAMPUS AND AMYGDALA, TOGETHER ESTABLISHING A CRITICAL YET MULTIFACETED ROLE FOR NON-STRIATAL DOPAMINE IN GOVERNING AFFECTIVE STATES, LEARNING AND DECISION-MAKING. AS RECENT EVIDENCE IMPLICATED NON-CANONICAL DOPAMINE PATHWAYS IN DORSAL HIPPOCAMPUS FUNCTION, THE PRESENTERS PROPOSED BELOW WILL DISCUSS WITH PARTICULAR ATTENTION THE PRECISE CIRCUIT ORIGIN OF THOSE LIMBIC DOPAMINE SIGNALS.
AVI MATARASSO, PHD STUDENT IN DR. BRUCHAS'S LAB AT UW, WILL FIRST PRESENT A COMPREHENSIVE AND COMPARATIVE MAPPING OF DOPAMINE AND NOREPINEPHRINE RELEASE DYNAMICS FROM THE LOCUS COERULEUS ACROSS SUBFIELDS OF THE HIPPOCAMPUS AND AMYGDALA IN RESPONSE TO APPETITIVE AND AVERSIVE STIMULI.
HYE SUN (SUNNY) CHOI, PHD STUDENT IN DR. KHEIRBEK'S LAB AT UCSF, WILL THEN DESCRIBE IN MORE DETAIL DOPAMINE SIGNALS IN THE DENTATE GYRUS IN THE CONTEXT OF ASSOCIATIVE LEARNING AND DISCRIMINATION TASKS, AND WILL IMPLICATE DOPAMINE NEURONS LOCATED IN THE DORSAL RAPHE NUCLEUS IN THESE PROCESSES.
ARTHUR GODINO, PHD STUDENT IN DR. NESTLER'S LAB AT MOUNT SINAI, WILL DETAIL HOW DOPAMINE REGULATES DOPAMINOCEPTIVE D1- OR D2-EXPRESSING NEURONS IN VENTRAL HIPPOCAMPUS TO ARBITRATE MOTIVATED APPROACH AND AVOIDANCE BEHAVIORS AT BASELINE, AS WELL AS THEIR DYSREGULATION BY CHRONIC STRESS AND DRUG EXPOSURE.
DR. DAMIEN KERSPERN, POSTDOCTORAL FELLOW IN DR. LUTAS'S LAB AT NIH/NIDDK, WILL CONCLUDE THE SESSION BY DISCUSSING THE UNIQUE ENCODING PROPERTIES OF MIDBRAIN DOPAMINE SIGNALS IN THE CENTRAL AMYGDALA DURING BOTH REWARD AND AVERSION CONDITIONING, ESPECIALLY BY CONTRAST TO THE NEIGHBORING BASOLATERAL AMYGDALA.

WEDNESDAY, JANUARY 31ST

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 15-16, FLOOR 1

REGULATION OF DIVERSE MOTIVATED BEHAVIORS BY THE HYPOTHALAMUS

CHAIRS: ADAM GORDON-FENNELL, FLAVIA BARBANO
PRESENTERS: FLAVIA BARBANO, ADAM GORDON-FENNELL, EDITA NAVRATILOVA, ADA EBAN-ROTHSCHILD

DECADES OF RESEARCH HAVE DEMONSTRATED THAT THE HYPOTHALAMUS IS A HIGHLY HETEROGENEOUS BRAIN STRUCTURE THAT IS CRUCIAL FOR MOTIVATED BEHAVIOR. RECENT ADVANCES HAVE REVEALED THAT THE HYPOTHALAMUS CONTAINS DISTINCT SUBPOPULATIONS OF NEURONS THAT CONTRIBUTE TO DISCRETE BUT INTERRELATED BEHAVIORS IMPORTANT FOR SURVIVAL. IN OUR PANEL, WE WILL DISCUSS CUTTING EDGE RESEARCH ON DISSECTING THE ROLE OF THE HYPOTHALAMUS IN AVERSION, CONSUMMATORY, AND SLEEP BEHAVIORS. DR. FLAVIA BARBANO (NATIONAL INSTITUTE ON DRUG ABUSE/NIH) WILL DISCUSS THE FUNCTION OF LATERAL HYPOTHALAMUS GLUTAMATE CELLS IN MODULATING VENTRAL TEGMENTAL AREA GLUTAMATE NEURONS TO SHAPE DEFENSIVE AND CONSUMMATORY BEHAVIOR, AND THE SWITCH BETWEEN THEM. DR. ADAM GORDON-FENNELL (UNIVERSITY OF WASHINGTON) WILL DESCRIBE THE TANDEM ROLE OF LATERAL HYPOTHALAMUS GABA AND GLUTAMATE CELLS IN THE REGULATION OF STRIATAL DOPAMINE RELEASE AND CONSUMMATORY BEHAVIORS. DR. ADA EBAN-ROTHSCHILD (UNIVERSITY OF MICHIGAN) WILL DISCUSS THE FUNCTIONS OF LATERAL HYPOTHALAMIC ENSEMBLES IN THE MOTIVATION TO PREPARE FOR SLEEP AND THE GATING OF SLEEP INITIATION AND INTENSITY. DR. EDITA NAVRATILOVA (UNIVERSITY OF ARIZONA) WILL PRESENT HER WORK ON THE PHYSIOLOGICAL ROLES OF HYPOTHALAMIC DYNORPHIN/KAPPA OPIOID RECEPTOR SIGNALING IN ELICITING AROUSAL AND HOW THIS SYSTEM BECOMES MALADAPTIVE IN CHRONIC PAIN CONDITIONS AND LEADS TO SLEEP DISRUPTIONS.

WEDNESDAY, JANUARY 31ST

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 17, FLOOR 1

PSYCHEDELICS FOR NEUROPSYCHIATRY: FROM BENCH TO BEDSIDE

CHAIR: PRAACHI TIWARI, ALAINA JASTER
PRESENTERS: ALEXANDER SMITH, ALAINA JASTER, PRAACHI TIWARI, NEIL SAVALIA

THERE HAS BEEN A RECENT RESURGENCE IN INTEREST IN THE THERAPEUTIC POTENTIAL OF PSYCHEDELICS FOR MENTAL DISORDERS. GIVEN THAT THIS FIELD IS STILL IN ITS INFANCY, IT IS CRUCIAL TO EXPLORE THE BEHAVIORAL, CIRCUIT, AND CELLULAR EFFECTS OF PSYCHEDELICS. THE PROPOSED PANEL WILL PRESENT FINDINGS ON ALL THESE LEVELS TO FOSTER DISCUSSION ON THE SCOPE OF WIDESPREAD USE OF PSYCHEDELICS IN MEDICINE. ALEX SMITH WILL FIRST PRESENT DATA EXPLORING THE IMPACT OF PSILOCYBIN, DOI, AND/OR DPT ON RELAPSE TO HEROIN SEEKING TRIGGERED BY CUES ASSOCIATED WITH PREVIOUS STRESSFUL LIFE EVENTS IN MICE. HE WILL ALSO DISCUSS IEG EXPRESSION DATA FROM WHOLE-BRAIN LIGHT-SHEET MICROSCOPY, FOCUSING ON NEURAL CIRCUITS ACTIVATED BY RELAPSE AND THESE COMPOUNDS. FOLLOWING THIS, ALAINA JASTER WILL DISCUSS HOW STRUCTURALLY DIFFERENT PSYCHEDELICS PRODUCE DISTINCT CHANGES IN BEHAVIORAL PHENOTYPES INVOLVED IN OPIOID REINFORCEMENT IN MICE, AS WELL AS DIFFERENCES ACROSS SEXES IN THEIR RESPONSE TO PSYCHEDELICS. SHE WILL PRIMARILY FOCUS ON THE ROLE OF THE 5-HT2A RECEPTORS, ESPECIALLY ON THE CORTICAL PYRAMIDAL NEURONS PROJECTING TO NUCLEUS ACCUMBENS, IN THESE BEHAVIORS. PRAACHI TIWARI WILL THEN PRESENT DATA ON THE NEUROANATOMICAL UNDERPINNINGS OF DOI IN AFFECTING ANXIETY-LIKE BEHAVIORAL RESPONSE IN RODENTS. SHE WILL DISCUSS THE ESSENTIAL ROLE OF 5-HT2A RECEPTORS ON PARVALBUMIN-POSITIVE INHIBITORY INTERNEURONS IN THE VENTRAL HIPPOCAMPUS IN DOI-EVOKED ANXIOLYTIC RESPONSE IN RODENTS. FINALLY, NEIL SAVALIA WILL DISCUSS PSILOCYBIN'S EFFECT ON NEURONAL STRUCTURE AND FUNCTION IN THE MOUSE FRONTAL CORTEX. HE WILL SHOW HOW PSILOCYBIN'S ACTIONS ON DENDRITIC CALCIUM AND LONG-TERM PLASTICITY DIFFER FOR SUBTYPES OF PYRAMIDAL NEURONS, SUGGESTIVE OF CIRCUIT AND CELL TYPE-SPECIFICITY THAT MAY RELATE TO PSILOCYBIN'S THERAPEUTIC EFFECTS. TOGETHER, THIS PANEL WILL EXPLORE THE WIDE ARRAY OF DATA AIMED TOWARDS UNDERSTANDING THE MECHANISMS UNDERLYING THE THERAPEUTIC EFFECTS OF PSYCHEDELICS AND THE TRANSLATIONAL VALIDITY OF THESE MODELS.

WEDNESDAY, JANUARY 31ST

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 6-8, FLOOR 2

EXERCISE YOUR MYELIN: INTERVENTIONS THAT ENHANCE MYELIN PLASTICITY AFTER INJURY OR DISEASE

CHAIR: EMILY PETRUS
PRESENTERS: ANNE WELLS, CHRISTINA MARION, TIMOTHY FAW, EMILY PETRUS

MYELIN FORMS FATTY SHEETS THAT WRAP AROUND AXONS TO ENHANCE INTER-NEURONAL COMMUNICATION. IMPORTANTLY, ADAPTATIONS IN MYELIN OPTIMIZE THE TIMING OF NEURAL TRANSMISSION AND ULTIMATELY ALTER NEURAL NETWORK FUNCTION BY MODULATING SPIKE-TIMING DEPENDENT SYNAPTIC PLASTICITY, THUS FORMING THE BASIS FOR COGNITIVE OR SKILL LEARNING. INJURY TO THE NERVOUS SYSTEM CAN NEGATIVELY IMPACT NEURONAL HEALTH, BUT ALSO THE QUALITY AND QUANTITY OF MYELINATED AXONS, BUNDLES, AND TRACTS. RECOVERY AFTER INJURY DEPENDS ON RESTORING OR REWIRING NEURONAL CONNECTIONS AND IS SUPPORTED BY MYELIN REPAIR. ACTIVITIES THAT HAVE A CAPABILITY TO ENHANCE MYELINATION AFTER INJURY INCLUDE EXERCISE, LEARNING NEW MOTOR SKILLS, AND ENRICHED SENSORY ENVIRONMENTS. THIS PANEL WILL DISCUSS THE MECHANISMS BY WHICH MYELIN ADAPTATIONS CAN BE INDUCED TO ENHANCE BEHAVIORAL RECOVERY. INJURY MODELS IN RATS, MICE, AND PEOPLE INCLUDE EARLY POSTNATAL ALCOHOL EXPOSURE (MODEL OF FETAL ALCOHOL SPECTRUM DISORDER), PERIPHERAL DENERVATION, AND SPINAL CORD INJURY, RESPECTIVELY. TECHNIQUES USED TO DETECT MYELIN PLASTICITY INCLUDE IMMUNOHISTOCHEMISTRY, SINGLE NUCLEUS RNA SEQUENCING, TRANSGENIC MOUSE MODELS, MAGNETIC RESONANCE IMAGING (MRI), AND FUNCTIONAL (BEHAVIORAL) READOUTS.
CHRISTINA MARION'S WORK EXPLORES HOW EXERCISE MODULATES MYELIN RECOVERY AFTER SPINAL CORD INJURY IN RODENTS. TIMOTHY FAW WILL COMPARE CLINICAL AND PRECLINICAL EVIDENCE FOR NOVEL EXERCISE TRAINING ON MYELIN PLASTICITY AFTER SPINAL CORD INJURY. EMILY PETRUS WILL DESCRIBE MYELIN DEFICITS AFTER PERIPHERAL DENERVATION AND SUBSEQUENT RESCUE AFTER MICE LEARN A NEW TASK.
THE STUDIES PRESENTED IN THIS PANEL HIGHLIGHT THE RELATIVELY NEW FIELD OF MYELIN PLASTICITY AND DESCRIBE EXCITING INTERVENTIONS THAT PROMOTE MYELIN FORMATION AND IMPROVE RECOVERY AFTER INJURY.

WEDNESDAY, JANUARY 31ST

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 9-10, FLOOR 2

TARGETING THE COMPLEMENT SYSTEM IN NEURODEGENERATION
CHAIRS: MARCELA PEKNA, JAN MULDER

PRESENTERS: MARCELA PEKNA, JAN MULDER, JOHN LEE, MILOS PEKNY

THE THERAPEUTIC OPTIONS FOR BRAIN INJURY AND NEURODEGENERATIVE DISORDERS ARE VERY LIMITED. THE COMPLEMENT SYSTEM MEDIATES NEUROINFLAMMATION AND DRIVES PROGRESSIVE LOSS OF SYNAPSES AND NEURONS IN ALZHEIMER'S DISEASE TYPE NEURODEGENERATION. COMPLEMENT HAS ALSO BEEN SHOWN TO CONTRIBUTE TO BLOOD-BRAIN BARRIER DYSFUNCTION ASSOCIATED WITH AGING AND TO AGGRAVATE TISSUE DAMAGE AFTER BRAIN TRAUMA OR STROKE. INHIBITION OF COMPLEMENT ACTIVATION THUS PRESENTS AN ATTRACTIVE THERAPEUTIC STRATEGY, AT LEAST FOR SOME OF THESE CONDITIONS. ON THE OTHER HAND, COMPLEMENT PROTEINS, COMPLEMENT ACTIVATION-DERIVED PEPTIDES AND MEMBRANE-BOUND COMPLEMENT RECEPTORS ARE ESSENTIAL FOR NORMAL CNS DEVELOPMENT, MAINTENANCE OF TISSUE HOMEOSTASIS, CLEARANCE OF NEURONAL DEBRIS AFTER INJURY AND REGULATION OF SEVERAL ASPECTS OF NEURAL PLASTICITY. IN ADDITION, RECENT FINDINGS SUGGEST THAT COMPLEMENT MAY EXERT DISTINCT EFFECTS AT DIFFERENT TIME POINTS AFTER INJURY (SUCH AS ACUTE VERSUS POST-ACUTE OR CHRONIC PHASE), IN DIFFERENT NEURODEGENERATIVE DISORDERS AND AT DIFFERENT STAGES OF A SPECIFIC NEURODEGENERATIVE CONDITION. WITH EMPHASIS ON THERAPEUTIC IMPLICATIONS AND CLINICAL TRANSLATION, MARCELA PEKNA WILL DISCUSS THE MULTIPLE ROLES OF C3AR SIGNALING IN REGULATING BRAIN TISSUE RESPONSES TO ISCHEMIA AND IN ISCHEMIC INJURY-INDUCED SECONDARY NEURODEGENERATION. TAKING ADVANTAGE OF THE PROTEOMICS AND TRANSCRIPTOMICS DATA ON THE DISTRIBUTION OF THE COMPLEMENT SYSTEM ACROSS TISSUES, CELL TYPES AND SPECIES GENERATED BY THE HUMAN PROTEIN ATLAS PROJECT, JAN MULDER WILL DEMONSTRATE THE POTENTIAL OF SPATIAL TRANSCRIPTOMICS AND INTEGRATION OF MULTI-OMICS DATA TO GAIN INSIGHTS INTO THE INVOLVEMENT OF THE COMPLEMENT SYSTEM IN STROKE AND FRONTOTEMPORAL DEMENTIA. JOHN LEE WILL HIGHLIGHT THE TRANSLATIONAL POTENTIAL OF C3AR AND C5ARI AS THERAPEUTIC TARGETS IN AMYOTROPHIC LATERAL SCLEROSIS. MILOS PEKNY WILL PRESENT THE CONCEPT OF DISEASE SUBTYPE-SPECIFICITY OF C3AR ROLES IN AMYOTROPHIC LATERAL SCLEROSIS AND DISCUSS THE IMPLICATIONS FOR PRECISION MEDICINE THERAPIES FOR THIS FATAL NEURODEGENERATIVE DISORDER.

THURSDAY, FEBRUARY 1ST

PANEL
7:30 A.M. - 9:30 A.M.
IMPERIAL BALLROOM, FLOOR 4

ENSEMBLE-SPECIFIC APPROACHES TO IDENTIFY CELL-TYPES, CIRCUITS AND MOLECULAR ALTERATIONS UNDERLYING REWARD-RELATED BEHAVIORS

CHAIRS: MARINE SALERY, RAJTARUN MADANGOPAL
PRESENTERS: ELIZABETH DONCHECK, ANA CLARA BOBADILLA, MARINE SALERY, RAJTARUN MADANGOPAL

LEARNED ASSOCIATIONS BETWEEN CUES AND THE REWARDING EFFECTS OF DRUGS PLAY A CRITICAL ROLE IN RELAPSE. ASSOCIATIVE MEMORIES, INCLUDING MALADAPTIVE DRUG MEMORIES ARE ENCODED WITHIN SPARSE POPULATIONS OF NEURONS TERMED NEURONAL ENSEMBLES. THIS PANEL WILL DEMONSTRATE THE USE OF ACTIVITY-DEPENDENT TOOLS TO INVESTIGATE THE ROLE OF NEURONAL ENSEMBLES IN MALADAPTIVE DRUG MEMORIES AND RELAPSE.
ELIZABETH DONCHECK (MUSC) WILL SHOW HOW USING HEAD-FIXED HEROIN SELF-ADMINISTRATION PAIRED WITH IN VIVO TWO-PHOTON CALCIUM IMAGING CAN RESOLVE DISCRETE NEURONAL ENSEMBLES IN THE PRELIMBIC CORTEX, DEFINED BY ACTIVITY DYNAMICS, THAT ARISE DURING CUE-INDUCED REINSTATEMENT. SHE WILL THEN DISSECT HOW DISRUPTING ENSEMBLE ACTIVITY THAT ENCODES AND DECODES DRUG-CUES SUPPRESSES REINSTATEMENT.
ANA CLARA BOBADILLA (CSU) WILL PRESENT A DUAL COCAINE AND SUCROSE SELF-ADMINISTRATION MODEL IN FOSICREERT2 MICE TO CHARACTERIZE COCAINE- AND SUCROSE-SEEKING ENSEMBLES' TRANSCRIPTOMES AND WILL DISCUSS HOW SPECIFIC TRANSCRIPTOMIC CHANGES CAN REFINE CLINICALLY RELEVANT APPROACHES TO DECREASE COCAINE-SEEKING WITHOUT ALTERING NON-DRUG REWARD-BASED POSITIVE REINFORCEMENT.
MARINE SALERY (MOUNT SINAI) WILL DESCRIBE THE REACTIVATION DYNAMICS AND MOLECULAR PROFILES OF COCAINE-RECRUITED ENSEMBLES IN ARC-CREERT2 MICE IN COCAINE-CONTEXT ASSOCIATIONS, USING SNRNA-SEQ APPROACHES TO SURVEY THE TRANSCRIPTOMIC SIGNATURE OF ENSEMBLES' RECRUITMENT.
RAJTARUN MADANGOPAL (NIDA IRP) WILL PRESENT USE OF THE CALCIUM-BASED ACTIVITY MARKER CAMPARI2 TO PERMANENTLY TAG COCAINE-MEMORY NEURONS IN RAT INFRALIMBIC CORTEX DURING THE FIRST MINUTE OF COCAINE RELAPSE. THEY WILL COMBINE TIME-LOCKED LABELING WITH SINGLE NUCLEI RNA SEQUENCING TO IDENTIFY COCAINE-MEMORY-SPECIFIC TRANSCRIPTIONAL SIGNATURES FOLLOWING COCAINE RELAPSE.
THIS SESSION WILL SHOWCASE STATE-OF-THE-ART APPROACHES TO INTERROGATE NEURONAL ENSEMBLE FUNCTION AND THEIR CONTRIBUTION TO THE DEVELOPMENT OF NOVEL STRATEGIES TO DISRUPT ADDICTION-RELATED PATHOLOGICAL MEMORIES.

THURSDAY, FEBRUARY 1ST

PANEL
7:30 A.M. - 9:30 A.M.
PEAK 6-8, FLOOR 2

BEHAVIORAL, NEURAL AND NEUROCHEMICAL DIFFERENCES IN DECISION MAKING: LET'S TALK ABOUT SEX

CHAIR: CATHARINE WINSTANLEY
PRESENTERS: ANDREW WIKENHEISER, CATHARINE WINSTANLEY, VALERIA GONZALEZ, JULIA COX

DECISION MAKING DEFICITS ARE A HALLMARK OF NUMEROUS PSYCHIATRIC DISORDERS, INCLUDING BIPOLAR DISORDER, ADDICTION DISORDERS, AND MAJOR DEPRESSION. MEN AND WOMEN DIFFER IN THEIR VULNERABILITY TO THESE DISORDERS, AND ALSO IN THE WAY THEY ARE MANIFEST. PARSING THE IMPACT OF BIOLOGICAL SEX FROM THAT OF GENDER CAN BE CHALLENGING IN RESEARCH USING HUMAN SUBJECTS. DECISION MAKING TASKS DESIGNED FOR USE IN LABORATORY ANIMALS MAY BE USEFUL IN DETERMINING WHETHER SEX DIFFERENCES EXIST ACROSS DIFFERENT DECISION-MAKING DOMAINS, AND ALSO IN PROBING THE NEURAL AND NEUROCHEMICAL BASES UNDERLYING THESE RESULTS. IN THIS PANEL, THE PRESENTERS WILL SHOWCASE DIVERSE APPROACHES TO MODELING DECISION-MAKING IN LABORATORY RATS. FIRST, DR. ANDREW WIKENHEISER WILL DISCUSS SEX DIFFERENCES IN DECISION MAKING ON A RECENTLY-DEVELOPED NATURALISTIC FORAGING TASK. THEN, DR. CATHARINE WINSTANLEY WILL SHARE RESULTS FROM BOTH PHARMACOLOGICAL CHALLENGES AND COMPUTATIONAL ANALYSES INDICATING SEXUALLY DIMORPHIC REGULATION OF DECISION MAKING ON THE CUED RAT GAMBLING TASK. DR. VALERIA GONZALEZ WILL THEN PRESENT DATA ON A TASK IN WHICH SUBJECTS PAY A REWARD COST FOR INFORMATION ABOUT REWARD, WITH CHEMOGENETIC EXPERIMENTS REVEALING A SEX-SPECIFIC ROLE FOR ANTERIOR CINGULATE CORTEX, AND NOT ORBITOFRONTAL CORTEX OR BASOLATERAL AMYGDALA, IN STABILIZING CHOICES INVOLVING SUCH INFORMATION. FINALLY, DR. JULIA COX WILL DISCUSS SEX DIFFERENCES IN THE ROLE OF ANTERIOR CINGULATE CORTEX NEURONS THAT PROJECT TO THE DORSOMEDIAL STRIATUM IN REGULATING MOTIVATION TO PERFORM A VALUE-BASED DECISION MAKING TASK.

THURSDAY, FEBRUARY 1ST

PANEL
7:30 A.M. - 9:30 A.M.
PEAK 9-10, FLOOR 2

REPAIRING THE CNS BY TARGETING THE GUT AND ENTERIC NERVOUS SYSTEM

CHAIR: WARREN ALILAIN
PRESENTERS: ALEXANDRA BYRNE, CEDRIC GEOFFROY, WARREN ALILAIN, KRISTINA KIGERL

THERE IS INCREASING EVIDENCE THAT THE BI-DIRECTIONAL GUT-CENTRAL NERVOUS SYSTEM (CNS) AXIS IS AN IMPORTANT FACTOR WHEN INVESTIGATING THE IMPACT OF NEURODEGENERATIVE DISEASE AND NEUROTRAUMATIC INJURY ON HEALTH AND RECOVERY. INDEED, THE SEVERITY AND EXTENT OF FUNCTIONAL LOSS AFTER CNS INJURY, AS WELL AS THE EFFICACY OF POTENTIAL THERAPEUTIC STRATEGIES, CAN BE INFLUENCED BY THE PERIPHERAL GUT SYSTEM. THIS PANEL WILL PRESENT THE LATEST FINDINGS AND DATA ON NEURAL INJURY AND ITS EFFECT ON THE GUT MICROBIOME AND GUT PATHOLOGY AND DYSFUNCTION. EQUALLY, PRESENTERS WILL ALSO SHOWCASE HOW MODULATING THE GUT MICROBIOME CAN SIMILARLY SHAPE LESION SEVERITY OR SIZE, NEURAL PLASTICITY AND REGENERATION, AND FUNCTIONAL RECOVERY (BOTH INTESTINAL AND NON-INTESTINAL). DR. BYRNE WILL BEGIN THE PANEL BY DISCUSSING THE RELEVANCE OF UNI-BACTERIAL DIETS AND MICROBIAL INFLUENCE ON THE INJURY RESPONSE IN C. ELEGANS. FOLLOWING THIS SESSION, DR. GEOFFROY WILL FURTHER EXPAND THIS DISCUSSION BY PRESENTING HOW TARGETING GUT METABOLITES AS A POTENTIAL THERAPEUTIC STRATEGY CAN PROMOTE GUT FUNCTION AFTER SPINAL CORD INJURY (SCI). THE CONCEPT OF TARGETING THE GUT TO PROMOTE FUNCTION WILL BE FURTHER EXPLORED WITH DR. ALILAIN PRESENTING DATA ON THE INFLUENCE OF THE GUT MICROBIOME AND DYSBIOSIS ON GUT HEALTH, AS WELL AS RESPIRATORY FUNCTION AFTER CERVICAL SCI. THE SESSION WILL BE CONCLUDED BY DR. KIGERL WHO WILL PRESENT AN IN-DEPTH METAGENOMIC ANALYSIS OF THE GUT MICROBIOTA FOLLOWING SCI WHICH CAN IN TURN LEAD TO DISCOVERY OF NOVEL THERAPEUTIC TARGETS. COLLECTIVELY, THESE PRESENTATIONS WILL HIGHLIGHT THE CRITICAL NATURE OF THE GUT-CNS AXIS AFTER DEVASTATING CNS INJURY AND HOW RESEARCHERS CAN EXPLOIT THIS RELATIONSHIP TO PROMOTE FUNCTIONAL RECOVERY AND IMPROVEMENT IN HEALTH.

THURSDAY, FEBRUARY 1ST

PANEL
7:30 A.M. - 9:30 A.M.
PEAK 14, FLOOR 1

SLIPPERY SLOPE: COMPLEX BIOLOGY OF SYNAPSES AND ITS IMPLICATION FOR SYNAPTIC FUNCTION AND DISEASE

CHAIRS: MARTIN HRUSKA, MATTHEW DALVA
PRESENTERS: MARTIN HRUSKA, JORIS DE WIT, ELVA DIAZ, MATTHEW DALVA

EXCITATORY SYNAPSES ARE THE FUNDAMENTAL CONNECTIONS BETWEEN NEURONS IN THE BRAIN UNDERLYING COGNITIVE FUNCTION. DISRUPTION OF MOLECULAR PROCESSES WITHIN PRE- AND POST-SYNAPTIC TERMINALS LEADS TO SYNAPTIC DYSFUNCTION THAT UNDERLIES VARIOUS DISORDERS OF THE BRAIN. USING A COMBINATION OF APPROACHES, THIS PANEL EXPLORES MOLECULAR AND CELLULAR MECHANISMS THAT REGULATE SYNAPSE DEVELOPMENT AND PLASTICITY, AND HOW DISRUPTION OF THESE PROCESSES MAY LEAD TO DISEASE. FOCUSING ON SUPER-RESOLUTION IMAGING OF FIXED AND LIVING NEURONS, DR. HRUSKA WILL DISCUSS THE ROLE OF SYNAPTIC NANOARCHITECTURE IN SELECTIVE SPINE VULNERABILITY IN THE A-BETA MODEL OF ALZHEIMER'S DISEASE. USING A COMBINATION OF IMAGING-BASED AND MOUSE GENETIC APPROACHES, DR. DE WIT WILL DISCUSS THE ROLE OF CELL ADHESION-MEDIATED POST-SYNAPTIC ORGANELLE DISTRIBUTION IN REGULATING DENDRITIC SPINE MATURATION AND ITS IMPLICATIONS FOR SPINE VULNERABILITY IN NEURODEGENERATIVE DISEASE. DR. DIAZ WILL PRESENT HOW THE AMPAR AUXILIARY FACTOR SYNDIG4 ESTABLISHES RESERVE POOLS OF GLUA1-AMPARS BY MAINTAINING SURFACE EXPRESSION AT PERISYNAPTIC SITES THAT ARE TARGETED TO SYNAPSES DURING LTP. DR. DALVA WILL CLOSE WITH A DISCUSSION OF NANOSCALE ORGANIZATION AND IMPACT OF LIQUID-LIQUID PHASE ON THE ORGANIZATION AND PLASTICITY OF DENDRITIC SPINE SYNAPSES.

THURSDAY, FEBRUARY 1ST

PANEL
7:30 A.M. - 9:30 A.M.
PEAK 15-16, FLOOR 1

A BED OF NAILS: THE CHALLENGE OF DISENTANGLING THE CIRCUITS AND FUNCTIONS OF THE BED NUCLEI OF THE STRIA TERMINALIS (BNST)

CHAIRS: SAMUEL CENTANNI, JASON RADLEY
PRESENTERS: ZOE MCELLIGOTT, SAMUEL CENTANNI, AMELIA DOUGLASS, JASON RADLEY

THE BNST IS A HETEROGENEOUS COLLECTION OF CELL GROUPS IN THE BASAL FOREBRAIN DEFINED BY EXTENSIVE AFFERENT INPUT FROM LIMBIC REGIONS SUCH AS THE INSULA, PREFRONTAL CORTEX, AND AMYGDALA, AND OUTPUT TO HYPOTHALAMIC AND OTHER LIMBIC STRUCTURES. WHILE VARIOUS FORMULATIONS OF THE BNST HAVE ATTRIBUTED IT AS PLAYING AN OVERARCHING ROLE IN THREAT UNCERTAINTY OR VALENCE DETECTION, THE COMPLEXITY OF CELL TYPES AND MACRO/MICROCIRCUIT REGULATION WARRANTS MULTIPRONGED STRATEGIES TO DISENTANGLE ITS DISCRETE FUNCTIONS. OUR PANEL WILL PRESENT DIFFERENT AND COMPLEMENTARY APPROACHES THAT COLLECTIVELY AIM TO UNDERSTAND HOW THIS DIVERSE BRAIN AREA MODULATES VARIOUS BEHAVIORAL AND EMOTIONAL STATES. FIRST, ZOE MCELLIGOTT (UNC) WILL PRESENT DATA ON UNIQUE MICROCIRCUIT REGULATION OF BNST SIGNALING VIA A GLUD-RECEPTOR MEDIATED TONIC CURRENT. NEXT, SAM CENTANNI (WAKE FOREST) WILL DISCUSS CIRCUIT-SPECIFIC MODULATION OF THE BNST BY AN UPSTREAM INSULA PROJECTION, AND HOW BASAL ACTIVITY IN THIS PATHWAY COULD BE A CIRCUIT BIOMARKER FOR SUBSEQUENT STRESS- AND ALCOHOL ABSTINENCE-INDUCED NEGATIVE AFFECT. AMELIA DOUGLASS (HARVARD) WILL PRESENT STUDIES ON HOW ACTIVATION OF AGRP ARCUATE HYPOTHALAMIC 'HUNGER NEURONS' CAN INHIBIT TONICALLY ACTIVE GABAERGIC AFFERENTS FROM THE BNST TO DRIVE ACTIVATION OF THE HPA AXIS DURING STARVATION. LASTLY, JASON RADLEY (UNIVERSITY OF IOWA) WILL HIGHLIGHT THE ROLE OF A PREFRONTAL–BNST PROJECTION IN MODULATING STRESS RESPONSES, ALONG WITH NEW EVIDENCE IMPLICATING THIS CIRCUIT IN THE CONSOLIDATION OF MEMORY STRENGTH AND PRECISION. COLLECTIVELY, OUR PANEL PRESENTS THE BNST'S ROLE AS MORE NUANCED AND COMPLEX THAN PREVIOUS FORMULATIONS, IN TERMS OF PROVIDING MULTIMODAL INTEGRATION OF UPSTREAM CIRCUIT INFORMATION, INTER-BNST MICROCIRCUIT REGULATION, AND IN COORDINATING EMOTIONAL STATUS AND GUIDANCE OF BEHAVIORAL OUTPUT.

THURSDAY, FEBRUARY 1ST

PANEL
7:30 A.M. - 9:30 A.M.
PEAK 17, FLOOR 1

NEURAL SYSTEMS REGULATING THE COMPETITION FOR CONTROL OVER MOTIVATED BEHAVIOR

CHAIR: RYAN LALUMIERE
PRESENTERS: JACQUELINE BARKER, AQILAH MCCANE, RYAN LALUMIERE, JAMIE PETERS

COMPETITION FOR CONTROL OVER BEHAVIOR REMAINS A FUNDAMENTAL ASPECT OF MOTIVATED BEHAVIORS AND CONTRIBUTES TO BOTH ADAPTIVE AND MALADAPTIVE OUTCOMES. YET THE NEURAL MECHANISMS THAT DETERMINE AND REGULATE THIS COMPETITION ARE NOT FULLY UNDERSTOOD. THIS PANEL WILL ADDRESS SUCH QUESTIONS ACROSS DIFFERENT TYPES OF MOTIVATED BEHAVIOR. DR. JACQUELINE BARKER WILL PRESENT WORK ON VENTRAL HIPPOCAMPAL CONTRIBUTION TO HABITUAL VERSUS MOTIVATED BEHAVIOR. IN VIVO ELECTROPHYSIOLOGICAL RECORDINGS FROM MICE TRAINED TO SELF-ADMINISTER SUCROSE ON EITHER HABIT- OR ACTION-PROMOTING SCHEDULES INDICATE ALTERED VENTRAL HIPPOCAMPUS (VHPC) ACTIVITY DURING THE DEVELOPMENT OF ABERRANT MOTIVATED BEHAVIOR THAT CAN BE MODULATED BY CLOSED-LOOP OPTOGENETIC INHIBITION OF THE VHPC. DR. AQILAH MCCANE WILL PRESENT FINDINGS REGARDING HOW CORTICOSTRIATAL NETWORKS INFLUENCE REWARD-SEEKING BEHAVIORS AND THE CONSEQUENCE OF ADOLESCENT ALCOHOL DRINKING ON THESE STRUCTURES. SHE WILL PRESENT RECENT WORK USING A CHEMOGENETIC STRATEGY AND IN VIVO ELECTROPHYSIOLOGY RECORDINGS TO INVESTIGATE HOW ORBITOFRONTAL CORTEX-DORSOMEDIAL STRIATUM CONNECTIONS MEDIATE RESPONSE INHIBITION, ALONG WITH DATA SHOWING HOW ADOLESCENT ALCOHOL DRINKING ALTERS THESE CONNECTIONS IN MALE AND FEMALE RATS. DR. RYAN LALUMIERE WILL PRESENT WORK FROM HIS LABORATORY REGARDING COCAINE SEEKING IN RATS. HIS FINDINGS SUGGEST AN IMPORTANT INTERACTION AMONG MULTIPLE CORTICOLIMBIC STRUCTURES IN LEARNING TO INHIBIT SUCH BEHAVIOR AND A POTENTIAL ROLE FOR THETA RHYTHMS IN THE INFRALIMBIC CORTEX IN MEDIATING SUCH INHIBITION. DR. JAMIE PETERS WILL PRESENT DATA ON DIVERGENT OUTPUTS FROM THE PREFRONTAL CORTEX THAT EXERT OPPOSING INFLUENCES ON HEROIN SEEKING BEHAVIOR. WHEREAS BOTH PREFRONTAL PYRAMIDAL NEURON SUBPOPULATIONS EXHIBIT SIMILAR PATTERNS OF HEROIN CUE REACTIVITY USING IN VIVO FIBER PHOTOMETRY, ONE APPEARS TO FUNCTION AS A DRIVER OF HEROIN SEEKING AND THE OTHER AS A LIMITER, USING OPTOGENETIC MANIPULATIONS.

PANEL
7:30 A.M. - 9:30 A.M.
PEAK II, FLOOR 2

SHORT TANDEM REPEATS IN NEURONAL FUNCTION AND NEUROLOGICAL DISEASE

CHAIR: PETER TODD, ANDY BERGLUND
PRESENTERS: ERIC WANG, GARY BASSELL, HANNAH SHORROCK, PETER TODD

OVER THE PAST 30 YEARS, SHORT TANDEM REPEAT EXPANSIONS HAVE EMERGED AS A COMMON CAUSE OF MANY NEUROLOGIC CONDITIONS, INCLUDING ALS, FRONTOTEMPORAL DEMENTIA, ATAXIA, MUSCULAR DYSTROPHY AND AUTISM. EXPANDED REPEATS AS DNA, RNA AND TRANSLATED PROTEINS CREATE DYNAMIC ELEMENTS THAT DRIVE DISEASE PATHOGENESIS. THESE SAME PROPERTIES ALLOW NORMAL SIZED REPEATS TO ACT AS MOLECULAR HANDLES WITH NATIVE ROLES IN NEURONAL FUNCTION. IN THIS SESSION CHAIRED BY DRS. PETER TODD (UNIVERSITY OF MICHIGAN) AND ANDY BERGLUND (UNIVERSITY OF ALBANY), FOUR SPEAKERS WORKING ACROSS A RANGE OF MODEL SYSTEMS AND DISEASE STATES WILL DESCRIBE HOW THE STRUCTURES OF REPETITIVE ELEMENTS AS RNA, DNA AND PROTEIN DIRECTLY INFLUENCE THEIR METABOLISM, BINDING PARTNERS, LOCALIZATION, TRANSLATION, AND DEGRADATION IN NEURONS. THEY WILL ALSO DISCUSS HOW REPEATS CREATE NOVEL TARGETS FOR MODULAR THERAPEUTIC DEVELOPMENT THROUGH USE OF EMERGING TECHNOLOGIES.
ERIC T. WANG (UNIVERSITY OF FLORIDA) WILL PRESENT WORK ON HOW THE RNA BINDING PROTEIN MUSCLEBLIND INTERACTS WITH CUG REPEATS TO CAUSE MYOTONIC DYSTROPHY THROUGH ALTERATIONS IN RNA SPLICING, STABILITY, TRANSPORT AND LOCALIZATION. GARY BASSELL (EMORY UNIVERSITY) WILL PRESENT STUDIES DELINEATING HOW FRAGILE X SYNDROME PATIENT DERIVED CEREBRAL BRAIN ORGANOIDS ALLOW MODELING OF CGG REPEAT-TRIGGERED SILENCING OF THE FRAGILE X GENE FMRI WITH SUBSEQUENT ALTERATIONS IN TRANSLATIONAL DYNAMICS THAT ARE POTENTIALLY TARGETABLE THERAPEUTICALLY. HEATHER SHORROCK (UNIVERSITY OF ALBANY) WILL DISCUSS HOW CAG REPEATS TRIGGER WIDESPREAD ALTERNATIVE SPLICING DYSREGULATION THAT PRECEDES SYMPTOM ONSET AND NEURODEGENERATION IN MODELS OF SPINOCEREBELLAR ATAXIA. LASTLY, PETER TODD WILL DISCUSS HOW EXPANDED REPEATS TRIGGER ABERRANT TRANSLATION IN THE ABSENCE OF AN AUG CODON (RAN TRANSLATION) TO GENERATE TOXIC PEPTIDES- BUT ALSO DISCUSS HOW THESE SAME PROCESSES ALSO ACT NORMALLY TO REGULATE TRANSLATION OF FMRP AND CONTROL DENDRITIC PROTEIN SYNTHESIS AND SYNAPTIC PLASTICITY.

THURSDAY, FEBRUARY 1ST

PANEL
7:30 A.M. - 9:30 A.M.
PEAK 12, FLOOR 2

BRIDGING THE GAP: EXPLORING BRAIN BIOMECHANICS AND NEUROSCIENCE SYNERGY

CHAIR: ROUZBEH AMINI
PRESENTERS: TURNER JENNINGS, MAHSA KARAMZADEH, PIROUZ KAVEHPOUR, ADITI DESHPANDE

RESEARCH RELATED TO BRAIN FUNCTION AND DISFUNCTION IS MOST OFTEN APPROACHED EITHER THROUGH THE LENS OF NEUROSCIENCE OR BIOMECHANICS, WITH LITTLE CROSSOVER. HOWEVER, SUCH AN APPROACH TENDS TO DECOUPLE THE BIOLOGICAL RESPONSE OF THE BRAIN FROM ITS UNDERLYING PHYSICS. IN THIS PANEL, WE AIM TO BRIDGE SUCH A GAP BY INTRODUCING MODERN TECHNIQUES AND RECENT RESEARCH IN THE FIELD OF BRAIN BIOMECHANICS OF INTEREST TO THE NEUROSCIENCE COMMUNITY. WE WILL DISCUSS RECENT ADVANCES IN NEUROIMAGING AND COMPUTATIONAL MODELING WHICH LINK PHYSICAL STIMULI TO NEUROLOGICAL CONDITIONS. WE WILL OUTLINE TECHNICAL CHALLENGES WHICH CAN BENEFIT FROM AN INTERDISCIPLINARY APPROACH COMBINING THE FIELDS OF BIOMECHANICS AND NEUROSCIENCE. TURNER JENNINGS WILL FIRST PRESENT AN ANALYSIS OF THE RESONANT VIBRATIONAL BEHAVIOR OF THE BRAIN AND ITS RELEVANCE TO MEDICAL IMAGING AND VIBRATION-BASED INTERVENTIONS. MAHSA KARAMZADEH WILL THEN DISCUSS APPLICATIONS OF PHASE CONTRAST MRI (PCMRI) TO MEASURE THE MOTION OF THE BRAIN DURING THE CARDIAC CYCLE IN CHIARI MALFORMATION TYPE I, AND HOW BRAIN TISSUE GEOMETRY AND DISPLACEMENT COMPARE WITH SYMPTOMOLOGY. DR. PIROUZ KAVEHPOUR WILL INTRODUCE HOW HIS TEAM MODEL CEREBROSPINAL AND BRAIN INTERACTION DURING TRAUMATIC BRAIN INJURIES WHILE CLOSELY EXAMINING TAU PROTEIN AGGREGATION. FINALLY, DR. ADITI DESHPANDE WILL PRESENT HIS FINDINGS ON HYPER-ACUTE CHANGES IN BRAIN PHYSIOLOGY AFTER BLUNT HEAD IMPACTS IN PRECLINICAL AND CLINICAL MODELS. THE WORK PRESENTED BY THE PANEL SPEAKERS WILL PROMOTE DISCUSSION OF TECHNIQUES AND PERSPECTIVES IN NEUROSCIENCE AND BIOENGINEERING AIMED AT INCREASING CROSS-FUNCTIONAL COLLABORATION.

THURSDAY, FEBRUARY 1ST

PANEL
4:30 P.M. - 6:30 P.M.
IMPERIAL BALLROOM, FLOOR 4

DOPAMINERGIC SIGNALS FOR PREDICTIVE LEARNING AND FLEXIBLE BEHAVIOR

CHAIR: SEAN OSTLUND
PRESENTERS: KATE WASSUM, DAVID MARTIN, MIHAELA IORDANOVA, DAVID BORTZ

TO EFFECTIVELY PURSUE GOALS IN A COMPLEX AND DYNAMIC ENVIRONMENT, WE MUST ENCODE AND CONTINUOUSLY UPDATE INFORMATION ABOUT IMPORTANT PAVLOVIAN (STIMULUS-OUTCOME) AND INSTRUMENTAL (ACTION-OUTCOME) CONTINGENCIES THAT WE ENCOUNTER AND USE THIS KNOWLEDGE TO FLEXIBLY MODIFY OUR ACTIONS. MIDBRAIN DOPAMINE NEURONS ARE STRONGLY IMPLICATED IN BOTH PREDICTIVE LEARNING AND BEHAVIORAL FLEXIBILITY. HOWEVER, MUCH REMAINS UNKNOWN ABOUT WHAT THE DOPAMINE SYSTEM ENCODES DURING SUCH LEARNING AND HOW THIS INFORMATION IS SHAPED BY AND RELAYED WITHIN DISTRIBUTED NEURAL CIRCUITS TO SUPPORT ADAPTIVE BEHAVIOR. PANELISTS WILL DISCUSS RECENT RESEARCH ADVANCING KNOWLEDGE IN THESE AREAS. KATE WASSUM (UCLA) WILL DISCUSS HOW DOPAMINE RELEASE IN THE BASOLATERAL AMYGDALA DRIVES ENCODING OF IDENTITY-SPECIFIC CUE-REWARD MEMORIES. DAVID MARTIN (UNIVERSITY OF MARYLAND) WILL PRESENT RECENT WORK EXAMINING HOW 5-HT2A RECEPTOR STIMULATION ALTERS REWARD PREDICTION ERROR SIGNALING BY NUCLEUS ACCUMBENS DOPAMINE RELEASE. MIHAELA IORDANOVA (CONCORDIA UNIVERSITY) WILL DISCUSS THE ROLE OF THE VENTRAL TEGMENTAL AREA DOPAMINE SYSTEM IN SIGNALING VALENCE PREDICTION ERRORS. DAVID BORTZ (UNIVERSITY OF PITTSBURGH) WILL DISCUSS HOW DORSAL STRIATAL DOPAMINE ENCODES OUTCOMES AND BEHAVIOR DURING WELL-LEARNED AND FLEXIBLE DISCRIMINATION TASKS AND HOW THE MEDIAL PREFRONTAL CORTEX AND MEDIAL SEPTUM INTERACT TO REGULATE THIS ACTIVITY. COLLECTIVELY, WE BELIEVE THIS PANEL WILL STIMULATE DISCUSSION AND NEW IDEAS ON HOW THE MIDBRAIN DOPAMINE SYSTEM CONTRIBUTES TO PREDICTIVE LEARNING AND FLEXIBLE BEHAVIOR.

THURSDAY, FEBRUARY 1ST

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 6-8, FLOOR 2

NEW INSIGHT INTO NEUROPEPTIDE DYNAMICS - FROM INDIVIDUAL EXOCYTOSIS EVENTS TO VOLUME TRANSMISSION

CHAIRS: LESLIE SOMBERS, ELYSSA MARGOLIS
PRESENTERS: LESLIE SOMBERS, PAUL SLESINGER, STEPHEN WEBER, MARTA SODEN

NEUROPEPTIDES WORK WITH NEURO- AND GLIO- TRANSMITTERS TO MODULATE CENTRAL AND PERIPHERAL NERVOUS SYSTEM ACTIVITY. WHILE A GREAT DEAL OF RESEARCH HAS FOCUSED ON HOW NEUROPEPTIDE RECEPTORS AFFECT NEURAL ACTIVITY, MUCH LESS IS UNDERSTOOD OF IN TERMS OF PEPTIDE DYNAMICS. NEUROPEPTIDES ARE GENERALLY CONCEPTUALIZED AS HAVING A BROAD ANATOMICAL INFLUENCE, DIFFUSING LONG DISTANCES FROM RELEASE SITES THUS ACTING VIA VOLUME TRANSMISSION. HOWEVER, MANY UNKNOWNS PERSIST INCLUDING THE FACTORS THAT LIMIT NEUROPEPTIDE DIFFUSION AND HOW NEUROPEPTIDE RELEASE AND DURATION OF ACTION COMPARE TO THOSE OF FAST-ACTING NEUROTRANSMITTERS. THIS PANEL WILL EXPLORE NEW FINDINGS ON FUNDAMENTAL ASPECTS OF NEUROPEPTIDE SIGNALING INCLUDING HOW TO DRIVE RELEASE, FACTORS LIMITING THE SPHERE OF INFLUENCE IN THE EXTRACELLULAR SPACE, AND THE SPATIOTEMPORAL DYNAMICS OF NEUROPEPTIDE SIGNALING. MARGOLIS WILL BRIEFLY PROVIDE CONTEXT FOR THE SESSION. SOMBERS WILL DISCUSS AMPEROMETRIC MEASUREMENTS OF INDIVIDUAL EXOCYTOSIS EVENTS RECORDED AT SINGLE CELLS, AND KEY DIFFERENCES OBSERVED BETWEEN THE KINETICS OF CATECHOLAMINES AND OPIOID NEUROPEPTIDES RELEASED FROM THE SAME POPULATION OF VESICLES. SLESINGER WILL DESCRIBE OPTICAL MEASUREMENTS USING PLASMONIC NANOVESICLES AND CELL-BASED NEUROTRANSMITTER FLUORESCENT ENGINEERED REPORTER (CNIFER), OR PACE, TO ESTIMATE THE SPATIOTEMPORAL SCALE OF SOMATOSTATIN-14 TRANSMISSION. WEBER WILL DESCRIBE A SMALL MICROFLUIDIC DEVICE THAT ELECTROOSMOTICALLY INFUSES PEPTIDES INTO, THROUGH, AND OUT OF THE TISSUE TO INFER EXTRACELLULAR PEPTIDASE ACTIVITY. FINALLY, SODEN WILL DISCUSS A CRISPR-BASED APPROACH TO ISOLATE PEPTIDE AND FAST NEUROTRANSMITTER FUNCTION IN CIRCUITS CONVERGING ONTO DOPAMINE NEURONS IN THE VENTRAL TEGMENTAL AREA. TOGETHER, THESE TALKS WILL PROVIDE NEW INSIGHT INTO OPEN QUESTIONS AND FUTURE DIRECTIONS IN THE FIELD.

THURSDAY, FEBRUARY 1ST

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 9-10, FLOOR 2

DECIPHERING THE NEURAL CODE FOR HIGH-LEVEL VISION

CHAIRS: MARK ELDRIDGE, BARRY RICHMOND
PRESENTERS: CHRIS BAKER, HAMIDREZA RAMEZANPOUR, MARK ELDRIDGE

HUMANS AND RHESUS MONKEYS SHARE MANY SIMILARITIES IN THE STRUCTURE OF THEIR VISUAL SYSTEMS. IN BOTH SPECIES, THE PERCEPTION, RECOGNITION, AND CATEGORIZATION OF OBJECTS, ANIMALS, AND PLACES ARE KNOWN TO BE SUPPORTED BY REGIONS OF THE INFERIOR TEMPORAL LOBE. THIS COLLECTION OF TALKS EMPLOYS IMAGING (IN HUMANS AND MONKEYS) AND MULTI-CHANNEL SINGLE-UNIT RECORDINGS (IN MONKEYS) TO PROVIDE INSIGHT INTO THE NEURAL MECHANISMS SUPPORTING HIGH-LEVEL VISION.
DR. CHRIS BAKER (NIMH, USA) WILL PRESENT IMAGING DATA IN HUMANS SHOWING THE NEURAL CORRELATES AND TIME COURSE OF REPRESENTATIONS OF THE PERCEPTION AND RECOGNITION OF FAMILIAR VS UNFAMILIAR STIMULI.
DR. HAMIDREZA RAMEZANPOUR (YORK UNIVERSITY, CANADA) HAS RECORDED MULTI-CHANNEL SINGLE-UNIT ACTIVITY FROM MONKEY INFEROTEMPORAL CORTEX AND USES ARTIFICIAL NEURAL NETWORKS TO DECODE HOW CATEGORY INFORMATION IS REPRESENTED DURING LEARNING.
DR. MARK ELDRIDGE (NIMH, USA) HAS RECORDED FROM MONKEY INFEROTEMPORAL CORTEX AND DOWNSTREAM REGIONS SIMULTANEOUSLY, AND WILL PROVIDE INSIGHT INTO THE NEURAL CODING OF CATEGORY LEARNING AND NOVEL OBJECT RECOGNITION.

THURSDAY, FEBRUARY 1ST

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 14, FLOOR 1

IN VIVO BRAIN RECORDINGS REVEAL CALORIE DENSE FOOD ITEMS RESHAPE REWARD CIRCUITRY DRIVING MALADAPTIVE BEHAVIOR

CHAIRS: RICHARD O'CONNOR, BRIDGET MATIKAINEN-ANKNEY
PRESENTERS: RICHARD O'CONNOR, BRIDGET MATIKAINEN-ANKNEY, MATT HOWE, KYLE BURGER

DYSREGULATED REWARD PROCESSING AND MALADAPTIVE BEHAVIORS ARE COMMON FEATURES OF MANY NEUROPSYCHIATRIC DISORDERS. RECENT TECHNOLOGICAL ADVANCES NOW ALLOW FOR HIGH-RESOLUTION IN VIVO RECORDING OF BRAIN FUNCTION IN CLINICAL AND PRECLINICAL SETTINGS DURING BEHAVIORAL TASKS RELEVANT TO MOTIVATED BEHAVIORS. THIS HAS FACILITATED RAPID PROGRESS IN OUR UNDERSTANDING OF THE NEURONAL ACTIVITY THAT GUIDE SUCH BEHAVIORS LEADING TO A COMPELLING BODY OF DATA SHOWING CONSUMPTION OF CALORIE-RICH, HIGHLY PALATABLE FOODS IMPART LASTING EFFECTS ON BRAIN REWARD CIRCUITS. TARGETING THESE DYSREGULATED SIGNALING PATHWAYS MAY BE A THERAPEUTIC APPROACH TO REVERSE MOTIVATIONAL ABNORMALITIES ASSOCIATED WITH A VARIETY OF NEUROPSYCHIATRIC DISORDERS, INCLUDING FEEDING DISORDERS. THIS PANEL WILL SHARE NEW RESEARCH ON THE NEUROADAPTATIONS IN THE BRAIN'S STRIATAL CIRCUITRY THAT ARE INDUCED BY PALATABLE FOOD, AND THE ROLE OF THESE CHANGES IN THE DEVELOPMENT OF A VARIETY OF MALADAPTIVE BEHAVIORS.
DR. RICHARD O'CONNOR (ICAHN SCHOOL OF MEDICINE) WILL PRESENT WORK HIGHLIGHTING HOW STRIATONIGRAL NEURONAL DYNAMICS DRIVE BEHAVIORAL ADAPTATIONS ASSOCIATED WITH CHRONIC OBESITY.
DR. BRIDGET MATIKAINEN-ANKNEY (RUTGERS UNIVERSITY) WILL EXPLORE HOW DIET-INDUCED OBESITY IMPACTS ENDOGENOUS OPIOID RECEPTOR-MEDIATED LONG TERM PLASTICITY MECHANISMS IN THE NUCLEUS ACCUMBENS.
DR. MATT HOWE (VIRGINIA TECH) WILL PRESENT DATA FROM INVASIVE NEURAL RECORDINGS IN HUMANS MEASURING MONOAMINE DYNAMICS IN RESPONSE TO SUGAR AND FAT.
DR. KYLE BURGER (UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL) WILL SHARE DATA COLLECTED USING FUNCTIONAL MRI IN HUMANS DEMONSTRATING HOW REGULAR CONSUMPTION OF SUGAR DRIVES ALTERATIONS IN STRIATAL RESPONSE TO ASSOCIATED SUGAR CUES AND INCREASES BEHAVIORAL MOTIVATION TO CONSUME SUGAR THUS LEADING TO PATTERNS THAT PUTATIVELY INCREASE THE RISK FOR OVEREATING THAT OCCUR PRIOR TO WEIGHT GAIN.

THURSDAY, FEBRUARY 1ST

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 15-16, FLOOR 1

BREAKING NEW TRAILS: NEW MOLECULAR AND VIRAL TECHNOLOGIES FOR SYSTEMS NEUROSCIENCE

CHAIR: OFER YIZHAR
PRESENTERS: OFER YIZHAR, CHRISTINA KIM, LIEF FENNO, RAAJARAM GOWRISHANKAR

PRECISION APPROACHES FOR OBSERVING AND CONTROLLING THE ACTIVITY OF DEFINED CNS CELL TYPES HAVE ENABLED DRAMATIC PROGRESS IN UNDERSTANDING THE STRUCTURE-FUNCTION RELATIONSHIP OF THE BRAIN. AMONG THESE, MOLECULAR AND VIRAL TECHNIQUES ENABLE AN UNPRECEDENTED DEGREE OF TEMPORAL AND GENETIC SPECIFICITY. PANELISTS WILL DISCUSS NEXT-GENERATION APPROACHES FOR NEUROSCIENCE, INCLUDING OPTOGENETIC TOOLS FOR EFFECTIVE TERMINAL SILENCING, ACTIVITY-TARGETED CELL ACCESS, COMPLEX VIRAL PAYLOAD DELIVERY, AND MULTIPLEXED SMALL MOLECULE FLUORESCENCE READ-OUT. THESE ADDRESS PREVIOUS LIMITATIONS IN THE MOLECULAR TOOLSET AND WILL FIND DIVERSE USE CASES ACROSS NEUROSCIENCE. OFER YIZHAR WILL DISCUSS DEVELOPMENT OF OPTICALLY-ACTIVATED, HIGH-POTENCY GPCRS FOR EFFECTIVE SYNAPTIC TERMINAL SILENCING, IN AWAKE BEHAVING ANIMALS. THESE ENABLE A DEGREE OF CONTROL BEYOND EXISTING OPTOGENETIC TOOLS BY LEVERAGING ENDOGENOUS SYNAPTIC MACHINERY TO INTERRUPT SYNAPTIC VESICLE FUSION. TINA KIM WILL DISCUSS DEVELOPMENT OF SYSTEMS FOR THE TARGETED MANIPULATION OF NEURONS DEFINED BY ANATOMY, RECENT ACTIVITY, AND TIME. SHE HAS PIONEERED THIS MULTIPLEXED NEURAL TARGETING APPROACH TO ENABLE TRANSCRIPTOMIC AND FUNCTIONAL ANALYSIS OF NEURONS IDENTIFIED AS ACTIVE DURING DISCRETE PERIODS OF BEHAVIORAL ACTIVITY. LIEF FENNO WILL DISCUSS DEVELOPMENT OF ENZYMATIC MANIPULATION OF AAV PAYLOADS TO ACHIEVE UNPRECEDENTED RESOLUTION IN THE EXPRESSION OF COMPLEX MOLECULAR PAYLOADS. THESE BRIDGE THE GAP BETWEEN TRANSCRIPTOMICS AND MOLECULAR NEUROSCIENCE TOOLS AND HAVE DRIVEN PROGRESS IN UNDERSTANDING THE ROLE OF MULTIPLY-DEFINED NEURAL SUBTYPES. RAAJ GOWRISHANKAR WILL DISCUSS IMPLEMENTATION OF MULTI-SPECTRAL, ALL-OPTICAL APPROACHES USING COMBINED OPTOGENETIC/NOVEL OPIOID BIOSENSORS TO CHARACTERIZE NEUROPEPTIDE INFLUENCE OF CIRCUIT ACTIVITY. THIS PANEL PROVIDES AN OPPORTUNITY TO DIRECTLY CONNECT WITH LABORATORIES DEVELOPING USEFUL REAGENTS, FOSTER COLLABORATION, AND DISCUSS EXPERIMENTAL DESIGNS OF INTEREST TO THE AUDIENCE.

THURSDAY, FEBRUARY 1ST

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 17, FLOOR 1

APRÉS-SEE: VISUALIZING DRUG EFFECTS WITH IN VIVO IMAGING TO ADVANCE THERAPEUTIC DEVELOPMENT

CHAIRS: BENJAMIN HALL, JONES PARKER
PRESENTERS: JONES PARKER, OLIVER MILLER, PAOLO BOTTA, LISA BEUTLER

RECENT ADVANCES IN, IN VIVO IMAGING THAT COMBINE FLUORESCENT BIOSENSORS WITH USER-FRIENDLY MEASUREMENT APPROACHES SUCH AS FIBER PHOTOMETRY AND MINIATURE MICROSCOPES HAVE BEEN EXPEDIENTLY ADOPTED BY BASIC RESEARCHERS. WHILE EARLY STAGES OF DRUG DEVELOPMENT REGULARLY RELY ON OPTICAL APPROACHES (E.G., FLUORESCENCE-BASED HIGH-THROUGHPUT SCREENING), ADOPTING NEW IN VIVO TECHNOLOGIES REQUIRES SCRUTINY, INCLUDING APPLICATION OF PHARMACOKINETIC AND PHARMACODYNAMIC UNDERSTANDING OF KNOWN DRUGS TO ENSURE PREDICTIVE VALUE OF SUCH TECHNIQUES.
A PANEL OF EXPERTS SPANNING BASIC RESEARCH AND PHARMACEUTICAL DEVELOPMENT WILL HIGHLIGHT THEIR EFFORTS IN THIS AREA. (1) DR. JONES PARKER (NORTHWESTERN UNIVERSITY) WILL DESCRIBE WORK ADDRESSING THE RIFT BETWEEN BEHAVIORAL READOUTS OF ANTIPSYCHOTIC DRUG EFFICACY AND THOSE OBTAINED BY IMAGING NEURAL SIGNALING IN THE DOPAMINE-ENRICHED STRIATUM. (2) DR. OLIVER MILLER (INSCOPIX, INC.) WILL DETAIL EFFORTS TO PARSE MAINSTAY, CANDIDATE, AND CLINICALLY FAILED ANTIDEPRESSANTS USING MINIATURE MICROSCOPES TO IMAGE CALCIUM AND NEUROTRANSMITTER DYNAMICS IN DEPRESSION-RELATED NEURAL CIRCUITS. (3) DR. PAOLO BOTTA (LUNDBECK, A/S) WILL DESCRIBE THE DEVELOPMENT OF A FUNCTIONAL MODEL TO PRECLINICALLY VALIDATE MIGRAINE TREATMENT CANDIDATES BASED ON IMAGING NEURONAL DYNAMICS AND VASCULATURE IN FREELY BEHAVING MICE BOTH WITH MINIATURE MICROSCOPES AND IN ANESTHETIZED ANIMALS USING FUNCTIONAL ULTRASOUND. (4) DR. LISA BEUTLER (NORTHWESTERN UNIVERSITY) WILL DISCUSS HER WORK USING FIBER PHOTOMETRY TO DETERMINE HOW OBESITY AND SUCCESSFUL ANTI-OBESITY MEDICATIONS ALTER CALCIUM ACTIVITY IN HYPOTHALAMIC FEEDING CIRCUITS IN RESPONSE TO GUT-BRAIN COMMUNICATION. DR BENJAMIN HALL WILL GIVE INTRODUCTORY REMARKS AND MODERATE DISCUSSION.
THE PANEL HIGHLIGHTS A GROWING AREA OF TRANSLATIONAL RESEARCH THAT BLENDS BASIC SCIENCE AND DRUG DEVELOPMENT. THE WORK PRESENTED WILL UNDERSCORE THE POTENTIAL IMPACT OF THESE APPROACHES IN THE DEVELOPMENT OF NEW THERAPEUTICS.

THURSDAY, FEBRUARY 1ST

PANEL
4:30 P.M. - 6:30 P.M.
PEAK II, FLOOR 2

EXPECTATIONS, CONTEXTUAL AND PLACEBO EFFECTS: BRAIN MECHANISMS

CHAIR: LUANA COLLOCA
PRESENTERS: PHILIP CORLETT, MATTHEW BANGHART, LIANE SCHMIDT, LUANA COLLOCA

EXPECTATIONS, CONTEXTUAL AND PLACEBO EFFECTS INFLUENCE THE COURSE OF MANY MEDICAL CONDITIONS, IMPACTING KEY MEASURES, INCLUDING LONG-TERM MORTALITY AND TREATMENT OUTCOMES. EXPECTATIONS ACCOUNT FOR A SIGNIFICANT PROPORTION OF THE OVERALL THERAPEUTIC EFFECT OF SOME PHARMACOLOGICAL TREATMENTS: UP TO 50% OF THE EFFICACY OF PAIN THERAPEUTICS MAY BE EXPECTATION DRIVEN (PLACEBO EFFECT). EXPECTATIONS ARE PARTICULARLY IMPORTANT IN RELATION TO ANTIDEPRESSANTS, ANTIPSYCHOTICS, AND PAIN THERAPEUTICS.
COLLOCA WILL INTRODUCE THE PANEL AND SPEAKERS WITH A FOCUS ON BRAIN MECHANISMS OF EXPECTATIONS ACROSS DISEASES.
CORLETT WILL PRESENT A NEW BRAIN IMAGING APPROACHES HE USES TO INTERPRET PSYCHOSES AND EXPECTATION. HE WILL EXPLAIN HOW MACHINE-LEARNING BASED PREDICTIVE MODELS CAN IMPROVE IDENTIFICATION OF CLINICAL SYMPTOMS AND ULTIMATELY DIAGNOSIS AND TREATMENT.
BANGHART WILL DISCUSS BRAIN CORTICAL AND SUBCORTICAL PATHWAYS THAT COORDINATE A FORM OF CONDITIONED PLACEBO ANTINOCICEPTION IN MICE INVOLVING EXPECTATIONS ABOUT PAIN. COLLOCA WILL OUTLINE THE STATE-OF-THE-ART OF PSYCHOLOGICAL AND NEUROBIOLOGICAL UNDERPINNINGS OF PLACEBO EFFECTS, FOCUSING ON POTENTIAL PREDICTORS OF THE PLACEBO EFFECTS, INCLUDING NEW PROMISING PHENOTYPES.
SCHMIDT WILL DESCRIBE HOW EXPECTATIONS ABOUT HUNGER AFFECT HUNGER SENSATIONS, HUNGER ADDRESSING DIETARY DECISION-MAKING, AND HOW THE BRAIN'S REWARD SYSTEM COMPUTES FOOD PREFERENCES UNDER HUNGER EXPECTATIONS. SHE WILL FURTHER LINK THIS WORK TO REAL WORLD PROBLEMS SUCH AS OBESITY AND THE COMPLEX INTERACTION BETWEEN THE BRAIN'S REWARD SYSTEM AND WEIGHT CHANGE.
COLLOCA WILL RESULTS FROM A RECENT STUDY SHOWING THAT ON A TIMESCALE OF MINUTES, ANTIDEPRESSANT PLACEBO EFFECTS THAT ARE MAINTAINED BY POSITIVE FEEDBACK LOOPS BETWEEN EXPECTANCIES AND MOOD IMPROVEMENT.

THURSDAY, FEBRUARY 1ST

PANEL
4:30 P.M. - 6:30 P.M.
PEAK 12, FLOOR 2

EMERGING BRAIN METABOLISM PARADIGMS IN MOOD DISORDERS: BRAIN TRANSCRIPTOMICS, DIURNAL EXPRESSION RHYTHMS, AND RELATIONSHIP TO COGNITION

CHAIRS: HARRY PANTAZOPOULOS, RAMMOHAN SHUKLA
PRESENTERS: KATERYNA MAKSYUTYNSKA, HARRY PANTAZOPOULOS, BARBARA GISABELLA, RAMMOHAN SHUKLA

METABOLIC DYSFUNCTION IS HIGHLY COMORBID WITH PSYCHIATRIC DISORDERS INCLUDING BIPOLAR DISORDER (BD), MAJOR DEPRESSIVE DISORDER (MDD) AND SCHIZOPHRENIA (SZ). EMERGING EVIDENCE SUGGESTS METABOLIC DYSFUNCTION MAY CONTRIBUTE TO BRAIN METABOLIC ALTERATIONS THAT UNDERLIE DISEASE SYMPTOMS AND MAY BE A PROMISING AVENUE FOR THERAPEUTIC STRATEGIES. DR. MAKSYUTYNSKA WILL DISCUSS RESULTS FROM A META-ANALYSIS DEMONSTRATING THAT METABOLIC DYSREGULATION IS ASSOCIATED WITH NEUROCOGNITIVE DYSFUNCTION. IN PARTICULAR, HE WILL PRESENT EVIDENCE FOR TYPE-2 DIABETES, INSULIN RESISTANCE, AND BODY MASS INDEX WITH COGNITIVE PERFORMANCE IN SUBJECTS WITH MOOD DISORDERS. DR. PANTAZOPOULOS WILL PRESENT TRANSCRIPTOMIC DATA DEMONSTRATING DIFFERENTIAL CHANGES IN METABOLIC PATHWAYS IN THE AMYGDALA OF SUBJECTS WITH BD, SZ, AND MDD. HE WILL ALSO DISCUSS PERTURBAGEN ANALYSIS RESULTS IDENTIFYING POTENTIAL THERAPEUTIC TARGETS FOR AMYGDALA METABOLIC ALTERATIONS IN THESE DISORDERS. DR. GISABELLA WILL PRESENT THE FIRST EVIDENCE FOR DIFFERENTIALLY ALTERED DIURNAL MOLECULAR RHYTHMS IN THE AMYGDALA OF SUBJECTS WITH BD, MDD, AND SZ. IN PARTICULAR, SHE WILL DESCRIBE EVIDENCE FOR ENHANCED MOLECULAR DIURNAL RHYTHMS AND ALTERED PHASE IN SUBJECTS WITH BD AND LOSS OF RHYTHMICITY IN SUBJECTS WITH MDD AND SZ. DR. SHUKLA WILL PRESENT EVIDENCE FROM A COMPARATIVE ANALYSIS OF MOLECULAR DATA FROM DIFFERENT EXPERIMENTAL SYSTEMS OF CHRONIC STRESS AND MDD IMPLICATING RIBOSOMAL PROTEIN GENES IN DEPRESSION. HE WILL DESCRIBE DATA SUGGESTING THAT STRESS INDUCED CHANGES IN RIBOSOMAL PROTEIN GENES MODIFY RIBOSOMAL STOICHIOMETRY, WHICH MAY CONTRIBUTE TO BRAIN METABOLIC DYSFUNCTION IN MDD.

PRESENTER DISCLOSURES

DISCLOSURES

Alilain, Warren:
NervGen Pharma: Contracted Research

Bainbridge, Jacci:
Biopharmaresearch: Grant

Berglund, Andy:
Dyne Therapeutics: Honoraria. Kate Therapeutics: Consultant. Juvena Therapeutics: Consultant. DE Shaw: Consultant. PepGen: Contracted Research. Syros: Contracted Research. Vertex: Contracted Research. Sanofi: Consultant. Mubadala Capital: Consultant. Agios: Contracted Research. Entrada: Consultant

Beutler, Lisa:
Eli Lilly: Stock / Equity - Publicly Traded Company

Boncyk, Christina:
Sedana Medical: Consultant

Bonn-Miller, Marcel:
Canopy Growth Corporation: Employee. Charlotte's Web: Employee. DeFloria, LLC: Board Member

Bredt, David:
Rapport Therapeutics: Founder, Board Member, Employee

Budney, Alan:
Canopy Growth: Advisory Board. Indivior: Consultant

Burdick, Katherine:
Merck: Advisory Board

Carr, Gregory:
LongTermGevity, Inc.: Advisory Board, Stock/Equity â“ Privately Held Company

Chen, Robert:
Abbvie: Consultant. Merz: Consultant. Ipsen: Consultant. Attune Neuroscience: Consultant

Cooper, Ziva:
True Terpenes: Other Financial or Material Support. Storz and Bickel: Other Financial or Material Support

Corlett, Philip:
Tetricus Labs: Board Member, Founder

Dougherty, Darin:
Medtronic: Contracted Research, Honoraria. Sage: Advisory Board. Boehringer-Ingelheim: Advisory Board. Innercosmos: Stock/Equity â“ Privately Held Company. Neurable: Stock/Equity â“ Privately Held Company. Intrinsic Powers: Stock/Equity â“ Privately Held Company

Finan, Patrick:
Ninnion Therapeutics: Advisory Board

Fricker, Lloyd:
Summit Pharma: Consultant. Spirify Pharma: Consultant

Garcia-Nafria, Javier:
Sosei Heptares Therapeutics: Contracted Research

Geoffroy, Cedric:
NeuroCreis: Founder. TanaTherapeutics: Founder

Hall, Benjamin:
H. Lundbeck A/S: Employee

Haney, Margaret:
Pleo Pharma: Advisory Board

Howe, Matt:
Takeda Pharmaceuticals: Consultant

Jaster, Alaina:
Terran Biosciences: Consultant

Kaye, Alfred:
Transcend Therapeutics: Contracted Research. Freedom Biosciences: Contracted Research

Land, Hunter:
Nalu Bioscience: Advisory Board. Alterola Biotech: Board Member

Lichtman, Aron:
Sea Pharmaceuticals LLC: Advisory Board

PRESENTER DISCLOSURES

DISCLOSURES

Malhotra, Anil:
Genomind, Inc: Consultant. Health Advances: Consultant. Iqvia Medtech: Consultant

Mantsch, John:
Promentis Pharmaceuticals: Founder

McElligott, Zoe:
Epicypher: Contracted Research

Miller, Oliver:
Inscopix: Employee

Napadow, Vitaly:
Cala Health: Consultant. Click Therapeutics: Consultant

Nichols, Charles:
2A Biosciences: Board Member, Founder, Other Financial or Material Support. NeuroPharmaka: Advisory Board. Double Blind: Advisory Board. Palo Santo: Advisory Board. LSU: Royalties

O'Donnell, Patricio:
Sage Therapeutics: Employee

Parker, Jones:
Karuna Therapeutics: Honoraria

Pekna, Marcela:
Merck KGaA: Consultant. Argenx: Advisory Board

Peters, Jamie:
Delix Therapeutics: Consultant

Raji, Cyrus:
CoreTechs: Consultant. Neurevolution LLC: Consultant. Voxelwise LLC: Consultant. Eli Lilly: Consultant

Rasband, Matthew:
Pipeline Therapeutics: Consultant

Seibyl, John:
Biogen, AbbVie, Life Molecular Imaging, GE Healthcare, LikeMinds, XingImaging, Invicro: Consultant. Realm IDX, XingImaging: Stock/Equity â“ Privately Held Company

Siddiqi, Shan:
Magnus Medical: Consultant. Brainsway: Stock / Equity - Publicly Traded Company. Neuronetics: Grant

Silverman, Daniel:
Syntermed: Other Financial or Material Support

Sinha, Rajita:
Aelis Farma: Contracted Research. Aptinyx Inc: Other Financial or Material Support. CT Pharma: Other Financial or Material Support. Menda Health: Advisory Board

Snyder, Gretchen:
Intra-Cellular Therapies Inc: Employee

Stacpoole, Sybil:
GSK: Stock / Equity - Publicly Traded Company. Astrazenica: Stock / Equity - Publicly Traded Company

Swanson, Thomas:
Sativa Science: Founder

Thomas, Brian:
Zynerba Pharmaceuticals: Consultant. Syqe Medical: Consultant. Biopharmaceutical Research Corporation: Consultant. Nalu Bio: Advisory Board. Cronos Group: Consultant. Bright Green: Advisory Board

Todd, Peter:
Denali Therapeutics: Consultant. Ionis Pharmaceuticals: Patent. UpToDate: Royalties

Tunbridge, Elizabeth:
Boehringer Ingelheim: Employee, Grant, Advisory Board. Biogen: Grant. J and J Innovations: Grant

Vandrey, Ryan:
Charlotte's Web: Consultant. Miraìa Pharmaceuticals: Advisory Board. Jazz Pharmaceuticals: Honoraria. Syqe Medical Ltd: Advisory Board. WebMD: Honoraria

PRESENTER DISCLOSURES

Vonder Haar, Cole:
Turner Scientific: Consultant

Wang, Eric:
Kate Therapeutics: Advisory Board, Consultant, Founder, Contracted Research. Design Therapeutics: Consultant. Entrada Therapeutics: Contracted Research, Contracted Research. Fluxion: Royalties

Weerts, Elise:
MyMD Pharmaceuticals Inc,: Contracted Research. MIRA Pharmaceuticals Inc: Contracted Research

Wenthur, Cody:
Psilera Inc: Contracted Research. Promega: Honoraria

THE FOLLOWING PRESENTERS HAD NOTHING TO DISCLOSE

Ackerman, Sarah
Adkins, DeAnna
Allen, Nicola
Alonso-Caraballo, Yanaira
Alvarez, Veronica
Amini, Rouzbeh
Apicella, Alfonso junior
Argyelan, Miklos
Averitt, Dayna
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Choudhry, Mashkoor
Chowdhury, Kawsar
Chu, Hong-yuan
Chung, Shinjae
Cohen, Akiva
Colloca, Luana
Corbit, Laura
Cox, Julia
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Dalva, Matthew
De Wit, Joris
Deleidi, Michela
Devilbiss, David
Diaz, Elva
Diba, Kamran

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