
The Sixth Annual Virtual
Rutgers Brain Health Institute
Symposium
Friday, Nov 19th & 20th 2020

The Sixth Annual Virtual BHI Symposium

Thurs Nov 19 & Fri Nov 20, 2020

Thurs Nov 19, 2020 Zoom link: https://rutgers.zoom.us/j/95188428981?pwd=Zm9GcmZrUkhUVWdxeVBKMmNjVTVoZz09

Meeting ID: 951 8842 8981; Passcode: bhi2020

Date & Time	Speaker	Title of Talk
Thurs, Nov 19 (11.30 AM – 12.45 PM)	Gary Aston-Jones, PhD *Director BHI* *Distinguished Professor of Psychiatry, RWJMS, RBHS* *Charlotte and Murray Strongwater Chair in Neuroscience & Brain Health*	*Welcome, BHI Overview & Town Hall To Discuss BHI Five Year Review*
Thurs, Nov 19 (1.00 PM – 1.20 PM)	Wayne Fisher, PhD *Director RUCARES* *Professor of Pediatrics, RWJMS, RBHS* *Henry Rutgers Endowed Chair* *BHI Core Faculty*	*Integrating Research And Practice In The Assessment And Treatment Of Autism Spectrum Disorders*
Thurs, Nov 19 (1.25 PM – 1.45 PM)	Cathleen Piazza, PhD *Director Pediatric Feeding Disorders Program at CSH* *Professor of Psychology, GSAPP, Rutgers-New Brunswick* *BHI Core Faculty*	*Integrating Research And Practice: An Intervention For Change-Resistant Behavior In Children With Autism As An Exemplar*
Thurs, Nov 19 (1.50 PM – 2.10 PM)	Miriam Rosenberg-Lee, PhD *Assistant Professor of Psychology, SASN, Rutgers-Newark*	*The Neural Basis Of Cognitive Strengths In Autism*
Thurs, Nov 19 (2.15 PM – 2.30 PM)	Zoom Break	Zoom Break
Thurs, Nov 19 (2.30 PM – 2.50 PM)	Emanuel DiCicco-Bloom, MD *Professor of Neuroscience & Cell Biology, RWJMS & CHINJ, RBHS*	*Defects In mTOR Signaling Mediate Common Neurite And Cell Migration Defects In Both Idiopathic And 16p11.2 Autism Neural Precursor Cells*
Thurs, Nov 19 (2.55 PM – 3.15 PM)	Steven Levison, PhD *Professor of Pharmacology, Physiology & Neuroscience, NJMS, RBHS, Director, Laboratory For Regenerative Neurobiology*	*Modeling The Effects Of Prenatal Infections On Neural Development And Behavior*
Thurs, Nov 19 (3.20 PM – 3.40 PM)	Mladen Roko Rašin, MD, PhD *Associate Professor of Neuroscience & Cell Biology, RWJMS, RBHS*	*Making Sense Of mRNA Landscapes: Translation Control In Neurodevelopment*

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Date & Time	Speaker	Title of Talk
Thurs, Nov 19 (3.45 PM – 4.05 PM)	Benjamin Samuels, PhD *Assistant Professor of Psychology, SAS, Rutgers-New Brunswick*	*Neural Circuits Mediating The Behavioral Effects Of Chronic Stress And Antidepressants In Male And Female Mice*
Thurs, Nov 19 (4.10 PM – 4.30 PM)	Ozlem Gunal, MD, PhD *Assistant Professor of Psychiatry, NJMS, RBHS*	*Cyfip1 Mediates Addiction Relevant Phenotypes In Mice*
Thurs, Nov 19 (4.35 PM – 4.55 PM)	Todd Mowery, PhD *Assistant Professor of Otolaryngology—Head and Neck Surgery, RWJMS, RBHS and BHI Core Faculty*	*Neural Mechanisms That Support Learning In Circuits With Significant Cellular Deficits*
Thurs, Nov 19, 5.00 PM	End of Symposium Day 1	*Virtual Cocktail Hour*

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Fri, Nov 20, 2020 Zoom link: https://rutgers.zoom.us/j/92822180849?pwd=MnBJbGtJRXRqYiswOUs2akY1OGoxQT09

Meeting ID: 928 2218 0849; Passcode: bhi2020

Date & Time	Speaker	Title of Talk
Fri, Nov 20 (9.00 AM – 9.20 AM)	David H. Zald, PhD *Professor of Psychiatry, RWJMS, RBHS, Director CAHBIR, Henry Rutgers Term Chair,* *BHI Core Faculty*	*Neuroimaging Networks for Translational Neuroscience*
Fri, Nov 20 (9.25 AM – 9.45 AM)	Mauricio Delgado, PhD *Professor and Chair of Psychology SASN, Rutgers-Newark*	*Reward Processing in the Human Brain*
Fri, Nov 20 (9.50 AM – 10.10 AM)	Laleh Najafizadeh, PhD *Associate Professor of Electrical and Computer Engineering* *SOE, Rutgers-New Brunswick*	*Data-Driven Methods for Understanding the Dynamics of Brain Function*
Fri, Nov 20 (10.15 AM – 10.35 AM)	Rafiq Huda, PhD *Assistant Professor of Cell Biology & Neuroscience, SAS, Rutgers-New Brunswick*	*Coupling Of Prefrontal Cortical Activity To Arousal Predicts Alcohol Consumption*
Fri, Nov 20 (10.40 AM – 11.00 AM)	Zoom Break	*Zoom Break*
Fri, Nov 20 (11.05 AM – 11.25 AM)	Vanessa Routh, PhD *Professor of Pharmacology, Physiology and Neuroscience, NJMS, RBHS*	*Hypothalamic Glucose Sensing Neurons: Multiple Functions, One Goal*
Fri, Nov 20 (11.30 AM – 11.50 AM)	Ying-Xian Pan, MD, PhD *Professor of Anesthesiology, NJMS, RBHS* *BHI Core Faculty*	*Biased Signaling At Multiple Mu Opioid Receptors Generated By Alternative Splicing Of OPRM1 Gene*
Fri, Nov 20 (12 Noon – 1.00 PM) Keynote Speaker	Stan B. Floresco, PhD *Professor of Psychology and Director of Neural Circuits and Cognition Laboratory, University of British Columbia, Vancouver, Canada.*	*Prefrontal-Subcortical Circuits Underlying Risk/Reward Decision Making*

Break for Virtual Lunch till 2 PM

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Meeting ID: 928 2218 0849; Passcode: bhi2020

Date & Time	Speaker	Title of Talk
Fri, Nov 20 (2.00 PM – 2.20 PM)	Radek Dobrowolski, PhD *Associate Professor of Biological Sciences, SASN, Rutgers-Newark*	*Impaired Nuclear Calcium Signaling Attenuates CREB-Mediated Neuronal Clearance in Alzheimer's Disease*
Fri, Nov 20 (2.25 PM – 2.45 PM)	Hyung Jin Ahn, PhD *Assistant Professor of Pharmacology, Physiology and Neuroscience, NJMS, RBHS, BHI Core Faculty*	*Fibrinogen As A Key Player For Cerebral Amyloid Angiopathy-Associated Vascular Pathology*
Fri, Nov 20 (2.50 PM – 3.10 PM)	Max Tischfield, PhD *Assistant Professor of Cell Biology and Neuroscience, SAS, Rutgers-New Brunswick and CHINJ*	*Brain Drain: Development Of Meningeal Lymphatic Networks And The Glymphatic System In Craniofacial Disorders*
Fri, Nov 20 (3.15 PM – 3.35 PM)	Stella Elkabes, PhD *Professor of Neurosurgery, NJMS, RBHS*	*Modulation Of Immune And Non-Immune Functions Of Astrocytes Following Spinal Cord Injury: Role Of Toll-Like Receptor 9*
Fri, Nov 20 (3.45 PM – 5.30 PM)	Student/Post-doc Poster Session	*Live Presentation in Zoom Breakout Rooms*

The Sixth Annual Virtual BHI Symposium

Student & Post-doc Presentation

Fri Nov 20, 2020 (3.45 PM- 5.30 PM)

Fri, Nov 20, 2020 Zoom link: https://rutgers.zoom.us/j/97237587543?pwd=TmJnL0dLRzVLWDJOM01PTlQ0TU9jUT09

Meeting ID: 972 3758 7543; Passcode: bhi2020

Name of Presenter	Title of Presentation	Presentation & Judge Time	Mentor(s)
Alessandro Bortolami	*Differences between the KCNB1 machinery complex and its KCNB1-R312H mutant found in epilepsy*	3.45-3.55	Federico Sesti
Anna Schneider	*Does neuromodulation result in reduction of circuit variability at the single cell level?*	4.00-4.10	Farzan Nadim
Dina Popova	*Functional impact of KCNJ6 variants on alcohol use disorder phenotypes in iPSC-derived human neurons*	4.15-4.25	Ron Hart
Elena Forzisi	*MAPK -mediated proapoptotic signaling by K+ channel integrin complexes*	4.30-4.40	Federico Sesti
Jackie Saenz	*Synaptojanin1 regulates Dopamine transporter trafficking via the PIP2/PI3K pathway*	4.45-4.55	Pingyue Pan
Jiyai Zheng	*Alcohol exposure induces depressive- and anxiety-like behaviors and neuroinflammation in the habenular nucleus of rats*	5.00-5.10	Jiang-Hong Ye
Joshua Stamos	*Manipulation of glucose concentration in Lateral Hypothalamus affects motivation for sucrose pellets in a task dependent fashion*	5.15-5.25	Kevin Beck
Julianne Price	*From Neurocardiac Signaling to Cognitive Recovery: A randomized clinical trial in women receiving outpatient treatment for alcohol and substance use disorders*	3.45-3.55	Marsha Bates & Jennifer Buckman
Kaushanie Fernandopulle	*Orexin drives motivation for palatable food via actions at orexin-1 receptor on VTA dopamine neurons*	4.00-4.10	Morgan James
Kimberly Wiersielis	*Sex differences in cognitive processing and anxiety-like behavior after intermittent fasting in aged mice*	4.15-4.25	Troy Roepke

Madhuvika Murugan	*Adenosine kinase regulates status epilepticus induced neurogenesis*	4.30-4.40	Detlev Boison
Malte Gueth	*Evidence of human parahippocampal theta activity during goal-directed spatial navigation: A combined EEG-fMRI study*	4.45-4.55	Travis Baker
Marialaina Nissenbaum	*Maternal T-cell Activation and Postnatal Behavioral and Microglial Changes to Staphylococcal Enterotoxins*	5.00-5.10	Alexander Kusnecov
Matthew Rich	*DBS-like stimulation of the nucleus accumbens shell induces presynaptic depotentiation at inputs on D2DR- but not D1DR-containing MSNs*	5.15-5.25	R. Chris Pierce
Pamela Hirschberg	*Ventromedial hypothalamic (VMH) neuronal nitric oxide synthase (nNOS)- glucose inhibited (GI) neurons may mediate the effects of estrogen on brown adipose tissue thermogenesis and white adipose beiging*	3.45-3.55	Vanessa Routh
Rodrigo Pena	*Theta-band resonance in a neocortical circuit*	4.00-4.10	Horacio Rotstein
Ryan Staples	*Simulating multiple sources of surface alexia in a computational model of reading*	4.15-4.25	William Graves
Sean Smith	*Human Operant Evaluations of Treatment Relapse*	4.30-4.40	Brian Greer
Stephanie Garcia	*Role of ketohexokinase in fructose sensing in the brain*	4.45-4.55	Andrew Thomas & Vanessa Routh
Talia Planas--Fontánez	*The mGluR5 agonist CHPG enhances recovery in mice subjected to experimental autoimmune encephalomyelitis (EAE)*	5.00-5.10	Cheryl Dreyfus
Tho Lai	*Developmental Role of Adenosine Kinase in the Cerebellum*	5.15-5.25	Detlev Boison
Xinyi Li	*Obesity effects on sensory evoked locus coeruleus (LC) neural responses and morphine withdrawal in rats*	3.45-3.55	Nick Bello

Mission Statement

The goal of the Brain Health Institute (BHI) is to develop neuroscience at Rutgers to become a highly translational and internationally preeminent research enterprise. New tools are transforming neuroscience, and these afford an unprecedented opportunity to create new treatments for central nervous system disorders. Neuroscience has been identified by Rutgers University as one of five signature areas for future focus and development. As part of this strategic plan, the BHI was established to become an internationally recognized center for basic, translational, and clinical research into the biological bases of human brain function and dysfunction. The BHI is the home for the overall Rutgers neuroscience initiative, and is a growing interdisciplinary institute consisting of more than 270 principal investigators with neuroscience laboratories across various campuses of Rutgers University and Rutgers Biomedical and Health Sciences. By supporting and coordinating neuroscience across all campuses, the BHI will unite Rutgers University's dynamic and diverse neuroscience community toward common goals:

- To create research programs focused on the biological underpinnings of the central nervous system's function and dysfunction.
- To develop treatments for these disorders using novel neuroscience tools.
- To establish a rich neuroscience resource in New Jersey that educates the public, clinicians, faculty, and students, as well as state, national, and international health officials.

BHI Strategic Plan & Accomplishments

The development of neuroscience at Rutgers by BHI, based on current research strengths, is focused on four areas and associated disorders: *Neurodevelopment* (e.g. autism spectrum disorder and schizophrenia, Tourette's), *Neurodegeneration and Injury* (e.g. multiple sclerosis, Parkinson's disease, Alzheimer's disease, spinal cord and traumatic brain injury), *Cognitive and Sensory Neuroscience* (e.g. dementias, aging, pain, auditory disorders), and *Motivational and Affective Neuroscience* (e.g. addiction, eating disorders, obesity, depression, anxiety). Rutgers currently has numerous well-funded investigators in each of the four focus areas that study brain processes at the cellular, circuit or behavioral levels. Many Rutgers neuroscientists are focused on translating the basic science-driven discoveries into clinical therapies to treat various neurological and neuropsychiatric disorders. To further develop these four focus areas, and facilitate translational research, BHI will use an institutional perspective to help realize the full potential of neuroscience research across Rutgers. BHI will recruit new faculty to strengthen current gaps in each area, provide pilot grant funding to support collaborative research, increase the visibility of the Rutgers neuroscience programs by hosting exceptional seminar speakers, and foster collaboration by hosting workshops, inter-campus exchange seminars and an annual neuroscience symposium. BHI will develop new research initiatives in critical areas that need new research and therapeutic insights, including a new addiction research center, an Alzheimer's and dementia research center and a center for autism research, education and services (described below). The BHI will also create state-of-the-art research infrastructure such as human brain imaging center and computational cognitive neuropsychiatry center to support multi-investigator, translational research across the institution.

The Five New Centers Launched by BHI

The Rutgers Center for Autism Research, Education and Services (RUCARES): Survey reports from Federal agencies suggest that 1 in 59 children in the US is diagnosed with Autism Spectrum Disorder (ASD); the rates are ~1 in 34 in New Jersey. Given the high incidence of ASD in New Jersey and the autism research and treatment expertise available at Rutgers, a Center of Excellence in Autism Research at Rutgers is urgently needed. Rutgers has considerable strengths in basic, clinical and translational autism research, with over 50 principal investigators working to develop new autism treatments. Rutgers faculty and students also work closely with the autism community in NJ, providing educational intervention and support services through the Douglass Developmental Disabilities Center and the newly created Rutgers Center for Adult Autism Services, and developing policy and performing public outreach through the Boggs Center on Developmental Disabilities. The new RUCARES will be responsible for coordinating and fostering basic and clinical research focused on diagnosing, treating and supporting patients with ASD. The goal is to develop a world-class autism research

center engaged in cutting edge basic research to identify mechanisms and biomarkers, produce novel interventional behavioral therapies, and create new technologies and services to support both pediatric and adult ASD patient population. Dr. Wayne Fisher was recruited as the inaugural director of both the RUCARES at BHI and CSH-RUCARES, a clinical entity within RUCARES that is a partnership with Children's Specialized Hospital (CSH). Dr. Fisher, also holds a Henry Rutgers Endowed Chair in the Department of Pediatrics at RWJMS. He was the director of the Center for Autism Spectrum Disorders at the Munroe-Meyer Institute at the University of Nebraska Medical Center and, previously, served as executive director of the Neurobehavioral Programs at the Kennedy Krieger Institute at Johns Hopkins University School of Medicine and the Marcus Behavior Center at the Marcus Institute in Atlanta, where he built clinical-research programs in autism and developmental disabilities. Dr. Brian Greer, recruited by BHI as a faculty in the Department of Pediatrics in RWJMS, serves as the assistant director of CSH-RUCARES, overseeing the Severe Behavior Program. In addition, Dr. Cathleen Piazza will join Rutgers as a professor in the Graduate School of Applied and Professional Psychology (GSAPP) and as a core member of the BHI. She will be the director of the Pediatric Feeding Disorders Program at CSH. As a world-renowned expert in pediatric feeding disorders, she will also join the professional teams in the small bowel/liver transplant and intestinal rehabilitation programs at CSH. The CSH-RUCARES and PFD programs are located at 888 Easton Avenue, Somerset, NJ and begins providing clinical services this month.

The Rutgers Center for Advanced Human Brain Imaging Research (CAHBIR): Advances in imaging technology now allow neuroscientists to non-invasively study structure, function and dynamical properties of the human brain. Using magnetic resonance imaging (MRI) methods neuroscientists are beginning to understand how brain structure and function are altered in disorders such as autism, schizophrenia, addiction, anxiety and depression, brain injury, neurodegeneration etc. This new knowledge is leading to the development of imaging biomarkers not only for diagnosis but also to determine efficacy and progress of treatments of various neurological and neuropsychiatric disorders. Rutgers neuroscientists have access to a diverse patient population and the expertise to carry out cutting edge analysis of brain functions and dysfunctions across the mental health spectrum. To fulfill this promise, BHI is developing a new brain imaging center (CAHBIR). The center will house a state-of-the-art 3Tesla (3T) Siemens MAGNETOM Prisma MRI instrument that will be dedicated for research. Dr. David H. Zald has been appointed as director of the new CAHBIR at the Rutgers Brain Health Institute. Dr. Zald is a professor and holds a Henry Rutgers Term Chair in the Department of Psychiatry in RWJMS. He was previously the Cornelius Vanderbilt Professor of Psychology and director of the Interdisciplinary Neuroscience Program for Undergraduates at Vanderbilt University. Dr. Zald joined Rutgers in May 2020. His responsibilities will include organizing the human brain imaging core facility to support research of faculty and trainees at Rutgers, RBHS, BHI, and the Center for Computational Cognitive Neuropsychiatry. Dr. Jeff Luci from University of Texas Austin was recently recruited as the Technical Director of CAHBIR. The new research Center, which will open in May 2020, will be located in the Staged Research Building on the Busch campus in Piscataway. The new research-dedicated 3T MRI scanner, which measures changes in blood flow, oxygen consumption and glucose use, will support research to non-invasively measure structure and activity of the human brain. The CAHBIR will help open new frontiers in human translational neuroscience at Rutgers. Pilot grant funding provided by the RU-New Brunswick Office of Vice Chancellor for Research and Innovation will help Rutgers New Brunswick faculty utilize the services offered by CAHBIR.

The Rutgers-Princeton Computational Cognitive Neuropsychiatry Center (CCNP): In spite of advances in genetics and basic neuroscience, our understanding of the brain mechanisms involved in psychiatric disorders remains in its infancy, seriously limiting our ability to develop desperately needed treatments for mental illness. Therefore, developing a better understanding of how the work that the brain does becomes disrupted, and how this leads to psychiatric problems, is now a major emphasis at the National Institute of Mental Health. It has been argued by leaders in the field that, at present, we do not fully understand the neurobiological bases for even a single symptom of a single psychiatric disorder. To address this important issue, researchers in the cognitive and brain sciences around the world forged interdisciplinary collaborations that resulted in the field of cognitive neuropsychiatry. Cognitive neuropsychiatry attempts to clarify the nature and patterns of brain activity that form the basis of specific symptoms, such as changes in mood, arousal, reality testing, threat perception, and other dimensions whose extremes represent mental illness. At the same time, great strides have occurred in computational neuroscience, a field of research that takes advantage of recent advances in computational methods and applies them to understanding brain function. Recently, a new approach has emerged from combining computational neuroscience with cognitive neuropsychiatry that is accelerating progress in this domain. This new field is called Computational Cognitive Neuropsychiatry. Computational cognitive neuropsychiatry is highly interdisciplinary and involves the use of mathematics and computer simulations to rapidly explore the effects of changes in individual biological variables, and their combinations, on the functioning of neural systems and human behavior. Computational cognitive psychiatry is very well-suited not only to understand mechanisms underlying complex normal brain functions, but also to delineate aberrant processes that underlie psychiatric disease endophenotypes, including problems in memory, attention and executive control. This exciting new field promises to provide a greater biological understanding of the complex dysfunctions that underlie psychiatric disease. The Rutgers-Princeton Center for Cognitive Computational Neuropsychiatry (CCNP) is a collaboration between the BHI and Princeton's Neuroscience Institute, created to pursue this exciting opportunity. CCNP is co-directed by Dr. Anna Konova (Rutgers) and Dr Yael Niv (Princeton Neuroscience Institute). The goal is to leverage the expertise in Princeton's department of Psychology and Neuroscience Institute, and in Rutgers' departments of Psychology, Psychiatry and Computer Science, Rutgers University Behavioral Health Care, Robert Wood Johnson Hospital, and the Rutgers Brain Health Institute, in a major collaborative initiative that has the potential to bring real and rapid progress to understanding the causes of psychiatric disorders, and will lead to novel therapies for treating these mental dysfunctions. The CCNP Core facility is located in Room V01, Research Tower, 675 Hoes Lane West, Piscataway. More information about services offered at the facility can be found at - https://ccnp.princeton.edu/about-ccnp/. The center currently has a pilot grant program to support investigators interested in using the services of the facility.

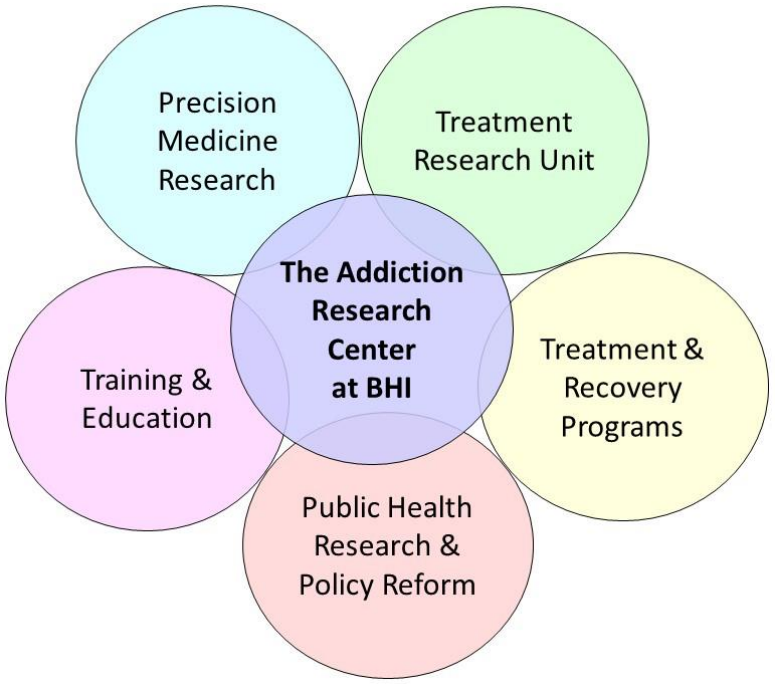
Rutgers Alzheimer's & Dementia Research Center (RUADRC): Alzheimer's disease (AD) and related dementias are a major cause of disability and death in the elderly. Approximately 6 million people have been diagnosed with AD and related dementias and the aging of America's population suggests that the number of Alzheimer's patients in the U.S. will, by 2050, increase to nearly 14 million people. Worldwide, approximately 40 million people have AD and related dementias. This number could also climb to nearly 120 million by 2050. As 5% of AD cases are familial and ~95% are sporadic, disease-modifying drugs that treat both sporadic and

familial AD are desirable. Despite recent advances in our understanding of basic biological mechanisms underlying AD and related dementias, we do not yet know how to prevent AD and related dementias, nor do we have an approved disease-modifying intervention. A major reason that these problems persist is that current animal models of AD and related dementias have not been able to predict the effectiveness of proposed therapies, so that many that have moved into clinical trials fail, which greatly slows the development of new therapies and increases their cost. Thus, there is a great need to develop the next generation of animal models (NexGeMo) of AD and related dementias to provide greater predictive power of potential therapies and thus accelerate the drug testing/clinical trial pipeline. The ultimate goals of the proposed RUADRC are:

- To develop therapies to cure AD and related dementias or, at the very least, effectively slow down the course of disease progression.
- To discover novel diagnostic and prognostic biomarkers that can forewarn the initiation of pathogenic processes before symptoms occur and also be used to monitor disease progression and treatment efficacy.

To achieve the above goals, research at RUADRC will focus on identifying disease mechanisms using genetic, cellular, organismal and behavioral approaches in animal and human model systems. Understanding of disease mechanisms will help uncover pathways that need to be targeted by drugs to achieve therapeutic efficacy. Development of relevant *in vitro* and *in vivo* models will be important for pre-clinical evaluation of novel drugs. A dementia clinic for patient recruitment, assessment and treatment will also be needed for translating research to clinic. The principal investigator at RUADRC, recruited by BHI, is Dr. Luciano D'Adamio, Herbert C. and Jacqueline Krieger Klein Endowed Chair in Alzheimer's Disease and Neurodegeneration Research, Professor of Pharmacology, Physiology & Neuroscience and Professor of Neurology at Rutgers New Jersey Medical School (NJMS) and Associate Director of Neurodegeneration and Injury at BHI. Dr. Ioana Carcea, a junior faculty recruited by BHI at NJMS, studies role of social learning in dementia by investigating oxytocin activity in aged and Alzheimer's disease rodent models. Dr. Hyung Jin Ahn, another BHI recruit, recently joined RUADRC and NJMS as a junior faculty. Dr. Ahn studies the role of cerebrovascular deficits in the etiology of AD and dementia. The Center is currently supported by multiple NIH grants and generous philanthropic support from Herbert C. and Jaqueline Krieger Klein as well as Rosalia Dattolo and Pasquale Amello Endowed Alzheimer's Research Fund established by Remember Me, Inc. Recently, Herbert Klein donated an additional $5 million gift, with a matching $2 million contribution from the RBHS Chancellor, to establish a new Krieger-Klein Endowed Chair in Neurodegeneration Research to help recruit and support a clinician-scientist faculty to serve as the Director of Krieger Klein Alzheimer's Disease and Cognitive Neurology Clinical Research Center. This recruitment is being led by the BHI and is underway

The Rutgers Addiction Research Center (RUARC): Our nation is in the midst of an unprecedented opioid epidemic. More people died from drug overdoses in 2014 than in any year on record, and the majority of drug overdose deaths (more than six out of ten) involved an opioid. The RUARC will build collaborations among scientists with the multidisciplinary expertise required to advance our understanding of the causes of opioid addiction` and other substance use disorders. As a component of the Brain Health Institute, RUARC will contain faculty in all Rutgers schools and campuses with expertise in addiction prevention, research, treatment, education, and public policy. A Treatment Research Unit (TRU), will be a key component of the RUARC. The TRU will tie together precision medicine research and clinical treatments by measuring treatment effectiveness as a function of genetics, age, gender, and



environment relevant to each individual addict. The TRU will collaborate with clinical entities across Rutgers as well as with the Rutgers Health Network, an integrated network of Rutgers' affiliated hospitals, community clinics, medical groups, wellness centers, and other affiliates across NJ, to provide a wide range of inpatient and outpatient research programs for drug dependent patients. Through the TRU, patients will benefit from substance use research while specialists advance knowledge and develop new therapies that are most effective for each of the many subsets of addiction patients. RUARC will be the only comprehensive addiction center in NJ with the capacity to impact the addiction epidemic through the diverse strengths of its members by integrating the following cutting edge approaches:

- Precision Medicine preclinical research and knowledge development that crosses multiple disciplines and addresses individual differences and needs in addiction treatment.
- Treatment and care of individuals and families coping with addiction.
- Public policy innovation and reform aimed at preventing development of drug use and at more effective avenues for addicts to obtain treatment.
- Inter-professional education of tomorrow's research, clinical, and criminal justice workforces from multiple disciplines in all aspects of addiction science.

We are recruiting a Director and other faculty for RUARC and TRU. To grow basic research in addiction at RUARC, BHI has recently recruited Dr. R. Christopher Pierce, from U Penn, as a Professor in Dept. of Psychiatry at RWJMS and Assistant Director of Neuroscience Training & Eductaion. In addition, Dr. Daniel Langleben, MD will be joining Rutgers as the Director of the TRU. Other faculty, recruited by BHI, with research interests in addiction, include Dr. Ying-Xian Pan (Professor, NJMS-Anesthesiology), Dr. Morgan James, (Assistant Professor, RWJMS-Psychiatry), Dr. Anna Konova (Assistant Professor, RWJMS/UBHC) and Dr. David Barker (Assistant Professor, RU-NB, SAS-Psychology).

Building a stronger, collaborative Rutgers Neuroscience Community

Modern neuroscience is a multidisciplinary field that integrates molecular and cell biology, genetics, physiology, pharmacology, psychology, biomedical engineering, computational science, statistics and other fields of science. For breakthroughs in basic research to be translated to the clinic, interdisciplinary collaborations are a must. Rutgers currently has over 250 neuroscience investigators, spread over multiple campuses across New Jersey, with expertise that span the entire spectrum of disciplines mentioned above. BHI supports the Rutgers neuroscience community by developing key core facilities, recruiting faculty to fill institutional gaps in expertise and by facilitating communication and collaborations between these Rutgers neuroscientists. BHI-

- Develops core facilities such as CCNP and CAHBIR.
- Jointly recruits faculty with departments and schools across Rutgers. We have recently recruited Dr. Todd Mowery and Dr. Mark Rossi as Assistant Professors of Otolaryngology and Psychiatry in RWJMS, respectively. Dr. Rossi was a joint recruitment with CHINJ. In addition, BHI jointly recruited Dr. Detlev Boison, Professor and Vice Chair of Research, and Dr. Yong Kim, Associate Professor, with the Department of Neurosurgery (RWJMS/NJMS). Other joint faculty recruitments with School of Pharmacy, RWJMS and NJMS are underway.
- Organizes focus area workshops that bring together neuroscientists across Rutgers to share their work and seek collaborations.
- Provides Pilot grant funding to novel projects which have principal investigators from different Rutgers campuses and Schools. In addition to fostering interdisciplinary collaborations, a goal of this funding program is to help the investigators convert the pilot grant projects to larger projects funded by extramural awards. Over 4 years, the pilot grant program awarded 33 grants totaling $1.32 million. BHI (RBHS & RU-NB), RU-Newark and NJIT contributed funding for 20 ($800,000), 10 ($400,000), and 3 ($120,000) awards, respectively. Based on the outcome data available for the first three years (2015-2017), the pilot grant program has been very successful. Pilot grant awardees used the information and preliminary data generated from the pilot grants to submit 41 extramural grant applications. Of these, 20 applications (~50% success rate) were awarded ~$13 million in total cost. The indirect costs generated by these extramural awards is ~4-fold more than the ~$1 million invested by the various entities over the 2015 to 2017 three-year period. In 2019, due to budgetary constraints and change in institutional priorities, RU-Newark and NJIT decided to disengage from the pilot program. The 2019 pilot program received a commitment from the Office of the VCRI, RU-NB and RBHS Chancellor to support 4 and 2 grant awards,

respectively. Following the external and internal review, BHI awarded 4 grants totaling $160,000, to faculty groups from RU-NB and RBHS. BHI continues to seek outcome data for the grant awarded in the last couple of years

- Hosts a Plenary Seminar series that brings prominent neuroscientists to various Rutgers campuses. These seminars are live webcast allowing Rutgers neuroscientists from both the host and remote sites to participate and learn about cutting-edge research in premier labs across the US. The BHI plenary seminar series brings exemplary neuroscientists from across the US to campus to speak and to meet with faculty and trainees. This not only provides a unique opportunity for Rutgers faculty and trainee to interact with high-caliber neuroscientists; but, also introduces the plenary speakers to ongoing neuroscience research at Rutgers. As these visitors recognize the strength of neuroscience at Rutgers, it helps increase the visibility of Rutgers neuroscience which, in turn, facilitates recruitment of faculty and trainees, publication of scientific articles and grant funding. The BHI plenary seminars are held at various Rutgers campuses and webcast live to all Rutgers campuses in NJ, including Rutgers-Newark, Rutgers-New Brunswick, Rutgers-NJMS, Rutgers-Camden and VA Research Center in East Orange. This allows faculty, students and staff across Rutgers to attend these seminars. Since 2015, the BHI Plenary seminar program has hosted over 40 speakers in various fields of neuroscience. As a measure of their research caliber, the average H-index of these speakers is ~85, an index score attained by ~10% of neuroscientist's world-wide. In addition to the plenary seminars, BHI created the Strongwater Endowed Lecture given by leaders in neuroscience including Dr. Bryan Roth (discoverer of the field of chemo-genetics) and the Directors of NIMH and NIAAA, Dr. Josh Gordon and Dr. George Koob, respectively.
- Holds an Annual Symposium that brings together faculty, post-docs, students and staff from neuroscience labs at Rutgers and neighboring institutions such as New Jersey Institute of Technology and Princeton. The day-long symposium includes talks by pilot grant awardees, Rutgers faculty and trainees, a keynote lecture and trainee poster session. Each year ~200 people attend the Annual BHI symposium. Keynote speakers have included world-renowned neuroscientists such as Dr. Pat Levitt (UCSF), Dr. György Buzsáki (NYU), Dr. Regina Carelli (UNC & Rutgers alumna), Dr. Richard Youle (NIH) and Dr. Eve Marder (Brandeis). This year's virtual BHI symposium Keynote Speaker will be Dr. Stan Floresco (University of British Columbia).
- In addition to the Annual BHI symposium, BHI has also hosted two Herbert and Jacqueline Krieger Klein symposiums on Alzheimer's Disease and Neurodegeneration at NJMS. Each symposium was attended by more than 80 people, including the donor Hon. Herb Klein and his family. The Klein symposium program included talks by Rutgers faculty and trainees engaged in Alzheimer's and neurodegeneration research and keynote lectures by leaders in the field of Alzheimer's disease and dementia, including Dr. Jie Shen (Harvard), Dr. Ottavio Arancio (Columbia), Domenico Pratico (Temple), and Dr. Riqiang Yan (University of Connecticut).
- Maintains a comprehensive website (brainhealthinstitute.rutgers.edu) that is kept current with useful information and resources including a searchable faculty expertise directory, funding opportunities, upcoming neuroscience events etc. BHI also has social media presence; using Twitter (**@BHI_Rutgers**), Facebook and LinkedIn to announce events and achievements of Rutgers neuroscientists.

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Keynote Speaker

Stan B. Floresco, PhD

Professor of Psychology and an Investigator at the Djavad Mowafaghian Centre for Brain Health at the University of British Columbia, Vancouver, Canada

"Prefrontal-Subcortical Circuits Underlying Risk/Reward Decision Making"

We routinely face decisions requiring evaluation and choice of different actions may or may not yield different types of rewards. These situations trigger competitive decision biases that reflect interplay between different medial prefrontal/orbital cortex, amygdalar and striatal nodes within the brain's dopamine system, which plays a critical role in action selection and reward processing. This lecture discusses some of the interactions between these circuits that shape decision biases and underlie conflicting urges when evaluating options that vary in terms of potential risks and rewards. Optogenetic studies revealed that phasic activity in subcortical circuitry linking the amygdala and the ventral striatum appears to promote choice towards more preferred rewards, and modify choices after non-rewarded actions. These biases are modified by prefrontal regions exert top-down control over the amygdala to temper these urges when riskier options are less profitable. Moreover, prefrontal activity occurring prior to action selection or after evaluation of their outcomes can differentially influence decision biases. In comparison, chemogenetic studies probing medial orbitofrontal cortical functions showed that distinct projections to the amygdala, ventral striatum, or cortico-cortical pathways to the prefrontal cortex enable flexible decision making and integration of reward history to promote optimal decision biases These findings provide insight into the dynamic competition between these cortical/subcortical circuits that shape our decision biases and underlie conflicting urges when evaluating options that vary in terms of potential risks and rewards.

Dr. Floresco received his BSc, MA and PhD from University of British Columbia. He completed his postdoctoral training at the University of Pittsburgh and then became a faculty in the Department of Psychology at University of British Columbia. Dr. Floresco's research focuses on neural circuits that facilitate different forms of learning, cognition and executive functioning. Using rodents as a model system, his work has a particular emphasis on interactions between the different brain regions that facilitate cognitive processes, including behavioral flexibility, cost-benefit decision making and reward-related learning. His research integrates traditional psychopharmacological, in-vivo neurophysiological and neurochemical techniques along with newer optogenetic and chemogenetic manipulations to elucidate the interactions between the prefrontal cortex and its key subcortical targets. Dysfunction in these systems has been implicated in a variety of disorders, including schizophrenia, depression and drug addiction. Dr. Floresco's work attempts to model how the normal brain solves certain types of problems, and then use this information to clarify the mechanisms that may underlie the impairments in cognitive and emotional functioning associated with these disorders. Dr. Floresco has published over 125 peer-reviewed articles with >17,000 citations (H-index of 68) and has won numerous teaching and research awards, including the 2019 ACNP Efron Award for outstanding basic research. He is an Associate Editor of leading neuroscience journals including, Psychopharmacology, Brain Research, Neuropsychopharmacology, Cognitive, Affective and Behavioral Neuroscience and on the editorial boards of prestigious journals in neuroscience.

Faculty Speakers

Wayne Fisher, PhD, BCBA-D
Henry Rutgers Endowed Chair
Director RUCARES and CSH-RUCARES,
Professor of Pediatrics
RWJMS, RBHS
BHI Core Faculty

Thurs, Nov 19 (1.00 PM – 1.20 PM)

Integrating Research and Practice in the Assessment and Treatment of Autism Spectrum Disorders

Integrating research and practice helps to ensure that our current patients receive the most up-to-date assessments and treatments, and it facilitates continual refinement of those services so that the patients we see in the future receive even better care. In this presentation, I will explain our plans for integrating research and practice as we grow the Rutgers University Center for Autism Research, Education, and Services (RU-CARES). As an exemplar, I will describe a line of translational research in our Severe Behavior Program designed to address the recalcitrant problem of treatment relapse in which destructive behavior exhibited by individuals with autism and related disorders increases after a period of successful treatment. This line of research involves the translation of a mathematical theory of behavior, called behavioral momentum theory, that postulates that the momentum of a response is analogous the momentum of a moving object, as characterized by Newtonian physics. I will show how behavioral-momentum equations can be used to generate novel hypotheses about preventing or mitigating treatment relapse in the form of resurgence of destructive behavior, and I will summarize the results of our research in this area thus far.

Cathleen Piazza, PhD, BCBA-D
Director Pediatric Feeding Disorders Program at CSH
Professor of Psychology
GSAPP, Rutgers-New Brunswick
BHI Core Faculty

Thurs, Nov 19 (1.25 PM – 1.45 PM)

Integrating Research and Practice: An Intervention for Change-Resistant Behavior in Children with Autism as an Exemplar

The intensive Pediatric Feeding Disorders Program at Children's Specialized Hospital will provide day-treatment services for children with severe feeding problems. The scientific, data-based approach the program uses facilitates the integration of research with practice. The professionals who are starting the program have a track record of conducting cutting-edge clinical research that has established empirical support for applied behavior-analytic interventions for feeding disorders. Their study on treatment of change-resistant feeding behavior in children with autism will serve as the exemplar of the seamless integration of research with practice for today's symposium.

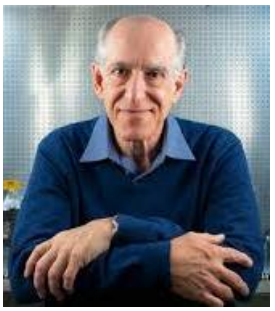
Miriam Rosenberg-Lee, PhD
Assistant Professor of Psychology
SASN, Rutgers-Newark

Thurs, Nov 19 (1.50 PM – 2.10 PM)

The Neural Basis of Cognitive Strengths in Autism

Autism spectrum disorders (ASD) are characterized by difficulties in social communication and repetitive and restrictive behaviors. Yet, the disorder is often accompanied by remarkable cognitive strengths in domains such as memory, spatial reasoning and musical ability. Understanding the neural basis of spared and enhanced abilities in ASD has the potential to elucidate mechanisms underlying both strengths and weakness in this population. Moreover, cultivating strengths, particularly in academic domains, like mathematics and reading, can contribute to improving life outcomes and supporting financial independence. Here, I present work examining enhanced arithmetic and word reading performance in children and college students with ASD. In both cases, reorganization of high-level visual processing areas in inferotemporal cortex (among other regions) underpinned these strengths. Further, these results point to mastery of symbolic systems, like letters and numbers, as a particularly potent learning modality in autism, but perhaps at a cost to other complex visual stimuli, such as faces.

Emanuel DiCicco-Bloom, MD
Professor of Neuroscience & Cell Biology
RWJMS & CHINJ, RBHS



Thurs, Nov 19 (2.30 PM – 2.50 PM)

Defects in mTOR Signaling Mediate Common Neurite and Cell Migration Defects in both Idiopathic and 16p11.2 Autism Neural Precursor Cells

Autism spectrum disorder (ASD) is defined by common behavioral characteristics, raising the possibility of shared pathogenic mechanisms. Yet, vast clinical and etiological heterogeneity suggests there may also be personalized phenotypes. Surprisingly, our iPSC studies find that six individuals from two distinct ASD-subtypes, idiopathic (I-ASD) and CNV 16p11.2 deletion (16pDel), have common reductions in neural precursor cell (NPC) neurite outgrowth and migration, even though DNA sequencing demonstrates no genetic overlap, and growth factor responses reveal subtype-specific impairments. To identify signaling defects that may contribute to these developmental defects, an unbiased phospho (P)-proteomic screen was performed. Surprisingly, despite the genetic heterogeneity, numerous shared P-peptides were identified between the autism subtypes including the mTOR pathway. mTOR signaling alterations were confirmed in all NPCs across both ASD-subtypes, and mTOR modulation rescued phenotypes in ASD and reproduced autism defects in controls. Thus, our studies demonstrate that distinct non-overlapping genetic variants converge on mTOR signaling defects that mediate consistent neurite and cell migration defects in two distinct ASD subtypes.

Steven Levison, PhD
Professor of Pharmacology, Physiology & Neuroscience
NJMS, RBHS
Director, Laboratory For Regenerative Neurobiology

Thurs, Nov 19 (2.55 PM – 3.15 PM)

Modeling the Effects of Prenatal Infections on Neural Development and Behavior

Epidemiologic studies have demonstrated that maternal immune activation secondary to viral and bacterial infections during the 3rd trimester of pregnancy increases levels of Interleukin-6 (IL-6) that is associated with an increased risk for autism, schizophrenia, cognitive dysfunction, ADHD and depression in their offspring. Therefore, we have injected IL-6 into mouse pups twice daily at a dose of 75 ng per injection to increase IL-6 plasma levels 2 fold. This elicited a small, but significant increase in body temperature but no effect on overall growth. At 3 weeks of age, the IL-6 injected pups showed reduced nose-to-nose and urogenital sniffing. Additionally, IL-6 injected animals exhibited increased self-grooming. At 6 weeks of age, the IL-6 injected mice were less social, as assessed by both social approach and novel social subject tests. IL-6 injected pups also exhibited increased anxiety as assessed using the elevated plus-maze and displayed a higher sensitivity to fear conditioning. At the cellular level, IL-6 stimulated the proliferation of a multi-potential progenitor and decreased the proliferation of two glial restricted progenitors. Fate mapping studies revealed decreased astrogliogenesis and decreased oligodendrogenesis in the frontal lobe.

Mladen Roko Rašin, MD, PhD
Associate Professor of Neuroscience & Cell Biology
RWJMS, RBHS

Thurs, Nov 19 (3.20 PM – 3.40 PM)

Making Sense of mRNA Landscapes: Translation Control in Neurodevelopment

The spatiotemporal differentiation of neural stem cells (NSC) into distinct neuronal subpopulations is critical for a properly functioning mammalian central nervous system. This intricate differentiation sequence requires precisely timed changes in gene expression (transcription) and ribosome centered protein synthesis (mRNA translation). The regulation of mRNA translation remains understudied in normal brain development, despite it being highly implicated in neurodevelopmental disorders like autism, epilepsy, and microcephaly. We and others have shown that the spatiotemporal specificity in translation of mixed mRNA landscapes is regulated in part by RNA binding proteins (RBPs). In particular, RBPs in the Elav protein family are major regulators of mRNA translation events, ribosome composition and neurodevelopment. However, there are still critical gaps in the field regarding the roles of RBPs in mRNA translation within NSCs and developing neurons. Therefore, the overall goal of our research is to characterize how distinct RBPs determine spatiotemporal translation events in normal and abnormal neurodevelopment. My presentation will focus on the current state and challenges of the field.

Benjamin Samuels, PhD
Assistant Professor of Psychology
SAS, Rutgers-New Brunswick

Thurs, Nov 19 (3.45 PM – 4.05 PM)

Neural Circuits Mediating the Behavioral Effects of Chronic Stress and Antidepressants in Male and Female Mice

Chronic stressful experiences can precipitate mood disorders in humans and maladaptive affective behaviors in rodents. However, most rodent chronic stress paradigms were designed in males and are less effective in females. First, I'll briefly describe two new stress paradigms that are effective in both male and female mice. Then, using those stress paradigms, I'll explain the importance of dentate gyrus granule cells in mediating the beneficial effects of antidepressants on avoidance behaviors. Finally, I'll explain the maladaptive effects of chronic stress on motivation and reward behaviors, which have high translational value for mood disorders such as depression.

Ozlem Gunal, MD, PhD
Assistant Professor of Psychiatry
NJMS, RBHS

Thurs, Nov 19 (4.10 PM – 4.30 PM)

Cyfip1 Mediates Addiction Relevant Phenotypes in Mice

Cocaine is a common drug of abuse that produces persistent changes in synaptic function and plasticity in the NAc, which results in addiction, but the cause of the differential predisposition to addiction remains largely unknown. Cytoplasmic FMR1-interacting protein (CYFIP 1) has been identified as a risk factor for several neuropsychiatric disorders including schizophrenia, intellectual disability, and autism in humans. To test if the cocaine related behavioral responses are affected when Cyfip1 levels are reduced, we performed open field tests in mice carrying a Cyfip1 mutation (Cyfip1+/-) and compared locomotor activity in control conditions and in response to cocaine. Cocaine-induced increase in locomotor response is blunted in Cyfip1+/- mice and in male mice more than female. A cocaine-conditioned place preference paradigm showed increased cocaine seeking in Cyfip1+/- mice. To add a self-controlling element and better simulate the pathophysiology of drug addiction in humans, we have used a reward-based touchscreen task. Preliminary results confirm the effect of Cyfip1 deficiency in reward-related decision-making. Clarifying Cyfip1's role in cocaine response and NAc plasticity, which is a previously unexamined target, may be relevant for a variety of disease-related genes with similar functions.

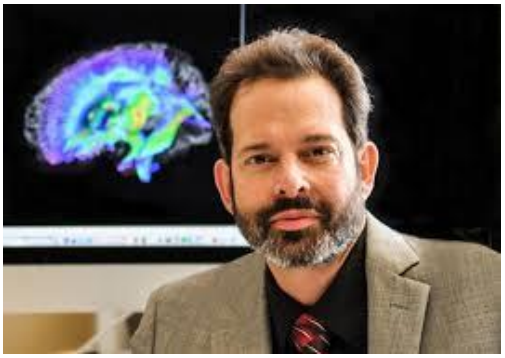
Todd Mowery, PhD
Assistant Professor of Otolaryngology—Head and Neck Surgery
RWJMS, RBHS
BHI Core Faculty

Thurs, Nov 19 (4.35 PM – 4.55 PM)

Neural Mechanisms that Support Learning in Circuits with Significant Cellular Deficits

The corticostriatal circuit has been identified as a vital pathway for associative learning. However, this circuit is permanently altered by a transient developmental sensory deprivation. How learning is maintained in such conditions is unclear. Here, we used whole cell recording from a functional corticostriatal slice preparation to measure changes to the cellular and synaptic properties of striatal medium spiny neurons as adult gerbils were learning a sound discrimination task. In both groups, learning was accompanied by the dichotomous trafficking of GABAA-α1 subunit containing receptors. Subsequently inhibitory tone in both groups moved towards the same mean during acquisition before returning to baseline as the animals mastered the task. Furthermore, a significant deficit to firing rate in the sensory deprived group was briefly compensated for by changes to intrinsic cellular properties during the acquisition phase of the task. The firing rate deficit in this group then re-emerged as the animals mastered the task. Together, these results demonstrate a form of learning related plasticity that allows significant cellular and synaptic deficits to be compensated for briefly. This novel form of plasticity has implications for a neural mechanism that support learning in many neurological disorders.

David H. Zald, PhD
Director, Center for Advanced Human Brain Imaging Research (CAHBIR),
Henry Rutgers Term Chair
Professor of Psychiatry, RWJMS, RBHS
BHI Core Faculty



Fri, Nov 20 (9.00 AM – 9.20 AM)

Neuroimaging Networks for Translational Neuroscience

Neuroimaging research has increasingly revealed the complex interplay of different brain networks in supporting different perceptual, affective and cognitive tasks. However, an understanding how this interplay shapes individual differences in ability, personality, and neuropsychiatric illness is only beginning to emerge. In this talk I will highlight features of circuits involved in motivated behavior and the ability of neuroimaging to provide a translation bridge from animal models to human behavior. The new Center for Advanced Human Brain Imaging Research (CAHBIR) on the Busch campus aims to facilitate such translational research and build upon the unique confluence of basic neuroscience and clinical research across the Rutgers community.

Mauricio Delgado, PhD
Professor and Chair of Psychology
Associate Director, Rutgers University Brain Imaging Center
SASN, Rutgers-Newark

Fri, Nov 20 (9.25 AM – 9.45 AM)

Reward Processing in the Human Brain

From winning a raffle to receiving praise from a colleague, the experience of reward elicits positive emotions, shapes our behavior and influences our emotional well-being. Central to processing rewards is the role of the striatum - the input unit of the basal ganglia and a key node in a putative human reward circuit. This talk will first describe early efforts aimed at characterizing a reward-related signal in the human striatum. We will then discuss how this signal can impact decision making and highlight how the surrounding social context (i.e., the level of closeness between individuals) can change reward-related responses and the inherent experience of a reward. Finally, we will focus on the beneficial effects that positive emotions can have on our ability to cope with negative affect elicited by acute stress.

Laleh Najafizadeh, PhD
Associate Professor of Electrical and Computer Engineering
SOE, Rutgers-New Brunswick

Fri, Nov 20 (9.50 AM – 10.10 AM)

Data-Driven Methods for Understanding the Dynamics of Brain Function

The human brain is a highly complex dynamic system. Achieving a complete understanding of how its anatomical structure supports a diverse range of functions, such as action, perception, and cognition, has been one of the major goals of neuroscience, but it is still far from reach. One of the obstacles in reaching this goal has been lack of computational techniques that can reliably describe the dynamic properties of the brain function when it is in action. In this talk, I will discuss the recent new computational techniques that have been developed in my lab for studying the dynamics of brain function and present their applications. .

Rafiq Huda, PhD
Assistant Professor of Cell Biology & Neuroscience
SAS, Rutgers-New Brunswick

Fri, Nov 20 (10.15 AM – 10.35 AM)

Coupling of Prefrontal Cortical Activity to Arousal Predicts Alcohol Consumption

Alcohol use disorder (AUD) exacts a major societal toll. AUD is highly comorbid with neuropsychiatric conditions characterized by hyperarousal (e.g., posttraumatic stress disorder), suggesting common underlying mechanisms. Top-down control from the prefrontal cortex (PFC), a critical hub for executive, cognitive, and emotional functions, is key for the regulation of alcohol consumption. Arousal exerts profound effects on cortical processing by engaging neuromodulation of excitatory and specific inhibitory cell types. Despite this, it is unclear whether and how arousal-mediated modulation of PFC circuits relates to alcohol drinking behaviors. Two-photon microscopy is ideally suited for studying cell-specific circuits. We addressed a major limitation of this technology by developing a novel behavioral paradigm for drinking in head-fixed mice. We recorded responses of layer 2/3 excitatory neurons in the PFC as mice voluntarily consumed alcohol, along with video recording of the pupil to track momentary fluctuations in arousal. Remarkably, we found that the coupling of arousal to ACC activity predicted the amount of alcohol consumed. This unique combination of technical and conceptual advances identifies cortical coupling to arousal as a potential biomarker for alcohol drinking and lay the groundwork for future studies to dissect the contribution of specific circuits in this process.

Vanessa Routh, PhD
Professor of Pharmacology, Physiology and Neuroscience
NJMS, RBHS

Fri, Nov 20 (11.05 AM – 11.25 AM)

Hypothalamic Glucose Sensing Neurons: Multiple functions, One goal

Since the brain is an obligate consumer of glucose, it is teleologically advantageous to have evolved neurons capable of sensing and responding to changes in extracellular glucose. Glucose-excited (GE) and glucose-inhibited (GI) neurons exist throughout the brain. Today's talk will focus on GI neurons in the ventromedial (VMH) and lateral (LH) hypothalamus. We have strong evidence that VMH GI neurons serve as part of an alarm system that raises blood glucose levels during life-threatening hypoglycemia. However, we hypothesize that these neurons serve multiple physiological roles in maintaining an adequate glucose supply for the brain. The evidence for a role of VMH GI neurons in maintaining fasting glucose levels as well as inhibiting processes that increase energy expenditure will be discussed. We further hypothesize that the LH orexin-GI neurons play a role in behaviors such as reward-based feeding and contribute to the difficulty maintaining weight loss after dieting. LH orexin-GI neurons may also play a role in wakefulness and arousal. Together, these data suggest a much more complex role for hypothalamic GI neurons in glucose homeostasis than simply as protection against iatrogenic insulin-induced hypoglycemia.

Ying-Xian Pan, MD, PhD
Professor of Anesthesiology
NJMS, RBHS
BHI Core Faculty

Fri, Nov 20 (11.30 AM – 11.50 AM)

Biased Signaling at Multiple Mu Opioid Receptors Generated by Alternative Splicing of OPRM1 Gene

Most clinically used opioids such as morphine and fentanyl, as well as drugs of abuse like heroin, act through the mu opioid receptors. The single-copy mu opioid receptor gene, OPRM1, undergoes extensive alternative pre-mRNA splicing, creating multiple splice variants or isoforms that are conserved from rodent to human. One type of the OPRM1 splice variants are the full-length 7 transmembrane (7TM) C-terminal splice variants, which have identical receptor structures including entire binding pocket, but contain a different intracellular C-terminal tail resulted from 3' alternative splicing. Biased signaling of GPCRs has been defined by evidences that different agonists can produce divergent signaling transduction pathways through a single receptor. We have demonstrated that a single mu agonist can induce differential G-protein or β-arrestin2 signaling through multiple 7TM splice variants. Particularly, exon 7-associated 7TM C-terminal variant showed greater β-arrestin2 bias for most mu agonists than MOR-1, an exon 4-associated variant, correlating with their roles in vivo suggested by using gene targeting mouse models. Our studies provide a new perspective on biased signaling at least for Oprm1, which perhaps is important for our understanding of the complex mu opioid actions in vivo where all the 7TM splice variants co-exist.

Radek Dobrowolski, PhD
Associate Professor of Biological Sciences
SASN, Rutgers-Newark

Fri, Nov 20 (2.00 PM – 2.20 PM)

Impaired Nuclear Calcium Signaling Attenuates CREB-Mediated Neuronal Clearance in Alzheimer's Disease

Inhibition of the autolysosomal system is one of the earliest changes in Alzheimer's disease (AD) brains. Consequent disruption of molecular trafficking and molecular clearance are causally linked to increased neuronal vulnerability and neurodegeneration. We find that a decrease of nuclear calcium levels and consequently cAMP response element-binding protein (CREB)-mediated expression of its target genes associated with the autolysosomal pathway is the underlying mechanism for attenuated molecular clearance and decreased neuroprotection in presenilin (PS) and Tau mutants. Expression of the CREB-target gene sestrin 2 (sesn2) in human AD neurons promotes autophagic clearance and neuronal survival under stress conditions. We hypothesize that PS1 and Tau mutants impair Ryanodine Receptor (RyR)-mediated control of nuclear calcium, therefore inhibiting CREB-mediated transcription of clearance genes, promoting buildup of neurotoxic proteins that accumulate in the AD brain. Our studies aim to characterize a novel pathway that drives formation of pathological hallmarks associated with AD. Induced pluripotent stem cell (iPSC)-derived human forebrain neurons and Drosophila melanogaster are used to assess the impact of nuclear calcium depletion and reduced pCREB signaling in molecular clearance during AD onset and progression. Nuclear calcium depletion in PS and Tau mutant neurons add an important dimension to the long-standing calcium hypothesis of AD.

Hyung Jin Ahn, PhD
Assistant Professor of Pharmacology, Physiology and Neuroscience
NJMS, RBHS
BHI Core Faculty

Fri, Nov 20 (2.25 PM – 2.45 PM)

Fibrinogen as a Key Player for Cerebral Amyloid Angiopathy-Associated Vascular Pathology

Cerebral amyloid angiopathy (CAA), where Aβ deposits around cerebral blood vessels, is a major contributor of vascular dysfunction in AD patient. However, the molecular mechanism underlying CAA formation and CAA-induced cerebrovascular pathology is unclear. Hereditary cerebral amyloid angiopathy (HCAA) is a rare familial form of CAA where mutations within the gene for the β-amyloid precursor protein (APP) causes an increase in vascular deposits of Aβ. Since the interaction between Aβ and fibrinogen increases CAA and plays an important role in cerebrovascular damage in AD, we investigated the role of the Aβ -fibrinogen interaction in HCAA pathology. We showed that the most common forms of HCAA-linked mutations, Dutch (E22Q) and Iowa (D23N), resulted in up to a 50-fold stronger binding affinity of Aβ for fibrinogen. In addition, the stronger interaction between fibrinogen and mutant Aβ s led to a dramatic perturbation of clot structure and delayed fibrinolysis. Immunofluorescence analysis of the occipital cortex showed an increase of fibrin(ogen)/ Aβ co-deposition as well as fibrin deposits in HCAA patients compared to early-onset AD patients and non-demented individuals. Our results suggest the HCAA-type Dutch and Iowa mutations increase the interaction between fibrinogen and Aβ and may lead to cerebrovascular pathologies observed in HCAA.

Max Tischfield, PhD
Assistant Professor of Cell Biology and Neuroscience
SAS, Rutgers-New Brunswick and CHINJ

Fri, Nov 20 (2.50 PM – 3.10 PM)

Brain Drain: Development of meningeal lymphatic networks and the glymphatic system in craniofacial disorders

Skull malformations are associated with cerebrovascular abnormalities that can cause serious complications for fluid balance in the CNS and brain health and function. We discovered that humans with abnormal skull development and inactivating mutations in the transcription factor TWIST1 also have dural cerebral vein malformations. Twist1 and Bmp2/Bmp4 conditional knock-out mouse models revealed that cerebral vein growth and remodeling is tightly coupled with skull development and dependent upon Bone Morphogenetic Protein (BMP) produced from surrounding bone and dura. Twist1 and BMP signaling is also necessary to integrate the development of dural lymphatic vessels (DLVs) with the skull, meninges, and cerebral blood vessels. These findings have clinical significance because DLVs are master regulators for tissue fluid homeostasis in the CNS and, as part of the brain's glymphatic system, are required for the drainage of macromolecules and waste from CSF. Furthermore, DLVs form a gateway between the CNS and peripheral immune system by facilitating the transport of brain-derived antigens and immune cells to the cervical lymph nodes. As such, their compromise may be associated with neuroimmune dysfunction, neurodegeneration, and cognitive impairments, underscoring the importance of addressing how DLV malformations arise and affect these processes. Thus, we aim to leverage our unique animal models to identify tissue-specific cellular interactions and signaling pathways that integrate the growth and function of DLVs with that of the surrounding environment in normal health and pathologic states.

Stella Elkabes, PhD
Director, Reynolds Family Spine Laboratory
Professor of Neurosurgery
NJMS, RBHS

Fri, Nov 20 (3.15 PM – 3.35 PM)

Modulation of Immune and Non-Immune Functions of Astrocytes following Spinal Cord Injury: Role of Toll-Like Receptor 9

The central nervous system (CNS) was historically considered an immune-privileged organ. However, this concept has changed as convincing evidence demonstrates that CNS infections and injuries as well as neurodegenerative diseases trigger innate immune responses in the brain and spinal cord (SC). Astrocytes and microglia are the principal intrinsic cell types that mount an innate immune response in CNS pathologies. This response is initiated by danger signals that activate pattern recognition receptors (PRRs). Toll-like receptors (TLRs) are the best-characterized family of PRRs, and are expressed in glia and neurons. Endogenous self-ligands released by stressed and damaged cells activate TLR signaling following CNS injury. This leads to release of inflammatory mediators and induction of sterile neuroinflammation. Investigations in our laboratory focus on the role of TLRs in traumatic spinal cord injury (SCI) with particular emphasis on TLR9. Previous studies indicated that intrathecal administration of a TLR9 agonist to mice sustaining a mid-thoracic SC contusion injury exacerbates the pro-inflammatory response and the functional outcomes of SCI. In contrast, intrathecal delivery of a TLR9 antagonist alleviates SCI-elicited neuropathic pain, bladder dysfunction and neuroinflammation. Studies to unravel the potential cellular and molecular mechanisms underlying these beneficial effects indicated that treatment with the TLR9 antagonist modifies the glial scar that forms around the lesion core. The antagonist attenuated astrocyte proliferation and increased the percentage of alternatively activated, neuroprotective M2 macrophages at the glial scar. Moreover, there was a reduction in the levels of chondroitin sulfate proteoglycans (CSPGs), inhibitors of axonal re-growth which are predominantly released by reactive astrocytes. These changes were paralleled by improved preservation of injured proximal axons. In vitro investigations indicated that direct antagonism of astroglial TLR9 hinders astrocyte proliferation by inhibiting the ERK/MAPK signaling pathway. Moreover, in astrocyte-macrophage co-cultures, the TLR9 antagonist enhanced the chemotaxis of macrophages and their polarization into the M2 phenotype through modulation of astrocyte-to-macrophage signals. Collectively, these findings suggest that treatment with the TLR9 antagonist creates a favorable milieu at the lesion site. This could be partly mediated by alterations in astrocyte function and in astrocyte-macrophage interactions.

Student/Post-doc Presentations

Breakout Room Presentation: Friday, Nov 20: 3.45-3.55 PM

Differences between the KCNB1 machinery complex and its KCNB1-R312H mutant found in epilepsy

Authors: Alessandro Bortolami and Federico Sesti

PI Name: Federico Sesti

Voltage-gated potassium channel (KCNB1, Kv2.1) is fundamental for neuronal excitability. Kv2.1 channel, which is abundantly expressed in the cortex and hippocampus, is one of the main actors in the intracellular signaling and it is essential for the correct cell life cycle. Specifically, this role is allowed by the interaction of Kv2.1 with other intramembrane proteins. The study of this signaling machinery is fundamental to understanding neuropathies, such as epilepsy, in which the mutation of this complex leads to altered neuronal function. Previous studies of our laboratory demonstrated that Kv2.1 is associated with integrin α5. Since integrins work as a dimer, applying coimmunoprecipitation and immunohistochemistry we observed a pool of different β integrins interacting with Kv2.1- α5, specifically β1 and β5. Our investigation of additional proteins intracellularly linked with Kv2.1-integrin complexes showed physical interactions with paxillin, vinculin and talin. Paxillin directly associates with the cytoplasmic tail of β-integrin and works as a scaffold protein. For this reason, we speculate that paxillin is linked to the channel complex throughout the β- integrin. To observe the alterations of this complex in epilepsy we compared WT-Kv2.1 mice with our epileptic mice model, which has a mutation in the channel's voltage sensor domain (R312H-Kv2.1). We finally identified structural differences in the R312H-Kv2.1 complex that we hypothesize are the reason for intracellular signaling alterations that may cause hyperactivity behavior and permanent functional and structural damage in neurons.

Breakout Room Presentation: Friday, Nov 20: 4.00-4.10 PM

Does neuromodulation result in reduction of circuit variability at the single cell level?

Authors: Anna C. Schneider, Dirk Bucher, Farzan Nadim

PI Name: Farzan Nadim

Neural circuits produce remarkably similar output across individuals. This is surprising since the underlying ionic currents, which give rise to the activity of the circuit, vary largely in the same cell type. Neural circuits operate in the presence of multiple neuromodulators in vivo. We hypothesize that neuromodulation plays a key role in reducing interindividual variability. We focused on the chemically isolated LP neuron of the crab stomatogastric nervous system. Only one copy of this neuron exists in each animal. LP produces rebound bursting oscillations driven by periodic inhibition from a group of pacemaker neurons. We measured excitability and rebound properties of LP in control saline and in the presence of one or two peptide modulators. We then compared the variability of these responses across preparations under the different modulatory conditions. Our results demonstrate that neuromodulators increased LP's excitability, decreased rebound latency, and changed rebound spiking structure. Furthermore, the application of even a single neuromodulator reduced the interindividual variability at the single-cell level. However, the addition of a second modulator did not additionally reduce variability. Funded by- . DFG SCHN 1594/1-1 & NIH MH060605

Breakout Room Presentation: Friday, Nov 20: 4.15-4.25 PM

Functional impact of KCNJ6 variants on alcohol use disorder phenotypes in iPSC-derived human neurons

Authors: Dina Popova, Mark Youssef, Petronio Zalamea, Jay Tischfield, Zhiping Pang, Ronald P. Hart.

PI Name: Ron Hart

A family-based study observed genome-wide association of heritable event-related oscillation deficits, often observed in alcoholics and in their offspring at high risk to develop alcoholism, with noncoding/synonymous single nucleotide polymorphisms (SNPs) in KCNJ6. This gene encodes GIRK2, a G-protein inward rectifying potassium channel responsible for regulating excitability of neurons. KCNJ6 variants have been associated with drug addiction and alcohol-related behaviors and is a target for ethanol. We hypothesize that alcoholism-associated KCNJ6 SNPs affect excitability of neurons, making them more vulnerable to the effects of alcohol. To test this hypothesis we obtained 8 human iPSC lines (4 affected/alcoholics/major allele and 4 unaffected/non-alcoholics/minor allele, sex balanced) from the Collaborative Study on the Genetics of Alcoholism (COGA) repository and prepared glutamatergic neurons using Ngn2 induction. Morphological and electrophysiological properties of neurons were examined in parallel with cytochemical detection of GIRK2 expression. We found that basal morphology and electrophysiological properties of neurons generated from major and minor allele carriers were unchanged. However, affected minor allele carriers show a reduction in GIRK2 expression, which was paralleled by increased excitability of the neurons. Single-cell RNAseq also identifies that KCNJ6 minor allele neurons exhibit increases in ribosomal and cholesterol pathways. We conclude that there are physiological differences between neurons from affected and unaffected subjects associated with excitability, possibly due to altered GIRK2 expression. Funded by NIH U10 AA008401

Breakout Room Presentation: Friday, Nov 20: 4.30-4.40 PM

MAPK -mediated proapoptotic signaling by K+ channel integrin complexes

Authors: Elena Forzisi and Federico Sesti

PI Name: Federico Sesti

Oxidative stress in association with high amounts of Reactive Oxygen Species (ROS) is a common feature observed in most neurodegenerative disorders such as Alzheimer Disease, traumatic brain injury and stroke. ROS act directly on neuronal macromolecules modifying their structural conformations and their functions leading to neuronal apoptosis. One of the macromolecules involved in this detrimental process is the voltage-gated K+ channel KCNB1. Our preliminary data shows that under oxidative conditions the channel forms oligomers and complexes with integrins alfa5 and they activate Ras GTPase among others signaling proteins. Although under normal condition and physiological stimuli the KCNB- integrin signaling modulates cell proliferation and survival; oxidative stress can trigger, through the same pathway, cell damage and apoptosis. Since one of the proteins related to oxidation of the channel is Ras, we speculate its involvement in the neurodegeneration process. The MAPK kinase cascade is the principal signal pathway of Ras, with downstream activation of Raf/ MEK/ ERK proteins. We investigated the activation of this cascade under hydrogen peroxide stimuli and selective inhibitors agents in CHO cells and mice brain samples that express WT-KCNB1 channel or a mutated form oxidation-resistant C73A- KCNB1. According to our hypothesis, we observed an increase in expression of RAF/MEK/ERK active form after the treatment and a significant connection between the KCNB1 channel oxidation and MAPK cascade set off. Pharmacological inhibition of the cascade inhibits KCNB1-mediated apoptosis. Together these data suggest that KCNB1 oligomerization leads to proapoptotic consequences by means of MAPK kinase pathway activation.

Breakout Room Presentation: Friday, Nov 20: 4.45-4.55 PM

Synaptojanin1 regulates Dopamine transporter trafficking via the PIP2/PI3K pathway

Authors: Jacqueline Saenz and Pingyue Pan

PI Name: Pingyue Pan

Parkinson's disease (PD) is a neurodegenerative disease characterized by the deterioration of dopaminergic neurons in the substation nigra. A long-standing question in the field is why dopaminergic neurons are vulnerable under PD-risk genetic conditions. Mutations of SYNJ1 (encoding synaptojanin1/synj1) are linked to families with parkinsonism. Synj1 is a key phosphatase of PI(4,5)P2, which is a membrane lipid essential for regulating neurotransmission. Dephosphorylation of PI(4,5)P2 by Synj1 assists in the clathrin coat removal from newly formed vesicles in neurons. Synj1 deficiency or inhibition of the PI3K pathway results in PI(4,5)P2 accumulation and impairs vesicle reformation. Recent studies from our lab and others have shown that Synj1 deficiency in mice led to dopamine neuron-specific synaptic defects, such as enlarged striatal dopaminergic terminals and impaired synaptic vesicle endocytosis. I now hypothesize that synj1 also regulates the recycling of dopamine transporter (DAT) via the PI(4,5)P2/PI3K pathway. Our preliminary data showed increased DAT immunofluorescence in the striatum of aged Synj1+/- mice. Consistently, DAT was increased in the soma and nerve terminals of cultured Synj1+/- dopamine neurons, however, the surface expression of DAT was reduced in Synj1-deficient conditions. PIP2 levels are specifically increased in Synj1 deficient midbrain neurons, but not cortical neurons. My recent data suggests that in cell lines, PIP2 levels can be manipulated at the membrane using pharmacological reagents targeting the PI3K pathway, which mimics Synj1 deficiency. I plan to use both pharmacological tools and genetic models to investigate if Synj1 regulates DAT surface expression via the PIP2/PI3K pathway. Funded by BHI pilot grant and the NIH supplement (3R01NS112390-02S1)

Breakout Room Presentation: Friday, Nov 20: 5.00-5.10 PM

Alcohol exposure induces depressive- and anxiety-like behaviors and neuroinflammation in the habenular nucleus of rats

Authors: Jiayi Zheng, Ding Li, Hualei Geng, Wanhong Zuo

PI Name: Jiang-Hong Ye

Alcohol use disorders (AUDs) often co-occur with other psychiatric conditions, including depressive disorders (DDs). The mechanisms underlying these disorders and their comorbidity remain unclear. Recently, interest in the lateral habenula, a small epithalamic brain structure, has increased because it can inhibit the dopamine and serotonin neurons in the midbrain reward center, the hypofunction of which is believed to be a critical contributor to the etiology of DDs and AUDs. Alcohol (EtOH)-induced neuroinflammation may play an essential role in the higher risk of DDs in alcoholics. To test whether AUDs can cause DDs and whether this involves changes in the neuroimmune factors, we conducted experiments on thirty six female Spray Dawley (SD) rats, which were randomly divided into two groups, EtOH treated and EtOH Naïve groups. They were treated with alcohol vapor or air for 4 weeks, following with alcohol or water intragastric administration for 10weeks. Behavioral tests for anxiety and depression were conducted 24 hours after the last EtOH/water session. We observed that the EtOH-treated group had significantly higher anxiety and depressive-like behaviors as reflected in the elevated plus-maze and open field. Besides, we observed a significant increase in the expression of inflammatory factors, such as IL-1β, IL6, and NLRP3 in the habenula of EtOH-treated rats. The future experiment will test whether these inflammatory factors in the habenula contribute to anxiety and depressive-like behaviors

Breakout Room Presentation: Friday, Nov 20: 5.15-5.25 PM

Manipulation of glucose concentration in Lateral Hypothalamus affects motivation for sucrose pellets in a task dependent fashion.

Authors: Joshua Stamos, Suraj B Teegala, Katherine Stalnaker, Vanessa H Routh, and Kevin D. Beck

PI Name: Kevin Beck

Lateral Hypothalamus (LH) is known to play an important role in motivation for food. However, the mechanism for this effect remains unclear. It has been shown that elevated body glucose levels has a satiating effect on hunger. It is also known that LH expresses glucose receptors. However, the connection between LH glucose concentration and motivation for food has never been explicitly shown. Here, we use microdialysis to modulate LH glucose concentration during two sucrose pellet self-administration tasks. We present preliminary data indicating that higher concentrations of glucose in LH lower the break point in a progressive ratio sucrose pellet self-administration task in a dose dependent fashion. High LH glucose concentrations (4mM) prevent sucrose pellet self-administration in a fixed ratio (FR) 32 self-administration design. However, changing LH glucose concentrations from normal to high levels during the FR 32 session has no effect on self-administration. These results indicate that once the FR task has begun the animal's behavior is no longer responsive to LH glucose concentration. These results bring up interesting questions about the nuanced nature of motivation for food reward. Funded by R01 DK103676.

Breakout Room Presentation: Friday, Nov 20: 3.45-3.55 PM

From Neurocardiac Signaling to Cognitive Recovery: A randomized clinical trial in women receiving outpatient treatment for alcohol and substance use disorders

Authors: Julianne Price, Anthony Pawlak, Evgeny Vaschillo, Julie Morgano, Sabrina Todaro, Sarah Grace Uhouse, Bronya Vaschillo, Jennifer Buckman, Marsha Bates

PI Name: Marsha Bates and Jennifer Buckman

Neurocognitive improvement is critical to successful recovery from alcohol and substance use disorders (ASUD) yet attempts at cognitive retraining have only been modestly successful. Many features of cognition and drinking behavior alike are arousal dependent. Resonance breathing (0.10 Hz), a slowed breathing technique that aligns the cardiovascular and neurocardiac signals, can modulate arousal and potentially improve cognitive function in a treatment-seeking population. In a randomized clinical trial, outpatient women with ASUD (N=77) completed in-lab cardiovascular and cognitive [Trail Making Task (TMT), Digit Symbol, and Stroop] assessments. They were then provided an app that either paced breathing to resonance or a faster-paced control (0.23 Hz) not associated with any therapeutic benefit. Following 8 weeks of app intervention, participants repeated the in-lab assessments. Cross-panel models examined pre-to-post cognitive performance considering intervention (active vs. control), frequency of app use, and pre-post cardiovascular function (previously reported). Those who were in the active condition (p=.08, ß= 1.70) and who used the app more frequently (p=.03, ß= 2.15) showed greater post-intervention performance on the TMT. Including cardiovascular function variables improved model fit but did not predict cognition. Utilization of a paced-breathing app is associated with improved cognitive performance in women with ASUD. While the underlying mechanisms are unclear, breath control may improve arousal modulation in times of stress through alignment of the neurocardiac and cardiovascular signals. Further study into the relationship between respiration, cardiovascular function, and neurocognition are needed to understand the process and improve implementation. Funded by the NIH (AA023667; MPI: M Bates, J Buckman). Dr. Price is funded through the Molecular Neuroscience of Alcohol and Drug Abuse Training T-32 (AA028254; PI: D Sarkar)

Breakout Room Presentation: Friday, Nov 20: 4.00-4.10 PM & 4.45-4.55 PM

Orexin drives motivation for palatable food via actions at orexin-1 receptor on VTA dopamine neurons

Authors: Kaushanie Fernandopulle, Sam Liu, Jackie Mehr, Shayna O'Connor, Nicholas T Bello, Gary Aston-Jones, Morgan H James

PI Name: Morgan James

Binge eating disorder (BED) is characterized by a sense of a loss of control over how much and what is consumed. The hypothalamic orexin (hypocretin) system has been linked to psychiatric disorders characterized by compulsive behaviors and has shown to be critical for motivated behavior across multiple reinforcers. Previous studies have shown reduced motivation for drugs of abuse following blockade of orexin-1 receptor (Ox1R) signaling in ventral tegmental area (VTA). Here we directly assessed the potential interaction between Ox1R and dopamine signaling in the expression of motivational endophenotypes relevant to BED. Female, TH-Cre+ rats were trained to lever press for sucrose on a behavioral economics paradigm, whereby the 'price' of a sucrose reward was increased across the session. Rats then received intra-VTA unilateral microinjections of an AAV5-Ox1R-shRNA virus (to knockdown Ox1R) or an AAV5-DIO-Kir virus (to silence dopamine-expressing cells). A third group ('disconnect' group) received both viruses in opposite hemispheres. Rats were then exposed to a binge-like eating paradigm, whereby they received access to sweetened fat for 30 min, twice a week for 4w; they were then re-tested on the behavioral economics paradigm. Rats were also tested on a task where the delivery sucrose pellets was paired with foot shock of escalating intensity. Rats that received unilateral injections showed a significant increase in motivation following binge compared to baseline; this was not observed in the disconnect group. Similarly, responding for foot shock-paired sucrose pellets was reduced in the disconnect group. These findings indicate that orexin peptides act at Ox1R on VTA dopamine neurons to drive enhanced motivation following binge-like eating.
Funded by BHI Pilot Grants to GAJ, MHJ and NTB; NIDA K99/R00 to MHJ; NIDA R01 to GAJ

Breakout Room Presentation: Friday, Nov 20: 4.15-4.25 PM

Sex differences in cognitive processing and anxiety-like behavior after intermittent fasting in aged mice

Authors: Kimberly Wiersielis, Yasrebi, A., Conde, K. & Roepke, T.A.

PI Name: Troy Roepke

Intermittent fasting (IMF) is associated with many health benefits in animal models and humans. Yet, little is known if an IMF diet affects mood and cognitive processing. In humans, IMF during Ramadan may alleviate anxiety. Here, we address the impact of IMF on hippocampal-dependent memory using the Y-maze and spatial object recognition (SOR), hippocampal-independent memory using novel object recognition (NOR), and anxiety-like behavior using the open field task (OFT) in middle-aged male (12 mo) and aged female (18 mo) mice. Y-maze data indicate that IMF males, but not females, perform worse in the identification of the unknown arm than same-sex controls, suggesting an IMF-induced deficit in interpreting spatial navigation routes. In the SOR task, which evaluates hippocampal-dependent object orientation, IMF females, but not males, exhibited a decrease in performance. In the NOR, which detect differences in hippocampal-independent memory, IMF males, but not females, performed better than their same-sex counterparts. Our results suggest that, in males, IMF results in deficits only in hippocampal-dependent tasks, yet an enhancement in performance when hippocampal-independent tasks are conducted. In females, only the hippocampal-dependent task of SOR was affected by IMF, suggesting IMF disrupts spatial object configuration. In the OFT, IMF male and female mice spent more time in the center zone, indicative of an anxiolytic phenotype. Our research suggests that IMF affects memory dependent upon age, sex, and hippocampal involvement, and induces an anxiolytic phenotype in both male and female aged mice.

Breakout Room Presentation: Friday, Nov 20: 4.30-4.40 PM

Adenosine kinase regulates status epilepticus induced neurogenesis

Authors: Madhuvika Murugan, Detlev Boison

PI Name: Detlev Boison

Adenosine kinase (ADK), a key enzyme in adenosine metabolism, plays a critical role in epilepsy. ADK exists in two isoforms – ADK-S is found in the cytoplasm and ADK-L is found in the nucleus. In epilepsy, the role of cytoplasmic ADK-S in regulating intra- and extracellular adenosine levels and thereby regulation of adenosine receptor dependent mechanisms is well known. However, recent evidence suggests a novel epigenetic mechanism by which the ADK-L isoform contributes to epileptogenesis and epilepsy progression. In this study, we assessed the spatiotemporal distribution of ADK isoforms in a kainic acid induced status epilepticus (KASE) model and investigated its role in the epigenetic regulation of SE-induced neurogenesis. To this end, brain tissue from 8-10-week-old C57BL/6 mice were collected at 0h, 2h, 1d, 3d and 7d time points following intrahippocampal KA injections. Immunohistochemistry with antibodies against ADK, Ki67 and DNA methyltransferase 1 (DNMT1) was performed to determine tissue ADK expression, number of proliferating cells and DNA methylation, respectively. Our results indicate a distinct cell and isoform specific expression pattern of ADK after status epilepticus (SE). Interestingly, the protein expression of ADK inversely correlated with SE-induced cell proliferation in the dentate gyrus, suggesting a critical role for ADK in stem cell proliferation possibly via epigenetic mechanisms. Many of these new cells are thought to integrate abnormally, potentially contributing to epileptogenesis, hence the role of ADK in neurogenesis, epilepsy development and maintenance warrants further investigation. Funded by- National Institutes of Health (NS065957, NS103740) and Citizens United for Research in Epilepsy (CURE Catalyst Award)

Breakout Room Presentation: Friday, Nov 20: 4.45-4.55 PM

Evidence of human parahippocampal theta activity during goal-directed spatial navigation: A combined EEG-fMRI study

Authors: Malte Gueth, Ravi D. Mill, Michael W. Cole, & Travis E. Baker

PI Name: Travis Baker

Parahippocampal theta activity has been credited to coordinate neural processes related to spatial navigation. Previously we found that feedback stimuli presented in a virtual maze environment elicited a burst of theta power over right-posterior areas of the human scalp (right-posterior theta: RPT), and was sensitive to the spatial trajectory (e.g. stronger theta for rightward turns). Further, source localization of this effect and a recent fMRI study pointed to a neural generator in the right parahippocampal cortex (rPHC). However, this interpretation is complicated by the inverse problem and the absence of time-frequency information in the hemodynamic response. Here, we addressed this issue using simultaneous EEG–fMRI recordings in 13 subjects navigating a virtual Maze No-maze task to find rewards. Consistent with previous work, RPT power was sensitive to the spatial location of the feedback, an effect only observed when the rewards were presented in a spatial environment. In the fMRI domain, spatial-related hemodynamic modulation was associated with activations of the spatial network, including the rPHC, as well as the hippocampus and precuneus. Further, feedback following rightward trajectories, relative to leftward trajectories, in the maze elicited stronger responses in a posterior cluster of the rPHC. Next, we entered parametric regressors based on frequency bands into a Linear Mixed Effects model. Hemodynamic responses in the posterior cluster of the rPHC during rightward navigation were exclusively predicted by RPT power. These results a role for PHC theta oscillations in encoding salient information for the purpose of spatial navigation.

Breakout Room Presentation: Friday, Nov 20: 5.00-5.10 PM

Maternal T-cell Activation and Postnatal Behavioral and Microglial Changes to Staphylococcal Enterotoxins

Authors: Marialaina Nissenbaum, Ruthy Glass, Nicholas Fox, Spencer Steigman, Diego Prado De Maio, Lori Covey, John Pintar, Huaye Zhang and Alexander W. Kusnecov

PI Name: Alexander Kusnecov

Maternal immune activation can be a neurodevelopmental disruptor. Recently, we found that maternal responses to T-cell "superantigens", Staphylococcal enterotoxins A (SEA) and B (SEB), induce deviations in normal offspring behavior. Two strains of pregnant female mice (C57BL/6 and BALB/c) received saline, SEA or SEB (200 μg/Kg) on embryonic day 12.5 (E12.5). Maternal enterotoxin treatment induced increased IL-2, IL-4, IL-6 and IFNγ levels, but no changes in IL-17A. In C57BL/6 pregnant females challenged with SEA or Saline at E12.5, SEA-selective T cell expansion was increased by 48hr, suggesting that T cell responses to SEs are active for several days during embryonic development. Postnatal behavioral assessments of juvenile offspring from SEA/SEB challenged mothers revealed strain-dependent differences in social behavior; BALB mice showed an increase, while C57BL/6 mice showed a decrease in social investigation. Both strains, however, showed delayed spatial learning (MWM), with SEA treatment in C57BL/6 mice also impairing radial arm maze learning. To determine if these effects are related to changes in postnatal microglial cell numbers and morphology, C57 mothers were given SEA or Saline on E10.5, E12.5 or E14.5. Quantitation across P7-P30 is being conducted in the hippocampus and prefrontal cortex. It is hypothesized that maternal immune-dependent alterations in microglial cell numbers in offspring may have a potential influence on synaptic pruning and/or dendritic spine density. Supported by MH104800, MH108994, and BHI.

Breakout Room Presentation: Friday, Nov 20: 5.15-5.25 PM

DBS-like stimulation of the nucleus accumbens shell induces presynaptic depotentiation at inputs on D2DR- but not D1DR-containing MSNs

Authors: Matthew Rich, Sarah E. Swinford-Jackson, Phillip J. Huffman, and R. Christopher Pierce

PI Name: Chris Pierce

Deep brain stimulation (DBS) within the nucleus accumbens (NAc) may suppress drug craving and relapse; but, the mechanisms underlying the efficacy of DBS remain unknown. Medium spiny neurons (MSNs), the major projection neurons of the NAc are subdivided based on the expression of either dopamine D1 receptors (D1DRs) or dopamine D2 receptors (D2DRs). Using optogenetic stimulation to mimic DBS we found that the relapse-attenuating behavioral effect was specifically driven by actions at D2DR-MSNs, indicating that DBS-induced suppression of cocaine reinstatement may be mediated by differential effects at the two MSN subtypes. To investigate cellular-specific mechanisms of DBS, we utilized transgenic rat lines that selectively express Cre recombinase in D1DR- or D2DR-containing neurons in combination with a Cre-dependent adeno-associated viral vector expression of eYFP. We then performed whole-cell patch clamp recordings from eYFP+ neurons (putative D1DR- or D2DR-MSNs) located in the medial NAc shell. Electrical stimulation (12 Hz) of NAc afferents evoked LTP-like postsynaptic responses in both D1DR- and D2DR-containing MSNs; however, prior cocaine experience occluded postsynaptic LTP in D1DR-MSNs. Additionally, measures of presynaptic plasticity were only altered in D2DR-MSNs. Paired pulse ratio and frequency of spontaneous excitatory postsynaptic currents (EPSCs) were significantly decreased following stimulation, suggesting a presynaptic depotentiation in D2DR- but not D1DR-MSNs. Taken together, our results show that DBS-induced attenuation of cocaine-seeking behavior is dependent on cell-type specific synaptic remodeling within the NAc shell. Supported by R01DA015214 and T32DA028874

Breakout Room Presentation: Friday, Nov 20: 3.45-3.55 PM

Ventromedial hypothalamic (VMH) neuronal nitric oxide synthase (nNOS)- glucose inhibited (GI) neurons may mediate the effects of estrogen on brown adipose tissue thermogenesis and white adipose beiging

Authors: Sarkar, P., Patel, V , Pamela Hirschberg, Vanessa Routh

PI Name: Vanessa Routh

Brown (BAT) and beige adipose tissue thermogenesis increases energy expenditure and protects against dietary obesity. Estrogen increases BAT thermogenesis, and beiging of white adipose tissue (bWAT) by activating lateral hypothalamic (LH) orexin (OX) neurons. This effect of estrogen is dependent on ventromedial hypothalamic (VMH) AMP-kinase (AMPK) inhibition by bone morphogenic protein 8B (BMP8B). AMPK inhibition is also required for estrogen's inhibitory effect on VMH glucose inhibited (GI) neurons. GI neurons are activated during periods of low energy such as fasting and hypoglycemia and signal to increase blood glucose levels. They may also play a role in energy homeostasis. Activation of VMH GI neurons in low glucose depends on AMPK-induced activation of neuronal nitric oxide synthase (nNOS). We hypothesize that VMH AMPK-dependent nNOS-GI neurons project to and inhibit LH OX neurons. Further, that BMP8B and estrogen activate LH OX neurons by inhibiting AMPK in VMH nNOS-GI neurons and preventing their activation during energy deficit. We test this hypothesis by injecting fluorescent retrograde tracers in the LH and using immunohistochemistry to determine whether retrobead positive VMH neurons express nNOS and the BMP8B receptor BMPR1a. Whole cell patch clamp recording was also used to determine whether retrobead expressing neurons were GI. We found that VMH nNOS and BMPR1a expressing neurons do project to the LH. Moreover, VMH GI neurons also project to the LH. These data suggest a role for AMPK-dependent VMH nNOS-GI neurons in the control of BAT thermogenesis and bWAT by estrogen and BMP8B.
Supported by F31DK126433-01 & R01DK10367

Breakout Room Presentation: Friday, Nov 20: 4.00-4.10 PM

Theta-band resonance in a neocortical circuit

Authors: Rodrigo Pena, Horacio G Rotstein

PI Name: Horacio G Rotstein

Sensory signals arriving from different areas are integrated into the neocortex. Oscillations at certain frequency bands are believed to coordinate activity in many areas. Resonance refers to the ability of a system to generate an amplified response for oscillatory inputs tuned to a specific frequency. Recent work showed the role of inhibition in the generation of theta (4-11 Hz) resonance in the neocortex. Optogenetic activation of interneurons induced theta-band-limited spiking in pyramidal neurons; however, direct optogenetic activation of pyramidal cells did not generate any resonance. To determine the mechanisms we constructed a biophysical model of the neocortex with pyramidal cells (PYR), parvalbumin-positive (PV) and somatostatin-expressing (SOM) interneurons. These cells are connected with exponential decaying synapses with short-term depression/facilitation. Every cell spontaneously fires while receiving a noise input. We apply periodic currents with different frequencies into PV cells and evaluate the PYR output. By applying oscillatory activation in PV, resonance was induced in PYRs whereas direct activation of PYRs did not show resonance, as experimentally reported. Our results highlight the importance of post-inhibitory rebound in order to transfer signals from PV to PYR cells. SOMs, adaptation, depression, and facilitation regulate these resonance effects. The effects can be explained by additional frequency filters that are added to the system: adaptation and facilitation act as a high-pass filter while depression acts as a low-pass filter. SOM cells regulate the low frequencies since they connect to other neurons through facilitation. Funded by NSF -DMS-1608077 (HGR).

Breakout Room Presentation: Friday, Nov 20: 4.15-4.25 PM

Simulating multiple sources of surface alexia in a computational model of reading

Authors: Ryan Staples, David C. Plaut, Jeffrey R. Binder, Olga Boukrina, Elizabeth B. Madden, A. M. Barrett, Nadine Martin, Argye E. Hillis, William W. Graves

PI Name: William Graves

The symptoms of surface alexia (an enhanced frequency-by-regularity interaction and the production of regularization errors) have been considered to result from damaged semantic representations. Surface errors can occur without impairment on semantic tasks. We use an artificial neural network (ANN) implementation of the triangle model of reading to examine the hypothesis that surface alexia with and without semantic impairment can be simulated in a single system. The model was a simple recurrent ANN. An orthographic input layer was fully connected to two hidden layers: one projecting to the phonological output layer and one to a semantic layer. This semantic layer projected onto a recurrent context layer and onto another hidden layer, which led to the phonological output layer. The trained model read 99.6% of the training set correctly and averaged 78.5% accuracy on held-out pseudowords. Each model initialization was lesioned at each of four locations (the orthography-phonology hidden layer and three locations along the semantic pathway) by removing 50% of the links into and out of the damaged layer. The model re-trained for 125 epochs. Lesions at multiple points along the semantic pathway caused larger frequency-by-regularity interactions (estimated with logistic regression) than orthography-phonology lesions ($t(14.037) = 3.117$, $p < 0.01$). Regularization errors occurred following semantic pathway lesions, but not orthography-phonology lesions ($t(110.7) = 7.626$, $p < 0.01$). These results demonstrate that lesions at multiple points along the semantic pathway produce the symptoms of surface alexia and provide a step towards modelling individualized therapies for acquired alexia. Funded by HD065839 (WWG).

Breakout Room Presentation: Friday, Nov 20: 4.30-4.40 and 4.45-4.55 PM

Human Operant Evaluations of Treatment Relapse

Authors: Sean Smith, and Brian D. Greer

PI Name: Brian Greer

Children with intellectual and developmental disabilities with limited communication skills often engage in problematic behavior to gain access to reinforcers. The most effective treatment for their problematic behavior is teaching them more communication skills. However, treatment relapse often occurs when an initially efficacious treatment is disrupted; for example, when the newly taught communication skills fail to produce reinforcers. This particular form of treatment relapse is called resurgence. Resurgence as Choice (RaC) is a quantitative model developed from animal models of treatment relapse, and recent research has demonstrated that RaC accurately predicts how multiple variables interact to produce different amounts of treatment relapse for nonhuman subjects. However, the accuracy of the quantitative model's predictions for human behavior is less clear. Evaluating the predictions made by RaC with human subjects can be problematic because it involves exposing participants to conditions that produce treatment relapse of potentially harmful behavior. We have developed a computer program that can manipulate each of the independent variables that RaC predicts to affect relapse, allowing researchers to translate findings from animal laboratories to human subjects safely using human operant preparations. Two especially important predictions made by RaC are that pretreatment and treatment durations will affect the magnitude of relapse. Evaluating the effects of these variables could have important applied implications for minimizing treatment relapse. Funded by R01HD079113, R01HD083214, and R01HD093734.

Breakout Room Presentation: Friday, Nov 20: 4.45-4.55 PM

Role of ketohexokinase in fructose sensing in the brain

Authors: Stephanie Garcia, Vanessa H. Routh, Andrew P. Thomas

PI Name: Vanessa H. Routh, Andrew P. Thomas

The introduction of high-fructose corn syrup has been associated with increased obesity and metabolic diseases. Thus, it is important to understand the effect of fructose on metabolic regulation and feeding. Fructose induces a paradoxical counterregulatory response leading to hyperglycemia, and activates CNS reward pathways without the satiation observed with glucose, resulting in enhanced food consumption. Interestingly, Fructose Sensing Neurons (FSNs), a subpopulation of neurons sensing and responding to fructose (identified by the Thomas lab), and Glucose Sensing Neurons (GSNs) show opposing effects on neuronal excitability. These monosaccharides are sensed through different metabolic pathways starting with glucokinase and ketohexokinase (KHK), respectively. In contrast to glucose metabolism, fructose phosphorylation by KHK is unregulated and can deplete ATP in the continuous presence of fructose. Based on behavioral and cellular evidence, we hypothesize that fructose and glucose metabolism lead to opposing effects on neuronal activity and feeding behavior; with KHK as a potential target for these differences. To understand the brain circuitry involved, we are mapping fructose-sensing regions with a KHK antibody. Expression has been found in CA1, CA2, CA3 and VMH, demonstrating potential fructose sensing in regions known for memory, learning, and homeostatic signaling. KHK knockout mice were used in a behavioral paradigm assessing motivation to seek food. No significant differences were found in these initial behavioral studies, suggesting KHK alone does not elicit a reward-seeking response. We continue to investigate fructose metabolic sensing in the CNS, including identification of fructose-sensing regions using calcium imaging.

Breakout Room Presentation: Friday, Nov 20: 5.00-5.10 PM

The mGluR5 agonist CHPG enhances recovery in mice subjected to experimental autoimmune encephalomyelitis (EAE)

Authors: Talia Planas--Fontánez, Y. Huang, S. Sathi, A. DeStefano, T. Sullivan, Cheryl F. Dreyfus

PI Name: Cheryl Dreyfus

Most treatments for demyelinating diseases, such as Multiple Sclerosis (MS), focus on targeting focal inflammatory lesions. However, remyelination treatments to enhance myelin repair mechanisms are still needed. Previous studies demonstrate that the general mGluR agonist, 1-amino-1,3-dicarboxycyclopentane (ACPD), enhances myelin proteins in a lesion site through production and release of BDNF from astrocytes, mediated through mGluR5. Recent work indicates that similar effects are elicited by intraperitoneal injection of the mGluR5 agonist, (R,S)-2-chloro-5-hydroxyphenylglycine (CHPG). Here, we assess the effects of CHPG in the MOG-EAE mouse model. Studies demonstrate that CHPG treatment (20mg/kg; i.p.; every other day) significantly reduces clinical scores of EAE mice. To define the role of astrocyte-derived mGluR5 in this process, effects of CHPG were examined in inducible-conditional hGFAP-CreERT2-mGluR5 fl/fl ROSA26 mice. Ablation of mGluR5 inhibits CHPG effects. Moreover, while EAE induction results in a significant decrease in BDNF (55%) and in PLP (58%) in the lumbar spinal cord, CHPG reverse deficits of these proteins to unlesioned control levels, suggesting the involvement of mGluR5 and BDNF. To determine which cells in EAE mice may be targets of CHPG action, several types were analyzed for the presence of mGluR5. Co-localization of mGluR5 with astrocytes and activated microglia was noted within lesion sites, indicating that these glial cells may be targets of CHPG actions. Targeting astrocyte-derived mGluRs might provide a new therapeutic opportunity in MS. Funded by NMSS RG4257B4/1, R01 NS03664, BMS Fellowship

Breakout Room Presentation: Friday, Nov 20: 5.15-5.25 PM

Developmental Role of Adenosine Kinase in the Cerebellum

Authors: Hoda Gebril, Amir Wahba, Xiaofeng Zhou, Emanuel DiCicco-Bloom, Tho Lai, Detlev Boison

PI Name: Detlev Boison

Adenosine acts as neuromodulator and metabolic regulator of the brain through a combination of adenosine receptor dependent and independent mechanisms. In the adult brain, adenosine is tightly regulated by its metabolic enzyme, adenosine kinase, existing in a cytoplasmic isoform ADK-S, and a nuclear isoform ADK-L. We recently discovered that ADK-L contributes to the regulation of neurogenesis, development, and plasticity of the adult hippocampus. Although the cerebellum is a highly plastic brain area with a delayed developmental trajectory, the role of ADK in the cerebellum remains obscure. This study was designed to investigate the developmental profile of ADK expression in the cerebellum and its role in developmental and proliferative processes. Using immunohistochemistry and Western Blot analysis, we found high levels of ADK-L expression during cerebellar development in cerebellar granular neuron precursors and Purkinje cells, which was maintained into adulthood, in contrast to cerebrum in which ADK-L expression is gradually reduced during development and largely restricted to astrocytes. In line with a functional role of ADK-L for cell proliferation, we found that the ADK inhibitor 5-iodotubercidin dose dependently blocked the proliferation of cerebellar granular precursors. Using double immunofluorescence analysis of the developing and the adult cerebellum, we showed that the expression of ADK-L associated with developing and mature Bergmann glial cells in the Purkinje layer and astrocytes in the three layers of cerebellar cortex. Together, our data demonstrated an association between neuronal ADK-L expression and developmental processes of the cerebellum, indicating a functional role of ADK-L for plasticity of the cerebellum. Funded by Dale Rice, and NS065957, NS103740 and CURE Catalyst Award to DB.

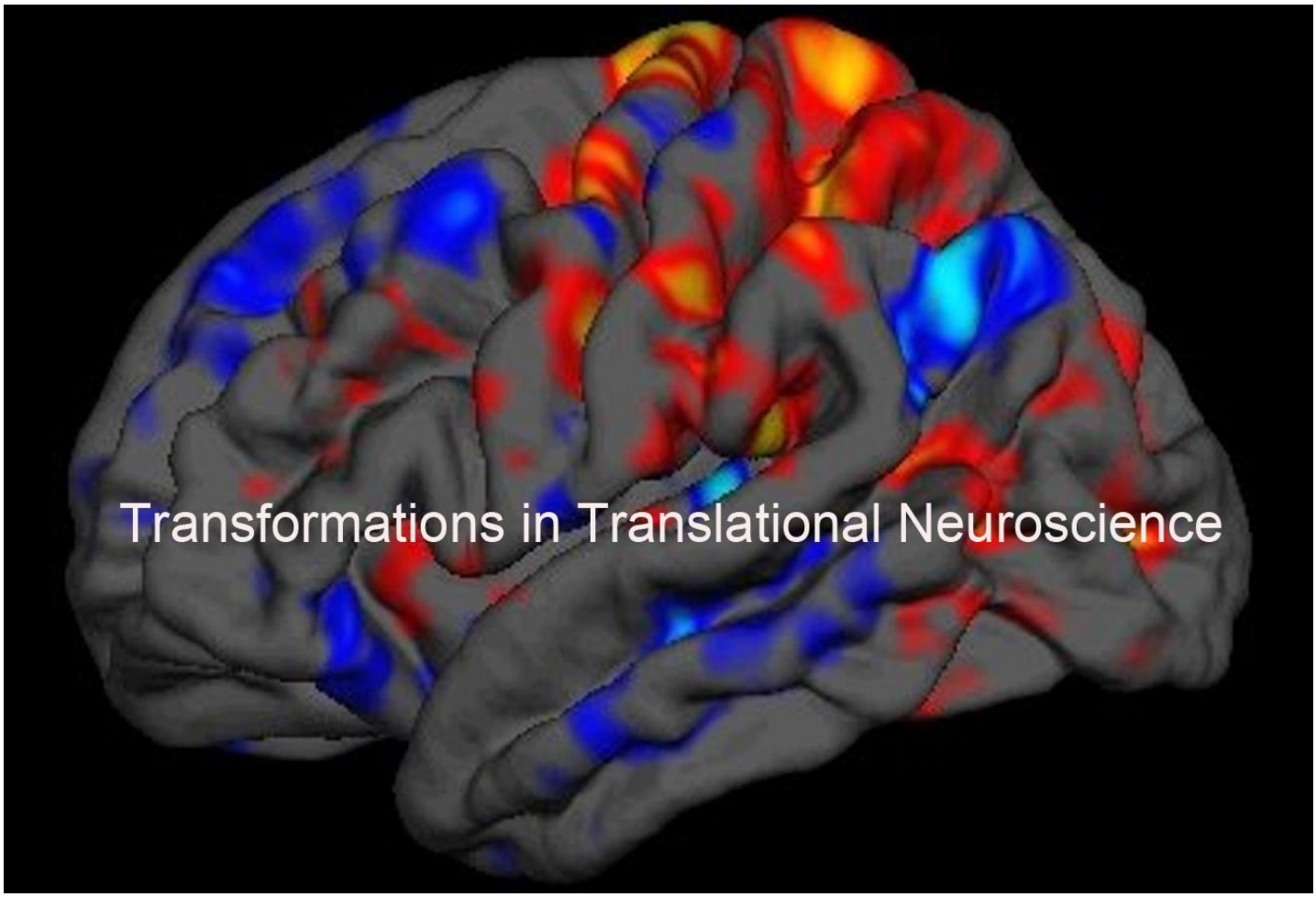
Breakout Room Presentation: Friday, Nov 20: 3.45-3.55 PM

Obesity effects on sensory evoked locus coeruleus (LC) neural responses and morphine withdrawal in rats

Authors: Xinyi Li, Chung-Yang Yeh, and Nicholas T. Bello

PI Name: Nick Bello

Locus coeruleus norepinephrine system (LC-NE) is implicated in a variety of cognitive processes, stress responsivity, and vulnerability to opioid misuse. This study aimed to examine the effects of obesity on LC activity and response to morphine withdrawal. Male obese prone (OP-CD) and obese resistant (OR-CD) rats (4 wks.) were fed high (HFD, 45% fat)- or low (LFD, 10% fat)- fat diets and underwent in vivo single unit electrophysiological recording under isoflurane anesthesia of LC activity at 14 weeks old (n= 31- 41 cells/ 6-7 rats). A separate group of Sprague Dawley (CD) rats (4 wks.) was placed on HFD and LFD for 18 weeks, received 5 days of saline or escalating doses of morphine (5- 15 mg/kg/BID, SC), and underwent 2 days of withdrawal. LC activity was subsequently measured on day 3 of withdrawal (n= 9- 19 cells/ 2- 6 rats). Electrophysiological recordings demonstrated increased sensory- evoked LC activity in OR-CD and LFD-fed OR-CD rats displayed higher evoked/ tonic activity (signal- to- noise ratio) than all other groups. Morphine treatment significantly reduced body weights and caloric intake in HFD- and LFD- fed CD rats and morphine withdrawal increased sensory- evoked LC activity. Signal- to- noise ratio revealed significant effects of diet and morphine treatment and morphine-treated HFD rat displayed the highest sensory-evoked activity. Two major health care issues are obesity and opioid misuse. These initial results suggest obesity to effect LC activity and LC neural responses to morphine withdrawal. Funded by USDA-NIFA NJ06180



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