

NIH Blueprint Workshop

**THE SCIENCE OF
INTEROCEPTION AND ITS ROLES
IN NERVOUS SYSTEM
DISORDERS**

April 16-17, 2019

Lister Hill Auditorium, NLM (Building 38A)
Bethesda, MD

Workshop Objectives

The objectives of this workshop are to identify gaps in research related to the science of interoception and its role(s) in nervous system disorders, and to develop strategies and recommendations to facilitate the advancement of this area of research. This workshop will bring together expertise from diverse fields including basic neuroscience, psychology, physiology, and clinical research to deliberate two important dynamic connections – the connections between the brain and body and the connection between basic research and human/clinical research. The primary focus areas for the workshop include the neural circuitry underlying the dynamic interactions between the central and peripheral nervous systems; interoceptive processes in associated diseases and disorders; effect of modulating interoceptive processes for potential interventions/therapies; and development of technologies and methodologies to enhance interoception research.

Workshop Planning Committee Members

National Center for Complementary and Integrative Health (NCCIH)

Dr. Wen G. Chen

Dr. Angela Arensdorf

Office of Behavioral and Social Science Research (OBSSR)

Dr. Dana Schloesser

National Institute on Alcohol Abuse and Alcoholism (NIAAA)

Dr. Changhai Cui

National Institute of Dental and Craniofacial Research (NIDCR)

Dr. Yolanda Vallejo

National Institute of Neurological Disorders and Stroke (NINDS)

Dr. Jim Gnadt

Dr. Michael Oshinsky

National Institute of Mental Health (NIMH)

Dr. Janine Simmons

Dr. Marjorie Garvey

National Institute on Aging (NIA)

Dr. Coryse St. Hillaire-Clarke

Dr. Lisbeth Nielsen

National Institute on Drug Abuse (NIDA)

Dr. Rita Valentino

National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

Dr. Victoria Spruance

National Cancer Institute (NCI)

Dr. Todd Horowitz

Dr. Paige Green

Agenda

April 16, 2019

- 8:30 AM **Welcome Remarks and Introduction**
Helene Langevin, Director of NCCIH
- 8:40 AM **Workshop Keynote:**
Ardem Patapoutian, Scripps Research
How do you feel? Role of sensing mechanical force in interoception
- 9:10 AM **Session 1: Neural Circuits Underlying Communication Between the Brain and the Body**
Session Chairs: *Janine Simmons (NIMH), Peter Strick (University of Pittsburgh)*
Rapporteur: *Gary Berntson (Ohio State University)*
Speakers:
Diego V. Bohorquez, Duke University
A gut choice
Zachary A. Knight, University of California, San Francisco
The neurobiology of thirst
Peter Strick, University of Pittsburgh
One example of the mind-body problem: circuits that link the cerebral cortex to the adrenal medulla
Richard D. Lane, University of Arizona
Limbic predictions gone awry: The role of maladaptive emotional avoidance in interoceptive insensitivity, persistent somatic symptoms and dyshomeostasis
- 11:30 AM ***Lunch***
- 12:30 PM **Session 2: Dynamics and Functions of the Central and Peripheral Nervous Systems in Interoception**
Session Chairs: *Lis Nielsen (NIA), Coryse St. Hillaire-Clarke (NIA), Lisa Barrett (Northeastern University)*
Rapporteur: *Karen Quigley (Northeastern University)*
Speakers:
Eliza Bliss-Moreau, University of California, Davis
Animal models of interoceptive neurobiology
Manos Tsakiris, University of London
Looking for the self outwith and within the body
Kyle Simmons, Johnson and Johnson

The insula: at the nexus of interoception and allostasis

Scott Kanoski, University of Southern California

The hippocampus: an interface between energy status signaling and memory function

2:30 PM **Break**

2:45 PM **Session 3: Modeling Disease, Alterations in Interoceptive Processes, and Comorbidities**

Session Chairs: *Changhai Cui (NIAAA), Rajita Sinha (Yale University)*

Rapporteur: *Bruno Bonaz (University of Grenoble, France)*

Speakers:

Paul J. Kenny, Icahn School of Medicine at Mount Sinai

Habenular Tcf712 links nicotine addiction to diabetes

Rita J. Valentino, NIDA

Visceral reactions

Martin P. Paulus, Laureate Institute for Brain Research

An active inference approach to interoceptive psychopathology

Emeran A. Mayer, University of California, Los Angeles

The Role of Gut Microbiome Brain Signaling in Interoception

4:45 PM **Wrap up**

5:00 PM **Adjourn**

April 17, 2019

8:45 AM **Workshop Keynote:**

Hugo Critchley, Brighton and Sussex Medical School

Disorders of interoception

9:15 AM **Session 4: Leveraging and Manipulating Interoception for Disease Intervention**

Session Chairs: *Victoria Spruance (NIDDK), Cynthia Price (University of Washington)*

Rapporteur: *Helen Weng (University of California, San Francisco)*

Speakers:

Lorenzo Leggio, NIAAA-NIDA

The gut in the brain: potential novel targets for the treatment of addictions

Jack L. Feldman, University of California, Los Angeles

Intero(re)ceptors affect breathing which affects everything else!

Jeanie Park, Emory University

Leveraging interoception to improve sympathetic function in chronic disease states

Vitaly Napadow, Harvard University/Massachusetts General Hospital

Therapeutic engagement of interoceptive pathways with respiratory-gated vagus nerve stimulation

Cynthia Price, University of Washington

Learning interoceptive awareness skills is linked to increased emotion regulation capacity and improved health outcomes

11:30 PM ***Lunch***

12:30 AM **Session 5: Technologies, Methodologies, and Biomarkers for Interoception Research**

Session Chairs: *Jim Gnadt (NINDS), Christof Koch (Allen Brain Institute)*

Rapporteur: Frederike Petzschner (University of Zürich, Switzerland)

Speakers:

Lisa Stowers, Scripps Research

Sensing and controlling urination from the brain

Rob W. Gereau, Washington University

Beyond the BRAIN: emerging technologies for measuring and manipulating cellular activity in the periphery

Warren Grill, Duke University

Interoceptive feedback from the urethra is essential to efficient voiding

Sarah Garfinkel, University of Sussex

Dissociating dimensions of interoception

2:30 PM ***Break***

2:45 PM **Session 6: Discussions - Future Directions & Recommendations**

Session Chairs: *Wen Chen (NCCIH), Dana Schloesser (OBSSR), and Angela Arensdorf (NCCIH)*

Speaker:

Sahib Khalsa, Laureate Institute for Brain Research

Charting a path forward for interoceptive neuroscience

Panelists: *Gary Berntson, Karen Quigley, Bruno Bonaz, Helen Weng, Frederike Petzschner*

4:45 PM **Wrap-up & Adjourn**

April 16, 2019

8:30 AM

Welcome Remarks and Introduction

Dr. Helene Langevin
Director of NCCIH

(Introduced by Dr. Wen G. Chen)



Helene Langevin, Director of National Center for Complementary and Integrative Health

Dr. Langevin was sworn in as director of the National Center for Complementary and Integrative Health on November 26, 2018. Prior to her arrival, she worked at the Osher Center for Integrative Medicine, jointly based at Brigham and Women's Hospital and Harvard Medical School, Boston. Dr. Langevin served as director of the Osher Center and professor-in-residence of medicine at Harvard Medical School since 2012. Dr. Langevin received an M.D. degree from McGill University, Montreal. She completed a postdoctoral research fellowship in neurochemistry at the MRC Neurochemical Pharmacology Unit in Cambridge, England, and a residency in internal medicine and fellowship in endocrinology and metabolism at The Johns Hopkins Hospital in Baltimore.

April 16, 2019

8:40 AM

Workshop Keynote One

Dr. Ardem Patapoutian

Scripps Research

(Introduced by Dr. Angela Arensdorf)



Ardem Patapoutian, Scripps Research Institute

Dr. Patapoutian is a professor in the Department of Molecular and Cellular Neuroscience at The Scripps Research Institute and a Howard Hughes Medical Institute investigator. The Patapoutian laboratory is interested in how we perceive physical stimuli such as temperature and pressure and employs innovative functional genomic techniques to identify and characterize novel ion channels and other sensors that translate mechanical energy into chemical signals. Piezocation channels discovered by the lab are expressed in tissues where mechanical forces influence biological processes such as touch; pain; hearing; cardiovascular, lung, and kidney function; and so on. The aim of the lab is to determine the roles of Piezos in these various scenarios and find new sensors of mechanical force. Dr. Patapoutian received his Ph.D. from the California Institute of Technology and was a postdoctoral fellow at

the University of California, San Francisco.

How do you feel? Role of sensing mechanical force in interoception

Interoception, the sense of internal state of the body, is now recognized to play an essential role in disparate physiological processes and diseases, and yet it is not understood at a deep level. We have limited knowledge on the relevant stimuli that are sensed for interoception, the circuitry of how this information is transmitted to the brain, and the consequences or output of these sensory signals. I will introduce interoception and focus on the first step in the process, which is the transduction or sensing of stimuli relevant for interoception. I will argue that mechanical forces are an important but largely ignored source in interoceptive input. Part of the reason why we understand so little about this process has been the lack of a molecular handle on mechanosensation. My lab identified PIEZO1 and PIEZO2, mechanically-activated cation channels that are expressed in many mechanosensitive cell types, including cranial sensory ganglia involved in interoception. Genetic studies established that PIEZO2 is the principal mechanical transducer for touch, proprioception. More recently, we have shown that PIEZOs play an essential role in baroreception (blood pressure sensing) and lung stretch. We think that future studies will illuminate the role of force sensing in various interoceptive processes including satiety, micturition, and gut function. This information will enable a deeper understanding of how our brain is aware of our internal self, and could lead to novel therapies for a wide range of physiological and psychological disorders.

April 16, 2019

9:10 AM – 11:30 AM

Session One

Neural Circuits Underlying Communication Between the Brain and the Body

Session Chairs

Dr. Janine Simmons (NIMH)

Dr. Peter Strick (University of Pittsburgh)

Rapporteur

Dr. Gary Berntson (Ohio State University)

Speakers

Dr. Diego V. Bohórquez (Duke University)

Dr. Zachary A. Knight (UCSF)

Dr. Peter Strick (University of Pittsburgh)

Dr. Richard D. Lane (University of Arizona)

10:10 AM – 10:30 AM

Break

10:30 AM – 11:30 AM

Summary and Panel Discussion



Janine Simmons, National Institute of Mental Health

Dr. Simmons is Chief of the Social & Affective Neuroscience Program within the Division of Neuroscience & Basic Behavioral Science at NIMH. Her program supports integrative systems-level approaches to understanding the neurobiological mechanisms governing emotion perception and regulation, stress and resilience, and social cognition and communication. Dr. Simmons also participates in NIMH's Research Domain Criteria (RDoC) working group, taking the lead for the Social Processes domain. She is NIMH's representative to the NIH Office of Behavioral and Social Sciences Research (OBSSR) and to the NIH Common Fund Science of Behavior Change (SOBC) initiative. Dr. Simmons attended Yale University, obtained her M.D., Ph.D. in Neurosciences from the UCLA School of Medicine, and completed a residency in General & Adult Psychiatry at Western Psychiatric Institute & Clinic.



Peter Strick, University of Pittsburgh

Dr. Strick is the Co-Director for the Center for Neuroscience, the Thomas Detre Professor & Chair of Neurobiology at the University of Pittsburgh, and the Scientific Director of the University of Pittsburgh Brain Institute. The Strick lab's research focuses on four major areas: the generation and control of voluntary movement by the motor areas of the cerebral cortex; the motor and cognitive functions of the basal ganglia and cerebellum; the neural basis for the mind-body connection; and unraveling the complex neural networks that comprise the central nervous system. Dr. Strick received his doctorate from the University of Pennsylvania; prior to joining the faculty of University of Pennsylvania he worked at the National Institute of Mental Health and in the departments of neurosurgery and physiology at the State University of New York-Medical Center.



Gary Berntson, Ohio State University

Dr. Berntson is an Emeritus Academy member of the Department of Psychology at Ohio State. His research interest is in the elucidation of the functional organization of brain mechanisms underlying behavioral and affective processes, with a special emphasis on autonomic regulation and social neuroscience. Recent collaborative research includes: a) the role of cognitive and social factors in autonomic regulation and immune functions, b) contribution of cortical/cognitive processes to anxiety, and the neural systems that mediate these relations, c) the impact of autonomic states on higher neural systems, d) the integrative organization of neurobehavioral, neuroendocrine, autonomic and immune systems, e) psychoneuroimmunology and the social neuroscience of health and disease, and f) the role of central nervous system structures in evaluative processes. Dr. Berntson received his Ph.D. from the University of Minnesota and was a postdoctoral fellow at Rockefeller University, New York.



Dr. Diego V. Bohórquez
Duke University

Dr. Bohórquez is an Assistant Professor in the Departments of Medicine and Neurobiology at Duke University. The Bohórquez laboratory's research is on uncovering how the brain recognizes food and bacteria in the gut, and how food and bacteria could be used to heal the brain from the gut. The primary focus is on dissecting the neural circuits that transform signals from food and/or bacteria in the gut into electrical inputs that modulate behaviors like the desire to eat. His laboratory is built on multidisciplinary expertise in viral vector genomics, neurophysiology, behavioral phenotyping, organoid cultures, and neuroimaging. Dr. Bohórquez received his Ph.D. from North Carolina State University and was a postdoctoral fellow in Neurogastroenterology at Duke University School of Medicine.

A gut choice

Our motivation to consume sugars is thought to arise at the surface of the gut. However, the neural circuits are unknown. The Bohórquez laboratory discovered a neural circuit linking gut to brain in one synapse. The circuit begins with a type of sensory epithelial cell that synapses with nerves. These epithelial cells are called neuropod cells. In the mouse small intestine, monosynaptic rabies virus infects neuropod cells and spreads onto vagal neurons that project to the nucleus tractus solitarius in the brainstem. This neural circuit is necessary and sufficient to transduce sensory signals from sugars. Silencing neuropod cells silences the ability of the animal to distinguish the caloric content in sugars. This gut sensor for calories is the portal for calories in nutrients to drive our motivation to eat.



Dr. Zachary Knight
University of California, San Francisco

Dr. Knight is an Assistant Professor in the Department of Physiology at the UCSF School of Medicine and a Robertson Neuroscience Investigator of the New York Stem Cell Foundation. The Knight laboratory's research is focused on three related topics: the control of hunger, thirst, and body temperature. A general principle emerging from their recent work has been the discovery that homeostatic circuits – long thought to function primarily by reacting to physiologic imbalances – utilize sensory cues to anticipate those physiologic changes and then adjust behavior preemptively. An ongoing interest of the lab is to understand how homeostatic circuits integrate sensory information from the outside world with internal signals arising from the body to generate and shape goal-directed behaviors. Dr. Knight earned his Ph.D. in Chemical Biology from UCSF and received postdoctoral training at Rockefeller University, New York.

The neurobiology of thirst

I will discuss neural mechanisms that regulate thirst, focusing on experiments in which we have imaged the activity of neurons in the lamina terminalis – a set of three small, interconnected forebrain nuclei that control fluid balance. These structures contain neurons that directly monitor the osmolarity of the blood and therefore are thought to be primary sensory neurons (interoceptors). We have shown that these neurons also receive rapid signals from the oropharynx that track fluid ingestion and from the gastrointestinal tract that report on the osmolarity of ingested fluid, which they integrate with bloodborne signals in order to dynamically regulate drinking behavior. I will draw parallels between this layered regulation of the thirst circuitry and the regulation of analogous neurons that control hunger.

One example of the mind-body problem: circuits that link the cerebral cortex to the adrenal medulla

Dr. Peter L. Strick

Modern medicine has generally viewed the concept of “psychosomatic” disease with suspicion. This is partly because no neural networks were known for the “mind,” conceptually associated with the cerebral cortex, to influence autonomic and endocrine systems that control internal organs. We recently used a unique tracing method to identify the areas of the cerebral cortex in the monkey that communicate through multisynaptic connections with the adrenal medulla, a major sympathetic effector. Our results identify three broad networks in the cerebral cortex that have access to the adrenal medulla. The largest network includes all of the cortical motor areas in the frontal lobe and portions of somatosensory cortex. These cortical areas are involved in all aspects of skeletomotor control from response selection to motor preparation and movement execution. This result suggests that there is a link between the descending control of muscles and the regulation of sympathetic output. This link could provide the neural substrate for the control of stress through “core” exercises, such as yoga and pilates.

The other two networks that influence the adrenal medulla originate from selected regions of anterior and mid cingulate cortex. Evidence from a variety of sources suggests that the mid cingulate regions are involved in cognitive control processes (e.g., awareness of errors, conflict, response selection), whereas the anterior cingulate regions are involved in the control of emotions. These cortical areas link cognitive processes and the control of affect with stress responses. This circuitry may mediate some of the effects of internal states like chronic stress and depression on organ function. Thus, our results in a nonhuman primate provide a concrete anatomical basis for psychosomatic illness where mental states can alter organ function.

We have performed similar experiments in the rat. Interestingly, many of the descending systems that influence the adrenal medulla in the monkey are absent in the rat. Specifically, inputs from several higher-order motor areas and from regions of cortex involved in cognitive control and affect are largely absent in the rat. These results suggest that rodent models have limited utility for examining the influences of higher order mental processes on sympathetic function.

Key Points:

1. The descending control over the adrenal medulla in monkeys originates from cortical areas involved in movement, cognition, and affect. Each network has a human equivalent.
2. There is a concrete neuroanatomical basis for psychosomatic illness where mental states can alter organ function.
3. Many of the cortical areas that influence the adrenal medulla in the monkey are absent in the rat.



Dr. Richard D. Lane
University of Arizona

Dr. Lane is a Professor of Psychiatry, Psychology, and Neuroscience at the University of Arizona, Tucson. He is a physician and clinical psychiatrist with a Ph.D. in experimental psychology. Dr. Lane is a medically-trained researcher with a serious interest in emotion research whose career has focused on advancing the understanding of the mechanisms by which emotion influences health outcomes. His laboratory has three inter-related research areas: 1) A cognitive-developmental model of individual differences in emotional experience and expression; studying the behavioral, neuroanatomical, and clinical correlates of emotional awareness and impairments in emotional awareness known as alexithymia or affective agnosia. 2) The neural basis of emotion and emotional awareness using PET and fMRI and its interaction with peripheral physiology, particularly vagal tone. 3) The mechanisms by which emotion triggers cardiac arrhythmias and

sudden cardiac death. Dr. Lane graduated with his MD from the University of Illinois Abraham Lincoln School of Medicine, and his Ph.D. from the University of Arizona.

Limbic predictions gone awry: the role of maladaptive emotional avoidance in interoceptive insensitivity, persistent somatic symptoms and dyshomeostasis

Functional somatic symptoms (FSS) constitute a major public health problem, accounting for 30 percent of all outpatient medical visits. Medical workups to rule out organic causes of these symptoms are a major health care cost. To the extent that these symptoms are interpreted as harbingers of serious illness, they constitute false interoceptive inferences. As such, a predictive processing framework is relevant.

Growing evidence suggests that maladaptive emotional avoidance, which comes in many varieties, often plays a role in FSS. Most commonly manifesting as anxiety or depression, these maladaptive emotional states often arise because of a failure to experience and express distressing emotions. This perspective on affective avoidance has been well described and substantiated by Barlow and colleagues, who have also developed effective treatment strategies. Since interoceptive perceptions derive from the brain's best guess about the causes of events in the body, a failure to recognize bodily sensations as due to distressing emotional states can be a potent source of false interoceptive inferences.

According to the EPIC (Embodied Predictive Interoceptive Coding) model of Feldman Barrett and Simmons, current bodily state arises from predictions, often affective in nature, about what will be needed in the immediate future to deal with current

environmental circumstances. Limbic activation arising in agranular anterior cingulate and anterior insular cortices issues visceromotor predictions that are sent downstream to visceromotor effectors and upstream to granular cortical structures to anticipate and mediate viscerosensory feedback and calculate prediction error. Because agranular cortices have limited capacity to receive feedback about prediction error, these visceromotor predictions tend to persist. Moreover, if the affective basis for the bodily arousal is not recognized, the ability to modify such predictions will be further impaired. This will additionally contribute to interoceptive insensitivity and result in deficits in the sense of allostatic self-efficacy, leading to fatigue, depression, and other false inferences about bodily state. Moreover, over time persistent physiological arousal will contribute to dyshomeostasis and increased risk for a variety of physical diseases.

Visceral sensations are predominantly transmitted to the central nervous system through the largely unmyelinated vagus. An eight-level hierarchy of vagal regulation has been described, characterized by an increasing capacity to recognize regularities over broader temporal and spatial scales as the hierarchy is ascended. The rostral anterior cingulate and medial prefrontal cortices, elements of the default network, participate in the conceptualization of emotional states that can help overcome maladaptive emotional avoidance and promote greater cardiac vagal tone. Given their strategic location and connectivity, these prefrontal areas are ideally situated to update and down-regulate agranular limbic areas.

Key Points:

1. Functional somatic symptoms are a major health care problem that can be attributed to false interoceptive inference.
2. Maladaptive emotional avoidance is a major source of affective dysregulation that can contribute to functional somatic symptoms and dyshomeostasis, increasing risk for a variety of physical diseases.
3. Agranular limbic cortices generate predictions about bodily state needs that contribute to bodily arousal and are relatively insensitive to feedback from prediction error.
4. The default network, particularly the rostral anterior cingulate and medial prefrontal cortices, participates in the conceptualization of avoided emotional states that can help overcome interoceptive insensitivity and the adverse health consequences with which they are associated.

April 16, 2019

12:30 PM – 2:30 PM

Session Two

Dynamics and Functions of the Central and Peripheral Nervous Systems in Interoception

Session Chairs

Dr. Coryse St. Hillaire-Clarke (NIA)

Dr. Lis Nielsen (NIA)

Dr. Lisa Barrett (Northeastern University)

Rapporteur

Dr. Karen Quigley (Northeastern University)

Speakers

Dr. Eliza Bliss-Moreau (University of California, Davis)

Dr. Manos Tsakiris (University of London)

Dr. W. Kyle Simmons (Johnson & Johnson)

Dr. Scott Kanoski (University of Southern California)

1:30 PM – 2:30 PM

Summary and Panel Discussion

2:30 PM – 2:45 PM

Break



Lis Nielsen, National Institute on Aging

Dr. Nielsen is Chief of the NIA Individual Behavioral Processes Branch, which supports behavioral, psychological and integrative biobehavioral research on the mechanistic pathways linking social and behavioral factors to health in mid-life and older age. Dr. Nielsen manages the Psychological Development and Integrative Science portfolio, which supports transdisciplinary research in affective science, health psychology, life-span developmental psychology, neuroeconomics and social neuroscience. She coordinates NIA research initiatives on midlife reversibility of risk associated with early life adversity, conscientiousness and healthy aging, socioemotional influences on decision-making, subjective well-being, and stress measurement. She serves on the Implementation Team for the trans-NIH Science of Behavior Change (SOBC) Common Fund Program and is the Project Scientist on the Midlife in the United States (MIDUS) Study. Dr. Nielsen has a Ph.D. in Cognitive Psychology and Cognitive Science from the University of Arizona and was a NRSA Postdoctoral Fellow in Psychology of Aging at Stanford University.



Coryse St. Hillaire-Clarke, National Institute on Aging

Dr. St. Hillaire-Clarke is a Program Director at NIA where she oversees the Sensory/Motor Disorders of Aging Program which supports research on mechanisms of normal aging and disease-related changes in motor, visual, auditory, somatosensory, proprioceptive, vestibular and chemosensory functions, as well as pain. She represents the Institute on several trans-NIH and trans-Agency working groups including the NIH Pain Consortium, the Interagency Modeling and Analysis Group, and the Music and Health Initiative Working Group. She also co-chairs the NIH Multisensory Research Working Group. Dr. St. Hillaire-Clarke received her Ph.D. in Neuroscience from Johns Hopkins University where she conducted research to identify the key cellular and molecular events that underlie the growth and survival of neurons in the peripheral nervous system.



Lisa Feldman Barrett, Northeastern University

Dr. Feldman Barrett is the University Distinguished Professor of Psychology and Director of the Interdisciplinary Affective Science Laboratory (IASLab) at Northeastern University. Dr. Barrett also holds research appointments in the Psychiatric Neuroimaging Program in the Department of Psychiatry and at the Martinos Center for Biomedical Imaging in the Department of Radiology at Massachusetts General Hospital /Harvard Medical School. Her current research takes a multidisciplinary approach to studying the nature of emotion from both psychological and neuroscience perspectives, incorporating insights from physiology, anatomy, anthropology and linguistics. Dr. Barrett's research led her to develop a predictive processing account of brain architecture and function which places allostasis, interoception, affect, and motivation at the core of the human mind, offering a trans-disorder approach to understanding mental and physical illness. Dr. Feldman Barrett received her undergraduate degree in psychology, with honors, at the University of Toronto and her Ph.D. in clinical psychology at the University of Waterloo.



Karen Quigley, Northeastern University

Dr. Quigley is a Research Associate Professor in the Department of Psychology at Northeastern University and Co-Director of the Interdisciplinary Affective Science Laboratory. Dr. Quigley's basic science work examines the psychophysiological correlates of affective experience including emotions and stress, the role of interoception in affective experience, and how we use peripheral physiological changes in constructing our affective experience. In earlier work, she co-authored a model for quantifying and assessing autonomic control of cardiovascular responses to stressors in animals and humans, validated noninvasive indices of autonomic control of the heart for use in children and adults, and examined the early life development of autonomic control of stressor-evoked cardiac function in an animal model.

This work was critical in demonstrating that the two main branches of the autonomic nervous system, the sympathetic and parasympathetic inputs to target organs are independently controlled, and therefore, that they should be separately measured. Dr. Quigley received her Ph.D. in Psychobiology from Ohio State University and received her postdoctoral training at Columbia University.



Dr. Eliza Bliss-Moreau
University of California, Davis

Dr. Bliss-Moreau is an Assistant Professor in the Department of Psychology at the University of California, Davis and a Core Scientist at the California National Primate Research Center. She is a psychologist with expertise in comparative and translational neurobiology and a focus on development and regulation of the neural systems that generate social behavior and affect in humans and nonhuman animals. Her lab is particularly interested in the interplay between autonomic and central nervous system activity during affective experience across the lifespan, both in health and disease states (e.g., following fetal Zika virus infection; in Alzheimer's disease). The Bliss-Moreau laboratory works with a variety of animal models in an effort to understand how environmental niches interact with affective processes to impact the function and interplay of the nervous systems. Dr. Bliss-Moreau received her Ph.D. from Boston College in Psychology and was a postdoctoral researcher at the University of California, Davis.

Animal models of interoceptive neurobiology

Understanding the dynamic interaction between the central and peripheral nervous systems in allostasis has important consequences for understanding a wide variety of psychological functions that are germane to human health and well-being. In this talk, I discuss the importance of animal models for answering mechanistic questions about physiological regulation, drawing on data from my lab on central nervous system and autonomic nervous system function in nonhuman primates. I discuss assumptions that have been present in the literature for decades, particularly about the structures in the central nervous system that regulate physiology, and how embracing those assumptions slows science. I conclude by highlighting topics on which intellectual energy and fiscal resources might have significant impact on human health.



Dr. Manos Tsakiris
University of London

Dr. Tsakiris is Professor of Psychology in the Department of Psychology, Royal Holloway, University of London and is leading the Lab of Action & Body. His research is highly interdisciplinary and uses a wide range of methods to investigate the neurocognitive mechanisms that shape the experience of embodiment and self-identity. Since 2016, he has been leading the interdisciplinary Body & Image in Arts & Science project at the Warburg Institute, and since 2017 the INtheSELF ERC Consolidator project at Royal Holloway that investigates the role of interoception for self- and social-awareness. Dr. Tsakiris studied psychology (BSc, Athens, Greece), philosophy (MSc in Philosophy of Mental Disorder, King's College, London, UK), and cognitive neuropsychology (MSc, University College London, UK) before completing his Ph.D. in psychology and cognitive neurosciences at the Institute of Cognitive Neuroscience, UCL.

Looking for the self outwith and within the body

From the perspective of psychological sciences, the question of selfhood is intimately linked to the question of body awareness. How do we become aware of our body and what are the implications of this body awareness for cognition, affect, and mental health? Going beyond the divide between the exteroceptive and interoceptive, recent empirical studies and models of interoceptive predictive coding have focused on the dynamic balance between these exteroceptive and interoceptive representations of the body. A wealth of recent evidence highlights their functional role and the implications of their interactions for our mental life. While exteroceptive processing underpins the malleability of body awareness, interoception provides a dynamic stability that sustains the core self. Having glimpsed the importance of the balancing act between exteroception and interoception for the developed self and its mental health, it is now time to study the ontogenetic development of the interoceptive self and its relation to other developing dimensions of self- and social awareness. That endeavor faces substantial research challenges that require methodological and theoretical advances and cross-disciplinary synergies.



Dr. W. Kyle Simmons
Janssen Research and Development

Dr. Simmons is the Director of the Mood Disorders Biomarkers Program within Janssen's Neuroscience Therapeutic Area. Prior to joining Janssen, he was a Principle Investigator at the Laureate Institute for Brain Research (LIBR) in Tulsa OK. While at LIBR, his research examined the neural bases of body-brain signaling, and how homeostatic signals from the body guide decision-making and influence emotion, both normatively and in psychiatric populations including depression and anorexia nervosa. A focus of his work has been the exploration of whether endocrine, metabolic, and immune signaling pathway markers can be used to identify clinically relevant subtypes of depression. Dr. Simmons completed his Ph.D. at Emory University and his postdoctoral fellowship in the Laboratory of Brain and Cognition at the National Institute of Mental Health Intramural Research Program.

The insula: at the nexus of interoception and allostasis

The insula is a central hub in a wider network of brain regions that support the perception of the body's homeostatic state and organization of allostatic behaviors. My talk will focus on findings demonstrating the insula's role in interoception of visceral signals, and how these signals are integrated with other neural systems, particularly those related to eating behaviors. I will present evidence that (1) visceral interoceptive and gustatory functions are colocalized in the insula, (2) the insula's gustatory and interoceptive circuitry is sensitive to peripheral metabolic signals, and (3) the insula's connectivity allows it to make this information available to the wider brain, thereby helping to guide allostatic behaviors. Given these findings, we can hypothesize that the ability to generate healthy behavioral responses to changes in interoceptive states should be related to the dynamic coupling between the insula and brain regions implicated in decisionmaking and reward. The talk will thus conclude with recent evidence that obesity is characterized by alterations in the relationship between hunger and the coupling of activity between the insula and key regions involved in reward and valuation, including the orbitofrontal cortex and ventral striatum. These findings, along with those shared by my fellow presenters in the session, suggest that failures to effectively integrate brain-body signaling into decisionmaking and behavior may contribute to some of our society's most costly diseases. A corollary of this, however, is that interventions aimed at improving the integration of interoception, decisionmaking, and behavior may be transformative to public health.



Dr. Scott Kanoski
University of Southern California

Dr. Scott Kanoski is an Associate Professor in the Department of Biological Sciences at the University of Southern California who studies the neurobiology of obesity onset, treatment, and pathophysiology. Dr. Kanoski's research applies multiple levels of analysis in rodent models, including behavioral, neuroanatomical, molecular, viral-based genetic, and neuropharmacological approaches. His research program is focused on discovering the underlying neural systems that regulate higher-order aspects of feeding behavior (e.g., learned, cognitive, reward), and to understand how these neural systems are negatively impacted by dietary and metabolic factors. Another primary focus of Dr. Kanoski's research is to discover the neurobiological mechanisms through which feeding related signals from the gastrointestinal tract influence memory and cognition, in part, through vagus nerve signaling. Dr. Kanoski received his M.S. and Ph.D. from Purdue University and was a postdoctoral fellow at the University of Pennsylvania.

The hippocampus: an interface between energy status signaling and memory function

The hippocampus controls fundamental learning and memory processes, including memory for visuospatial navigation (spatial memory) and memory for autobiographical events (episodic memory). Emerging evidence reveals that hippocampal-dependent memory function is regulated by various peripheral biological systems that are traditionally known for their roles in appetite and body weight regulation. These findings are consistent with a model in which feeding behavior and hippocampal-dependent memory function are closely linked. Indeed, recent findings reveal that interoceptive energy status cues communicate from the gut to the brain to promote hippocampal-dependent spatial and episodic memory. More specifically, we highlight a pathway through which gastrointestinal-derived signals are communicated via the vagus nerve to the hippocampus through multiorder neural circuitry to promote episodic memory function via neurotrophic and neurogenic mechanisms. These results are consistent with a framework that it is evolutionarily advantageous to encode and recall critical features surrounding feeding behavior, including the spatial location of a food source, social factors, postabsorptive processing, and other episodic elements of a meal.

April 16, 2019

2:45 PM – 4:45 PM

Session Three

Modeling Disease, Alterations in Interoceptive Processes, and Comorbidities

Session Chairs

Dr. Changhai Cui (NIAAA)

Dr. Rajita Sinha (Yale University)

Rapporteur

Dr. Bruno Bonaz (University of Grenoble, France)

Speakers

Dr. Paul J. Kenny (Icahn School of Medicine at Mount Sinai)

Dr. Rita J. Valentino (NIDA)

Dr. Martin P. Paulus (Laureate Institute for Brain Research)

Dr. Emeran A. Mayer (UCLA)

3:45 PM – 4:45 PM

Summary and Panel Discussion

4:45 PM – 5:00 PM

Wrap up and Adjourn



Changhai Cui, National Institute on Alcohol Abuse and Alcoholism

Dr. Cui is a Program Director in the Division of Neuroscience and Behavior, NIAAA. She manages an alcohol research portfolio focusing on the neurobiology of alcohol use disorders at the molecular, cellular, and circuitry levels, including neuromodulation, neuroimmune interaction, signaling transduction, and neurotechnology. Dr. Cui is involved in trans-NIH activities, such as the NIH Blueprint for Neuroscience Research and the Brain Research through Advancing Innovative Neurotechnologies Initiative. She has been the team lead for a Blueprint team to develop and implement the Blueprint Science Initiative on understanding the dynamic neuroimmune interactions in the transition from normal CNS function to disorders. Dr. Cui received her B.S./M.S. in biochemistry/biophysics from Peking University, China, and Ph.D.

in biochemistry from University of Wisconsin-Madison. She had postdoctoral training in molecular and cellular neuroscience of nicotinic acetylcholine receptors and glutamate receptors at the Salk Institute and the National Institutes of Health.



Rajita Sinha, Yale University

Dr. Sinha is the Foundations Fund Professor of Psychiatry and Professor in the Child Study Center and of Neuroscience at the Yale University School of Medicine. She is also the Director of the Yale Interdisciplinary Stress Center which focuses on understanding sex-specific pathways of stress, emotions, addictive behaviors and their effects on chronic diseases and health outcomes. She is an expert in sex-specific neurobiological mechanisms underlying stress and reward *across the lifespan*, from in children, to adults and older adults, and its associated peripheral and central adaptations in stress and reward pathways that increase risk of and relapse to substance use disorders. More recently, she is making discoveries on the link between stress and metabolic adaptations in obesity that drive highly palatable food craving

and intake and the applications of mindfulness-based stress-eating interventions to improve obesity outcomes. Dr. Sinha received her Ph.D. in Biological Psychology from Oklahoma University Health Sciences and further training in Clinical Psychology from Yale University.



Bruno Bonaz, University of Grenoble, France

Dr. Bonaz is a Professor of Gastroenterology in the Grenoble Faculty of Medicine and Hospital in Grenoble, France. Additionally, he is the President of the International Society of Autonomic Neuroscience. Dr. Bonaz's research is focused on brain-gut interactions, both at the pre-clinical and clinical level, focusing on irritable bowel syndrome and inflammatory bowel diseases with a special interest on the role of stress and the autonomic nervous system in the pathophysiology of such diseases. In particular, he is working on the anti-inflammatory (anti-TNF) properties of the vagus nerve (VN) through VN stimulation (VNS) and has shown that VNS has an anti-inflammatory role in a model of colitis in rats and, in a translational approach, has recently published the first pilot study of VNS in patients with active Crohn's disease.



Dr. Paul J. Kenny
Icahn School of Medicine at Mount Sinai

Dr. Kenny is the Ward-Coleman Professor and Chairman of The Nash Department of Neuroscience and Director of the Drug Discovery Institute at the Icahn School of Medicine at Mount Sinai. Dr. Kenny is also co-founder of Eolas Therapeutics, Inc., a company focused on developing novel medications for drug addiction. Dr. Kenny serves as a Senior Editor for The Journal of Neuroscience. Prior joining the Icahn School of Medicine at Mount Sinai, Dr. Kenny was on the faculty of The Scripps Research Institute in Jupiter, Florida. Research in Dr. Kenny's laboratory is focused on understanding the molecular neurobiology of drug addiction, obesity, and schizophrenia. Dr. Kenny is a graduate of Trinity College Dublin, where he earned a degree in Biochemistry. He completed his Ph.D. in neuropharmacology at King's College London. Dr. Kenny completed his postdoctoral training at The Scripps Research Institute in La Jolla, CA.

Habenular Tcf712 links nicotine addiction to diabetes

The neuropeptide glucagon-like peptide-1 (GLP-1) was shown recently to enhance sensitivity of medial habenula (mHb) neurons to nicotine and thereby exert inhibitory control over nicotine intake. Little is known about the intracellular mechanisms through which GLP-1 acts. Here, we tested the hypothesis that the transcription factor Tcf712, considered a core component of the GLP-1 signaling cascade, regulates the actions of nicotine on mHb neurons to control nicotine intake. We found that Tcf712 is highly enriched in the mHb and, using a new line of *Tcf712* mutant rats, that Tcf712 deficiency increases nicotine self-administration behavior. CRISPR-mediated cleavage of *Tcf712* in the mHb similarly increased nicotine self-administration in mice. Using whole-cell electrophysiological recordings and RNA sequencing, we found that Tcf712 regulates the recovery of nicotinic acetylcholine receptors in the mHb from nicotine-induced desensitization through a mechanism involving local cAMP signaling. Notably, both *TCF7L2* mutations and a history of tobacco smoking increase the risk of type 2 diabetes through unknown mechanisms. We found that doses of nicotine that activate the mHb increased blood glucose levels in rodents and that Tcf712 knockdown in the mHb blocked this effect. Moreover, repeated exposure to hyperglycemic doses of nicotine elevated circulating levels of insulin and glucagon and induced diabetes-like disruption of blood glucose homeostasis. *Tcf712^{mut}* rats were resistant to nicotine-induced perturbations in blood glucose homeostasis. Together, these findings demonstrate that Tcf712 regulates the stimulatory effects of nicotine on mHb neurons to control nicotine intake and hyperglycemic responses to the drug, potentially explaining the link between *TCF7L2* mutations and diabetes and tobacco smoking.



Dr. Rita J. Valentino
National Institute on Drug Abuse

Dr. Valentino is currently the Director of the Division of Neuroscience and Behavior at NIDA. Her career spans over 30 years of academic research and leadership experience in neuropsychopharmacology, stress neurobiology, and drug addiction. Dr. Valentino is particularly recognized for her research on the effects of stress on neural systems, cognition and behavior, the impact of sex, age and coping style on behavioral and cognitive health and mechanisms underlying communication between the brain and pelvic viscera. She is a Fellow of the American College of Neuropsychopharmacology and a member of the Scientific Advisory Board of the Brain Behavior Foundation. She is also the Editor-in-Chief of *Neurobiology of Stress*. Dr. Valentino received a Ph.D. in Pharmacology from the University of Michigan. She then went on to do a postdoctoral fellowship at the University of North Carolina and a second postdoctoral fellowship at the Salk Institute.

Visceral reactions

Ascending circuits convey information about the state of viscera to the cortex so that behavior and cognitive functions are coordinated with visceral activity. These same circuits provide a route through which pathological processes in viscera can affect brain activity and produce comorbid central and peripheral symptoms. One example of this is the ascending circuitry that processes information from the pelvic viscera. Barrington's nucleus, the pontine micturition center, receives information from bladder afferents and is positioned to relay this information to the cortical-projecting norepinephrine (NE) nucleus, locus coeruleus (LC). In the rat, in anticipation of micturition, LC-cortical projections are activated, and LC-cortical coherence is increased in theta frequency. This signal is thought to facilitate voiding preparatory behaviors such that micturition can occur in safe and socially appropriate environments. Pathological conditions of the bladder, such as partial bladder outlet obstruction (pBOO), that resemble features of benign prostatic hypertrophy lock the LC-cortical circuit in this anticipatory state. This is characterized by (1) persistent cortical arousal, (2) theta oscillation associated with non-micturition-related bladder contractions, and (3) a loss of the cortical response to bladder emptying. These electrophysiological signatures may underlie sleep disturbances, the sensation of urgency, and incontinence, respectively. They also have the potential to affect brain processing and responding to other sensory inputs. The central processing of bladder information and consequences of pBOO on the brain exemplify the critical role of circuits that underlie interoception in healthy and disease states.



Dr. Martin P. Paulus
Laureate Institute for Brain Research

Dr. Paulus is the Scientific Director and President of the Laureate Institute for Brain Research (LIBR) in Tulsa, OK. Prior to joining LIBR in May 2014, he had been a Professor in the Department of Psychiatry at the University of California San Diego (UCSD) and the Director of Telemental Health at the Veterans Affairs San Diego Health Care System . LIBR focuses on using neuroscience approaches to develop better assessments for diagnosis or prognosis of mental health problems and to develop neuroscience-based novel interventions. Dr. Paulus' research focuses on pragmatic academic psychiatry, i.e., how to use neuroscience-based measurements to generate individual level predictions that can be useful for clinicians. Moreover, Dr. Paulus is interested in whether computational approaches can be useful to better develop an explanatory basis for psychiatric disorders that can be submitted to rigorous scientific examination.

An active inference approach to interoceptive psychopathology

Interoception refers to the process by which the nervous system senses and integrates signals originating from within the body, providing a momentary mapping of the body's internal landscape and its relationship to the outside world. Active inference is based on the premise that afferent sensory input to the brain is constantly shaped and modified by prior expectations. In this review we propose that interoceptive psychopathology results from two primary interoceptive dysfunctions: first, individuals have abnormally strong expectations of situations that elicit bodily change (i.e., hyperprecise priors), and second, they have great difficulty adjusting these expectations when the environment changes (i.e., context rigidity). We will present data and evidence of how these dysfunctions potentially manifest in mental illness and how interventions aimed at altering interoceptive processing can help the brain create a more realistic model of its internal state.



Dr. Emeran A. Mayer
University of California, Los Angeles

Dr. Mayer is the director of the Gail and Gerald Oppenheimer Family Center for Neurobiology of Stress. He is currently PI of a NIH Center grant on sex differences in functional GI disorders, on a consortium grant of brain bladder interactions, and a RO1 grant on brain imaging in IBS. Dr. Mayer is a regular member of the NIDDK CIMG study section, has been president of the Functional Brain Gut group, and Associate Editor of Gastroenterology. Dr. Mayer has a career long interest in clinical and research aspects of brain body interactions, with a focus on brain gut interactions in health and disease. Besides being a widely recognized expert for functional GI disorders. Dr. Mayer received his MD/PhD degrees from the Ludwig Maximilian's University in Munich, Germany. He completed his residency at the Vancouver General Hospital in Vancouver, Canada, and his GI fellowship training at the UCLA/VA Wadsworth Training Program.

The Role of Gut Microbiome Brain Signaling in Interoception

Converging evidence from behavioral and neuroimaging studies supports a model of aberrant processing of interoceptive information in several brain networks underlying this phenomenon. Sensory signals from the body, including the gut and its microbiome, are processed and integrated in medullary pontine nuclei before they reach the sensorimotor network. The great majority of homeostatic visceral interoceptive signals do not engage the emotional arousal and central executive networks, and are not consciously perceived. The salience network, including the anterior insula in close interaction with the pontine locus coeruleus, assesses and predicts the threat of such signals to the homeostasis of the organism. In cases of perceived threat, ascending noradrenergic pathways from the locus coeruleus cause widespread changes the excitability of cortical brain regions, including key regions of the salience network. The engagement of the salience network in response to perceived threat shifts activity from the default mode network to the executive control network and increases the functional connectivity with the sensorimotor and emotional arousal networks. Recent neuroimaging studies in urological chronic pelvic pain conditions (UCPPS) and irritable bowel syndrome (IBS) have confirmed alterations in the functional connectivity between several networks and with the brainstem, and a possible role of gut microbial signals. Symptom improvement in response to cognitive behavioral therapy in IBS is associated with a normalization of this abnormal functional connectivity between these networks, which is associated with changes in the microbiome. The proposed model incorporates a body of animal and human behavioral observations, including symptom-related anxiety, catastrophizing, and overlap of pain conditions referred to different parts of the body.

April 17, 2019

8:45 AM

Workshop Keynote Two

Dr. Hugo Critchley

Brighton and Sussex Medical School

(Introduced by Dr. Dana Schloesser)



Dr. Hugo Critchley
Brighton and Sussex Medical School

Dr. Critchley is Chair in Psychiatry at Brighton and Sussex Medical School and co-director of the Sackler Centre for Consciousness Science, University of Sussex. Dr. Critchley's human neuroscience research is focused on central autonomic control and interoception relevant to emotion. His research addresses brain-body interactions, particularly in the regulation of normal and abnormal emotion, and combines techniques from autonomic/cardiovascular physiology, neuroimaging and cognitive neuroscience. Dr. Critchley trained in Physiology and Medicine in the University of Liverpool and received his doctorate in Psychological Studies at the University of Oxford. He undertook specialist training in psychiatry at Institute of Psychiatry and Institute of Neurology, in parallel with research fellowships including a Wellcome Trust Senior Research Fellow in Clinical Science.

Disorders of interoception

I will discuss interoception as viscerosensory signaling and processing. A set of distinct frameworks for characterizing disorders of other sensory systems might be applied to categorize disorders of interoception.

I will present a dimensional classification of interoceptive disorders that begins at the level of the interoceptors, through afferent pathways, central encoding and decoding, the interface with action, affect, and cognition, through to the consciously accessible psychological representations of internal bodily signals.

Normal interoceptive processing can underpin the experience of symptoms and fuel the expression of physical and psychological disorders. Examples of these will be discussed. Moreover, redundancy in bodily signaling and control might drive mechanisms through which pathological states are maintained.

I aim to illustrate how dysfunctions at these different levels are expressed as clinical disorders, using select examples, and consider how particular mechanisms can be tested and potentially targeted.

April 17, 2019

9:15 AM – 11:30 AM

Session Four

Leveraging and Manipulating Interoception for Disease Intervention

Session Chairs

Dr. Victoria Spruance (NIDDK)

Dr. Cynthia Price (University of Washington)

Rapporteur

Dr. Helen Weng (UCSF)

Speakers

Dr. Lorenzo Leggio (NIAAA-NIDA)

Dr. Jack L. Feldman (UCLA)

Dr. Jeanie Park (Emory University)

Dr. Vitaly Napadow (Harvard University/MGH)

10:15 AM – 10:30 AM

Break

10:30 AM – 11:30 AM

Summary and Panel Discussion



Victoria Spruance, National Institute of Diabetes and Digestive and Kidney Diseases

Dr. Spruance is a Presidential Management Fellow/Program Specialist at NIDDK in the Division of Kidney, Urologic and Hematologic Diseases (KUH). She oversees the R13 conference grant portfolio and serves as the KUH representative to the Minority Affairs Advisory Committee. Her broad scientific interests include stem cell therapeutics, as well as the neural control of renal, urologic, and hematologic functions. Dr. Spruance received her Ph.D. in the laboratory of Dr. Michael Lane at Drexel University in the Department of Neurobiology and Anatomy. She completed her doctoral thesis on the use of progenitor cell transplantation to enhance plasticity and respiratory

function following cervical injury.



Cynthia Price, University of Washington

Dr. Price's program of research is focused on the study of a mind and body intervention that she developed called Mindful Awareness in Body-oriented Therapy (MABT), an innovative mindfulness-based approach designed to teach interoceptive awareness skills to promote self-care and emotion regulation. She has been the Principal Investigator on multiple MABT studies for populations including people in recovery from post-traumatic stress disorder, and substance use disorder. Integral to her program of research has been ongoing work related to conceptual development of interoceptive awareness. She developed the Scale of Body Connection (SBC) to address the need for a self-report measure of body awareness for use in mind and body research. The SBC measures two related but distinct constructs: body

(interoceptive) awareness, and bodily dissociation. In addition, she is a co-author on the Multidimensional Assessment of Interoceptive Awareness, developed to assess multiple aspects of interoceptive awareness in mind-body research.



Helen Weng, University of California, San Francisco

Dr. Weng is an Assistant Professor of Psychiatry at UCSF with faculty appointments at the Osher Center for Integrative Medicine and Neuroscape Center. Trained as a neuroscientist and clinical psychologist, her research focuses on developing new neuroscientific tools to understand how compassion and mindfulness meditation may improve health. Her research demonstrated that short-term compassion meditation increases both altruistic and neural responses to suffering, suggesting that compassion is a skill that may be trained. Currently she is developing and validating the EMBODY Task, which applies machine learning techniques to functional MRI data to identify mental states of interoception during meditation. This approach yields novel metrics of attention

during meditation such as percentage time engaged in interoception, which will give the field unprecedented power in elucidating the attentional mechanisms through which meditation may improve health.



Dr. Lorenzo Leggio

**National Institute on Alcohol Abuse and Alcoholism,
National Institute on Drug Abuse**

Dr. Leggio is a Senior Investigator at the National Institutes of Health Intramural Research Program and serves as the Chief of the Section on Clinical Psychoneuroendocrinology and Neuropsychopharmacology, a joint NIAAA and NIDA laboratory. Dr. Leggio's laboratory conducts clinical and translational inpatient and outpatient studies to identify possible novel medications for addiction. His group uses a combination of state-of-the-art, innovative bio behavioral and pharmacological procedures performed under well-controlled human laboratory conditions. Collaborative bed-to-bench approaches are also employed using behavioral, pharmacological, and transgenic animal models. Dr. Leggio and his team are particularly interested in the role of the gut-liver-brain axis in alcohol- and drug-seeking behaviors. His laboratory has recently expanded its research looking at the role of the gut microbiota in

heavy drinkers with a special emphasis on the relationships between alcohol-related seeking behaviors and the microbiota-gut-brain axis.

The gut in the brain: potential novel targets for the treatment of addictions

Alcohol and substance use disorders represent leading causes of morbidity and mortality worldwide. However, treatment options, including pharmacotherapies, are limited in number and efficacy. Accumulating evidence suggests that elements of the gut-brain axis, such as neuroendocrine pathways and the gut microbiome, are involved in the pathophysiology of addictions and therefore may be investigated as potential therapeutic targets. One pathway that has begun to be examined in this regard is the ghrelin system, especially in alcohol use disorder (AUD). Observational studies indicate that endogenous levels of the stomach-derived peptide ghrelin are positively associated with craving for alcohol, subjective responses to alcohol, and brain activity in response to alcohol cues. Knockout rodent models suggest that deletion of the ghrelin peptide or receptor gene leads to reduction of alcohol intake and other alcohol-related outcomes. Different research groups have found that ghrelin administration increases, while ghrelin receptor (GHS-R1a) blockade reduces alcohol intake and other alcohol-related outcomes in rodents. Ghrelin administration in heavy-drinking individuals increases alcohol craving and self-administration and modulates brain activity in response to alcohol reward anticipation. PF-5190457, a GHS-R1a blocker, has been shown to be safe and tolerable when coadministered with alcohol. Furthermore, preliminary results suggest that this compound may reduce cue-elicited craving for alcohol in heavy-drinking individuals – a finding in need of replication. Collectively, the existing literature supports further examination of the ghrelin system as a therapeutic target for addictions.



Dr. Jack L. Feldman
University of California, Los Angeles

Dr. Feldman is a Distinguished Professor in Neurobiology at UCLA and a member of the Brain Research Institute. A central problem confronting neuroscientists is to understand how molecular, synaptic, and cellular properties of individual neurons in densely interconnected networks result in behaviors ranging from hitting a baseball, playing the piano, reading or writing a book, taking an exam, regulating blood pressure or reproduction, or doing research. The Feldman laboratory has developed a model system that enables them to perform unique studies that directly address this problem. They investigate the neural basis for respiration in the isolated neonate rat brainstem, a preparation that offers simultaneous access to cellular, synaptic, and network properties. They intend to understand how homeostatically regulated breathing movements occur, and in course, principles of integrative organization in the nervous system.

Intero(re)ceptors affect breathing, which affects everything else!

Breathing underlies regulation of blood gases (oxygen and carbon dioxide) and when awry, e.g., sleep apnea, pulmonary disease, can result in significant pathologies. Moreover, breathing is emerging as a critical factor that can modulate emotional state and cognitive function. Essential for the proper function of breathing are numerous interoceptors, including oxygen sensors in the carotid body, stretch and other mechanoreceptors in the lung, and carbon dioxide sensors in the brain. I will describe the various pathways and mechanisms by which these interoceptors influence breathing and/or the interoception of breathing, and how breathing can induce or affect nervous system disorders.



Dr. Jeanie Park
Emory University

Dr. Park is an Associate Professor of Medicine and of Physiology at Emory University School of Medicine. She is also a Staff Physician at the Atlanta Veterans Affairs Medical Center. Dr. Park's research focus is in neurogenic control of the circulation in disease states characterized by high cardiovascular risk. Specifically, her interest is in the regulation of the sympathetic nervous system and its role in increasing cardiovascular disease risk in patients with chronic renal failure, hypertension, obesity, stress-related disorders such as posttraumatic stress disorder, and smokers. Dr. Park received her M.D. from the University of Alabama in Birmingham. She then completed her internship/residency in Internal Medicine at Washington University and Barnes-Jewish Hospital, St. Louis, MO. She then had a Clinical Fellowship in Nephrology and Hypertension at the University of California, Los Angeles and a Research Fellowship in the Division of Nephrology at the University of Southern California and University of

California, Los Angeles.

Leveraging interoception to improve sympathetic function in chronic disease states

Interoception refers broadly to the sensing of the internal state of the body. This presentation will highlight examples of leveraging interoception to improve sympathetic nervous system overactivity and regulation in chronic disease states that are characterized by increased cardiovascular disease risk. For example, patients with posttraumatic stress disorder (PTSD) have exaggerated increases in sympathetic activation during mental stress and impaired arterial baroreflex sensitivity. Device-guided slow breathing, in which respiratory rates are lowered via a biofeedback device, engages interoception by bringing awareness to breathing sensations and activating afferent pathways in the lung, leading to reflex reductions in sympathetic activity and improvements in arterial baroreflex sensitivity in PTSD. As a second example, patients with chronic kidney disease (CKD) have substantially increased cardiovascular risk in part due to chronic overactivation of the sympathetic nervous system. Prior work has shown that mindfulness meditation, including breathing awareness and body scan, acutely lowers sympathetic activity and blood pressure in untrained African-American men with CKD. Increased interoception, particularly of breathing, may ameliorate sympathetic overactivity via conscious (e.g., awareness of breathing sensations) and unconscious afferent pathways (e.g., activation of pulmonary stretch receptors) and could potentially be leveraged to improve sympathetic function and regulation in patients characterized by increased cardiovascular risk. Whether such interoceptive interventions lead to sustained improvements in autonomic function and ultimately to improved clinical outcomes should be investigated in future studies.



Dr. Vitaly Napadow
Harvard University/Massachusetts General Hospital

Dr. Napadow is an Associate Professor at the Martinos Center for Biomedical Imaging at Massachusetts General Hospital and Harvard Medical School in Boston, MA, where he is also the Director of the Center for Integrative Pain Neuroimaging. Dr. Napadow also holds a secondary appointment at the Pain Management Center at Brigham and Women's Hospital. He received his Ph.D. in biomedical engineering from the Harvard-MIT Health Sciences and Technology program. Dr. Napadow's laboratory has pioneered the application of non-invasive neuroimaging techniques to better understand the brain circuitry underlying aversive perceptual states, particularly chronic pain, and to better understand how nonpharmacologic therapies ameliorate these states. Autonomic homeostatic circuitries play an important role in the processing of somatosensory, cognitive, and affective factors, influencing

the malleable experience of pain, and the Napadow Lab has applied human functional and structural neuroimaging to explore how vagal pathways, in particular, modulate pain perception.

Therapeutic engagement of interoceptive pathways with respiratory-gated vagus nerve stimulation

Biological rhythms entrain physiological activity throughout the body, and the respiratory rhythm is known to impact cognitive, emotional, and sensory processing. The pathways that link respiratory signaling with higher brain function arise from both brainstem respiratory centers and cardiorespiratory stretch receptors, which generate interoceptive processing in the neocortex. Specifically, the vagus nerve directs interoception-related afference to the brainstem, and clinical neuromodulation approaches have targeted such pathways with vagus nerve stimulation. In fact, transcutaneous Vagus Nerve Stimulation (tVNS) is a promising therapy for several visceral and brain disorders including migraine, depression, and visceral pain. As the primary afferent relay for the vagus nerve lies in the medulla and is differentially influenced by different phases of the respiratory rhythm, we have proposed that Respiratory-Gated Vagal Afferent Nerve Stimulation (RAVANS) can enhance brainstem targeting, leading to enhanced clinical outcomes. We recently reported (Sclocco et al., 2019; Garcia et al., 2018) that tVNS targeting of the main vagal afferent nucleus, NTS, in the brainstem can be enhanced by gating stimulation to the respiratory rhythm, suggesting that tVNS can be used to therapeutically interface neuromodulation with the interoception system. This talk will explore how respiratory rhythm and vagus nerve physiology may inform therapeutic neuromodulation, and suggest new synergistic approaches by which RAVANS tVNS can be coupled with other interventions that direct attention to respiratory rhythms, such as mindfulness meditation training.

Learning interoceptive awareness skills is linked to increased emotion regulation capacity and improved health outcomes

Dr. Cynthia Price

Brain imaging studies and neurocognitive models suggest the importance of interoception for emotion regulation to support behavior change, yet little is known about targeting interoceptive skill development through intervention research. Research on the intervention Mindful Awareness in Body-oriented Therapy (MABT) helps to close this gap. A mind-body approach, MABT was designed to teach interoceptive skills to promote emotion regulation, involving an incremental approach to facilitate development of interoceptive awareness skills. Delivered individually, the approach allows therapists to assess regulatory responses to sensory experience and to scaffold the training process in the face of baseline difficulty through a combination of psychoeducational, somatic, and mindfulness approaches. This presentation will present overall findings from multiple MABT studies demonstrating that people with high levels of distress can learn interoceptive skills in a relatively short period; likewise, integration of these skills in daily life is consistently high over extended study periods. In a recently completed NIDA-funded RCT to examine MABT as an adjunct to women's substance use disorder treatment (N=187), those who received MABT showed significantly increased respiratory sinus arrhythmia (RSA) at rest immediately post intervention, and this effect was maintained through the 12-month followup compared to treatment as usual (TAU) and an active control condition. Substance use, the primary outcome, also showed a significant long-term effect for MABT compared to TAU. The significant improvements in interoceptive awareness and concomitant improvements in emotion regulation capacity and reduction in substance use are consistent with neurocognitive models that link interoception to positive behavior change in SUD. These results point to the role of interoceptive training for improved health.

April 17, 2019

12:30 PM – 2:30 PM

Session Five

Technologies, Methodologies, and Biomarkers for Interoception Research

Session Chairs

Dr. Jim Gnatd (NINDS)

Dr. Christof Koch (Allen Brain Institute)

Rapporteur

*Dr. Frederike Petzschner (University of Zürich,
Switzerland)*

Speakers

Dr. Lisa Stowers (Scripps Research)

Dr. Robert W. Gereau IV (Washington University)

Dr. Warren M. Grill (Duke University)

Dr. Sarah Garfinkel (University of Sussex)

1:30 PM – 2:30 PM

Summary and Panel Discussion

2:30 PM – 2:45 PM

Break



Jim Gnatd, National Institute of Neurological Disorders and Stroke

Dr. Gnatd is a NINDS Program Director in Systems and Computational Neuroscience and Team Lead for the NIH BRAIN Integrative and Quantitative Approaches, has worked in systems and cognitive neuroscience and neuroengineering for over 35 years. He has been a principal in the NIH BRAIN Initiative since its inception in 2014 and he co-leads a team of trans-NIH Program Directors in the “understanding circuits” part of the initiative. Dr. Gnatd manages an NIH funding portfolio that includes quantitative and systems neuroscience, programs in integrated, team-science approaches, and in intracranial opportunities for investigative human neuroscience. In addition, he has been involved in NIH and National Science Foundation initiatives in computational neuroscience, multisensory integration, interoception, and

mechanisms of manual therapies. In collaboration with NIH review offices, Dr. Gnatd has developed tools to understand the precision of NIH review scoring, and methods to convey its margins of uncertainty. Prior to taking the position at NINDS, Dr. Gnatd was a NIH-funded investigator working on sleep physiology related to narcolepsy, quantitative neurophysiologic approaches in cognitive neuroscience, systems engineering to understand neural circuit dynamics, and neurological etiologies of eye behavior pathologies.



Christof Koch, (Allen Brain Institute)

Since receiving his Ph.D. on biophysical modeling of retinal ganglion cells and dendritic spines on cortical neurons in 1982 under T. Poggio and V. Braitenberg, he has had an abiding interest in understanding the physical basis of computation in the brain, with a particular focus on neocortex, thalamus and claustrum, and on visual processing, and visual perception, attention and consciousness, as evidenced by his textbook and monographs on these topics (*Biophysics of Computation: Information Processing in Single Neurons*, 1999; *The Quest for Consciousness: A Neurobiological Approach*, 2004 and *Consciousness: Confessions of a Romantic Reductionist*, 2012). For more than a quarter of a century he led a laboratory at Caltech focused on these topics. He has published

more than 300 papers in the peer-reviewed literature. Frustrated the lack of reproducibility in biology, he left Caltech 10 years ago to direct a large-scale (330 scientists and staff), focused, and high-throughput effort to identify and catalogue all cortical cell types in mouse and human cortex using single-cell transcriptional, morphological, electrical, and connectional properties and to build cellular-level Brain Observatory using optical and electrical recording in behaving mice.



Frederike Petzschner, University of Zürich, Switzerland

Dr. Petzschner is a Senior Scientist at the Translational Neuromodeling Unit (TNU) at the University of Zurich and ETH Zurich. Before coming to Zurich, she obtained a M. Sc. Hon. Degree in Physics, followed by a Ph.D. in Neuroscience at the Graduate School of Systemic Neurosciences at the LMU Munich and the Bernstein Center for Computational Neuroscience in Munich. In her research, Dr. Petzschner combines computational models of learning, decision-making and perception with measurements of human behavior and brain function (EEG & fMRI). In her work she focuses on studying the perception of the body (interoception) and reward and structure learning in the context of

psychosomatic disorders, addiction, and Obsessive-compulsive disorder. Since 2015 she is one of the organizers of the international Computational Psychiatry Course in Zurich attracting more than 150 students annually.



Dr. Lisa Stowers
The Scripps Research Institute

Dr. Stowers is a Full Professor in the Department of Molecular and Cellular Neuroscience at The Scripps Research Institute. The Stowers laboratory has developed in-depth knowledge and experience to study the logic of the olfactory system. They are identifying the coding logic of all aspects of the system: (1) specific pheromone chemosignals that generate stereotypic behavior (2) sensory neurons that detect pheromones and other specialized chemosignals (3) the neural and molecular mechanisms in the brain that result in stereotypic behavior. They are studying several independent stereotypic behaviors in the mouse: male-male aggression, pup-suckling, inter-species fear, female reproductive behavior, and scent marking. Analysis of these behaviors in parallel will enable them to determine the

neural mechanisms that specify each behavior as well as the common mechanisms that underlie general principles of stereotypic behavior.

Sensing and controlling urination from the brain

How does the brain transform sensory information into complex behavior? The objective of our work is to identify the relevant neurons across the brain that are necessary to produce a relatively simple motivated behavior to study and identify fundamental principles underlying coding. Sensory-to-behavior circuits must contain a variety of neural computations such as those that determine the identity and meaning of the sensed cues, gauge internal state, remember previous experience, and command muscle action. However, without knowing all of the parts of a model circuit, studying where and how these computations occur has proven difficult. Currently, complete circuit structure underlying most behaviors is largely unknown, and no complete model circuit has been traversed through the mouse limbic system. Therefore, study of neural coding relies on investigation of single brain regions, such as subdivisions of the amygdala or hypothalamus. Such focus may be akin to blind men touching different parts of an elephant; without perceiving the entirety, interpretation may become distorted. Here we propose that sensation-to-motivated-behavior employs an entire circuit and its study as a whole will accelerate understanding. We are overcoming this bottleneck by leveraging the systematic control of the mouse's olfactory system to elicit urine-marking behavior as an ideal model circuit. Upon smelling females, male mice are motivated to intentionally deposit copious urine marks to advertise their sexual availability. To investigate how this motivated circuit encodes behavior, we have begun to identify the primary neural nodes that underlie the sensory-to-muscle transformation to generate behavior. We expect that once completed we will be able to determine the activity patterns of the relevant neurons in relationship to the behavior and to each other. We anticipate that full knowledge of the parts and activity patterns of the complete circuit will provide a crucial first step to understanding how sensory systems, the brain, and the body collectively generate behavior.



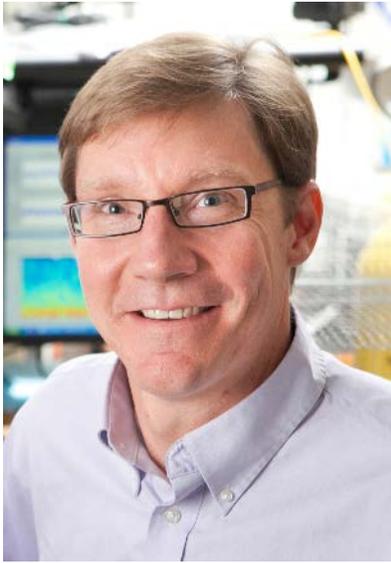
Dr. Robert W. Gereau IV
Washington University

Dr. Gereau is a researcher interested in determining the cellular and molecular changes that underlie the development of chronic pain conditions. His lab utilizes a combination of behavioral studies, patch clamp electrophysiology, optogenetics, in vivo imaging, molecular, and genetic approaches to understand the signaling pathways, cells and circuits involved in nervous system plasticity that underlies pain sensitization. The lab mission is to identify novel approaches to reverse this maladaptive plasticity to provide new therapeutic strategies to reduce pain and its impact on patient quality of life. Work in the lab also includes clinical science aimed at translating findings from the lab into new or improved therapies for patients with pain. These studies include comparative studies of human physiology to preclinical models, as well as healthy human volunteer studies aimed at establishing proof of concept for novel analgesic therapies based on findings from the laboratory. Recent

work in the Gereau lab has included work to develop novel technologies enabling the measurement and manipulation of neuronal activity in freely moving animals. In a collaborative effort with the materials science lab of Dr. John Rogers, at Northwestern University, Gereau has helped to develop battery-free, wireless implants for optogenetic manipulation, microfluidic delivery of drugs, and measurement of a variety of physiological parameters. The most recent iterations enable the measurement of end-organ function, algorithms to identify pathological dysfunction and deliver corrective neuromodulation in a closed-loop system.

Beyond the BRAIN: emerging technologies for measuring and manipulating cellular activity in the periphery

Interoception relies on integration of a variety of signals originating in diverse tissues in the body. Insights into mechanisms of interoception rely therefore on the ability to measure and manipulate activity of a variety of cell types in diverse tissue environments. Much progress has been made over the past few years in the development of new technologies to measure and manipulate cellular activity and signaling, thanks largely to coordinated efforts in the BRAIN Initiative. Much of this technology is focused on activity or signaling in the brain, and therefore specifies a unique set of design parameters. These tools are often not easily adapted to the peripheral nervous system and other peripheral tissues, as would be needed in the context of studying many aspects of interoception. This presentation will discuss newly adapted technologies for measuring and manipulating cellular function in the periphery, with a focus on devices developed to study peripheral nerves and visceral organs, including the bladder.



Dr. Warren M. Grill
Duke University

Dr. Grill is the Edmund T. Pratt, Jr. School Distinguished Professor of Biomedical Engineering at Duke University. His research interests are in neural engineering and neuromodulation and include design and testing of electrodes and stimulation techniques, the electrical properties of tissues and cells, and computational neuroscience with applications to restoration of bladder function, treatment of movement disorders with deep brain stimulation, and electrical stimulation for treatment of pain. He is Co-Founder, Director, and Chief Scientific Officer of NDI Medical, a medical device incubator, and Co-Founder, Director, and Chief Scientific Officer of DBI, which is commercializing a novel approach to brain stimulation for neurological disorders. Dr. Grill serves as a Consultant to the Neurological Devices Panel of the FDA Medical Devices Advisory

Committee and on the editorial boards of *Brain Stimulation*, *Journal of Neural Engineering*, and *Current Opinion in Biomedical Engineering*. Dr. Grill received his B.S. in biomedical engineering from Boston University and a Ph.D. in biomedical engineering from Case Western Reserve University.

Interoceptive feedback from the urethra is essential to efficient voiding

The principal functions of the lower urinary tract are to store and expel urine (continence and micturition, respectively). Urinary retention is the inability to empty the bladder completely, and may result from bladder hypocontractility, increases in outlet resistance, or both. Sensory innervation of the urethra transmits information related to flow, and we sought to determine the role of this feedback in coordinated voiding. We combined urethral anesthesia and selective nerve transection to reveal that feedback from pudendal afferents is required for efficient voiding, and the loss of pudendal sensory activity leads to a reduction in voiding efficiency. Subsequently, we demonstrated that electrical stimulation of sensory fibers in the pudendal nerve could improve bladder emptying in an animal model of urinary retention. An initial clinical translation of these results to humans demonstrated the feasibility of delivering intraurethral electrical stimulation as a means to determine whether electrical activation of pudendal nerve afferents may provide a new approach to restore efficient bladder emptying in persons with nonobstructive urinary retention.



Dr. Sarah N Garfinkel
University of Sussex, England

Dr. Garfinkel is a Professor in Clinical and Affective Neuroscience, BSMS, University of Sussex. Her research centers on heart-brain interactions and interoceptive processing, with a particular focus on how alterations in interoception can influence emotion, memory, and anxiety. Using a variety of techniques (fMRI, autonomic monitoring and manipulation, behavioral testing) she determines how dimensions of interoception are altered in different clinical conditions. The Garfinkel laboratory's current research focuses on interoceptive processing in autism, anxiety, and schizophrenia. Their research demonstrates how dimensions of interoception (subjective, objective, and metacognitive indices) can be dissociated, and highlights how they map on to different clinical symptoms. Dr. Garfinkel received her Ph.D. in Experimental Psychology from the University of Sussex, England.

Dissociating dimensions of interoception

Interoception describes the afferent signaling, central processing, and neural and mental representation of internal bodily signals. This talk will detail methods that delineate and assess dimensions of interoception, with a focus on (1) behavioral accuracy (i.e., the accuracy with which internal bodily sensations such as heartbeats can be detected); (2) subjective report (i.e., self-assessed measures of perceived interoceptive aptitude); (3) interoceptive metacognitive awareness, the mathematical computation of the correspondence between subjective and objective measures of interoception, to denote "interoceptive insight"; and 4) neural measures to assess interoception, which include fMRI and EEG, such as heartbeat evoked potentials (HEP). Using methods to time-lock stimuli to distinct physiological signatures and/or phases, the (5) preconscious impact of afferent signals can also be assessed. These dimensions of interoception are informative, as they map onto cognitive and emotion processing. They are also differentially and selectively disrupted in distinct clinical disorders, and thus offer mechanistic insights with implications for novel treatments.

April 17, 2019

2:45 PM – 4:45 PM

Session Six

Discussions - Future Directions and Recommendations

Session Chairs

Dr. Wen G. Chen (NCCIH)

Dr. Dana Schloesser (OBSSR)

Dr. Angela Arensdorf (NCCIH)

Speaker

Dr. Sahib Khalsa (Laureate Institute for Brain Research)

Panelists

Dr. Karen Quigley

Dr. Bruno Bonaz

Dr. Helen Weng

Dr. Frederike Petzschner

4:45 PM – 5:00 PM

Wrap-up and Adjourn



Wen Chen, National Center for Complementary and Integrative Health

Dr. Chen is the Chief of NCCIH's Basic and Mechanistic Research Branch in Complementary and Integrative Health in the Division of Extramural Research. Dr. Chen's portfolio includes research and training programs related to fundamental and translational science research on acupuncture, meditation, and music and art interventions. Dr. Chen currently represents NCCIH at multiple trans-NIH and interagency working groups and committees. She is the NCCIH Program Representative on the NIH Pain Consortium and is heavily involved in the trans-NIH HEAL Initiative on behalf of NCCIH. She also serves as a working group member for the NIH Common Fund initiative on Stimulating Peripheral Activity to Relieve Conditions, a member of the Trans-NIH Music and Health Working Group, a member of the Collaborative Research in Computational Neuroscience, and a member of the NIH Blueprint/BRAIN Initiative Marmoset Working Group. Dr. Chen is also leading the NIH Blueprint Interoception Working Group. Dr. Chen's areas of expertise include neurobiology, molecular biology, biochemistry, pain, sensory and motor systems, and epigenetics. She earned a Ph.D. in Biological Chemistry and Molecular Pharmacology from Harvard University. She also earned a master's degree in medical sciences as part of the Harvard-Markey Medical Scientist training program at Harvard Medical School. Dr. Chen did her postdoctoral training in proteomics at Massachusetts Institute of Technology.



Dana Schloesser, NIH Office of Behavioral and Social Sciences Research

Dr. Schloesser is a Health Scientist Administrator at the NIH OBSSR focusing on the neurosciences across the NIH institutes, centers, and offices, particularly where they intersect with the behavioral and social sciences. She is currently involved in the BRAIN Initiative, BluePrint for Neuroscience Research, the Sleep Research Coordinating Committee, the Myalgic Encephalomyelitis/Chronic Fatigue Syndrome Working Group, and the Adolescent Brain Cognitive Development Study. Dana came to OBSSR from the National Institute of Neurological Disorders and Stroke (NINDS) in Channels, Synapses, and Neural Circuits, where she was a Health Scientist Administrator. During her time at NINDS, she was involved in programmatic efforts involving chronic fatigue, epilepsy, and the BRAIN Initiative. Prior to NINDS, she was an American Association for the Advancement of Science (AAAS) Fellow at OBSSR with a focus on behavioral neurosciences.



Angela Arensdorf, National Center for Complementary and Integrative Health

Dr. Arensdorf is a Health Science Policy Analyst within the Office of Policy, Planning and Evaluation (OPPE) at NCCIH. In this role, Dr. Arensdorf is involved in the strategic planning, coordination, evaluation, and implementation of select NCCIH activities. Prior to joining NCCIH in her current role, Dr. Arensdorf was an AAAS Science and Technology Policy Fellow at NCCIH. She received her B.S. in biology and biochemistry from Clarke University, a Ph.D. in cell and molecular biology from the University of Iowa, and postdoctoral training in cellular signaling at St. Jude Children's Research Hospital. Dr. Arensdorf's scientific expertise is in gene regulation, endoplasmic reticulum stress responses, GPCR biology, Hedgehog signaling, and bioinformatics.



Dr. Sahib S. Khalsa
Laureate Institute for Brain Research

Dr. Khalsa is the Director of Clinical Studies at the Laureate Institute for Brain Research and an Assistant Professor at Oxley College of Health Sciences at the University of Tulsa. His research examines how people feel their heartbeat, how the human brain maps cardiac sensation, and whether there is dysfunctional cross-talk between the heart and brain in psychiatric and cardiovascular illnesses. A major focus has been the application of pharmacological approaches to perturb cardiovascular sensations using isoproterenol, a peripheral beta-adrenergic agonist akin to adrenaline. By pairing isoproterenol infusions with a rating dial to assess momentary subjective experience, they have shown that they can successfully elicit and measure changes in heartbeat perception in every individual. To date, Dr. Khalsa's studies have suggested that the conscious perception of the heartbeat (i.e.,

interoceptive awareness) is influenced by long-term meditation practice, is reduced in normal aging, is exaggerated in eating disorders, and is mediated by both somatosensory afferents from the skin and a network that includes the insular and anterior cingulate cortices. Ongoing projects examine the neural basis of heart-brain communication in eating and anxiety disorders and test the influence of novel body-based therapeutic interventions on illness severity and time course. Over the long term, these and future studies aim to address the question "How can re-establishing a functional dialogue between the body and brain improve human health?" Dr. Khalsa received his M.D. and Ph.D. in Neuroscience from the University of Iowa and residency in Psychiatry at the University of California Los Angeles.

Charting a path forward for interoceptive neuroscience

In November 2016 a gathering of interoception experts from around the world met at the first Interoception Summit with the goal of accelerating progress in understanding the role of interoception in mental health. The meeting discussions were organized around four themes: interoceptive assessment, interoceptive integration, interoceptive psychopathology, and the generation of a roadmap that could serve as a guide for future endeavors. This talk will present an overview of the consensus generated by the meeting and highlight recent findings from the emerging area of "interoceptive neuroscience" that provide insight into the pathways and mechanisms underlying brain-body communication in health and in nervous system disorders. However, despite this recent progress there are still many roadblocks obstructing our understanding of interoception. Successfully exploring the frontiers of inner space will require conceptual and methodological advances, an interdisciplinary approach, models that can be tested in preclinical and clinical settings, and above all, commitment from funding agencies to support such work. Some potential approaches for moving interoceptive neuroscience forward will be discussed.

Additional Planning Committee Member Biosketches:



Todd Horowitz, National Cancer Institute

Dr. Horowitz is a cognitive psychologist, with a B.S. from Michigan State University (1990) and a Ph.D. from the University of California, Berkeley (1995). From 1995 to 2012, he worked at Brigham and Women's Hospital and Harvard Medical School, before moving to NCI, where he is now a Program Director in the Division Cancer Control and Population Sciences. He has published over 70 peer-reviewed research papers on visual perception and attention, including basic research as well as applications to the study of Parkinson's Disease, autism, driving, and airport baggage screening. Currently, he is working to engage cognitive psychologists and vision scientists with problems in cancer control, such as improving medical image interpretation, studying the cognitive effects of cancer and cancer treatments, and improving the

effectiveness of visual health communications.



Michael L. Oshinsky, National Institute of Neurological Disorders and Stroke

Dr. Oshinsky joined NINDS in 2014 as the Program Director for Pain and Migraine Research. As a Program Director at NINDS, Dr. Oshinsky is responsible for research and administrative issues related to migraine, other headache disorders, neuropathic pain, peripheral and central mechanisms that mediate pain, central processing of pain, disease-related pain disorders, and therapeutic pain devices. Dr. Oshinsky received a bachelors in biology with a concentration in neuroscience from Brandeis University. He earned his Ph.D. in neurobiology and behavior from Cornell University. He received his postdoctoral training as an NIH-sponsored postdoctoral fellow at the University of Pennsylvania. He was an Associate Professor in the Department of Neurology at Thomas Jefferson University from 2001-2014 before joining NINDS. During those years he was the Director of Preclinical Research at the Jefferson Headache Center and directed an NIH-funded

research program aimed at developing and characterizing animal models of headache. In 2011, Dr. Oshinsky was awarded the Harold G. Wolff Award for headache research.