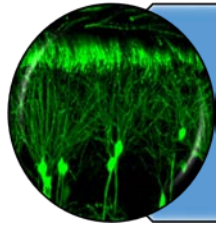




Faculty Research

2019



Research at the Tulane Brain Institute

Research at the Tulane Brain Institute is centered around four research themes built on identified strengths that are advanced by transdisciplinary teams made up of Brain Institute faculty, postdoctoral fellows, and students from across the University. Themes are supported through investment in infrastructure and programmatic initiatives with the goal of developing physical and intellectual clusters of research excellence.

Memory & Cognition

Brain Institute scientists are exploring brain mechanisms that support memory and cognition. Researchers are examining how memories are made and stored in the brain and how these processes change during normal and pathological aging. Ongoing research into neural processes underlying typical and atypical cognitive development and function has implications for understanding autism, attention deficit hyperactivity disorder, and schizophrenia.

Neurodegenerative Disease, Neural Injury & Repair

Brain Institute scientists are conducting research on neurodegenerative disease and neural injury resulting from trauma or stroke. Researchers are examining mechanisms underlying age-related dementias including Alzheimer's disease. Experiments are underway testing the use of adult stem cells as potential avenues for treatment of neurodegenerative diseases such as multiple sclerosis. The work of Tulane neuroscientists is leading to new discoveries regarding risk factors and treatments of stroke.

Hormone-Brain Interactions

Brain Institute scientists are exploring the impact of hormones on the brain. Research investigating stress and the effects of stress hormones on the brain has implications for understanding depression, anxiety disorders, and posttraumatic stress. The study of how hormones such as estrogens and androgens impact the brain across the lifespan may lead to the understanding of mechanisms by which males and females have different biological vulnerabilities to brain disorders.

Brain-Body Health

Brain Institute scientists are exploring the role of the brain in health and disease. Scientists are examining how the nervous system is involved in the regulation of the body's glucose levels and related implications for treating diabetes. Researchers are investigating the role for the brain in the development and treatment of hypertension and obesity. Tulane neuroscientists have developed a new drug to treat pain that may be a safer, non-addictive alternative to current pain medications.

To learn more about research at the Tulane Brain Institute, please explore our *Faculty Research Profiles*.

Brain Institute Faculty Research Groups

Memory & Cognition

Dr. Lydia Bazzano

Dr. Daniel Burnston

Dr. Paul Colombo

Dr. Jill Daniel

Dr. Laurie Earls

Dr. Jonathan Fadok

Dr. Hai Huang

Dr. Michal Jazwinski

Dr. Jeffrey Lockman

Dr. Andrew MacLean

Dr. Julie Markant

Dr. Ricardo Mostany

Dr. Stephen Nelson

Dr. Jeffrey Rouse

Dr. Michael Scheeringa

Dr. Laura Schrader

Dr. Yu-Ping Wang

Dr. James Zadina

Neurodegenerative Disease, Neural Injury & Repair

Dr. Lydia Bazzano

Dr. Bruce Bunnell

Dr. David Busija

Dr. Aaron Dumont

Dr. Michal Jazwinski

Dr. Prasad Katakam

Dr. Andrew MacLean

Dr. Michael Moore

Dr. Ricardo Mostany

Dr. Stephen Nelson

Dr. Gregory Stewart

Dr. James Zadina

Hormone-Brain Interactions

Dr. Paul Colombo

Dr. Jill Daniel

Dr. Stacy Drury

Dr. Sarah Lindsey

Dr. Franck Mauvais-Jarvis

Dr. Michael Scheeringa

Dr. Laura Schrader

Dr. Jeffrey Rouse

Dr. Jeffrey Tasker

Dr. James Zadina

Brain-Body Health

Dr. David Busija

Dr. Paul Colombo

Dr. Andrei Derbenev

Dr. Stacy Drury

Dr. Sarah Gray

Dr. Suttira Intapad

Dr. Sarah Lindsey

Dr. Jeffrey Lockman

Dr. Franck Mauvais-Jarvis

Dr. Andrew MacLean

Dr. Stryder Meadows

Dr. Gregory Stewart

Dr. Jeffrey Tasker

Dr. Yu-Ping Wang

Dr. James Zadina

Dr. Andrea Zsombok

Tulane Brain Institute
Faculty
Research Profiles
(in alphabetical order)

Lydia Bazzano, M.D., Ph.D.

Lynda B & H Leighton Steward Professor in Nutrition
Director, Center for Lifespan Epidemiology
Associate Professor of Epidemiology
Clinical Assistant Professor of Medicine

Brain Institute Research Groups

Memory & Cognition; Neurodegenerative Disease,
Neural Injury & Repair

Broad Research Goals

Identifying risk factors, timing and subpopulations for intervention that could reduce the incidence of stroke and cognitive decline in later life and improve the rate of successful aging for persons across the nation and world-wide.

Research Overview

The number of individuals within U.S. population that are older than 65 years is estimated to grow from 39 million in 2008 to 88.5 million in 2050, and the number of those older than 85 years old is expected to increase from 5.7 million to 19 million¹. It is critical that healthcare costs and morbidity and mortality associated with the diseases of aging are minimized, and this is most effectively done through maintaining optimal physical and cognitive health. The integrity of the vascular system is essential for healthy aging. Subclinical changes in the structural and functional components of the vascular system occur simultaneously with subtle changes in cognition (memory and mental sharpness), before clinical disease becomes apparent. Early life factors, from birth through childhood and adolescence, may play an important role in cognitive performance by way of affecting the vascular system.



Dr. Lydia Bazzano and members of the Bogalusa community



In the Bogalusa Heart Study we are examining the influence of cardiovascular risk factors and aging of the circulatory system on cognitive function and stroke events. This will assist in identifying risk factors, timing and special groups that may benefit from intervention that could reduce the rate of cognitive decline in later life. This study is a unique opportunity to determine if cardiovascular health in childhood and young adulthood affect cognitive function in mid-life and later through aging of the heart and blood vessels. The Bogalusa Heart Study is unique in the nation and the world in having data collected from childhood to middle age (over 40 years) on cardiovascular health in both African-Americans and Caucasians. This research is currently funded by the National Institute on Aging.

Dr. Bazzano has published more than 100 peer-reviewed research papers and has experience in designing and conducting both observational studies and randomized controlled trials in the community. Her published research on cognitive and brain health includes “Effects of early blood pressure reduction on cognitive function in patients with acute ischemic stroke”

(<http://www.ncbi.nlm.nih.gov/pubmed/27412188>) and “Postural hand tremor and incident hypertension in young to middle-aged adults: the Bogalusa heart study”

(<http://www.ncbi.nlm.nih.gov/pubmed/27136316>).

¹ US Census Bureau. (2010). *The Next Four Decades – The Older Population in the United States: 2010 to 2050*. Retrieved from <https://www.census.gov/prod/2010pubs/p25-1138.pdf>

Bruce A. Bunnell, Ph.D.

Director, Tulane Center for Stem Cell Research and Regenerative Medicine
Professor, Department of Pharmacology
Chair, Division of Regenerative Medicine, Tulane National Primate Research Center



Brain Institute Research Group

Neurodegenerative Disease, Neural Injury & Repair

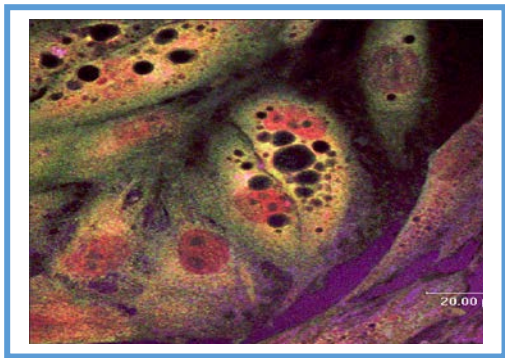
Broad Research Goals

The goal is to utilize stem cell, gene therapy and/or tissue engineering approaches for the development and application of novel treatments for neurodegenerative diseases, including Multiple Sclerosis and Krabbe's disease.

Research Overview

Stem cells as a treatment for Multiple Sclerosis. My research group has been investigating the therapeutic efficacy and mechanisms of actions for stem cell-based therapies derived from adult fat tissue as a treatment for Multiple Sclerosis (MS). These stem cell therapies have demonstrated comprehensive improvements in an animal model this common neurodegenerative disease. In MS, an autoimmune response is elicited against myelin, an integral component of the central nervous system, which results in cognitive and vision problems, fatigue, and progressive loss of motor function. This preclinical research has shown functional recovery, robust modulation of the immune system, and anti-inflammatory effects following therapy, and the in-depth mechanisms facilitating these improvements are currently being elucidated.

Pathology and treatment of Krabbe's disease. Globoid cell leukodystrophy (GLD; also known as Krabbe's disease) is a rapidly progressing inborn metabolic neurological disease. GLD is defined by the deficiency of a key enzyme in the lysosome. The missing enzyme normally breaks down several macromolecules known as galactolipids, including galactosylceramide, a major sphingolipid of the white matter of the brain and spinal cord. The absence of this enzyme results in the accumulation of a molecule, psychosine, that is toxic to cells in the brain, spinal cord and peripheral nerves. The end result is a markedly shortened life span in humans and animals with this disease. The incidence of Krabbe's disease in humans, specifically, in the United States is 1 in 100,000 live births. A nonhuman primate model of Krabbe's disease exists at the Tulane National Primate Research Center. Dr. Bunnell is exploring several innovative therapeutic strategies for Krabbe's disease in the nonhuman primate model including stem cell interventions and gene therapies in collaboration with investigators across the globe.



Adult mesenchymal stem cells isolated from human fat after undergoing adipose differentiation

Dr. Bunnell's research is funded by the National Institutes of Health, National Science Foundation and the *Marko Spark Innovation Research Fund*.

Daniel C. Burnston

Assistant Professor / Philosophy Department

Brain Institute Research Groups

Memory & Cognition

Broad Research Goals

To understand the relationship between psychological concepts and emerging results from systems neuroscience; to explicate how it is possible to localize function in complex neural networks, and how localized parts contribute to psychological functioning.



Research Overview

Dr. Burnston's work assesses conceptual issues at the intersection of philosophy, psychology, and neuroscience. Particular focus is on the relationship between the mental states posited in psychological and everyday explanation of behavior, and the functioning of the brain systems that produce these behaviors. More specific issues include the question of whether and how neural systems represent the world, whether psychological categories such as "intention," can be localized in the brain, and the nature of scientific explanation in neuroscience.

One line of Dr. Burnston's research focuses on everyday "folk" categories such as 'belief' and 'intention', and what role these categories should play in neural explanations of behavior. On "realist" views of these categories, intentions are discrete structures in the brain which stand in causal relationships to the motor systems that carry out the behavior. Burnston, along with several collaborators, argues for a systematic view of these concepts, on which they are neither purely fictions (as some have contended), nor are they isolable brain processes that directly cause and control behavior. Categories such as 'intention' in fact include a number of dissociable connotations, each of which play a role in explaining behavior. But the category does not name a distinct, action-controlling neural state.

A second line of research addresses whether it is possible to "localize" functions in the brain, while granting the highly dynamic, interactive, and network-dependent nature of brain function. Burnston defends a "contextualist" approach to localization, arguing that we can still isolate parts of the brain and describe their particular functional capacities, but that these explanations must be phrased in terms of the shifting interactions between a given area and other environmental and neural factors. Ongoing work explores the relationship between this view of functional explanation and traditional notions from cognitive science, such as 'computation' and 'representation'.

Dr. Burnston has received funding from the National Science Foundation and from the KLI theoretical biology institute in Vienna, Austria. He publishes in both philosophical and empirical journals. More information is available at: <http://danburnston.tulane.edu/>

David W. Busija, Ph.D. M.D. [Hon]

Regents Professor and Chair, Department of Pharmacology

Brain Institute Research Groups

Neurodegenerative Disease, Neural Injury & Repair; Brain-Body Health

Broad Research Goals

To elucidate the mitochondrial mechanisms in regulation of the neurovascular unit during health and disease.

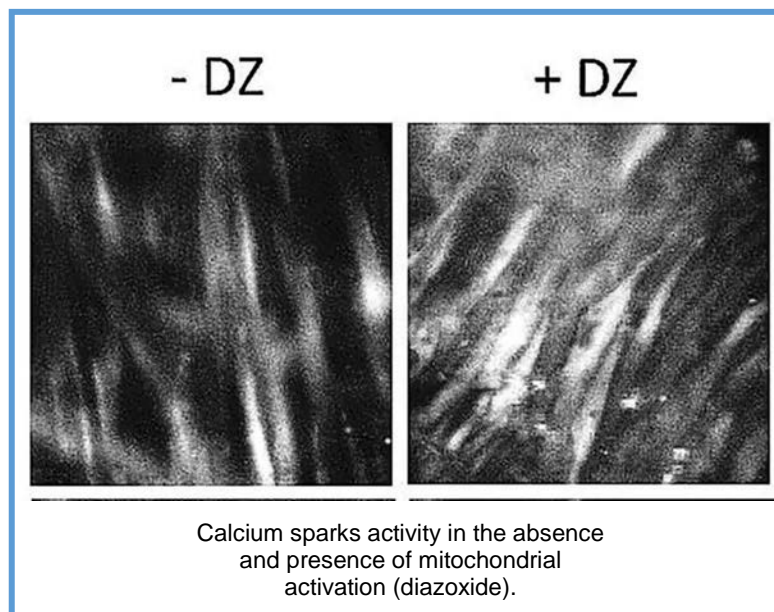
Research Overview

Dr. Busija directs a well-established, diverse research program that focuses on: 1) The mechanisms involved in the regulation of the cerebral circulation in health and disease; 2) The mechanisms of damage to the brain following injury; 3) Therapeutic strategies to restore normal cerebral vascular responses during disease processes such as insulin resistance and ischemia/reperfusion; and 4) Development of methods to protect cells of the neurovascular unit (endothelium, smooth muscle, perivascular nerves, astroglia, neurons, etc.) against potentially lethal stimuli. These seemingly unrelated topics are unified by the focus on the role of mitochondria. Activation of mitochondria promotes dilation of cerebral arteries by mechanisms involving increases in



Dr. David Busija

calcium spark activity and subsequent stimulation of calcium activated potassium channels in vascular smooth muscle. The dilation of vascular smooth muscle is augmented by global increases of calcium in endothelium and neurons with the subsequent release and diffusion of nitric oxide. Insulin resistance, a condition that usually precedes the development of type II diabetes, is able to reduce dilation to mitochondrial activators, probably as a result of local inflammatory processes and increased cellular and tissue levels of reactive oxygen species. Targeting mitochondria with activators of ATP sensitive potassium channels on the inner mitochondrial membrane protects cells of the neurovascular unit by reducing increases in the production of reactive



oxygen species and by limiting the calcium surges following exposure to lethal stimuli. Insulin resistance impairs the ability of cells of the cardiovascular system to be protected due to impairment of mitochondrial function.

Paul J. Colombo, Ph.D.

Associate Professor, Department of Psychology

Brain Institute Research Groups

Memory & Cognition; Hormone-Brain Interactions;
Brain-Body Health

Broad Research Goals

Our overall goal is to understand how musical experience influences neural development and adult brain plasticity in order to improve therapeutic interventions for healthy childhood development, and for cognitive and memory disorders.



Paul Colombo and members of the laboratory

Research Overview

New Orleans has a unique and vibrant musical culture, and members of this laboratory use musical training as a model system to study brain plasticity. Experience-dependent plasticity associated with musical training generalizes beyond auditory processing to influence cognitive functions including attention, working memory, and inhibitory control. In one line of investigation, we study effects of musical training on executive functions, and on neural activity measured by EEG. In another line of research, we study effects of musical training on stress reactivity measured behaviorally and biochemically. Most recently, results of studies in young subjects have been used to formulate and test music-related interventions for preventing and ameliorating age-associated cognitive decline.

We also study effects of music-based mentoring on neural, cognitive, and social development. Studies conducted in collaboration with community partners The Roots of Music, and Make Music NOLA, examine the effects of music-based mentoring on executive functions, self-efficacy, and the neurobiological mechanisms underlying the impact of music training on behavior and cognitive functions.

For more information: <https://www.youtube.com/watch?v=Agcy2eNhATw&feature=youtu.be>

Research supported by the National Science Foundation, Tulane University Program for Research Support, the Tulane University Center for Public Service, and the Carol Lavin-Bernick Faculty Research Grant Program.

Jill M. Daniel, Ph.D.

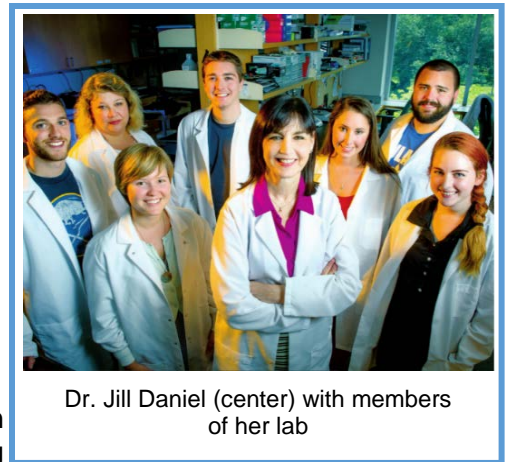
Director, Tulane Brain Institute
Professor, Department of Psychology

Brain Institute Research Groups

Memory & Cognition; Hormone-Brain Interactions

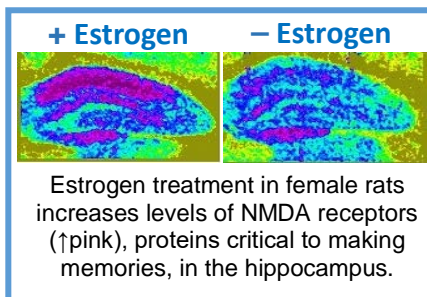
Broad Research Goals

To determine how estrogens and androgens impact the brain and cognition across the lifespan with the goal of understanding contributions of these hormones to the specific biological vulnerabilities that males and females have to brain disorders



Research Overview

Estrogens and the aging brain. Women have increased risk of Alzheimer's disease and other age-related dementias as compared to men. It is hypothesized that the loss of estrogen at menopause contributes to this increased risk. Research in the Daniel lab showed that administration of estrogen begun during a critical window following loss of ovarian function has positive impacts on memory and the hippocampus, a brain area important for memory. The goal of ongoing research is to determine long-term consequences for memory and the brain of short-term exposure to estrogens during middle-age such as that used by women during the menopausal transition. Results demonstrate that short-term treatment with estrogen during middle-age in female rats results in lasting memory enhancements and increases in levels of estrogen receptors and other proteins important for memory in the hippocampus. Effects persist long after estrogen treatment is terminated. Increased levels of estrogen receptors in the hippocampus of aging females, even in the absence of estrogen, are associated with improved memory. Mechanisms by which estrogen receptors impact memory in the absence of estrogens and the associated implications for female cognitive aging is the focus of current work.



Male vulnerability to disorders of impulse control. Males as compared to females have increased incidence of disorders characterized by decreased impulse control including ADHD and addiction. Research in the Daniel lab is providing evidence of potential brain mechanisms that contribute to this sex difference. Results show that in a rat model, males compared to females are more likely to choose immediate small rewards over delayed large rewards and less likely to inhibit premature responding. Further, males as compared to females have decreased connections between the prefrontal cortex, a brain area involved in impulse control, and the dorsal striatum, an area involved in control of motor output. Current work is exploring functional consequences of this brain sex difference and is examining how androgens and estrogens act during critical developmental periods to differentially organize brain areas involved in impulse control in males and females. The ultimate goal is to understand how biological sex interacts with individual risk factors to impact vulnerability to disorders characterized by deficits in impulse control.

Dr. Daniel's research is funded by the National Institutes of Health and has been featured in local and national media outlets. (See <http://www.cbsnews.com/videos/estrogen-shown-to-have-anti-aging-effect-on-the-brain/>)

Andrei V. Derbenev, Ph.D.

Associate Professor, Department of Physiology

Brain Institute Research Group

Brain-Body Health

Broad Research Goals

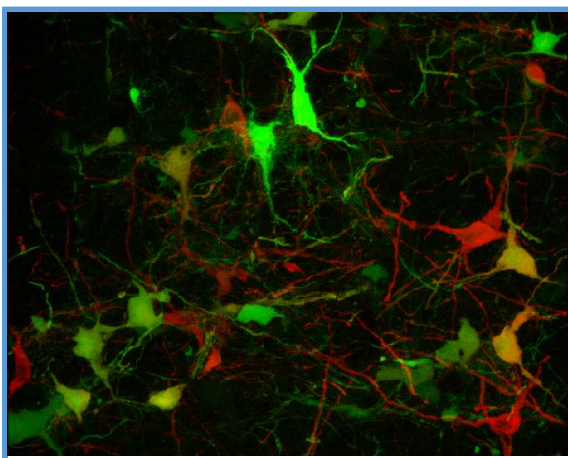
Dr. Derbenev's laboratory studies how the brain regulates blood pressure. The studies focus on identification of neurotherapeutic approaches to restore the function of specific neurons and neural circuits which are dysfunctional in hypertension and obesity.



Dr. Andrei Derbenev

Research Overview

Dr. Derbenev's laboratory focuses on understanding the essential relationship between the brain and blood pressure control in health and disease. The brain is directly involved in the regulation of blood pressure, largely through actions of neurons and neural circuits that control kidney function, heart and vasculature.



Kidney-related neurons in the brainstem.

Dr. Derbenev's laboratory focuses on a region of the brain, the RVLM (rostral ventrolateral medulla) that controls fight-or-flight response, and is largely involved in the regulation and maintenance of blood pressure. Indeed, an increased activity of those neurons is known to exist in many forms of hypertension. Dr. Derbenev's work involves identification of specific neuronal population using viral neuro-tracing methods and electrophysiology. Using these techniques the laboratory determines the underlying mechanisms involved in the neural control of blood pressure. Studying these brain area is the initial step to develop new strategies to control blood pressure via the brain.

Blood pressure and endocannabinoids. Dr. Derbenev's laboratory also studies how cannabinoids - the compounds of cannabis (another name for marijuana) - affect a brainstem area involved in blood pressure control. These studies focus on the role of cannabinoid and other cell surface proteins and their involvement in blood pressure control.

Dr. Derbenev's research is funded by the National Institutes of Health; Heart, Lung, and Blood Institute and has been featured in local media outlets.

(See <http://www2.tulane.edu/som/departments/physiology/research/andrei-derbenev-research.cfm>; <https://tulane.edu/researcher-explores-effects-cannabinoids-blood-pressure>).

Stacy Drury, M.D. Ph.D.

Associate Director, Tulane Brain Institute
Vice Chair of Research/ Department of Pediatrics
Remigio Gonzalez MD Professor of Child Psychiatry

Brain Institute Research Groups

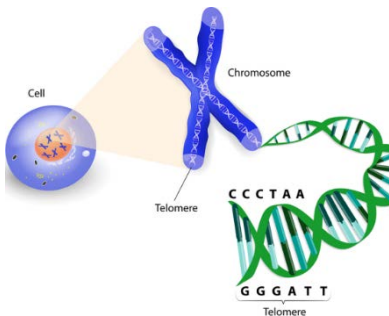
Brain-Body Health; Hormone-Brain Interactions

Broad Research Goals

To better understand how the interaction between early life adversity with genetic and epigenetic factors influences child health and development. The lab also explores how caregiving and the broader community environment can provide protective buffering to children against the lasting negative effects of early life stress.

Research Overview

Early life, including the prenatal period, represents one of the most critical developmental time periods. During the first years of life the brain undergoes rapid changes, rapidly growing and changing to prepare the child for the experiences and environments that they expect to encounter throughout their lives. Research now clearly finds that even the prenatal environment has direct effects on the development of the child, some of which occur through epigenetic changes. After a child is born the early caregiving a child receives serves as a critical developmental regulator of both child behavior and biology. Sensitive and responsive caregiving has been shown to shape children's physiologic stress response systems, guiding how they respond to later stressors. This same sensitive caregiving also influences epigenetic and cellular factors. Research in the Drury lab has demonstrated the impact of caregiving, abuse, neighborhood violence, and maternal prenatal smoking, among other factors, on telomeres, the cellular aglet cap at the end of every chromosome.



Telomeres are the cellular clock, marking aging and stress within the cell, that capture a myriad of different stress exposures and are potentially predictive of future health risks. Efforts to decrease the lasting, cross-domain, health effects of toxic stress, child maltreatment, and violence need to not only look at the outside of children but also protect the inside biological factors to ensure life-long health.

Dr. Stacy Drury and members of her research team



Dr. Drury's research is currently funded by NIMH, NIMHD, and The Bill and Melinda Gate Foundation. She has previously received funding from the Dr. Harry Seneca Trust, NARSAD, The Harvard Center of the Developing Child, NIEHS, SAMSHA and the Tulane Oliver Fund. Her work has been featured in the Washington Post: ("Violence at home puts a genetic stamp on kids and may lead to health problems.")

<http://m.washingtonpost.com/news/to-your-health/wp/2014/06/18/violence-at-home-puts-a-genetic-stamp-on-kids-and-may-lead-to-health-problems/>) and the Wall Street

Journal (John S Dykes: "How dickensian childhood leaves genetic scars.")

<http://online.wsj.com/article/SB10001424052702304363104577390462225369908.html?KEYWORDS=telomere>)

Aaron S. Dumont, M.D., M.B.A.

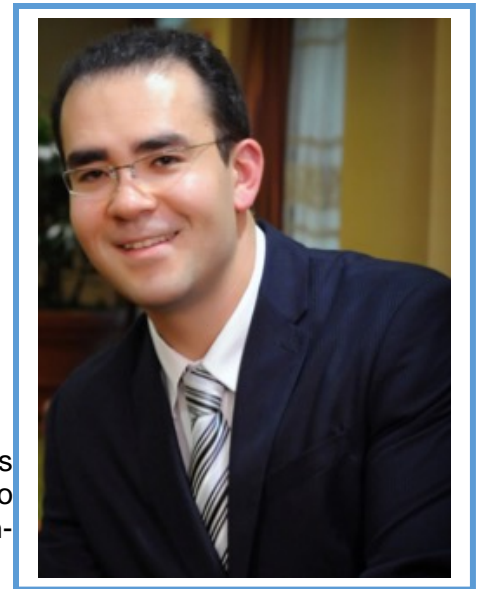
Charles B. Wilson Professor & Chair,
Department of Neurosurgery
Director, Tulane Center for Clinical Neurosciences

Brain Institute Research Group

Neurodegenerative Disease, Neural Injury & Repair

Broad Research Goals

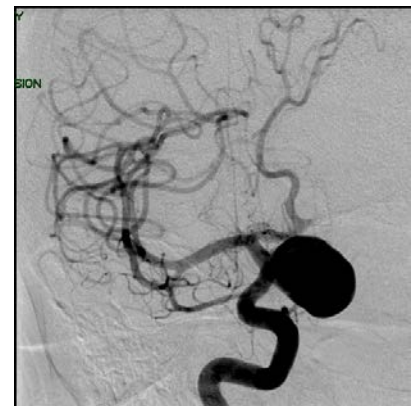
The overall goal of the laboratory is to understand mechanisms leading to the formation and rupture of cerebral aneurysms and to translate this knowledge to the development of minimally and non-invasive therapies for this potentially devastating condition.



Research Overview

Cerebral aneurysms are an outward bulging and weakness of the wall of brain blood vessels. Aneurysms may rupture resulting in a devastating stroke with bleeding in the fluid space around the brain and within the brain (subarachnoid hemorrhage and intracerebral hemorrhage). Despite efforts to improve treatments, cerebral aneurysms continue to be fatal for many. Additionally, the majority of survivors are left with permanent disability preventing these patients from returning to their former lives. Understanding which aneurysms may bleed and developing better treatments (including minimally invasive and non-invasive/medical therapies) is critical for the future of patients afflicted with this disease.

The research conducted in this laboratory focuses on the role of inflammation and oxidative stress in the formation, progression and rupture of cerebral aneurysms. To understand potential mechanisms within these pathways, the laboratory conducts *in vitro* experiments using cultured cerebral vascular smooth muscle cells to elucidate molecular events that may lead to blood vessel wall breakdown and the formation and ultimately rupture of these lesions. The laboratory also examines such mechanisms in a mouse model of cerebral aneurysm formation and rupture. Identified mechanisms contributing to aneurysm formation and rupture are then targeted with novel technology and drugs/non-invasive therapies with the ultimate goal of translating this to improving the treatment of human cerebral aneurysms.



The work in this laboratory has been supported by the National Institute of Neurological Disorders and Stroke (NINDS), the Neurosurgery Research and Education Foundation, the New York Academy of Medicine and the Charles B. Wilson Endowed Chair at Tulane University.

Laurie Earls, Ph.D.

Assistant Professor, Department of Cell and Molecular Biology

Brain Institute Research Group

Memory & Cognition

Broad Research Goals

The goal of the Earls laboratory is to understand how the molecular processes governing memory change with age and how this impacts vulnerability to disease



Dr. Laurie Earls with her lab

Research Overview

As we age, our cognitive abilities change; however, studies on the molecular pathways involved in memory have historically been conducted in the young brain. Therefore, little is known about how these processes change as the brain ages. Research in the Earls lab is showing that there are specific pathways that regulate brain function differentially with age, and that this affects the age of onset for diseases of memory and cognition.

The 22q11.2 Deletion Syndrome (22q11DS) is the second most common chromosomal disorder after Down Syndrome. A variety of psychiatric deficits arise in 22q11 patients as they age, including cognitive deficits, anxiety, and an increased risk for schizophrenia. The Earls Lab studies how brain function changes with age in 22q11DS, and has identified multiple mechanisms of vulnerability to disease in affected brains. This has led to two major discoveries.

Age-dependent changes in miRNA targeting

microRNAs are small molecules that have the capacity to influence the expression of large cohorts of genes. We are just beginning to understand that the targets of a given microRNA change with cellular context and with age. The Earls Lab is studying the mechanisms that govern miRNA targeting and how these are involved in the aging brain.

Novel small peptides involved in age-related cognitive decline

Our genome encodes small peptides that have heretofore remained undiscovered due to their small sizes. The Earls Lab is characterizing one such gene, the Plasticity-Associated Neural Transcript Short (Pants). Pants negatively regulates neural function and memory with age, so that loss of Pants improves brain function. Understanding the mechanisms by which this small peptide impacts our memories with age may be beneficial not only for individuals with 22q11DS, but also for all those experiencing age-related memory loss.

Dr. Earls' research is funded by the National Institutes of Mental Health and the Brain and Behavior Research Foundation.

Jonathan P. Fadok, Ph.D.

Assistant Professor, Department of Psychology

Brain Institute Research Groups

Memory & Cognition

Broad Research Goals

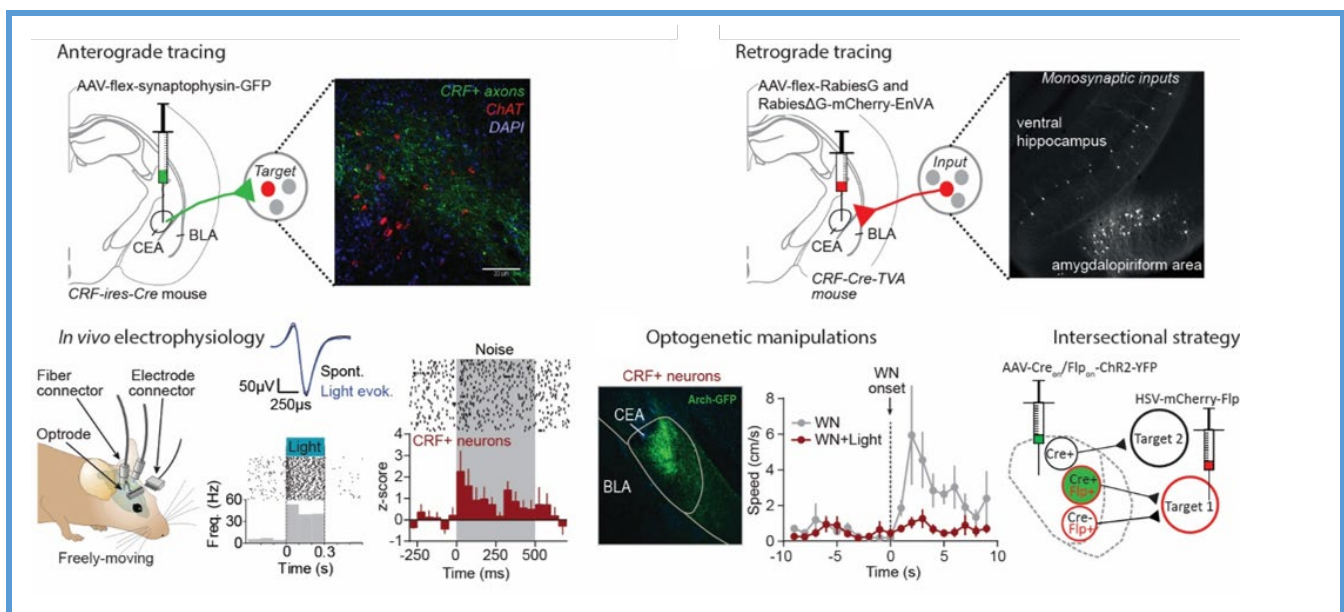


The Fadok laboratory is focused on understanding how neuronal circuits interact to control learning and adaptive behavior. A fundamental goal of the laboratory is to discover the neurobiological mechanisms underlying emotional states, with the hope of identifying novel targets and strategies for therapeutic intervention designed to alleviate mental illness.

Research Overview

Survival of an organism is contingent upon selection of appropriate behavioral responses in the face of rapidly changing environmental stimuli. This depends on learning about predictors of possible positive and negative outcomes, and on mounting an adaptive behavioral response. Understanding how activity in defined neuronal circuits (identified using molecular markers and anatomical connectivity) mediates appetitive (positive) and aversive (negative) learning, as well as how these circuitries are distinct or overlapping, is a central question in the Fadok laboratory.

Using a multidisciplinary approach that combines advanced neuroanatomical tracing techniques, behavior, neurophysiological recordings, and methods to manipulate brain function, the Fadok lab is dissecting the neuronal circuitry of appetitive and aversive learning with a focus on interactions between brain areas and cell types. Ultimately, elucidating these mechanisms at the level of defined neurons and circuits is fundamental, not only for developing a basic understanding of memory processes in the brain, but also to inform a mechanistic approach to psychiatric conditions associated with dysfunctional appetitive or aversive circuits, including anxiety and mood disorders.



Fadok, et al. (2017) A competitive inhibitory circuit for selection of active and passive fear responses. *Nature*. 542(7639): 96-100. Read-only link: <http://rdcu.be/oWjif>

Maria J. Galazo, Ph.D.

Assistant Professor / Cell and Molecular Biology

Brain Institute Research Groups

Memory & Cognition; Neurodegenerative Disease & Recovery

Broad Research Goals

Dr. Galazo's research aims at understanding the mechanisms controlling the development and function of neural circuits underlying high cognitive skills such as sensation, learning, and memory. Her work involves using a variety of molecular, cellular, and electrophysiological approaches, like manipulation of gene expression, RNAseq, and *in vivo* recording and control of neural activity in behaving animals.



Research Overview

Brain functions and behavior are the result of coordinated activity of neural circuits assembled during brain development. A variety of genetic, activity-dependent, and environmental mechanisms regulate neural circuit formation. Dr. Galazo's lab aims to understand the interplay between mechanisms acting at the genetic, cellular, and network levels regulating neural circuit formation and emergence of cognitive functions. Also, her lab studies how disruptions of these developmental mechanisms lead to neurological disorders, and explores the application of principles governing circuit formation to repair lesioned or degenerating brain circuits.

Selected Publications

Rodriguez-Muela, N., Litterman, N.K., Norabuena, E.M., Mull, J.L., **Galazo M.J.**, Sun, C., Ng, S.Y., Makhortova, N.R., Macklis, J.D., Rubin, L.L. (2017) *Single-Cell Analysis of SMN Reveals its broader role in neuromuscular disease*. **Cell Reports** 18 (6): 1484-1498.

Galazo, M.J., Emsley, J.G, and Macklis, J.D. (2016) *Corticothalamic Projection Neuron Development beyond Subtype Specification: Fog2 and Intersectional Controls Regulate Intraclass Neuronal Diversity*. **Neuron** 91 (1): 90-106.

Rodriguez-Tornos, F.M., Briz, C.G., Weiss, L., Sebastián, A., Ares, S., Navarrete, M., Frangeul, L., **Galazo, M.J.**, Jabaudon, D., Esteban, J.A., and Nieto, M. (2016) *Cux1 Enables Interhemispheric Connections of Layer II/III Neurons by Regulating Kv1-Dependent Firing*. **Neuron** 89 (3): 494-506.

Greig, L.C. *, Woodworth, M.B. *, **Galazo, M.J.**, Padmanaban, H., and Macklis, J.D. (2013) *Molecular logic of neocortical projection neuron specification, development and diversity*. **Nature Reviews Neuroscience** 14 (11): 755-69. *Co-first authors.

Jabaudon, D., Shnyder, S.J., Tischfield, D.J., **Galazo, M.J.**, and Macklis, J.D. (2011) *ROR β induces barrel-like neuronal clusters in the developing neocortex*. **Cerebral Cortex** 22 (5): 996.

Galazo, M.J., Martinez-Ceredeno, V., Porrero, C., and Clasca, F. (2008) *Embryonic and postnatal development of the layer I-directed ("matrix") thalamocortical system in the rat*. **Cerebral Cortex** 18 (2): 344-63.

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<https://www.elsevier.com/books/axons-and-brain-architecture/rockland/978-0-12-801393-9>

Sarah A. O. Gray, Ph.D.

Assistant Professor / Department of Psychology
Clinical Assistant Professor / Department of Psychiatry & Behavioral Sciences



Brain Institute Research Groups

Brain-Body Health

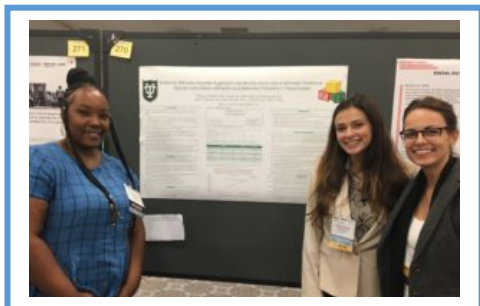
Broad Research Goals

To understand the developmental consequences of early life adversity, with a specific focus on intergenerational processes.

Research Overview

Adverse childhood experiences (ACEs) are significant risk factors for mental illness across the lifespan – risks that extend to the next generation. Dr. Gray's research focuses on examining these pathways of transmission among both parents and young children who have experienced early adversity, such as witnessing family or community violence. She takes a multilevel approach to her work, integrating narrative, behavioral, and physiological measurement to understand how risk for mental illness and resilience is transmitted across generations through both behavioral and biological pathways. For example, her work has demonstrated that mothers' experiences of early adversity and prenatal stress have implications for infants' and preschoolers' autonomic physiology during parent-child interactions.

As a clinical psychologist, she is interested in translating these research interests directly into clinical practice. Along with some of her Brain Institute collaborators, she is launching an NIH-funded clinical trial to investigate whether a preventive intervention for parents and young children called Mom Power can shift self-regulation in both parents and children at the physiological and behavioral level.



Dr. Gray's students present their research at the International Society for Traumatic Stress Studies

Dr. Gray has published broadly on topics related to early-emerging psychopathology, family processes, and trauma, and her work has been funded by the National Institutes of Health, the Brain & Behavior Foundation, and the American Psychoanalytic Association. She is the recipient of a ZERO TO THREE Leaders for the 21st Century Fellowship and a NARSAD Young Investigator award and was recently recognized with an Early Career Research Contributions Award from the Society for Research in Child Development. More information about her lab's work can be found at cfl.tulane.edu.

Hai Huang, Ph.D.

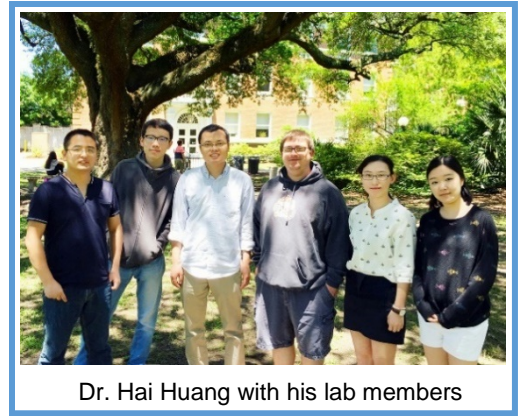
Assistant Professor, Department of Cell & Molecular Biology

Brain Institute Research Group

Memory & Cognition

Broad Research Goals

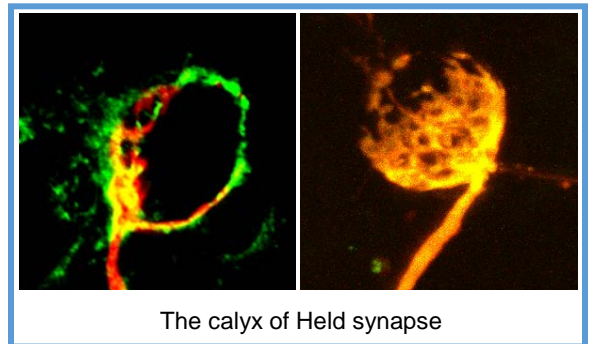
To understand the synaptic mechanisms for auditory information processing, and how noise and hearing loss affect neuronal function at central auditory system.



Research Overview

Our brain utilizes subtle differences in intensity, spectral, and timing cues between two ears to localize sound sources. Auditory information is encoded by action potentials phase-locked to the sound at high rates with sub-millisecond accuracy at the auditory brainstem. Dr. Huang's laboratory aims to identify key mechanisms that support reliable and precise signaling transmission by utilizing calyx of Held, one of the largest synapse in mammalian brain, and also expanding to other conventional synapses in the central auditory system.

Noise-induced hearing loss is rapidly becoming a greater concern as more people live in urban, acoustically enriched environments for extended hours. Besides about 0.2% children in the United States are born with a detectable level of hearing loss in one or both ears, as many as 16% adolescents aged 12 to 19 have reported some hearing loss that linked to loud noise. Noise-induced hearing loss is primarily caused by damage or loss of auditory hair cells within the cochlea. In response to the decreased sensory input, the central nervous system undergoes compensatory changes that alter sensory function, including alterations of neuronal excitability and synaptic transmission. The second major research in Dr. Huang's laboratory is to study how noise exposure and hearing loss affect central auditory function.



Dr. Huang's research is funded by the National Institute on Deafness and Other Communication Disorders of the U.S. National Institutes of Health.

Suttira Intapad, Ph.D.

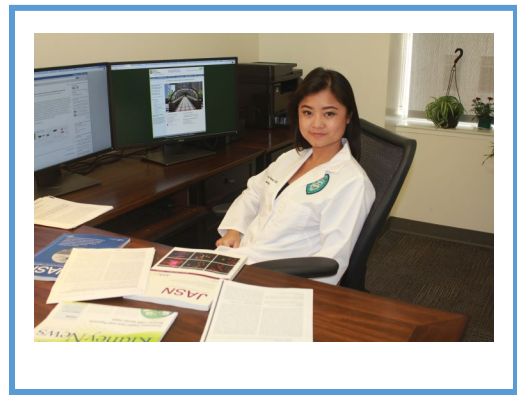
Assistant Professor / Department of Pharmacology

Brain Institute Research Groups

Brain-Body Health

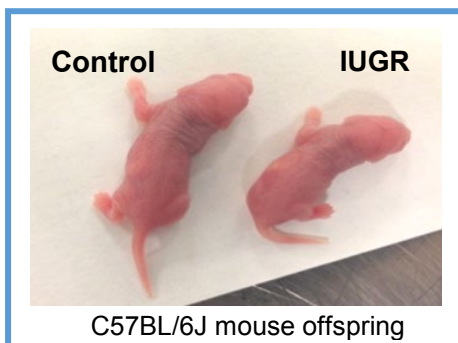
Broad Research Goals

To determination of signaling mechanisms that link low birth weight and cardiometabolic diseases.



Research Overview

Early life experiences *in utero* have lasting consequences for cardiovascular health. Low birth weight (LBW) is a crude marker of an adverse *in utero* environment and is associated with hypertension and obesity; these are risk factors for cardiovascular disease later in life. However, the mechanisms linking LBW and high blood pressure are unclear. Low birth weight (LBW) impacts 8.2% of all babies born in the United States with African American infants being two times more likely to be born LBW relative to Caucasian infants. LBW and cardiovascular disease are highly prevalent in the Southeastern United States where the prevalence for LBW is >16% in African Americans. The brain leptin signaling pathway has been suggested to play a role in metabolic dysfunction and hypertension in obese human and experimental animals. Activation of brain leptin receptor increases sympathetic nerves activities and blood pressure. Whether the brain leptin receptor signaling pathway is involved in the developmental programming of hypertension in LBW individuals is unknown. In this project, we aim to investigate the role of leptin signaling specifically in pro-opiomelanocortin (POMC) neurons in the hypertension of LBW



C57BL/6J mouse offspring

mouse offspring. I will use my new mouse model of LBW or intrauterine growth restriction (IUGR), which is induced by placental insufficiency, to mimic the major cause of LBW in the Western world in conjunction with site-specific knockout mice. The role of negative regulators of leptin signaling protein-tyrosine phosphatase 1B (PTP1B) and suppressor of cytokine signaling 3 (SOCS3) and the downstream cascade [melanocortin 4 receptor (MC4R) and renal nerves] of leptin signaling will also be determined in my experiments. Understanding of the mechanisms that contribute to hypertension in offspring exposed to complications during pregnancy from reduced uterine perfusion

may lead to potential clinical considerations for the prevention and management of blood pressure in LBW individuals.

Dr. Intapad's research is currently funded by the American Heart Association and American Society of Nephrology. For more information please visit

<https://www2.tulane.edu/som/departments/pharmacology/intapad.cfm>

S. Michal Jazwinski. Ph.D.

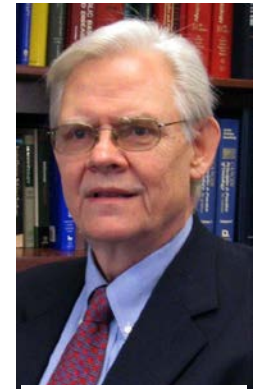
Professor, Department of Medicine

Brain Institute Research Groups

Memory & Cognition; Neurodegenerative Disease, Neural Injury and Repair

Broad Research Goals

To elucidate the genetic and environmental factors that determine unhealthy aging and can contribute to cognitive decline and the development of degenerative brain disorders



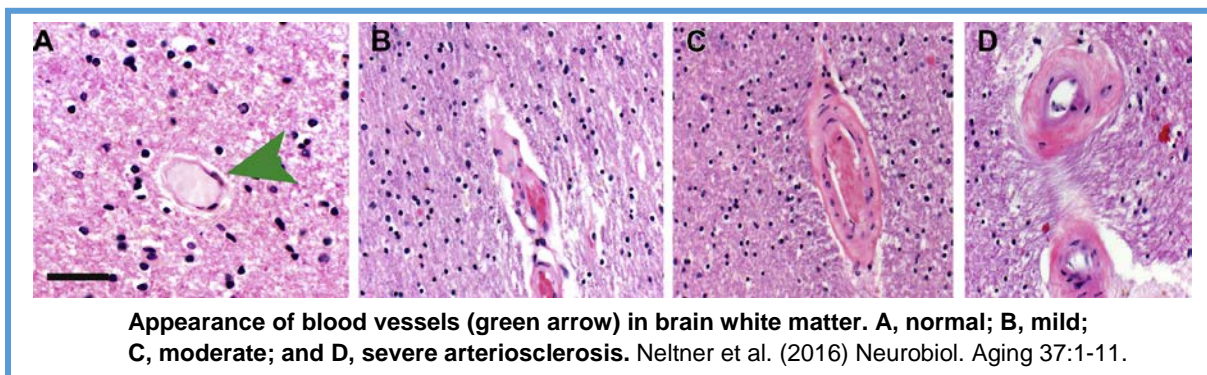
Dr. Jazwinski

Research Overview

Frailty can be quantified objectively and loss of cognitive ability is one of its components. Certain features of energy metabolism are associated with the exponential increase in frailty in the later years of life, and there are differences in how this plays out in males and in females. The genes that underlie these differences are distinct, as well, including cell death genes in males and genes that alter the characteristics of energy metabolism in females.

Affect, or how one experiences feelings and emotions, has a genetic component in centenarians. Events much earlier in life modify the way genes have this impact. One of these genes is a known risk factor for Alzheimer's disease.

Brain pathologies in centenarians are neither universal nor homogeneous. Sclerosis of a brain region essential for learning and the presence of a novel gene variant are associated with moderate or severe arteriosclerosis throughout the brain.



Appearance of blood vessels (green arrow) in brain white matter. A, normal; B, mild; C, moderate; and D, severe arteriosclerosis. Neltner et al. (2016) *Neurobiol. Aging* 37:1-11.

The above are some of the areas of focus in Dr. Jazwinski's research.

Dr. Jazwinski's research is funded by the National Institutes of Health. His recent paper (DOI:10.1159/000443793) on the association of cell death genes with features of unhealthy aging was designated "Editor's Choice – free access," by the journal.

Prasad V.G. Katakam, M.D. Ph.D.

Assistant Professor, Department of Pharmacology

Brain Institute Research Groups

Neurodegenerative Disease, Neural Injury & Repair

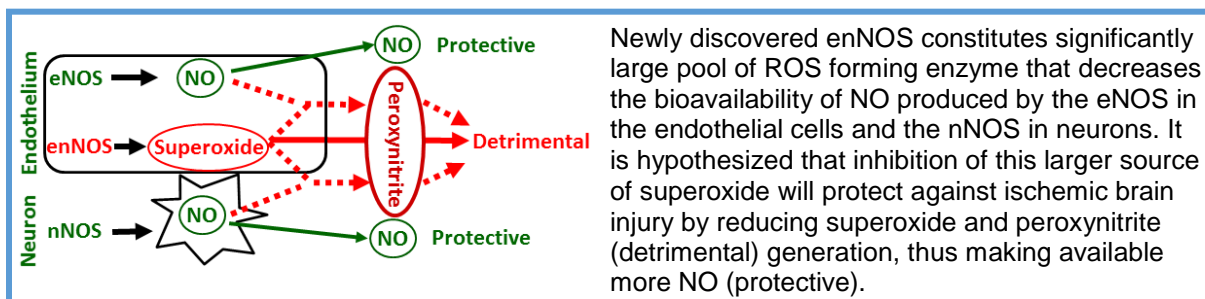
Broad Research Goals

To determine how nitric oxide synthase isoforms regulate brain microvascular function under physiological conditions and also under pathological states such as stroke and diabetes.

Research Overview

Vascular Actions of Insulin. Insulin is a metabolic hormone. Research by Katakam lab has extensively studied the vascular actions of insulin in normal and insulin resistant conditions in arteries of the brain. Insulin resistance is a condition where tissues become resistant to insulin's actions which ultimately leads to type 2 diabetes. Insulin resistance has been linked to many diverse diseases of the brain (Alzheimer's disease and Vascular Cognitive Impairment) and cardio-vascular system (hypertension, ischemic heart disease, stroke etc.). Vascular actions of insulin involve promoting contraction of vascular wall (vasoconstriction) as well as relaxing the vessels (vasodilation). Katakam lab has shown that, in insulin resistant state, the beneficial effects of insulin (vasodilation) are diminished and deleterious effects of insulin (vasoconstriction) are promoted. The focus of the research is to examine the mechanisms underlying the potential harmful effects of insulin in cerebral arteries of diabetic rats.

Nitric Oxide Synthase Biology. There are three known isoforms of nitric oxide synthase (NOS) that catalyzes the formation of nitric oxide, namely endothelial (eNOS), neuronal (nNOS), and inducible (iNOS) isoforms. Katakam laboratory has discovered a functional variant of nNOS in brain microvascular endothelial cells (enNOS) that is distinct from the other known NOS isoforms. What is unique about this new nNOS is that it produces superoxide instead of nitric oxide under physiological conditions. The focus of the research is to examine the mechanisms underlying the function of endothelial nNOS isoform and its role in stroke and diabetes.



Brooke Hamling (2nd Yr), Venkata Sure (4th Yr), Prasad Katakam, and Wesley Evans (3rd Yr) (from L to R).

Dr. Katakam's research is funded by National Institutes of Health, American Heart Association, and Louisiana Board of Regents Support Fund.

Sarah Lindsey, Ph.D.

Assistant Professor, Department of Pharmacology

Brain Institute Research Groups

Hormone-Brain Interactions; Brain-Body Health

Broad Research Goals

To define and dissect estrogen receptor signaling to ultimately improve beneficial responses to menopausal hormone therapy while reducing adverse effects.

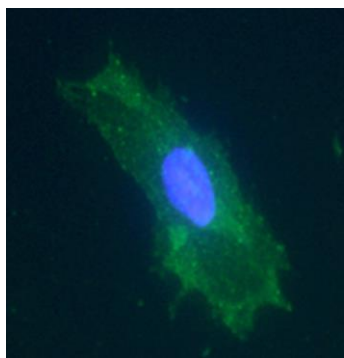
Research Overview



Lab members: Hallie Spooner, Dr. Sarah Lindsey, Dillion Hutson, Jen Duong, Mary Wilkinson, Dr. Benard Ogola, Dr. Margaret Zimmerman, and Caleb

Effects of estrogen on cognitive and cardiovascular health: The loss of endogenous estrogens that occurs with menopause is associated with both a decrease in cognition and an increase in blood pressure. Despite the fact that menopausal therapy improves brain function, recent clinical trials revealed adverse cardiovascular effects. In collaboration with the Daniel lab, Dr. Lindsey found that midlife estrogen treatment is beneficial for both cognition and blood pressure but induces kidney damage. Our future goal is to determine whether alternative treatments, such as drugs that target specific estrogen receptors, improve the profile of hormone therapy to give women the confidence to use this treatment when it significantly improves their quality of life.

Membrane-Initiated Estrogen Signaling: The Lindsey lab is particularly focused on a newly discovered estrogen receptor called GPER that induces rapid effects (within minutes). The hypothesis is that targeting only these receptors may induce the beneficial effects of estrogen in the brain and body without inducing heart disease and cancer. The lab also assesses how estrogens in the environment, such as those found in chemicals used to make pesticides and plastics, may interfere with the actions of this receptor. The overall goal is to elucidate the therapeutic potential of GPER, the changes in this pathway that occur with aging and disease, and the impact of environmental estrogens on its beneficial effects.



GPER immunostaining in an isolated smooth muscle cell.

Estrogen and PTSD: Estrogen also plays an important role in modulating the response to stress. Recent epidemiological evidence suggests a link between post-traumatic stress disorder (PTSD) and cardiovascular disease, particularly in females. Importantly, estrogen loss exacerbates the development and progression of both diseases. In collaboration with the Schrader lab, the goal is to identify symptoms that precede the development of PTSD as well as targets for therapeutic intervention. The central hypothesis is that traumatic stress in the presence of cardiovascular irregularities promotes PTSD and decreases circulating estrogen. This decrease in estrogen in turn exacerbates symptoms but can be treated with estrogen therapy.

Dr. Lindsey's research is currently funded by the NIH-NHLBI. For more information please visit <http://lindseylab.tulane.edu>.

Jeffrey J. Lockman, Ph.D.

Professor, Department of Psychology
Lila L. and Douglas J. Hertz Chair in Psychology

Brain Institute Research Groups

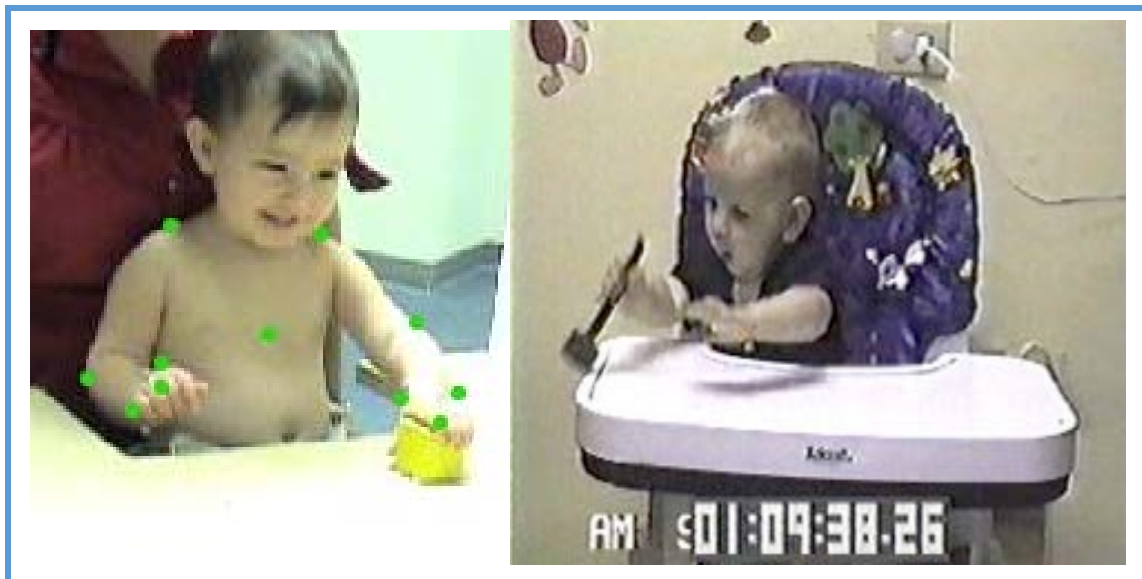
Memory & Cognition; Brain-Body Health

Broad Research Goals

The goal of our research is to understand the development of tool use, motor behavior and body knowledge in infants and young children and how these behavioral developments relate to brain development. This work can be used to inform understanding of children with motor difficulties and children with Autism Spectrum Disorder.

Research Overview

Our lab focuses on how infants and young children develop basic motor skills and what these achievements can tell us about early brain development. Using motion-tracking technology, our lab has developed state-of-the-art measures of early motor behavior to chart the development of hand function, manual skill and body knowledge. This work has the potential to document infants who may be at risk for motor delays or Autism Spectrum Disorder, at a time when early intervention efforts can be most helpful.



This research has been supported by grants from the National Institutes of Health. Please follow the accompanying link for a video produced by the American Psychological Association on Dr. Lockman's research and lab: <https://www.youtube.com/watch?v=JqXGbrgE6cc>

Andrew G. MacLean, Ph.D.

Assistant Professor, Department of Microbiology & Immunology
Division of Comparative Pathology, Tulane National Primate
Research Center



Brain Institute Research Groups

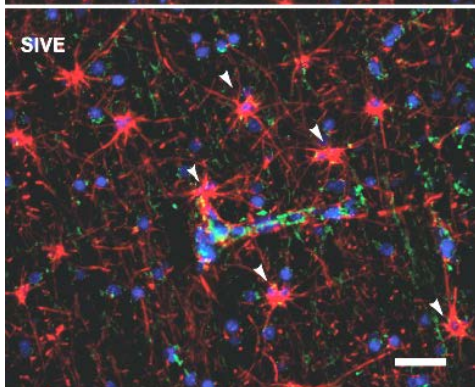
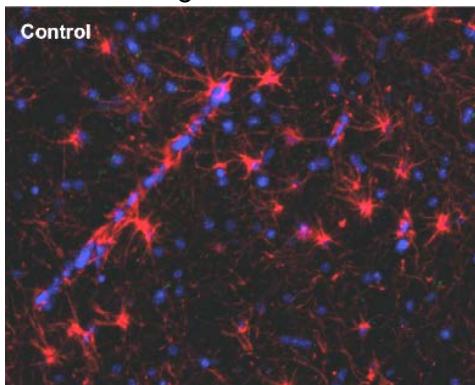
Memory & Cognition; Neurodegenerative Disease, Neural Injury & Repair; Brain-Body Health

Broad Research Goals

The MacLean lab seeks to understand the cellular mechanisms of glial activation and blood-brain barrier disruption in the development of diseases. These include infectious diseases (HIV, Dengue, Zika, Chikungunya) and behavioral conditions (Autism Spectrum Disorder, Self-Injurious Behavior, Addiction).

Research Overview

The brain is functionally separated from the rest of the body by a structure called the blood-brain barrier. This consists of endothelial cells and glia. Activation of the endothelial cells can cause the barrier to cease functioning, causing imbalances within the brain. Glial cells regulate the function of the endothelial cells, and constitute the majority of the cells inside the human brain. Despite their abundance, we know surprisingly little about how glia function in the initiation of disease. Understanding the mechanisms of endothelial-glia interactions has become an important line of investigation in neuroscience. Exciting recent work from the field has demonstrated central roles for both of these cell types in the development and resolution of disease. Moreover, glial cells appear to be primary responders to neurodegenerative disease, but whether they are directly affected by disease, are responding to disease, or are in fact driving the disease remains unclear. Defining the precise roles that glia play will be a crucial step if we wish to understand how the nervous system functions in health and disease.



Activation of glia (red) and endothelial cells during HIV-associated brain inflammation. Normal brains have very low levels of the inflammatory protein TLR2 (green). It is apparent that brains of monkeys infected with virus have much higher levels of TLR2 (green) on glia and endothelial cells.

This work has been supported by the National Institutes of Health, including the National Center for Research Resources, the Office of the NIH Director, the National Institute for Mental Health, and the National Institute on Drug Abuse. Projects have also received support from the Veterans' Administration, the Louisiana Board of Regents, and Tulane University.

Julie Markant, Ph.D.

Assistant Professor, Department of Psychology

Brain Institute Research Group

Memory & Cognition

Broad Research Goals

To understand how brain development supports attention, learning, and memory interactions during infancy and early childhood, with the goal of determining how these normative cognitive processes are altered in cases of atypical development (e.g., autism, ADHD).



Dr. Julie Markant (center) with members of her lab.

Research Overview

Infants and young children rapidly learn new information as they explore their surroundings, despite the fact that as adults we only rarely explicitly direct their attention to the most meaningful information in the environment. Dr. Markant's research uses eye tracking, neuroimaging, and genetic methods to examine the cognitive and neurobiological mechanisms that support this efficient, incidental learning during infants' and children's exploration of the visual world. Dr. Markant's research specifically focuses on the intersection between two cognitive processes, selective attention and memory, during early development. Selective attention involves focusing on relevant information and ignoring distracting information. During the first year of life infants develop increasing control over selective attention so that they can more easily ignore irrelevant information. Dr. Markant's research has shown that this increasing control over attention also supports improved learning and memory during infancy. Using neuroimaging methods with adult participants, Dr. Markant has shown that this link between selective attention and enhanced learning can be attributed to stronger neural signals in brain regions that represent the images that are learned in the context of controlled selective attention. In other words, ignoring distracting information helps you see the meaningful information more clearly, which in turn supports a more distinct memory for that information. Dr. Markant has also shown that genetic variants affecting dopamine signaling in frontostriatal networks are related to individual differences in selective attention and learning performance during infancy and continue to predict attention and memory performance into early childhood. Dr. Markant is currently examining how infants use previously learned information to efficiently guide selective attention, with the goal of understanding reciprocal attention-memory interactions during early development that may support cumulative learning over the course of development.

More information about Dr. Markant's research and The Learning & Brain Development Lab is available at <https://lbdlab.tulane.edu>.

Franck Mauvais-Jarvis, M.D.

Price-Goldsmith Professor of Nutrition
Professor, Department of Medicine, Section of Endocrinology

Brain Institute Research Groups

Hormone-Brain Interactions; Brain-Body Health

Broad Research Goals

Our goal is to discover novel mechanisms and/or therapeutic avenues for diabetes and obesity. We are especially interested in the development of gender-based medicines to prevent the diseases.



Research Overview

The Mauvais-Jarvis lab focuses on gender differences and the role of male and female hormones in metabolic diseases. We study the mechanisms underlying energy and glucose homeostasis and how this balance is altered in diabetes, obesity and metabolic syndrome. Our approach focuses on both sexes and includes basic research in cell culture and pre-clinical animal models, translational research and patient-oriented clinical research. Our goals are to develop gender-based approaches to prevent/treat diabetes, obesity and related metabolic disorders.

The Mauvais-Jarvis' lab is currently funded by the National Institutes of Health and the American Diabetes Association. For more information, please see lab website.

<http://www2.tulane.edu/som/departments/medicine/endocrinology/diabetes-research/Lab/mauvais-jarvis-lab-index.cfm>

Stryder Meadows, Ph.D.

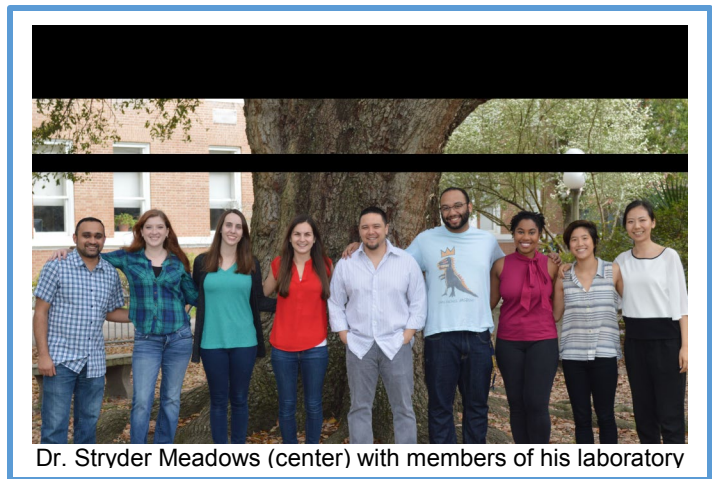
Assistant Professor
Dept. of Cell and Molecular Biology
Stepping Stone Foundation Early Career
Professor

Brain Institute Research Groups

Brain-Body Health

Broad Research Goals

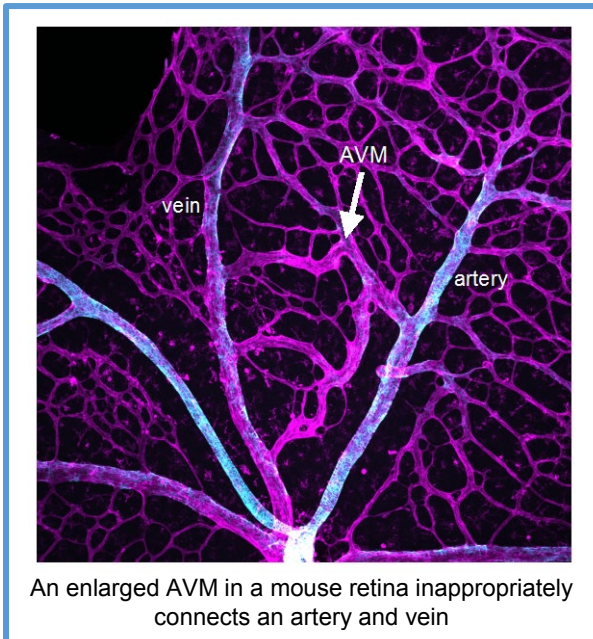
The focus of the laboratory is to elucidate the molecular pathways underlying vascular development and disease, including the formation of arteriovenous malformations, which can form in the brain and regularly occur in Hereditary Hemorrhagic Telangiectasia patients.



Research Overview

Dr. Meadows' laboratory aims to understand the molecular mechanisms responsible for the formation of arteriovenous malformations related to Hereditary Hemorrhagic Telangiectasia (HHT). HHT is a vascular disorder that affects 1 in 5000 people, with many patients developing AVMs in major organs, including the brain (10% of patients). Arteriovenous malformations are inappropriate, fragile

connections between arteries and veins that can hemorrhage leading to stroke and even death. The Meadows laboratory utilizes genomic sequencing techniques and a mouse model of HHT, whereby AVMs form in the retina (an extension of the brain), to uncover genes involved in the pathogenesis of arteriovenous malformations. Dr. Meadows' research is currently pursuing several candidate factors as therapeutic targets for arteriovenous malformations related to HHT, however these studies will also have an impact on brain arteriovenous malformations not associated with HHT. Work in the Meadows laboratory has identified a signaling pathway that when therapeutically targeted in a mouse model of HHT results in the prevention and alleviation of arteriovenous malformations.



Dr. Meadows' research is funded by the Department of Defense, National Institutes of Health - National Heart,

Lung, Blood Institute and the American Heart Association.

Lab website: <https://meadowslab.squarespace.com>

Publications: <https://www.ncbi.nlm.nih.gov/sites/myncbi/1z10cltFCZnQe/bibliography/47938653/public/?sort=date&direction=ascending>

Michael J. Moore, Ph.D.

Associate Professor, Department of Biomedical Engineering

Brain Institute Research Group

Neurodegenerative Disease, Neural Injury & Repair

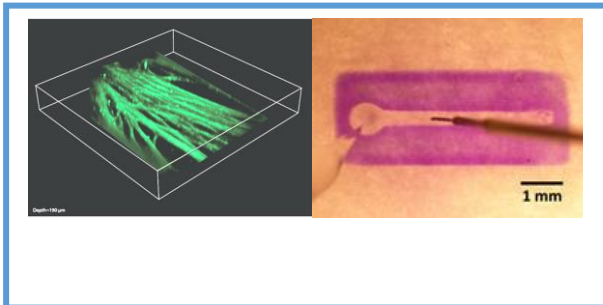
Broad Research Goals

The focus of our laboratory is to develop microscale tissue models of the nervous system. These models are being utilized for studying neurodegenerative disorders, and as tools for testing experimental drugs and for screening drugs and other chemicals for neurotoxicity.



Research Overview

Microengineered living tissue models of demyelinating disorders: Multiple sclerosis, which affects the brain and spinal cord, and peripheral nerve disorders such as Charcot Marie Tooth disease and Guillain-Barré syndrome, lead to degeneration of myelin, which is a protective sheath that surrounds nerve fibers and enables them to conduct impulses rapidly. When this protective sheath is damaged, it can lead to an array of neuropathological symptoms, such as loss of sensation, vision loss, muscle weakness, and loss of coordination. Unfortunately, there are no cures and very few treatment options for these disorders. Because these disorders involve the complex interactions of a variety of cell types,



it can be difficult to study these disorders in animal models, which do not predict human outcomes very well. Our model systems are unique because their 3D structure enables a type of electro-physiological testing that is analogous to nerve conduction testing, which is used in the clinic to diagnose and characterize these disorders. These models also make it easier to parse the contributions of different cell types and to test potential treatments.

High-content models for drug discovery and toxicity screening: More than 90% of experimental neurological drugs that go to clinical trials fail to reach the market. One of the main reasons for this shortcoming is that the animal models currently used in preclinical drug development do not very well predict human biology. Some studies can be done on human cells cultured in Petri dishes, but the information gained from these screens is limited because cell physiology changes when cultured on hard, smooth surfaces. We are developing living tissue models made from human cells that have a 3D structure more similar to actual human nervous tissue. The structural and functional changes observed in these models is similar to the kind of information typically obtained from animal studies, but these are living human tissues, so their predictive value may be higher than that for animal studies. These efforts are being translated to real-world drug screening through a partnership with our spin-off company, AxoSim Technologies.

Dr. Moore's research is funded by grants from the National Institutes of Health, the National Science Foundation, the Center for Advancing Science in Space and the Marko Spark Innovation Research Fund, as well as through a partnership with AxoSim Technologies (<http://axosim.com/>). Dr. Moore's Laboratory website: <http://www.tulane.edu/~mooremj>.

Ricardo Mostany, Ph.D.

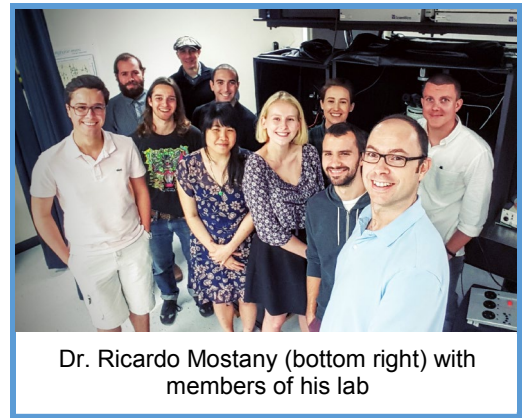
Assistant Professor, Department of Pharmacology

Brain Institute Research Groups

Memory & Cognition; Neurodegenerative Disease, Neural Injury & Repair

Broad Research Goals

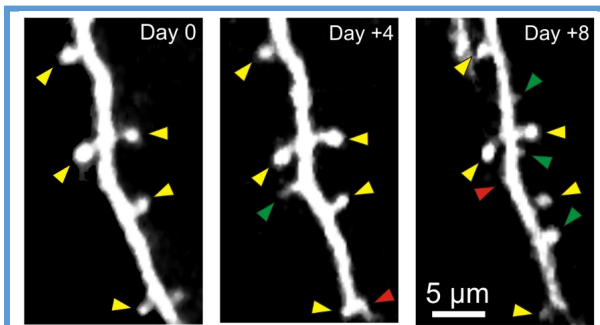
Mechanisms of synaptic plasticity in the aging brain and their role in memory and learning, Alzheimer's disease, and in recovery after stroke.



Dr. Ricardo Mostany (bottom right) with members of his lab

Research Overview

Synaptic plasticity in the aging brain. The decline in brain performance occurring during aging negatively impacts the degree of independence, number of injuries, and fatal accidents of normally aging people. Unfortunately, the neural mechanisms mediating this progressive decline are poorly understood. Using cutting-edge imaging techniques and transgenic mice, Dr. Mostany studies if the contacts between neurons are differentially affected by age, and if the brain's ability to create long-lasting synapses is reduced with aging. Studies from his lab show both increased number and reduced



Two-photon excitation time-lapse imaging of dendritic spines from the same cortical neuron acquired 4 days apart. Stable (yellow arrowheads), gained (green), and lost dendritic spines (red) are depicted.

stability of dendritic spines (i.e., the sites of excitatory synapses) in the cerebral cortex of aged mice compared with the results from young mice. The Mostany Lab studies if these alterations are the result of a progressive deterioration of the activity of inhibitory interneurons and is testing this hypothesis using electrophysiological recordings of these neurons in brains from young and aged mice. His lab also investigates the synaptic dynamics associated with experience and learning of new tasks to test the hypothesis that the aged brain uses different mechanisms than the young brain to store and recall information. In addition, while advancing age is a main risk factor for developing Alzheimer's disease, the mechanisms behind age-related brain decline are

poorly understood. Furthermore, little is known about the deficits in synaptic plasticity occurring during the progression of the pathology in Alzheimer's disease. Deciphering the mechanisms underlying this decline in brain performance will provide the basis for understanding the reason behind the shift from healthy brain aging to the degenerative processes observed in this disease.

Stroke and neuroprotection. The lack of pharmacological treatments for stroke, restricted to acute clot-buster interventions aimed to restore blood flow to ischemic brain regions as soon as possible, makes stroke the fifth leading cause of death and the leading cause of long-term adult disability in North America. The Mostany Lab is studying mechanisms to protect the brain during the ischemic episode by promoting the activity of specific subsets of neurons. These studies have the potential for the development of therapeutic interventions designed to protect the ischemic brain from further progression of the damage.

Dr. Mostany's research is currently funded by the *National Institute on Aging*, *Louisiana Board of Regents*, *Elsa U. Pardee Foundation*, *Tulane Brain Institute Research Fund Award*, and the *Tulane University Oliver Fund Scholars Award*. Mostany Lab's Website: <http://mostanylab.tulane.edu/>

Stephen Nelson, M.D, Ph.D.

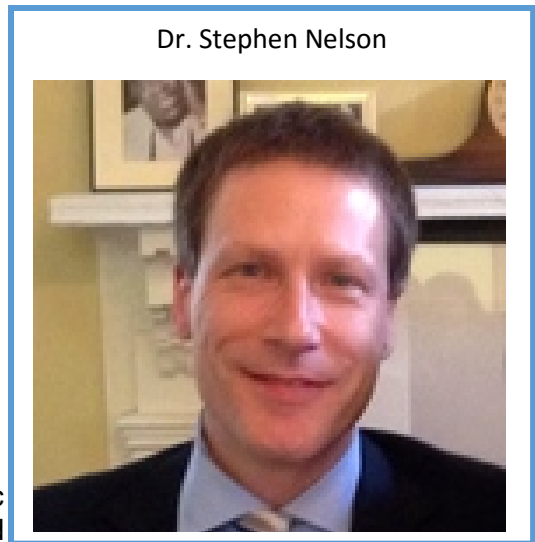
Associate Professor of Pediatrics, Neurology, Neurosurgery and Psychiatry
Division Head, Pediatric Neurology

Brain Institute Research Groups

Memory & Cognition; Neurodegenerative Disease, Neural Injury & Repair

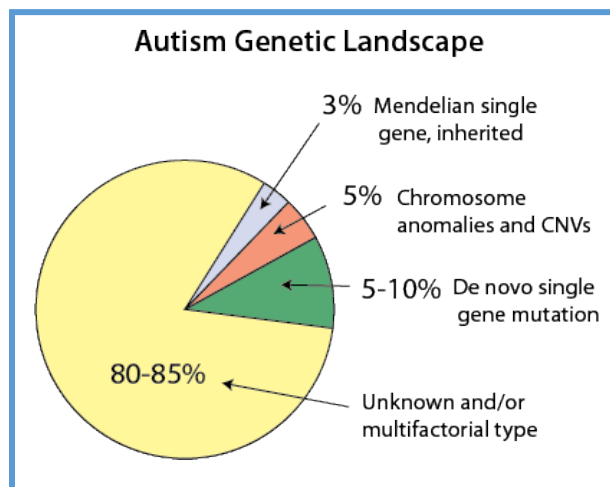
Broad Research Goals

As a clinician interested in the intersection between genetic variation and treatment approaches in autism, I am focused on enhancing our understanding of how determination of key rare and common genetic variations and copy numbers influence the presentation, treatment and family history for both autism and epilepsy.



Research Overview

Dr. Nelson's clinical practice focuses on autism, neurodevelopmental disorders, and epilepsy. In his clinical research, he has created an extensive database of genetic variants and clinical presentations for a range of different clinical outcomes, using this data to drive clinical decisions, provide novel information about familial risk, and identify symptom clusters that correlate with novel genetic variations. This has provided valuable information in determining the optimal management of intractable epilepsy patients, whether by specific antiepileptic combinations, ketogenic diet, and Vagus nerve stimulator.



Jeffrey Rouse, M.D

Assistant Professor, Department of Psychiatry and Behavioral Sciences



Brain Institute Research Groups

Memory and Cognition; Hormone-Brain Interactions

Broad Research Goals

As a board-certified forensic psychiatrist and the Orleans Parish Coroner, my academic interests include the neuroanatomical risk factors for violence, the application of biomarkers to forensic risk assessment, functional and structural neuroimaging of brain regions and networks involved in emotion regulation, and the use of real-time functional magnetic resonance imaging (rt-fMRI) neurofeedback as a research and clinical tool.

Research Overview

In collaboration with Dr. Jeremy Cohen, Assistant Professor in the Department of Psychology at Xavier University of Louisiana, our shared goal is the application of neuroimaging as a tool to understand the structure and function of the human brain in emotion regulation.

Currently, we are utilizing a freely accessible, existing neuroimaging dataset of rt-fMRI neurofeedback experiment. Real-time neurofeedback of neuroimaging is a newly emerging technology that permits a person in a brain scanner to observe and alter intentionally their own brain activity in specific regions. This technique can be used to enhance or dampen the response of specific brain networks and has been utilized in preliminary work in cognitive enhancement, addictive disorders, post-traumatic stress disorder (PTSD) and schizophrenia, and others. Our interest lies in the utility of this technology as applied to emotional regulation neural networks and in identifying what individual factors may underlie an individual's ability to self-regulate neural activity

In addition, recently we have received pilot funding through the NIH BUILD program at Xavier to obtain our own fMRI data to investigate the neural basis of social cooperation and implicit bias, the phenomenon of unconscious preference for one social group over another. Our project will employ fMRI to observe the functional brain networks involved when a person plays a cooperative game with a partner. The person in the scanner will play this game, entitled the Trust Game, with a partner of the same ethnicity and with a partner of a different ethnicity. Not only will we measure how performance in the game itself may differ depending on the ethnicity of the partner, but also we will measure how the large scale networks of the brain may differ accordingly. We will then also collect from each player psychological information regarding a player's style of thinking and style of emotional control, levels of stress-related hormones in saliva, and direct, reaction-time based measurements of implicit bias. All these measurements will then be tested to see if they can explain any differences we may find in the brain networks according to a match or mismatch between a player and the partner's ethnicity. Finally, we will investigate whether players can successfully regulate the activity of certain regions of the brain we hypothesize are involved in these complex social interactions, using rt-fMRI neurofeedback.

Michael S. Scheeringa, M.D.

Vice Chair of Research
Venancio Antonio Wander Garcia, IV, M.D. Chair in Psychiatry

Brain Institute Research Groups

Memory & Cognition; Hormone-Brain Interactions

Broad Research Goals

Posttraumatic stress disorder (PTSD) including diagnostic criteria, randomized clinical trials, autonomic regulation, HPA axis regulation, cognitive factors, memory, genetics, and personalized treatment. Dr. Scheeringa also has developed and validated a diagnostic interview and treatments for very young children.



Michael S. Scheeringa, M.D.

Research Overview

Dr. Scheeringa has authored numerous scientific papers and book chapters on posttraumatic stress disorder (PTSD) in young children over the last 21 years. He has conducted five federally-funded projects on traumatized youth to assess their psychiatric symptoms, neurobiological profiles, and family functioning. He has conducted randomized clinical trials to treat PTSD in preschool children and older youth.

His current research includes studying the neurobiological reactivity of youth during cognitive behavioral therapy for PTSD and anxiety disorders.

Dr. Scheeringa's work has been supported by NIMH, ACYF, and NARSAD. For more information, the link to his lab is <http://medicine.tulane.edu/departments/psychiatry/research/dr-scheeringas-lab>

Laura Schrader, Ph.D.

Associate Professor, Department of Cell and Molecular Biology

Brain Institute Research Groups

Memory & Cognition; Hormone-Brain Interactions

Broad Research Goals

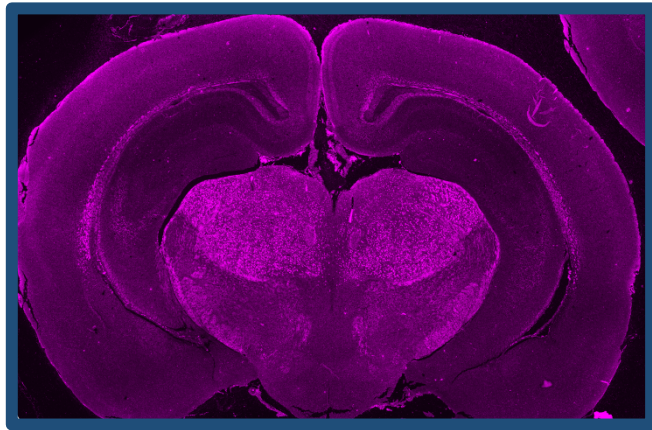
To understand the influence of the interaction of genes and environment on the developing and adult brain.



Dr. Laura Schrader, seated on right, and her lab.

Research Overview

The research in Dr. Schrader's lab is focused on two main topics. The first focus seeks to determine factors that modulate expression and function of ion channels, and this includes investigations at both the genomic and protein levels. The goal of this research is to understand how the cells of the brain intrinsically regulate neuronal excitability and synaptic communication, particularly during pathological conditions. We are currently investigating the role of *Shox2*, a transcription factor that is important for development, in neuronal excitability and developmental neuropathologies, such as autism and epilepsy. In addition, we are testing the involvement and modulation of a particular potassium channel in a mouse model of Fragile X Syndrome, the most common monogenic form of autism.



***Shox2* expression in the mouse brain.** *Shox2* is highly expressed in the thalamus, an area of the brain important for relaying sensory, motor, and cognitive information to the rest of the brain.

The second focus of the lab investigates sex differences in the regulation of signaling cascades in the hippocampus and other areas of the brain in chronic and acute stress. Approximately twice the number of women experience stress disorders compared to men, and neurobiological mechanisms likely contribute to this dichotomy. We are currently investigating cellular mechanisms and signaling cascades that may underlie the divergence of these mechanisms in males and females. This approach may lead to improved individualized pharmacological intervention to enhance protective pathways and/or decrease activity of pathways with negative effects in various neuropathological conditions such as: depression, anxiety and posttraumatic stress disorder (PTSD).

Funded by NSF, NIH, Tulane Brain Institute Research Fund Award, and Simons Foundation

Gregory W. Stewart, M.D.

W. Kennon McWilliams Professor in Sports Medicine / Orthopaedics
Associate Professor, Physical Medicine and Rehab / Orthopaedics

Brain Institute Research Groups

Neurodegenerative Disease & Recovery; Brain-Body Health

Broad Research Goals

Our primary goal at this time is the development of a well-known and widely recognized center for the study of mild TBI and a brain repository for the purpose of studying traumatic brain injury on both the gross anatomical as well as histological level. We are also interested in studying the long-term effect of participation in high-impact sports on brain health and cognition in order to better understand the potential effects of head injury sustained during these sports later in life.

Research Overview

We work with athletes from all walks of life- from high school to retired professional athletes- to understand the short and long-term effects of sports on brain health, both at the cognitive level, as well as at the physiological level. Specifically, we are interested in the effects of sports-related head trauma on brain function and long-term brain health. Much of our research centers on studying the results of concussive head injury in athletes, as well as identifying means by which to identify and understand the effects of sub-concussion forces sustained during sports activities. Currently, the diagnosis of chronic traumatic encephalopathy (CTE) can only be definitively made post-mortem and has not been widely studied. In fact, only recently was a consensus for the diagnosis of TBI determined and published. Thus, we seek to understand the progression of sports-related traumatic brain injury (TBI) on a comprehensive physiological level, as well as to help determine factors in living patients that may help physicians to more effectively diagnose and manage TBI, both symptomatically and in terms of addressing the disease itself. Additionally, we are interested in helping to develop methods of concussion prevention in all athletes, whether they are high school-aged athletes participating in extramural sports or professional athletes at the most elite levels of training. Our research group is focused largely on establishing a brain repository dedicated largely to the hopes of providing new information for the growing body of gross anatomical and histological research regarding TBI.



Jeffrey Tasker, Ph.D.

Professor, Department of Cell and Molecular Biology
Catherine and Hunter Pierson Chair in Neuroscience

Brain Institute Research Groups

Hormone-Brain Interactions; Brain-Body Health

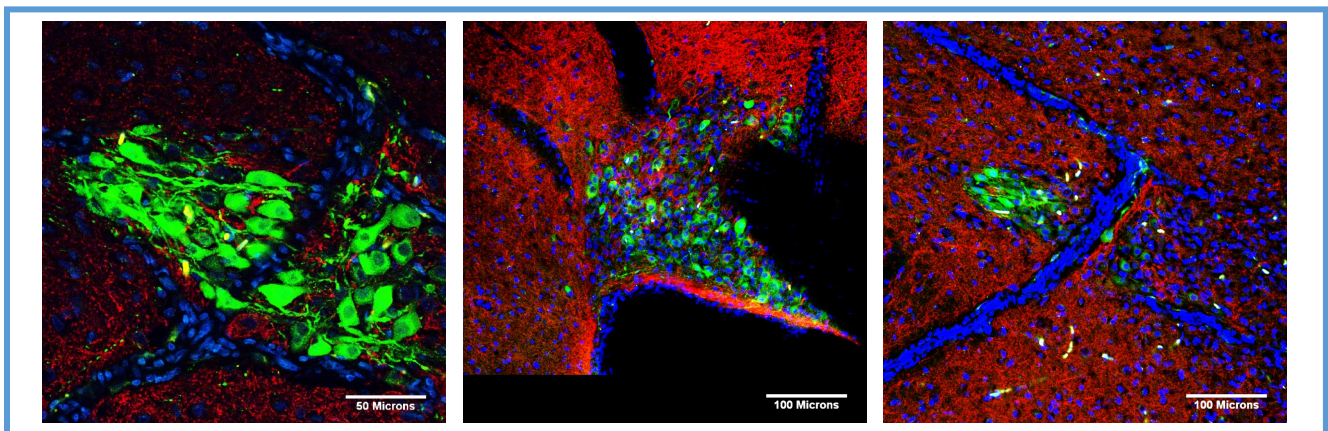
Broad Research Goals

The overarching goal of research in the Tasker lab is to understand how the brain controls physiological balance, or homeostasis, via the brain-body reciprocal interface.



Research Overview

The Tasker lab is studying the effects of acute and chronic stress on the brain as well as interactions between stress, energy metabolism and fluid homeostasis. Stress leads to changes in brain signals and neural circuit activity that are beneficial in the short term, but that can cause damage to brain cells and pathological modifications in brain circuitry if the stress is chronic or traumatic in nature. The Tasker lab uses rats and mice as models to study stress-induced brain plasticity underlying human psychiatric disease states such as depression, anxiety, and posttraumatic stress disorder. Their current focus is on signaling in the brain by the stress hormone corticosteroid, which they discovered to cause endocannabinoid production and to contribute to stress adaptation under normal conditions and stress pathology following conditions of chronic stress. They are also currently studying how traumatic stress leads to increased alcohol consumption by altering endocannabinoid signaling in the amygdala.



Potassium-chloride co-transporter labeling (red) in the hypothalamic paraventricular nucleus (left and right) and supraoptic nucleus (middle) of a transgenic rat expressing green fluorescent protein in vasopressin neurons. Blue fluorescent labeling of nuclei, including neurons, glia and blood cells.

The research performed in the Tasker lab has been funded for nearly 25 years by grants from the National Institutes of Health, the National Science Foundation, the American Heart Association and the state of Louisiana. Dr. Tasker holds the Catherine and Hunter Pierson Endowed Chair in Neuroscience, which he has used to support cutting edge exploratory brain research in his lab. He was awarded the School of Science and Engineering Outstanding Researcher award in 2015 for his lab's work on stress and the brain. He has mentored 18 PhD students in Neuroscience and Cell and Molecular Biology, and has supervised 15 post docs.

Yu-Ping Wang, Ph.D.

Professor, Biomedical Engineering
Director, Multiscale Bioimaging and Bioinformatics Lab.

Brain Institute Research Groups

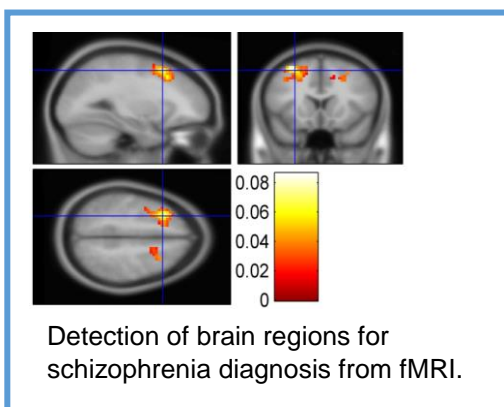
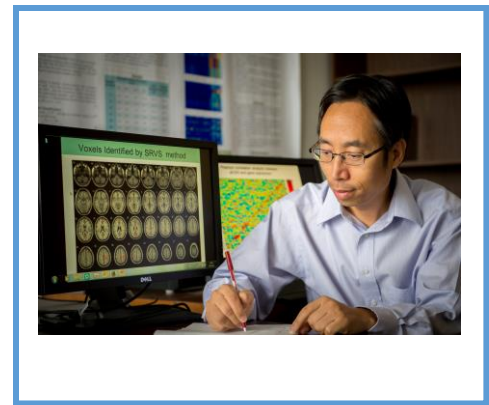
Memory & Cognition; Brain-Body Health

Broad Research Goals

To develop computational approaches for the detection of biomarkers from multiscale genomic and imaging data, in order to explore the association between genetic variations and brain functions and behaviors, and further integrate these data for more precise diagnosis of multiple mental illnesses.

Research Overview

Utilizing multiscale and multimodal brain imaging and genetic techniques such as fMRI imaging and SNP arrays, complementary information can be fused for comprehensive and systematic diagnosis of complex diseases. However, these brain imaging and genetic data are of different nature, format, organization and structure and are produced by different platforms at various scales; fusion of these heterogeneous data has been difficult. The goal of Dr. Wang's laboratory has been the development of novel computational approaches to correlate and integrate multimodal MRI imaging with genomic data while incorporate biological knowledge and their interaction networks for the detection of biomarkers, and to apply and validate the detected biomarkers for the identification of risk genes/gene modules and for the improved diagnosis of subtle patient subgroups. Three of our ongoing NIH projects include: 1) to study the correlation between multiple brain imaging (e.g., structural and functional MRI) and genomic data (e.g., SNPs and DNA methylation) for the detection of epistasis factors or interaction networks; 2) to integrate multiscale imaging and genomic data, especially incorporating epistasis factors, for the identification of biomarkers, from which risk genes can be better detected; 3) to apply the detected biomarkers for the classification of multiple mental illnesses (e.g., *as schizophrenia, Unipolar, and bipolar disorders*) that are currently based on symptoms and are often misdiagnosed.



Dr. Wang's laboratory is also part of an NSF supported consortium including New Mexico, Nebraska, and Louisiana on developmental chronnecto-genomics (Dev-CoG), whose overarching goal is to advance our understanding of childhood brain connectivity by developing new analytic approaches to study brain connectivity over short and long periods of time (the chronnectome) via multiple imaging modalities (e.g., fMRI, MEG) as well as their genetic underpinnings. Changes in brain connectivity during childhood are both relatively rapid and poorly understood, especially with respect to time-varying connectivity or oscillatory behavior as well as their relationship to genetic factors.

Dr. Wang's research has been funded by both NIH and NSF, and featured in many media reports. To learn more about his group's research, please visit his website at <http://www.tulane.edu/~wyp/>

James E. Zadina, Ph.D.

Senior Research Career Scientist,
Department of Veterans Affairs
Professor, Departments of Medicine and
Pharmacology

Brain Institute Research Groups

Brain-Body Health; Neurodegenerative
Disease, Neural Injury & Repair; Hormone-
Brain Interactions; Memory & Cognition



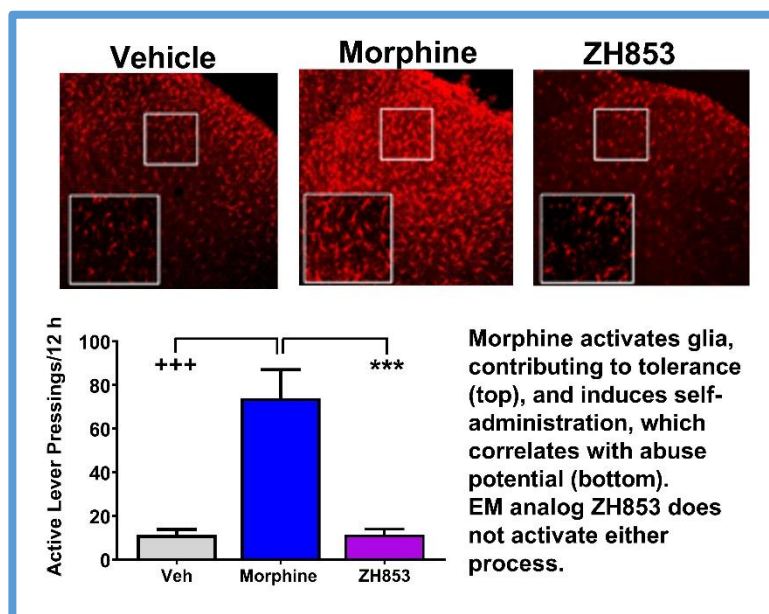
Dr. James Zadina (back left) and lab members

Broad Research Goals

To improve understanding of opioids and their mechanisms of action. To develop new pain medications with reduced side-effects, especially abuse liability.

Research Overview

Opioids are the most effective therapy for moderate to severe pain, but their use is limited by risk of addiction, potentially fatal respiratory depression, and other major side effects. A long-standing goal of opioid research is to separate effective analgesia from dangerous side effects.



In a novel approach, we engineered and tested chemical modifications of a natural brain opioid (endomorphin), discovered in our lab in 1997, with the goal of optimizing analgesic effectiveness and minimizing side effects. In animal studies, one of these compounds, ZH853, produced analgesic effectiveness equal to, and in several cases greater than morphine, while showing reduced or absent abuse liability, respiratory depression, motor impairment, tolerance, and proinflammatory (glial activation) effects.

These results were recently published ([doi:10.1016/j.neuropharm.2015.12.024](https://doi.org/10.1016/j.neuropharm.2015.12.024)) and have been featured in local, national and international media outlets including

AAAS and Nature outlook: http://www.eurekalert.org/pub_releases/2016-01/tu-snd012816.php
http://www.nature.com/nature/outlook/pain/index.html?WT.mc_id=TWT_NA_1607_PAIN/

A comprehensive plan has been developed to raise funds to conduct FDA-required preclinical studies and enter clinical trials. Our laboratory continues to investigate the mechanisms by which this compound is distinct from morphine and produces its highly favorable profile. In addition, a publication is in press showing that it is highly effective in models of multiple types of pain. This work was funded by the Dept. of Veterans Affairs, Dept. of Defense, Office of Naval Research, and the Louisiana Board of Regents.

Andrea Zsombok, Ph.D.

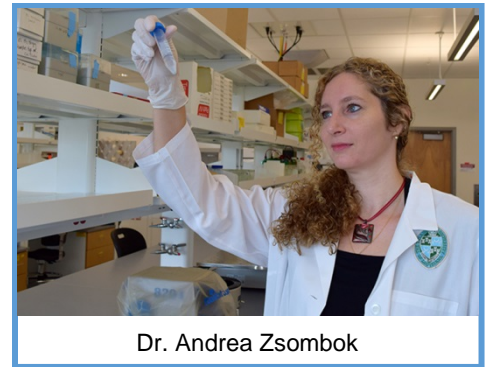
Associate Professor, Department of Physiology

Brain Institute Research Group

Brain-Body Health

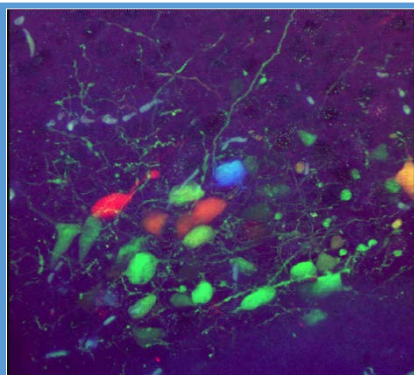
Broad Research Goals

To identify neurotherapeutics for the treatment of diabetes



Research Overview

Dr. Zsombok's laboratory focuses on the fundamental relationship between the brain and glucose control in health and diabetes. Brain regulation of glucose homeostasis has always been a potentially important avenue for diabetes research and treatment, and the recent availability of precise new experimental approaches has now made this potential a reality. Manipulation of specific neurons with viral gene delivery or the availability of retrograde viral tracers allowing identification of tissue specific neurons offers a revolutionary approach for the control of glucose levels.



Retrograde viral labeling was used to identify liver-related (green) and stomach-related (red) neurons.

TRPs and glucose control. Dr. Zsombok's laboratory investigates neural circuits in the hypothalamus and brainstem and examines the role of cell surface proteins (e.g., TRPV1) and their contribution to glucose metabolism. TRPV1, which is activated by capsaicin, the pungent ingredient of hot pepper, was shown to have beneficial effects on whole body metabolism including glucose levels. The studies conducted in her laboratory investigate neurons that convey to the liver the need to store or release sugar, a mechanism, which is altered in diabetes. Her studies established the properties of liver-related neurons, identified TRPV1 as a novel regulator of the brain-liver connections, and showed that the brain-liver circuitry is altered in diabetic condition. This may contribute to the impairment of control of liver glucose production, which is well known in diabetes. Therefore, identification of the key elements of the brain-liver circuitry

is the first step in developing new pharmacological targets and strategies for glucose management.

Antipsychotics and diabetes. Treatment with atypical antipsychotics (e.g., olanzapine) is associated with metabolic side effects including weight gain and glucose dysregulation. A variety of brain sites and mechanisms have been proposed as contributors to the side effects. A recent study from Dr. Zsombok's laboratory demonstrated that olanzapine has a powerful effect on brainstem neurons. The findings also could provide compelling explanation for why females are more sensitive to antipsychotic-induced metabolic disturbances than their male counterparts.

Dr. Zsombok's research is funded by the National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases and has been featured in local and national media outlet. (See <http://medicalxpress.com/news/2015-04-unraveling-link-diabetes-brain.html>)



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