

2017 McKnight Memory & Cognitive Disorder Awards [Bulk]

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NEWS RELEASE

THE McKNIGHT ENDOWMENT FUND FOR NEUROSCIENCE

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McKNIGHT AWARDS \$1.2 MILLION FOR STUDY OF BRAIN DISORDERS

FOR IMMEDIATE RELEASE (Minneapolis, December 16, 2016)-The McKnight Endowment Fund for Neuroscience has selected four projects to receive the 2017 Memory and Cognitive Disorders Awards. The awards will total \$1.2 million over three years for research on the biology of brain diseases, with each project receiving \$300,000 between 2017 and 2019.

The Memory and Cognitive Disorders Awards support innovative research by U.S. scientists who are studying neurological and psychiatric diseases, especially those related to memory and cognition. The awards encourage collaboration between basic and clinical neuroscience to translate laboratory discoveries about the brain and nervous system into diagnoses and therapies to improve human health.

The awards will support studies of genes and areas of the brain involved in neurological disorders such as Alzheimer's disease, autism spectrum disorders, and addiction. "This year's McKnight MCD awards represent a range of powerful and multidisciplinary studies that will help us understand the brain basis of memory including disease states when memory or other aspects of higher cognitive function fail," said Wendy Suzuki, Ph.D., chair of the awards committee and Professor of Neural Science and Psychology at New York University.

The awards are inspired by the interests of William L. McKnight, who founded The McKnight Foundation in 1953 and wanted to support research on diseases affecting memory. His daughter, Virginia McKnight Binger, and The McKnight Foundation board established the McKnight neuroscience program in his honor in 1977.

Up to four awards are given each year. This year's awardees are:

* **Donna J. Calu, PhD, Assistant Professor in the Department of Anatomy and Neurobiology, University of Maryland, School of Medicine**

Individual Differences in Attention Signaling in Amygdala Circuits

* **Fred H. Gage, PhD, Professor, The Salk Institute for Biological Studies, and Matthew Shtrahman, MD, PhD, Assistant Professor, University of California, San Diego**

Using Deep In Vivo Two-Photon Ca²⁺ Imaging to Study Temporal Pattern Separation

* **Gabriel Kreiman, PhD, Associate Professor of Ophthalmology and Neurology, Children's Hospital Boston, Harvard Medical School**

Behavioral, Physiological and Computational Mechanisms Underlying Episodic Memory Formation in the Human Brain

* **Boris Zemelman, PhD, Assistant Professor of Neuroscience, and Daniel Johnston, PhD, Professor of Neuroscience and Director of the Center for Learning and Memory, University of Texas at Austin**

Prefrontal Dysfunction in Fragile X Syndrome

With 71 letters of intent received this year, the awards are highly competitive. A committee of distinguished scientists reviews the letters and invites a select few researchers to submit full proposals. In addition to Suzuki, the committee includes Robert Edwards, MD, University of California, San Francisco; Howard Eichenbaum, PhD, Boston University; Ming Guo, MD, PhD, UCLA; Rich O'Brien, MD, PhD, Duke University; Steven E. Petersen, PhD, Washington University in St. Louis; and Matthew Shapiro, PhD, Mount Sinai School of Medicine.

Letters of intent for the 2018 awards are due by March 27, 2017. For more information, see

www.mcknight.org/neuroscience

ABOUT THE McKNIGHT ENDOWMENT FUND FOR NEUROSCIENCE

The McKnight Endowment Fund for Neuroscience is an independent organization funded solely by The McKnight Foundation of Minneapolis, Minnesota, and led by a board of prominent neuroscientists from around the country. The McKnight Foundation has supported neuroscience research since 1977. The foundation established the Endowment Fund in 1986 to carry out one of the intentions of founder William L. McKnight (1887-1978). One of the early leaders of the 3M Company, he had a personal interest in memory and its diseases.

The Endowment Fund makes three types of awards each year. In addition to the Memory and Cognitive Disorders Awards, they are the McKnight Technological Innovations in Neuroscience Awards, providing seed money to develop technical inventions to advance brain research; and the McKnight Scholar Awards, supporting neuroscientists in the early stages of their research careers.

2017 McKnight Memory and Cognitive Disorders Awards

Donna J. Calu, PhD, Assistant Professor in the Department of Anatomy and Neurobiology, University of Maryland, School of Medicine

Individual Differences in Attention Signaling in Amygdala Circuits

Dr. Calu's research is driven by her desire to understand individual vulnerability to addiction, which is manifest in the addicts' compulsion to seek and take drugs even in the face of known negative consequences of drug abuse. Generally, humans modify their behavior when outcome values suddenly get better or worse than expected, but the ability to modify behavior when situations get worse is compromised in addicted individuals. To better understand the addiction vulnerable phenotype it is critical to understand how individuals differ prior to any exposure to drugs of abuse. Dr. Calu's lab uses animal models to study the brain mechanisms underlying sign-tracking and goal-tracking individual differences in rats. Sign-trackers show heightened motivational drive triggered by food and drug-associated cues, while goal-trackers use cues to guide flexible responding based on the current value of the outcome. Dr. Calu is recording real-time activity of individual amygdala neurons to examine how they fire when sign- and goal-trackers perform tasks that violate their expectations for reward. She is also selectively inhibiting neurons to examine the role of amygdala pathways in driving attention towards cues in the face of negative consequences. Dr. Calu will consider her team's findings as they relate to understanding individual vulnerability to and prevention of addiction.

Fred H. Gage, PhD, Professor, The Salk Institute for Biological Studies, and Matthew Shtrahman, MD, PhD, Assistant Professor, University of California, San Diego

Using Deep In Vivo Two-Photon Ca²⁺ Imaging to Study Temporal Pattern Separation

Drs. Gage and Shtrahman are exploring how the hippocampus distinguishes similar experiences to form discrete memories, a process termed pattern separation. Specifically, they are investigating how the hippocampus processes dynamic sensory information that varies with time during memory formation. They will focus their studies on the dentate gyrus, a region within the hippocampus thought to be critical for pattern separation and one of only two regions within the mammalian brain that generates new neurons throughout life. Gage and Shtrahman will use two-photon calcium imaging to probe the activity of newborn neurons in this deep brain region to better understand this important brain function. Understanding these mechanisms will provide crucial insights into why our ability to learn and remember declines with age and how hippocampal disease leads to significant memory impairment in disorders such as Alzheimer's disease and schizophrenia.

Gabriel Kreiman, PhD, Associate Professor of Ophthalmology and Neurology, Children's Hospital Boston, Harvard Medical School

Behavioral, Physiological and Computational Mechanisms Underlying Episodic Memory Formation in the Human Brain

By showing movie clips to individuals and determining what they are able to remember from the viewing, Dr. Kreiman and his team endeavor to understand how episodic memories are made.

Episodic memories "constitute the essential fabric of our lives," he says, encompassing everything that happens to an individual and ultimately forming the basis of who we are. Since episodic memory formation is too complex to be tracked in real life, Kreiman uses movies as a proxy, since people develop emotional associations with characters as they do in the real world. Kreiman and his team are quantitatively studying the behavioral filtering mechanisms that lead to remembering versus forgetting and building a computational model predicting what movie content will and will not be memorable to subjects. Kreiman is collaborating with Dr. Itzhak Fried at UCLA, whose work with epilepsy patients provides an opportunity to study neuronal spiking activity in the hippocampus during episodic memory formation. Their work is significant given that cognitive disorders affecting memory formation have devastating consequences that to date cannot be treated with drugs, behavioral therapies, or other approaches.

Boris Zemelman, PhD, Assistant Professor of Neuroscience, and Daniel Johnston, PhD, Professor of Neuroscience and Director of the Center for Learning and Memory, University of Texas at Austin

Prefrontal Dysfunction in Fragile X Syndrome

Austin Center for Learning and Memory researchers Daniel Johnston and Boris Zemelman have teamed up to study the role of the prefrontal cortex (PFC) in Fragile X Syndrome (FXS). FXS results from a mutation in a gene called *fmr1* and a loss of a protein called FMRP, disrupting neuronal function. FXS is the most common inherited form of intellectual disability and most common monogenic cause of autism. Using a mouse model in which the *fmr1* gene has been deleted, the Johnston lab has been studying a simple working memory-like behavior called trace eye-blink conditioning, in which pairing a visual cue with a non-contiguous air puff leads to anticipatory eyelid closure. Interestingly, mice lacking the *fmr1* gene and the protein FMRP are unable to learn this task. In this project, the investigators will use viruses designed by Zemelman to remove or replace FMRP in specific neurons of the PFC, and then examine animal behavior, the complement of neuronal proteins and the firing patterns of selected PFC cells. Long-term, their research holds promise for clinical approaches to FXS and autism by determining optimal cell targets for therapeutic interventions.

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