

brain waves

Newsletter of the
Brain Research Foundation
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Brain Research Foundation

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Allen Institute for Brain Science

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Annual Neuroscience Day

Winners of the 10th Annual Neuroscience Day Poster Presentation are:

Graduate Student

Constanza Cortes
The University of Chicago

Bruce Howng
The University of Chicago

Brian Theyel
The University of Chicago

William Zeiger
The University of Chicago

Post Doctoral Fellow

Lisa Jungbauer, Ph.D.
University of Illinois at Chicago

Clinical Research

Alexandrina Gomes
The University of Chicago

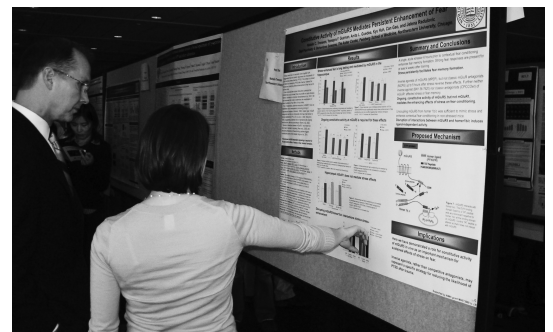
On December 12, 2008, the Brain Research Foundation sponsored its 10th Annual Neuroscience Day. This event is held every year to promote the interaction of neuroscientists and to learn about new, exciting research through poster presentations and lectures. This unique forum is intended to provide all members of the Chicago-land neuroscience community the opportunity to share research interests and to stimulate scientific interactions between laboratories.

The day was a huge success. 74 posters were presented from a variety of areas of study, including Alzheimer's disease, depression, Huntington's disease and schizophrenia. The posters gave a brief summary of recent research that graduate students and postdoctoral fellows were conducting around Chicago. Each participant was on hand to explain their work. Judges from various Chicago institutions graded the posters and the top presenters were awarded \$500 for their outstanding work.

Scientific lectures followed the presentations. Our guest speakers were: D. James Surmeier, Ph.D. from Northwestern University, Scott T. Brady, Ph.D. from the University of Illinois at Chicago, Jeffrey H. Kordower, Ph.D. from Rush University Medical Center, Nicholas G. Hatsopoulos, Ph.D. from the

University of Chicago, and the Keynote speaker was Robert C. Malenka, M.D., Ph.D. from Stanford University School of Medicine. Sangram S. Sisodia, Ph.D., from the University of Chicago, was the moderator for this event. We would like to thank all of them for helping to make this an extremely informative and well received event.

Our 2009 Neuroscience Day will be postponed until 2010 since the Society for Neuroscience will hold its annual meeting in Chicago during that time. The Society is the world's largest organization of researchers dedicated to advancing understanding of the brain. This is the first time Chicago will be hosting this event which is estimated to have 32,000 attendees—all meeting and discussing the latest neuroscience research.



Dr. D. James Surmeier (left) and Dr. Natalie Tronson (right)

dear friends

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In these difficult times, it is crucial for an organization to remain connected to its donors and to stay relevant. The Foundation continues to support groundbreaking research but sometimes that isn't enough. Every few years, we must re-evaluate the Foundation as a whole: our programs, our fundraising, and even our visibility in the community. We must strive to be the best for our donors who believe in what we do.

You will read in this issue about how our Seed Grant Program has expanded to greater Chicago. The Foundation saw a need in the Chicago neuroscience community and was determined to help support worthy projects that have the potential of obtaining funding from the National Institutes of Health or other outside sources. We are pleased to be able to support such talented researchers and only wish that we were capable of funding even more.

This past year, we were presented with an opportunity to partner with a prestigious organization, the Allen Institute for Brain Science, to promote advancements in brain research and to facilitate the discovery of new scientific knowledge. We saw an opportunity for a philanthropic partnership that focused on a one-time, joint fundraising effort in Chicago to raise awareness

and financial support for the complementary work of our two organizations. You can read more about the partnership and the visibility that it provides later in this newsletter.

In order to raise awareness, raise funds and stay relevant, we need to tell our story and be easy to find. Our foundation is dependent on contributions from people who come to know us through our trustees, our friends, our publications and our website. We are extremely pleased that the respected medical and pharmaceutical advertising agency, AbelsonTaylor, has generously donated their services to renew how the Brain Research Foundation is perceived by our donors, scientists and the general public. They will help create new branding that will enhance the look and feel of the Foundation. Specifically, this will result in a newly designed website and a more cohesive feeling to everything we do.

These are exciting times at the Foundation. Every level of support is appreciated. We hope you will continue to think of us in your giving plans.

Sincerely,

Terre A. Sharma, Ph.D.
Executive Director

in the spotlight

Brain Research Foundation Scientific Review Committee

The Brain Research Foundation Scientific Review Committee was established to review our annual seed grant applications. This committee is made up of six researchers from several institutions throughout greater Chicago. Their scientific expertise was invaluable when reviewing the 2009 Brain Research Foundation Seed Grant proposals. Following is a brief description of each reviewer's research interests:

The size and complex shapes of many neurons present unique challenges in delivering essential components to the right places in the right amounts. An efficient set of intracellular transport processes known as axonal transport are required

to generate and maintain the functional architecture of neurons. Recent evidence suggests that many late onset neurodegenerative diseases, including Alzheimer's, Huntington's and Parkinson's disease, as well as ALS, are the result of disruptions in this trafficking of proteins essential for neuronal function. Remarkably, these often involve changes in the regulation of motor proteins and targeting of cargoes carried by axonal transport. Based on these approaches, **Dr. Scott Brady's** lab is identifying novel pathogenic mechanisms and new therapeutic targets by studying these changes in neuronal transport mechanisms.

(continued on page 4)



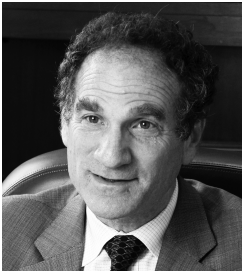
Dr. Scott Brady
University of Illinois
at Chicago

in the spotlight

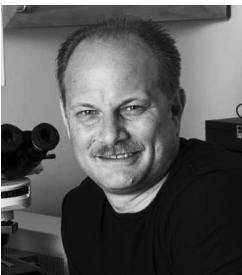
(continued from page 1)



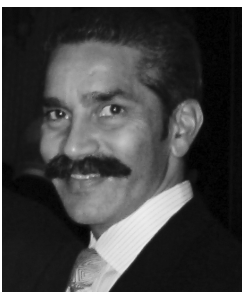
Dr. Nicholas Hatsopoulos
The University of Chicago



Dr. John Kessler
Northwestern University



Dr. Jeffrey Kordower
Rush University Medical Center



Dr. Sangram Sisodia
The University of Chicago



Dr. D. James Surmeier
Northwestern University

Dr. Nicholas Hatsopoulos' research focuses on the neural basis of motor control and learning. He is investigating what features of motor behavior are encoded and how this information is represented in the collective activity of neuronal ensembles in the motor cortex. He is also interested in what way these representations change as motor learning occurs. To answer these questions, the electrical discharge of many motor cortical neurons is simultaneously recorded using multi-electrode arrays and correlated with motor behavior. The encoding properties of individual motor cortical neurons are being studied to determine how these single cell properties relate to higher-order representations involving groups of neurons. The possibility that changes in functional connectivity among neurons may occur during motor learning is also being explored. Finally, various decoding strategies are being developed by which the activities of neural ensembles can be used to predict the behavior of the animal. Ultimately, this research may lead to neural prosthetic technologies that will allow people with spinal injuries or other severe motor disabilities to use brain signals to control either a cursor on a computer screen, a robot device, or even their own arm.

Dr. John Kessler's laboratory focuses on the biology of embryonic stem cells and neural stem cells. He is interested in defining mechanisms regulating neuronal and glial differentiation of stem/progenitor cells, and on understanding how growth factors promote neuronal and glial survival and phenotypic expression. These studies seek to identify the cytokines that regulate stem cell proliferation and differentiation, to define the intracellular signals that transduce their effects, and to understand how the effects of different growth factors are integrated by the progenitor cell. Although the principal focus of these studies is on definition of mechanisms underlying stem cell differentiation, a significant effort is also devoted to applying molecular neurobiology to clinical problems. Specifically they are developing techniques for the treatment of spinal cord injury and stroke.

Dr. Jeffrey Kordower is a leading researcher in the fields of gene therapy, neural transplantation, nonhuman primate models of neurodegenerative disease and experimental therapeutic strategies for Parkinson's and Huntington's disease. In 1995, he made the pioneering demonstration that fetal transplants can survive in patients with Parkinson's disease; a paper that was published in *The New England Journal of Medicine*. In 2000, he published

the lead article in *Science*, demonstrating for the first time that gene delivery of a trophic factor called GDNF can prevent degeneration and restore function in nonhuman primate models of Parkinson's disease. Dr. Kordower is a Scientific Advisory Board (SAB) Member for numerous biotechnology companies and foundations, including a founding member of the SAB for the Michael J. Fox Foundation. Currently his main interests involve gene therapy and cell replacement strategies using stem cells in rodent and nonhuman primate models of Parkinson's and Huntington's disease.

Dr. Sangram Sisodia's laboratory studies the molecular and cellular basis of Alzheimer's disease (AD), the most common cause of senile dementia. AD affects neurons in the neocortex, hippocampus and basal forebrain and affected brain regions contain abundant levels of senile plaques composed of amyloid, derived from amyloid precursor proteins (APP). Early-onset, familial forms of AD (FAD) are caused by inheritance of genes encoding mutant variants of presenilin 1 (PS1), presenilin 2 (PS2), and APP. Research in his laboratory has focused on understanding the normal biology of PS1 and PS2, and the molecular and cellular mechanisms by which mutant PS and APP cause AD. To explore these issues, his laboratory has employed cellular and biochemical approaches, as well as transgenic and gene targeted mouse models. The mouse models have offered important insights into disease pathogenesis and his laboratory has discovered critical genetic and environmental factors that influence these processes.

The research in **Dr. D. James Surmeier's** lab revolves around the question of how neuromodulators shape the excitability of basal ganglia neurons. The basal ganglia is a richly interconnected set of nuclei that regulate motor and cognitive behaviors. Disorders in basal ganglia function underlie a wide variety of psychomotor disorders including Parkinson's disease, dystonia, Huntington's disease, schizophrenia and Tourette's syndrome. In many of these diseases, the principal defect appears to involve an alteration in dopaminergic signaling. For example, the symptoms of Parkinson's disease are a consequence of the death of dopaminergic neurons that innervate one of the basal ganglia nuclei, the striatum. Using a combination of optical, electrophysiological and molecular approaches, Dr. Surmeier has made great strides in understanding the impact of neuromodulators, like dopamine, on basal ganglia function that will hopefully lead to new therapeutic strategies for diseases like Parkinson's disease.

Seed Grants: Growing Discovery

For the past 29 years, the Brain Research Foundation has been supporting neuroscientists through our annual Fay/Frank Seed Grant Program. These grants are one of the most important and productive things the Foundation does to support promising investigative leads. The program provides start-up money to launch an innovative project that will likely become competitive for federal funding.

This year, the Seed Grant Program was expanded to reach more neuroscientists by opening the grants up to all eligible neuroscientists in the greater Chicago area. We envision having even more impact on neuroscience and hope you continue to support this investment in the future. Following are two summaries of the 2009 Seed Grant projects:

Seizure-like Activity Driving the Progression of Alzheimer's Disease



Dr. Dean M. Hartley
Department of Neurological
Sciences,
Rush University Medical Center

Alzheimer's disease (AD) is a progressive brain disorder characterized by the formation of two pathological features, plaques and tangles. Research has shown that these two abnormal pathologies of the brain develops in a very characteristic pattern over time. A key to understanding AD is to understand how this progression occurs. **Dr. Dean M. Hartley's** (Department of Neurological Sciences at Rush University Medical Center) working model is that brain cells become "hyperactive," similar to the activity measured during very mild seizures; this abnormal activity then causes the characteristic AD pathology to develop in this area. Moreover, this hyperactivity travels to other regions by specific connections causing a cascade of hyperexcitability and subsequent AD pathology; this specific hyperactivity drives the progressive pathology in the brain. Studies have reported seizure-like activity in AD patients and animal models of AD; in fact, recent studies in animal models of AD have shown a type of "silent seizure," suggesting there is an undetected hyperactivity in the AD brain. Dr. Hartley will test his hypothesis by placing sensitive monitoring

devices in a mouse model of Alzheimer's and determine if the sequence of the developing pathology is preceded by hyperactivity. To further understand this problem, drugs that block this hyperactivity, including anti-seizure medications, will be administered testing the drug at different time periods. This will help in understanding if hyperactivity is involved, and also if interrupting hyperactivity at specific time may block "downstream" areas from developing AD pathology. A better understanding of this relationship is warranted and may be extremely valuable in identifying mechanisms responsible for this devastating disease. Most importantly, this understanding may suggest that drugs blocking or reducing hyperactivity in the brain may be able to stop the initiation or progression of the disease; currently we are only treating the symptoms. The potential of this research is that antiepileptic drugs, which block neuronal hyperexcitability, may be useful in treating AD. Because these drugs are currently used to treat epilepsy, they could be rapidly transitioned to the treatment of AD.

2009 Seed Grant Recipients

Raj Awatramani, Ph.D.

Department of Neurology,
Northwestern University
The Developmental Basis of
Dopaminergic Neuron Diversity

Thomas C. Bozza, Ph.D.

Department of Neurobiology and
Physiology, Northwestern University
Optogenetic Analysis of Mammalian
Olfactory Circuits

Jianhua Cang, Ph.D.

Department of Neurobiology and
Physiology, Northwestern University
Organization and Development of
Motor Maps in the Mouse Superior
Colliculus

Dane M. Chetkovich, M.D., Ph.D.

(Winner of Margaret Hoover Fay
Epilepsy Seed Grant)
Department of Neurology,
Northwestern University
Gene Therapy for Treatment
of Epilepsy

Anis Contractor, Ph.D.

Department of Physiology,
Northwestern University
In Vivo Analysis of the Role of FMRP
in Dendrite Maturation and Plasticity in
the Somatosensory Cortex

Jaime García-Añoveros, Ph.D.

Department of Anesthesiology,
Northwestern University
Insm1 in Terminal Neurogenic
Proliferation

Christian R. W. Hansel, Ph.D.

Department of Neurobiology,
The University of Chicago
The Role of AMPA Receptor (GluR2)
Trafficking in Cerebellar Plasticity in
Adult Mice: An Imaging Study

Dean M. Hartley, Ph.D.

Department of Neurological Sciences,
Rush University Medical Center
The Role of Seizure-like Activity
Driving the Progression of
Alzheimer's Disease

Benjamin B. Lahey, Ph.D.

Department of Health Studies,
The University of Chicago
Functional Neurobiology of Harsh
Maternal Parenting

Jill A. Morris, Ph.D.

(Winner of Women's Council
Seed Grant)
Department of Pediatrics,
Northwestern University/Children's
Memorial Research Center
Deciphering the Roles of DISC1
Isoforms in Embryonic Brain
Development

Puneet Opal, M.D., Ph.D.

Department of Neurology,
Northwestern University
Epigenetics in Spinocerebellar Ataxia

P. Hande Ozdinler, Ph.D.

Department of Neurology,
Northwestern University
Investigation of Molecular and Genetic
Controls over Cell-Type Specific
Vulnerability of CSMN in ALS

Jeremy Amiel Rosenkranz, Ph.D.

Department of Cellular and Molecular
Pharmacology,
Rosalind Franklin University of
Medicine and Science
Chronic Stress Causes Pathology of
K⁺ Channels in Amygdala Neurons

Marc W. Slutzky, M.D., Ph.D.

Department of Neurology,
Northwestern University
A Brain-Machine Interface Based on
Movement-Related Potentials from
Epidural vs. Subdural Signals

Geoffrey T. Swanson, Ph.D.

Department of Molecular
Pharmacology and Biological
Chemistry,
Northwestern University
The Role of Kainate Receptors in
Oligodendrocyte Toxicity

Understanding the Genetic Basis of Schizophrenia



Dr. Jill A. Morris
Department of Pediatrics,
Northwestern University/
Children's Memorial
Research Center

Schizophrenia is a devastating neurodevelopmental illness, which affects 1% of the population and is associated with high rates of morbidity and mortality. Schizophrenia is characterized by multiple symptoms including hallucinations, delusions and social withdrawal. Although drugs are available to treat some of the symptoms of schizophrenia, the profound side effects make non-compliance a major issue and often result in relapse and hospitalization. Schizophrenia is believed to have a neurodevelopmental origin in that patients demonstrate early cognitive impairments, behavioral dysfunction in childhood and adolescence, abnormalities in central nervous system (CNS) development, and no demonstrative neurodegeneration. One of the contributing factors to abnormal neurodevelopment in schizophrenia is thought to be a genetic insult. Therefore, understanding the genetic and developmental basis of schizophrenia is critical for discovering treatments.

Multiple schizophrenia susceptibility genes have been identified including DISC1 (Disrupted in Schizophrenia 1). DISC1 was initially identified in a large Scottish family with members who suffered from schizophrenia, bipolar disorder and recurrent major depression. DISC1's association with schizophrenia has been confirmed in other population and family studies. Genetic studies

have also indicated a DISC1 association with bipolar affective disorder, autism and Asperger syndrome. There are multiple forms of DISC1 expressed in the developing brain.

Dr. Jill A. Morris, Department of Pediatrics at Northwestern University, plans to examine the function of these multiple DISC1 variants during development. It may be that disrupting the function of a specific DISC1 variant determines if an individual has increased susceptibility to schizophrenia, bipolar affective disorder or autism.

Dr. Morris' lab will determine the developmental defects in the developing mouse brain due to the loss of different Disc1 isoforms. Studies in the developing mouse have demonstrated prominent expression of mouse Disc1 in the hippocampus as well as expression in the developing cerebral cortex, hypothalamus, cerebellum and olfactory bulbs. These are brain regions that have been implicated in schizophrenia pathogenesis. The disruption of different DISC1 isoforms during development may result in varying phenotypes. This very novel research will greatly aid in the understanding of DISC1's role in major psychiatric disorders.

brain matters

Achieving Breakthroughs from Collaboration



(from left) Kathryn Johnson, Bruce Johnson, Nathan Hansen, Dr. Allen Jones

On Thursday, November 13, 2008, Kathryn and Bruce Johnson hosted a stimulating reception about a unique partnership for discovery. To better understand the brain's possibilities, find cures for hundreds of neurological diseases and accelerate new discoveries, the Brain Research Foundation joined forces with the Allen Institute for Brain Science. This partnership combined the entrepreneurial business model of the Allen Institute for Brain Science with the Brain Research Foundation's foresight over fifty years ago to invest in neuroscientists pursuing cutting edge research. The ultimate goal: to facilitate the discovery of new scientific knowledge that will result in improved treatments and cures for diseases such as Alzheimer's, multiple sclerosis, autism, brain tumors and spinal cord injuries.

Representatives from both organizations explained how important brain research is and how each group is filling critical funding gaps not met in the neuroscience community. One important way the Brain Research Foundation delivers this is through

our Seed Grant Program, which provides start-up money for studies that have the potential to develop into comprehensive research projects suitable for larger grant proposals. The Allen Institute for Brain Science tackles leading-edge projects, such as the Allen Mouse Brain Atlas and their latest project the Allen Human Brain Atlas, that fuel innovation and discovery for countless pioneering scientists.

It is imperative that brain research receives the funding that it needs to hasten the search for cures. Through support of its donors, the partnership of these two visionary organizations will lead to advances in understanding of brain function and treatment of brain-related disorder. Together we can make a difference; together we can translate science into action.

If you would like to support this partnership please call 312.759.5150.

If you would like more information, please visit www.alleninstitute.org and www.brain-map.org.

For more information on the Brain Research Foundation, please call 312.759.5150 or visit our website at www.theBRF.org

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