# Our unique approach covers all brain disorders.

**Brain Research Foundation** 2010-2011 Annual Report

Our quest to understand how the brain works is leading to answers that advance our knowledge about all neurological disorders.


rophic lateral sclerosis (ALS)
Alzheimer's diseas
Down syndro
coma
Huntington's disease
autism
brain tumor
Rett syndrome
stroke
cquired brain injurie
aphasia
arcolepsy
epilepsy
erebral palsy
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dyslexia
aneurysm
Parkinson's disease
on deficit hyperactivity disorder
Cruetzfeldt-Jakob disease
leep disorder
dementia
concussion

When Dr. Frederic Gibbs co-founded the Brain Research Foundation in 1953, he was investigating the treatment of epilepsy. But instead of establishing a foundation focused solely on epilepsy, he recognized that discoveries about how the brain and nervous system function would eventually lead to understanding the many diseases that result when they are compromised.

He was a visionary then and the BRF continues to support his vision today. By focusing on research and education that are disease-neutral, we move science closer to answers that will one day lead to prevention and cures.

## To Our Brain Research Foundation Friends

Our 2010-2011 Annual Report focuses on the extraordinary scientific research and educational programs we have supported. Unlike other research foundations, we promote exploration and education that are disease-neutral. The work the Foundation does advances our understanding of brain function and all neurological disorders. From Alzheimer's disease to autism, the spectrum of research is both wide and exciting.

In this economic environment it is even more crucial that we continue our mandate to fund research at increasing levels. Innovative researchers are finding few, if any, resources to support the important work they're doing. By providing consistent funding and support to these scientists, the Foundation has been able to play an integral role in helping advance cutting-edge science and technologies. Our goal is to enable research to evolve from discovery, to application, to testing, and finally, to treatment of patients.

We take calculated risks. Our contributions to scientists through our successful Seed Grant Program provide funding for new directions in research. In the past two years, the Brain Research Foundation has awarded nearly $1.3 million in seed grants to 32 doctors and scientists dedicated to understanding the brain. Our funding of innovative ideas is truly yielding novel results.

As we celebrate the 30th anniversary of our Seed Grant Program, we take stock of the program's accomplishments. Our seed grants have enabled researchers to answer many questions about the brain and how it works. In many instances these results allow the investigators to obtain additional funding that permits them to continue to expand their research and validate their hypotheses. Our seed grant recipients, and researchers throughout the world, will build on the knowledge gained through BRF seed grant funding; our comprehension of the brain and neurological disorders will grow exponentially.

In addition to our annual Seed Grant Program, we have broadened our funding scope by awarding larger grants to distinguished investigators. Through our support of work conducted by highly experienced and productive scientists, the BRF makes possible extremely innovative research that promises to lead to significant findings. The Foundation awarded Drs. Xavier Castellanos and Paul Greengard $150,000 each. Dr. Castellanos' work at New York University is focused on understanding ADHD. Dr. Greengard of Rockefeller University is developing technology that will lead to better understanding of the molecular mechanisms behind Parkinson's disease. The outcomes of these projects will have a major impact on the understanding of ADHD, Parkinson's disease and other related neurological disorders.

In addition to funding research, the BRF mission is to further educate researchers and the general public about scientific progress and brain-related issues. In December of 2010, we hosted our 11th Neuroscience Day—an annual event through which neuroscientists and graduate students learn about exciting new research. The Foundation also began an educational program focused on concussive injuries in children

and adolescents in sports. We will continue to build awareness, support and understanding around these important topics.

Our mission to advance the understanding of brain function and treatment of brain-related disorders guides each mile of our journey as a foundation. With your support, we look forward to continuing our important work in the years to come. Every dollar invested by our donors is used to move us closer to treatments and eventual cures.

Sincerely,

Terre A. Constantine, Ph.D.
Executive Director

Nathan Hansen
President

# Innovative ideas

For 30 years, the Brain Research Foundation has awarded annual grants through our Fay/Frank Seed Grant Program. This program invests in worthy, innovative neuroscience research, funding promising investigations that drive advances in our knowledge of how the brain functions. Seed grants, which are $40,000 one-year awards, provide support for novel scientific hypotheses that may not be funded by other sources. It is our seed grant funding which allows the researchers to gather the much-needed preliminary data that will enable them to obtain additional outside grants to continue their work.

The success of this program varies from year to year but there are always successes. Each year seed grant recipients publish in scientific journals. Each year seed grant recipients obtain additional outside funding. Each year the seed grant projects answer questions about the brain, even if the results are sometimes unexpected.

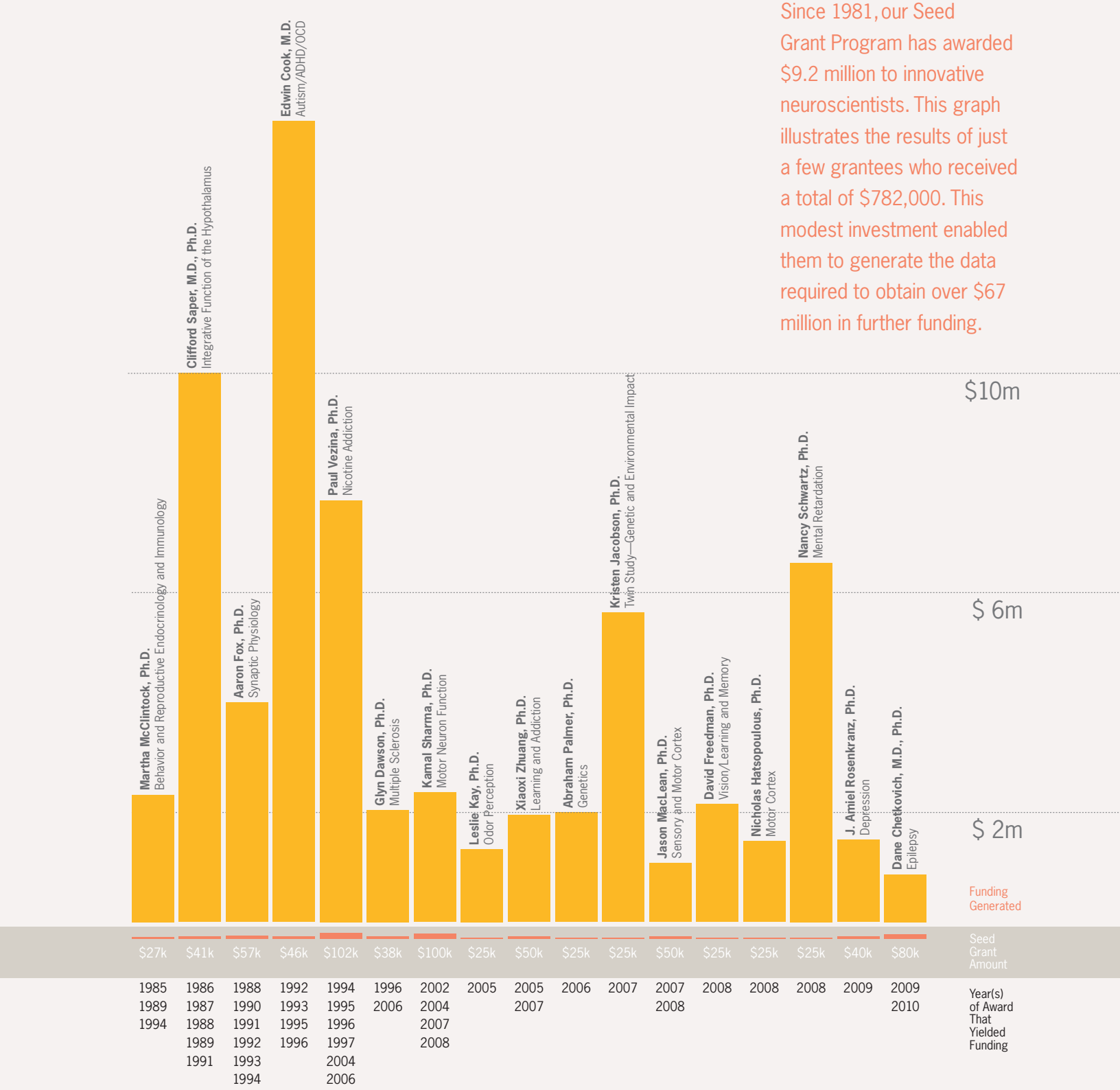
The Foundation is taking a calculated risk, supporting a project in its early stages, with the understanding that some outcomes may be ground-breaking and others may not–but all results generate findings that help advance the understanding of the brain.

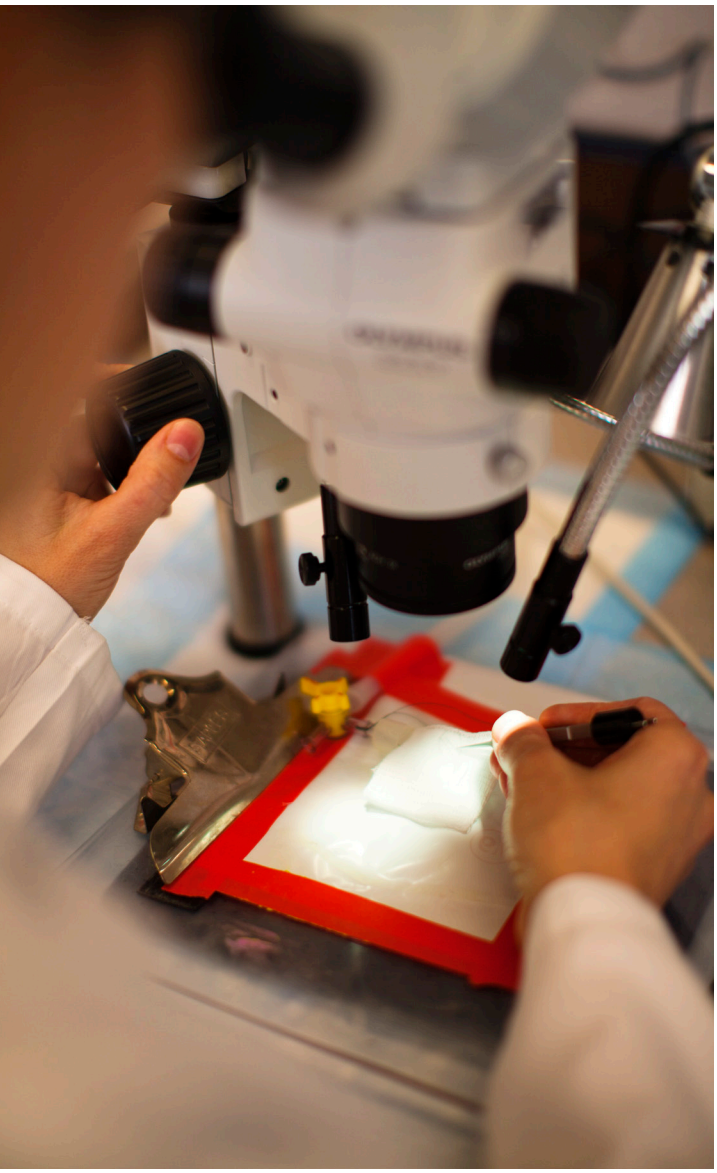
This is a risk the Foundation is willing to take and has been taking since 1981. Since its inception, the Seed Grant Program has distributed $9.2 million to neuroscientists. This support and commitment is critical to the scientific community and to those suffering from neurological disorders. The Brain Research Foundation is extremely proud that it plays a key role in supporting the research that will have a profound influence on the quality of human life.

The four seed grant recipients we have highlighted in this report illustrate the breadth of science we will be advancing as well as the successes that have already been achieved or are on the horizon.

# Limitless possibilities

Since 1981, our Seed Grant Program has awarded $9.2 million to innovative neuroscientists. This graph illustrates the results of just a few grantees who received a total of $782,000. This modest investment enabled them to generate the data required to obtain over $67 million in further funding.






A Ardelt, MD, PhD
Neurointensive Care

## Agnieszka A. Ardelt, M.D., Ph.D.

Assistant Professor, Department of Neurology, The University of Chicago

**Her investigations into neurorepair will support Dr. Ardelt's clinical work with stroke patients and also have the potential to advance the treatment of other brain disorders.**

Suffering a stroke leaves most people with few options other than to cope with the effects of irreversible brain damage. Physical rehabilitation is the only alternative after failure of preventative efforts such as diet and exercise, drug therapy or stent surgery to clear a blockage. In addition to preventing strokes, stents can treat them. However, the window of time for stent therapy to effectively reverse a stroke is so small that most patients survive a stroke with varying degrees of disability.

But what if there were a way for the brain to repair itself in the aftermath of a stroke and return to its former capacity? Dr. Agnieszka A. Ardelt, assistant professor of neurology at the University of Chicago, will explore that possibility with her Brain Research Foundation Seed Grant. She has designed a study that will determine whether introducing into brain cells the protein Hu antigen R (HuR), which stabilizes messenger RNA and thereby regulates gene expression, will improve function—days, weeks or months after a stroke occurs.

Dr. Ardelt will use the middle cerebral artery occlusion model for studying ischemic stroke in mice. She will investigate recovery at early (24 and 72 hours) and late (30 days) time points, comparing the genetically manipulated animals that express HuR to wild type or normal mice. Dr. Ardelt expects to see smaller lesions in the genetically manipulated mice, illustrating augmentation of cerebral neuroprotection and neurorepair. This repair should improve long-term functional outcome.

Dr. Ardelt will then try to identify more specific clues to how the stroke-damaged brain might repair itself. She will test various molecules that are relevant to neurorepair to determine if they change from having a beneficial role to a detrimental one during a stroke. The study will identify the tipping point at which positive new cell regeneration could morph into negative effects such as seizures and tumors.

Dr. Ardelt's hope is that her work will not only help patients recover from strokes more readily but that it will help individuals with other brain disorders like multiple sclerosis.

Looking at how a damaged brain repairs itself holds great promise for understanding brain disorders that are the result of sudden injury. Insight could lead to long-lasting solutions that will help patients suffering from a stroke or traumatic brain injury as a result of a serious accident or military injury. Dr. Ardelt's hope is that her work will not only help patients recover from strokes more readily but that it will help individuals with other brain disorders like multiple sclerosis, where HuR may regulate the expression of beneficial genes.

# 30 years of progress

"If we want neuroscience research to progress—if we want new findings in epilepsy or Alzheimer's disease, stroke, multiple sclerosis—then it requires an investment. The BRF's investment is small. But I've been able to turn that small investment into a ten-fold increase in amount of money that's available to do our research. When we're successful in translating this into further funding and expanding our investigation, it's really a ten-to-one matching system for us."

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

Associate Professor of Neurology,
Northwestern University
2009, 2010 Seed Grant Recipient

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

Associate Professor, Department of Neurology, Northwestern University

**BRF-funded seed grant research leads Dr. Chetkovich to exponential advancements not just in his study of epilepsy but other researchers' understanding of both epilepsy and mood disorders as well.**

Details surrounding a pair of Brain Research Foundation grants awarded in 2009 and 2010 to Dr. Dane Chetkovich for his epilepsy studies tell a compelling story about how our seed grant money yields valuable and far-reaching results.

Dr. Chetkovich has parlayed both of his grant studies into substantial additional funding. And through collaboration and sharing of technology, his work has led to improved understanding of how abnormal brain function leads to epilepsy.

Epilepsy is characterized by recurrent seizures that occur spontaneously. At its worst, epilepsy leads to disability, reduced quality of life and increased risk of sudden death. While therapeutic drugs and even surgery have improved the lives of many patients with epilepsy, such treatments often come at a cost. There are others who are resistant to these therapies and are still searching for relief.

Dr. Chetkovich used his 2009 and 2010 BRF seed grant money to approach this disease from two different perspectives.

In his 2009 seed grant study, Dr. Chetkovich tested his hypothesis that the presence of a specific protein in the brain might stop epilepsy. His lab engineered a virus to deliver the gene of that protein into the brain cells of epileptic mice. The experiments progressed quickly and demonstrated that viral gene therapy was indeed a viable approach to stopping epilepsy in mice.

Dr. Chetkovich used the data he generated from this $40,000 BRF seed grant to obtain a National Institutes of Health (NIH) award in the amount of $450,000. He then took the next step in the funding process by applying for a second, larger NIH grant. If his proposal is successful, he could receive an additional $1.2 million for a project that BRF funded when it was just an innovative idea. The Foundation's $40,000 investment has the potential to generate 40 times more in additional funding. This additional funding allows Dr. Chetkovich to continue to advance his study of epilepsy at an even more rapid pace.

Dr. Chetkovich's 2010 seed grant project created a novel mouse model of epilepsy. Based on his previous results, Dr. Chetkovich hypothesized that if his lab disrupted a regulatory protein in the brain, it would cause seizures. Deleting that protein from a strain of mice proved his hypothesis correct—the genetically altered mice displayed seizures.

With this new data, he obtained another early stage NIH grant for $420,000.

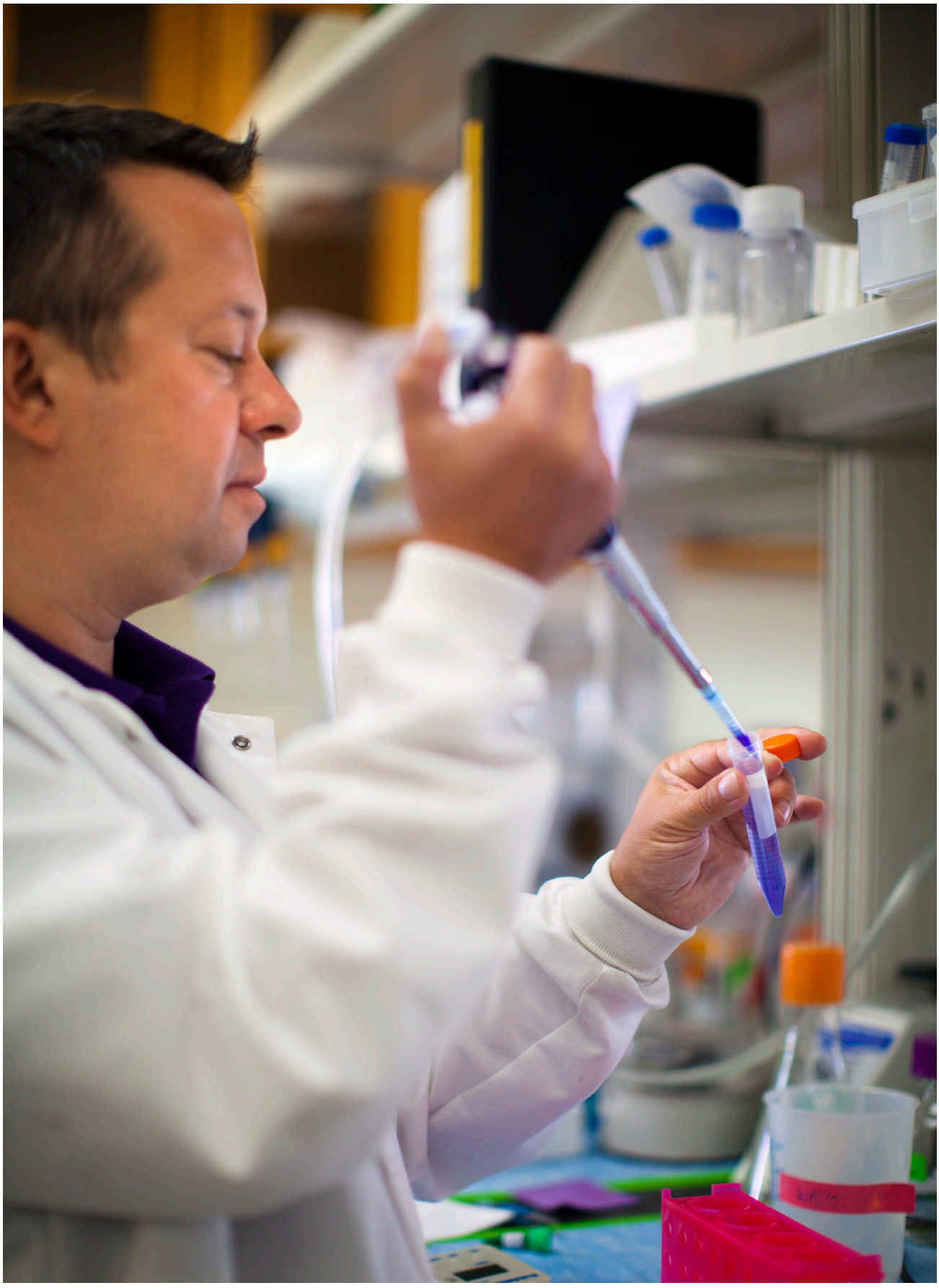
This novel mouse model has been an invaluable tool for researchers studying epilepsy. Dr. Chetkovich has shared his model with other scientists in Chicago, Texas, Germany, Switzerland and London. The BRF seed grant has not only advanced Dr. Chetkovich's research in epilepsy but also the research of national and international neuroscientists.

The Foundation's initial $40,000 investment into epilepsy research has the potential to generate over 40 times more in additional funding.

In addition to generously giving his mouse model to others working in the field of epilepsy, Dr. Chetkovich is sharing it with scientists working on depression. It is now thought that the regulatory protein associated with epilepsy is also involved in mood regulation.

The innovative progress of Dr. Chetkovich's work illustrates the key role the Brain Research Foundation plays in promoting better understanding of the brain through grants that help advance science exponentially—providing knowledge and discovery that impact a wide range of neuroscience research.

BRF seed grants have far-reaching implications. In the case of Dr. Chetkovich, results he generated through his 2009 and 2010 seed grants enabled him to get additional funding from the NIH. This, in turn, has accelerated the pace of his research, bringing him closer to a new treatment for epilepsy and affording him the opportunity to share his methodology internationally with scientists exploring both epilepsy and depression.



## Peter Penzes, Ph.D.

Associate Professor, Department of Physiology, Northwestern University

**Insight from Dr. Penzes' research will help scientists understand how connections in brain cells are disrupted in autism, and may uncover a viable therapeutic target that has real potential as an orally administered drug.**

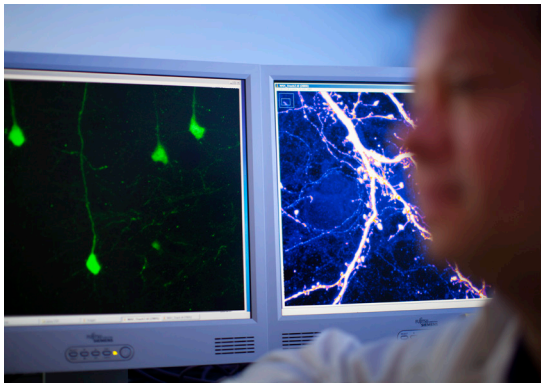
Autism spectrum disorder (ASD) is a physical condition that affects children at an alarmingly high rate. One in 110 children will be diagnosed with autism. Abnormal social interaction, language difficulties and repetitive actions are all characteristics of autistic behavior. Autism also impairs a child's ability to learn.

Exactly why autism occurs in one child and not another is unknown to scientists, although a combination of genetics and environment may play a role. Scientific evidence suggests that autism is caused by a malfunction of the connections, or synapses, between brain cells.

Recently, Peter Penzes, Ph.D., an associate professor of physiology at Northwestern University determined that a molecule, mutations in which have been genetically associated with autism, is involved in synapse development and remodeling in nerve cells.

Dr. Penzes will use his $40,000 BRF seed grant to further characterize the role of this molecule in mice. A strain of mice genetically engineered to be deficient in this molecule will be used to determine how such a shortage affects behavior, as well as brain physiology. Experiments will show how the molecule signals and regulates synapse development and behavior in a functioning organism. The research will also test predictions for how this molecule is associated with ASD. His research will focus on the frontal cortex, an area of the brain typically associated with psychiatric disorders, including ASD.

To study synapse development, Dr. Penzes will use fluorescent microscopy to observe and measure nerve cells in mouse brain slices. These cells will express a yellow fluorescent protein that will allow for the visualization of the connections between nerve cells.



*In his study of synapse development, Dr. Penzes is using fluorescent microscopy to observe and measure nerve cells. Pictured here are cells that express a fluorescent protein, enabling him to observe the connections between nerve cells.*

The behavioral portion of the study will involve observing genetically altered mice that exhibit many of the social characteristics of autism without any unusual physical manifestations. Mice will be tested for how they exhibit core behaviors such as social interaction, nesting and juvenile play, as well as how they communicate. A variety of maze tests will assess learning capacity and response to change.

Insights from Dr. Penzes' research will help scientists understand the electrical connections in brain cells that may be disrupted in autism cases. Understanding biological mechanisms that trigger autism can lead to the identification of potential targets for therapy. Targeting this molecule may be fruitful because it has a high likelihood of oral bioavailability and low toxicity in humans.

The knowledge realized through Dr. Penzes' research may lead to better understanding of other neurodevelopmental disorders. Defects similar to the alterations in synapses prevalent in autism are also present in mental retardation, fragile-X syndrome and Down syndrome.

## Orly Lazarov, Ph.D.

Associate Professor, Department of Anatomy and Cell Biology, The University of Illinois at Chicago

**Dr. Lazarov's investigation of neurogenesis in adult stem cells will lead to greater understanding of Alzheimer's disease.**

When Dr. Orly Lazarov sought to understand certain cellular processes associated with the aging brain, she entered uncharted territory. With only a few milestones to guide her, Dr. Lazarov has navigated a new path of understanding about how a deficiency in a protein indicates a lack of new cellular growth and how this may play a role in Alzheimer's disease.

Through a 2010 Brain Research Foundation seed grant, the BRF took a calculated risk that allowed Dr. Lazarov to explore a theory previously supported only through observation. The resulting scientific study confirmed her hypothesis that this protein is somehow related to age-related cognitive impairments. A second BRF seed grant in 2011 allows Dr. Lazarov to build on her initial research.

In her first seed grant study, Dr. Lazarov identified the need to understand a metabolic process involving a protein that appeared to play a role in regeneration of brain cells. Very little was known about how this protein functions, as well as how an associated metabolic process regulates the ongoing regeneration of brain stem cells that is crucial for healthy and vibrant brain activity.

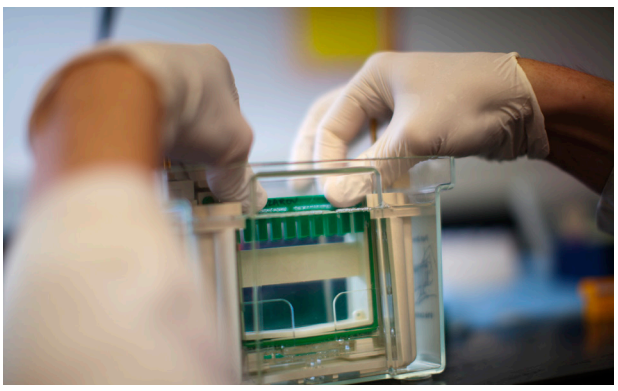
Dr. Lazarov tested her initial theory in two ways. First she analyzed whether the metabolized study protein affects maintenance, self-renewal and proliferation of brain stem cells. Follow-up experiments confirmed untested observations that the protein as it metabolized leads to regeneration of a specific type of stem cell. This cell type is located deep in an area of the brain that nurtures new cell birth. Prior related experiments have indicated that this type of protein is reduced in Alzheimer's patients.

In her initial experiments, Dr. Lazarov shed light on new information about how cells develop in the adult brain. She found that additional amounts of a little-studied protein bolster new cell development under certain conditions. What remains unknown is how this protein interacts in the wider environment.

Identifying impediments to new brain cell growth may help scientists understand other types of degenerative brain diseases, particularly those that emerge in otherwise healthy adults, such as Parkinson's disease, epilepsy and amyotrophic lateral sclerosis (ALS).

Her second round of experiments will measure protein levels as they decline in the aging brain, evaluate the reasons behind this decline and assess whether reduced levels of this protein are a factor in diminished new cell development. Experiments will also attempt to identify the specific molecules that interact with this protein as they metabolize into new cells.

Mice with metabolic deficiencies associated with the study protein have exhibited multiple brain defects. This indicates that Dr. Lazarov's studies have the potential to provide useful information for other neuroscience research. Identifying impediments to new brain cell growth may help scientists understand learning and memory and other types of degenerative brain diseases, such as Parkinson's disease and amyotrophic lateral sclerosis (ALS).



## 2010 Seed Grant Recipients

**Rajeshwar B. Awatramani, Ph.D.**
*Department of Neurology, Northwestern University*
The developmental basis of dopaminergic neuron diversity

**Dane M. Chetkovich, M.D., Ph.D.**
*Department of Neurology, Northwestern University*
Role of TRIP8b in epilepsy
*Margaret Hoover Fay Epilepsy Seed Grant Awardee*

**Anis Contractor, Ph.D.**
*Department of Physiology, Northwestern University*
The role of beta2* nicotinic receptors in natural reward mechanisms

**David J. Freedman, Ph.D.**
*Department of Neurobiology, The University of Chicago*
Neuronal circuit mechanisms of visual feature integration

**Jaime García-Añoveros, Ph.D.**
*Department of Anesthesiology, Northwestern University*
CRZF1 in Te migration and differentiation of Cajal-Retzius cells

**Liang-Wei Gong, Ph.D.**
*Department of Biological Sciences, University of Illinois at Chicago*
The regulation of dynamin and actin polymerization in endocytic vesicle biogenesis

**Jay A. Gottfried, M.D., Ph.D.**
*Department of Neurology, Northwestern University*
Perceptual coding of natural odors in the human brain

**Elizabeth A. Grove, Ph.D.**
*Department of Neurobiology, The University of Chicago*
Novel approach to gene manipulation in a cerebral cortical signaling center
*Women's Council Seed Grant Awardee*

**Jaime Grutzendler, M.D.**
*Department of Neurology, Northwestern University*
Embolus extravasation: a link between vascular and Alzheimer's pathology

**Orly Lazarov, Ph.D.**
*Department of Anatomy and Cell Biology, University of Illinois at Chicago*
Regulation of neural stem cells by amyloid precursor protein metabolites in the adult brain

**Puneet Opal, M.D., Ph.D.**
*Department of Neurology, Northwestern University*
Role of VEGF in spinocerebellar ataxia type 1

**Lei Wang, Ph.D.**
*Department of Psychiatry and Behavioral Sciences, Northwestern University*
Development of a calcium-sensitive MRI probe for neural activity

**Jack Waters, Ph.D.**
*Department of Physiology, Northwestern University*
Pre-and postsynaptic effects of muscarinic acetylcholine receptors in somatosensory neocortex

**Anthony R. West, Ph.D.**
*Department of Neuroscience, Rosalind Franklin University*
Phosphodiesterase 10A as a novel therapeutic target in the treatment of levodopa-induced dyskinesias

## 2011 Seed Grant Recipients

**Ravi Allada, M.D.**
*Department of Neurobiology and Physiology, Northwestern University*
Circadian clocks and neurodegeneration

**Agnieszka A. Ardelt, M.D., Ph.D.**
*Department of Neurology, The University of Chicago*
Could HuR, a regulator of growth factor mRNAs, improve outcome after ischemic stroke?
*Women's Council Seed Grant Awardee*

**Thomas Bozza, Ph.D.**
*Department of Neurobiology and Physiology, Northwestern University*
Analysis of trace amine-associated receptor cluster deletion mice

**Anjen Chenn, M.D., Ph.D.**
*Department of Pathology, Northwestern University*
N-cadherin regulation of the adult neural stem cell niche

**Yuanyi Feng, M.D., Ph.D.**
*Department of Neurology, Northwestern University*
Molecular genetic analysis of filamin functions in cerebral cortical development

**Jay A. Gottfried, M.D., Ph.D.**
*Department of Neurology, Northwestern University*
Perceptual coding of natural odors in the human brain

**Christian Hansel, Ph.D.**
*Department of Neurobiology, The University of Chicago*
Is there a cerebellar component of autism? A study using the 'chromosome 7 duplicated' (Dup) mouse model

**Orly Lazarov, Ph.D.**
*Department of Anatomy and Cell Biology, University of Illinois at Chicago*
Regulation of neural stem cells by amyloid precursor protein metabolites in the adult brain

**Gianmaria Maccaferri, M.D., Ph.D.** *Department of Physiology, Northwestern University*
Cell type-specific alterations in a genetic animal model of Rett syndrome

**Michela Marinelli, Ph.D.**
*Department of Cellular and Molecular Pharmacology, Rosalind Franklin University*
Habenular modulation of dopamine neurons and its relevance for cocaine addiction

**James A. Mastrianni, M.D., Ph.D.**
*Department of Neurology, The University of Chicago*
Treatment of genetic prion disease by mutation-selective RNAi

**Gerardo A. Morfini, Ph.D.**
*Department of Anatomy and Cell Biology, University of Illinois at Chicago*
Effects of mutant huntingtin on cytoplasmic dynein phosphorylation and function

**Peter Penzes, Ph.D.**
*Department of Physiology, Northwestern University*
Validation of synaptic targets in autism spectrum disorders

**Indira M. Raman, Ph.D.**
*Department of Neurobiology and Physiology, Northwestern University*
Sensorimotor processing in the zebrafish cerebellum

**Jamie D. Roitman, Ph.D.**
*Department of Psychology, University of Illinois at Chicago*
Effect of adolescent alcohol consumption on risk-preference and neural encoding of risky rewards

**Gordon M. G. Shepherd, M.D., Ph.D.**
*Department of Physiology, Northwestern University*
Cortical mechanisms in a mouse model of amyotrophic lateral sclerosis

**Geoffrey T. Swanson, Ph.D.**
*Department of Molecular Pharmacology and Biological Chemistry, Northwestern University*
Galectin modulation of excitatory transmission

**Jack Waters, Ph.D.**
*Department of Physiology, Northwestern University*
Nicotinic modulation of the excitability of neocortical pyramidal neurons

# 30 years of innovation

"I am glad to hear that the BRF is still giving its seed grants. When I was at the University of Chicago, during the early days of this program this was a very important means of funding new research initiatives, especially by young faculty who were just starting up, or by senior faculty who wanted to get into a new field. In fact, I have emulated the program on a smaller scale at Harvard, where we give similar seed grants to our faculty each year."

Clifford Saper, M.D., Ph.D.

James Jackson Putnam Professor of Neurology and Neuroscience, Harvard Medical School
1986, 1987, 1988, 1989, 1991 Seed Grant Recipient

# Expanded funding

In 2011, the Brain Research Foundation expanded its funding to support even more ground-breaking research. In addition to our annual Seed Grant Program, the Foundation awarded two larger grants to distinguished investigators. By selecting projects from highly experienced and productive scientists, the BRF hopes to provide the start-up funding for novel approaches to understanding the brain that will lead to significant findings. Drs. Xavier Castellanos and Paul Greengard were chosen to receive $150,000 each to pursue exciting research in attention deficit hyperactivity disorder (ADHD) and Parkinson's disease, respectively.

Long-time friends of the Brain Research Foundation who wanted a way to broaden their family's contribution to advance neuroscience made these inaugural grants possible. This generosity acted as a catalyst to establish the BRF Scientific Innovations Award that was officially created in fiscal year 2012.

The intent of this new awards program is to support research ideas or strategies that are so cutting edge that they may not yet be considered for other sources of funding. The Foundation expects these grant will yield exciting results that will form the basis of submissions for major grants funding and lead to significant publications in high impact journals. The Scientific Innovations Award will fund any area of the full spectrum of brain function and disease, including ADHD, autism spectrum disorder, Parkinson's disease, Alzheimer's disease, epilepsy, schizophrenia, mood disorders, ALS, and many others.

## Paul Greengard, Ph.D.

Vincent Astor Professor, Laboratory of Molecular and Cellular Neuroscience of the Comparative Bioscience Center, Rockefeller University

**A 2000 Nobel Prize winner, Dr. Greengard is developing innovative technology that will lead to better understanding of the molecular mechanisms behind Parkinson's disease.**

Paul Greengard, Ph.D., professor of molecular and cellular neuroscience at Rockefeller University, designed a study to help scientists understand how Parkinson's disease destroys brain cells. Results from this work should pave the way for research to identify better treatments for the disease.

Parkinson's disease (PD) inhibits movement, causes tremors, and may lead to early death. Parkinson's disease is incurable and worsens over time. The medications that are prescribed for PD attempt to control the symptoms of the disease. No drugs yet exist to slow or stop the inevitable deterioration of brain cells that control body movement. Existing PD drugs have limited results and become less effective over time. Currently prescribed drugs for PD carry frequent and often intolerable adverse effects, exhibited by abnormal involuntary movement.

The exact cause of PD is unknown but several factors appear to play a role, including genetics and environment. Scientists know that PD strikes by killing dopamine-producing cells in a specific region located in the middle of the brain, an area called the substantia nigra pars compacta. Dopamine is a signaling molecule that regulates normal movement of the human body. What puzzles scientists is why PD does not attack dopamine-producing cells that exist in an adjacent, but separate, brain region called the ventral tegmental area.

Technical limitations have prevented researchers from solving the mystery of why dopamine-producing cells in one brain region are susceptible to PD, while cells in a nearby region are resistant. The two brain regions are so closely intermingled that efforts to isolate them with scalpels and lasers,

even under powerful microscopes, traumatize brain tissue. Studies involving compromised tissue samples have led to inconclusive results.

A strain of genetically modified mice will eliminate the need to use cutting tools to isolate the different brain regions. Mice in this study will be bred to carry a green fluorescent protein that will exist in the dopamine-producing cells in two specific areas of the brain. One set of mice will have the green florescent protein in the region where PD attacks dopamine-producing cells. Another group of mice will have the identifying protein in the region with PD-resistant cells.

Dr. Greengard is using his 2011 BRF $150,000 grant to compare the properties of these two cell groups. This comparison study will help scientists unravel the key molecular steps responsible for the selective death of dopamine-producing cells and gain clues about the key proteins responsible.

Samples will undergo microarray analysis in which thousands of molecules in a biological sample will be analyzed at the same time. That will allow a large amount of data to be assembled into two lists: one showing molecules that are specific to the dopamine-producing cells that are attacked in PD and the other showing molecules that are specific to the dopamine-producing cells that are PD-resistant.

Dr. Greengard expects to identify specific receptor proteins and enzymes that are a factor in Parkinson's disease and also identify areas that would be most receptive to new drug treatments and other innovative therapies.

Dr. Greengard expects to identify specific receptor proteins and enzymes that are a factor in PD. This knowledge would elucidate areas that would be most receptive to new drug treatments and other innovative therapies for PD.

This innovative technology could not only be used to better understand the molecular mechanisms behind PD, it could be used to uncover mechanisms in other neurological disorders like Alzheimer's disease, schizophrenia and depression.

## F. Xavier Castellanos, M.D.

Neidich Professor of Child and Adolescent Psychiatry at NYU Langone Medical Center and Nathan Kline Institute

**Dr. Castellanos is elucidating the neuroscience of ADHD and its relationship to substance abuse through genetic studies and sophisticated brain imaging.**

Attention-deficit/hyperactivity disorder (ADHD) is a psychiatric condition that, until recently, has defied scientific understanding. Scientific research of a disease aims to identify causes or connect symptoms to underlying physiology. Such methods are traditionally less effective for understanding a syndrome, such as ADHD, which is characterized by multiple symptoms that frequently occur together.

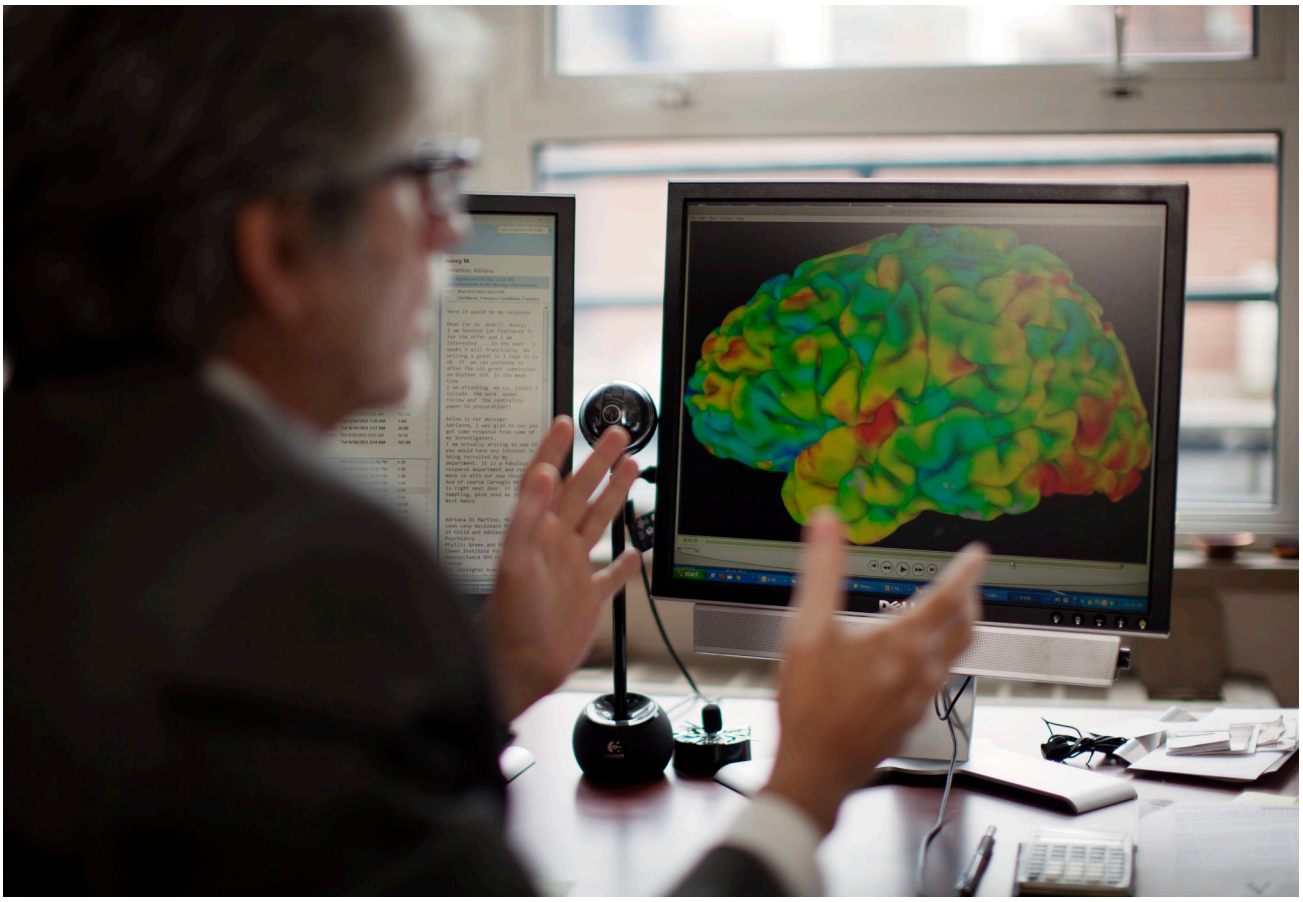
Recent progress in the fields of neuroimaging and genetics make it possible for scientists to answer fundamental questions that will lead to better diagnosis, treatment and prevention of ADHD. After a dozen years and an international effort, researchers have identified a gene, Latrophilin-3 (LPHN3), related to the tendency to manifest ADHD. LPHN3 is thought to be linked to a particular type of ADHD that is associated with a high likelihood of developing conduct disorder, nicotine addiction, and substance abuse disorders (SUD) including alcoholism.

Dr. Castellanos has designed a project using MRI to study people who carry the risk gene for ADHD.

The Brain Research Foundation awarded F. Xavier Castellanos a $150,000 grant to launch a project that that will lay the foundation for long-term research into ADHD. Dr. Castellanos, a physician and researcher with New York University and the Nathan Kline Institute for Psychiatric Research, has designed a research project using functional magnetic resonance imaging (fMRI) to study people who carry the risk gene for ADHD and are also prone to substance abuse. The study will involve only individuals who carry informative variations of the risk gene for ADHD and who have been diagnosed with ADHD. It will compare fMRI scans of substance abusers and non substance abusers. Analyses of brain imaging data will focus on areas of the brain implicated in ADHD and in which the risk gene for ADHD is strongly expressed.

Since the grant was awarded, scientists have learned more about this specific gene and its relationship with ADHD. Specifically, they have identified variations in the gene that appear to predict even more strongly which people diagnosed with ADHD will also have substance abuse. Dr. Castellanos and his colleagues will genetically characterize participants into four relevant subgroups. One group will include substance abusers with a high-risk type of ADHD gene; substance abusers with a low-risk type; and two separate groups of non substance abusers, one high-risk and one low-risk. These individuals will undergo fMRI to yield data that will identify commonalities, as well as differences, among the subgroups.

Identification of a gene is only an initial step. Identifying which specific variations in a gene are responsible for differences in biological function can be like finding a needle in a haystack. But learning how this gene functions and malfunctions in some types of ADHD will likely reveal much about the disorder overall.



# Advocate for knowledge

In addition to providing research funding, the Brain Research Foundation supports educational programs for researchers, families struggling with debilitating brain disorders and the general public.

Each year, the Foundation hosts Neuroscience Day 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 members of the neuroscience community the opportunity to share research interests and to stimulate scientific interactions between laboratories.

In 2010, the BRF launched an educational program on sports-related brain injuries in youth. The Foundation began networking with local schools and leaders in the youth sports field to help educate school and community sports administrators, coaches, and parents of young athletes about concussions.

As with all the work we do, the Foundation's educational programming focuses on the critical importance of understanding the way the brain and nervous system work and builds awareness of the brain-related issues that impact all our lives.

## Protecting student athletes

Brain injuries related to youth sports activities are of increasing concern in communities across the country. The Brain Research Foundation identified a need for more education and research on the topic of sports-related concussions. A better understanding among coaches, medical professionals, parents and students will ultimately lead to safer experiences for young athletes.

A concussion is a type of brain injury, or TBI, caused by a bump, blow, or jolt to the head that can change the way your brain normally works. Concussions can occur from a fall or a blow to the body that causes the head and brain to move quickly back and forth. Any person suspected of suffering a concussion needs to be seen by a health care professional, as immediate care may speed recovery. While concussions are often described as mild brain injuries, repeated injuries or a severe concussion may lead to long-lasting problems with movement, learning and speaking.

According to the Centers for Disease Control and Prevention (CDC), children and teens are more likely to get a concussion and take longer to recover than adults. In addition, athletes who have ever had a concussion are at increased risk for another. A study by the Brain Injury Association of America and the CDC reported that 40.5% of athletes who suffer concussions return to play before it is safe to do so.

To launch the BRF's initiative, a panel discussion was held at the Foundation's Discovery Dinner in November 2010. Chicago Alderman Ed Burke was in attendance and learned of the national movement to adopt new laws related to the care of young athletes with head injuries. He and his aldermanic colleague Latasha Thomas made a motion that the City of Chicago adopt an ordinance requiring any Chicago student-athlete who exhibits signs, symptoms, or behaviors associated with a concussion be removed from a game or practice and barred from returning without written medical clearance. Schools not enforcing the ordinance would risk losing their water and sewage exemption. The ordinance was passed by the City Council in January of 2011.

Simultaneously, a movement was underway in Springfield to put into law similar protection for students across the state. In late July of 2011, BRF Executive Director Dr. Terre Constantine attended Governor Pat Quinn's signing of the Protecting Our Student-Athletes Act.

The Brain Research Foundation worked with the Chicago Public Schools to help educate its administrators and coaches on how to identify head injuries in young athletes and what steps they should take if they suspect a student has a concussion.

Dr. Carrie Jaworski, (left) head team physician with Northwestern University, made presentations on behalf of the BRF at two meetings of administrators and coaches in April of 2011 and subsequently had her presentation taped so that all involved in the sports program of CPS could participate. The BRF also provided clipboards with CDC concussion information and CDC posters on the topic to all Chicago Public Schools.

## Letter from the Treasurer

The Brain Research Foundation is a strong, viable organization with a concrete mission. Due to an increase in financial contributions and wise investment strategies, we increased our funding of research by more than $500,000. This was due in part to a generous anonymous contribution of $300,000 and the increase in net revenue from our Discovery Dinner.

In fiscal year 2011, the Brain Research Foundation expanded its Fay/Frank Seed Grant Program to the full State of Illinois. This important program provides start-up funds to researchers for innovative investigations that have the potential to lead to new understanding and treatments of neurological disorders. We were pleased to be able to increase the total program funding by $120,000 to a total of $720,000, enabling us to better help researchers initiate new projects. We also began funding larger grants of $150,000 to further the work of more experienced researchers in neuroscience. Two of these grants were awarded in fiscal year 2011.

The following is a summary of our income and major expenses for fiscal years 2010 and 2011. In addition, we have provided a condensed balance sheet for those fiscal years. In the two years since our last report we added over $3 million in assets to the Foundation. In 2011, we improved our donor base and had an increase in donor contributions of $2.1 million. This increase came from enhanced investment performance and charitable supporters of the Foundation, including a generous contribution of $1.8 million from the Pioneer Fund in Denver. Our total assets at the end of fiscal year 2011 were in excess of $14 million. We encourage you to review our audited financial statements on our website or contact the Brain Research Foundation office.

With the support of the Board of Trustees, staff and donors, the Brain Research Foundation continues to be a financially strong organization that provides critical funding for exciting new research projects and valuable educational programs.  We will work hard to sustain your support and fulfill our mission.

Sincerely,

David H. Fishburn
Treasurer

# 57 years of support

"There are very few sources of funding for people doing depression research. Most private foundations that fund research into brain disorders tend to have a very specific focus—for instance, the Parkinson's or Alzheimer's foundations. So having access to a foundation that's able to decide exactly what type of work it wants to fund, and supports an incredibly broad spectrum of research, has been tremendously important to me and my colleagues."

J. Amiel Rosenkranz, Ph.D.

Assistant Professor of Cellular and Molecular Pharmacology, Rosalind Franklin University
2009 Seed Grant Recipient

## Financial Statements

**Highlights of Income Statement**
Years Ended June 30, 2010 and June 30, 2011

| | 2010 | 2011 |
|---|---|---|
| Beginning net assets | $ 8,391,988 | $ 11,033,268 |
| Return of grant funds/reversal of liability | 1,984,917 | - |
| Interest on returned grant funds | 200,353 | - |
| Contributions | 466,429 | 2,597,249 |
| Interest and dividends | 321,230 | 401,437 |
| Net realized gain (loss) on investments | (72,935) | 177,176 |
| Change in net unrealized gain on investments | 962,020 | 1,687,936 |
| **Total** | **$ 12,254,002** | **$ 15,897,066** |
| | | |
| Expenses | | |
| Program services | $ 763,703 | $ 1,259,518 |
| Supporting services | 457,031 | 472,822 |
| Total | $ 1,220,734 | $ 1,732,340 |
| | | |
| **Total net assets** | **$ 11,033,268** | **$ 14,164,726** |

## Financial Statements (continued)

**Statement of Financial Position**
As of June 30, 2010 and 2011

| Assets | 2010 | 2011 |
|---|---|---|
| Cash | $ 6,578 | $ 46,095 |
| Current prepaid expenses and deposits | 22,720 | 25,026 |
| Investments | 11,000,863 | 14,080,462 |
| Contributions receivable | 53,525 | 50,000 |
| Property and equipment | 16,518 | 28,184 |
| Other assets | 55,651 | 5,651 |
| **Total** | **$ 11,155,855** | **$ 14,235,418** |

| Liabilities and Net Assets | 2010 | 2011 |
|---|---|---|
| Liabilities | | |
| Accounts Payable and Accrued Expenses | $ 122,587 | $ 70,692 |
| Total liabilities | $ 122,587 | $ 70,692 |
| | | |
| Net Assets | | |
| Unrestricted | $ 7,979,783 | $ 8,972,647 |
| Unrestricted-Board-designated | 2,702,715 | 3,149,106 |
| Temporarily restricted | 350,770 | 542,973 |
| Permanently restricted | - | 1,500,000 |
| Total net assets | $ 11,033,268 | $ 14,164,726 |
| | | |
| **Total** | **$ 11,155,855** | **$ 14,235,418** |

# Our heartfelt thanks

Support from our Board of Trustees, corporations, foundations, longtime friends, and new donors enables us to fulfill our important mission of understanding brain function in children and adults.

Those included on the following pages gave financial contributions from July 1, 2009, through June 30, 2011. With their help, we continue to fund research and educational programs that lead to new treatments, prevention and eventual cures for neurological disorders.

Thank you.

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