

# Klerman and Freedman Prizes



2011 Klerman Prize  
Prizewinner  
Chadi Calarge, M.D.



Brian D'Onofrio, Ph.D.  
Honorable Mention



Jennifer S. Silk, Ph.D.  
Honorable Mention



2011 Freedman Prize  
Prizewinner  
Alexandre Bonnin, Ph.D.



Alberto Bacci, Ph.D.  
Honorable Mention



Andrew Pieper, M.D., Ph.D.  
Honorable Mention

*A reception and dinner  
to present the*

*17th Annual  
Klerman Prize*

*14th Annual  
Freedman Prize*

*and the*

*2nd Annual  
Visionary Philanthropist  
Award*

**July 29, 2011**

**Le Parker Meridien Hotel**  
119 West 56th Street  
New York, N.Y.

# Welcome

Welcome to the 2011 Klerman and Freedman Prize presentation ceremony. This annual event recognizes outstanding early achievements by young scientists conducting basic and clinical neurobiological research with the support of NARSAD Young Investigator Grants awarded by the Brain & Behavior Research Foundation.

This evening's honorees have shown exceptional promise in their pursuit of deeper understanding of the human brain to ultimately conquer mental illness.

Toward that goal, NARSAD Grants provide initial funding for able researchers at different stages of their careers to try new ideas and forge new pathways in pilot projects deemed premature or too 'out of the box' by other funders. Each of the six recipients of the 2011 Klerman and Freedman Prizes has gone on to obtain significant additional support from other funding agencies.

The seeking out and selecting of recipients of grants and awards bestowed by the Brain & Behavior Research Foundation is the responsibility of its Scientific Council. This volunteer group of scientific leaders has guided the work of the Foundation since its inception as the National Alliance for Research on Schizophrenia and Depression, or NARSAD. The change of name to the Brain & Behavior Research Foundation was made to better reflect the broad scope of its support for research across all mental illness.

Visit [www.bbrfoundation.org](http://www.bbrfoundation.org) or call 516-829-0091 to learn more.

## Our mission:

The Brain & Behavior Research Foundation is committed to alleviating the suffering of mental illness by awarding grants that will lead to advances and breakthroughs in scientific research.

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# The Prizes

The Klerman and Freedman Prizes pay tribute to Drs. Gerald L. Klerman and Daniel X. Freedman, whose legacies as researchers, teachers, physicians and administrators indelibly influenced neuropsychiatry. Their outstanding contributions continue to inspire scientists who knew them as well as those just entering the field.

Below and in the following pages, read more about the lives and work of Drs. Klerman and Freedman, and about the achievements of the Young Investigators we honor today.

## The Klerman Prize

The Klerman Prize, which honors exceptional clinical research by a Young Investigator, was established in 1994 by Myrna Weissman, Ph.D., in memory of her late husband, Gerald L. Klerman, M.D.

A distinguished psychiatric researcher and mentor at the National Institute of Mental Health (NIMH) and a member of the faculties of Yale, Harvard and Cornell Universities, Dr. Klerman served from 1977 to 1980 as chief administrator at the Alcohol, Drug Abuse and Mental Health Administration.

Dr. Klerman joined NIMH in 1959, in the early days of psychopharmacology. He was a central figure in the psychopharmacology service center's collaborative study of phenothiazine as a treatment for acute schizophrenia and in the program on the psychobiology of depression. Dr. Klerman led in planning multisite studies defining affective and anxiety disorders, and developing and evaluating treatments. While pioneering in studies of psychotropic medications, he also developed and tested interpersonal psychotherapy, a treatment now used throughout the world.

Dr. Weissman is herself an eminent depression researcher at Columbia University and the New York State Psychiatric Institute. She received NARSAD Distinguished Investigator Grants in 1991, 2000 and 2005 and the Selo Prize for Outstanding Achievement in Affective Disorders Research in 1994.

A committee of the Brain & Behavior Research Foundation Scientific Council selects the prizewinner(s). The Klerman Prize Committee is chaired by Robert M.A. Hirschfeld, M.D., of the University of Texas Medical Branch at Galveston. Other committee members include: Martin B. Keller, M.D., Brown University; Rachel G. Klein, Ph.D., New York University; Nina R. Schooler, Ph.D., State University of New York, Downstate; and Karen Dineen Wagner, M.D., Ph.D., University of Texas Medical Branch at Galveston.



## 2011 Klerman Prizewinner

Chadi Calarge, M.D.  
University of Iowa

### 2007 NARSAD Young Investigator Grant

Metabolic and Hormonal  
Abnormalities in Children  
Treated with Risperidone:  
A Two-Year Follow-Up Study

Chadi Calarge, an associate professor in the department of psychiatry at the University of Iowa, pursues research aimed at better understanding the effects of psychotropic drugs used in the treatment of children and adolescents, and how these drugs can be made safer and more effective. This is an area of considerable concern as the number of children being prescribed these drugs increases.

Dr. Calarge received his premedical and medical training at the Lebanese University, which awarded him the M.D. degree in 1998. He completed residencies in general psychiatry and child and adolescent psychiatry at the University of Iowa, and joined the University's faculty in 2005. His time in residency coincided with a period of expanded use with young people of psychotropic drugs such as antipsychotics and antidepressants, with attendant concerns regarding possible long-term deleterious effects on their health and development.

Among the adverse effects Dr. Calarge is examining and hoping to find interventions for are the weight increases and other metabolic changes induced by antipsychotic medications that are linked to cardiovascular disease. He is working to chart the scope of such effects during long-term treatment and to identify demographic, clinical and genetic factors that may make some individuals more susceptible to adverse effects.

## Dedicated Researcher Tracks Youths to Determine Long-Term Impact of Psychotropic Medication

Dr. Calarge has received two NARSAD Young Investigator Grants from the Brain & Behavior Research Foundation. The first, awarded in 2005, funded a cross-sectional study to evaluate the long-term skeletal effects of risperidone, the antipsychotic most commonly prescribed for children and adolescents. The 2007 grant supported a follow-up assessment of the participants in the original research sample.

Like most antipsychotics, risperidone elevates a hormone called prolactin that when produced in excess is associated with low bone mass. Almost all bone-mass accrual occurs by the time of young adulthood and determines one's lifelong risk for osteoporosis. Dr. Calarge's research, which he believes to be the first to explore skeletal effects of psychotropic drugs in youths, used state-of-the-art imaging to investigate the impact of risperidone-induced hyperprolactinemia on bone mass.

These studies have led to the development of an extensive dataset that includes a comprehensive review of the participants' developmental and treatment history. This information now opens the way for Dr. Calarge and his colleagues to explore questions related to the safety of psychotropics, and to look for safety-enhancing interventions. Currently, the researchers are examining the efficacy of supplementation with calcium and vitamin D to optimize bone mass in youths who are receiving risperidone.

Based on the preliminary data acquired through this research, Dr. Calarge's group has recently launched a large study, one of several in his lab now being funded by the National Institute of Health, exploring whether selective serotonin reuptake inhibitors (or SSRIs), a group of commonly used antidepressants, also interfere with skeletal development.

*“The contribution of the Brain & Behavior Research Foundation funding support to my career and research cannot be overstated. The work has resulted in more than two dozen presentations, posters and publications with several additional ones in preparation. The findings generated four grants from the National Institute of Health with a value of approximately \$3.5 million in direct costs with an additional \$1.5 million in indirect costs. Thank you to the Brain & Behavior Research Foundation.”*

*– Chadi Calarge, M.D.*



## 2011 Klerman Prize Honorable Mention

Brian D'Onofrio, Ph.D.  
Indiana University-Bloomington

Brian D'Onofrio, an associate professor of clinical psychology in the department of psychological and brain sciences at Indiana University-Bloomington, explores the mechanisms through which environmental risk factors influence child, adolescent and adult psychiatric problems such as major depressive disorder, conduct disorder, substance abuse and schizophrenia.

Dr. D'Onofrio received his undergraduate degree in psychology at the University of Virginia in 1997. He studied psychiatric and behavior genetics at Virginia Commonwealth University before returning to the University of Virginia, where he was awarded a Ph.D. in clinical psychology in 2005. As part of his doctoral training, he completed a clinical internship at Harvard Medical School/Children's Hospital Boston. He joined the Indiana University faculty in 2005.

Using a variety of experimental approaches, Dr. D'Onofrio and his colleagues study the processes that underlie the associations between environmental risk factors and psychiatric problems. They use genetically informed designs to detail how genetics and environment act and interact; longitudinal (long-term) analyses to examine the development of children's adjustment over time; and intervention studies to observe how different conditions influence family dynamics. Currently, the lab is investigating the consequences for severe psychiatric problems of such early risk factors as maternal smoking and stress during pregnancy, the causes and consequences of early pubertal development, risky sexual behavior and teenage childbearing.

**2007 NARSAD  
Young Investigator  
Grant**  
Quasi-Experimental Studies  
of the Intergenerational  
Transmission of Major  
Depression

## Identifying the Genetic and Environmental Factors That Can Make Depression ‘Hereditary’

Dr. D’Onofrio’s NARSAD Young Investigator Grant funded a project aimed at helping to identify environmental and genetic mechanisms underlying the transmission of major depressive disorder from parents to their offspring. To do so, he conducted secondary data analyses (analysis of research by others) of two studies, one done in Australia and one in Sweden. The Children of Twins design was used to explore genetic factors, environmental risks that increase the likelihood of depression in both parents and offspring, and environmental factors specifically related to offspring exposure to parental depression. The research compared the offspring of identical and fraternal twins in which one member of the twin pair had a history of depression and the other twin did not, and also close relatives of the twins differentially exposed to parental depression, to help specify processes that explain the inter-generational transmission of depression.

The first study, recently published in *Psychological Medicine*, suggests that the mechanisms through which parental depression influences offspring depends on the behavioral/emotional construct being explored, and the association between parental depression and offspring depression was independent of confounding genetic and environmental factors. By contrast, the results suggest that genetic factors passed from parents to offspring accounted for the correlation between parental depression and offspring conduct problems. A second study suggests that the mechanisms through which parental depression influences offspring social competence, a risk factor for subsequent depression, depends on whether it was the mother or the father who was depressed.

*“The NARSAD Young Investigator Grant given by the Brain & Behavior Research Foundation was instrumental in helping me build strong collaborations with international researchers. From these collaborations I have been able to assist in the creation of a large, population-based study in Sweden. These efforts helped to secure additional funding from the National Institute of Child Health and Human Development, the National Institute on Drug Abuse, the National Institute of Mental Health and the Swedish Council (Medicine). The NARSAD Grant also enabled me to focus on the policy implications of my research by working as a member of the British Academy Policy Centre’s Social Science and Family Policies working group.”*

*– Brian D’Onofrio, Ph.D.*



## 2011 Klerman Prize Honorable Mention

Jennifer S. Silk, Ph.D.  
University of Pittsburgh

Jennifer Silk is an associate professor in the department of psychiatry at the Western Psychiatric Institute and Clinic of the University of Pittsburgh School of Medicine. She also directs the University of Pittsburgh's Developmental Affective Science Collective, an initiative that fosters research and training related to affective development and affective disorders.

A 1997 graduate of the University of Virginia, Dr. Silk earned a Ph.D. in clinical psychology in 2002 from Temple University, where she received the Georgoudi Award for Outstanding Doctoral Dissertation. She completed a pre-doctoral clinical psychology fellowship and a postdoctoral fellowship, both at the Western Psychiatric Institute and Clinic, and joined the University of Pittsburgh faculty in 2005. She was awarded a National Institute of Mental Health–mentored Research Scientist Development Award to investigate social and neurobiological risk factors for the intergenerational transmission of depression.

Nearly half of children with a depressed parent will experience an episode of major depression by late adolescence, with the percentage rising as high as 60 percent by the age of 25. In her research, Dr. Silk is examining the ways in which young people with anxiety or depression, or at risk for developing these disorders, process social emotional information, such as peer rejection or parental criticism, and how social processes may exacerbate or compensate for neurobiological risk for affective disorders. And she is eager to investigate how information stemming from such research can be applied to help improve treatments for these disorders.

## 2007 NARSAD Young Investigator Grant

Neural and Social  
Mechanisms of Altered  
Emotion Regulation Among  
Adolescents at High Risk  
for Depression

## Young Scientist Pioneers Study With Adolescents to Discover Triggers for Affective Disorders

For her 2007 NARSAD Young Investigator Grant project, Dr. Silk identified a pattern of decreasing pupil size in the eyes of young people with major depressive disorder, or those who are at risk for it, when they viewed emotionally charged information. Those whose pupil size decreased the most had marked difficulty in managing their negative emotions during interactions with their parents and when assessed on aspects of their daily life. This finding was published in 2007 in the *American Journal of Psychiatry*.

To investigate the neural underpinnings of her discovery, which may indicate a biomarker for depression, Dr. Silk combined two methodologies: pupillometry, which measures changes in pupil diameter, together with functional brain neuroimaging. Applying these techniques with depressed or at-risk young subjects, she observed that decreased pupillary response coincided with decreased activity

in the rostral anterior cingulate cortex, a brain area involved in the management of emotions, suggesting a lessened ability among these youths to engage regulatory brain regions in the processing of emotional information. She is interested in determining whether this deficit could be addressed with behavioral and/or psychopharmacological interventions.

Dr. Silk is currently directing a project funded by the National Institute on Drug Abuse to develop interdisciplinary methods for measuring emotion regulation in adolescence. She recently received an NIMH grant to investigate why so many anxious youths develop depression during adolescence. She also leads an NIMH-funded project looking into how an understanding of emotion regulation processes can be used to improve cognitive behavioral therapy for childhood anxiety disorders.

*“The NARSAD Grant from the Brain & Behavior Research Foundation allowed me to collect data on a potential biomarker for depression risk that could have implications for depression screening or therapeutic interventions. The support was instrumental in helping me learn to conduct a functional neuroimaging study and to compete successfully for NIH funding in this area. Also, by making it possible for me to collect preliminary data on responses to parental criticism and praise, the NARSAD Grant helped me to obtain another NIH grant focused on this topic.”*

*– Jennifer S. Silk, Ph.D.*

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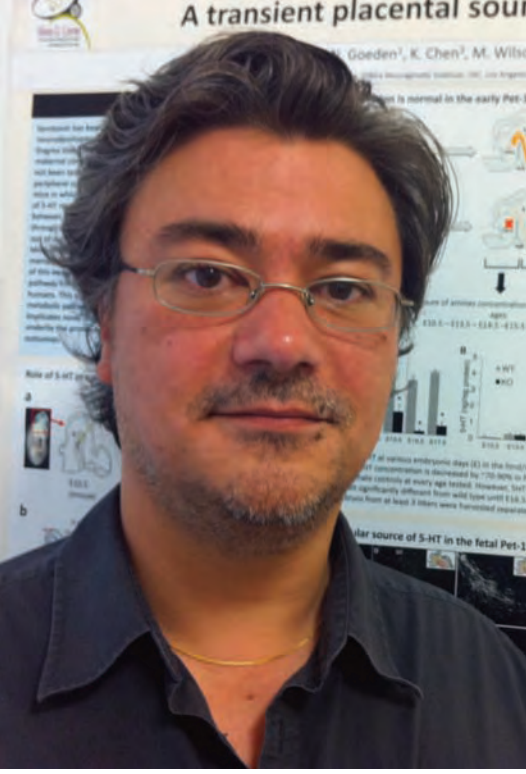
## The Freedman Prize

The Freedman Prize honors the late Daniel X. Freedman, M.D., a pioneer in biological psychiatry and psychopharmacology and a founding member of the Brain & Behavior Research Foundation Scientific Council. It is presented to a Young Investigator for outstanding basic studies.

Dr. Freedman's work at Yale University and at the National Institute of Mental Health in the 1950s led to a novel view of the reactions of brain systems to both internal and external signals that could be aided by drugs. He discovered the first link of hallucinogens to brain neurotransmitters — serotonin. He served on the University of Chicago faculty for 18 years and subsequently at UCLA as the Judson Braun Professor of Psychiatry and Pharmacology.

Scientific Council Member Jack D. Barchas, M.D., Barklie McKee Henry Professor and chair of the department of psychiatry at Weill Medical College of Cornell University and psychiatrist-in-chief of the New York Weill Cornell Medical Center of New York-Presbyterian Hospital, was a colleague of Dr. Freedman at Yale. He remembers that among Dr. Freedman's early interests was the mechanism of action of hallucinogens. "Freedman provided the first evidence that brain serotonin was changed by LSD," Dr. Barchas said. "It was important and pioneering research that has had an enormous impact both in terms of the direct finding and the ideas that grew out of it."

A committee made up of the Brain & Behavior Research Foundation Scientific Council members is responsible for selecting the awardee(s). The Freedman Prize Committee is chaired by Ariel Y. Deutch, Ph.D., of Vanderbilt University. Other committee members include: Joseph T. Coyle, M.D., Harvard University; Ronald S. Duman, Ph.D., Yale University; Fritz A. Henn, M.D., Ph.D., Brookhaven National Laboratory; Peter W. Kalivas, Ph.D., Medical University of South Carolina; Husseini K. Manji, M.D., Johnson & Johnson PRD; Eric J. Nestler, M.D., Ph.D., Mount Sinai School of Medicine; and Bryan L. Roth, M.D., Ph.D., University of North Carolina at Chapel Hill.



## 2011 Freedman Prize

Alexandre Bonnin, Ph.D.  
University of Southern California

Alexandre Bonnin is an assistant professor of research at the University of Southern California. His research is aimed at understanding the ways in which interactions between mother and fetus affect fetal brain development and the risk of developing mental illness in the postnatal period and in adult life.

The recipient of a Ph.D. in neuroscience in 1999 from the University of Paris and the Pasteur Institute in France, Dr. Bonnin completed postdoctoral fellowships in neurobiology at the University of California-Irvine and Vanderbilt University before joining the University of Southern California in 2009.

Using mice as their experimental model, Dr. Bonnin and colleagues are focusing on the role of abnormal serotonin neurotransmission in the programming of neurodevelopmental disorders. Nerve cells, or neurons, communicate in the brain via chemical neurotransmitters that travel down axons, which are wire-like projections on a signaling neuron from which the cell's message is dispatched to a receiving neuron. The multiple actions of serotonin in the fetal brain suggested to Dr. Bonnin that the neurotransmitter plays an important role in the development of brain and behavior disorders.

This idea is supported by the lab's recent genetic studies showing that disruption of serotonin signaling during a restricted period of fetal development results in long-term behavioral dysfunction lasting into adulthood.

**2007 NARSAD  
Young Investigator  
Grant**  
Serotonin Modulates Axon  
Guidance Mechanisms  
During Brain Development  
supported by Research Partner,  
The Essel Foundation

## Breakthrough Discoveries of In Utero Brain Development and Its Links to Mental Illness

Dr. Bonnin is the recipient of two NARSAD Young Investigator Grants awarded by the Brain & Behavior Research Foundation. His initial efforts uncovered a new role for the neurotransmitter serotonin in the fetal brain. This in turn led to a surprising discovery that for the first time establishes a direct link between the maternal-fetal interface and fetal brain development.

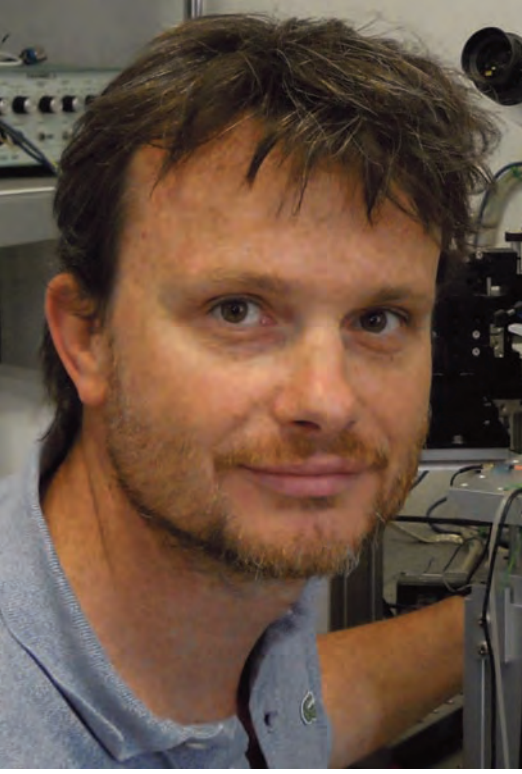
Dr. Bonnin and his team have demonstrated that serotonergic signaling in utero is important for the precise topographic arrangement of axons on neurons involved in communication between the thalamus and the cortex. The thalamus conveys a range of sensory information, including motor signals to the cortex, which is the center of higher thinking processes in the brain. This finding points to serotonergic modulation of axon guidance mechanisms as important in the fine-tuning of fetal brain wiring. This function of serotonin signaling was demonstrated by manipulating the expression of serotonin receptors in fetal mice brains.

The investigation of the source of serotonin in fetal brains led to the discovery of an early placental source of the neurotransmitter and indications that genetic or environmental factors that alter placental serotonin synthesis and delivery to the fetus could affect fetal brain wiring.

In current research, supported by his 2010 NARSAD Young Investigator Grant, Dr. Bonnin has been expanding his studies of how maternal- and placental-derived neurotransmitters and other molecules impact the development of serotonin-relevant and other circuits implicated in brain and behavior disorders. He is also working toward a better understanding and reduction of the adverse effects on fetal brain development of therapeutic drugs taken by pregnant women, in particular the most commonly prescribed antidepressants, the selective serotonin reuptake inhibitors, or SSRIs. In utero exposure to SSRIs induces disturbances to offspring ranging from neonatal irritability to poor psychomotor development during childhood.

*“Thanks to the data generated using my 2007 NARSAD Young Investigator Grant given by the Brain & Behavior Research Foundation, I recently obtained a grant from the National Institute of Child Health and Human Development. This enabled me to develop an ex vivo placental perfusion system and discover the placental source of serotonin in utero. These results were recently published in the journal Nature.”*

*– Alexandre Bonnin, Ph.D.*



## 2011 Freedman Prize Honorable Mention

Alberto Bacci, Ph.D.

Brain and Spine Institute (ICM), Paris

Alberto Bacci, a senior group leader at the Brain and Spine Institute (ICM) in Paris, France, studies the cellular physiology of microcircuits within the cortex of the brain: how they connect and contribute to brain network activities. Within the cerebral cortex, the constant computation of incoming sensory information is integrated to provide a coherent representation of the world – to generate all cortical-related activities, ranging from the simplest behavior to the most sophisticated cognitive function.

Dr. Bacci earned a master's degree in biological sciences and a Ph.D. in pharmacology and experimental therapeutics, awarded in 2000, from the University of Milan, Italy. After completing postdoctoral training in neurophysiology at Stanford University in 2005, he joined the European Brain Research Institute in Rome as Group Leader. He was recently appointed to his current post at ICM.

The research Dr. Bacci directs is focused on an extremely heterogeneous population of nerve cells, called GABAergic neurons, or interneurons, which secrete the neurotransmitter GABA (gamma-aminobutyric-acid). Neurotransmitters are the chemical messengers dispatched from one neuron to another to activate or inhibit activity in the receiving cell. GABA is the brain's primary inhibitory neurotransmitter. GABAergic neurotransmission is fundamental for integrating and filtering incoming information and providing a code used by neurons to perform sophisticated computational operations.

## 2007 NARSAD Young Investigator Grant

Parvalbumin Modulation  
of Inhibitory Synaptic  
Transmission and Network  
Oscillations in the Neocortex

supported by Research Partner,  
The Test Endowment

## Understanding the Brain's Circuitry and What Might Cause Symptoms of Schizophrenia

In schizophrenia, GABAergic interneurons called parvalbumin (PV)-positive are disrupted. This cell class is critical for the generation of a wide range of rhythmic activities believed instrumental in synchronizing neuronal assemblies during perception, attention and sensory representation. It is likely that in schizophrenia the specific ability of PV+ interneurons to control and synchronize disparate cortical circuits is affected, possibly underlying many symptoms of the disorder.

In his NARSAD project, Dr. Bacci and his group provided evidence of novel modes of PV+ interneuron neurotransmission. They found that asynchronous release of the neurotransmitter altered the capability of target neurons to integrate specific inputs into a reliable and faithful output. These results suggest that specific activities of PV+ interneurons might change the network coding strategy to propagate information with potentially important consequences for information processing in the cerebral cortex.

Another aspect of this research also provided insights into a persistent form of self-inhibition induced by repeated firing activity in single neurons. This phenomenon is caused by synthesis and release of endogenous cannabinoids by and onto the same neuron; that is, the cell puts itself to sleep for several minutes. The Bacci team found that a similar endocannabinoid-mediated self inhibition was present in around 30 percent of particular neurons in the cortical area called the neocortex. In addition to self-modulation, single neuron activation induced long-term depression of inhibitory inputs. Such effects could play important roles in the modulation of neocortical networks. Cannabis (marijuana) abuse is a risk factor for schizophrenia in predisposed individuals, and the endogenous cannabinoid system is altered in people with schizophrenia. The results were published in *PLoS Biology*, *The Journal of Neuroscience* and *Nature Neuroscience*.

*“The NARSAD Young Investigator Grant given by the Brain & Behavior Research Foundation contributed essential resources when I moved from Stanford University to the European Brain Research Institute, helping me to set up my laboratory and start my independent career as a principal investigator. Scientifically, the award expanded my scope and allowed me to start new research lines that are now funded by the European Research Council. The NARSAD Grant was essential for securing my tenure at the European Brain Research Institute, and I am sure played a major role when I successfully competed for a senior group leader position at the Brain and Spine Institute.”*

*– Alberto Bacci, Ph.D.*



## 2011 Freedman Prize Honorable Mention

Andrew A. Pieper, M.D., Ph.D.  
University of Texas Southwestern  
Medical Center at Dallas

Andrew Pieper is an assistant professor of psychiatry and biochemistry at the University of Texas Southwestern Medical Center at Dallas, where he pursues research aimed at elucidating molecular mechanisms of neuropsychiatric disease. His focus is on the role of neuronal PAS domain protein 3, or NPAS3, a molecule in the brain that has been implicated in a number of brain and behavior disorders, including schizophrenia.

A 1992 graduate in biology and chemistry from Earlham College, Dr. Pieper earned his M.D. degree and a Ph.D. in neuroscience from Johns Hopkins University School of Medicine in 2001. Following internship in internal medicine and two years of residency training in psychiatry at Hopkins, he completed his residency at the University of Texas Southwestern Medical Center at Dallas, where he became a research fellow in 2005 and assistant professor in 2006.

NPAS3 is a transcription factor: it participates in transcribing the instructions in a gene from DNA to RNA for activation in a cell. Dr. Pieper's impetus for studying NPAS3 stemmed from findings that the gene for NPAS3 was disrupted in some people with schizophrenia and bipolar disorder. During his postdoctoral fellowship, he and his mentor, Dr. Steven McKnight, discovered that NPAS3 controls critical aspects of normal adult hippocampal neurogenesis, the process through which new neurons arise in the hippocampus, a brain region critical to memory. NPAS3 controls the survival of newborn hippocampal neurons in the adult brain; in NPAS3-deficient mice, adult hippocampal neurogenesis is virtually eliminated.

### NARSAD 2007 Young Investigator Grant

Investigation of the Role of  
the Brain-Specific Transcription  
Factor Neuronal PAS Domain  
Protein 3 (NPAS3) in  
Hippocampal Neurogenesis

## Discovering – and Understanding – the Process of Hippocampal Neurogenesis Points Toward Novel Treatments

In research supported by a NARSAD Grant in 2007 from the Brain & Behavior Research Foundation, Dr. Pieper determined that in NPAS3-deficient mice the almost complete lack of functional hippocampal neurogenesis is associated with a substantially smaller than normal dentate gyrus, a key sub-region of the hippocampus. He learned that the deficit in hippocampal neurogenesis in NPAS3-deficient mice is actually due to elevated levels of apoptosis of newborn NPAS3-deficient neural precursor cells. (Apoptosis is a process of cell death occurring through injury or cell suicide.) He further showed that newborn cells that do survive in NPAS3-deficient mice are poorly formed and function poorly.

In schizophrenia and depression, disease progression is often characterized by decrease in the size of the hippocampus. Based on the hypothesis that deficient hippocampal neurogenesis might be a contributing factor to some symptoms in schizophrenia, such as the cognitive

deficits for which there are currently no treatments, Dr. Pieper and his team initiated specially designed, nontraditional screening methods to try to identify new compounds that would augment hippocampal neurogenesis. They succeeded in uncovering a novel series of proneurogenic, neuroprotective compounds in animal models of disorders that included schizophrenia, cognitive decline with aging, Huntington's disease and Parkinson's disease. These results have been published in the journals *Cell* and the *Journal of the American Chemical Society*.

Dr. Pieper was awarded a second NARSAD Young Investigator Grant in 2009 to pursue the study of these neuroprotective, proneurogenic molecules as potential candidates for drug development for treatment of brain and behavior disorders. In addition to those cited above, the laboratory is conducting screening projects related to other disorders, including obsessive compulsive disorder, Rett syndrome and autism.

*“I am most grateful for the generous support I received through the NARSAD Young Investigator Grant given by the Brain & Behavior Research Foundation. This support was vital to the success of the early stages of my independent research program as a new faculty member.”*

*– Andrew A. Pieper, M.D., Ph.D.*



George B. Handran, Esq.

## The 2011 Visionary Philanthropist Award

*honoring*

The Trustees of the  
Sidney R. Baer, Jr. Foundation  
George B. Handran, Esq.  
and U.S. Bank

In 2002, when Sidney R. Baer, Jr., died, the Trustees of his estate were faced with the prospect of how to best utilize the funds he left for the benefit of mental health. He wanted to help others who suffer from mental illness as he had during his lifetime. Some of his ideas were discussed while he was alive, and one that interested him was funding medical research.

By good fortune, the Trustees were directed to the Brain & Behavior Research Foundation (then NARSAD), and a valuable partnership was formed that has provided a powerful opportunity to learn about medical research and fund incredibly exciting work. Initially, the Baer Foundation was offered several investigators who met the general criteria of the Foundation, and they were funded as part of the Research Partners Program. As the relationship strengthened, personal connections with the grantees were formed, and visits were made to their labs to learn more about their work.

The Young Investigator Grantees have moved on to become Independent and Distinguished Investigators. Additionally, there have been a number of grants made to young scientists working in the labs of other Grantees previously funded by the Baer Foundation. There have also been meetings between the Trustees and a number of the Brain & Behavior Research

To have the benefit of the Brain & Behavior Research Foundation Scientific Council vet the best applications for NARSAD Grants, and then to have complete discretion in selecting scientists to fund is a unique and phenomenal opportunity to support the vision of the Sidney R. Baer, Jr. Foundation.

Foundation Scientific Council members, greatly enriching their knowledge and information about mental health research.

The Trustees have come to realize that the most difficult task is to decide which and how many of the Brain & Behavior Research Foundation Young Investigators to fund based on the funding available.

During this long and fruitful partnership, not only have specific grants been made to selected investigators, but the Baer Foundation has also sponsored annual public mental health research symposia in St. Louis and Boston, featuring NARSAD Grantees as speakers. This has enabled the Foundation to bring new knowledge to a public audience that might not otherwise be able to acquire such information.

The acknowledgment from Grantees as to how much they have appreciated the support given at a crucial time in their burgeoning careers has convinced the

trustees that the Young Investigator Grantee who will later receive National Institute of Mental Health, National Institutes of Health, and other major funding will continue to grow and contribute to science. One Trustee remembers a comment made by a grateful Grantee who will be a devoted schizophrenia researcher for life, that she just needed the encouragement to “take the big leap!” How much more rewarding can a philanthropist’s life be?

In 2004, with the help and advice of Connie Lieber, then president of the Brain & Behavior Research Foundation, and Herbert Pardes, M.D., president of the Scientific Council, the Brain & Behavior Research Foundation created the Sidney R. Baer, Jr. Award for Innovative Research in Schizophrenia, to honor Mr. Baer’s memory. It is awarded annually to a Young Investigator who is selected by that year’s recipient of the Lieber Award for Outstanding Achievement in Schizophrenia Research.

### **Our mission:**

The Brain & Behavior Research Foundation is committed to alleviating the suffering of mental illness by awarding grants that will lead to advances and breakthroughs in scientific research.

### **How we do it:**

100% of all donor contributions for research are invested in NARSAD Grants leading to discoveries in understanding causes and improving treatments of disorders in children and adults, such as depression, bipolar disorder, schizophrenia, autism, attention-deficit hyperactivity disorder, and anxiety disorders like obsessive-compulsive and post-traumatic stress disorders.

### **Our credentials:**

Over a quarter of a century, we have awarded nearly \$300 million worldwide to more than 3,300 scientists carefully selected by our prestigious Scientific Council.

### **Our vision:**

To bring the joy of living to those affected by mental illness – those who are ill and their families and friends.