

# The Quarterly

Fall 2014

 **BRAIN & BEHAVIOR**  
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FOCUS ON:

**SUICIDE  
PREVENTION**



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**Cover: (clockwise from top left): a)** Dr. Oz presenting The Pardes Humanitarian Prize to Dr. Herbert Pardes. **b)** Dr. Eric Kandel, Jeff Borenstein, Foundation President & CEO and Dr. Oz. **c)** J. John Mann, M.D., at Columbia University where he studies suicide risk and suicide prevention (p. 6). **d)** Dr. Kay Redfield Jamison, Keynote Presenter at the Brain & Behavior Research Foundation Scientific Symposium. **e)** Dr. Herbert Pardes, President, Scientific Council (p. 48).

**Jeffrey Borenstein, M.D.**

President & CEO  
Brain & Behavior Research  
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Robin Williams's tragic suicide this past August has brought renewed focus to the critical public discussion about suicide. The loss of such a beloved and renowned celebrity is a stark reminder that hopelessness and despair can affect anyone. According to the Centers for Disease Control and Prevention (CDC), nearly 40,000 Americans die by suicide each year and the rates have not decreased in 60 years. While the great majority of people with a mental illness do not die by suicide, of those who do, more than 90 percent have a diagnosable mental illness.

By funding research grants to identify the brain mechanisms that cause mental illness, and in some cases to understand specifically what causes someone to attempt suicide—and what can be done to effectively intervene—the Brain & Behavior Research Foundation is committed to reducing the loss of life from psychiatric illness. We present some very promising examples of current research in this issue.

Kay Redfield Jamison, Ph.D., Professor of Psychiatry at The Johns Hopkins School of Medicine and 2010 recipient of the Foundation's Productive Lives Award, lives with bipolar disorder and, years ago, barely survived a suicide attempt. Dr. Jamison was the keynote speaker at this year's New York City Mental Health Research Symposium on October 24th, at which recipients of the Foundation's 2014 Outstanding Achievement Prizes reported on their research. Dr. Jamison offered an important message of hope. The prizewinners were honored at the Foundation's National Awards Dinner that evening (see pp.40-47).

The lion's share of credit for the Foundation's hugely successful model belongs to our Scientific Council and its founding and ongoing President, Herbert Pardes, M.D. This year, in recognition of his extraordinary vision and lifelong commitment to human health and well-being, the Foundation inaugurated the Pardes Humanitarian Prize (see pp.48-49). The first Pardes Prize was presented to Dr. Pardes by Dr. Mehmet Oz, at the Awards Dinner in the presence of hundreds of Foundation friends and supporters.

I extend the Foundation's thanks to all of you who attend our events, read our publications, share your stories and concerns and contribute the financial support essential to the realization of Dr. Pardes's vision and the Foundation's mission to increase the possibilities for all to live full, productive lives.

Sincerely,

A handwritten signature in black ink, appearing to read 'Jeffrey Borenstein, M.D.', written in a cursive style.

Jeffrey Borenstein, M.D.  
President & CEO

# Research Discoveries in the News

## A Promising Predictor for Suicide Identified

A team that includes three Foundation-funded researchers reported they have identified a biomarker (biological predictor) that, in preliminary tests, predicted suicidal behavior with an accuracy of 80 percent or higher. The potential biomarker can be detected in a simple blood test and appears to predict the progression from thinking about suicide to acting on such thoughts.

Suicide claims the lives of nearly 40,000 Americans annually, representing a rate of the population that has not declined in the last 60 years. In 2011, suicide was the tenth leading cause of death for Americans. These facts motivated **Zachary A. Kaminsky, Ph.D.**, of The Johns Hopkins School of Medicine, a recipient of a 2010 NARSAD Young Investigator Grant, who led a team that also included **Holly C. Wilcox, Ph.D.** and **Jennifer L. Payne, M.D.**, two prior recipients of Young Investigator grants. Their discoveries were published in *The American Journal of Psychiatry* on July 30th.

Brain tissue samples of people who have died by suicide have long been available at a small number of brain tissue banks. In recent years, these precious resources have been studied with increasingly sophisticated genomic tools. Studying these samples, Dr. Kaminsky and colleagues found that the activity level of the SKA2 gene was consistently below normal in cells of the prefrontal cortex (the seat of judgment and impulse control) in those who had died by suicide. The team found that a common variant of the SKA2 gene, in which one DNA

“letter” is substituted for another, makes that gene susceptible to an “epigenetic”\* chemical change that can lower its activity level. Such changes occur when chemical groups—in this case, a molecule of methyl (CH<sub>3</sub>)—attach to the gene, preventing it from being expressed.

Dr. Kaminsky is especially interested in epigenetic changes that can promote suicidal pathology. Evidence from the research enabled the team to create a model blood test and try it in two small groups of living people, including people known to be at risk for suicide. The test looks for reduced SKA2 activity, which, the team hypothesizes, is caused by an epigenetic change that prevents brain cells from properly regulating receptors for glucocorticoid stress hormones, most notably cortisol. Abnormal cortisol levels have previously been linked with suicidal behavior.

The hypothesis is that the drop in SKA2 activity in people who die by suicide indicates an inability to properly regulate the response to stress. In people with the telltale SKA2 variation, there is a high risk of suicidal ideation progressing to suicidal action in the presence of a stressor, the team suggests.

According to Dr. Kaminsky and colleagues, “early screening of those at risk for suicidal ideation and suicide attempt may be possible, allowing for the identification of people at risk, proactive treatment, and stress and anxiety reduction.”

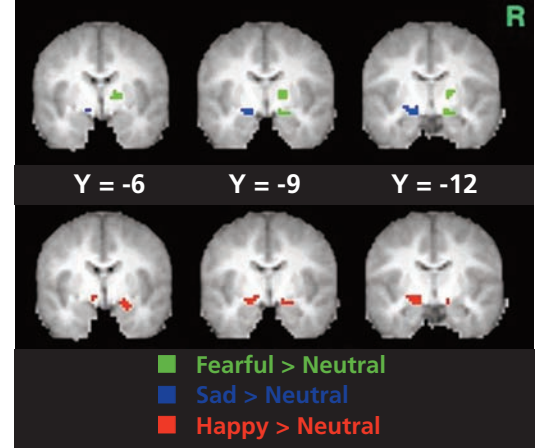


**TAKE AWAY:** Researchers have identified a biomarker that may predict who will progress from thinking about suicide to attempting it.

Zachary Aaron Kaminsky, Ph.D.; Holly C. Wilcox, Ph.D.; Jennifer L. Payne, M.D.

\* Refer to glossary on page 52.

# Possible Early Predictor of Mental Health Risk



Over the last two decades, researchers have learned that severe stress experienced early in life can change the brain in ways that affect behavior well into adulthood. New research led by **Deanna M. Barch, Ph.D.**, of Washington University in St. Louis, a 2013 NARSAD Distinguished Investigator Grantee, has made progress in identifying these brain changes in young children. Her colleagues in this work include **Joan L. Luby, M.D.** and **Kelley N. Botteron, M.D.**, who have received multiple grants from the Foundation.

The team reported their findings in the July 2014 issue of the *Journal of the American Academy of Child & Adolescent Psychiatry*. The results suggest that hyperactivity in the limbic areas of the brain—those involved in emotions and behavior—may be a biomarker (or biological predictor) that doctors can use to identify children exposed to stress and trauma that are likely to go on to develop stress-related disorders.

It is more difficult to study young children than adults when it comes to mental health. Abuse of a child or a child’s caretaker is likely hidden and many children cannot articulate their symptoms. For these reasons, an objective biomarker of stress and trauma would be of immense value.

Dr. Barch’s team selected a group of children aged three to five years old who were given initial psychiatric evaluations. Some of the children were deemed to be “healthy controls,” others had been subjected to stress or trauma, and some had already developed disorders such as depression.

As these children grew to ages seven to 12 they were given functional magnetic resonance imaging (fMRI) brain scans to measure the level of activity in the brain while they responded to pictures of faces. The faces

Above: These fMRI brain scans made by Dr. Barch and colleagues show that children’s brain activity response to faces that showed emotion of all kinds—negative faces (green areas), sad faces (blue areas) and happy faces (red areas)—increases in proportion to the amount of cumulative stress a child has experienced. (across, from L to R: less stress to more stress).

expressed the gamut of emotions from fearful, sad, or neutral to happy.

Most important, perhaps, was the observation that children who had experienced life stress or trauma showed higher levels of limbic brain activity than did healthy children. Unexpectedly, the specific areas of the brain that were overactive differed, depending on whether the child had experienced stress or trauma.

In all of the children who had experienced stress, an important part of the limbic system, the amygdala\*, was hyperactive when pictures were shown of faces displaying emotion. Activity was normal when the face lacked emotion. Children who had experienced trauma showed over-activity when shown sad faces, but not other “emotional” faces. Children diagnosed with depression and those with other psychiatric illnesses showed abnormal activity in different parts of the limbic areas.

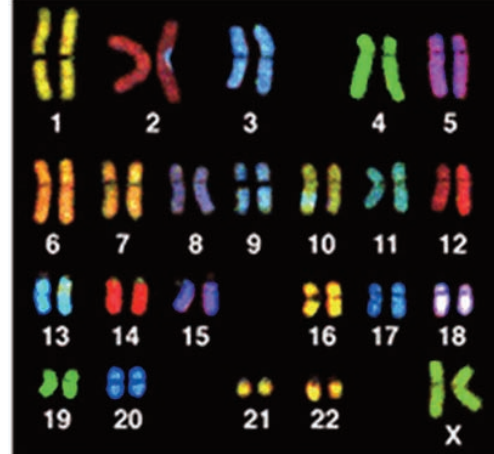
Their findings, the authors state, “suggest that limbic hyperactivity may be a biomarker of early life stress and trauma in children and may have implications in the risk trajectory for depression and other stress-related disorders.” This new work may be providing a pathway for early diagnosis and intervention in stress-related psychiatric illness.



Deanna M. Barch, Ph.D.; Joan L. Luby, M.D.; Kelley N. Botteron, M.D.

**TAKE AWAY:** New research findings could lead to tools for earlier diagnosis and intervention for those susceptible to developing stress-related mental illness.

# Developing Risk Profiles for Schizophrenia



Above: In studying genomes of people with schizophrenia, researchers identified 108 previously unidentified locations among the 23 human chromosomes where DNA errors were associated with the illness.

Results of the largest study ever undertaken to understand the genetics of schizophrenia appeared in the prestigious journal *Nature* on July 24th. Thomas Insel, M.D., Director of the National Institute of Mental Health, said that “a giant step forward” had been taken toward a better understanding of the genetics of schizophrenia, which could ultimately lead to better identification of those at risk of developing the illness, and to the development of new treatments.

Hundreds of scientists participating in the international Psychiatric Genomics Consortium (PGC) contributed to the mammoth study, which analyzed blood samples contributed by 36,989 people with schizophrenia and 113,075 healthy controls of diverse races and ethnicities. The bottom line: variations relative to the norm in 108 different genetic “loci” (locations containing genes along the full length of the human genome) were associated in this sample with the occurrence of schizophrenia. The loci were among genes expressed in the brain and in neurons—about three-fourths of the variations detected in the study are active mainly or exclusively in cells of the brain.

One of the key team members was **Patrick Sullivan, M.D.**, of the University of North Carolina, recipient of a 2010 NARSAD Distinguished Investigator Grant and winner of this year’s Lieber Prize for Outstanding Achievement in Schizophrenia Research. Dr. Sullivan organized the psychiatric genetics community into the PGC in 2007, and it now consists of more than 500 investigators across 80 institutions in 25 countries. One of the team leaders was **Michael O’Donovan, M.D., Ph.D.**, of Cardiff University, United Kingdom, the 2012 Lieber Prizewinner. First author on the paper is this year’s recipient of the Sidney R. Baer, Jr. Prize for Inno-

ative and Promising Schizophrenia Research, **Stephan Ripke, M.D.**, of the Broad Institute.

Only 25 of the 108 genome locations had previously been associated with schizophrenia; 83 were new and will lead to much follow-up. Some of the 25 locations previously noted suggest defects in genes that have been consistently associated with higher risk for schizophrenia. One such gene, *DRD2*, tells cells in the brain how to encode a protein that serves as a receptor (docking port) for the neurotransmitter dopamine.\* Those receptors are the targets of all known antipsychotic medications, the first of which was discovered some 60 years ago.

Other genes previously linked with the illness and pinpointed in the new study include those involved in transmission of glutamate—the brain’s key “excitatory” neurotransmitter—and in synaptic plasticity, the process in which communication nodes between neurons in the brain gain and lose strength in response to different stimuli and conditions.

Possibly the most intriguing result was an association with genes related to the generation of the body’s innate immune system. This will fuel efforts, which have been increasing, to study the possible role of immunity in schizophrenia causation and what might be done to prevent it.



**TAKE AWAY:** Largest genetic study of schizophrenia to date identifies new links that could lead to more effective interventions and possibilities for prevention.

Patrick F. Sullivan, M.D., FRANZCP; Michael O’Donovan, M.D., Ph.D.; Stephan Ripke, M.D.

\* Refer to glossary on page 52.

# Reliably Predicting Who is at Risk of Suicide

**A Career Devoted to Identifying the  
Brain Biology Associated with Suicide**



J. John Mann, M.D., of Columbia University, is one of a small number of neuroscientists who have quietly transformed our understanding of suicide over the last three decades. A member of the Foundation's Scientific Council and a 2008 recipient of a NARSAD Distinguished Investigator Grant, Dr. Mann, together with colleagues, has published hundreds of studies that are building a biological science to understand what leads to—and what might prevent—suicide.

## **J. John Mann, M.D.**

Paul Janssen Professor of Translational  
Neuroscience in Psychiatry and Radiology

Vice Chair for Research,  
Department of Psychiatry  
Columbia University

Director of Research and Director of  
Molecular Imaging and Neuropathology  
Division  
New York State Psychiatric Institute

2008 NARSAD Grantee

Foundation Scientific Council Member

In the United States, the suicide rate has remained virtually unchanged in 60 years. In 2011, the most recent year for which data are available, nearly 40,000 suicides were reported. It is the tenth leading cause of death for Americans. There are behavioral warning signs that have been associated with increased risk of suicide: behavior and symptoms of recurrent major depressive episodes, expressions of hopelessness and negativity, impulsive behavior and a pattern of impaired decision making and problem solving.

Early in his career, Dr. Mann, The Paul Janssen Professor of Transla-

tional Neuroscience in Psychiatry and Radiology at Columbia University, realized the behavioral warning signs weren't doing enough to help those at risk. He began his journey to find ways to more reliably predict who might attempt suicide and to develop means to more effectively intervene. Working with postmortem human brain tissue early on, Dr. Mann set out to discover what was different in the brains of people who had suffered from major depression and taken their own life. His team and other colleagues discovered abnormally low levels of the neurotransmitter serotonin\*, a message-transmitting chemical that is the target of



**“There’s also a potential role for brain imaging. There may be 20 different ways to arrive at disordered neural circuitry in the cortex, which predicts suicide risk. We may not fully understand how all of these occur for a long time. But we may be able to scan people right now to predict the probability.”**

today’s widely used SSRI (selective serotonin reuptake inhibitor) antidepressant medicines such as fluoxetine (Prozac®) and paroxetine (Paxil®). These medications are designed to increase brain serotonin signals.

Dr. Mann and a colleague noticed, critically, that in people who had died by suicide, serotonin was low—not only in those who suffered from major depression, but also in other disorders including schizophrenia, bipolar disorder and anxiety. In depressed people who had taken their life, “there were abnormalities that were confined to areas of the brain involved in decision making and the ability to restrain oneself,” Dr. Mann explains. These areas in the frontal part of the brain are called the orbitofrontal cortex and the anterior cingulate cortex.

This early evidence contributed to a theory of suicide aimed at prediction. Called the stress-diathesis theory of suicide risk, it focuses on the impact of stress upon people who are biologically predisposed to handle stress poorly. In the presence of stress—whether a sudden psychosocial trauma and/or acute episode of a psychiatric illness—people with specific brain abnormalities appear predisposed to, and are at higher risk of, suicide.

“Our research highlighted the predisposition, which had been overlooked,” says Dr. Mann. “Once you took the list of things associated with suicides, and divided it into these two domains of stress and predisposition, everything we knew became more meaningful. There is the stressor part, or life events; and there is the way you cope when things go wrong.”

Some major advances have been made with the introduction of functional imaging of the living brain. “It led us to think: Well, what’s going on in the brain of a person who hasn’t died of suicide but might?” Dr. Mann says. Additional insight has also been obtained with gene-sequencing technologies, which have begun to flesh out what risk might be genetic. The overall contribution of genetic factors to the predisposition portion of suicide risk is estimated to be as high as 50 percent. Epigenetic factors—chemical modifications of DNA that change gene activity—also seem to be implicated in predisposition risk.

Several lines of suicide research point to aberrations in the human stress-response system, referred to by scientists as the HPA axis (for the hypothalamus, the pituitary and the adrenal glands that regulate the stress response). “HPA dysfunction is linked to depression and unstable

mood, changes in cognition and decision making,” Dr. Mann says. “One thing that distinguishes serious, often lethal suicide attempts from non-lethal ones is an individual who retrieves disproportionately negative memories. In problem solving, these people cannot rethink the problem; there is cognitive rigidity. We often hear such people say, ‘There’s no way out; I’m stuck.’ This is due to deficits in cognitive processing.”

Serotonin deficiency likely contributes to these deficits. In addition to transmitting messages between neurons, serotonin enhances the release of growth hormones in the brain such as BDNF\* (brain-derived neurotrophic factor). “BDNF causes neurons to get bigger, to form more connections,” says Dr. Mann. It also causes new nerve cells to be born in the hippocampus. Low serotonin affects all these vital processes.

“I can see blood tests becoming an important part of screening for suicidal patients,” Dr. Mann says. “There’s also a potential role for brain imaging. There may be 20 different ways to arrive at disordered neural circuitry in the cortex, which predicts suicide risk. We may not fully understand how all of these occur for a long time. But we may be able to scan people right now to predict the probability,” he says.

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\* Refer to glossary on page 52.

## Volunteers Needed for “Paradigm-Shifting” Study on Rapid Antidepressant

“Becoming suicidal is not a fluke. And it’s not just because of the circumstances someone has experienced,” says Dr. J. John Mann. Using combat veterans as an example, he emphasizes the component of biological predisposition that determines “how resilient you happen to be” when trauma or stress occurs.

“A NARSAD Distinguished Investigator Grant enabled me to get pilot data for this, and that led to a major NIH grant. Some of my group’s most creative and original ideas would never have gotten off the ground if it had not been for the paradigm-shift approach that the Foundation encourages.”

To the extent this vulnerability is determined by genes, serotonin deficiency, problems in the brain’s dopamine\* or noradrenergic pathways\*, problems in cellular docking ports for stress hormones called glucocorticoid receptors, or other problems in the stress-response system, the current thinking is that it takes more than severe trauma to make someone determined to act on suicidal thoughts. Dr. Mann gives this example: many people enter combat; about 20 percent develop PTSD or major depression. “But of that 20 percent, only a fraction will have additional vulnerability that places them at higher risk for suicide: poor decision making, excessive pessimism, impaired problem solving. Those dysfunctions are not about the severity of the stressor—we can find examples of all soldiers in the same unit being exposed to the same trauma. They are about individual biological predisposition.”

At some point, Dr. Mann hopes that advanced brain imaging, measures of decision making and blood tests for biomarkers of elevated suicide risk can screen for people predisposed

in this way. Such tests might, for example, be given to soldiers before being sent into combat.

More immediately, Dr. Mann is excited about a potential medication to reverse high suicide risk in select patients who are depressed. His group and others at Columbia University are currently seeking patients to take part in two NIH-funded clinical trials for ketamine\*. Dr. Mann invites patients aged 18 to 65 with major depression but no history of other psychiatric illness to inquire about participating. For more information call 646-774-5788.

“Ketamine does two things to people with major depression that are different from all the other antidepressants now in use,” says Dr. Mann. “First, when it gets people better, it gets them a lot better. Second, it does this in a couple of hours. This is a paradigm shift in the way we think antidepressants can work.”

Ketamine inhibits the NMDA receptor, which is ubiquitous in the brain. Originally used as an anesthetic, ketamine in higher doses has side effects such as dissociative symptoms\*, like those seen in psychosis. However, the clinical trials use a low-dose pharmaceutical derivative of ketamine whose one-time administration in the studies is carefully controlled, and side effects are milder and transient. In one of the two trials, ketamine is compared to another medication, midazolam, to determine its impact, if any, on suicidal thoughts. In a second clinical trial, the brain is imaged in real time as ketamine is administered via an IV to study how the brain chemistry changes with the medication’s astonishingly rapid antidepressant effect.

“The Foundation has been really important in our field, and this is an example,” Dr. Mann says. “Our idea of doing an imaging study in real time of patients being given ketamine would not have been funded by NIMH without some pilot data. A NARSAD Distinguished Investigator Grant enabled me to get pilot data for this, and that led to a major NIH grant. Some of my group’s most creative and original ideas would never have gotten off the ground if it had not been for the paradigm-shift approach that the Foundation encourages.”

### HAVE A QUESTION?

Send questions for Dr. Mann to [asktheresearcher@bbrfoundation.org](mailto:asktheresearcher@bbrfoundation.org). Select questions and answers will be in the next issue of *The Quarterly*.

Please note that the researcher cannot give specific recommendations or advice about treatment; diagnosis and treatment are complex and highly individualized processes that require comprehensive face-to-face assessment.

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## Surviving Psychiatric Illness: Suicide Risk Assessment and Prevention

WITH:

**J. JOHN MANN, M.D.**

Columbia University



WHEN:

**December 16, 2014**  
**2:00 P.M. EST**

MODERATOR:

**Jeffrey Borenstein, M.D.**

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### Kerry Ressler, M.D., Ph.D.

Professor, Psychiatry and Behavioral Sciences, Emory University School of Medicine

Co-Director, Trauma Clinic, Fulton County Behavioral Sciences

Investigator, Howard Hughes Medical Institute

2002, 2005 NARSAD Grantee

2009 Freedman Prize for Exceptional Basic Research by a Young Investigator

Foundation Scientific Council Member

#### **Knowing that trauma can occur at any time to anyone, is there any way to prevent post-traumatic stress disorder (PTSD)?**

We don't know with certainty, but the leading ideas are related to the idea of secondary prevention. If the unexpected trauma cannot be prevented in the first place, we hope to be able to prevent the untoward consequences of that trauma—PTSD, depression, substance abuse, and other disorders that can occur in the aftermath of trauma. What is particularly exciting about this line of research is that decades of work in the field of learning and memory have shown that new memories—even traumatic memories—are not consolidated, or made permanent,

ANSWERS TO:

## *Ask the Researcher*

immediately. Rather, there is a period of hours to days in which potential interventions, from psychological to pharmacological, may be used to prevent the over-learning of the initial trauma memory and thus prevent PTSD and related disorders.

#### **What happens if someone has “blocked out” the specifics of a trauma—or it happened so long ago that the details are fuzzy—but they have the behavioral symptoms of PTSD? Is it still possible to treat them?**

Yes, they will still respond to pharmacotherapy. Right now, SSRIs remain the first line agent, even though a number of other medications are under study. Additionally, exposure-based psychotherapy can still be quite effective. Often, patients find as they start talking about even the fuzzy memories around the edge, more and more components of the memory and accompanying emotions will return and be available for processing and habituation. Furthermore, cognitive and skills-training components of cognitive and dialectical behavioral therapy as well as approaches such as EMDR can all help to access and diminish symptoms. The important thing is for patients to know that there are a number of options available that can help and to be persistent in seeking recovery.

#### **What do you see as the most promising development for PTSD on the horizon?**

I think the new developments that are the nearest are likely those that prevent PTSD development in the early hours after the trauma in the emergency department or on the battlefield, during the “golden hours” mentioned in the original interview article. There are already a number of exciting ideas being tested or soon to be tested, and the biology of memory consolidation is more mature than many other areas of stress biology. A second area that is terrifically exciting derives from the rapidly developing molecular neurobiology of fear circuitry, including amygdala\* and connected limbic brain areas. It appears that there are certain “fear off” and “fear on” networks within the microcircuitry of these regions. As we better understand the receptors and other molecular identities of these cell types, rational drug design and targeting could lead to specifically activating the endogenous “fear off” network or inhibiting the brain’s “fear on” network. Overall, I’m hopeful that the combination of progress in molecular pharmacology along with greater understanding of fear learning, memory and behavior will lead PTSD to being one of the first psychiatric illnesses to be understood from molecule to mind, with rational treatments translated from bench to bedside.

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- 2 COLUMBIA UNIVERSITY \$23.7M
- 3 HARVARD UNIVERSITY \$23.5M
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**34**  
COUNTRIES, INCLUDING THE U.S.

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- 3 UNITED KINGDOM
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The all-volunteer **Foundation Scientific Council** is comprised of 150 leading experts across disciplines in brain & behavior research who review grant applications and recommend the most promising ideas to fund. The group includes:

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- 47 MEMBERS OF THE INSTITUTE OF MEDICINE

# In Fight to Prevent Suicide, the Foundation Helps Identify Causes and Develop Preventative Techniques

## NARSAD Grantees Study Genetics, Use New Technologies, Test Prevention Methods

The Brain & Behavior Research Foundation is proactive in its awarding of research grants related to the study of suicide each year. This feature highlights the work of several recent NARSAD Grantees taking diverse approaches to understand what biology and brain activity lead to suicide and to identify specific techniques to avert the tragic loss of life.

One of the most hopeful approaches in reducing the number of suicides involves finding a reliable way to predict who is at what doctors call “imminent risk.” A powerful way to address this begins with better understanding genetic factors, which are estimated to account for up to 50 percent of total risk. Researchers are making steady progress in identifying the complex relationships between variations in a person’s genetic material and illnesses of all kinds. There is an additional complication that applies to suicide—the fact that more than 90 percent of people who die by suicide have a diagnosable mental illness.

2008 NARSAD Young Investigator Grantee **Vincenzo De Luca, M.D.**, of the University of Toronto, in his comprehensive 2012 book chapter on “The Neurobiological Basis of Suicide” that he co-authored with several colleagues, discusses the difficulty of teasing out genetic factors specifically related to suicide risk from those re-

lated to any “background” psychiatric conditions an individual may have. Broad scans of the human genome, called genome-wide association studies\*, have turned up some possible links between specific gene variations and suicide, but it has been hard to corroborate results from different studies. Potential ways to get more useful results, say Dr. De Luca and colleagues, include efforts to study interactions among multiple genes—since only very rarely do “risk” genes act alone. Dr. De Luca and others are now also engaged in studying the impact of epigenetic\* factors in altering gene expression. Epigenetic factors change the “expression,” or activity levels, of genes without changing the order of DNA letters in the genome. Comprehensively understanding epigenetic modifications of gene activity, in addition to identifying those genes linked to suicide risk, could lead to more effective diagnostic tools that could in turn enable more effective interventions for those at highest risk.

Dr. Gilbert hopes biological predictors will enhance the tools available to clinicians to identify individuals at greatest risk of suicide.

Dr. Renaud's ultimate goal is to develop standard, effective clinical interventions as well as suicide prevention guidelines for public health officials to follow.

A number of studies have identified clinical behavioral warning signs that are associated with an increased likelihood of suicide attempt/ completion including aggression, and impulsivity. 2010 NARSAD Young Investigator Grantee **Alison Gilbert, Ph.D.**, of Zucker Hillside Hospital in New York, and her colleagues have been using NARSAD Grant support to study the role of impulsivity in suicide attempters with bipolar disorder. As a group, patients with bipolar disorder are more impulsive than healthy individuals, even during periods of relative affective remission. This trait-like impulsivity has been linked with changes in brain functioning in specific regions, including the orbitofrontal cortex (an area in the front of the brain responsible for decision making).

Dr. Gilbert is taking brain images of the white matter—tracts that connect various brain regions to one another—with an imaging method called diffusion tensor imaging. She is comparing the images from patients with bipolar disorder who have and who have not made a suicide attempt. Her hypothesis is that there will be reduced integrity in the white matter in the orbitofrontal cortex of the brain in those who have attempted suicide versus those who have not. The goal of her study is to use brain imaging to identify reliable biological markers to predict suicide risk in combination with behavioral measures, including impulsivity. Her hope is that these predictors will enhance the tools available to clinicians to identify individuals at greatest risk of suicide.

Preventative techniques on “the front lines” with primary care doctors and mental health professionals, could have a major impact in preventing suicide. This is the subject of research by 2008 NARSAD Young Investigator Grantee **Johanne Renaud, M.D.**, of McGill University in Canada. She has studied how young people at high risk in Quebec are served by “the system.” Between 1995 and 2005, 422 youths under age 18 died of suicide in the province; only one-third received services from youth centers, and only about one-fourth had any psychiatric help in the year preceding suicide.

Dr. Renaud was recognized in 2012 with the Foundation's Klerman Prize, Honorable Mention for demonstrating that, although most children and adolescent suicide completers suffer from a diagnosable mental illness, a significant proportion of them are left without appropriate healthcare support (including psychiatric consultation, psychotherapy and pharmacotherapy) in the period preceding their suicide. Results from her NARSAD Grant-supported work published in October in the *Canadian Journal of Psychiatry* show that the most important gap in having received appropriate health care support still exists among young people suffering from depression and substance use disorders. Her findings can already inform policies in mental health services and suicide prevention, and her ultimate goal is to develop standard, effective clinical interventions as well as suicide prevention guidelines for public health officials to follow.



**Vincenzo De Luca, M.D.**  
2008 NARSAD Young Investigator Grantee

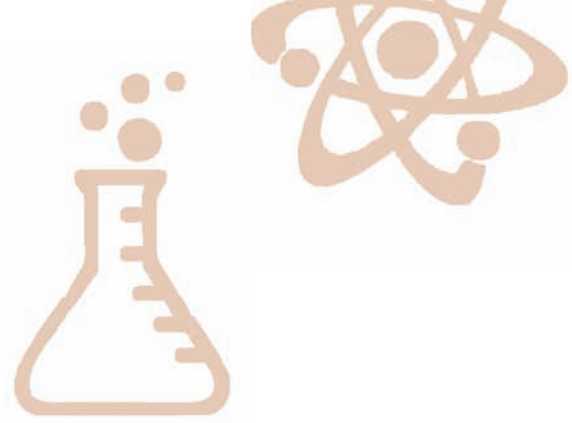


**Alison Gilbert, Ph.D.**  
2010 NARSAD Young Investigator Grantee



**Johanne Renaud, M.D.**  
2008 NARSAD Young Investigator Grantee  
2012 Klerman Prize Honorable Mention

# New Treatments/ Therapies



## Computerized Screening Tool for Youth Suicide Risk Coming Soon

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A team of scientists, including 2001 NARSAD Distinguished Investigator Grantee David A. Brent, M.D., is developing a computerized screening tool to be used in hospital emergency departments (EDs) across the country. The goal is to avert youth suicides, the second leading cause of death among teens aged 12 to 17 in the United States. The team aims to refine algorithms that can predict which youth are most likely to attempt suicide and then develop a personalized screening tool in which each question is based on the individual's previous responses. Once the effectiveness of the new screening tool is confirmed, the hope is that it will help save lives.

Source: *Science Update*, September 23, 2014

## Genetic Link to PTSD Could Help in Prevention and Treatment

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A new study has demonstrated a link between variants in the ADRB2 gene, childhood trauma and an elevated risk for post-traumatic stress disorder (PTSD) in adulthood. The findings are significant for the study of PTSD and for treatment and prevention of stress-related illnesses. Israel Liberzon, M.D., a 1997 NARSAD Young Investigator Grantee at the University of Michigan and first author of the study, says that "by understanding how PTSD develops, we are better positioned to employ effective prevention and intervention strategies in the military and beyond. With these data, we will help patients suffering from the strains of PTSD earlier on, and prevent unnecessary pain, suffering and stress."

Source: *JAMA Psychiatry*, August 27, 2014, online

## Research Supports Deep Brain Stimulation for Resistant OCD

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For the 40 percent to 60 percent of people with treatment-resistant obsessive-compulsive disorder (OCD), deep brain stimulation could be an important new option. In this treatment, known as DBS, electrical stimulation is delivered via electrodes placed in specific areas of the brain. A team of scientists, led by 2009 NARSAD Young Investigator Grantee Clement Hamani, M.D., Ph.D., has reviewed the research on DBS for OCD and concluded that, while the samples are small and larger studies need to be conducted, bilateral (both sides of the brain) stimulation of the subthalamic nucleus and the nucleus accumbens regions could improve symptoms for those patients with OCD who have not responded to other treatments.

Source: *Neurosurgery*, October 2014



# THE POWER OF A RESEARCH PARTNERSHIP



Virginia and Mark Silver

Eleonore Beurel, Ph.D.

Virginia Silver, a member of the Foundation's Board of Directors, and her husband, Mark Silver, M.D., have a research partnership with 2013 NARSAD Young Investigator Grantee Eleonore Beurel, Ph.D., of the University of Miami. Dr. Beurel is working to help usher in a new generation of better, more effective medications for the treatment of mood disorders.

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*"Our daughter was diagnosed five years ago with clinical depression and severe anxiety disorder. Although now stabilized and living a happy, productive life, I came to realize that if it weren't for research, she would not have had the medications that have worked for her. We were drawn to support the Brain & Behavior Research Foundation because we believe so strongly that research has to be supported for the sake of our children's children—and for all the generations down the road." — Virginia Silver*

For information on becoming a Research Partner or to support research in other ways, please call (800) 829-8289 or visit our website at [bbrfoundation.org/research-partner](http://bbrfoundation.org/research-partner)



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# Frequently Asked Questions

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## on SUICIDE PREVENTION

**Q:** **Is it possible to predict who will attempt suicide?**

**A:** There are warning signs.<sup>1</sup> People who talk about suicide or say they have “no reason to live,” or those in unbearable pain—psychological or physical—should be taken seriously. According to the American Foundation for Suicide Prevention, a person’s suicide risk is greatest if his or her behavior is new or has increased, especially if it is related to a painful event or loss. Withdrawal, calling people to say goodbye or increased use of alcohol or drugs are a few other such warning signs. Scientists are working to create a blood test that would offer an objective way to help predict who is at risk of attempting suicide. Foundation-funded researchers—Zachary A. Kaminsky, Ph.D., recipient of a 2010 NARSAD Young Investigator Grant; Holly C. Wilcox, Ph.D. and Jennifer L. Payne, M.D.—have recently identified a potential biomarker (biological predictor) to predict the progression from thinking about suicide to acting on such thoughts.<sup>2</sup>

**Q:** **Are there any national efforts to address suicide prevention?**

**A:** The National Alliance for Suicide Prevention was launched in 2010 as a public-private collaborative effort to champion suicide prevention as a national priority; it is led by The Honorable John M. McHugh, Secretary of the Army (public sector co-chair) and The Honorable Gordon H. Smith, President and CEO of the National Association of Broadcasters (private sector co-chair). In 2014, the Alliance released “A Prioritized



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Research Agenda for Suicide Prevention,” which outlines the research areas that show the most promise in helping to reduce the rates of suicide, and a “Suicide Research Prioritization Plan of Action” that is currently underway. The Foundation’s NARSAD Grants on suicide are included in this work and will be part of an online searchable database of all suicide-related research.<sup>3</sup>

**Q:** **Has suicide been linked to anything beyond feelings of despair?**

**A:** Yes, some abnormalities in the brain can put a person at a higher risk of attempting suicide. A leader in this research, J. John Mann, M.D., of Columbia University, a member of the Foundation’s Scientific Council and a 2008 recipient of a NARSAD Distinguished Investigator Grant, studied the brains of deceased patients who suffered major depression and died by suicide. Many of them had low levels of the neurotransmitter serotonin, a message-transmitting chemical that is the target of widely-used antidepressant medications such as fluoxetine (Prozac®) and paroxetine (Paxil®).<sup>4</sup> Reduced levels of serotonin contribute to other brain abnormalities that can raise the risk of suicide such as a dysregulation of the stress-response system and deficits in cognitive processing, or thinking.<sup>5</sup> Much other research is underway to identify the brain activity or malfunctioning that can identify who is at highest risk of attempting suicide as well as to develop the most effective intervention methods.

**Q:** **I’m worried that a loved one may be contemplating suicide. What should I do to help him?**

**A:** First, you should know that studies show people do not start thinking about suicide just because someone asks them about it. Tell your loved one that you are worried and want to help. Be direct and non-judgmental. Don’t be afraid to ask whether they are thinking about suicide. If they have a plan to do so it could indicate that they need help right away. The American Foundation for Suicide Prevention suggests a number of steps you should take:<sup>1</sup>

- Do not leave the person alone. Have them call the Suicide Prevention Lifeline at 1-800-TALK (8255)
- Remove lethal weapons and drugs.
- Call or escort them to an emergency room, counseling service, or psychiatrist.
- In an emergency, call 911.

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SOURCES:

<sup>1</sup> American Foundation for Suicide Prevention, [www.afsp.org](http://www.afsp.org)

<sup>2</sup> The American Journal of Psychiatry, July 30, 2014

<sup>3</sup> For more information on the National Alliance for Suicide Prevention, go to [actionallianceforsuicideprevention.org/NSSP](http://actionallianceforsuicideprevention.org/NSSP)

<sup>4</sup> J. John Mann, “The serotonergic system in mood disorders and suicidal behavior,” *Philosophical Transactions of the Royal Society of London*, Feb. 25, 2013. Free download at [ncbi.nlm.nih.gov/pmc/articles/PMC3638390/](http://ncbi.nlm.nih.gov/pmc/articles/PMC3638390/)

<sup>5</sup> K Heeringen, JJ Mann, “The neurobiology of suicide,” *The Lancet Psychiatry*, Volume 1, Issue 1, Pages 63 - 72, June 2014

# An Agonizing Journey and a “Blessing”

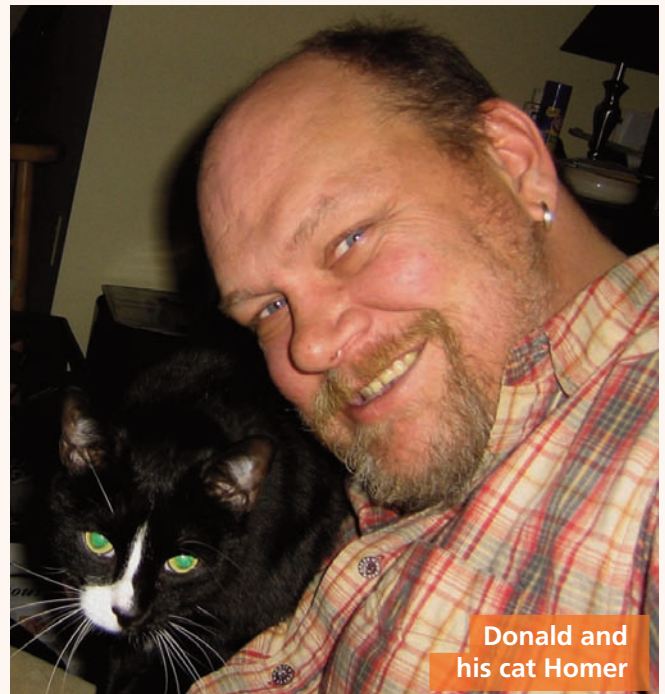
## A Family Works to Improve Crisis Intervention and Support Research

Janet and Donald Boardman, Sr., remember with chilling clarity the last time their son Donald, Jr., had to be hospitalized against his will.

“When the sheriffs came,” Janet says, “he was in our back yard, very ill, very angry, and when he started walking away, pushing his way through the sheriffs, one of them hit him with a billy stick. Then they pushed him down, put handcuffs on him and pepper-sprayed him.” As the spray drifted into the house, Mrs. Boardman, and her younger daughter, Kate, watched him being taken away—again.

For years the Boardmans, like many families in similar circumstances, lived with the anguish and frustration of trying to protect a loved one with schizophrenia, often from himself. Their son refused or abandoned treatment, due to side effects and ineffectiveness, and denying that there was anything wrong with him. What medications he did take rarely worked, or not for long. Before lasting help finally came in the form of the antipsychotic medication clozapine (Clozaril®), Donald, Jr., had gone through periods of homelessness, suicidal thoughts, 15 hospitalizations, eight of them involuntary, and an arrest for assault, which put him in the justice system where a sympathetic judge helped to focus him on compliance with his treatment plan.

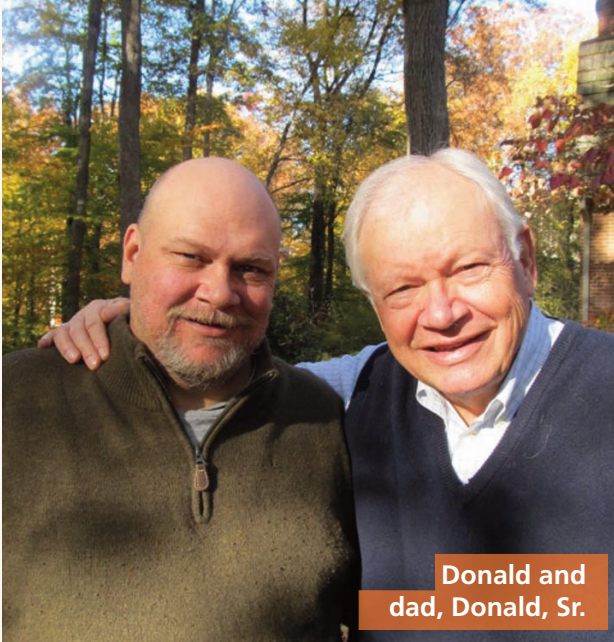
His illness was exacerbated by factors common in mental illness. The lack of insight into their illness, medically termed anosognosia, occurs in about half of people with schizophrenia. Another factor is marijuana, that Don began to smoke, his parents believe, as an attempt at self-medication. Research has been showing that for young people with a



Donald and his cat Homer

genetic vulnerability to developing schizophrenia, it can be a trigger. In 1986, at age 17, two years after the depression that had first led his parents to seek psychiatric help for him, Donald, Jr., started smoking marijuana and, not long after, exhibited “suicidal ideation and behavior” and was hospitalized.

By 21, he was severely psychotic. The agonizing journey had begun in earnest.



Donald and  
dad, Donald, Sr.

**“Seeing positive treatments that have come from research is a blessing,” says Donald, Sr.**

“It takes a while to get your mind around the fact that this is going to be ongoing and life is never going to return to normal,” Janet says.

Donald Boardman, Sr., who had had a successful 30-year career as a real estate financial officer and CPA, retired early, in part, he says, to help with his son’s care. “I went into nonprofit work in the area of special needs housing and homeless services, and both Jan and I became active in NAMI.”

NAMI, the National Alliance on Mental Illness, runs programs to help families and those with mental illness learn about and cope with mental illness. Donald, Sr., served on the NAMI Maryland state board for six years, as did Janet on the local board in Montgomery County, Maryland, where they live. She and a colleague, both educated in nursing, initiated the NAMI Family-to-Family Education Program for the county.

Their son’s last encounter with the sheriffs led Janet to become an instructor in Crisis Intervention Team Training, a national program that helps teach law enforcement personnel about dealing with people who have a mental illness. As part of the training, Janet explains, they spend an hour being bombarded with “virtual voices” to “get a sense of what it’s like to have schizophrenia.”

The Boardmans have supported the Brain & Behavior Research Foundation for the past 15 years. In 2013, Donald, Sr., joined the Foundation’s Board



Donald and mom,  
Janet, on the golf course,  
Captive Island, Florida

of Directors and recently served on the organizing committee for the Discovery to Recovery Conference, held in Washington, D.C., in September. At the conference he found “notable” the emphasis by several speakers on early detection and treatment for mental illness. “I couldn’t help wondering,” he says, “whether we’d have had a less traumatic progression if there had been such an emphasis when we were in the early stages of Don’s illness.”

The Boardmans’ faith in research is understandable. Their son’s recovery was due in large measure to the work of Foundation Scientific Council Member Herbert Y. Meltzer, M.D., the principal investigator on the trials that led to the approval of the use of clozapine for treatment-resistant schizophrenia. With clozapine and supplemental antidepressant and anti-anxiety medication, the voices in Donald, Jr.’s head, while not completely gone, became controllable.

Today, at 45, Donald, Jr., lives on his own in Baltimore, near his doctors at the Sheppard Pratt Health System. He has a job, which he has held for 12 years, driving for a pharmacy. He lives about an hour away from his parents, who are in touch daily, visit frequently and continue to provide emotional and financial support. Sisters Anne and Kate are also in regular touch.

Says Donald, Sr., “Seeing positive treatments that have come from research is a blessing.”

# The 27<sup>th</sup> Annual National Awards Dinner

October 24, 2014, The Pierre Hotel, New York City

## Eight Researchers Honored With the Annual Brain & Behavior Research Foundation Outstanding Achievement Prizes

The Outstanding Achievement Prizes, presented in five categories, are among the most prestigious awards in the field of psychiatric research. Selection of prize recipients is made by committees of the Foundation's Scientific Council—a volunteer group of 150 distinguished leaders in brain and behavior research.



**“I am profoundly honored to be selected as a Lieber Prize winner by my distinguished colleagues. We are entering a new era of the neuropsychiatric and genomic revolutions, where advanced bioinformatics and other evolving technologies will help us to integrate brain, behavioral and genomic data about schizophrenia that we only imagined was possible in the past. I’ve always believed that context is crucial in complex scientific matters. The generosity of my family, colleagues, patients and their families, and people like Connie and Steve Lieber, have facilitated the sense of scientific, community and social responsibility that enhances all of our endeavors. Thank you all.”**

### David Braff, M.D.

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Dr. Braff is Distinguished Professor of Psychiatry and Director of the Schizophrenia Program at the University of California San Diego School of Medicine. He is Director and Lead Scientist of the National Institutes of Health (NIH) multi-site Consortium on the Genetics of Schizophrenia (COGS), designed to identify the genetic basis of neurophysiologic and cognitive abnormalities of schizophrenia.

William E. Bunney, Jr., M.D., Lieber Prize Selection Committee Chair, extols Dr. Braff's schizophrenia research as having had “worldwide influence on animal and human studies.” As one measure of his influence in the field, Dr. Braff has been reported by the Institute for Scientific Information (ISI) as being in the top half of the top one percent of most cited neuropsychiatric researchers. A dedicated clinician as well as researcher, he is the attending physician for over 12,000 patients with schizophrenia and other mental disorders. In his

investigations, Dr. Braff has applied brain imaging technology and genetic and genomic tools to dissect the abnormal neural circuits and brain architecture of schizophrenia. He has worked to identify brain biomarkers of the cognitive and physiological deficits schizophrenia imposes, and behavioral and genetically determined targets for developing new medications and psychosocial therapies.

A 1970 graduate of the Perelman School of Medicine at the University of Pennsylvania, Dr. Braff completed psychiatric and research training at Yale University and the University of California, San Francisco. He has served as a Councilor and President of the American College of Neuropsychopharmacology, and Councilor, Executive Secretary and President of the Society of Biological Psychiatry, which awarded him its gold medal for lifetime research accomplishments.



**THE LIEBER PRIZE  
FOR OUTSTANDING  
ACHIEVEMENT IN  
SCHIZOPHRENIA  
RESEARCH**

Established in 1987 by  
Constance Lieber, Foundation President  
Emerita, and Stephen Lieber, Chair of  
the Foundation’s Board of Directors.

**2014 Lieber Prizewinners**

**David Braff, M.D.**

University of California-San Diego School  
of Medicine

2007 NARSAD Distinguished  
Investigator Grantee

**Patrick F. Sullivan, M.D.,  
FRANZCP**

University of North Carolina-Chapel Hill

2010 NARSAD Distinguished  
Investigator Grantee

**“I am honored, humbled, and terrifically appreciative of being selected as a co-winner of the 2014 Lieber Prize. It is my deep hope that the work that led to my selection will continue so that we can greatly expand our knowledge of the basis of schizophrenia so that these new findings will, in turn, lead to advances that improve the lives of people living with schizophrenia and other serious mental disorders.”**



**Patrick F. Sullivan, M.D., FRANZCP**

As a psychiatric geneticist, Dr. Sullivan works to decode the molecular and cellular consequences of the genetic variation underlying schizophrenia. He heads large, multinational projects across a range of disorders, dividing his time between Sweden, where he is a Professor at the Karolinska Institutet, and the University of North Carolina, where he is the M. Hayworth & Family Distinguished Professor of Psychiatry and UNC Professor of Genetics and Psychiatry, as well as the Director of the Center for Psychiatric Genomics.

Dr. Sullivan is a founder and the lead investigator of the Psychiatric Genomics Consortium (PGC), in which 300 scientists from 70 institutions in 19 countries are conducting mega-analyses, involving 90,000 participants, of genetic risk for schizophrenia, depression, autism, bipolar disorder and attention-deficit hyperactivity disorder. The PGC, says Dr. Bunney, Lieber Prize Selection Committee Chair, has made “remarkable progress defining over 100 potential risk loci that meet genome-wide significance and which were among

genes expressed in the brain and in neurons.” Dr. Sullivan is also the principal investigator for a Swedish genetic study of 10,000 patients with schizophrenia and bipolar disorder, one of the few projects looking into the impact of environmental factors in these disorders.

Among his seminal findings, Dr. Sullivan uncovered a role for calcium biology in the etiology of schizophrenia and bipolar disorder. His research provided evidence supporting a pathway regulated by a microRNA, one of a class of small molecules shown to play key roles in gene expression.

Dr. Sullivan received his M.D. from the University of California, San Francisco, in 1988. He completed a residency in psychiatry at Western Psychiatric Institute and Clinic at the University of Pittsburgh and a fellowship at the Royal Australian and New Zealand College of Psychiatrists (FRANZCP).



**THE COLVIN PRIZE  
FOR OUTSTANDING  
ACHIEVEMENT IN  
MOOD DISORDERS  
RESEARCH**



“Receiving the Colvin Prize is a tremendous honor, both for me and for the colleagues with whom I worked over the past two decades to advance understanding of the neurobiology of bipolar disorder. While this prize affirms the significance of our past work, it also inspires and invigorates our current and future research, which we hope will improve the lives of people affected by bipolar disorder by leading to the discovery and development of new treatments.”

### Wayne C. Drevets, M.D.

Dr. Drevets’s pioneering neuroanatomical and neuro-imaging studies have greatly advanced the identification and delineation of abnormalities of brain structure and function in patients with unipolar and bipolar disorders, which has had a major impact on the treatment of these disorders. In 2012, following a distinguished 20-year career in academia, he became a Scientific Vice President and Disease Area Leader in Mood Disorders at Janssen Research & Development, of Johnson & Johnson, Inc., working toward the goal of developing faster, more effective antidepressants that will be effective for more patients.

Among the contributions noted by Robert Post, M.D., Colvin Prize Selection Committee Chair, Dr. Drevets’s identification of abnormalities in the subgenual anterior cingulate cortex in patients with depression has advanced the use of deep brain stimulation for the treatment of resistant depression (by targeting that area) and his imaging studies helped identify brain areas involved in the fast-acting antidepressant effects

of the medication ketamine. Dr. Drevets also demonstrated that lithium corrects the abnormal reductions in gray-matter volume in the cerebral cortex observed in patients with bipolar disorder.

Before moving to Janssen, Dr. Drevets held the Oxley Foundation Chair in Neuroscience Research at the University of Oklahoma, where he was founding President and Scientific Director of the Laureate Institute for Brain Research.

Dr. Drevets received his medical degree from the University of Kansas School of Medicine in 1983. He did a residency in psychiatry and a fellowship at the Washington University School of Medicine in St. Louis, and subsequently served on the faculties of Washington University and the University of Pittsburgh and later as Chief of the Section on Neuroimaging in Mood and Anxiety Disorders of the National Institute of Mental Health Intramural Research Program.



First awarded in 1993, this prize has been known successively as the Selo Prize, Falcone Prize and Bipolar Mood Prize. It was re-named in 2012 to honor a longtime Foundation supporter, the late Oliver D. Colvin, Jr., who bequeathed the largest single contribution in the Foundation’s history.

**2014 Colvin Prizewinners**

**Wayne C. Drevets, M.D.**

Janssen Research & Development  
 Johnson & Johnson, Inc.  
 1996 NARSAD Young Investigator Grantee  
 1999 NARSAD Independent Investigator Grantee

**Fritz A. Henn, M.D., Ph.D.**

Icahn School of Medicine at Mount Sinai

**“Winning the Colvin Prize for research in affective disorders was a total surprise and enormous honor. That my peers feel our work merits recognition is the greatest reward after a lifetime of work aimed at understanding and better treating major mental illness.”**



**Fritz A. Henn, M.D., Ph.D.**

In a wide-ranging career as researcher, clinician and scientific administrator, Dr. Henn has moved from research that created unique animal models of depression for brain exploration to his current efforts to design and test better treatments for human depressive illness, which he is leading in dual professorial posts at Cold Spring Harbor Laboratory and the Icahn School of Medicine at Mount Sinai.

Dr. Henn conducted his work on animal models in the 1990s, in Germany, where he was Professor of Psychiatry at the University of Heidelberg and simultaneously served as Director of the Central Institute of Mental Health in Mannheim.

Of particular importance among the models he developed were two mouse strains, in one of which mice were helpless when confronted with an escapable aversive stimuli, mimicking many symptoms of human depression; and the other in which mice were resistant to stress and able to quickly learn how to escape. He went on to elaborate the neurotransmitters and neural pathway involved in this learned helplessness model of depression.

“Emanating from this work,” Dr. Post, Colvin Prize Selection Committee Chair, explains, “he identified a little-known discrete area of brain that was hyperactive in both depressed animals and humans—the lateral habenula. If activity in this area is normalized, the animals no longer show depression-like behavior. He now has found a potential chemical treatment that decreases activity in the lateral habenula in animals and is conducting a clinical trial of it in patients with depression. This site is also being studied with deep brain stimulation for patients with refractory depression.

Dr. Henn earned a Ph.D. in biochemistry and biophysics at Johns Hopkins University and completed his M.D. and residency in psychiatry at Washington University School of Medicine. After returning from his posts in Germany, he served briefly as Associate Director of Brookhaven National Laboratory before joining Cold Spring Harbor in 2007. Among many honors, he received the Federal Cross of Merit, awarded by the President of Germany.



**THE RUANE PRIZE  
FOR OUTSTANDING  
ACHIEVEMENT IN  
CHILD & ADOLESCENT  
PSYCHIATRIC RESEARCH  
RESEARCH**

Established in 2000 by philanthropists Joy and William Ruane to recognize significant advances in research toward the understanding and treatment of early-onset brain and behavior disorders.

**2014 Ruane Prizewinner**

**Anita Thapar, M.D., Ph.D.**  
Cardiff University School of Medicine,  
UK



**“I am deeply honored and excited to be awarded the Ruane Prize this year. This award provides a huge boost to me and my team and hopefully others in my field. I have been very fortunate with wonderful mentors and colleagues and an exceptionally supportive family. I feel tremendously passionate about child and adolescent psychiatry and my drive to push forward is because of the patients I see, their families and their stories. This prize serves as further inspiration and I am really glad for our field that there is this type of recognition.”**

**Anita Thapar, M.D., Ph.D.**

Dr. Thapar M.D., Ph.D., was the first Professor in Child and Adolescent Psychiatry in Wales, appointed in 1999 at the Cardiff University School of Medicine. There she founded and heads the Academic Section of Child and Adolescent Psychiatry of the Institute of Psychological Medicine and Clinical Neurosciences and Developmental Disorders at the Medical Research Council (MRC) Centre for Neuropsychiatric Genetics and Genomics.

Dr. Thapar’s research has focused mainly on attention-deficit hyperactivity disorder (ADHD). More recently, she has been looking into adolescent depression and familial risk, focusing on the processes that contribute to cross-generational transmission and the mechanisms of resilience. Of her work, Daniel S. Pine, M.D., Ruane Prize Selection Committee Chair, states: “Anita Thapar’s contributions to child psychiatry are notable for a rare combination of breadth and depth.”

In early twin studies, Dr. Thapar and her team helped to establish the strong genetic component in ADHD, and later identified large, rare chromosomal deletions and duplications associated with risk for developing ADHD that overlap with genetic risks for autism and schizophrenia. She has designed novel ways to examine interactions between genetic and environmental factors involved in the risk for ADHD.

Dr. Thapar graduated from the University of Wales College of Medicine and was awarded an MRC Clinical Research Training Fellowship in Genetic Epidemiology and Child Psychiatry. After completing a Ph.D., she became Senior Lecturer in Child and Adolescent Psychiatry at the University of Manchester before her appointment to Cardiff University. She is a Fellow of the Royal College of Psychiatrists and of the U.K. Academy of Medical Sciences.



**THE GOLDMAN-RAKIC PRIZE FOR OUTSTANDING ACHIEVEMENT IN COGNITIVE NEUROSCIENCE**

Created by Constance and Stephen Lieber in memory of the renowned neuroscientist Patricia Goldman-Rakic after her untimely accidental death in 2003.

**2014 Goldman-Rakic Prizewinner**

**Richard L. Huganir, Ph.D.**

Johns Hopkins University  
School of Medicine

1999 NARSAD Distinguished Investigator Grantee

**“It is a great privilege to win the Goldman-Rakic Prize for Cognitive Neuroscience Research. Dr. Goldman-Rakic was a pioneer in our understanding of the biological basis of memory and how these processes are involved in cognitive disorders. This has been my life long career goal as well—to understand how memory is encoded in the brain and how these mechanisms are disrupted in cognitive disorders. I am honored to be associated with her legacy as well as with the outstanding previous winners of the Goldman-Rakic Prize.”**



**Richard L. Huganir, Ph.D.**

Dr. Huganir is Professor in the Departments of Biological Chemistry and of Pharmacology and Director of the Solomon H. Snyder Department of Neuroscience at the Johns Hopkins University School of Medicine and Co-Director of The Johns Hopkins Medicine Brain Science Institute. His research focuses on synapses and the cellular and molecular mechanisms that regulate the transmission of signals across the synapse and throughout the brain.

Through studies concentrating on the receptors that mediate the response of neurons to neurotransmitters released at synapses, Dr. Huganir has shown that regulation of receptor function is a major mechanism for regulation of neuronal connectivity and critical for many higher brain processes, including learning and memory, as well as for brain development.

“Dr. Huganir and his colleagues have a profoundly advanced understanding of the molecular mechanisms underlying the regulation of neurotransmitter receptor

function,” says Jack D. Barchas, M.D., Chair of the Goldman-Rakic Prize Selection Committee. “It has vital importance to studies of the causes of and potential new treatments for disorders such as schizophrenia, autism, dementias, mental retardation and addictions. Dr. Huganir was influenced by the work of Patricia Goldman-Rakic and the results of his studies would have been of great interest to her.”

A member of the Institute of Medicine and of the National Academy of Sciences, Dr. Huganir holds a Ph.D. in biochemistry and molecular and cell biology from Cornell University. After completing a postdoctoral fellowship at Yale University School of Medicine with Nobel Laureate and Foundation Scientific Council member Paul Greengard, Ph.D., he joined the Greengard laboratory at The Rockefeller University. He moved to Johns Hopkins in 1988. Dr. Huganir has been a Howard Hughes Medical Institute Investigator since 1988.



**THE SIDNEY R. BAER, JR. PRIZE FOR INNOVATIVE AND PROMISING SCHIZOPHRENIA RESEARCH**

Established in 2005, this prize is funded by the Sidney R. Baer, Jr., Foundation, and is awarded to young scientists selected by the year's Lieber Prizewinners.

**2014 Baer Prizewinners**

**Gregory A. Light, Ph.D.**

University of California-San Diego  
2003 and 2006 NARSAD Young Investigator Grantee  
2013 NARSAD Independent Investigator Grantee

**Stephan Ripke, M.D.**

Psychiatric Genomics Consortium

This year, **Gregory A. Light, Ph.D.**, was selected by Dr. Braff, and **Stephan Ripke, M.D.**, was selected by Dr. Sullivan to receive The Sidney R. Baer, Jr. Prize.



**"I am deeply honored to receive the Brain & Behavior Research Foundation Baer Prize for Innovative and Promising Research in Schizophrenia Research. My research would not have been possible without the generous support of NARSAD Grants at critical junctures of my career. This award strengthens my resolve to continue to develop treatment strategies that will ameliorate, prevent, and perhaps even cure schizophrenia and related psychotic illnesses in the next stages of my career. That I will be able to receive this honor alongside Dr. David Braff, an inspirational mentor, colleague and friend, is extraordinarily meaningful."**

**Gregory A. Light, Ph.D.**

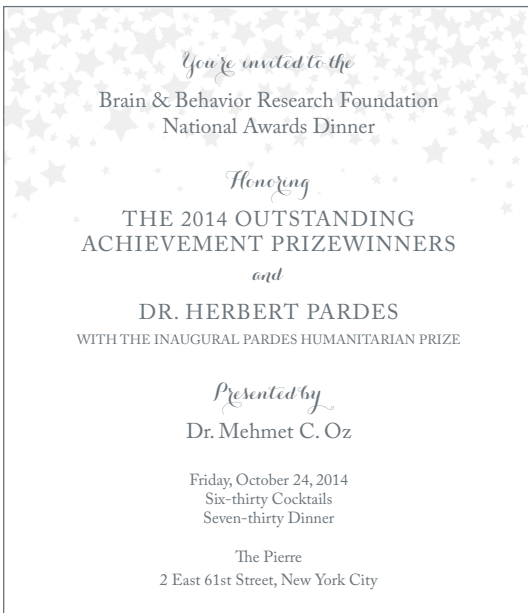
Dr. Light is an Associate Professor of Psychiatry at the University of California, San Diego (UCSD), Associate Director of the UCSD Schizophrenia Research Program, which Dr. Braff directs, and UCSD Site Coordinator for the NIH Consortium on the Genetics of Schizophrenia (COGS), a multi-institutional program under Dr. Braff's direction. He is also Associate Director of the Clinical Neuroscience and Genomics Unit of the San Diego Veterans Affairs Department.

Of his protégé, Dr. Braff has written: "Dr. Gregory Light's elegant series of 'NextGen' neurophysiological studies suggest that careful analyses of the electrical signals of brain activity, measured using electroencephalography (EEG), may reveal important harmonic relationships in the activity of brain circuits. The underlying premise is a simple one—that brain function is expressed by circuits that fire, and therefore generate

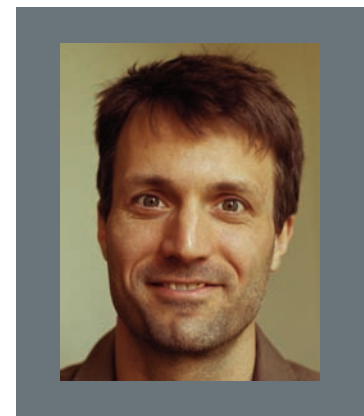
oscillating EEG signals at different frequencies in a symphonic array.

"Abnormalities in the structure and function of brain circuits would be reflected in cacophonous music, chords where the musical 'notes' are firing at the wrong rate (pitch), volume (amplitude) or timing. It is increasingly evident that schizophrenia is a disorder characterized by disturbances in the 'music of the brain hemispheres.'"

Dr. Light received a B.A. degree, summa cum laude, from Nazareth College and a Ph.D. in clinical neuropsychology under a joint doctoral program of UCSD and San Diego State University. He completed post-doctoral training in biological psychiatry and neuroscience before joining the UCSD faculty.



“Discovering that I was awarded the Baer Prize for Innovative and Promising Schizophrenia Research filled me with joy, pride and humility. I accept this prize on behalf of the numerous collaborators and patients, without whom the Psychiatric Genomics Consortium would not be possible. As a result of the immense collaborative efforts of the PGC, I believe that we are now on the path towards making seminal discoveries into the biology of this devastating disease. New therapeutic targets are imminent and the support of this prize will have a great impact on realizing this goal.”



## Stephan Ripke, M.D.

Dr. Ripke is the statistical analyst for the Psychiatric Genomics Consortium (PGC), a large, international collaboration created and led by Dr. Sullivan that is working to pinpoint the genetics of schizophrenia and other psychiatric disorders. From 2008 until returning to his native Germany this past summer, Dr. Ripke was at the Broad Institute of the Massachusetts Institute of Technology and Harvard University and Massachusetts General Hospital. He is continuing his association with the PGC at the Charité Universitätsmedizin Berlin, the oldest and most prominent hospital and medical school in Berlin.

Dr. Sullivan states: “Dr Ripke has been at the center of genomic discovery for schizophrenia since 2008. He designed, implemented and ran the genomic analysis pipeline that is the cornerstone of the efforts of the Psychiatric Genomics Consortium. He has made multiple critical contributions to our knowledge of the

genetic basis of schizophrenia, bipolar disorder and autism.”

Dr. Ripke performs the combined analysis of the raw genetic data from PGC members, which involves some 100 datasets from research groups from many countries. The computer pipeline he created standardizes data, imputes missing values, performs the final analysis and brings the results into a displayable format tool. One such tool, RICOPILI, is used for visualizing regions of interest in select genome-wide association studies data sets.

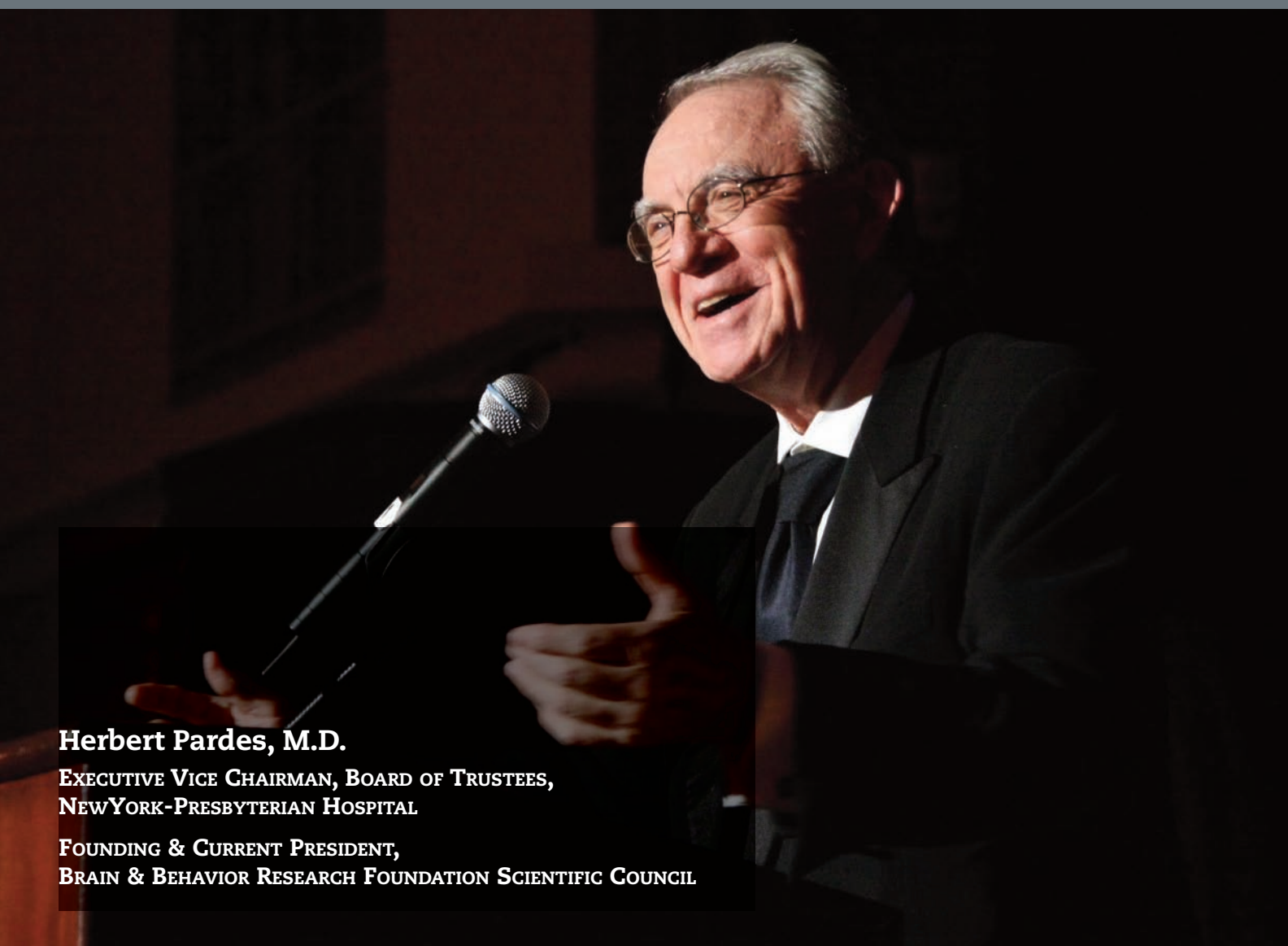
A magna cum laude graduate of the University of Hamburg, Germany, where he subsequently earned his medical degree, Dr. Ripke completed medical residency in Berlin, and then joined the Max Planck Institute of Psychiatry, in Munich, as a statistical geneticist before his appointment to the Broad Institute.



# THE INAUGURAL PARDES HUMANITARIAN PRIZE

# 2014

This prize honors those individuals who have had a powerful impact on many aspects of mental health. Characteristics of the recipient include a focus on humanitarianism as well as important contributions to education, prevention, research, administration, clinical care, mentoring and advocacy for policies in support of mental health. Dr. Herbert Pardes is our first honoree.



## **Herbert Pardes, M.D.**

**EXECUTIVE VICE CHAIRMAN, BOARD OF TRUSTEES,  
NEW YORK-PRESBYTERIAN HOSPITAL**

**FOUNDING & CURRENT PRESIDENT,  
BRAIN & BEHAVIOR RESEARCH FOUNDATION SCIENTIFIC COUNCIL**



Nationally recognized for the breadth of his expertise in education, research, clinical care and health policy, Dr. Pardes is a national spokesman for academic medical centers, for transformation of healthcare in an empathic, humanistic and patient-centered direction and for the power of technology and innovation to dramatically improve 21st century medicine. He is engaged at local, state and federal levels working on legislation to ensure the best medical and mental healthcare to all who need it.

A noted psychiatrist and outspoken advocate for mental health, Dr. Herbert Pardes has led the Foundation's distinguished 150-member Scientific Council since its inception in 1986. He is a former Director of the National Institute for Mental Health (NIMH) and former President and CEO (2000-2011) of the then newly merged NewYork-Presbyterian Hospital (1997), where he continues to serve as Executive Vice Chairman of the Board of Trustees.









Top:  
 Dr. Oz presenting The Pardes Humanitarian Prize to Dr. Herbert Pardes; Dr. Eric Kandel, Jeff Borenstein, Foundation President & CEO and Dr. Oz



Right:  
 Foundation President Emerita, Constance E. Lieber; National Awards Dinner Committee Co-Chairs, Suzanne Golden and Virginia Silver



Bottom:  
 Dr. Kay Redfield Jamison, Keynote Presenter at the Brain & Behavior Research Foundation Scientific Symposium earlier that day; Dr. Pardes with sons Lawrence and James



# Glossary

**amygdala:** (pp.4, 10) An almond-shaped structure located deep within the brain's medial temporal lobe (one in each hemisphere of the brain). The amygdala is part of the limbic system and is known to play a key role in the processing of emotions. Mental illnesses, including anxiety, autism spectrum disorder, depression, post-traumatic stress disorder, and phobias are suspected of being linked to abnormal functioning of the amygdala.

**BDNF (brain-derived neurotrophic factor):** (p.7) Growth-factor proteins that spur the birth of neurons in the brain and enhance the formation of synapses (connections between neurons), a process important in brain plasticity, or the capacity of the brain to repair and adapt to change. Studies in rodents have shown that exposure to chronic stress can lower BDNF levels and cause pathology in the hippocampus, a brain area critical in learning and memory, and whose dysfunction has been linked with depression in people. Successful antidepressant therapy is thought to raise BDNF levels. Many studies have focused on various negative impacts on brain function resulting from mutations in the gene that encodes the BDNF protein.

**dissociative symptoms:** (p.8) Those in which perceptions of sight and sound are distorted and a feeling of detachment—dissociation—is experienced. Sometimes described as out-of-body experiences. Dissociative symptoms can be induced by drugs (such as ketamine) but they are also among the symptoms reported by some sufferers of post-traumatic stress disorder (PTSD).

**dopamine:** (pp.5, 8) A neurotransmitter in the brain that can activate five types of dopamine receptors (D1, D2, D3, D4, D5) located on neurons (dopamine neurons) that are specifically activated by dopamine. It is a key element of the brain's reward system and is also believed to play a central role in the learning of new motor skills. Reduced dopamine concentrations in the prefrontal cortex are thought to contribute to ADHD and some symptoms of schizophrenia.

**epigenetic:** (p.3, 32) Refers to groups of molecules that attach to the double helix of DNA, "marking" or "tagging" it and helping to determine whether a given gene is switched "on" or "off," or the degree to which a gene that is switched on "expresses" itself (by giving a cell instructions to manufacture more or less of a specific protein).

**genome-wide association studies:** (p.32) Such studies often involve thousands of subjects and compare the genetic material of healthy individuals with people who have a particular illness. The hope of researchers in such studies is to identify DNA irregularities—misspellings in the genetic code—in people with the illness that do not occur, or occur much less frequently, in healthy people. Such differences are potential clues about genetic contributions to the illness. Genome-wide association studies are criticized by some for being inconsistent: genes supposedly linked with illnesses have not been identified in similar studies of the same illness.

**ketamine:** (p.8) A molecule that is an antagonist of the so-called NMDA class of nerve-cell receptors. It has been used primarily for inducing and maintaining general anesthesia, along with sedatives. It has also been used to treat depression in people diagnosed with bipolar disorder who have not responded to other antidepressants. Ketamine has been used experimentally, too, in treatment of refractory major depression, producing therapeutic effects in a matter of hours. This medication is controversial because of its potential side effects such as hallucinations and high blood pressure. Much research is underway to understand its mechanism of action and develop similarly functioning alternative medications.

**noradrenergic pathway:** (p.8) The system involving norepinephrine, or noradrenaline, in the transmission of nerve impulses. This adrenaline-like molecule is released from noradrenergic neurons and binds to adrenergic receptors. In addition to its role as a neurotransmitter, norepinephrine can also act as a hormone. It affects parts of the brain, such as the amygdala, where attention and responses are controlled. Along with epinephrine, norepinephrine also underlies the fight-or-flight response.

**serotonin:** (p.6) A neurotransmitter, or chemical messenger of the nervous system, which, when improperly produced or regulated, is thought to be involved in a range of mental illnesses, including depression. Serotonin is the target of today's widely used SSRI (selective serotonin reuptake inhibitor) antidepressant medicines such as fluoxetine (Prozac®) and paroxetine (Paxil®). These medications are designed to increase brain serotonin signals.



# With a Will... There's a Way to Help

A gift to the Foundation supports cutting-edge mental health research and future breakthroughs. There are many ways to support the Brain & Behavior Research Foundation during your lifetime and one particularly meaningful way is through planned giving.

## Name the Brain & Behavior Research Foundation as a beneficiary of your:

- Will or Trust
  - IRA or other retirement plan
  - Life insurance policy
  - Life income or other planned gift
- (Charitable Gift Annuity, Charitable Remainder Trust, Charitable Lead Trust or Remainder Interest in a personal residence)

For more information, please visit [bbrfoundation.org/plannedgiving](http://bbrfoundation.org/plannedgiving) or call 800-829-8289

## Making a Bequest

Bequests and other planned gifts have a profound and lasting impact on the scientific field in the form of the Brain & Behavior Research Foundation NARSAD Grants program and your gift helps incentivize the field of research by funding Young, Independent and Distinguished Investigators around the globe.

*100% of all donations for research are invested in NARSAD Grants, thanks to the generosity of two family foundations.*

Sign up for eNews:   
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# Investing in Breakthroughs — To Find a Cure

## OUR MISSION:

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

## OUR VISION:

To bring the joy of living to those affected by mental illness—those who are ill and their loved ones.

## 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, schizophrenia, anxiety, autism, and bipolar, attention-deficit hyperactivity, post-traumatic stress and obsessive-compulsive disorders.

## OUR CREDENTIALS:

For more than a quarter of a century, we have awarded over \$320 million worldwide to more than 3,800 scientists carefully selected by our prestigious Scientific Council.