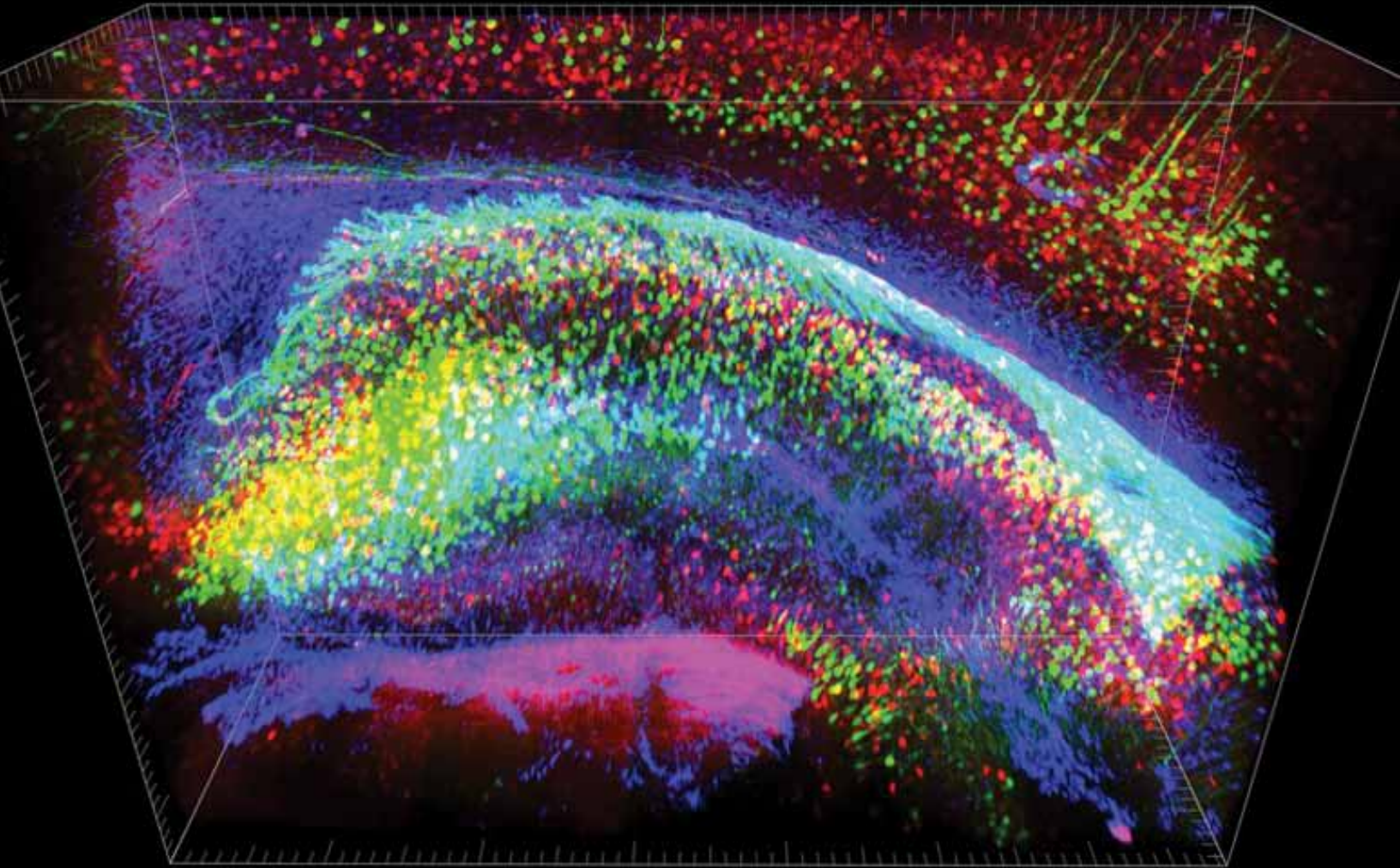


Annual Report 2013

 **BRAIN &
BEHAVIOR**
RESEARCH FOUNDATION
Awarding **NARSAD** Grants



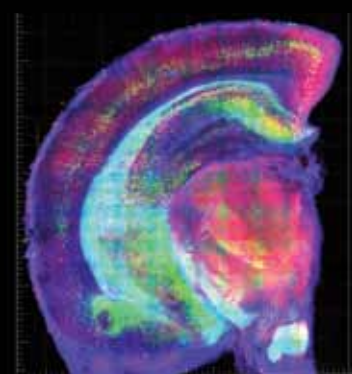
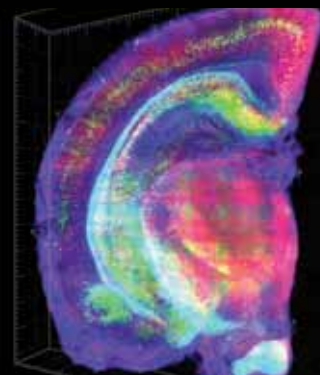
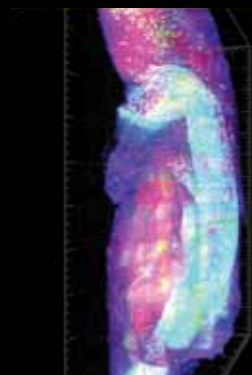
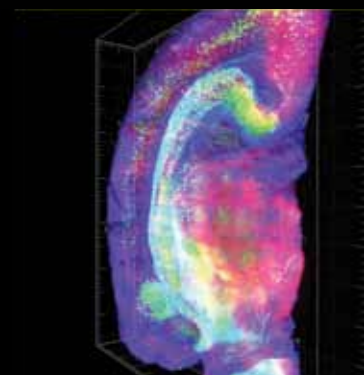
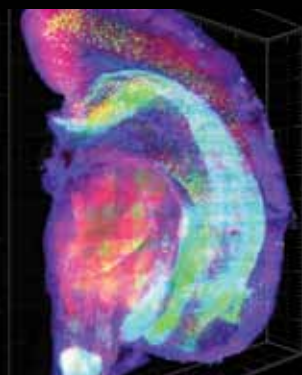
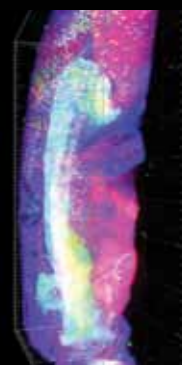
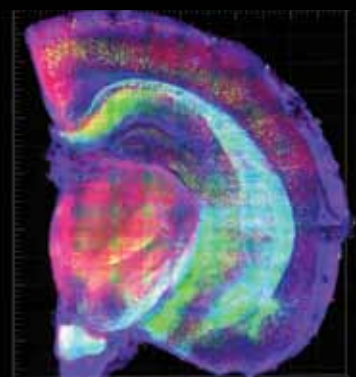
Transformative Research Improving Lives

FROM DISCOVERY TO RECOVERY

Cover and this page:

Stills from a video showing a mouse brain in unprecedented detail using the breakthrough new technology, CLARITY, developed by Karl Deisseroth, M.D., Ph.D. at his Stanford University lab. CLARITY enables researchers to obtain high-resolution three-dimensional imagery of the postmortem brain by rendering the brain essentially transparent. With this new technology, it is possible to see in detail the complex fine wiring and essential features underpinning function while also offering a global perspective of brain structure.

Dr. Deisseroth received the Foundation's 2013 Goldman-Rakic Prize for Outstanding Achievement in Cognitive Neuroscience for his groundbreaking work in developing new technologies that are revolutionizing brain and behavior research.



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 grants have proven to work as catalysts for extraordinary discoveries. Grantees report that their initial NARSAD* Grant led to subsequent funding on average 11 to 19 times the original grant amount.

*The organization was formerly known as NARSAD or the National Alliance for Research on Schizophrenia and Depression.

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Leadership Letter

Dear Foundation Supporters,

2013 was a year of substantial progress in brain and behavior research that will improve the lives of our loved ones. In April, the White House announced a major new public-private collaboration—the BRAIN (Brain Research through Advancing Innovative Neurotechnologies) Initiative—to “unlock” the mysteries of the brain and map its activity and functioning. This new Initiative acknowledges the unprecedented rate of advancement in neuroscience and the crucial role of new technologies in discovering how the brain functions and can dysfunction. The White House cited optogenetics, developed by Dr. Karl Deisseroth at Stanford with the early support of a Foundation NARSAD Grant, as one of the “landmark discoveries” that make this the right time to support a broad-based research program to find new ways to treat, cure, and even prevent brain disorders.

Funding discoveries that lead to deeper understanding of the brain and better ways of treating, curing and ultimately preventing mental illness has been the mission of the Brain & Behavior Research Foundation since its founding in the 1980s as the National Alliance for Research on Schizophrenia and Depression (NARSAD). Over time, Foundation-funded research has expanded to encompass the full range of mental illnesses, including addiction, anxiety, attention-deficit hyperactivity disorder, autism, bipolar disorder, eating disorders, post-traumatic stress disorder and others. The achievements made through our NARSAD Grants have helped structure the field of psychiatric research and continue to lead to breakthroughs. “From discovery to recovery” is how we encapsulate our mission: investing in cutting-edge research projects to improve the lives of those with mental illness.

Some of the major discoveries made by NARSAD Grantees in 2013, in basic research, new technologies and next-generation therapies, are highlighted in this report. Among them are findings that identify potential new triggers for depression and targets for its treatment; that hold out hope for early diagnosis and preventative measures for mental illness; that offer potential new ways to treat the negative symptoms of schizophrenia, such as loss of motivation and social withdrawal; and that demonstrate how to help those with serious mental illness take off weight and maintain a healthy lifestyle.

The quest to decipher the brain’s mysteries is a constant one. You will read about the innovative work of Dr. Kirsty Spalding at Karolinska Institutet in Sweden that led to the first ever quantification of neurogenesis, the growth of new brain cells, generated throughout human life. Dr. Marina Picciotto at Yale identified a signaling system in the brain that may be a root cause of depression and could transform the treatment of that illness. The latest breakthrough technology developed at Dr. Karl Deisseroth’s lab, called CLARITY, is also presented. These are just a few examples of the broad and inspiring work that is happening all over the country and the world.

Some members of our Community have also taken the courageous step of recounting their personal journeys toward recovery from mental illness. We share their stories of perseverance, coupled with their unshakeable conviction of the possibility

scientific research offers to fundamentally change what it means to live with a mental illness. We are very grateful for the example they set through their open sharing.

Innovation and advances, as any venture capitalist knows, involve risk management. NARSAD Grant projects are selected by members of the Foundation's all-volunteer Scientific Council, comprised of 146 leading neuroscientists across disciplines in brain and behavior research, including two Nobel Laureates and four former Directors of the National Institute of Mental Health. These men and women are uniquely qualified to identify new research projects that may be unproven but offer potential for significant breakthroughs. They recommend the most promising ideas to invest in, whether proposed by budding early career neuroscientists or by established scientists seeking to explore new paths. NARSAD Grants, awarded on three levels, Young Investigator, Independent Investigator and Distinguished Investigator, provide crucial support for investigators to pursue new ideas that may not get funded elsewhere.

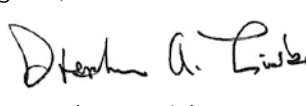
The Brain & Behavior Research Foundation can take managed risks because it is funded solely by private contributions, 100 percent of which are invested directly into NARSAD Grants for research; operational expenses are funded by two family foundations. In 2013 the Foundation awarded grants totaling \$17.3 million: 200 NARSAD Young Investigator Grants of \$60,000 each for a two-year period, 40 Independent Investigator Grants of \$100,000 each for two years and 15 Distinguished Investigator Grants of \$100,000 for one year.

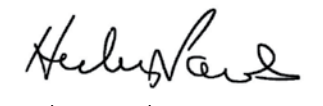
The Foundation's supporters know, usually from personal experience, the toll that mental illness takes. They understand the immense challenge of unlocking the mysteries of the brain that hold the key to better understanding and treatment of mental illness. With the Foundation's model of investing in cutting-edge ideas, identified with the expertise and insight of the Scientific Council, and made possible through private contributions from the Foundation's donor Community, we are making significant progress to improve the lives of those with mental illness. NARSAD Grants often support seeds of breakthrough ideas, and innovative researchers in their very early stages, which very possibly would never see the light of day without the initial NARSAD Grant support.

Your continued support at this time can make more of an impact than ever before with the confluence of public and private support for brain and behavior research spurred by the BRAIN Initiative. This is the era we will realize life-changing breakthroughs. Let's hasten the progress.

With sincere thanks and regards,


Jeffrey Borenstein, M.D.
President and CEO


Stephen A. Lieber
Chair, Board of Directors


Herbert Pardes, M.D.
President, Scientific Council





FROM DISCOVERY TO RECOVERY

Since 1987, the Foundation has awarded nearly \$310 million in its NARSAD Grants to more than 3,700 scientists around the world. Research projects aim to identify the causes and develop better treatments to improve the lives of those with mental illness.



BASIC RESEARCH

to understand what happens in the brain
to cause mental illness

NEW TECHNOLOGIES

to advance or create new ways of
studying and understanding the brain

NEXT GENERATION THERAPIES

to reduce symptoms of mental illness
and retrain the brain

Left: Parvalbumin-expressing neurons, a special kind of inhibitory interneuron linked to schizophrenia, as seen in a video from a human brain using the new technology CLARITY.



Innovative Methodology by Foundation Grantee Quantifies New Brain Cells in Adult Humans

KIRSTY SPALDING, PH.D.

Assistant Professor

Department of Cell and Molecular Biology

Karolinska Institutet, Sweden

It was believed for a long time that the human brain didn't change much once mature. That belief has been turned on its head over the course of the past fifteen years. With the support of a 1998 NARSAD Grant, Bruce S. McEwen, Ph.D., of The Rockefeller University, demonstrated that the brain can "remodel" its architecture and adapts to experience. Foundation Scientific Council Member Fred H. Gage, Ph.D., of the Salk Institute, and colleagues also demonstrated in 1998 that there is "neurogenesis" (the birth of new neurons) in the adult human hippocampus. This new study, published in the June 6th, 2013 issue of the journal *Cell*, quantifies for the first time the number of new neurons produced in adult humans.

2007 NARSAD Young Investigator Grantee Kirsty L. Spalding, Ph.D., and colleagues at Sweden's Karolinska Institutet demonstrated by "carbon-dating" neurons in preserved postmortem brains that the average adult generates 1,400 new hippocampal neurons every day in the prime of life; a rate that does not vary greatly over time and corresponds

with a turnover of almost two percent every year. Neurogenesis was confirmed in a single brain region, the hippocampus, and only in one subregion within it called the dentate gyrus. Reduced neurogenesis in this region is believed to be associated with depression, bipolar disorder, schizophrenia and some anxiety disorders.

The Karolinska team hypothesized that they could "carbon-date" neurons in preserved post-mortem brains since between 1945 and 1963 nuclear weapons were tested openly at above-ground sites. This increased atmospheric levels of Carbon-14 (^{14}C) and essentially "stamped" the DNA of all cells with ^{14}C (and other elements in the atmosphere) at the time of their birth. The researchers had already successfully carbon-dated a variety of other cells over the past decade, including fat cells. They eventually were able to refine the process to a point that it became sensitive enough to measure tiny amounts of ^{14}C in small hippocampus samples.

As the hippocampus is a region heavily implicated in many brain and behavior disorders, the new findings offer exciting proof of the brain's potential to recover from dysfunction throughout life.

Above: Dr. Spalding at work in her lab in Stockholm, Sweden.



Discovery of How Antidepressants Work Leads toward Improved Depression Treatments

HONGJUN SONG, PH.D.

Professor, Neurology & Neuroscience and Director, Stem Cell Program,
Institute for Cell Engineering,
Johns Hopkins University School of Medicine

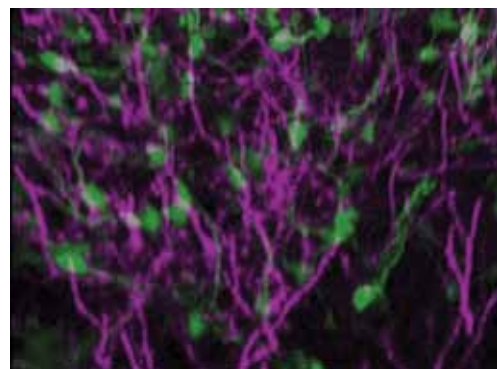
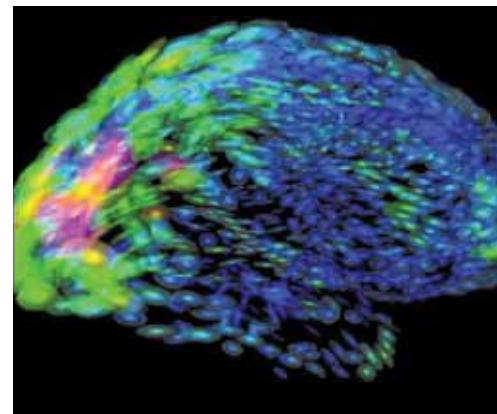
Building on findings from stem cell research in 2011 that helped explain how the brain can regenerate, NARSAD Grantees performed a sophisticated series of experiments and analyses that led them to discover a protein that helps electroconvulsive therapy (ECT) and antidepressant medications work. It was known that these therapies work by stimulating stem cell development in the brain, but it was not known how. The protein identified is produced by an inhibitor gene (sFRP3), known to regulate neural stem cells and the creation of new neurons. It appears that both antidepressant medication and ECT reduce the amount of protein produced by the sFRP3 gene, which then stimulates neural stem cell activity and the growth of new neurons.

The results of this new work may enable a personalized medicine approach to predict an individual's likely response to antidepressant treatment based on their genetic code as well as provide a

new target for the development of next generation therapies. The findings were published online in *Molecular Psychiatry* on Dec. 4, 2012 and in *Cell Stem Cell* on Feb. 7, 2013.

"Previous studies have shown that antidepressants and electroconvulsive therapy both activate neural stem cells in the adult brain to divide and form new neurons," commented NARSAD Grantee Hongjun Song, Ph.D. "What we were missing were the specific molecules linking antidepressant treatment and stem cell activation."

Other NARSAD Grantees involved in these studies include Mi-Hyeon Jang, Ph.D., Kimberly M. Christian, Ph.D., Guo-li Ming, M.D., Ph.D. and Mikhail V. Pletnikov, M.D., Ph.D. of the Johns Hopkins University; René Hen, Ph.D., Columbia University; and Elisabeth B. Binder, M.D., Ph.D., Max Planck Institute of Psychiatry.



Top: Video still from the lab of Hongjun Song, Ph.D. at Johns Hopkins University. Stem cells in the adult brain contribute to the development of new neurons that affect learning, memory and mood regulation.

Above: Video still from the lab of Hongjun Song, Ph.D. showing stem cells in purple and new neurons in green.



“I believe that research will change what it means to have a mental illness and will make it possible to treat an illness of the brain as well as an illness of the body.”

Nothing to be Ashamed of

On February 29, 2000, Albert Bensimon, then in his early fifties, stepped into the waters off Laguna Beach, California, and kept on walking. He remembers getting “pretty far out until the water was up to my neck. I honestly don’t know what stopped me.”

Bensimon (pictured left with his mother) had been battling major depression for years. His constant task as his family of origin’s disaster control manager had taken a heavy toll: coping with an out-of-control sister with schizophrenia, grieving a brother who vanished and is believed murdered, helping a father diagnosed with Alzheimer’s disease and a mother continuing to live in denial.

Al credits the right mix of talk therapy and medication with helping him re-engage in life and his work in computers and sales after his suicide attempt. But what helped me the most,” he says, “was my wife Pat’s consistent support. ... It was she who forcefully suggested I see a psychiatrist, and it was she who found the right one.” He also says that it is critical “to be brutally candid with oneself and others, to not try to mask, hide or diminish the fact that you—or they—need help.”

Today, Al and Pat live in Georgia near their daughter, now married and a successful corporate lawyer. Their first grandchild was born last August. Their son and his family live in southwest Florida. Life, says Al, is pretty good.

Al explains why he has supported the Foundation for over two decades: I believe that research will change what it means to have a mental illness and will make it possible to treat an illness of the brain as well as an illness of the body.”

NARSAD Grantee and Team Discover New Depression Trigger and Treatment Target

MARINA PICCIOTTO, PH.D.

Charles B. G. Murphy Professor of Psychiatry
Professor of Neurobiology and Pharmacology
Assistant Chair for Basic Science Research, Psychiatry
Yale University School of Medicine

For decades, many scientists have favored a theory of depression that stresses the impact of abnormally low levels of a signal-carrying chemical, called serotonin. In new research at Yale University, Dr. Marina Picciotto led a team of researchers in the discovery that increases in a signaling chemical called acetylcholine may be central in causing depression, leading to a new hypothesis that it is the disruption of acetylcholine, and not only serotonin or other neurotransmitters, that sets depression in motion. Targeting acetylcholine disruption may be a way to treat the root cause of depression and could lead to more effective treatments.

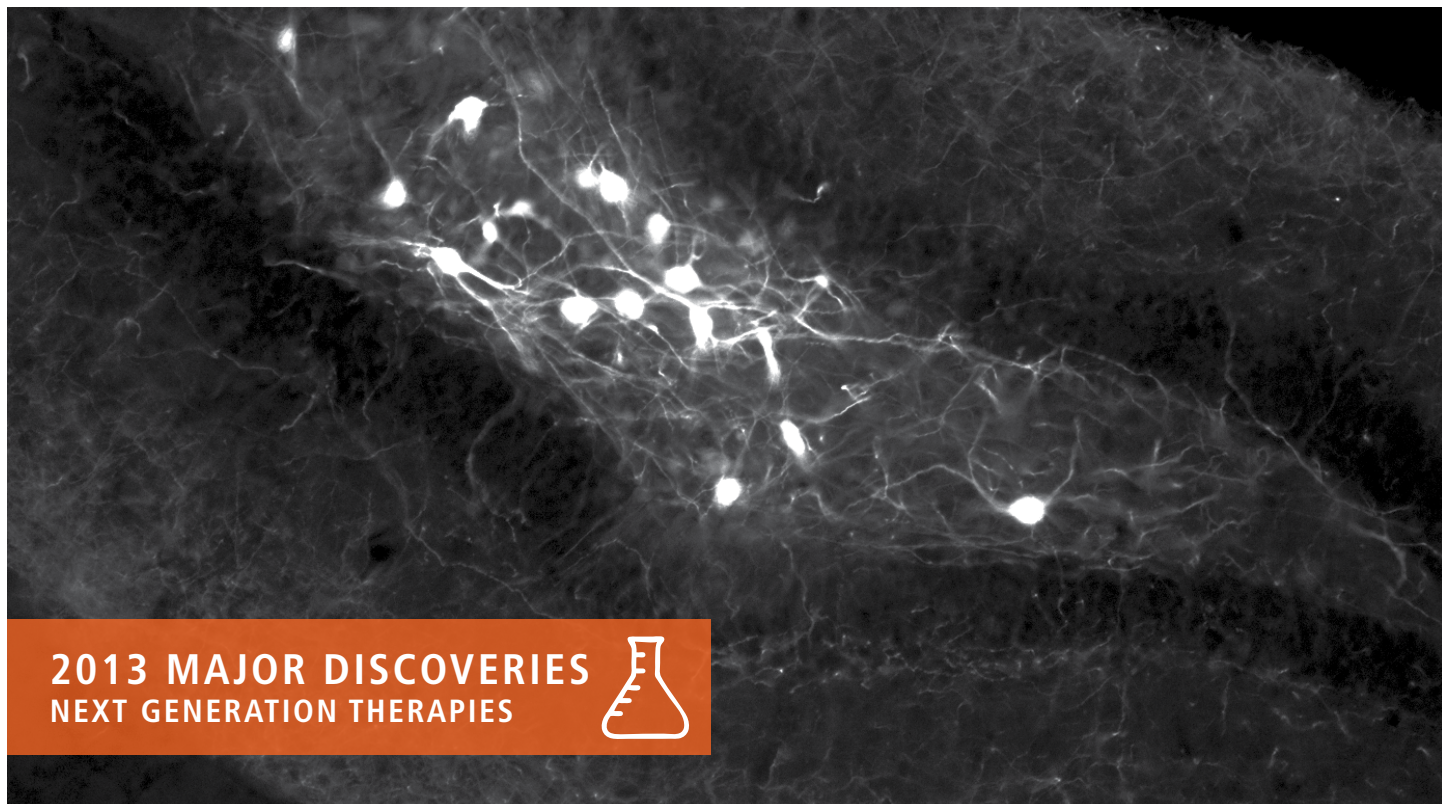
"Serotonin may be treating the problem," Dr. Picciotto explained, "but acetylcholine disruption may be a primary cause of depression. If we can treat the root cause, perhaps we can get a better response from the patient."

The Yale team's experiments demonstrate that abnormally

high levels of acetylcholine in the brain can cause depression and anxiety symptoms in mice. In the brains of non-depressed mice—and people—an enzyme called acetylcholinesterase (AChE) is produced to lower acetylcholine levels. The team showed that when depressed mice were given Prozac®, a common antidepressant medication that regulates serotonin levels, AChE levels were raised, and abnormally high levels of acetylcholine were thus brought under control. By experimentally blocking the "ports," called receptors, where acetylcholine molecules "dock" with nerve cells in the brain, the team was able to reverse depression in mice.

The Yale team also demonstrated that interruptions in acetylcholine signaling in the brain area called the hippocampus—important in memory and mood—promote depression and anxiety in mice. Further research studies can now be undertaken to determine if medications that target acetylcholine are more effective in treating depression.

Below: Higher power magnification of hippocampal neurons expressing the AAV-AChE-shRNA-GFP construct. Individual neuronal cell bodies and their processes can be seen in the dentate gyrus of the hippocampus.





Over lunch ... Dr. Kim expressed ... his deep feelings for the challenges that people like Rebecca face as the motivation for his studies.

Supporting Science That Will Make a Difference in Their Daughter's Life

In August, Harryet and Stuart Ehrlich took a mini-vacation from their home in New Jersey to Baltimore, Maryland. The highlight of their trip was a stop at the Johns Hopkins University School of Medicine Department of Psychiatry and Behavioral Sciences to meet NARSAD Young Investigator Grantee Sun-Hong Kim, Ph.D.

The Ehrlichs (pictured above with their daughter Rebecca) and Dr. Kim are Research Partners, participants in a Brain & Behavior Research Foundation program that matches major donors with scientists in a common area of interest. The Ehrlichs' daughter Rebecca has struggled for much of her life with the symptoms of bipolar disorder. Dr. Kim's research aims to find an explanation of disturbances that occur in the developing brain as neural pathways are laid down. These disturbances are implicated in mental illness.

The Ehrlichs found the meeting with Dr. Kim "exciting and unexpectedly moving." As they recount: "It's hard to explain the power of the connection we felt getting to know a scientist who has the potential to make a difference in our daughter's life, as well as the lives of so many others who struggle every day. Visiting Sun-Hong's lab, meeting his team and listening intently to understand as best we could what his research is intended to achieve was far more than we had expected to experience."

Over lunch the Ehrlichs got to know their Research Partner on a more personal level as Dr. Kim expressed his appreciation for his first grant, making it possible for him to launch his independent research, and his deep feelings for the challenges that people like Rebecca face as the motivation for his studies.

With Cutting Edge Technology, New Way to Reduce Anxiety Symptoms Discovered

RENE HEN, PH.D.

Professor of Psychiatry, Neuroscience, Pharmacology
Director, Division of Integrative Neuroscience, Department of Psychiatry
New York State Psychiatric Institute
Columbia University Medical Center (CUMC)

Foundation Scientific Council Member and three-time NARSAD Grantee, Rene Hen, Ph.D. of Columbia University led a team of researchers that may have found a way to reduce anxiety in post-traumatic stress disorder and panic disorder, without negatively affecting learning. The research team utilized a cutting-edge new technology called optogenetics developed by Karl Deisseroth, M.D., Ph.D. of Stanford University with the support of a 2005 NARSAD Young Investigator Grant. Results of the study were published in the *journal Neuron* on March 6, 2013.

With the use of optogenetics, the researchers were able to selectively activate neurons in the dentate gyrus region of the brain (a portion of the hippocampus) and found for the first time that they could reduce symptoms of anxiety in mice without affecting learning. The dentate gyrus has been known to play a key role in learning and some evidence has suggested it may contribute to anxiety. "But until now no one has been able to figure out how the hippocampus could be

involved in both processes," explained Dr. Hen.

The researchers discovered that elevating cell activity in the dorsal dentate gyrus region increased the animals' desire to explore their environment but also disrupted their ability to learn. Elevating activity in the ventral dentate gyrus region lowered their anxiety, with no effect on learning. "It turns out that different parts of the dentate gyrus have somewhat different functions, with the dorsal portion largely dedicated to learning and the ventral portion dedicated to anxiety," said lead author Mazen A. Kheirbek, Ph.D., a NARSAD Young Investigator Grantee and postdoctoral fellow in neuroscience at CUMC.

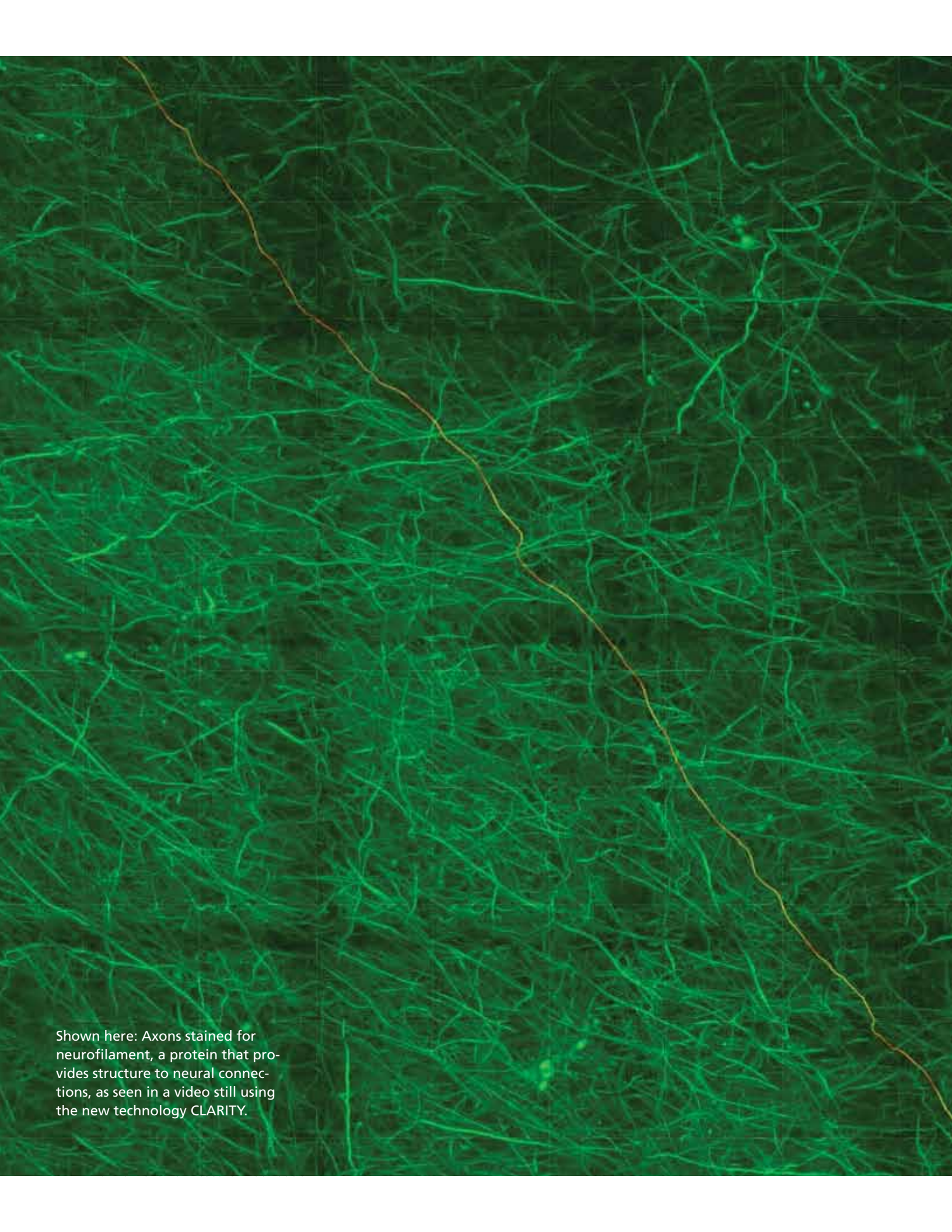
"The therapeutic implication is that it may be possible to relieve anxiety in people with anxiety disorders by targeting the ventral dentate gyrus, perhaps with medications or deep-brain stimulation, without affecting learning," said Dr. Hen.

Below: Optogenetics is a new technology that has revolutionized systems neuroscience by providing precise control over brain circuitry in awake, behaving animals. Optogenetics involves the use of light to rapidly open and close the membrane channels that make neurons fire and cease firing and allows for observation of the effects on behavior. Developed at the lab of Karl Deisseroth, M.D., Ph.D. with the support of a 2005 NARSAD Young Investigator Grant.



2013 MAJOR DISCOVERIES
NEW TECHNOLOGIES



A high-resolution micrograph showing a complex, dense network of green-stained axons. The axons are thin, thread-like structures that crisscross the entire field of view. A single, thicker, yellowish line runs diagonally from the top left towards the bottom right, standing out from the green network. The background is dark, making the green and yellow structures highly visible.

Shown here: Axons stained for neurofilament, a protein that provides structure to neural connections, as seen in a video still using the new technology CLARITY.

New 3-D Imaging Technology Promises Breakthroughs in Brain Research

KARL DEISSEROTH, M.D., PH.D.

Professor of Bioengineering and of Psychiatry and Behavioral Sciences, Stanford University School of Medicine

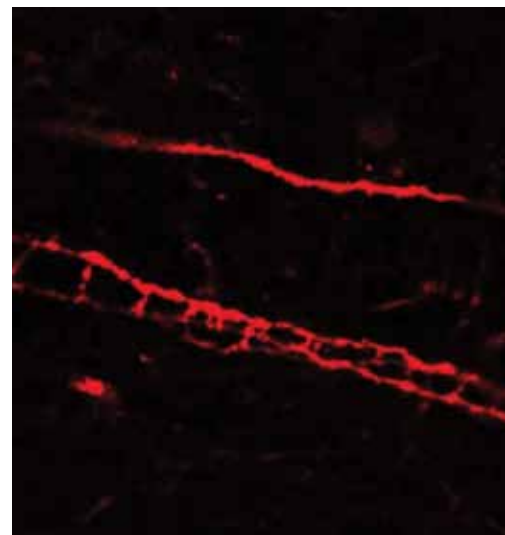
Foundation Scientific Council Member and former NARSAD Grantee, Karl Deisseroth, M.D., Ph.D., led a team at Stanford in developing a new experimental method they are calling “CLARITY,” that enables researchers for the first time to obtain high-resolution three-dimensional imagery of the brain. The new method, as reported April 10, 2013 in *Nature*, renders the brain essentially transparent, making it possible to see in detail its complex fine wiring and essential features underpinning the functioning of the brain while also offering a global perspective of brain structure.

Prior to CLARITY, creating a 3-D image of the brain required carving its tissue into hundreds or thousands of hair-thin slices, scanning images of the slices in microscopic detail, and then painstakingly realigning the sections. Now a 3-D view of all the complex circuitry in the brain is possible while all of the important structures of the brain remain intact and in place (neurons, axons, dendrites, synapses, proteins, nucleic acids, etc.). By replacing the brain’s fat with a clear gel, CLARITY turns the opaque and impenetrable

brain transparent and permeable. The hydrogel also importantly holds the brain’s anatomy intact and because it is permeable, the brain can be stained to localize proteins, neurotransmitters and genes at a high resolution.

“Studying intact systems with this sort of molecular resolution and global scope—to be able to see the fine detail and the big picture at the same time—has been a major unmet goal in biology, and a goal that CLARITY begins to address,” says Dr. Deisseroth. The new imaging technology can be used to make any organ transparent, but it was the challenges of imaging the brain that motivated Dr. Deisseroth, who hopes to dissect psychiatric disorders such as schizophrenia, depression and autism.

“If CLARITY is a predictor, the next few years could be a period of rapid new insights into brain structure and function,” commented Thomas Insel, M.D., Director of the National Institute of Mental Health. “One can barely begin to imagine how tools like CLARITY will change our concepts of how the brain works in health and disease.”



Above: Video still of a donated human brain from a patient with autism as seen with the new technology CLARITY.

2013 MAJOR DISCOVERIES
NEW TECHNOLOGIES



Foundation-Funded Study Identifies Schizophrenia Early Warning Sign

SCOTT A. SCHOBEL, M.D., M.S.
Adjunct Associate Research Scientist
Division of Translational Imaging
New York State Psychiatric Institute
Columbia University Medical Center

A diagnosis of schizophrenia is often preceded by a “prodromal” phase of the illness, in which milder symptoms are present for weeks or even years before developing into full-blown psychosis. With the use of brain imaging technology, a study funded in part by a NARSAD Young Investigator Grant to Scott A. Schobel, M.D., M.S., shows that elevated levels of the neurotransmitter glutamate in the hippocampus region of the brain may cause the transition to psychosis in people at high risk for developing schizophrenia. The study was published April 10, 2013 in *Neuron*.

Dr. Schobel and team conducted brain imaging to examine the hippocampus of people who sought psychiatric help for symptoms like mild perceptual hallucinations or delusions that did not reach the threshold of full psychosis. The study volunteers were imaged twice—at the beginning of the study, and again nearly two and a half years later, after 40% of the subjects had been diagnosed with a psychotic disorder.

In the patients who later developed psychosis, increased glutamate activity was associated with some hippocampal abnormalities during the prodromal phase, but these abnormalities were much more pronounced following a diagnosis. In addition, the degree of hippocampal abnormality during the prodromal phase could be used to predict the amount of time before a patient developed psychosis. Taken together, the findings strongly suggest that increased glutamate activity can be an early warning sign for hippocampal dysfunction that will progress during the transition from prodromal to full-blown psychosis.

The researchers also tested the mechanism behind these alterations using brain imaging in animal models, finding that increasing glutamate activity also produced similar patterns of hippocampal abnormalities—and schizophrenia-like symptoms—in rodents. This suggests that controlling glutamate levels in high risk individuals or those in the early stage of illness could be an effective preventive and/or therapeutic strategy.

Below: Hippocampus of a human brain illuminated with multiple fluorescent proteins.
© WBUR Boston NPR



Heartache and Hard-Won Progress

Miriam Katowitz and Arthur Radin were able to provide their children with a good home and excellent education, but discovered that they could not provide a bulwark against mental illness. Their older son, David, had his first psychotic episode during his first semester at college.

Now 44, David lives with schizophrenia, and over the ensuing years, he and his family have experienced both heartache and hard-won progress. After a harrowing beginning in which he was treated with haloperidol, which worsened his condition and left him with traces of tardive dyskinesia, a side effect that causes involuntary, tic-like movements, he has been stabilized on risperidone, one of the atypical antipsychotic medications. The development of this class of medications was sparked by the work of Brain & Behavior Research Foundation Scientific Council Member Herbert Meltzer, M.D., with the support of a 1988 NARSAD Grant. Although not effective for all patients, these antipsychotics have been life-saving for millions of patients who respond positively to them.

The onset of David's illness coincided with the founding of NARSAD, now the Brain & Behavior Research Foundation. Miriam and Arthur learned of its existence through "an ad in the paper," Miriam recalls. "We gave a little money, and then we thought, 'what else can we do?'"

Since that time, the couple's involvement has grown with the organization. They believe that scientific research offers the best hope for families like theirs. Arthur has served on the Foundation's Board of Directors for five years, the last three years as its Treasurer. And, since 1997, as participants in the Research Partners Program, which pairs donors with scientists working in a field of interest to the donors, the couple has supported 11 NARSAD Young Investigator Grantees working on various aspects of schizophrenia.



© Kate Burton

Miriam and Art believe that scientific research offers the best hope for families like theirs.

Behavioral Therapy Program Achieves Weight Loss for People with Mental Illness

GAIL L. DAUMIT, M.D., M.H.S.

Associate Director, Welch Center for Prevention,
Epidemiology and Clinical Research
Associate Professor of Medicine
Johns Hopkins University

NARSAD Grantees Gail L. Daumit, M.D., M.H.S.; Faith B. Dickerson, Ph.D., M.P.H.; and Richard W. Goldberg, Ph.D., launched the longest and largest randomized behavioral weight loss trial in participants with mental illness that's ever been done. Project "ACHIEVE" was tailored especially for people with mental illnesses, such as bipolar disorder, schizophrenia and depression. Results of the study, published in *The New England Journal of Medicine* on April 25, 2013, show that people with serious mental illnesses lose weight and can keep it off through a modified lifestyle intervention program.

"Patients with serious mental illness have an extremely high risk of premature mortality—about three times higher than the overall population—and about 80% are overweight or obese," said Dr. Daumit, the study's lead author. "They really need weight loss programs." One issue is the antipsychotic

(or psychotropic) medications these patients take that are known to increase appetite and cause weight gain.

Project ACHIEVE was based on lifestyle changes known to be effective in the general population, and was amended to account for cognitive and behavioral challenges present in mental illness. The study had almost 300 participants who used an average of 3 psychotropic medications each. Half were placed in a program focused on improving eating and exercise habits while the other half received no special training. Those in the intervention group lost an average of 7 pounds over the course of the study and continued to maintain the loss.

The researchers report that these results are very consistent with results from weight loss programs with the general public. "The change that we measured was weight and we saw that physical health change," said Dr. Daumit. "But we also saw participants that felt better about themselves overall."

Below: Still from video depicting Project "Achieve" showing patients with mental illness participating in the lifestyle intervention program. Courtesy of Gail Daumit, M.D., M.H.S.



2013 MAJOR DISCOVERIES
NEXT GENERATION THERAPIES





Researchers Find Way to Increase Neuroplasticity & Treat “Negative” Symptoms of Schizophrenia

JOSEPH T. COYLE, M.D.
Eben S. Draper Professor of Psychiatry and Neuroscience
Harvard Medical School

Recent research at McLean Hospital and Harvard University Medical School, led by Joseph T. Coyle, M.D., a NARSAD Distinguished Investigator Grantee and Foundation Scientific Council Member, shows a very promising possibility for the future treatment of the “negative” symptoms of schizophrenia by improving neuroplasticity—the ability of the nerve cell networks in the brain to physically adapt to changing conditions. Negative symptoms in schizophrenia include decrease in motivation, lack of attention, emotional flatness, memory loss and social withdrawal.

The researchers worked with mice to determine if they could find a cluster of abnormalities known to affect the brain’s hippocampus in people with schizophrenia. The mice were genetically engineered to have very low N-methyl-D-aspartate (NMDA) receptor activity in the brain, a condition suspected to be linked to impaired synaptic plasticity, memory formation and the negative symptoms of schizophrenia.

In a paper published in the May 31, 2013 issue of *Proceedings of the National Academy of Sciences*, Dr. Coyle and colleagues reported that the mice with low NMDA receptor activity “displayed impaired hippocampal plasticity, as well as the morphological [shape], neurochemical and cognitive abnormalities consistent with what is observed in schizophrenia.” Then they went further. The mice used in the experiments had only about 10 percent of normal NMDA receptor activity because they had been engineered to lack D-serine, one of two molecules needed to activate the receptors. When the researchers treated the mice with D-serine, NMDA receptor function in the hippocampus was restored. Over time, all of the observed hippocampal symptoms proved reversible.

While not the sole cause of schizophrenia, the ability to reverse low activity (“hypoactivity”) in NMDA receptors in the brain in mice suggests it may be possible to develop D-serine-based treatments for use in that could prove to be a breakthrough in the treatment of schizophrenia.

Above: Dr. Coyle at work in his lab in Boston, Massachusetts.



Historic Study Finds Brain Scans Can Guide Depression Treatment Decisions

HELEN S. MAYBERG, M.D.

Professor of Psychiatry, Neurology and Radiology
Emory University School of Medicine

Using positron emission tomography (PET) scan images, researchers have identified specific brain activity that can potentially predict whether people with major depressive disorder (MDD) will best respond to an antidepressant medication or psychotherapy.

Helen S. Mayberg, M.D., Foundation Scientific Council Member, led the study. Dr. Mayberg pioneered work using PET scans to better understand depression with her first NARSAD Young Investigator Grant in 1991, and went on to demonstrate that the subcallosal cingulate (or “Brodmann Area 25”) region of the brain is a key locus of pathology in depression. Dr. Mayberg is now well known for her innovative work in piloting deep brain stimulation (DBS) to target Area 25 to treat patients with resistant depression—a study she undertook with the support of a NARSAD Distinguished Investigator Grant in 2002.

In the current study, published in the June 12, 2013 issue of *JAMA Psychiatry*, Dr. Mayberg and colleagues sought to

identify a biomarker (biological predictor) that could identify which type of treatment a patient would benefit from based on the individual’s brain activity. After having an initial baseline PET scan, 33 patients completed 12 weeks on escitalopram (a common antidepressant medication) and 34 patients completed 12 weeks of cognitive behavioral therapy (or CBT, a specific type of “talk therapy”). Using the pre-treatment PET scans, they compared the scan patterns in those patients as a function of their treatment type and response.

The researchers found that in the 38 patients who had clear outcomes, there was lower-than-normal activity in a brain region called the right anterior insula linked with remission after CBT and poor response to the antidepressant drug. Overactivity of the same region was linked with remission after drug treatment and poor response to CBT. The results of this new work are of historic importance. The data clearly suggest that treatment decisions might be based on a patient’s brain state, offering a first potential biomarker for treatment selection.

Below: Helen S. Mayberg, M.D. of Emory University School of Medicine.



With Persistence, Recovering from Depression

Twenty years ago, Steven Addlestone, then a recent graduate of Vanderbilt University Law School, had just begun his practice with a major Atlanta law firm and was newly engaged to his law-school sweetheart. It should have been one of the happiest times of his life.

But seemingly out of the blue he spiraled into a major depression that lasted four months. As his moods yo-yoed beyond his control, Mr. Addlestone (pictured above with his wife, Claire; son Ethan and daughter Emily) went from one treatment to another without much success. It would be 12 years before his doctor, Paul Holtzheimer, M.D., a former trainee of Foundation Scientific Council Member, Helen Mayberg, M.D., and a 2007 NARSAD Young Investigator Grantee, was able to stabilize his symptoms.

What sustained him during those years and made it possible for him to function was the support he received from his doctors, family and colleagues who, he says, “understood what was going on and were willing to work with me. There’s still a lot of stigma attached to mental illness,” he says, “and often people don’t seek treatment because they’re embarrassed at having a ‘weakness’ they don’t want to admit.”

Now, at 44, having had no major relapses for the past seven years and feeling “really well,” Mr. Addlestone holds a post as senior counsel at a Fortune 500 company in Kingsport, Tennessee, where he lives with his wife, Claire, and their teenage son and daughter. The family continues to enthusiastically support the Brain & Behavior Research Foundation, saying: “We think it is all so promising. We marvel how far research and treatment have come just since I started having my problems. It’s really uplifting.”



“There’s still a lot of stigma attached to mental illness,” he says, “and often people don’t seek treatment because they’re embarrassed at having a ‘weakness’ they don’t want to admit.”





fMRI Brain Scans May Help Diagnose Depression in Preschoolers

JOAN L. LUBY, M.D.
Professor of Psychiatry
Director, Early Emotional Development Program
Washington University of St. Louis (WUSTL) School of Medicine

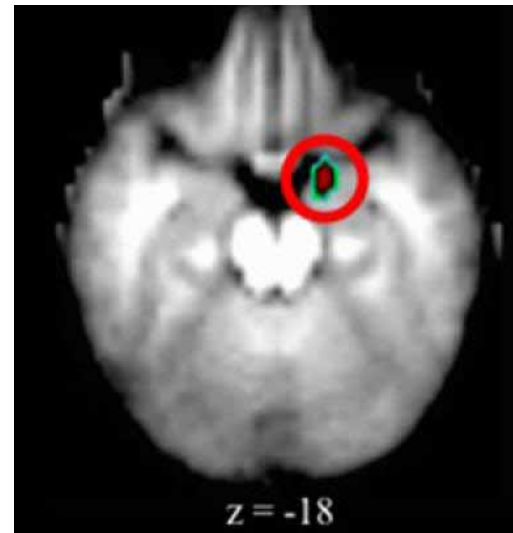
Brain scan studies of people from elementary school age right up through older adulthood have identified activity patterns associated with depression in a key brain region for emotional processing and regulating known as the amygdala. In a first-of-its-kind study of the preschool age group, a research team at Washington University of St. Louis (WUSTL) School of Medicine, including Brain & Behavior Research Foundation NARSAD Grantees Joan L. Luby, M.D. and Deanna M. Barch, Ph.D., used functional magnetic resonance imaging (fMRI) to study the amygdala activity of depressed four to six year olds.

The researchers set out to make and compare highly-detailed images of brain activity in 23 non-medicated preschoolers with depression and 31 non-depressed peers. As has been done with other age groups, the children were shown pictures of peoples' faces with happy, sad, fearful and neutral expressions. The scans of preschoolers with depression showed much more activity (more blood flow) in the amygdala no matter what facial expression the

child viewed. This is a contrast to findings in the non-depressed preschoolers and provides the earliest evidence yet of changes in brain function in young children with depression.

The researchers report that their findings—published in the July issue of the *Journal of the American Academy of Child & Adolescent Psychiatry*—could lead to identification and treatment of depressed children earlier in the course of the illness, potentially preventing recurring and long-lasting consequences of depression.

Drs. Luby and Barch are early emotional development experts with an interest in the developmental trajectories of mental illness and causes, treatments and early intervention to allow for better outcomes. Deanna M. Barch, Ph.D. is Professor of Psychology, Psychiatry and Radiology, WUSTL and Center Director, The Conte Center for Neuroscience of Mental Disorders, a collaboration between Washington, Yale and Johns Hopkins universities.



Above: Brain scans of preschoolers with depression revealed elevated activity in the amygdala (the small area in the red circle) when compared with scans of young children exhibiting no signs of depression. (credit: Washington University School of Medicine)

Opposite page: Joan L. Luby, M.D. demonstrates play therapy with a preschooler. (credit: Mark Gilliland)

WELCOME

TO OUR NEWEST MEMBERS OF THE SCIENTIFIC COUNCIL

The Scientific Council is comprised of 146 leaders across disciplines in brain and behavior research who volunteer their time to review NARSAD Grant applications and select the most promising research projects to fund.



ANISSA ABI-DARGHAM, M.D.

Professor of Clinical Psychiatry and Radiology, Columbia University College of Physicians and Surgeons
Director of the Division of Translational Imaging and Director of Clinical and Imaging Research
Lieber Center for Schizophrenia Research
New York State Psychiatric Institute

Dr. Abi-Dargham's research has focused on using molecular imaging techniques (SPECT and PET) to study the pathophysiology of schizophrenia, schizophrenia spectrum disorders, addiction (alcoholism and more recently cannabis dependence) and co-morbid schizophrenia with addiction. Her research has resulted in findings describing the complex alterations of dopamine transmission in schizophrenia and has shown increased striatal dopamine release in schizophrenia. This has become one of the most established findings of schizophrenia research and is now being tested as a biomarker for risk in patients displaying early symptom signs ("prodromal" patients).

Dr. Abi-Dargham is from Beirut, Lebanon where she received her medical degree at St. Joseph University's Medical School.

NARSAD Grants: Young Investigator 1993 and 1997; Independent Investigator in 2000;
Distinguished Investigator in 2008

Foundation Prizes: 2002 Klerman Honorable Mention Prize for Exceptional Clinical Research by a Young Investigator



GARY ASTON-JONES, PH.D.

William E. Murray Endowed Chair of Excellence in Neuroscience
and Director of the Cognitive Neuroscience Center and the Neuroscience Institute
Medical University of South Carolina

Dr. Aston-Jones's research focuses on the modulation of reward behavior, addiction and cognitive functions by ascending brain monoamine and peptide systems, and uses neurophysiology, neuroanatomy and behavioral neuropharmacology in animal studies. He has directed a well-funded lab for more than 20 years and chaired the Neurobiology of Motivated Behavior study section at National Institutes of Health. He and his colleagues have recently described a role for the brain noradrenergic locus coeruleus system in decision and behavioral flexibility, as well as a key role for the neuropeptides orexin/hypocretins in reward processing and addiction.

Dr. Aston-Jones earned his Ph.D. in Neurobiology from the California Institute of Technology with Floyd Bloom, and was a Postdoctoral Fellow at the Salk Institute.



KAREN F. BERMAN, M.D.

Senior Investigator and Chief of the Clinical Brain Disorders Branch
and the Section on Integrative Neuroimaging
NIMH Intramural Research Program, National Institutes of Health

Dr. Berman's research group conducts translational investigations, using multimodal neuroimaging to bridge the gap between neurogenetic, molecular, cellular, and system-level mechanisms of brain dysfunction in neuropsychiatric disorders, with particular focus on neurodevelopmental and genetically-sourced disorders such as schizophrenia and Williams syndrome. The group also studies the effects of gonadal steroid hormones on brain function.

Dr. Berman received her M.D. degree at St. Louis University, completed a medical internship at Washington University in St. Louis and did her residency training in psychiatry at the University of California at San Diego. Dr. Berman also completed residency training in nuclear medicine at the NIH Warren G. Magnusen Clinical Center and is board certified in both psychiatry and nuclear medicine.

NARSAD Grants: Independent Investigator in 2000



JOHN G. CSERNANSKY, M.D.

Lizzie Gilman Professor and Chair in the Department of Psychiatry and Behavioral Sciences
Northwestern University Feinberg School of Medicine

Dr. Csernansky's research interests include in vivo neuroimaging of neuropsychiatric disorders, especially schizophrenia and Alzheimer's disease; clinical trials of cognition-enhancing drugs and the development of valid animal models for neuropsychiatric disorders. Dr. Csernansky has over 250 peer-reviewed publications and has also authored several chapters and books.

Prior to joining the faculty at Northwestern University, Dr. Csernansky served as the Gregory B. Couch Professor of Psychiatry at Washington University School of Medicine, and secured National Institutes of Health funding there to establish a Conte Center for the Neuroscience of Mental Disorders, focused on improving understanding of the neurodevelopmental origins of schizophrenia.



NATHANIEL HEINTZ, PH.D.

Investigator, Howard Hughes Medical Institute
James and Marilyn Simons Professor
Laboratory of Molecular Biology
The Rockefeller University

Research in Dr. Heintz's laboratory aims to identify the genes, circuits, cells, macromolecular assemblies and individual molecules that contribute to the function and dysfunction of the mammalian brain. Dr. Heintz and his colleagues have developed a suite of novel approaches based on the manipulation of bacterial artificial chromosomes (BACs) to investigate the histological and functional complexities of the mammalian brain in vivo and to understand how these mechanisms become dysfunctional in disease.

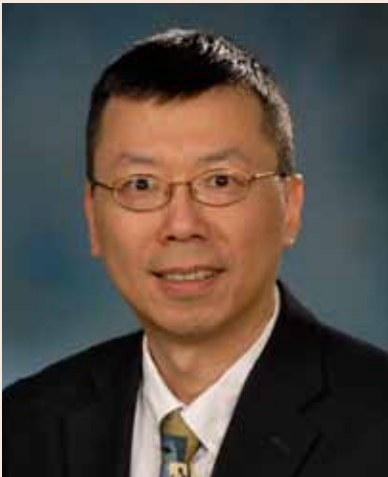
Dr. Heintz received his B.A. in biology from Williams College; Ph.D. from the State University of New York, Albany; and worked as a postdoctoral fellow at Washington University in St. Louis prior to joining the faculty at Rockefeller University in 1983.

I am most proud of my early discovery that hippocampal volume was lower in patients with depression compared with controls, and was ameliorated by antidepressant treatment... I am happy that it gave credence to depression as a brain disease. I have had many clinicians thank me for helping them take care of their patients.

—Yvette I. Sheline

SCIENTIFIC COUNCIL INCLUDES:

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- 4 FORMER DIRECTORS OF THE NATIONAL INSTITUTE OF MENTAL HEALTH
- 13 MEMBERS OF THE NATIONAL ACADEMY OF SCIENCES
- 20 CHAIRS OF PSYCHIATRY & NEUROSCIENCE DEPTS AT LEADING MEDICAL INSTITUTIONS
- 45 MEMBERS OF THE INSTITUTE OF MEDICINE



ELLIOTT HONG, M.D.

Professor of Psychiatry; Director, First Episode Psychosis Clinic; Chief, Neuroimaging Research Program at the Maryland Psychiatric Research Center (MPRC)
Director, Center for Brain Imaging Research
University of Maryland School of Medicine

Dr. Hong is a practicing psychiatrist in addition to a neuroscientist studying the causes of and treatments for brain illnesses. His motivation for conducting research is to integrate clinical needs into basic research, and to translate genetic, imaging, and neurophysiological findings into improved diagnostic and treatment methods for individuals with schizophrenia and other severe mental illnesses.

Dr. Hong completed his medical studies at Sun Yat-Sen University of Medical Sciences, Faculty of Medicine, in Guangzhou, China. He practiced psychiatry in China for several years before moving to the US where he completed graduate studies in medical/psychiatric anthropology at the University of North Carolina at Chapel Hill and then repeated a residency in psychiatry at the University of Maryland.

NARSAD Grants: Young Investigator in 2004



PAUL H. PATTERSON, PH.D.

Anne P. and Benjamin F. Biaggini Professor of Biological Sciences
California Institute of Technology (Caltech)

Much of the research in Dr. Patterson's laboratory involves the study of interactions between the nervous and immune systems. Dr. Patterson began his work in developmental neurobiology with studies of dissociated neuronal cultures while on the faculty at Harvard Medical School. After moving to Caltech, his group developed a mouse model of mental illness based on the risk factor of maternal infection. Dr. Patterson's group is also testing various types of gene therapy for treatment of mouse models of multiple sclerosis and Huntington's disease. This includes novel viral vectors for delivery to the brain.

Dr. Patterson grew up in Chicago, attended Grinnell College in Iowa, and obtained his Ph.D. at The Johns Hopkins University in biochemistry.

NARSAD Grants: Distinguished Investigator in 1999



YVETTE I. SHELINE

Professor of Psychiatry and Radiology
 Director, Center for the Neuroscience of Depression and Stress (CNDS)
 University of Pennsylvania Perelman School of Medicine

Dr. Yvette Sheline is known for her pioneering studies of hippocampal volume loss in major depression and the moderating effects of antidepressant treatment, work widely cited in psychiatric literature. Her research has also integrated structural/functional neuroimaging with depression course, neuropsychological correlates, and treatment outcomes. She seeks to determine how depression affects the brain using neuroimaging techniques, and to understand how stress produces functional dysregulation. Dr. Sheline investigates treatment effects of antidepressants and cognitive behavioral therapy on emotion-induced fMRI activity in PTSD and depression; longitudinal effects of treatment on neuropsychological and brain structural variables in late-life depression; and modifiers of brain amyloid binding in normal aging and preclinical Alzheimer's Disease.

Prior to joining the faculty at Penn, Dr. Sheline was Professor of Psychiatry and Director, Center for Depression Stress & Neuroimaging at Washington University School of Medicine in St. Louis.

NARSAD Grants: Young Investigator in 1998 and Independent Investigator in 2002 and 2005

Foundation Prizes: 2002 Klerman Prize Honorable Mention for Exceptional Clinical Research by a Young Investigator



MYRNA M. WEISSMAN, PH.D.

Diane Goldman Kemper Family Professor of Epidemiology in Psychiatry
 College of Physicians and Surgeons and Mailman School of Public Health
 Columbia University
 Chief, Division of Epidemiology, New York State Psychiatric Institute

Dr. Weissman's research focuses on understanding the rates and risks of mood and anxiety disorders using methods of epidemiology, genetics, neuroimaging, and the application of these findings to develop empirically-based treatments and preventive intervention. She directs a 3-generation study of families at high and low risk for depression and directs a multi-center study to determine the impact of maternal remission from depression on offspring. Dr. Weissman is one of the principal investigators in a multi-centered study to find biomarkers of response to the treatment of depression and was one of the developers of Interpersonal Psychotherapy, an evidenced-based treatment for depression.

Prior to joining the faculty at Columbia, Dr. Weissman was a Professor of Psychiatry and Epidemiology at Yale University School of Medicine and Director of the Depression Research Unit.

NARSAD Grants: Distinguished Investigator 1991, 2000 and 2005

Foundation Prizes: 1994 Selo Prize for Outstanding Achievement in Affective Disorders Research (renamed the Colvin Prize in 2012)

NARSAD 2013 Independent Investigator Grants

487 ▶ 40 ▶ 4M
APPLICATIONS GRANTS \$ FUNDED

Forty mid-career scientists from 10 countries and 34 institutions will pursue innovative research related to depression, bipolar disorder, schizophrenia, anxiety and post-traumatic stress disorder.

"The range of project proposals this year was exceptional in its variety of new approaches to understand and treat mental illness. Tackling the illnesses of the brain remains science's most daunting challenge and requires these cutting-edge approaches that the Brain & Behavior Research Foundation has been supporting for 27 years with its NARSAD grants. Each year we build upon the growing body of knowledge about the brain and its functioning and come closer to finding cures."

Robert M. Post, M.D.
Chair, NARSAD Independent Investigator Grant Selection Committee
Brain & Behavior Research Foundation Scientific Council
Head, Bipolar Collaborative Network
Professor of Psychiatry, George Washington School of Medicine

“Recent evidence of gene-environment interplay supports the need for environmental interventions, even for highly heritable disorders. We hope our research will provide the groundwork to conduct a larger multi-site study of early prevention in the children of parents with bipolar disorder ...”

Mark A. Ellenbogen, Ph.D.

BASIC RESEARCH

BIPOLAR DISORDER

Anabel Martinez-Aran, Ph.D.
Institut D'investigacions Biomèdiques August Pi i Sunyer (IDIBAPS)

DEPRESSION

Robert C. Thompson, Ph.D.
University of Michigan

Qin Wang, M.D., Ph.D.
University of Alabama at Birmingham

POST-TRAUMATIC STRESS DISORDER (PTSD)

Julia A. Chester, Ph.D.
Purdue University

SCHIZOPHRENIA

Alessandro Bertolino, M.D., Ph.D.
University of Bari

Peng Jin, Ph.D.
Emory University

Carsten Korth, M.D., Ph.D.
University of Düsseldorf

Antonieta Lavin, Ph.D.
Medical University of South Carolina

Todd Lencz, Ph.D.
The Feinstein Institute for Medical Research

Daniel J. Mueller, M.D., Ph.D.
Centre for Addiction and Mental Health,
University of Toronto

Brien P. Riley, Ph.D.
Virginia Commonwealth University

MULTIPLE DISORDERS

Alon Chen, Ph.D.
Weizmann Institute of Science

Todd Denton Gould, M.D.
University of Maryland

Andrew L. Gundlach, Ph.D.
University of Melbourne

Yasushi Nakagawa, M.D., Ph.D.
University of Minnesota

NEW TECHNOLOGIES

BIPOLAR DISORDER

Manon H. J. Hillegers, M.D., Ph.D.
Utrecht University

Beny Lafer, M.D., Ph.D.
University of São Paulo

DEPRESSION

Christopher G. Beevers, Ph.D.
University of Texas at Austin

SCHIZOPHRENIA

Dost Öngür, M.D., Ph.D.
Harvard University

NEXT GENERATION THERAPIES

DEPRESSION

Charles L. Raison, M.D.
University of Arizona

Jonathan P. Roiser, Ph.D.
University of London

Gabrielle Rudenko, Ph.D.
University of Michigan

John A. Wemmie, M.D., Ph.D.
University of Iowa

SCHIZOPHRENIA

Christopher R. Bowie, Ph.D.
Queen's University Belfast

Ariel Graff-Guerrero, M.D., Ph.D.
Centre for Addiction and Mental Health,
University of Toronto

Gregory A. Light, Ph.D.
University of California, San Diego

Alessandro Usiello, Ph.D.
Ceinge Biotechnologie Avanzate

Xiang Yang Zhang, M.D., Ph.D.
Baylor College of Medicine

MULTIPLE DISORDERS

Elizabeth W. Twamley, Ph.D.
University of California, San Diego

Analia Bortolozzi, Ph.D.
Institut D'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS)

DIAGNOSTIC TOOLS/EARLY INTERVENTION

BIPOLAR DISORDER

Mark A. Ellenbogen, Ph.D.
Concordia University

Michael F. Grunebaum, M.D.
Columbia University

Vivian Kafantaris, M.D.
The Feinstein Institute for Medical Research

DEPRESSION

Heather C. Abercrombie, Ph.D.
University of Wisconsin

James E. Swain, M.D., Ph.D.
University of Michigan

POST-TRAUMATIC STRESS DISORDER (PTSD)

Ananda B. Amstadter, Ph.D.
Virginia Commonwealth University

SCHIZOPHRENIA

Deepak C. D'Souza, M.D.
Yale University

Stephen J. Glatt, Ph.D.
State University of New York
Upstate Medical University

Christine I. Hooker, Ph.D.
Harvard University

Oliver D. Howes, M.D., Ph.D.
Institute of Psychiatry,
King's College London

NARSAD 2013 Young Investigator Grants

1,199 ▶ **200** ▶ **11.8M**
APPLICATIONS GRANTS \$ FUNDED

Marking our 27th year of bestowing transformative research grants on young scientists in brain & behavior research, we are very proud to announce \$11.8 million in 200 new two-year grants. NARSAD Young Investigator Grants enable early career scientists to garner pilot data for innovative ideas before they have “proof of concept” for their work. This year, a record-breaking 1,199 applications were received.

The Foundation has awarded \$204.4 million in 3,497 research grants to Young Investigators since 1987. This investment in early career scientists’ bold, outside-the-box research ideas has reached across the world to 33 countries.

Please consider investing in a Research Partnership with our new Investigators.

For more information, visit: bbrfoundation.org/research-partner.

BASIC RESEARCH

ANXIETY

Martin Levesque, Ph.D.
Laval University

Natalina Salmaso, Ph.D.
Yale University

Demetrio Sierra, Ph.D.
Massachusetts General Hospital,
Harvard University

Xiaojing Ye, Ph.D.
New York University

ANXIETY AND DEPRESSION

Kate D. Fitzgerald, M.D.
University of Michigan

Katharina Kircanski, Ph.D.
Stanford University

Heide Klumpp, Ph.D.
University of Illinois at Chicago

Jodi Lukkes, Ph.D.
McLean Hospital, Harvard University

Katie A. McLaughlin, Ph.D.
Children's Hospital, Boston

Alina Patke, Ph.D.
The Rockefeller University

Yonejung Yoon, Ph.D.
Weill Cornell Medical College,
Cornell University

ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD)

Nicola M. Grissom, Ph.D.
University of Pennsylvania

Julie S. Haas, Ph.D.
Lehigh University

Maria Kharitonova, Ph.D.
Children's Hospital, Boston

Hagai Maoz, M.D.
Tel Aviv University

AUTISM SPECTRUM DISORDER (ASD)

Jyothi Arikath, Ph.D.
University of Nebraska Medical Center

Guy Horev, Ph.D.
Cold Spring Harbor Laboratory

Christelle Golzio, Ph.D.
Duke University

Alaine C. Keebaugh, Ph.D.
Emory University

Ji-Ann Lee, Ph.D.
University of California, Los Angeles

Lucas Matt, Ph.D.
University of California, Davis

Tabrez J. Siddiqui, Ph.D.
University of British Columbia

Courtney L. Thaxton, Ph.D.
University of North Carolina, Chapel Hill

BIPOLAR DISORDER (BP)

June Gruber, Ph.D.
Yale University

Shizhong Han, Ph.D.
University of Iowa

Maria De Las Mercedes Perez-Rodriguez, M.D., Ph.D.
Icahn School of Medicine at Mount Sinai

Hyung W. Nam, Ph.D.
Mayo Clinic

DEPRESSION

Nicole L. Baganz, Ph.D.
Vanderbilt University

Adrienne J. Betz, Ph.D.
Quinnipiac University

Paul R. Burghardt, Ph.D.
University of Michigan

Erin C. Dunn, Sc.D., M.P.H.
Massachusetts General Hospital,
Harvard University

Jian Feng, Ph.D.

Icahn School of Medicine at Mount Sinai

Ellen K. Grishman, M.D.

University of Texas Southwestern Medical Center at Dallas

Tamar Lea Gur, M.D., Ph.D.

University of Pennsylvania

Avram Holmes, Ph.D.

Harvard University Medical School

Jianxiong Jiang, Ph.D.

Emory University School of Medicine

Ilia N. Karatsoreos, Ph.D.

Washington State University, Vancouver

Stephanie H. Parade, Ph.D.

Brown University

Christophe Proulx, Ph.D.

University of California, San Diego

Crystal E. Schiller, Ph.D.

University of North Carolina, Chapel Hill

Anne L. S. Teissier, Ph.D.

Research Foundation for Mental Hygiene, Inc., Columbia University

Brent J. Thompson, Ph.D.

University of Texas Health Science Center, San Antonio

Anne Venner, Ph.D.

Beth Israel Deaconess Medical Center, Harvard University

POST-TRAUMATIC STRESS DISORDER (PTSD)

Jonathan D. Morrow, M.D., Ph.D.
University of Michigan

SCHIZOPHRENIA

Sandra Ahrens, Ph.D.
Cold Spring Harbor Laboratory

Hannah E. Brown, M.D.
Massachusetts General Hospital,
Harvard University

Solange P. Brown, M.D., Ph.D.
Johns Hopkins University

Sarah E. Canetta, Ph.D.
Columbia University

Ioana Carcea, M.D., Ph.D.
New York University School of Medicine

Anne L. Collins, Ph.D.
University of North Carolina, Chapel Hill

Jennifer M. Coughlin, M.D.
Johns Hopkins University

Juan A. Gallego, M.D.
The Feinstein Institute for Medical Research

Kazuo Hashimoto-Torii, Ph.D.
Children's National Medical Center

Xiao-Hong Lu, Ph.D.
University of California, Los Angeles

Heline Mirzakhania, Ph.D.
University of California, San Diego

Amanda C. Mitchell, Ph.D.
Icahn School of Medicine at Mount Sinai

Lauren V. Moran, M.D.
Massachusetts General Hospital,
Harvard University

Semanti Mukherjee, Ph.D.
The Feinstein Institute for Medical Research

Jess Nithianantharajah, Ph.D.
University of Edinburgh

Katie L. Nugent, Ph.D.
Maryland Psychiatric Research Center,
University of Maryland

Melissa L. Perreault, Ph.D.
Centre for Addiction and Mental Health,
University of Toronto

Todd F. Roberts, Ph.D.
University of Texas Southwestern Medical
Center at Dallas

Juan Song, Ph.D.
Johns Hopkins University School of Medicine

Theodoros Tsetsenis, Ph.D.
Stanford University

MENTAL ILLNESS—GENERAL

Mulugeta S. Abebe, Ph.D.
Columbia University

Frederic Ambroggi, Ph.D.
University of California, San Francisco

Laura M. Fiori, Ph.D.
University of Ottawa

Judy Liu, Ph.D.
Children's National Medical Center

MULTIPLE DISORDERS

Beth E. Cohn, M.D.
University of California, San Francisco

Christina Gross, Ph.D.
Emory University

Benjamin Y. Hayden, Ph.D.
University of Rochester

Jia Sheng Hu, Ph.D.
University of California, San Francisco

Soo Young Kim, Ph.D.
University of California, Berkeley

Torsten Klengel, M.D.
Max Planck Institute for Psychiatry

Pan Li, Ph.D.
Johns Hopkins University

Machteld C. Marcelis, M.D., Ph.D.
Maastricht University

Nadine M. Melhem, Ph.D.
University of Pittsburgh

Frederick C. Nucifora, Ph.D., D.O., M.H.S.
Johns Hopkins University

Fereshteh, S. Nugent, Ph.D.
Uniformed Services University of the Health
Sciences

Edwin C. Oh, Ph.D.
Duke University

Angela R. Ozburn, Ph.D.
University of Pittsburgh

Dirk J. A. Smit, Ph.D.
Vrije Universiteit Amsterdam

Joyce So, M.D., Ph.D.
Centre for Addiction and Mental Health,
University of Toronto

Eli A. Stahl, Ph.D.
Icahn School of Medicine at Mount Sinai

Bin Xu, Ph.D.
Columbia University

OTHER

Addiction

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Families, friends and individuals living with a mental illness, from around the globe, team-up in a variety of ways—from community walks to gingerbread-house-building competitions—to support the foundation by raising funds for research. We are grateful to our community leaders!

\$75,000+

7th Annual Chrissy's Wish Memorial Golf Outing

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Combined Statement of Financial Position

DECEMBER 31,

2013

ASSETS	
Cash and cash equivalents	\$ 9,825,107
Investments, at fair value	9,951,960
Contributions receivable, net	1,873,281
Other receivable	87,031
Pledges receivable, net	2,247,449
Prepaid expenses	19,868
Assets held in charitable remainder trusts	1,404,297
Fixed assets, net	101,242
Security deposits	77,110
	\$ 25,587,345

LIABILITIES & NET ASSETS	
Liabilities:	
Accounts payable and accrued expenses	\$ 269,558
Grants payable	12,578,705
Accrued compensation	42,426
Annuities payable	861,080
Charitable gift annuities payable	360,716
<i>Total Liabilities</i>	<i>14,112,485</i>
Net Assets:	
Unrestricted	2,142,098
Unrestricted - board designated endowment	4,509,262
Temporarily restricted	100,000
Permanently restricted	4,723,500
<i>Total Net Assets</i>	<i>11,474,860</i>
	\$ 25,587,345

2013 FINANCIAL SUMMARY:

We are pleased to report on the financial position and results of the Brain & Behavior Research Foundation for 2013. We remain appreciative and thankful for the commitment of Foundation leadership, dedicated staff, volunteers and our strong donor support base that allows the Foundation to perform its vital work. We are indebted to the Foundation Scientific Council, our distinguished research leaders covering virtually every major discipline within brain and behavior science, who volunteer their expertise to select and recommend the most promising grant projects to fund.

Contributions held firm in 2013 and we continued to receive major support from bequests for which we are deeply grateful for the generosity of the individuals and their families. We would also like to acknowledge the extraordinary bequest in 2012 from the late Oliver D. Colvin, Jr. that continues to support our efforts at the Foundation. These donations further the Foundation's mission to alleviate the suffering caused by mental illness by awarding grants that will lead to advances and breakthroughs in scientific research.

Combined Statement of Activities

YEAR ENDED DECEMBER 31		2013
SUPPORT AND REVENUE		
Contributions	\$	7,060,748
Contribution of services		1,310,739
Bequests		4,417,319
Net realized and unrealized gains on investments		697,782
Net appreciation of assets held in charitable remainder trusts		271,676
Dividend and interest income		344,568
Annuities due		25,073
Total Support and Revenue		14,127,905
EXPENSES		
Program Services:		
Research grants and awards		8,915,971
Scientific advancement		1,641,936
Program support		2,077,225
<i>Total Program Services</i>		<i>12,635,132</i>
Supporting Services:		
Fundraising*		877,139
Administration*		1,661,858
<i>Total Supporting Services</i>		<i>2,538,997</i>
Total Expenses		15,174,129
Change in Net Assets:		(1,046,224)
Net Assets, Beginning of year		12,521,084
Net Assets, End of year	\$	11,474,860

*All fundraising and administration expenses are funded by specially designated grants.

With our strong financial posture, we are positioned for a future of accelerating research accomplishments to help those living with mental illness to live more full and productive lives. Our leadership in funding mental health research continued in 2013, as the Foundation awarded NARSAD Grants bringing the total investment in mental health research to over \$300 million since inception.

Thanks to the generosity of two family foundations, all supporting services were once again underwritten in 2013. This allows for donations targeted for research to go directly to funding NARSAD Grants. The financial report shown herein has been summarized from our 2013 audited financial statements. The Foundation's complete audited financial statements and our most recent IRS Form 990 are available online at bbrfoundation.org or contact our office at 800.829.8289 for copies of the material.



The Hollister Family, long-time supporters of the Brain & Behavior Research Foundation

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
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- 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 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 gifts help incentivize the field of research by funding Young, Independent and Distinguished Investigators around the globe.

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

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BEHAVIOR**
RESEARCH FOUNDATION
Awarding **NARSAD** Grants

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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

Over a quarter of a century, we have awarded nearly \$310 million worldwide to more than 3,700 scientists carefully selected by our prestigious Scientific Council.