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# Quarterly

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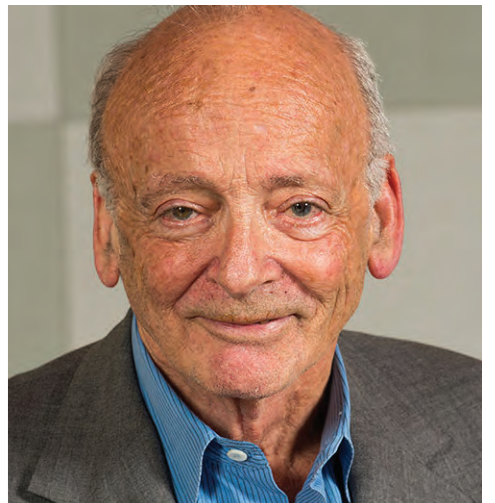
PRESENTING THE INDEPENDENT INVESTIGATORS



Mothers' Depression and  
its Impact on Their Children  
with **MYRNA WEISSMAN, PH.D.**



NFL Player  
**KEITH O'NEIL**  
Living with Bipolar Disorder



Parenting:  
Suicide Prevention in Young People  
**DAVID SHAFFER, M.D.**

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**Credit:** Images courtesy of Myrna M. Weissman, Ph.D., Foundation Scientific Council member; Keith O'Neil; David Shaffer, M.D.; and the Foundation Researchers.

**Jeffrey Borenstein, M.D.**

President & CEO  
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As a psychiatrist I have seen the devastating effects that a suicide has on surviving family members. I have also seen how people who have thoughts of suicide can regain their health and hope with appropriate treatment.

Unfortunately, suicide is the 10th leading cause of death in the United States. Tragically, for people between the ages of 15 to 34, suicide is the second leading cause of death.

Suicide research funding totals a yearly average of \$72 million (40,000 annual deaths) compared to \$222 million for influenza research (31,000 annual deaths) and \$304 million for high blood pressure research (56,000 annual deaths) according to the National Institutes of Health.

Since 1987, the Brain & Behavior Research Foundation has funded 59 grants specifically on suicide and many others on related topics such as depression. Unlike government sources of funding, philanthropic funding is sometimes able to support more cutting-edge research. Three Foundation grantees serve as examples of pioneering research on suicide:

**Dr. Zachary Kaminsky** of Johns Hopkins University is investigating the possibility of a blood test, including proteins that may be markers of suicide risk.

**Dr. J. John Mann** of Columbia University is studying neurotransmitters, as well as behaviors that lead to and might prevent suicide. Dr. Mann is most excited about potential medications to reverse high suicide risk in select patients who are depressed. Currently, he is overseeing two clinical trials for ketamine as a possible treatment for major depression. According to Dr. Mann and researchers in other institutions, ketamine acts rapidly—within a couple of hours. It is an example of a new push to find agents and methods that act quickly in those patients they help.

**Dr. Daniel Weinberger** of the Lieber Institute for Brain Development at Johns Hopkins University, as well as investigators at other institutions are researching gene expression changes as potential biomarkers for suicidality, which may then provide potentially relevant insight for the development of prevention and treatment approaches.

While none of these developments have yet been converted to practical use in clinical assessment and care, they suggest future possibilities. One of our major goals has to be to develop additional advanced scientific findings and then transmit that information to the breadth of the medical profession.

We must continue to bridge the gap from bench science to translational science and to clinical care.

We must use what we learn as a much needed catalyst to change the dialogue on mental illness and put substantial dollars into research funding. It is only through support for research that we can alleviate the pain and suffering mental illness can cause families, and find the advances and breakthroughs that will result in better treatments and hope for cures.

Sincerely,

A handwritten signature in black ink, appearing to read "Jeffrey Borenstein". The signature is written in a cursive, flowing style.

Jeffrey Borenstein, M.D.  
President & CEO

# Research Discoveries in the News

## Two Studies Pursue An Elusive Goal: Predicting Who Will Make A Suicide Attempt

Attempting suicide is among the strongest risk factors for future suicide completion. Thus there is great value in knowing which people are most likely to attempt suicide in the future, and to predict who among these attempters will ultimately die by suicide. These are among the leading goals of investigators.

Two recently published studies by 2013 NARSAD Young Investigator **James Bolton, M.D.**, of the University of Manitoba, and colleagues, report progress, but remind us how difficult it is to predict suicidal behavior. One of the new studies is about people who were referred to psychiatric staff at two large hospital emergency departments; the other, about suicidal behavior in a large sample of people from the general population diagnosed with major depressive disorder (MDD).

On June 6th, Dr. Bolton and colleagues reported in the *Journal of Nervous and Mental Disease* the fate of 6,919 referrals to psychiatric services in two Manitoba hospitals over a 3-year period. Ultimately, 3,939 patients formed the basis of the study's analysis, of which 104 returned to the ER after a suicide attempt within 6 months of their original ER visit.

After evaluating an extensive list of factors, the team concluded there were only two measures with predictive power regarding future suicide attempts: a history of suicidal thinking and previous suicide attempts. Still, neither of these factors, or other factors such as depression or hopelessness that did

correlate to some degree with future attempts, could predict which specific patients would attempt suicide again. The two measures have a public health value, in helping to broadly guide evaluation and treatment, but no predictive value in individual cases.

A second paper by Dr. Bolton and colleagues, based on a U.S. survey of 34,000 non-institutionalized adults, appeared in the April-June 2015 issue of the *Archives of Suicide Research*. The researchers examined how stressful life events were associated with suicidal behavior. Focusing on the 6,004 survey respondents who had MDD, the team found a relationship between stressful life events—especially interpersonal problems with friends, coworkers or relatives, and severe financial difficulty—and the likelihood of a future suicide attempt.

The team noted that “despite the significant association found between some stressful life events and suicidal behaviors,” each of them, taken individually, has a relatively low “predictive” value—less than 10 percent. While they are important warning flags, particularly in someone thought to be at risk for suicide, stressful events cannot themselves predict whether a particular person is going to make a suicide attempt. Importantly though, these risk factors can guide evaluation: “Doctors should ask about recent stressful life events as part of their risk assessment of depressed persons,” the team concludes, “and may consider additional supportive psychotherapeutic approaches as part of their depression management.”



**TAKEAWAY:** Researchers have found important connections between risk factors and future suicide attempts, but it remains very difficult to predict suicidal behavior at the individual level.

James Bolton, M.D.

# Looking For Clues in Reward Circuits of Bipolar and Depressed Patients

When people with bipolar disorder experience depressive episodes, the reward circuits in their brains show impairments similar to those that affect people diagnosed with major depressive disorder (MDD), scientists reported March 13th in the journal *Neuropsychopharmacology*. When these circuits are weakened, people's ability to experience pleasure diminishes.

Most clinical studies exploring how depression affects the brain have focused on people with MDD. Because patients with the two disorders may respond differently to antidepressant medications, it's important to understand the neurobiology of both groups in order to develop effective treatments.

A team\* of scientists at the University of Pennsylvania and the National Institute of Mental Health, led by 2010 NARSAD Young Investigator grantee **Theodore Satterthwaite, M.D.**, and **Daniel H. Wolf, M.D., Ph.D.**, a 2005 Young Investigator Grantee, used functional magnetic resonance imaging (fMRI) to compare how the brain's reward circuits work in depressed patients with the two disorders. Their analysis included 23 people with bipolar depression, 22 with major depressive disorder, and 32 healthy controls.

The researchers first examined reward circuits while study participants played a card game in which they earned money by correctly guessing whether cards were red or black. Money was lost for incorrect guesses. In healthy participants, winning money activated the reward-processing parts of their brains more strongly than losing money. These responses were less robust for depressed patients. The more severe a patient's depression, regardless of their clinical diagnosis, the less their reward system responded. The team also examined reward circuits in their resting state, when study participants were not performing any activity expected to activate those parts of the brain.

In patients with bipolar disorder and major depressive disorder, connections between different reward-processing regions of the brain were weaker than they were in people without depression. This weakening was greater in patients with more severe depression in both groups.

The scientists did find differences between the two groups of depressed patients. Winning money activated a reward center—the ventral striatum—more strongly in patients with bipolar disorder than it did in those with major depressive disorder. And the strength of certain circuit connections was stronger in patients with bipolar disorder than it was in patients with major depressive disorder. These differences might reflect the two groups' different risks for manic episodes, during which reward responses appear to be heightened rather than dampened, the scientists say.

Why is it so important to distinguish among brain responses to reward? First, symptoms of depression—which may be more linked to reward-system dysfunction such as loss of pleasure—tend to be less responsive to standard treatments. “Attenuated reward system response may therefore evolve to be a useful biomarker in drug discovery and clinical trials for mood disorders,” Dr. Satterthwaite says. Second, because many people with bipolar disorder first seek clinical help during depressive episodes, identifying differences between bipolar disorder and major depressive disorder could help ensure patients are accurately diagnosed from the start and receive treatment specifically designed to relieve their symptoms.

\*Additional Foundation-funded team members:

**Claudia F. Baldassano, M.D.**, 2003 Young Investigator (YI)

**Yvette I. Sheline, M.D.**, 1998 YI, 2002 and 2005

Independent Investigator; Scientific Council (SC) Member

**Ruben C. Gur, Ph.D.**, 2007 Distinguished Investigator (DI)

**Raquel E. Gur, M.D.**, 1999 DI

**Ellen Leibenluft, M.D.**, SC Member



**TAKEAWAY: A new study sheds light on the neurobiological differences between bipolar disorder and major depression, which could lead to more targeted treatments.**

Theodore Satterthwaite, M.D.; Daniel H. Wolf, M.D., Ph.D.

# Parent's History of Suicide Attempts Helps Predict Suicide Attempts In Children

As public health experts debate the best ways to reduce suicides—a top-five leading cause of death among Americans aged 10 to 54 in 2013—new research calls attention to the importance of early intervention based on long-term risk factors.

In a study published in the February 2015 issue of *JAMA Psychiatry*, a team led by NARSAD Scientific Council member and 2008 Distinguished Investigator grantee **J. John Mann, M.D.**, probed the extent to which suicidal behavior in a parent gets passed on to children. The investigators tracked 701 children of 334 people diagnosed with mood disorders for an average of six years to identify factors that predicted suicide attempts among the children.

The research team also included 2001 NARSAD Distinguished Investigator grantee **David A. Brent, M.D.**, 2013 Young Investigator grantee **Nadine M. Melhem, Ph.D.**, and 1996 and 1998 Young Investigator grantee **John G. Keilp, Ph.D.**

The investigators found that having a parent who had attempted suicide made it nearly five times more likely that one of their children would make an attempt. It has been known that both genetic and non-genetic factors related to the predisposition for suicidal behavior or to psychiatric illnesses that trigger suicidal behavior, are transmitted in families. This study sought to identify the factors responsible for such familial transmission.

Suicide attempts were more likely among those children who, like their parents, were diagnosed with a mood disorder such as major depression or bipolar disorder. Such diagnoses appear to be needed for the manifestation of suicidal behavior, about a year before the first attempt. Most people diagnosed

with depression do not attempt suicide because they do not have a predisposition to suicidal behavior.

Independent of family history of depression, impulsive and aggressive behavioral traits among the children also made it more likely that they will attempt suicide. This indicates a greater propensity to act on emotions. Those with pronounced aggressive and impulsive traits are also more likely to be diagnosed with a mood disorder; the combination puts them at greater risk for a suicide attempt.

These findings highlight the importance of three long-term risk factors in predicting suicide attempts: a family history of suicide attempts, a family history of mood disorders, and a personal history of impulsive aggression. It's important that such families focus on early detection and treatment of mood disorders and aggressive-impulsive traits, the researchers say.

In recent months, public officials have taken steps to make it more difficult for people to attempt suicide. There are plans to build suicide-prevention structures around San Francisco's Golden Gate Bridge and New Jersey's George Washington Bridge.

Efforts on all fronts may be needed to address troubling recent developments in suicide research, including the increase found in suicide rates among African American children between 1993 and 2012, as reported in *JAMA Pediatrics* on May 18th. This was a period in which suicide rates went down among white children.



**TAKEAWAY: Suicidal behavior in a parent is passed on to children, making early detection and treatment of mood disorders critically important.**

J. John Mann, M.D.; David A. Brent, M.D.

# Depression in Mothers

## A Landmark, 30-Year Study Rewrites the Book on Mothers' Depression and Its Impact on Their Children



### 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  
Foundation Scientific Council Member  
NARSAD Grants:  
Distinguished Investigator 2005, 2000 and 1991  
1994 Falcone Prize in  
Affective Disorders Research

These days, when Myrna Weissman, Ph.D., addresses her colleagues in medicine about her life's work—the study of depression, and the impact of a mother's depression on her children—she has to go out of her way to remind them how much things have changed since she was a graduate student in the mid-1970s.

The conventional wisdom back then, she says, “was that children didn't get depressed, and that depression, generally, was a disorder of menopausal women.” In 1978 a major medical journal published an article that asserted, “The notion of a syndrome of childhood depression rests largely on surmise.”

In large part because of studies performed by Dr. Weissman and her fellow scientists over the past three decades, we now know how wrong those assumptions were.

Children indeed can become depressed, and depression itself—which affects women about twice as often as men—typically begins in the years just after puberty and peaks before age 35. This period includes the prime childbearing years for women. The fact remains that women can become depressed during menopause, but what Dr. Weissman and her

colleagues discovered was that, for many women, the disorder begins earlier in life.

The other ground-shifting finding to emerge from Dr. Weissman's work is that, in many cases, the children of depressed mothers are themselves negatively affected by their mothers' condition. Just as important, when depressed mothers are successfully treated, the mental health of their children also improves. It's a discovery that points directly to a way to prevent depression in the rising generation (see page 8).



## When depressed mothers are successfully treated, the mental health of their children also improves.

### A Life's Work

Dr. Weissman trained at Yale University to be an epidemiologist—an expert in the prevalence and patterns of diseases in large populations. She is now Professor of Epidemiology in Psychiatry at Columbia University and Chief of the Division of Epidemiology at the New York State Psychiatric Institute. A three-time recipient of NARSAD Distinguished Investigator Grants (1991, 2000, 2005), Dr. Weissman is also a member of the Foundation's Scientific Council.

After graduate school, she became involved in an effort to discover the rates of psychiatric disorders in the community. "At the time, there was no authoritative population data, for instance, on the prevalence of depression or anxiety disorders," Dr. Weissman says. She helped conduct a survey of some 18,000 people in New Haven, Connecticut and four other communities around the U.S. that showed depression was more common and began much earlier in life than was previously believed.

"As an epidemiologist," she recalls, "I was interested in the early signs of the disorder and in prevention." With that in mind, in 1982 Dr. Weissman embarked on a study that would define her career and change conventional wisdom. She calls it "the high-risk study." Its purpose was to enroll patients with moderate to severe depression and to follow their

offspring over time—and do the same with an age-matched group of non-depressed healthy people who would serve as controls. The idea was to watch the children of depressed parents, their mothers especially, to see whether the children developed depression or other psychiatric symptoms more frequently than children of non-depressed parents.

This "first wave" of the high-risk depression study showed that depression was "highly familial," says Dr. Weissman—meaning that having a mother or father with moderate to severe depression significantly raised the odds that a child would also develop symptoms. The other main finding was that depression symptoms were uncommon before puberty but that there was a big rise after puberty, in adolescence.

### The Long View

Ten years later Dr. Weissman and her colleagues repeated the study, following the same patients and controls, as well as some new recruits. "The findings were sustained," she remembers. "It wasn't that we began to see children in the low-risk population start to get depressed at the 10-year mark; just as in the first wave, we saw that the rates were always higher in the high-risk group." Moreover, children of depressed parents, when they began to show symptoms, did not show symptoms of other

psychiatric ailments. "It was specific: they had depression."

At the 20-year mark, Dr. Weissman and her colleagues once more revisited the families enrolled in the high-risk study. This time the scientists began to incorporate newly available tools in an attempt to understand the biology of depression. At this interval, in addition to exams and interviews with participants, brain-wave studies called EEGs were performed. In later iterations of the study—at the 30- and 35-year marks, respectively—MRI scans were performed and DNA collected from those willing to donate samples. These technologies are now central in efforts by Dr. Weissman and her colleagues to identify biomarkers—biological indications of depression—to aid diagnosis and treatment.

The original results of the high-risk study have held up across the decades. Not only is the study rare for its longevity, that very longevity has made it possible to study the children of the children of the original high-risk parents, and now their children too. "Our findings have been confirmed by us and reconfirmed by others," Dr. Weissman says.

The other major fruit of the high-risk study, regarding the impact of a mother's depression on the mental health of her children, is explained in the accompanying story.

## When Mom Gets Better, So Do Her Kids

In 2006, a large federally-funded study focusing on treatment of depressed people was completed. Called STAR\*D (Sequenced Treatment Alternatives to Relieve Depression), it involved more than 4,000 patients who had not been helped by a first round of treatment with antidepressants. While the study was in progress, Dr. Weissman and her colleagues started an offshoot study, called STAR\*D-Child. It focused directly on the question of how the successful treatment of depressed mothers affected their children.

Dr. Weissman hopes to see psychiatric care integrated with primary care, to treat depressed mothers and so many others who otherwise might go undiagnosed and untreated.

The results, reported over a period of years since 2006, have been clear: when mothers are treated and their depression lifts, their children benefit, both in the near-term and over the long haul. In studies of this kind, a reduction in depression symptoms to the point that few remain, is considered a "remission."

Not only is the degree of remission important, so too is the timing. In the STAR\*D-Child study, children with depressed moms fared best when their mothers responded to treatment within three months. But the effects

### HAVE A QUESTION?

Send questions for Dr. Weissman 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.

were also positive for children whose mothers responded to treatment a few months later. In a 2011 report, Dr. Weissman and colleagues noted that one year after remission, 77 percent of mothers were still in remission. Overall, more than two mothers in three got better within a year when they were given the proper treatment and follow up.

The best news about this research concerns the children of these mothers. "Externalizing" behaviors and other psychiatric symptoms decreased significantly in children whose mothers got better, whether early or later on. The conclusion in 2011 was no different than what the same team offered in 2006, at the time of their first report: "These findings support the importance of vigorous treatment for depressed mothers in primary care or psychiatric clinics and suggest the utility of evaluating the children, especially children whose mothers continue to be depressed."

Dr. Weissman hopes to see psychiatric care integrated with primary care, to treat depressed mothers and so many others who otherwise might go undiagnosed and untreated. As the co-developer of an important and increasingly popular form of psychotherapy called IPT, she believes such integration is a realistic possibility.

IPT stands for interpersonal psychotherapy, and a person can be helped by it in as few as three sessions. The first session is devoted to evaluating a person's specific problems; the second session, to finding a way to support the person, if needed over an extended period, for instance by telephone; in the third session, patients with persisting symptoms are assigned to regular treatment. For Dr. Weissman, the point is that many who need help can be helped quickly. "Treatment doesn't need to be a long-term affair," she says.

# Ask the Researcher

**My husband's sister has schizophrenia and I'm afraid that if we have children they could be affected too. How high is the risk of this happening?**

In general, large and carefully conducted studies tell us that the absolute risk is not high. The vast majority of people who have a relative with schizophrenia do not get the disease. In many circumstances, the increase in risk is from around one percent to a few percent. A more complete answer for you and your husband requires more information and perhaps even the involvement of a medical geneticist or genetic counselor. There are a few rare instances where a more definitive answer might be possible.

**I think it's wonderful that you got a consortium of scientists to work together to find answers on schizophrenia. What progress do you expect in the next five years?**

In July 2014, the Psychiatric Genomics Consortium published a landmark paper that identified over 100 different genetic clues for schizophrenia. This paper used genetic information from 36,000 people with schizophrenia. The Consortium is now doing genetic assays to increase this number to 62,000 people with

schizophrenia. We expect to complete this work in a few months, and the results should be available in 2016. Right now, we are now writing a grant application to increase this number to 100,000 people with schizophrenia. We hope to complete this work within four years.



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

Professor, Karolinska Institutet  
M. Hayworth & Family Distinguished  
Professor of Psychiatry  
Professor of Genetics & Psychiatry  
Director, Center for Psychiatric Genomics  
University of North Carolina, Chapel Hill  
2014 Lieber Prize for Outstanding  
Achievement in Schizophrenia Research  
NARSAD Grant:  
Distinguished Investigator 2010

## The Importance of Clinical Trials

Clinical trials are a vital part of research and at the heart of all medical advances. Clinical trials look at new ways to prevent, detect, or treat mental and physical illnesses.

Choosing to take part in clinical research is an important personal decision about your interests, needs, and expectations of the research. For basic information about clinical trials, and to help you make a decision about whether to participate, visit "NIH Clinical Research Trials and You" at [nih.gov/health/clinicaltrials/](http://nih.gov/health/clinicaltrials/).

Another helpful website is [ClinicalTrials.gov](http://ClinicalTrials.gov), a searchable registry and results database of federally and privately supported clinical trials, including those supported by the Foundation. Mental health clinical trials are conducted in nearly every state in the U.S. and in many countries internationally. To find out whether an actively recruiting study may be near you, talk to your healthcare team. Your doctor or nurse can inform you about clinical trials that might be right for your situation or that of a loved one.

# 2015 Independent Investigator Grants

315 ▶ 40 ▶ \$3.9M  
APPLICATIONS GRANTS AWARDED FUNDED



## Robert M. Post, M.D.

Head, Bipolar Collaborative Network  
Professor of Psychiatry  
George Washington School  
of Medicine  
Foundation Scientific Council  
Member

Forty mid-career neuroscience researchers from 30 institutions in 16 countries have been chosen to receive a total of \$3.9 million in funding from The Brain & Behavior Research Foundation. The grants fund [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), and [next-generation therapies](#) (that reduce symptoms of mental illness and ultimately cure and prevent brain and behavior disorders.) The Foundation's Independent Investigator Grants provide each scientist with \$50,000 per year for up to two years to support their work during the critical period between the start of the research and the receipt of sustained funding.

We are delighted to support these researchers' work and are pleased to introduce them to you in the pages that follow.

Every year, applications are reviewed by members of the Foundation's Scientific Council, led by Robert M. Post, M.D., Scientific Council Member and Chair of the Independent Investigator Grant Selection Committee. The Council is composed of 150 leading experts across disciplines in brain and behavior research who volunteer their time to select the most promising research ideas to fund. We are very grateful to them and to all of our donors whose contributions make the awarding of these grants possible.

**BY THE NUMBERS** SINCE 1987

Awarded to Scientists



**\$328 MILLION**

Grants

**4,800+**

The breakdown of our grantees since 1987

- 3,697 Young Investigators
- 748 Independent Investigators
- 379 Distinguished Investigators



Universities &  
Medical Centers

**518**



Countries,  
Including the U.S.

**34**

**150 Scientific Council Members**

The all-volunteer *Foundation Scientific Council* is composed 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:

- 47 Members of the Institute of Medicine
- 21 Chairs of Psychiatry & Neuroscience Departments
- 13 Members of the National Academy of Sciences
- 4 Recipients of the National Medal of Science
- 4 Former Directors of the National Institute of Mental Health
- 2 Nobel Prize Winners

## BASIC RESEARCH



NARSAD Grants fund **Basic Research** to understand what happens in the brain to cause mental illness

### ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD)



**Satinder K. Singh, Ph.D.**, Yale University, will investigate the molecular structure of the dopamine transporter /PICK1 complex. The dopamine transporter is responsible for reuptake of the neurotransmitter dopamine from neuronal synapses. Defects

in dopamine signaling are suspected to play a role in attention-deficit hyperactivity disorder, and commonly prescribed drugs for ADHD boost dopamine levels by blocking its transporter. Dr. Singh hypothesizes that the PICK1 protein keeps the transporter in check in healthy cells, and that mutations in the dopamine transporter prevent interaction between the two proteins.

“Success in this research will open up a new chapter in the molecular understanding of ADHD. Second, and perhaps more importantly, it may lead to the development of novel, structure-based therapeutics.” —**Satinder K. Singh, Ph.D.**

### BIPOLAR DISORDER (BD)



**Tomas Hajek, M.D., Ph.D.**, Dalhousie University, will investigate whether diabetes and prediabetes contribute to structural damage to the brain in people with bipolar disorder. If a causative link

exists, better monitoring and treatment of these metabolic conditions could slow brain aging in people with bipolar disorder.

“This NARSAD Grant will allow us to investigate whether diabetes or prediabetes are risk factors for brain changes in bipolar disorder. Identifying modifiable causes of brain alterations in this disorder would be the first step toward prevention or treatment.” —**Tomas Hajek, M.D., Ph.D.**

### DEPRESSION



**Chadi A. Calarge, M.D.**, Baylor College of Medicine, will investigate the relationship between gut bacteria and depression. He will focus on bacteria that produce an enzyme called tryptophanase, which breaks down a precursor of the neurotransmitter

serotonin. Elevated levels of tryptophanases have been associated with a number of neuropsychiatric conditions.

“This research might open the way for the emergence of new treatment options for depression and anxiety, using pre- and probiotics.” —**Chadi A. Calarge, M.D.**

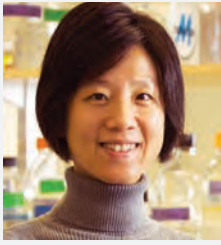


**Ming-Hu Han, Ph.D.**, Icahn School of Medicine at Mount Sinai, will study the ventral tegmental area (VTA) of the brain, one area where changes to neural circuitry have been linked

to depression. The VTA is a major part of the brain's reward circuitry. Dr. Han will investigate how cells in the lateral hypothalamus, a brain area involved in the body and brain's responses to stress, communicate with the VTA.

## BASIC RESEARCH *(cont.)*

### DEPRESSION *(cont.)*



**Yingxi Lin, Ph.D.**, Massachusetts Institute of Technology, will look for clues about what makes some people develop depression in response to social stressors, whereas others are resistant. Using a mouse model of depression, she will analyze differences between the brains of animals that are susceptible or resistant to developing depression-like symptoms

when confronted with social stress.

“This study will identify circuit components that are critical for depressive behaviors and will lay the foundation for future research to uncover the basic circuit mechanisms underlying depression.”

—Yingxi Lin, Ph.D.

### MOOD DISORDERS



**Samer Hattar, Ph.D.**, Johns Hopkins University, has discovered a neural pathway by which light directly influences mood, independent of the biological clock and sleep. He will use his NARSAD Grant to identify the brain regions that negatively alter mood and cognition when people are exposed to irregular light patterns, such as during shift work or traveling across time zones.

“Our laboratory is defining the retinal and brain circuits that mediate the effects of light on mood and learning and memory.”

—Samer Hattar, Ph.D.



**Gregg D. Stanwood, Ph.D.**, Florida State University, will investigate the role of dopamine D2 receptors in regulating brain development. There is evidence that misregulation of these receptors causes developing neurons to migrate improperly and can have long-term consequences on behavior.

“With this NARSAD Grant my group will investigate the mechanisms through which dopamine D2 receptors impact brain development and contribute to the prodromal foundations of mental health disorders.”

—Gregg D. Stanwood, Ph.D.

### POST-TRAUMATIC STRESS DISORDER (PTSD)



**Tanja Jovanovic, Ph.D.**, Emory University, will examine areas of the brain related to processing fearful emotions. These areas are known to be altered in PTSD and are activated in individuals with a variant of a gene called FKBP5 that increases risk for PTSD. Changes in chemical “tags” on the gene (methyl molecules) have been noted following childhood trauma. Dr. Jovanovic’s team will

compare brain activation of FKBP5 and the status of these methyl marks, in children with and without trauma exposure.

“This study will significantly contribute to the development of early intervention strategies for children at high risk for developing anxiety and depression disorders.”

—Tanja Jovanovic, Ph.D.

**PTSD** (cont.)



**Bo Li, Ph.D.**, Cold Spring Harbor Laboratory, aims to elucidate the mechanisms that cause abnormal fear processing in anxiety disorders such as PTSD. He will use his NARSAD Grant to investigate brain

circuits in the anterior insular cortex and the amygdala, brain regions that are activated during the experience of fear and that are hyperactive in people with anxiety disorders.

“The support from the Brain & Behavior Research Foundation, through this NARSAD Independent Investigator Grant, is essential for us to get this project off the ground.” —**Bo Li, Ph.D.**



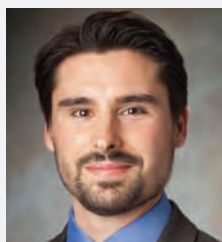
**Rajesh Narendran, M.D.**, University of Pittsburgh, will investigate the role of nociceptin, a brain chemical thought to counteract stress and anxiety, in protecting against PTSD. He will use PET scans to image the brains

of college women who have experienced sexual violence and determine whether there are differences in the numbers of nociceptin receptors between women who developed PTSD and those who did not.

“We are very excited to have the opportunity to evaluate the role of the anti-stress neuropeptide nociceptin in individuals with PTSD and resilience.”

—**Rajesh Narendran, M.D.**

**SCHIZOPHRENIA**



**Alan Anticevic, Ph.D.**, Yale University, will combine laboratory and clinical studies to better understand the disruptions to neural networks that give rise to schizophrenia. Lack of knowledge about the biological processes underlying schizophrenia’s onset limits progress in developing treatment for the early phases of the disorder, when intervention is vital.

“This project has implications for the rational design of treatments for schizophrenia.”

—**Alan Anticevic, Ph.D.**



**Murray J. Cairns, Ph.D.**, University of Newcastle, will use genetic clues to search for the biochemical mechanisms that give rise to schizophrenia. He will investigate how cell function is affected by specific genetic variations in regions of the genome that the Psychiatric Genomics Consortium has associated with the disorder.

“This project will explore the biological function of disease-associated changes in gene expression.”

—**Murray J. Cairns, Ph.D.**



**Ana Luisa M. Carvalho, Ph.D.**, University of Coimbra, will investigate whether abnormalities in the stargazin protein in people with schizophrenia disrupt the ability of neural circuits to adapt to changes in the environment. She will use mouse models to test the cellular and behavioral effects of specific variations in the CACNG2 gene that encodes stargazin, which she identifies in patients with the disorder. She will also image

“Schizophrenia is a devastating mental disorder that affects about one percent of the population.”

—**Ana Luisa M. Carvalho, Ph.D.**

the brains of both mice and patients to test how brain chemistry and connectivity are affected by stargazin mutations.



SCHIZOPHRENIA (cont.)



**Michael Andrew Fox, Ph.D.**, Virginia Tech, will investigate how cells known as parvalbumin-expressing interneurons form inhibitory synapses, through which they can dampen the activity of other brain cells. Defects in inhibitory synapses from these cells have been strongly linked to autism, epilepsy, and schizophrenia. Understanding the molecular signals

that guide their formation could aid in the development of treatments for these disorders.

“We lack a clear understanding of the molecular mechanisms responsible for the formation of inhibitory synapses. Here we aim to elucidate novel molecular signals that underlie the formation of these important synapses.”

—**Michael Andrew Fox, Ph.D.**



**Wen-Jun Gao, M.D., Ph.D.**, Drexel University College of Medicine, will evaluate whether reduced signaling from brain cells called parvalbumin-containing fast-spiking interneurons causes problems with short-term memory. Inhibitory signaling from these cells is thought to be diminished in people with schizophrenia.

Dr. Gao’s team will explore ways to enhance their activity and determine whether this improves cognitive function in a mouse model of the disorder.

“This study will address a fundamental question of whether augmenting inhibition is sufficient to ameliorate cognitive symptoms in schizophrenia that are involved in impaired inhibitory circuitry.”

—**Wen-Jun Gao, M.D., Ph.D.**



**Jacob M. Hooker, Ph.D.**, Massachusetts General Hospital, Harvard University, will measure epigenetic dysfunction in the human brain using a new PET radiotracer for histone deacetylase (HDAC) that his lab developed. His team will associate changes in HDAC with changes in brain function using a brain-specific simultaneous MR-PET scanner. The research will clarify

the role of HDAC in diseases including Alzheimer’s and schizophrenia.

“I am thrilled to have been selected for a NARSAD Grant and even more thrilled to advance our neurochemical imaging studies using the support the award provides.”

—**Jacob M. Hooker, Ph.D.**



**Christopher Barnaby Nelson, Ph.D.**, Orygen Youth Health Research Centre (OYHRC), University of Melbourne, wants to improve understanding of the vulnerability factors and mechanisms that lead to psychotic disorders, in order to develop new tools to identify young people who are at the highest risk of developing these conditions. He is planning

a clinical study to analyze the relationship between certain cognitive disturbances and the disturbed sense of self experienced by people with schizophrenia. The study will assess the value of a range of clinical, cognitive, and psychophysiological measures in predicting psychotic disorders.

“The study may result in an improved ability in the health care system to identify young people at risk of these disorders and implement preventive interventions.”

—**Christopher Barnaby Nelson, Ph.D.**

SCHIZOPHRENIA (cont.)



**Francesco Papaleo, Ph.D.**, Italian Institute of Technology, will investigate how variations in the dystrobrevin-binding protein 1 gene affect an individual's response to antipsychotic drugs. The gene affects the expression of dopamine D2 receptors, which are implicated in the onset of schizophrenia symptoms and targeted by every antipsychotic drug currently in clinical use.

“Genetic screening can be used as a base to implement more effective and personalized therapeutical strategies in schizophrenia.”

—**Francesco Papaleo, Ph.D.**



**Kevin M. Spencer, Ph.D.**, VA Boston Healthcare System, Brockton, Harvard University, is studying anomalies in brain activity patterns that are characteristic of schizophrenia. He aims to determine what causes increased spontaneous gamma oscillations in the brains of people with schizophrenia and whether this activity is related to or increases the risk of psychosis.

“The results of this project will help facilitate the development of new treatments for schizophrenia.”

—**Kevin M. Spencer, Ph.D.**



**Joseph Ventura, Ph.D.**, University of California, Los Angeles, will evaluate the effects of inflammation on cognition in patients with schizophrenia. He will examine whether inflammation influences patients' response to cognition-enhancing treatments, particularly aerobic exercise. There is evidence to suggest that regular aerobic exercise can improve learning and memory in some people with schizophrenia.

“The evaluation of inflammatory processes could provide useful predictors of treatment response and suggest new intervention targets for cognitive deficits in schizophrenia patients.”

—**Joseph Ventura, Ph.D.**

Dr. Ventura will investigate whether inflammation levels can be used to predict whether an individual patient will experience these benefits.



**Stanislav S. Zakharenko, M.D., Ph.D.**, St. Jude Children's Research Hospital, is investigating age-dependent regulation of a neural circuit the brain uses to detect and analyze auditory information. The circuit may be misregulated in people with schizophrenia, causing auditory hallucinations. Dr. Zakharenko's experiments are designed to help explain why these hallucinations arise later in life.

“I am honored and thrilled to receive the NARSAD Independent Investigator Grant. This funding will enable my lab to investigate the molecular mechanisms that drive the changes in brain circuits associated with schizophrenia. We are eager and excited to get these experiments underway!”

—**Karen Zito, Ph.D.**



**Karen Zito, Ph.D.**, University of California, Davis Medical Center, will examine the cellular and molecular mechanisms that stabilize dendritic spines on the surface of neurons. The numbers of these spines, which facilitate neuron-to-neuron communication, are reduced on the brain cells of people with schizophrenia.

SUICIDE



**Daniel Paul Dickstein, M.D.**, Brown University, will seek to identify brain activity patterns that can be used to identify children who are at high risk for

suicide. He will use functional MRI scans to evaluate changes in brain circuits relating to peer acceptance and attitudes towards suicide in two group of children—one group without psychiatric illness and one group of children engaged in self-injury, which is a potent risk factor for a first-time suicide attempt.

“Without the Brain & Behavior Research Foundation’s willingness to take a risk and to invest in our research project with a NARSAD Grant, we would be unable to conduct our cutting-edge study.”

—Daniel Paul Dickstein, M.D.

TIC DISORDERS



**Christopher J. Pittenger, M.D., Ph.D.**, Yale University, will use a mouse model developed in his lab to investigate the brain abnormalities that underlie Tourette

syndrome and other tic disorders. His team will explore atypical features they have observed in the mice that affect the neurotransmitter GABA and supporting brain cells called oligodendrocytes.

“Disorders such as Tourette syndrome lead to great suffering and are difficult to treat. We aim to put the pathophysiological analysis of Tourette syndrome on a more solid footing and establish a paradigm for the evaluation of models that will be applicable to other conditions.”

—Christopher J. Pittenger, M.D., Ph.D.

# Meet the Scientist

A Virtual Q&A Discussion

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July 14

**BORDERLINE PERSONALITY DISORDER**

**D. Bradford Reich, M.D.**

Harvard Medical School



August 19

**ADDICTION**

**Nora D. Volkow, M.D.**

National Institute of Drug Abuse, National Institutes of Health



September 8

**NEW APPROACHES IN TREATING DEPRESSION**

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

Cold Spring Harbor Laboratory, Icahn School of Medicine at Mount Sinai



October 13

**MOOD DISORDERS**

**Carrie E. Bearden, Ph.D.**

University of California, Los Angeles



November 10

**SCHIZOPHRENIA**

**Carol A. Tamminga, M.D.**

University of Texas Southwestern Medical School



December 15

**AUTISM AND NEW FINDINGS**

**Joseph Buxbaum, Ph.D.**

Icahn School of Medicine at Mount Sinai



**MODERATOR:**

**Jeffrey Borenstein, M.D.**

President & CEO, Brain & Behavior Research Foundation  
Host of the PBS TV series “Healthy Minds”



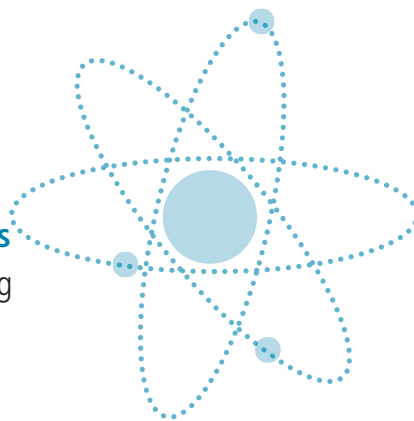
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## NEW TECHNOLOGIES

NARSAD Grants fund **New Technologies** to advance or create new ways of studying and understanding the brain



### DEPRESSION



**Gilles R.C. Pourtois, Ph.D.**, Ghent University, will evaluate whether people with depression whose symptoms include severe anhedonia—an inability to experience pleasure—are less likely than others to benefit from treatments that involve

non-invasive brain stimulation. The research could help explain how a specific form of transcranial magnetic stimulation—accelerated theta burst stimulation of the left dorsolateral prefrontal cortex—improves the symptoms of depression for about 40 percent of patients..



**Laura Rachel Stroud, Ph.D.**, The Miriam Hospital, Brown University, is seeking methods to identify infants whose mothers' severe depression puts them at risk for developing brain problems and major

depressive disorder. Using three-dimensional ultrasound, she will look for brain, endocrine, and behavioral changes in the fetus that are associated with major depressive disorder in mothers and can be detected during pregnancy.

“This project seeks to establish valid neurophysiological (ERP-related) biomarkers of anhedonia in order to improve the treatment (based on neurostimulation) of major depressive disorder.” —**Gilles R.C. Pourtois, Ph.D.**

“In order to halt the inter-generational cycle of major depressive disorder, novel approaches are needed to delineate mechanisms and earliest markers of child risk.” —**Laura Rachel Stroud, Ph.D.**

### SCHIZOPHRENIA



**Judith Gault, Ph.D.**, University of Colorado, Denver, is investigating deep brain stimulation (DBS) as a potential treatment for schizophrenia. To evaluate the effectiveness of DBS in treating schizophrenia, researchers first need to identify abnormal circuits in the brain that might benefit from therapeutic stimulation. Dr. Gault will assess neuronal activity in the brains of patients who are undergoing DBS treatment for Parkinson's disease to identify regions involved in a phenomenon called auditory gating. Auditory gating is impaired in most people with schizophrenia, and these circuits may be good targets for DBS.

“Ultimately, our intent is to identify nodes integral to inform the development of deep brain stimulation for the treatment of schizophrenia.”

—**Judith Gault, Ph.D.**

## MULTIPLE DISORDERS



**Adam Kepecs, Ph.D.**, Cold Spring Harbor Laboratory, will take advantage of new light-based genetic tools to monitor and manipulate the activity of cells that release the neurotransmitter serotonin in mice. Serotonin levels are modulated by drugs to treat depression, anxiety, panic disorder, chronic pain, and other psychiatric conditions, but the chemical's precise effects remain unclear. Dr. Kepecs'

experiments are designed to clarify how serotonin-releasing cells affect behavior.



**Kirsty Millar, Ph.D.**, University of Edinburgh, will study neural precursor cells that her lab has grown from skin cells donated by a family with a significant genetic risk of developing schizophrenia or severe depression. Dr. Millar will use the cells to identify genes whose activity is altered by the chromosomal rearrangement in the at-risk family, and use that information to identify altered biological

pathways that may contribute to the development of disease.



**Jason James Radley, Ph.D.**, University of Iowa, is studying how chronic stress leads to prolonged increases in the stress hormone cortisol. Cortisol increases alertness and thinking abilities, but chronically high levels can have negative effects on health and contribute to the development of several psychiatric conditions. Dr. Radley will use new light-based tools to identify neural circuits that regulate the release of

cortisol and determine whether stimulating these circuits can reduce its levels in a rat model of chronic stress

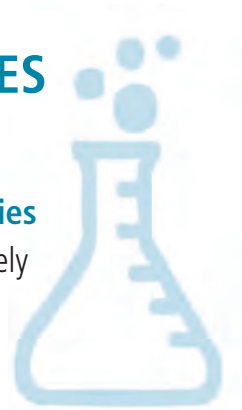
"I am delighted to receive this funding which builds upon the generosity of members of a Scottish family that has donated biopsies to generate induced pluripotent stem cell-derived neurons." —**Kirsty Millar, Ph.D.**

"We hope that scientific advances in this area will enable a better understanding of the chicken-and-egg relationship between abnormal cortisol levels and psychiatric illnesses."

—**Jason James Radley, Ph.D.**

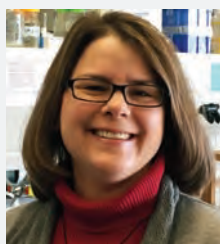


# NEXT GENERATION THERAPIES



NARSAD Grants fund **Next Generation Therapies** to reduce symptoms of mental illness and ultimately cure and prevent brain and behavior disorders

## AUTISM SPECTRUM DISORDER (ASD)



**Suzanne Paradis, Ph.D.**, Brandeis University, will investigate the potential of a protein her lab discovered, Sem4D, to restore the balance of excitation and inhibition in the brain. Neurons in the brain connect with one another via two kinds of synapses—excitatory synapses, which promote information propagation, and inhibitory synapses, which prevent it. The balance between excitatory and inhibitory synapses is

thought to be disrupted in the brains of people with autism. Sem4D causes new inhibitory synapses to form very rapidly, suggesting it may be a useful therapeutic.

“It is our hope that investigating this process will yield insight into new therapeutic avenues for restoring inhibition in the brain, and ultimately, novel treatments for these disorders.”

—Suzanne Paradis, Ph.D.

## BIPOLAR DISORDER (BP)



**Jean-Martin Beaulieu, Ph.D.**, Laval University, will investigate the molecular mechanism that makes lithium an effective treatment for bipolar disorder. The drug, which has been used since 1949, can cause serious side effects if its use is not carefully monitored. Determining its molecular mechanism is a first step toward developing alternative treatments that are safer or more effective.

“This project constitutes a step toward the rational discovery of selective therapeutic agents for the treatment of bipolar disorder.”

—Jean-Martin Beaulieu, Ph.D.



**Christopher E. Ramsden, M.D.**, National Institute of Neurological Disorders and Stroke will explore how omega-6 and omega-3 fatty acids in the diet affect the symptoms of bipolar disorder and migraines. Dr. Ramsden has found that changing dietary levels of these fatty acids can reduce both pain and psychological distress in patients with chronic headaches, and is now testing whether the same diet can

benefit people with bipolar disorder. He will use his NARSAD Grant to investigate the molecular mechanisms that link omega-6 and omega-3 fatty acids to causes of bipolar disorder and migraines in the central nervous system.

“This NARSAD Grant will help us elucidate molecular mechanisms linking abnormal brain lipid metabolism to the pathogenesis of bipolar disorder and migraine headaches.”

—Christopher E. Ramsden, M.D.

## DEPRESSION

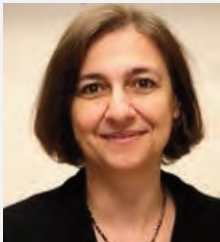


**Venetia Zachariou, Ph.D.**, Icahn School of Medicine at Mount Sinai, will investigate the mechanism of antidepressant drugs that target the glutamate system. Glutamate-targeting drugs are fast acting and effective for many patients who have not responded to classical antidepressants. Understanding their cellular effects could help identify targets for new therapies and reveal factors that determine individual responses to treatment.

“We want to further understand the key protein interactions and signal transduction adaptations involved in the actions of ketamine-like antidepressants.”

—**Venetia Zachariou, Ph.D.**

## POST-TRAUMATIC STRESS DISORDER (PTSD)

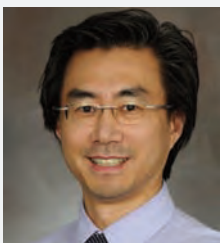


**Adriana Feder, M.D.**, Icahn School of Medicine at Mount Sinai, will evaluate the effectiveness of the anesthetic ketamine for treating PTSD. Dr. Feder's team has shown that the severity of PTSD symptoms decreases with a single sub-anesthetic dose of ketamine, and will now test whether repeated ketamine treatment can maintain an improvement in symptoms over a prolonged period.



**Ilan Harpaz-Rotem, Ph.D.**, Yale University, will test whether prolonged exposure therapy is more beneficial to people with PTSD when it follows a dose of ketamine. Prolonged exposure therapy, which involves helping people confront their memories and feelings about a trauma in a safe way, is considered the most effective treatment for PTSD. There is emerging evidence that the anesthetic ketamine not only relieves PTSD symptoms but also temporarily increases the brain's capacity to rewire its connections, suggesting a window of opportunity to enhance the effects of behavioral therapy.

## SCHIZOPHRENIA



**Raymond Y. Cho, M.D., M.Sc.**, University of Texas Health Science Center at Houston, will investigate whether transcranial direct current stimulation (tDCS) improves motivation and emotional expression in people with schizophrenia. There is evidence that tDCS—the application of weak, virtually unnoticeable electrical currents over the scalp—can reduce auditory hallucinations, but its effects on the cognitive symptoms of schizophrenia have not been assessed.



**Dean Francis Salisbury, Ph.D.**, University of Pittsburgh School of Medicine, will work to develop simple biomarkers to aid in detecting the early stages of a psychotic break in individuals with schizophrenia. Early identification is essential for treatments that could prevent the emergence of psychosis and its life-long debilitating effects.

“We are grateful for this NARSAD Grant which will help us to develop new neurophysiological tests to detect the presence of psychosis.”

—**Dean Francis Salisbury, Ph.D.**

## MULTIPLE DISORDERS



**Jay A. Gottfried, M.D., Ph.D.**, Northwestern University, will test whether fear memories can be selectively reactivated and weakened during sleep, and whether this reduces specific fears when a person is awake. The ability to target specific memories for transformation during sleep could be beneficial for treating post-

traumatic stress disorder, specific phobias, and other anxiety disorders.



**Sachin Patel, M.D., Ph.D.**, Vanderbilt University, will research the role of a lipid produced by the nervous system, 2-arachidonoylglycerol (2-AG), in protecting against depression during stress. 2-AG activates the same receptor in the brain that is targeted by tetrahydrocannabinol (THC),

the psychoactive compound in marijuana. In animal studies, lack of 2-AG produces anxiety, social interaction deficits, and an inability to experience pleasure. Dr. Patel seeks to determine whether enhancing 2-AG levels could be an effective strategy for treating stress-related psychiatric disorders.

“Our proposed work will yield significant insights into the neural plasticity of emotional memories, with promise for guiding future translational work in the areas of psychiatric illness, anxiety, and pathological fear.”

—Jay A. Gottfried, M.D., Ph.D.

“Our ultimate aim is to develop novel cannabinoid-based therapeutic approaches for major depression and anxiety disorders.”

—Sachin Patel, M.D., Ph.D.

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# THE POWER OF A RESEARCH PARTNERSHIP



Frances and Bob Weisman

Danielle M. Andrade, M.D.

Frances and Bob Weisman have a Research Partnership with Danielle M. Andrade, M.D., of the University Health Network at the University of Toronto, a 2010 NARSAD Young Investigator grantee.

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*“Supporting research is essential in order to advance our knowledge as to how the brain works and what can go wrong to cause mental illness. Focused research is certain to lead to relief and comfort for the millions who struggle daily with these illnesses. Our participation for over 20 years with the Foundation, and as Research Partners for the past 14 years, gives us the opportunity to support and motivate the endeavors of the Young Investigators who are focused on these complex issues.”*

—The Weismans

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# A Downward Spiral Leads to Uplift

## Former NFL Player Helps Others After Facing His Diagnosis



### Keith O'Neil

Former NFL Player & Super Bowl Champion  
President & Founder,  
4th and Forever Foundation

Dreams and reality were always at odds for Keith O'Neil. With a former NFL player for a father and an early love for the game, he longed to play professional football, even as a child. "I always had a dream about playing in the league," he says.

But severe anxiety clouded that childhood vision. "I couldn't sleep at night," he recalls. "My mind would just keep going." Around age 12, he began having suicidal thoughts—not crafting plans, but staring at the bottles in his parents' medicine cabinet. "I'd want to die," he says. "I'd want everything just to end."

His parents knew he was moody, but because he would snap out of it, they never suspected an underlying illness. The symptoms receded during high school, and his love for football—the competition, camaraderie, and physicality—flourished.

Keith attended Northern Arizona University on an athletic scholarship, playing football for all four years. But the symptoms resumed, and he turned to alcohol. "I needed a release from the stress I put on myself," he says. "I think drinking was a coping mechanism."

Just as his NFL dream came true—he joined the Dallas Cowboys after college—an old reality returned. Constantly anxious, he didn't sleep for five nights straight during rookie training. "I was a mess," he recalls. Gradually, he learned to manage his symptoms by preparing himself for sleep and sticking to a routine. He played with the Cowboys for two years.

When the Indianapolis Colts picked him up in 2005, Keith realized another dream: playing under revered coach Tony Dungy. But the anxiety worsened. He couldn't stop

## Through 4th And Forever, Keith is realizing a new dream, easing the way for others and reducing the stigma surrounding mental illness.

thinking about the playbook, yet kept forgetting plays. He worried about days ahead and days past. He knew he had to make a decision: "I was going to quit the NFL or I was going to get help," he says.

Keith confessed to Dungy not only about his present state but also his lifelong anxiety. Dungy rallied his staff to help. Keith began taking anti-anxiety medication and continued to play. In his fourth year with the team, the Colts won the Super Bowl.

His new reality soon came crashing down. He and his wife, Jill, who he'd met in college, returned to his hometown of Buffalo, New York. Keith got a job in medical device sales, and Jill became pregnant. But her miscarriage in December 2010 triggered a severe manic episode. After a few days of euphoria—he spent money, he felt great—Keith became paranoid and delusional. He thought a "higher being" was tapping his computer, phone, and even his thoughts. He hallucinated.

Lucid enough to know something was wrong, he researched his symptoms online and diagnosed himself with cyclothymia—a mood disorder in which emotions swing between mild depression and hypomania, or elevated mood. His friend's mother, a psychologist, urged him to seek psychiatric help. The symptoms worsening, Jill had to make the appointment. "Without the support of my wife and family I don't know what would have happened to me," Keith says. Within a week, he had a clinical diagnosis of bipolar 1 disorder—severe mood swings from mania to depression—and began medication.

There was still an uphill battle to climb. Coping with the reality of his illness and medication side effects, Keith sank into an 18-month-long depression that persisted even after the birth of his son, Conor, in April 2012.

That summer, Keith met Steven L. Dubovsky M.D., a psychiatrist at the University of Buffalo. Dr. Dubovsky prescribed lithium, oxcarbazepine (Trileptal) and aripiprazole (Abilify), which "really made all the difference in the world," says Keith. "I still deal with my moods but I'm as healthy as I can get."

As he regained his life, Keith learned how many other people suffer from mental illness, often in silence. In October 2013, he founded 4th And Forever, a non-profit organization dedicated to raising awareness, providing education, and funding research. Today, Keith travels the country speaking with communities and high school students. He has served as the keynote speaker at two *Foundation Discovery to Recovery: A Path to Health Minds* conferences; in September, 2014 in Washington DC and in February, 2015 in Los Angeles where he spoke about his experience and living a productive life.

Although Keith sometimes has normal performance anxiety before big talks, "the reaction I get from the crowd is well worth it," he says.

Through 4th And Forever, Keith is realizing a new dream, easing the way for others and reducing the stigma surrounding mental illness. "I want to do something to help, to say 'I went through this and it's okay to talk about it.'"

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# FREQUENTLY ASKED QUESTIONS

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## *on* SUICIDE

Q  
A

### **Do adolescents die as a result of suicide more often than adults?**

No. Adolescents and younger adults—up to age 25—have consistently lower rates of suicide completion than older adults.<sup>1</sup> The U.S. Centers for Disease Control and Prevention, which calculates the suicide rate among Americans each year, reported in 2013 that there were 10.9 suicide deaths for every 100,000 people aged 15 to 24. This is the second lowest suicide rate among the U.S. population, with only children aged 14 and younger completing fewer suicides. The highest suicide rate was 19.1 deaths among 100,000 people aged 45 to 64. As of 2011, however, the CDC also reports that suicide is the second leading cause of death among people aged 15 to 24. Suicidal thoughts and planning, as well as suicide attempts, are also more common among people aged 18 to 29 compared to adults aged 30 or older.<sup>2</sup>

Q  
A

### **What are some of the most common risk factors in adolescent suicide?**

Having a psychiatric disorder such as depression or bipolar disorder is one of the biggest risk factors for suicide at any age. Other important risk factors for adolescent suicide include a family history of suicidal behavior or psychiatric disorders, a history of physical or sexual abuse, and alcohol or drug abuse. A teen's risk rises when he or she has access to a way to complete suicide, such as easy access to a firearm. Life stresses such as parents' divorce or a friend or family member's death, or ongoing stresses from harassment or bullying, can add to the risk of completing suicide. Scientists are also examining adolescents and others to see if there are any biological or chemical signs in the brain that can be used to predict a person's risk of suicide. 2008 NARSAD Young Investigator grantee Vincenzo De Luca, M.D., of the University of Toronto has been studying changes in genes that may be linked to the risk of suicide, including genes that help to regulate serotonin, a message-transmitting chemical that plays a large role in many mood disorders.<sup>3</sup> 2015 NARSAD Independent Investigator grantee Daniel Paul Dickstein, M.D., of Brown University, is looking at functional MRI scans to search for changes in brain circuits in adolescents who have injured themselves deliberately—a behavior that puts them at higher risk of a suicide attempt.<sup>4</sup> Dr. Dickstein hopes that these brain scans could be used someday to identify children at high-risk for suicide.

## **Q How does a family history of suicide contribute to an adolescent's risk of suicide?**

**A** Scientists know that some psychiatric disorders that raise the risk of suicide, such as depression, schizophrenia, and bipolar disorder, can run in families. This is one indirect way that a family history could increase a teen's risk of suicide. Some studies of twins also suggest that a tendency toward suicide could be inherited separately from any inherited disease such as depression.<sup>5</sup> Apart from specific diseases, 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, and his fellow researchers have noted that impulsive aggression, which has been linked to suicide risk, is a behavior that appears to run in families.<sup>6</sup> Some researchers also think that a family suicide may serve as something like a "role model" for adolescents who may already be at high risk for suicide as the result of a psychiatric disorder or other stresses.

## **Q I've heard that reports of suicide in the media can be "contagious," especially for young people. Is there any truth to that?**

**A** Yes. Many studies, including a 2012 report that examined 56 earlier research papers, show that media coverage of a suicide can lead to increases in suicidal thoughts and attempts and completed suicides among people who read about or watch coverage of the suicide.<sup>7</sup> This contagion effect is especially strong among people aged 15 to 24, if the media coverage somehow "glamorizes" the suicide or provides detailed information on how the suicide was completed. Journalists have partnered with suicide prevention organizations and public health experts to develop guidelines for reporting on suicide that minimize the contagion effect.<sup>8</sup>

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

<sup>2</sup> U.S. Centers for Disease Control and Prevention, Understanding Suicide. [http://www.cdc.gov/violenceprevention/pdf/suicide\\_factsheet-a.pdf](http://www.cdc.gov/violenceprevention/pdf/suicide_factsheet-a.pdf)

<sup>3</sup> C.C. Zai et al., "Genetic Factors and Suicidal Behavior" in *The Neurobiological Basis of Suicide*. Free download at [www.ncbi.nlm.nih.gov/books/NBK107191](http://www.ncbi.nlm.nih.gov/books/NBK107191)

<sup>4</sup> K.L. Kim et al., "Psychiatric and self-injury profiles of adolescent suicide attempters versus adolescents engaged in nonsuicidal self-injury" *Suicide and Life-Threatening Behavior*, Volume 45, Pages 35-50, February 2015.

<sup>5</sup> American Foundation for Suicide Prevention. [www.asfp.org](http://www.asfp.org)

<sup>6</sup> D.A. Brent et al., "Peripubertal suicide attempts in offspring of suicide attempters with siblings concordant for suicidal behavior" *American Journal of Psychiatry*, Volume 160, Pages 1486-1493, August 2003.

<sup>7</sup> M. Sisask and A. Värnik, "Media roles in suicide prevention: a systematic review" *International Journal of Environmental Research and Public Health*, Volume 9, Pages 123-38, 2012.

<sup>8</sup> For more information on the guidelines, visit <http://reportingonsuicide.org>

# Parenting

## Advice for Parents on Suicide and Suicidal Behavior in Young People



### David Shaffer, M.D.

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David Shaffer, M.D., is the Irving Philips Professor of Child Psychiatry and Professor of Psychiatry and Pediatrics at The College of Physicians & Surgeons, Columbia University. He is the Chief of the Division of Child and Adolescent Psychiatry at Columbia University Medical Center. Dr. Shaffer, a recipient of the 2006 Brain & Behavior Research Foundation Ruane Prize for Outstanding Achievement in Child and Adolescent Psychiatric Research and a 1992 NARSAD Distinguished Investigator Grantee, is a pioneer in the study of suicide and was the lead investigator in developing the Children's Global Assessment Scale (C-GAS). He has led a team of colleagues and investigators in developing and modifying the Diagnostic Interview Schedule for Children (DISC) and the Columbia Teen Screen.

**Over the course of your career, you have made a number of major discoveries about suicide. Let's discuss some of these in the context of giving advice to parents. First, at what age does thinking about suicide—"suicidal ideation"—begin? It is not common in young children, correct?**

Suicidal ideation doesn't carry an awful lot of weight at a very young age. And suicidal behavior—as distinguished from talking about it—is very, very rare in young children. You rarely see suicide attempts before puberty. The nature of most attempts in the young child are basically doing things that one's parents say are dangerous. These are things that children have learned will generate a response. If you want to scare your parents, you sit on the window ledge, or walk into traffic. The truth is, pre-pubescent

children have got a different brain, it works in a completely different way, and their ability to express a full range of emotions and to plan things and do all the things that go into a successful suicide are just not available until adolescence. There are big leaps in cognitive abilities that come with adolescence—the ability to empathize with others, the ability to generalize, etc.

### **If I am the parent of a child who is troubled and I fear he or she is contemplating suicide, what should I be thinking and doing?**

What I often say to parents in this situation is: what's making the child think about that? Is there a family history? Is it exposure to somebody else who has committed suicide who might be setting an example or generating imitation? Has the child made direct threats? Each of those has ramifications. Regarding threats, one normally takes passive remarks such as "Oh, I'd rather be dead"—remarks in which one doesn't say, "I'm going to kill myself"—as having not an awful lot of prognostic significance.

But here are things that you do worry about: risk factors that exist within the family—a family history of suicide; if the kid is drinking a lot, getting drunk—alcohol is a very major stimulus of suicide; if there are available methods in the household—a gun collection for example; if there's any evidence that the child has poor emotional control—if he loses his temper very frequently, or easily gets upset; further, if there are crises, or significant "challenges"—it could be an examination, or having to appear in court, or it could be a planned separation by the parents. Such looming events often serve as a marker for a planned suicide. By marker I mean pending events that generate stresses that brew in the kid's mind, and may result in an anticipatory suicide. Such thinking is much more related to "I'd rather be dead than have to face... XYZ" than someone pondering whether life is worth living or having existential doubts.

To summarize, I think one wants to know about the child's usual mood; whether they're doing anything dangerous. For a kid you're worried about, alcohol is about as dangerous as you can get. Are there available methods? And, importantly, what has the underlying history of the child been like?

### **Of those who attempt suicide, what portion have diagnosable psychiatric conditions such as depression?**

A fairly high proportion, whether or not they have actually been diagnosed.

### **I have seen figures as high as 90 percent. Do you trust that number?**

No. I think it understates the impact of what I would call a stress-event—a current stress that is really worrying the person. Some people who experience stressors don't have a psychiatric diagnosis, but they are ill-equipped to deal with the particular stress.

### **What are some popular misconceptions about suicide?**

Referring back to the statistics showing how common it is in adolescence to have thoughts about suicide or to make an attempt: some people, without looking at what the figures mean, assume that if you make an attempt then "you've got suicide in you." People often regard suicidality as a permanent mood state—you're walking around thinking about suicide all day long. But this is not how it happens. Thinking about suicide is episodic, and very brief. Many people will have such episodes, which are then dispelled by the rest of life—things turning out better than expected or simply changing their mind. There's also a widespread belief that there's nothing you can do to stop a suicide, because if you stop someone from doing it one way, they'll find another way. But there is no evidence of that. In fact, the evidence is contrary to

that. When you make access to a particular method more difficult, you don't see increases in other methods.

### **Some of your earliest work showed the importance of emulation and imitation in suicide attempts.**

Yes. There were young people who had committed suicide and next to their body were photos of people, usually famous, who previously had done the same. A sociologist confirmed this after Marilyn Monroe's death. An extensive look revealed that the more coverage a notable suicide received in the press, the greater the imitation effect. What is sometimes called the cluster effect is explained by the fact that at any given time, suicidal ideation is extremely common and so there are a large pool of people thinking about it. In nearly all cases, people don't act on the thought. But when you have a role model, a famous person who commits suicide, and the press coverage depicts it as a tragedy, and not a crime, it glamorizes the act. Seeing this, it's possible for some people to think, "Look, she's a heroine now!"

### **What should we do about this phenomenon?**

I think the moral is, the less talk about suicide, the better. Rather than the reverse. I think most of our work on press coverage supports that.

### **Less talk on whose part?**

On everybody's part. Suicide is not an intuitive thought or action that occurs to everybody. It is given value and usage. Sometimes, accounts of a suicide will go so far as to describe in detail what the person did. Young children and adolescents have relatively few approved options, if they want to assert themselves. Troubled kids, I mean. If you're in a school in which a student has committed suicide, the general advice is, let there be a prayer, or a discussion about something terrible that's happened, some tragedy that's affected this lovely boy who we all knew and loved—and that's that. In other places, people start talking about the causes. And once you get a big

assembly where everyone is talking about causes, you get an amazing amount of scapegoating—perhaps understandably. So you get teachers who are blamed; other kids are made to be scapegoats; so are parents. Quite a lot of damage can be done. I don't think there's any evidence that this damage is a good thing.

### **This brings to mind the recent suicide "clusters" that were reported among high school teens in Palo Alto, California, in the heart of high-pressure Silicon Valley.**

The important thing is: most kids who commit suicide are facing some kind of problem. I would suggest that rather than blame the educational environment or the culture at large, it is more useful to think more about the situation in which the affected child finds himself. The right thing for a parent to do is to help the troubled child and give advice on how they can get out of the fix they are in. I think the most important message for parents is: when a kid is talking about suicide, or when a kid leaves a piece of paper on the desk that has the word suicide in it, or even may threaten suicide, the thing to do is not to start immediately on life and death, but to try and get some understanding of the event that is either looming or has taken place, that is worrying the kid. And then try to work through some options and also to demonstrate support. Suicide equals a worry about something, not necessarily a giving up on everything.

Very often the worry will be made worse by parental distress—by the parent who says, "Oh, that is something you should be worried about." Parents must try to get things into a less lethal, less threatening kind of mode.

### **How?**

The way you move in that direction is, you say, "OK, now we've got this problem between you and so-and-so....What kinds of things have you thought of to get over this?" You can then get the kid to be the parent. Then: when we've gone through the whole long list of things that could be done, "Which do we think is the best?" So it's really very basic;



you try to get the kid involved by letting him ask questions as well as give you answers; and you try to show that the kind of anxieties he's having are very common in life.

When I'm teaching medical residents, I always say: when a kid has an "event," that's a goldmine for you. All of a sudden, out of the blue, they do something. If you can really explore the things which upset them, and the nature of their response, you're getting to something treatable.

### **And what kind of treatments are available?**

CBT—cognitive behavioral therapy—is one method that is used. There has been a good deal of interest recently in an even shorter course of therapy, called IPT—interpersonal psychotherapy. (Its co-developer and champion is Foundation Scientific Council member Dr. Myrna Weissman, profiled on page 6 of this issue). It starts off in a very intriguing way: you write a list of who are the most important people in your life. The therapist takes them up, one by one, and says, "Now, if you have to think of any problem you have with that person, what is it?" That's the first session. There's some evidence that the first session does all the work. You're restoring some kind of proportionality to the situation, bringing it back into normal life, in a way.

### **Is it a way of saying, "These people are important to me—I realize that I really don't want to die"?**

I don't think I would bring the word "die" into it at all. Because I think once you start introducing a bridge between a common problem and death, you're really just reinforcing the value of it, almost normalizing death as a potential response to a common problem.

### **If a parent is concerned, then, and the child has issues, should a therapist be consulted?**

The word therapist is used so broadly. I think you want a psychiatrist because the real issue is you want somebody who's good at making a diagnosis. And



that's the specialty of psychiatry. Also, many clinical psychologists are extremely well educated and I think they are very much in tune with diagnosis. They don't get into medication, but they know which kinds of disorders require medication. Often they are available within the school and then they can actually influence irritants to the child which are occurring in the school.

### **You've made us more aware of the potential danger of talking about suicide. If I am the parent of a troubled child and I've heard your remarks—"less talk about suicide is better"—now I'm scared to bring it up.**

I don't think that's a terrible thing. I think you may want to bring it up because it has happened to somebody else. I think the parts of suicide that you do want to bring up are not necessarily the tragic components, because those can increase the martyr-like role of somebody who has taken their life. The parts to discuss are what's known about the difficulties that this person had in their life.

Most important, I think you want to get into the habit of having your child coming to you with a problem. A lot of liberal parents are very reasonable about that. And they're good listeners. The thing you want, above all, is for the kid to talk to you and you to talk to the kid. You've got to develop that—a strategy of being a good listener. And it's easy. You just say, "Oh, that's interesting. Tell me more about that—what happened?"

# Glossary

**EEG:** Electroencephalography, a method for recording electrical activity in the brain.

**externalizing behaviors:** Behavioral problems that appear in a child's outward relations, with those around him or her. They can take a variety of forms such as conduct problems, noncompliance, aggression toward peers, high activity level, and poor regulation of impulses. Often contrasted with internalizing behaviors, which include withdrawal, anxiety, inhibition and depressed mood.

**fMRI:** A variant of magnetic resonance imaging, which enables researchers to make key measurements of activity and function in the resting brain.

**interpersonal psychotherapy (IPT):**

A short course of psychotherapy co-developed by Foundation Scientific Council member Myrna Weissman, M.D. IPT focuses on an individual's specific vulnerability to social stressors. In as few as three sessions, patients have been able to regain control of mood and functioning.

**MRI:** Magnetic resonance imaging. A procedure in which radio waves and a powerful magnet linked to a computer are used to create detailed pictures of areas inside the body. MRI is especially useful for imaging the brain, the spine, the soft tissue of joints, and the inside of bones. Also called magnetic resonance imaging, NMRI, and nuclear magnetic resonance imaging.

**psychosis:** A severe mental disorder in which a person loses the ability to recognize reality or relate to others. The person is not able to cope with the demands of everyday life. Symptoms include being paranoid, having false ideas about what is taking place or who one is, and seeing, hearing, or feeling things that are not there.

**subclinical:** An illness or disorder that is not severe enough to present definite or readily observable symptoms.



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