

# 2024 Leading Research Achievements

by BBRF Grantees, Prizewinners & Scientific Council Members

Presented in order of publication.



Basic Research; Diagnostic Tools/Early Intervention: **Suicide Prevention**

## Suicide Risk Fluctuates Across the Menstrual Cycle, Affecting Different Women Differently



**Tory A. Eisenlohr-Moul, Ph.D.**

*University of Illinois, Chicago*

2018 BBRF Young Investigator

*Journal: American Journal of Psychiatry*

January 1, 2024

The new research reveals how suicide risk fluctuates not only in correspondence with the menstrual cycle and shifting hormone levels, but also how symptoms fluctuate daily within individuals and how impacts vary from person to person. "While past suicide research has highlighted broad psychopathological and sociodemographic factors as predictors of suicide risk, our study reveals an acute peri-menstrual risk period for suicidal ideation and planning," the team wrote. This, they said, "presents an opportunity for biological and psychosocial intervention."

Next-Generation Therapies: **PTSD, Depression, Anxiety**

## Preliminary Trial of Psychoactive Drug Ibogaine Yields 'Initial Evidence' for Powerful Therapeutic Potential



**Nolan R. Williams, M.D.**

*Stanford University*

2024 BBRF Colvin Prize

2019 BBRF Klerman Prize

2018, 2016 BBRF Young

Investigator

*Journal: Nature Medicine*

January 5, 2024

In a small, preliminary clinical test in military veterans, researchers obtained "initial evidence" suggesting the psychoactive compound ibogaine, when co-administered with magnesium to boost safety, "could be a powerful therapeutic" to safely treat a variety of psychiatric symptoms, including PTSD, depression, anxiety, and suicidality, which can emerge following traumatic brain injury.

The research team included **Jennifer Keller, Ph.D.**, 2009 BBRF Young Investigator.

Basic Research: **Anxiety**

## In Childhood Anxiety, CBT Helps By Normalizing Hyperactive Brain Circuits, Study Finds



**Simone P. Haller, D. Phil**

*National Institute of Mental Health*

2020 BBRF Young Investigator

*Journal: American Journal of Psychiatry*

January 24, 2024

A study of brain network and circuit responses in young people with anxiety disorders who were treated with cognitive behavioral therapy (CBT) suggests how the therapy helps to normalize some (but not all) irregularities likely involved in generating anxiety symptoms. This in turn suggests how CBT and possible adjuncts to it might be modified to improve outcomes. Among the team's findings: CBT may more effectively target cortical circuits, while subcortical dysfunction (including in limbic areas like the amygdala) may lag in responsivity and/or might require more direct interventions to alter exaggerated defensive reactions.

The research team included: **Ned H. Kalin, M.D.**, BBRF Scientific Council; **Rany Abend, Ph.D.**, 2019 BBRF Young Investigator; **Katharina Kircanski, Ph.D.**, 2013 BBRF Young Investigator.

Basic Research: **Depression**

## How Immune Activation May Alter the Brain and Cause Depression-Related Behavior During Chronic Social Stress



**Scott J. Russo, Ph.D.**

*Icahn School of Medicine at Mount Sinai*

BBRF Scientific Council  
2008, 2006 BBRF Young Investigator

This research indicates a specific mechanism through which stress and immune activation combine to alter behavior. A protein called MMP8, released during chronic social stress in mice by circulating immune cells, was able to invade the brain and alter the shape of the space between neurons. This can adversely affect the nucleus accumbens and possibly other brain areas. In mouse experiments, this mechanism was causally linked with social avoidance, an adverse behavioral change seen in human depression.

The research team included: **Eric J. Nestler, M.D., Ph.D.**, BBRF Scientific Council, three-time BBRF prize winner, and 1996 BBRF Distinguished Investigator; **James W. Murrough, M.D.**, 2009 BBRF Young Investigator; **Eric M. Parise, Ph.D.**, 2021 Young Investigator; **Romain Durand-de Cuttoli, Ph.D.**, 2022 BBRF Young Investigator; **Lyonna F. Parise, Ph.D.**, 2022 BBRF Young Investigator; **Long Li, Ph.D.**, 2021 BBRF Young Investigator; **Kenny L. Chan, Ph.D.**, 2022 BBRF Young Investigator.



**Flurin Cathomas, M.D.**

*Mount Sinai / Psychiatric University Hospital Zurich*

2020 BBRF Young Investigator

Journal: *Nature*  
February 7, 2024

Basic Research: **Eating Disorders**

## Food-Seeking Circuit in the Brain That Can Override Hunger or 'Fullness' Signals May Shed Light on Eating Disorders



**Fernando M.C.V. Reis, Ph.D.**

*University of California, Los Angeles*

2022, 2018 BBRF Young Investigator

Researchers discovered that a specific group of neurons in a region of the brainstem (called the periaqueductal grey or PAG) previously associated with fear, when activated, induces mice to forage and eat even when they are not hungry—especially rewarding highly caloric foods. The research could provide important insights into eating disorders such as binge eating disorder and anorexia nervosa.

The research team included **Jonathan C. Kao, Ph.D.**, 2020 BBRF Young Investigator; **Alcino J. Silva, Ph.D.**, a 1999 BBRF Independent Investigator.



**Avishek Adhikari, Ph.D.**

*University of California, Los Angeles*

2014 BBRF Young Investigator

Journal: *Nature Communications*  
March 7, 2024

Next-Generation Therapies: **Autism Spectrum Disorders**

## A Stem Cell-Based Therapeutic ‘Rescue Strategy’ is Developed for Timothy Syndrome, an Autism Spectrum Disorder



**Sergiu P. Pasca, M.D.**

*Stanford University*

2017 BBRF Independent

Investigator

2012 BBRF Young Investigator

Journal: *Nature*

April 24, 2024

Published experiments demonstrated a potential therapeutic “rescue strategy” using stem cell technology for the neurodevelopmental disorder Timothy Syndrome (TS), one of the autism spectrum disorders. By modifying messenger RNA activity for a gene involved in disease pathology, researchers prevented the emergence of disease pathology in human neurons implanted in living mice. Those neurons were generated with stem cell technology that Dr. Pasca and several other grantees have pioneered over the years—the technological predicate to this rapid translation to illness-relevant experiments.

Next-Generation Therapies: **Schizophrenia**

## New First-in-Class Schizophrenia Medicine Reduced Positive and Negative Symptoms in Decisive Phase 3 Trials



**Steven M. Paul, M.D.**

*(Lancet and JAMA Psychiatry papers)*

BBRF Scientific Council Emeritus

KarXT (xanomeline-trospium), a new medicine for treating schizophrenia—one that appears to help reduce both positive and negative symptoms of the illness—performed well in two phase 3 clinical trials reported in 2024 that contributed to the drug’s approval by the FDA in September (its trade name is Cobenfy). It is the first antipsychotic treatment that does not target the D2 dopamine receptor, targeting instead two muscarinic receptors called M1 and M4 with the aim of indirectly impacting the balance between the dopamine and acetylcholine systems, including in the brain’s striatum, which in turn might help therapeutically address pathology that gives rise to psychosis.



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

*(JAMA Psychiatry paper)*

BBRF Scientific Council

2011 BBRF Lieber Prize;

2010, 1998 BBRF Distinguished

Investigator

Journals:

*JAMA Psychiatry*, May 1, 2024

*The Lancet*, January 13, 2024

The research team in the *Lancet* paper included **Christoph U. Correll, M.D.**, 2007 BBRF Young Investigator.

Basic Research; Next-Generation Therapies: **PTSD, Anxiety, Depression**

## Study of One Psychedelic Drug Suggests How It Might be Modified to Eliminate Psychedelic Effects While Retaining Therapeutic Ones



**Lyonna F. Parise, Ph.D.**

*Icahn School of Medicine at Mount Sinai*

2022 BBRF Young Investigator

Journal: *Nature*

May 8, 2024

A detailed study of how the psychedelic drug 5-MeO-DMT interacts with receptors for the neurotransmitter serotonin has suggested that a modified version of the drug that targets the serotonin 1A receptor may not generate psychedelic effects while preserving some of the potential therapeutic effects attributed in various studies to psychedelics in depression, PTSD, and other illnesses.

This research was co-led by Daniel Wacker, Ph.D., of the Icahn School of Medicine at Mount Sinai, and Dalibor Sames, Ph.D., of Columbia University. The team included **Scott J. Russo, Ph.D.**, BBRF Scientific Council and 2008, 2006 BBRF Young Investigator.

Basic Research; Next-Generation Therapies: **Bipolar Disorder**

## Experiments Point to Possible Next-Gen Drug Therapies for Bipolar Disorder, Including for Lithium Non-Responders



**Anouar Khayachi, Ph.D.**

*McGill University*

2022 BBRF Young Investigator

Journal: *The Lancet*  
June 1, 2024

Researchers used stem cell-based technology to study differences in cells sampled from bipolar disorder (BD) patients who respond to lithium vs. those who do not. This led to discovery of two ways to reduce hyperactivity in neurons, a characteristic problem in BD. The research suggests that activation of Akt, a signaling pathway, and AMPK, a protein complex, could be targets for next-gen therapeutics for BD. Personalized medicine for BD, if realized, could address the lag between diagnosis and therapy selection, and reduce the risk of suicide. The research also suggests one possible way of addressing lithium non-response.

Co-leaders of the research team included **Guy A. Rouleau, M.D., Ph.D.**, 2010 BBRF Distinguished Investigator; and **Martin Alda, M.D., FRCPC**, 2020 BBRF Colvin Prize winner and a 2003 and 1999 BBRF Independent Investigator.

New Technologies: **Deep-Brain Stimulation**

## Team Develops an Innovative, Implantable Ultrasound Device to Stimulate Neurons in Deep-Brain Regions



**Canan Dagdeviren, Ph.D.**

*Massachusetts Institute of Technology*

2018 BBRF Young Investigator

Journal: *Nature Communications*  
June 4, 2024

Researchers developed and tested a tiny, implantable neurostimulation device that uses ultrasound to modify the activity of neurons deep in the brain. The neural stimulator, called ImpULS, could become “a potent neuromodulatory tool” for therapeutic applications ranging from major depression to Alzheimer’s.

The research team included **Steve Ramirez, Ph.D.**, 2016 BBRF Young Investigator.

Diagnostic Tools/Early Intervention: **Depression**

## Network Connectivity Patterns in High-Risk Pre-Adolescents Correctly Predicted Depression Symptom Onset 2 Years Later



**Dylan G. Gee, Ph.D.**

*Yale University*

2015 BBRF Young Investigator

Journal: *Developmental Cognitive Neuroscience*  
June 4, 2024

Imaging scans from over 1,700 of the 11,000+ children enrolled in the NIMH’s Adolescent Brain Cognitive Development Study (ABCD) revealed connectivity patterns in the scans of healthy 9- and 10-year olds with parental history of depression that predicted the onset of depression symptoms only 2 years later. This addresses the pressing need to identify predictive neural markers for development of depression prior to the onset of adolescence, especially among children at high familial risk.

The research team included **Taylor J. Keding, Ph.D.**, 2023 BBRF Young Investigator; **Jutta Joormann, Ph.D.**, 2006 BBRF Young Investigator.



Diagnostic Tools/Early Intervention; Next-Generation Therapies: **Bipolar Disorder**

## Researchers Develop 'Mood Instability' Measures to Re-Think How Best to Care for Bipolar Disorder Patients



**Sarah H. Sperry, Ph.D.**

*University of Michigan*

2022 BBRF Young Investigator

Journal: *Nature Mental Health*  
August 8, 2024

Evidence based on mood records from 603 bipolar disorder patients collected over 10 years or longer calls into question the assumption in clinical medicine that periods between low and high mood in bipolar disorder are ones of "normal" mood. The team's finding of considerable "mood instability" between major episodes of depression and mania/hypomania could lead to future efforts to treat such mood fluctuations and in so doing potentially improve quality of life for patients.

**Melvin G. McClinnis, M.D., FRCPsych**, 1999 BBRF Independent Investigator and 1992 BBRF Young Investigator, was a co-author of the paper.

Next-Generation Therapies: **Bipolar Disorder**

## Evidence Grows of the Effectiveness of Rapid-Acting Brain Stimulation to Treat Bipolar Depression



**Nolan R. Williams, M.D.**

*Stanford University*

2024 BBRF Colvin Prize  
2019 BBRF Klerman Prize  
2018, 2016 BBRF Young Investigator

Three papers appearing in 2024 (two by Dr. Williams and colleagues; the other by Dr. Sheline's team) have provided clinical trial-based evidence of the effectiveness and safety of rapid-acting non-invasive brain stimulation therapy to treat people suffering from severe, treatment-resistant bipolar depression. This is of particular importance given the greatly elevated risk of suicide among adults with BD (estimated at 10% - 15% or higher). The three trials involved applications of individually targeted iTBS (intermittent theta-burst stimulation) given 10 times daily in short sessions separated by about 1 hour and continuing over 5 days. The SAINT iTBS-based protocol developed by Dr. Williams's team was approved by the FDA for commercialization in treating major depression in 2022. The trials thus far in depressed BD patients have generated similarly high rates of treatment response and remissions.

The Sheline team included **Nicholas L. Balderston, Ph.D.**, 2021 BBRF Klerman Prize, 2021 and 2018 BBRF Young Investigator; and **Robin Cash, Ph.D.**, 2020 BBRF Young Investigator. Among co-authors of one the Williams papers was **Peter Zandi, Ph.D., MPH, MHS**, a 2004 BBRF Young Investigator.



**Yvette I. Sheline, M.D.**

*University of Pennsylvania*

BBRF Scientific Council  
2005, 2002 BBRF Independent Investigator  
1998 BBRF Young Investigator

Journals:

Williams et al:

*Journal of Affective Disorders*,  
August 16, 2024

*Brain Stimulation*, March 4, 2024

Sheline et al:

*JAMA Psychiatry*, July 10, 2024

Diagnostic Tools/Early Intervention; Next-Generation Therapies: **Addiction**

## A Possible Biomarker for Cocaine Misuse and a Novel Treatment for Cocaine Addiction Based on Compound in Rosemary



**Kevin T. Beier, Ph.D.**

University of California Irvine  
School of Medicine

2017 BBRF Young Investigator

Journal: *Neuron*  
August 16, 2024

Researchers found that activity of certain neurons in the brain's globus pallidus can predict behavioral responses to cocaine in mice. This potential biomarker also suggests a possible basis for novel treatment of cocaine and other substance abuse: administration of carnosic acid obtained from rosemary extract. Currently, there are no effective therapeutics for dependence on psychostimulants like cocaine.

The research team included **Jason Aoto, Ph.D.**, 2016 BBRF Young Investigator.

Next-Generation Therapies: **PTSD, Depression**

## tDCS Non-Invasive Brain Stimulation Fares Well in Trials for PTSD and Major Depression



**Mascha van 't Wout-Frank, Ph.D.**

Brown University

2010 Young Investigator

Two clinical trials co-led by BBRF grantees demonstrate the versatility and potential effectiveness of transcranial direct current stimulation (tDCS), a low-power form of non-invasive brain stimulation, in reducing symptoms of PTSD and major depressive disorder. tDCS uses direct current applied to the scalp to alter neural activity in the cortex and can be used in home-based self-administered applications. The depression study (Dr. Fu and colleagues) was a demonstration of that possibility—users self-administered the treatments over 20 weeks, but were monitored constantly via teleconference. Dr. van 't Wout-Frank and colleagues separately reported encouraging results of a double-blinded, randomized, placebo-controlled trial using tDCS to treat U.S. military veterans with warzone-related PTSD.



**Cynthia H. Y. Fu, M.D., Ph.D.**

King's College London, UK

2006, 2002 Young Investigator

Journals:  
Fu et al: *Nature Medicine*,  
October 21, 2024  
van 't Wout-Frank et al:  
*JAMA Psychiatry*, March 6, 2024

Dr. Fu's colleagues included **Allan H. Young, M.D., Ph.D.**, 2000 BBRF Independent Investigator; and **Jair Soares, M.D., Ph.D.**, a 2002 BBRF Independent Investigator and 1999 and 1997 BBRF Young Investigator. Dr. van 't Wout-Frank's team was co-led by **Noah S. Philip, M.D.**, 2024 BBRF Distinguished Investigator, and included **Amanda Arulpragasam, Ph.D.**, 2024 BBRF Young Investigator, and **Benjamin D. Greenberg, M.D., Ph.D.**, 2000 BBRF Independent Investigator.

Basic Research; Next-Generation Therapies: **Addiction**

## A Strategy to Sharply Blunt Addictive Reward From Opioids While Retaining Their Pain-Relieving Properties



**Francis S. Lee, M.D., Ph.D.**

Weill Cornell Medicine

BBRF Scientific Council  
2010 BBRF Independent  
Investigator  
2005, 2002 BBRF Young  
Investigator

Journal: *Science Advances*  
November 29, 2024

Researchers administered the drug JZL184 in mice to raise levels of 2-AG, a naturally occurring neuromodulator in the endocannabinoid system. This greatly reduced reward from opioids but had no impact on opioids' pain-relieving properties, suggesting a possible adjunctive therapy to reduce opioid addiction in pain patients.

The research team included **Conor Liston, M.D., Ph.D.**, 2013 BBRF Young Investigator; **Virginia M. Pickel, Ph.D.**, 2001 BBRF Distinguished Investigator; **Lisa A. Briand, Ph.D.**, 2015 BBRF Young Investigator; and **Kristen Pleil, Ph.D.**, 2017 BBRF Young Investigator.

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