2025 Leading Research Achievements
by BBRF Grantees, Prizewinners & Scientific Council Members
Presented in order of publication.

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

Next-Generation Therapies: Autism, Schizophrenia, Neurodevelopmental Disorders

Proof-of-Concept Test for an RNA-Based Therapy to Prevent Effects of a Devastating Autism-Related Gene Mutation

Marta Biagioli, Ph.D.

University of Trento, Italy

2015 BBRF Young Investigator

Journal: *Molecular Therapy*
March 5, 2025

Researchers reported progress in developing an RNA-based therapy to treat neurodevelopmental disorders, including some autism spectrum disorders (ASDs). They synthesized a long non-coding RNA (lncRNA) molecule designed to bind to a messenger RNA for the gene CHD8, with the effect of increasing production of the CHD8 protein. This is a way of addressing an insufficiency of that protein in neurons of people with a devastating CHD8 gene mutation that disables one copy of the gene and can lead to macrocephaly, or enlarged head size, in a subset of people with ASDs. Dr. Biagioli noted possible implications of such RNA-based therapies beyond the CHD8 syndrome and ASD, with potential impact "for a large repertory of currently incurable neurologic conditions caused by reduced levels of target protein[s]."

The research team included **Christelle Golzio, Ph.D.**, 2013 BBRF Young Investigator.

Basic Research, Next-Generation Therapies: Eating Disorders

Loss of Pleasure From High-Fat Food That Paradoxically Supports Obesity Is Traced to a Brain Signaling Pathway Involving Neurotensin

Stephan Lammel, Ph.D.

University of California, Berkeley

2015 BBRF Young Investigator

Neta Gazit Shimoni, Ph.D.

University of California, Berkeley

2021 BBRF Young Investigator

Journal: *Nature*
March 26, 2025

The new research helps explain a paradox: why individuals acclimated to high-fat food begin to get less pleasure from it yet continue to eat it and become obese. The team demonstrated that chronic consumption by mice of a high-fat diet alters hedonic feeding behaviors and disrupts signaling in the pathway connecting the lateral nucleus accumbens (NAc) and the ventral tegmental area (VTA). The disruption affects neurotensin, a signaling protein, and influences the progression of obesity. Further experiments showed that targeting neurotensin signaling in the NAc-VTA pathway may be a way to regulate food intake and support healthy weight maintenance—perhaps without disrupting other essential functions mediated by neurotensin, which include regulation of pain and body temperature.

Next-Generation Therapies: Schizophrenia, Bipolar Disorder, Depression

Team Modifies LSD Molecule to Capture Potential Therapeutic Effects While Limiting Hallucinations
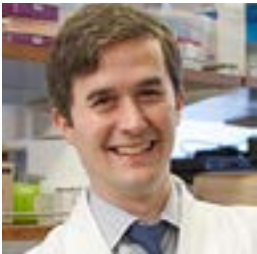
William A. Carlezon, Jr., Ph.D.

*Harvard Medical School
McLean Hospital*

BBRF Scientific Council

2007, 2005 BBRF Independent
Investigator
1999 BBRF Young Investigator

Conor Liston, M.D., Ph.D.

Weill Cornell Medicine

BBRF Scientific Council
2013 BBRF Young Investigator

Journal: *Proceedings of the
National Academy of Sciences
(PNAS)*
April 14, 2025

Three BBRF grantees were part of a team led by Dr. David E. Olson reporting that a slight modification of the LSD molecule produced a distinct drug, named JRT, which appears to have little or no hallucinogenic potential yet retains some of the potentially powerful pro-cognitive therapeutic impact of LSD and other hallucinogens, in addition to having potentially anti-depressant properties. These specific effects suggest that an optimized version of JRT or drugs with similar structural modifications may have the potential to address the negative and cognitive symptoms of schizophrenia, and more broadly, the team said, may be useful in "treating [other] illnesses unlikely to be addressed by psychedelics, including bipolar disorder and psychosis in neurodegenerative diseases."

The research team included **Alex S. Nord, Ph.D**., 2015 BBRF Young Investigator.

Next-Generation Therapies: Depression, Anxiety, PTSD

Non-invasive Ultrasound Brain Modulation Therapy Shows Potential to Treat Mood, Anxiety, Trauma, Across Diagnoses in Pilot Trial

Gregory A. Fonzo, Ph.D.

The University of Texas at Austin

2019 BBRF Young Investigator

Journal: *Molecular Psychiatry*
April 24, 2025

Researchers reported results of a pilot study of low-intensity transcranial focused ultrasound (tFUS), a non-invasive type of brain stimulation, which they tested for safety and therapeutic potential in 29 patients with a variety of mood, anxiety, and trauma-related disorders, as well as 23 healthy controls. tFUS uses focused high-frequency soundwaves to directly stimulate areas of the brain that lie beneath the cortex, including structures involved in mood disorders. Participants in the unblinded pilot clinical trial, most in their early 20s, had overlapping diagnoses: major depression (16); bipolar disorder (10); alcohol use disorder (4); panic disorder (2); anxiety disorders (23); PTSD (10). The team "observed a significant reduction in a general measure of negative-affect symptoms" in the participants, with moderate-to-large effect sizes. Larger trials with placebo comparisons can now follow, exploring diagnostic specificity, the optimal number of treatment sessions, and durability of therapeutic effects.

The research team included **Charles B. Nemeroff, M.D., Ph.D.**, BBRF Scientific Council member, BBRF Selo Prize winner and 2003, 1996 BBRF Distinguished Investigator.

Diagnostic Tools/Early Intervention: Depression, Childhood Mental Health

Sleep Disturbances in Preadolescents Predicted Increased Depression Severity, Self-Harm Behaviors the Following Week

Caroline P. Hoyniak, Ph.D.

Washington University in St. Louis

2022 BBRF Young Investigator

Journal: *Research on Child and Adolescent Psychopathology*
May 14, 2025

The researchers obtained evidence establishing a potentially predictive connection between disturbances in sleep and the occurrence of depression and self-harming behaviors in preadolescent children. Their most important finding was that weekly self-reports of trouble sleeping predicted reports of increased depression severity and engagement in self-harm behaviors the following week. Also, reports of fatigue predicted increased depression severity the following week. "Clinicians working with preadolescents with or at risk for depression and/or self-harm behaviors should regularly assess difficulty sleeping and fatigue," the team advised.

The paper's senior authors were **Joan L. Luby, M.D.**, winner of the BBRF Klerman and Ruane Prizes and 3-time BBRF grantee; and **Deanna Barch, Ph.D.**, BBRF Lieber Prize winner and 4-time BBRF grantee. Both are members of BBRF's Scientific Council.

Next-Generation Therapies: Addiction

Alcohol-Regulating Hormone Delivered in Combination With GLP-1 Drug Has Potential Application in Alcohol Use Disorder

E. Zayra Millan, Ph.D.

University of New South Wales, Sydney, Australia

2020 BBRF Young Investigator

Journal: *Neuropsychopharmacology*
May 26, 2025

Animal experiments with a long-lasting analog of the liver-produced hormone FGF21 indicated how it modulates the brain to curtail alcohol consumption. Notably, the analog altered behaviors involving alcohol consumption. In both sexes, it weakened the intensity of responses following presentation of alcohol-related cues, and reduced the motivation of individual animals to seek alcohol. The impacts of the compound were augmented when combined with a GLP-1 stimulating drug, suggesting a potential future treatment for alcohol use disorder. Separately, trials are currently under way to test drugs such as Wegovy and Ozempic that stimulate the GLP-1 receptor to treat people with alcohol use disorder.

Basic Research: PTSD

Brain Changes Underlying PTSD Are Revealed in Detailed Analysis at the Single-Cell Level

Matthew J. Girgenti, Ph.D.

Yale School of Medicine

2023, 2019 BBRF Young Investigator

Journal: *Nature*
June 18, 2025

A study empowered by advances in technology has provided what is likely the most detailed account to date of biological changes that take place in the brain when someone has post-traumatic stress disorder (PTSD). The new findings shed light on PTSD pathology, identify specific and potentially targetable genetic, cell-type, and functional alterations, and also indicate factors distinguishing brain changes in PTSD vs. major depressive disorder. The data that contributed to the team's analysis was derived from over 2 million individual cells sampled from postmortem brains donated by patients' families.

The research team included: BBRF Scientific Council members including the Council's Vice President, **John H. Krystal, M.D.**, BBRF Colvin Prize winner and 3-time BBRF grantee; **David A. Lewis, M.D.**, BBRF Leiber Prize winner and 2008 BBRF Distinguished Investigator; and **Kristen J. Brennand, Ph.D.**, 2-time BBRF grantee and Maltz Prize winner. Also on the team were **Alicia Che, Ph.D.**, 2019 BBRF Young Investigator; **Nenand Sestan, M.D., Ph.D.**, 2012 BBRF Distinguished Investigator, 2006 Young Investigator; **Paul E. Holtzenheimer, M.D.**, 2016 BBRF Independent Investigator, 2007 Young Investigator; **Jill R. Glausier, Ph.D.**, 2015 BBRF Young Investigator; and **Daniel Levey, Ph.D.**, 2019 BBRF Young Investigator.

Diagnostic Tools/Early Intervention: Depression, Suicide Prevention, Childhood Mental Health

Addictive Use of Phones, Social Media, & Video Games Is "Common" in Young Adolescents and Linked to Risk for Suicidal Behaviors and Worse Mental Health, Study Finds

J. John Mann, M.D.

New York State Psychiatric Institute

Columbia University Medical Center

2022 BBRF Colvin Prize
2008 BBRF Distinguished Investigator

Journal: *Journal of the American Medical Association (JAMA)*
June 18, 2025

Using 4 years of interim data from an ongoing study of mental health and brain development in over 11,000 American children and adolescents, researchers found that "high" or "increasing" addictive use of screen-based activities is not only commonplace, but is also associated with two to three times higher rates of suicidal ideation, suicidal behaviors, and other mental health problems, compared with those with "low" addictive or much weaker habitual screen use. The study calls urgent attention to the issue of developing effective preventive and treatment approaches for those youth who become addicted to their screens.

Diagnostic Tools/Early Intervention: Depression, Suicide Prevention, Childhood Mental Health

More Screen Time in Childhood Followed By Depression in Early Adolescence Is Linked to Less Sleep and White Matter Changes

João Paulo Lima Santos, M.D.

University of Pittsburgh

2021 Young Investigator

Journal: *JAMA Pediatrics*
June 23, 2025

A study based on data from nearly 1,000 young people, ages 9-13, suggests how the amount of time spent on screens each day—TVs, computers, mobile phones, videogames—impacts depression risk at age 13. The study related screen use to sleep patterns and the structure of the brain's white matter. More daily screen time in late childhood (ages 9-10) was associated with more depressive symptoms in early adolescence (age 13). The screen time/depression relationship, in turn, was found to be related to short sleep and diminished coherence of a particular white matter tract type, cingulum bundles. White matter is a key factor, the team suggested, in understanding how screen time interacts with sleep to impact depression risk by age 13. "These findings underscore the importance of fostering healthy screen time habits and prioritizing adequate sleep to support emotional and brain development," they said.

The research team included **Amelia Versace, M.D.**, 2009 BBRF Young Investigator, and **Cecile D. Ladouceur, Ph.D**., 2006 BBRF Young Investigator.

Basic Research: Autism, Schizophrenia, Neurodevelopmental Disorders

For the First Time, Researchers Model a Crucial Phase of Early Human Brain Development—the Forging of Connections Across the Developing Spinal Cord

Sergiu P. Pasca, M.D.

Stanford University

2017 BBRF Independent Investigator
2012 BBRF Young Investigator

Journals:
Science, July 17, 2025
Nature, April 9, 2025

Using stem cell-based technology to create living models of human brain development—called "assembloids," formed by integrating brain organoids based on several human cell types—researchers for the first time succeeded in modeling the process through which specialized cells in the embryonic neural tube guide axons crossing from one side of the emerging spinal cord to the other, establishing bilateral connectivity. This provides insight into brain development as well as problems that can cause neurodevelopmental disorders. In a *Nature* paper published in April, Dr. Pasca and colleagues reported success in building a functioning model of the human neural sensory pathway, a platform for studying the pathophysiology of sensory-related symptoms. Problems with interpreting signals coming into the brain from sensory organs is an important issue in schizophrenia and bipolar disorder with psychosis, and can also occur in ADHD, autism, and depression.

The research team in both papers included **Neal D. Amin, M.D., Ph.D**., 2021 BBRF Young Investigator. The team on the *Nature* paper included **Kevin W. Kelley, M.D., Ph.D.**, 2024 BBRF Young Investigator.

Next-Generation Therapies: PTSD, Depression

Study Sheds Light on MDMA's Prosocial Effects & Lower Abuse Potential

Robert C. Malenka, M.D., Ph.D.

Stanford University School of Medicine

2010 BBRF Goldman-Rakic Prize
2007 BBRF Distinguished Investigator
1992, 1990 Young Investigator

Drs. Malenka, Eshel, and Boris D. Heifets provided evidence explaining why the amphetamine-like psychotropic compound MDMA at low doses has reduced abuse potential compared with other amphetamines, and why it and a variant form called R-MDMA appear to generate pro-social effects, which are potentially useful in treating PTSD, depression, and other illnesses.
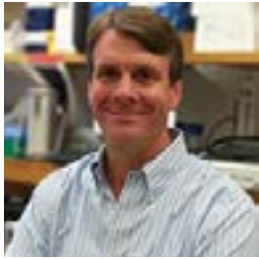
Neir Eshel, M.D., Ph.D.

Stanford University School of Medicine

2023, 2020 BBRF Young Investigator

Journal: *Molecular Psychiatry*
July 24, 2025

A Way to Repair a "Leaky" Blood-Brain Barrier (BBB) is Tested

Stewart A. Anderson, M.D.

University of Pennsylvania Perelman School of Medicine

BBRF Scientific Council
2016 BBRF Independent Investigator
2002, 1995 BBRF Young Investigator
1999 BBRF Freedman Prize winner

Journal:
Science Translational Medicine
August 20, 2025

Researchers tested a way to potentially repair the integrity of the blood-brain barrier (BBB), the protective membrane that separates the brain from the bloodstream. Leaks in the BBB have been linked with neurodevelopmental illnesses including schizophrenia and autism, as well as stress-related depression and anxiety. In experiments using stem cell-based technology the team found that mitochondria, the cellular energy "factories," are dysfunctional in the BBB in a genetic illness called 22qDS syndrome, associated with intellectual disability, autism, and ADHD—but also, possibly, in other disorders in which BBB integrity is impaired. When treated with the FDA-approved drug bezafibrate, stem cell-derived human BBB cells showed improved mitochondrial generation of ATP and reduced BBB "leakiness."

The research team included **Adam J. Rossano, M.D., Ph.D.**, 2023 BBRF Young Investigator.

New Research Underlines the Importance of Recognizing Mood Instability Between 'Major Episodes' in Bipolar Disorder

Sarah H. Sperry, Ph.D.

University of Michigan

2022 BBRF Young Investigator

Journal: *Nature Mental Health*
September 22, 2025

New research underlines the importance of "mood instability" occurring between major mood episodes in bipolar disorder. 481 patients followed over 5 years fell into three distinct mood instability subgroups, "high," "moderate," and "low," each predicting future clinical and functional outcomes. Over 78% were in the high or moderate groups, suggesting mood instability is a non-trivial factor in understanding the patient experience. The study confirms and extends preliminary findings reported last year. High mood instability correlated with the most severe outcomes in year 6. Compared with those in the low instability class, those in the high instability class had worse family and work functioning, poorer mental health functioning, and higher suicidal ideation in year 6. The team argues for implementing patient-reported mood assessment measures which could potentially reveal significant—and treatable—mood instability between major episodes.

The research team also included **Melvin G. McInnis, M.D.**, 1999 BBRF Independent Investigator and 1992 BBRF Young Investigator; and **Ivy F. Tso, Ph.D.**, 2018 BBRF Young Investigator.

Diagnostic Tools/Early Intervention; Next-Generation Therapies: Depression, Anxiety. Childhood Mental Health

Smartphone Sensors + ChatGPT Successfully Tracked & Predicted Symptoms in Adolescents with Anhedonia

Christian Webb, Ph.D.

McLean Hospital
Harvard Medical School

2018, 2015 BBRF Young Investigator

Journal: *NPP—Digital Psychiatry and Neuroscience*
October 13, 2025

While smartphones can passively collect rich behavioral data (with users' consent) by tracking patterns of movement and activity, and while Large Language Model (LLM)-based tools like ChatGPT can analyze text with impressive accuracy, it is unclear whether they can provide insight into the emotional or motivational aspects of an individual user's behavior. This question was addressed in a pilot study examining the two technologies in the context of a talk therapy called behavioral activation (BA), which aims to reduce the classic depression symptom of anhedonia by targeting patterns of avoidance and withdrawal and by increasing engagement with rewarding activities. The team recruited 38 adolescents, ages 13–18, to receive 12 weekly hour-long individual BA therapy sessions targeting their anhedonia. A subset of 13 participants also contributed passive smartphone data, collected continuously via built-in accelerometer and GPS sensors. Every other week during treatment all participants completed a "burst" of real-time assessments ("ecological momentary assessments") over 5 consecutive days via 2-3 surveys delivered each day via a smartphone app and analyzed by ChatGPT. The researchers concluded that LLM-based assessments can indeed provide "clinically relevant insights based on language generated outside the therapy room, offering scalable and unobtrusive ways to monitor therapeutic processes in patients' daily lives" even as in-person therapy is being delivered.

The research team also included: **Diego A. Pizzagalli, Ph.D**., BBRF Scientific Council, 2017 BBRF Distinguished Investigator, 2008 BBRF Independent Investigator; and **Erika E. Forbes, Ph.D.**, 2014 BBRF Independent Investigator, 2006 BBRF Young Investigator.

Next-Generation Therapies: Obsessive-Compulsive Disorder (OCD)

Deep-Brain Stimulation Guided by Brain Mapping Resulted in Rapid & Acute Reduction in Severe OCD Symptoms in Trial Patient

Andrew Moses Lee, M.D., Ph.D.

University of California, San Francisco

2020 BBRF Young Investigator

Andrew D. Krystal, M.D.

University of California, San Francisco

1997, 1993 BBRF Young Investigator

Journal: *Translational Psychiatry*
October 31, 2025

A research team developed and tested in a first patient a novel protocol designed to identify optimal personalized brain stimulation targets for severe, treatment-resistant OCD. Once identified, the team used these targets to guide precise implantation of a deep-brain stimulation (DBS) device whose subsequent activation resulted in rapid and acute reduction of the patient's OCD symptoms (62% lower 6 months after the procedure). Both the mapping of brain targets via implanted electrodes and insertion of the DBS device were invasive procedures involving brain surgery; but the targets identified in this highly treatment-resistant patient, if they are replicated in other such patients, may also prove useful in targeting non-invasive brain stimulation therapies such as TMS.

The research team included: **Joline M. Fan, M.D.**, 2022 BBRF Young Investigator.

The Brain & Behavior Research Foundation is committed to alleviating the suffering caused by mental illness by awarding scientific research grants that will ultimately enable people to live full, happy, and productive lives.

BBRF funds the most innovative ideas in neuroscience and psychiatry to better understand the causes and develop new ways to effectively treat brain and behavior disorders. These illnesses include addiction, ADHD, anxiety, autism, bipolar disorder, borderline personality disorder, depression, eating disorders, OCD, PTSD, schizophrenia, as well as research in suicide prevention.

Since 1987 BBRF has awarded $475 million to fund over 6,800 grants to more than 5,700 leading scientists around the world working to develop improved treatments, cures, and methods of prevention for mental illness.

100% of every dollar donated for research goes to research. BBRF's operating expenses are covered by separate foundation grants.

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70k
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5,700
researchers

Our 70,000 donors have joined together in the great challenge of modern medical science–overcoming mental illness.

Since 1987 the Foundation has awarded $475 million to fund more than 6,800 grants.

Grants have been given to 5,700 leading scientists around the world.