

2022 Leading Research Achievements

by BBRF Grantees, Prizewinners & Scientific Council Members

Presented in order of publication.



Next-Generation Therapies: **Depression**

Discovering How tDCS Brain Stimulation Therapeutically Modifies Brain Circuits in Depression



Evangelia G. Chrysikou, Ph.D.

Drexel University

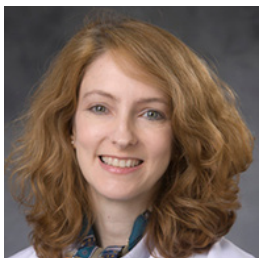
2015 BBRF Young Investigator

Journal: *Biological Psychiatry: Cognitive Neuroscience & Neuroimaging*
January 1, 2022

Researchers found mechanistic evidence supporting the ability of tDCS (transcranial direct current stimulation), a form of non-invasive brain stimulation, to help patients with moderate to severe depression. Among other things, they showed that tDCS influences connections between the medial prefrontal cortex and the amygdala, both of which have been implicated in emotional processing and emotion regulation. Results represent an important step toward understanding mechanisms of action of tDCS as a potentially safe, low-cost, and effective treatment for depression.

Next-Generation Therapies: **Depression**

Non-Invasive TMS Brain Stimulation Activates Deep-Brain Region Important in Depression



Sarah H. Lisanby, M.D.

National Institute of Mental Health; Duke University

BBRF Scientific Council; 2010 BBRF Distinguished Investigator; 2003 Independent Investigator; 1996 Young Investigator; 2001 BBRF Klerman Prize

Journal: *NeuroImage*
January 1, 2022

Individually targeted transcranial magnetic stimulation (TMS) was used to activate an important depression-related target located deep within the brain. This suggests the potential of non-invasive stimulation therapies to reach important brain areas previously thought beyond their reach, in depression and other psychiatric illnesses.

The research team included: **Zhi-De Deng, Ph.D.**, 2017 BBRF Young Investigator

Basic Research: **Depression, Anxiety, PTSD, Borderline Personality Disorder**

Researchers Identify a Neural Signature Centrally Important in Restructuring Negative Self-Beliefs



Trevor Steward, Ph.D.

University of Melbourne, Australia

2020 BBRF Young Investigator

Journal: *Molecular Psychiatry*
January 1, 2022

Little is known about what happens in the brain when CBT or other therapies succeed in helping patients in the task of cognitive reappraisal. This research describes a novel neural signature that comes into play when a person restructures negative self-beliefs and proposes a new theory about brain mechanisms responsible for enabling people to sustain complex mental representations of the self. The findings have potential implications for targeting brain stimulation treatments to help alleviate symptoms of self-impairing negative self-beliefs.

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

Evidence That Cognitive Behavioral Therapy Can Help People With Insomnia Who Also Are Depressed or Anxious



Lauren D. Asarnow, Ph.D.

*University of California,
San Francisco*

2019 BBRF Young Investigator

*Journal: Current Psychiatry
Reports
January 21, 2022*

A large body of research has demonstrated the effectiveness of CBT-I, a specialized form of cognitive behavioral therapy, in treating chronic insomnia in adults without psychiatric co-morbidities. Dr. Asarnow and colleagues conducted a review of recent research and found evidence of the importance of treating insomnia symptoms in people who also suffer from either depression, anxiety, or PTSD. Comorbid participants of such trials who did experience an improvement in insomnia symptoms were more likely to have better depression outcomes; more research is needed to determine how it impacts symptoms in anxiety and PTSD.

Next-Generation Therapies: **Addiction**

A Molecule Tested in Higher Primates Reduced Alcohol Consumption By Half



Kyle H. Flippo, Ph.D.

University of Iowa

2019 BBRF Young Investigator

*Journal: Cell Metabolism
February 1, 2022*

Administering a hormone called FGF21, researchers were able to reduce alcohol consumption by about 50% in monkeys exhibiting a strong preference for alcohol. The experiments also provided evidence of a liver-to-brain circuit that specifically regulates alcohol consumption.

The research team included **Brad A. Grueter, Ph.D.**, 2016 and 2014 BBRF Young Investigator.

Next-Generation Therapies: **Schizophrenia, Psychosis**

Comprehensive Analysis Suggests Metacognitive Training Can Be Effective in Schizophrenia and Psychotic Disorders



Martin Lepage, Ph.D.

McGill University

2002 BBRF Young Investigator

*Journal: JAMA Psychiatry
March 23, 2022*

A meta-analysis of 43 prior clinical trials testing metacognitive training (MCT) for psychosis concluded MCT is an effective treatment, with benefits still evident in patients 1 year following the end of MCT sessions. In MCT, a therapist or facilitator enters into discussions with a group of patients, seeking to discover what they believe about their own thoughts. MCT targets maladaptive thinking styles common to psychosis, which include jumping to conclusions, inflexibly holding on to beliefs, and being overconfident in initial judgments.

The research team included **Steffan Moritz, Ph.D.**, 2014 BBRF Independent Investigator, 2008, 2005 Young Investigator.

Basic Research: **Schizophrenia**

Important New Research on Schizophrenia Genetics Provides Strongest Evidence to Date of Problems at the Brain's Synapses



Tarjinder Singh, Ph.D.

Columbia University

2019 BBRF Young Investigator

Journal: *Nature*

April 8, 2022

In two papers published concurrently, an international team composed of hundreds of scientists provided the most comprehensive picture to date of how variations in the human genome affect schizophrenia risk. Their work contains some of the most compelling indications linking the illness with problems at the synapse—the gaps across which neurons in the brain communicate.

The research teams included several dozen recipients of BBRF grants, members of the BBRF Scientific Council, and recipients of BBRF annual prizes for outstanding achievement in research. Among senior members of the team were **Michael C. O'Donovan, M.D., Ph.D.**, 2012 BBRF Lieber Prize winner; **Stephan Ripke, M.D., Ph.D.**, 2015 BBRF Young Investigator and 2014 BBRF Baer Prize winner; and **Patrick Sullivan, M.D., FRANZCP**, 2014 BBRF Lieber Prize winner.

Basic Research: **Schizophrenia**

Stem Cell Technology Helps Identify a Potential Causal Mechanism in Schizophrenia That Could Be Targeted



Lorna A. Farrelly, Ph.D.

Icahn School of Medicine at Mount Sinai

2019 BBRF Young Investigator

Journal: *Nature Communications*

April 22, 2022

Using stem-cell technology, researchers identified an aberrant gene-regulation pattern called hyperacetylation that may be causally involved in some cases of schizophrenia. Acetyl molecules attach to DNA packaging proteins to encourage or repress gene activation. Hyperacetylation means that there are too many acetyl molecules attaching to bundles of DNA called histones, causing one or more genes to be abnormally regulated. The team identified a specific protein, BRD4, which, if blocked or repressed, might help alleviate the severity of the aberration.

The research team included: included **Kristen Brennand, Ph.D.**, BBRF Scientific Council, 2018 BBRF Maltz Prize, 2016 BBRF Independent Investigator, 2012 Young Investigator; **Carol A. Tamminga, M.D.**, 2011 BBRF Lieber Prize winner, 2010 and 1998 BBRF Distinguished Investigator; **Ian Maze, Ph.D.**, 2014 BBRF Young Investigator.

Next-Generation Therapies: **Depression**

Video Game-Based Intervention Helped Reduce Cognitive Deficits in Depressed Patients



Richard S.E. Keefe, Ph.D.

Duke University

BBRF Scientific Council; 2003 BBRF Independent Investigator; 1995, 1991 Young Investigator

Journal: *American Journal of Psychiatry*

April 12, 2022

Researchers testing a novel video game-based intervention in depressed patients found that it can reduce the severity of an important form of cognitive deficit—the ability to remain engaged and pay attention to a task over a sustained interval.

The research team included **Amit Etkin, M.D., Ph.D.**, 2012 BBRF Young Investigator.

Basic Research: **Addiction**

Researchers Discover Potentially Targetable Brain Circuit Controlling Cocaine Withdrawal Anxiety and Relapse



Kevin Beier, Ph.D.

*University of California Irvine
School of Medicine*

2017 BBRF Young Investigator

*Journal: Cell Reports
May 3, 2022*

Researchers discovered an extended brain circuit involved in cocaine addiction. The circuit regulates withdrawal anxiety and the urge to take cocaine again. Distinct from reward circuits driven by dopamine, the newly identified circuit might be targeted by novel therapeutic agents to reduce the negative affect that develops during withdrawal as well as to prevent relapse.

Basic Research: **All Mental Illnesses**

Precise Imaging Reveals How a Key Receptor's Signaling Is Modulated—A Spur to Improving Psychiatric and Other Drugs



Wesley B. Asher, Ph.D.

Columbia University

2014 BBRF Young Investigator

*Journal: Cell
May 12, 2022*

Researchers have obtained powerful new insights into mechanisms involved in GPCRs, cellular receptors whose signaling is implicated in many psychiatric disorders. GPCRs are the target of one-third of all approved drugs, including therapeutics prescribed for psychiatric disorders such as schizophrenia, bipolar disorder, and depression. The dopamine D2 receptor, which is the target of all current antipsychotic medicines, is a GPCR, for example. The research will aid efforts to improve the action of drugs that interact with GPCRs, including psychiatric drugs, to make them more effective and/or to reduce side effects.

The study's senior author was **Jonathan Javitch, M.D., Ph.D.**, BBRF Scientific Council, 2010 Distinguished Investigator, 2003 Independent Investigator, 1992, 1990 Young Investigator.

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

A Circuit Causally Linked With Spontaneous Nicotine Addiction Remissions May Be a Powerful Addiction Treatment Target



Shan H. Siddiqi, M.D.

Harvard Medical School

2022 BBRF Klerman Prize
2019 BBRF Young Investigator

*Journal: Nature Medicine
June 3, 2022*

By studying 129 people who were addicted to nicotine at the time they suffered brain damage, a team of researchers has identified a brain network they believe is causally linked with remission from nicotine addiction and that can be targeted with non-invasive brain stimulation.

The research team included **Nora D. Volkow, M.D.**, BBRF Scientific Council; Director, National Institute on Drug Abuse.

Next-Generation Therapies: **PTSD**

Clinical Trial Comparing Different Forms of Exposure and Drug Therapy in Combat Veterans with PTSD Is Step Toward Individualized Treatment



Francis S. Lee, M.D.

Weill Cornell Medicine

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

Journal: Translational Psychiatry
July 22, 2022

In a step toward precision medicine, a clinical trial found that two forms of exposure therapy enabled combat veterans to significantly reduce PTSD symptoms. Whether or not a patient also experienced depression affected which form of treatment was more effective. Those carrying either of two common genetic variations affecting processes that may impact fear extinction also showed evidence of having distinct therapy responses.

The research team included: **Barbara O. Rothbaum, Ph.D.**, 2012 BBRF Distinguished Investigator; **Christopher Reist, M.D.**, 1996 and 1993 BBRF Young Investigator; **Tanja Jovanovic, Ph.D.**, 2015 BBRF Independent Investigator, 2010 Young Investigator; **Seth D. Norholm, Ph.D.**, 2002 BBRF Young Investigator; **Charles E. Glatt, M.D., Ph.D.**, 2003 and 2001 BBRF Young Investigator.

Basic Research: **Depression, Anxiety, PTSD**

Researchers Identify Molecule That Orchestrates Association of Events With Positive and Negative Memories



Kay M. Tye, Ph.D.

Salk Institute for Biological Studies

BBRF Scientific Council Emeritus,
2016 BBRF Freedman Prize,
2013 BBRF Young Investigator

Journal: Nature
July 20, 2022

Researchers discovered that neurotensin, a neurotransmitter, orchestrates a process in the brain's amygdala that enables us to assign positive and negative "tags" to specific memories. Targeting this molecule might be the aim of future treatments for individuals who fixate on or overstress negative memories.

The team included **Kerry J. Ressler, M.D., Ph.D.**, BBRF Scientific Council, 2009 BBRF Freedman Prize, 2005 and 2002 BBRF Young Investigator; **Romy Wichmann, Ph.D.**, 2016 BBRF Young Investigator; **Cody A. Siciliano, Ph.D.**, 2017 BBRF Young Investigator; **Xin Jin, Ph.D.**, 2018 BBRF Young Investigator; **Anna Beyeler, Ph.D.**, 2015 BBRF Young Investigator.

Next-Generation Therapies: **ADHD**

Home-Based tDCS Brain Stimulation Treatments Reduced Inattention in Adults with ADHD



Douglas Teixeira Leffa, M.D., Ph.D.

Universidade Federal do Rio Grande do Sul, Brazil

Journal: JAMA Psychiatry
August 3, 2022

Researchers have obtained promising results in a clinical trial of a home-based non-invasive brain stimulation treatment for adults with ADHD. The treatment, using low-power transcranial direct current stimulation (tDCS) technology, was associated with lower inattention symptoms in patients.

The research team included: **Joan Camprodon, M.D., Ph.D., MPH**, 2010 BBRF Young Investigator; **André Brunoni, M.D., Ph.D.**, 2013 BBRF Young Investigator.

Next-Generation Therapies: **Depression**

FDA Clears SAINT Rapid-Acting Brain Stimulation Approach for Those Suffering From Resistant Major Depression



Nolan R. Williams, M.D.

Stanford University

2019 BBRF Klerman Prize
2018, 2016 BBRF Young Investigator

*FDA announcement made
September 6, 2022*

The FDA gave clearance for a commercial application of the SAINT brain stimulation protocol developed by Dr. Williams and colleagues. In a recent clinical trial, SAINT enabled 79 percent of patients with refractory major depression to achieve remission after only 5 days of accelerated non-invasive treatments.

Next-Generation Therapies: **Suicide Prevention**

Folic Acid Supplements Were Associated With Lower Suicidality in Large Database Study



J. John Mann, M.D.

*Columbia University/NY State
Psychiatric Institute*

BBRF Scientific Council;
2022 BBRF Colvin Prize;
2008 BBRF Distinguished Investigator

*Journal: JAMA Psychiatry
September 28, 2022*

In a promising lead in suicide prevention, researchers found that in a cohort of over 866,000 people prescribed folic acid supplements over 5 years, there was a 44% lower rate of suicidal events during periods when the supplements were being taken vs. when they were not being taken.

Next-Generation Therapies: **Depression**

Adding an Antibiotic Improved Brain Stimulation Results in Depression



**Alexander McGirr M.D.,
Ph.D.**

University of Calgary, Canada

2018 BBRF Young Investigator

*Journal: JAMA Psychiatry
October 12, 2022*

By providing 2 weeks of antibiotic therapy using the drug d-cycloserine during a 4-week treatment course with iTBS, a form of non-invasive brain stimulation, researchers were able to show significantly improved outcomes in patients with moderate to severe major depression.

Basic Research: **All Mental Illnesses**

Lab-Grown Human Neurons Transplanted into the Rat Brain Grew, Connected, and Promise to Shed Light on Psychiatric Illness



Sergiu Pasca, M.D.

Stanford University

2017 BBRF Independent Investigator; 2012 Young Investigator

Journal: *Nature*
October 12, 2022

Researchers grew organoids composed of human cortical neurons and transplanted them into the rat sensory cortex. The human cells integrated functionally into the rat brain—could receive sensory stimulation and drive behavior. The same approach enabled the team to study pathology in human cells transplanted from patients with a neuropsychiatric disorder, a strategy that can also be applied in other disorders.

The research team included: **Karl Deisseroth, M.D., Ph.D.**, BBRF Scientific Council, 2013 BBRF Goldman-Rakic Prize winner, 2007 and 2005 BBRF Young Investigator; **Felicity Gore, Ph.D.**, 2019 BBRF Young Investigator; **Neal D. Amin, M.D., Ph.D.**, 2021 BBRF Young Investigator

Next-Generation Therapies: **Depression**

After 'Priming' with Ketamine, Patients Receiving Self-Esteem Training Had Extended Antidepressant Benefits, Study Finds



Robert H. Howland, M.D.

University of Pittsburgh

1991 BBRF Young Investigator

In a randomized placebo-controlled clinical trial, ketamine's rapid antidepressant effect which normally fades within a week was still present after 30 days for treatment-resistant participants who received a single ketamine injection and 4 days of computer-administered self-esteem training.



Sanjay J. Mathew, M.D.

Baylor College School of Medicine

2009 BBRF Independent Investigator;
2006, 2001 Young Investigator

Journal: *American Journal of Psychiatry*
December 1, 2022

BRAIN & BEHAVIOR

RESEARCH FOUNDATION

Awarding **NARSAD** Grants

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.

For more than 35 years BBRF has awarded more than \$440 million to fund 6,400 grants to more than 5,300 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.

Research for Recovery



For 35 years the Brain & Behavior Research Foundation has fostered new research pathways and transformative breakthroughs.



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



Since 1987 the Foundation has awarded \$440 million to fund more than 6,400 grants.



Grants have been given to 5,300 leading scientists around the world.