

2023 Leading Research Achievements

by BBRF Grantees, Prizewinners & Scientific Council Members

Presented in order of publication.



Next-Generation Therapies: **Borderline Personality Disorder, Suicidality**

Talk Therapy + Brain Stimulation Reduced Suicidal Ideation in Patients with Borderline Personality Disorder and Treatment-Resistant Depression



Anthony C. Ruocco, Ph.D., C.Psych.

University of Toronto

2014 BBRF Young Investigator

In a clinical trial, individuals with borderline personality disorder (BPD) and co-occurring major depression and suicidal ideation, when treated with dialectical behavior therapy (DBT) and concurrent magnetic seizure therapy (MST), experienced a rapid, clinically meaningful reduction in suicidal ideation at 5 weeks that was sustained at 4-month follow-up.

The research team included: **Zafiris J. Daskalakis, M.D., Ph.D.**, BBRF Scientific Council, 2008 BBRF Independent Investigator, 2006 and 2004 Young Investigator; and **Daniel M. Blumberger, M.D.**, 2010 BBRF Young Investigator. Dr. Ruocco's 2014 BBRF Young Investigator grant, devoted to the work reported in the new paper, was supported by The Families for Borderline Personality Disorder Research.



Jenna M. Traynor, Ph.D.

McLean Hospital / Harvard University

2022 BBRF Young Investigator

Journal: Nature Mental Health
January 19, 2023

Diagnostic Tools / Early Intervention: **Autism Spectrum Disorders**

Four Subtypes of Autism Spectrum Disorder Are Distinguished, Helping to Explain Individual Differences in Symptoms



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

Weill Cornell Medicine

2013 BBRF Young Investigator

Journal: Nature Neuroscience
March 9, 2023

Researchers used a large set of neuroimaging data to identify distinct sets of alterations in functional connectivity that may help explain differences among people with autism spectrum disorder (ASD). A cohort of 299 individuals with ASD "clustered" into four subgroups, each with distinct patterns of atypical functional connectivity in ASD-related neural networks affecting verbal ability, social affect, and repetitive behaviors and restricted interests. The findings promise to advance the search for new treatments.

Basic Research: **OCD**

Functional Connectivity Brain Changes Involving Links Between Cognition and Motor Function Are Discerned in OCD Patients



Odile van den Heuvel, M.D., Ph.D.

Amsterdam University Medical Center, Netherlands

2009 BBRF Young Investigator



Paul M. Thompson, Ph.D.

University of Southern California

2017 BBRF Distinguished Investigator

Journal: Molecular Psychiatry
May 2, 2023

A large international team investigated brain-wide functional connectivity differences using MRI data of 1,024 OCD patients and 1,028 healthy controls. They found widespread functional connectivity aberrations in people with OCD, notably in the sensorimotor network. These could reflect impairments in suppressing irrelevant sensory, cognitive, and motor information, which may contribute to the inability of patients to inhibit undesired thoughts and images and repetitive behaviors and thoughts.

The research team included: team co-leader **Dan J. Stein, Ph.D., FRCPC**, 1991 BBRF Young Investigator; **Alan Anticevic, Ph.D.**, 2015 BBRF Klerman Prize winner, 2015 BBRF Independent Investigator and 2012 Young Investigator; **Chiang-Shan R. Li, M.D., Ph.D.**, 2009 BBRF Young Investigator; **Erika L. Nurmi, M.D., Ph.D.**, 2008, 2010 BBRF Young Investigator; **Christopher Pittenger, M.D., Ph.D.**, 2015 BBRF Independent Investigator, 2009, 2007 Young Investigator; **Blair H. Simpson, M.D., Ph.D.**, 2010 BBRF Independent Investigator; **Emil R. Stern, Ph.D.**, 2008 BBRF Young Investigator; **Philip R. Szeszko, Ph.D.**, 2009 BBRF Independent Investigator, 2003, 1998 Young Investigator; **Hein J. F. van Marle, M.D., Ph.D.**, 2022, 2018 BBRF Young Investigator

Basic Research, Diagnostic Tools/Early Intervention: **Substance Use Disorder, Schizophrenia**

In Young Men, Up to 20% of Schizophrenia Might Be Prevented If Cannabis Use Disorder Is Not Present



Nora Volkow, M.D.

Director, National Institute on Drug Abuse/NIH

BBRF Scientific Council

Journal: Psychological Medicine
May 4, 2023

Using Danish national health records of 6.9 million individuals born in the country over 5 decades, investigators found that cannabis use disorder (CUD) is contributing to a “steadily increasing proportion” of schizophrenia cases—a figure, in young men, they “conservatively” estimate at 15% for 2021. Such cases might have been preventable if CUD had not been present, they said. In young males, aged 21-30, and possibly up to age 40, the proportion of schizophrenia cases that may now be avoided if CUD is not present “may even be as high as 25% to 30%,” they added. For this reason, the team considers CUD to be “a major modifiable risk factor for schizophrenia, particularly among males.”

Brain Changes Related to Adolescent Cannabis Use Are Found to Persist Into Young Adulthood



Matthew D. Albaugh, Ph.D.

University of Vermont

2020 BBRF Young Investigator

Journal: Molecular Psychiatry
June 28, 2023

Brain changes related to adolescent initiation of cannabis were found in this follow-up study to have persisted into young adulthood. This was true especially in brain areas rich in type 1 cannabinoid receptors—the same areas that undergo the greatest age-related cortical thickness changes during adolescence. The team identified potential indirect effects on psychotic symptoms at age 22 associated with thickness changes in temporal areas of the brain. The research provides a foundation for neurodevelopmentally informed models of cannabis exposure.

The research team included: **Henrik Walter M.D., Ph.D.**, 2017 BBRF Distinguished Investigator; **Robert Whelan, Ph.D.**, 2015 BBRF Young Investigator; **Alexandra Potter, Ph.D.**, 2009 BBRF Young Investigator

Basic Research: **Long COVID**

Gliosis, an Immune Response to Brain Injury, Is Found in Brains of Recovered COVID Patients With Lasting Depression and Cognitive Symptoms



Jeffrey H. Meyer, M.D., Ph.D.

University of Toronto

2015 BBRF Distinguished Investigator; 2000 and 1998 Young Investigator

Journal: *JAMA Psychiatry*
May 31, 2023

Researchers studying recovered COVID patients with lingering depression and cognitive symptoms (COVID-DC) found evidence of gliosis, an immune response to brain injury. Most affected were two brain regions: the ventral striatum and dorsal putamen. Higher readings in the latter area also were found to correlate with motor slowing. This result suggests it may be worthwhile to test several drugs now in development to reduce gliosis in COVID-DC (i.e., “long COVID”) patients.

The research team included: **Romina Mizrahi, M.D., Ph.D.**, 2014 BBRF Independent Investigator and 2010 BBRF Young Investigator; **Nathan Kolla, M.D., Ph.D.**, 2013 BBRF Young Investigator; and **M. Ishrat Husain, MBBS, M.D.**, 2019 BBRF Young Investigator

Next-Generation Therapies: **PTSD**

In PTSD, Evidence That a Single Ketamine Infusion May Enhance Extinction of Recalled Traumatic Memories



Ilan Harpaz-Rotem, Ph.D.

Yale University

2015 BBRF Independent Investigator

Journal: *Neuropsychopharmacology*
June 3, 2023

What if traumatic memories could be rewritten—overwritten and replaced with other memories, or modified so that the memory-induced fear response to the original trauma is extinguished? A pilot study generated evidence that a single ketamine infusion may have enhanced extinction of traumatic memories, following their initial retrieval, in PTSD patients. Ketamine combined with talk therapy is a potential novel future intervention for PTSD and anxiety disorders, the researchers suggested.

The research team included: **John H. Krystal, M.D.**, BBRF Scientific Council, 2019 BBRF Colvin Prize, 2006, 2000 BBRF Distinguished Investigator, 1997 BBRF Independent Investigator; and **Ben Kelmendi, M.D.**, 2016 BBRF Young Investigator

Next-Generation Therapies: **Depression**

Rapid-Acting Pill to Treat Postpartum Depression is Approved



Marlene Freeman, M.D.

*Massachusetts General Hospital
Harvard Medical School*

2000, 1998 BBRF Young Investigator

Journal: *American Journal of Psychiatry*
July 28, 2023

The FDA on August 4th approved the first short-course, rapid-acting oral treatment for patients with postpartum depression (PPD). Called zuranolone (marketed as Zuruvae), it is given in pill form for 14 days and begins to reduce severe PPD symptoms in as little as 3 days. Because of its accessibility, zuranolone is an important advance. The first-ever rapid-acting medicine for postpartum depression, brexanolone, on the market since 2019, is administered via continuous infusion in a medical facility. A number of past BBRF grantees performed research laying the groundwork for these new rapid-acting PPD therapies, among them three-time grantee **Cynthia Neill Epperson, M.D.**, who mapped changes in cortical levels of the inhibitory neurotransmitter GABA across the menstrual cycle and in postpartum women. The new therapies act upon one of the cellular receptors for GABA.

Diagnostic Tools / Early Intervention: **Psychosis, Schizophrenia**

A Connectivity Signature Predicting Response to Antipsychotic Therapy is Identified in First-Episode Psychosis Patients



Anil K. Malhotra, M.D.

Feinstein Institutes for Medical Research/Zucker Hillside Hospital

BBRF Scientific Council, 2006 and 2001 BBRF Independent Investigator; 1999 Young Investigator

Journal: American Journal of Psychiatry

August 30, 2023

Researchers reported encouraging news in the search for biomarkers to predict treatment response to antipsychotics in individuals with first-episode psychosis. The predictors the team found using functional brain imaging involved connectivity between the cerebellum and the cerebral cortex, where lower connectivity at baseline predicted better response to antipsychotics. Cerebellar-cortical hyper-connectivity in psychosis may result from dysregulation of dopamine in cortical cognitive systems, the team said. Predictors for individualized response to antipsychotic treatment can help find the best treatment more rapidly, and thus increase the likelihood of better long-term outcomes for first-episode patients.

The research team included: first author **Hengyi Cao, Ph.D.**, 2018 BBRF Young Investigator; **Todd Lencz, Ph.D.**, 2013 BBRF Independent Investigator and 2001 Young Investigator; **Juan A. Gallego, M.D.**, 2013 BBRF Young Investigator; **Anita D. Barber, Ph.D.**, 2009 BBRF Young Investigator; **Delbert G. Robinson, M.D.**, 2005 BBRF Independent Investigator

Next-Generation Therapies: **Schizophrenia**

Anti-Inflammatory Medicine Reduced Positive Symptom Severity in Chronic Schizophrenia Patients with Elevated Inflammatory Markers



Thomas W. Weickert, Ph.D.

2016 BBRF Independent Investigator

Cynthia S. Weickert, Ph.D.

2004 BBRF Independent Investigator
2001, 1999 Young Investigator



*SUNY Upstate Medical University
Neuroscience Research Australia
University of New South Wales*

Journal: Brain, Behavior and Immunity

October 15, 2023

A small clinical trial tested the approved anti-inflammatory drug canakinumab in a group of chronic schizophrenia patients with elevated blood markers of inflammation. The team found that a single injection of the drug (150mg) “was effective in reducing a peripheral marker of inflammation [C-reactive protein, CRP].” Levels of CRP declined continuously for the first 4 weeks post-injection and were significantly reduced at all times through 8 weeks relative to baseline levels. This was accompanied by a measurable reduction considered significant in the severity of positive symptoms—hallucinations, delusions, and odd or intrusive thoughts.

The research team included: **Rhoshel Lenroot, M.D.**, 2003 BBRF Young Investigator; **Julia Lappin, MBChB, MRCPsych**, 2008 BBRF Young Investigator

Next-Generation Therapies: **Depression**

Precisely Targeting and Predicting the Impact of TMS Brain Stimulation for Depression with Combined TMS/fMRI



Desmond J. Oathes, Ph.D.

University of Pennsylvania

2016 BBRF Young Investigator

Journal: Nature Mental Health

November 27, 2023

Using a combination of preliminary TMS pulses and simultaneous functional MRI scanning, researchers identified a predictor of response to non-invasive rTMS brain stimulation therapy in depression. The more a preliminary TMS pulse showed that activity in a deep-brain structure called the subgenual anterior cingulate cortex (sgACC) was reduced, the greater the response to 3 days of rTMS therapy. Potential implications include precisely targeting treatments to relieve specific psychiatric symptoms; and the ability to predict patient response before TMS therapy begins.

The research team included **Yvette I. Sheline, M.D.**, 2005 and 2002 BBRF Independent Investigator, 1998 BBRF Young Investigator