

Leading Research Achievements by Foundation Grantees in 2017

LISTED IN CHRONOLOGICAL ORDER





Neurofeedback App Improves Early Cognitive Deficit in People with High Psychosis Risk

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

Jimmy Choi, Psy.D.

The Institute of Living at Hartford Hospital, Connecticut
2010 Young Investigator Grant

Problems with mental processing speed are common among people at high risk for psychosis, and are thought to be related to broader deficits in social functioning. In a randomized clinical trial involving 62 people at high risk for psychosis, researchers enhanced participants' processing speed using a neurofeedback training program and saw improvements in social behaviors which persisted for as much as two months. The training was done using a tablet-based program, in which the difficulty levels of tasks was personalized. The program tracks participants' eyes and uses movements of their pupils to adjust the difficulty of a task. In addition to improving social functioning, it's thought that addressing early manifestations of cognitive deficit may diminish the risk of conversion to psychosis, delay it, or attenuate symptom severity when it does occur.

Journal: *Psychiatric Rehabilitation Journal*, February 15, 2017

*Other BBRF grantees on the research team included: 2002, 1999 Young Investigator Cheryl Corcoran, M.D.; Scientific Council Member, 1995 Independent Investigator, and 1990 Young Investigator Daniel C. Javitt, M.D., Ph.D.; and Scientific Council Member, 2000 Distinguished Investigator Godfrey D. Pearlson, M.D.

Brain Abnormalities Linked to Suicidal Behavior in Young People with Bipolar Disorder

Basic Research: **Bipolar Disorder, Suicide Prevention**

Hilary P. Blumberg, M.D.

Yale University School of Medicine
Scientific Council Member
2006 Klerman Prizewinner
2006 Independent Investigator Grant
2002 Young Investigator Grant

A study of adolescents and young adults aged 14-25 with bipolar disorder has found structural and functional differences in the brains of those with the disorder who have attempted suicide compared with those who have not. About half of people who have bipolar disorder make at least one suicide attempt. The differences uncovered in the study could help researchers identify young people who are at greatest risk. MRI analysis found that parts of the brain regulating emotion and impulses were smaller and less active in those who had attempted suicide, and that white matter connecting those regions was also diminished.

Journal: *American Journal of Psychiatry*, February 21, 2017

*Other BBRF grantees on the research team included: 2016 Young Investigator Jie Liu, Ph.D.; and 2012, 2008 Young Investigator Fei Wang, Ph.D.



Dr. André R. Brunoni

Dr. Daskalakis

Discovery of Four Depression “Biotypes” Could Help Target Treatments

Diagnostic Tools & Early Intervention: **Depression**

Conor Liston, M.D.

Weill Cornell Medical College

2016 Freedman Prize Honorable Mention

2013 Young Investigator Grant

A large new brain-scan study identified four categories of biological activity, or “biotypes,” of depression that may help doctors choose more effective treatments—just as a blood test might guide treatment of cancer or heart disease. When researchers used a machine learning program to divide over 450 depression patients into categories based on biomarkers in their brain activity patterns (after the patients received “resting state” fMRI scans), they found four categories associated with distinct sets of clinical symptoms. In comparative terms, brains of patients who had depressive anxiety tended to have fewer connections in networks involved in responses to fear and negative emotional stimuli. Those with difficulty feeling pleasure had more connections in networks that regulate reward processing and control over movement.

Journal: *Nature Medicine*, April 10, 2017

*Other BBRF grantees on the research team included: Scientific Council Member, 2015 Ruane Prizewinner BJ Casey, Ph.D.; 2010 Young Investigator Marc J. Dubin, M.D., Ph.D.; 2016 Young Investigator Amit Etkin, M.D., Ph.D.; 2012 and 2009 Young Investigator Jennifer Keller, Ph.D.; Scientific Council Member, 1995 Independent Investigator and 1991 Young Investigator Helen S. Mayberg, M.D.; 2016 Young Investigator Desmond Jay Oathes, Ph.D.; 2002 Distinguished Investigator and 1998 Independent Investigator Alvaro Pascual-Leone, M.D., Ph.D.; and Scientific Council Member, 2005 Falcone Prizewinner Alan F. Schatzberg, M.D.

Deep Transcranial Magnetic Stimulation (dTMS) Could Help Treat Bipolar Depression

Next-Generation Therapies: **Bipolar Disorder**

André R. Brunoni, M.D., Ph.D.

University of São Paulo, Brazil

2013 Young Investigator Grant

Z. Jeff Daskalakis, M.D., Ph.D.

Centre for Addiction and Mental Health,
University of Toronto, Canada

Scientific Council Member

2008 Independent Investigator Grant

2006, 2004 Young Investigator Grant

Deep transcranial magnetic stimulation (dTMS), a non-invasive procedure that uses magnetic fields to stimulate brain cells, may be useful when added to medication to treat bipolar depression. If these results, based on a study involving 50 patients, are confirmed in further studies, dTMS could join the limited options available for treating bipolar depression, in which resistance to treatment is two times higher than in major (unipolar) depression. dTMS has already been shown to improve symptoms in patients with major depression. Half of those enrolled in the study received the treatment, which involved 20 dTMS sessions held over four weeks; the other patients received a version of the treatment in which no magnetic fields were generated.

Journal: *Neuropsychopharmacology*, April 26, 2017



Dr. Rodriguez



Dr. Simpson



Early Test Shows: Experimental Drug May Have Potential to Relieve OCD Symptoms Quickly and with Few Side Effects

Next-Generation Therapies: **OCD**

Carolyn I. Rodriguez, M.D., Ph.D.

Stanford University School of Medicine
2017 Klerman Prize Honorable Mention
2014, 2009 Young Investigator Grant

Helen Blair Simpson, M.D., Ph.D.

Columbia University College of Physicians and Surgeons
2010 Independent Investigator Grant
2005 Young Investigator Grant

A pilot study suggested that rapastinel, an experimental drug currently being evaluated for the treatment of major depression, may relieve the symptoms of obsessive-compulsive disorder (OCD) rapidly and with few side effects. Seven patients were given a single dose of the drug. Within hours of treatment, reductions were noted in the severity of patients' obsessions and compulsions, as well as symptoms of anxiety and depression. The effects were not long-lasting, enduring less than a full week. The researchers turned to rapastinel because they previously found that some OCD patients had received rapid relief when treated with the experimental drug ketamine. It has been used to rapidly lift severe depression, but has significant side-effects.

Journal: *American Journal of Psychiatry*, May 22, 2017

Animal Studies Suggest a New Path to Fast-Acting Antidepressant

Next-Generation Therapies: **Depression**

Abraham A. Palmer, Ph.D.

University of California, San Diego
2006, 2003 Young Investigator Grant

Animal research has uncovered a drug development strategy that could lead to a new type of antidepressant medication. Researchers suggest that inhibiting an enzyme called GLO1 could have fast-acting antidepressant effects, relieving patients' symptoms in a matter of days. In a mouse study, GLO1 activity was reduced by genetic manipulation and by administering two different chemical inhibitors. This appears to boost factors that enhance signaling between neurons. The investigators are now working with medicinal chemists to try to develop better GLO1-inhibiting compounds. These could give rise to a new, faster-acting treatment for depression—an alternative, perhaps to approaches centered on the experimental fast-acting compound called ketamine, which has undesirable side-effects.

Journal: *Molecular Psychiatry*, June 12, 2017

*Other BBRF grantees on the research team included: 2016 Independent Investigator, 2012 and 2007 Young Investigator Stephanie Dulawa, Ph.D.; and 2016 Young Investigator Marcia J. Ramaker, Ph.D.



New Technique Lets Researchers Watch Human Brain Circuits Begin to Wire-Up

New Technology: **Autism, Schizophrenia**

Sergiu P. Pasca, M.D.

Stanford University

2017 Independent Investigator Grant

2012 Young Investigator Grant

Scientists have devised a new system that lets them watch human neurons grown in the lab find and form connections with their signaling partners, an essential process in developing human brains. The process of “wiring up” is thought to go awry in a number of serious disorders, including autism, epilepsy and schizophrenia—but it’s hard to study. The new technique focused on the connections formed by cells called interneurons. These neurons spend months growing and migrating to their ultimate brain destinations during fetal development and in the cortex play an indispensable “braking” role in communication between neurons. By learning how to recreate those processes in lab dish-based “spheroids,” the team already has been able to recreate pathology seen in a disorder called Timothy syndrome and correct it using experimental drugs. It’s an example of how the technique can be used in studying other brain disorders.

Journal: *Nature*, July 18, 2017

*Other BBRF grantees on the research team included 1991 Young Investigator Joachim F. Hallmayer, M.D.

Ketamine Rapidly Reduced Suicidal Thoughts in People with Depression

Next-Generation Therapies: **Depression, Suicide Prevention**

Samuel Wilkinson, M.D.

Yale University School of Medicine

2016 Young Investigator Grant

A single dose of ketamine, the anesthetic drug that has been found to have fast-acting antidepressant effects, can significantly reduce suicidal thoughts in patients with depression for up to a week, researchers discovered. The findings are based on data from 167 patients who participated in 10 previous studies on ketamine’s effects. All received a single dose of the drug or a placebo drug, administered intravenously. This “meta-analysis”—a study of multiple other studies—suggests that the drug not only reduces patients’ overall depression; it also appears to be particularly effective at countering suicidal thoughts.

Journal: *American Journal of Psychiatry*, October 10, 2017

*Other BBRF grantees on the research team included: 2013 and 2009 Young Investigator Michael H. Bloch, M.D., M.S.; 2015 Independent Investigator and 2002 Young Investigator Adriana Feder, M.D.; 2009 Independent Investigator, 2006 and 2001 Young Investigator Sanjay J. Mathew, M.D.; 2009 Young Investigator James W. Murrough, M.D., Ph.D.; 2014 Distinguished Investigator, 2007 Independent Investigator and a 2001 and 1999 Young Investigator Gerard Sanacora, M.D., Ph.D.; and 2011 Bipolar Mood Disorders Awardee, 2005 Independent Investigator and 1996 Young Investigator Carlos A. Zarate, Jr., M.D.



Dr. Sit



Dr. Wisner



Study Shows Exposure to Bright Light at Midday Reduces Depression in Patients with Bipolar Disorder

Next-Generation Therapies: **Bipolar Disorder, Depression**

Dorothy K.Y. Sit, M.D.

Northwestern University
2013, 2002 Young Investigator Grant

Katherine L. Wisner, M.D., M.S.

Northwestern University
1998 Independent Investigator Grant

Light therapy can be an effective treatment for seasonal depression, but there has been concern that the treatment might induce mania in people with bipolar disorder. In a newly reported trial, involving 46 people, no manic episodes were reported, despite daily exposure to bright light. After six weeks of treatment, 68 percent of those who received bright light therapy experienced a remission of their depression. In contrast, only 22 percent of those in the placebo group achieved remission. Treatments were administered midday, beginning with 15 minutes of light exposure and increasing daily until treatments reached a duration of one hour. The light dose was similar to that used to treat seasonal affective disorder. In an earlier trial in which treatments were given in the morning, some patients became manic, suggesting timing of the treatments may be important.

Journal: *American Journal of Psychiatry*, October 16, 2017

New Analysis Finds Behavioral Therapy Should Be Combined with Medication to Relieve Severe Anxiety in Children

Next-Generation Therapies: **Bipolar Disorder, Depression**

Michael Howard Bloch, M.D., M.S.

Yale Child Study Center
2013, 2009 Young Investigator Grant

Both therapy and anti-anxiety medications can help relieve the symptoms of anxiety in children and adolescents. But children whose anxiety symptoms are severe likely need both, a new study indicates. The finding was the result of closer investigation of the 448 children and adolescents with generalized, social, or separation anxiety disorders who participated in the CAMS clinical trial, 220 of whom had severe symptoms. The team found that these patients achieved remission during the trial only if they received a combination of sertraline and cognitive behavior therapy. For those with severe anxiety, remission rates following medication or behavioral therapy alone were similar to those of study participants who received a placebo. This analysis also revealed that anxiety was most resistant to treatment in children from lower socioeconomic backgrounds and in those who had been diagnosed with obsessive-compulsive disorder.

Journal: *Journal of Clinical Child & Adolescent Psychology*, November 14, 2017

*Other BBRF grantees on the research team included: 2013 Young Investigator Eli R. Lebowitz, Ph.D.; and 2017 Young Investigator Jerome H. Taylor, M.D.

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