Top 10 Discoveries in 2013 by NARSAD Grantees

**Kirsty Spalding, Ph.D.**  
Karolinska Institutet, Stockholm, Sweden  
*2007 NARSAD YI*  
Retrospective Analysis of Cell Turnover in the Brain, in Schizophrenia and Mood Disorders

**Basic Research: General Mental Illness**  
Innovative Methodology Quantifies New Neurons in Adult Humans  
By carbon dating birth dates of neurons in the human hippocampus*, Dr. Spalding and team have, for the first time, been able to identify the number of new neurons generated in adult brains, furthering the idea that new neurons support cognitive functions throughout life and reinforces the possibility of enhancing this process to treat psychiatric illnesses.  
*Journal: Cell, June 6, 2013*

**Marina Picciotto, Ph.D.**  
Yale University  
*2004 NARSAD II*  
Nicotinic Acetylcholine Receptors: Novel Targets for Antidepressant Development

**Next Generation Therapies: Depression**  
Discovery of New Depression Trigger and Treatment Target  
Dr. Picciotto led a team of researchers in the discovery that a signaling chemical called acetylcholine may be central in causing depression, leading to a new hypothesis that it is the disruption of acetylcholine, and not serotonin*, which sets depression in motion. Targeting acetylcholine disruption may be a way to treat the root cause of depression and could lead to more effective treatments.  
*Journal: PNAS, February 11, 2013*

**Rene Hen, Ph.D.**  
Columbia University Medical Center  
*2003 NARSAD DI*  
Antidepressants and Neurogenesis in the Adult Hippocampus

**New Technologies: Anxiety**  
New Way to Reduce Anxiety Symptoms Discovered  
Using optogenetics*, Dr. Hen led a group of researchers in the discovery that selective activation of the dentate gyrus, a portion of the hippocampus, can reduce anxiety in people with post-traumatic stress disorder and panic disorder without negatively affecting the ability to learn. By targeting this area with medication or deep brain stimulation it may be possible relieve anxiety with no negative effects.  
*Journal: Neuron, March 6, 2013*

**Karl Deisseroth, M.D., Ph.D.**  
Stanford University  
*2005 NARSAD YI*  
Mechanism and Significance of Excitation-Neurogenesis Coupling

**New Technologies: General Mental Illness**  
3D Imaging Technology Promises Breakthroughs in Brain Research  
Dr. Deisseroth and team developed CLARITY, a new imaging technology that provides high-resolution, 3D images of the brain making it possible for scientists to simultaneously look at “the big picture” and fine details of the brain’s complex fine wiring and essential features. Rendering the brain transparent, may lead to new insights into brain structure and function shedding light on the underlying causes of mental illnesses.  
*Journal: Nature, April 10, 2013*

**Scott A. Schobel, M.D.**  
Columbia University Medical Center  
*2008 NARSAD YI*  
Cross-Species Imaging of Hippocampal Subregion Metabolism in Schizophrenia and Mouse Models of Disease

**Early Intervention: Schizophrenia**  
Foundation-Funded Study Identifies Schizophrenia Early Warning Sign  
Using neuroimaging, Dr. Schobel discovered that high levels of the neurotransmitter glutamate in the hippocampus region of the brain may cause the transition to psychosis in people at high risk for developing schizophrenia. This suggests that increased glutamate activity can be an early warning sign for schizophrenia, and that controlling glutamate levels may be an effective preventive and/or therapeutic strategy.  
*Journal: Neuron, April 10, 2013*
Top 10 Discoveries (continued)

Gail L. Daumit, M.D., M.H.S.
Johns Hopkins University
2010 NARSAD II
Mobile Phone Interactive Technology for Weight Loss: A Pilot Study in Persons with Serious Mental Illness

Next Generation Therapies: Depression
Behavioral Therapy Program Achieves Weight Loss for People with Mental Illness
Project Achieve, the first weight loss clinical trial with people with serious mental illnesses, was led by Dr. Daumit to account for cognitive and behavioral challenges present in mental illness. She found that people with serious mental illnesses can lose weight and keep it off through a modified lifestyle intervention program. Journal: The New England Journal of Medicine, April 25, 2013

Joseph T. Coyle, M.D.
Harvard Medical School
2004 NARSAD DI
Defining the Role of D-serine, An NMDA Receptor Modulator, in Cognition and Behavior

Basic Research: Schizophrenia Negative Symptoms
Researchers Find Way to Increase Neuroplasticity and Treat “Negative” Symptoms of Schizophrenia
Dr. Coyle and team were able to reverse schizophrenia-like negative* symptoms in genetically engineered mice by giving them D-serine, one of two molecules required to activate NMDA receptors. This supports the theory that low activity in these receptors can cause negative symptoms in people with schizophrenia and indicates they may be reversible. Journal: PNAS, May 31, 2013

Helen S. Mayberg, M.D.
Emory University
2002 NARSAD DI
Deep Brain Stimulation for Refractory Major Depression

Next Generation Therapies: Depression
Historic Study Finds Brain Scans Can Guide Depression Treatment Decisions
Using PET scan imaging, Dr. Mayberg and colleagues identified specific activity in the right anterior insula of the brain that can potentially predict whether people with major depressive disorder will better respond to antidepressant medication or psychotherapy. A patient’s biology rather than behavioral symptoms could decide treatment. Journal: JAMA Psychiatry, June 12, 2013

Joan L. Luby, M.D. and Deanna Barch, Ph.D.
Washington University School of Medicine
2008 NARSAD II (Joan Luby)
Serotonin Transporter Polymorphisms and Course of Preschool Onset Depression

New Technologies: Depression
fMRI Brain Scans May Help Diagnose Depression in Preschoolers
In a first-of-its-kind study, Drs. Luby and Barch used functional MRIs to compare images of activity in the amygdala* in non-medicated preschoolers with depression and preschoolers who were not depressed. Scans of preschoolers with depression showed more activity in the amygdala, providing the earliest evidence yet of changes in brain function in children with depression. Journal: Journal of the American Academy of Child & Adolescent Psychiatry, July 2013

Hongjun Song, Ph.D.
Johns Hopkins University
2008 NARSAD II
Role of sFRP3 in Antidepressant-Induced Adult Hippocampal Neurogenesis and Behavior

Next Generation Therapies: Depression
Discovery of How Antidepressants Work Leads Toward Improved Depression Treatments
Dr. Song and co-researchers have discovered a protein that helps electroconvulsive therapy (ECT) and antidepressant medications work, possibly enabling predictive tests of an individual’s response to antidepressant treatment based on their genetic code and providing a new target for the development of improved treatments. Journal: Molecular Psychiatry, December 4, 2012

Type of NARSAD Grant:  
YI - Young Investigator  |  DI - Distinguished Investigator  |  II - Independent Investigator

*hippocampus: an area of the brain key to memory and learning.
*serotonin: a signal-carrying chemical of which low levels have long been associated with depression.
*optogenetics: a cutting-edge technology that allows scientists to selectively activate neurons in the brain and observe the corresponding behavior.
*negative symptoms of schizophrenia: decreased motivation, lack of attention, emotional flatness, memory loss, social withdrawal.
*amygdala: region of the brain that controls emotional processing and regulating.