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

NEW YORK MENTAL HEALTH RESEARCH SYMPOSIUM

Friday, October 24, 2014
Kaufman Music Center
129 West 67th Street
New York, NY

Welcome

We are delighted to welcome you to the 27th Annual New York City Mental Health Research Symposium. Today you will hear presentations by the eight 2014 Brain & Behavior Research Foundation Outstanding Achievement Prizewinners and two exceptionally promising NARSAD Young Investigator Grantees. Together they will take you on a tour of the frontiers of neuroscience.

We are also very pleased to present Kay Redfield Jamison, Ph.D., Professor at Johns Hopkins School of Medicine and Co-Director of the Johns Hopkins Mood Disorders Center, who will speak of her lifelong experience with bipolar disorder. In her Keynote Presentation, "A Life in Moods," she will share what has helped her overcome the burdens of her illness to live a full and productive life.

Throughout the day, you will learn about the breakthrough findings from multinational collaborations on the genetics and genomics of schizophrenia and other mental illnesses that are paving the way toward more targeted and effective treatments. You will also hear about trials for more tailored treatments for bipolar disorder and depression, including one using light therapy. A leader in child and adolescent psychiatry will present the latest on attention-deficit hyperactivity disorder, in both understanding of how the illness develops and how to better treat it.

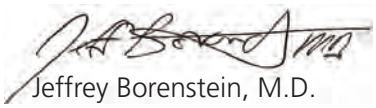
The Outstanding Achievement Prizes are selected by special Committees of the Foundation's Scientific Council, a volunteer group of 150 professionals across disciplines in brain and behavior research, who also select each year's NARSAD Grantees. The projects selected by the Council are chosen specifically to open new frontiers in research and fund innovative projects that may not be supported elsewhere. Through this model of research grant selection, the Foundation fills a gap in funding that has resulted in some of the most important advances in the field.

Since 1987, the Foundation has awarded over $320 million in NARSAD Grants to more than 3,800 scientists worldwide. Funded by private donations, 100 percent of contributions to the Foundation go directly into research funding.

Thanks to Otsuka Pharmaceuticals, Inc., Sunovion and Janssen Pharmaceuticals, Inc., for their charitable support for this year's Symposium. To learn more about the Foundation, visit bbrfoundation.org or call us at (800) 829-8289.

Enjoy your day!

Sincerely,



Jeffrey Borenstein, M.D.
President & CEO

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Morning Program
9:00 a.m. - 12:30 p.m.: Outstanding Achievement Prizewinner Presentations

12:30 p.m. - 1:30 p.m.: Lunch Break

Afternoon Program:
1:30 p.m. - 2:15 p.m.: Keynote Address

2:15 p.m. - 4:30 p.m.: Outstanding Achievement Prizewinner Presentations and Young Investigator Presentations

NEW YORK CITY MENTAL HEALTH RESEARCH SYMPOSIUM

MODERATOR

**Founding Member,
Brain & Behavior Research
Foundation Scientific Council**

Chair, Klerman Prize Selection Committee for Exceptional Clinical Research by a Young Investigator

2002 NARSAD Distinguished Investigator Grantee

2003 Falcone Prize (now the Colvin Prize) for Outstanding Achievement in Mood Disorders Research

Robert M.A. Hirschfeld, M.D.

**Titus H. Harris Chair
Harry K. Davis Professor
Professor and Chair, Department of Psychiatry
University of Texas Medical Branch**

Dr. Hirschfeld, who previously headed the National Institute of Mental Health Mood, Anxiety and Disorders Research Branch, is internationally recognized for his research on the diagnosis and treatment of depression, bipolar disorder and anxiety disorders. With colleagues, he developed the Mood Disorder Questionnaire, the most widely used screening instrument for bipolar disorder.

Dr. Hirschfeld served as chair of the original and revision versions of the American Psychiatric Association's Workgroup to develop practice guidelines for treatment of patients with bipolar disorder. He was chief of the Mood, Anxiety and Personality Disorders Research Branch and Clinical Director of the Depression Awareness, Recognition and Treatment (D/ART) program of the National Institute of Mental Health.

Among his honors, Dr. Hirschfeld received the Klerman Lifetime Research Award and Jan Fawcett Humanitarian Award from the National Depressive and Manic-Depressive Association (now known as the Depression and Bipolar Support Alliance), and the Klerman Award for Panic Disorder from the World Psychiatric Association.

Dr. Hirschfeld has been organizing the annual Brain & Behavior Research Foundation New York City Mental Health Research Symposium since its inception in 1988.

COMMENTATOR

**Founding Member,
Brain & Behavior Research
Foundation Scientific Council**

Chair, Outstanding Achievement Prize Selection Committee on the Goldman-Rakic Prize for Outstanding Achievement in Cognitive Neuroscience Research

Jack D. Barchas, M.D.

**Chair and Barklie McKee Henry Professor of Psychiatry
Weill Cornell Medical College
Psychiatrist-in-Chief, Weill Cornell Medical Center
NewYork-Presbyterian Hospital and Payne Whitney Clinic**

An established leader in advancing understanding of neuroregulators and their relation to stress Dr. Barchas's research has dealt with neuroregulators; substances that act as neurotransmitters or as regulators of neuronal function. The research program has included identification of biochemical pathways, molecular regulation and genetics of neuroregulators, as well as study of their relation to behavior and stress.

Dr. Barchas spent 25 years at Stanford University where he was the Nancy Pritzker Professor and Director of the Pritzker Laboratory, an interdisciplinary program centered on fundamental aspects of systems and behavioral neurobiology. Immediately before coming to Cornell, he spent almost four years at the UCLA Medical School as Dean for Neuroscience and then also for Research Development, dealing with all areas of biomedical research. Involved in public policy and academic issues, he was Chair of the Board on Biobehavioral Science and Mental Disorders for the Institute of Medicine of the National Academies and served as editor of Archives of General Psychiatry.

MORNING SESSION

9:00 a.m. - 12:30 p.m.

PRESENTATIONS:
2014 OUTSTANDING ACHIEVEMENT PRIZEWINNERS

Patrick Francis Sullivan, M.D., FRANZCP
University of North Carolina, Chapel Hill
Lieber Prize | Schizophrenia Research

David L. Braff, M.D.
University of California, San Diego Medical Center
Lieber Prize | Schizophrenia Research

Stephan Ripke, M.D.
Charité - Universitätsmedizin Berlin
Sidney R. Baer, Jr. Prize | Innovative and Promising Schizophrenia Research

Gregory Light, Ph.D.
University of California, San Diego
Sidney R. Baer, Jr. Prize | Innovative and Promising Schizophrenia Research

Wayne C. Drevets, M.D.
Janssen Research and Development
Johnson & Johnson, Inc.
Colvin Prize | Mood Disorders Research

Fritz A. Henn, M.D., Ph.D.
Cold Spring Harbor Laboratory
Colvin Prize | Mood Disorders Research

Progress in Schizophrenia: Three Stories

Patrick F. Sullivan, M.D., FRANZCP
Professor, Karolinska Institutet
M. Hayworth & Family Distinguished Professor of Psychiatry
Professor of Genetics & Psychiatry
Director, Center for Psychiatric Genomics
University of North Carolina, Chapel Hill

2014 Lieber Prize for Outstanding Achievement in Schizophrenia Research

NARSAD Grant: Distinguished Investigator 2010

After a century of uncertainty, in the past year there has been substantial progress in identifying the genetic basis of schizophrenia. The field has struggled greatly to find a methodology whose application yielded consistently replicated results.

There are three important stories that Dr. Sullivan will relate in his presentation. The first story is about the unprecedented international collaborations that made these advances possible. The Psychiatric Genomics Consortium (PGC) was founded in 2007. Now in its eighth year, the PGC is the largest consortium in the history of psychiatry with more than 700 scientists; it represents the largest biological experiment in the history of psychiatry (with currently more than 200,000 subjects) and is arguably the most successful.

The second story concerns the findings themselves. The consortium recently reported the identification of 108 genomic loci for schizophrenia. The findings implicate genetic variation near the type 2 dopamine receptor (the molecular target of antipsychotic medications), calcium signaling and several biological processes highly relevant to the function of the synapse. These findings provide insights into the fundamental biology of schizophrenia. The published work for schizophrenia is exceptional, but yet larger studies are in progress and should provide far greater insights.

The third story is about the ways scientists can now get beyond "finding genes" to "using genes" in order to improve diagnosis, treatment and even prevention. Dr. Sullivan will discuss the potential clinical and therapeutic relevance of these findings.

Dr. Sullivan received his M.D. from the University of California, San Francisco and completed a residency in psychiatry at Western Psychiatric Institute and Clinic at the University of Pittsburgh. He also completed a fellowship at the Royal Australian and New Zealand College of Psychiatrists (FRANZCP).

Deconstructing and Overcoming Schizophrenia: Genes, Neural Circuits and Improving Outcomes

David L. Braff, M.D.
Distinguished Professor of Psychiatry
University of California, San Diego

2014 Lieber Prize for Outstanding Achievement in Schizophrenia Research

NARSAD Grant: Distinguished Investigator 2007

Dr. Braff has pursued and extended our understanding of the neurobiology, genomic architecture, and treatment of schizophrenia via a number of major research projects. These projects include a long-standing National Institute of Mental Health (NIMH) and NARSAD Grant-funded translational research program which has been continuously funded for over 30 years. In addition, Dr Braff, a NARSAD Distinguished Investigator Grantee, is the Director of the NIMH Consortium on the Genetics of Schizophrenia (COGS), working with many distinguished colleagues at over 10 sites to identify the behavioral (endophenotype) and genomic deficits associated with schizophrenia.

Endophenotypes are quantitative and heritable neurocognitive and neurophysiological biomarkers that showl aboratory- based deficits in schizophrenia patients. These neuroscience-based neurophysiological and neurocognitive behavioral measures are analyzed via cutting edge techniques including genotyping; gene expression; gene sequencing; stem cell research identifying genetic deficits and then repairing or "rescuing" these deficits using state-of-the-art techniques; and other promising neuroscience methods. Cumulatively, the COGS and UCSD translational research cohort of over 5,000 subjects represents probably the largest neuroscience-based behavioral and genomically studied schizophrenia cohort available to researchers who want to use emerging methods to fully understand the molecular, biological, and genomic, as well as the functional and outcome deficits, in schizophrenia.

Dr. Braff and COGS colleagues have conducted detailed genomic studies of the neurocognitive and neurophysiological deficits as well as clinical features and outcomes of patients and families with schizophrenia. One advantage of this strategy that merges neuroscience measures with genomics is that each patient is extensively studied using state-of-the-art neurophysiological and neurocognitive techniques to fully characterize them behaviorally. This means that when a genomic abnormality is identified, there is an informatics basis to understand how the genes are expressed behaviorally and in real-world function. The driving concept is that while we have a rapidly increasing base of facts about schizo-phrenia, integrating these facts is a major challenge and one that is necessary to integrate our research findings into better patient care.

The quantifiable schizophrenia-related neurophysiological and neurocognitive endophenotypes are heritable, and along with genomic information can open unique pathways to understanding the origins of schizophrenia. In a complementary manner, the relationship of endophenotype and related genomic deficits to real-world functional deficits offers targets for development of new treatments designed to reverse and ultimately detect and prevent the neurocognitive and functional disabilities of schizophrenia.

A 1970 graduate of the Perelman School of Medicine at the University of Pennsylvania, Dr. Braff completed psychiatric and research training at Yale University and the University of California, San Francisco.

Breakthrough in Pinpointing the Genetics of Schizophrenia through Large, International Collaboration

Stephan Ripke, M.D.
Statistical Analyst
Psychiatric Genomics Consortium
Charité - Universitätsmedizin Berlin

2014 Sidney R. Baer, Jr. Prize for Innovative and Promising Schizophrenia Research

In recent years, GWAS (genome-wide association studies) have provided a great deal of biological insight into the genetic underpinnings for a diverse range of common diseases. Moreover, GWAS are beginning to be useful in distinguishing subgroups of affected individuals. Consequently, GWAS may be used as an important tool for predictive research and the refinement of related phenotypes.

Taken together, the results so far confirm GWAS as a successful analytical tool. The psychiatric genetics field, while largely unsuccessful in the beginning, understood the importance of collaboration early on and began extensive sharing of raw genotypes by 2007. After initial successes in 2011, this consortium, The Psychiatric Genomics Consortium (PGC), quickly grew and collected genotypic data for more than 150,000 individuals. A second grant funded genotyping of more than 100,000 individuals.

The PGC continues to expand and currently encompasses approximately 100 centers with over 1,000 contributing and active researchers. The PGC published among the most successful GWAS analyses in the biomedical field with hundreds of genome-wide significant findings. Many other genetic consortia have learned from the success of the PGC and are beginning to adopt a similar approach to data sharing and collaboration.

In his presentation, Dr. Ripke will describe initial results from GWAS for a range of psychiatric illnesses, identifying which components have been critical for its success and what has been learned from both failures and successes. He will explain why the most important step to scientific progress in human genetics of complex traits is collaboration and exchange of data. In a world where data (in this case genotype data) becomes available in enormous amounts, and where computer power increases significantly via computer clusters and cloud computing, it has been essential to bring everybody together to produce robust findings.

Dr. Ripke earned his M.D. at the University of Hamburg, Germany, did his residency in Berlin, and then joined the Max Planck Institute of Psychiatry as a statistical geneticist. He began his association with the PGC at the Broad Institute of MIT and Harvard University and continues it now at the Charité Universitätsmedizin Berlin, the oldest and most prominent hospital and medical school in Berlin.

Biomarker-Guided Treatment of Schizophrenia

Schizophrenia affects approximately one percent of the world's population, strikes early in life and is highly disabling, resulting in profound long-term suffering in patients and their loved ones. In recent years, advances in neuroscience have transformed our understanding of impaired brain functions in schizophrenia. Despite substantial progress, diagnosis and treatment decisions are still largely based on subjective patient reports, clinician inferences about patient inner experiences and behavioral observation, rather than informed by objective, reliable laboratory-based tests.

In his presentation, Dr. Light will describe a translatable electroencephalography (EEG) test called mismatch negativity (MMN) that is regarded as a breakthrough "biomarker" (biological predictor) that offers great promise for improving our understanding and treatment of schizophrenia.

MMN accounts for nearly half of the variance in clinical symptoms, cognitive abilities and level of psychosocial functioning, and merges advances in neuroscience with important practical clinical issues. This measure is also sensitive to medication effects and predicts response to some interventions. MMN also substantially improves the prediction of which individuals at high clinical risk for developing schizophrenia actually develop this devastating illness. Thus, MMN can contribute to personalized, next-generation biomarker-guided treatment strategies aimed at ameliorating or even preventing the onset of schizophrenia.

Dr. Light received a Ph.D. in clinical neuropsychology under a joint doctoral program of UCSD and San Diego State University. He completed postdoctoral training in biological psychiatry and neuroscience before joining the UCSD faculty.

Gregory Light, Ph.D.

Associate Professor of Psychiatry, University of California, San Diego (UCSD)

Associate Director, Schizophrenia Research Program, UCSD Site Coordinator, National Institute of Health Consortium on the Genetics of Schizophrenia
UCSD Associate Director, Clinical Neuroscience and Genomics Unit
San Diego Veterans Affairs Department

2014 Sidney R. Baer, Jr. Prize for Innovative and Promising Schizophrenia Research

NARSAD Grants:
Young Investigator 2003, 2006
Independent Investigator 2013

Neuroimaging of Bipolar Disorder Reveals Abnormalities of Brain Structure and Function: Implications for Novel Therapeutics

Wayne C. Drevets, M.D.
Vice President
Mood Disease Area Leader,
Neuroscience Therapeutic Area
Janssen Research & Development
Johnson & Johnson, Inc.

2014 Colvin Prize for Outstanding Achievement in Mood Disorders Research

Foundation Scientific Council Member

NARSAD Grants: Young Investigator 1996, Independent Investigator 1999

Prizes: 2000 Freedman Prize Honorable Mention for Exceptional Basic Research by a Young Investigator

Dr. Drevets will discuss how the biological basis of bipolar disorder is being elucidated progressively by converging evidence from studies of brain function and structure, and of genetic and other types of molecular biomarkers.

One of the technologies that enabled these endeavors involved biomedical imaging tools, such as positron emission tomography (PET) and magnetic resonance imaging (MRI), which provided the means to noninvasively investigate brain function, structure and chemistry in patients suffering from bipolar disorder. These technologies also facilitated complementary research in healthy individuals aimed at characterizing the brain circuits that normally regulate the cognitive-behavioral domains affected in bipolar disorder, such as emotional experience, mood regulation and social processing.

Taken together, the findings from research conducted using these technologies has shown that the brain circuits that function normally to modulate emotional behavior, stress responses and reward processing are altered profoundly in patients with bipolar disorder relative to healthy controls. Notably, the abnormal patterns of functional activity and tissue volume loss in these circuits in patients with bipolar disorder are impacted variably by drugs that produce mood stabilizing or antidepressant actions. The effects of these medications on brain imaging measures and molecular assays from patients with bipolar disorder, as well as on experimental animals subjected to repeated stress, are beginning to guide the discovery of new drugs, which potentially will more effectively maintain symptom remission and promote illness recovery.

Dr. Drevets received his M.D.from the University of Kansas School of Medicine, completed residency in psychiatry and a fellowship at the Washington University School of Medicine in St. Louis. He served on the faculties of Washington University and the University of Pittsburgh and as Chief of the Section on Neuroimaging in Mood and Anxiety Disorders of the National Institute of Mental Health Intramural Research Program. Before moving to Janssen, he held the Oxley Foundation Chair in Neuroscience Research at the University of Oklahoma, where he was founding President and Scientific Director of the Laureate Institute for Brain Research.

New Ideas for the Design of an Effective Antidepressant

Fritz A. Henn, M.D., Ph.D.

Professor
Cold Spring Harbor Laboratory

Professor of Psychiatry
Icahn School of Medicine at Mount Sinai

2014 Colvin Prize for Outstanding Achievement in Mood Disorders Research

Foundation Scientific Council Member

Depression is one of the leading health problems in the world, causing more disability than any other class of illness including heart disease or cancer. Dr. Henn's approach to study depression—what causes it and how to better treat it—was to attempt to develop an animal model that mirrored the disease and included a stress component and a genetic component, as major depressive illness does.

Dr. Henn approached this by adding genetic vulnerability to the learned helplessness model of depression in animal models. Looking at how the brain of the "helpless" and "non-helpless" (or resilient) animals differed, Dr. Henn and his colleagues found that activating the lateral habenula, a small structure above the thalamus in the brain, caused depressive symptoms. Activation of the habenula was also seen in depressed human patients.

The lateral habenula controls reward perception and directly controls the mono-amines, dopamine, serotonin and nor-epinephrine, which appear to play a role in depression. An overactive habenula inhibits reward perception and serotonin activation, and blocking this activity with deep brain stimulation reversed it in animals and people.

Dr. Henn found that over-activity of the lateral habenula is due to increased glutamate activity at nerve endings. This increased glutamate also destroys nerve endings in the cortex. One approach to new antidepressants is to increase the reuptake of glutamate and Dr. Henn and his group are currently attempting to do this in a medication trial with patients.

Finally, what is the molecular basis of the habenular activation? Using proteomics, Dr. Henn found one protein responsible and showed that down-regulating this protein led to the immediate loss of depressive symptoms, thus providing another target for a truly effective antidepressant.

Dr. Henn earned a Ph.D. in biochemistry and biophysics at Johns Hopkins University and completed his M.D. and residency in psychiatry at Washington University School of Medicine. After returning from research posts in Germany, for which he received the Federal Cross of Merit awarded by the President of Germany, he served briefly as Associate Director of Brookhaven National Laboratory before joining Cold Spring Harbor Laboratory in 2007.

AFTERNOON SESSION

1:30 p.m. - 4:30 p.m.

KEYNOTE ADDRESS: A Life In Moods
Kay Redfield Jamison, Ph.D.
Johns Hopkins University School of Medicine

PRESENTATIONS:
2014 OUTSTANDING ACHIEVEMENT PRIZEWINNERS

Anita Thapar, M.D., Ph.D.
Cardiff University School of Medicine, UK
Ruane Prize | Child and Adolescent Psychiatric Research

Richard L. Huganir, Ph.D.
Johns Hopkins University School of Medicine
Goldman-Rakic Prize | Cognitive Neuroscience

PRESENTATIONS:
YOUNG INVESTIGATOR GRANTEES

Dorothy K.Y. Sit, M.D.
Unviersity of Pittsburgh

Jennifer Marie Coughlin, M.D.
Johns Hopkins University

KEYNOTE ADDRESS
A Life in Moods

Kay Redfield Jamison, Ph.D.

Dalio Family Professor in Mood Disorders
Professor of Psychiatry
Johns Hopkins University School of Medicine

Co-director
Johns Hopkins Mood Disorders Center

Honorary Professor of English
University of St. Andrews, Scotland

2000 Falcone Prize for Outstanding Achievement in Affective Disorders Research (now named The Colvin Prize for Outstanding Achievement in Mood Disorders Research)

2010 Brain & Behavior Research Foundation Productive Lives Awardee

Dr. Jamison is the co–author of the standard medical text on manic-depressive (bipolar) illness, which was chosen as the most outstanding book in biomedical sciences by the American Association of Publishers, and author of *Touched with Fire, An Unquiet Mind, Night Falls Fast, Exuberance,* and *Nothing Was the Same.* Her memoir about her experiences with manic-depressive illness, *An Unquiet Mind,* was cited by several major publications as one of the best books of 1995; it was on *The New York Times* Bestseller List for more than five months and translated into twenty–five languages. *Night Falls Fast: Understanding Suicide* was a national bestseller, translated into twenty languages, and selected by *The New York Times* as a Notable Book of 1999. Her book *Exuberance: The Passion for Life,* was selected by *The Washington Post, The Seattle Times,* and *The San Francisco Chronicle* as one of the best books of 2004 and by *Discover* magazine as one of the best science books of the year. Her most recent book, *Nothing Was the Same,* was selected as one of the best books of 2009 by *The Washington Post.*

Dr. Jamison did her undergraduate and doctoral studies at the University of California, Los Angeles where she was a National Science Foundation Research Fellow, University of California Cook Scholar, John F. Kennedy Scholar, United States Public Health Service Pre-doctoral Research Fellow, and UCLA Graduate Woman of the Year. She also studied zoology and neurophysiology at the University of St. Andrews in Scotland.

Dr. Jamison, formerly the director of the UCLA Affective Disorders Clinic, was selected as UCLA Woman of Science. She is recipient of the American Suicide Foundation Research Award, the UCLA Distinguished Alumnus Award, the UCLA Award for Creative Excellence, the Siena Medal, the Endowment Award from the Massachusetts General Hospital/Harvard Medical School, the Fawcett Humanitarian Award, the Steven V. Logan Award for Research into Brain Disorders from the National Alliance for the Mentally Ill, the William Styron Award from the National Mental Health Association, the Yale University McGovern Award for excellence in medical communication, and the David Mahoney Prize from Harvard University. She has been awarded numerous honorary degrees, selected as one of five individuals for the public television series "Great Minds of Medicine", and chosen by *Time* magazine as a "Hero of Medicine". She was Distinguished Lecturer at Harvard University in 2002 and the Litchfield Lecturer at the University of Oxford in 2003. She is the recipient of the Lewis Thomas Prize and a MacArthur Genius Award.

The Search for Causes of Attention-Deficit Hyperactivity Disorder and Why It Matters

Anita Thapar, M.D., Ph.D.
Professor of Child & Adolescent Psychiatry,
Institute of Psychological Medicine and Clinical Neuro-sciences and MRC Centre for Neuropsychiatric Genetics and Genomics
Cardiff University, UK

2014 Ruane Prize for Outstanding Achievement in Child and Adolescent Psychiatric Research

Attention-deficit hyperactivity disorder (ADHD) is a childhood-onset neurodevelopmental disorder with multiple adverse impacts that begin in childhood and continue into adult life. Dr. Thapar will talk about her research journey, which has focused on investigating the causes and outcomes of ADHD. As a practicing child and adolescent psychiatrist, she finds this process continues to be strongly influenced by the experiences of those affected and the realization that we need scientific evidence to influence practice.

Dr. Thapar will describe her discoveries in the mid-1990s of the strong genetic contribution to ADHD and its later outcomes. These discoveries were informed by studies of genetically identical and non-identical twins. She will then shift into her more current, 21st century work discuss her team's molecular genetic discoveries on ADHD. Findings highlight the genetic overlap of ADHD with schizophrenia and autism spectrum disorder, as well as with population variability in communication impairments.

No complex disorder is explained by genes alone. Disentangling the contribution of genes and environment requires unusual quasi-experimental designs because many important environmental risks are interdependent on genetic contributions. Dr. Thapar will talk about some of the approaches she and her team have used to identify important early environmental risk factors and the discoveries made from them. These cover prenatal factors as well as later social environmental factors that influence outcomes.

Dr. Thapar's most recent research focuses on disaggregating the ADHD clinical presentation into meaningful subtypes that help understand links between genes, ADHD and the brain mechanisms that contribute to adverse outcomes. Throughout the discussion of her research journey and discovery highlights, she will highlight why these research findings matter.

Dr. Thapar completed her medical degree and training in psychiatry in Wales. As an MRC Centre for Neuropsychiatric Genetics and Genomics fellow, she completed a Ph.D. in genetic epidemiology, after which she became a Senior Lecturer in Child and Adolescent Psychiatry at the University of Manchester. She returned to Cardiff University to take up the Chair and Head of Academic Section in Child & Adolescent Psychiatry.

Understanding How the Brain "Fires and Wires" and Creates Memories

Recent research has revealed that many cognitive disorders such as schizophrenia, autism and depression are "synaptopathies," diseases of the synapse. Synapses are the tiny gaps between neurons through which messages are transmitted from cell to cell. Many studies have found that synaptic transmission between neurons in the brain is disrupted in these disorders, affecting the circuits involved in higher brain processes such as learning, cognition, mood and intelligence.

Dr. Huganir has been studying the molecular mechanisms involved in normal synaptic transmission and how in brain disorders synaptic transmission is altered. He has focused on neurotransmitter receptors—proteins that mediate the response to neurotransmitters in the brain—to analyze how they work and are regulated to modify synaptic connections, neuronal circuits and behavior.

Dr. Huganir will discuss his research that has shown that these receptors can be regulated by chemical modifications in the cell that increase or decrease receptor function, dramatically altering synaptic connectivity, circuits and behavior. In addition, he will present studies on the identification and characterization of a large complex of molecules that interact with neurotransmitter receptors to regulate their function. His studies have demonstrated that regulation of neurotransmitter receptor function is a major mechanism for the synaptic plasticity underlying higher brain function including learning, memory, fear and cognition.

Most recently, these receptors and their interacting molecules have been implicated in studies of schizophrenia, autism, intellectual disability and PTSD. Dr. Huganir is now investigating the role of these receptors and interacting molecules in these cognitive disorders by generating mouse models of these diseases and studying how synaptic transmission and plasticity, as well as the animals' behavior, is altered. The goal of these studies is to identify potential novel targets for the therapeutic treatment of these debilitating brain disorders.

Dr. Huganir completed a Ph.D. in biochemistry and molecular and cell biology at Cornell University followed by a postdoctoral fellowship at Yale University School of Medicine with Nobel Laureate and Foundation Scientific Council member Paul Greengard, Ph.D. He joined the Greengard laboratory at The Rockefeller University and then moved to The Johns Hopkins University in 1988. He is a Howard Hughes Medical Institute Investigator since 1988.

Richard L. Huganir, Ph.D.
Professor of Biological Chemistry and of Pharmacology
Director of the Solomon H. Snyder Department of Neuroscience
Johns Hopkins University School of Medicine

Co-Director, Johns Hopkins Medicine Brain Science Institute

2014 Goldman-Rakic Prize for Outstanding Achievement in Cognitive Neuroscience

NARSAD Grant: Distinguished Investigator 1999

Light Therapy for Bipolar Disorder: A Promising Treatment Option May Unveil Hints about the Underlying Biology

Dorothy K.Y. Sit, M.D.
Assistant Professor of Psychiatry
Western Psychiatric Institute and Clinic
University of Pittsburgh Medical Center

NARSAD Grant:
Young Investigator 2013

Bipolar disorder (BP) is a major public health concern. Having BP is often associated with reduced quality of life, increased medical illness, chronic disability and an increased risk for suicide. Studies have uncovered effective medications for the mania phase of BP, but there are few treatments for the depressive phase (bipolar depression) with considerable possible side effects, including heightened risk of metabolic disorders (obesity, diabetes and hyperlipidemia) and the induction of mania or what is referred to as rapid cycling (having four or more episodes of major depression, mania, hypomania, or mixed states, all within a year).

More than two decades of literature have provided support for the efficacy of light therapy for seasonal affective disorder. Published preliminary data from research Dr. Sit conducted together with Dr. Katherine Wisner, former NARSAD Young Investigator Grantee, and colleagues, suggested that midday light therapy can provide antidepressant effects for women with non-seasonal bipolar depression. Building on that data, Dr. Sit investigated the efficacy of midday light therapy in a clinical trial; initial findings from the treatment study indicated robust effects with a significant reduction in depression levels and increased remission rates with midday light therapy versus an inactive comparator.

In the course of the study, Dr. Sit encountered an intriguing finding. Very depressed patients with BP with otherwise normal ophthalmic health had significant impairment in visual perception. Vision tests indicated patients had reduced sensitivity to contrast (light-dark transitions) and were unable to perceive images or patterns with a dim or washed out appearance. The difference in visual perception between patients and controls was large enough to suggest the reduction in contrast sensitivity was not a random finding.

Dr. Sit is extending these findings, with the support of her NARSAD Grant, by conducting a novel study examining neural and visual biomarkers in male and female patients with BP who receive light therapy so as to begin to understand the possible brain mechanism underlying the response to light treatment in BP. Abnormal responses that normalize with light treatment could point towards a novel mechanism for the therapeutic effects of light and inform a new approach to predict a subgroup of patients with altered photic processing who might derive increased benefit from light therapy.

Dr. Sit received her medical degree from the University of Toronto, School of Medicine and completed her residency in family medicine at the Icahn School of Medicine at Mount Sinai and the University of Toronto. She completed her psychiatry residency as well as a fellowship in psychopharmacology at the University of Massachusetts Medical School.

Does Inflammation Play a Role in Schizophrenia?

Jennifer M. Coughlin, M.D.

Assistant Professor of Psychiatry and Behavioral Sciences
The Johns Hopkins University School of Medicine

NARSAD Grant: Young Investigator 2013

Recent schizophrenia research supports a model wherein molecular brain changes in late adolescence contribute to the onset and early progression of the illness. Studies further implicate oxidative stress and altered immune pathways even in early stages of schizophrenia, suggesting that these two systems may play a role in disease development. Much of this research-to-date demonstrates changes in oxidative stress and pro-inflammatory markers in peripheral tissues, but it is unclear whether those changes reliably reflect changes in brain tissue. One limitation of studies using brain tissue obtained at autopsy from patients with schizophrenia is that such patients usually have had longstanding disease and chronic exposure to medications, limiting the assessment of disease markers in early-stage disease.

Central nervous system (CNS) biomarkers (biological predictors) for schizophrenia are badly needed to enable early detection and intervention; Dr. Coughlin's research is working toward that end. Building on preliminary findings, she has been examining a large collection of cerebrospinal fluid (CSF), the fluid that bathes the brain, for changes in levels of inflammatory proteins and markers of oxidative stress. Those CSF samples were collected from patients during their first episode of psychosis and from patients assessed as at risk for schizophrenia.

Dr. Coughlin will present recent results regarding characterization of neurochemical mediators of oxidative stress and inflammation in CSF compared to healthy individuals. She will also introduce complementary molecular brain imaging techniques that she has been applying to study inflammation in early stages of schizophrenia. Through parallel use of biochemical assays of CSF and molecular imaging, she aims to validate the role of inflammation in schizophrenia by repeatedly interrogating the CNS directly for evidence of abnormal immune signal and oxidative stress over the course of early-stage illness.

Ultimately, Dr. Coughlin hopes to aid in further identification of biomarkers relevant to the pathophysiology of schizophrenia, and develop other molecular imaging techniques to detect and quantify changes in those markers in living patients. Such methods may enable scientists to further understand the relationship between molecular systems and altered neurotransmission in schizophrenia, ultimately informing concrete strategies for early detection and intervention.

Dr. Coughlin obtained her medical degree from the University of Maryland School of Medicine and completed residency training in psychiatry at the Johns Hopkins University School of Medicine, where she also completed a fellowship in molecular psychiatry.

Scientific Council

150 MEMBERS

- **2** NOBEL PRIZE WINNERS
- **4** FORMER DIRECTORS OF THE NATIONAL INSTITUTE OF MENTAL HEALTH
- **13** MEMBERS OF THE NATIONAL ACADEMY OF SCIENCES
- **21** CHAIRS OF PSYCHIATRY & NEUROSCIENCE DEPTS. AT LEADING MEDICAL INSTITUTIONS
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