# 2017 INTERNATIONAL MENTAL HEALTH RESEARCH SYMPOSIUM

Friday, October 27, 2017 9:00am-4:30pm

**Kaufman Music Center** 129 West 67<sup>th</sup> Street New York, NY 10023





#### Welcome

Welcome to our International Mental Health Research Symposium. Today we will hear from the Foundation's 2017 Outstanding Achievement Prizewinners and two exceptional Young Investigator Grantees, on topics ranging from schizophrenia and addiction to childhood interventions and the brain circuitry behind mood disorders.

The Outstanding Achievement Prizewinners are selected by special committees of the Foundation's Scientific Council, a volunteer group of 177 pre-eminent mental health professionals across disciplines in brain and behavior research, who also select each year's Young Investigator, Independent Investigator and Distinguished Investigator Grantees. Since 1987, the Foundation has awarded \$380 million to fund more than 5,500 grants to more than 4,500 scientists around the world. These awards are made specifically to fill a gap in funding innovative research that may not be supported elsewhere, but is vital for advancement in the fields of neuroscience and psychiatry.

We are pleased this year to present Herbert Pardes, M.D., as our Keynote Speaker. Dr. Pardes is Executive Vice Chairman of the NewYork-Presbyterian Hospital Board and the Founder and President of the Brain & Behavior Research Foundation's Scientific Council. Nationally recognized for broad expertise in education, research, clinical care and health policy, today he will offer his thoughts on breakthrough opportunities for mental health.

We would like to extend special thanks to our sponsors The Allergan Foundation and Sunovion Pharmaceuticals, Inc. for their charitable support of this year's symposium.

We hope today's conference will inspire you. Our shared commitment to advance science will change what it means to live with a mental illness and open possibilities for more people to live full, happy, and productive lives. In our 30th anniversary year, I thank you for your ongoing support to help us get closer to realizing this vision.

Sincerely,

Jeffrey Borenstein, M.D. President & CEO

Brain & Behavior Research Foundation

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# INTERNATIONAL MENTAL HEALTH RESEARCH SYMPOSIUM



#### Robert M.A. Hirschfeld, M.D.

DeWitt Wallace Senior Scholar

Professor of Psychiatry Weill Cornell Medical College, Cornell University

NewYork-Presbyterian Hospital

Founding Scientific Council Member

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

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

2002 Distinguished Investigator Grant

Prior to joining Weill Cornell in April 2015, Dr. Hirschfeld served for 25 years as Professor and Chair of the Department of Psychiatry at the University of Texas Medical Branch in Galveston. He previously led the Mood, Anxiety and Disorders Research Branch at the National Institute of Mental Health, and is internationally recognized for his research on the diagnosis and treatment of depression, bipolar disorder

and anxiety disorders. With colleagues, Dr. Hirschfeld developed the Mood Disorder Questionnaire, the widely used screening instrument for bipolar disorder. He received a 2002 Distinguished Investigator Grant and 2003 Falcone Prize (re-named the Colvin Prize in 2012) for Outstanding Achievement in Mood Disorders Research from the Brain & Behavior Research Foundation

#### Commentator



#### Myrna Weissman, Ph.D.

Diane Goldman Kemper Family Professor of Epidemiology in Psychiatry Columbia University College of Physicians & Surgeons

Scientific Council Member

1994 Selo Prize in Depression Research (now the Colvin Prize)

2005, 2000, 1991 Distinguished Investigator

Dr. Weissman is a Professor of Epidemiology in Psychiatry, College of Physicians and Surgeons and the Mailman School of Public Health at Columbia University and Chief of the Division of Epidemiology at New York State Psychiatric Institute (NYSPI). She is a member of the Sackler Institute for Developmental Psychobiology at Columbia. Until 1987, she was a Professor of Psychiatry and Epidemiology at Yale University School of Medicine and Director of the Depression Research Unit. She has been a Visiting Senior Scholar at the Institute of Medicine, National Academy of Sciences in Washington, D.C. She received a Ph.D. in epidemiology from Yale University School of Medicine in 1974.

Her research is on understanding the rates and risks of mood and anxiety disorders using methods of epidemiology, genetics, neuroimaging, and the application of these findings to develop and test empirically based treatments and preventive intervention. Her current interest is in bringing psychiatric epidemiology closer to translational studies in the neurosciences and genetics. She directs a 3-generation study of families at high and low risk for depression who have been studied clinically for over 30 years and who are participating in electropsychology and imaging studies. She has directed these multi-centered studies to determine the impact of maternal remission from depression on offspring. She is one of the Principle Investigators in a multi-centered study to find biomarkers of response to the

treatment of depression and other disorders with over 100 clinical trials of efficacy. Along with her late husband Gerald Klerman she developed Interpersonal Psychotherapy, an evidence-based treatment for depression. Studies using IPT have been carried out worldwide and a manual for group IPT is available through the World Health Organization.

Dr. Weissman has been a consultant to many private and public agencies, and is a member of the Institute of Medicine, National Academy of Science. She has been the author or a co-author of over 600 scientific articles and chapters, and 11 books. She has been the recipient of numerous grants from NIMH, the Foundation and numerous awards for her research. She is on. the editorial board of several journals including JAMA Psychiatry.

In April 2009, she was selected by the American College of Epidemiology as 1 of 10 epidemiologists in the United States who has had a major impact on public policy and public health. The summary of her work on depression appears in a special issue of the Annals of Epidemiology, Triumphs in Epidemiology. In January 2016, she was listed as one of the 100 highly cited authors in Google Scholars Citation.

### MORNING SFSSION

9:00am-12:30pm

#### **Outstanding Achievement Prizewinners**

The Prevention of Relapse with Medication: A Statistical Perspective John M. Davis, M.D.

University of Illinois at Chicago

**Toward Personalized Medicine** in Schizophrenia: Clinical Trials Targeting Specific Biomarkers and **Patient Populations** 

Deanna L. Kelly, Pharm.D., BCPP University of Maryland School of Medicine

The Brain Circuitry of Bipolar Disorder: A View from Brain Scanning Research

Hilary P. Blumberg, M.D. Yale School of Medicine

Mechanisms of Mood Disorder in the Human Brain: Neural Targets for New Treatments

Mary L. Phillips, M.D., M.D. (Cantab) University of Pittsburgh, Western Psychiatric Institute and Clinic

Recovery from Severe **Psychosocial Deprivation** 

Nathan A. Fox. Ph.D.

The University of Maryland, College Park

Charles A. Nelson III, Ph.D. Harvard Medical School & Boston Children's Hospital

Charles H. Zeanah, Jr., M.D. Tulane University School of Medicine

### AFTERNOON SESSION

1:30pm-4:30pm

#### Keynote Speaker

Are There Breakthrough Opportunities For Mental Health?

Herbert Pardes, M.D.

Executive Vice Chair, Board of Trustees NewYork-Presbyterian Hospital

President, Brain & Behavior Research Foundation Scientific Council

#### **Outstanding Achievement Prizewinners**

Addiction as Brain Disorder of Self-Control

Trevor W. Robbins, Ph.D. University of Cambridge, UK

#### **Young Investigator Grantees**

Harnessing the Microbiota-Gut-Brain Axis During Pregnancy to Improve Mother and Child's Health

Mary C. Kimmel, M.D.

University of North Carolina at Chapel Hill

Brain Development and the Immune System: The Basic Science of Stress

Anna V. Molofsky, M.D., Ph.D.

University of California, San Francisco

# THE PREVENTION OF RELAPSE WITH MEDICATION: A STATISTICAL PERSPECTIVE

#### LIEBER PRIZE FOR OUTSTANDING ACHIEVEMENT IN SCHIZOPHRENIA RESEARCH



John M. Davis, M.D.
Gilman Professor of Psychiatry and Research
Professor of Medicine
University of Illinois at Chicago

In the late 1960s, antipsychotics were becoming widely used to treat acute episodes of schizophrenia, but the long-term use of the drugs to prevent recurrence was controversial. despite many trials scattered throughout the literature. To take a closer look at this problem, Dr. Davis devised a statistical method in the early 1970s (now called meta-analysis) to combine results from multiple controlled trials. This was the first meta-analysis in psychiatry and psychology, and the second in internal medicine.

In drawing together the literature, Dr. Davis showed massive consistent evidence that longterm antipsychotic treatment could prevent many recurrences of acute psychotic episodes and that long-term lithium prevented relapses of both the manic and depressive phases of bipolar disorder. Although there were only a few studies of the prophylactic effects of longterm antidepressant use to prevent future episodes of depression, the results consistently showed a prophylactic effect as well. These findings have been replicated many times and have stood the test of time. The FDA now requires long-term maintenance trials for approval of new drugs. In subsequent years, meta-analysis became widely used, particularly with the formation of the worldwide Cochrane collaboration in the 1990s. Dr. Davis also wrote about the limitations of maintenance medication at the time and will discuss limitations of its current use.

Before antipsychotics were discovered, some patients had a psychotic episode, but recovered spontaneously and never had a relapse. Dr. Davis also showed that initially all antipsychotics were equally effective, but later when the antipsychotic drug clozapine was discovered, that some were more efficacious. More recently he and his colleagues have used network meta-analysis to compare the relative efficacy or side effect liability of many antipsychotics to better summarize efficacy and safety. He has also shown that meta-analysis can clarify contradictory results of similar but not identical interventions, where one can be efficacious and the other ineffective, which helps identify the mechanism responsible for the difference. He will illustrate this with studies on prevention of heart attacks and strokes. Dr. Davis will review recent work on the regulation of the expression or repression of a gene (epigenetics) as well as other biochemical mechanisms that may lead to the development of new drugs.

John M. Davis attended Princeton University, received his medical degree from Yale University School of Medicine, interned at Massachusetts General Hospital, and went back to Yale for his psychiatric residency. He received his research training at the National Institute of Health. He is now in the department of psychiatry at the University of Illinois at Chicago School of Medicine.

# TOWARD PERSONALIZED MEDICINE IN SCHIZOPHRENIA: CLINICAL TRIALS TARGETING SPECIFIC BIOMARKERS AND PATIENT POPULATIONS

#### 2017 MALTZ PRIZE FOR INNOVATIVE & PROMISING SCHIZOPHRENIA RESEARCH



Deanna L. Kelly, Pharm.D., BCPP

Professor of Psychiatry University of Maryland School of Medicine

Affiliate Professor University of Maryland School of Pharmacy

Director, Treatment Research Program Maryland Psychiatric Research Center

President College of Psychiatric and Neurologic Pharmacists (CPNP) While there have been many significant and meaningful advances in the field of schizophrenia in the past decade, the development of novel treatments for people with this illness has been a slower process. Translating new findings to the level of medication development is less than ideal and optimizing outcomes for patients are hindered by a lack of personalized strategies.

Most treatments available currently have been studied without regard to the heterogeneity of schizophrenia. This means that treatments we currently use have not been tailored to specific patient groups or populations but rather based on the diagnostic criteria of the DSM-5 and studied in everyone the same way. We know that schizophrenia presents very differently and that there is a wide range of different levels of treatment response and different adverse effects, with many people not achieving optimal outcomes.

Dr. Kelly and her Treatment Research Program team at the Maryland Psychiatric Research Center have focused on treatment-oriented research that strives to optimize and best treat patients in a more personalized way. Specifically, she has been one of the few clinical trial researchers focused specifically on the biologic differences and side effects of women with schizophrenia. She is also working on a large multinational clinical trial targeted at treating people with the medication clozapine, where she is focused on better using this medication and safely showing its efficacy in a population of African descent patients who may have a genetic predisposition to certain side effects.

Additionally, she has been working with a collaborative team from Johns Hopkins University and Harvard to examine a subgroup of people

with schizophrenia who have a high degree of inflammation and have a unique immune response to gliadin, a protein found in wheat and other foods. Dr. Kelly and her colleagues have shown that certain antibodies formed in response to gliadin are high in some, but not all people with schizophrenia and these same people may have improvements in inflammation and psychiatric symptoms with removal of gluten from the diet. She and her colleagues are working on a large confirmatory study where they hope to prove the effectiveness in the specific schizophrenia population having this antibody biomarker and they hope to better understand the reasons why it may be effective.

Deanna L. Kelly is Professor of Psychiatry at University of Maryland Baltimore School of Medicine and Affiliate Professor in the School of Pharmacy. She is currently Director and Chief of the Treatment Research Program at the Maryland Psychiatric Research Center. Dr. Kelly received her bachelor's and doctoral degrees in pharmacy at Duquesne University. She completed residency training in psychiatric pharmacy practice at the University of Maryland.

# THE BRAIN CIRCUITRY OF BIPOLAR DISORDER: A VIEW FROM BRAIN SCANNING RESEARCH

#### 2017 COLVIN PRIZE FOR OUTSTANDING ACHIEVEMENT IN MOOD DISORDERS RESEARCH



#### Hilary P. Blumberg, M.D.

John and Hope Furth Endowed Professor of Psychiatric Neuroscience Professor of Psychiatry, Radiology and Biomedical Imaging and in the Child Study Center

Director, Mood Disorders Research Program Yale University School of Medicine

Scientific Council Member

Klerman Prize for Exceptional Clinical Research 2006

2006 Independent Investigator 2002 Young Investigator

Millions of individuals worldwide suffer from bipolar disorder (BD) and many will lose their lives to suicide. Dr. Blumberg has dedicated her research career to getting these individuals better help by elucidating causes of BD and contributing to critically-needed new methods for early detection, intervention and prevention. She will present her state-ofthe-art brain scanning research that has had tremendous impact on the field in advancing knowledge about brain circuitry of BD. Among her important pioneering contributions were some of the first demonstrations of differences in the functioning of emotional brain circuitry in individuals while they were experiencing manic or depressive symptoms of BD.

Using innovative brain scanning methods, she has shown structural differences in the gray matter nodes, and integrity of the white matter wiring, in emotion brain circuitry underlying its different functioning. She has used innovative, integrative approaches with neuroimaging to show negative influences of genetic variations and early life stress (such as child abuse and neglect), and salutary influences of pharmacological and non-pharmacological interventions on the structure and function of the circuitry.

Dr. Blumberg is perhaps best known for her pioneering work in these areas of research in youths with BD. This has included research evidence of differences in the trajectories of development of the brain circuitry during adolescence that has shaped the view of BD as a disorder of neurodevelopment and of adolescence as an important period. Her more recent areas of study include some of the first multi-modality research on the brain circuitry of suicide risk in adolescents and young adults, changes in the brain in BD with age later in life, and with her

Brain Emotion Circuitry-Targeted Self-Monitoring and Regulation Therapy (BE-SMART) psychobehavioral treatment. For individuals who are suffering from and are at risk for BD. Dr. Blumberg's research brings great hope that on the horizon are new methods for early detection, targeted treatments, improved prognosis and prevention of BD progression and suicide.

Hilary P. Blumberg is the John and Hope Furth Endowed Professor of Psychiatric Neuroscience, Professor of Psychiatry, Radiology and Biomedical Imaging and in the Child Center at the Yale School of Medicine. She is Director of the Yale Mood Disorders Research Program that brings together scientists from multiple disciplines across the campus to study mood and related disorders. She graduated summa cum laude in neuroscience from Harvard University and completed her medical degree, psychiatry training and specialty training in research in neuroimaging of neuropsychiatric disorders at Cornell University Medical College.

# MECHANISMS OF MOOD DISORDER IN THE HUMAN BRAIN: NEURAL TARGETS FOR NEW TREATMENTS

#### 2017 COLVIN PRIZE FOR OUTSTANDING ACHIEVEMENT IN MOOD DISORDERS RESEARCH



#### Mary L. Phillips M.D., M.D. (Cantab)

Pittsburgh Foundation-Emmerling Endowed Chair in Psychotic Disorders

Professor in Psychiatry and Clinical and Translational Science University of Pittsburgh, Western Psychiatric Institute and Clinic

Scientific Council Member

2005 Independent Investigator

Bipolar disorders affect up to 4.5 percent of Americans, and are the fourth leading cause of disability worldwide. People with these disorders not only suffer from difficulties in controlling emotions, and severe mood episodes, but are also especially sensitive to rewards. Unfortunately, it is often difficult to correctly diagnose people with these disorders, as they are often diagnosed with other psychiatric illnesses, in particular, depression. It also remains challenging to identify people who are at future risk for bipolar disorders, as there are no clear biological measures of these debilitating disorders. The development of new treatments for bipolar disorders has been slow because of these problems.

Dr. Phillips' laboratory uses different types of brain imaging techniques to examine the brain mechanisms underlying development of bipolar disorders in people across childhood and adulthood. Their goal is to identify patterns of abnormal brain activity in people with bipolar disorders, in order to identify brain-based markers of these disorders. These brain-based markers can then be used to improve accuracy in diagnosing people with these disorders; identify people who are at future risk of developing these disorders before major mental health problems arise; and guide development of new treatments for people suffering from these disorders.

Dr. Phillips' team has shown that the cross-talk between brain regions important for experiencing emotions (subcortical regions) and brain regions important for controlling emotions (prefrontal cortical regions) is disrupted in children and adults with bipolar disorders, and likely underlies the difficulty in controlling emotions experienced by people with these disorders. They have also shown that a particular prefrontal cortical region, the left ventrolateral prefrontal cortex, is overactive in people with bipolar disorders when they are asked to take part in a gambling task. This pattern of abnormal brain response is not present in people with depression. This brain region is important for learning about the chance of rewarding events happening in the future—for example, winning money. The fact that this region is overactive in people with bipolar disorders during gambling suggests that people with these disorders may be abnormally sensitive to the chance of future rewards, and is a promising brain-based marker of bipolar disorders. Dr. Phillips' team is now using this marker to help develop new treatments, including new brain stimulation treatments, for bipolar disorders.

Mary L. Phillips is the Pittsburgh Foundation-Emmerling Endowed Chair in Psychotic Disorders, and Professor in Psychiatry and Clinical and Translational Science in the University of Pittsburgh. She heads the Clinical and Translational Affective Neuroscience Program in the Department of Psychiatry at the University of Pittsburgh. Dr. Phillips trained in Medicine at Cambridge University, UK, and in Psychiatry at the Maudsley Hospital and the Institute of Psychiatry, King's College, University of London, UK.

# RECOVERY FROM SEVERE PSYCHOSOCIAL DEPRIVATION

#### 2017 RUANE PRIZE FOR OUTSTANDING ACHIEVEMENT IN CHILD & ADOLFSCENT PSYCHIATRIC RESEARCH



Nathan A. Fox, Ph.D.

Distinguished University Professor

Chair, Department of Human Development and Quantitative Methodology

Neuroscience and Cognitive Sciences Program University of Maryland, College Park

2007 Distinguished Investigator



Charles A. Nelson III. Ph.D.

Professor of Pediatrics and Neuroscience

Professor of Psychology in Psychiatry Harvard Medical School

Professor of Education Harvard Graduate School of Education

Richard David Scott Chair in Pediatric Developmental Medicine Research

Director of Research, Division of Developmental Medicine Boston Children's Hospital



Charles H. Zeanah, Jr., M.D.

Mary Peters Sellars Polchow Chair in Psychiatry

Vice Chair for Child and Adolescent Psychiatry Professor of Psychiatry and Pediatrics

Director of the Institute for Infant and Early Childhood Mental Health

Tulane University School of Medicine

Experience is the engine that drives much of postnatal brain development. When children are deprived of key (i.e., experience-expected) experiences, particularly during critical periods of development, brain and behavioral development can be derailed. There is perhaps no more egregious form of deprivation than being raised in large, state-run institutions.

In the presentation by the Ruane recipients, Dr. Nelson will introduce the Bucharest Early Intervention Project (BEIP), launched 17 years ago and based in Bucharest, Romania. In the BEIP, three groups of Romanian children are being studied: infants abandoned to institutions and who remain in institutional care; infants abandoned to institutions but then placed in high quality foster care; and infants who have never been institutionalized. These three groups have been studied through age 16, with a 20-year follow up being planned. Dr. Nelson will discuss the project's conceptual framework, experimental design, the ethics involved in conducting this work and the nature of the intervention deployed.

Dr. Fox will discuss the effects of institutionalization on BEIP children's behavior and brains, noting whether there were effects in these domains as a function of the intervention that were sustainable over time, and if timing effects such as the age at which children were removed from an institution and placed into families mattered. He will also identify factors in the lives of the children that affected developmental outcomes, including the number of transitions and disruptions in a child's caregiving context. The pattern of results from the Bucharest Study suggest that early adversity has lasting effects upon behavior and brain. Removal from adversity, particularly early in life, appears to remediate some but not all of the effects of early adversity.

The project has extended previous findings by showing that serious disturbances of attachment and psychopathology were evident as early as three to four years in children who had experienced early deprivation. As Dr. Zeanah will discuss, emotional disorders, aggressive behavior disorders and inattention/overactivity were evident in early childhood among children who had been deprived. Randomization to foster care led to substantial reductions in emotional disorders, especially for girls. Later in childhood, children who had histories of institutional rearing showed signs of social communication problems that were as severe as children with autism, though most did not have other features of autism spectrum disorder. Foster care significantly reduced these social abnormalities. By early adolescence, there were significantly fewer signs of aggressive behavior disorders and signs of callousness for boys who had been placed in foster care in early childhood.

Both boys and girls who had been randomized to foster care showed fewer signs of attachment disorders. Throughout the study, quality of foster care, stability of foster care, and early placement in foster care substantially enhanced recovery for children who had experienced deprivation.

Nathan A. Fox is a Distinguished University Professor in the Department of Human Development and Quantitative Methodology and Neuroscience and Cognitive Sciences Program at the University of Maryland. He received a bachelor's degree in Political Science at Williams College and his Ph.D. in Psychology and Social Relations from Harvard University, and was a Postdoctoral Fellow in Cross-Cultural Child Development at Harvard.

Charles A. Nelson III is a Professor of Pediatrics and Neuroscience and Professor of Psychology in the Department of Psychiatry at Harvard Medical School, and Professor of Education in the Harvard Graduate School of Education. He also holds the Richard David Scott Chair in Pediatric Developmental Medicine Research at Boston Children's Hospital, and is Director of Research in the Division of Developmental Medicine. He received his undergraduate degree from McGill University, master's degrees from the University of Wisconsin and his Ph.D. from the University of Kansas, all in psychology.

Charles H. Zeanah, Jr. is the Mary Peters Sellars Polchow Chair in Psychiatry, and serves as Vice Chair for Child and Adolescent Psychiatry, and Professor of Psychiatry and Pediatrics at the Tulane University School of Medicine. He directs of the Institute for Infant and Early Childhood Mental Health also at the Tulane University School of Medicine. He received his bachelor's degree in English and his M.D. from Tulane University. He completed a pediatric internship at the University of Virginia, a residency in general psychiatry at Duke University and a fellowship in child and adolescent psychiatry and a research fellowship at Stanford University.

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# ARE THERE BREAKTHROUGH OPPORTUNITIES FOR MENTAL HEALTH?

#### Herbert Pardes, M.D.

Executive Vice Chairman of the Board, NewYork-Presbyterian Hospital

President, Brain & Behavior Research Foundation Scientific Council

Many factors today are increasing the attention to mental health. Critical is how the collective field of constituent support (patients, families, healthcare professionals and all concerned citizens) will use these opportunities to dramatically improve care for people with psychiatric disorders taking advantage of transformative new research and clinical developments and their translation to mental health care.

Dr. Herbert Pardes is Executive Vice Chairman of the NewYork-Presbyterian Hospital Board and President of the Brain & Behavior Research Foundation Scientific Council. Nationally recognized for broad expertise in education, research, clinical care and health policy, he is a vigorous advocate of highest

quality care for all patients, academic medical centers, empathic care and technology innovation to transform medicine.

He was NewYork-Presbyterian Hospital and Healthcare System President and CEO from 1999-2011. Dr. Pardes was Vice President for Health Sciences and Dean of the College of Physicians and Surgeons at Columbia University from 1989-1999. A noted psychiatrist, he served as Director of the National Institute of Mental Health and U.S. Assistant Surgeon General during the Carter and Reagan administrations, and has been President of the American Psychiatric Association and a National Academy of Medicine member.



# ADDICTION AS BRAIN DISORDER OF SELF-CONTROL

2017 GOLDMAN-RAKIC PRIZE FOR OUTSTANDING ACHIEVEMENT IN COGNITIVE NEUROSCIENCE



Trevor Robbins, Ph.D.

Professor, Cognitive Neuroscience University of Cambridge

Director

Behavioural and Clinical Neuroscience Institute

Drug addiction, involving alcohol and nicotine as well as illicit drugs such as cocaine and heroin, constitutes a major socioeconomic burden worldwide, not only upon the individual but also upon their families and society in general, including drug-related crime. Addiction is difficult to treat because of its relapsing nature. Just when an addict appears to have abstained from drug-taking, events plunge them back into escalating drug binges; they appear to lack "willpower" to resist these urges.

We generally support those of our smoking friends attempting to "give up" when they show by the dint of their "willpower" they can resist the infernal urge to smoke. However, in general the lay citizen tends not to be sympathetic to addicts, especially those on illicit drugs, assuming their behavior to be caused initially by a degree of moral deviance in the pursuit of transient pleasure or relief, compounded subsequently by this failure of "self-control." Much understanding from basic neuroscience research in experimental animals, and subsequently in volunteering humans, has established that initial effects of many drugs of abuse are mediated by an ancient subcortical reward system in the brain served by the chemical messenger dopamine which provides initially strong motivation for drug-seeking, but may then become more automated and habitual. and hence even harder to control

What then do we mean by self-control, how is it mediated by the brain, and how does it bear on the causation of addiction and its resistance to treatment? We know from sophisticated psychological measures that addiction is often associated with impaired self-control. We also know that self-control is mediated by specific brain networks headed by the frontal lobes of the brain responsible for our higher powers of

intelligence and thinking. A major question is whether impairments in self-control are caused by impairment of these neural networks by drug abuse or whether they were pre-existing and hence contribute to the tendency to take drugs in vulnerable individuals. Dr. Robbins will provide evidence for both types of effect, by investigations of non-drug abusing relatives of drug addicts, large samples of healthy adolescents, and appropriate animal models. He will also discuss whether this realization of the brain basis of "willpower" may possibly help in the treatment and management of drugaddicted individuals.

Trevor Robbins is a Professor of Cognitive Neuroscience at the University of Cambridge and Director of the Behavioural and Clinical Neuroscience Institute. He received his bachelor's, master's and doctoral degrees in psychology from the University of Cambridge. He is a Fellow for the Royal Society (FRS).

# HARNESSING THE MICROBIOTA-GUTBRAIN AXIS DURING PREGNANCY TO MPROVE MOTHER AND CHILD'S HEALTH



Mary C. Kimmel, M.D.

2016 Young Investigator

Assistant Professor Medical Director, Perinatal Psychiatry Inpatient Unit University of North Carolina at Chapel Hill Antenatal depression or prenatal depression (AND) and postpartum depression (PPD) can result in significant illness and death for mother and child, but current options for prevention, diagnosis and treatment are limited. An emerging area of research in mental health is the study of the gut microbiota (the bacteria and other organisms that populate the intestinal tract), which might serve as a biomarker and novel treatment target for AND and PPD. Furthermore, the microbiome may serve in communicating information from mother to child and be important in the child's development.

While there has been research of the microbiome changing across pregnancy, studying the microbiome, especially the gut microbiota, in relation to perinatal depression and anxiety is new. In a preliminary feasibility study of thirty women, many women were found to be using different forms of probiotic pills and dietary choices in hopes of improving their health—a finding especially true for women with histories of depression and anxiety. Women with histories of anxiety had elevated symptoms on a depression screener in the third trimester. Some of the women in the study developed PPD. Microbial composition is being explored in relation to different trajectories of symptoms and to AND and PPD.

Clinical work on a specialized Perinatal Psychiatry Inpatient Unit (PPIU) that treats women with severe forms of perinatal depression and anxiety, and outpatient work in a specialized perinatal psychiatry clinic, will show where more information is needed to improve outcomes for mother, baby and family. In her talk, Dr. Kimmel will discuss her ongoing project to analyze microbial composition over the course of pregnancy by following a sample of

50 women (35 women with and 15 women without histories of major depression or anxiety disorders) across the perinatal period, and to study the relationship of the microbiome to stress reactivity of mother and child six to eight weeks postpartum. She will also discuss how information about the microbiome might be combined with other genomics research to improve the ability to create personalized treatments.

Mary Kimmel serves as Assistant Professor of Psychiatry and Medical Director of the Perinatal Psychiatry Inpatient Unit at the University of North Carolina at Chapel Hill. She received her bachelor's degree from Northwestern University and her medical degree from Drexel University, subsequently serving as Chief Resident and Fellow in the Department of Psychiatry and Behavioral Sciences at Johns Hopkins University. Her research focuses on improving diagnosis, treatment and preventative measures for postpartum depression.

# BRAIN DEVELOPMENT AND THE IMMUNE SYSTEM: THE BASIC SCIENCE OF STRESS



Anna V. Molofsky, M.D., Ph.D.
Assistant Professor of Psychiatry
University of California, San Francisco
2016 Young Investigator

In many mental health conditions, stress and trauma can trigger the emergence of symptoms or worsen their severity. The developing brain is particularly vulnerable, and it is thought that during this period stress can become encoded in synapses—the essential connections between nerve cells in the brain. Dr. Molofsky's research group aims to understand how brain synapses form and how stress impacts this process. Her lab is particularly interested in the long unappreciated brain cells known as "glia." These cells play key roles in brain development and are also the first responders when the brain is under stress.

Dr. Molofsky's project stems from the discovery that glial cells produce a potent immune signal that triggers brain synapses to get "eaten" away. Dr. Molofsky's research into this immune signaling pathway will address the hypothesis that the immune system is both essential during brain development, and an important regulator of the brain's stress response. These studies may lead to future strategies to protect the developing brain from stress and to restore synapse balance in psychiatric disorders.

Dr. Molofsky is a psychiatrist and neuroscientist at the University of California, San Francisco, where she is currently an Assistant Professor in the Department of Psychiatry and the Weill Institute for Neurosciences. Her research group is focused on cellular and molecular mechanisms of brain development, and her clinical focus is in psychotherapy. She obtained her bachelor's degree in Neuroscience and Chemistry from Amherst College, and her M.D. and Ph.D. degrees from the University of Michigan. She completed her psychiatry residency and postdoctoral fellowship at the University of California. San Francisco.

#### **177** Members (7 Emeritus)

- 2 Nobel Prize Winners
- **2** Former Directors of the National Institute of Mental Health as well as the current Director
- **4** Recipients of the National Medal of Science
- 13 Members of the National Academy of Sciences
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- 52 Members of the National Academy of Medicine

#### SCIENTIFIC COUNCIL

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