2019 INTERNATIONAL MENTAL HEALTH RESEARCH SYMPOSIUM

Friday, November 1, 2019
9:00am–4:30pm

Kaufman Music Center
New York, NY

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

More than 30 Years of Research for Recovery

Mission

The Brain & Behavior Research Foundation is committed to alleviating the suffering caused by mental illness by awarding grants that will lead to advances and breakthroughs in scientific research.

We fund leading-edge research for mental health that:

- **Patients** require to recover
- **Parents** desire for their children
- **Psychiatrists** need to provide better care
- **Pioneering Scientists** depend upon to make new discoveries
- **Philanthropists** can point to with pride

Our goal: new treatments, cures, and methods of prevention.

Vision

To dramatically improve the lives of those living with mental illness, ultimately enabling them to live full, happy, and productive lives.

100% of all donor contributions for research are invested in BBRF grants that lead to discoveries in understanding the causes and improving treatments for brain and behavior disorders in children and adults including addiction, ADHD, anxiety, autism, bipolar disorder, borderline personality disorder, depression, eating disorders, OCD, PTSD, schizophrenia, and suicide prevention.

For more than 30 years the Brain & Behavior Research Foundation has fostered new research pathways and transformative breakthroughs.

Our 70,000 donors have joined together in the great challenge of modern medical science — overcoming mental illness.

Since 1987 the Foundation has awarded more than $408 million to fund more than 5,900 grants.

Grants have been given to more than 4,800 leading scientists around the world.

Welcome

Welcome to our International Mental Health Research Symposium.

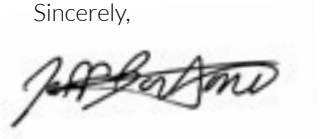
Today we will hear presentations from the Brain & Behavior Research Foundation's 2019 Outstanding Achievement Prize-winners on topics that will include depression, bipolar disorder, ADHD, and schizophrenia. The Outstanding Achievement Prizewinners are selected by special committees of the BBRF Scientific Council, a volunteer group of 184 mental health experts across disciplines in brain and behavior research who review all Foundation grant applications and recommend the most promising ideas to fund.

Since 1987, the Foundation has awarded more than $408 million to fund more than 5,900 grants to more than 4,800 scientists around the world. These awards are made specifically to fund innovative research that may be not be supported elsewhere, but is vital for advancement in the fields of neuroscience and psychiatry. **100% of every dollar donated for research is invested in our research grants.** Our operating expenses are covered by separate foundation grants.

We are pleased this year to have Dr. William Carpenter as our Keynote Speaker. Dr. Carpenter is a member of the BBRF Scientific Council, a past BBRF prizewinner and grant recipient, and is the winner of the 2019 Pardes Humanitarian Prize in Mental Health. He has been a transformative force in psychiatry for over 40 years. Throughout his career, Dr. Carpenter has taken a person-centered, rather than an illness-centered view of schizophrenia which has led to more compassionate care for people with this illness. He has played a critical role in shifting the focus of treatment to the earliest stages of the illness, when interventions may have their most profound impact and maximize the likelihood of recovery.

We hope today's Symposium will inspire you. Thank you for joining us in our commitment to dramatically improve the lives of those with mental illness and ultimately enable more people to live full, happy, and productive lives.

Sincerely,



Jeffrey Borenstein, M.D.
President & CEO
Brain & Behavior Research Foundation

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MODERATOR

Robert M.A. Hirschfeld, M.D.

BBRF Founding Scientific Council Member

2002 Distinguished Investigator
2003 Falcone Prizewinner for Outstanding Achievement in Mood Disorders Research

Dr. Robert Hirschfeld is a Professor of Psychiatry and the DeWitt Wallace Senior Scholar in the Department of Psychiatry at Weill Cornell Medical College. Prior to joining the Weill Cornell Department of Psychiatry in April 2015, he served for nearly 25 years as Professor and Chair of the Department of Psychiatry at the University of Texas Medical Branch in Galveston where he conducted research, treated patients, and provided educational programs for medical students and residents. Before coming to Texas, Dr. Hirschfeld spent 18 years at the National Institute of Mental Health, where he was Chief of the Mood, Anxiety, Personality Disorders Research Branch.

Dr. Hirschfeld is renowned internationally for his research on the diagnosis and treatment of bipolar disorder and depression. He developed the Mood Disorder Questionnaire (MDQ), the most widely used screening instrument for bipolar disorder in the world.

Dr. Hirschfeld has authored nearly 300 scientific papers and abstracts in leading scientific and medical journals, and has contributed chapters on mood and anxiety disorders in four major psychiatric textbooks, as well as in nearly two dozen other books on psychiatry. He served as Chair of the original American Psychiatric Association Guidelines for Treatment of Patients with Bipolar Disorders as well as the revision of the document.

Dr. Hirschfeld received his Bachelor of Science degree from the Massachusetts Institute of Technology in 1964, and his M.D. degree from the University of Michigan in 1968. He completed his residency in Psychiatry at Stanford University Medical Center in 1972 and received a Master of Science in Operations Research from Stanford University in the same year. He was certified in Psychiatry by the American Board of Psychiatry and Neurology in 1975.

Dr. Hirschfeld is the recipient of numerous honors, including the 2010 Award for Research in Mood Disorders from the American College of Psychiatrists, the Edward A. Strecker, M.D. Award from the University of Pennsylvania, the Gerald L. Klerman Lifetime Research Award from the National Depressive and Manic Depressive Association, the Jan Fawcett Humanitarian Award from the National Depressive and Manic Depressive Association, the Special Presidential Commendation from the American Psychiatric Association, and the Gerald L. Klerman Award for Panic Disorder from the World Psychiatric Association. Dr. Hirschfeld serves on Board of the American Foundation for Suicide Prevention. He also is a member of the Scientific Advisory Board of the Depression and Bipolar Support Alliance and the Scientific Advisory Board of the ADAA.

Morning Session

9:00am–12:10pm

Early-Life Determinants of Schizophrenia & Other Psychiatric Disorders

Alan S. Brown, M.D., M.P.H.

Columbia University Irving Medical Center / New York State Psychiatric Institute

Thalamo-Cortical Interactions in Cognition

Christoph Kellendonk, Ph.D.

Columbia University Irving Medical Center / New York State Psychiatric Institute

Preventing Schizophrenia – 'Thinking the Unthinkable'

John J. McGrath, M.D., Ph.D.

The University of Queensland / Queensland Centre for Mental Health Research

Decision Making & Neuropsychiatry: What Can We Learn from the Decisions We Make?

James P. Kesby, Ph.D.

The University of Queensland

The Shape of Discovery: Ketamine for Treatment-Resistant Depression

Dennis S. Charney, M.D.

Icahn School of Medicine at Mount Sinai

Afternoon Session

1:20pm–4:30pm

Keynote Speaker

William T. Carpenter, Jr., M.D.

New Thoughts About Mental Illness: Implications for Discovery & Treatment

Resilient Brains: Adaptive Brain Mechanisms in Bipolar Disorder

Sophia Frangou, M.D., Ph.D., F.R.C.Psych

Icahn School of Medicine at Mount Sinai

Ketamine: Imagining New Ways to Treat Depression

John H. Krystal, M.D.

Yale University

Developmental Psychopathology & Stigma Reduction: A Synthesis

Stephen P. Hinshaw, Ph.D.

University of California, Berkeley / University of California, San Francisco

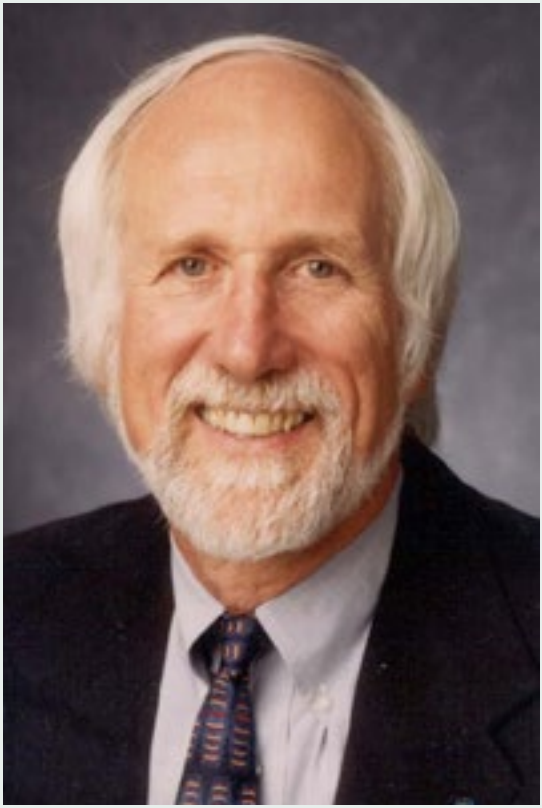
Harnessing Hippocampal Neurogenesis to Improve Cognition and Mood

René Hen, Ph.D.

Columbia University / New York State Psychiatric Institute

KEYNOTE PRESENTATION

New Thoughts About Mental Illness: Implications for Discovery & Treatment



William T. Carpenter, Jr., M.D.

Maryland Psychiatric Research Center

Professor of Psychiatry and Pharmacology

University of Maryland School of Medicine

Dr. William Carpenter is a luminary in the field of psychiatry who has tirelessly advocated for resources for research on mental illness and for reducing stigma. His vision, scientific productivity, leadership, and advocacy have helped shape our understanding of schizophrenia and other forms of serious mental illness.

Dr. Carpenter's professional interests include phenomenology, etiology, pathophysiology, anatomy, and treatment. He has made original and fundamental contributions in psychopathology, assessment methodology, testing of novel treatments, and research ethics. He has served as Principal Investigator on five NIMH-funded center grants and has received three BBRF Distinguished Investigator awards. He provided expert testimony in the case of the United States Government v. John Hinckley and in 1989 was a member of the State Department delegation to inspect the political use of psychiatry in the Soviet Union. Dr. Carpenter is the Editor-in-Chief for *Schizophrenia Bulletin*, has served on many editorial boards and advisory committees, and has authored more than 400 publications. He is past president of the American College of Neuropsychopharmacology and was instrumental in the founding of the Brain & Behavior Research Foundation, where he is a member of the Scientific Council and Chairs the Program Committee.

Today, Dr. Carpenter will discuss various examples of how deconstruction of psychiatric syndromes provides opportunity for discovery.

He offers this example: For over 100 years schizophrenia has been viewed as a specific disease. This appears not to be the case, however, and advancing knowledge about the illness has been slow. Forty years ago, a clinical syndrome status for schizophrenia was proposed, one that would recognize differences among individual patients. It has remained for the 21st century to break away from the "disease-entity" paradigm and reconceptualize the psychopathology. The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) recognizes syndrome status for schizophrenia, and symptom dimensions that cross diagnostic boundaries. Clinical high-risk concepts based on early detection of vulnerability to psychosis present the opportunity for prevention of a full psychotic disorder but also acknowledge substantial heterogeneity with different therapeutic needs across cases.

The NIMH introduced the Research Domains Criteria to relate behavioral constructs to neural circuits in order to increase knowledge on mechanisms underlying psychopathology in disorders. Another program, called HiTOP, conceptualizes psychopathology developmental patterns that identify traits underlying groups of disorders. Computational approaches have initiated studies that may substantially alter the organization of psychopathology.

These new concepts, Dr. Carpenter suggests, may lead to better understanding of mechanisms and provide new targets for therapeutic discovery for treatment. Industry and regulatory bodies are preparing for a new era in conceptualizing therapeutics.

2019 LIEBER PRIZE FOR OUTSTANDING ACHIEVEMENT IN SCHIZOPHRENIA RESEARCH

Early-Life Determinants of Schizophrenia and Other Psychiatric Disorders

Alan S. Brown, M.D., M.P.H.

Professor of Psychiatry and Epidemiology

Director, Unit in Birth Cohort Studies

Vagelos College of Physicians and Surgeons

Columbia University Irving Medical Center

New York State Psychiatric Institute

2015 BBRF Distinguished Investigator

2004, 2000 BBRF Independent Investigator

1996, 1994 BBRF Young Investigator

Dr. Alan S. Brown's principal area of research is the epidemiology of prenatal risk factors for schizophrenia and other psychiatric disorders.

He has over 25 years of experience in large-scale collaborative birth cohort studies of prenatal and other early-life exposures in relation to schizophrenia, autism spectrum disorders, and other psychiatric illnesses among offspring. Risk factors that he has studied include maternal infectious, inflammatory, toxic, hormonal, nutritional, and antidepressant exposures.

Dr. Brown is the founder and principal investigator of the Finnish Prenatal Studies (FiPS), a series of investigations based on a national birth cohort of over 2 million individuals. He has made several new scientific discoveries by analyzing stored maternal serum samples drawn during pregnancy for specific biological markers among offspring with schizophrenia and other psychiatric disorders. Among these findings, he demonstrated that a mother's exposure to infections, inflammation, smoking, and low thyroid hormone levels are related to an increased risk of schizophrenia in the offspring. Moreover, he has demonstrated that maternal exposure to the insecticide DDT is associated with risk of autism.

Dr. Brown will discuss how, early in his career, he was drawn to the field of epidemiology. He went on to examine whether fetal environmental exposures might predispose to schizophrenia. In his work with birth cohorts, large samples of individuals born to mothers whose serum had been stored during their pregnancies were followed up for schizophrenia and other psychiatric disorders later in life. Among his findings he discovered relationships between the later risk of schizophrenia and prenatal biomarkers of exposures such as inflammation, smoking, thyroid hormone deficiency, and low iron and folic acid levels. He will discuss his current efforts, also aimed at better understanding how various risk factors might operate to cause schizophrenia and other psychiatric disorders; estimating the degree to which they contribute to the illness; and applying this new knowledge to generate interventions for prevention and treatment.

2019 MALTZ PRIZE FOR INNOVATIVE &
PROMISING SCHIZOPHRENIA RESEARCH

Thalamo-Cortical Interactions in Cognition

Christoph Kellendonk, Ph.D.

Associate Professor of Pharmacology in Psychiatry
Columbia University
New York State Psychiatric Institute

2008, 2002 BBRF Young Investigator

Dr. Christoph Kellendonk received his Ph.D. from the University of Heidelberg, Germany. For his postdoctoral studies he joined the laboratory of Dr. Eric Kandel (BBRF Scientific Council member and Nobel laureate), where he became interested in studying how brain circuitry regulates behaviors relevant for psychiatric disorders.

Dr. Kellendonk's laboratory uses mouse genetic tools to better understand the biology that underlies cognitive and negative symptoms of schizophrenia. While the positive symptoms —which include disordered thought processes, hallucinations and delusions—are the most characteristic feature of the disorder, they are difficult to model in the mouse. In contrast, cognitive and negative symptoms of the disorder—including deficits in working memory and motivation—have behavioral readouts in mice that are relatable to humans. Cognitive and negative symptoms are poorly understood and difficult to treat, and their severity is a strong predictor of the long-term prognosis of patients with schizophrenia.

Dr. Kellendonk's laboratory takes observations made in patients with schizophrenia (e.g., from brain imaging or epidemiological studies) and then seeks to model these observations as closely as possible in the mouse. One important finding from the laboratory is that chronic antipsychotic medication in the adult mouse leads to specific changes in the anatomy and functional balance of basal ganglia circuitry that is affected in schizophrenia. Brain imaging studies informed by these mouse studies are currently being performed in patients to determine whether the same anatomical and functional changes are observed. Another important finding showed that thalamic input to the cortex is necessary for sustaining cortical activity during working memory, a cognitive ability impaired in patients. Boosting thalamic function in the mouse enhances short-term working memory, thereby identifying the thalamus as a potential target for therapeutic interventions for improving cognitive deficits.

Today, Dr. Kellendonk will present data from mouse studies that establish a causal relationship between thalamic function and working memory, a key cognitive deficit in patients with schizophrenia. As he will explain, mechanistic studies further suggest that the thalamus interacts with the prefrontal cortex to sustain cortical activity necessary for working memory.

2019 LIEBER PRIZE FOR OUTSTANDING ACHIEVEMENT IN SCHIZOPHRENIA RESEARCH

Preventing Schizophrenia—'Thinking the Unthinkable'

John J. McGrath M.D., Ph.D.

Niels Bohr Professor
Aarhus University

Director
Queensland Centre for Mental Health Research, The University of Queensland

Conjoint Professor
Queensland Brain Institute

Dr. John McGrath is a psychiatrist interested in discovering the causes of serious mental illnesses. His research aims to generate and evaluate non-genetic risk factors for schizophrenia.

Dr. McGrath has forged productive cross-disciplinary collaborations linking risk-factor epidemiology with developmental neurobiology. For example, he and his colleagues have made discoveries linking prenatal vitamin D and later risk of mental illness in children. In addition, he has supervised major systematic reviews of the epidemiology of schizophrenia.

Dr. McGrath was awarded a John Cade Fellowship by the Australian National Health and Medical Research Council. In 2016 he was also awarded a Niels Bohr Professorship by the Danish National Research Foundation.

Today's talk will focus on an ambitious goal—the primary prevention of schizophrenia. In the last two decades, substantial progress has been made in understanding the epidemiology of schizophrenia. With respect to risk factor epidemiology, several potentially modifiable risk factors have been linked to the risk of schizophrenia (e.g., early cannabis use, trauma exposure, paternal age, low vitamin D, prenatal infection, obstetric complications). By way of example, the research linking low prenatal vitamin D and risk of schizophrenia will be summarized. Dr. McGrath will suggest that it is now time to sharpen our hypotheses and design the next generation of studies to refine our understanding of the modifiable risk factors for schizophrenia; that it is time we 'think the unthinkable'—that the primary prevention of schizophrenia is a tractable research question of considerable public health importance.

2019 MALTZ PRIZE FOR INNOVATIVE AND PROMISING SCHIZOPHRENIA RESEARCH

Decision-making and Neuropsychiatry: What Can We Learn From the Decisions We Make?"

James P. Kesby, Ph.D.

University of Queensland Amplify Fellow

Queensland Brain Institute; University of Queensland Centre for Clinical Research; The University of Queensland

Dr. James P. Kesby obtained his Ph.D. at the University of Queensland, studying the developmental risk factors for schizophrenia in animal models. His postdoctoral training was under the tutelage of Professor Athina Markou at the University of California San Diego, where he focused on the cognitive deficits associated with methamphetamine dependence and HIV disease in both animal models and human datasets. He is currently a postdoctoral fellow in the Queensland Brain Institute at the University of Queensland, under the mentorship of Professors Darryl Eyles and John McGrath.

Dr. Kesby's research examines how dysfunction in a region of the brain called the associative striatum produces hallucinations and delusions (psychosis) and contributes to poor decision-making in people with schizophrenia. He uses a range of experimental approaches to manipulate brain circuits and neurochemistry in animal models during decision-making tests. These studies are demonstrating that the underlying brain dysfunction associated with psychosis can also impair cognitive function. Cognitive and psychotic symptoms have long been viewed as separate entities. Dr. Kesby's research highlights that these two symptom groups are not separate and feature overlapping neurobiology that can be targeted with future treatment options.

His current research is testing decision-making in people with psychosis and schizophrenia. For these studies, he asks people who are experiencing psychotic symptoms to choose the best option in various scenarios on a computer program. This provides a range of information about why people with schizophrenia make poor decisions, and in combination with functional brain imaging, can provide an idea as to which brain areas are responding differently. By using similar tests of decision-making in people with psychosis and in animal models after circuit-based manipulations, Dr. Kesby's translational approach aims to leverage the strength of basic research synergistically with outcomes obtained from direct patient-based clinical studies.

Today, Dr. Kesby will talk about building on knowledge of the neurotransmitter dopamine and its role in cognition to identify better treatments for schizophrenia. In schizophrenia, increased dopamine activity in the associative striatum is present prior to diagnosis and is central to the expression of psychotic symptoms. However, the associative striatum also integrates cortical inputs that are critical for the decision-making impairments in schizophrenia. According to Dr. Kesby, this makes the associative striatum an interface between psychotic and cognitive symptoms, providing a tantalizing opportunity for interventions that improve a broader spectrum of symptoms.

2019 COLVIN PRIZE FOR OUTSTANDING ACHIEVEMENT IN MOOD DISORDERS RESEARCH

The Shape of Discovery: Ketamine for Treatment-Resistant Depression

Dennis S. Charney, M.D.

Dean
Icahn School of Medicine at Mount Sinai

President for Academic Affairs
Mount Sinai Health System

BBRF Scientific Council Member Emeritus

Dr. Dennis S. Charney is a world expert in the neurobiology and treatment of mood and anxiety disorders, having made fundamental contributions to the understanding of the causes of human anxiety, fear, and depression, and the discovery of new treatments for mood and anxiety disorders. His research on depression has led to discovery of new and novel therapies for treatment-resistant depression including ketamine and EMFT (Emotional Faces Memory Task), the first digital treatment for depression.

Dr. Charney has been honored with many of the major awards in his field for his scientific research, including World's Most Influential Scientific Minds 2014 and 2015, was ranked 48 out of 1,360 of Most Highly Cited Life Science Researchers in the World. His discovery with his co-inventors of the use of intranasal ketamine for the treatment of treatment-resistant depression was named by Cleveland Clinic on its Top 10 list of 2017 Health Care Innovations. He holds three U.S. Patents, and 19 U.S. and Foreign Patent Applications, 10 of which are licensed to two companies. He has published 785 articles and book chapters, and 16 books, including *Resilience: The Science of Mastering Life's Greatest Challenges*, and Charney & Nestler's *Neurobiology of Mental Illness, 5th Edition*. Dr. Charney was elected to the National Academy of Medicine in 2000, and the National Academy of Inventors in 2017.

Today, Dr. Charney will discuss the discovery of ketamine as a treatment for resistant depression. The discovery of ketamine raises questions about the process of discovery, which Dr. Charney will address. These include: What types of environments facilitate discovery? What is the optimal size of research groups? How did the science come together that led to the initial trials? What opposition existed? What was the initial reaction?

2019 COLVIN PRIZE FOR OUTSTANDING ACHIEVEMENT IN MOOD DISORDERS RESEARCH

Resilient Brains: Adaptive Brain Mechanisms in Bipolar Disorder

Sophia Frangou, M.D., Ph.D., FRCPsych

Research Chair in Brain Health,
University of British Columbia

Professor of Psychiatry,
Icahn School of Medicine at Mount Sinai

2008 BBRF Independent Investigator

2002 BBRF Young Investigator

Dr. Sophia Frangou received her Master's Degree in Neuroscience and her Ph.D. from the University of London, UK, and completed her psychiatry training at the Maudsley Hospital, UK.

Her work has greatly advanced the understanding of the pathophysiology of bipolar disorder, particularly in relation to genetic and familial risk. She has made groundbreaking contributions to the characterization of brain mechanisms of resilience in those at high familial risk for bipolar disorder. Dr. Frangou has authored more than 200 papers and has written or contributed to 10 books on mental illness. In 2016, she published *Women in Academic Psychiatry: A Mind to Succeed*, to promote women psychiatrists aiming for academic leadership positions.

Dr. Frangou is a fellow of the European Psychiatric Association (EPA), the Royal College of Psychiatrists, and the American Psychiatric Association. She is the founding chair of the Neuroimaging Section of the EPA and the Neuroimaging Network of the European College of Neuropsychopharmacology, and is current chair of the Panamerican Division of the Royal College of Psychiatrists. She co-chairs the Lifespan Working Group of the Enhancing NeuroImaging Genetics Through Meta-Analysis (ENIGMA) consortium and the consortium for the investigation of Psychopathology and Allostatic Load Across the Lifespan (PALS). She is editor for *European Psychiatry* and *Human Brain Mapping* and member of the editorial board of major scientific journals.

Regarding today's presentation, Dr. Frangou says: "Recognizing the factors that promote resilience in the presence of significant genetic risk is very important, as it shifts the focus from illness to resilience. Many factors may contribute to resilience in relatives of people with bipolar disorder. These can be psychological (e.g., good coping skills), social (e.g., supportive relationships), and biological. My research group has focused on identifying the biological 'signature' of resilience by studying differences in brain anatomy and function between patients and their well relatives." Her research suggests that it is possible to find biomarkers of disease and resilience to bipolar disorder, paving the way for the development of interventions that may mitigate the risk of this disorder.

2019 COLVIN PRIZE FOR OUTSTANDING ACHIEVEMENT IN MOOD DISORDERS RESEARCH

Ketamine: Imagining New Ways to Treat Depression

John H. Krystal, M.D.

Robert L. McNeil, Jr. Professor of Translational Research, Professor of Psychiatry, Neuroscience, and Psychology; Co-Director of the Yale Center for Clinical Investigation; Chair, Department of Psychiatry, *Yale University School of Medicine;*

Chief, Psychiatry and Behavioral Health
Yale-New Haven Hospital;

Director, Clinical Neuroscience Division
VA National Center for PTSD;

Director
NIAAA Center for the Translational Neuroscience of Alcoholism

BBRF Scientific Council Member

2006, 2000 BBRF Distinguished Investigator

1997 BBRF Independent Investigator

Dr. John H. Krystal is a leading expert in the areas of alcoholism, post-traumatic stress disorder, schizophrenia, and depression. His work links psychopharmacology, neuroimaging, molecular genetics, and computational neuroscience to study the neurobiology and treatment of these disorders. He is best known for his role in the discovery of the rapid antidepressant effects of ketamine in depressed patients.

He is a member of the U.S. National Academy of Medicine. He also serves in a variety of advisory and review capacities for NIAAA, NIMH, Wellcome Trust, BBRF, the Broad Institute, and the Karolinska Institutet.

By 1957, all of the commonly prescribed antidepressant classes were discovered. Since then, depression research focused on monoamine signaling systems based in primitive parts of the brain: dopamine, serotonin, norepinphrine, and acetylcholine, largely ignoring the unique biology of higher brain centers. By the 1990s, Dr. Krystal's mentor and colleague, Dr. Dennis Charney, found reason to question the centrality of monoamines to depression. This led them to hypothesize that the signaling mechanisms employed by higher brain centers, particularly glutamate and GABA signaling, might be critical to depression and its treatment.

How could glutamate signaling be studied in people? This was the focus of Dr. Krystal's laboratory. He developed the use of ketamine as a probe of the biology of depression, discovering its remarkably rapid and robust antidepressant effects in depressed patients. When Janssen Pharmaceuticals received FDA approval for the s-isomer of ketamine (esketamine), it was clear that they had created new hope for people with depression and had jumpstarted depression research.

Today's presentation will highlight the rationale for the initial ketamine study, the initial findings in depressed patients, and the subsequent clinical studies (including the Spravato trials) that have shaped our understanding of the role of ketamine in the management of treatment-resistant symptoms of depression and potentially other indications (suicide risk, PTSD). It will also follow the thread of basic neuroscience studies that have aimed to identify the specific neural signaling mechanisms through which ketamine produces its therapeutic effects. Dr. Krystal will suggest that ketamine may be the prototype for a new class of rapidly-acting antidepressant medications that build from what the field is learning about ketamine.

2019 RUANE PRIZE FOR OUTSTANDING ACHIEVEMENT
IN CHILD & ADOLESCENT PSYCHIATRIC RESEARCH

Developmental Psychopathology and Stigma Reduction: A Synthesis

Stephen P. Hinshaw, Ph.D.

Professor of Psychiatry and Vice-Chair for Child and Adolescent Psychology
The University of California, San Francisco

Professor of Psychology
The University of California, Berkeley

Dr. Stephen Hinshaw received his A.B. from Harvard in 1974 and his Ph.D. in clinical psychology from UCLA in 1983. He completed his postdoctoral fellowship at the Langley Porter Institute of the University of California, San Francisco, in 1985. His research focuses on developmental psychopathology, multimodal treatment strategies for youth with externalizing disorders (focusing on the family and peer-related processes that produce optimal change), and mental illness stigma. He has authored over 360 articles and chapters plus 12 books, including (with Richard Scheffler) *The ADHD Explosion: Myths, Medication, Money, and Today's Push for Performance* (Oxford University Press, 2014), and (as sole author) *Another Kind of Madness: A Journey through the Stigma and Hope of Mental Illness* (St. Martin's Press, 2017).

Dr. Hinshaw's research focuses on evidence-based assessment and treatment of youth with attention-deficit hyperactivity disorder (ADHD) and related disruptive behaviors, the interplay of neurobiological vulnerability and environmental contexts (especially parenting practices and peer relationships) in explaining the onset and maintenance of such conditions, and the contribution of deficits in executive function to later maladjustment. Through a multilayered program of work he has altered the field's fundamental perspective from a narrow focus on symptoms and heritability to a broader view of context, development, and competencies. He is the world's leader in investigating girls and women with ADHD. His Berkeley Girls with ADHD Longitudinal Study (BGALS) is the largest such investigation in existence. Among key findings: the major risk for self-injury in girls with ADHD as they mature into adulthood, which is explained in part by factors like poor response inhibition, peer rejection, and early trauma.

In today's talk, after highlighting the current mental health crisis—particularly rising rates of suicide, mood disorders, ADHD, and functional impairments in children and adolescents—Dr. Hinshaw will discuss his work with neurodevelopmental disorders and disruptive behavior disorders, emphasizing the strong neurobiological risk for such conditions while highlighting the role of peer relationships and optimal parenting strategies in predicting resilient outcomes. In terms of treatment, he will discuss the need for combinations of pharmacologic and psychosocial interventions to address those at highest risk. The talk features the example of Dr. Hinshaw's father, a philosopher whose lifelong, misdiagnosed, and professionally silenced bipolar disorder affected the entire family and led Dr. Hinshaw into clinical psychology and mental health.

2019 GOLDMAN-RAKIC PRIZE FOR OUTSTANDING ACHIEVEMENT IN COGNITIVE NEUROSCIENCE RESEARCH

Harnessing Hippocampal Neurogenesis to Improve Cognition and Mood

René Hen, Ph.D.

Professor of Psychiatry, Neuroscience and Pharmacology
Columbia University

Director, Division of Systems Neuroscience
New York State Psychiatric Institute

BBRF Scientific Council Member

2009, 2003 BBRF Distinguished Investigator

1998 BBRF Independent Investigator

Dr. René Hen was born in Strasbourg, France, and received his Ph.D. from University Louis Pasteur under the mentorship of Pierre Chambon. After a postdoctoral stay in Richard Axel's laboratory at Columbia University, Dr. Hen became an assistant professor in Strasbourg. He then returned to Columbia University, where he is presently a professor of pharmacology, psychiatry, and neuroscience and the director of the division of systems neuroscience at the New York State Psychiatric Institute.

Dr. Hen's laboratory is using animal models to elucidate the neural substrates that underlie mood and anxiety disorders. He has been studying the mechanism of action of antidepressant medications as well as hippocampal neurogenesis for the past 25 years and he has a strong background in molecular biology, pharmacology, gene-targeting technologies, and in behavioral studies.

In today's talk, Dr. Hen will explain how his lab has approached the problem of determining the mechanism through which antidepressant medications work. In trying to resolve this mystery, Dr. Hen studied the neural targets of antidepressants, including the effects on different serotonin receptors and the processes downstream from them. The Hen lab's discovery that antidepressants increase neurogenesis in the dentate gyrus area of the hippocampus, and that manipulations that countered this increase caused a partial loss of antidepressant effect, set the stage for two lines of research, which he will explain. One was mechanistic; the other, therapeutic. Dr. Hen will explain how, with collaborators in the New York State Psychiatric Institute, he is attempting to translate these discoveries to a clinical setting.

OUR SCIENTIFIC COUNCIL

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12 Members of the National Academy of Sciences
4 Recipients of the National Medal of Science
3 Former Directors of the National Institute of Mental Health and the current Director
1 Nobel Prize Winner

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