New Research: Mood Disorders

February 27, 2013 | Bipolar Disorder [1], Schizophrenia [2], Geriatric Psychiatry [3], Major Depressive Disorder [4], Addiction [5]

A recent symposium brought together some of the nation’s leading experts to talk about promising advances in psychiatry and to address areas where progress has faltered.

A recent symposium exploring causes of mood disorders, novel treatments, and proposals for how to bring new drugs to market was held at the Icahn School of Medicine at Mount Sinai (MSSM) in New York City. Supported by the Deborah Elkins Foundation, the goal was to bring leading experts together to talk about promising advances in psychiatry and to address areas where progress has faltered. Wayne Goodman, MD, Chair of Psychiatry at MSSM, noted, “The symposium is part of a broader initiative at Mount Sinai to influence and encourage basic discoveries in neuroscience, better understand the causes of major psychiatric disorders, and develop innovative treatments.”

Below is a list of presenters, in order of appearance:
• Dennis Charney, MD
• Pamela Sklar, MD, PhD
• Scott J. Russo, PhD
• Vilma Gabbay, MD
• Maurizio Fava, MD
• Andrew D. Krystal, MD
• Charles Kellner, MD
• Wayne Goodman, MD
• Dan V. Iosifescu, MD
• Fritz Henn, MD, PhD
• James Murrough, MD

For a summary of the Keynote Address, please click here.

Keynote Address
Dennis Charney, MD, Anne and Joel Ehrenkranz Dean of the Icahn School and an international expert in the study of resilience, depression, and PTSD, called for a revolution in the way mental illness is studied. He expressed the need for better understanding of the function of genes related to mental illness and how they relate to behavior and environment and the need for a diagnostic system based on cause or disease pathology that adequately predicts illness course and response to therapy. He discussed the importance of new prevention and treatment strategies as well.

“Identification of new molecular targets for drug development for psychiatric disorders has stalled, and we are still treating the symptoms of disease rather than the disease itself,” said Dr Charney. “We also need new psychosocial therapy paradigms, better ways to diagnose, new preventative measures for individuals at high risk for psychiatric disorders, and to break down the barriers to diagnosis and treatment in the community. We have all of the components to achieve these goals at Mount Sinai.”

Dr Charney highlighted several ongoing projects at MSSM and elsewhere, such as optogenetics, which uses a beam of light to control brain cell activity and can modulate mental illness in a mouse.
model. He discussed promising research at MSSM on the use of ketamine as a rapidly acting drug in patients with treatment-resistant depression and how stem cells can be used in a model of depression rather than animals. He highlighted a proposal of a new diagnostic system that uses genetic and personal characteristics and environmental factors to identify mental illness and establish an individual signature of disease. Panels and presentations followed Dr Charney’s remarks.

For a summary of the Panel on Translational Research in Depression, please click here.

**Panel: Translational Research in Depression**
- Pamela Sklar, MD, PhD, Chief, Division of Psychiatric Genomics at MSSM, is a principal investigator in the Psychiatric Genome-Wide Association Study Consortium, the world’s largest consortium in psychiatry working to identify the genes associated with bipolar disorder. She discussed the importance of sample size in designing trials to understand bipolar disorder, and as a result, the need for collaboration. The PGC schizophrenia and bipolar disorder groups have now identified more than 50 new genetic loci for schizophrenia and bipolar disorder. These results should spur further biological investigations. In particular, Dr Sklar’s group has identified calcium channel signaling as implicated in bipolar disorder, and are planning to evaluate the efficacy of a calcium channel blocker, isradipine, a drug used to control hypertension, in the treatment of bipolar disorder.
- Scott J. Russo, PhD, Assistant Professor in Neuroscience at MSSM is studying depression as a whole-body disease caused by an inflammatory response from the immune system, rather than dysfunction in the brain. His lab transplanted the bone marrow of depressed mice into healthy mice and found that these previously healthy mice exhibited signs of depression after experiencing a mild stressor. They also found that mice with immune cells that release more of a protein called interleukin-6 in response to a toxin developed a more severe depression-like response to the stress.
- Vilma Gabbay, MD, Chief of the newly opened Pediatric Mood and Anxiety Disorder Program, said childhood mental illness is almost an epidemic, and that many adults with treatment-resistant depression have initial onset in their teen years. Dr Gabbay’s team is studying anhedonia, or the inability to experience pleasure, as it is pervasive in most mental illnesses in teens. For a summary of New Approaches to the Development of Rapidly-Acting Treatments, please click here.

**Presentation: New Approaches to the Development of Rapidly-Acting Treatments for Mood Disorders**
- Maurizio Fava, MD, Slater Family Professor of Psychiatry, Harvard Medical School, suggested redesigning earlier phase clinical trials by keeping these trials smaller. He suggested the traditional double-arm trial with an experimental group and placebo group, but after this phase is complete, splitting the placebo group into a secondary experimental and placebo group. For a summary of Strategies for Optimizing Early Phase Trials of Novel Drugs in Mood and Anxiety Disorders, please click here.

**Presentation: Strategies for Optimizing Early Phase Trials of Novel Drugs in Mood and Anxiety Disorders**
- Andrew D. Krystal, MD, Professor of Psychiatry, Duke University Medical Center, indicated that now is a time of tremendous discovery, but the cost and failure rates of drug development are both rising, particularly for central nervous system and oncology drugs. Phase III is the most expensive phase of clinical trials and by the time a drug makes it to a Phase III and fails, a pharmaceutical company may have already invested close to a billion dollars. The cost of having such high failure rates in Phase III is leading many companies to pull back from, or out of, CNS drug development. Since Phase II is the gatekeeper to Phase III, Dr Krystal suggested that the parameters for approval in Phase II need to be more stringent. Study designs need to be more efficient, failure needs to be established more quickly, and proof of concept needs to be established earlier. In order to improve the cost benefit ratio of drug development, more money needs to be invested in the earlier phases in order to create more successful Phase II results. For a summary of Novel Treatments for Mood and Anxiety Disorders, please click here.

**Panel: Novel Treatments for Mood and Anxiety Disorders**
- Charles Kellner, MD, Professor of Psychiatry at MSSM, spoke about a nationwide study that MSSM is leading along with Duke University, called PRIDE (Prolonging Remission in Depressed Elderly). PRIDE will determine whether medications alone or medications and ECT work best to prevent depressive relapse and to improve quality of life for older people with severe mood disorders.
• Wayne Goodman, MD, Chair of Psychiatry and Dan V. Iosifescu, MD, Director of the Mood and Anxiety Disorders Program, spoke to the emerging use of medical devices in lieu of drugs to help treat disorders and continuing research into “differing modalities of delivering charges to the brain,” including new magnetic stimulation technologies. Dr. Goodman spoke about deep-brain stimulation as a promising treatment for psychiatric disorders.

• Fritz Henn, MD, PhD, Professor of Psychiatry and James Murrough, MD, Assistant Professor of Psychiatry at MSSM, spoke to the efficacy of ketamine versus midazolam as a rapidly-acting antidepressant, presenting results showing favorable short-term safety profiles of single-infusion ketamine.

For more information, please visit http://www.mssm.edu/departments-and-institutes/psychiatry.

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