This presentation will review recent findings in these studies, and discuss the potential implications of this work for prevention and treatment.

5. PSYCHIATRY IN THE NEW MILLENNIUM

S.E. Hyman
National Institute of Mental Health, Bethesda, Maryland

Psychiatry enters the new millennium grappling with complexity at many levels. Gone are many simple ideas, for example, that there is “a gene for schizophrenia” or “a gene aggression”. Gone are simple ideas that related single neurotransmitters to mental disorders. Gone too are the ideas that correlated circumscribed brain regions with particular cognitive or emotional functions. Instead behavioral tendencies and risk of mental disorders turn out to be genetically complex, involving the interaction of multiple genes and nongenetic factors—indeed our comfortable picture of genes acting in simple additive ways, and of their product, proteins, acting in simple linear signaling pathways has proven woefully inadequate. At the same time, it is clear that the brain must be understood in terms of distributed information processing, with its cellular components being remarkably plastic. Not only is it the case that synapses are constantly being physically remodeled by the environment, but contrary to old dogmas, neurogenesis in the mature brain is now an established fact. Even clinical trial design must adapt to the need to generalize to a complex “real world”. These new views introduce new needs for computation and informatics, and for new models to replace the old. Ultimately, however, with our new ideas and new technologies, we will be on track to answer the central age-old questions of psychiatry: How is the human brain built? How does it change over the life span? What are the precise genetic and environmental risk factors for mental illnesses? What are the pathophysiologies that produce the symptoms and disabilities? How do our treatments, including psychotherapy work? What objective markers can we discover to monitor the progression of the pathophysiology and the effects of treatment? How will we discover preventive measures and cures that will be effective in diverse populations and settings?

6. AN UPDATE ON NEW SOMATIC TREATMENTS FOR DEPRESSION—ECT, TMS, VNS, DBS

M.S. George (1), H.A. Sackeim (2), A.J. Rush (3), R. Kumar (4)

(1) Medical University of South Carolina, Charleston, SC 29425; (2) Columbia University College of Physicians & Surgeons, New York State Psychiatric Institute, New York, NY 10032; (3) University of Texas Southwestern Medical Center, Dallas, TX 75390-9086; (4) Colorado Movement Disorders Center, Englewood, CO 80110

Recently, several new brain stimulation methods have been introduced with reported antidepressant effects. These improvements in older technologies (ECT), or invention of new approaches (TMS-transcranial magnetic stimulation, VNS-vagus nerve stimulation, DBS-deep brain stimulation) build on advances in functional neuroimaging and improved knowledge of the brain circuits involved in regulating mood and anxiety. This workshop will involve brief presentations of recent data in each of these fields, although full presentation of the findings with each tool are also presented at other parts of the Biological Psychiatry Meeting (Drs. Sackeim (ECT) and Kumar (DBS)-Sat. Morning). Following the brief presentations of the newest findings in each field, the workshop will focus critical discussion on common issues across these fields. These include but are not limited to the following:

- the effects of different frequencies, pulse widths and dose on brain function,
- relative invasiveness and known side effects of each approach, the potential for studies in normal subjects as opposed to pathology,
- future use of the techniques in informed algorithms of clinical treatment (what to use when and in what order, if and when they are approved for clinical use),
- progress in using animal models of depression to understand these new tools,
- and using imaging techniques to understand the brain effects of the technologies and measure effectiveness.

7. GABA/GLUTAMATE DYSREGULATION IN DEPRESSION

H. Murck (1), I.A. Antonijevic (1), F. Petty (2), P. Skolnick (3), R.S. El Mallakh (4)

(1) Max-Planck-Institute of Psychiatry, Munich 80804, Germany; (2) Vet. Affairs Med Ctr., Univ. Texas Southwestern Med Center, Dallas, Texas, 75235; (3) Eli Lilly & Co, Indianapolis, IN 46285; (4) University of Louisville School of Medicine, Louisville, Kentucky 40292

Robust biological markers of depression are endocrine changes, especially hypercortisolism, and changes in the sleep EEG, especially a more disrupted
sleep with a disinhibition of rapid-eye-movement (REM)-sleep and a decrease in slow-wave-sleep (SWS). As Dr. Murck will present, there is evidence that an overactivity of glutamatergic and decline of GABAergic neurotransmission is involved in these phenomena. Moreover total sleep deprivation, having an antidepressive efficacy, seems to act at these systems. Dr. Antonijevic will then focus on the importance of gender differences in sleep endocrine regulation with regard to depression. An involvement of the GABAergic system will be discussed. The sleep-EEG findings will lead to the assumption of changes in the polarization level of thalamocortical cells, which might be related to the action of the Na-K-ATPase. The involvement of this enzyme in the pathophysiology of depression, particularly as it relates to bipolar illness, is summarized by Dr. El Mallakh. As the Na-K-ATPase is also involved in the reuptake of glutamate and GABA changes in the activity of this enzyme could be involved in the dysregulation of both neurotransmitter systems. Evidence for the NMDA receptor as a target for commonly used antidepressive substances from binding studies and the efficacy of NMDA receptor antagonist in animal models of depression will be presented by Dr. Skolnick. Arguments for the importance of the GABAergic system in the pathophysiology of depression are presented by Dr. Petty showing data from animal models, from clinical and genetic studies, and the usefulness of GABAergic agents as antidepressant medication.

### 8. NUTS AND BOLTS MAGNETIC RESONANCE SPECTROSCOPY: A GUIDE TO QUANTITATIVE MEASUREMENT OF CEREBRAL NEUROCHEMISTRY


(1) Wayne State University School of Medicine, Detroit, MI, 48201, (2) McLean Hospital, Harvard University, Belmont, MA, 02718, (3) Nathan Kline Research Institute, Orangeburg, NY, 10962, (4) University of Washington, Seattle, WA 98105

Magnetic Resonance Spectroscopy (MRS) has emerged as a powerful tool for in vivo measurement of cerebral neurochemistry. Recent advances in MRS technology and their subsequent automation have enabled this technology to become widely available at most medical centers. The goal of this workshop is to provide a nuts and bolts guide which will enable investigators with new access to MRS technology to acquire, analyze, and quantitate MRS data. The attendee of the workshop will be guided through each step of the process necessary to obtain quantitative MRS measurements of cerebral neurochemistry for research investigations. Topics to be addressed in this workshop include goal oriented pulse sequence and parameter choices, spectral fitting techniques, voxel tissue segmentation, and neurochemical quantitation. In addition, participants will be taught strategies to avoid common MRS pitfalls and to recognize artifacts in their MRS data. This will be followed by a panelist discussion and subsequent audience question/answer session on the limitations and potential of MRS technology. Participants will be provided with a brief “nuts and bolts guide” and a list of commercial and public domain software tools available for the analysis of MRS data.

### Neurochemical Brain Imaging Findings in Mood Disorders

**Thursday, May 11, 12:15 PM–2:15 PM**

**Location**: Gold Coast

**Chair**: Jair C. Soares

**Co-Chair**: Robert B. Innis

### 9. NEUROCHEMICAL BRAIN IMAGING FINDINGS IN MOOD DISORDERS


(1) Dept of Psychiatry, Univ. of Pittsburgh, Pittsburgh, PA 15213; (2) Dept of Psychiatry, Yale University, West Haven, CT 06516; (3) Dept of Psychiatry, Harvard University, Belmont, MA 02178

Linked to developments in the methodologies for in vivo neurochemical brain imaging studies, important new possibilities for investigations on the pathophysiology of neuropsychiatric disorders have become available. These methodologies have in recent years been applied to studies in mood disorders. This workshop will include leading investigators in this area, who will review recent advances in this field, and perspectives for future developments. Dr. Renshaw will discuss new magnetic resonance spectroscopy (MRS) studies that examine brain adenosine metabolism in affective disorder patients. Dr. Soares will present results from ongoing studies that utilize 1H MRS and 7Li MRS to study in vivo brain neurochemistry and the pharmacokinetics of lithium as related to the pathophysiology of bipolar disorder, and the mechanisms of action of lithium. Dr. Anand will review his most recent findings from investigations that examine the role of the dopaminergic system in the pathophysiology of mood disorders. Dr. Drevets will discuss his findings from ongoing PET studies of the SHT1A system in unipolars and bipolar disorder individuals. Last, Dr. Innis will moderate a discussion centered on the specific presentations, on related methodological issues, and on possibilities for future developments. Overall, the workshop should provide invaluable new information regarding in vivo applications of neurochemical brain imaging methods to investigate the pathophysiology of mood disorders. It should be a very useful source of new information in this area for researchers working on this field and related ones.

### The Interaction Between the Immune System and Psychiatric Disorders

**Thursday, May 11, 12:15 PM–2:15 PM**

**Location**: Water Tower

**Chair**: Mark H. Rapaport

**Co-Chair**: Cheryl M. Wong