FRIDAY, MAY 15

PLENARY SESSION
Plasticity Based Therapeutics
Friday, May 15, 2009 8:00 AM - 10:00 AM
Location: Regency Ballroom - 3rd Floor
Chair: Husseini Manji

268. Neural Systems Involved in Fear Extinction: Implications for Psychotherapy

Michael Davis

Psychiatry Emory, Atlanta, GA

In our laboratory we study the physiological bases of learning and memory and brain areas involved in fear, anxiety and stress. To simplify this question, we work with a reflex behavior that is readily quantifiable and known to be altered by prior experience. In many species, including man, a loud noise elicits a startle response, which occurs very rapidly. We have determined the neural pathway that mediates acoustic startle in the rat, which consists of three synapses in the brainstem and spinal cord. Although startle is very fast and has a relatively simple circuit, it is exquisitely sensitive to changes in the environment, to drugs, as well as prior learning, such as fear conditioning. Startle thus provides a brainstem and spinal reflex system that is modulated by higher brain systems. Using electrical stimulation or single unit recording in unanesthetized animals we are determining the points within this pathway where certain environmental events, drugs, or prior learning affect neural transmission. Pathways involved in fear conditioning are being delineated using mechanical and chemical lesions, electrical brain stimulation and anterograde and retrograde tracing techniques. These involve sensory inputs to a part of the brain called the amygdala, which projects directly to the startle circuit. We have found that excitatory amino acid receptors in the amygdala play a critical role in fear conditioning. Currently we are evaluating the role of various second messenger systems in the amygdala in fear conditioning. We are also using viral vector gene transfer to over-express various proteins in the amygdala to see how they participate in fear conditioning. Other studies seek to determine where peptides, such as corticotropin releasing hormone, or dopamine agonists, act to increase startle amplitude, and whether different parts of the brain may be involved in fear vs. anxiety. We are also interested in processes involved in the suppression of fear because an inability to suppress fear and anxiety occurs in many psychiatric patients. To do this we study brain areas and neurotransmitters in involved in fear extinction as well as conditioned inhibition, a direct test of fear inhibition we can now measure in rats and humans. We have found that a protein in the amygdala called the NMDA receptor is critical for fear extinction and that a drug that facilitates the function of this protein called D-cycloserine, facilitates extinction in rats and psychotherapy in humans.

269. Thinking Differently About Schizophrenia

Bita Moghaddam

Neuroscience, University of Pittsburgh, Pittsburgh, PA

Bita Moghaddam, PhD is Professor of Neuroscience, Psychiatry, and Pharmaceutical Sciences at the University of Pittsburgh. She is the author of nearly 100 scientific papers and has extensive expertise in using animal models to study the cellular basis of cognitive constructs that are critical to psychiatric disorders including schizophrenia. She has a longstanding track record of involvement in successful translational research and is an effective educator and mentor. She has established novel biochemical models for the mechanisms by which the hallucinogen PCP produces psychotic symptoms that mimic schizophrenia. Her work has led to the discovery of the first non-monoamine targeting compound for treatment of schizophrenia. She was the Co-Director of the Center for Neuroscience Graduate Training Program at the University of Pittsburgh (2005-2007) during which time she initiated several effective changes related to the curriculum and the recruitment of students to this program. Her research has been funded continuously since 1991 including a MERIT award from NIMH. She is the recipient of many prestigious awards including ACNP's Efron award for excellence in research related to Neuropsychopharmacology the Paul Janssen Schizophrenia Research Award from the Collegium Internationale Neuro-Psychopharmacologicum,. She serves on numerous editorial and advisory boards as well as national and local educational and service oriented committees.

270. Plasticity Based Therapeutics for the Treatment of Severe Mood Disorders

Carlos Alberto Zarate

National Institute of Mental Health, Bethesda, MD

Carlos A. Zarate, M.D. is Chief of Experimental Therapeutics of the Mood and Anxiety Disorders Program at the National Institute of Mental Health (NIMH). Dr. Zarate completed his residency training in psychiatry at the Massachusetts Mental Health Center/Brockton VAMC division. He later completed a fellowship in Clinical Psychopharmacology at McLean Hospital of the Consolidated Department of Psychiatry, Harvard Medical School and remained on staff at McLean Hospital as the Director of the Bipolar and Psychotic Disorders Outpatient Services and Director of the New and Experimental Clinic. From 1998 to 2000 Dr. Zarate was the Chief of the Bipolar and Psychotic Disorders Program at the University of Massachusetts Medical School. In 2001, he joined the Mood and Anxiety Disorders Program at NIMH. His achievements and awards include the Ethel-DuPont Warren Award and Livingston Awards, Consolidated Department of Psychiatry, Harvard Medical School; Outstanding Psychiatrist Research Award, Massachusetts Psychiatric Association; Program for Minority Research Training in Psychiatry, APA; the National Alliance for Research on Schizophrenia and Depression Young Investigator Award; National Alliance for Research on Schizophrenia and Depression Independent investigator award; and the National Institutes of Health Director's Award Scientific/ Medical. Dr. Zarate's research focuses on the pathophysiology and development of novel therapeutics for treatment-resistant mood disorders as well as the study of biosignatures of treatment response.

271. Stress-Induced Plasticity in Amygdala: Therapteutic Implications for Affective Disorders Sumantra Chattarji

National Centre for Biological Sciences, Bangalore, India

Sumantra Chattarji received his Master's degree in Physics from the Indian Institute of Technology. He then went on to do a PhD in Neuroscience, under the supervision of Terry Sejnowski, at the Johns Hopkins University and Salk Institute. After post-doctoral research at Yale University, he started his own laboratory at the National Centre for Biological Sciences, India in 1999. His laboratory studies the effects of stressful experiences on cells and synapses in the amygdala. His research has identified several novel neural correlates of stress-induced plasticity in the amygdala, which are strikingly different from those observed in the hippocampus. He is a visiting scientist at the Picower Institute for Learning & Memory at MIT, where he collaborates with Susumu Tonegawa. He is a member of the Council of the Molecular and Cellular Cognition Society and serves on the editorial board of the Journal of Neurophysiology. He was awarded the International Senior Research Fellowship by The Wellcome Trust in 2003 and the FRAXA Vision 2008 Award by the Fragile X Research Foundation.

PRESIDENTIAL LECTURE
Friday, May 15, 2009 10:30 AM - 11:30 PM
Location: Regency Ballroom - 3rd Floor
Chair: Husseini Manji

272. Gene-Environment Interdependencer

Michael Rutter

Institute of Psychiatry, London, United Kingdom

Professor Sir Michael Rutter is Professor of Developmental Psychopathology at the Institute of Psychiatry, Kings College, London. He has been a consultant psychiatrist at the Maudsley Hospital since 1966, and was Professor of Child Psychiatry at the Institute of Psychiatry from 1973 to 1998. He set up the Medical Research Council Child Psychiatry Research Unit in 1984 and the Social, Genetic and Developmental Psychiatry Centre 10 years later, being honorary director of both until October 1998. His research has included the genetics of autism; the study of both school and family influences on children's behaviour; the links between mental disorders in childhood and adult life; epidemiological approaches to test causal hypotheses; and gene-environment interplay. He was Deputy Chairman of the Wellcome Trust from 1999 to 2004, and has been a Trustee of the Nuffield Foundation since 1992. He was elected a Fellow of the Royal Society in 1987 and an honorary member of the British Academy in 2002. He was a Founding Fellow of the Academia Europaea and the Academy of Medical Sciences, of which he is currently Clinical Vice-President. He has received numerous international honours and has published some 40 books and over 400 scientific papers and chapters.

WORKSHOP
Psychopharmacogenetics: A New Era of Rational Treatment in Psychiatry?
Friday, May 15, 2009 12:30 PM - 2:00 PM
Location: Regency A - 3rd Floor
Chair: Martin Alda*
Moderator: James L. Kennedy**

*Supported by CIHR
**Supported by CIHR

273. Psychopharmacogenetics: A New Era of Rational Treatment in Psychiatry?

Gonzalo Laje[1], Martin Alda[2], Carolin Opgen-Rhein[3], Daniel J. Mueller[4]

[1]NIMH, Bethesda, MD, [2]Dalhousie University, Halifax, NS, Canada, [3]Charité - University Medicine, Berlin, Germany, [4]CAMH, Dept. of Psychiatry, Univ. of Toronto, Toronto, ON, Canada

Dr Laje: The Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study followed prospectively a cohort of 1915 individuals who were treated with the SSRI citalopram and provided DNA. Patients were assessed biweekly to evaluate severity and tolerability. Dr. Laje will present candidate gene (sampling 68 genes) and genome-wide association study (using 109,435 markers) in a subset of this cohort (n=338) to test for genetic variation associated with tolerability. Dr. Alda: Response to long term lithium treatment has been associated with several clinical factors, including family history of bipolar disorder and response to lithium in affected relatives. The available data support the view that responders to lithium constitute a core bipolar phenotype particularly suitable for gene-mapping efforts. These findings as well as methodological considerations will be discussed in the presentation. Dr. Opgen-Rhein: Antipsychotic-induced weight gain is likely modulated by genetic factors. We analyzed important candidate genes, including the 5-HT2C, insulin induced gene G (INSIG), glutamic acid decarboxylase (GAD2) and the leptin gene in a German sample. One 5-HT2C promoter marker genotype showed strong association with weight gain (p=.005) Dr. Mueller: Polymorphisms of the CYP2D6 and CYP2C19 genes have been genotyped by use of the Roche AmpliChip in 40 OCD patients, and 30 schizophrenia patients. CYP2D6 rapid metabolizers were significantly more often antidepressants non-responders (p=.01). The schizophrenia CYP2D6 extensive metabolizers showed improved positive symptoms whereas the intermediate metabolizers had worsening of positive symptoms. In other analyses, the cannabinoid-1-receptor gene was associated with antipsychotic induced weight gain in a sample of 209 patients.

WORKSHOP
A Multi-Modal Approach to Understand Risk, Resilience, and Relapse Biomarkers in Mood Disorders
Friday, May 15, 2009 12:30 PM - 2:00 PM
Location: Regency B - 3rd Floor
Chair: Zubin Bhagwagar*
Moderator: Mary Louise Phillips**

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274. A Multi-Modal Approach to Understand Risk, Resilience, and Relapse Biomarkers in Mood Disorders

Helen S. Mayberg[1], Kiki Chang[2], Mary Louise Phillips[3], Zubin Bhagwagar4

[1]Emory University, Atlanta, GA, [2]Stanford University, Stanford, CA, [3]University of Pittsburgh, Pittsburgh, PA, [4]Yale University, New Haven, CT

Advances in neuroimaging modalities allow unparalleled access to molecular mechanisms and neural circuits to understand the neurobiological basis of psychiatric disorders with a recent focus on mood disorders. Using these techniques it is now possible to consider the evolution of mood disorders in various stages of development and in various populations. The main question that this workshop will address is: Is it possible to use multimodal neuroimaging paradigms to determine biomarkers modulating resilience, risk and relapse in the development of mood disorders. Imaging modalities to be discussed will include functional, structural and spectroscopic magnetic imaging together with molecular imaging using positron emission tomography. There biomarkers are specific, discriminating neural circuits involved in recovery and relapse and this panel will model the available approaches. The discussion in the workshop will focus on the development of biomarkers for risk, recovery, resilience, and relapse in mood disorders which may inform clinical decisions and help in the better treatment of patients with these chronic illnesses. Kiki Chang (Stanford) will present novel longitudinal data in children at risk for bipolar disorder to focus on specific neurobiological and genetic mechanisms for risk and resilience. Helen Mayberg (Emory) will present new data on imaging biomarkers predictive of treatment response in MDD patients. Mary Phillips (Pittsburgh) will highlight new functional neuroimaging data in adults with, and in adolescents at risk for, bipolar disorder and MDD. Zubin Bhagwagar (Yale) will present a novel approach synthesizing a number of dysfunctional modalities mediating recovery and relapse in MDD to develop a model of vulnerability to MDD focusing on a number of biomarkers.