260. Prevention of Alzhiemer's Disease: Rationale, Pathobiology, and Current and Future Studies

Steven T. DeKosky

University of Pittsburgh, Pittsburgh, PA

Dr. DeKosky is Professor and Chair of the Department of Neurology, and Director of the Alzheimer's Disease Research Center (ADRC) at the University of Pittsburgh. His clinical research includes differential diagnosis, neuroimaging, and genetic risks of Alzheimer's disease and trials of new medications. His basic research centers on structural and neurochemical changes in human brains in normal aging and dementia. Dr. DeKosky was a member of the National Board of Directors of the Alzheimer's Association for 8 years, the last 4 as Vice-Chair. He was re-elected to the National Board in 2003 after 1 year off. He was the Chair of the Alzheimer's Association Medical and Scientific Advisory Council from 1997 to 2002. He now chairs the Professional Advisory Board of the Greater Pittsburgh Chapter of the Alzheimer's Association and was a Founding Member of the Lexington-Blue Grass Chapter of the Alzheimer's Association. In 2002 he was elected Chair of the Medical and Scientific Advisory Panel of Alzheimer's Disease International (ADI), the international organization of national Alzheimer's Associations. Dr. DeKosky is principal investigator of a national multicenter study of 3,000 subjects in a double-blind, placebo controlled trial of Ginkgo biloba, funded by the NIH. He has served as a consultant to the FDA and to a number of pharmaceutical companies. In 2003 he was appointed to the Peripheral and Central Nervous System (PCNS) Advisory Committee of the FDA. Dr. DeKosky served on the National Institute on Aging Neuroscience Review Committee and chaired the committee from 2000-2001. Dr. DeKosky has served as Chair of the Section on Geriatrics of the American Academy of Neurology (AAN). He chaired the recent AAN Practice Parameters Committee for Early Detection, Diagnosis and Management of Dementia. He was an Examiner in Neurology for the American Board of Psychiatry and Neurology (ABPN) for over 15 years and served as a member of the ABPN Part I (Written) Examination Committee for 10 years. In 2002 he was elected to the Neurology Council of the ABPN; he is one of the eight neurologists who oversee board certification in the US. He has received a Teacher Investigator Development Award from the NINDS, the Presidential Award of the American Neurological Association, and is listed in "The Best Doctors in America." He has published over 200 peer-reviewed articles and book chapters.

261. Genetic and Clinical High-Risk Strategies in Understanding Vulnerability to Psychosis

Tyrone D. Cannon

Psychology, UCLA, Los Angeles, CA

Tyrone D. Cannon earned his bachelor's degree at Dartmouth College (1985) and his doctoral degree at the University of Southern California (1990). He spent a year in clinical training at the UCLA Neuropsychiatric Institute (1990-1991), before taking his first academic appointment in the Department of Psychology at the University of Pennsylvania, where he was promoted to associate professor with tenure in 1997. He joined the faculty at UCLA in 1999 as the Staglin Family Professor of Psychology, Psychiatry and Biobehavioral Sciences, and Human Genetics. Professor Cannon's work on the genetic, neural, and cognitive bases of schizophrenia has been continuously funded by NIH since 1991. Since joining the faculty at UCLA, Professor Cannon has established a new center for the prevention of schizophrenia in at-risk youth and a Center for Adolescent onset Schizophrenia, both based in the Neuropsychiatric Institute at UCLA. The primary aims of Dr Cannon's research are to discover the causes of schizophrenia and to develop effective treatment and prevention strategies based on an understanding of the genetic and neural mechanisms that give rise to the disorder.

Supported by NIH

262. Fragile X: Perspectives from Birth through Aging

Randi J. Hagerman

University of California, Davis, Davis, CA

Randi Hagerman, M.D., is a developmental and behavioral pediatrician who has the Tsakopoulos-Vismara Endowed Professor of Pediatrics at the University of California at Davis, Medical Center. She is also the Medical Director of the M.I.N.D. Institute, which stands for Medical Investigation of Neurodevelopmental Disorders. She is an internationally recognized clinician and researcher in developmental and behavioral pediatrics and her area of expertise is fragile X syndrome. She has spent over 20 years doing clinical work and research regarding this syndrome, particularly, in molecular clinical correlations and treatment endeavors. She has written several books on fragile X syndrome, including a third edition of Fragile X Syndrome: Diagnosis, Treatment and Research, which was published in 2002 by Johns Hopkins University Press. She also wrote Neurodevelopmental Disorders: Diagnosis and Treatment (1999 - Oxford University Press), which covers a broad array of disorders that impact cognitive development and behavior, and documents multidisciplinary interventions including medical, psychopharmacological and educational treatments. Dr. Hagerman co-founded the National Fragile X Foundation in Denver, Colorado, in 1984; and, presently, is on the Board and the Scientific and Clinical Advisory Committee of the National Fragile X Foundation. She is also a scientific adviser to the Conquer Fragile X Foundation; and, she is on the Advisory Board of both the Northern and the Southern California Fragile X Associations.

263. Maternal Care, DNA Methylation and Gene Expression

Michael J. Meaney

Department of Psychiatry, McGill University, Montreal, Canada

Michael J. Meaney is a James McGill Professor of Medicine at Douglas Hospital Research Centre of McGill University and Director of the Maternal Adversity, Vulnerability and Neurodevelopment Project as well as the Developmental Neuroendocrinology Laboratory of McGill University. Meaney was educated at Loyola College of Montreal and received his PhD from Concordia University (Montreal) with post-doctoral training at The Rockefeller University in New York. on the effects of early experience on gene expression and development. Meaney¹s research focuses on the effects of early experience on gene expression and development research. The program is multidisciplinary and includes studies of behaviour and physiology, to molecular biology and genetics. The primary objective of these studies is to define the processes that govern gene environment interactions. He has authored over 225 journal articles and has been the recipient of a Scientist Award from the Canadian Institutes for Health Research (CIHR) and a Distinguished Scientist Award from the National Alliance for Research in Schizophrenia and Affective Disorders. He currently holds a CIHR Senior Scientist Award. Graduates from Meaney¹s lab hold faculty appointments across North America and Europe, including Queen's University, University of California at Berkley, University of British Columbia, University of Michigan, and the RIKEN Institute.

PRESIDENTIAL INVITED LECTURE

Neurophysiology of Reward

Friday, May 20, 11:00 AM - 12:00 PM

Location: Grand Ballroom

Chair: Jeffrey A. Lieberman

264. Neurophysiology of Reward

Wolfram Schultz

Department of Anatomy, University of Cambridge, Cambridge, United Kingdom

Dr. Schultz received his medical degree from the University of Heidelberg in Germany. Dr. Schultz is currently a Wellcome Principal Research Fellow and

Professor of Neuroscience in the Department of Anatomy at University of Cambridge, United Kingdom. Prior to this position, he held the positions of Assistant, Associate Professor and Professor of Neurophysiology at the Institute of Physiology, University of Fribourg, Switzerland. Dr. Schultz did postdoctoral work at the Dept. of Histology, Karolinska Institute, in Stockholm, Sweden; the Laboratory of Neurobiology, Dept. of Physiology, State University of New York at Buffalo, U.S.A. (with Sir John C. Eccles); and the Section of Neurobiology, Max-Planck-Institute for Biophysical Chemistry, Göttingen, Germany (with O. D. Creutzfeldt). He has been a Visiting Scientist at Karolinska Institute, Stockholm, Sweden; University of Cambridge, UK; Tokyo Metropolitan Institute for Neurosciences, Japan; and Tamagawa University, Machida, Tokyo, Japan

WORKSHOP
Dysfunction of Reward Systems in Psychopathology: Clinical and Research Implications
Friday, May 20, 12:30 PM - 2:00 PM
Location: Georgia 3
Chair: Paul A. Newhouse
Moderator: Monique Ernst

265. Dysfunction of Reward Systems in Psychopathology: Clinical and Research Implications

Alexandra S. Potter[1], Martin P. Paulus[2], June Corwin[3], Eveline A. Crone[4]

[1]Psychiatry, University of Vermont, Burlington, VT, [2]Psychiatry, University of California, San Diego, La Jolla, CA, [3]Psychiatry, New York University School of Medicine, New York, N, [4]Center for Mind and Brain, University of California, Davis, Davis, CA

While research on the cognitive aspects of psychiatric disorders has traditionally focused on learning and memory, it is being increasingly recognized that aberrations in decision-making and sensitivity to reward may play a very significant role in the expression of psychopathologic behaviors. Recent advances have allowed these impairments in decision-making to be modeled and/or examined by a variety of psychological, mathematical, neuroimaging, and pharmacological means. This workshop will illustrate how distinct dysfunction in motivation and reward-related processes affects certain psychopathologies. This approach to provide an understanding of the different aspects of altered motivated behaviors in psychiatric disorders promises to open new avenues of research and guide novel treatment strategies. Discussion will be directed towards the application of various investigative strategies to particular psychiatric disorders and/or the development of additional approaches. Input will be sought regarding other disorders that would be useful to investigate utilizing current approaches. Monique Ernst will demonstrate how neuroimaging can be used to examine risk taking and reward in pediatric anxiety disorders. Eveline Crone will present neuroimaging data from children and adults to demonstrate developmental changes in subcomponents of decision-making. Additionally, the relation between autonomic measures and brain activity will be discussed. Martin Paulus will present decision data on schizophrenia and substance abuse disorders. Alexandra Potter will discuss recent advances in examining the neurochemical mediation of inhibitional failure and reward sensitivity in ADHD utilizing pharmacologic probes of the nicotinic chiolinergic system. Finally, June Corwin will present several theoretical models and their associated measures of decision making that have been shown to differentiate among patients with dementia, affective disease, and amnesia, and will demonstrate their applicability to a range of other problems associated with response to contingency.

Supported by National Institute on Aging, Netherlands Science Foundation (NWO), NIMH, Targacept Inc., NIH (DA13186, DA016663 MPP)

WORKSHOP
Glutamate as a Therapeutic Target in Fear and Anxiety: Preclinical Rationale and Future Clinical Directions
Friday, May 20, 12:30 PM - 2:00 PM
Location: Georgia 4
Chair: Jack M. Gorman
Moderator: Sanjay J. Mathew

266. Glutamate as a Therapeutic Target in Fear and Anxiety: Preclinical Rationale and Future Clinical Directions

Michael Davis[1], Andrew W. Goddard[2], Anantha Shekhar[2], Darryle D. Schoepp[3], Sanjay J. Mathew[4]

[1]Psychiatry, Emory University, Atlanta, GA, [2]Psychiatry, Indiana University, Indianapolis, IN, [3]Neuroscience Research, Eli Lilly and Company, Indianapolis, IN, [4]Psychiatry, Mount Sinai School of Medicine, New York, NY

An emerging literature has suggested a role for glutamate in fear extinction and anxiety disorders. NMDA receptors within the amygdala likely play a critical role in conditioned fear extinction. D-cycloserine (DCS), a partial glycine site agonist at the NMDA receptor, facilitated extinction in rats, and enhanced habituation in the exposure-based treatment of height phobia. This translational workshop will address several unanswered questions in this area: (1) Given the suggestion that involvement of NMDA receptors in extinction is time-dependent, what is the optimal duration and timing of NMDA modulators, and do these approaches enhance extinction learning only in the setting of psychotherapy? Dr. Andrew Goddard, Indiana University, will present clinical data using DCS in social phobia and Dr. Michael Davis, Emory University, will present data using DCS in rodent and human phobic conditions; (2) What is the role for non-NMDA receptor glutamate modulators (AMPA, metabotropic) in enhancing extinction and treating anxiety disorders? Dr. Darryle Schoepp, Eli Lilly and Company, will present data implicating multiple mGLU receptor subtypes as targets for anxiety drugs. (3) Plasticity enhancing agents with varied effects on glutamatergic neurotransmission have been proposed as novel antidepressants; what role might they serve in phobic disorders and which should be studied? Dr. Sanjay Mathew, Mount Sinai, will present a trial of the glutamate release inhibitor riluzole in generalized anxiety disorder and its effects on neuronal viability using MRS; Dr. Anantha Shekhar, Indiana University, will present basic data demonstrating the regulation of synaptic plasticity by glutamate mechanisms in pathological anxiety states.

Supported by NARSAD, NIMH NSF

INTEGRATED RESEARCH SESSION
Environmental Risk Factors and Apoptosis in Neurodevelopmental Disorders: Basic and Clinical Data
Friday, May 20, 12:30 PM - 2:00 PM
Location: Georgia 5
Chair: Lars F. Jarskog
Co-Chair: Henry A. Nasrallah

267. Apoptotic Proteins in Frontal Cortical Development: Implications for Neurodevelopmental Disorders

Lars F. Jarskog

Psychiatry, Univ. of North Carolina - Chapel Hill, Chapel Hill, NC

Background: Apoptosis is very active during normal brain development. It is estimated that ~50% of all neurons formed in the CNS die by apoptosis in early life. Apoptosis has also been implicated in the pathophysiology of several neurodevelopmental disorders. Pathological activation of apoptosis during development can lead to changes in neuronal numbers and/or connectivity in adult brain. Pro- and anti-apoptotic proteins interact to regulate apoptosis. In