10. THE INTERACTION BETWEEN THE IMMUNE SYSTEM AND PSYCHIATRIC DISORDERS

M.H. Rapaport (1), C. Wong (2), R. Yehuda (2), M. Lavia (3)

(1) Psychopharmacology Research Program, UCSD, La Jolla, CA 92037; (2) Bronx VAMC, Bronx, NY 10468; (3) Medical University of South Carolina, Charleston, SC 29425

This workshop focuses on evidence suggesting that there are interactions between immune system and psychiatric disorders. Two of the presentations will emphasize work led by Dr. Yehuda and Dr. Wong done in collaboration with Dr. Ester Sternberg and Dr. Mark Rapaport investigating the interactions between neuroendocrine and immune function in PTSD. These presentations demonstrate that the paradoxical biological findings observed in the neuroendocrine function in PTSD may lead to altered immune function. The third presentation will be by Dr. Mariano Lavia and Dr. Bruce Lydiard who find a significant decrease in immune function associated with anxiety disorders. Dr. Lavia has found a decreased number of interleukin-2 receptor positive lymphocytes in cultures of anti CD-3 stimulated peripheral blood mononuclear cells in patients with panic disorder and that these patients are more likely to develop colds. These patients have normalization of immune function with successful pharmacotherapy. In the fourth presentation Dr. Rapaport will present data demonstrating that cytokine activation is present in a minority of stabilized schizophrenic patients. Further Dr. Rapaport will discuss data about the interaction between changes in cytokine levels and the presence of autoantibodies. In particular the presence of an autoantibody to a 60-kilodalton heat shock protein. The intention behind this workshop is to facilitate discussion about the interaction between immune system and psychiatric disorders.

New Directions in Cortical Electrophysiology: From Basic Neuroscience to Clinical Research

Thursday, May 11, 12:15 PM–2:15 PM
Location: New Orleans
Chair: Gerard E. Bruder
Co-Chair: Nashaat N. Boutros

11. NEW DIRECTIONS IN CORTICAL ELECTROPHYSIOLOGY: FROM BASIC NEUROSCIENCE TO CLINICAL RESEARCH

G.E. Bruder (1), D.C. Javitt (2), R.W. McCarley (3), B.I. Turetsky (4)

(1) New York State Psychiatric Institute, New York, NY 10032; (2) Nathan Klein Institute for Psychiatric Research, Orangeburg, NY 10962; (3) Harvard Medical School, Department of Psychiatry, Brockton VA Medical Center, Brockton, MA 02301; (4) University of Pennsylvania, Department of Psychiatry, Philadelphia, PA 19104

Event-related potential (ERP) and quantitative electroencephalographic (EEG) techniques provide a means of probing basic neurophysiologic function. Recent developments in high-density electrode arrays, source localization, and combined measurement of ERPs and functional magnetic resonance imaging (fMRI) provide new ways for studying abnormalities of brain function in schizophrenia and affective disorders. Reductions of auditory ERPs have been consistently observed in schizophrenia, beginning about 100 milliseconds after stimulus onset (N1) and extending to later cognitive potentials (P3). Dr. Javitt will focus on early negative ERPs, including N1 and mismatch negativity (MMN), generated in auditory cortex. His studies in monkeys indicate the deficits of NMDA receptors play a role in the N1 and MMN reductions in schizophrenia. Dr. McCarley will present data on synchronization of EEG to auditory stimuli of different rates, which is used to investigate gamma frequency entrainment in schizophrenia. A neural circuit model of deficient recurrent inhibition, involving blocking effects at NMDA receptors on GABAergic interneurons, is presented to account for “steady state” EEG gamma deficits in schizophrenia. Dr. Turetsky will illustrate the use of combined ERP and fMRI techniques to study oddball and novelty P3 responses of healthy individuals and patients with schizophrenia. Measures of P3 subcomponents and fMRI hemodynamic activations are used to probe the physiologic networks underlying normal and abnormal information processing. Lastly, Dr. Bruder will present evidence of electrophysiologic differences between responders and nonresponders to treatment with the SSRI antidepressant fluoxetine. The findings suggest that individual differences among depressed patients on measures of regional hemispheric activation may be of value as predictors of therapeutic response to antidepressants.

12. SEX AND BRAIN DEVELOPMENT

D.R. Rubinow, P.J. Schmidt, L. Zhang

Behavioral Endocrinology Branch, NIMH, Bethesda, MD 20892-1276

Consistent with the importance of reproductive behavior for survival of the species, the gonadal steroids are major regulators of neural function and brain development. Investigation of these regulatory effects has revealed both mechanisms and principles that underlie emergent behavioral properties. First, activation effects of gonadal steroids comprise both acute, signal transduction-mediated and classical, intracellular receptor-mediated actions, the latter including modulation of the synthesis of the synthetic and metabolic enzymes for neurotransmitters, neuropeptides, neuroeffector receptors, and second messengers. Second, gonadal steroids create a context that influences both formation of neurocircuitry and acute neural response. These actions are largely inferred from three types of observations: structural and functional sexual dimorphisms; changes in neural response during reproductive endocrine change (e.g. the ovulatory cycle); and modulation of response to hormone manipulation (e.g. castration). In fact, all stages of neuronal development—neurogenesis, growth, migration, differentiation, and synaptic organization—are modulated by gonadal steroids. Third, gonadal steroids organize the brain during critical developmental windows. Androgen blockade, for example, alters 5-HT1A receptor m-RNA but not GABA receptor subunit expression during the last prenatal week, while the opposite is observed during the fourth postnatal week. Fourth, the effects of gonadal steroids are context dependent and differ as a function of environment, prior exposure, age, and genotypic characteristics. Studies of the effects of gonadal steroids on behavior promise to help answer the critical question in human behavioral endocrinology: Why do different individuals respond differently to ostensibly the same stimulus?