Insights from basic neurobiology

Hormonal effects on extra- and intraneural mechanism: an integrative approach

Huda Akil

Mental Health Research Institute, University of Michigan, Michigan, MI 48109 USA

Key words: Steroids, Depression; Stress

This overview will examine the current status of our understanding of the limbic-hypothalamo-pituitary-adrenal (LHPA) axis in stress and depression. From molecular approaches to circuit studies, from laboratory animals to humans in clinical situations, the field has gathered a great deal of information about the interface The picture that emerges is both exciting and complex This lecture will attempt to highlight the following: (a) what is firmly known about the brain control of the LHPA axis and its potential role in depression; (b) some areas of conflicting views; (c) some questions for the future.

The presentation will end with a discussion of how much animal stress studies can help in understanding major depression, and with speculation about the potential role of specific brain structures and circuits in the expression of the disease.

Norepinephrine and serotonin transporters: molecular insights into antidepressant targets

Randy D. Blakely

Department of Anatomy and Cell Biology, Emory University School of Anatomy, Atlanta, GA 30322, USA

Key words Norepinephrine, Serotonin, Transport, Gene regulation, Antidepressants

Norepinephrine (NE) and serotonin (5HT) transporters are highly related members of a large and expanding gene family of carrier proteins whose unifying function is the catalysis of plasma membrane cotransport of substrates (neurotransmitters, neuromodulators, osmolytes) with Na^+ and Cl^-. Although a basic understanding of the activity of NE and 5HT transporters has been appreciated for decades, the intrinsic molecular structure of these proteins and their regulation remains inferred rather than defined For example, the native structure of monoamine transporters, their precise cellular localization, and direct or indirect modulation as a consequence of receptor activation are largely matters of conjecture. Transporter-specific antibodies are now revealing previously unappreciated features of carrier structure and in combination with studies focused on gene regulation, are being applied to reveal the potential for carrier plasticity, likely to be relevant for genetically or pharmacologically altered synapses.

A neurodevelopmental perspective on altered cortical circuits in schizophrenia

Francine M. Benes

Laboratory for Structural Neuroscience, McLean Hospital, Belmont, MA, USA, and Department of Psychiatry and Program in Neuroscience, Harvard Medical School, Boston, MA, USA

Key words Cingulate cortex, Schizophrenia, GABA; Glutamate

Recent studies have demonstrated microscopic changes in corticolimbic regions of schizophrenic (SZ) brain. In the anterior cingulate cortex (ACCx), several differences have been noted, and these have included (a) a decreased density of neurons, but not glial cells, (b) a preferential decrease in the density of non-pyramidal neurons, particularly in layer II; (c) a selective increase of $GABA_A$ receptor binding activity on pyramidal cell bodies in layers II and III, but not V and VI; (d) an increase of NFP200K-immunoreactive vertical axons in layers II and IIIa; and (e) an increased density of glutamate-immunoreactive small calibre fibers with a vertical orientation Taking together these various differences noted in ACCx of SZs, the data seem to fit a working model in which there are two separate abnormalities: a decrease of GABAergic inhibition and an increase of glutamatergic excitation. The fact that the changes were consistently observed in layer II is in support of the neurodevelopmen-