

Biological Psychiatry

A Journal of Psychiatric Neuroscience and Therapeutics

IN THIS ISSUE-APRIL 15TH

Synchrony Abnormalities in Schizophrenia

We normally have no difficulty recognizing our own thoughts and actions. For example, we appear to “tag” our speech and filter it from our sensory experience so that we are not distracted by it. Similarly we recognize our thoughts and do not experience them as externally generated. **Ford et al.** (pages 736–743) provide electrophysiologic evidence that the brain marks self-generated actions with preparatory epochs of gamma oscillations, as measured by electroencephalography (EEG). In schizophrenia, deficits in the generation of these preparatory gamma oscillations in neural activity are associated with symptoms of avolition and apathy.

The administration of drugs that block *N*-methyl-D-aspartate (NMDA) glutamate receptors transiently produces some effects in humans that resemble schizophrenia. Would these drugs produce schizophrenia-like alterations in cortical electrical activity in rodents? **Pinault** (pages 730–735) now reports that non-competitive NMDA receptor antagonists dose-dependently increase the power (200–400%) of spontaneously occurring γ oscillations in the rat neocortex. This effect occurs at doses that are comparable to those that produce cognitive deficits and schizophrenia-like symptoms in humans.

Deficits in the presence of high frequency (gamma) EEG oscillations during the processing of different types of information may provide insights into which neural pathway is most impaired in schizophrenia. **Spencer et al.** (pages 744–747) report that while individuals performed a visual target detection (oddball) task, the early visual-evoked gamma oscillation is reduced. In contrast, the early auditory-evoked gamma oscillation was normal in people with schizophrenia.

Prepulse inhibition (PPI) of the startle reflex is a measure of sensorimotor gating that is deficient in schizophrenia patients. Drugs that activate dopamine receptors cause similar PPI deficits in rats. **Shilling et al.** (pages 748–758) discovered that rat strains differing in sensitivity to these PPI deficits also differ in the expression of many genes within one particular brain region, the nucleus accumbens. Many of these genes have been implicated in the vulnerability to schizophrenia.

Glutamate System Dysfunction in Schizophrenia

Do antipsychotic medications contribute to loss of a type of supporting cell, astrocytes, in the cerebral cortex of individuals with schizophrenia? **Konopaske et al.** (pages 759–765) determined the total number of two types of supporting cells, oligodendrocytes and astrocytes, in the parietal cortex of monkeys exposed chronically to haloperidol or olanzapine. In contrast to expectations, they found significantly fewer astrocytes,

but not oligodendrocytes, in both groups of antipsychotic-exposed monkeys. Given the important role for astrocytes in modulating glutamate neurotransmission, these findings raise questions about the impact of antipsychotic treatment upon disturbances in glutamate neurotransmission in schizophrenia.

Oni-Orisan et al. (pages 766–775) used western blot analysis and in situ hybridization to assess expression of vesicular glutamate transporters 1 and 2 (VGLUT1-2) in the prefrontal cortex of subjects with schizophrenia and a healthy comparison group. A significant decrease in VGLUT1 protein was found in the anterior cingulate cortex (ACC) suggesting a decrease in presynaptic release of glutamate in this region. These findings support a growing literature implicating abnormalities of the ACC in schizophrenia.

Attentional Control in Schizophrenia & High-Risk Individuals

Reilly et al. (pages 776–783) report that antipsychotic-naïve first episode schizophrenia patients who demonstrate reduced attention also exhibit impaired response inhibition. These effects persisted after treatment with second-generation antipsychotic medications and clinical stabilization, suggesting that impairments in attention and response inhibition are traits that do not vary with standard treatments or symptom levels.

Groom et al. (pages 784–792) provide new insights into the nature of cortical contributions to attention impairments in schizophrenia and attention deficit hyperactivity disorder (ADHD). They examined two physiologic indicators of brain activity (P300, N200) with EEG. They found that individuals with schizophrenia had reduced P300 and N200 amplitude, siblings of people with schizophrenia had reduced P300 amplitude but not reduced N200 amplitude, and people with ADHD had reduced N200 but not reduced P300 amplitude. Together, these data suggest that attention deficits in ADHD and schizophrenia may be partially dissociated at the level of circuitry dysfunction.

Schizophrenia and Cerebral Asymmetry

Kawasaki et al. (pages 793–800) examined cortical brain asymmetry using voxel-based morphometry and found abnormal lateralization patterns in the planum temporale and pars triangularis in the patients with schizophrenia. These findings may reflect a perturbation in the lateralization process underlying left cerebral dominance for language.

Inflammatory Syndrome in Schizophrenia?

Potvin et al. (pages 801–808) performed a meta-analysis to test the hypothesis that an imbalance in the function of two sets of CD4+ T helper lymphocytes (Th1, Th2) in favor of the Th2

lymphocytes contributes to immune system dysfunction associated with schizophrenia. The results suggest that an increase occurs in interleukin-1 receptor antagonist (IL1RA), soluble interleukin-2 receptor (sIL-2R), and interleukin-6 (IL-6) levels and a decrease in interleukin-2 (IL-2). No significant effects were obtained for interferon- γ (IFN- γ), interleukin-4 (IL-4), interleukin-1 β (IL-1 β), tumor necrosis factor- α (TNF- α), soluble interleukin-6 receptor (sIL-6R) and interleukin-10 (IL-10). These findings are not consistent with Th2 predominance and provide evidence of an inflammatory syndrome in schizophrenia.

Psychosis Risk from Maternal Exposure to Herpes Simplex Virus

Buka *et al.* (pages 809–815) obtained maternal serum samples stored over 40 years for a large sample of persons with psychosis ($n = 200$) and 544 matched controls. Offspring of mothers who were infected with herpes simplex virus type 2, particularly mothers who may have had repeated exposure to the virus during pregnancy, were at significantly increased risk for the development of psychosis. These findings may have implications for the primary prevention of schizophrenia and other psychoses.