In this Issue

Volume 75, Number 4, February 15, 2014

A brief summary of the articles appearing in this issue of *Biological Psychiatry*.

Special Issue: Neuroimmune Mechanisms Related to Psychosis

Although the causes of schizophrenia remain unknown, it is increasingly clear that the immune system plays an important role. A family of immune proteins called major histocompatibility complex I (MHCI) molecules may mediate both genetic and environmental contributions to schizophrenia through direct effects on brain development. This review by **McAllister** (pages 262–268) summarizes our current understanding of MHCI expression and function in the developing brain, as well as its involvement in altering brain connections following exposure to an environmental risk factor for schizophrenia, from the perspective of how these roles for MHCI might contribute to its pathogenesis.

Recent reports suggest that psychiatric diseases like schizophrenia or other primary psychotic disorders could, in some cases, be caused by an antibody-mediated attack on key proteins expressed in brain neurons, particularly *N*-methyl-D-aspartate receptors. **Coutinho *et al.*** (pages 269–275) critically review the evidence that exists in the literature for "autoimmune psychosis", using the criteria that have been applied to other antibody-mediated neurological conditions such as myasthenia gravis.

The major histocompatibility complex is one of the most investigated, genetically diverse regions of the genome. In their review, **Corvin and Morris** (pages 276–283) describe the genetic evidence implicating this region in schizophrenia susceptibility. Interestingly, the locus may not play such a significant effect in risk for other psychiatric disorders. Translating these findings into biological insight poses challenges, not least in identifying how many signals are contributing to this association and localizing risk to specific genes.

Deakin *et al.* (pages 284–291) review the neuroimmunology of neuronal cell surface antibodies associated with central nervous system disorders, and their importance and relevance to psychotic disorders. They concentrate on the particular association between *N*-methyl-D-aspartate receptor antibodies and primary psychotic illness, including the clinically relevant implications for psychiatric practice.

All current medications for schizophrenia are believed to act through similar mechanisms, but their effectiveness is limited, particularly with regard to negative and cognitive symptoms. A new theory of schizophrenia suggests that a class of immunomodulatory proteins in the immune system known as cytokines may increase risk for schizophrenia. **Girgis *et al.*** (pages 292–299) review the scientific evidence which supports the involvement of cytokines in schizophrenia and give specific examples of how this knowledge can be translated into new treatments for schizophrenia.

Benros *et al.* (pages 300–306) summarize the epidemiological evidence that indicates that a broad range of autoimmune diseases involving multiple organ systems are associated with psychosis. Autoimmune diseases are characterized by self-reactivity and immune responses which can also affect the brain and induce psychiatric symptoms, such as psychosis. However, the associations could also be caused by shared genetic factors or common environmental triggers such as infections. Nonetheless, the authors recommend that autoimmune diseases should be considered by clinicians in the treatment of individuals with psychotic symptoms.

The review by **Meyer** (pages 307–315) summarizes ongoing research exploring the consequences of prenatal immune activation on neurodevelopmental processes in rodent systems. These animal models are pivotal for establishing causal relationships and for identifying mechanisms that affect normal brain development in the event of early-life immune exposures. An important refinement of these models is the incorporation of multiple etiologically relevant risk factors by combining prenatal immune challenges with specific genetic manipulations or additional environmental adversities.

Horváth and Mirnics (pages 316–323) review immune system transcript disturbances in the brain of subjects with schizophrenia, and discuss these disturbances in the context of genetic vulnerability and environmental insults. They also contemplate the potential origin of the immune system gene expression changes, particularly in the context of the neurodevelopmental hypothesis of the disease. Converging evidence suggests that serpin peptidase inhibitor, clade A member 3 (SERPINA3) and interferon inducible transmembrane protein (IFITM) family transcripts are upregulated in schizophrenia, and potentially important contributors to the disease process itself. As the *IFITM* gene family is primarily expressed in the endothelial cells and meninges, and as the meninges play a critical role in interneuron development, they suggest that these two non-neuronal cell populations might play an important role in schizophrenia pathophysiology.

Immune mediated mechanisms may play a key role in a subgroup of patients with psychosis. **Bergink *et al.*** (pages 324–331) review autoimmunity, microglia, monocytes, T cells and their cytokines in affective and non-affective psychosis. Evidence suggests that if biomarkers exist for immune abnormalities in psychosis, they may be found in monocyte inflammatory activation, reduced T cell numbers and TH1 skewing. The authors conclude with presenting an immune mediated two-hit model for psychosis.

Children born to mothers who had an infection during pregnancy are at increased risk of being later diagnosed with schizophrenia or autism. Mouse models that experimentally activate the maternal immune system during pregnancy produce pups with abnormal brain and behavioral development. Here, **Bauman *et al.*** (pages 332–341) describe a novel nonhuman primate model of maternal immune activation using a modified form of the viral mimic, poly IC. Compared with control animals, rhesus monkey offspring prenatally exposed to maternal immune activation demonstrate repetitive behaviors and altered social/communication development.

0006-3223/$36.00
http://dx.doi.org/10.1016/j.biopsych.2013.12.007