In This Issue

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

Review: Genetic Animal Models of Schizophrenia

The development of informative animal models for schizophrenia has been hindered by lack of knowledge into the underlying pathophysiology. However, recent large genetic studies have identified eight copy number variants that increase schizophrenia risk, five of which have now been modeled in animals, facilitating study of the biological consequences. **Forsingdal *et al.*** (pages 13–24) review and compare findings from these copy number variant models and discuss their potential for identification of schizophrenia-related biology and novel drug targets.

The Immune System and Psychosis

Prefrontal cortex (PFC) immune activation is associated with schizophrenia, but the role of the nuclear factor-κB (NF-κB) complex, which controls expression of immune markers, remains unclear. Here, **Volk *et al.*** (pages 25–34) examined signaling pathways for the NF-κB transcriptional complex in the PFC in schizophrenia. They report higher transcript levels for NF-κB family members, activation receptors, and kinases in human subjects with schizophrenia, but not antipsychotic-exposed monkeys or mice exposed prenatally to maternal immune activation. These findings suggest that higher NF-κB activity in schizophrenia may contribute to elevated levels of immune markers that are regulated by NF-κB transcriptional activity.

In this meta-analysis, **Cullen *et al.*** (pages 35–48) found an overall positive association between non-neurological autoimmune disorders and psychosis that is consistent across study designs and psychiatric diagnoses. For individual disorders, they detected positive associations for pernicious anemia, pemphigoid, psoriasis, celiac disease, and Graves' disease, and negative associations for ankylosing spondylitis and rheumatoid arthritis. This analysis supports the widely reported relationship between non-neurological autoimmune disorders and psychosis, and suggests that monitoring of individuals with specific autoimmune disorders for early signs of psychosis is warranted.

Motor Circuitry Abnormalities in Schizophrenia

Schizophrenia is associated with motor inhibition deficits, which are often attributed to motor cortex dysfunction. PFC regulates motor cortex and also shows abnormalities in persons with schizophrenia. Here, **Du *et al.*** (pages 49–59) used multiple imaging and brain stimulation techniques in patients with schizophrenia to illustrate that reduced short-interval intracortical inhibition is modulated by PFC–motor cortex connectivity. These data identify the circuitry underlying this commonly observed motor deficit in schizophrenia and provide further support for its candidacy as a biomarker of inhibitory dysfunction.

Brain Network Dynamics in Schizophrenia

The neurobiology of psychosis remains poorly understood. Applying a theoretical systems–neuroscience framework to human brain imaging data from two independent cohorts, **Supekar *et al.*** (pages 60–69) test the triple-network saliency model of schizophrenia, which posits that dysregulated functional organization of three key neurocognitive networks contributes to psychosis in schizophrenia. They report that dynamic cross-network interactions centered at the salience network correlated with positive, but not negative, symptoms and could reliably distinguish patients with schizophrenia from healthy control subjects. These data provide support for the model and further inform the framework used to characterize aberrant brain dynamics in psychosis.

Thalamic Microstructural Change in Early Psychosis

Multiple abnormalities of the thalamus are implicated in schizophrenia pathophysiology, but evidence regarding specific alterations in thalamic nuclei has largely been limited to postmortem investigations. **Cho *et al.*** (pages 70–78) used multimodal neuroimaging approaches to investigate specific microstructural changes in thalamic nuclei in patients with first-episode psychosis. Relative to healthy subjects, patients showed reduced microstructural complexity in thalamic regions connected to the orbitofrontal cortex and lateral temporal cortex. Structural complexity in the orbitofrontal cortex–connected thalamic region correlated with spatial working memory in patients. These data provide in vivo evidence of thalamic microstructural abnormalities in early psychosis.

Antipsychotic Effects on Dopamine Function

The presynaptic dopamine system has been implicated in both the etiology of psychosis and antipsychotic treatment response. However, the effect of antipsychotic medication on the dopamine system remains unclear. In this positron emission tomography study of individuals with first-episode psychosis, **Jauhar *et al.*** (pages 79–87) found no change in dopamine synthesis capacity before and 5 weeks after commencement of antipsychotic treatment. Further, change in symptoms was not associated with change in dopamine synthesis capacity. These data suggest that the therapeutic effects of antipsychotic medication are not related to alterations in dopamine synthesis capacity.

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