In This Issue

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

Reviews: Prefrontal Cortical Actions and Cognitive Functioning

Inhibitory gamma-aminobutyric acid (GABA) transmission within the frontal lobes has been proposed to play a key role in the regulation of cognitive and emotional processes. Disruptions in GABA signaling have been observed in the brains of patients with schizophrenia, but how this may relate to cognitive dysfunction associated with the disease is unclear. In this review, **Tse *et al.*** (pages 929–939) provide a summary of recent preclinical studies demonstrating a key role for prefrontal cortical GABA transmission in regulating numerous cognitive functions disrupted in schizophrenia.

Psychostimulants are an effective treatment for attention-deficit/hyperactivity disorder. In this review, **Spencer *et al.*** (pages 940–950) discuss recent evidence demonstrating a pivotal role of the prefrontal cortex (PFC) in the cognition-enhancing and therapeutic actions of psychostimulants. This work indicates that clinically-relevant doses of psychostimulants preferentially act in the PFC to elevate noradrenergic $\alpha 2$ and dopaminergic D1 receptor signaling. Understanding these PFC-mediated procognitive actions of low-dose psychostimulants may help guide clinical and public policy, in addition to development of novel treatments for conditions associated with PFC dysregulation.

Using Event-Related Potentials for Psychosis Prediction

In this paper, **Bodatsch *et al.*** (pages 951–958) systematically review event-related potentials as predictive markers of psychosis development. They also conducted a meta-analysis, which reveals that certain event-related potentials, duration mismatch negativity in particular, may be promising candidates for improving the prediction of psychosis onset. The authors conclude that this approach has the potential to provide an estimation of the remaining time until psychosis onset and could also inform approaches that are targeted towards psychosis prevention.

Protein Expression and Regulation in Schizophrenia: Glutamate and NOS1AP

MacDonald *et al.* (pages 959–968) investigated synaptic protein network alterations linked to dendritic spine loss in schizophrenia using auditory cortex gray matter tissue. Many proteins showed altered expression in individuals diagnosed with schizophrenia, which were predominately associated with the glutamate synapse. Compared with control subjects, synaptic protein co-expression was significantly decreased in subjects with schizophrenia, with the exception of a small group of postsynaptic density proteins, for which co-expression was increased and inversely correlated with spine loss. These findings highlight the complexity of alterations to glutamate signaling protein networks in schizophrenia.

Nitric oxide synthase 1 adaptor protein (NOS1AP) is encoded by a putative schizophrenia susceptibility gene. It is overexpressed in postmortem brains from subjects with schizophrenia. Here, **Carrel *et al.*** (pages 969–978) report that NOS1AP overexpression during rat embryonic development delays neuronal migration and decreases dendritic growth, resulting in aberrant neuronal connectivity. These data are consistent with alterations observed in patients with schizophrenia and suggest that NOS1AP plays an important role in neurodevelopment.

Clinical Trial: Brain Stimulation Fails to Improve Negative Symptoms

To date, there are no treatments that specifically target the negative symptoms of schizophrenia. **Wobrock *et al.*** (pages 979–988) conducted a multicenter, randomized, controlled clinical trial to evaluate the efficacy of high-frequency repetitive transcranial magnetic stimulation to treat negative symptoms of schizophrenia. Treatment was applied to the dorsolateral prefrontal cortex, a region where reduced activation has been linked to negative symptoms. They observed no difference in symptom improvement between active and sham treatment, which establishes the need for the development of new stimulation paradigms for the treatment of negative symptoms in schizophrenia.

Psychosis Risk: Brain Network Structural Covariance

Heinze *et al.* (pages 989–996) investigated whole-brain structural covariance patterns within eight major brain networks in individuals at high risk for developing psychosis. Compared with healthy controls, high-risk participants displayed reduced covariance in the default mode network and increased covariance in the motor and executive control networks. In addition, altered covariance was observed in the salience, executive control, auditory, and motor networks in high-risk participants who transitioned to psychosis, compared with those who did not transition. Despite these subtle connectivity alterations, results suggest that structural networks remain largely intact in individuals at risk for psychosis.

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