In this Issue

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

Schizophrenia, Context, and Memory

In their review of memory studies of schizophrenia, **Libby *et al.*** (pages 944–950) use quantitative procedures to test the contribution of recollection and familiarity to retrieval impairments in schizophrenia. Contrary to previous conclusions of a selective recollection versus familiarity impairment, the authors found that both processes were affected, with large recollection and intermediate familiarity deficits. Results suggest that both retrieval processes should be targeted for treatment, and that pathophysiology involves multifocal medial temporal lobe and/or prefrontal cortex dysfunction.

Manoach *et al.* (pages 967–975) utilized the temporal precision of magnetoencephalography to demonstrate that, compared with healthy controls, patients with schizophrenia are impaired in using contextual information to produce brain activation in some regions (anterior cingulate cortex) and they generate increased activity in other cortical regions when preparing to perform a strategy-driven eye movement task (antisaccade) compared to a sensory guided task (prosaccade). Their findings suggest that impaired use of context to mobilize cognitive control contributes to behavior that is stimulus-bound and error-prone rather than flexibly guided by context in schizophrenia.

Risk for Schizophrenia: Cognition and Brain Development

Schizophrenia is associated with IQ impairments that appear to have a substantial genetic contribution, but no study has demonstrated that these impairments can be attributed to schizophrenia's polygenic architecture. **McIntosh *et al.*** (pages 938–943) examined genome-wide association study data from a cohort who were cognitively assessed at ages 11 and 70. They report that individuals carrying a higher polygenic risk load for schizophrenia had a lower IQ at age 70 but not at age 11. A greater load of schizophrenia risk variants was also associated with a greater decline in lifelong cognitive ability. These findings suggest that common genetic variants may underlie both cognitive aging and risk of schizophrenia.

In a multi-site family study, **Calkins *et al.*** (pages 976–984) investigated whether particular neuropsychological abilities in schizophrenia patients predicted performance in their biological relatives. The authors found that all neurocognitive abilities were heritable, and that male patients' performance, especially spatial processing and face memory, predicted the performance of their siblings and mothers. The results suggest that even abilities that generally have a strong sex advantage (spatial processing for men; face memory for women) may be genetically informative in schizophrenia families.

Moorhead *et al.* (pages 985–992) investigated brain development over time in young people with intellectual impairment, and thus, at increased risk of schizophrenia. Within this group, they found that the occurrence of psychotic symptoms was associated with reduced tissue volumes in the medial temporal lobes. Similar developmental changes have been observed in familial and symptomatic populations also know to be at enhanced risk of psychosis, suggesting that these medial temporal changes may be central to the development of schizophrenia regardless of the nature of the vulnerability state.

Psychosis and Immune System Dysregulation

Fineberg and Ellman (pages 951–966) review evidence suggesting that immune alterations are associated with risk of schizophrenia and schizophrenia-related brain alterations. Findings from human and animal studies linking proinflammatory cytokines and immune-related genes to schizophrenia and brain abnormalities found in schizophrenia are reviewed and discussed using a life course perspective, examining the contribution of inflammation from the fetal period to disorder presentation. Unexplored areas and future directions, including the interplay between inflammation, genes, and environmental factors, are discussed.

Miller *et al.* (pages 993–999) performed a meta-analysis of blood lymphocyte parameters in schizophrenia, considering effects of clinical status and antipsychotic treatment. They found abnormalities in drug-naïve first-episode psychosis, suggesting an effect that may be independent of antipsychotic medications. While some parameters (CD4/CD8) appear to be state markers for acute exacerbations of psychosis, others (CD56) may be trait markers. They conclude, however, that more well-controlled longitudinal studies and correlations with clinical features are needed.

Postpartum psychosis is a severe mood disorder occurring within 4 weeks after delivery, a period of heightened immune responsiveness and an altered endocrine set point. **Bergink *et al***. (pages 1000–1007) investigated immune activation in women with first-onset postpartum psychosis, healthy postpartum women, and nonpostpartum women. They identified a dysregulation of the neuro-immuno-endocrine axis in women with postpartum psychosis, including elevated monocyte/macrophage activity and reduction of T cell numbers. These data support the hypothesis that disturbances in the endocrine and immune systems may represent a vulnerability factor for postpartum psychosis.

Transcranial Magnetic Stimulation for Hallucinations

Hoffman *et al.* (pages 1008–1014) conducted a randomized, sham-controlled clinical trial for patients with schizophrenia and severe auditory/verbal hallucinations utilizing repetitive transcranial magnetic stimulation (rTMS) to target Wernicke's area and the right homologous area. Additional stimulation during a masked phase was delivered to the site appearing to produce greater improvement. This protocol demonstrated some clinical benefit favoring rTMS over sham stimulation, particularly for patients whose motor threshold was consistently detected. Level of hallucination salience was predictive of site-specific rTMS response, and level of nondominant motor impairment positively correlated with rTMS response to the nondominant site.

Brain Effects of Cognitive Remediation Therapy in Schizophrenia

Penadés *et al.* (pages 1015–1023) used multimodal magnetic resonance imaging to investigate the impact of cognitive remediation therapy on brain activation and structural connectivity patterns in patients with schizophrenia. They found changes suggesting an improvement in the efficiency of central executive and default networks and observed an increase in white matter integrity in the genu of the corpus callosum after treatment. Functional and structural changes were also correlated.

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Oxidative Stress Exacerbates Schizophrenia-Like Phenotypes

Growing evidence suggests that oxidative stress may play a significant role in the pathogenesis of schizophrenia. Using a corticolimbic interneuron-specific *N*-methyl-D-aspartate receptor hypofunction mouse model, **Jiang *et al.*** (pages 1024–1034) explored whether oxidative stress contributes to social isolation-induced schizophrenia-like phenotypes. Their findings suggest that the failure of antioxidant defense mechanisms in fast-spiking parvalbumin interneurons leads to abnormal elevation of reactive oxygen species in the cortex. This failure of oxidative stress mechanisms may contribute to the exacerbation of schizophrenia-like behavioral phenotypes in this animal model.