In This Issue

Volume 92, Number 4, August 15, 2022

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

Immune Response and Psychiatric Disorders

Autoimmune psychosis may be caused by anti-neuronal autoantibodies, but findings have been mixed. Using tissue-based assays, **Endres *et al.*** (pages 261–274) analyzed cerebrospinal fluid and serum samples from patients with schizophreniform and affective syndromes. The authors detected novel anti-neuronal autoantibodies in cerebrospinal fluid of 18% of patients that followed 5 principal patterns, including against vascular structures, granule cells, myelinated fibers, Purkinje cells, and astrocytes. These findings suggest that the spectrum of autoantibodies in these patient groups may be broader than previously thought.

Anxiety disorders are common in individuals with psychosis, but whether anxiety in childhood is a risk factor for later psychosis remains unclear. Both disorders have been associated with elevated levels of C-reactive protein, a marker of inflammation. Analyzing data from a longitudinal cohort, **Morales-Muñoz *et al.*** (pages 275–282) found that persistently high levels of generalized anxiety at the ages of 8, 10, and 13 years is associated with increased odds of psychosis at age 24. This association was mediated by C-reactive protein level, suggesting that stress-activated inflammatory mechanisms may play a role in the link between anxiety and psychosis.

Evidence suggests a link between infection and neuropsychiatric disorders, but it is unclear whether there is a shared genetic basis underlying this relationship. Here, **Shorter *et al.*** (pages 283–290) report that infection diagnoses showed genetic correlation with multiple psychiatric disorders. Polygenic risk scores for infection were associated with increased risk of attention-deficit/hyperactivity disorder, major depressive disorder, and schizophrenia. Infections accounted for a small proportion of the risk for mental disorders conferred by infection polygenic risk score. Overall, these data indicate that infection polygenic factors may have only small effects on risk for mental disorders.

Genetics, Brain Structure, and Neuropsychiatric Risk

Schizophrenia is highly heritable and is associated with alterations in brain morphology. Yet, studies have shown little or no genetic correlation between schizophrenia and brain structure. Here, using novel biostatistical tools, **van der Meer *et al.*** (pages 291–298) identified substantial genetic overlap between schizophrenia and brain structure, which may have previously been obscured through standard genetic approaches because results indicated mixed directions of effects. Further, the authors showed that a polygenic score based on the shared genetic architecture was able to predict schizophrenia. These data advance our knowledge of schizophrenia's genetic complexity.

The cerebral cortex plays a role in many perceptual, cognitive, and affective processes that are disrupted in mental illness. Here, **Patel *et al.*** (pages 299–313) integrated fetal single-cell and bulk-tissue gene expression data with case-control differences in cortical surface area for several psychiatric disorders, including schizophrenia and attention-deficit/hyperactivity disorder. The authors found that across 11 cortical regions, group differences were associated with genetic expression profiles specific to radial glia and intermediate progenitor cells. Additional analyses revealed an intersection of these genes with those implicated in a number of prenatal risk factors. These data suggest that differential growth of the cerebral cortex in utero may relate to increased risk of later developing mental illness.

Hippocampal shape is altered in schizophrenia, but the mechanism by which surface deformations occur is not well understood. In this shape analysis, **Roeske *et al.*** (pages 314–322) illustrate that shape deformations of hippocampal subfield CA1 can be attributed to an incomplete inversion of the hippocampus, an atypical anatomic pattern that occurs during fetal brain development. This finding suggests a potential neurodevelopmental mechanism for the hippocampal shape differences that are often observed in schizophrenia.

PDZD8 Disruption Causes Cognitive Impairment

The protein PDZD8 is a component of the endoplasmic reticulum, an organelle with important functions in all animal cells. Here, **Al-Amri *et al.*** (pages 323–334) identified loss-of-function mutations in *PDZD8* as the cause of a developmental disorder characterized by intellectual disability with autistic features in 2 families of first-cousin marriages. Further work demonstrated that targeted disruption of PDZD8 impaired long-term memory in fruit flies and mice. These findings reveal a possible pathophysiological mechanism of syndromic intellectual disability.

ISSN: 0006-3223