# In This Issue

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

### Neural and Metabolic Correlates of Psychotic Experiences

Psychotic-like experiences (PLEs) in childhood are associated with greater risk of psychosis in adulthood, but the neural correlates of childhood PLEs are not yet clear. **Karcher *et al.*** (pages 7–15) investigated the relationship between brain network connectivity and PLEs using data from a cohort of school-age children. The authors report that increased PLEs were associated with reduced connectivity in cingulo-opercular, default mode, and cinguloparietal networks. PLEs were also associated with impaired connectivity between the cerebellum and both the cingulo-opercular and cinguloparietal networks. These same networks have been linked to psychotic disorders in adulthood, suggesting that psychosis-related functional connectivity alterations may be present as early as 9 years of age.

Psychotic symptoms exist on a continuum. Here, **Sabaroedin *et al.*** (pages 16–24) investigated whether functional connectivity of dorsal corticostriatal circuitry, which is disrupted in patients and individuals at high risk for psychosis, is associated with PLEs in a nonclinical community sample of adults. The authors found that reduced connectivity between the dorsal striatum and prefrontal and motor cortices was correlated with subthreshold delusions and hallucinations, suggesting that altered connectivity of the dorsal corticostriatal circuit extends to the subclinical domain of positive-symptom PLEs.

Metabolic dysregulation has been identified in adults with schizophrenia and, more recently, in children who later developed a psychotic disorder. In an extension of that recent work, **Madrid-Gambin *et al.*** (pages 25–34) used lipidomic and proteomic approaches in the same general-population cohort to investigate whether such alterations are also present in children who later report PLEs. The authors detected alterations in 16 lipids and one protein between the control and PLE groups, providing evidence for an early biological signature of later psychotic experiences.

### B Vitamins in First-Episode Psychosis

Levels of homocysteine, an amino acid regulated by intake of folic acid and B vitamins, are elevated in individuals with schizophrenia. Studies have shown that increased intake of B vitamins decreases homocysteine and improves symptoms in people with schizophrenia. In this randomized, double-blind, placebo-controlled, 12-week trial, **Allott *et al.*** (pages 35–44) report that a B-vitamin supplement containing folic acid, $B_{12}$, and $B_6$ reduced homocysteine levels in patients with first-episode psychosis but did not improve overall symptoms or neurocognition. However, B-vitamin supplementation did show specific effects in a measure of concentration, and in select cognitive domains among female patients and patients with affective psychosis.

### Schizophrenia Gene Coexpression Predicts Treatment Response

Schizophrenia risk variants may regulate gene expression, which may then relate to clinical outcomes. **Pergola *et al.*** (pages 45–55) investigated this hypothesis by studying the coexpression networks of schizophrenia risk genes in human postmortem prefrontal cortex messenger RNA datasets. The authors report that a gene coexpression pathway overrepresenting schizophrenia risk genes predicted approximately 6% of the variance in short-term response to olanzapine treatment in patients with schizophrenia. These data indicate that genome-wide convergence of schizophrenia risk genes in a specific coexpression module may translate into interindividual variability of treatment response.

### Advanced Paternal Age and Schizophrenia

Advanced paternal age has been associated with schizophrenia. However, debate remains whether this effect is caused by transmission of increased paternal age–related de novo mutations or whether it can be explained by the confounds of selection into late fatherhood. **Wang *et al.*** (pages 56–64) sought to address this by using polygenic risk scores to control for paternal and maternal genetic vulnerability to schizophrenia in a sample of patients with schizophrenia with no known family history of major psychiatric disorders. The association of paternal age with early-onset schizophrenia in offspring remained after adjustment for parental predisposition, providing support that advanced paternal age plays an independent role in the risk for schizophrenia.

### Brain Structure and Psychopathology

The cerebellum is implicated in numerous mental disorders, including schizophrenia and depression, but its role in the developmental stages of psychopathology remains unclear. Using machine learning and magnetic resonance imaging in an adolescent community sample, **Moberget *et al.*** (pages 65–75) found that individual differences in cerebellar anatomy could predict both cognitive function and psychopathology. Additionally, cerebellar morphology showed association with psychosis symptoms, conduct problems, and anxiety but not other symptom domains. Further, these associations were stronger for the cerebellum than for other cerebral anatomical features, suggesting a crucial role for the cerebellum in the early manifestation of severe mental illness.

 

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