In This Issue

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

Copy Number Variants Across Disorders

Rare copy number variants (CNVs) confer high risk for neurodevelopmental disorders, including autism spectrum disorder and schizophrenia. Focusing on both convergent and locus-specific effects across these variants, **Silva *et al.*** (pages 341–361) summarize emerging findings from cognitive and neuroimaging studies in human cohorts, animal models, and in silico pathway models. The authors highlight the need to integrate multiomics knowledge (e.g., transcriptomics, genomics, and proteomics) with findings from neuroimaging and clinical data in order to identify major disease mechanisms that may be common across high-risk genetic variants.

Shared genetic factors have been identified between bipolar disorder, schizophrenia, and autism spectrum disorder. **Kushima *et al.*** (pages 362–374) performed a cross-disorder analysis of genic and regulatory CNVs in these disorders. The authors found that bipolar disorder differed from schizophrenia and autism spectrum disorder in CNV burden, characteristics of CNVs linked to neurodevelopmental disorders, and regulatory CNVs. The authors also identified shared molecular mechanisms, including those related to chromatin biology, across the 3 disorders, providing insight into their genetic pathogenesis.

Neuroimaging Alterations in Relatives and Patients

Schizophrenia and bipolar disorder share clinical and genetic characteristics, and both disorders are highly heritable. Thus, investigation of unaffected relatives offers a unique opportunity to understand potential risk mechanisms. In this meta-analysis, **Cattarinussi *et al.*** (pages 375–384) pooled data from structural and functional magnetic resonance imaging studies on unaffected relatives of individuals with schizophrenia or bipolar disorder. The authors found both shared and distinct alterations in thalamocortical circuitry, regions that have been implicated in cognitive and emotional regulation. These results implicate the thalamus as a common region associated with risk for these disorders.

The cerebellum is implicated in psychosis, but the course of cerebellar-related alterations in relation to illness stage, specific diagnosis, and cognition remains unclear. In this cross-sectional structural magnetic resonance imaging study, **Moussa-Tooks *et al.*** (pages 385–395) found no differences in cerebellar structure between healthy participants and those with psychosis, regardless of diagnosis or illness stage, in contrast to prior work. However, the authors did find smaller cerebellar volumes in psychosis among individuals with impaired premorbid cognitive ability. These findings highlight the high heterogeneity of psychosis and suggest that early developmental insults may play a role in cerebellar abnormalities in psychosis.

Visual Alterations in Psychosis

Impairments of the visual system are implicated in psychotic disorders. Here, **Türközer *et al.*** (pages 396–406) found structural reductions in visual cortex subregions of individuals with psychosis and their first-degree relatives, compared with healthy control subjects. Some reductions showed regional specificity in female probands and some showed correlation with cognitive impairments and peripheral inflammatory markers. These findings add to the evidence suggesting that the visual system is disrupted in psychosis.

Prior work has identified deficits in gamma band oscillations during visual processing in psychosis, but the processes underlying these alterations are not fully understood. Here, **Mancini *et al.*** (pages 407–418) analyzed electroencephalography data from individuals with 22q11.2 deletion syndrome, which is associated with genetic risk for psychosis, who completed a visual task. Compared with a control group, deletion carriers showed decreased oscillatory responses to visual stimuli in the gamma and theta bands, while alpha/beta desynchronization was intact. These data provide insight into the neurobiology of visual deficits in this genetic syndrome.

Mechanisms of Treatment Resistance in Schizophrenia

Treatment resistance affects a significant proportion of patients with schizophrenia. Olanzapine has shown effectiveness for treatment-resistant schizophrenia (TRS), but therapeutic results vary by individual patient, with the mechanisms underlying this resistance not well understood. Using pharmacogenomics and induced pluripotent stem cells from patients with TRS, **Sun *et al.*** (pages 419–433) identified a microRNA-mediated neuregulin-1–dependent mechanism of olanzapine resistance in TRS, which provides a potential novel biomarker of and molecular target for TRS.

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