In This Issue

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

Review: Deubiquitinating Enzymes and Neurodevelopmental Disorders

Protein ubiquitination is a widespread protein modification that directs protein degradation. A family of deubiquitinating enzymes (DUBs) opposes this activity, and many of these enzymes are implicated in neurodevelopmental disorders. In this review, **Jolly *et al.*** (pages 614–625) describe the current genetic and functional evidence that links multiple DUBs with brain development. Further, the authors highlight how knowledge of DUB function is illuminating new therapeutic paradigms to overcome neurodevelopmental disorders underpinned by loss of protein abundance.

Review: Predictive Modeling in Autism

Autism spectrum disorder (ASD) is a heterogeneous neurodevelopmental condition. Improved understanding of the brain-based characteristics of ASD could help guide clinical research. Here, **Horien *et al.*** (pages 626–642) review studies that have used magnetic resonance imaging functional connectivity data to predict autism phenotypes. The authors discuss how issues related to autism-specific study and analysis design can affect the biological and clinical utility of predictive modeling methods. The authors highlight the need for predictive modeling studies that use dimensional and subtyping approaches, which may help address the heterogeneity of ASD and yield novel insights into the biological underpinnings of autism.

Artificial Intelligence: Brain Biomarkers of ASD

ASD is among the most common neurodevelopment disorders, but the neurobiology of ASD is still poorly understood, in part because of high heterogeneity and inconsistent findings. Using large-scale human brain imaging data from 3 independent cohorts coupled with artificial intelligence techniques, **Supekar *et al.*** (pages 643–653) found reproducible functional brain biomarkers, including in the posterior cingulate cortex and precuneus, that accurately distinguished individuals with ASD from neurotypical control subjects and that were able to predict individual differences in core social and communication symptoms. These findings highlight the utility of such approaches in advancing our knowledge of brain biomarkers of neuropsychiatric psychopathology.

Sex Differences in ASD Subgroups

Sex differences in the diagnosis of ASD are marked, but it is possible that such discrepancy in prevalence between the sexes is related to symptom heterogeneity and/or measurement bias. In this longitudinal study of children who had a sibling diagnosed with ASD, **Burrows *et al.*** (pages 654–662) identified a balanced 1:1 male to female ratio in a "high-concern" group based on scores of social communication and restricted and repetitive behaviors. These data suggest that girls may be equally likely to demonstrate elevated ASD traits and highlight an approach that may be useful in better understanding the development of ASD symptoms across early childhood.

Maternal Behavior and Preterm Outcomes

Infants born very prematurely often require life-saving care. Both illness and procedure-related injuries early in life have been related to altered brain development and poorer outcomes, but positive maternal interactions may improve cognitive and language outcomes in these infants. In this longitudinal study of children born very preterm, **Miller *et al.*** (pages 663–673) demonstrated that supportive and responsive behavior from mothers was related to higher scores on cognitive and language assessments at 3-year follow-up among children who showed less mature cortical gray matter at term-equivalent age. These data suggest that promoting greater maternal sensitivity may be an avenue through which neurodevelopment could be improved for children born very preterm.

The Cerebellum in ASD

The cerebellum is a structure that contains more than half the neurons of the brain. Previous studies have reported inconsistent findings in this region in individuals with ASD. Using multiple approaches to analyze data from a large multicenter study, **Laidi *et al.*** (pages 674–682) found no differences in the anatomy of the cerebellum between individuals with ASD and control individuals. These findings suggest that cerebellar anatomy may be unaffected in ASD.

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