In This Issue

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

Neonatal Immune Biomarkers for Autism

The identification of an early biomarker for autism spectrum disorder (ASD) would promote earlier diagnosis and intervention, and possibly lead to improved outcomes. **Heuer *et al.*** (pages 255–264) tested blood samples taken from newborns and found that interleukin-6 and interleukin-8 levels were increased in children who were later diagnosed with ASD, compared with a matched general population control group. Other neonatal immune markers were increased in children with ASD compared with children who were later diagnosed with developmental delay. These data suggest that children who are diagnosed with ASD may have higher neonatal levels of immune activity, and that development of newborn blood testing for inflammatory markers might lead to tools that provide the ability to assess ASD risk at birth.

Genetics of ASD

ASD is highly heritable. **Pain *et al.*** (pages 265–273) conducted a transcriptome-wide association study to identify genes that are expressed at different levels in individuals diagnosed with ASD. This was achieved by testing whether genetic variation more common in those with ASD also influences gene expression levels. The authors identified 14 differentially expressed genes in ASD, including *XRN2*, *CTSB*, and *PDIA6*, providing novel insight into the underlying biology of this disorder.

Heterozygous deletion of the *TSHZ3* gene has previously been linked to an ASD syndrome in humans, and to ASD-like behavior in mice. Using a novel transgenic mouse model, **Chabbert *et al.*** (pages 274–285) show that targeted neuronal inactivation of *Tshz3* shortly after birth leads to ASD-like behavior, electrophysiological and synaptic changes in cortical projection neurons, impaired corticostriatal transmission, and altered expression of numerous genes linked to ASD and other neurodevelopmental deficits. These results suggest that *TSHZ3* may play a critical postnatal role in ASD pathogenesis.

Assortative Mating in ASD

Assortative mating, a system in which individuals with similar traits or genotypes mate together more frequently than would be expected by chance, has been hypothesized to play a role in ASD. **Connolly *et al.*** (pages 286–293) used kinship coefficients to examine genetic relatedness in spouse pairs compared with nonspouse pairs from two genome-wide association study datasets. The authors found evidence of assortative mating in multiplex ASD families (i.e., that contain one or more ASD family member), but not in families with only one ASD family member, providing support for the assortative mating hypothesis.

Genotype-Phenotype Relationships: Cognition in Humans and Flies

Habituation learning is believed to serve as a sensory filter required for higher cognition, but the underlying genetics and relevance to disease are poorly understood. From among an established list of genes implicated in intellectual disability with or without comorbid ASD, **Fenckova *et al.*** (pages 294–305) identified more than 100 genes that are required for habituation learning in *Drosophila*. In addition, the authors discovered Ras-MAPK signaling as a mechanism that oppositely regulates habituation in inhibitory versus excitatory neurons. These data suggest that habituation deficits may represent an endophenotype for intellectual disability with comorbid ASD.

Genetic deletions on chromosome 15 (BP1-BP2) are associated with increased risk for neurodevelopmental disorders, including schizophrenia, epilepsy, and developmental delay. Using a web-based cognitive test battery, **Woo *et al.*** (pages 306–314) identified reading- and math-related cognitive deficits in deletion carriers, but not in their noncarrier spouses. Separate work in flies revealed that reduction in *Cyfip* dosage, one of the genes in the deletion, is associated with associative and habituation learning deficits. These results provide insight into cognitive outcomes associated with BP1-BP2 deletions and demonstrate the utility of a remote phenotyping tool for characterizing a geographically distributed population of research subjects.

Connectomics in ASD and ADHD

ASD and attention-deficit/hyperactivity disorder (ADHD) are commonly comorbid, and both are associated with complex structural and functional brain abnormalities. **Lake *et al.*** (pages 315–326) used a data-driven, subject-level, connectome-based predictive modeling approach to identify brain–behavior associations that are predictive of symptom severity. The authors found widespread disorder-specific and shared neurofunctional pathologies and identified functional connectivity patterns that were able to independently predict clinical measures of ASD and ADHD symptom severity.

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