In This Issue

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

Clinical Presentations of Mutations in the Autism Risk Gene *ADNP*

Sequencing studies of individuals with autism spectrum disorder (ASD) and intellectual disability (ID) have frequently identified de novo mutations in *ADNP*, a gene that plays a role in embryonic development. Beyond their identification, these ASD/ID syndromes must then be clinically defined. Using a worldwide cohort, **Van Dijck *et al.*** (pages 287–297) provide a clinical characterization of Helsmoortel-Van der Aa syndrome, a complex neurodevelopmental disorder caused by *ADNP* mutations. They report that these individuals share clinical features, including ID, ASD, speech and motor delay, facial characteristics, and multiple medical comorbidities, that are distinctive from other ASD/ID syndromes. Further, individuals carrying the p.Tyr719* mutation were more severely affected, suggesting that these features may be mutation dependent.

Tourette Syndrome Polygenic Risk Scores Predict Tics

The genetics of Tourette syndrome, a disorder characterized by motor and vocal tics, is not yet well understood, but it is thought that common genetic variants may be involved. **Abdulkadir *et al.*** (pages 298–304) used data from a recent genome-wide association study to calculate Tourette syndrome–based polygenic risk scores, which predicted the presence of tics in a general population cohort of children. There was no association with obsessive-compulsive disorder, attention-deficit/hyperactivity disorder, or ASD. These data suggest that multiple common variants may be involved in a broad tic phenotype.

Endogenous DISC1 Interactome in Neural Development

The DISC1 protein has been implicated in neurodevelopmental disorders and has been intensely investigated, but identification of the endogenous DISC1 interactome has not been determined. Here, **Wilkinson *et al.*** (pages 305–316) generated a $DISC1^{FLAG}$ induced pluripotent stem cell line using advanced genome editing and further differentiated these cells into neural progenitor cells and astrocytes. Using these models, the authors determined cell type-specific DISC1 interactomes, which clustered into numerous functional modules consistent with the known functions of DISC1. Additionally, they found that the human neural progenitor cell DISC1 interactome was enriched for nonsynonymous mutations in schizophrenia.

Parental Infection and Offspring Mental Disorders

Maternal infection during pregnancy has been associated with increased risk for schizophrenia and ASD in offspring. Using a population-based registry to analyze exposure to both maternal and paternal infections, **Lydholm *et al.*** (pages 317–325) found similarly increased risks of mental disorders in the offspring after exposure to maternal infections before, during, and after pregnancy, compared to unexposed children. The risk of mental disorders was greater for infections requiring hospital contact. These data provide further insight into the link between parental infection and offspring risk for mental disorders but suggest that the pregnancy period itself is not associated with a greater risk.

Early Parenting Intervention and Child Neurodevelopment

Early adverse experiences negatively impact neurodevelopment, but it remains unclear whether early interventions can normalize developmental trajectories in at-risk children. **Bick *et al.*** (pages 326–335) used data from a randomized clinical trial of a parenting intervention program for families with infants and toddlers monitored for maltreatment. They found that higher levels of early home adversity are associated with more immature patterns of cortical function in middle childhood, as measured with electroencephalography. Relative to a control intervention, children from families assigned to an early parenting program showed more neurotypical profiles in middle childhood. These findings suggest that early parenting intervention programs may convey protective effects on long-term neurodevelopment in children exposed to adverse environments.

Structural Connectivity in Disruptive Behavior Problems

Studies of white matter connectivity in children with disruptive behavior have yielded inconsistent results, possibly owing to the trait's heterogeneity. Using diffusion tensor imaging and a multidimensional approach to disruptive behavior problems, **Bolhuis *et al.*** (pages 336–344) observed that global white matter microstructure was reduced in preadolescents with higher levels of delinquent behavior, but not in those with physical aggression, irritability, or disobedient behavior problems. Multiple individual tracts contributed to this global association, including the uncinate and cingulum. These data help advance the search for the neurobiological correlates of childhood disruptive behavior.

Amino Acid Dysregulation in ASD

ASD is highly heterogenous, with no reliable diagnostic biomarkers. Evidence has suggested an association between dysregulation of branched-chain amino acids and the behavioral characteristics of ASD. Here, **Smith *et al.*** (pages 345–354) compared plasma metabolites in children with ASD and typically developing children, and then identified three amino acid dysregulation metabotypes associated with ASD. Combined, these metabotypes were present in ~16% of the subjects with ASD and showed high specificity and positive

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predictive value. These metabolic data may help lead to the development of diagnostic tests for the early identification of subsets of children with ASD.

Brain Stimulation Modifies Response Inhibition

Response inhibition is a decision-making process that reflects one's ability to stop a suboptimal action. This ability is often impaired in psychiatric disorders, such as substance use disorders and obsessive-compulsive disorder, reflecting a form of impulsive behavior. Cortical paired associative stimulation is a type of transcranial magnetic stimulation that can induce cortical synapse plasticity. Here, **Kohl *et al.*** (pages 355–363) used this technique in healthy volunteers to show that it can also be used to modify response inhibition as a function of age. These findings showed specificity to targeted cortico-cortical and cortico-subcortical inhibitory networks, suggesting that this technique may be useful within psychiatry.