In This Issue

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

Autism Genotypes and Phenotypes

Identifying genetic variants that increase risk for autism and are common in the population remains a great challenge. Several approaches have been proposed to improve detection of these risk variants, including the selection of subgroups of individuals based on symptom characteristics. **Chaste *et al.*** (pages 775–784) examined the impact of such clinical homogeneity on genetic homogeneity using a well-characterized sample of autism spectrum disorder (ASD). No genome-wide significant associations were identified, suggesting that analysis of clinical phenotypes is not a productive path for which to discover genetic risk variants in ASD.

In this study, **Hanson *et al.*** (pages 785–793) clarify the phenotype of 16p11.2 deletion through the examination of psychiatric and developmental presentation in both children and adults with de novo and inherited recurrent ~600 kb chromosome 16p11.2 deletions. They report that individuals with the 16p11.2 deletion have high rates of psychiatric and developmental disorders, including developmental coordination disorder, phonological processing disorder, language disorders, and ASD. These individuals also provide a genetically well-defined group to study the emergence of developmental difficulties, particularly those associated with the broader autism phenotype.

Resting State Network Abnormalities in ASD

Cortical connectivity patterns are abnormal in ASD, but much remains unknown about the nature of these abnormalities. **Kitzbichler *et al.*** (pages 794–804) used magnetoencephalography to study functional connectivity in resting state networks in ASD. The ASD group showed more integrated, efficient, and distributed networks in the α and γ bands, whereas the typically developing group showed more integrated, efficient, and clustered networks in the β band. Overall, these findings suggest that network abnormalities in ASD are both complex and widespread, are more likely in subnetworks that include the frontal lobe, and are consistent within, but not between, frequency bands.

Genetic Mutations Contribute to Neurodevelopmental Disorders

SYNGAP1 mutations are linked to several developmental brain disorders, including intellectual disability, schizophrenia, and ASD. Here, **Aceti *et al.*** (pages 805–815) demonstrate that *Syngap1* mutations in mice alter the structural growth and maturation of developing cortical pyramidal neurons. These developmental insults, which included accelerated dendritic growth and premature slowing of dendritic spine dynamics, were linked to disruptions in cortical circuitry. These findings suggest that alterations in neuronal growth during critical periods of synaptogenesis may be a common process contributing to distinct neurodevelopmental disorders.

Cav1.3, a member of a calcium channel family, regulates important functions in the brain, including neuronal excitability and neuronal development. Two mutations in its gene, *CACNA1D*, have recently been identified in patients with ASD but not in their unaffected family members. Using a whole-cell patch-clamp technique to study the related functional consequences, **Pinggera *et al.*** (pages 816–822) show that both mutations abnormally increase Cav1.3 function, suggesting that *CACNA1D* gain-of-function mutations may play a causal role in the development of ASD.

Maternal Immune Activation Produces Abnormal Social Attention

Maternal infection during pregnancy is associated with an increased risk of having a child later diagnosed with schizophrenia or autism. Rhesus monkey offspring prenatally exposed to maternal immune activation, in which a modified form of the viral mimic poly IC is used, have recently been shown to display abnormal repetitive behaviors, altered communication, and atypical social interactions. Using eye-tracking in these same animals, **Machado *et al.*** (pages 823–832) now demonstrate that, compared with control monkeys, prenatally-exposed monkeys show abnormal gaze patterns when viewing faces of conspecifics. These data suggest that this nonhuman primate model may improve translation between animal models and complex human developmental disorders.

Autism and Head Circumference Growth in Infancy

Evidence suggests a link between autism and increased growth of head circumference during early infancy, but the dynamic features of such growth have been more difficult to characterize. **McKeague *et al.*** (pages 833–840) conducted a case-control study using data from national well-baby clinics in Finland. From 2-4 months of age, they found a strong association between accelerated head circumference growth and autism, but only among cases with comorbid intellectual disability, and irrespective of acceleration in height and weight. After 6 months of age, associations emerged between autism and accelerated growth in height and weight.

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