In This Issue

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

Review: Modeling Autism Using Human Neurons

Understanding the mechanisms underlying autism spectrum disorder (ASD) has been slowed by the limited availability of research specimens. Here, **Muotri** (pages 642–649) reviews applications of human induced pluripotent stem cell technology, capable of reprogramming somatic cells from people with autism and generating "minibrains" in a dish. Despite its limitations, this human model approach offers an opportunity to test specific hypotheses about autism pathology in order to progress this field of inquiry.

Translating Neurogenomics Into New Therapeutics

Our understanding of the genetic variation that contributes to the risk for schizophrenia, bipolar disorder, and other neuropsychiatric disorders has advanced in recent years. While these findings are attractive starting points to derive disease biology insights and novel therapeutic candidate mechanisms, the path from genetic locus to testable clinical hypothesis is poorly defined. In this review article, **Wendland and Ehlers** (pages 650–656) provide an overview and an industry perspective and detail a set of challenges that must be addressed to efficiently translate this genetics knowledge into novel therapeutics.

Visual and Motor Alterations in ASD

Children with ASD exhibit motor deficits and impairments in learning from visual feedback. Using resting-state functional magnetic resonance imaging, **Nebel *et al.*** (pages 633–641) demonstrate that visual and motor systems are intrinsically more out-of-sync in children with ASD compared to typically developing children. Moreover, visual-motor asynchrony is related to the severity of autistic traits. These findings provide support for a neural link between motor and social deficits in ASD.

Altered visual patterns are hallmarks of ASD, but whether eye-tracking indices can be used to detect or identify biomarkers has been unclear. Using eye-tracking technology in toddlers, **Pierce *et al.*** (pages 657–666) found that a subtype of toddlers with ASD who strongly prefer geometric images, relative to toddlers with ASD who prefer social images, have more severe symptoms. This gaze profile was not present in typically developing toddlers or those with other delays. These data suggest that visual preference for geometric images may be an early biomarker for a more severe subtype of ASD.

Microcircuit Disruptions in Autism

Genetic findings in autism have suggested that abnormalities may be present in deep layer microcircuits in the prefrontal cortex. **Luongo *et al.*** (pages 667–675) report that cholinergic receptor stimulation with carbachol decorrelates patterns of activity generated by prefrontal cortex neurons in normal mice, but that this effect is absent in two mouse models of autism. This microcircuit-level disruption in neural activity may contribute to the attentional deficits observed in autism and may represent a novel therapeutic target.

Frontal Tract Abnormalities in Early ASD

Frontal lobe abnormalities have been linked to social, emotional, and language deficits, but whether they are present early in ASD development has been unclear. **Solso *et al***. (pages 676–684) examined the microstructure and volume of frontal lobe pathways using diffusion tensor imaging in toddlers with ASD. Compared with typically developing toddlers, they report that multiple frontal pathways display axonal overconnectivity and abnormal growth trajectories. These early age-related changes may contribute to later functional underconnectivity and impaired behaviors in ASD.

Neurobiology of Female Aggression

Impulsive aggression has been linked to structural plasticity in the nucleus accumbens, but the underlying mechanisms, particularly in females, remain unclear. Using a female hamster model, **Been *et al.*** (pages 685–692) link escalation of aggression to a signaling cascade of metabotropic glutamate receptor 5 activation, decreased phosphorylation of fragile X mental retardation protein, and increased synaptic scaffolding proteins. These findings suggest that targeting metabotropic glutamate receptor regulation of synaptic plasticity may be a promising therapeutic approach for the treatment of pathological aggression.

Oxytocin-Induced Changes in Cerebral Blood Flow

Paloyelis *et al.* (pages 693–705) used arterial spin labeling to quantify and visualize the effects of intranasal oxytocin in the resting human brain. Compared to those who received placebo, healthy volunteers who received oxytocin displayed neural activation in limbic and related areas of the brain involved in social-emotional information processing, delineating an oxytocinergic network. These data also provide a spatiotemporal profile of oxytocin-induced changes in cerebral blood flow, which may be used to guide future experiments and clinical applications.

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