In This Issue

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

Error Processing and Inhibitory Control in OCD

The ability to adaptively regulate behavior is achieved through error processing and inhibitory control. **Norman *et al.*** (pages 713–725) performed an image-based meta-analysis of functional neuroimaging studies of error processing and inhibitory control in patients with obsessive-compulsive disorder (OCD). Relative to healthy control subjects, patients showed cingulo-opercular hyperactivation during error processing as well as cingulo-opercular and orbito-striato-thalamic hypoactivation and impaired performance during inhibitory control. The authors suggest that this pattern of neurocognitive abnormalities may underlie the inability to stop compulsive behaviors in OCD, whereby errant behaviors remain uncorrected by deficient inhibitory control networks.

Brain Stimulation for OCD: Target Sites and Connectivity

Deep brain stimulation (DBS) has emerged as a promising treatment for patients with severe treatment-resistant OCD, but the most effective target sites have yet to be identified. In this randomized double-blind trial, **Tyagi *et al.*** (pages 726–734) directly compared DBS of the ventral capsule/ventral striatum (VC/VS) and the anteromedial subthalamic nucleus (amSTN) in six patients with severe OCD. OCD symptoms were reduced to the same extent by DBS at each site. DBS of amSTN, but not VC/VS, improved cognitive flexibility. VC/VS DBS was more effective at improving mood. Magnetic resonance imaging tractography suggested that these different behavioral effects reflect DBS modulation of distinct brain networks.

Neuromodulation therapies have been successfully employed to alleviate symptoms in OCD, but it remains unclear which networks are associated with clinical improvement. In this study, **Baldermann *et al.*** (pages 735–743) used models that were able to cross-predict clinical outcome of DBS for OCD in two independent datasets consisting of patient-specific and normative connectome data. Further, they calculated a model of optimal connectivity encompassing the lateral and medial prefrontal cortices that was able to predict outcome in the overall sample. These findings may help guide DBS targets to achieve beneficial outcomes in patients with OCD.

Infections and Risk of Self-harm

Inflammation and infections are associated with mental disorders and suicide. In this nationwide register-based cohort study, **Gjervig Hansen *et al.*** (pages 744–751) found an increased risk of deliberate self-harm among individuals treated with anti-infective agents for infection compared with individuals with no infections. This increased risk showed a dose-response relationship and persisted for up to 5 years after the last infection, even after adjustment for multiple confounds. Risk was further increased for those with infections requiring hospitalization. These findings indicate that less severe infections treated with anti-infective agents are associated with an increased risk of deliberate self-harm; additional research will be important to identify the underlying causal mechanisms.

Electrophysiology and Genotype in Angelman Syndrome

Angelman syndrome is a genetic disorder characterized by impaired brain development, intellectual disability, and seizures. Using electroencephalography, **Frohlich *et al.*** (pages 752–759) found elevated theta power and diminished beta power in affected children with a deletion genotype, compared with those with a nondeletion genotype. These data indicate that patterns of electrical brain activity in Angelman syndrome may differ based on the numbers of affected genes and that abnormal theta and beta oscillations may underlie the more severe clinical phenotype caused by deletion.

Aberrant Signaling Mechanisms in Autism and Parkinson's Disease

Autism spectrum disorder occurs more frequently in boys than girls, but the genetic and molecular causes of this bias remain unknown. *CC2D1A* mutations are associated with autism spectrum disorder. In this study, **Zamarbide *et al.*** (pages 760–768) observed an altered molecular signaling cascade and spatial memory deficits that were present in *Cc2d1a*-deficient male mice, but not *Cc2d1a*-deficient female mice. Restoration of the signaling via a pharmacologic inhibitor rescued the behavioral deficits. These data suggest that male-specific signaling mechanisms in the hippocampus may play a role in male-biased neurodevelopmental disorders.

Death-associated protein kinase 1 (DAPK1) has been implicated in the pathogenesis of diverse neurodegenerative diseases. Using a chronic Parkinson's disease mouse model, **Su *et al.*** (pages 769–781) report a novel regulatory pathway of miR-26a/DAPK1. They found that loss of miR-26a enhances the translation of DAPK1, which leads to abnormal hyperphosphorylation of α-synuclein, dopaminergic neuron loss, and motor disability. Genetic deletion of DAPK1 in dopaminergic neurons or peptide-induced blockade of α-synuclein phosphorylation reversed the phenotype, suggesting that this pathway may serve as a novel therapeutic target for Parkinson's disease.

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