In this Issue

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

Novel Treatment Targets for Cognitive Dysfunctions

β adrenergic receptor signaling plays a major role in learning and memory. **Dang *et al.*** (pages 179–188) evaluated whether formoterol, a long-acting β2 adrenergic receptor agonist, could improve cognitive function in a mouse model of Down syndrome. They found dentate gyrus atrophy and loss of β adrenergic signaling in the hippocampus of Down syndrome mice. Formoterol treatment improved cognitive function and was associated with improvements in synaptic density and dendritic complexity. These data suggest that improving β2 signaling may be a successful strategy in the treatment of cognitive disabilities in people with Down syndrome.

Studies have suggested that metabotropic glutamate receptor 5 (mGluR5) inhibition corrects multiple phenotypes related to fragile X symptoms. **Michalon *et al.*** (pages 189–197) used functional magnetic resonance imaging to investigate the effects of chronic treatment with CTEP, an mGluR5 inhibitor. Fragile X mice showed no significant changes in mGluR5 expression levels compared with wild-type mice, but CTEP treatment restored their learning deficits and fully or partially normalized neuronal activity in the amygdala and thalamic structures. These data advance our understanding of the pathophysiology of fragile X, and highlight the potential of functional imaging as a biomarker of fragile X treatment response.

Intellectual disability is a defining characteristic of fragile X syndrome that is not ameliorated by currently available therapies. **Franklin *et al.*** (pages 198–206) show that administration of glycogen synthase kinase-3 inhibitors normalizes impaired long-term potentiation in the dentate gyrus and several cognitive tasks in a mouse model of fragile X syndrome. These data suggest that glycogen synthase kinase-3 inhibitors should be further studied as potential therapeutic agents for patients with fragile X syndrome.

Clinical Trial of AZD3480: Treatment for Adult Attention-Deficit/Hyperactivity Disorder

Potter *et al.* (pages 207–214) conducted a within-subjects, randomized, placebo-controlled, double-blind trial of AZD3480, a nicotinic agonist, in adults with attention-deficit/hyperactivity disorder (ADHD). They report that response inhibition and ADHD symptoms were significantly improved following two weeks of treatment with 50 mg of AZD3480. The dose was well-tolerated with no serious adverse events. These results support the potential use of nicotinic agonists as treatments for adult ADHD.

Antioxidant Supplementation for Smith-Lemli-Opitz Syndrome

Smith-Lemli-Opitz syndrome (SLOS) is caused by a defect in cholesterol biosynthesis and commonly manifests as autism spectrum disorder. In SLOS, accumulation of the cholesterol precursor, 7-DHC, and its oxidation products are critical for the emergence of pathophysiology. Using fibroblasts from human SLOS patients and a mutant mouse SLOS model, **Korade *et al.*** (pages 215–222) show that an antioxidant mixture and vitamin E supplementation decrease the accumulation of toxic 7-DHC-derived oxysterols and reverse disease-related gene expression changes.

Autism: Mathematic Strengths and Social Weaknesses

Autism is associated with social and communicative deficits, but it can also be accompanied by cognitive strengths. **Iuculano *et al.*** (pages 223–230) investigated mathematical abilities and brain activity patterns in children with high-functioning autism and IQ-matched typically developing children. Both groups engaged similar brain areas and overall levels of activation did not differ. However, the children with autism displayed superior numerical problem solving abilities, which was characterized by a unique pattern of brain organization. This insight could be used to improve educational, professional and social outcomes for individuals with autism.

Infants naturally show a preference for human contact, including faces and voices. Using eye-tracking, **Shic *et al.*** (pages 231–237) report that 6-month old infants later diagnosed with an autism spectrum disorder show difficulties attending to scenes containing faces and look away from informative facial features when the face is talking. These findings suggest that, even in the first months after birth, infants later diagnosed with autism are impaired in their ability to regulate attention to complex social stimuli, and may be experiencing an altered social experience at a critical developmental point.

Genetic Link Between Theta Activity and ADHD

ADHD is associated with increased reaction time variability and altered electrophysiological activity during cognitive control tasks. **McLoughlin *et al.*** (pages 238–247) investigated the underlying relationships in a sample of adolescent twins and found that theta activity, an electroencephalographic measure of cognitive control, is genetically related to both ADHD and reaction time variability. This finding supports a genetic link between the cognitive control system and ADHD, and identifies a genetically related neurophysiological marker of reaction time variability in ADHD.

White Matter Microstructure: Relationship Between Age and Cognition

Peters *et al.* (pages 248–256) examined the functional correlates of age-related differences in white matter microstructure across a wide age range (ages 8-68), using diffusion tensor imaging. From childhood into early adulthood, differences in fractional anisotropy of the cingulum were associated with executive functioning, whereas fractional anisotropy of the inferior fronto-occipital fasciculus was associated with visual learning and global cognitive performance via speed of processing. These findings indicate a role for protracted development of long-range white matter connections in neurocognitive maturation.

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