IN THIS ISSUE

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

Effects of Early-Life Stress

McLaughlin *et al.* (pages 1008–1015) report that children raised in deprived rearing environments display a developmental trajectory of frontal electroencephalographic asymmetry characterized by a prolonged period of greater activation in the right hemisphere as compared to the left. This developmental pattern predicted the onset of internalizing psychopathology in childhood. Exposure to adverse early-life environments can alter the trajectory of brain development in children, culminating in heightened risk for psychopathology, highlighting the importance of early interventions to mitigate the effects of these adverse environments.

Early-life stress is known to have long-term effects on the hypothalamic-pituitary-adrenal (HPA) axis, including reduced reactivity in adulthood. Compared to control children, **Ouellet-Morin *et al.*** (pages 1016–1023) report that maltreated/bullied children had lower cortisol responses to stress, which was associated with increased social and behavioral problems. These findings emphasize the need to better understand the mechanisms underlying this blunted reactivity and its potential impact on development and functioning.

Stress, Anxiety, and Serotonin

The early-life stress of maternal separation is associated with enhanced serotonin type 2 (5-HT2) receptor function, perturbation of neuronal circuit responses to stress and increased anxiety behavior. **Benekareddy *et al.*** (pages 1024–1032) now provide evidence that treatment with ketanserin, a 5-HT2 receptor antagonist, prevents the development of anxiety-related behavior and dysregulated gene expression in the prefrontal cortex observed in maternally separated rats.

Murrough *et al.* (pages 1033–1038) report reduced serotonin transporter availability within the amygdala in patients with posttraumatic stress disorder (PTSD) using positron emission tomography and the novel serotonin transporter-selective radiotracer [^{11}C]AFM. Lower serotonin transporter availability was associated with higher levels of anxiety and depression symptoms in PTSD patients. These results provide novel evidence for abnormalities in the serotonin transporter and amygdala function in PTSD.

Serotonin 1B (5-HT1B) receptor agonists exacerbate obsessive-compulsive disorder (OCD) symptoms in patients and induce OCD-like behavior in mice. **Shanahan *et al.*** (pages 1039–1048) show that orbitofrontal 5-HT1B receptors are necessary and sufficient to induce OCD-like behavior in mice, and that serotonin reuptake inhibitor pharmacotherapy reduces OCD-like behavior by desensitizing orbitofrontal 5-HT1B receptors. These findings suggest an essential role for orbitofrontal 5-HT1B receptors in OCD pathophysiology and treatment.

Attention bias modification, a technique to alter cognitive biases, is used as a therapy for anxiety disorders. **Fox *et al.*** (pages 1049–1054) randomized healthy adults to receive either positive bias or negative bias training. They found that individuals with a low-expression form of 5-HTTLPR, the serotonin transporter gene, relative to those with the high-expression form, developed stronger biases regardless of training type, suggesting that allelic variation influences differential sensitivity to interventions.

Cortisol Response Before Trauma Exposure

It has been suggested that dysregulated HPA axis function may be involved in the development of PTSD, but few studies have evaluated its function before trauma exposure. In this prospective study of police recruits, **Inslicht *et al.*** (pages 1055–1062) found that greater cortisol awakening response during academy training predicted greater peritraumatic dissociation and acute stress disorder symptoms over the first 3 years of police service, suggesting a possible pre-exposure risk factor for later symptoms.

Role Impairments Due to Insomnia

Hajak *et al.* (pages 1063–1073) examined associations of insomnia with days out of role in a large population-based sample. A significant association was found between insomnia and increased number of days out of role controlling for comorbid conditions. Insomnia accounted for 13.6% of all days out of role and had relatively stable associations with days out of role across subsamples of respondents who varied in number of comorbid conditions.

Exploring Anxiety Phenotypes

In an effort to identify phenotype-specific alterations of anxiety, **Filiou *et al.*** (pages 1074–1082) employed a quantitative proteomics and metabolomics approach to compare mouse lines with high, normal, and low anxiety-related behavior. They found protein, metabolite, and pathway differences, revealing a key role for mitochondria in the modulation of anxiety-related behavior. The data also provided a panel of potential candidate biomarkers for anxiety disorders.

Brain Alterations in Fear and Anxiety

Zarei *et al.* (pages 1083–1090) performed a structural and diffusion tensor magnetic resonance imaging study of pediatric-onset OCD to explore whether it constitutes a neurobiologically or clinically different subtype of OCD. Adolescents with OCD displayed a wide range of changes in gray matter, white matter, and subcortical structures compared to adolescent controls. These changes are broadly consistent with, but more extensive than, those identified in the adult OCD literature.

PTSD is associated with anterior cingulate cortex (ACC) abnormalities, which may in turn be associated with deficits in emotion regulation. The Val158Met polymorphism in the catechol-*O*-methyltransferase gene, which regulates dopamine in the frontal lobe, may moderate ACC integrity in PTSD. **Schulz-Heik *et al.*** (pages 1091–1096) tested this hypothesis in Vietnam and Persian Gulf War veterans with or without PTSD. Their findings indicate that the polymorphism moderates the effect of PTSD-related processes on ACC volume.

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