In This Issue

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

Corticotropin-Releasing Factor and Anxiety

Corticotropin-releasing factor (CRF), which is expressed in the amygdala, plays a role in stress and psychopathology. **Kalin *et al.*** (pages 345–355) used viral vector technology and multimodal neuroimaging to investigate the role of CRF amygdala systems in mediating pathological anxiety in nonhuman primates. They report that, compared with control monkeys, monkeys with chronic CRF overexpression had increased anxiety that led to functional and structural changes in anxiety-related neural circuits. This translational work implicates increased activity in CRF systems in the pathophysiology of primate anxiety.

Recent evidence in rodents has shown that stress-induced CRF promotes anxiety through decreasing the levels of the endocannabinoid anandamide and thereby reducing inhibitory tone in the amygdala. Using an imaging genetics strategy in young adults, **Demers *et al.*** (pages 356–362) show that genetic polymorphisms associated with differential anandamide (*FAAH*) and CRF (*CRHR1*) signaling modulate amygdala function and mediate risk for anxiety disorders. These data provide translational evidence that the molecular interactions between anandamide and CRF regulate amygdala function and anxiety.

Metabolic Syndrome and Posttraumatic Stress Disorder in Veterans

Posttraumatic stress disorder (PTSD) is associated with increased risk for metabolic syndrome, a cluster of conditions that increases risk for heart disease, stroke, and other serious health problems. Using magnetic resonance imaging in young U.S. military veterans who had been deployed, **Wolf *et al.*** (pages 363–371) found that PTSD is associated with greater metabolic syndrome severity, which, in turn, is associated with widespread reductions in cortical thickness. These results raise concerns about the potential for premature age-related health decline in this population, highlighting the need to identify effective interventions to reduce PTSD-related health consequences.

Trauma and Intergenerational Methylation

Epigenetic mechanisms have been implicated in the intergenerational transmission of stress effects in animals, but not yet in humans. **Yehuda *et al.*** (pages 372–380) examined methylation of *FKPB5*, a stress-related gene, in Holocaust-exposed parents and their adult offspring. Compared with Jewish control subjects, Holocaust survivors demonstrate higher methylation, whereas their offspring show lower methylation, at the same site. Methylation levels between parents and their offspring were correlated. These findings reflect the transmission of biological traits that might be trauma-related from parent to child, but the directional change suggests that offspring may make epigenetic modifications in response to trauma-induced alterations in the parent.

Neural and Behavioral Responses to Stress

Natural disasters increase risk of psychopathology, although most exposed individuals remain resilient. Using event-related potential data, **Kujawa *et al.*** (pages 381–389) report that neural reactivity to emotional images prospectively predicted children's internalizing and externalizing symptoms following Hurricane Sandy. Among children exposed to higher hurricane-related stress, increased reactivity to unpleasant images predicted greater externalizing symptoms, whereas increased reactivity to pleasant images predicted lower symptoms. These findings suggest that the neural processing of emotional information contributes to risk and resilience in response to stress.

Thigmotaxis is the tendency to stay close to walls when exploring an open space and is a reliable measure of fear in most animals. **Walz *et al.*** (pages 390–397) used precise global positioning data in an effort to translate this knowledge to humans. During both an open-field test and a natural city walk, patients with agoraphobia showed enhanced thigmotaxis compared with control participants. This study validates the translational potential of the open-field test and reveals that the evolutionary behavior of thigmotaxis is related to the pathologic fear of open spaces in humans.

Oxytocin and Stress

Evidence has been mixed regarding the impact of genetic variation in the oxytocin receptor gene (*OXTR*) on stress responding. **Dannlowski *et al.*** (pages 398–405) assessed brain imaging correlates of this interaction in healthy participants and identified a decrease of ventral striatum gray matter volume with increasing levels of maltreatment experience in *OXTR* G-allele homozygotes, but not A-allele carriers. Reduced ventral striatum gray matter volume was also associated with lower levels of prosocial traits. These data suggest that the detrimental effects of childhood maltreatment on brain structure are dependent upon *OXTR* variation.

Oxytocin can have a wide range of effects on anxiety. **Steinman *et al.*** (pages 406–414) found that social defeat stress increased the activity of oxytocin neurons in the bed nucleus of the stria terminalis in female, but not male, mice. Intranasal oxytocin administration reduced social interaction in female mice naïve to defeat, similar to levels observed in stressed female mice. These results suggest that sex-specific effects of stress on oxytocin neurons may contribute to sex-specific behavioral responses to stress.

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