In this Issue

Volume 71, Number 7, April 1, 2012

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

Stress-Related Pathophysiology

Increases in levels of the inflammatory cytokine interleukin-6 (IL-6) have been associated with stress. Here, **Garcia-Oscos *et al.*** (pages 574–582) demonstrate that IL-6 administration reversibly decreases the ratio between synaptic inhibition and excitation. The use of two animal models of stress in vivo produced similar results, which were inhibited by an IL-6 blocker of trans-signaling, suggesting that IL-6 plays a pivotal role in stress modulation of central synaptic function.

Using a learned helplessness paradigm in mice, **Zhou *et al***. (pages 583–592) report that inescapable foot shocks activated the transcription factor FoxO3a in brain. Activation was accompanied by a reduction of Akt activity and an increase in active glycogen synthase kinase-3β (GSK3β). Inhibition of GSK3β reduced shock-induced behaviors, FoxO3a nuclear accumulation, and FoxO3a transcriptional activity. These findings suggest that a GSK3β FoxO3a complex in brain is involved in stress-induced behavior disturbances, and disrupting this signaling complex may have implications in the treatment of stress-related disorders.

Imaging: Emotion Processing and Rumination

van Tol *et al.* (pages 593–602) investigated brain activation in patients with major depression, common anxiety disorders, or both during a memory task containing negative and positive words. Their findings show that depression, anxiety or both are associated with decreased activation of the hippocampus during the encoding of positive, but not negative, words. This was observed irrespective of illness severity, medication use, or regional brain volume and indicates that hippocampal blunting may represent a common vulnerability factor for depression and anxiety.

Using functional magnetic resonance imaging, **Hulvershorn *et al.*** (pages 603–610) investigated brain activation in response to negative emotional stimuli in unmedicated depressed, manic and euthymic bipolar subjects. An increased activation in mood generating regions was observed in all three phases of bipolar disorder compared to healthy controls, although there were regional differences across mood states. The cortical mood regulating areas showed abnormal activation particularly in the manic state.

Zhu *et al.* (pages 611–617) evaluated resting-state default mode network functional connectivity in first-episode, treatment-naive young adults with major depressive disorder and healthy controls. They report a pattern of dissociation in patients, with increased connectivity in anterior regions associated with rumination, but decreased connectivity in posterior regions associated with overgeneral autobiographical memory. These findings highlight the relationship between altered resting-state default mode network connectivity and self-related features of depression.

Depression: Functional Links in BDNF and ADCY7

Changes in brain-derived neurotrophic factor (BDNF) expression have been associated with mood disorders and cognitive decline. Using a combination of techniques, **Hing *et al.*** (pages 618–626) found that a polymorphism near *BDNF* occurs within a regulatory sequence (BE5.2) that modulates BDNF promoter 4 (BP4) activity following cell depolarization. However, the BE5.2 alleles differed significantly in their abilities to affect BP4 activity. Considering the critical role of BP4 in normal mood and cognition, this study suggests a functional link between *BDNF* gene regulation, mood disorders and cognitive decline.

Joeyen-Waldorf *et al.* (pages 627–632) identified similar changes in the expression of a gene, *ADCY7*, in the amygdala between a mouse model of a depressive-like syndrome (serotonin transporter knockout mice) and postmortem samples from human subjects with major depression. Translating these results, they show that *ADCY7* genetic variation in healthy human subjects biases threat-related amygdala reactivity. Together, these results implicate *ADCY7* in the modulation of mood regulation and, possibly, risk for depression.

Mechanisms: Hormones and Antidepressant Effects

Ovarian hormones may contribute to the increased vulnerability to depression in women as well as to antidepressant response. **Benmansour *et al.*** (pages 633–641) found that estrogen and/or progesterone administered acutely to rats inhibits the ability of selective serotonin reuptake inhibitors to block the serotonin transporter. Examining the receptor mechanisms underlying these effects, they also report that targeting of estrogen receptor beta or G-protein coupled receptor 30 may promote the beneficial effects of estrogen without its associated diminution of antidepressant efficacy.

Carrier and Kabbaj (pages 642–651) investigated the molecular mechanisms underlying the antidepressant effects of testosterone within the hippocampus, a fundamental structure in the etiology of depression. Testosterone replacement in gonadectomized adult male rats had antidepressant-like effects with no effects on hippocampal cell proliferation or survival. They also found a testosterone-dependent regulation of hippocampal extracellular signal-regulated kinase 2 expression, implicating ERK2 function in mediating the antidepressant effects of testosterone.

Forward Model Dysfunction in Obsessive-Compulsive Disorder

Using electroencephalography to test inhibitory gating, **Gentsch *et al.*** (pages 652–659) found reduced N1 suppression in the event-related brain potential during actively generated, relative to passively observed, feedback in patients with obsessive-compulsive disorder, suggesting a failure in the prediction and sensory gating of the consequences of their own actions. The increased mismatch between expected and actual outcomes may explain patients' feelings of incompleteness even after properly executed actions and the augmented search for control.

0006-3223/$36.00