IN THIS ISSUE

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

Gene Expression: QKI and Retinoic Acid

A new study of human brain tissue from suicide victims may provide insights into the neurobiology of suicide. **Klempan *et al.*** (pages 824–831) provide evidence for reduced QKI gene expression levels and levels of the QKI protein in the brains of suicide victims with major depression compared to controls, across multiple brain regions. No evidence of genetic or epigenetic changes in the vicinity of the QKI locus was identified. These alterations suggest that deficits in myelination-related pathways may underlie multiple psychiatric disorders.

Linking multiple levels of research, a new report may provide insights into the association between the administration of retinoic acid (RA), a derivative of Vitamin A commonly prescribed to treat acne, and depression. Investigating postmortem hippocampal tissue from individuals with affective disorders, RA signaling pathways in a rodent model of depression, and corticotropin-releasing hormone (CRH) expression in cultured neuroblastoma cells, **Chen *et al.*** (pages 832–839) found that RA receptor-α may play an important role in affective disorders by regulating the activity of hypothalamic CRH neurons.

Social and Cognitive Aspects of Behavior and Decision-Making

Chandler *et al.* (pages 840–846) provide new insight into impaired decision-making associated with bipolar disorder. The authors examined how people made choices when situations were framed as gains or losses. They found that bipolar disorder patients did not simply make risky choices. While they made more risky choices for increased gains when dilemmas were couched in positive terms, they were more conservative in their decision-making in order to avoid high-probability losses. Thus, bipolar disorder is associated with biased but not simply disinhibited risky decision-making.

There is new evidence that the interplay between the amygdala and the prefrontal cortex influences the way that people react to emotionally ambiguous facial expressions. **Blasi *et al.*** (pages 847–853) studied brain circuit activity with functional magnetic resonance imaging (fMRI) while people evaluated pictures of faces expressing various emotions. Their results suggest that increased amygdala reactivity and differential functional coupling with prefrontal regions shapes decisions made in response to socially ambiguous cues.

To evaluate the neural correlates of emotional instability, **Koenigsberg *et al.*** (pages 854–863) compared fMRI signals in patients with borderline personality disorder (BPD) and healthy individuals as they attempted to reduce the intensity of their responses to emotional stimuli by changing their appraisal of these stimuli. They found that when BPD patients tried to control their responses to emotional stimuli by obtaining emotional distance from these stimuli, they showed reduced activation in the intraparietal sulcus and dorsal anterior cingulate as well as reduced attenuation of amygdala activation. These findings suggest that BPD patients may inadequately engage brain regions involved in the cognitive control of emotion.

Envy and schadenfreude (gloating over another's misfortune) are social emotions, widely agreed to be a symptom of the social tendency to compare one's pay-offs with those of others. **Shamay-Tsoory *et al.*** (pages 864–870) evaluated the effects of oxytocin or placebo administration on the intensity of these emotions in participants who played a game of chance. They found that oxytocin increased feelings of envy and schadenfreude. These findings suggest a more complex role for oxytocin in social behavior than simply enhancing social affiliation.

Inflammation a Risk Factor for Fatigue

In a community-based study, **Cho *et al.*** (pages 871–878) found that high plasma levels of C-reactive protein (CRP), a biomarker of low-grade systemic inflammation, predicted fatigue five years later in the general population. Additionally, CRP predicted fatigue in the subgroup of participants without medical disorders, and a persistent elevation of CRP was more important than a transient elevation in predicting fatigue. This indicates that low-grade systemic inflammation, especially its persistent form, may be a risk factor for fatigue, unexplained by the co-existence of medical disorders.

Cortisol and Cognitive Deficits in Depression

Major depression is often associated with cognitive deficits and elevated levels of stress hormones. Investigating a sample of medication-free depressed patients and healthy controls, **Hinkelmann *et al.*** (pages 879–885) suggest that increased secretion of salivary cortisol is partly responsible for the cognitive deficits associated with depression.

Brain Network Dysfunction in Affective Disorders

Diffusion tensor imaging (DTI) enables the detection of microscopic structural abnormalities in white matter that might be associated with affective disorders. In their systematic review, **Sexton *et al.*** (pages 814–823) found that DTI studies of affective disorders consistently identify reduced anisotropy in the frontal and temporal lobes and tracts of subjects with affective disorders relative to control subjects.

A new study provides insights into how Behavioral Activation Therapy, a form of psychotherapy designed to promote the experience of positive emotions, works to treat depression. **Dichter *et al.*** (pages 886–897) studied brain circuit activation with fMRI in patients with depression and healthy controls as they performed a Wheel of Fortune game. The authors found that after three months of psychotherapy, 75% of the depressed patients showed substantial improvement in mood and increased activation of cortical, striatal, and limbic regions during the selection, anticipation, and receipt of reward. These findings suggest that this psychotherapy increases the activation of circuitry associated with motivation and reward as depressed patients begin to experience more pleasure in their lives.

Brody *et al.* (pages 898–901) had smokers with and without a history of depression smoke a cigarette during positron emission tomography involving the dopamine 2/3 radiotracer ^{11}C-raclopride. The authors found that smokers with a history of depression showed evidence of greater smoking-related displacement of ^{11}C-raclopride, indicating that they have heightened smoking-induced dopamine release compared to non-depressed smokers. Also, the greater the smoking related dopamine release, the more depression and anxiety the subjects experienced. Together, these data suggest that depressed smokers may be more vulnerable to continued smoking because of enhanced dopaminergic responses to smoking and the associated impact on mood and reward.

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