In This Issue

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

Addiction Neuroscience Framework

This review by **Kwako *et al.*** (pages 179–189) proposes a framework for an Addictions Neuroclinical Assessment that incorporates functional domains derived from the neural mechanisms of addiction. Three domains—executive function, incentive salience, and negative emotionality—tied to different phases in the cycle of addiction form the core functional elements of addictive disorders. The authors assert that measurement of these domains, by collecting multidimensional neuroimaging, genetic, and clinical data, will provide the foundation for an understanding of variation and shared mechanisms in addictive disorders.

Nicotine Cessation: Effects of Metabolism and Dopamine Function

Individual differences in the rate of nicotine metabolism affect smoking behavior and quitting success. To clarify the mechanisms underlying these associations, **Falcone *et al.*** (pages 190–197) utilized functional magnetic resonance imaging to examine neural responses to smoking cues during the first 24 hours of a quit attempt in treatment-seeking smokers. They report that normal, compared to slow, metabolizers of nicotine exhibited heightened abstinence-induced neural responses to smoking cues, which were associated with cravings to smoke. These data provide insight into the increased relapse rates of smokers with normal nicotine metabolism.

Rademacher *et al.* (pages 198–206) used positron emission tomography to examine the striatal dopamine system, which is known to play a central role in addiction, in smokers before and after abstinence. Compared with nonsmokers, smokers initially showed reduced capacity to synthesize dopamine, but these differences disappeared after 3 months of abstinence. These results suggest that alterations in presynaptic dopamine function in smokers can normalize after prolonged abstinence.

Cellular Mechanisms of Addiction

Astrocytes play an important role in nervous system function, yet the influence of cocaine use on astrocytes is still unclear. **Scofield *et al.*** (pages 207–215) used high-resolution fluorescent imaging of individual astrocytes to generate three-dimensional rendering and computations of morphometric features following cocaine self-administration and extinction in rats. They report that extinction is associated with reduced astrocyte size, reduced GFAP expression, and decreased colocalization with nucleus accumbens synapses. These data enhance our understanding of cocaine-induced adaptations in synaptic communication and plasticity, mechanisms that may underlie relapse vulnerability.

Disturbances in cannabinoid receptor signaling have been linked to emotional and cognitive dysregulation. In addition, hippocampal abnormalities are linked to psychopathology in schizophrenia. Using a combination of in vivo electrophysiology and behavioral pharmacology in rats, **Loureiro *et al.*** (pages 216–225) demonstrate that activation of CB_1 receptors in the ventral hippocampus modulates neuronal activity within the nucleus accumbens and regulates both emotional salience processing and social cognition. These data provide new insight into the role of cannabinoid transmission in neuropsychiatric disorders.

N-acetylcysteine for Drug Abstinence

Evidence suggests that *N*-acetylcysteine may promote abstinence from cocaine, but the mechanisms underlying its potential therapeutic benefit are unknown. In an animal model of addiction, **Ducret *et al.*** (pages 226–234) demonstrate that daily *N*-acetylcysteine treatment promotes abstinence in the face of punishment and restores control over cocaine intake at relapse in rats with long access to self-administration. These effects were associated with normalized levels of the glutamate transporter GLT-1 and plasticity mechanisms in the nucleus accumbens and dorsolateral striatum.

Reward and Learning in the Nucleus Accumbens

The opioid system, which is regulated in part by the RGS family of proteins, mediates the rewarding effects of drugs of abuse, but the precise contributing mechanisms are unclear. **Sutton *et al.*** (pages 235–245) demonstrate that RGS7 regulates behavioral responses to morphine, in addition to morphine reward in striatal, but not dopaminergic, neurons. RGS7 also moderates changes in neuronal excitability and synaptic plasticity induced by opioid exposure. Together, these data identify a novel role for RGS7 in the control of opioid-mediated reward.

Addiction is driven in part by powerful associations between drugs and environmental stimuli predictive of drug experiences. Neuronal ensembles, or small populations of sparsely distributed neurons, are thought to encode these types of learned associations. The study by **Whitaker *et al.*** (pages 246–256) reveals that when animals learn to associate environmental cues with the effects of cocaine, synapses within neuronal ensembles in the nucleus accumbens shell are silenced. This process may reduce the ability of these ensembles to represent new information about the environment, perhaps contributing to the persistence of addiction-related learning.

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