In this Issue

Volume 72, Number 10, November 15, 2012

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

Examining Risks of Δ9-Tetrahydrocannabinol Exposure

Adolescent marijuana use is associated with subsequent abuse of other drugs, but neurobiological mechanisms underlying such vulnerability are unknown. Using rodent models, **Tomasiewicz *et al.*** (pages 803–810) demonstrate that viral manipulations of the gene coding for the endogenous opioid, proenkephalin, in the nucleus accumbens, a key reward brain region, directly regulates adult heroin self-administration behavior associated with adolescent Δ9-tetrahydrocannabinol (THC) exposure. Additionally, they demonstrate that adolescent THC use alters epigenetic regulation of proenkephalin in adulthood that could underlie long-term behavioral disturbances.

Although cannabis consumption is a relatively common behavior, only a small proportion of users develop clinically significant or persisting psychotic symptoms. Genetic variation may contribute to cannabis psychosis susceptibility. This experiment built on the observation that the AKT1signaling pathway responds to THC and modulates signaling via dopamine receptors, thought to be involved in some forms of psychosis. **Di Forti *et al.*** (pages 811–816) carried out a case control study in first-episode psychosis patients and controls which demonstrated that the *AKT1* rs2494732 genotype influences the risk of psychotic disorders in cannabis users, thus confirming a recent report.

Review: Striatum's Role in Antisocial Behavior and Psychopathy

Glenn and Yang (pages 817–822) review evidence that abnormalities in the striatum may confer risk for antisocial behavior and psychopathic traits. The authors suggest that the volume of the striatum is increased in antisocial and psychopathic individuals, and that functioning is also increased in specific contexts. They also discuss genetic and environmental factors that may contribute to the development of abnormalities in the striatum.

Treatments for Alcohol Dependence

Dopamine is a chemical brain messenger critically important in reward and motivation. Long-term alcohol consumption leads to a dysregulated dopamine system. **Steensland *et al.*** (pages 823–831) found that OSU6162, a dopamine D2 receptor partial agonist, decreased voluntary ethanol intake and seeking as well as prevented relapse in rats chronically exposed to alcohol. OSU6162 may attenuate the rewarding properties of ethanol and may serve as a potential new medication for alcohol dependence.

Current medications for alcohol dependence, including naltrexone and acamprosate, are not effective for all patients. More research is needed to identify for whom these medications work best. In their clinical trial of multiple treatments for alcohol dependence, **Fucito *et al.*** (pages 832–838) found that alcohol dependent smokers had better drinking outcomes on naltrexone than placebo, whereas alcohol dependent nonsmokers had similar drinking outcomes regardless of treatment. Therefore, smoking status may be a factor for clinicians to consider when prescribing medication for alcohol dependence.

Reward, Behavior, and Cognition

Testosterone may be an early fetal programming mechanism influencing later susceptibility to several neuropsychiatric conditions. Using functional magnetic resonance imaging (fMRI) in 8–11 year old male children, **Lombardo *et al.*** (pages 839–847) found that increased fetal testosterone measured in amniotic fluid predicted reward system sensitivity to positively, compared to negatively, valenced facial cues. Furthermore, increased fetal testosterone predicted increased behavioral approach tendencies via its influence on the reward system. These results suggest testosterone may be an important fetal programming mechanism in conditions that differentially affect the sexes and affect the brain's reward system, emotion processing, and approach behavior.

The low level of response, or low sensitivity, to alcohol is a characteristic that predicts later alcoholism. Prior brain imaging analyses have indicated that low-response subjects process cognitive information differently. Using fMRI in low and high alcohol-responsive individuals, **Paulus *et al.*** (pages 848–855) demonstrate that the same unique problem-solving patterns are seen for an emotional-based task, indicating that the low level of response may reflect broad-based underlying thought processes.

Chronic cocaine use is associated with cognitive deficits that may increase the likelihood of relapse. **Gould *et al.*** (pages 856–863) examined the effects of current cocaine use and abstinence on brain function and cognition in monkeys with a long history of cocaine self-administration. Cocaine-experienced monkeys showed several deficits in cognitive performance compared to control animals and imaging studies documented several brain regions that responded differently during these tasks. Abstinence from cocaine significantly improved cognition. These data suggest that addiction treatments designed to enhance cognition may promote addiction recovery.

Body image disturbance is a core characteristic of anorexia nervosa (AN) and affected individuals also display visuospatial difficulties. **Favaro *et al.*** (pages 864–870) explored resting-state functional connectivity of brain networks involved in visuospatial and somatosensory processing in active and recovered women with AN and healthy controls. They found hypoconnectivity within the ventral visual network in both AN groups and a hyperconnectivity within the somatosensory network in the active AN group. These findings may help explain the lack of integration between visual and somatosensory perceptual information which contributes to body image disturbance.

Dose-Related Drug Effects: Methylphenidate and Salvinorin A

Ranganathan *et al.* (pages 871–879) characterized the dose-related behavioral, subjective, cognitive, endocrine, cardiovascular and electrophysiological effects of Salvinorin A, a highly selective kappa opiate receptor that is often used recreationally, in healthy humans. Salvinorin A produced psychotomimetic effects and perceptual alterations, increased plasma cortisol and prolactin, and reduced resting electroencephalogram spectral power, but did not produce euphoria, cognitive deficits or changes in vital signs. The effects had a rapid onset, were transient and of brief duration, and were not dose-related. Salvinorin A administration was well tolerated without acute or delayed adverse effects.

0006-3223/$36.00
http://dx.doi.org/10.1016/j.biopsych.2012.09.008

Despite its regular use in children, methylphenidate's effects on developing prefrontal circuitry are still not well understood. Examining neuronal excitability and synaptic transmission in developing prefrontal cortical neurons, **Urban *et al.*** (pages 880 – 888) found that methylphenidate produced significant depressive effects on pyramidal neurons in juveniles, while exerting excitatory effects in adult rats. Minimum clinically-relevant doses also produced depressive effects in juvenile rats. These findings suggest that juvenile prefrontal cortex is highly sensitive to methylphenidate and that doses outside the clinical range may result in long-lasting changes to prefrontal functions.