Biological Psychiatry

A Journal of Psychiatric Neuroscience and Therapeutics

In this Issue-August 1st

New Treatment Paths for Addiction

Using an animal model, **Chaudhri *et al.*** (pages 203–210) found that the context in which alcohol-associated cues are experienced influences the ability of those cues to trigger relapse. Specifically, re-exposure to the context in which the original association between the cue and alcohol was formed leads to relapse. When extinction of responding to the alcohol cue occurs in multiple distinct contexts, the power of the previous alcohol-associated context to renew cue-triggered alcohol-seeking is diminished.

Using rats genetically selected for their innate propensity to excessive alcohol drinking, **Economidou *et al.*** (pages 211–218) found that dysregulation of the nociceptin/orphanin FQ system in the amygdala contributes to the propensity to drink alcohol. The involvement of the amygdala in this process suggests that nociceptin/orphanin FQ may be involved in the stress-related vulnerability to drinking.

Drug dependence and withdrawal are clinically important features of opiate addiction and also represent a dramatic example of neural plasticity. **Sharf *et al.*** (pages 175–183) demonstrate molecular and neural mechanisms by which a specific neuropeptide signal, orexin, participates and promotes withdrawal symptoms. These findings raise the possibility that orexin receptor antagonists might play a role in the treatment of opiate withdrawal symptoms.

Tourette's: Corticospinal System and Comorbidity Genetics

Gilles de la Tourette syndrome (GTS) is characterized by tics (involuntary movements and noises). Using transcranial magnetic stimulation, **Orth *et al***. (pages 248–251) now report that GTS is associated with reduced cortical excitability (reflected in a more shallow input/output curve) and reduced short-interval cortical inhibition. Among patients diagnosed with GTS, greater cortical excitability was associated with more tics. Thus, reduced cortical excitability may be, in some way, protective against tic behaviors.

Grados *et al.* (pages 219–225) performed a latent class analyses on a large sample of pairs of siblings where one or both of the siblings carried the diagnosis of GTS to identify subtypes of this disorder. They found evidence supporting the existence of the following subtypes: 1) GTS alone; 2) GTS with obsessive-compulsive disorder (OCD) and; 3) GTS with OCD and attention-deficit/hyperactivity disorder (ADHD). Only the GTS + OCD + ADHD class was highly heritable.

Reward System Dysfunction

Alcoholism, as with other addictive behaviors and substance abuse, may be linked with dysfunction of the reward system. Using magnetic resonance imaging (MRI), **Makris *et al.*** (pages 192–202) measured volumes of reward system brain regions in non-drinking alcoholics and found structural deficits, associated with years of heavy drinking and memory function. However, the severity of the brain structure deficits improved with length of abstinence from drinking.

Mice with targeted deletion of the hypothalamic neuropeptide, melanin-concentrating hormone (MCH), have a metabolic phenotype associated with increased energy expenditure and resistance to diet-induced obesity. In this study, **Pissios *et al.*** (pages 184–191) show that the mesolimbic dopamine system (reward circuitry) is also dysregulated in these mice leading to abnormal responses to drugs and food. These data link homeostatic (hypothalamus) and reward-related (mesolimbic dopamine system) circuits.

Obestatin Levels in Obesity and Anorexia

Nakahara *et al.* (pages 252–255) investigated fasting obestatin, which is reported to inhibit appetite and gastric motility, and ghrelin levels in patients with obesity and anorexia nervosa (AN). Obestatin was negatively correlated with body mass index, glucose, insulin, leptin, and homeostasis model assessment of insulin resistance (HOMA-R), and was positively correlated with acyl-ghrelin and desacyl-ghrelin. Both obestatin and ghrelin were increased in the AN group and decreased in the obese group. These findings suggest that obestatin is a nutritional marker reflecting body adiposity and insulin resistance.

Memory Functioning: Roles of Dopamine and Oxytocin

Dopamine neurotransmission modulates hippocampal and prefrontal cortex neuronal activity during memory performance. Using functional MRI, **Bertolino *et al.*** (pages 226–234) demonstrate that there are interactive effects of variation in two dopamine-related genes, the gene coding for the dopamine transporter (DAT) and the dopamine-metabolizing enzyme catechol-*O*-methyltransferase (COMT), upon hippocampal and prefrontal cortical activation during memory tasks.

Oxytocin has been shown to enhance social recognition in animals. **Guastella *et al.*** (pages 256–258) administered oxytocin or a placebo to human males and then presented happy, angry, and neutral human faces. Participants returned the following day to make memory judgments for seen and never seen faces. Results showed that oxytocin enhanced memory for happy faces over angry and neutral faces, indicating that it may enhance bonding in humans by strengthening the encoding of positive social information.

0006-3223/08/$34.00

BIOL PSYCHIATRY 2008;64:171–172

Prepulse Inhibition is Modulated by D_3 Receptors

Dopamine is released by brain cells to signal an important event but certain dopamine receptors (D_3) inhibit its release. **Roussos *et al.*** (pages 235–240) show for the first time that our ability to detect and process important sensory information is influenced by variation in a gene that codes for the D_3 dopamine receptor. People with the gene variant which produces the most active D_3 receptor are faster in detecting, but worse in processing, salient information from among distracting stimuli.

MRI Findings of PINK1 Carriers

Mutations in the *PINK1* gene can cause psychiatric and movement-related symptoms of Parkinson's disease (PD). **Reetz *et al.*** (pages 241–247) performed structural high-resolution MRI, which revealed specific cerebral gray matter degeneration of limbic and frontal structures in *PINK1* mutation carriers which were also correlated with clinical psychiatric syndrome scores. The results support the hypothesis that limbic and frontal gray matter alterations could explain the various psychiatric features observed in *PINK1* mutation carriers.