



American College of Neuropsychopharmacology

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Social Stressors Can Be Powerful Triggers for Cocaine Use

Scientists Study How Brief Stress Can Intensify the Desire for Cocaine

NASHVILLE, TN (December 7, 2009) – Rodents that are exposed to episodes of brief social stress become sensitized to the effects of cocaine and are more likely to binge on the drug, according to an abstract presented at the American College of Neuropsychopharmacology's (ACNP) annual meeting today. Researchers have identified a promising model for explaining the effects of brief versus prolonged stress episodes in the brain's reward system.

Dr. Klaus Miczek and his team at Tufts University studied two different types of social stress and their effects on areas of the brain associated with inhibition, memory and pleasure. They examined the social stress response by measuring changes in two chemicals: BDNF, a factor that promotes nerve cell growth and is important for learning and memory, and dopamine, a neurotransmitter linked with pleasure and novelty in the brain's mesolimbic system. They wanted to see how the brain reacts to differently-timed stressful situations and whether this reaction would affect the self-administration of cocaine.

Scientists created two models to simulate brief and prolonged stress. In the first model, over 10 days, individual rats were exposed to four brief periods with an aggressive rat in an adjacent cage. To simulate prolonged stress, over a five-week period, a subordinate rat was placed in a special cage so it could see, hear and smell a dominant rat, leaving it in constant fear of attacks. In both cases, the rats could self administer cocaine by pressing a bar for intravenous injections.

Researchers were surprised to find big differences in how different lengths of exposure to stress affected the brain's reward system. "Rats that were exposed to episodes of brief stress had a greater response to cocaine and were more likely to binge on the drug," said Klaus Miczek, PhD, Tufts University and ACNP member.

Miczek explained that brief stress increased BDNF and dopamine activity in the brain, which in turn led to a greater "high" from cocaine. However, rats exposed to prolonged stress released lower levels of dopamine, and were less likely to self administer cocaine, which produces a "high" by increasing the dopamine effects. In fact, they experienced signs of depression including a lack of pleasure exhibited by refusing sugar

and having poor weight gain. They also showed a blunted dopamine response to cocaine. They became passive and experienced a lower dopamine release.

“These two extremes indicate that this is a very promising model to study the effects of brief stress episodes in contrast to prolonged episodes that are continuous and unpredictable,” added Miczek.

The study of social stress promises to translate readily to other species including humans. Social stresses induce biochemical or cellular changes in the brain and an understanding of these changes can help identify targets for treatment. Among the new features of the current research is the focus on intracellular signaling pathways that regulate gene expression and how they are profoundly altered by episodes of social stress. These findings may help lead to the development of medications that can prevent or reverse the intensifying effects of stress on cocaine use.

Miczek cautioned that these studies need to be replicated in other species – and ultimately in the human population. Miczek’s work is funded by the National Institute on Drug Abuse.

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ACNP, founded in 1961, is a professional organization of more than 700 leading scientists, including four Nobel Laureates. The mission of ACNP is to further research and education in neuropsychopharmacology and related fields in the following ways: promoting the interaction of a broad range of scientific disciplines of brain and behavior in order to advance the understanding of prevention and treatment of disease of the nervous system including psychiatric, neurological, behavioral and addictive disorders; encouraging scientists to enter research careers in fields related to these disorders and their treatment; and ensuring the dissemination of relevant scientific advances.