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Gene therapy reduces cocaine use in rats

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Researchers at the U.S. Department of Energy's Brookhaven National Laboratory have shown that increasing the brain level of receptors for dopamine, a pleasure-related chemical, can reduce use of cocaine by 75 percent in rats trained to self-administer it. Earlier research by this team had similar findings for alcohol intake. Treatments that increase levels of these chemicals - dopamine D2 receptors -- may prove useful in treating addiction, according to the authors. The study will be published online April 16 and will appear in the July 2008 issue of *Synapse.*

"By increasing dopamine D2 receptor levels, we saw a dramatic drop in these rats' interest in cocaine," said lead author Panayotis (Peter) Thanos, a neuroscientist with Brookhaven Lab and the National Institute on Alcohol Abuse and Alcoholism (NIAAA) Laboratory of Neuroimaging. "This provides new evidence that low levels of dopamine D2 receptors may play an important role in not just alcoholism but in cocaine abuse as well. It also shows a potential direction for addiction therapies."

The D2 receptor receives signals in the brain triggered by dopamine, a neurotransmitter needed to experience feelings of pleasure and reward. Without receptors for dopamine, these signals get "jammed" and the pleasure response is blunted. Previous studies at Brookhaven Lab have shown that chronic abuse of alcohol and other addictive drugs increases the brain's production of dopamine. Over time, however, these drugs deplete the brain's D2 receptors and rewire the brain so that normal pleasurable activities that stimulate these pathways no longer do - leaving the addictive drug as the only way to achieve this stimulation.

The current study suggests that cocaine-dependent individuals may have their need for cocaine decreased if their D2 levels are boosted. Thanos' lab previously demonstrated dramatic reductions in alcohol use in alcohol-preferring rats infused with dopamine D2 receptors. Thanos hypothesized that the same would hold true with other addictive drugs.

The researchers tested this hypothesis by injecting a virus that had been rendered harmless and altered to carry the D2 receptor gene directly into the brains of experimental rats that were trained to self-administer cocaine -- the same technique used in the earlier alcohol study. The virus acted as a mechanism to deliver the gene to the nucleus accumbens, the brain's pleasure center, enabling the cells in this brain region to make receptor proteins themselves.

The scientists examined how the injected genes affected the rats' cocaine-using behavior after they had been taking cocaine for two weeks. After receiving the D2 receptor treatment, the rats showed a 75 percent decrease in self-administration of the drug. This effect lasted six days before their cocaine self-administration returned to previous levels.

"This adds another piece to the puzzle of the complex role of dopamine D2 receptors in addiction," said Thanos.

Source: Brookhaven National Laboratory