Nicotine triggers the same brain reward circuitry as opiates

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In experiments with mice, researchers have found that nicotine triggers the same neural pathways that give opiates such as heroin their addictively rewarding properties--including associating an environment with the drug's reward. However, unlike opiates, nicotine does not directly activate the brain's opiate receptors, but activates the natural opioid reward pathway in the brain.

The researchers, led by Julie Blendy of the Transdisciplinary Tobacco Use Research Center (TTURC) at the University of Pennsylvania, said their findings suggest more effective ways that opiate blockers could be used to help smokers quit.

In their experiments reported in the June 16, 2005, issue of Neuron, the researchers administered nicotine to mice and analyzed the levels of a protein called CREB--known to control genes involved in the reward pathway of opiates and other abused drugs. They found that not only was CREB activated in the reward regions of the nicotine-treated animal's brains, but also that the drug naloxone, which blocks the opiate receptors, blocked CREB activation. Also, mutant mouse strains lacking the opioid receptor did not show an increase in CREB activity when they received nicotine.

The researchers also studied the relationship among nicotine, the environment, and this reward pathway. They conditioned mice to associate a specific test chamber with receiving nicotine, finding that the mice would prefer to stay in that chamber when given a choice. The

researchers found that just placing the conditioned mice in the chamber activated CREB. They also found that naloxone blocked this conditioned increase in CREB, and that mutant mice lacking CREB or pretreated with naloxone did not show any reward response to nicotine.

However, naloxone did not block the chamber choice of mice conditioned with cocaine, found the researchers, indicating that cocaine activates the brain reward pathway in a different way from nicotine and opiates.

"The present results demonstrate that nicotine-associated environmental stimuli can activate the same molecular signal transduction molecules as the drug itself," wrote Blendy and her colleagues. They wrote that the activation of CREB "is evident not only after acute and repeated nicotine administration, but also following exposure to an environment in which the animal has previously received nicotine."

The researchers noted that clinical studies of opioid receptor blockers to relieve cigarette cravings "so far have produced mixed results, ranging from ineffectiveness at smoking cessation to mild reduction in the desire to smoke."

The researchers wrote that their findings "suggest that the timing and context of opioid receptor antagonist administration are critical for determining the effectiveness of blocking nicotine reward . . . . Given the results reported here, clinical studies designed to evaluate administration of opioid antagonists just prior to cues associated with smoking could lead to a more promising treatment regimen."

Source: Cell Press