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Rat study suggests why teens get hooked on cocaine more easily than adults

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New drug research suggests that teens may get addicted and relapse more easily than adults because developing brains are more powerfully motivated by drug-related cues. This conclusion has been reached by researchers who found that adolescent rats given cocaine – a powerfully addicting stimulant – were more likely than adults to prefer the place where they got it. That learned association endured: Even after experimenters extinguished the drug-linked preference, a small reinstating dose of cocaine appeared to rekindle that preference – but only in the adolescent rats.

The research, performed at McLean Hospital, Harvard Medical School's largest psychiatric facility, was reported in the April issue of *Behavioral Neuroscience*, published by the American Psychological Association.

Evidence that younger brains get stuck on drug-related stimuli reinforces real-world data. Epidemiological studies confirm that of people in various age groups who experiment with drugs, teens are by far the most likely to become addicted. Thus, the new findings may be useful in developing new treatments for youthful addiction.

In the study, psychologists Heather Brenhouse, PhD, and Susan Andersen, PhD, who directs McLean's Developmental Psychopharmacology Laboratory, introduced rats that were 38 or 77 days old (equivalent to 13 or 20 human years) to an apparatus with one central and two larger side chambers that had different flooring, wall colors and lighting. For three days in a row, the researchers injected the

rats with saline solution in the morning and placed them in one side chamber for an hour. Four hours later, they injected them with a preference-forming dose of cocaine (either 10 or 20 mg per kg of weight, to assess two doses known to be habit-forming) and placed them in the opposite-side chamber for an hour. Conditioning this way kept the rats from associating the symptoms of withdrawal with the non-drug chamber.

On Day 4, the researchers let the rats freely explore the entire apparatus in a drug-free state for 30 minutes, to test for "conditioned place preference" for the chamber where they got cocaine. Brenhouse and Andersen calculated how long each rat spent in the drug-paired side relative to total time spent on either side. They repeated the procedure every 24 hours until each animal's place preference was extinguished, when the time they spent in the drug-paired chamber was cut in half – suggesting no lingering preference for either side.

Relative to adults, adolescent rats required around 75 percent more trials to extinguish a preference for the place where they were given the drug.

After each rat's last extinction trial, the researchers waited 24 hours, injected a low 5 mg/kg "priming" dose of cocaine, and put it back in the apparatus to test for place preference. During this test for "reinstatement" of extinguished preferences, adolescent rats showed a significantly greater renewed preference than did adults for the drug-paired chamber. Those that had originally learned on a 10 mg/kg dose of cocaine showed 40 percent greater reinstatement than the few adult rats that showed a place preference at the lower dose.

Interestingly, both adolescent and adult rats who were conditioned at the 20 mg/kg dose renewed their place preference to a similar degree. Brenhouse and Andersen view this as a sign that adolescents form stronger memories for even less potent rewards. Thus, they wrote,

"Adolescent vulnerability to addiction involves robust memories for drug-associated cues that are difficult to extinguish." They speculate that the context of drug use is more salient to adolescents, perhaps because the frontal cortex is still developing.

Brenhouse and her fellow researchers found in prior studies that during adolescence, dopamine – a neurotransmitter that signals "reward" – may trigger more focused messages traveling from the frontal-cortex area involved with learning to a central area involved with reward and addiction. This biochemical express lane, which appears to fade as the brain matures, may result in the adolescent brain's capacity for building stronger memories for rewarding stimuli -- including the people, places and events associated with addicting drugs.

This heightened salience, say Brenhouse and Andersen, "may require atypical strategies for drug abuse intervention during the adolescent period, such as extended treatment that involves substitution with different rewards, for example, exercise or music." Brenhouse wonders whether teens may learn best when rewards are involved. "Harnessing their acute ability to learn well and form strong associations with stimuli that predict rewards may be helpful," she says. "In addition, it may be important to realize that adolescents might need longer treatment programs."

Source: American Psychological Association