

Emotional 'bummer' of cocaine addiction mimicked in animals

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Cocaine addicts often suffer a downward emotional spiral that is a key to their craving and chronic relapse. While researchers have developed animal models of the reward of cocaine, they have not been able to model this emotional impact, until now.

Regina Carelli and colleagues report experiments with rats in which they have mimicked the negative affect of cocaine addiction and even how it drives greater cocaine use. They said their animal model could enable better understanding of the emotional motivations of cocaine addiction and how to ameliorate them.

The researchers reported their findings in the March 13, 2008, issue of the journal *Neuron*, published by Cell Press.

The researchers started with the well-known phenomenon that rats will tend to avoid a taste that is paired with self-administration of a drug such as cocaine. Also, it was known that the greater avoidance of the taste was associated with greater drug self-administration.

In their experiments, the researchers squirted a grape- or orange-flavored sweet solution into the mouths of rats. After squirting one flavor, the rats were given a chance to press a lever to obtain cocaine; after the other taste, pressing the lever delivered only a saline solution.

The researchers measured the rats' response to the flavors by analyzing video of their expressions and measuring the electrical activity of a muscle involved in the licking response.

They found that the rats developed an aversion to the normally enjoyable taste that was associated with cocaine, compared to the saline-associated taste. They also found that the greater the measured aversion, the quicker and more

frequently the rats pressed the lever to obtain cocaine.

The researchers also found that the aversive taste excited activity in a brain region called the nucleus accumbens, which is associated with expression of motivated behaviors.

The researchers wrote that their findings demonstrated that it is possible to induce a "negative affective state" in the animals that predicts the motivation to take cocaine. They said their finding "also is provocative because it bridges two well-known drug-abuse phenomena. The first, that drug-associated cues elicit drug seeking, has been well documented in humans and animal models. The second, that negative affect drives drug seeking, has been well described by human addicts but is difficult to model in animals. The importance of this study lies in this animal model's potential to define and then ameliorate the motivational properties of negative affect evoked by drug-associated stimuli and thereby decrease the drive for the drug," they wrote.

In a preview of the article in the same issue of *Neuron*, Donna Calu and Geoffrey Schoenbaum wrote that the relationship between the taste aversion and increased drug taking "lends strong support to the proposal that triggering of aversive affective states by drug-associated cues plays a role in drug-seeking behavior and provides a novel behavioral model in which to investigate the circuit basis of this phenomenon."

Source: Cell Press

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