Neuropsychopharmacology www.nature.com/npp

RESEARCH HIGHLIGHT

Not worth the wait: cocaine alters reward processing in the nucleus accumbens

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Neuropsychopharmacology (2018) 43:2333–2334; https://doi.org/10.1038/s41386-018-0094-9

Poor decision making is a hallmark of addiction. This is clear from the fact that addicts accept many risks and make great sacrifices in order to use drugs like cocaine despite the fleeting pleasure they get from this activity. However, long-term drug users are also prone to making poor choices in other areas of their life, like engaging in unprotected sex and reckless driving. This fits with a growing body of laboratory research showing that cocaine addicts process the costs and benefits of their actions differently than healthy non-users, and are specifically more likely to accept a small but immediate reward rather than wait for a large reward—a bias indicative of *impulsive decision making* (for review, see ref. [1]).

Determining the behavioral and neural mechanisms of impulsive decision making is an important goal of addiction research, and recent studies have shown that merely allowing rats to self-administer cocaine disrupts the way they make decisions about non-drug rewards [1], suggesting that repeated drug exposure leads to long-term alterations in the function of neural circuits that normally mediate adaptive decision making. In the current issue of *Neuropsychopharmacology*, Burton et al. [2] build on this body of work to investigate whether cocaine-induced changes in decision making are accompanied by changes in the way rewards are processed by the nucleus accumbens (NAc), a region that is strongly implicated in both decision making and cocaine addiction.

Rats in this study were trained to perform a clever behavioral task in which they were asked to choose between two sucrose rewards that differed in value in one of two ways: for some training blocks, rewards differed only in the time between action selection and reward delivery (short- vs. long-delay trials), whereas for other blocks, both rewards were delivered quickly, but differed in size (small- vs. large-reward trials). Prior to the final testing phase, separate groups of rats were trained to self-administer cocaine or sucrose pellets on a different task, allowing the researchers to investigate how this drug-taking experience impacted rats' ability to make decisions based on differences in reward delay and size. Consistent with a bias towards impulsive choice, cocaine-exposed rats were highly sensitive to delays in reward delivery, showing a stronger preference for the short-delay reward than drug-naive rats when choosing between it and the long-delay reward. Cocaine-exposed rats also made more mistakes when they were instructed to choose the lesser of the two rewards, regardless of whether its low value was related to its delay or size. Such findings fit with previous reports from this group indicating that chronic cocaine intake makes rats more sensitive to differences in reward value, particularly when this involves an increase in waiting time [3].

The crucial step forward by Burton et al. [2] was to show that cocaine-exposed rats also exhibited changes in task-related NAc activity. In the drug-naive (sucrose-only) group, many NAc neurons increased their rate of firing during periods of reward retrieval and consumption, and this activity was strongly modulated by *reward value*, in that high-value rewards elicited more rapid firing than low-value rewards, regardless of whether their value was based on a difference in reward delay or size. In addition to encoding value, NAc neurons also exhibited *directional-tuning*, in that they fired at a higher rate when a reward was delivered in their 'preferred' location, either the left or right food well. Now, given that the cocaine group showed greater behavioral sensitivity to differences in reward value, one might expect their NAc neurons to show even more extreme value encoding, perhaps firing at an exaggerated rate during the collection of high-value rewards, but just the opposite was observed. The cocaine group had significantly fewer reward-responsive NAc neurons (21% vs. 30%, for control group), and those reward-responsive neurons that were identified in this group tended to show *weaker* value encoding and directional tuning. The one important exception to this pattern was that NAc activity in the cocaine group showed steeper delay discounting. Specifically, reward-responsive neurons in the NAc of cocaine-exposed rats were highly sensitive to delays in reward delivery, with firing rates tracking relatively subtle changes in the waiting time for delayed rewards.

This report by Burton et al. [2] helps fill in our understanding of the neural processes associated with poor decision making in addiction. Their findings complement other recent findings that cocaine-exposed rats show weaker phasic NAc *dopamine release* in response to non-drug rewards [4], suggesting that reinforcement learning processes in this region are disrupted by long-term drug use. Of course, because such findings are correlational in nature, it remains to be experimentally determined if the effects of repeated cocaine intake on decision making are causally mediated by attenuated reward-related neural activity (or dopamine release) in the NAc. Furthermore, the dysregulation of NAc function described by Burton et al. [2] is likely to be only one piece of the puzzle. Determining how drug-induced neuroadaptations in the NAc relate to changes in the function of other structures implicated in adaptive decision making, such as the prefrontal cortex and dorsal striatum, should be an important aim for future research.

It is also worth noting that Burton et al. [2] found that cocaine-exposed rats were generally *quicker* to make decisions, an effect that was apparent across all trial types. This finding is more in line

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Received: 1 May 2018 Accepted: 2 May 2018
Published online: 29 May 2018

with an *exaggerated* motivational response (or a failure to inhibit behavior) than a *deficit* in reward processing. Although the authors did not describe any neural correlates of this behavioral phenomenon, previous studies have shown that repeated cocaine exposure increases rats' motivational response to food-paired cues, an effect that has been linked to potentiated—rather than diminished—task-related neural activity [5] and dopamine release [6] in the NAc. Such findings speak to the multifaceted nature of drug addiction—a disorder that involves complex, bidirectional alterations in emotional and motivational function. While this study by Burton et al. [2] sheds new light on processes underlying the prolonged effects of cocaine exposure on delay discounting, there is much left to learn about how such drug experiences impact the control of motivated behavior, and why they affect some NAc functions so differently than others.

ACKNOWLEDGEMENTS

The authors are supported by the NIH grants AG045380, DK098709, and MH106972.

ADDITIONAL INFORMATION

Competing interests: The authors declare no competing interests.

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