American College of Neuropsychopharmacology

www.nature.com/npp

RESEARCH HIGHLIGHT

The complexity of drug choice: rats prefer alcohol over social interaction

David N. Kearns[1] ✉

Neuropsychopharmacology (2023) 48:583–584; https://doi.org/10.1038/s41386-022-01469-0

Recently, there has been much interest in choice between drugs and social reinforcement. This interest was stimulated by the fascinating results of experiments showing that, when given a choice, rats greatly preferred brief periods of social interaction with a fellow rat over intravenous infusions of drugs including methamphetamine and heroin, independently of drug dose [1]. Even after extended or intermittent access drug self-administration, procedures which result in addiction-like behavior, introduction of social interaction as an alternative to heroin or methamphetamine caused rats to abstain from the drug. That rats, even ones showing signs resembling addiction, would give up these drugs when offered the chance to interact with a peer suggests that social interaction is an extremely powerful reinforcer in rats.

In a new study published in this issue of *Neuropsychopharmacology*, Marchant et al. [2] report the intriguing and unexpected finding that when given a mutually exclusive choice between unsweetened oral alcohol and social interaction, rats preferred alcohol. The authors themselves noted that they were surprised by this outcome and performed a series of tests to further investigate the effect. When it was the only reinforcer available, social interaction supported operant response rates well above inactive lever response rates, confirming that it was an effective reinforcer. Yet persistent preference for alcohol was observed when pitted against social interaction in choice. This preference could only be abolished when the price of alcohol (i.e., the effort to obtain it) was greatly increased, when the concentration of alcohol was reduced to zero or near zero, or when rats were given free access to alcohol prior to the choice session. Marchant et al.'s rigorous and systematic investigations into the effect confirm that it is a reliable one.

Marchant et al. discuss several possible explanations for the seemingly difficult to reconcile findings that rats prefer alcohol over social reinforcement, but prefer social reinforcement over other drugs that have been tested. The most intriguing of these is that choice depends on the specific interactions between the particular drug and non-drug alternative offered. Indeed, previous experiments have shown that the experience of a drug in a choice situation can alter the value of the non-drug option and thereby greatly affect the allocation of behavior between the drug and non-drug alternative [3]. Specifically, choosing between cocaine and saccharin while under the influence of cocaine resulted in exclusive cocaine choice in rats, due to the anorexic effects of cocaine devaluing the saccharin alternative; in contrast, heroin appeared to increase the value of saccharin, leading not to exclusive preference but instead to regular consumption of both reinforcers (and increased consumption of saccharin when a large heroin dose was used) [3].

It is likely that such reinforcer interactions in choice situations are bidirectional—i.e., non-drug alternatives may also alter the value of the drug reinforcer. Of relevance to Marchant et al.'s findings, there is evidence suggesting that brief opportunities to socialize may increase motivation for alcohol. Previous research found that occasional, experimenter-controlled presentations of a social peer, using a guillotine door and screen arrangement like that used in recent social choice studies, greatly increased unsweetened alcohol drinking in rats [4]. In Marchant et al.'s study, subjects did not exclusively choose alcohol and so also experienced occasional presentations of a social peer—the difference was that the subjects, rather than the experimenter, controlled when those would happen. It may be that occasional opportunities to socialize—or perhaps even just hearing and smelling the partner rat behind the door—increases the reinforcing value of alcohol. This type of reinforcer interaction could potentially explain the alcohol preference observed by Marchant et al. in their study.

In the dozen years since Ahmed's [5] seminal paper describing the validity problem in experiments where taking the drug is the only option, many studies using drug vs. non-drug alternative choice procedures have been published. The more we learn about the factors controlling drug choice, the more we see how complex choice behavior can be. Established theoretical frameworks for understanding choice behavior (e.g., the Matching Law) provide some insight, but they were based on observations of subjects choosing between the same reinforcer (usually food) available on different schedules, in different amounts, or after different delays. Choice between two reinforcers of different kinds, as is studied in drug vs. non-drug reinforcer choice experiments, is more complicated. Not only does such choice depend on the price, amounts, and delays to the two options, but, as suggested by recent studies (including the one by Marchant et al.) choice behavior will also depend on the particular drug and non-drug alternatives offered and the way in which they interact, with each potentially enhancing or diminishing the reinforcing value of the other.

The potential complexity of choice is great, even with just two choice options, as used in current animal models of drug choice. The human drug-taking situation may obviously involve many more options, thereby multiplying the number of factors determining drug choice. Understanding behavior within such a

[1]Department of Psychology, American University, Washington, DC, USA. ✉email: kearns@american.edu

Received: 20 September 2022 Accepted: 21 September 2022
Published online: 5 October 2022

complex system will be a formidable task, but a necessary one if we are to have a complete understanding of drug-taking behavior. Research like that by Marchant et al.'s study published in this issue take us closer to that goal.

REFERENCES

1. Venniro M, Zhang M, Caprioli D, Hoots JK, Golden SA, et al. Volitional social interaction prevents drug addiction in rat models. Nat Neurosci. 2018;21:1520–9.
2. Marchant NJ, McDonald AJ, Matsuzaki R, van Mourik Y, Schetters D, De Vries T. Rats choose alcohol over social reward in an operant choice procedure. Neuropsychopharmacology. 2022 https://doi.org/10.1038/s41386-022-01447-6.
3. Vandaele Y, Cantin L, Serre F, Vouillac-Mendoza C, Ahmed SH. Choosing under the influence: a drug-specific mechanism by which the setting controls drug choices in rats. Neuropsychopharmacology. 2016;41:646–57.
4. Tomie A, Uveges JM, Burger KM, Patterson-Buckendahl P, Pohorecky LA. Effects of ethanol sipper and social opportunity on ethanol drinking in rats. Alcohol Alcohol. 2004;39:197–202.
5. Ahmed SH. Validation crisis in animal models of drug addiction: beyond non-disordered drug use toward drug addiction. Neurosci Biobehav Rev. 2010;35:172–84.

AUTHOR CONTRIBUTIONS

DK wrote and edited the manuscript and approved the final version.

FUNDING

This work was supported by NIDA award DA055572.

COMPETING INTERESTS

The author declares no competing interests.

ADDITIONAL INFORMATION

Correspondence and requests for materials should be addressed to David N. Kearns.