## **Editorial**

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# Why did the kitten cross the road? A meditation on positive versus negative reinforcement in addiction

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Why did the kitten cross the road? One possibility is that there is something better on the other side (e.g., warm sun or sun-paired cue) (Box 1a). A second possibility is that there is something lacking or depleting on the first side (e.g., temperature sapping cold). Distinguishing between these possibilities is challenging and cannot be answered by experimental designs using positive versus negative reinforcement.<sup>1-3</sup> If the kitten is more likely to cross the road following temperature changes on the opposite side, it is called positive reinforcement. If the behaviour is emitted following temperature changes on the starting side, it is called negative reinforcement. Yet in both scenarios the kitten is approaching the warmer side.

So, why did the kitten cross the road? As a start, the kitten is unlikely to cross unless it has evidence that the other side is preferable; i.e., in and of itself, cold temperature might trigger a motivational state, but it will lack direction unless the kitten has either previously associated the other side with warmth or can feel the radiating heat.

Does the magnitude of temperature differential matter? If the difference is small, there might be little motivation to cross. If the difference is large, the motivation to approach could be greater. Most work suggests that this differential is more important than the absolute values, a phenomenon called a "contrast effect." Indeed, the relative difference between options is more important than the absolute reward for prompting nucleus accumbens dopamine release<sup>4</sup> and motivated behaviours.<sup>5-9</sup>

There has been much discussion about whether these processes are relevant for understanding clinically problematic drug seeking. This includes proposals that repeated substance use initially occurs because the individual is seeking reward but later switches to avoidance of withdrawal symptoms. However, most evidence suggests that, in and of themselves, abstinence syndromes are low motivational states. <sup>10,11</sup> With further experience, withdrawal symptoms may come to serve as occasion setters (Box 1b), increasing striatal dopamine release <sup>12,13</sup> and the ability of drug-paired cues to elicit approach. <sup>11,13,14</sup>

#### Box 1. Notes

- a. The original title was "Why did the chicken cross the road?" but evidently chickens prefer cooler temperatures. Too complicated.
- b. Occasion setters promote the ability of other stimuli to elicit a
  response and may or may not have conditioned effects of their own.
   For our eponymous kitten, grey skies could be occasion setters that
  augment the temperature contrast effect.

### Box 2. Implications for addiction research and clinical practice

Much of the impetus for this essay comes from a debate about how withdrawal symptoms affect drug-seeking behaviours. It is proposed here that there are 2 main effects: (i) signalling that it is time to obtain drug, and (ii) heightening the contrast between available options. The development of these withdrawal-promoted effects constitutes an addition to the accumulating number of stimuli that can trigger drug seeking rather than a "switch" from approach to avoidance. Indeed, interventions that provide little more than an easing of withdrawal symptoms demonstrate poor clinical efficacy including high rates of morbidity and mortality; <sup>22,23</sup> despite this, they are disconcertingly common. <sup>23,24</sup>

Together, this evidence suggests that debates about positive versus negative reinforcement are largely semantic and uninformative. The relevant processes are more complex than captured by these terms; <sup>11,14-20</sup> people with severe addictions alternate between high and low reward-seeking states; <sup>17-21</sup> and their drug seeking, per se, continues to reflect approach behaviours, now invigorated by the contrasting alternatives and elevated readiness to respond (Box 2).

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## References

- Baron A, Galizio M. Positive and negative reinforcement: Should the distinction be preserved? Behav Anal 2005;28:85-98.
- Baron A, Galizio M. The distinction between positive and negative reinforcement: use with care. Behav Anal 2006;29:141-51.
- Michael J. Comment on Baron and Gazlio (2005). Behav Anal 2006; 29:117-9.
- Genn RF, Ahn S, Phillips AG. Attenuated dopamine efflux in the rat nucleus accumbens during successful negative contrast. *Behav Neurosci* 2004;118:869-73.
- Crespi LP. Quantitative variation of incentive and performance in the white rat. Am Psychol 1942;55:467-517.
- 6. Reynolds GS. Behavioral contrast. J Exp Anal Behav 1961;4:57-71.
- Beninger RJ, Kendall SB. Behavioral contrast in rats with different reinforcers and different response topographies. J Exp Anal Behav 1975;24:267-80.
- Toates F. Motivational systems. New York: Cambridge University Press, 1986.
- Venniro M, Zhang M, Caprioli D, et al. Volitional social interaction prevents drug addiction in rat models. Nat Neurosci 2018;21:1520-9.
- Stewart J, Wise RA. Reinstatement of heroin self-administration habits: morphine prompts and naltrexone discourages renewed responding after extinction. *Psychopharmacology (Berl)* 1992;108:79-84.
- Shaham Y, Rajabi H, Stewart J. Relapse to heroin-seeking in rats under opioid maintenance: the effects of stress, heroin priming, and withdrawal. J Neurosci 1996;16:1957-63.

- Kojori ES, Naganawa M, Ramchandani VA, et al. Contributions of opioid receptors to striatal dopamine release during naloxone precipitated withdrawal [poster]. American College of Neuropsychopharmacology Annual Meeting; 2020 Dec. 8.
- 13. Shi Z, Jagannathan K, Padley JH, et al. The role of withdrawal in mesocorticolimbic drug cue reactivity in opioid use disorder. *Addict Biol* 2020; doi: 10.1111/adb.12977.
- Hutcheson DM, Everitt BJ, Robbins TW, et al. The role of withdrawal in heroin addiction: enhances reward or promotes avoidance? *Nat Neurosci* 2001;4:943-7.
- 15. Stolerman I. Drugs of abuse: behavioural principles, methods and terms. *Trends Pharmacol Sci* 1992;13:170-6.
- 16. Stewart J. Psychological and neural mechanisms of relapse. *Philos Trans R Soc Lond B Biol Sci* 2008;363:3147-58.
- Leyton M, Vezina P. Dopamine ups and downs in vulnerability to addictions: a neurodevelopmental model. *Trends Pharmacol Sci* 2014;35:268-76.
- 18. Robinson TE, Berridge KC. The incentive sensitization theory of addiction: some current issues. *Philos Trans R Soc Lond B Biol Sci* 2008;363:3137-46.
- King A, Vena A, Hasin DS, et al. Subjective responses to alcohol in the development and maintenance of alcohol use disorder. *Am J Psychiatry* 2021; doi.org/10.1176/appi.ajp.2020.20030247.
- Koob GF, Volkow ND. Neurobiology of addiction: a neurocircuitry analysis. *Lancet Psychiatry* 2016;3:760-73.
- Zilverstand A, Huang AS, Alia-Klein N, et al. Neuroimaging impaired response inhibition and salience attribution in human drug addiction: a systematic review. *Neuron* 2018;98:886-903.
- Chang Z, Lichtenstein P, Larsson H, et al. Substance use disorders, psychiatric disorders, and mortality after release from prison: a nationwide longitudinal cohort study. *Lancet Psychiatry* 2015;2:422-30.
- Wakeman SE, Larochelle MR, Ameli O, et al. Comparative effectiveness of different treatment pathways for opioid use disorder. *JAMA Netw Open* 2020;3:e1920622.
- 24. Fletcher AM. *Inside rehab: the surprising truth about addiction treatment and how to get help that works.* New York: Viking Penguin; 2013.