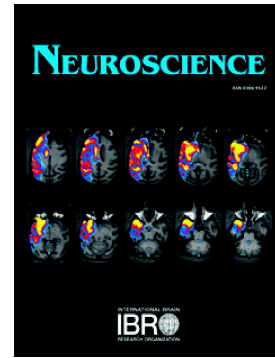


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Dopamine signaling is critical for supporting cue-driven behavioural control

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Key words: learning, memory, action, mesolimbic dopamine, reward

Abstract

Mesolimbic dopamine has been implicated in reward learning. Fischbach-Weiss and Janak (this issue) use optogenetics to attenuate dopamine signaling and study its role in cue-driven motivated behaviour.

The role of dopamine (DA) in reward learning and reinforcement is well-established (Wise, 2004). Yet, efforts continue in attempt to shed light on the specific mechanisms that are modulated by DA signaling. Indeed, the ventral tegmental area (VTA) DA signal has been linked to one of the most fundamental teaching algorithms in learning, namely error-correction (Rescorla and Wagner, 1972; Sutton and Barto, 1990; Schultz et al., 1997). Studies has provided both correlational (Waelti et al., 2001) and causal evidence for the role of VTA DA in associative learning, with optogenetic activation or inhibition of VTA DA neurons enhancing or disrupting learning, respectively (Steinberg et al., 2013; Chang et al., 2016; 2017; Keiflin et al., 2017; Maes et al., 2019). Beyond this, DA has also been linked to a number of reward-dependent behavioural and psychological constructs including action initiation, vigor, effort, motivation, incentive salience and incentive learning (Berridge, 2007; Wassum et al., 2013; Ostlund et al., 2014; Hamid et al., 2016; Ko and Wanat, 2016). Here, Fischbach-Weiss and Janak (2019) integrate Pavlovian and instrumental influences over behaviour to investigate the effect of reward-paired VTA DA signaling attenuation on reward-seeking and cue-dependent behavioural control.

In an elegant set of studies, the authors used optogenetics to attenuate reward-evoked dopamine signaling and examine its effect on established behaviour using a high and a low-effort task. In the high-effort task, mice nose-poked on a progressive ratio schedule to earn a high-fat food reward, whereas in the low-effort task a single nose-poke earned the mice the same reward. Prior to reward delivery, an auditory cue signaled the end of response requirement (particularly in the case of the high-effort task) and reward availability. DA neuron inhibition at the time of reward consumption led to a reduction in nose pokes, an increase in the time taken to collect rewards after cue presentation, and a reduction in overall rewards earned, while leaving the frequency of reward port-entries unaffected. These data show that reward-paired reduction in DA signaling led to an impairment in using the reward-predicting cue to guide behavior. In the high-effort task

this made the mice less efficient. In the low-effort task, the instrumental action and the cue-driven response were disrupted at different temporal windows, with the decline in action following the cue-driven response. This suggests that while the cue-driven response is quickly disrupted when followed by a reward that is paired with DA signaling attenuation, the instrumental response may still remain supported by the cue until the secondary reinforcing properties of the latter are reduced.

To determine the specificity of the dopaminergic manipulation on cue learning, the authors trained mice on a two-cue forced-choice task in which a left or a right nose-poke was followed by an auditory stimulus that predicted reward availability in the reward port. Attenuation of the dopamine signal during reward delivery following one nose-poke but not the other led to a cue-specific increase in the time taken to collect the available reward in the port following cue presentation. The specificity of the behavioural effect to the cue that preceded the reward-paired dopamine manipulation is important because it suggests that attenuating the dopamine signal during reward does not devalue the reward per se, or else the mice would have taken longer to collect the reward following both cues. Interestingly, the delay in responding persisted following DA-inhibition trials, in that subsequent nose-poke initiation took longer compared to control trials following no inhibition, thereby also suggesting a persistent effect of the dopamine manipulation.

These results join a number of findings that speak to the role of dopamine in maintaining an established response based on either instrumental or Pavlovian associations (Wise et al., 1978; Franklin and McCoy, 1979; Dickinson et al., 2000). However, the temporal specificity of the optogenetic dopamine manipulation in the studies by Fischbach-Weiss and Janak (2019) is centered on reward consumption and is unlikely to spill over to other task states. The fact that states preceding reward consumption were selectively affected by the manipulation is consistent with reinforcement-learning accounts of DA function, and represents an important advancement in understanding how VTA DA neurons control reward-related behaviour.

* I have read and have abided by the statement of ethical standards for manuscripts submitted to Neuroscience

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