Sugar consumption can be reduced by tonic activation of dopamine reward pathway

Rewarding (pleasurable) and aversive events give us dissimilar perceptions, which powerfully shape our decisions and therefore behavioral outcomes. In fact, chemical changes, which take place in our brain, are very different under these opposite circumstances. Dopamine is a natural substance that belongs to a class of molecules called neurotransmitters whose role is to mediate communication between nerve cells in the brain. A number of previous studies have shown that dopamine release in a small brain region called the “nucleus accumbens” causes, or at least is coincident with, feelings of pleasure and reward. Therefore, dopamine is often thought of as the “reward chemical”. A number of recent studies have revealed that increases in dopamine release within nucleus accumbens are critical for triggering behaviors directed at obtaining drugs of abuse, like cocaine, and natural rewards, like sweet tastants. However, this increased release needs to occur with a specific pattern, characterized by rapid, transient and relatively large rises in extracellular dopamine concentrations. This happens when the cells that release dopamine fire at high frequencies (>30 Hz). Recently, we demonstrated that if dopamine cells are experimentally driven to fire at a low frequency (5 Hz) for a relatively long time (minutes), dopamine is released with a very different pattern (lower concentrations which persists for a longer time). Interestingly, we discovered that this low frequency dopamine signaling, termed “tonic” release, dampens alcohol intake in rats, possibly by preventing the large, transient dopamine spikes that are associated with drug and alcohol consumption. In this study, we explored whether driving dopamine activity into this tonic mode affects natural reward consumption in a similar fashion.

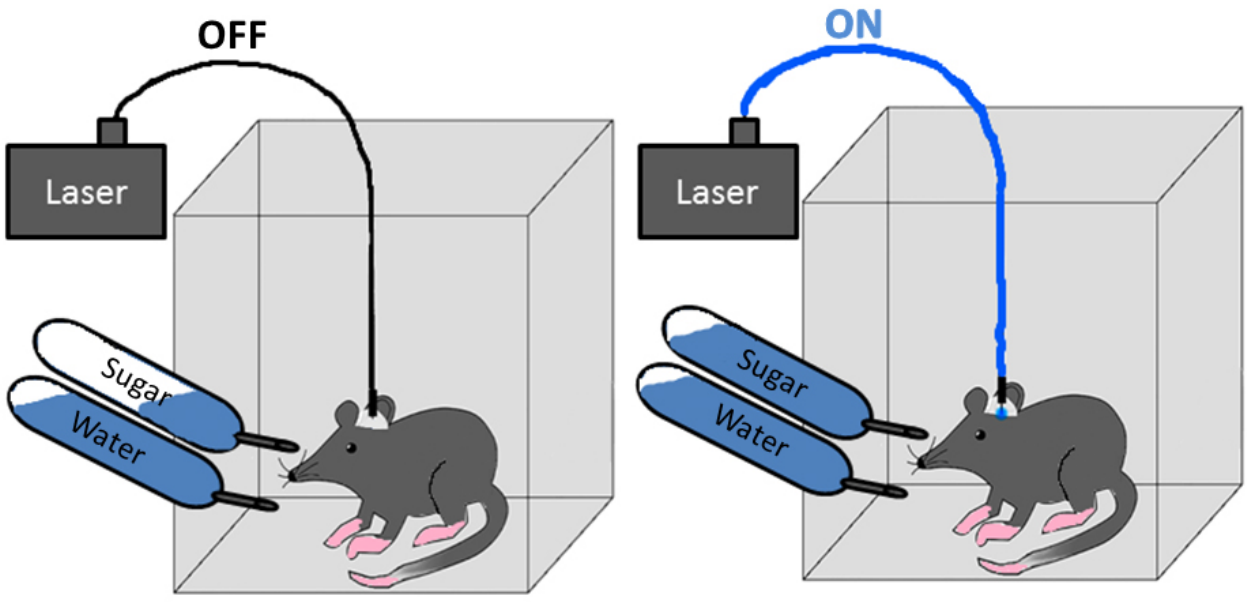

Fig. 1. Schematic of the behavioral set-up designed to evaluate the effect of optogenetic stimulation of the VTA-nucleus accumbens dopamine circuit on consummatory behaviors.

To test this idea, rats were given the opportunity to consume either water or a sucrose (sugar) solution over multiple 30-min testing periods. They quickly established a stable baseline of drinking with a higher preference for sucrose. We then used a technique called “optogenetics”, which allowed us to selectively activate dopamine neurons but not any other kind of cells. To do so, subjects were injected with a virus that selectively expressed a light-sensitive protein called channelrhodopsin-2 (ChR2) in dopamine neurons. This protein is activated by blue light applied through an implanted optical fiber connected to a laser. When activated, ChR2 excites the cells they are expressed in, causing them to fire action potentials. Therefore, by delivering low frequency blue laser pulses onto the neurons expressing ChR2, we could selectively activate these cells, inducing tonic patterns of dopamine release in the rat nucleus accumbens during the drinking sessions (Fig. 1). When these tonic pulses of blue light were delivered during the first 10 minutes of a drinking session, rats drank significantly less from the sucrose bottle, while their water consumption was not changed. Interestingly, rats did not compensate for their diminished sucrose intake when the laser stimulation was terminated for the last 20 minutes of the drinking sessions. These findings reveal that the effect of tonic dopamine release was relatively long lasting and was not limited to the period when it was being released. As noted earlier, similar results were previously obtained when rats were allowed to choose between alcohol and water. Furthermore, identical behavioral consequences (decreased sucrose intake, but not water) were observed following stimulation of the ventral tegmental area (VTA), where dopamine cell bodies are located, or the nucleus accumbens, which receives strong dopaminergic innervation from the VTA. Based on these findings, we concluded that tonic dopamine activity within the VTA-nucleus accumbens circuit plays a causal role in the inhibition of consummatory behavior directed at a natural reward.

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