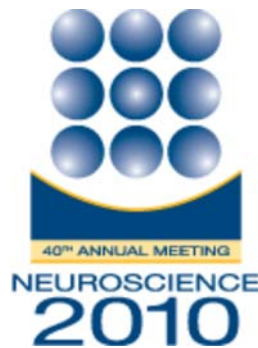


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Presentation Abstract

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Title: Optical activation of dopamine neurons for 200 milliseconds is sufficient for operant reinforcement

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Abstract: Dopamine neurons of the ventral midbrain are activated for about 200 ms following onset of reward stimuli. This brief dopamine signal could be sufficient for positive reinforcement of associated stimuli and actions. There are three lines of evidence in favor of this hypothesis. First, dopamine neurons signal “reward prediction error,” which has the appropriate characteristics for a reinforcement signal. Second, electrical stimulation of the dopamine cell body region is positively reinforcing and evokes a transient dopamine signal that resembles natural dopamine signals. However, it is known that the electrical stimulation activates non-dopamine neurons as well, and the role of dopamine in electrically-induced reinforcement has remained a topic of debate. Third, pharmacological and other manipulations that selectively activate dopamine receptors for minutes or longer are sufficient for positive reinforcement. A technique has recently been developed that allows optical stimulation of genetically targeted neurons with temporal control in the range of milliseconds (Boyden et al., 2005). Because of its potential for neuronal specificity and temporal precision, this technique enables a definitive test of the hypothesis described above. Tsai and colleagues (2009) recently demonstrated that this technique is effective in activating dopamine neurons. They also showed that repeated stimulation of dopamine neurons over a period of 30 minutes was sufficient for inducing conditioned place preference, a Pavlovian form of positive reinforcement. Whereas in their experiments, both the conditioned stimulus and

the reinforcer were spread over a 30 minute period, in a typical operant reinforcement situation, a transient action is reinforced by a transient reward event occurring just moments later. We have virally delivered the light-activated cation channel channelrhodopsin-2 (ChR2) into the ventral tegmental area of DAT-Cre mice (Backman et al., 2006), using an AAV-FLEX vector (Atasoy et al., 2008). A single pulse of 473 nm blue light (477 mW/mm² irradiance at fiber tip) was delivered for 200 ms immediately following each nose poke. This has so far been sufficient to condition operant responding in 5 mice. Both the time course of the development of operant responding, and the breakpoint on a progressive ratio schedule, were roughly similar to that found for food reward in hungry animals. Thus we provide compelling evidence that a single brief burst of dopamine, with a temporal profile closely resembling the response of dopamine neurons to natural reward stimuli, is sufficient for operant reinforcement.

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