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Dopamine release drives motivation, independently from dopamine cell firing

Ali Mohebi¹ and Joshua D. Berke¹

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Despite decades of study, fundamental aspects of dopamine biology are still being revealed.

Dopamine release in the forebrain has at least two distinct functions: it invigorates current behavior (motivation) [1] and influences future behavior (learning) [2]. The learning role seems, at least in part, to involve brief bursts of dopamine cell firing signaling reward prediction errors [3]. This “phasic” dopamine signal helps adjust future reward expectations, through the modification of synaptic strengths in forebrain targets [4]. This is a compelling account of reinforcement learning mechanisms, but does not describe how dopamine achieves more immediate motivational functions.

It has been argued that motivation is mediated by distinct, slower changes in “tonic” dopamine cell firing. This now appears not to be the case [5]. In rats working for sugar rewards, we directly compared the firing of optogenetically identified midbrain dopamine cells (in the ventral tegmental area) with forebrain dopamine release (measured using microdialysis, voltammetry, and optical sensors). We found that dopamine release increases with reward expectation—and thereby enhances the animals’ willingness to expend effort [1, 5]. Crucially, however, we found no corresponding change in dopamine cell firing.

Instead, this motivational aspect of dopamine release seems to be locally controlled within forebrain subregions. In both striatum and cortex we found specific “hotspots” (nucleus accumbens core and ventral prefrontal cortex) where dopamine release covaried with reward expectation [5]. These spatial foci stand in contrast to the canonical concept of dopaminergic reward prediction errors being “broadcast” throughout the forebrain.

There are many mechanisms that can achieve local control of dopamine release [6], most obviously the nicotinic acetylcholine receptors on dopamine terminals. The axons of striatal cholinergic interneurons form a very dense network of release sites closely intermingled with dopamine varicosities. Artificial stimulation

of striatal cholinergic neurons very rapidly evokes dopamine release.

Although the local control of dopamine release has long been studied, its functional and computational significance is only now coming into focus. A better understanding of how dopamine release is regulated in behaving animals may provide a critical foundation for our understanding of neurological and psychiatric disorders, and the development of novel pharmacological therapies.

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ADDITIONAL INFORMATION

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¹Department of Neurology and Weill Institute for Neurosciences, University of California, San Francisco, USA
Correspondence: Joshua D. Berke (joshua.berke@ucsf.edu)