

Heretical thoughts about the role of dopamine neurons in the quest for rewards

Health, well being, and reproductive success are impacted by the ability to predict the consequences of actions and to chart a course that maximizes benefits while minimizing costs. One of the principal phenomena used to study cost-benefit decision making and its neural underpinnings was discovered at McGill in the early 1950s: Rats and other animals will work indefatigably for rewarding electrical stimulation, even to the neglect of physiological needs and at significant energetic costs. Such determined pursuit of a costly, illusory benefit has been taken as an analog of addiction and has been attributed to the artificial activation of neural circuitry that normally subserves the rewarding effects of natural goal objects, such as food. Convergent evidence seems to point to phasic activation of dopamine neurons as the critical causal event in intracranial self-stimulation and to support a series model of brain-reward circuitry: The rewarding electrical stimulation activates highly excitable, non-dopaminergic neurons that provide input to dopaminergic cell bodies. The demonstration that rodents will also work for direct, selective, optical activation of dopaminergic neurons has been taken as confirmation. If so, the story of intracranial self-stimulation is a closed book that tells a simple story. I will argue the contrary on the basis of computational modeling and data from behavioral and electrochemical experiments in which reward seeking is measured as a function of the strength and cost of electrical or optical brain stimulation. These results challenge the series model and imply that the book remains open. The plot line has taken an unexpected turn: could rewarding electrical stimulation and optical activation of dopamine neurons produce behaviors that appear similar but arise from neural signals that converge on the behavioral final-common path along functionally and neurally distinct routes?