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HOT TOPIC

Striatal Dopamine: The Cement of the Brain?
Jeong H, Taylor A, Floeder JR, et al. Mesolimbic dopamine release conveys causal associations. Science 2022;378:eabq6740.

… and as these [Resemblance, Contiguity, and Causation] are the only ties of our thoughts, they are really to us the cement of the universe, and all the operations of the mind must, in a great measure, depend on them.
—David Hume, Abstract of *A Treatise of Human Nature*

The brain is increasingly conceptualized as a set of "predictive processing" systems comparing internal models of the world with sensory experiences and action outcomes. The seminal work of Wolfram Schultz et al[1] identified striatal dopamine as an important component of predictive processes, indicating that phasic striatal dopamine transients embody reward prediction error (RPE) signals for reinforcement learning. Schultz's work is thought to validate a specific class of predictive processing models: temporal difference reinforcement learning (TDRL) algorithms. TDRL calculates state value as the value of current outcomes plus a weighted sum of predicted future outcomes. Cues predicting "good" outcomes therefore acquire intrinsic value. Dopamine transients are suggested to represent the difference between the state value at t and the predicted value from $t-1$, the RPE.

Although TDRL models have mostly been studied during Pavlovian or instrumental conditioning, they appear to generalize to motor control.[2] Phasic dopamine signaling is likely degraded in Parkinson's disease (PD) and not restored by levodopa. This probably explains levodopa-refractory fine motor control deficits in PD.[3] However, TDRL models have conceptual limitations.[4] They deal poorly with the passage of time and generate an internal model of downstream cue associations. How does this happen with truly novel cues? With manifold potential cues, how to manage the multiplicity of internal models?

Jeong et al[5] propose a different model of predictive striatal dopaminergic signaling: adjusted net contingency for causal relations (ANCCR; "anchor"), a Humean device for detecting and acting on causal relationships. ANCCR looks for cues preceding a target; TDRL looks for outcomes following a cue. In ANCCR, phasic dopamine signals a "meaningful causal target" instead of RPE to retrospectively identify meaningful cues. ANCCR and TDRL often make similar predictions, but Jeong et al[5] identified nine predictions to differentiate these models. When tested in variations of a mouse Pavlovian task, all experiments favored ANCCR over TDRL.

The ANCCR model is complex and rests on numerous assumptions. The supporting experiments used simple tasks, assessing dopaminergic signaling only in ventral striatum in a small number of mice. Nonetheless, many of these findings probably generalize to dorsal striatal signaling directly relevant to PD. The work of Jeong et al[5] is highly likely to provoke considerable discussion, perhaps actual controversy, signaling the increasing and fruitful role of formal theory in the neurosciences.

Data Availability Statement

Data sharing not applicable - no new data generated

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