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REWARD

Calculating error

> each input area conveys diverse signals to the VTA

Dopaminergic neurons in the ventral tegmental area (VTA) compute the reward prediction error (RPE): the value of an actual reward minus that of the predicted reward (as signalled by a preceding cue). The VTA receives inputs from many different brain areas, but what each of these inputs contributes to RPE computation is unclear. Now, Watabe-Uchida and colleagues show that these input neurons show a wide range of different response profiles to cues and rewards.

The authors trained mice to associate different odours with one of four outcomes presented 2 seconds later: a reward with 90% probability, a reward with 50% probability, no reward or an aversive air puff. The authors then injected a rabies virus encoding channelrhodopsin 2 (ChR2) into the VTA of these mice such that neurons presynaptic to VTA dopaminergic neurons would also express ChR2. The authors took electrophysiological recordings from several brain regions (mostly situated around the medial forebrain bundle) that are known to send projections to the VTA, and, in doing so, they identified 205 (light-responsive) monosynaptic VTA inputs.

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These 205 neurons could be broadly divided into five 'clusters' based on their responses to the reward-predicting cues and the subsequent reward. For example, some clusters showed different profiles of excitation in response to reward cues and/or reward, whereas another cluster exhibited a sustained suppression of activity following the reward cue. Neurons of each cluster were identified in each of the VTA-projecting areas that were tested, indicating that each input area conveys diverse signals to the VTA.

Next, the authors investigated what RPE-relevant information was transmitted by these inputs. Few neurons encoded only the actual reward (10 of 205) or only reward expectation (26 of 205). By contrast, a large proportion of the inputs (79 of 205) was influenced by both the reward expectation and the actual reward. Again, neurons encoding these different RPE components were distributed across the probed brain areas.

In addition, some neurons (36 of 205) showed responses to rewards expected at 90% probability that were suppressed more than responses to rewards expected at 50% probability, mimicking the RPE signal itself. A small number of input neurons (8 of 205) showed 'complete RPE' coding: that is, they too showed expectation-dependent suppression, as well as reward-cue responses and reward-omission responses. Thus, a considerable number of inputs transmit RPE-like signals.

Finally, the authors generated a linear model to reconstruct VTA neuron activity using the recorded activity of individually weighted input neurons and found that the inputs are highly redundant: removing any one of the input areas did not substantially affect the activity of the modelled dopaminergic neuron. Together, these results demonstrate that RPE inputs to the VTA project from distributed areas, have different response profiles and often carry a mixture of information.

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ORIGINAL ARTICLE Tian, J. *et al.* Distributed and mixed information in monosynaptic inputs to dopamine neurons. *Neuron* http://dx.doi.org/10.1016/j.neuron.2016.08.018 (2016)
FURTHER READING Schultz, W. Dopamine reward prediction-error signalling: a two-component response. *Nat. Rev. Neurosci.* **17**, 183–195 (2016)