Distinct Flavors of Prediction Error Signals in Forebrain Cholinergic and Midbrain Dopaminergic Neurons during Reinforcement Learning

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Presentation Abstract Summary Basal forebrain (BF) cholinergic (ChAT) neurons project throughout cortex and, by modulating cortical plasticity, may support learning. Yet the principles governing ChAT neuron activation have remained obscure. Recent work from our lab revealed that ChAT neurons respond rapidly (~20ms) to reinforcers (reward, punishment) and are modulated by reinforcement expectation or surprise, analogous to dopaminergic reward prediction error (RPE). Therefore we hypothesized that ChAT neurons provide an unsigned, cortical counterpart to dopaminergic RPE. To test this, we simultaneously monitored BF ChAT and midbrain dopamine (DAT) neurons using fiber photometry in a cued, probabilistic outcome task. We confirmed that ChAT neurons respond alike to reward and punishment. With learning, ChAT neurons acquired responses to predictive stimuli and showed diminished responses to expected outcomes, hallmarks of a prediction error. Using dual fiber measurements in a reversal learning paradigm, we observed a striking but partial correspondence between DAT and ChAT signals within and across learning trials. Our results demonstrate that BF ChAT neurons provide a cortical prediction error signal computationally distinct from but coordinated with dopaminergic RPE.

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