

Chen Institute Symposium 2025

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Talk title: *The direct and indirect pathways oppositely control cortical activity along the decision axis*

Abstract: The two principal basal ganglia pathways - termed direct and indirect - are thought to oppositely modulate cortical activity via their distinct projection patterns. While this cortico-basal ganglia-thalamic loop is considered a major organizing principle of the forebrain, if and when the two pathways exert opposing control of cortical activity is not clear. Here, we record simultaneously from anterior cingulate cortex (ACC) and dorsomedial striatum (DMS) while inhibiting direct or indirect pathway neurons (in DMS) as mice perform an accumulation-of-evidence task in which the manipulations produce opposing decision biases. Inconsistent with the classic model, both manipulations produce heterogeneous responses in cortex, with a bias towards excitation. However, the two pathways exert opponent and selective influence over the subpopulation of cortical neurons that encode accumulated sensory evidence, the task-relevant decision variable. The direction of the modulation depends on a neuron's tuning to ipsilateral versus contralateral evidence, such that the net effect is to produce opposite shifts in coding along the decision axis. In contrast, striatal pathways have minimal influence over other cortical neurons, including those with binary tuning for the animal's selected choice (left or right action). When mice are not accumulating evidence, due to either a task variation or to a change in strategy, the opposing influence of striatal pathways on cortical representations diminishes. Thus, our results support an updated classic model, in which basal ganglia pathways modulate cortical activity based on the target neuron's functional tuning, so as to generate opponent shifts not in overall activity but in the task-relevant decision variable.