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BASAL GANGLIA

Pathways for action

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Two basal ganglia pathways — the direct, striatonigral pathway and the indirect, striatopallidal pathway — have been proposed to regulate the performance of actions through opposing roles in the initiation of actions and the maintenance of ongoing actions; however, recent studies have begun to challenge this view. Now, Tecuapetla, Costa and colleagues show that patterns of coordinated activity within these pathways regulate action performance.

The authors set out to examine how the activities of the direct and indirect pathways affect action initiation. To do so, they expressed archaerhodopsin or channelrhodopsin 2 — to allow optogenetic silencing or activation of neurons, respectively — in dorsolateral striatum neurons in one or the other or both of these pathways in mice. These animals were then trained to press a lever in bouts to obtain a reward.

Optogenetic inhibition of both pathways simultaneously led to an increase in the latency of the trained animals to press the lever for the first time in a bout, indicating that striatal activity is required for the proper initiation of this action. Interestingly, selective inhibition of either pathway also increased the latency to the first lever press by the same magnitude, suggesting that activity in both pathways is required for action initiation.

Increasing the firing rate of one or both of these pathways through optogenetic activation also led to an increase in the latency to press the lever. This finding suggests that the patterns of activities in these pathways are critical for action initiation, arguing against the proposal that action initiation is determined by increased activity in the direct pathway and decreased activity in the indirect pathway.

Video analysis of the animals during the manipulation of activity in these pathways revealed that they may have different roles in action initiation. Disruption of normal activity in the direct, striatonigral pathway simply increased the time it took for the animals to initiate pressing; that is, the animals stayed close to the lever. By contrast, altering activity in the indirect, striatopallidal pathway led animals to abort lever presses and leave the vicinity of the lever.

The authors next examined the roles of the two pathways in ongoing actions, by manipulating activity in one or both of these pathways after the first lever press in the sequence. They found that inhibition of one or both pathways led to a reduction in the number of lever presses during the period of the light stimulus, indicating that activity of both pathways is required for action performance. Further video analysis indicated that inhibition of the indirect pathway was linked to an increase in the number of abortions of further lever pressing.

Subtly increasing the activity in the direct pathway promoted lever pressing after action initiation, whereas subtle increases in indirect-pathway activity had no effect on ongoing lever pressing. Larger increases in the frequency of stimulation of either pathway disrupted ongoing lever pressing, although again, only with indirect-pathway activation was abortive behaviour observed.

Together, these findings support a revised view of how these pathways interact to regulate action performance. The authors suggest that through coordinated patterns of activities the direct pathway promotes the initiation and continued performance of actions, whereas the indirect pathway allows these actions to be performed by suppressing other behaviours.

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ORIGINAL ARTICLE Tecuapetla, F. *et al.* Complementary contributions of striatal projection pathways to action initiation and execution. *Cell* **166**, 703–715 (2016)