



How Cortical and Thalamic inputs to the Sensorimotor striatum guide motor sequence execution

Cheshta Bhatia 1, Bence Olveczky 1

1 Department of Organismic and Evolutionary Biology, Harvard University

The brain's ability to sequence movements enables rich and adaptive behavior, such as playing piano sonatas from sheet music. However, such flexibility can result in slow and error-prone performances [1,2]. Practicing the same motor sequence repeatedly can render its execution fast, effortless, and 'automatic' [3,4,5]. The sensorimotor striatum (DLS) within the Basal Ganglia underlies both flexible and automatic sequence execution, yet the roles of cortical (motor cortex, MC) and thalamic inputs to DLS in executing motor sequences and whether and how these depend on task demands is unclear.

One possibility is that extensive practice of the same sequence transfers control to the thalamostriatal pathway, such that the sequence can be unambiguously defined in terms of how past (thalamus) begets future behavior (DLS) [6]. However, if there are competing demands for flexibility, such that the elements used in overtrained behavior are also used in other sequences, this could prevent subcortical consolidation of overtrained behavior, rendering it dependent on MC inputs to DLS [7]. To test our hypothesis, we probed neural circuits in expert rats trained to perform motor sequences of three lever presses. We trained two cohorts of rats - one, in which rats were overtrained to perform a single sequence (automatic-only), and second, in which rats performed the same motor sequence also in a visually-guided context (flexible+automatic). We chronically silenced thalamostriatal projections in both cohorts using an intersectional viral approach and observed that performance and kinematics were disrupted in the automatic-only cohort. Interestingly, automatic sequence execution in the flexible+automatic cohort was unaffected. One downside of this technique is that it also silences collateral projections. To specifically target Thalamic inputs to DLS, we use transient optogenetic inhibition using eOPN3 and observed the same result. Optogenetic silencing of corticostriatal projections in rats performing the flexible+automatic task impaired kinematics in both modes but only disrupted automatic sequencing.

Together, this work provides insights into the hierarchical control of motor sequences, showing

that the thalamostriatal circuit controls automatic sequence execution only when there are no demands for flexibility. However, if there is a need to flexibly re-use motor elements, the execution of automatic sequences is controlled by corticostriatal projections.

motor sequence execution, neural circuits, Sensorimotor striatum (DLS), flexible vs automatic behavior, ontogenetic inhibition (eOPN3)