Normal and Parkinsonian Control of Motor Programs in Pallidal and Subthalamic Networks of Basal Ganglia

(1-page summary)

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The basal ganglia (BG) play a significant role in motor control. Nevertheless, the physiological mechanisms responsible for this control as well as the pathophysiology responsible for Parkinson's disease (PD) motor symptoms remain unclear. In studies of the relationships between behavior and neural activity in the BG, recordings have revealed many different patterns of activity, differently (and somewhat inconsistently) timed in relation to movement onset. Based on a series of experimental observations, Mink suggested that the function of the BG is to control competing motor programs, inhibiting those that interfere with the voluntary movement being executed, and focusing disinhibition on this desired movement. This hypothesis was further supported by several experimental observations. Modeling of the BG's role in motor control requires a study of how BG networks respond to cortical input to influence thalamocortical circuits responsible for motor control.

In our modeling circuits we have subsets of subthalamic nucleus and external and internal segments of Globus Pallidus, each of which represents a transiently formed group of neurons. Each subset is represented by a conductance-based model for the corresponding types of neurons. Input from the cortex and striatum determine which subset in their target structures are to be activated or suppressed. The connectivity of the circuit is based on the known anatomy of BG. To find values appropriate for the present modeling study, synaptic strength was adjusted in a series of simulations in such a way that the patterns of activity of the modeled neurons are physiologically reasonable.

Because our goal was to develop a model relevant both to normal behavior and behavioral deficits in PD, we chose to simulate motor switching (e.g. simple opposing movements such as reaching and withdrawing or pronation/supination of the simple neurological exam), which is critically impaired in PD. We simulated the dynamics of the model circuit by switching corticostriatal input from one set of network subsets to the complementary one. In the context of Mink's theory PD results in an inability to correctly inhibit unwanted and support wanted motor programs, leading to akinesia, bradykinesia and rigidity. The modeling was developed to elucidate possible mechanisms for both normal motor control and the pathophysiology associated with PD. Akinesia-like behavior, which is the primary symptom of PD, is exhibited in the model network when all subsets of internal segment of Globus Pallidus become active and significantly inhibit thalamocortical circuits, thus preventing facilitation of any motor program. This situation was observed during numerical simulation of the modified model network under the influence of competing corticostriatal inputs. The modeling allowed for the identification of those biologically-relevant modifications of the network (both in cellular properties and circuitry), which can be responsible for slowness of movement in PD.