CHAPTER 12 - FUNCTIONAL NEUROANATOMY OF THE BASAL GANGLIA

Though the traditional model of frontal-basal ganglionic connectivity positing five segregated, parallel loops needs updating, the basic model remains a useful heuristic for understanding neurobehavioral dysfunction in movement disorders. The five circuits are named according to their function or site of frontal origin: the motor circuit originating in the supplementary motor area, the oculomotor circuit originating in the frontal eye field, and the lateral orbitofrontal, anterior cingulate, and dorsolateral prefrontal circuits. The first two circuits are important in motor function, whereas the latter three circuits are important in cognition and behavior. Behavioral deficits associated with pathology of the three circuits have been outlined: dorsolateral - poor organizational and memory search strategies, stimulus-boundedness, impaired cognitive flexibility, dissociations in verbal and manual behavior; orbitofrontal - personality change, mood disorders, environmental dependency, and obsessive-compulsiveness; anterior cingulate - impaired motivation and ineffective response inhibition.

Several points bear emphasizing about functional correlates of fronto-subcortical circuit dysfunction. One, in neurodegenerative conditions, cognitive and behavioral syndromes are likely to be complex because multiple circuits are often disrupted. Two, although broad statements about anatomic-functional correlates can be advanced, details are less well worked out and controversial. For example, there is little debate that patients with PD often demonstrate executive dysfunction. What remains debated, is the extent to which executive deficits account for other (e.g., memory) deficits. Three, some have proposed that circuits are open and interconnected. Even if closed, the circuits have open components, allowing for the possibility that cognitive dysfunction reflects disruption of afferent and/or efferent connections between the open component and another structure. A simplified illustration of the key pathophysiology in PD is presented in Supplemental Figure 1.
In PD, diminished dopaminergic innervation of the striatum (esp. the putamen) results in decreased activity of inhibitory projections from the striatum to the substantia nigra (pars reticulata) and internal globus pallidus. These structures' consequently increased inhibitory effect on the external globus pallidus, together with increased activity in the inhibitory projections from the striatum to the external globus pallidus, lead to a decrease in the inhibitory effect exerted by the external globus pallidus's projections on the subthalamic nucleus. The subthalamic nucleus's overactive excitatory projections to the internal globus pallidus/substantia nigra (pars reticulata), together with the already diminished inhibition of the internal globus pallidus/substantia nigra pars reticulata by striatal projections, lead to excessive inhibition of the ventrolateral thalamus. This, in turn, leads to a diminution of the excitatory thalamic influence on motor cortex.

In HD, there is a preferential loss of inhibitory, GABA-ergic projections from the striatum (esp. caudate) to the external globus pallidus. The external globus pallidus' inhibitory control over the subthalamic nucleus is thus enhanced. Increased inhibition of the subthalamic nucleus in turn results in reduction of this structure's excitatory influences on substantia nigra pars reticulata and internal globus pallidus. The internal globus pallidus and substantia nigra pars reticulata thus have a diminished inhibitory influence on thalamus, which in turn leads to overactivation of excitatory projections from thalamus to motor cortex.