

Functional Neuroanatomy of the Basal Ganglia

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Case-Based Questions (please see page 3 for answers)

1.	A 38-year-old man with a history Huntington's disease in multiple paternal relatives presents for evaluation of depression and suicidal ideation. His wife notes that he has been increasingly irritable, with random outbursts of temper. He appears restless and fidgety at the time of evaluation, with subtle choreiform movements in the left arm. Which one of the following abnormalities is likely to be present in this patient?
a.	A decrease in the intensity of glutamatergic signals from the frontal lobe to the striatum
b.	An increase in the intensity of GABAergic signals from the external (lateral) globus pallidus to the subthalamic nucleus
c.	A decrease in the intensity of glutamatergic signals from the thalamus to the cerebral cortex
d.	An increase in the intensity of GABAergic signals from the internal (medial) globus pallidus to the thalamus
e.	An increase in the intensity of GABAergic signals from the external (lateral) globus pallidus to the internal (medial) globus pallidus

2.	A 52-year-old man presents for evaluation of aching and "stiffness" in the neck, back and hips. Clinical evaluation reveals a subtle resting tremor in the right hand and a shuffling gait. He responds slowly when asked to perform rapid voluntary movements. His wife notes that he has become less mobile over the past year and tends to eat meals much more slowly than he used to. A consulting neurologist suggests a trial of L-Dopa, which results in some improvement in his symptoms. Which one of the following abnormalities was likely present in present in this patient at the time of initial evaluation?
a.	Decreased activity of glutamatergic neurons projecting from the subthalamic nucleus to the internal (medial) segment of the globus pallidus
b.	Increased activity of GABAergic neurons projecting from the striatum to the external (lateral) segment of the globus pallidus
c.	Decreased activity of GABAergic neurons projecting from the internal (medial) segment of the globus pallidus to the thalamus
d.	Increased activity of GABAergic neurons projecting from the external (lateral) segment of the globus pallidus to the subthalamic nucleus
e.	Increased activity of glutamatergic neurons projecting from the thalamus to the cerebral cortex

3.	A 64-year-old woman slips on an icy patch and falls backwards, striking her occiput squarely on the surface of the sidewalk. She is found unconscious by a neighbor and transported by ambulance to a local hospital. Radiographic studies reveal evidence of contusions involving the orbital frontal surfaces of each cerebral hemisphere. Which afferent projections to the basal ganglia would most likely be directly damaged by this patient's brain injury?
a.	Projections to the dorsal putamen
b.	Projections to the ventral pallidum
c.	Projections to the body of the caudate nucleus
d.	Projections to the ventral striatum
e.	Projections to the dorsal head of the caudate nucleus

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Question 1 Correct Answer and Rationale: B: An increase in the intensity of GABAergic signals from the external (lateral) globus pallidus to the subthalamic nucleus

Rationale: A characteristic feature of classical Huntington's disease is a preferential loss of GABAergic D2 receptor-expressing medium spiny neurons in the striatum projecting to the external globus pallidus. This loss of inhibitory projections results in increased activity of GABAergic neurons in the lateral globus pallidus that project to the subthalamic nucleus.

Question 2 Correct Answer and Rationale: B: Increased activity of GABAergic neurons projecting from the striatum to the external (lateral) globus pallidus

Rationale: Based on the patient's presenting symptoms and improvement after L-Dopa administration, the clinical diagnosis is the of Parkinson's disease, with a loss of dopaminergic projections from the pars compacta of the substantia nigra to medium spiny neurons in the striatum. Dopamine normally has an excitatory influence on D1 striatal neurons projecting to the internal (medial) globus pallidus and an inhibitory influence on D2 striatal neurons projecting to the external (lateral) globus pallidus. With a loss of dopaminergic input, the activity of D2 striatal neurons would be expected to increase.

Question 3 Correct Answer and Rationale: D: Projections to the ventral striatum

Rationale: The orbital frontal cortex is a component of the so-called limbic loop of the basal ganglia. Most cortical afferents from this region project to the ventral striatum