Lecture #11 Basal Ganglia

Question 1: What is the genetic or biochemical cause of most instances of Parkinson's disease?

a) Somatic mutation of the Pk1 gene

b) Unknown

c) Intracellular damage due to low intracellular Ca++

d) Genetic mutation of the Pk1 gene

e) Methylation of the Pk1 gene

HINT:

Parkinson’s disease has no cure or prevention

EXPLANATION:

The causes of the large majority of Parkinson’s disease cases are unknown. The extent to which genetics vs environment is at fault is unknown. Dozens of genes are correlated with Parkinson’s disease, and many environmental factors are weakly correlated with Parkinson’s disease. Excess internal Ca++ has been suggested as causative, alpha-synuclein and tau protein may be causative. PINK1 gene mutations are a rare cause of Parkinson’s disease.

ANSWER: ['Unknown']

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Question 2: Excitatory glutamate output projects from which basal ganglia neuron type, nuclear division, or nucleus, etc.?

a) globus pallidus external segment

b) subthalamic nucleus

c) globus pallidus internal segment

d) D1 striatal projection neurons

e) D2 striatal projection neurons

HINT:

The excitatory step is part of the indirect pathway and hyperdirect pathway

EXPLANATION:

There is only one glutamatergic excitatory basal ganglia nucleus, the subthalamic nucleus. The subthalamic nucleus is part of the indirect and hyperdirect paths, receiving input from the external segment of the globus pallidus and from the cerebral cortex hyperdirect path. The output of the subthalamic nucleus excites the inhibitory output nuclei of the basal ganglia.

ANSWER: ['subthalamic nucleus']

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Question 3: How is adenylate cyclase activity (in response to dopamine) affected in striatal projection neurons expressing D1 receptors vs those expressing D2 receptors, respectively?

a) Increased vs decreased

b) Increased vs increased

c) Unaffected vs increased

d) Decreased vs increased

e) Decreased vs decreased

HINT:

D1=excitatory, D2=inhibitory

EXPLANATION:

Both D1 and D2 receptors are G protein coupled receptors. Adenylate cyclase activity is one of the main targets. D1 receptors increase adenylate cyclase activity, D2 receptors decrease adenylate cyclase activity. These can be regarded as excitatory and inhibitory effects, respectively.

ANSWER: ['Increased vs decreased']

Lecture #11 Basal Ganglia

Question 4: Which provide the main input to the internal segment of the globus pallidus (GPi)?

a) Substantia nigra pars reticulata (SNr) neurons

b) Substantia nigra pars compacta (SNc) neurons

c) Subthalamic nucleus (STN) neurons

d) D1 striatal projection neurons

e) D2 striatal projection neurons

HINT:

The direct pathway is involved

EXPLANATION:

There are two main pathways through the basal ganglia, the movement exciting direct path and the movement inhibiting indirect path. Both paths begin with the projection of cerebral cortex layer 5 neurons to the striatum of the basal ganglia, the caudate and putamen nuclei. Corticostriate neurons synapse on GABA-ergic striatal projection neurons that express either D1 or D2 type dopamine receptors. The D1 cells project the direct path to the basal ganglia inhibitory output nuclei, the internal segment of the globus pallidus and the substantia nigra pars reticulata. The output nuclei are inhibited by the direct pathway input, reducing their inhibition of movement. This disinhibition facilitates movement. The D2 cells project the indirect path to the external segment of the globus pallidus. The indirect path continues with a projection from the external segment to the subthalamic nucleus, the only excitatory glutaminergic basal ganglia nucleus. The subthalamic nucleus projects to the basal ganglia output nuclei. The extra inhibitory step in the indirect pathway makes it inhibitory to movement. The indirect pathway excites the inhibitory basal ganglia output nuclei, discouraging movement. Dopamine projected to the striatum from the substantia nigra pars compacta excites D1 receptors, and thus excites the direct pathway, and it inhibits D2 receptors, and thus inhibits the indirect pathway. The two effects combine to make dopamine a powerful excitatory factor in promoting movement.

ANSWER: ['D1 striatal projection neurons']

Lecture #11 Basal Ganglia

Question 5: Which lists the indirect pathway through the basal ganglia via the correct structures in the correct order?

a) neocortex>striatum>globus pallidus external segment>ventral thalamus>neocortex

b) neocortex> ventral thalamus >globus pallidus internal segment>striatum>neocortex

c) neocortex>substantia nigra >ventral thalamus>neocortex

d) neocortex>striatum>globus pallidus external segment>subthalamic nucleus>globus pallidus internal segment>ventral thalamus>neocortex

e) neocortex>striatum>globus pallidus internal segment>ventral thalamus>neocortex

HINT:

Two inhibitory steps are required before the output nuclei

EXPLANATION:

There are two main pathways through the basal ganglia, the movement exciting direct path and the movement inhibiting indirect path. Both paths begin with the projection of cerebral cortex layer 5 neurons to the striatum of the basal ganglia, the caudate and putamen nuclei. Corticostriate neurons synapse on GABA-ergic striatal projection neurons that express either D1 or D2 type dopamine receptors. The D1 cells project the direct path to the basal ganglia inhibitory output nuclei, the internal segment of the globus pallidus and the substantia nigra pars reticulata. The output nuclei are inhibited by the direct pathway input, reducing their inhibition of movement. This disinhibition facilitates movement. The D2 cells project the indirect path to the external segment of the globus pallidus. The indirect path continues with a projection from the external segment to the subthalamic nucleus, the only excitatory glutaminergic basal ganglia nucleus. The subthalamic nucleus projects to the basal ganglia output nuclei. The extra inhibitory step in the indirect pathway makes it inhibitory to movement. The indirect pathway excites the inhibitory basal ganglia output nuclei, discouraging movement. Dopamine projected to the striatum from the substantia nigra pars compacta excites D1 receptors, and thus excites the direct pathway, and it inhibits D2 receptors, and thus inhibits the indirect pathway. The two effects combine to make dopamine a powerful excitatory factor in promoting movement.

ANSWER: ['neocortex>striatum>globus pallidus external segment>subthalamic nucleus>globus pallidus internal segment>ventral thalamus>neocortex']

Lecture #11 Basal Ganglia

Question 6: The output from the globus pallidus external segment (pars externa) is which?

a) Dopaminergic

b) GABA-ergic

c) Axons that project to spinal cord motor neurons and interneurons

d) Glutamatergic

e) Axons ending primarily in motor cortex

HINT:

The subthalamic nucleus is the only glutaminergic nucleus of the basal ganglia

EXPLANATION:

There are two main pathways through the basal ganglia, the movement exciting direct path and the movement inhibiting indirect path. Both paths begin with the projection of cerebral cortex layer 5 neurons to the striatum of the basal ganglia, the caudate and putamen nuclei. Corticostriate neurons synapse on GABA-ergic striatal projection neurons that express either D1 or D2 type dopamine receptors. The D2 cells project the indirect path to the external segment of the globus pallidus. The indirect path continues with a projection from the external segment to the subthalamic nucleus, the only excitatory glutaminergic basal ganglia nucleus. The subthalamic nucleus projects to the basal ganglia output nuclei. The extra inhibitory step in the indirect pathway makes it inhibitory to movement. The indirect pathway excites the inhibitory basal ganglia output nuclei, discouraging movement.

ANSWER: ['GABA-ergic']

Lecture #11 Basal Ganglia

Question 7: Which is the LEAST likely sign of Parkinson's disease?

a) Bradykinesia

b) Intention tremor

c) Hypometria in gait

d) Akinesia

e) Resting tremor

HINT:

contrast Parkinson’s disease with cerebellar disease

EXPLANATION:

The common signs of Parkinson’s disease include bradykinesia or akinesia, hypometria, loss of balance, rigidity, mask-like face, and often a relatively rapid tremor at rest. The resting tremor contrasts with cerebellar signs, which are commonly an intention tremor at the end of movements, hypermetria, decomposition of movements into component parts, and a drunken gait. Oculomotor signs are rare in Parkinson’s disease and common in cerebellar disease.

ANSWER: ['Intention tremor']

Lecture #11 Basal Ganglia

Question 8: The output from the globus pallidus internal segment (pars interna) is which?

a) Dopaminergic

b) Glutamatergic

c) Axons ending primarily in motor cortex

d) Axons that project to spinal cord motor neurons and interneurons

e) GABA-ergic

HINT:

The subthalamic nucleus is the only glutaminergic nucleus of the basal ganglia

EXPLANATION:

The substantia nigra pars reticulata and the internal segment of the globus pallidus are the two output nuclei of the basal ganglia. Both are GABA-ergic inhibitory nuclei that inhibit the ventral thalamus and therefore motor areas of cortex.

ANSWER: ['GABA-ergic']

Lecture #11 Basal Ganglia

Question 9: What is the early motor sign of Huntington's disease?

a) Uncontrolled movements or chorea

b) Intention tremor and/or decomposition of movement

c) Bradykinesia or akinesia

d) Tremor

e) Oculomotor paresis and/or saccadic suppression

HINT:

The indirect path in basal ganglia is first damaged, with predictable motor effects

EXPLANATION:

Huntington’s disease first affects D2 receptor-expressing striatal projection GABA neurons of the indirect pathway. The indirect path inhibits movements, and early Huntington’s disease is characterized by the loss of inhibition causing uncontrolled dance-like movements, Huntington’s chorea.

ANSWER: ['Uncontrolled movements or chorea']

Lecture #11 Basal Ganglia

Question 10: The output from D1 receptor expressing striatal projection neurons is which?

a) Enkephalinergic

b) Glutamatergic excitatory

c) GABA-ergic inhibitory

d) Neuromodulatory, either excitatory of inhibitory depending on context

e) Dopaminergic excitatory

HINT:

The subthalamic nucleus is the only glutaminergic nucleus of the basal ganglia

EXPLANATION:

Both D1 and D2 receptors are G protein coupled receptors. Adenylate cyclase activity is one of the main targets. D1 receptors increase adenylate cyclase activity, D2 receptors decrease adenylate cyclase activity. These can be regarded as excitatory and inhibitory effects, respectively.

ANSWER: ['GABA-ergic inhibitory']

Lecture #11 Basal Ganglia

Question 11: The two main output targets of the striatum of the basal ganglia are which?

a) Substantia nigra pars reticulata (SNr) and subthalamic nucleus (STN)

b) Substantia nigra pars compacta (SNc) and substantia nigra pars reticulata (SNr)

c) Substantia nigra pars compacta (SNc) and subthalamic nucleus (STN)

d) External and internal segments of the globus pallidus (GPe and GPi)

e) Internal segment of the globus pallidus (GPi) and substantia nigra pars reticulata (SNr)

HINT:

Both are inhibitory outputs to inhibitory neurons

EXPLANATION:

Corticostriate neurons synapse on GABA-ergic striatal projection neurons that express either D1 or D2 type dopamine receptors. The D1 cells project the direct path to the basal ganglia inhibitory output nuclei, the internal segment of the globus pallidus and the substantia nigra pars reticulata. The D2 cells project the indirect path to the external segment of the globus pallidus.

ANSWER: ['External and internal segments of the globus pallidus (GPe and GPi)']

Lecture #11 Basal Ganglia

Question 12: Which neurotransmitter is supplied by structures that lie one just dorsal to the crus cerebri and the other in the midbrain tegmentum, ventrally near the midline?

a) Histamine

b) Dopamine

c) Serotonin

d) Norepinephrine

e) Acetylcholine

HINT:

Consider the subdivisions of the midbrain seen in a cross section axial or horizontal view

EXPLANATION:

The two major sources of dopamine as a neuromodulator are the substantia nigra pars compacta and ventral tegmental area in the midbrain. The substantia nigra lies immediately dorsal to the most ventral crus cerebri and ventral to the midbrain tegmentum. The ventral tegmental area lies along the midline of the midbrain in a roughly defined ventral to dorsal band through the tegmentum.

ANSWER: ['Dopamine']

Lecture #11 Basal Ganglia

Question 13: What is the most likely function of the hyperdirect pathway?

a) Providing a pinpoint focus of inhibition to block a specific response commanded by the direct pathway

b) Shortening the latency of excitatory signals through the direct pathway

c) Inhibitory sculpting of direct pathway excitation

d) Stronger excitation of movement than the direct pathway

e) Roughly equivalent in excitation of movement to direct pathway activation

HINT:

The hyperdirect pathway projects from cerebral cortex to the subthalamic nucleus

EXPLANATION:

In addition to the direct and indirect pathways through the basal ganglia, there is a ‘hyperdirect’ pathway from cerebral cortex directly to the subthalamic nucleus, thus bypassing two inhibitory steps of the indirect pathway. The effects of the hyperdirect path are expected to be similar to those of the indirect path, inhibiting movement and sculpting the correct movement by inhibiting similar incorrect movements.

ANSWER: ['Inhibitory sculpting of direct pathway excitation']

Lecture #11 Basal Ganglia

Question 14: What is a (are) major direct output(s) of the substantia nigra pars reticulata and internal segment of the globus pallidus?

a) Spinal cord ventral horn

b) Motor cortex

c) Substantia nigra pars compacta and external segment of the globus pallidus

d) Ventral thalamus

e) Association cortex

HINT:

Identify the output nuclei of the basal ganglia

EXPLANATION:

The output nuclei of the basal ganglia are the globus pallidus internal segment and the substantia nigra pars reticulata. They project GABA-ergic axons to the ventral thalamus, mainly to the ventral anterior nucleus. This inhibits the ventral thalamus and inhibits the motor cortical areas that the ventral thalamus excites.

ANSWER: ['Ventral thalamus']

Lecture #11 Basal Ganglia

Question 15: Which lists the direct pathway through the basal ganglia via the correct structures in the correct order?

a) neocortex>substantia nigra>ventral thalamus>neocortex

b) neocortex>striatum>globus pallidus external segment>subthalamic nucleus>globus pallidus internal segment>ventral thalamus>neocortex

c) neocortex>ventral thalamus>globus pallidus internal segment>striatum>neocortex

d) neocortex>striatum>globus pallidus external segment>ventral thalamus>neocortex

e) neocortex>striatum>globus pallidus internal segment>ventral thalamus>neocortex

HINT:

The external segment of the globus pallidus and the subthalamic nucleus are not involved

EXPLANATION:

There are two main pathways through the basal ganglia, the movement exciting direct path and the movement inhibiting indirect path. Both paths begin with the projection of cerebral cortex layer 5 neurons to the striatum of the basal ganglia, the caudate and putamen nuclei. Corticostriate neurons synapse on GABA-ergic striatal projection neurons that express either D1 or D2 type dopamine receptors. The D1 cells project the direct path to the basal ganglia inhibitory output nuclei, the internal segment of the globus pallidus and the substantia nigra pars reticulata. The output nuclei are inhibited by the direct pathway input, reducing their inhibition of movement. This disinhibition facilitates movement. The D2 cells project the indirect path to the external segment of the globus pallidus. The indirect path continues with a projection from the external segment to the subthalamic nucleus, the only excitatory glutaminergic basal ganglia nucleus. The subthalamic nucleus projects to the basal ganglia output nuclei. The extra inhibitory step in the indirect pathway makes it inhibitory to movement. The indirect pathway excites the inhibitory basal ganglia output nuclei, discouraging movement. Dopamine projected to the striatum from the substantia nigra pars compacta excites D1 receptors, and thus excites the direct pathway, and it inhibits D2 receptors, and thus inhibits the indirect pathway. The two effects combine to make dopamine a powerful excitatory factor in promoting movement.

ANSWER: ['neocortex>striatum>globus pallidus internal segment>ventral thalamus>neocortex']

Lecture #11 Basal Ganglia

Question 16: What neurological disorder is most closely associated with loss of the subthalamic nucleus?

a) Huntington's disease

b) Parkinson's disease

c) Essential tremor

d) Tardive dyskinesia

e) Hemiballism

HINT:

The subthalamic nucleus excites the basal ganglia output nuclei to increase inhibition of movement

EXPLANATION:

A stroke or tuberculosis can damage the subthalamic nucleus on one side. This lowers excitation of the inhibitory basal ganglia output nuclei, resulting in the uncontrolled release of large flinging limb movements, hemiballism.

ANSWER: ['Hemiballism']

Lecture #11 Basal Ganglia

Question 17: What is the main neurotransmitter of the substantia nigra pars reticulata neurons?

a) D1

b) GABA

c) Glutamate

d) Dopamine

e) D2

HINT:

The substantia nigra pars reticulata is one of the output nuclei of the basal ganglia

EXPLANATION:

The substantia nigra pars reticulata and the internal segment of the globus pallidus are the two output nuclei of the basal ganglia. Both are GABA-ergic inhibitory nuclei that inhibit the ventral thalamus and therefore motor areas of cortex.

ANSWER: ['GABA']

Lecture #11 Basal Ganglia

Question 18: Which provide the main input to the external segment of the globus pallidus (GPe)?

a) D1 striatal projection neurons

b) D2 striatal projection neurons

c) Subthalamic nucleus (STN) neurons

d) Substantia nigra pars reticulata (SNr) neurons

e) Substantia nigra pars compacta (SNc) neurons

HINT:

The indirect pathway is involved

EXPLANATION:

There are two main pathways through the basal ganglia, the movement exciting direct path and the movement inhibiting indirect path. Both paths begin with the projection of cerebral cortex layer 5 neurons to the striatum of the basal ganglia, the caudate and putamen nuclei. Corticostriate neurons synapse on GABA-ergic striatal projection neurons that express either D1 or D2 type dopamine receptors. The D1 cells project the direct path to the basal ganglia inhibitory output nuclei, the internal segment of the globus pallidus and the substantia nigra pars reticulata. The output nuclei are inhibited by the direct pathway input, reducing their inhibition of movement. This disinhibition facilitates movement. The D2 cells project the indirect path to the external segment of the globus pallidus. The indirect path continues with a projection from the external segment to the subthalamic nucleus, the only excitatory glutaminergic basal ganglia nucleus. The subthalamic nucleus projects to the basal ganglia output nuclei. The extra inhibitory step in the indirect pathway makes it inhibitory to movement. The indirect pathway excites the inhibitory basal ganglia output nuclei, discouraging movement. Dopamine projected to the striatum from the substantia nigra pars compacta excites D1 receptors, and thus excites the direct pathway, and it inhibits D2 receptors, and thus inhibits the indirect pathway. The two effects combine to make dopamine a powerful excitatory factor in promoting movement.

ANSWER: ['D2 striatal projection neurons']

Lecture #11 Basal Ganglia

Question 19: What is the most direct early cause of the signs of Huntington's disease?

a) Loss of D1 receptor expressing striatal projection neurons

b) Loss of substantia nigra pars compacta dopamine neurons

c) Loss of D2 receptor expressing striatal projection neurons

d) Loss of substantia nigra pars reticulata dopamine neurons

e) Loss of neurons throughout cerebral cortex

HINT:

The indirect path in basal ganglia is first damaged, with predictable motor effects

EXPLANATION:

Huntington’s disease first affects D2 receptor-expressing striatal projection GABA neurons of the indirect pathway. The indirect path inhibits movements, and early Huntington’s disease is characterized by the loss of inhibition causing uncontrolled dance-like movements, Huntington’s chorea.

ANSWER: ['Loss of D2 receptor expressing striatal projection neurons']

Lecture #11 Basal Ganglia

Question 20: The two main output nuclei of the basal ganglia are which?

a) Substantia nigra pars reticulata (SNr) and subthalamic nucleus (STN)

b) Substantia nigra pars compacta (SNc) and substantia nigra pars reticulata (SNr)

c) External and internal segments of the globus pallidus (GPe and GPi)

d) Substantia nigra pars compacta (SNc) and subthalamic nucleus (STN)

e) Internal segment of the globus pallidus (GPi) and substantia nigra pars reticulata (SNr)

HINT:

The output nuclei are the point of convergence of the direct and indirect pathways

EXPLANATION:

The internal segment of the globus pallidus (GPi) and substantia nigra pars reticulata (SNr) are the inhibitory output nuclei of the basal ganglia. Corticostriate neurons synapse on GABA-ergic striatal projection neurons that express either D1 or D2 type dopamine receptors. The D1 cells project the direct path to the basal ganglia inhibitory output nuclei, the internal segment of the globus pallidus and the substantia nigra pars reticulata. The output nuclei are inhibited by the direct pathway input, reducing their inhibition of movement. This disinhibition facilitates movement. The D2 cells project the indirect path to the external segment of the globus pallidus. The indirect path continues with a projection from the external segment to the subthalamic nucleus, the only excitatory glutaminergic basal ganglia nucleus. The subthalamic nucleus projects to the basal ganglia output nuclei. The extra inhibitory step in the indirect pathway makes it inhibitory to movement. The indirect pathway excites the inhibitory basal ganglia output nuclei, discouraging movement.

ANSWER: ['Internal segment of the globus pallidus (GPi) and substantia nigra pars reticulata (SNr)']

Lecture #11 Basal Ganglia

Question 21: Which is the hyperdirect pathway?

a) Striatum to substantia nigra pars compacta

b) Cerebral cortex to substantia nigra pars reticulata

c) Cerebral cortex to substantia nigra pars compacta

d) Cerebral cortex to subthalamic nucleus

e) Striatum to substantia nigra pars reticulata

HINT:

The hyperdirect path acts like the indirect path but skips two of the inhibitory steps

EXPLANATION:

In addition to the direct and indirect pathways through the basal ganglia, there is a ‘hyperdirect’ pathway from cerebral cortex directly to the subthalamic nucleus, thus bypassing two inhibitory steps of the indirect pathway. The effects of the hyperdirect path are expected to be similar to those of the indirect path, inhibiting movement and sculpting the correct movement by inhibiting similar incorrect movements.

ANSWER: ['Cerebral cortex to subthalamic nucleus']