Chapter 43. The Basal Ganglia
Basal ganglia in history

Parkinson’s disease

Huntington’s disease
Parkinson’s disease

1817

Parkinson’s disease (PD) is a degenerative disorder of the central nervous system mainly affecting the motor system. Early in the course of the disease, the most obvious symptoms are movement-related; these include shaking, rigidity, slowness of movement and difficulty with walking and gait. Later, thinking and behavioral problems may arise, with dementia commonly occurring in the advanced stages of the disease, and depression being the most common psychiatric symptom.
Structure of Basal ganglia
Structures in Basal Ganglia

- Striatum
- Globus pallidus
- Substantia nigra
- Subthalamic nucleus
Structures in Basal Ganglia

- Striatum
- Globus pallidus
- Substantia nigra
- Subthalamic nucleus
- Caudate nucleus
- Putamen
- External segment
- Internal segment
- Pars reticulata
- Pars compacta
What are the structures in BG?
Caudate nucleus

Long C-shaped structure.
Head, body and tail regions
The putamen is a round structure located at the base of the forebrain (telencephalon). The putamen and caudate nucleus together form the dorsal striatum. It is also one of the structures that comprises the basal ganglia.
The globus pallidus (Latin for "pale globe") also known as paleostriatum or dorsal pallidum, is a sub-cortical structure of the brain.
The substantia nigra is a brain structure located in the mesencephalon (midbrain) that plays an important role in reward and movement. Substantia nigra is Latin for "black substance", reflecting the fact that parts of the substantia nigra appear darker than neighboring areas due to high levels of neuromelanin in dopaminergic neurons.
Monkey basal ganglia
Human basal ganglia
Neurons in Basal Ganglia
Medium spiny neurons (MSNs), also known as spiny projection neurons, are a special type of GABA-ergic inhibitory cell representing 95% of neurons within the human striatum, a structure located in the basal ganglia.

The medium spiny neurons are medium-sized neurons (~15 microns in diameter, ~12-13 microns in the mouse) with large and extensive dendritic trees (~500 microns in diameter).
Neurons in basal ganglia

- GABAergic neurons
  - Medium spiny neuron (MSN)

- Cholinergic neurons
  - Tonically active neurons (TAN)

- Glutamatergic neurons
MSN circuit in Striatum

TAN
MSN circuit in Striatum

To dendrite shaft
- Dopamine neuron
- To dendrite spine
- Cortex
- To dendrite shaft & shaft
  - Thalamus

Around axon hillock
- Large interneuron (TAN)
- To cell body
- Inhibitory interneuron

Figure 43-3 The medium spiny neurons in the striatum have extrinsic and intrinsic inputs. Glutamatergic inputs from the cerebral cortex and dopaminergic inputs from the substantia nigra pars compacta terminate on dendritic spines of medium spiny neurons. The reward-related dopaminergic inputs are thought to modulate the strength of cortical inputs and to play a role in synaptic changes and reinforcement learning in the striatum. Glutamatergic inputs from the thalamus end on the spines and shafts of dendrites of medium spiny neurons. Medium spiny neurons also receive cholinergic and GABAergic input from interneurons in the striatum.
Circuit of Basal Ganglia
Basal ganglia circuit
-Basic circuit

Cortex => Striatum => GP => PPN => motor output

Direct & Indirect pathways

Hyperdirect pathway

Loop circuit

Figure 43-2 The basal ganglia–thalamocortical circuitry. The circuitry of the basal ganglia includes the striatum (here represented by one of its components, the putamen), the external and internal segments of the globus pallidus (GPe and GPi, respectively), the substantia nigra pars reticulata (not shown) and pars compacta (SNC), and the subthalamic nucleus (STN). Cortical input enters the striatum and subthalamic nucleus. Basal ganglia output is conveyed to several thalamic nuclei (the centromedian and parafascicular nuclei and the ventral anterior and ventral lateral nuclei) and the pedunculopontine nucleus. Excitatory connections are shown in red, inhibitory pathways in gray. The dopaminergic SNC projection to the striatum regulates corticostratial transmission along direct and indirect pathways.
Basal ganglia circuit
-Basic circuit
Basal ganglia circuit
-Basic circuit

Hyperdirect pathway

Why?
Neuronal activity in BG

**Inhibitory**

**Excitatory**

A. Cortex

B. Direct pathway

C. Indirect pathway

Motor output (e.g. SC)

Movement control
Value processing
Decision-making
Neuronal activity in BG

What’s the advantage of this circuit?
Parallel circuits of basal ganglia
Various regions in cortex
Concept of parallel anatomical circuit
Example BG circuits from 4 distinct areas of frontal cortex
Functions
In parallel circuits

Loop circuit

What’s the advantage of parallel processing?
Functions of BG

- Action selection
- Movement preparation
- Motor execution
- Sequential movement
- Voluntary movement
- Memory-guided movement
- Reinforcement learning
Action selection is a way of characterizing the most basic problem of intelligent systems: what to do next. In artificial intelligence and computational cognitive science, "the action selection problem" is typically associated with intelligent agents and animats—artificial systems that exhibit complex behaviour in an agent environment.
**Figure 43-6** Areas of the brain with movement-related activity. PET images show significant levels of activity in human volunteers performing a sinusoidal arm movement. The images are shown superimposed on corresponding structural MRI images. The "ipsilateral" and "contralateral" hemispheres are in relation to the moving arm. (Adapted, with permission, from Turner et al. 1998.)

**A.** Movement-related activity in the cortex covers large portions of the primary sensorimotor, dorsolateral and mesial premotor, and dorsal parietal cortices, predominately contralateral to the moving extremity. Activity related to the rate of movement is restricted to a small band of cortex surrounding the contralateral central sulcus.

**B.** Movement-related activity in the basal ganglia and thalamus is seen in motor-related portions of the basal ganglia and thalamus primarily on the side contralateral to the moving arm. Rate-related activity is restricted to the posterior globus pallidus.

**C.** A large portion of the anterior cerebellum ipsilateral to the moving arm is active during movement. Movement-related activity is seen in a band covering the mesial portions of the cerebellum.
Dopamine neurons
DA neuron activity
In reinforcement learning

**Reward prediction error signal**

- Unexpected reward signal
- Prediction (expectation)
- Error signal

Reward information is processed by specific neurons in specific brain structures. Reward neurons produce internal reward signals and use them for influencing brain activity that controls our actions, decisions and choices.
D1R or D2R-mediated circuit in BG

D1R: direct pathway
D2R: Indirect pathway
D1R & D2R signaling
Neuronal activity in BG

Dopamine neuron

B Direct pathway

C Indirect pathway

D1R

D2R

(+)

(-)

(+)

(+) (-)

(+) (-)

Inhibitory

Excitatory

GO

NOGO
Questions
1. When use the D2R blocker?
2. When block the D2R-containing neurons by optogenetics?
Parkinson’s disease

**Parkinson's disease** (PD) is a long-term degenerative disorder of the central nervous system that mainly affects the motor system. The symptoms generally come on slowly over time. Early in the disease, the most obvious are shaking, rigidity, slowness of movement, and difficulty with walking.
Figure 43-8  Loss of dopamine in the striatum in Parkinson disease. Positron emission tomography (PET) images of $^{18}$F-DOPA uptake in the striatum in a normal subject and in a twin of a Parkinson patient show the extent of dopamine metabolism. In the twin, $^{18}$F-DOPA uptake in the putamen was reduced when the subject was asymptomatic and more severely reduced five years later when symptomatic. (Adapted, with permission, from Brooks 2000.)
Figure 43-9 Abnormalities in the pattern of neuronal firing in the basal ganglia of parkinsonian monkeys. Raster plots show continuous data recordings from selected representative neurons situated in the structures portrayed at the left.
MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) is a prodrug to the neurotoxin MPP+, which causes permanent symptoms of Parkinson’s disease by destroying dopaminergic neurons in the substantia nigra of the brain.

MPTP causes Parkinsonism in primates including humans. Rodents are much less susceptible.
What is wrong in the right circuit and how to cause the Parkinsonian symptom?
What’s the L-DOPA & its function? Side effects?
The Globus Pallidus Sends Reward-Related Signals to the Lateral Habenula

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