Basal Ganglia

Each day we are doing thousands of movements, from walking to writing and so many more. Have you ever wondered which system is responsible for organizing and smoothening all these movements? The answer to that question lies within the structure called **basal ganglia**.

The basal ganglia are a collection of subcortical structures consisting of several connected nuclei located in the brain. They are called the caudate nucleus, putamen, globus pallidus, subthalamic nucleus, and substantia nigra (the last two are only functionally connected and related to this system).

Two major pathways emerge from the basal ganglia, which project onto various structures of the brain, communicating with them. They are called the **direct** (excitatory) **and indirect** (inhibitory) **pathways**. This article will explain both of them, and also provide you with some relevant clinical aspects about them and the basal ganglia.

Key Facts

Basal ganglia – Nuclei: caudate nucleus, putamen, globus pallidus, subthalamic nucleus, substantia nigra (last two are functionally connected) // Function: movement modulation

Direct Pathway

Pathway: cortex > stratum > globus pallidus > thalamus > motor cortex /// Fuction – increse in motor activity /// Type – excitatoy

Indirect Pathway

Pathway: cortex > striatum > globus pallidus > subthalamus > globus pallidus > thalamus > motor cortex /// Function – decrease in motor activity /// Type – inhibitory

Basics

Basal ganglia are big subcortical structures consisted of several connected nuclei that are located within the telencephalon, mesencephalon, and diencephalon. Basal ganglia are a part of the **extrapyramidal system** and they participate in the movement modulation.

Input signals from the cortex are processed within the basal ganglia, which then create a focused output signal that ends up within the motor neurons of the **frontal lobe** and brainstem. These signals serve for **planning** and proper **execution of a movement**.

Unlike the cerebellum, basal ganglia do not receive input signals from the spinal cord, but, they are directly connected to the cerebral cortex.

Basal ganglia consist of five pairs of nuclei. Anatomy of the basal ganglia at the first glance may seem confusing, so let's list the nuclei in order to remember them easily:

- Caudate nucleus
- Putamen
- Globus pallidus
- Subthalamic nucleus and substantia nigra are also functionally connected to this system.

The afferent portion of the basal ganglia is called **striatum**. This structure consists of the **putamen** and the **caudate nucleus**. Internally to the putamen is the **globus pallidus**, and both of them (the putamen and the globus pallidus) used to be known as the **lentiform nucleus**.

The globus pallidus is functionally different than the striatum, in a way that it functions as the efferent portion of the basal ganglia. Globus pallidus has two functionally different parts: **inner globus pallidus** (or the internal segement of the globus pallidus) and **external globus pallidus** (or the external segment). From the striatum, the two main pathways from the basal ganglia arise, which are called the **direct** and **indirect pathway**. The direct pathway is excitatory and is in charge for the initial part of the movements, while the indirect pathway is inhibitory and it prevents the unnecessary movements.

Direct pathway

The direct pathway starts from the **striatum** (caudate nucleus and putamen). The neurons of the striatum are excited by the cortex. These neurons however, are **inhibitory neurons** and their axons go to the internal globus pallidus. These inhibitory fibers use the gamma-aminobutyric acid (**GABA**) as their main inhibitory neurotransmitter.

The neurons from the **internal globus pallidus** send their axons to the **thalamus**, and they are also inhibitory. These fibers going from the pallidum to the thalamus form two fascicles of the white matter called **ansa lenticularis** and **lenticular fasciculus**, that before entering the thalamus fuse into one pathway called **thalamic fasciculus**.

From the thalamus, excitatory pathways go to the cortex (**prefrontal**, **premotor** and **supplementary cortex**) where they affect the planning of the movement by synapsing with the neurons of the **corticospinal** and **corticobulbar tracts**.

So, we mentioned four anatomical pathways:

- **Cortex - striatum**
- **Striatum - globus pallidus**
- **Globus pallidus - thalamus**
- **Thalamus - motor cortex**

Physiologically speaking, the **first and the last one, are excitatory**, whereas the **second and the third are inhibitory**. This is important for understanding the function of the basal ganglia.

This entire system functions on the principle of **positive feedback**. How?

Well, since the two of the inhibitory synapses are serially connected, that means that the first inhibitory neuron (striatum) suppresses the activity of the second inhibitory neuron (globus pallidus). The result of this is a reduction of the inhibitory influence that the globus pallidus has over the thalamus, so-called **disinhibition of the thalamus**, which is equivalent to the excitation of the motor cortex.

So general function of the direct pathway of the basal ganglia is to excite the motor cortex or to increase the motor activity.

Indirect pathway

This pathway also rises from the **striatum**. Inhibitory neurons from the striatum synapse with the external segment of the **globus pallidus**. The neurons of the external segment of the globus pallidus send inhibitory fibers to the **subthalamus**. Additionally, the subthalamus sends excitatory projections back to the internal segment of the globus pallidus.

So functionally the striatum inhibits the external globus pallidus, and that causes a disinhibition of the subthalamus.

For that reason, the neurons of the subthalamus become more active, and they excite the internal segment of the globus pallidus. So finally this loop inhibits the thalamic nuclei.

The final result of this pathways is a decreased activity of the cortical motor neurons, and consequential **suppression of the extemporaneous movement**.

Modulation of the basal ganglia

Neuronal circuits that modulate the function of the basal ganglia are:

- The **nigrostriatal pathway**
- The **thalamostriatal pathway**

Nigrostriatal pathway

This pathway projects from the **substantia nigra pars compacta** to the **striatum**, and it utilizes the neurotransmitter **dopamine**. This pathway has the modulatory effect on the basal ganglia, with dopamine facilitating the motor loop in these two ways:

- It excites the direct pathway
- It inhibits the indirect pathway

The different effect on the direct and indirect pathway is explained by the activation of the different dopamine receptors that are located within the neurons of the striatum. There are two types of dopamine receptors, D1 and D2, which respond differently when stimulated with dopamine. Stimulation of D1 results with the excitation of the neuron, while the stimulation D2 results with inhibition.

D1 receptors are found on the striatal neurons that give rise to the **direct pathway**. On the other hand, **D2 receptors** are found on the neurons whose axons form the **indirect pathway**. So the final effect of the nigrostriatal pathway is the promotion of the direct pathway and at the same time the inhibition of the indirect pathway.

The activity of the neurons within the pars compacta substantia nigra is related to the reward system and behavioral stimuli, so it is thought that they play a role in some forms of motor learning.

Thalamostriatal fibers

These fibers arise from the **intralaminar nuclei of the thalamus** and terminate primarily in the striatum. Besides that, some fibers terminate in the globus pallidus and in the subthalamic nucleus.

Highlights

- Direct and indirect pathways have the opposite effects on the **thalamus** and the **globus pallidus-substantia nigra complex**.
- The activation of the **direct pathway** reduces the inhibition of the thalamus and excites the motor cortex.
- On the other hand, the activation of the **indirect pathway** increases the inhibition of the thalamus, which leads to the inhibition of the motor cortex.

Clinical aspects

Disorders of the basal ganglia are classified into two categories:

- **Hypertonicity**, that is an abnormal increase of the muscle tone in response to passive stretch. As we have learned so far, when the indirect pathway of the basal ganglia is stimulated, it sends signals to the motor cortex and brainstem, which ultimately inhibit muscle tone. Following a lesion of the basal ganglia, this inhibitory influence is lost and hypertonicity is manifested contralateral to the side of the lesion.
- **Dyskinesia** is a presence of the unintentional purposeless movements. Dyskinesias are classified further as:
  - Hypokinesia
  - Hyperkinesia

Hyperkinetic disorders

These disorders are caused by a disturbance of the indirect loop that causes a loss of the inhibition of the thalamic neurons, which ultimately results in excess cortical activity and movement. They are presented as:

- **Tremor**, that is a rhythmic, low amplitude movement that may be manifested as the nodding of the head, or in the hands and feet.
- **Chorea** is a sequence of rapid involuntary movements involving mostly the hands and feet, the tongue, and facial muscles.
- **Hemiballismus** is a condition where the patient exhibits involuntary ballistic (violent striking) movements on only one side of the body, that affect only the proximal muscles of a limb.
- **Ballismus** is the equivalent to the hemiballismus, with the difference that it affects the entire body. It is the most extreme type of the dyskinesia .

Huntington's disease is a rare inherited condition that manifests with severe chorea and hemiballismus that develop over the time. The neuropathological substrate of the disease is the degeneration of the striatal neurons that give rise to the indirect pathway.

Hypokinetic disorders

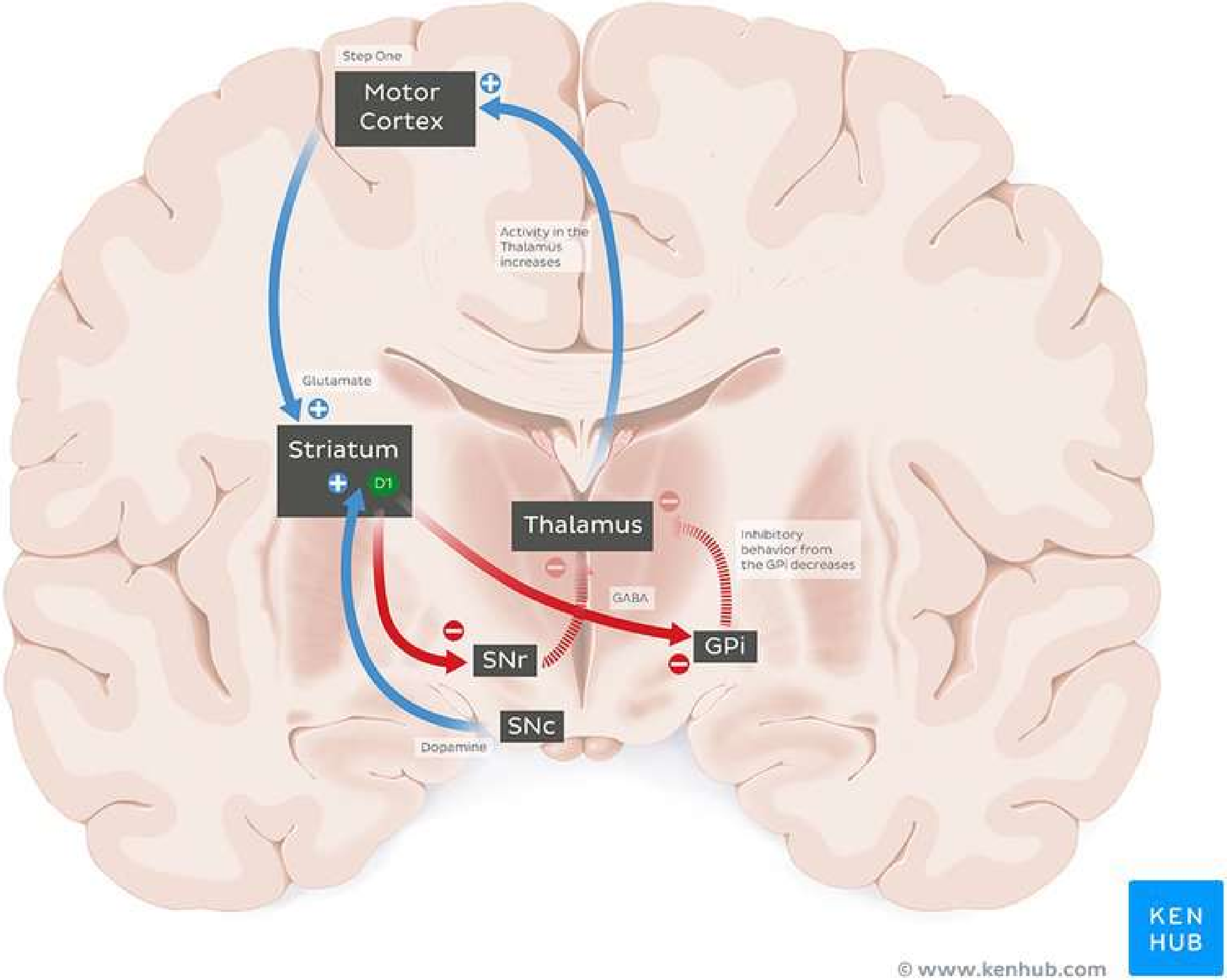
These disorders result from the degeneration of the neurons that form the direct pathway. Since this is the pathway that serves for the planning of the movement, the problems that patients will have been presented in two forms:

- **Bradykinesia** that is presented with slow movement

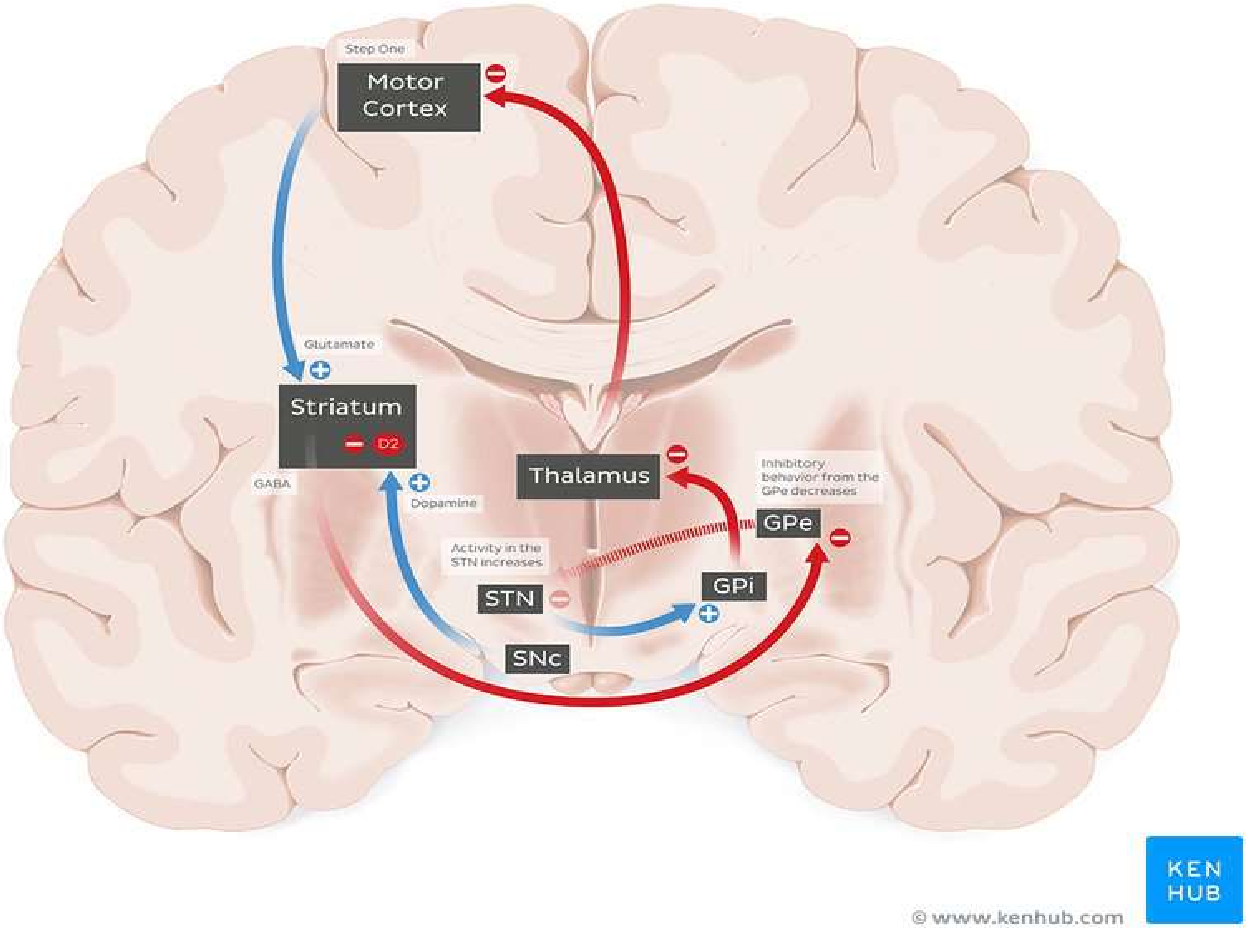
- **Akinesia** that is presented with the inability to move at all because the individual is unable to plan or to direct a movement toward a desired position or target.

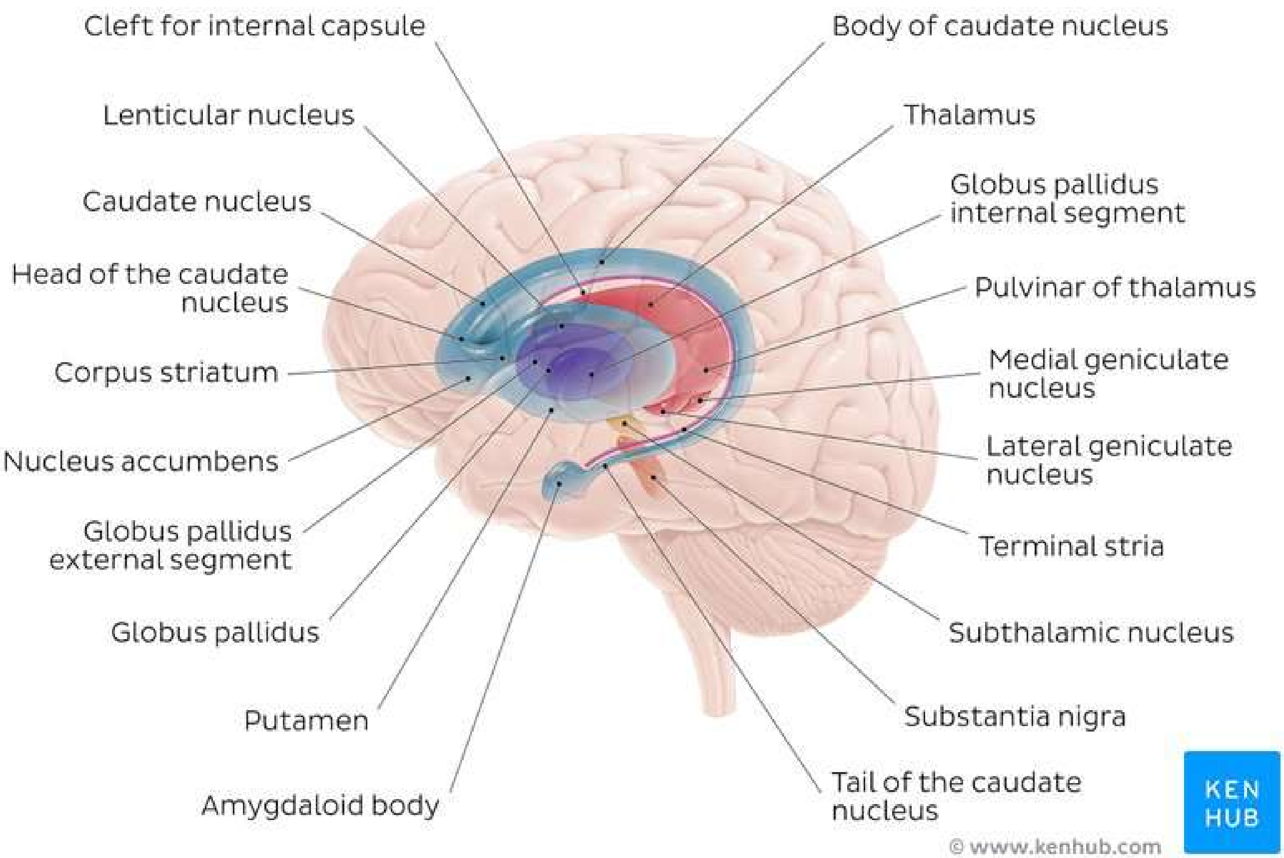
Parkinson's disease is the most prevalent disorder associated with the basal ganglia. It is the result of the degeneration of the dopaminergic neurons of the pars compacta of the substantia nigra. This is actually the place of origin of the nigrostriatal pathway that is essential for the promotion of the direct pathway of the basal ganglia. Because of its damage, the excitation of the supplementary motor area which is of key significance for the movement planning, is lost.

Direct Pathway of the Basal Ganglia



Indirect Pathway of the Basal Ganglia




Cleft for internal capsule
Lenticular nucleus
Caudate nucleus
Head of the caudate nucleus
Corpus striatum
Nucleus accumbens
Globus pallidus external segment
Globus pallidus
Putamen
Amygdaloid body
Body of caudate nucleus
Thalamus
Globus pallidus internal segment
Pulvinar of thalamus
Medial geniculate nucleus
Lateral geniculate nucleus
Terminal stria
Subthalamic nucleus
Substantia nigra
Tail of the caudate nucleus
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