Physiology 435 team

PHYSIOLOGY OF BASAL GANGLIA & REGULATORY MECHANISMS

Objectives:

- Appreciate **different nuclei** of basal ganglia.
- Know different **neurotransmitters** that have a role in basal ganglia functions.
- Appreciate general **functions** of basal ganglia.
- Diagnose basal ganglia disorders.

Done by:

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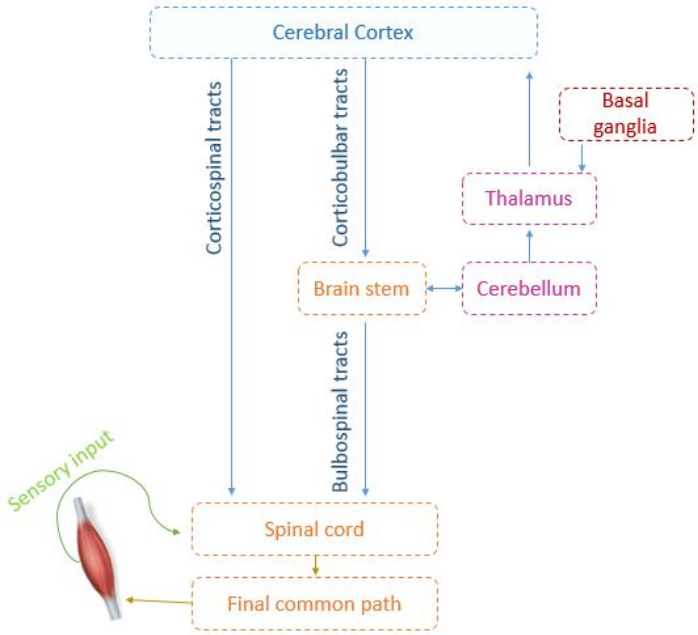
Color index: Important - Further explanation - Doctors Notes - Numbers.

*Please check out this link before viewing the file to know if there are any additions or changes.

Motor Activity Control

Overview of Motor Activity Control:

The Cerebral Cortex is sending signals to the brain stem, and then finally to the skeletal muscle for movement. At the same time, the thalamus is receiving signals from both Basal Ganglia and the cerebellum. The function of this is to calculate the beginning and the end of the movement.

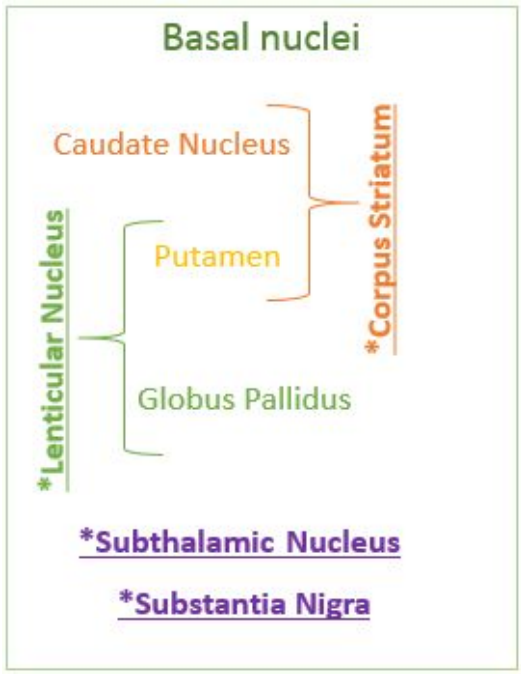


So, which structure will first give us the Action Potential? The Basal Ganglia.

Why? Because it is in charge of "planning" before moving by counting the distance and time. If there is a defect, the movement itself becomes slow. The person wouldn't know where to start and stop. They will have muscle rigidity, and if you push them, they wouldn't be able to stop, unless someone helps them. That is the end course of the disease.

Components and Functional Anatomy of the Basal Ganglia

The basal ganglia are ***subcortical*** nuclei of grey matter located within the white matter in the interior part of cerebrum near about base.



The Nuclei of the Basal Ganglia:

- **Caudate Nucleus**
- **Putamen**
- **Globus Pallidus**

Caudate Nucleus + *Putamen* = **C**orpus Striatum

Globus pa**ll**idus + *Putamen* = **L**enticu**l**ar nucleus

Structures related to the basal ganglia:

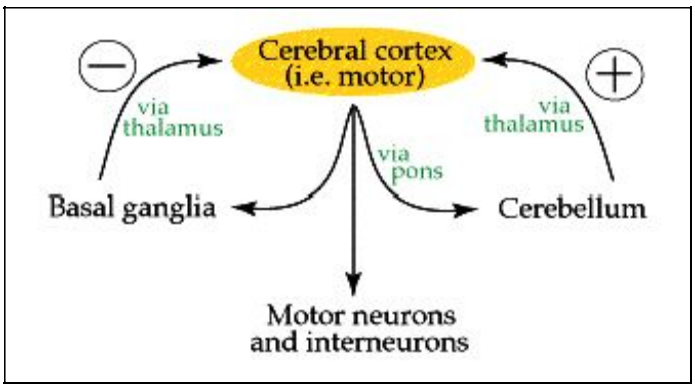
- **Subthalamic Nucleus**
- **Substantia Nigra**

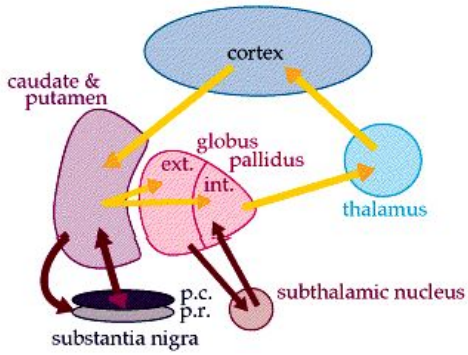
2-Minute Neuroscience: Basal Ganglia (Duration: 1:59)

Connections of the Basal Ganglia

There are 3 important types of connections to remember:

Main **input** to the basal ganglia	Main **output** from the basal ganglia	Connections **between** parts of basal ganglia
Input projects from the **cerebral cortex** (motor area) → **NEOSTRIATUM**[1]	Is via the **thalamus** → **cerebral cortex** (motor area)	**The Basic Circuits:** Motor, Cognitive, Limbic, and Oculomotor Loops.



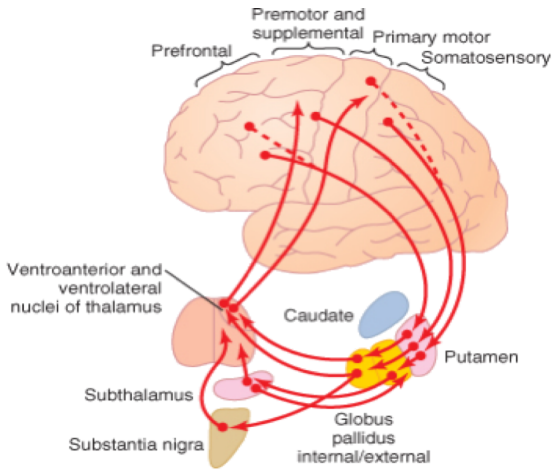


Basic Circuits of Basal Ganglia

Motor loop (Putamen circuit)	Concerned with learned movement Things that you learn in at an early age e.g. writing, holding a spoon When you want to learn something new, you have to **Put** an effort to **Learn**
Cognitive[2] loop (Caudate circuit)	Concerned with **cognitive control** of sequences of motor pattern. Basically it is concerned with **motor intentions** Using stored information in your memory to respond to a stimulus, e.g. running away from a fire.
Limbic loop	Involved in giving motor expression to emotions like smiling, aggressive or submissive Posture You need your **Limbs** to stand and have proper **posture**, so stand tall and **smile**
Oculomotor loop	Concerned with voluntary eye movement [saccadic[3] movement]

[1] A term for the caudate nucleus and putamen, i.e., Corpus Striatum
[2] cognition means thinking process using sensory input with information ***already stored in memory***
[3] a small rapid jerky movement of the eye especially as it jumps from fixation on one point to another (as in reading)

1- The Putamen Circuit: امشوا مع الصوره مره بيسهل



Pathway:

- **Input from:** Cerebral cortex, i.e.

Premotor, **supplementary motor** and **Somatosensory cortex**.

- **Passes through:**

After receiving the input, the pathway passes to the putamen firstly, then to the globus pallidus , ending in the **thalamus** "ventroanterior and ventrolateral nuclei" before sending out the output.

- **Output from:**

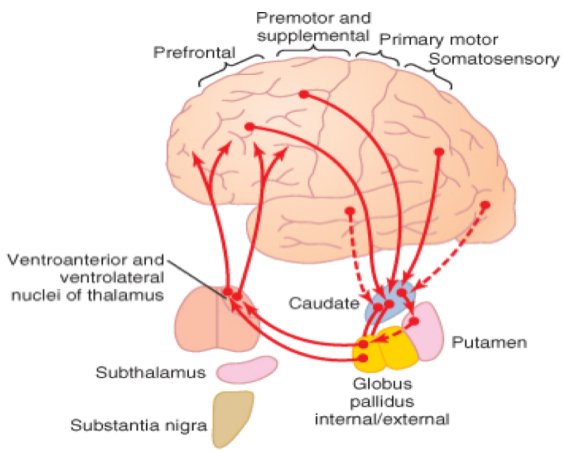
Premotor, supplementary motor and **primary cortex**.

Thus, putamen circuits has its input mainly from these parts adjacent to the primary motor cortex but not much from the primary motor cortex itself.

Functions:

- **Executes Learned Patterns of Motor Activity**
- Basal ganglia function in association with the **corticospinal system** to control complex patterns of motor activity.
  - ★ **Examples are:**
    - Writing of letters of the alphabet.
    - Cutting paper with scissors.
    - Hammering nails.
    - Shooting a basketball through a hoop.
    - Passing a football.
    - Throwing a baseball.
    - The movements of shoveling dirt.
    - Most aspects of vocalization.
    - Controlled movements of the eyes.
    - Virtually any other of our skilled movements, most of them performed subconsciously.

2-The Caudate Circuit: امشوا مع الصوره مره بيسهل



Pathway:

- **Input from:** Association areas.
- **Passes through:** After receiving the input, the signals pass to the caudate nucleus firstly, then to globus pallidus, ending in the **thalamus** before sending out the output
- **Output from:** Prefrontal, premotor and supplementary motor area.

Functions:

- **Cognitive Control of Sequences of Motor Patterns.**
  - ***Recall:*** *Cognition means the thinking processes of the brain, using both sensory input to the brain plus information already stored in memory.* Thoughts are generated in the mind by a process called **cognitive control of motor activity**.
  - **Example:** A person seeing a lion approach and then responding instantaneously and automatically by
    (1) turning away from the lion.
    (2) beginning to run.
    (3) even attempting to climb a tree.

  Thus, cognitive control of motor activity determines subconsciously, and within seconds, which patterns of movement will be used together to achieve a complex goal.

- **Change the Timing and to Scale the Intensity of Movements.**

  Two important capabilities of the brain in controlling movement are:
  1. To determine how rapidly the movement is to be performed.
  2. To control how large the movement will be.
  - **Example:** A person may write the letter "a" slowly or rapidly.

Also, he or she may write a small "a" on a piece of paper or a large "a" on a chalkboard. Regardless of the choice, the proportional characteristics of the letter remain nearly the same.

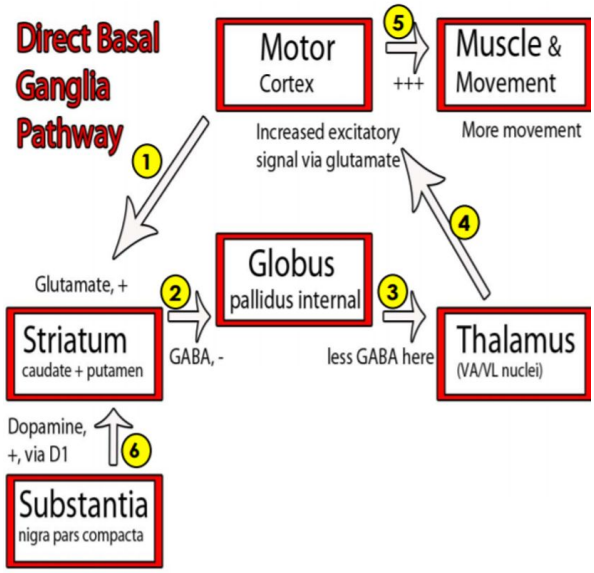
يعني بيكون الشكل النهائي للحرف هو نفسه، الشيء الوحيد اللي تغير الحجم أو سرعة الشخص في الكتابة، بس النتيجة هي نفسها.
كلام كثير بس لازم نحطه الشكوى لله.. أهم شي بالوظائف يوصلكم مفهوم اللي بالأحمر.. كودات = اسد + حرف الاي

Basal Ganglial Pathways Direct and Indirect

Direct Pathway "Excitatory Pathway":

امشوا مع الصوره مره بيسهل

1. **Motor Cortex** sends out **excitatory** (Glutamate) input to Striatum (**St**).
2. The **St**, as a result, sends out **inhibitory** (GABA) to the Globus Pallidus Internal (**GPi**).
3. **GPi** sends **less inhibitory** (GABA) input to the **Thalamus.** بما انه لس انهبتوري يعني بتظل متحفزه
4. Resulting the **Thalamus** to send **excitatory** (Glutamate) input back to the **Motor Cortex.**
5. **Increase** in motor activity :).



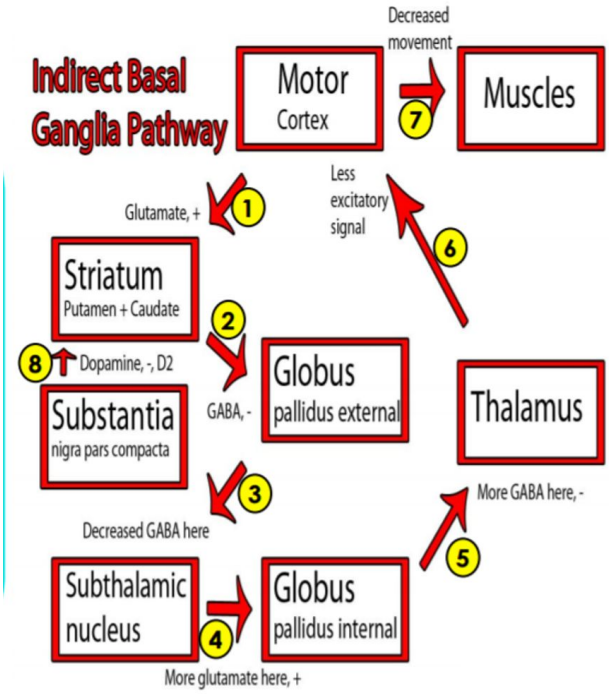
*+SNPC (Substantia Nigra Pars Compacta) is involved by sending Dopamine to St, which will bind to DA1 receptor which is **excitatory**.*

The basal ganglia - The direct pathway (Khan academy channel) (Duration:10:46) very helpful start from 4:28

Indirect Pathway "Inhibitory Pathway":

امشوا مع الصوره مره بيسهل

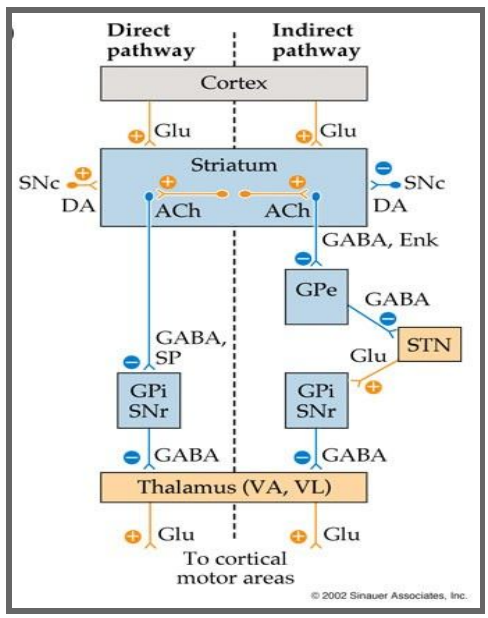
1. **Motor Cortex** sends out **excitatory** (Glutamate) to Striatum (**St**) to excite it.
2. The **St**, as a result, sends out **inhibitory** (GABA) to the Globus Pallidus External (**GPe**)
3. **GPe** will send **less inhibitory** (GABA) to Subthalamic Nucleus (**SThN**).
4. **SThN** will send **excitatory** (Glutamate) to **GPi**
5. **GPi** will send **inhibitory** (GABA) to **Thalamus**
6. Thalamus will send **less excitatory** Glutamate to Motor Cortex
7. **Decreased** motor activity



+SNPC (Substantia Nigra Pars Compacta) is involved by sending Dopamine to St, which will bind to DA2 receptor which is ***inhibitory***

[The basal ganglia - Concepts of the indirect pathway](#) (Duration: 8:42)(Khan academy channel)

Both Direct and Indirect Pathways:



Think of it this way:

The cortex sends **excitatory** impulses by GLU in both pathways, the striatum then sends **inhibitory** impulses in both pathways (using GABA), the thalamus **receives inhibitory** impulses and **sends** to the cortex **excitatory** impulses in both pathways, either directly from GPi in the direct pathway, or indirectly through GPe, SThN & GPi in the indirect pathway. **The cortex' motor activity ultimately depends on the signals reaching the GPi**, when the inhibitory signals (sent by GPi) are inhibited as in the direct pathway, the thalamus gets less inhibition and can send the motor cortex more signals and hence the motor activity of the cortex would **increase**. while in the indirect pathway the inhibitory GPi is excited, the thalamus gets more inhibition and thus can send less signals, the motor activity would therefore **decrease**.

Function: Direct and indirect pathway of basal ganglia sharpens signals and make them stronger.

- **How do they work cooperatively?** اضافته الدكتوره هالسنه وموب موجود بسلايدات الأولاد

For example: if you want to concentrate on writing.

The direct pathway= facilitate the movement= induce action potential.

The indirect pathway=suppress unnecessary movements= inhibit action potential.

- **Why do we need this sharp selective mechanism?** اضافته الدكتورة هالسنة وموب موجود بسلايدات الأولاد

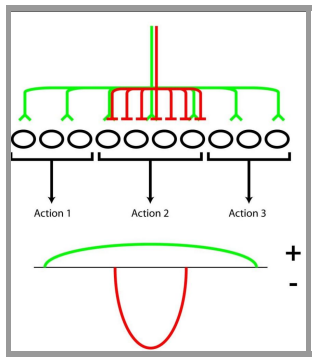
  There are many stimuli around us , however we can make a single action for one stimuli and ignore the unnecessary ones .This is a selection mechanism that work in big and small scales.

  E.g. To look to the right or to the left? How far to look?

Summary of direct and indirect pathways.	
Direct pathway	**Indirect pathway**
Facilitate the movement	**Suppress** the movements
Dopamine acts on **D1** receptor (facilitate strong, phasic inputs - suppress weak inputs).	Dopamine acts on **D2** receptors(suppress the striatal activity)
GPi inhibition.	**GPi excitation.**
Focused and robust.	Widespread and diffuse.
Co-activation of these pathways facilitates action selection through center-surrounded mechanisms .	

الصورة اضافتها الدكتورة هالسنة وميب موجوده بسلايدات الأولاد

The green fibers are the indirect pathway , they are widespread and diffused.
While the red fibers are the direct pathway, they are few and concentrated.
The red fibers induce action potential while the green maintains the resting membrane potential.
*If there is a defect in this mechanism we will have **tremors**.



Metabolic characteristics of basal ganglia:

- **high oxygen consumption.**
- **High copper content.**

- **Wilson's disease (copper poisoning) :**
  - **Autosomal recessive** where there is **lentiform nucleus degeneration** in basal ganglia.
  - There is copper accumulation in liver , retina and lentiform nucleus, Due to decreased levels of **ceruloplasmin** [4]protein.

*Patients will have liver problems as well such as jaundice.

Functions and disorders of basal ganglia:

❖ **Function of basal ganglia :** control / plan/ programme movements and cognition[5].

❖ **What will happen in Basal ganglia defect?**

Ataxia[6] , speech problems, posture and gait problems and mental problems.

❖ **Basal ganglia disorders:**

Movement disorders :

Parkinson's disease.	substantia nigra degeneration	Hypokinetic	Pill rolling rest **tremors** **Lead pipe** rigidity akinesia[7]
Hemiballismus	Hemorrhagic destruction of contralateral subthalamic N. destruction. Hypertensive patients.	Hyperkinetic	Wild movements of half(hemi) of the body
Athetosis	Corpus striatum & thalamus hypomyelination.	Hyperkinetic	Slow, ,**writhing** movements in appendicular muscles
Chorea	**striatum** atrophy.	-	Multiple, **random**, **quick** movements in appendicular muscles.
Huntington's disease	-	Hyperkinetic	-
Drug induced (Neuroleptics ,MPTP)	-	Hypokinetic	-

★ **Extra:**

hemiballismus happens because of an artery problem of subthalamus.Since subthalamus didn't receive enough blood it will go into infarction this leads to a problem in signals transmission in cortex fibers then problems in fibers from cortex to spinal cord (that cross).

An infarction in the subthalamus will cause wild movement in the contralateral part of the body.

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[4] Ceruloplasmin is an important protein of copper metabolism
[5] Thinking process using information already stored in memory.
[6] Loss of control of body movements:range,force,direction..etc.
[7] Loss of voluntary movements.

PARKINSON'S DISEASE

- First described by james parkinson.
- Degeneration of dopaminergic neurons nigrostriatal (of substantia nigra and striatum(caudate & putamen)
    - they used Methyl Phenyl Tetrahydro Pyridine (MPTP) on animals experiment. The oxidant MPP+ is toxic to substantia nigra so it causes parkinson's in the animals.

- Features:

Tremors - Rigidity - Akinesia & bradykinesia - Postural changes - Speech changes.

- Treatment: L-levodopa "for more details check out pharmacology lecture".

★ References:

- 435 girls slides and notes.
- 434's teamwork.
- Guyton and hall textbook of medical physiology 12th edition.
- NEUROANATOMY 5th edition.
- Wikipedia.
- Ganong's Review of Medical Physiology (Twenty-Third Edition).