CNS

Doctor 2021

Anatomy

Sheet (3)

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Basal Nuclei

- Slides will be in purple, doctor's note in black.

Brain is divided into forebrain, midbrain & hindbrain. We talked previously about midbrain & hindbrain so the upcoming lectures will be about forebrain.
Forebrain is composed of telencephalon (cortex, under neath subcortical white matter & gray matter within the white matter) and diencephalon (thalamus, epithalamus, subthalamus & hypothalamus).
In this lecture we will start with the gray matter within the subcortical white matter which is a group of nuclei called (BASAL NUCLEI) and they mainly have motor function.

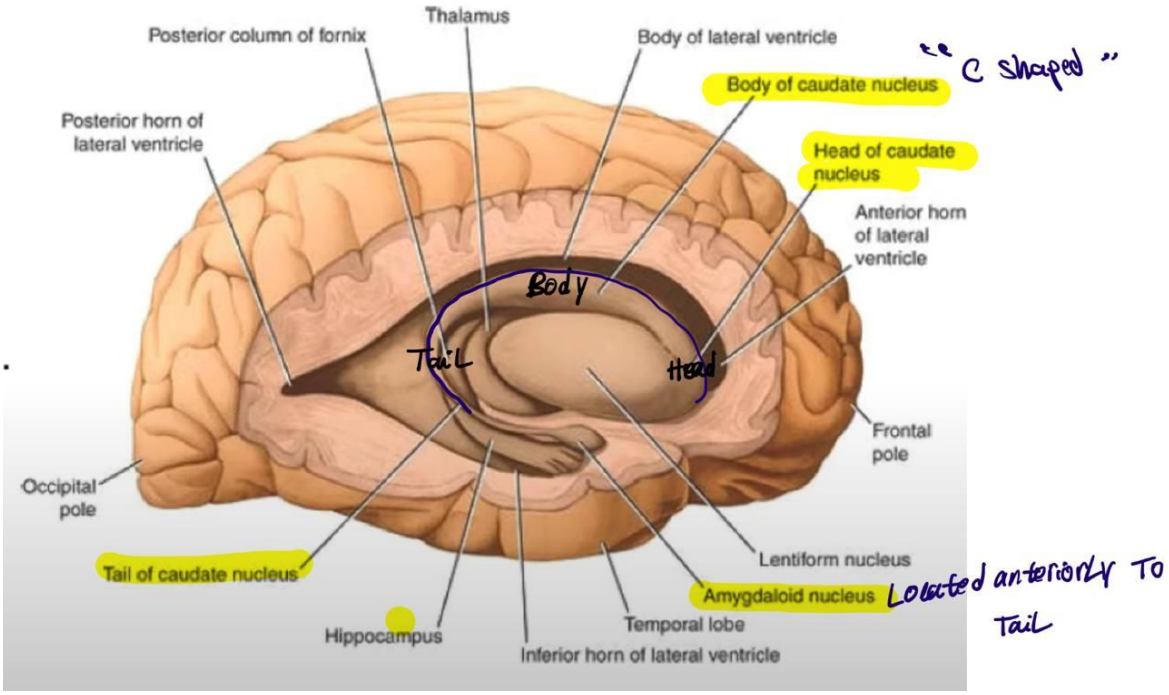
-Previously it was called basal ganglia, but we said before that ganglia means cell bodies in PNS, while nuclei cell bodies in CNS, so the most precise name is basal nuclei.

- Basal nuclei:

collection of masses of gray matter situated within each cerebral hemisphere.

- Divided generally into:

- ✓ Corpus striatum
  - Caudate nucleus **(it has a "C" shape with head, body & tail)**
  - Lentiform nucleus **(wedge shape مثل حبة العدس)**
    Lentiform is divided into lateral part called (putamen nucleus) & medial/inner called (globus pallidus)
- ✓ Amygdaloid nucleus **(at the end of caudate's tail)**
- ✓ Claustrum

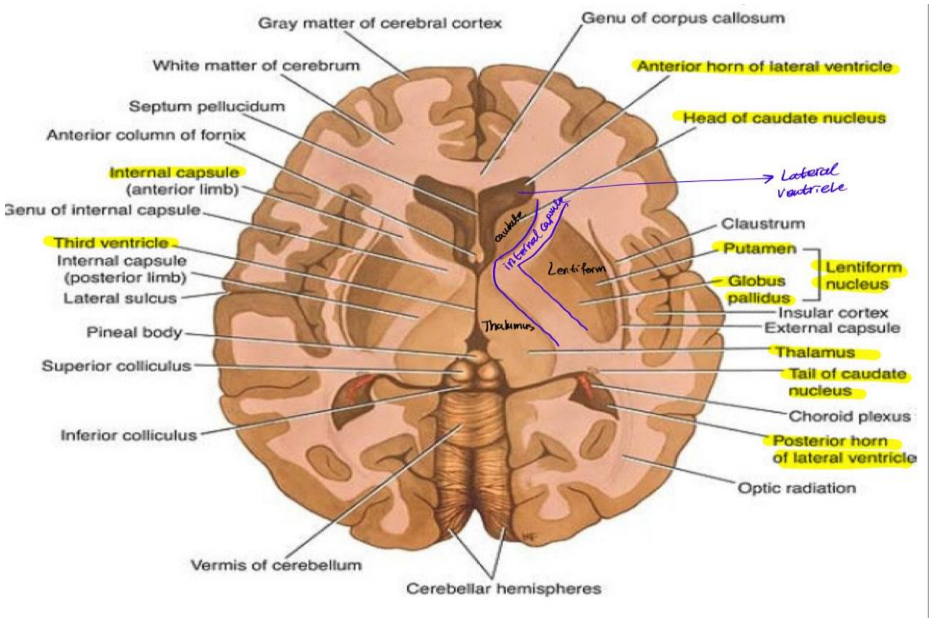


- Corpus striatum

Divided by internal capsule (a band of nerve fibers) into:

- Caudate nucleus
- Lentiform nucleus

Remember that internal capsule is the narrow area where tracts pass through before projecting from thalamus into cortex. notice the figure below, thalamus is located on either sides of 3rd ventricle (cavity of diencephalon). Internal capsule separates thalamus & caudate medially from lentiform laterally.

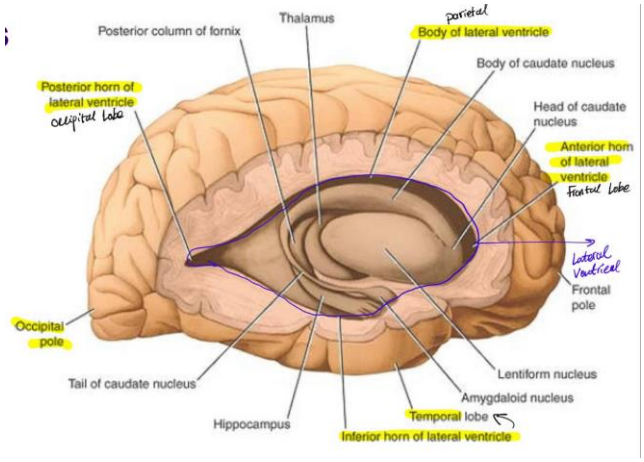


- **Caudate nucleus** (1st part of corpus striatum)
  large C-shaped mass of gray matter, closely related to the lateral ventricle and lies lateral to the thalamus (formed of head, body & tail).
  - ✓ Head: large and rounded and forms the lateral wall of the anterior horn of the lateral ventricle **(head is at level of frontal lobe).**
  - ✓ Body: long and narrow and is continuous with the head in the region of the interventricular foramen. forms part of the floor of the body of the lateral ventricle.

Interventricular foramen/ foramen of Monro is the passageway between 3rd ventricle and lateral ventricles.

- ✓ Tail: long and slender and is continuous with the body in the region of the posterior end of the thalamus. It follows the contour of the lateral ventricle and continues forward in the roof of the inferior horn of the lateral ventricle. It terminates anteriorly in the amygdaloid nucleus.

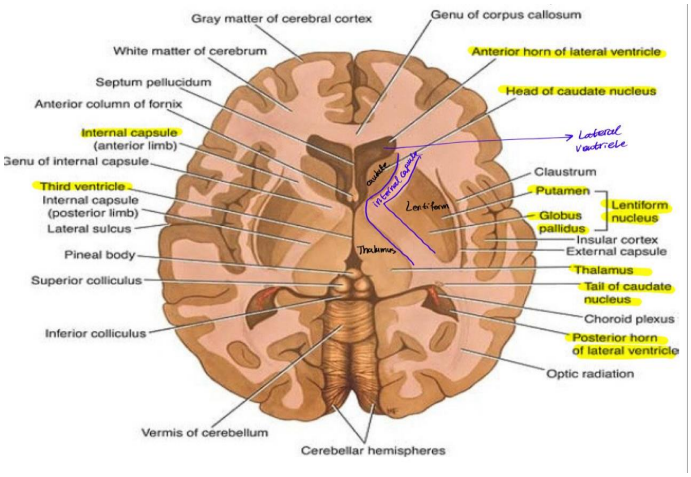
SAGITTAL SECTION



Lateral ventricle is C shaped; it has anterior horn in frontal lobe, body in parietal lobe, posterior horn in occipital lobe and inferior horn in temporal lobe.

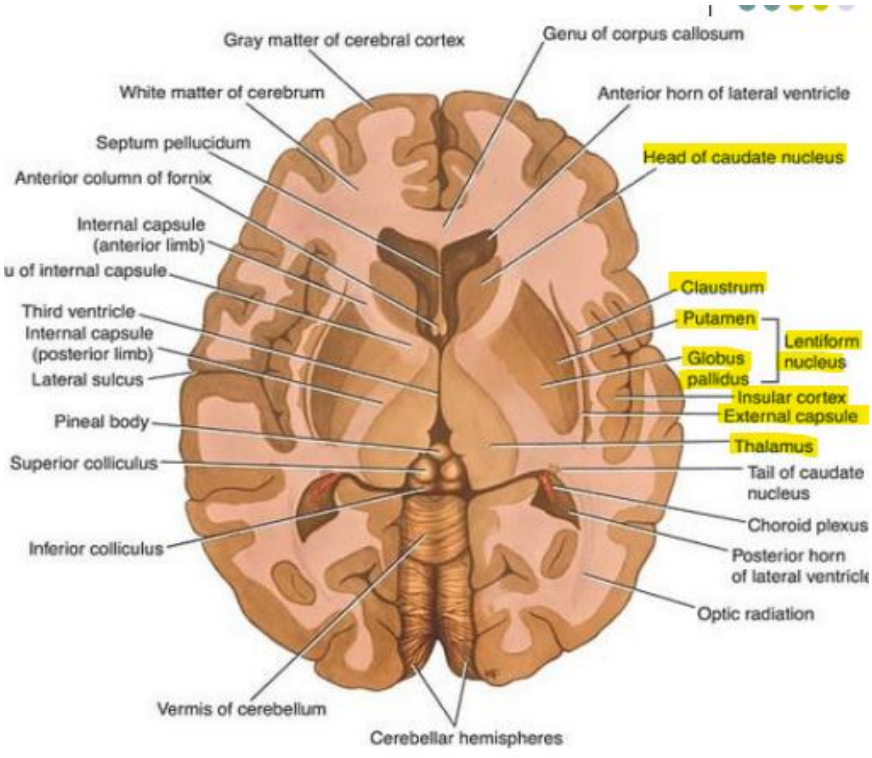
Caudate has a relationship with lateral ventricle, the transverse section shows how head of caudate is related to the lateral wall of lateral ventricle, posteriorly you can see tail of caudate related to inferior horn of lateral ventricle.

TRANSVERSE SECTION



- **Lentiform nucleus** (2nd part of corpus striatum)
  - ✓ It has two parts, putamen nucleus (darker lateral part) & globus pallidus (lighter medial part).
  - ✓ wedge-shaped (lateral part is wider than medial part) mass of gray matter whose broad convex base is directed laterally and whose blade is directed medially.
  - ✓ Medially: internal capsule (separating caudate & thalamus medially from lentiform laterally).
  - ✓ Laterally: external capsule (thin sheet of white matter), which separates it from the claustrum (last part of basal nuclei).
  - ✓ Divided into:
    - Putamen nucleus: a larger, darker lateral portion
    - Globus pallidus: inner lighter portion, it's divided into:
      - Internus
      - Externus

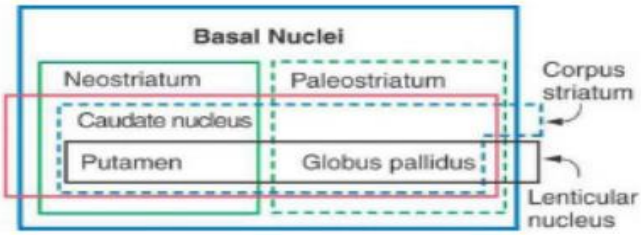
      (they are not clear in the picture below, but functionally they are different)
  - ✓ Claustrum: thin sheet of gray matter that is separated from the lateral surface of the lentiform nucleus by the external capsule and lateral to the claustrum is the subcortical white matter of the insula.

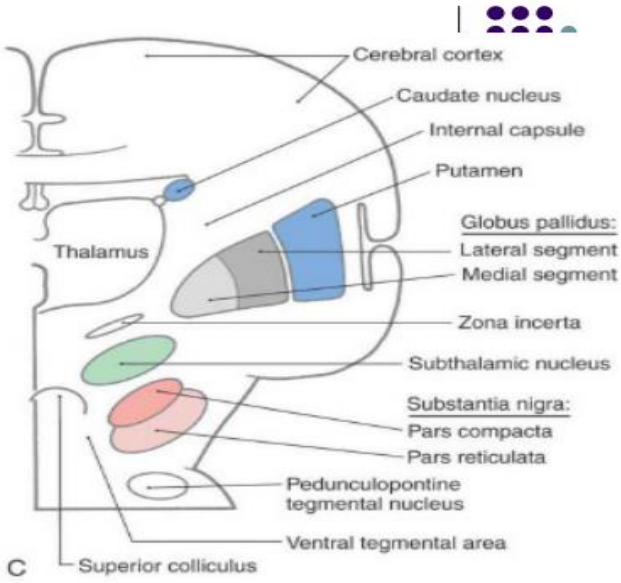


So, here is how nuclei are arranged from inside to outside:

- **Caudate & thalamus are most medial**
- **internal capsule (white matter)**
- **Lentiform (gray matter)**
- **external capsule (white matter)**
- **Claustrum (part of basal nuclei)**
- **subcortical white matter of insula**
- **Insular cortex (most lateral, it's part of cortex but hidden in the lateral fissure which separates temporal lobe from frontal & parietal superiorly)**

Note: in the previous pages we have talked about basal nuclei from anatomical point of view, now we will start with the functional aspect, but before we will make another classification.





- **Putamen + globus pallidus = lentiform nucleus** } **ANATOMICAL CLASSIFICATION**
- **Putamen + globus pallidus + caudate = corpus striatum**

- **Caudate + putamen = Neostriatum** } **FUNCTIONAL CLASSIFICATION**
- **Globus pallidus = paleostriatum**

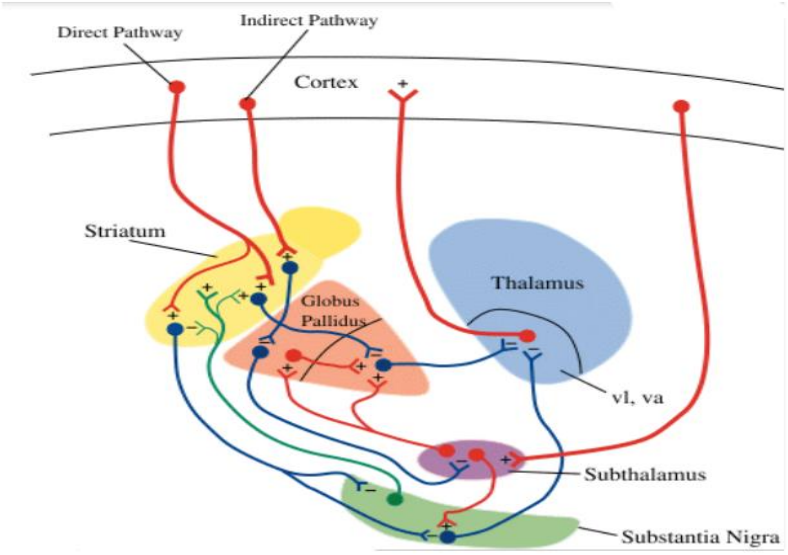
NOTE: striatum = neostriatum

Basal nuclei are mainly motor. Remember the descending tracts in which UMN is controlling LMN. However, the motor system is more complex. In cortex, before activation of UMN & LMN, there will be consultation with areas related to motor which their main function is fine tuning & coordination. Just like cerebellum.
Basal nuclei have relatively similar functions, there will be cross talk between cortex & basal nuclei before activation of UMN & LMN, and this is called motor loops.

Motor loops are divided into direct pathway & indirect pathway, and both start in motor cortex and return to motor cortex.

- Direct pathway

- **keys of the picture:**
  - **Red: excitatory (+)**
  - **Blue: inhibitory (-)**
  - **Green: modulatory**



The direct pathway starts by neurons their cells bodies found in cortex and they go down to striatum (neostriatum: caudate & putamen).

The beginning of direct pathway is called corticostriate (the term implies where it has started and finished; from cortex to striatum). This neuron is excitatory, it will excite an inhibitory neuron called striatopallidal (from striatum to globus pallidus internus). And this inhibitory neuron inhibits a neuron called pallidothalamic which is also inhibitory.
The net result of inhibition of an inhibitory neuron is activation of the last neuron which is called thalamocortical.

Note: globus pallidus has two parts; internus & externus.

➢ Mechanism of disinhibition:

- Activation of excitatory neuron; the net result is excitation.
- Activation of inhibitory neuron; inhibition.
- Inhibition of inhibitory neuron; excitation.

مثل الرياضيات بالزبط، (+ = - × -) / (- = + × -)

So, the direct pathway starts with excitatory fibers (corticostriate) which excites inhibitory fibers (striatopallidal) which produces GABA (inhibitory), so the next neuron (pallidothalamic) will be inhibited producing less GABA.

In other words, the 4th neuron (the thalamocortical fibers; their cell bodies are found in thalamus and they're projecting towards cortex, will escape inhibition). So, normally they're tonically active and the effect of pallidothalamic fibers on them is inhibitory.

المثال كأنك عم تسوق سيارة على منحدر، عشان السيارة تمشي مافي داعي للبنزين فقط بترفع رجلك عن البريك ولحالها بتمشي، هون صار نفس الاشي لما انرفع عنهم البريك لحالهم اشتغلوا

So normally, thalamocortical fibers are active and firing, the fibers coming from globus pallidus internus to thalamus are inhibitory (break). Activation of direct pathway means that thalamocortical fibers escape inhibition.

The net effect of direct pathway is excitatory, it increases the activity of the thalamus and consequently activates cortex.

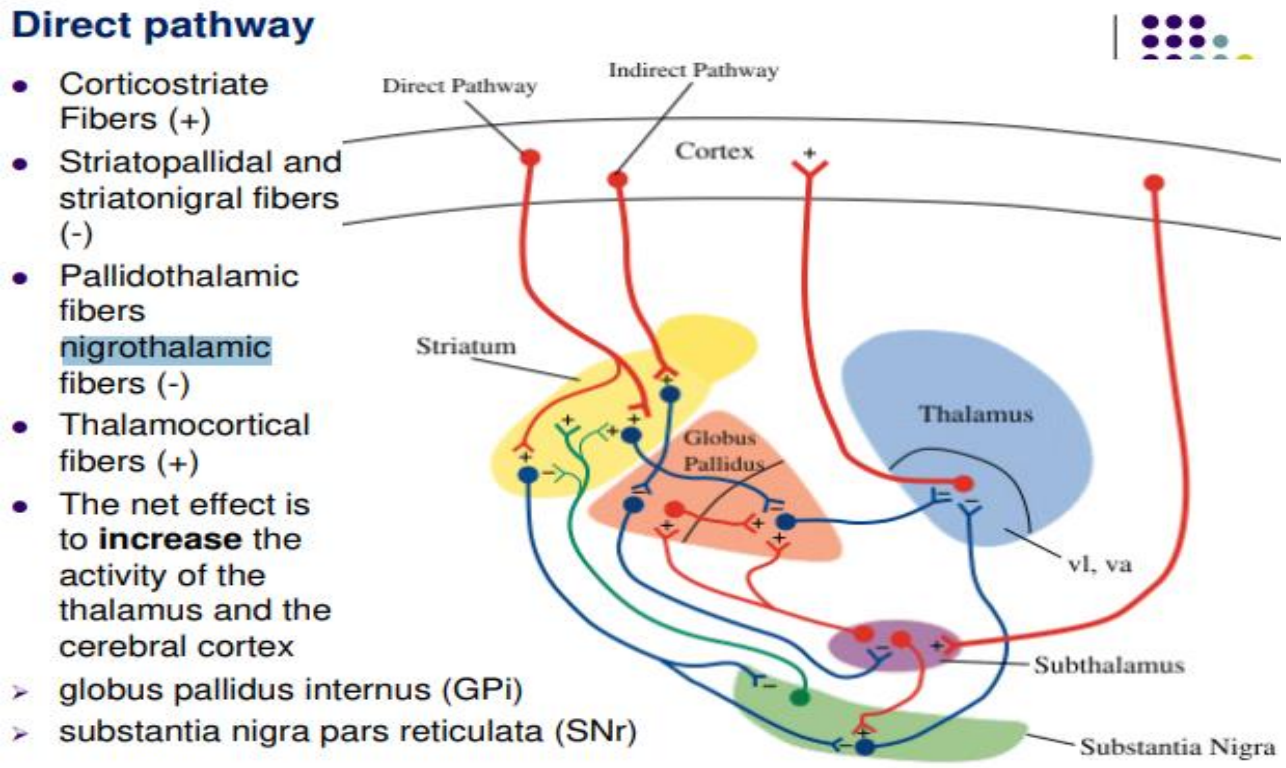
(+) . (-) . (-) . (+) = +

Globus pallidus internus (GPi) is very similar to substantia nigra pars reticulata (SNr). Substantia nigra is anatomically mid brain but functionally basal nuclei, it has motor function.

Substantia nigra is two parts: pars reticulata & pars compacta.

Reticulata is exactly like GPi (same connection & function). It's inhibitory on thalamus, specifically in va (ventral anterior nuclei) & vl (ventral lateral nuclei) which contain thalamocortical fibers.

Note: no fibers reach cortex before passing in thalamus (motor & sensory).



- **Indirect pathway** "it has an extra loop"

It's just like direct, but it has an extra loop in structure called subthalamus.

Anatomically, subthalamus is part of diencephalon. However, functionally it's related to basal nuclei, and it has motor function.

Like direct pathway, Indirect pathway begins from corticostriate fibers (+), which excite striatopallidal fibers.

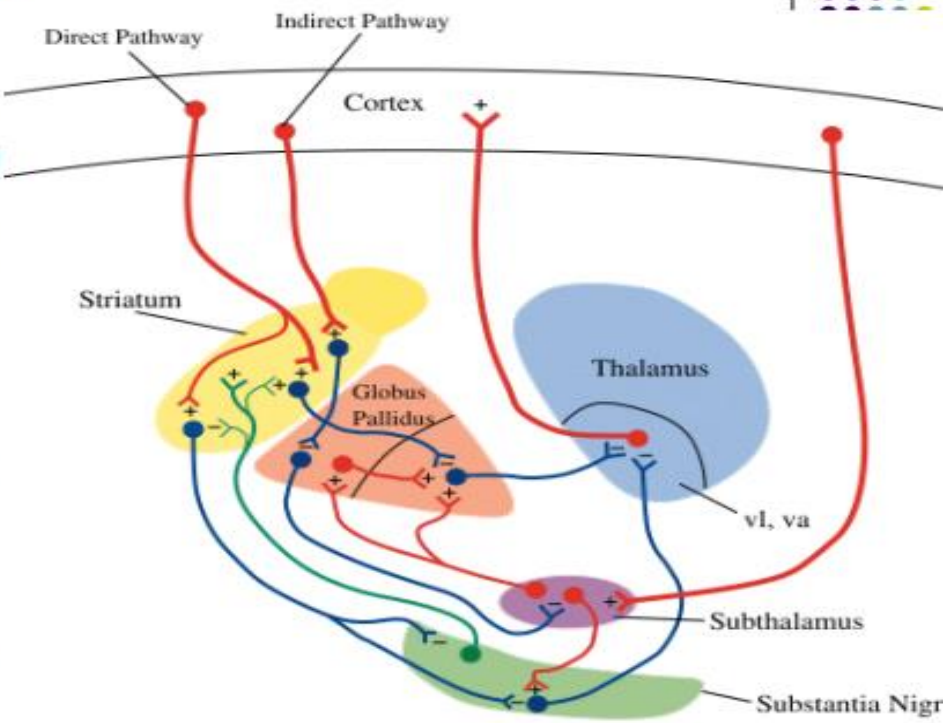
Striatiopallidal fibers go to globus pallidus externus (in direct they were going to internus), from externus an inhibitory fibers called pallidosubthalamic go to the subthalamus. And from subthalamus the subthalamopallidal fibers go to globus pallidus internus.

Extra loop

Then it continues like the direct pathway, but because of extra loop the net effect of indirect pathway is inhibitory (decreasing the activity in thalamus & cerebral cortex).

Indirect pathway

- Corticostriate Fibers (+)
- Striatopallidal (-)
- Pallidosubthalamic fibers (-)
- Subthalamopallidal fibers (+)
- Pallidothalamic fibers nigrothalamic fibers (-)
- Thalamocortical fibers (+)
- The net effect is to **decrease** the activity of the thalamus and the cerebral cortex

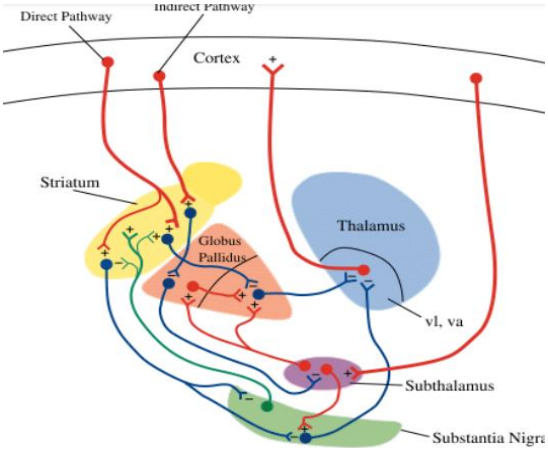


Through this increase and decrease, both direct & indirect pathways contribute to fine tuning in basal nuclei.

➢ Role of substantia nigra

We said that substantia nigra has mainly two parts: reticulata (SNr) & compacta (SNc). Reticulata has the same function as globus pallidus internus, while compacta is modulatory, it produces dopamine to neostriatum.

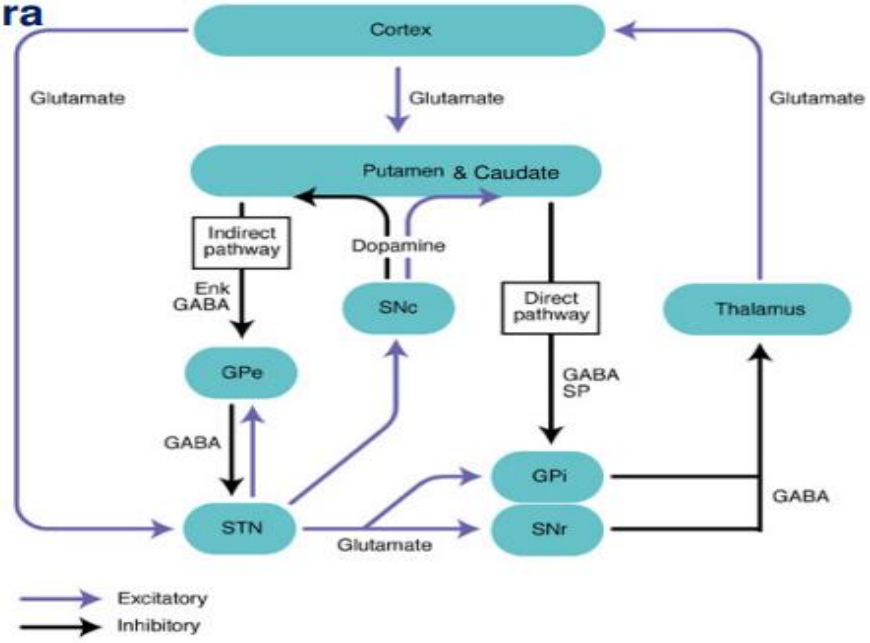
Look at the green fibers arising from substantia nigra/pars compacta, those are dopaminergic neurons reach striatum and give excitatory & inhibitory fibers.



The effect of dopamine (excitatory/inhibitory) depends on the receptor. There are two dopaminergic receptors: D1 & D2
Net effect of dopamine on direct pathway is excitatory & inhibitory on indirect pathway. So, pars compacta help to initiate the movement.

Role of Substantia nigra

- Substantia nigra pars reticulata (SNr) functionally similar to GPi
- Substantia nigra pars Compacta (SNc)
  - Releases dopamine in neostriatum
  - Excitatory to direct pathway (D1 receptors)
  - Inhibitory to indirect pathway (D2 receptors)



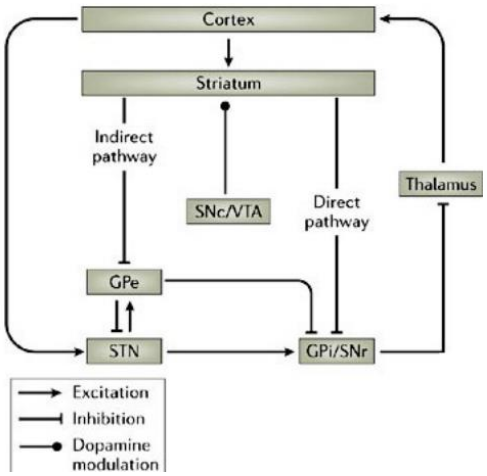
Note: Basal ganglia receive no direct input from or output to the spinal cord.

Basal nuclei have no direct relationship with spinal cord, they send & receive signals from cortex. Cerebellum receive input from spinal cord but there is no output from cerebellum to spinal cord.

- Functions of basal ganglia

In general function of basal ganglia are:

1. **regulation of voluntary muscle movement (direct & indirect pathways are responsible of fine tuning)**
2. **learning motor skills. Basal nuclei have software/ stored programs responsible of motor skills that all people can do without thinking like walking. Those motor skills can be improved like car driving.**



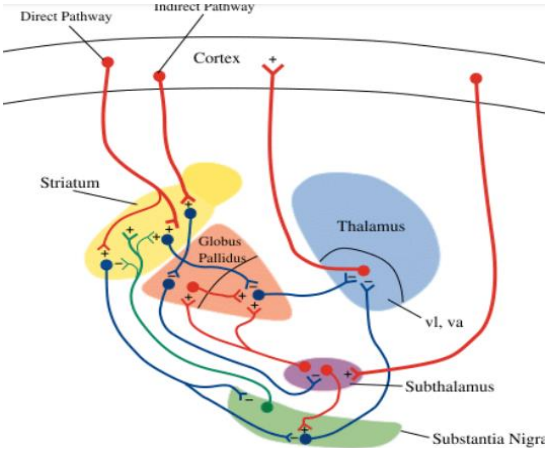
3. Preparation for the movements by controlling the axial and girdle movements of the body.

Disinhibition is the Primary Mode of Basal Nuclear Function

Problems in basal nuclei can be *hyperkinetic* (increase in movement) & *hypokinetic* (decrease in movement)

- ## Parkinson's disease

Progressive disease because of degeneration of dopaminergic neurons in substantia nigra which leads to a hypokinetic problem.



Net effect of dopaminergic neurons arising from pars compacta towards striatum is excitatory to direct & inhibitory to indirect. If the amount of dopamine is reduced and those fibers are degenerated the opposite will happen, the direct will be inhibited and the indirect will be active.

The direct pathway is responsible for movement initiation, so without dopamine there will be difficulty in movement initiation (bradykinesia).

- **Bradylinseia: difficulty in movement initiation.**
- **Akinesia: cannot move at all.**

- **Signs and symptoms include tremors, rigidity & bradykinesia.**
- **Rigidity is just like symptoms of UMN lesions since the activity of cortex is decreased.**
- **Tremors in Parkinson's are static tremors (exist even without movement) while in cerebellum they are intentional tremors (just with movement).**

Go through picture below:

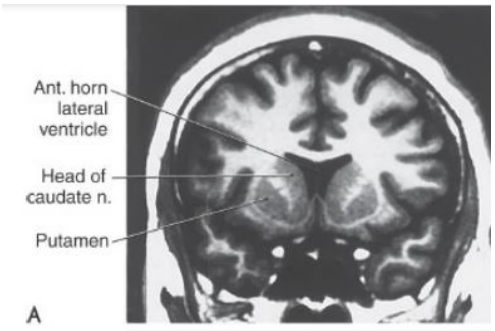
Parkinson Disease

- Progressive disease of unknown cause
- Neuronal degeneration in the **substantia nigra**
- Reduction in the release of the neurotransmitter dopamine within striatum
- signs and symptoms:
  - **Tremor**
    - slow and occurs most obviously when the limbs are at rest
  - **Rigidity**
    - present to an equal extent in opposing muscle groups
  - **Bradykinesis**
    - difficulty in initiating (**akinesia**) **and** performing new movements

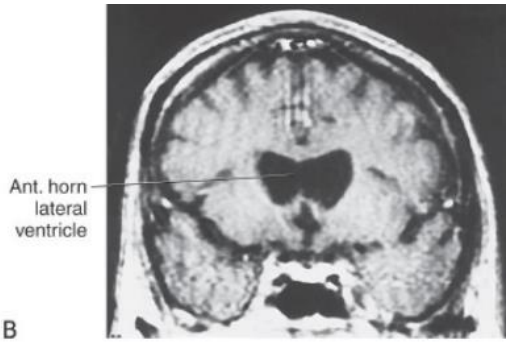
- Huntington disease

Inherited genetic disease, due to gene defect in chromosome no.4, it includes degeneration of striatonigral inhibiting pathway. If this inhibitory pathway is degenerated, as result neurons in substantia nigra will escape inhibition (totally the opposite of Parkinson's disease). So, it results no inhibition of dopaminergic neurons, more dopamine is produced which lead to involuntary movements of extremities (choreiform movement) & in extreme cases patients will get dementia.

The picture on the left shows what happens in Huntington, it's a frontal section showing caudate nucleus and it's normal.



This picture shows enlarged lateral ventricle due to caudate degeneration.



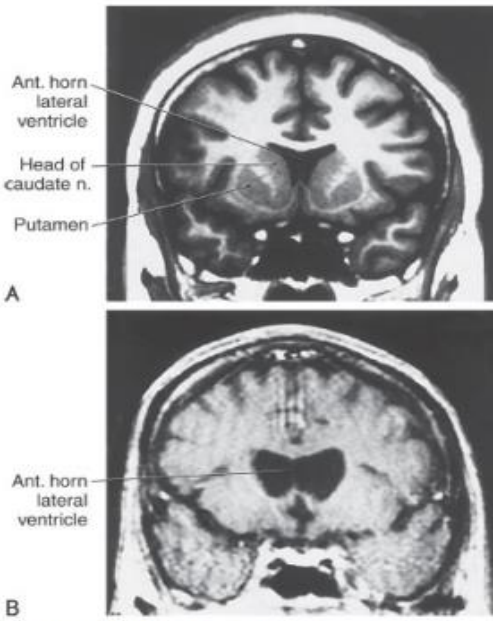
Go through the slide for revision:

Huntington disease

- Inherited disease, single gene defect on chromosome 4.
- Degeneration of the **striatonigral-inhibiting pathway**.
- This results in the dopa-secreting neurons of the substantia nigra becoming overactive; thus, the nigrostriatal pathway inhibits the caudate nucleus and the putamen
- Signs and symptoms:

1- **Choreiform movements:** first appear as involuntary movements of the extremities and twitching of the face (facial grimacing). Later, patient becomes immobile and unable to speak or swallow.

2- **Progressive dementia:** occurs with loss of memory and intellectual capacity.



➢ Computed tomography scans show enlarged lateral ventricles due to degeneration of the caudate nuclei.

V1