VAGUS ACADEMIC TEAM

BAU-Medicine

Sheet no. 14
Lecture Date: 3/3/2021
Lecture Title: Motor pathways II
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If you come by any mistake (whether it be spelling, grammatical or scientific) while browsing this sheet, kindly report it to the Academic team Facebook account.

The dr. pointed main structures in almost every picture .

Basal Ganglia

- The basal ganglia includes the (major nuclei) **caudate, putamen and globus pallidus** , and a number of closely related nuclei .
- There are other nuclei related to basal ganglia :

1. **Subthalamic nucleus** (some classify it as a part of epithalamus, but the dr prefers to classify it as basal nuclei) .
2. **Substantia nigra** in the midbrain .
3. **Claustrum** .
4. **Amygdala** .

- They influence motor system primarily through projections to upper motor neurons .
- Motor deficits depend on the specific nucleus damaged .
- Understanding the neurochemistry of basal ganglia drives the development of clinical treatment .

Basal Nuclei (Ganglia)

Ganglia : collection of cell bodies in PNS (outside central nervous system) .
Nuclei : collection of cell bodies in CNS .
Here *ganglia* is an exception; some books still use ganglia instead of nuclei .

The function of basal nuclei :
*At the beginning we said that they are part of the control system (they are very important for adjusting the orders that exit from cerebral cortex).
*The major connection of them (the efferent fibers) go to the cortex (final target); because their effect is on the initiator (cerebral cortex) ,and they have a station before they go to cerebral cortex which is the thalamus.
*Hierarchical control system is a form of the control system (control system includes basal nuclei and cerebellum) .

Basal Ganglia

- They control **fine movement** and sometimes **initiation of movement** (start movement rapidly), but if there is a damage the initiation becomes slow .

  Example of damage : Parkinson disease .
- The basal ganglia act as :
  - **Brake against involuntary movement (fine movement):**

    In Parkinson : if the patient want to move his hand to the right , his hand will not go to the right, instead it will make a random movement .
  - **Switch to turn on a fixed action pattern (initiation of movement):**

    The movement will take long time to move .
- Their direct output is to the VA(ventral anterior) of the thalamus :
  - Projects primarily to area 6 (premotor & supplementary motor areas) .
  - The afferent of VA are the efferent of basal nuclei .
  - From the basal nuclei go to VA then go to cerebral cortex (make movement) .

Basal Ganglia Terminology

- **Striatum (neostriatum)** = caudate + putamen (they are separated from each other but in specific region they meet) .
- **Lentiform nucleus** = putamen + globus pallidus (they are continuous in the center) .
- **Corpus striatum** = caudate + lentiform
- **Basal ganglia** = corpus striatum + amygdala
- **Globus pallidus** = pallidum = paleostriatum (old name) .
- **Claustrum (+subthalamic nucleus & substantia nigra)** are sometimes included with the basal ganglia .
- Basal ganglia is included by the **extrapyramidal system** .

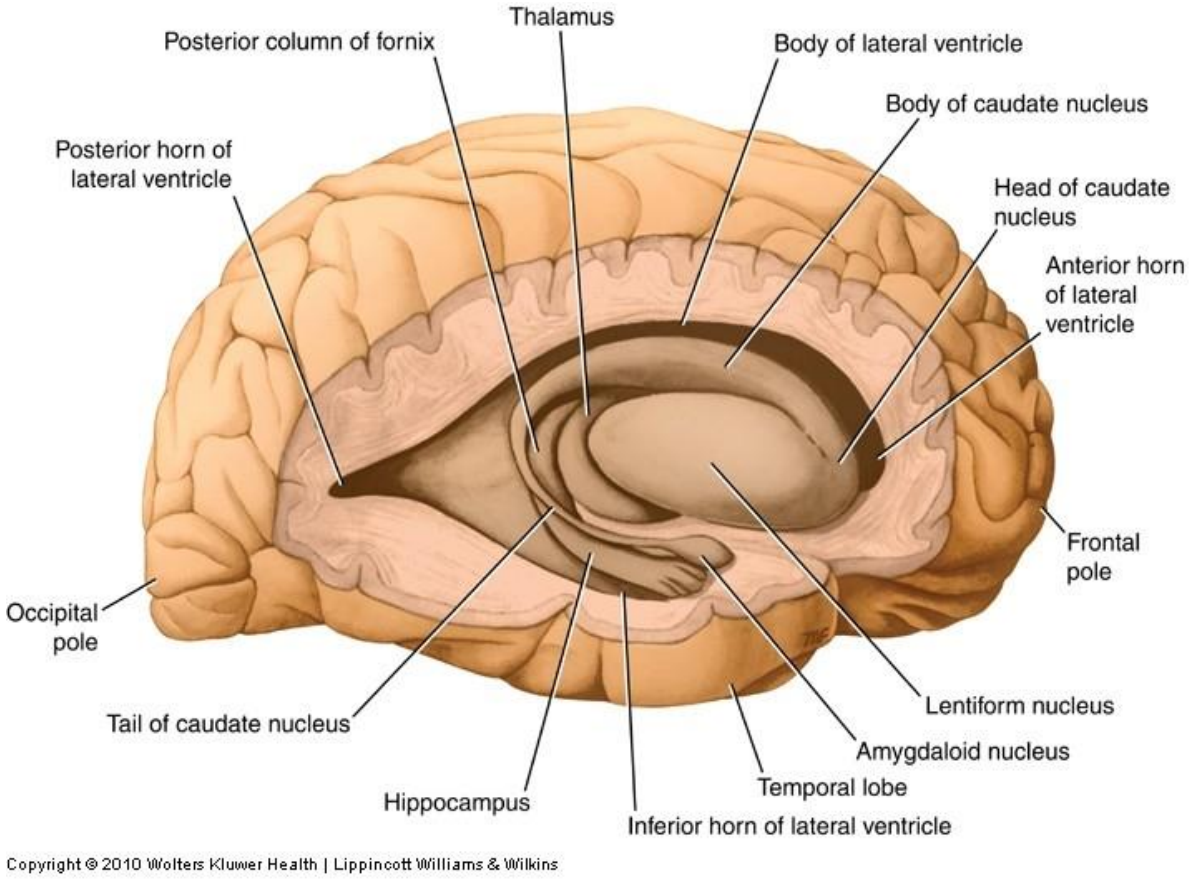
Basal Ganglia : Gross Anatomy

- **Caudate Nucleus** (c-shaped) :

* Parts :

** head : it's the most anterior part and it's close to the anterior horn and the body of lateral ventricle . (the head is big and gets smaller) .

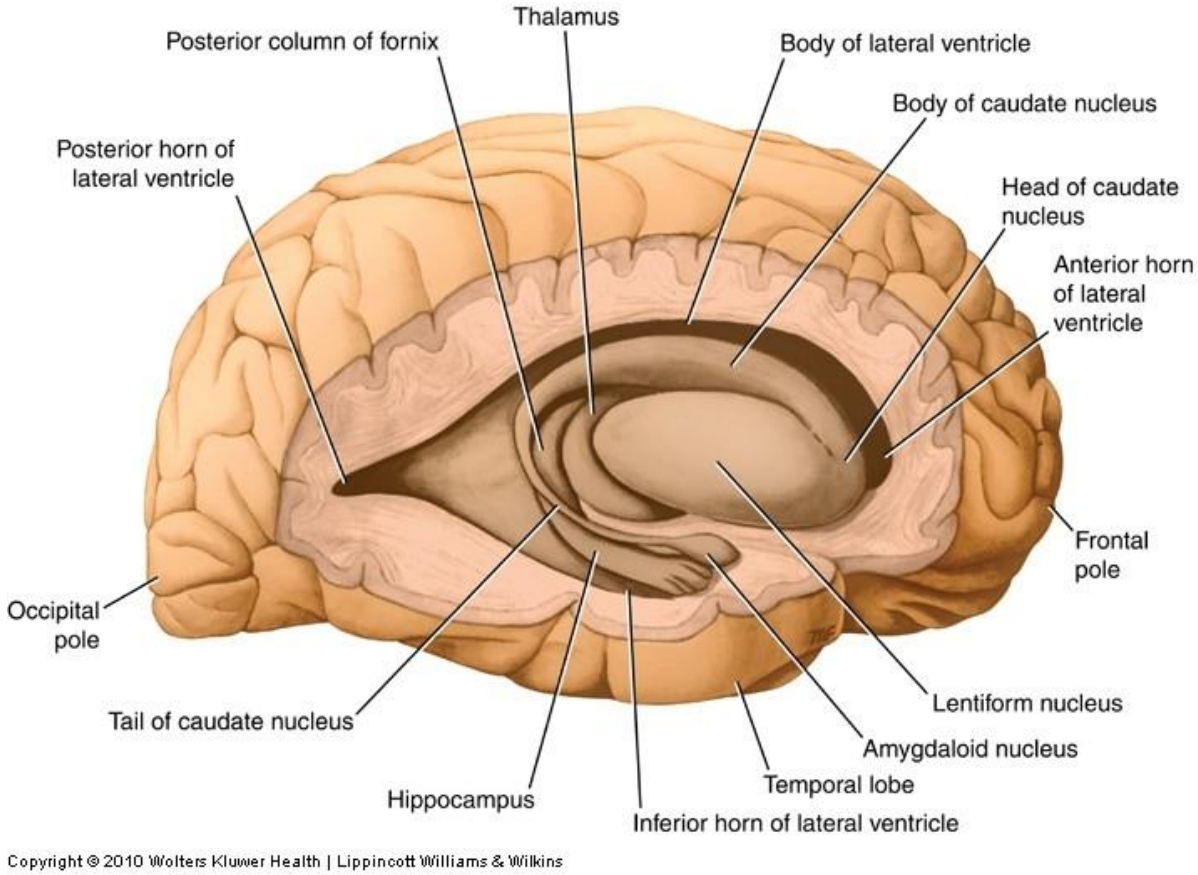
**tail : walks with the lateral ventricle and the inferior horn of the lateral ventricle .



- **Caudate Nucleus :**

* Location :

We said that the caudate nucleus and putamen are separated, but in a specific region they meet so the anterior part of putamen and the most anterior inferior part of the head of caudate meet with each other, the region where they meet is called ((**nucleus accumbense : responsible for attention**)) .



* Relations of caudate nucleus :

1- **lateral ventricle** : internal lateral to the lateral ventricle (internal because the c-shape of the caudate is smaller than the c-shape of the lateral ventricle) .

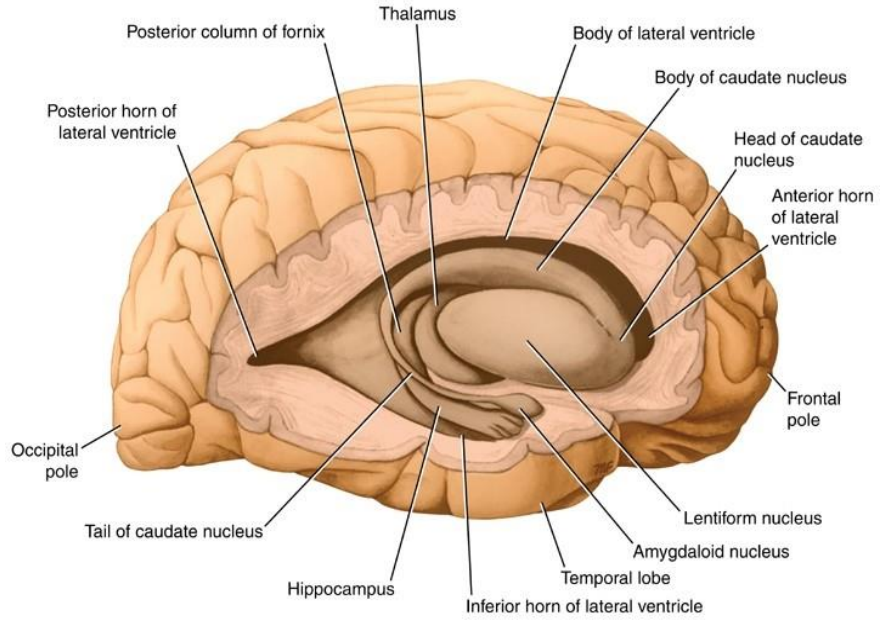
2- **amygdaloid nucleus** : the tail walks and skips the hippocampus, continues walking until it reaches the anterior of the temporal lobe where the amygdaloid nucleus is. (ends posteriorly to amygdala) .

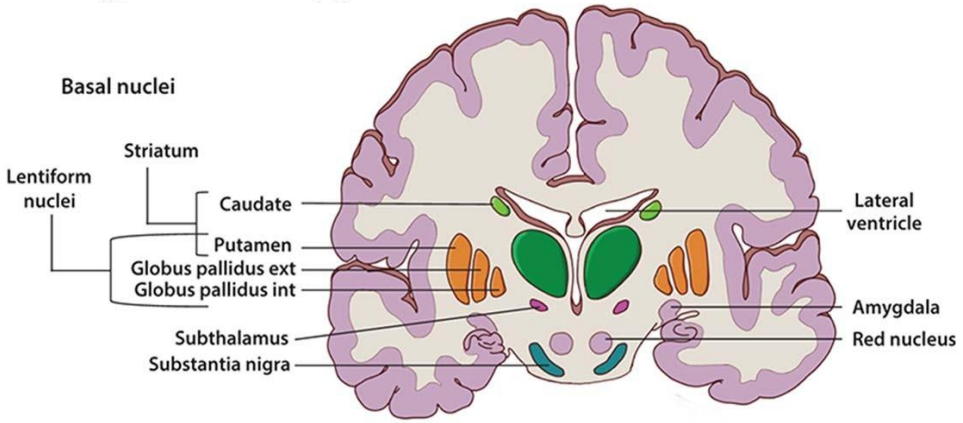
**So the caudate starts at the frontal lobe ⟶ parietal lobe ⟶ temporal lobe and walks with lateral ventricle .

** the c-shaped head of the caudate starts big and gets smaller, that's why in the coronal section or transverse section we will see 2 parts of the c-shape .

• Lentiform nucleus :

* Parts
  - Putamen .
  - Globus pallidus :-
    - Internal (GPi) .
    - External (GPe) .
* Shape : lentils or pyramidal (From the outside it is big and on the medial side it gets smaller) .
* Location : in the picture we see putamen from lateral view. From The anterior view of the brain we see first putamen, more posteriorly we see globus pallidus .
* Relations
  - External & internal capsules .
  - Claustrum
  - (putamen) is lateral to the thalamus, between it and the thalamus there is an internal capsule .
  - It's internal to the caudate nucleus .





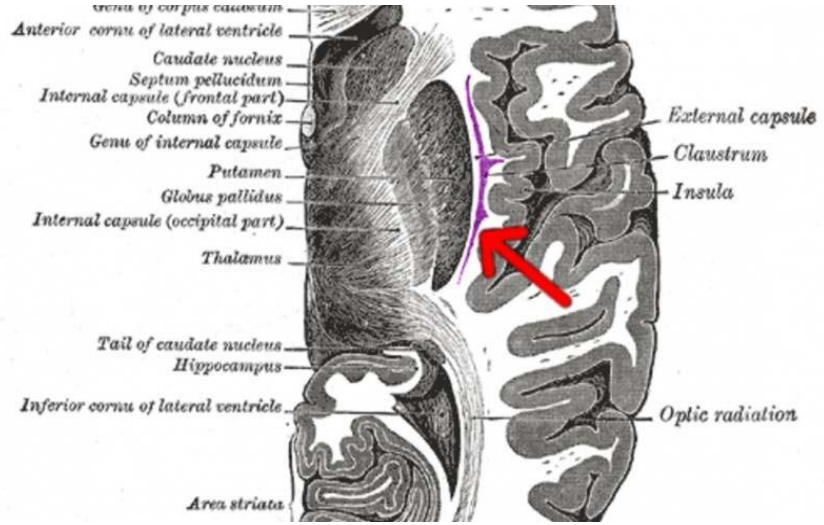
- Amygdaloid nucleus .
- Subthalamic nucleus .
- Substantia nigra :

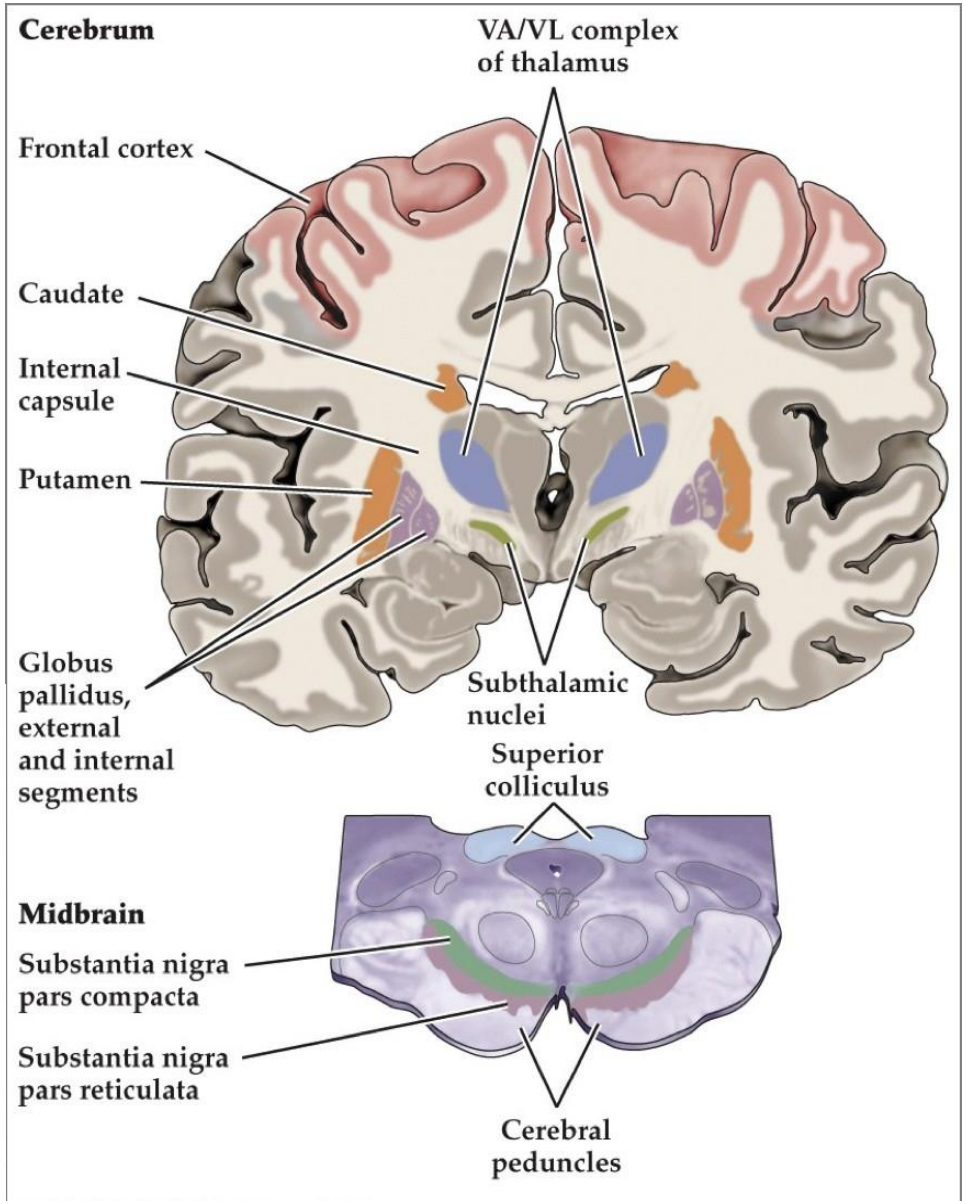
  1/ Pars reticulata (SNr)

  most anterior part, and near cerebral peduncles

  2/ Pars compacta (SNc)

  posterior part
- Claustrum .





1- **Amygdaloid nucleus**: most anterior part of the temporal lobe , it's anterior to hippocampus and anterior to the tail of caudate nucleus . (part of the limbic system *emotions*)

2- **Subthalamic nucleus** : it's below the thalamus and near to substantia nigra (large nucleus starts from the inferior part of midbrain to the superior part of midbrain until the diencephalon) .

*Lentiform is medial to the insula.

*Claustrum (gray mater small island) is between insula and putamen.

*between claustrum and putamen there is an **external** capsule (white mater).

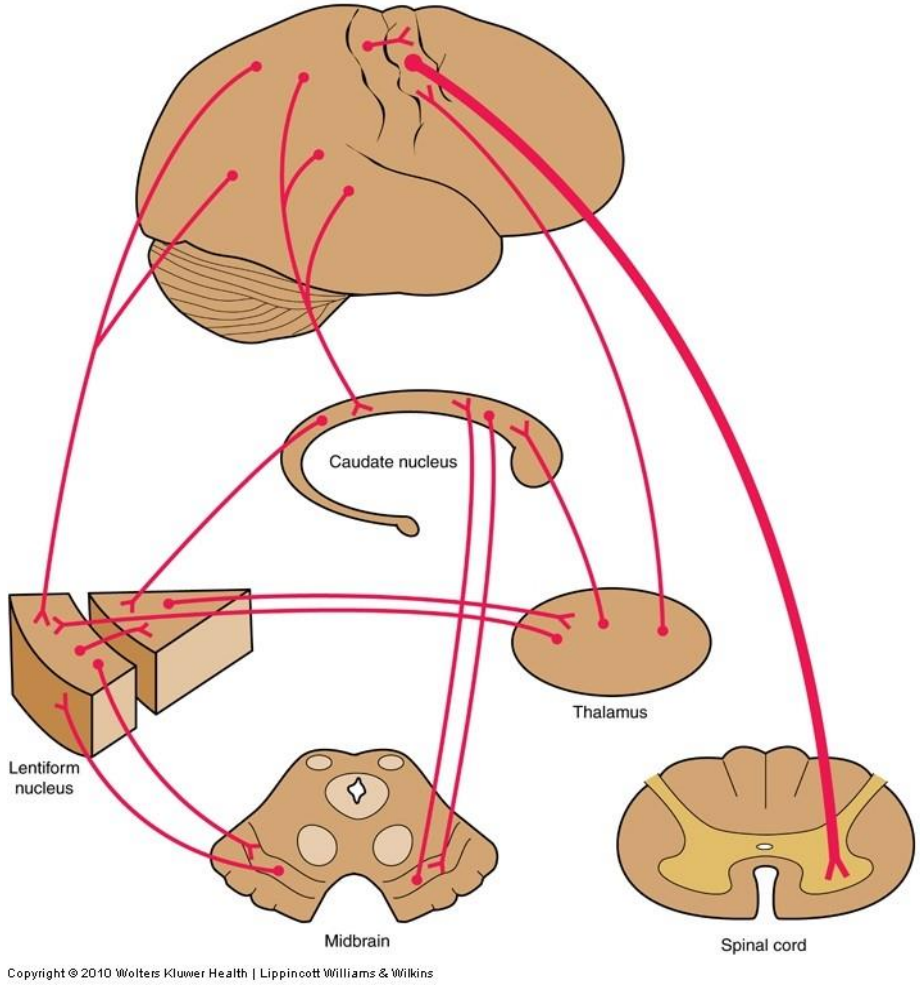
*between claustrum and insula there is an **extreme** capsule (white mater).

From medial to lateral :

Thalamus → internal capsule → globus pallidus → putamen → external capsule → claustrum → extreme capsule → insula .

Basal Ganglia Circuitry

- Basal ganglia has a specific circuit that froms its action which is important for tuning the orders that exit from the cerebral cortex .
- **Inputs (afferent)**
  - Most inputs enter the striatum (according to the basal ganglia circuit, putamen and caudate function together) .
  - These inputs are excitatory .
- **Outputs (efferent)**
  - Most leave (last decision) from Gpi & SNr
  - Most go to VA nucleus of the thalamus, which projects to motor cortex
  - The outputs are GABAergic and inhibitory
    - VA excites motor cortex, leading to movements .
    - Increase basal ganglia output will inhibit the VA and reduce overall movements .



* The circuit starts from :
Inputs come from cerebral cortex & thalamus to striatum then to GPi then leave to the ventral anterior (VA) of the thalamus, then to the the motor cortex .

* the basic function of basal nuclei is to inhibit the ventral anterior, and the relation between VA and motor cortex is excitatory .

* more inputs to the cortex from AV → more excitation to the cortex .

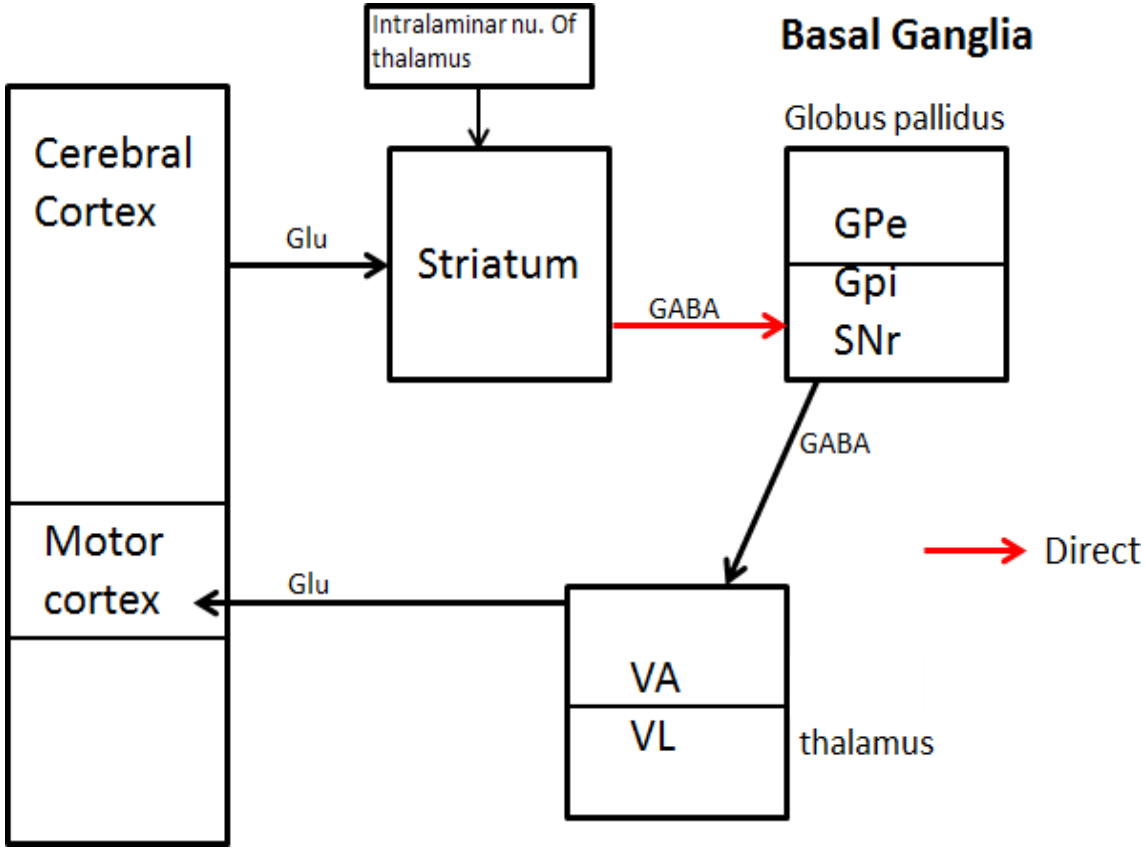
* more action of basal ganglia leads to less action of AV (because it inhibits AV).. So less action of the cortex .

Basal Ganglia Circuitry
Intrinsic Circuits

- Large number of connections between components of the basal ganglia
- Can be grouped into (one increases and the other decreases the output to GPi) :
  - Direct pathway
  - Indirect pathway
- These pathways affect the VA activity (final target) and thus the motor cortex activity

The Direct Pathway

- Cortical activity → ↑direct pathway → ↓Gpi activity → ↑ VA activity
- <u>Activity in the direct pathway leads to increased motor cortex activity and increased movements</u>

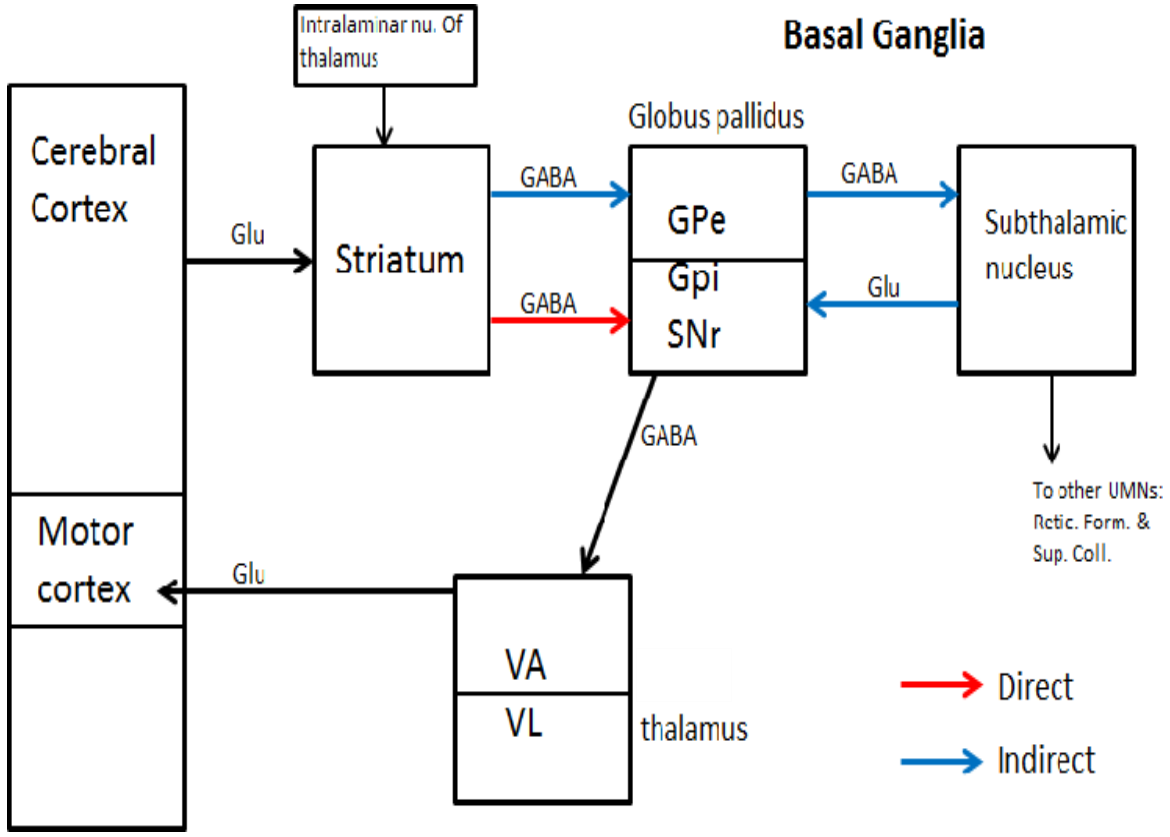


In direct pathway : the striatum gives GABA(-) to GPi and GPi gives GABA(-) to AV; so negative with negative become positive, that means that the direct pathway makes **disinhibition** ⟶ increase the activity of the motor cortex .
SO,,From striatum to GPi

- Uses GABA, which inhibits another GABAergic projection (GPi to VA) .

The Indirect Pathway

- Goes from striatum to GPe (GABA) to the subthalamic nucleus (GABA) .
- Subthalamic nucleus to Gpi (Glu) .
- ↑ activity in the cortex → ↑ activity of subthalamic nu. → ↑ GPi → ↓ VA activity → ↓ motor cortex activity .



indirect pathway : striatum gives GABA(-) to GPe (GPe is functionally connected with subthalamic nucleus) , then GPe gives GABA(-) to subthalamic ,then subthalamic gives GLU(+) to GPi, then GPi gives GABA(-) to the AV .

So negative with negative become positive ,then positive with positive become positive , then positive with negative gives NEGATIVE .

SO, increasing the activity of GPi means **increase of inhibition** .

Indirect pathway makes inhibition (decrease in AV leads to decrease in the motor cortex function) .

* From striatum to GPi
  - Uses GABA, which inhibits another GABAergic projection (GPi to VA)
    - Disinhibition

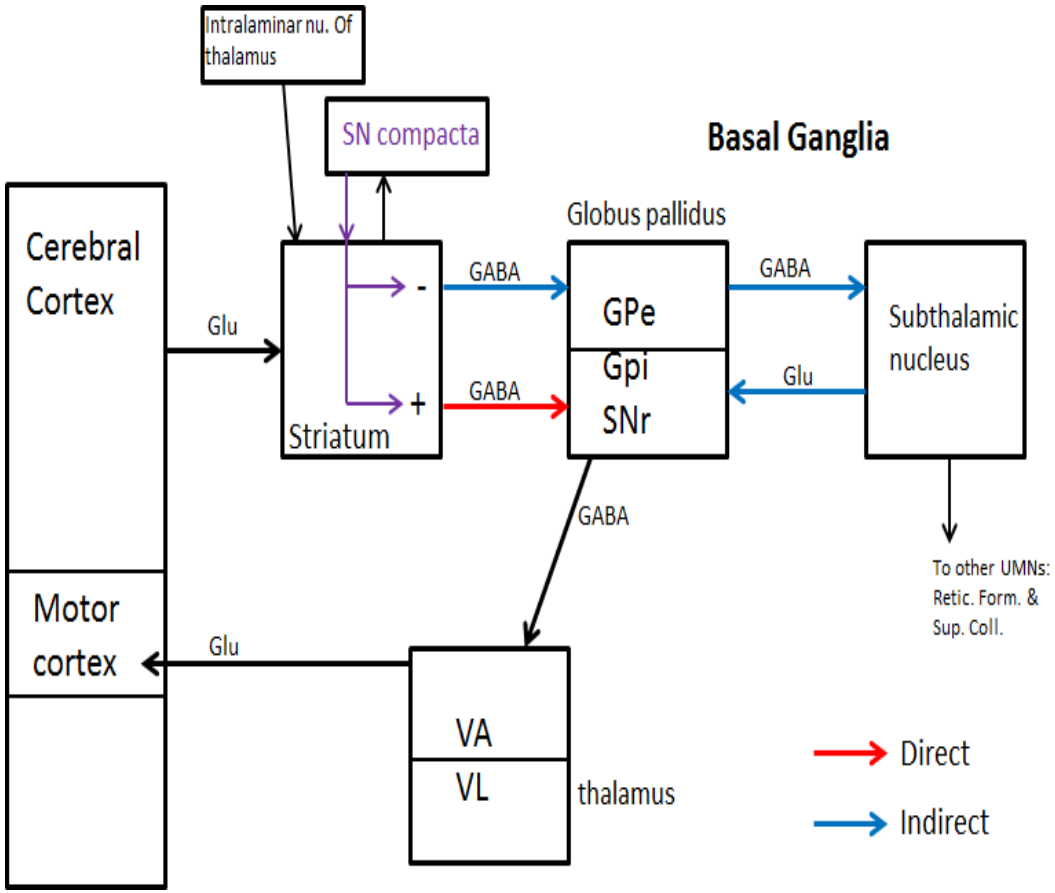
Basal Ganglia Circuitry

- The direct pathway increase movements .
- The indirect pathway decrease movements .
- Normal behavior requires a balance between the direct and indirect pathways .
- All pathways are uncrossed
  - Right basal ganglia modulate right cortex and affect movements on the left side of the body
- Acetylcholine is used by the interneurons in the striatum
  - It affects the output of the direct and indirect pathways .
  - It's a target for drug therapy .

Nigrostriatal Pathway

- In the striatum different cell types give rise to the direct and indirect pathways .
- Both cell types receive dopaminergic input from SN pars compacta (SN compacta uses dopamine as a neurotransmitter) .
- These cells have different receptors for DA
  - For **direct** pathway, DA **excites** the striatal cells (that means excitation of direct pathway)
  - For **indirect** pathway, DA **inhibits** the striatal cells (inhibition of indirect pathway)

  Net result is ***excitation*** (because we already know that direct pathway makes excitation and indirect pathway makes inhibition, here we make excitation to the direct pathway and inhibition to the indirect pathway) .
- Thus the nigrostriatal pathway ↑ the activity of the VA and motor cortex
- PD (Parkinson disease : nigro striatal degeneration) leads to
  - ↓ direct pathway activity
  - ↑ indirect pathway activity
  - ↓ activity of VA and motor cortex



Cerebellum

Cerebellum

- The cerebellum is essential for normal movements .
- It affects motor behavior by affecting UMNs (upper motor neurons) .
- Has a direct effect on the motor cortex itself like the basal ganglia by the ventral lateral nucleus .
- It has another direct effect on other upper motor neurons (cortex or other than cortex) like vestibular nucleus (vestibulospinal tract)
- It receives inputs from all over CNS (all ascending neurons send a copy to the cerebellum by spinocerebellar tract) and all descending orders also send a copy to cerebellum .
- The cerebellum acts as a comparator
  - Compares intended actions (data from cerebral cortex) to the actual movements (sensory data) .
  - Sends corrective signals into the descending motor pathways .

If you planned to move your leg in a certain way but you were about to fall, the cerebellum directly compares between the intended order and the real action, based on that it will adjust the movement so that you don't fall .

Cerebellar Function

- It affects all movements, it is important in :
  - Balance (connection with vestibular nuclei (direct/indirect , in/out) .
  - Locomotion (generally affecting cerebrum) .
  - Simple & complex movements .
  - Eye movements (3^{rd}, 4^{th},6^{th} cranial nerves send info toward it) .
- Site of motor learning
  - Important for learning new motor skills and adjusting movements to changing sensory inputs . (learning skills depends on correcting mistakes)

Cerebellar Anatomy Gross Anatomy

- Location .....

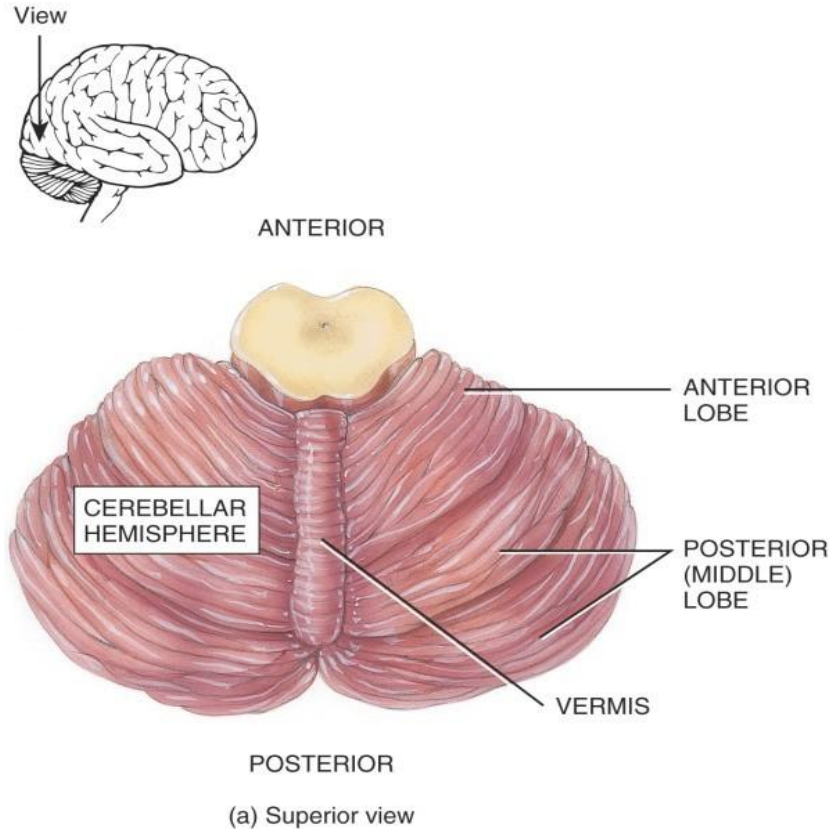
*Posterior to the brain stem .

*posterior inferior to the cerebrum .

*transverse fissure separates cerebellum from cerebrum .

*found within the posterior cranial fossa .

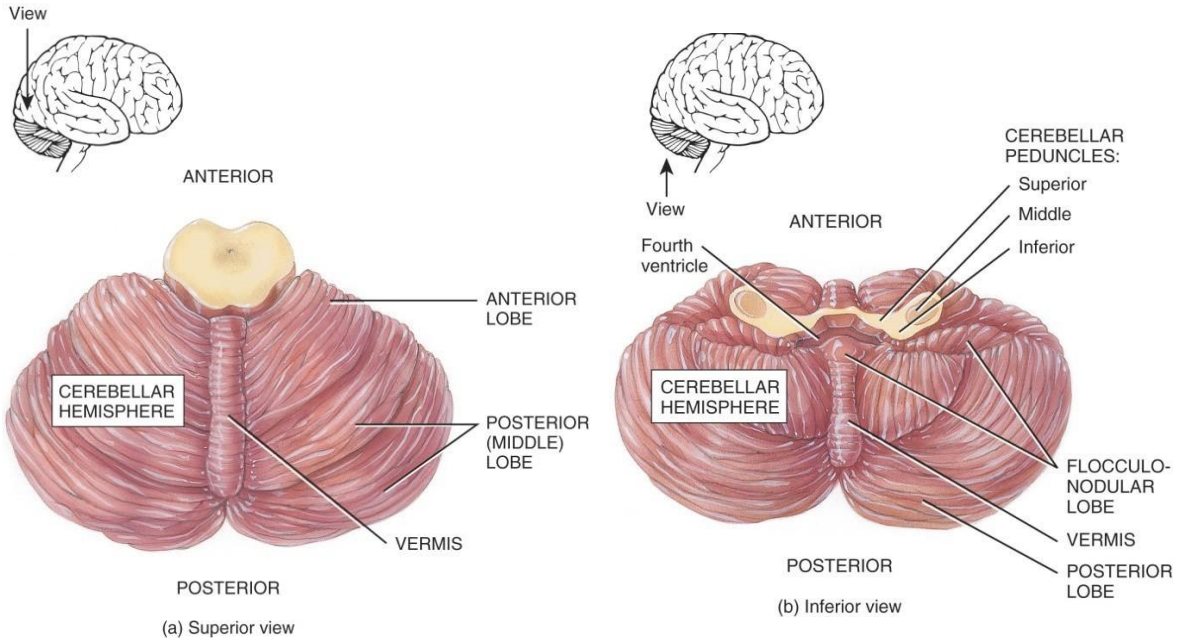
- Relations .....
- The cerebellum consists of two hemispheres
- The hemispheres are connected by vermis

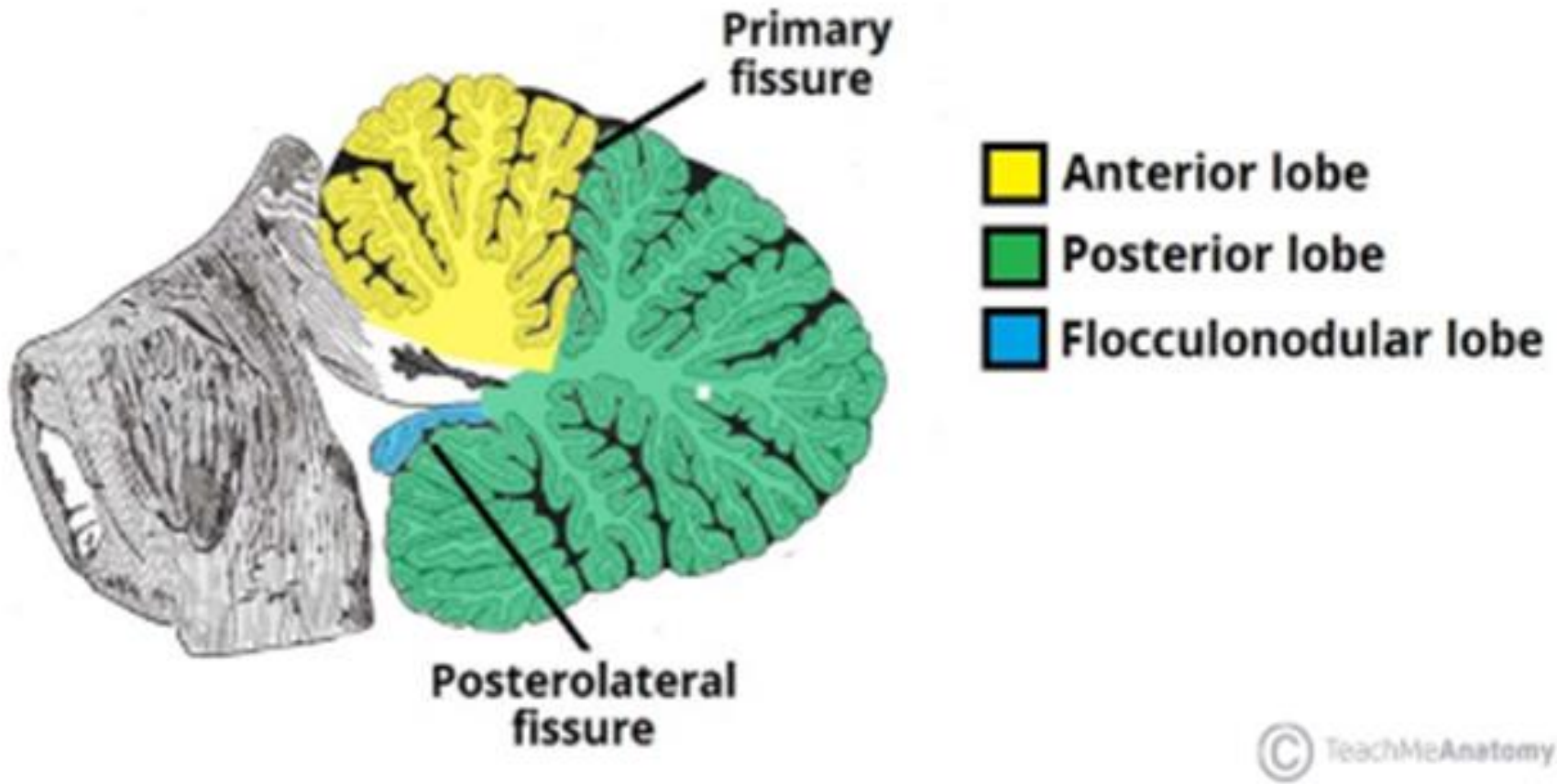


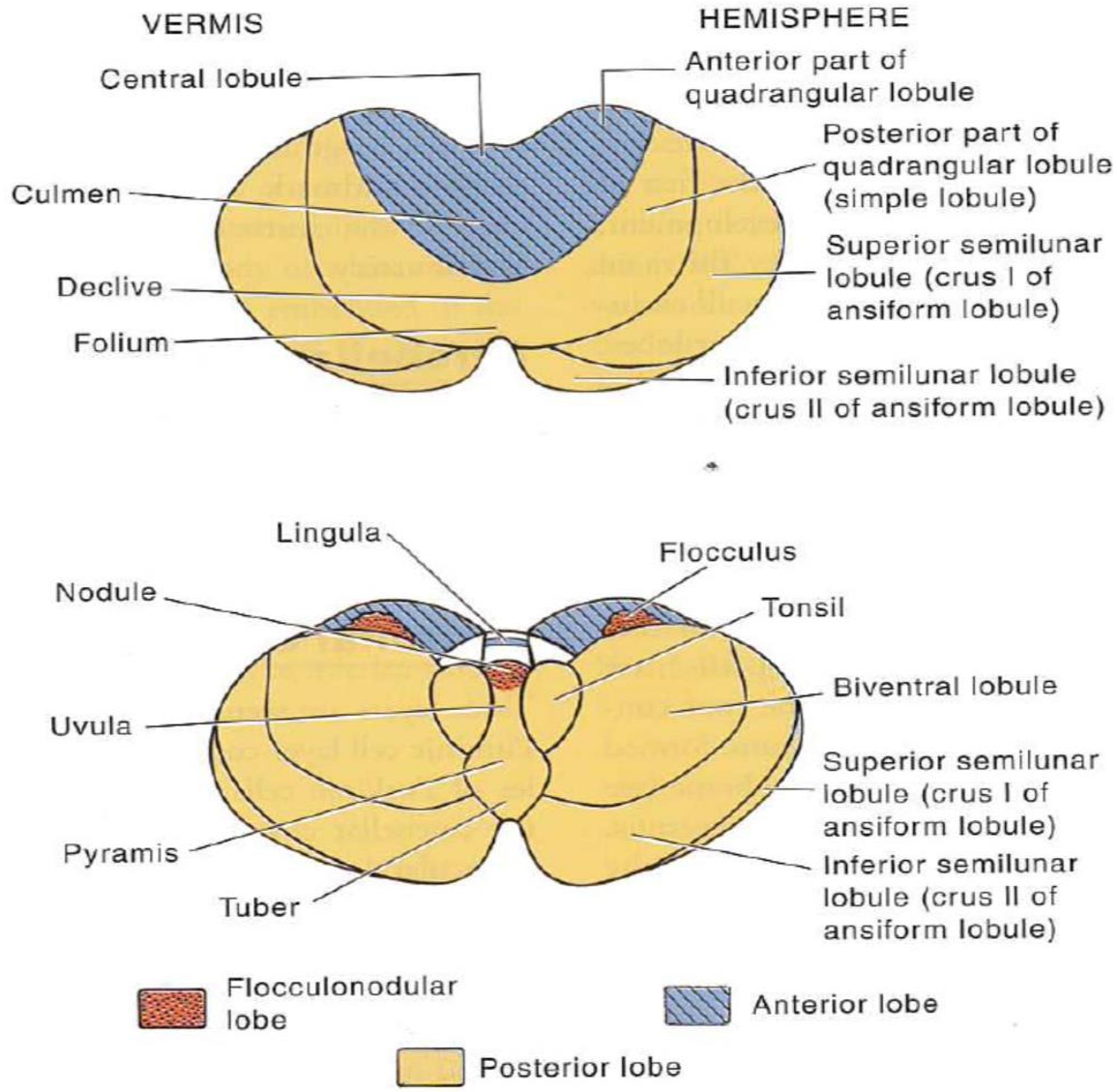
(a) Superior view

- Three main lobes :
  - Anterior lobe (superiorly located) .
  - ➢ Primary fissure : separates between anterior and posterior lobes .
  - Posterior lobe (middle lobe) : the largest .
    - Cerebellar tonsils: (inferiorly) bulgy area near foramen magnum, sometimes herniation occurs here .
    - Most of cerebellum is posterior lobe .
  - ➢ Posterolateral fissure (uvulonodular fissure) seperates posterior lobe from flocculonodular lobe .
  - Flocculonodular lobe (nodular part of vermis and floccular gyri) .

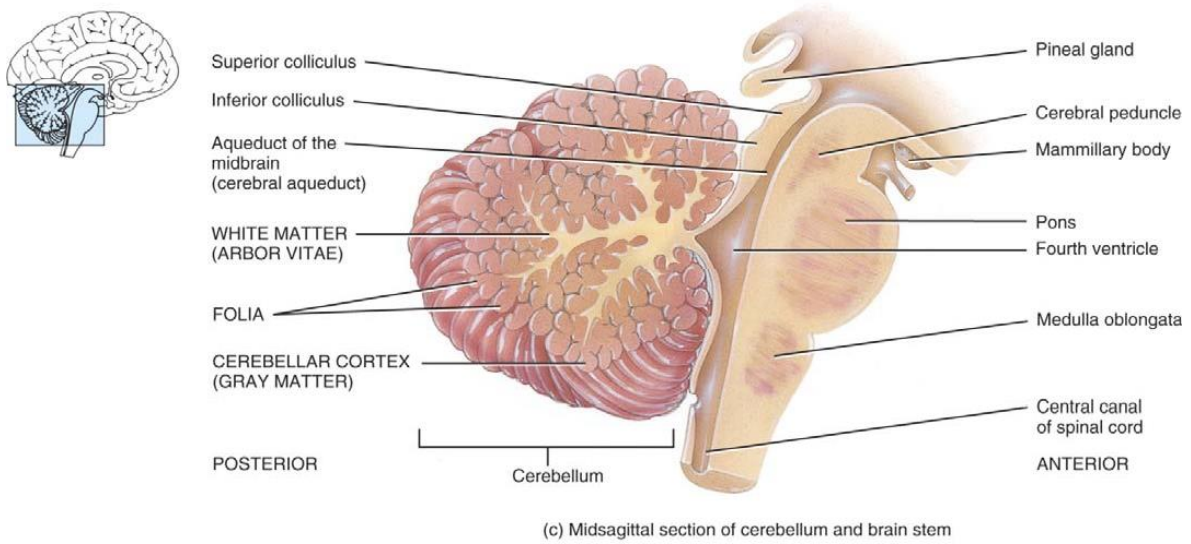
Nodular part of vermis is the most anterior inferior part which is near the brainstem






VERMIS
HEMISPHERE
Central lobule
Anterior part of quadrangular lobule
Posterior part of quadrangular lobule (simple lobule)
Culmen
Superior semilunar lobule (crus I of ansiform lobule)
Declive
Folium
Inferior semilunar lobule (crus II of ansiform lobule)
Lingula
Flocculus
Nodule
Tonsil
Biventral lobule
Uvula
Superior semilunar lobule (crus I of ansiform lobule)
Pyramis
Inferior semilunar lobule (crus II of ansiform lobule)
Tuber
Flocculonodular lobe
Anterior lobe
Posterior lobe

Cerebellum: Internal Structure



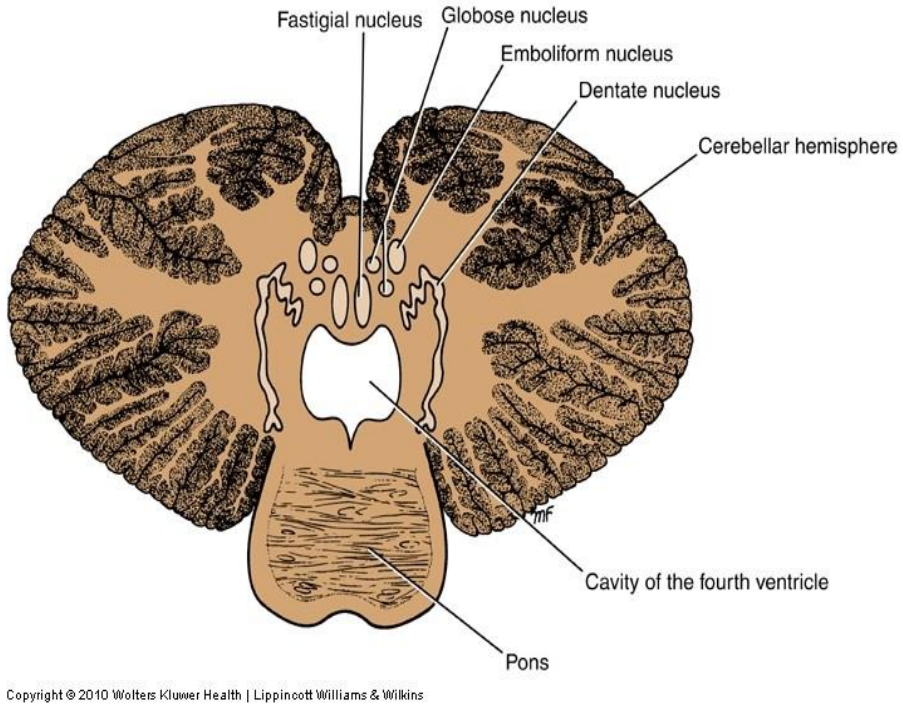
(c) Midsagittal section of cerebellum and brain stem

- Content (grey matter + white matter) :
  - Cerebellar cortex (folia) convoluted externally & central nuclei are grey matter
  - Arbor vitae = tree of life = white matter (cerebellar nuclei) .

Cerebellar Anatomy

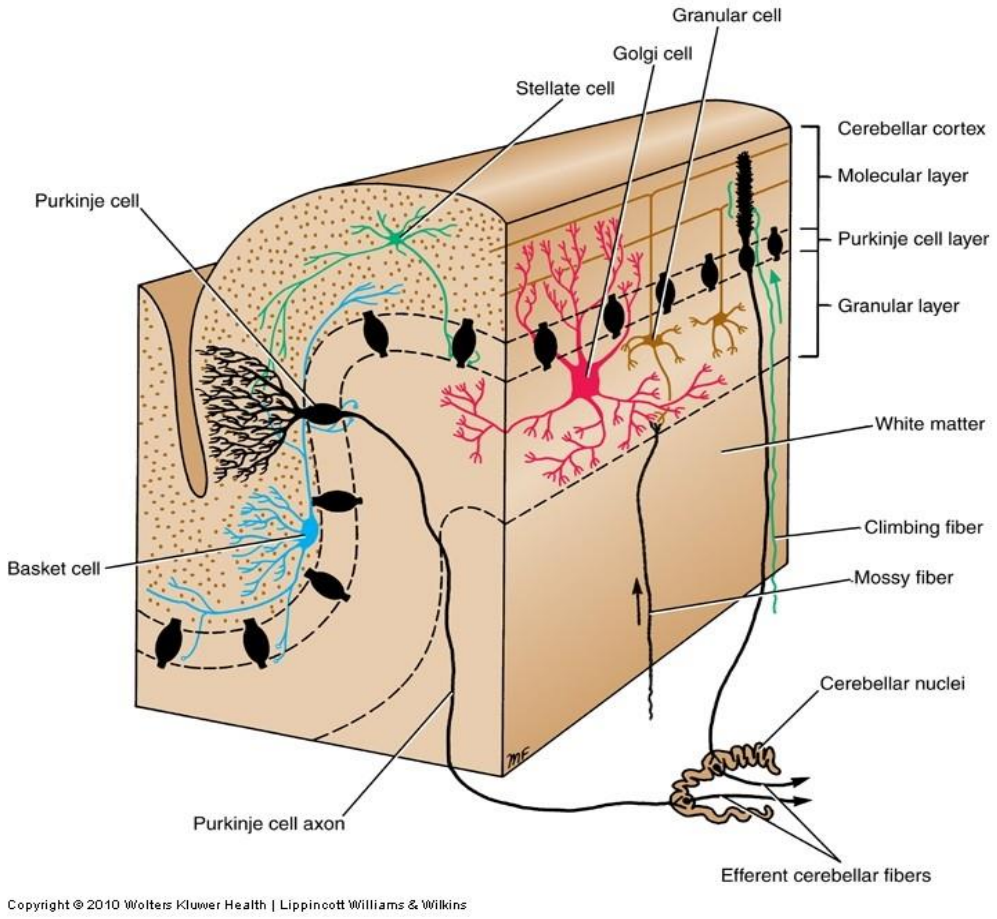
- Cerebellum includes a cortex & deep nuclei
- The deep nuclei are the major source of output from the cerebellum
- Four nuclei from medial to lateral
  - Fastigial
  - Globose
  - Emboliform
  - Dentate (largest one) it has a shape like the shape of the inferior olivary nucleus (we can see it with naked eye) .

Together called Interposed nuclei



Cerebellar Cortex

- Cerebellar cortex includes 5 cell types in 3 layers
- Five cell types
  - Inhibitory cells (4 cells)
    - **Purkinje cells** (large/efferent of cerebellar cortex & mostly go to the cerebellar nuclei), **basket cells** (molecular layer), **Golgi cells** (granule layer) and **stellate cells** (molecular layer) .
  - Excitatory cells (1 cell)
    - **Granule cells** (in granule layer)
- Three layers
  - Molecular layer (basket and stellate cells)
  - Purkinje cell layer
  - Granule cell layer (golgi cell)



Cerebellar Inputs

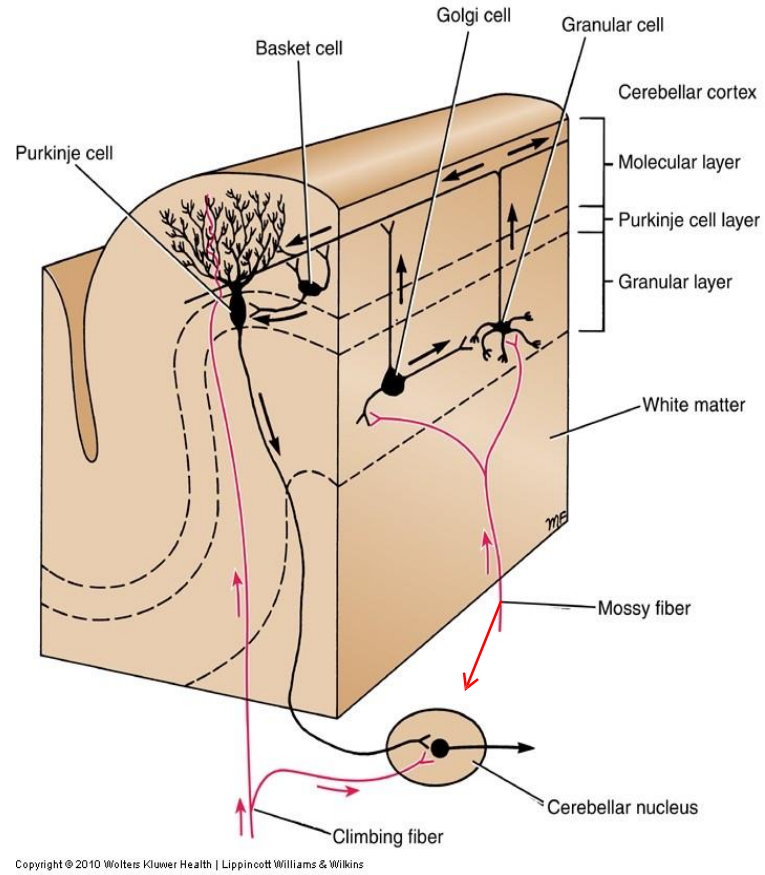
- The **main target** of input fibers is the cerebellar cortex, but there is a copy that goes to the cerebellar nuclei .
- **Inputs** to the cerebellum

  1- Climbing fibers

  - From inferior olivary complex (olivocerebellar fibers) .
  - Decussate .
  - Enter from Inferior cerebellar peduncle .

  2- Mossy fibers

  - All remaining inputs: spinal cord, vestibular n. & nuclei, and pontine nuclei .
  - Part of them enter from middle cerebellar peduncle , others from inferior and small amount enter from superior cerebellar peduncle .
- Each type of input fibers **branches :**
  - Branch to deep nuclei
  - Branch to cerebellar cortex

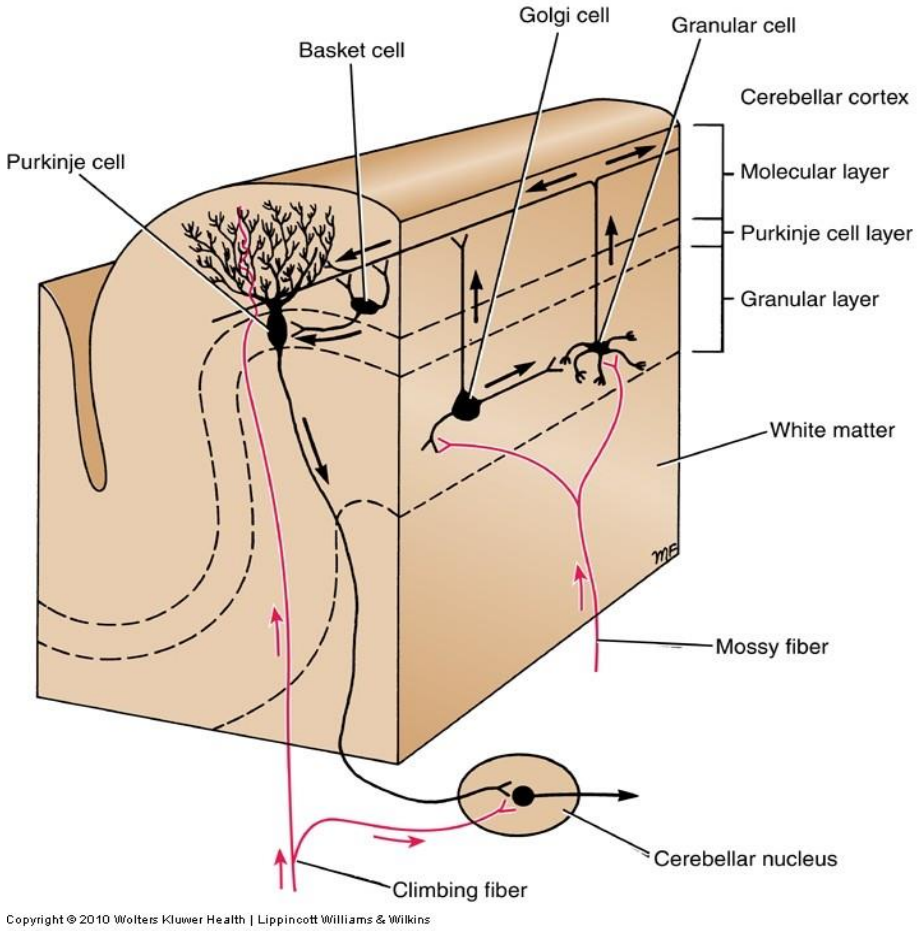


Cerebellar Circuit

- The basic cerebellar circuit includes :
- **Main excitatory loop**
- **Inhibitory cortical side loop**

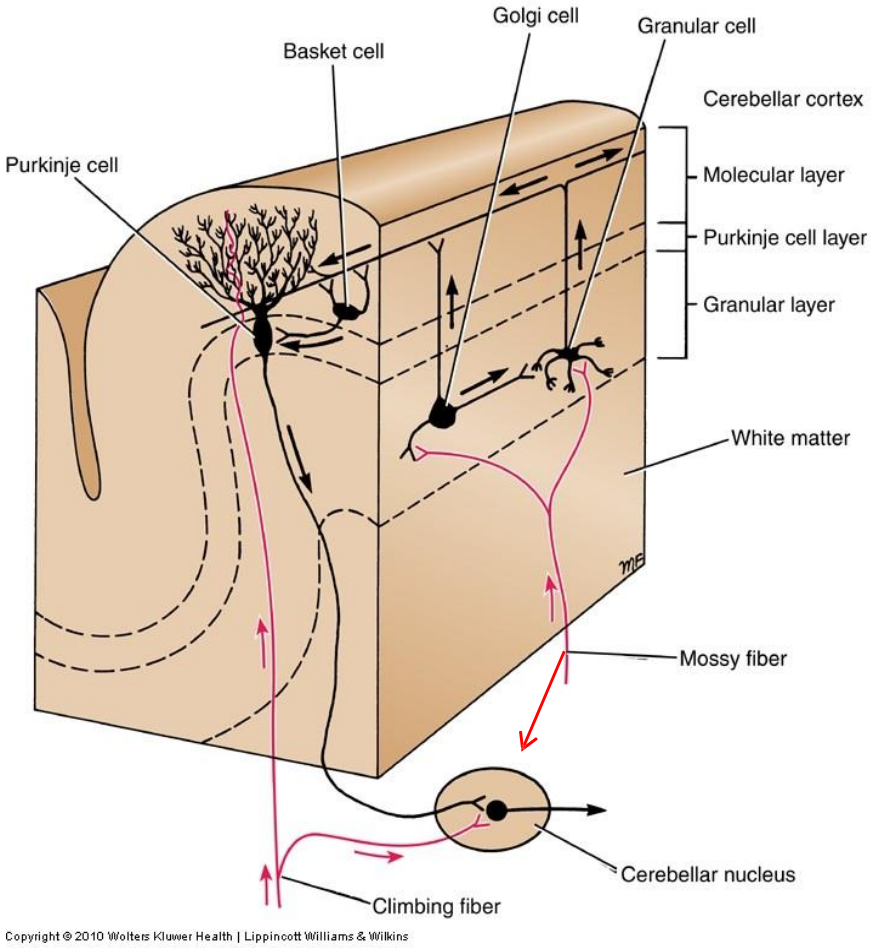
- (inputs from mossy and climbing cells = excitatory , output from cerebellar nuclei (efferent from cerebellum) = excitatory , inputs/output from purkinje to/from the cortex of cerebellar nuclei = inhibitory) .

- Increase cerebellar cortex output >> excitation from cerebellum in general decreases .



The Main Excitatory Loop

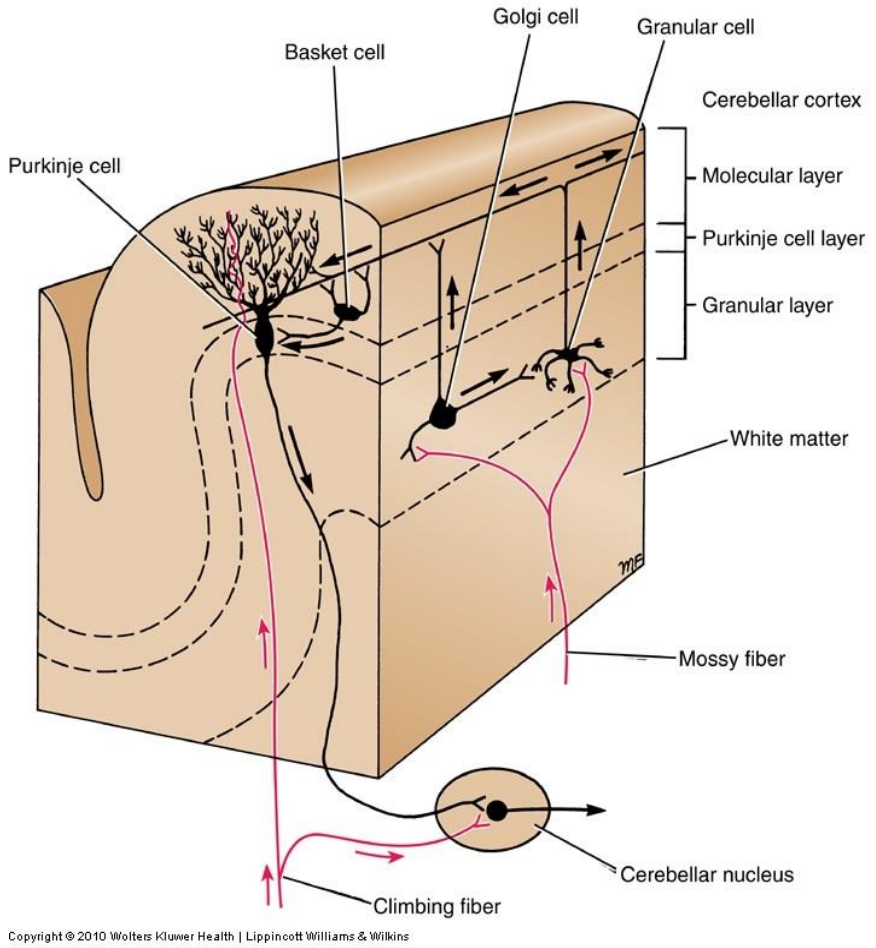
- Includes the input and the deep cerebellar nuclei
- Both the inputs & the cells of the deep nuclei are excitatory



The Inhibitory Cortical Side Loop

- Serves to modulate the activity in the deep cerebellar nuclei .
- **Mossy & climbing fibers** are inputs to cerebellar cortex
  - Climbing fibers contact Purkinje cells directly
  - Mossy fibers contact granule cells
- **Granule cells contact Purkinje cells**

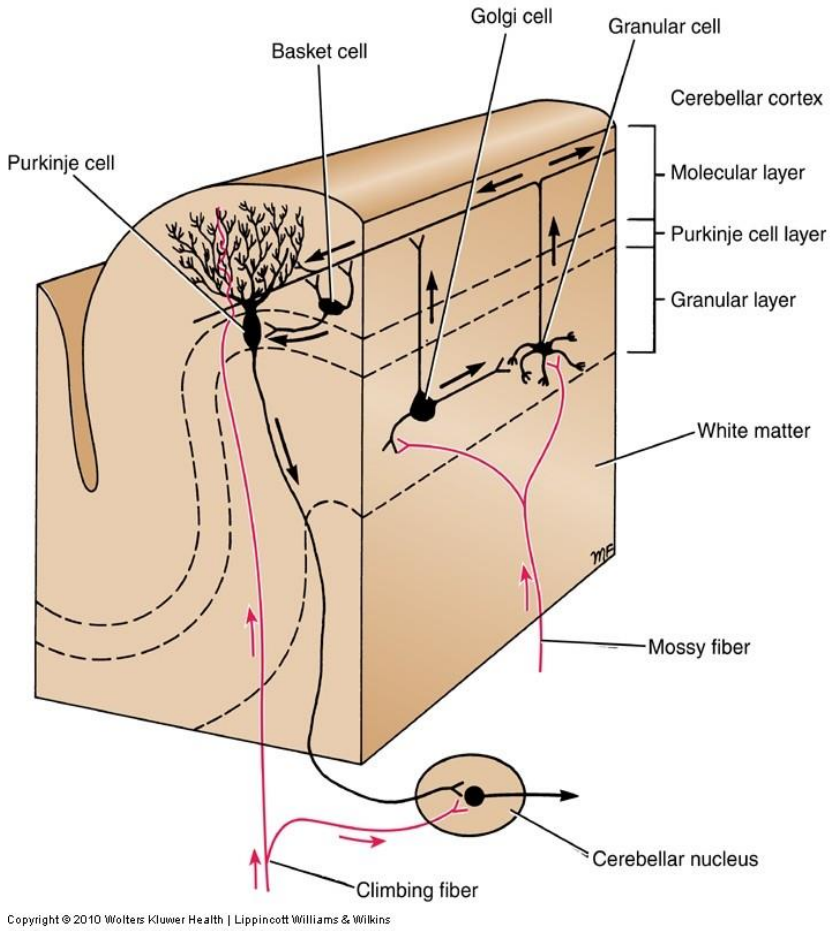
➢ Output of cerebellar cortex (Purkinje fibers) depend on the mossy & climbing fibers



The Inhibitory Cortical Side Loop

- Remaining cells (**Golgi, basket & stellate**) are <u>inhibitory</u> interneurons
  - Alter granule & Purkinje cells
- Purkinje cells (cerebellar cortex output) are inhibitory
  - Purkinje cells targets :
    - deep cerebellar nuclei & vestibular nuclei

➢ <u>Thus cerebellar output is driven by the main excitatory loop and limited by the inhibitory cortical side loop (2 modulations) .</u>

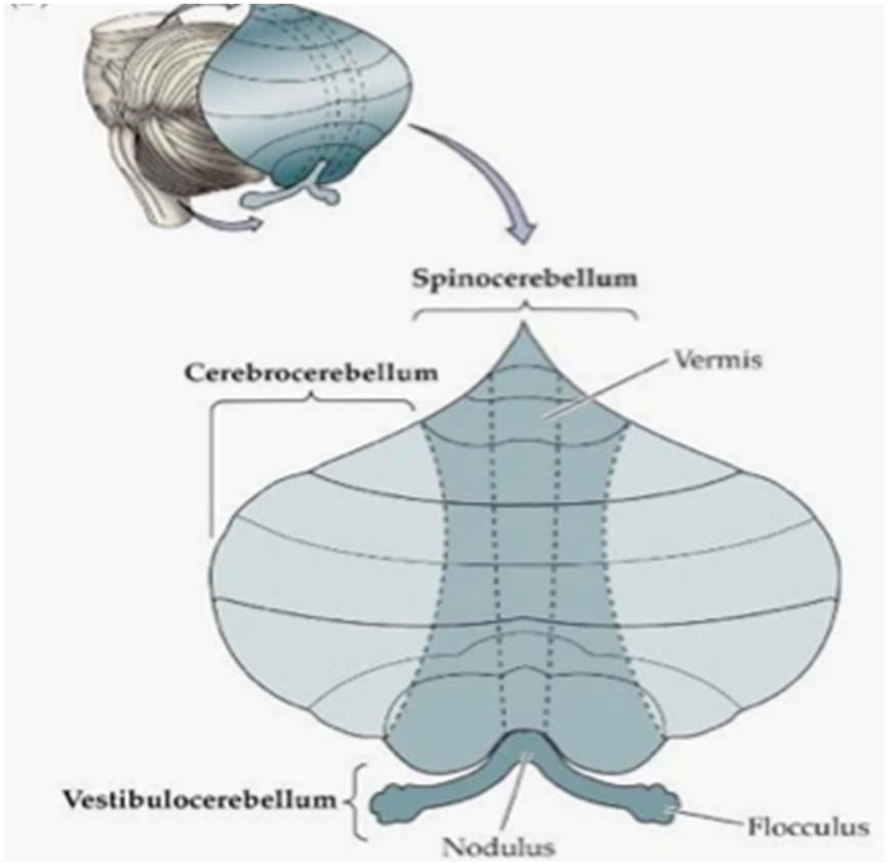


Cerebellar Functional Divisions

The doctor skipped the next 3 slides .

the dr. only mentioned colored words here

1. Vestibulocerebellum
   - Flocculonodular lobe & fastigial nu.
   - Balance, eye movements
2. Spinocerebellum
   - Vermis & paravermal parts of hemispheres & interposed nuclei (emboliform & globose)
   - Motor execution
3. Cerebrocerebellum
   - Lateral hemispheres & dentate nu.
   - Motor planning



Vestibulocerebellum

Function

- Balance & eye movements

Inputs

- Vestibular n. fibers
- Vestibular nuclei
- Inferior olive

Deep nucleus

- Fastigial nucleus

Outputs (From fastigial nu. & Purkinje cells)

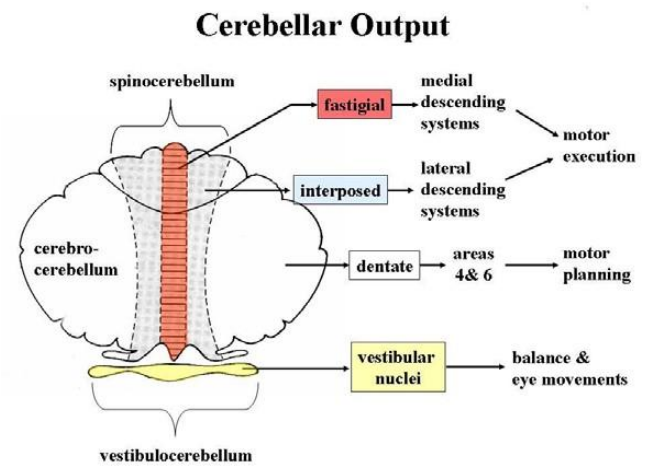
- Vestibular nuclei
- Reticular formation
- VL of thalamus

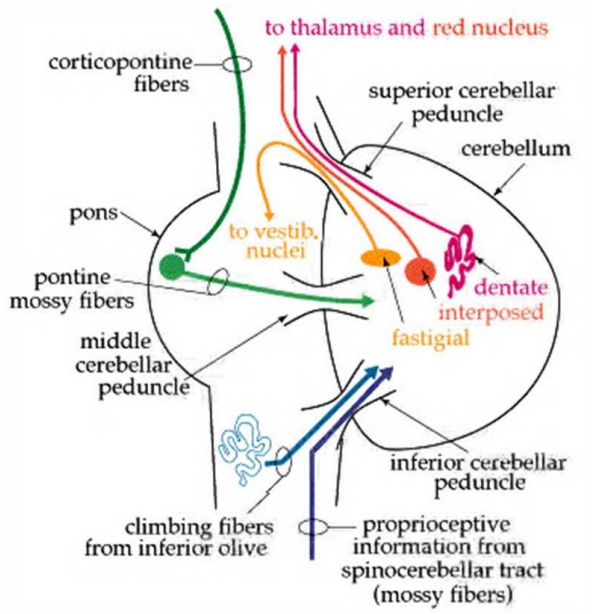
Part of motor system targeted

- UMNs of medial pathway

Major signs of damage

- Staggering or falling, nystagmus





Spinocerebellum

Function

- Execution of movement
  - Compensates for changes in load, regulates muscle tone, guides limb movement, helps maintain posture
- Organized somatotopically
  - Head & trunk – vermis
  - Limbs – paravermal areas

Inputs

- Spinal & trigeminal inputs
- Inferior olive

Deep nucleus

- Fastigial & interposed nuclei

Outputs

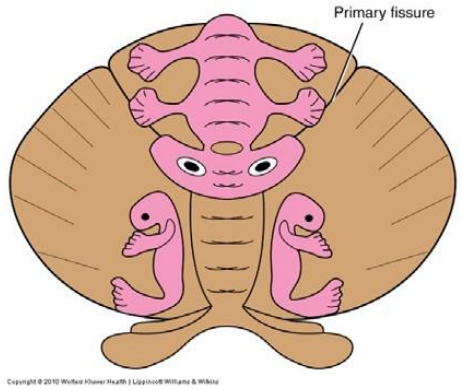
- Vermis
  - Reticular formation & Vestibular nu.
- Paravermal
  - Red nucleus, VL of thalamus & Inferior olive

Part of motor system targeted

- UMNs of medial & lateral pathways

Major signs of damage

- Staggering gait, intention tremor



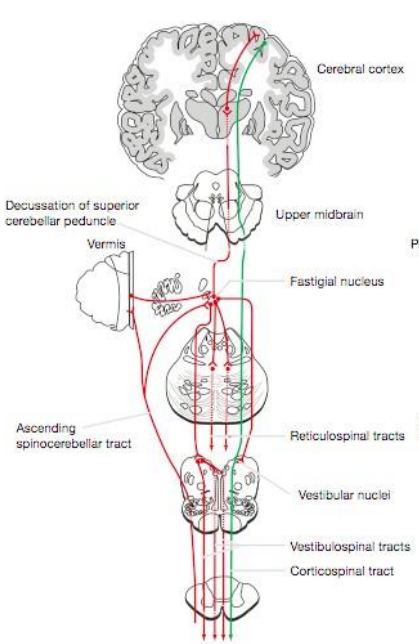


Fig. 9-1. Spinocerebellum—vermis.

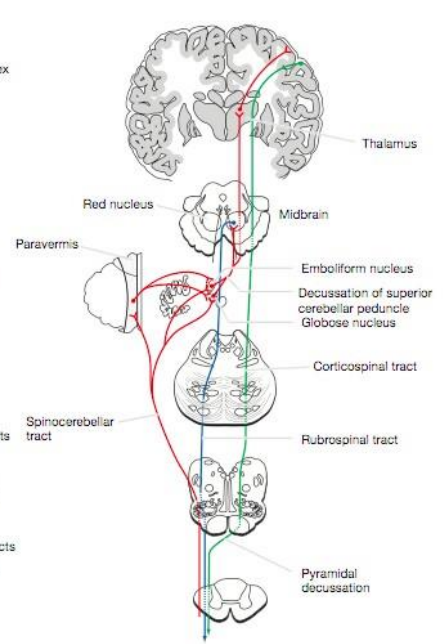


Fig. 9-2. Spinocerebellum—paravermis.

Cerebrocerebellum

Function

- Coordination, planning of voluntary movements

Inputs

- Pontine nuclei (relaying information from sensory & motor cerebral cortex)
- Inferior olive

Deep nucleus

- Dentate nucleus

Outputs

- Red nucleus (to inferior olive, back to cerebellum)
- VL of thalamus

Part of motor system targeted

- Motor cortex (via VL)

Major signs of damage

- Decomposition of movements

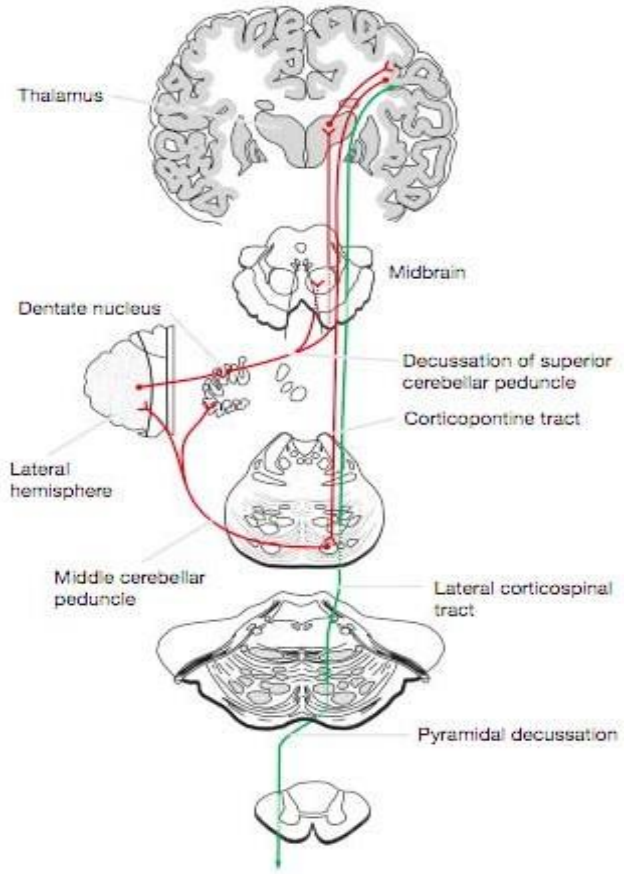


Fig. 9-3. Cerebrocerebellum.

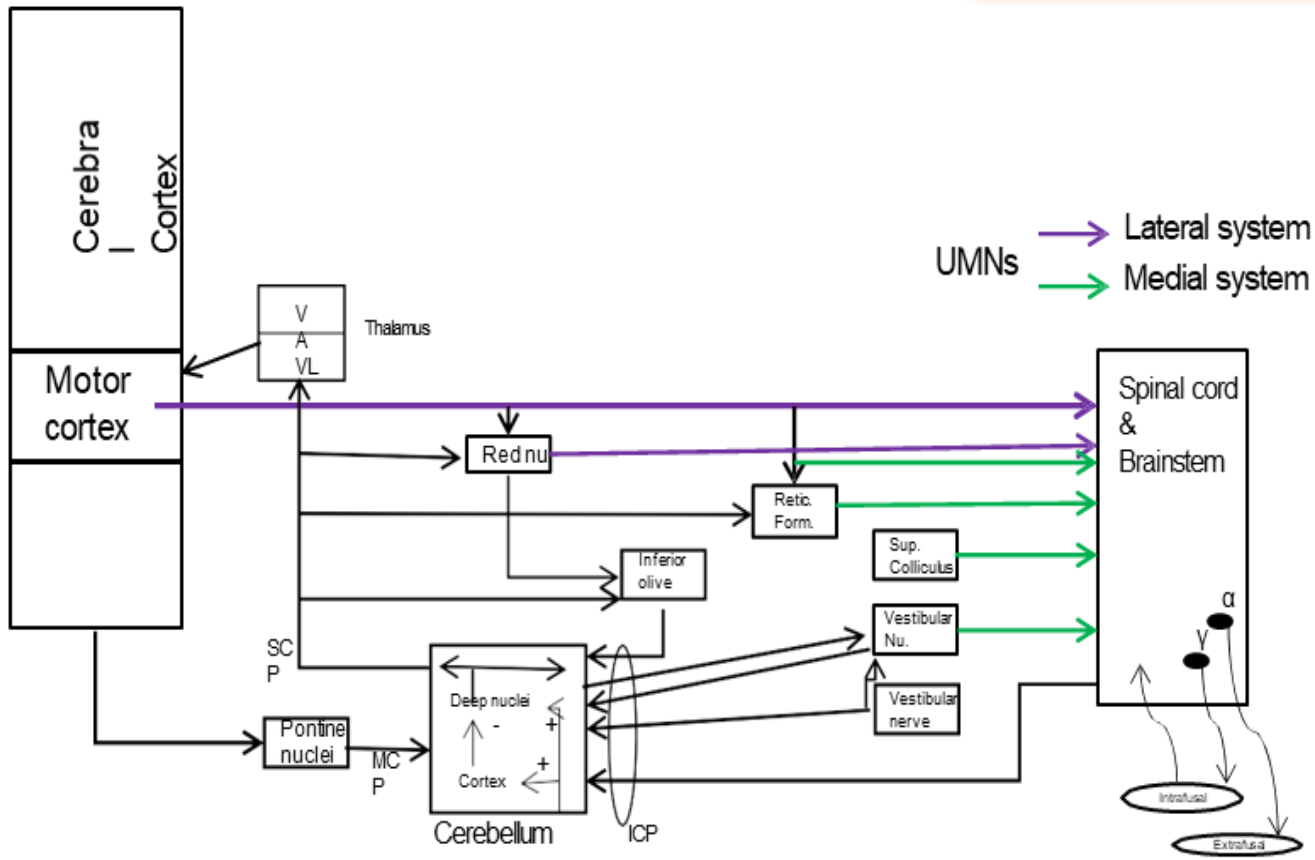
Cerebellar Peduncles

Peduncle	Major inputs to cerebellum Fibers from:	Major outputs from cerebellum Fibers to:
Inferior - Restiform body - Juxtarestiform body	Inferior olive (climbing fibers) Dorsal spinocerebellar tract Cuneocerebellar tract Vestibular nerve Vestibular nuclei	Vestibular nuclei
Middle (brachium pontis)	Pontine nuclei (relay inputs from cerebral cortex)	None
Superior (brachium conjunctivum)	Ventral spinocerebellar Rostral spinocerebellar	Red nucleus VL thalamus Reticular formation Inferior olive

Purkinjie fibers go to cerebellar nuclei, but some fibers go to vestibular nuclei (exception)

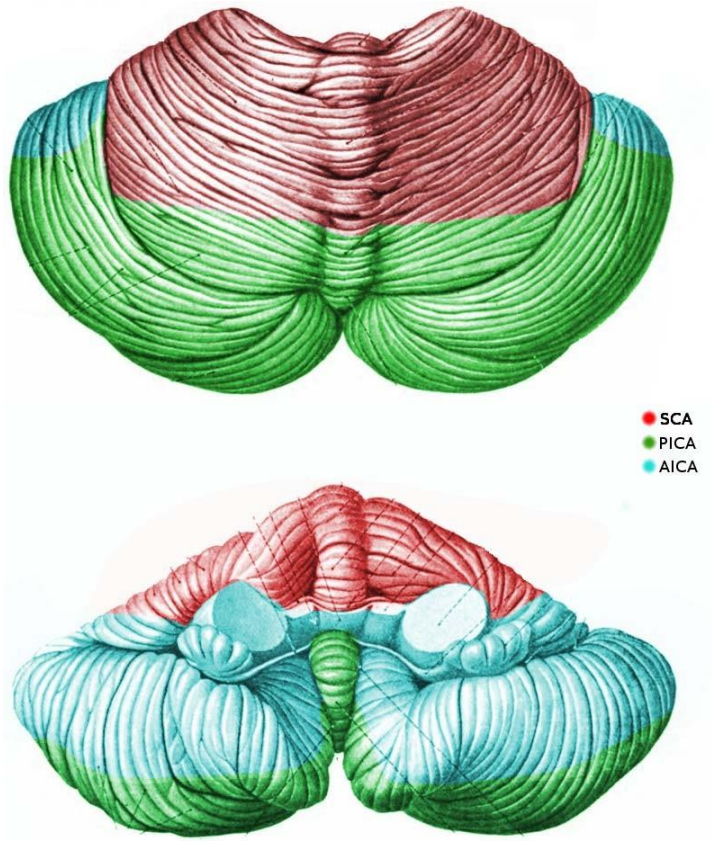
Cerebellar Circuitry

ICP: inferior cerebellar peduncle.
MCP: middle cerebellar peduncle.
SCP : superior cerebellar peduncle.



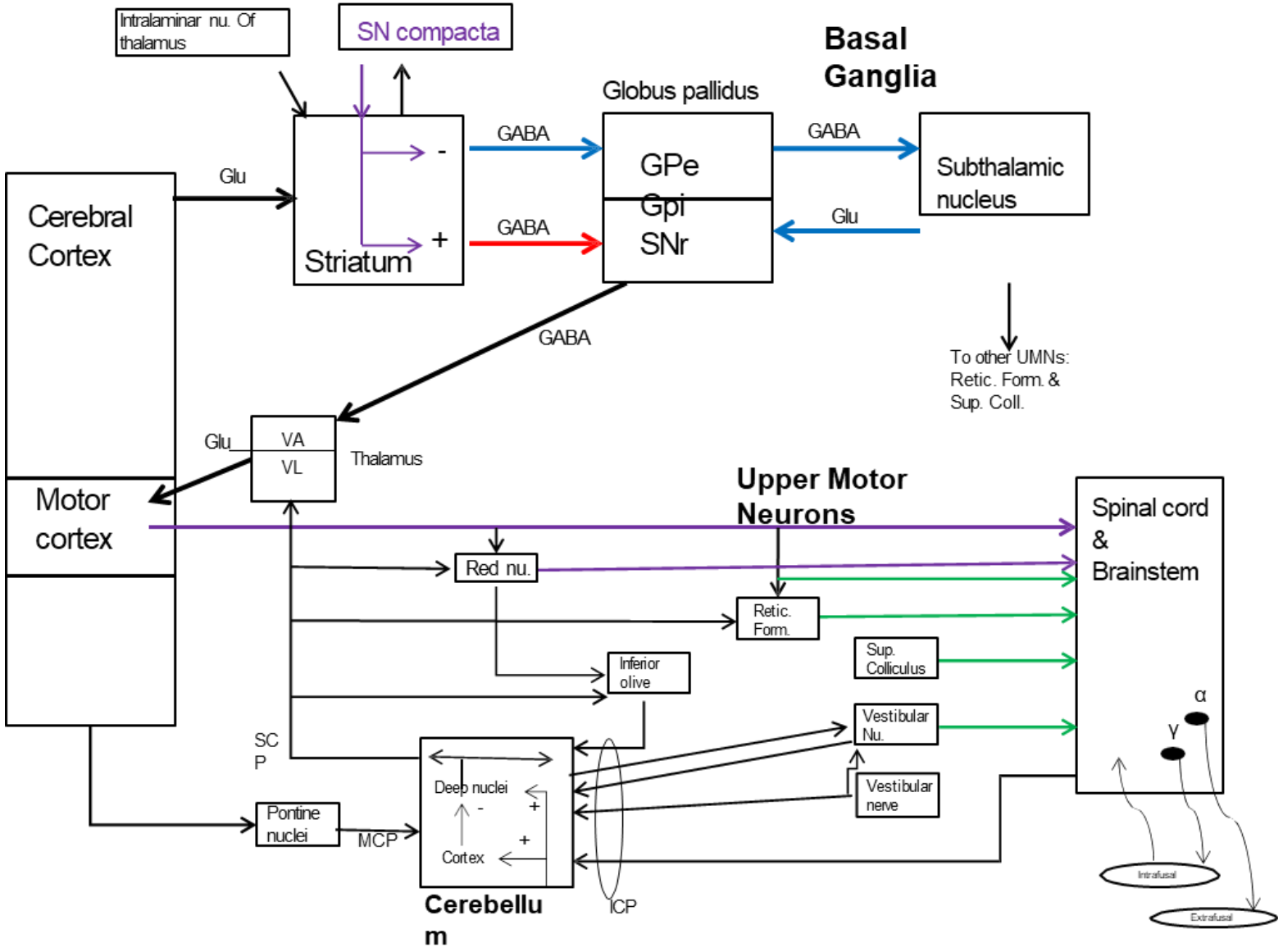
Blood Supply of Cerebellum

- **SCA (anterior lobe)**
  - Superior cerebellar hemispheres
  - Superior vermis
  - Dentate nucleus
  - Most of white matter
  - Superior cerebellar peduncle
- **AICA (posterior part)**
  - Middle cerebellar peduncle
  - Flocculus
  - Anteroinferior surface of the cerebellum
- **PICA (inferior of posterior part +foleccula)**
  - Posteroinferior cerebellar hemispheres
  - Inferior portion of the vermis
  - Inferior cerebellar peduncle



Please refer to the last mins of the record to understand what's required ☺

Motor System



Thank you