Cerebellum and Basal Ganglia

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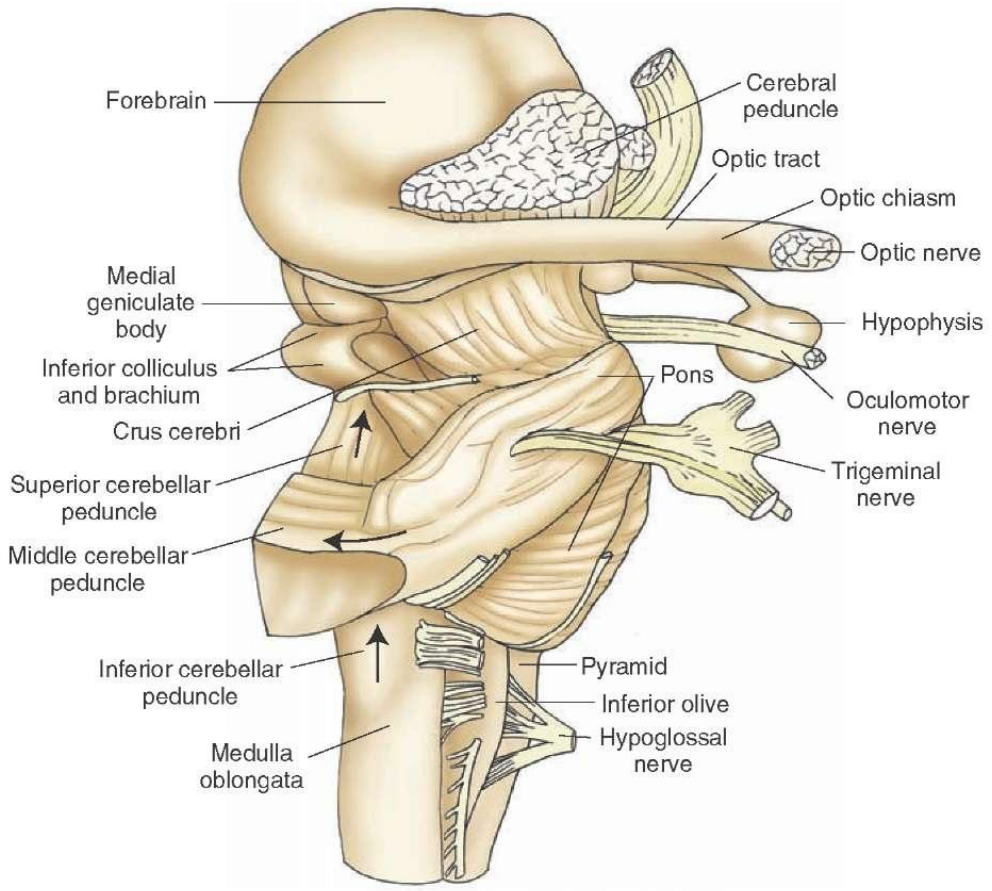
Cerebellum

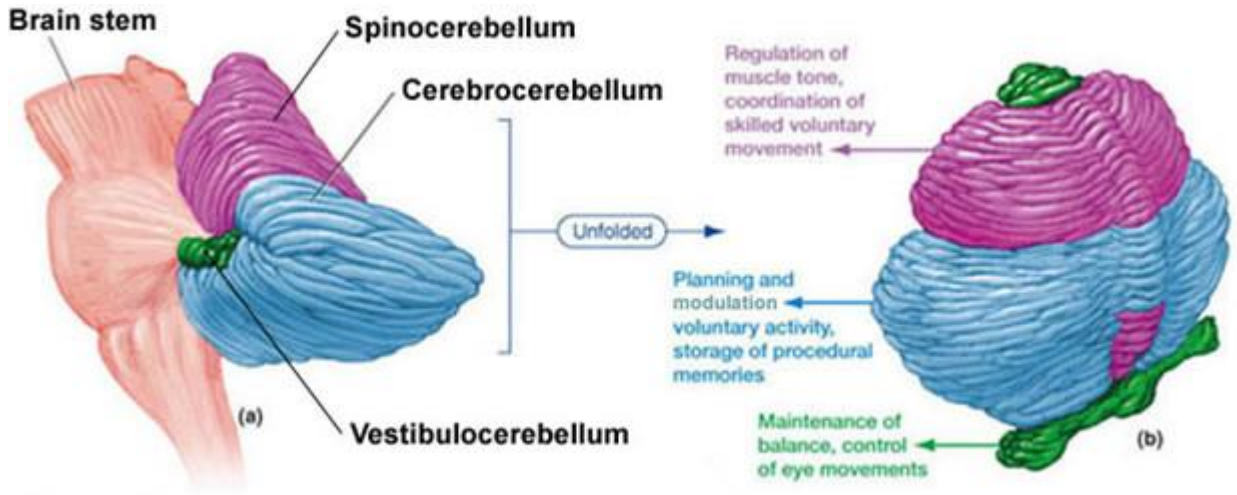
- *Association of the movements* - **synergy of the movement**
- *Maintenance of the posture with respect to one s position in space*
- *Maintenance of the tension or firmness (or tone) of the muscle*

- 150 g, 10% of total neuronal mass
- Posterior cranial fossa
- Is attached to the brainstem by three peduncles
- Inferior and middle peduncles are mainly cerebral afferents, whereas superior peduncles are cerebral efferents



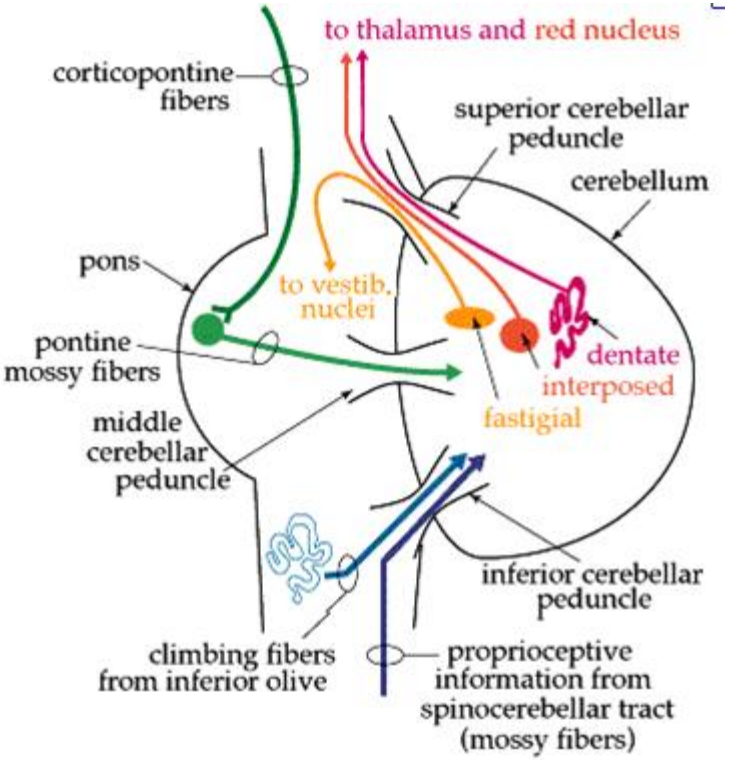
Cerebrall cortex

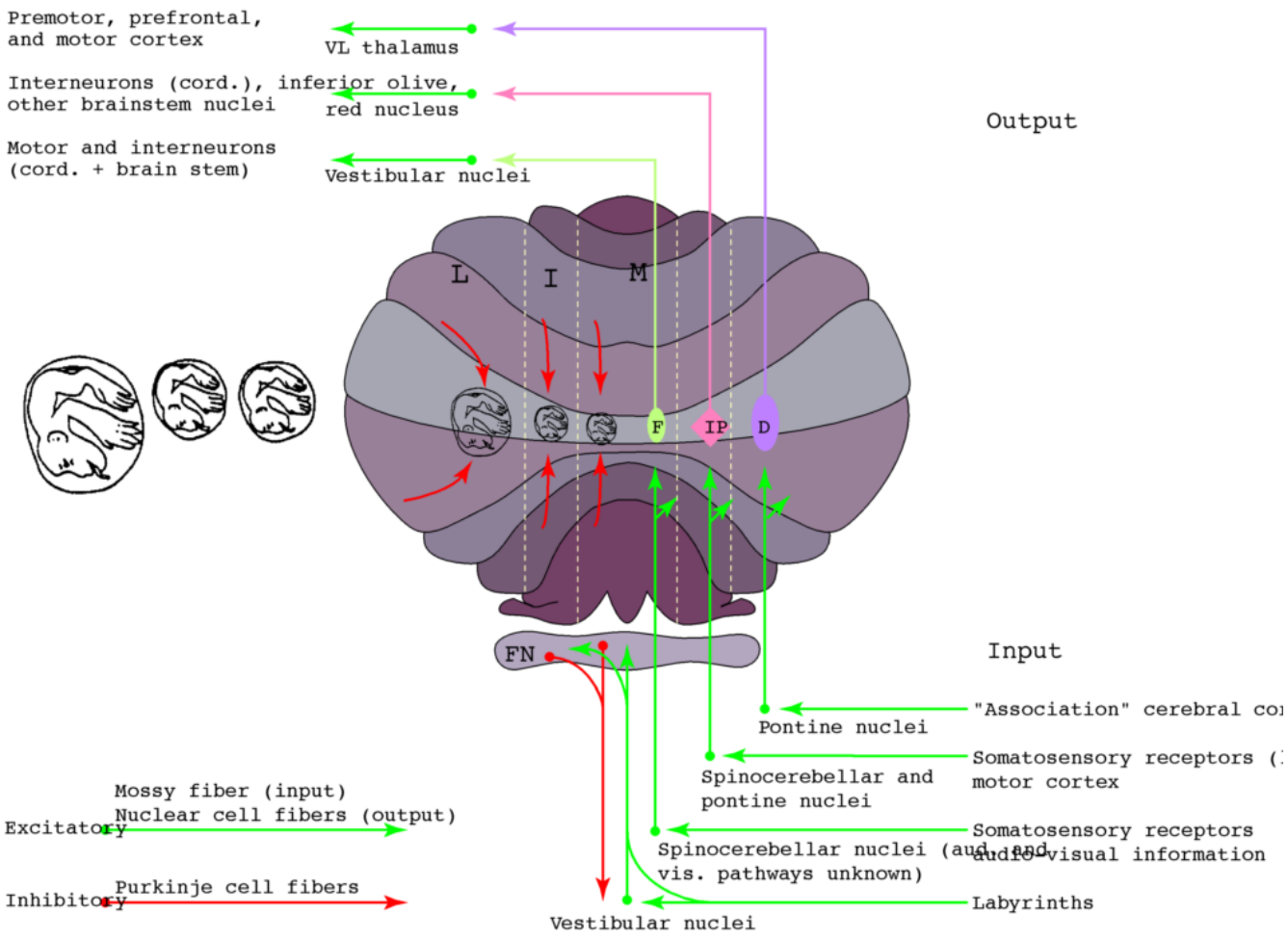
- Consists **of three lobes**:
- ***Anterior***: primary fissure separates from the posterior lobe; receives major spinal cord inputs; is referred as ***SPINOCEREBELLUM***
- ***Posterior:*** is separated from the flocculonodular lobe by a posterolateral fissure; is referred as ***CEREBROCEREBELLUM***
- ***Flocculonodular lobe:*** filogenetically is the most primitive; receives major inputs from the vestibular system; is referred as ***VESTIBULOCEREBELLUM***


Brain stem
Spinocerebellum
Cerebrocerebellum
Vestibulocerebellum
(a)
Unfolded
Regulation of muscle tone, coordination of skilled voluntary movement
Planning and modulation voluntary activity, storage of procedural memories
Maintenance of balance, control of eye movements
(b)

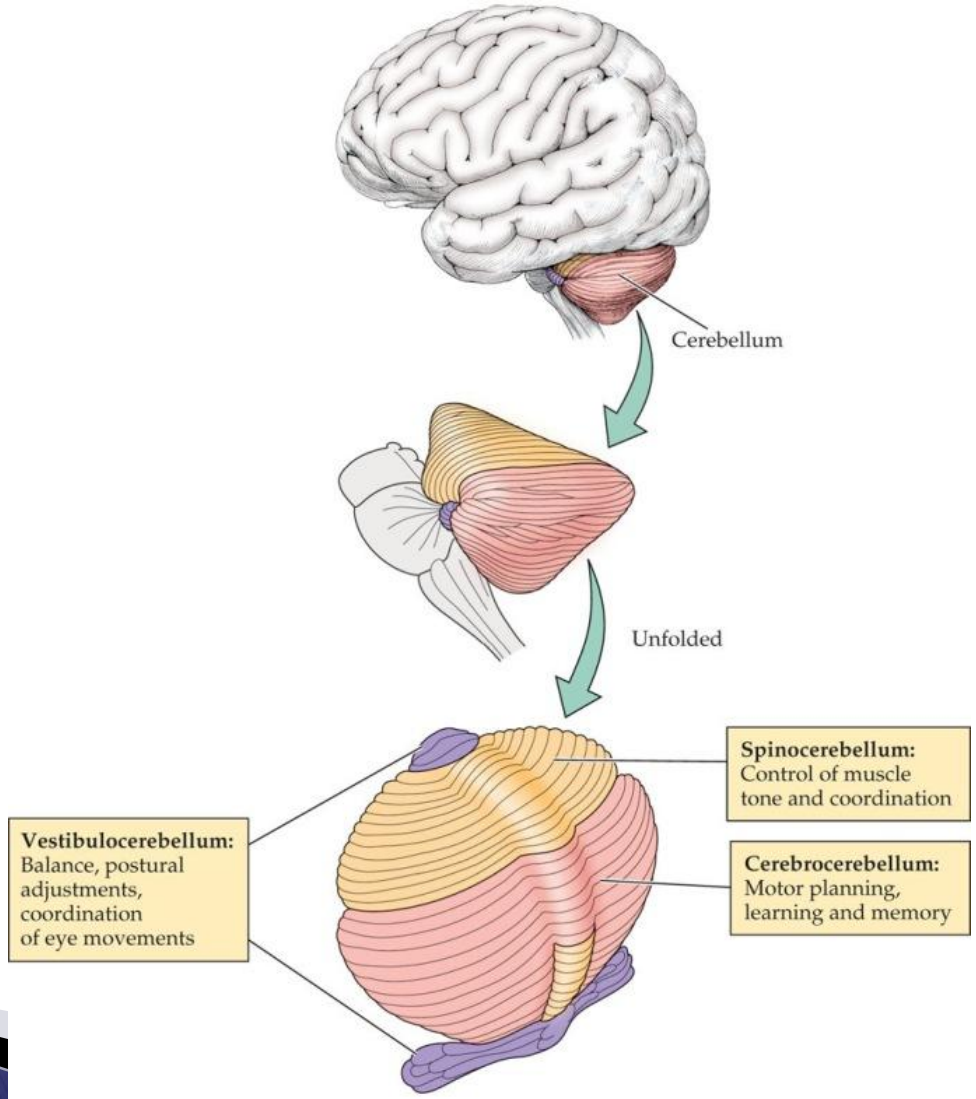
DEEP CEREBELLAR NUCLEI

- Medial structure is called ***FASTIGIAL NUCLEUS***
- Lateral structure is called ***DENTATE NUCLEUS***
- Between previous two is ***INTERPOSED NUCLEI (MEDIAL STRUCTURE IS CALLED GLOBOSE NUCLEUS AND LATERAL STRUCTURE IS CALLED EMBOLIFORM NUCLEUS)***



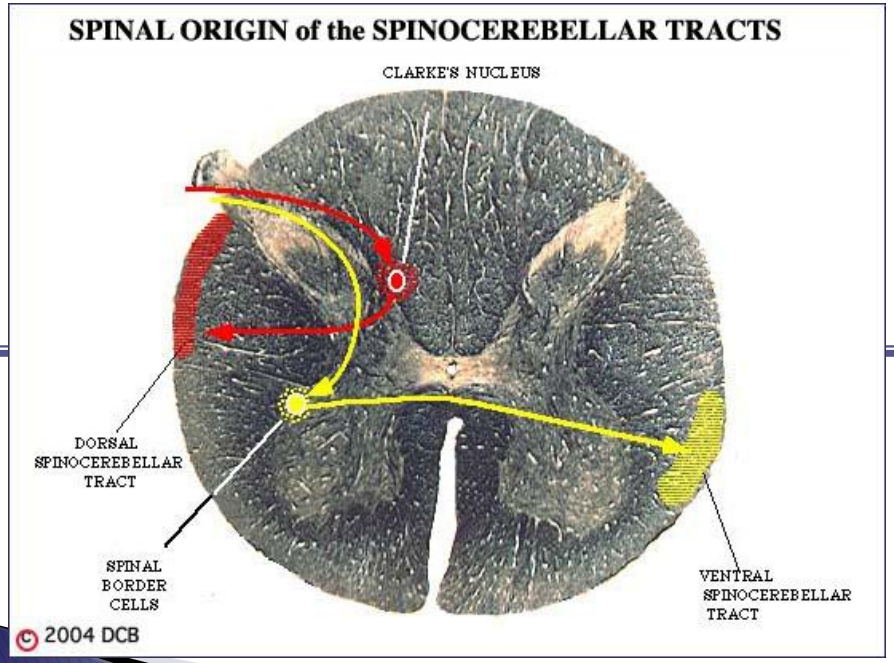


AFFERENT PROJECTIONS TO THE CEREBELLUM



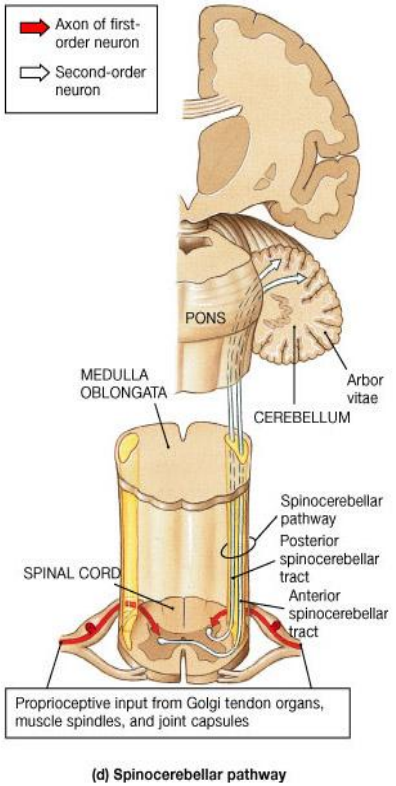
Afferent connections of the cerebellum

- **SPINOCEREBELLUM (spinal cord)**
- Provides control of muscle tone and movement
- Pathways include: spinocerebellar tract – dorsal and ventral
  cuneocerebellar tract
  rostral spinocerebellar tract



Dorsal (posterior) spinocerebellar tract

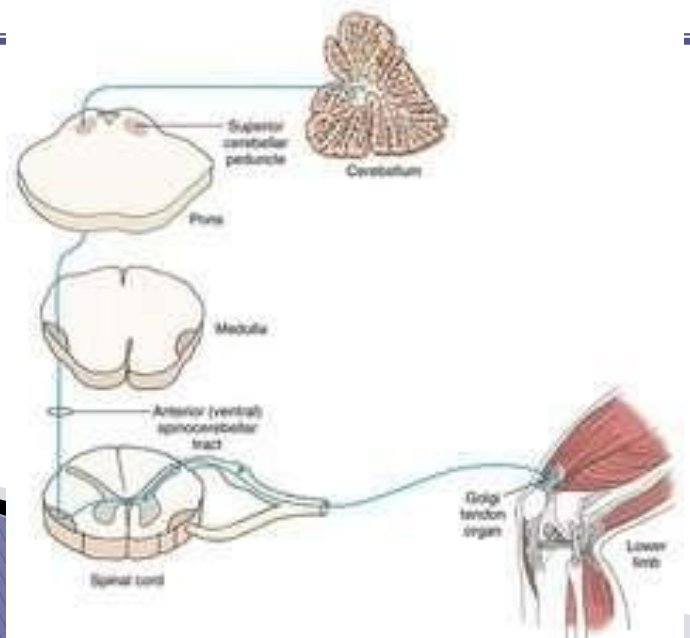
- **Origins** from the muscle spindles and Golgi tendon organs from the lower limbs
- **Passes** through inferior cerebellar peduncle
- **Terminates** in medial part of ipsilateral anterior lobe and adjacent portions of the posterior lobe

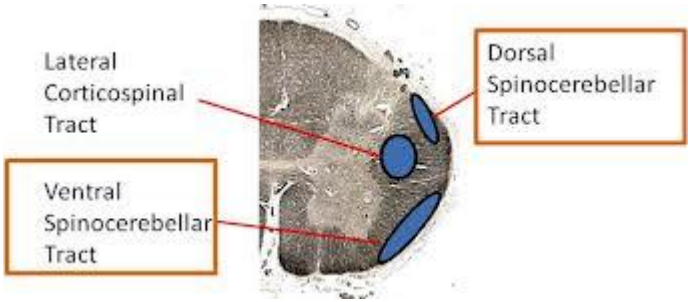


(d) Spinocerebellar pathway

Ventral (anterior) spinocerebellar tract

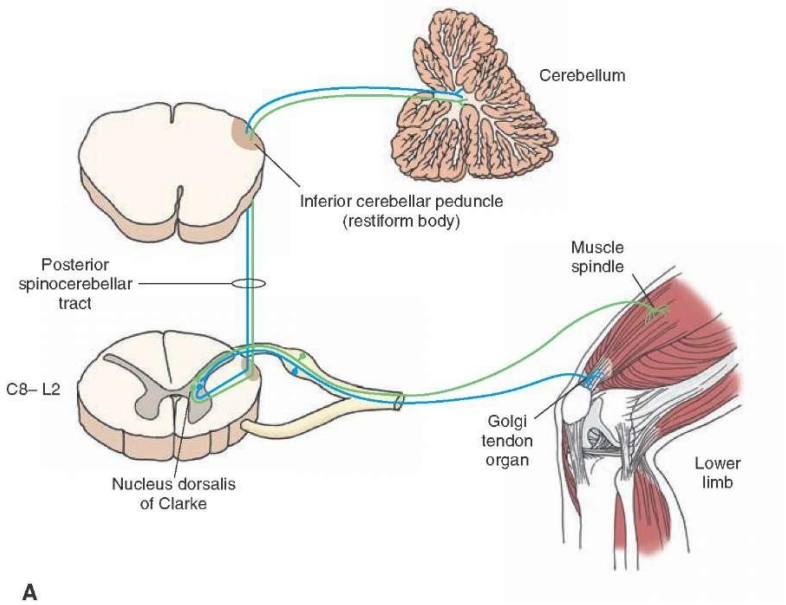
- **Origins** from the Golgi tendon organs detecting whole limb movement
- **Passes** through superior cerebellar peduncle
- **Terminates** close to the regions where dorsal pathway terminate

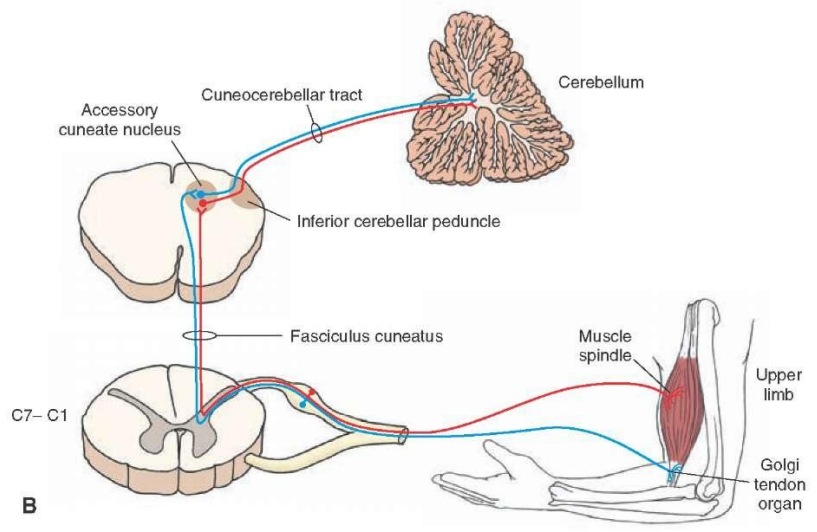




Cuneocerebellar tract

- Upper limb equivalent to the dorsal spinocerebelar tract
- **Origins** from the muscle spindles and Golgi tendon organs from the upper limbs
- **Terminates** in medial part of ipsilateral anterior lobe and adjacent portions of the posterior lobe



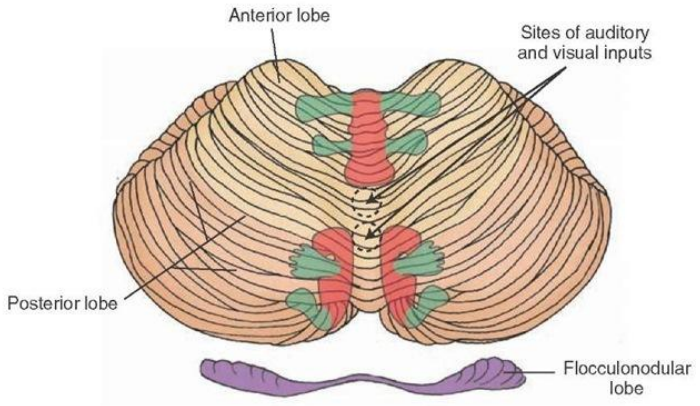


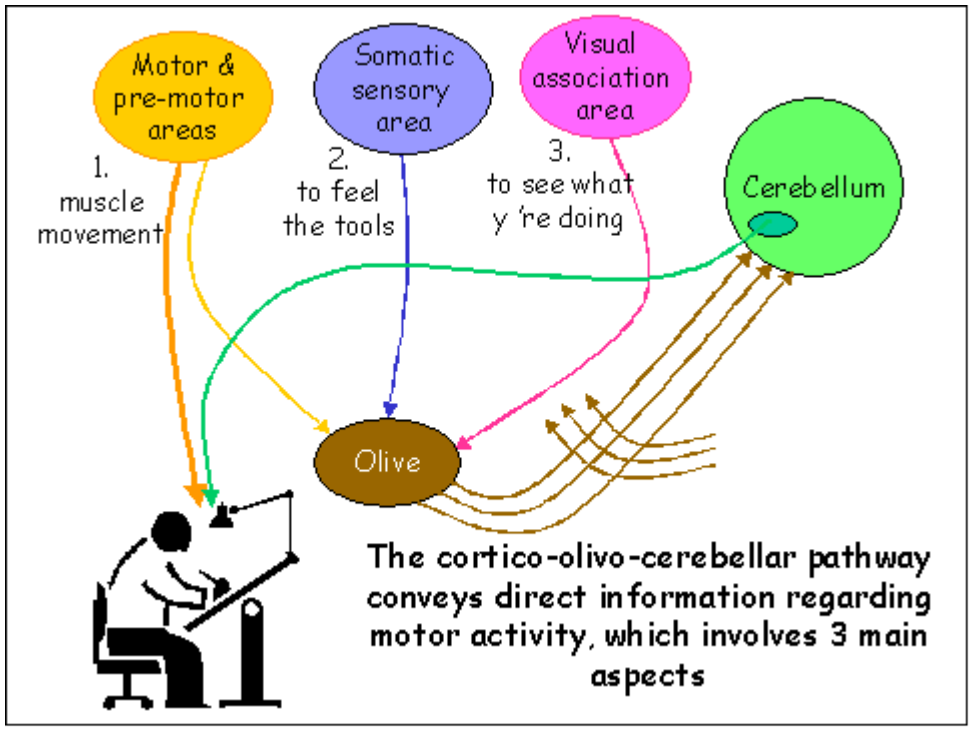
Rostral spinocerebellar tract

- Upper limb equivalent of the ventral spinocerebellar tract not yet identified in humans
- Provides whole upper limb movement to the anterior lobe from the upper limb

Afferents from brainstem

- **INFEROR OLIVARY NUCLEUS**
- **Receives inputs from the spinal cord (CUTANEOUS AFFERENTS, JOINT AFFERENTS, AND MUSCLE SPINDELS) and from cerebral cortex (AXONS PASSES TO THE CONTRALATERAL CEREBELLAR CORTEX VIA INFERIOR CEREBELLAR PEDUNCLES TERMINATING SOMATOTOPICALLY WITHIN THE ANTERIOR AND POSTERIOR LOBES)**




Motor & pre-motor areas
Somatic sensory area
Visual association area
Cerebellum
1. muscle movement
2. to feel the tools
3. to see what y 're doing
Olive
The cortico-olivo-cerebellar pathway conveys direct information regarding motor activity, which involves 3 main aspects

Vestibular system afferents

- Receives signals from the otolith organ (macula of saccule and utricle) and semicircular canals
- Enters cerebellar cortex via monosynaptic (called juxtarestiform body) or dysinaptic pathway (mainly from medial and inferior vestibular nuclei)
- Provides information about the position of the head in space at any time point given

Reticular formation afferents

- Regulate extensor muscle tone, coordinate movements, maintain erect posture
- Arise from the ***lateral and paramedian reticular nuclei*** of the medulla and from the ***reticulotegmental nucleus*** of the pons
- Serves as a relay for the cerebral cortical inputs to the vermal and paravermal region of the anterior and posterior lobes of the cerebellar cortex

Afferents from cerebral cortex

- There are several ways:
- 1) comes from cortex to the red nucleus
- 2) is from red nucleus to the ipsilateral inferior olivary nucleus
- 3) from inferior olivary nucleus to the contralateral cerebellar hemisphere

RED NUCLEUS

- Serves as relay from cortex to the spinal cord
- Activates the flexor motor system
- Red nucleus ⟶ inferior olivary nucleus ⟶ contralateral anterior and posterior lobes of cerebellar cortex

- **Deep pontine nuclei**
- Arises from the frontal lobe (motor system)
- Parietal, temporal and visual cortices provides sensory system information
- Parietal system provides planning and programming information
- Temporal and occipital lobes provide information about auditory and visual system

Other inputs to the cerebellar cortex

- **TECTUM-** provides auditory and visual information projecting to the pontine nuclei then through middle cerebellar peduncle to the cerebellar cortex
- **TRIGEMINAL SYSTEM-** information from the muscles of the face and jaw from the mesencephalic trigeminal nucleus
- **MONOAMINERGIC SYSTEM-** modulator of the cerebellar cortical neurons

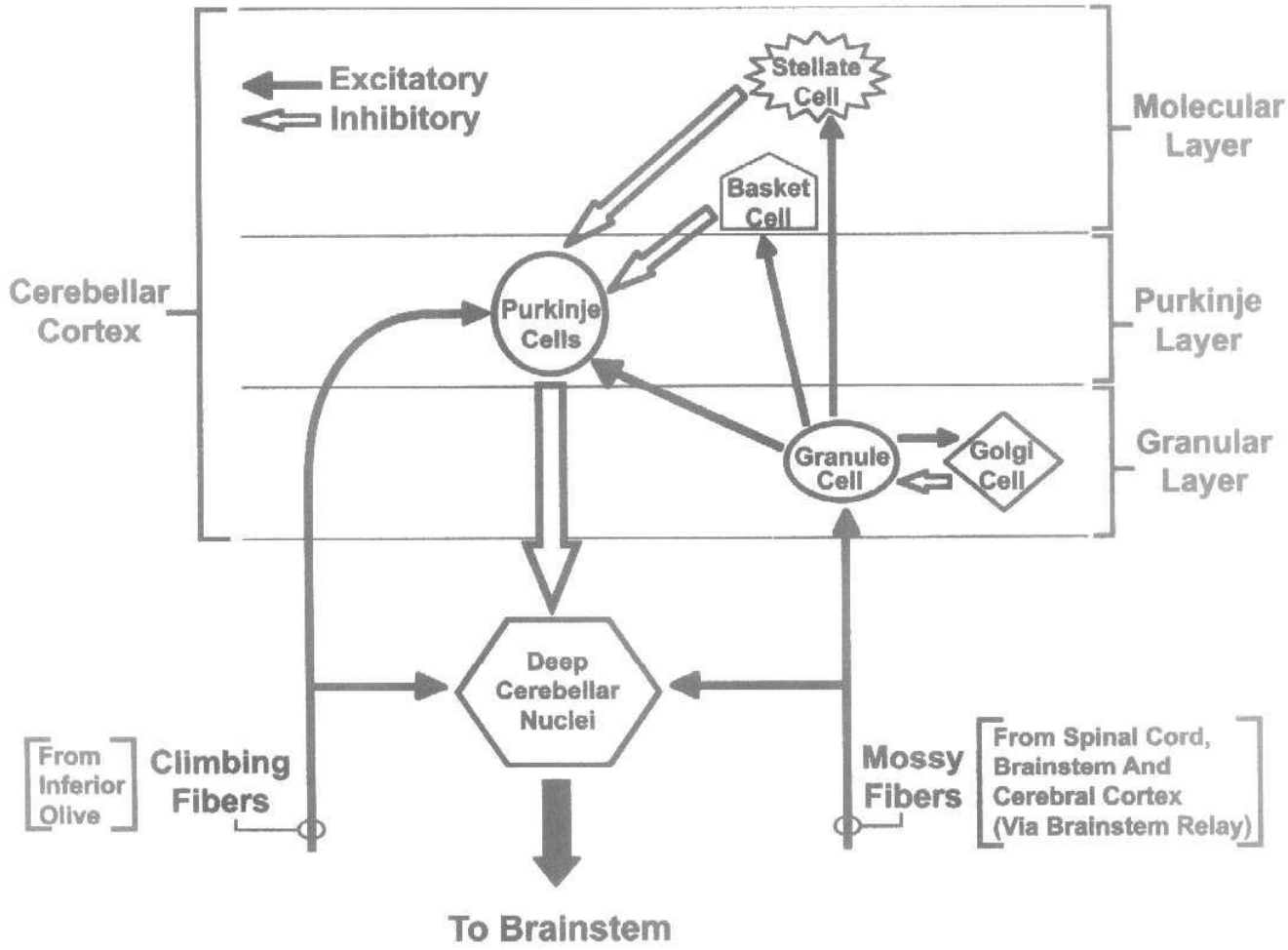
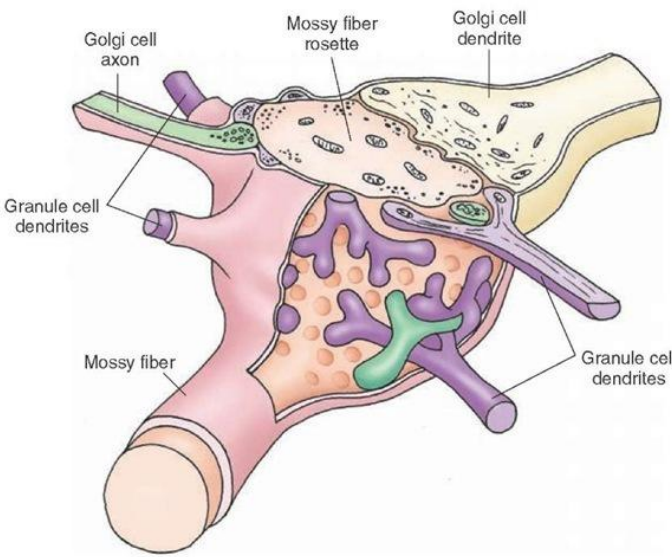
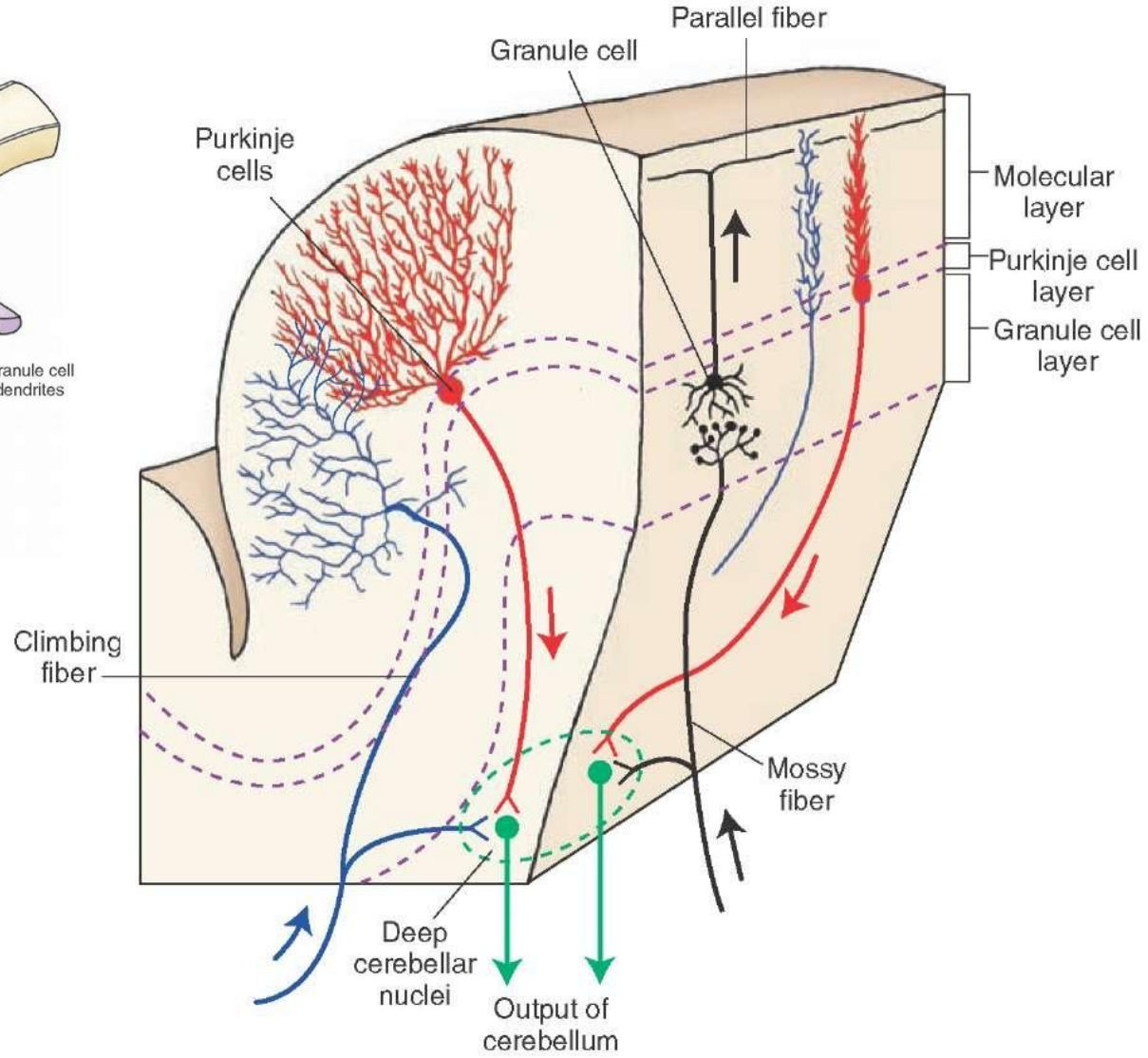


Fig. 7. Simplified diagrammatic representation of the afferent, intracerebellar, and efferent circuitry of the cerebellum, illustrating excitatory and inhibitory components.

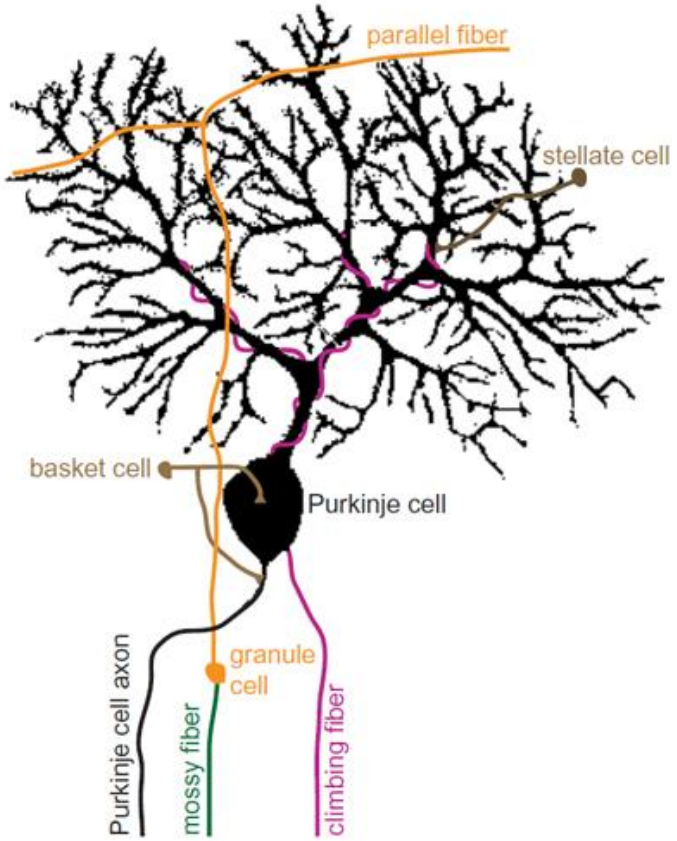
AFFERENT FIBERS - MOSSY AND CLIMBING FIBERS

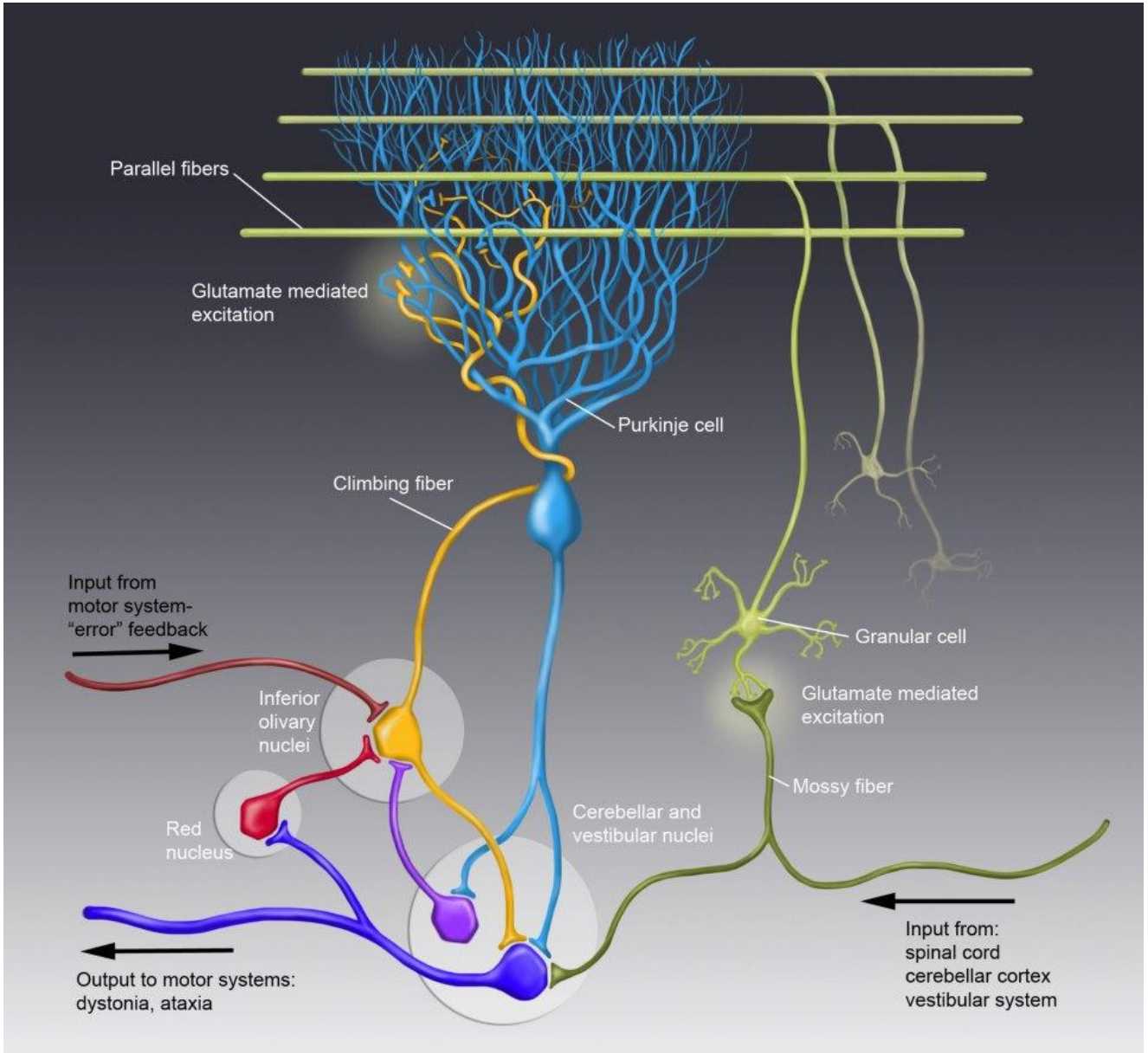
- **MOSSY FIBERS**
- They give rise to many branches in the granular layer
- They terminate forming mossy fiber rosettes; focus of a cerebellar glomerulus (synaptic connection of mossy fiber axons, granule cells dendrites and Golgi axon terminals
- They are **excitatory (glutamate)** and arise from all CNS regions with exception of the inferior olivary nucleus


Golgi cell axon
Mossy fiber rosette
Golgi cell dendrite
Granule cell dendrites
Mossy fiber
Granule cell dendrites


Parallel fiber
Granule cell
Purkinje cells
Molecular layer
Purkinje cell layer
Granule cell layer
Climbing fiber
Mossy fiber
Deep cerebellar nuclei
Output of cerebellum

- **CLIMBING FIBERS**
- Arise from inferior olivary nucleus and reach molecular layer to make synapse with dendrites of Purkinje cells
- Aspartate is neurotransmitter that is believed to be released on terminals of climbing fibers




Parallel fibers
Glutamate mediated excitation
Purkinje cell
Climbing fiber
Input from motor system- "error" feedback
Granular cell
Glutamate mediated excitation
Inferior olivary nuclei
Mossy fiber
Red nucleus
Cerebellar and vestibular nuclei
Input from: spinal cord cerebellar cortex vestibular system
Output to motor systems: dystonia, ataxia

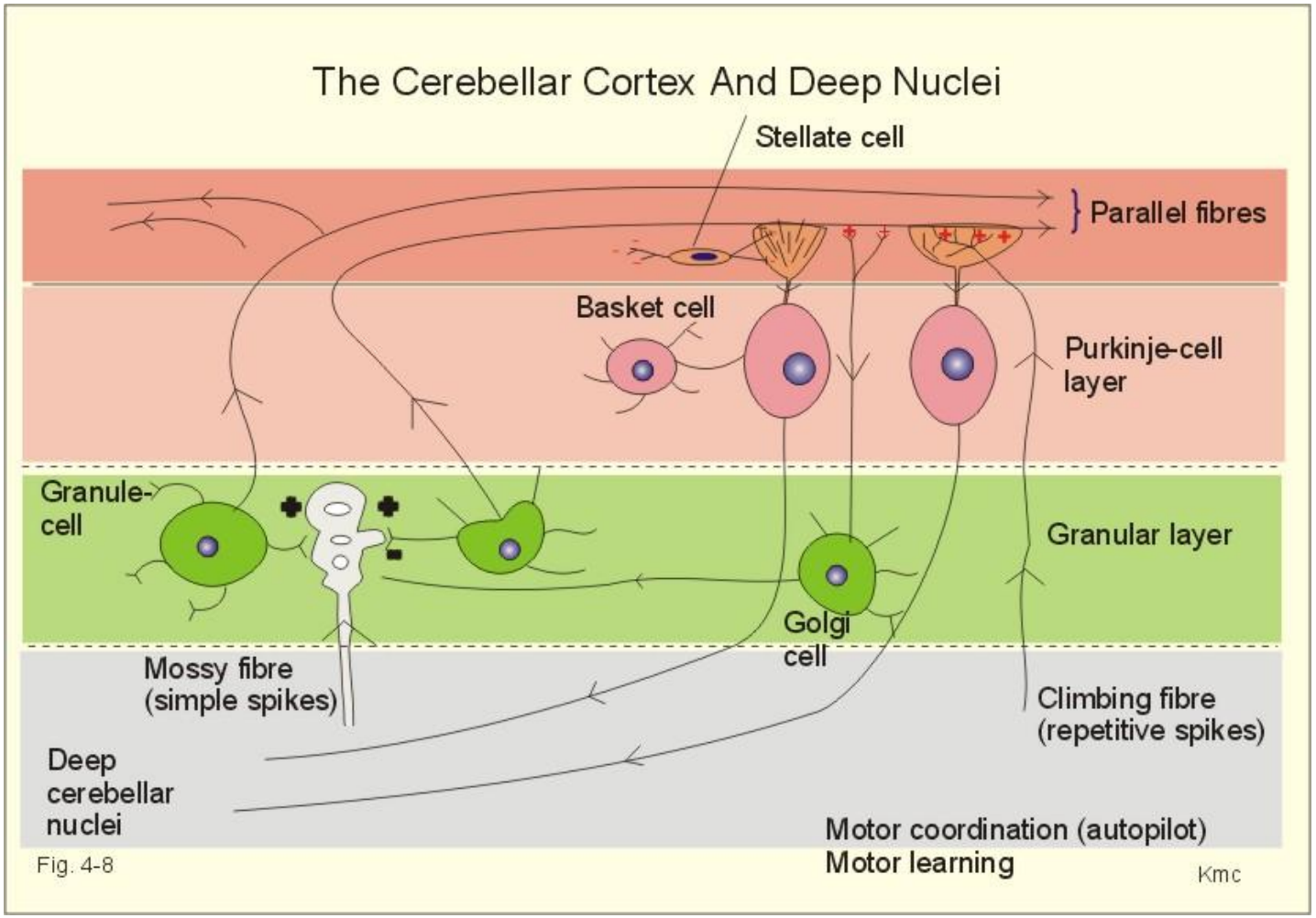
Cerebellar cortex

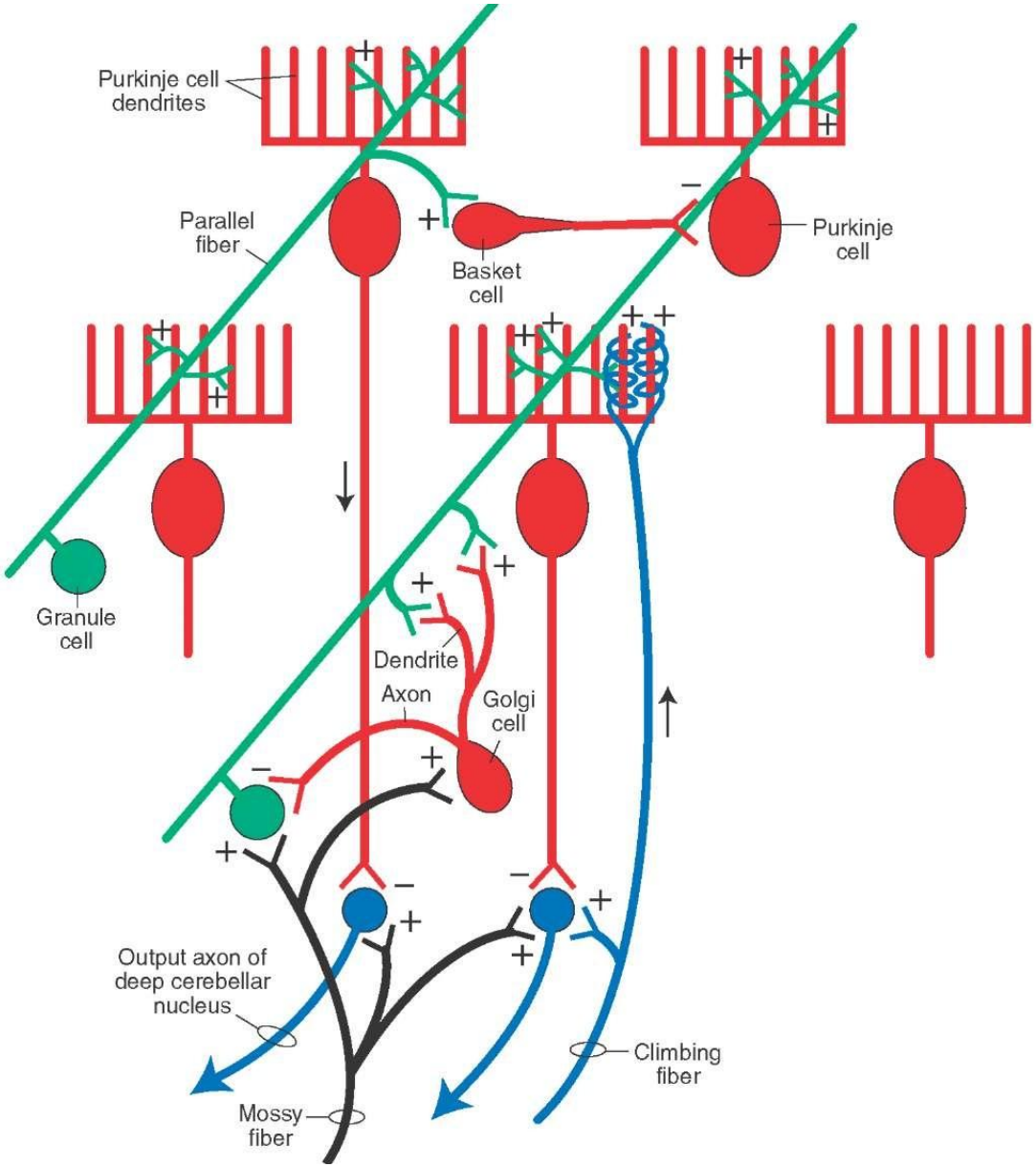
- ***Consists of three cell layers:***
- ***Granular cell layer***
- ***Purkinje cell layer***
- ***Molecular cell layer***

- ***Granular cell layer***

- ***granule cells; excites dedrites of Purkinje cells (glutamate)***
- ***Golgi cells; inhibits (GABA) granule cells and makes synaptic contact with axon terminals of mossy fiber***

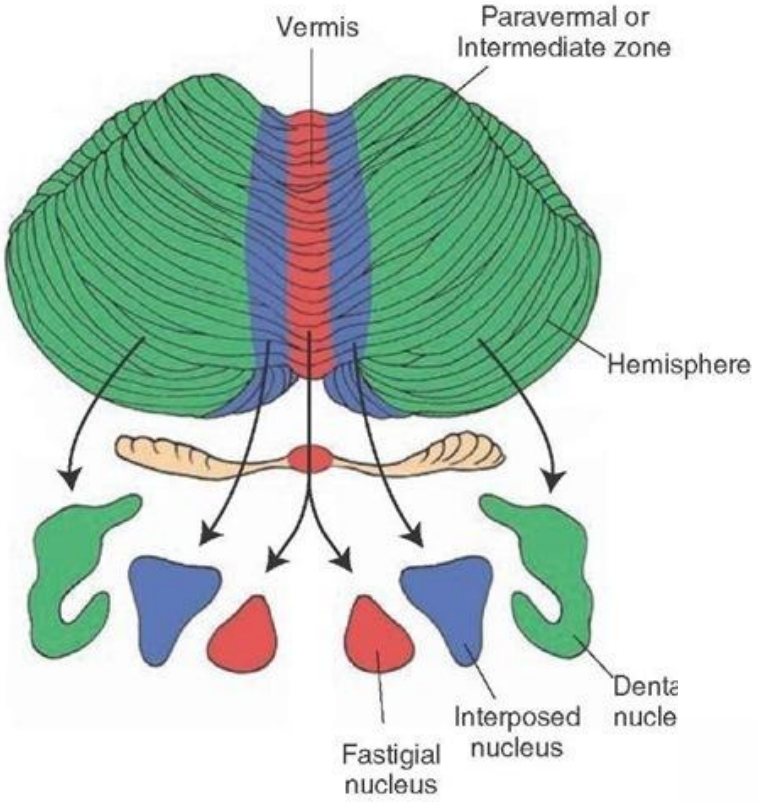
- ***Purkinje cell layer***
- Contains one cell type, Purkinje cells; these are only projecting neurons of the cerebellum; they are inhibitory cell type (GABA)
- ***Molecular cell layer***
- Contains dendrites of Purkinje cells, parallel fibers and two other types referred to as basket cells (inhibitory cells)


The Cerebellar Cortex And Deep Nuclei
Stellate cell
Parallel fibres
Basket cell
Purkinje-cell layer
Granule-cell
Granular layer
Golgi cell
Mossy fibre (simple spikes)
Climbing fibre (repetitive spikes)
Deep cerebellar nuclei
Motor coordination (autopilot)
Motor learning
Fig. 4-8
Kmc

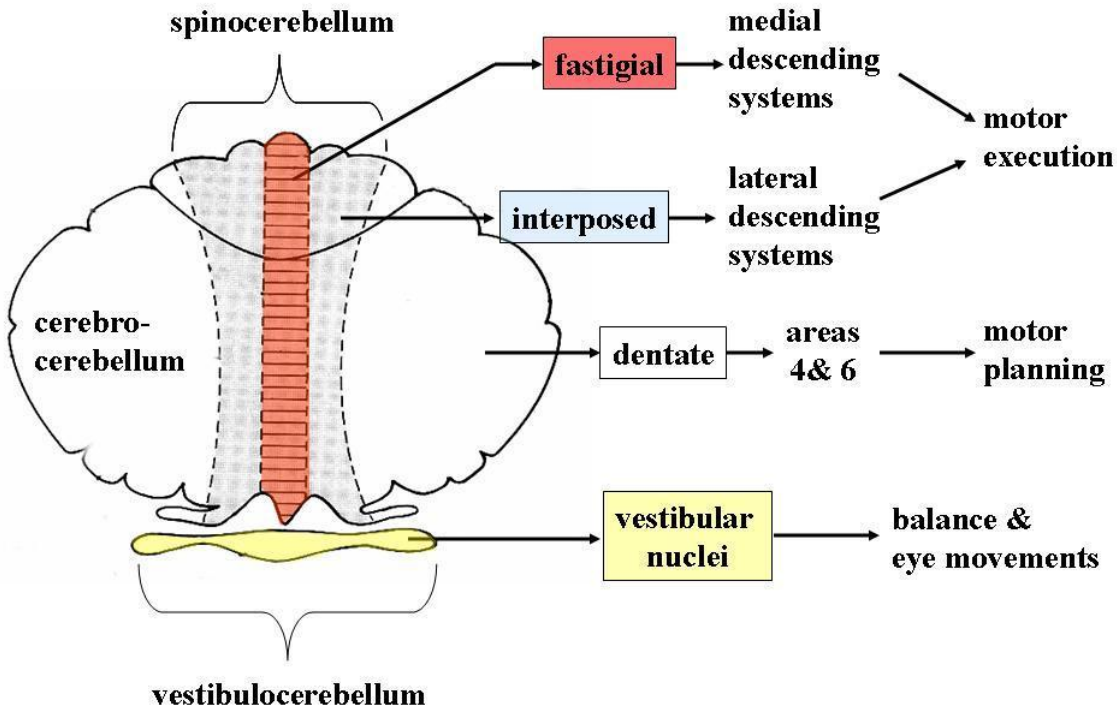

Purkinje cell dendrites
Parallel fiber
Basket cell
Purkinje cell
Granule cell
Dendrite
Axon
Golgi cell
Output axon of deep cerebellar nucleus
Climbing fiber
Mossy fiber

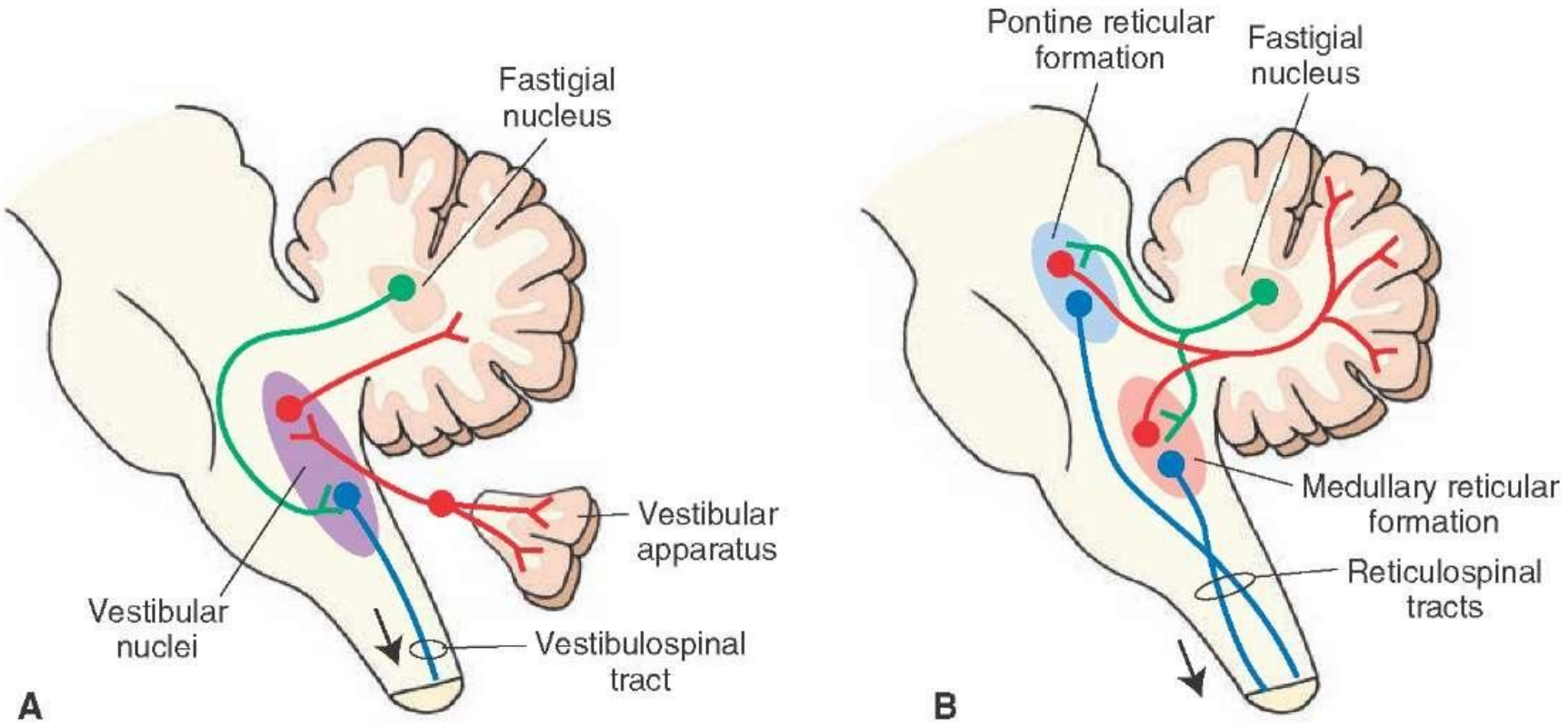
Efferent projections of the cerebellar cortex

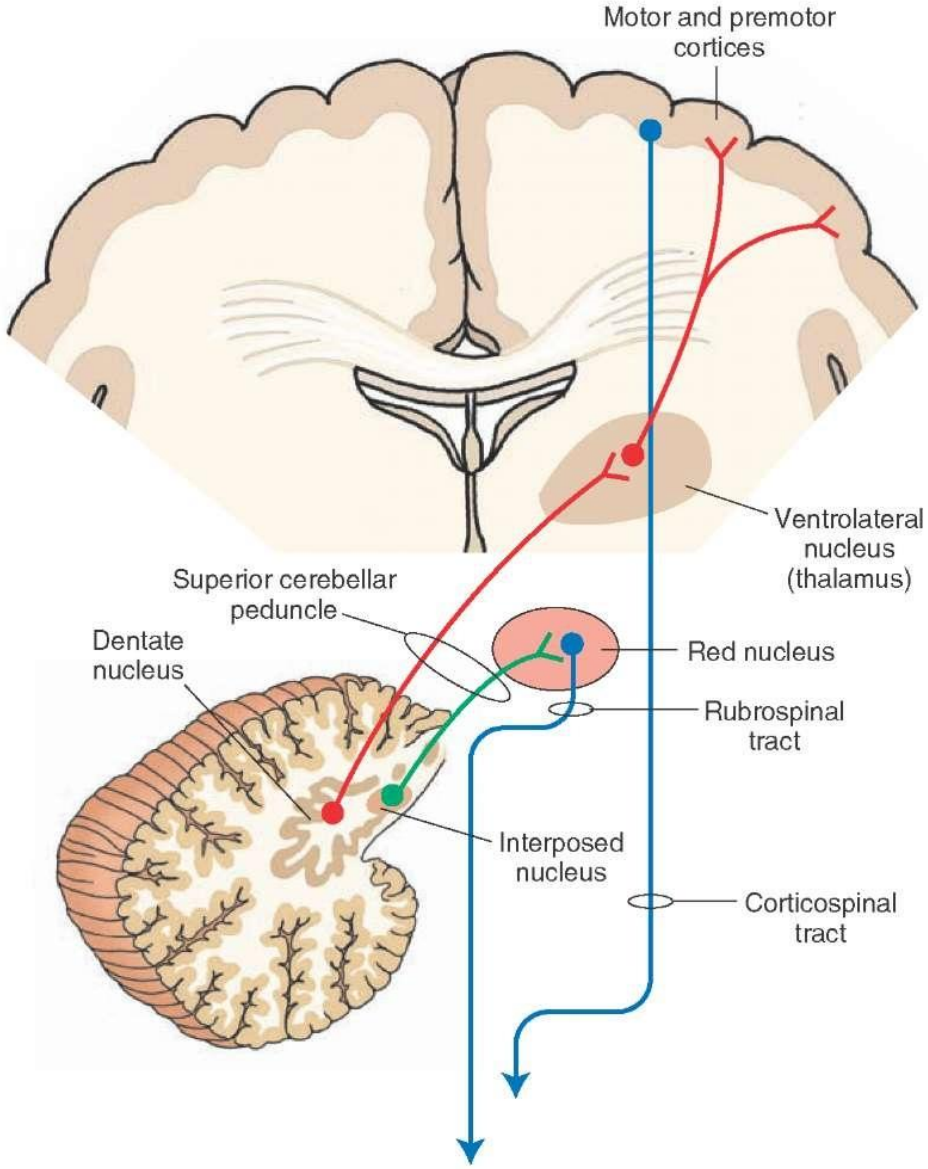
- Cortex transmits its signals to the deep cerebellar nuclei via **Purkinje cell axon (inhibitory)**
- Purkinje cell projections to the deep cerebellar nuclei are topographically arranged
- Purkinje cells associated with **VESTIBULOCEREBELLUM AND SPINOCEREBELLUM** projects to the **fastigial nucleus**
- Purkinje cells associated with the **CEREBROCEREBELLUM** project to the **interposed nucleus and dentate nuclei**

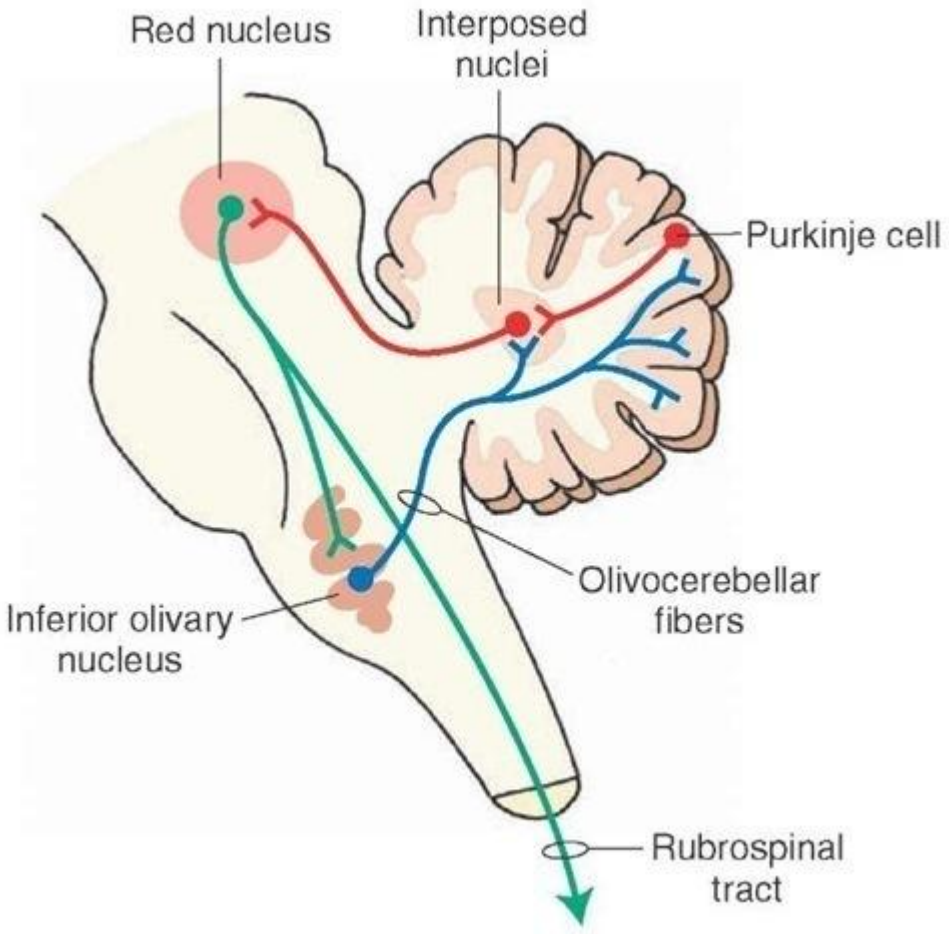


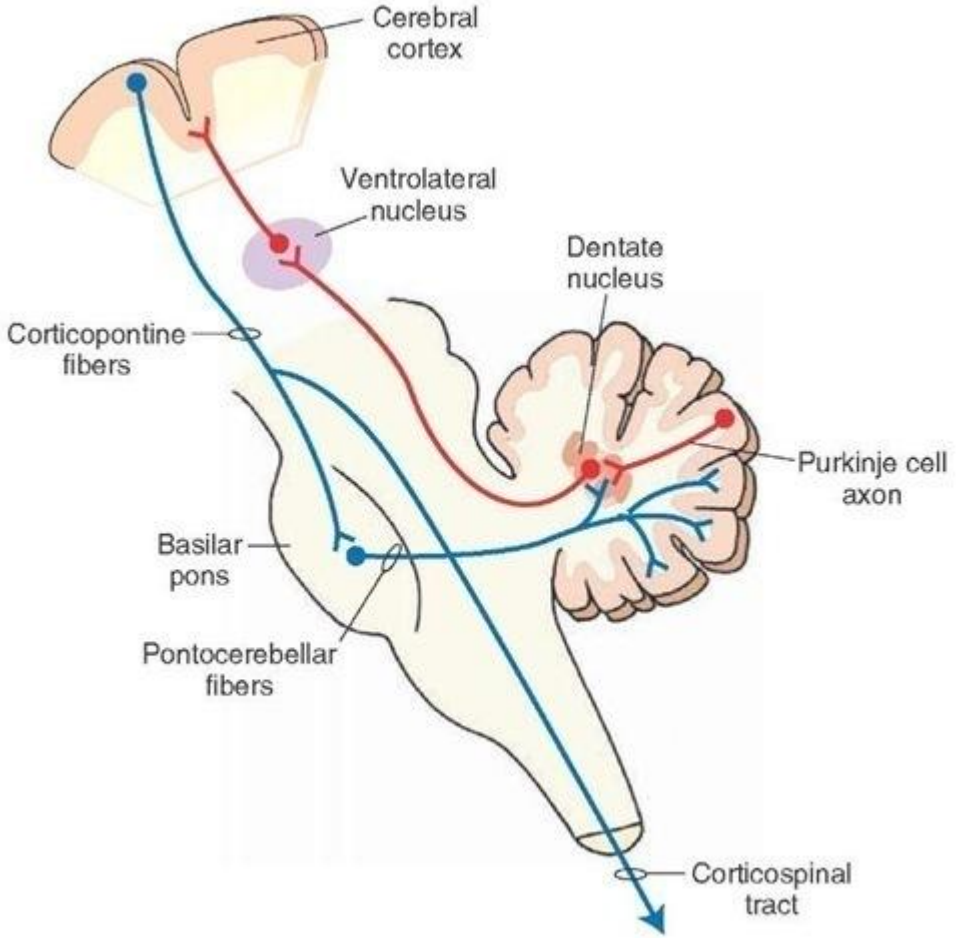
Cerebellar Output

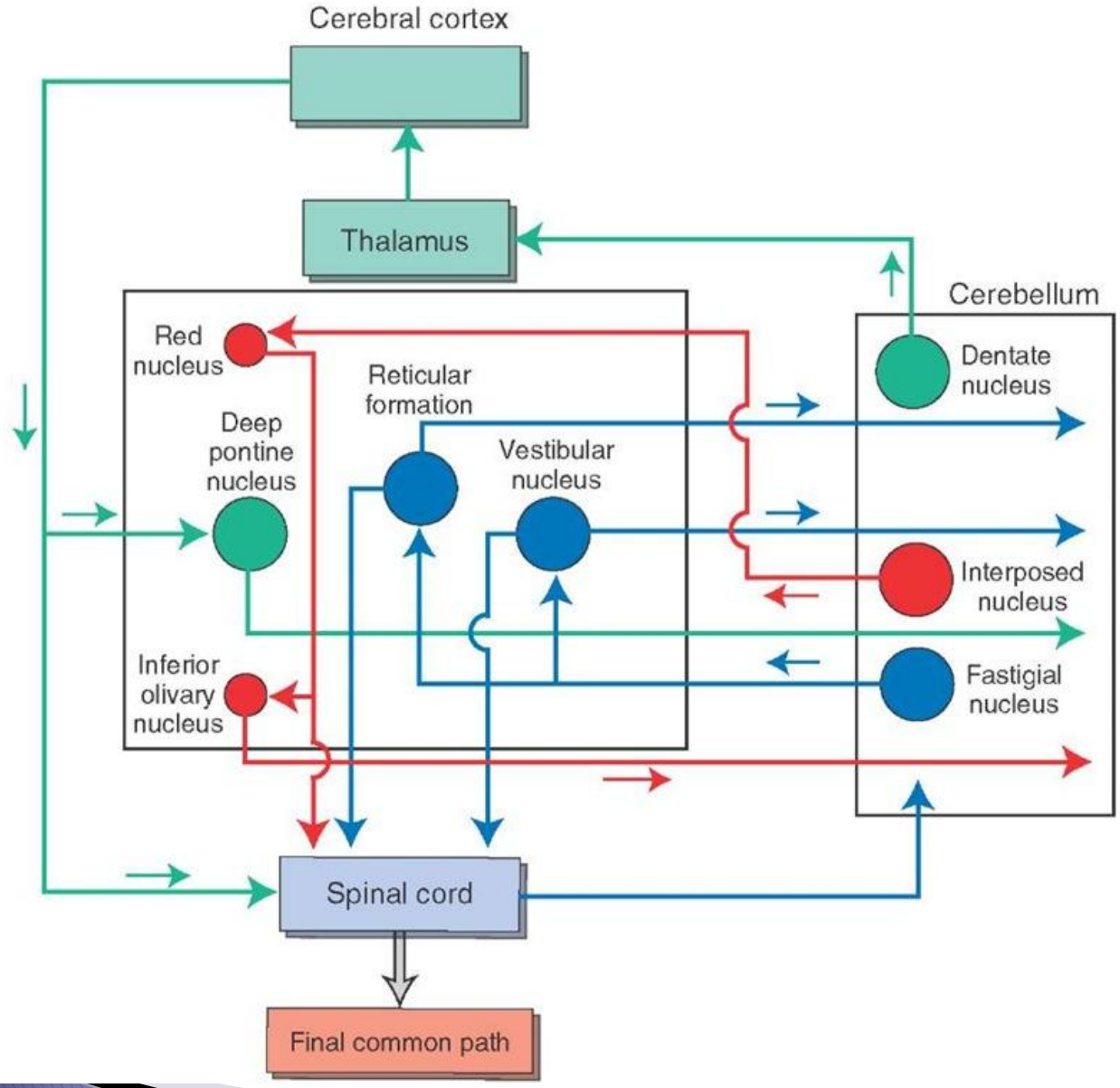



Fastigial nucleus
Vestibular apparatus
Vestibular nuclei
Vestibulospinal tract
A
Pontine reticular formation
Fastigial nucleus
Medullary reticular formation
Reticulospinal tracts
B


Motor and premotor cortices
Ventrolateral nucleus (thalamus)
Superior cerebellar peduncle
Dentate nucleus
Red nucleus
Rubrospinal tract
Interposed nucleus
Corticospinal tract


Red nucleus
Interposed nuclei
Purkinje cell
Olivocerebellar fibers
Inferior olivary nucleus
Rubrospinal tract


Cerebral cortex
Ventrolateral nucleus
Dentate nucleus
Corticopontine fibers
Purkinje cell axon
Basilar pons
Pontocerebellar fibers
Corticospinal tract


Cerebral cortex
Thalamus
Cerebellum
Red nucleus
Reticular formation
Deep pontine nucleus
Vestibular nucleus
Dentate nucleus
Interposed nucleus
Fastigial nucleus
Inferior olivary nucleus
Spinal cord
Final common path

Motor learning and the cerebellum

- Primary regions involved in motor learning include the mossy and climbing fiber connections that are made with Purkinje cell
- Each of sensory modalities that projects to the cerebellum (visual, vestibular, auditory and somatosensory) contribute to the learning process within the cerebellum

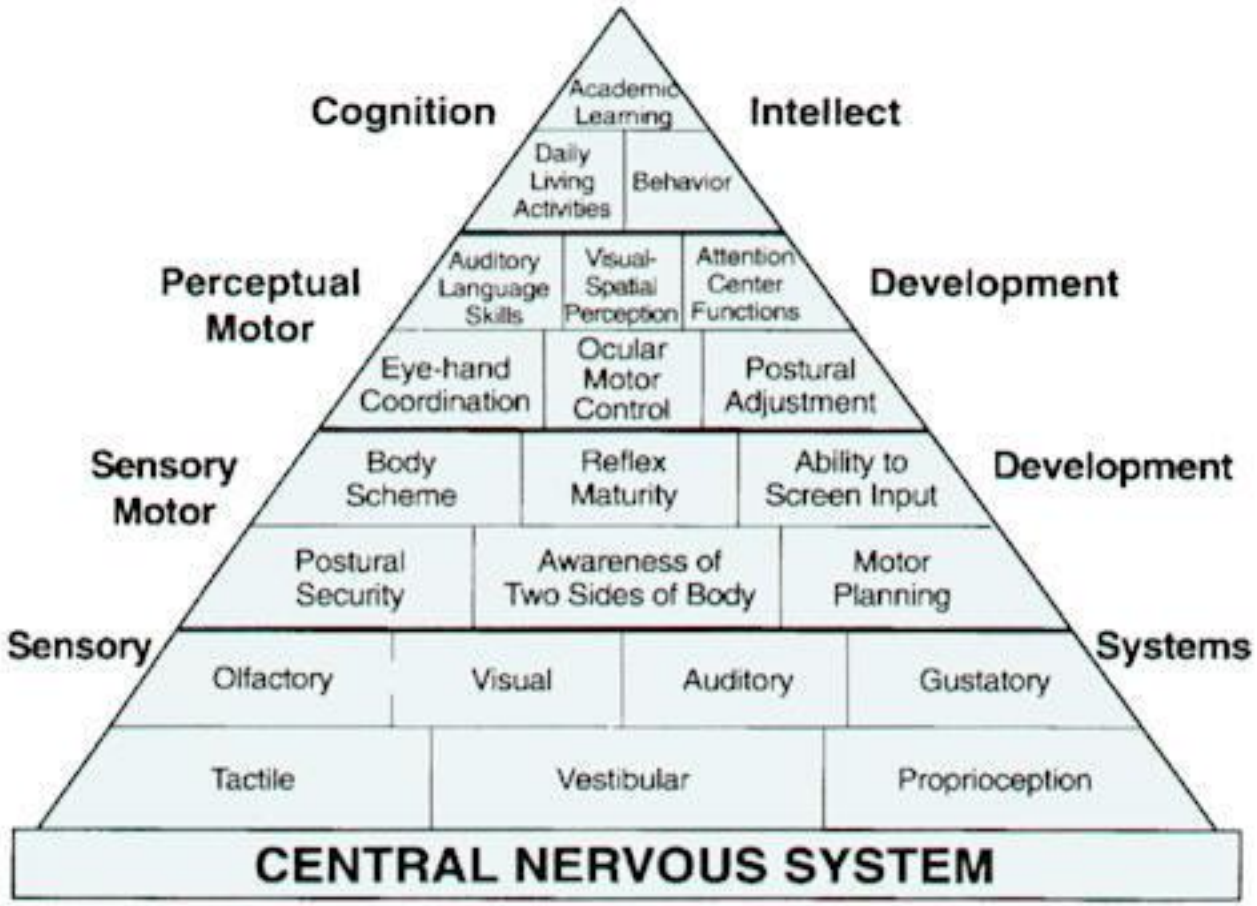
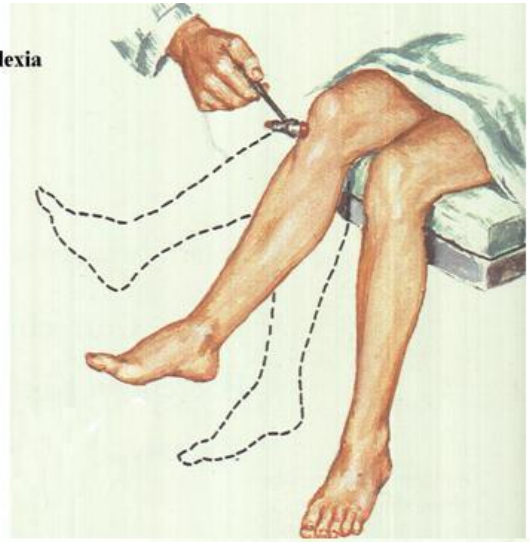


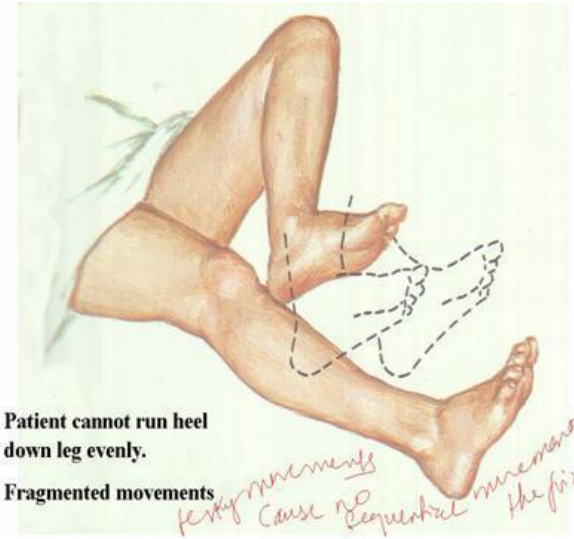
Figure 5. Pyramid of Learning. (Williams & Shellenberger, 1-4)

Cerebellar disorders

- ***ATAXIA***
- Involves the cerebellar hemispheres or disruption of the feedback circuit between the cerebellar cortex and the cerebral cortex
- If the damage involves flocculonodular lobe or the vermal region of posterior or anterior lobes patient will display gait ataxia (they walk with legs widely separated); these symptoms are often seen in cases of alcoholic cerebellar degeneration preferentially affecting the anterior lobe

Hyper-reflexia
& clonus





Patient cannot run heel
down leg evenly.

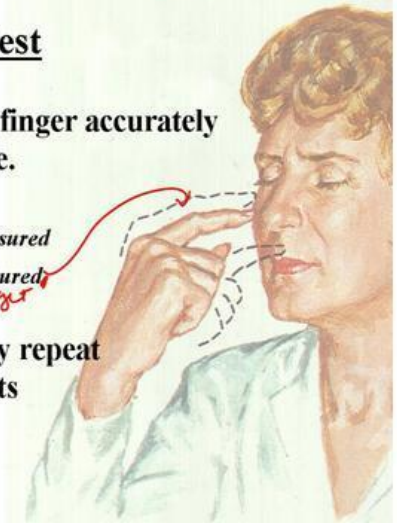
Fragmented movements

Finger-to-Nose Test

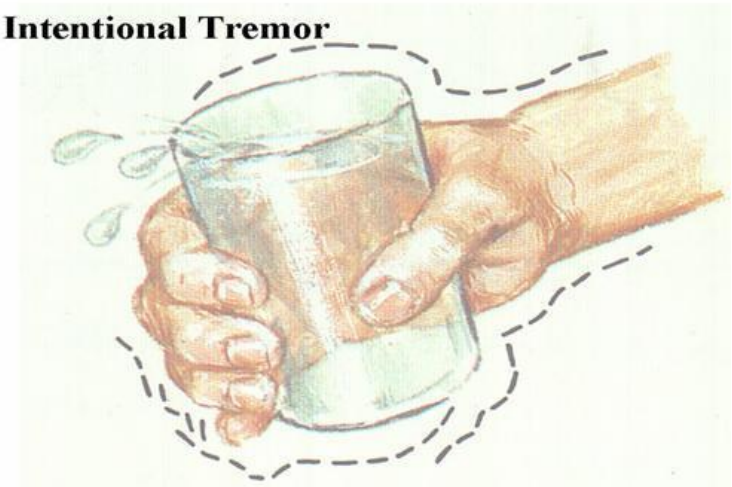
Patient cannot direct finger accurately
to nose with eyes close.
(dysmetria)

- *a. hypometria: under measured*
- *b. hypermetria: over measured*

Patient cannot rapidly repeat
alternating movements
(adiadochokinesia)



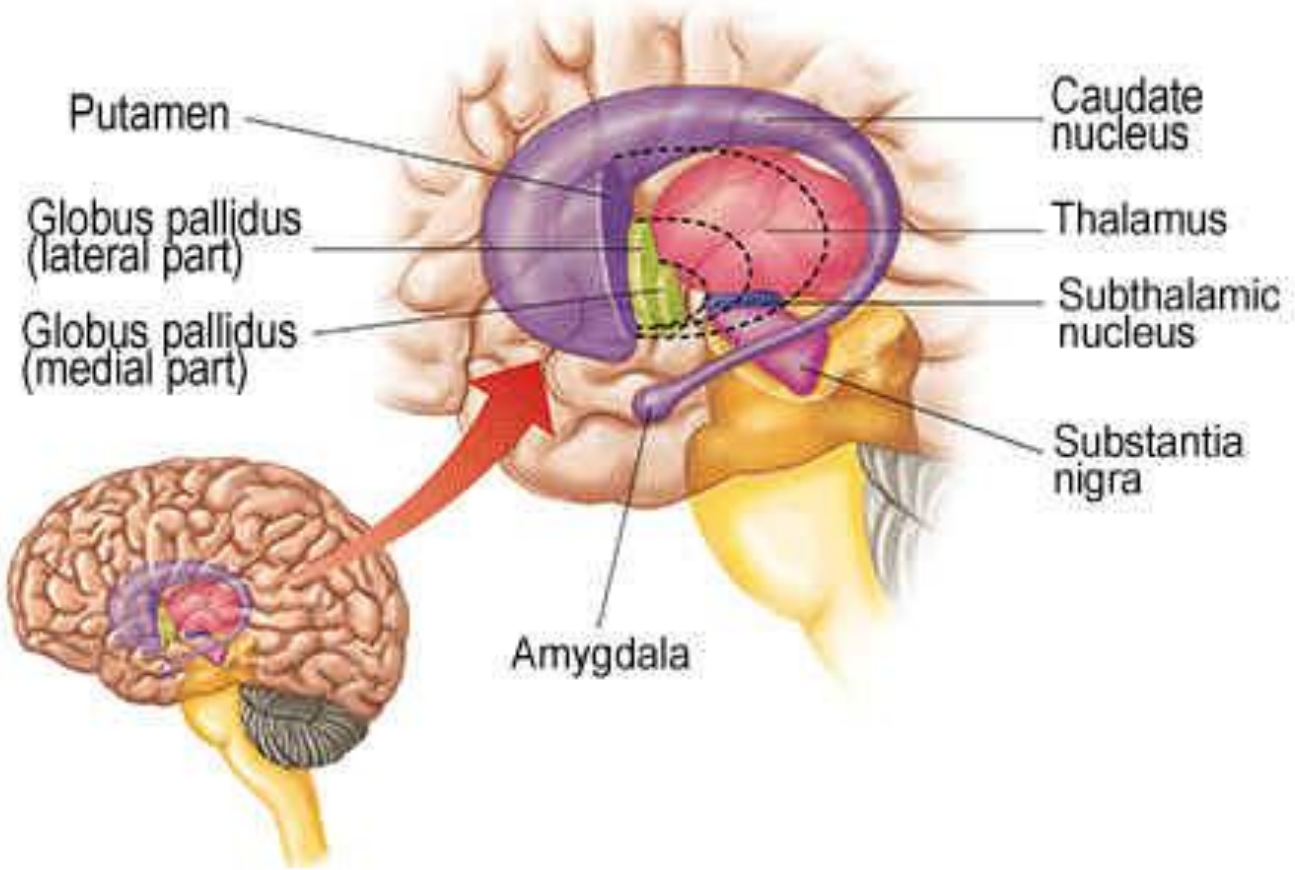
Intentional Tremor



- **HYPOTONIA**
- Has been associated with damage to parts of the cerebellar cortex
- The precise mechanism underlying this disorder remains unknown
- Because the outputs to a brainstem structure are typically excitatory, such lesion may cause loss of excitation to the lateral vestibular nucleus, resulting in loss of excitatory input to spinal cord motor neurons and subsequent hypotonia

- **CEREBELLAR NYSTAGMUS AND GIAT ATAXIA**
- Lesions of the vermal region of the cerebellar cortex or fastigial nucleus can result in cerebellar nystagmus


Gait ataxia with "tandem" gait
Finger-finger test (intention tremor)
Dysdiadochokinesis
Dysmetria (hypermetria)
Postural test for position sense
Test for gaze-evoked nystagmus
Rebound phenomenon
Saccades; gaze-evoked and rebound nystagmus


Putamen
Globus pallidus (lateral part)
Globus pallidus (medial part)
Caudate nucleus
Thalamus
Subthalamic nucleus
Substantia nigra
Amygdala

The Basal Ganglia

- Primary function of the basal ganglia is to provide a feedback mechanism to the cerebral cortex for the initiation of the motor response
- Reduces or dampens the excitatory inputs to the cerebral cortex

COMPOSTION OF THE BASAL GANGLIA

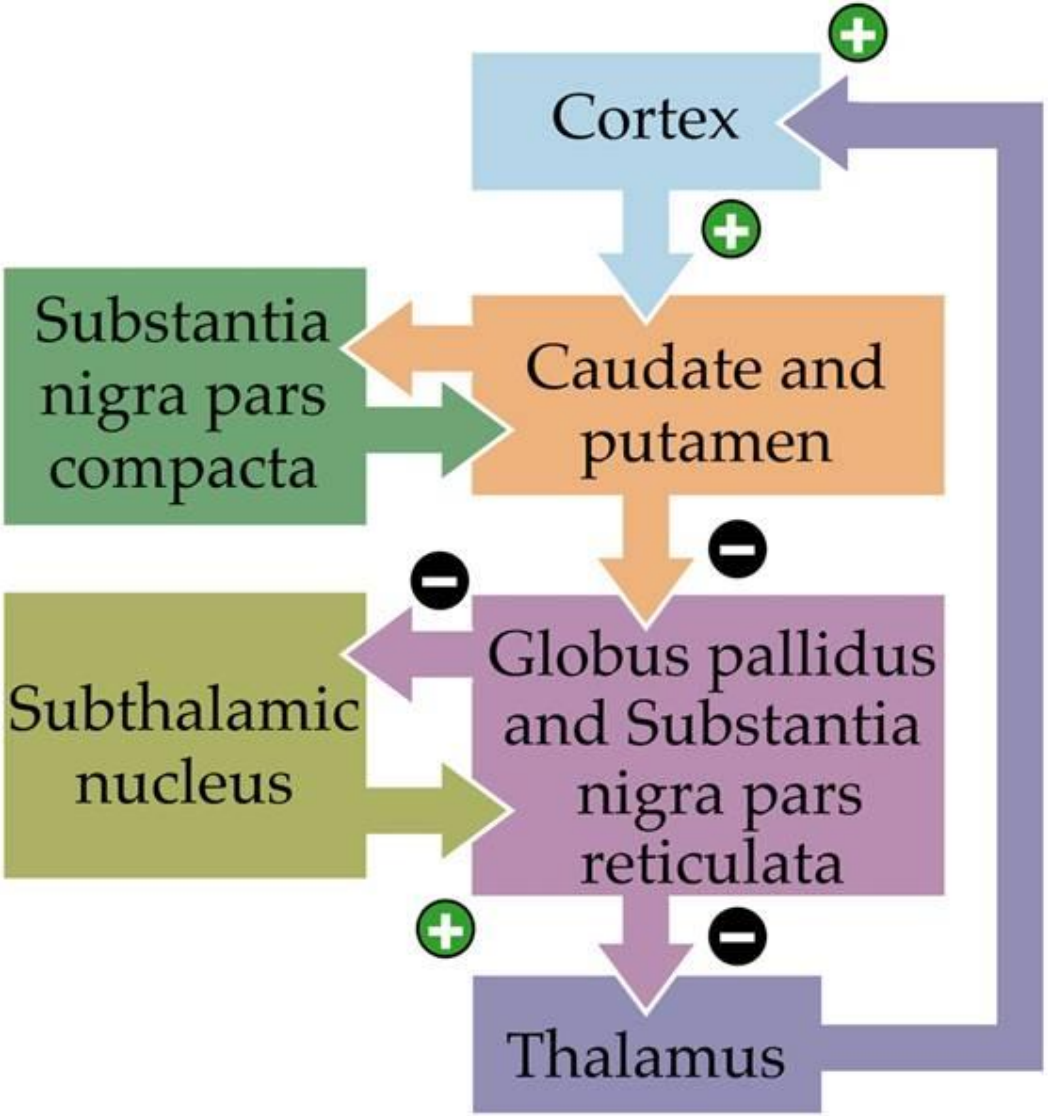
- **CONSISTS OF:**

- **NEOSTRIATUM** (caudate nucleus and putamen)=***AFFERENT PART***
- **PALEOSTRIATUM** (globus pallidus)
- **SUBTHALAMIC NUCLEUS**
- **SUBSTANTIA NIGRA** (pars reticulata and pars compacta)

AFFERENT SOURCES OF THE BASAL GANGLIA

- Arises from cerebral cortex (motor, sensory, limbic system)
- Inputs from primary motor, secondary motor and primary somatosensory regions project to the **PUTAMEN (MOTOR FUNCTION)**
- Inputs from cortical association regions, frontal eye fields and limbic regions of the cortex project to the **CAUDATE NUCLEUS (**INPUTS INVOLVED IN COGNITION, EYE MOVEMENTS AND EMOTINAL CORRELATES OF MOVEMENTS**)**

BASAL GANGLIA

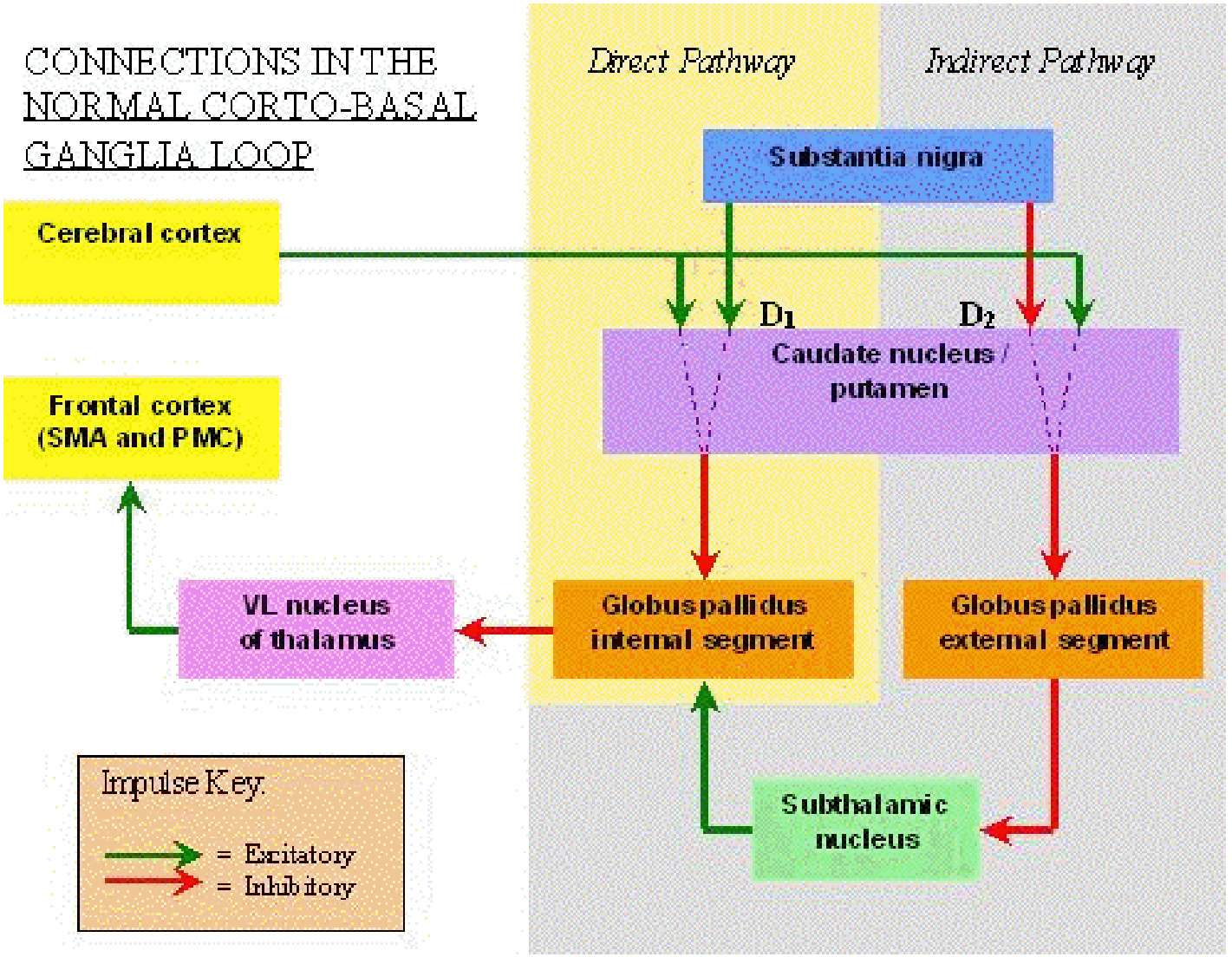


- **Centromedian nucleus** of the thalamus is the source of an indirect cortical input to the striatum (**thalamostriate fibers**)

- PROJECTIONS FROM THE NEOCORTEX AND TAHALAMUS END AS **STRIOSOME** (contains peptides such as substance P, somatostatin, and encephalin;) and they are surrounded by a larger compartment referred as a **MATRIX** (acetylcholinesterase rich)

INTERNAL CONNECTION OF THE BASAL GANGLIA

- 1) connections of the neostriatum with the globus pallidus)
- ✓ THERE ARE TWO PROJECTIONS, ONE TO THE INTERNAL (MEDIAL) PART OF THE GLOBUS PALLIDUS (GABA) AND ONE TO THE EXTERNAL (LATERAL) PART OF THE GLOBUS PALLIDUS (GABA)
- ✓ THERE ARE TWO PATHWAYS, DIRECT AND INDIRECT PATHWAY


CONNECTIONS IN THE NORMAL CORTO-BASAL GANGLIA LOOP
Direct Pathway
Indirect Pathway
Substantia nigra
Cerebral cortex
D1
D2
Caudate nucleus / putamen
Frontal cortex (SMA and PMC)
VL nucleus of thalamus
Globus pallidus internal segment
Globus pallidus external segment
Subthalamic nucleus
Impulse Key
= Excitatory
= Inhibitory

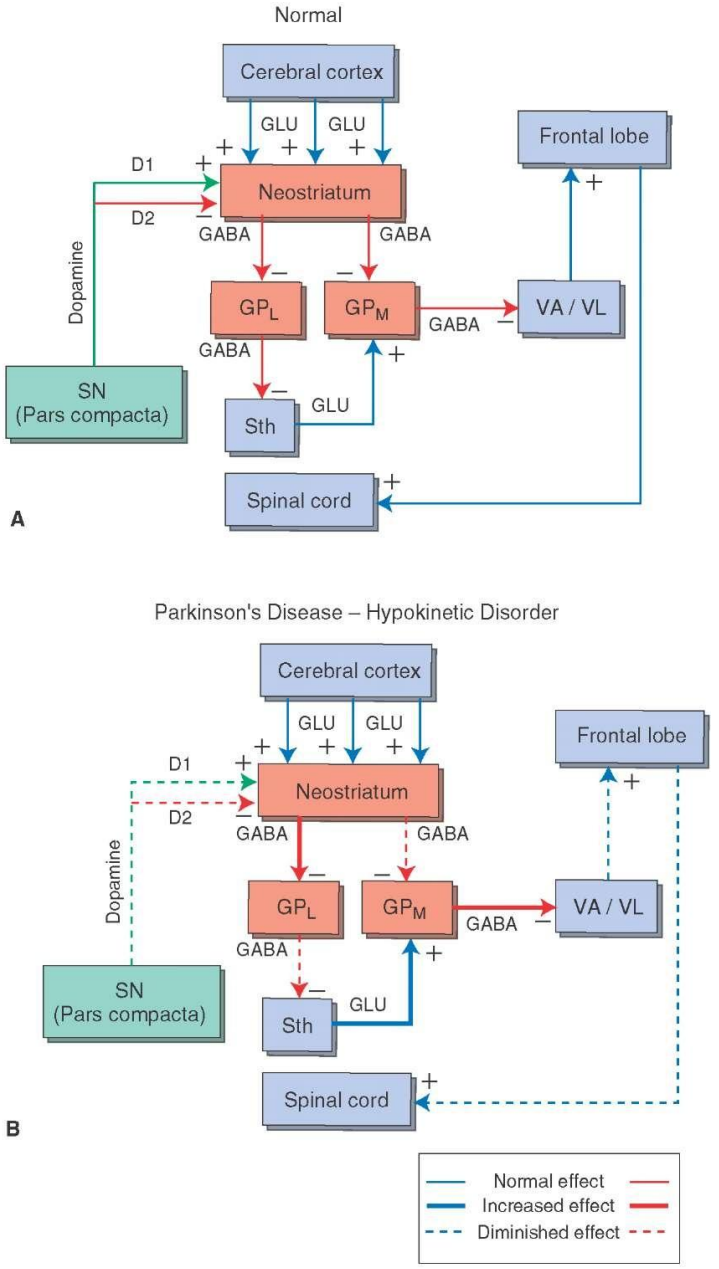
CONNECTIONS OF THE NEOSTRIATUM WITH THE SUBSTANTIA NIGRA

- Neostraitum projects to the **pars reticulate** **(GABA AND SUBSTANCE P)**
- Projections to the neostriatum arises from **pars compacta** **(DOPAMIN)**
- Pars reticulate also projects to the thalamus, superior colliculus and locally to the pars compacta

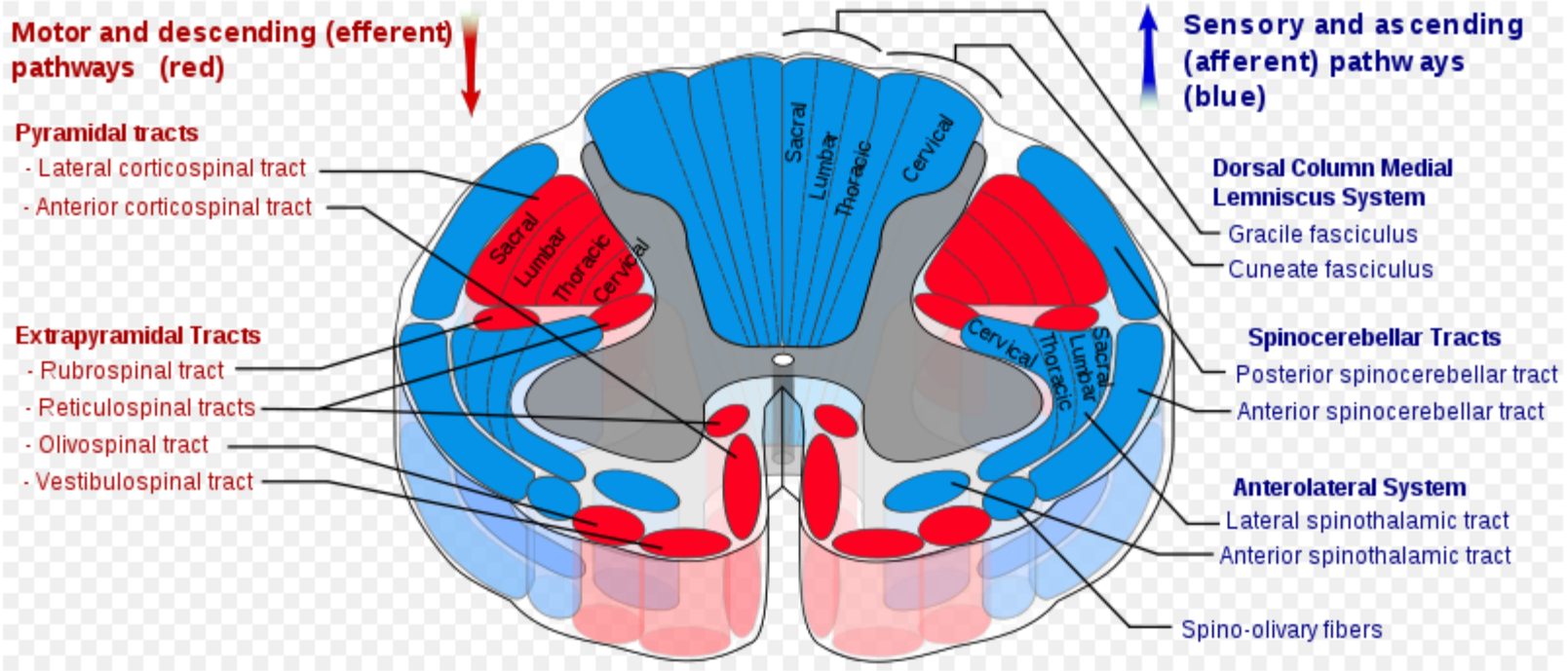
OUTPUT OF THE BASAL GANGLIA

- **FIRST PATHWAY**, *ANSA LENTICULARIS*, arises from the medial pallidal segment, projects to the red nucleus, then turns rostrally to enter the thalamus
- **SECOND PATHWAY**, *LENTICULAR FASCICULUS*, arises from the medial pallidal segment, exits pallidum dorsally, they also enter the thalamus et the end
- **THIRD OUTPUT PATWAY**, *FROM SUBSTANTIA NIGRA*

FUNCTIONAL MECHANISMS OF THE BASAL GANGLIA

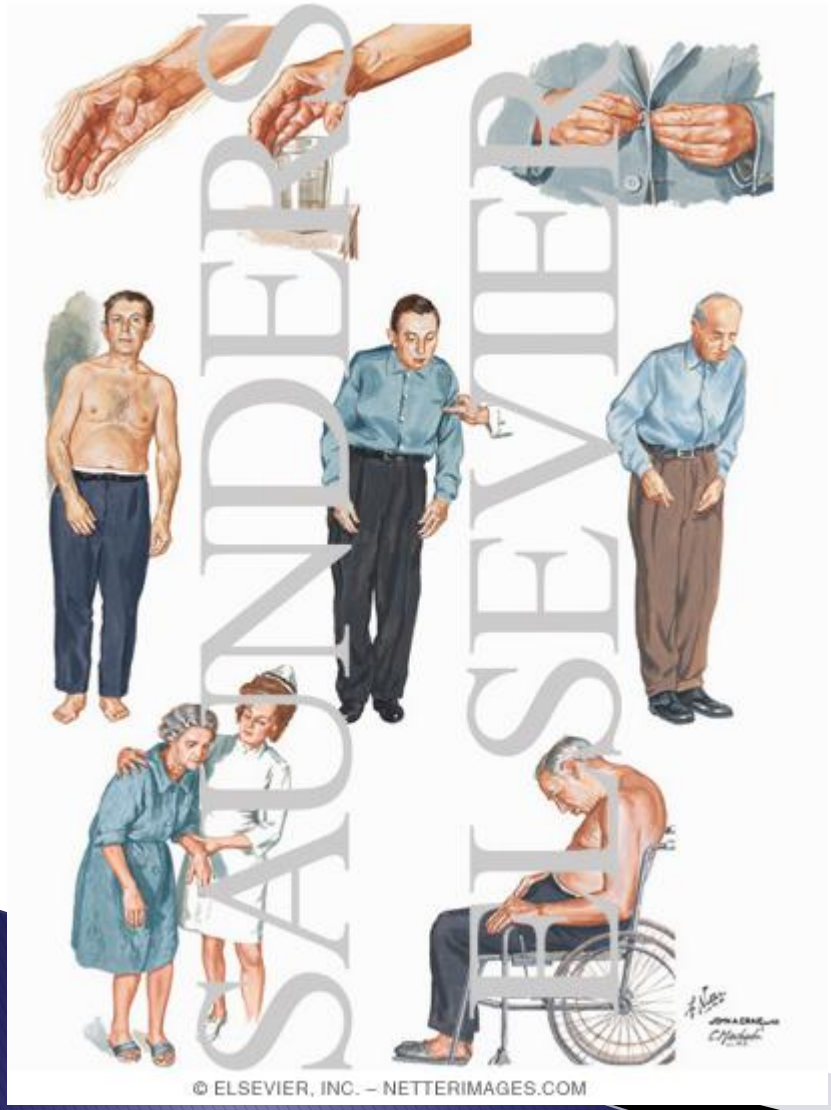


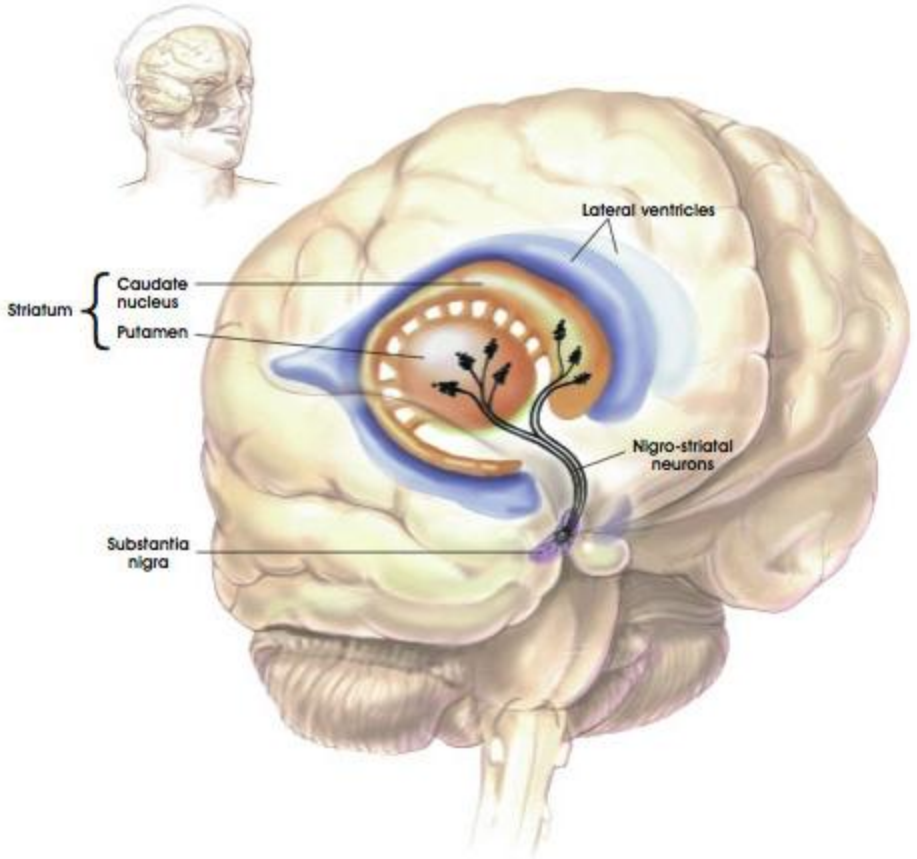
Clinical symptoms of lesions of the basal ganglia



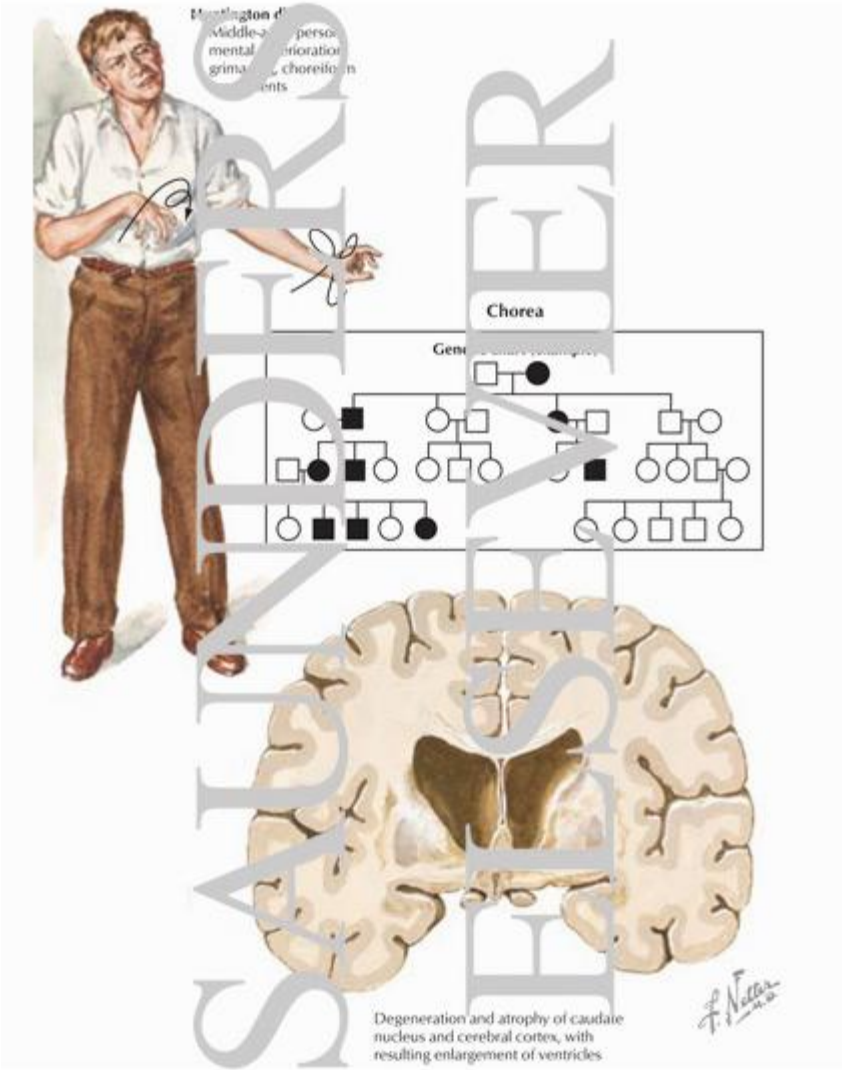
Full resolution (SVG file, nominally 874 × 376 pixels, file size: 140 KB)

Extrapyramidal symptoms could be the consequences of antipsychotic drugs usage





PARKINSON DISEASE



HUNTINGTON DISEASE

The genetics of Huntington's disease

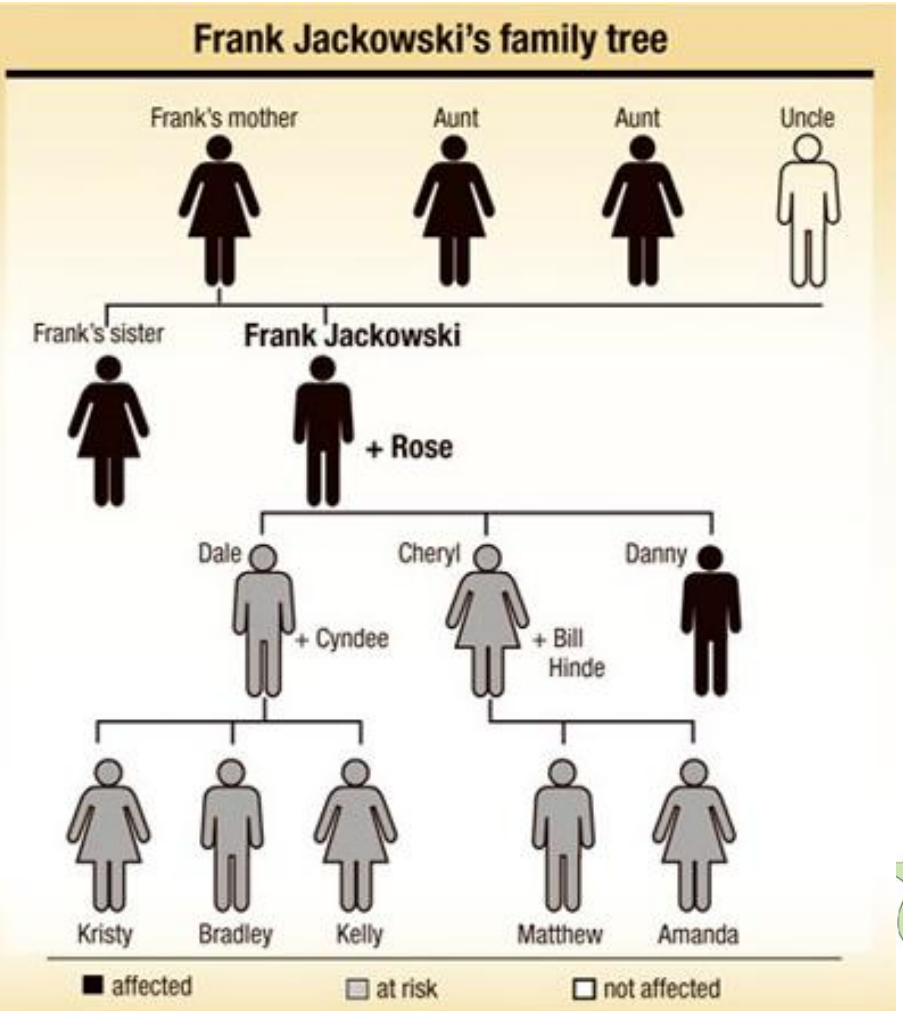
Huntington's disease is a **degenerative neurological condition** that comes from a dominant mutation in a gene on the fourth chromosome.

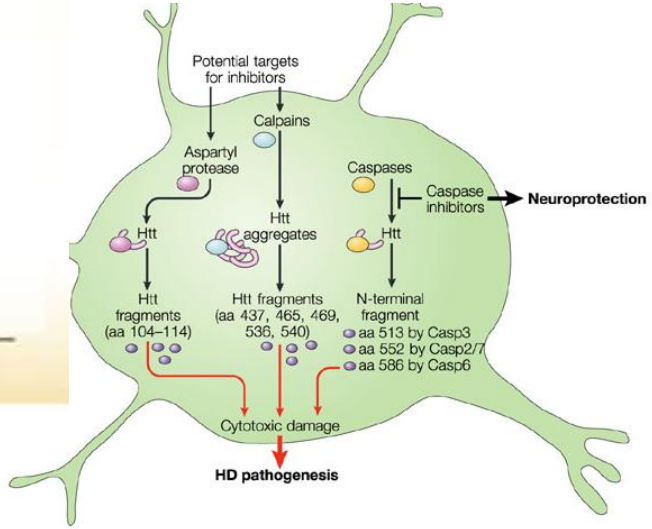
Each person has two copies of the Huntington's gene, one inherited from each parent. A person needs **only one** abnormal copy to develop the disease.

Parents randomly give one of their two copies to each child. A child of a parent who has Huntington's disease has a **50 percent** chance of inheriting the abnormal copy from that parent.

A grandchild of a person with Huntington's disease has a **25 percent** risk if the gene status of the parent is unknown.

Source: Huntington's Outreach Project for Education at Stanford University





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