CEREBELLUM AND CEREBELLAR LESIONS

REQUIRED READING: Blumenfeld, Chapter 15 Cerebellum and Powerpoint with comments

LEARNING OBJECTIVES: after studying this chapter, students should be able to:

1. Explain the overall function of the cerebellum and the role it plays in motor control.
2. Describe the cerebellar anatomy: surfaces, fissures, and lobes.
3. Explain the histological organization of the cerebellar cortex and name the cells found in each layer.
4. Describe the functional cerebellar regions.
5. Indicate the origin and name of the afferent pathways providing inputs to the cerebellum.
6. Explain the cerebellar processing.
7. Indicate the important efferent or output fibers passing through each of the cerebellar peduncles and their function.
8. Describe the deficits associated with damage to the cerebellum or the cerebellar peduncles.
9. Name the blood vessels that supply the cerebellum and explain the deficits that result from their occlusion.
10. Briefly explain other acute/chronic cerebellar disorders

OVERVIEW

We will focus here on the functional organization and significance of the cerebellum: the functional divisions, the cerebellar pathways and some of the deficits associated with their damage.

Refer to the Blumenfeld textbook for the above indicated learning objectives.

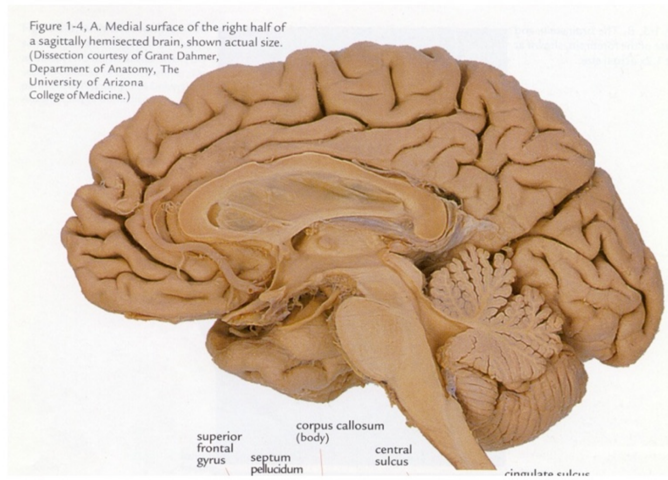
Comments on the Power Point presentation

Slides 3, 4 – Describes the functions of the cerebellum

OBJ. # 1

Cerebellar Functions

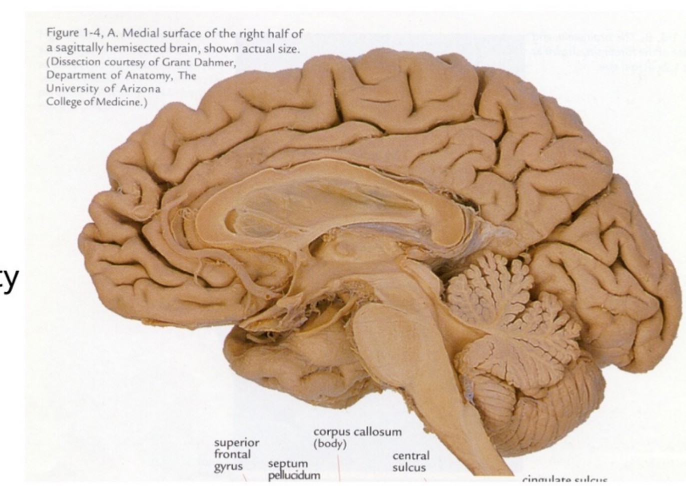
- Control of ongoing movement
  - Contribute to motor planning
  - Detecting motor error
  - Correct the error during movement
  - Stores the correction as memory
- Controls posture and gait
- Helps to regulate muscle tone



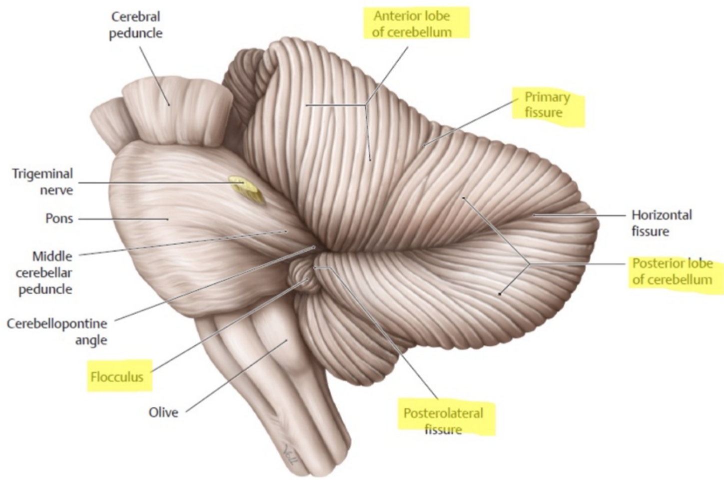
OBJ. # 1

Cerebellar Functions

- Monitor and modulate motor activity originating in other structures.
- Ex: At the end of a movement, automatic excitation of antagonist muscles and inhibition of agonist muscles – allows limbs to arrive at a precise location in space.



Slides 5 - 8: Introductory review of the cerebellar anatomy – for a good and concise cerebellar anatomy review- See chapter 15 in Blumenfeld

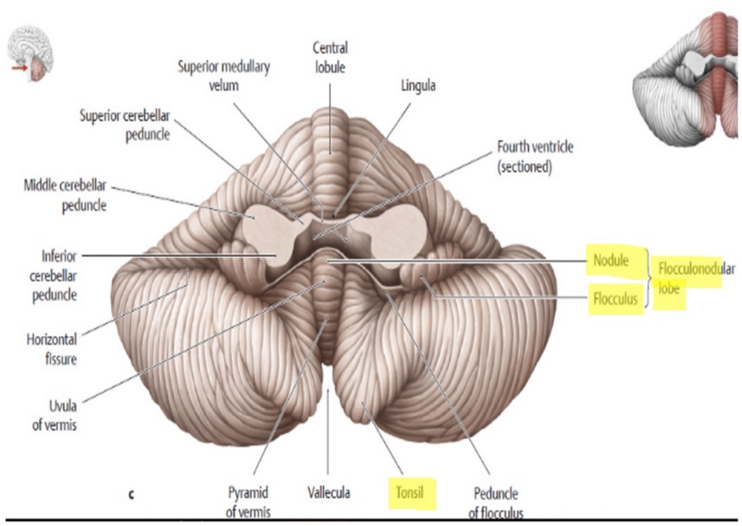


Cerebellar Anatomy

- **3 lobes**: **anterior**, **posterior** and **flocculonodular**
- **2 fissures**: **primary** and **posterolateral**
- **3 surfaces**: **superior**, **inferior**, and **ventral**

★ There is a horizontal fissure, however it has no clear functional or clinical significance

OBJ. # 2



Cerebellar Anatomy

- **3 lobes**: **anterior**, **posterior** and **flocculonodular**
- **2 fissures**: **primary** and **posterolateral**
- **3 surfaces**: **superior**, **inferior**, and **ventral**

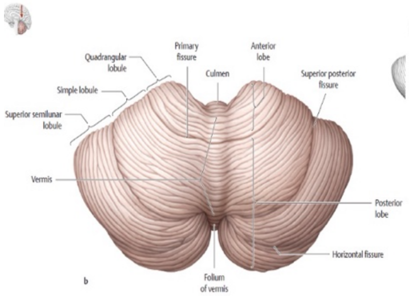
★ There is a horizontal fissure, however it has no clear functional or clinical significance

OBJ. # 2

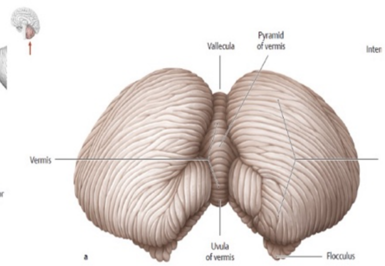
Cerebellar Anatomy

OBJ. # 2

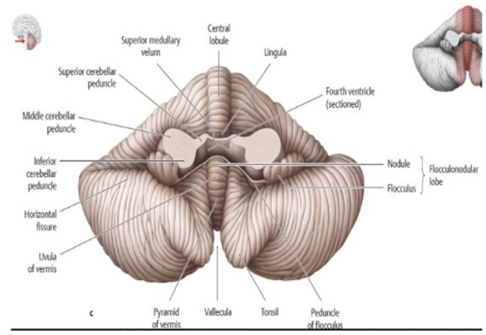
Superior surface



Inferior surface

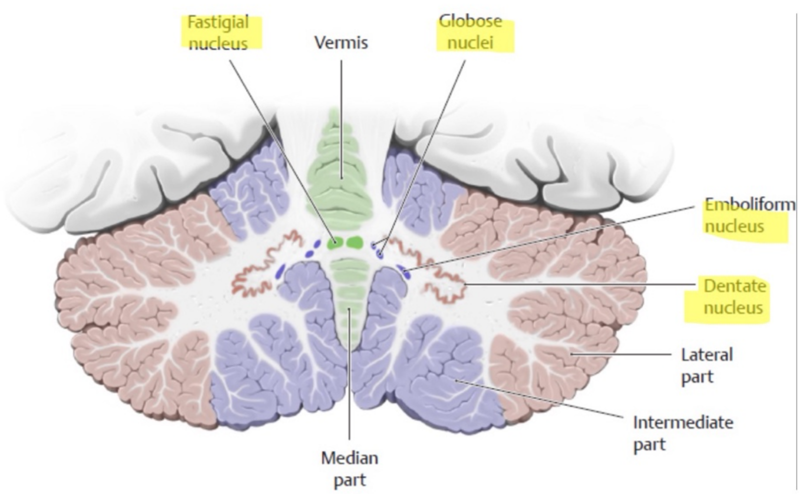


Ventral surface



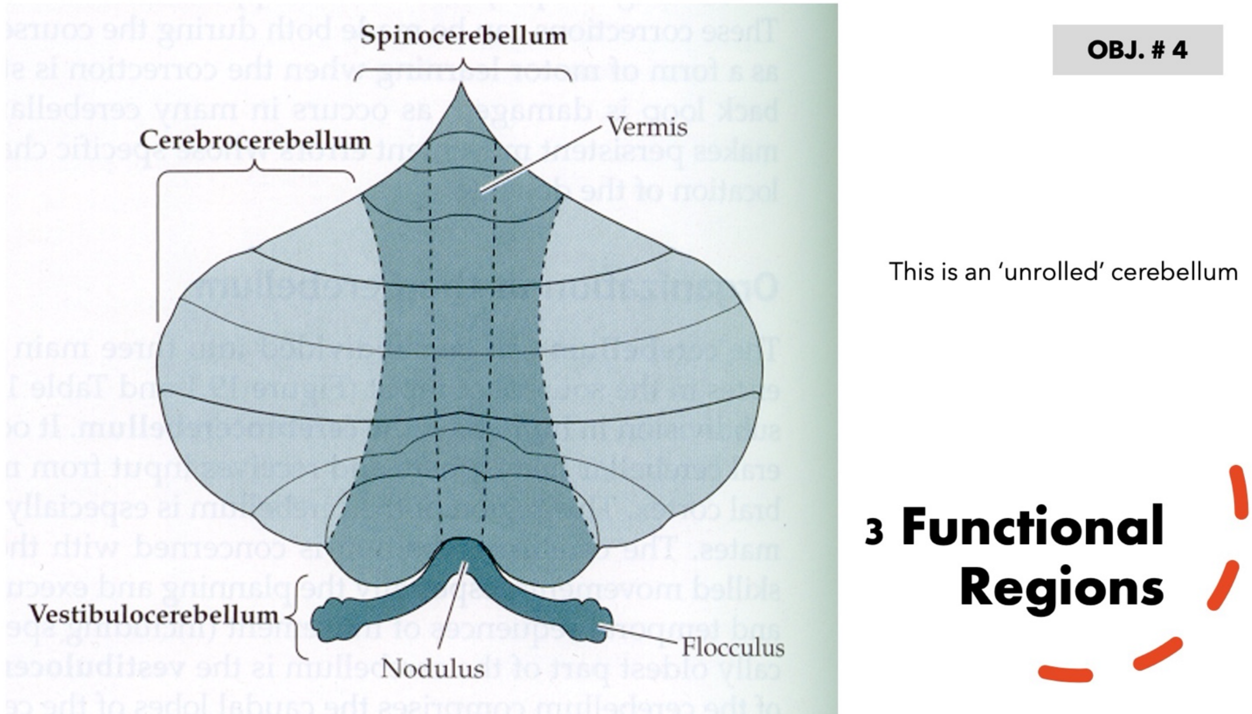
Cerebellar Anatomy

OBJ. # 2



- 4 deep cerebellar nuclei: **dentate, emboliform, globose,** and **fastigeal**.
- **The 4 vestibular nuclei are considered part of the deep cerebellar nuclei because they project directly to the cerebellum**

Slide 9 – A schematic view of the cerebellum in an ‘unrolled’ view. Imagine this image rolled along the horizontal axis such that the flocculus and nodulus are tucked into the center of the role.

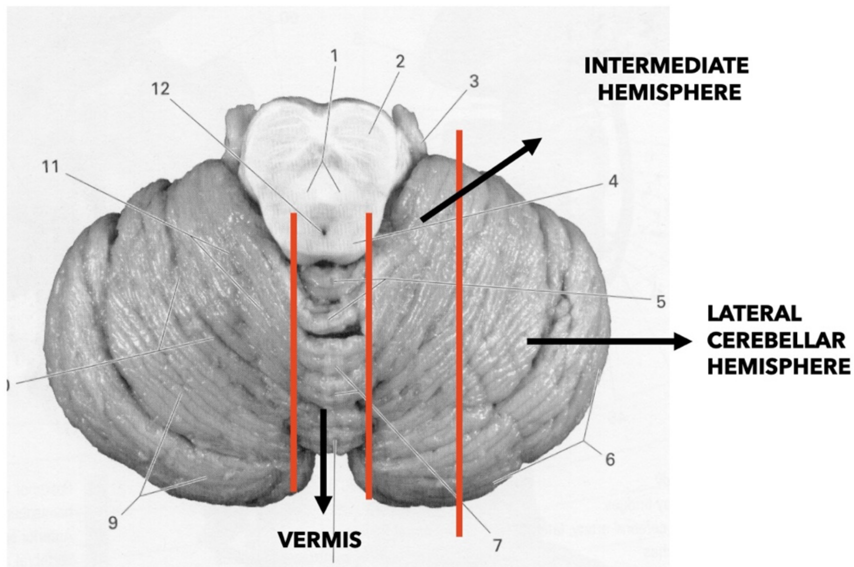


Slide 10 - 12 - These slides show the division of the cerebellum into functional areas:

- Spinocerebellum = the superior vermis and paravermal area;
- Cerebrocerebellum or Pontocerebellum = the lateral cerebellar hemisphere;
- Vestibulocerebellum = the flocculo-nodular lobe and the inferior vermis.

3 Functional Regions

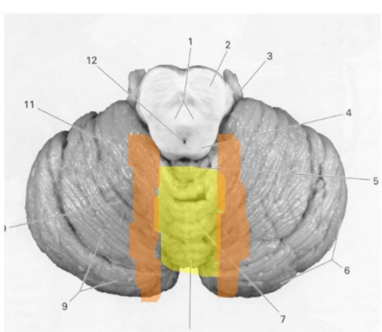
OBJ. # 4



OBJ. # 4

Cerebellar Functional Areas

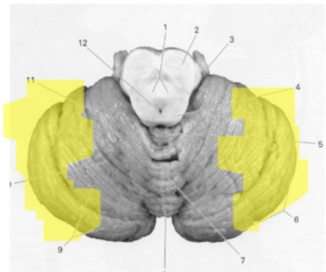
Spinocerebellum – developmentally older structure:

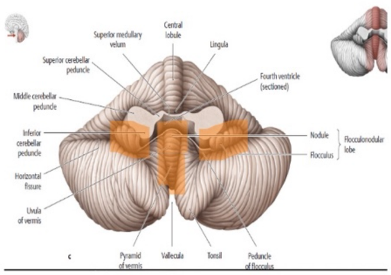


Superior Vermis → **Posture and axial muscle coordination/ Balance, gait and muscle tone**

Intermediate Hemispheres → **Motor coordination of limb movements**

OBJ. # 4





Cerebellar Functional Areas

Cerebrocerebellum

Lateral Cerebellar Hemispheres → **Motor planning + motor learning**

Vestibulocerebellum

Flocculonodular Lobe + Inferior Vermis → **Vestibulo-ocular Coordination and balance**

The main function of the cerebellum is to make corrections to the ongoing movement. To do that, the cerebellum needs to receive information from the cortex (descending motor pathways) regarding the movement to be performed next, and what is the motor plan for its execution. Then, the cerebellum needs to receive information from the spinal cord to verify that the movement is being performed as planned. If this is not the case, the cerebellum will attempt to correct the movement, and the correction will be stored as memory. Because the cerebellar outputs don’t directly reach the spinal cord or the cortex, the correction occurs through communications with the different descending pathways that terminate in the spinal cord

Slide 13 - This slide shows the 3 layers of the cerebellar cortex. The cerebellar cortex is composed of 3 layers, from outer to inner: molecular layer, Purkinje cell layer, and granule layer.

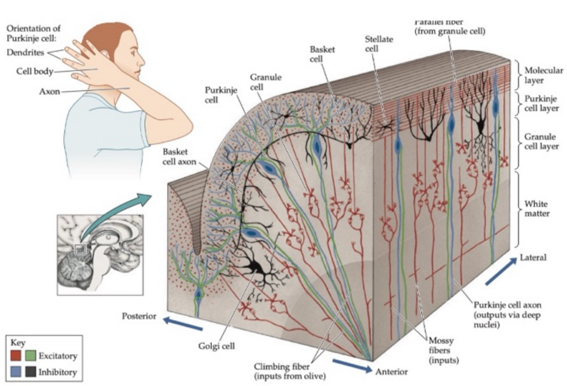
• The molecular layer contains mostly fibers and only 2 types of inhibitory interneurons: the stellate and basket cells. The fibers present here are the dendrites of the main cell in the cerebellar cortex: the Purkinje cells. Other fibers parallel to the surface of the cortex are the axons of granule cells, which cell bodies are in the granule cell layer.

• The Purkinje cell layer contains the cell bodies of the Purkinje cells, which dendrites extend as a tree from the cell body into the molecular layer. The Purkinje cell axons exit the cortex and enter the white matter to terminate synapsing with neurons in the deep cerebellar nuclei.

• The granular layer consists of 2 types of neurons: the inhibitory Golgi type 2 and the very abundant excitatory granule cells. These cells receive inputs from the inferior cerebellar peduncle that ended synapsing in specialized structures named glomeruli form by the granule cell dendrites and Golgi cell axons. The Golgi type 2 cell dendrites project to the molecular layer. The axons of the granule cells, the so-called parallel fibers, in the molecular layer form excitatory synapses with Purkinje cell dendrites. Each Purkinje cell is influenced by as many as a million granule cells and the inhibitory inputs from basket and stellate interneurons to produce a single electrical impulse, which is inhibitory.

OBJ. # 6

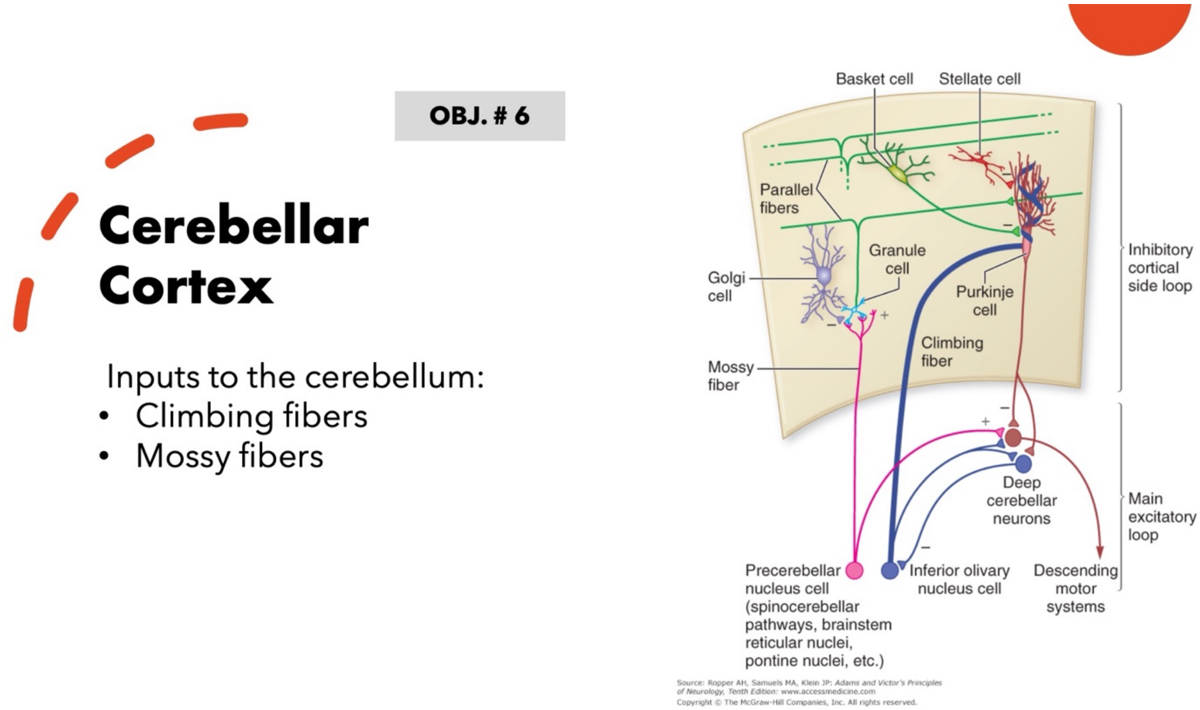
Cerebellar Cortex Cellular Organization



3 Layers from outer to inner:

- Molecular
    - Mostly contains granule cell axons
    - Dendrites of purkinje cells
    - Some interneurons
- Purkinje cell
    - Contains the purkinje cells!
    - Second largest cells in the CNS
    - Only axons to leave the cerebellar cortex
    - Purkinje cells use GABA as neurotransmitter -> all output from cerebellar cortex is inhibitor
- Granule cell
    - Densely populated with granule cells and other interneurons, nearly as many cells as the rest of the nervous system
    - Only excitatory neuron in cerebellum (glutamate)

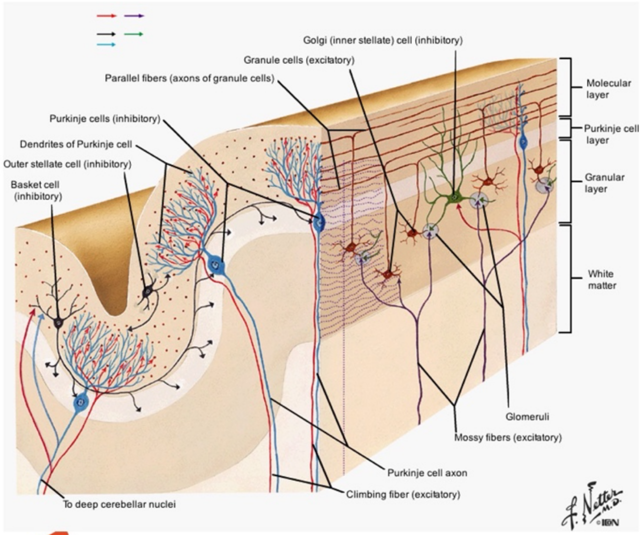
Slide 14, 15: Input fibers reaching the cerebellar cortex are of 2 different types: climbing and mossy fibers depending on their behavior as they enter the cerebellar cortex. As all of these fibers enter the cerebellum, they bifurcate to send one direct branch to the deep cerebellar nuclei while the other branch terminates in the cerebellar cortex. All inputs are excitatory.



The fibers known as **climbing** fibers only come to the cerebellum from the inferior olivary nucleus and terminate wrapping around the dendrites of Purkinje cells in the molecular layer, as indicated in the diagram. This is the reason why they are called climbing! **Mossy** fibers make up most of the other inputs; as they enter the cerebellar cortex, they make synapses with the granule and Golgi type II cells at the synaptic glomeruli in the granule cell layer. Granule cells axons project to the molecular layer to synapse with Purkinje cell dendrites. In the molecular layer these axons divide into 2 branches, each traveling parallel to the cerebellar surface. They are named parallel fibers and they contact Purkinje cells in their way. Stellate and basket cells also project to the dendrites of the Purkinje cells. Purkinje cells integrate all the information available to produce a cortical output which is sent to the deep cerebellar nuclei. This cortical output is inhibitory and is transmitted by the axons of the Purkinje cells.

Cerebellar Afferents:

OBJ. # 6



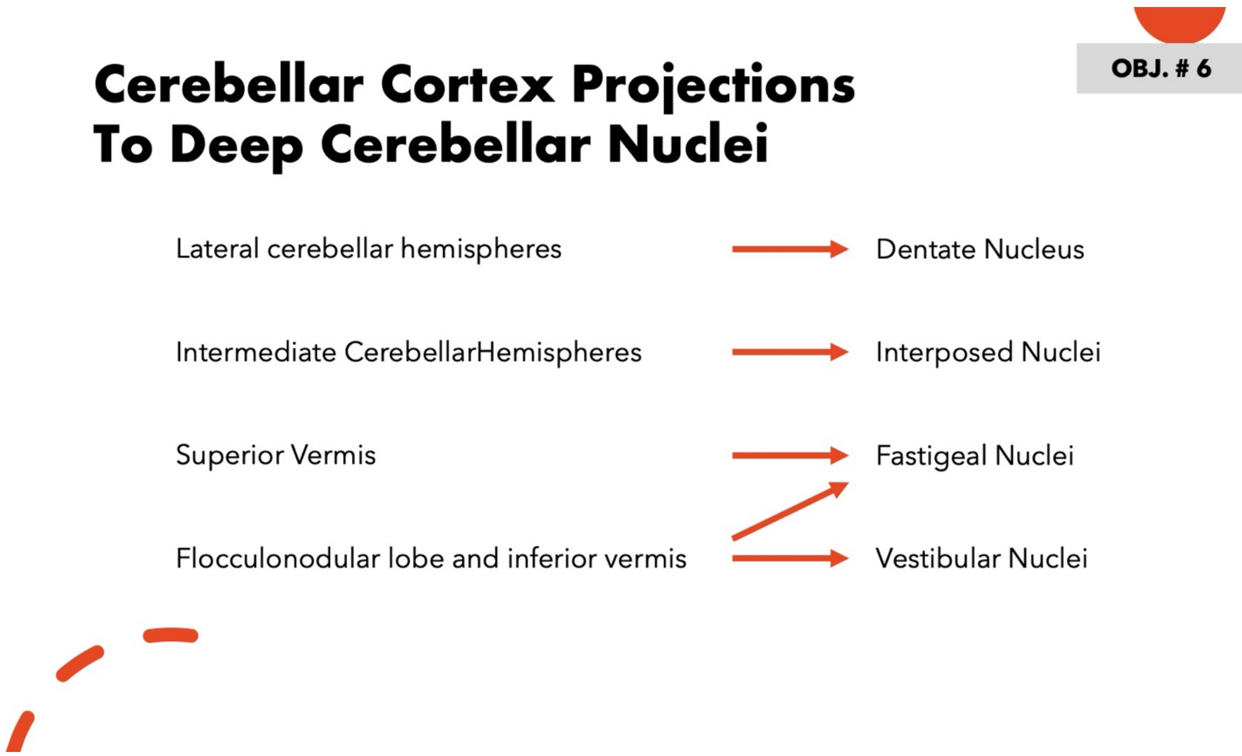
Mossy fibers:

- Enter via ICP and MCP
- Coming from pontocerebellar, spinocerebellar, and vestibulocerebellar tracts
- Form excitatory (glutamate) synapses on granule cells

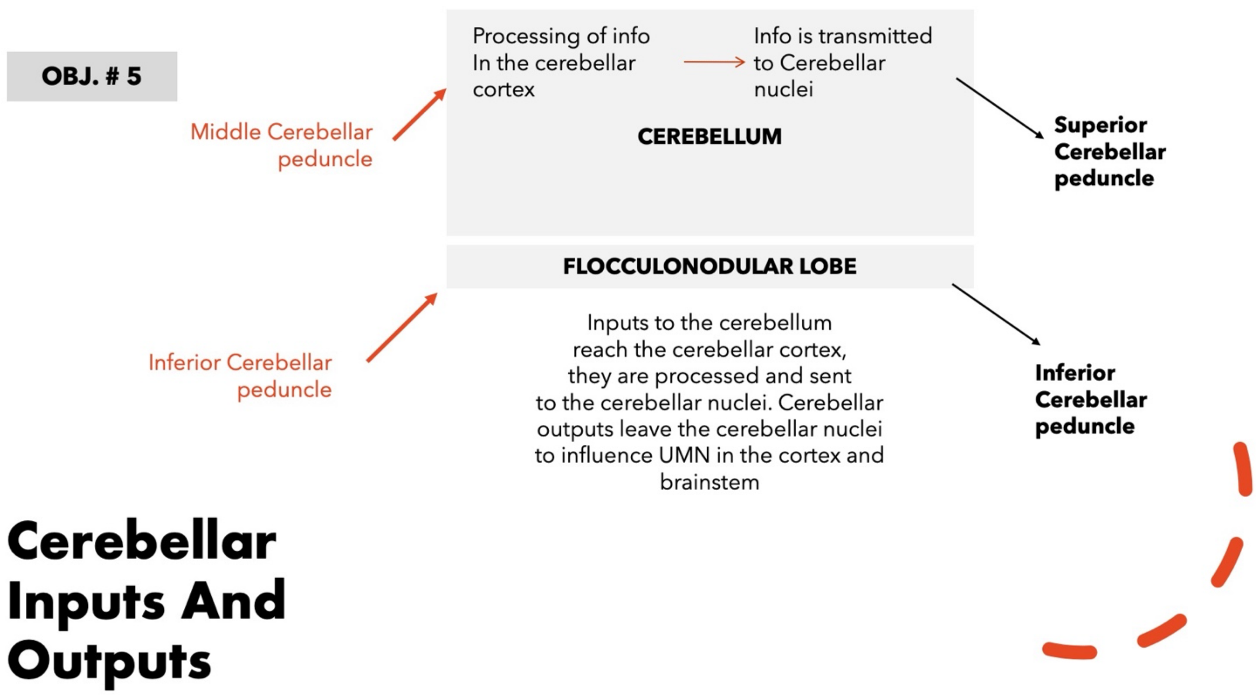
Climbing fibers:

- Enter via ICP
- Projected from olivary nuclei (olivocerebellar tracts)
- Excitatory input directly on purkinje cells
- Important for motor learning

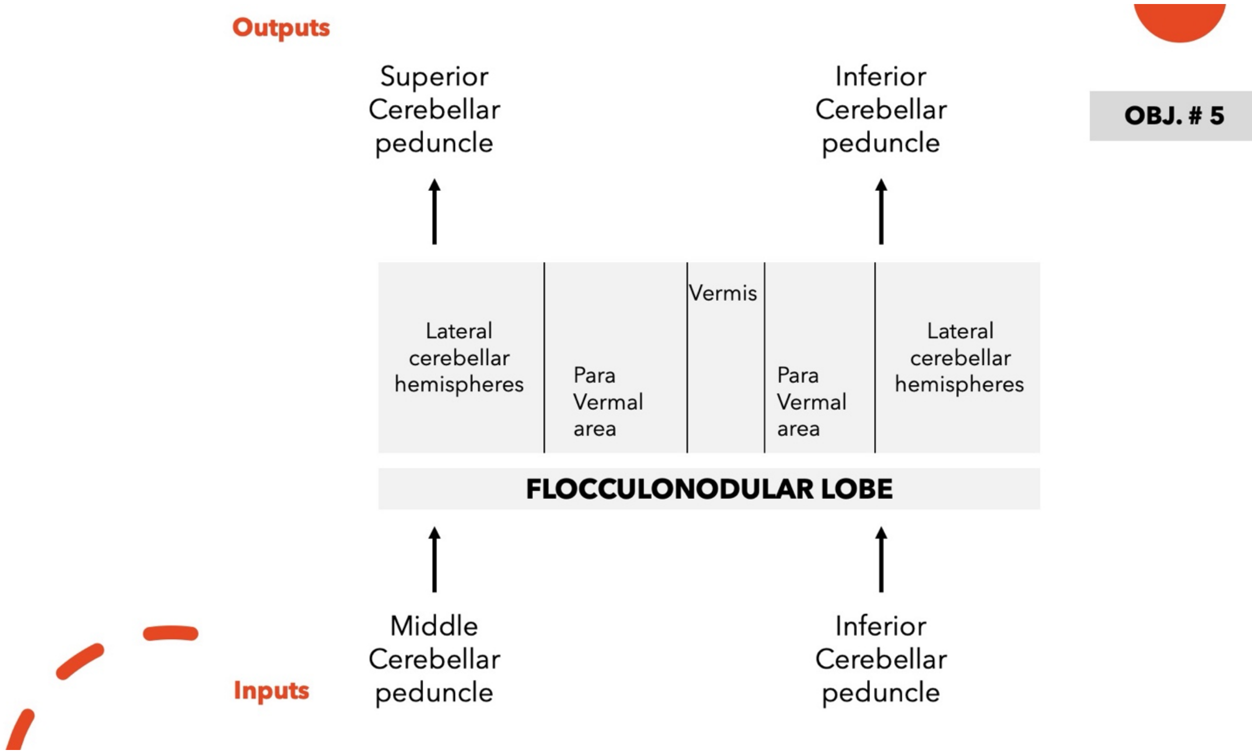
Slide 16 – The Purkinje cells of the different cortical cerebellar areas project to each one of the 3 deep cerebellar nuclei. Remember that it is the job of the deep cerebellar nuclei to create the final output pathways that leave the cerebellum to influence motor movement. Here we see how the more lateral cortical areas project to the more lateral deep cerebellar nuclei and the more medial areas project to the more medial nuclei.



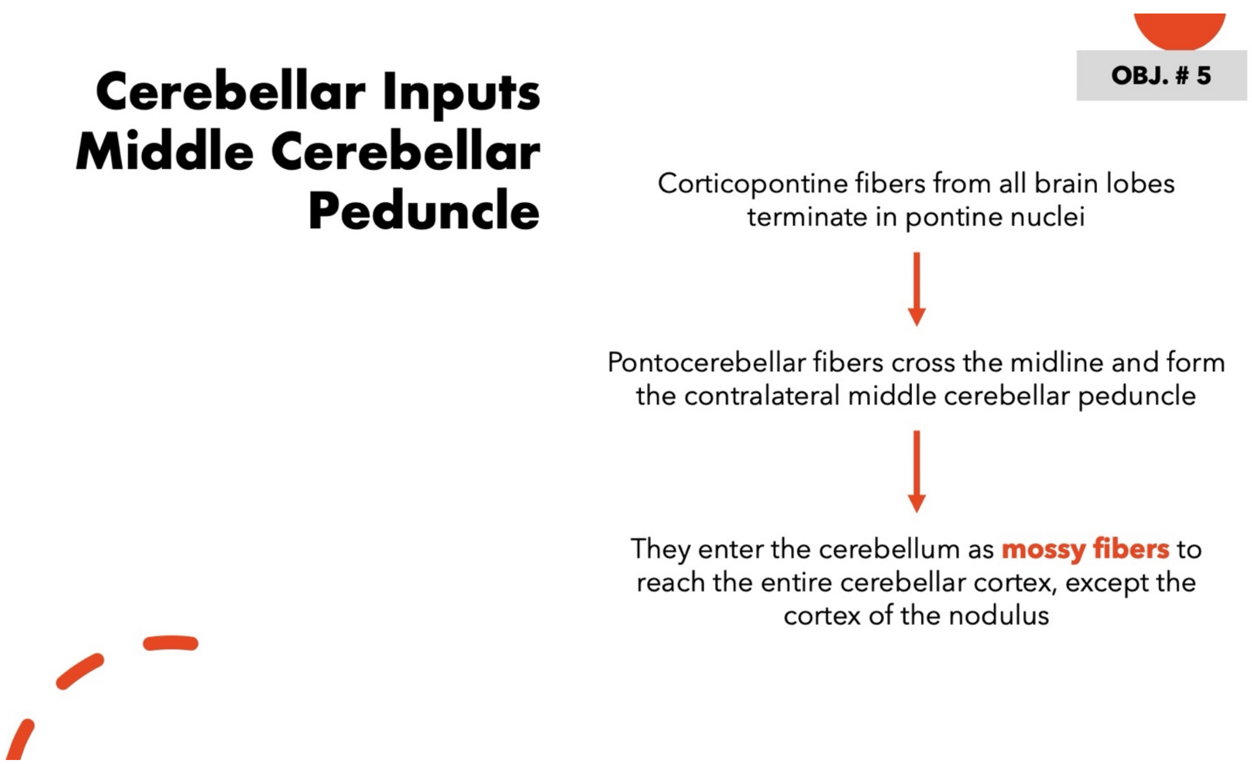
Slide 18 is a diagram showing the cerebellar processing of information. Input fibers transmitting information from different CNS locations come to the cerebellum and reach the cerebellarcortex. The information is processed in the cerebellar cortex to generate a cerebellar output. This output is sent to the deep cerebellar nuclei where it is combined with inputs to the deep nuclei to produce a final cerebellar output that is excitatory. This excitatory output leaves the cerebellum through the superior and inferior cerebellar peduncles.



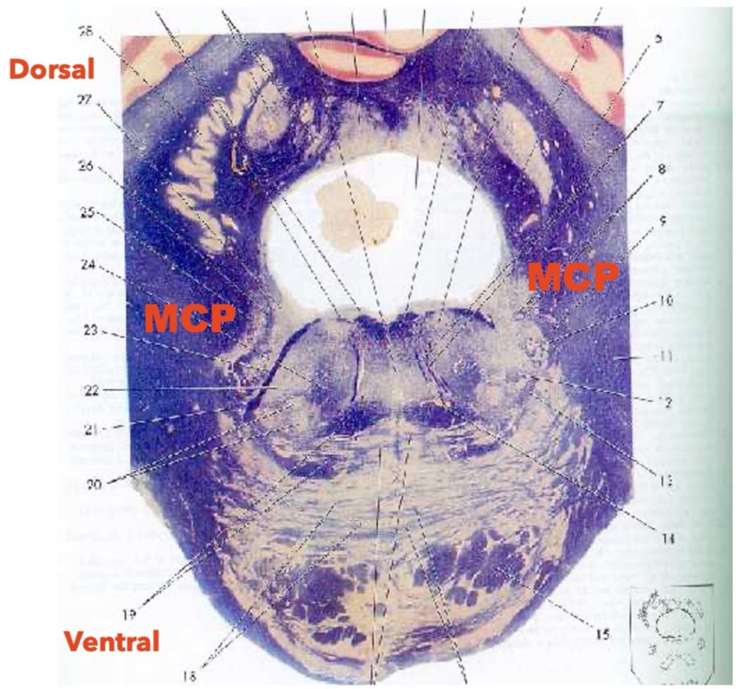
Slide 19 - Schematic of the cerebellum showing functional divisions, indicating the main cerebellar peduncles carrying inputs and outputs.



Slide 20 - Shows the input pathways to the cerebellum through the middle cerebellar peduncle. This pathway brings information from the cortex about a planned movement.



Slide 21 - Section though the caudal pons showing the massive middle cerebellar peduncle (MCP).



OBJ. # 5

Slide 22 - Inputs to the cerebellum also come through the inferior cerebellar peduncle (ICP). This slide refers to the 3 spinocerebellar tracts bringing to the cerebellum unconscious proprioceptive information from the spinal cord. These pathways tell the cerebellum how the planned movement is being performed. Notice that one of these pathways: the ventral spinocerebellar tract enters the cerebellum with the superior cerebellar peduncle not with the inferior cerebellar peduncle. These pathways represent the unconscious proprioception and convey the same information from the body that is transmitted to the cortex with the DCML pathway.

Cerebellar Inputs
Inferior Cerebellar Peduncle

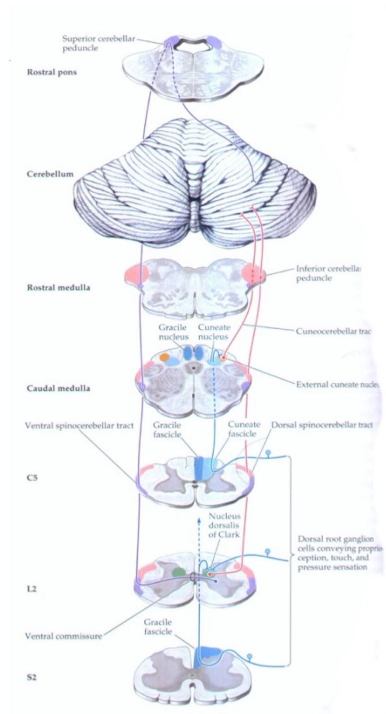
OBJ. # 5

- **Spinocerebellar fibers** travel in several tracts.
  - Dorsal spinocerebellar tract
  - Ventral spinocerebellar tract
  - Cuneocerebellar tract
  - Rostral spinocerebellar (we don't know much about this pathway)
- They convey sensory information about limb proprioception from all levels of the spinal cord. The fibers terminate mostly in the paravermal area and superior vermis as mossy fibers

Slide 23 – Diagram taken from Blumenfeld showing the pathways of the 3 major spinocerebellar tracts.

OBJ. # 5

Spinocerebellar Fibers



Slide 24 - The olivocerebellar tracts also reach the cerebellum through the ICP. These fibers are coming from the contralateral olivary nucleus in the medulla.

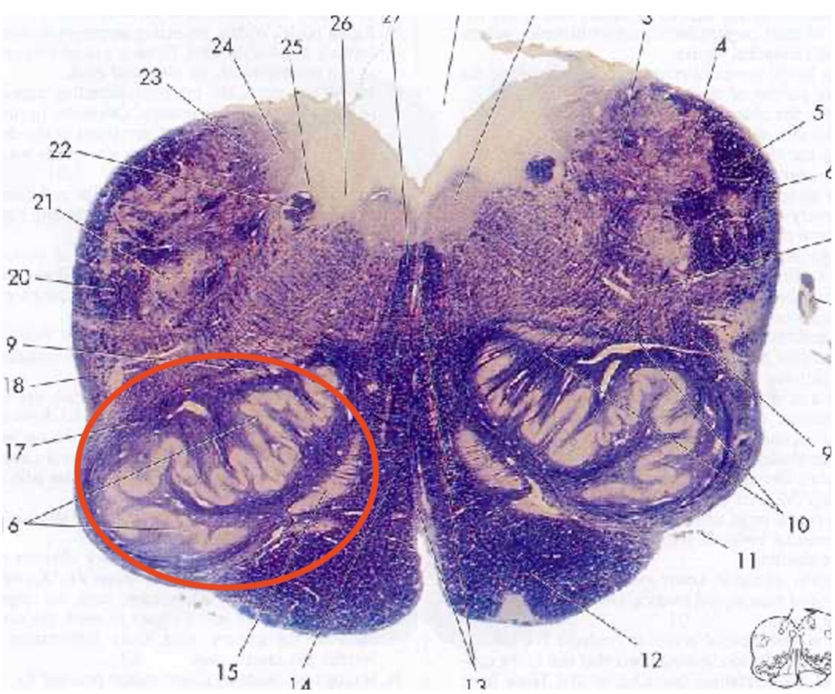
Cerebellar Inputs
Inferior Cerebellar Peduncle

OBJ. # 5

Spinocerebellar fibers travel in several tracts. They convey sensory information about limb movement from all levels of the spinal cord. The fibers terminate mostly in the intermediate zone and superior vermis as mossy fibers

Olivocerebellar fibers cross the midline to enter the contralateral cerebellum as **climbing fibers** to terminate in the entire cerebellar cortex

Slide 25 shows a section through the mid-medulla showing the inferior olivary nucleus from where the olivocerebellar fibers originate. These fibers cross the medulla and enter the contralateral ICP



OBJ. # 5

Inferior Olivary Nucleus

Slide 26 - Other important input through the ICP is the primary and secondary vestibular fibers, described in this slide. These fibers come to the cerebellum from the 4 vestibular nuclei located in the upper medulla and caudal pons.

Cerebellar Inputs
Inferior Cerebellar Peduncle

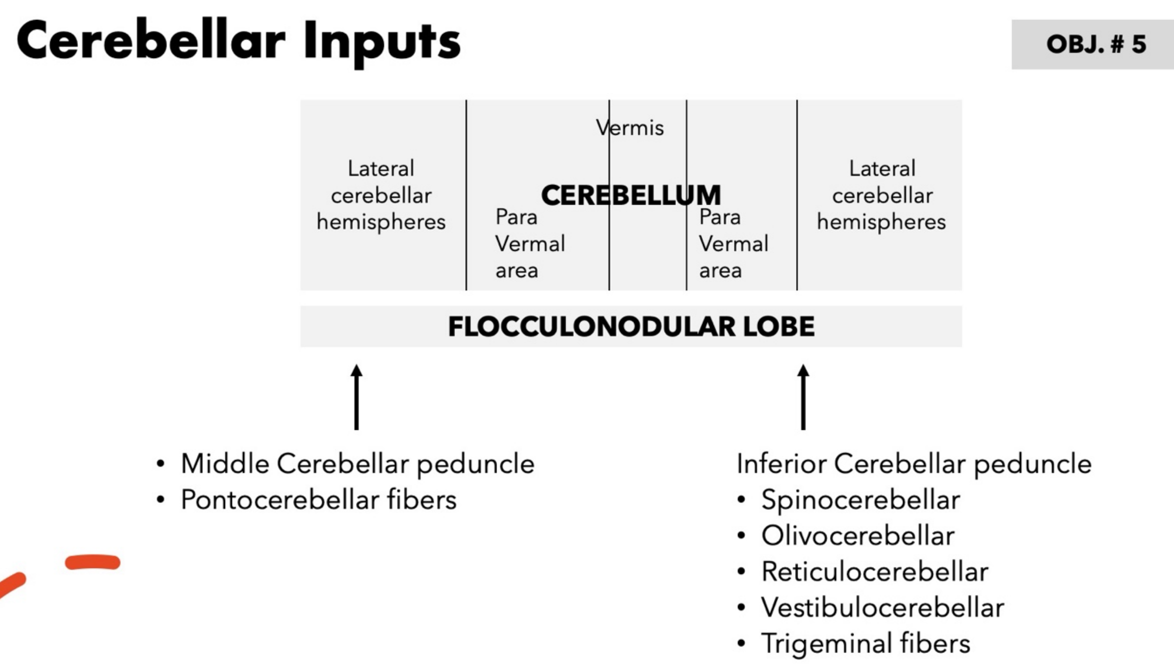
OBJ. # 5

Spinocerebellar fibers travel in several tracts. They convey sensory information about limb movement from all levels of the spinal cord. The fibers terminate mostly in the intermediate zone and superior vermis as mossy fibers

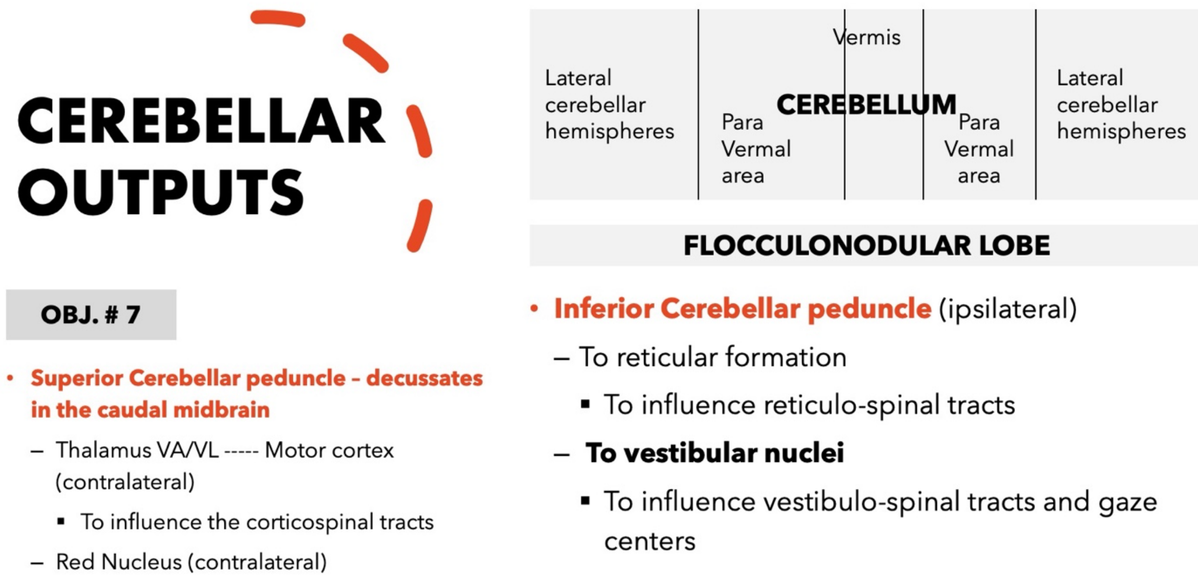
Olivocerebellar fibers cross the midline to enter the contralateral cerebellum as climbing fibers to terminate in the entire cerebellar cortex

Primary and secondary vestibular fibers project via the juxtarestiform body, a subtract of the inferior cerebellar peduncle, as **mossy fibers** to terminate in the flocculonodular lobe and inferior vermis

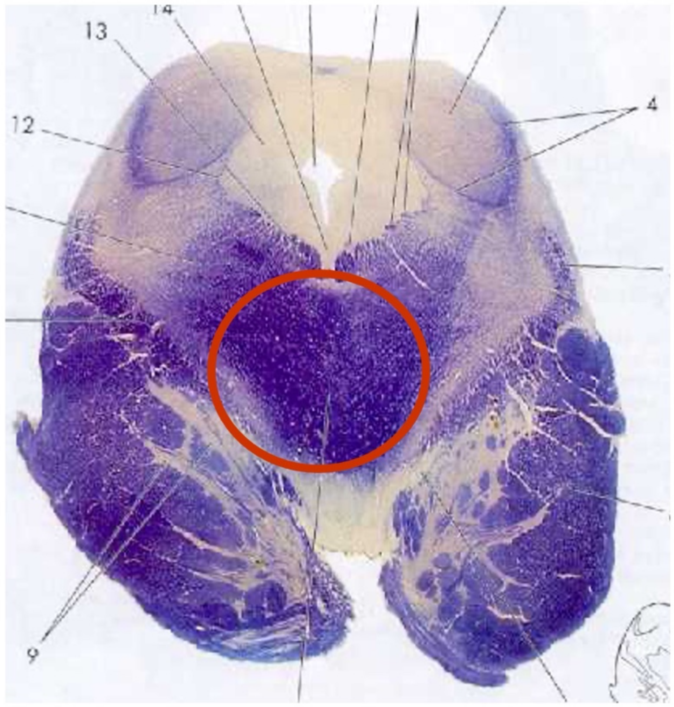
Slide 27 – Diagram summarizing the main inputs to the cerebellum through the middle and inferior cerebellar peduncles



Slide 28 – Now we move to the cerebellar outputs. Most cerebellar output fibers exit through the superior cerebellar peduncle (SCP), however, a small but very important set of fibers, mostly projecting to the vestibular nuclei, do so through the ICP. Some fibers in the ICP also terminate in the reticular formation of the medulla. The SCP fibers influence movement indirectly; **the cerebellar pathways do not project directly to either the motor cortex or the spinal cord.** Cerebellar pathways influence brainstem nuclei that in turn project to the spinal cord such as the medial and lateral vestibulospinal tracts. Fibers exiting through the SCP decussate in the caudal midbrain to terminate in different nuclei contralaterally, indirectly influencing motor control.



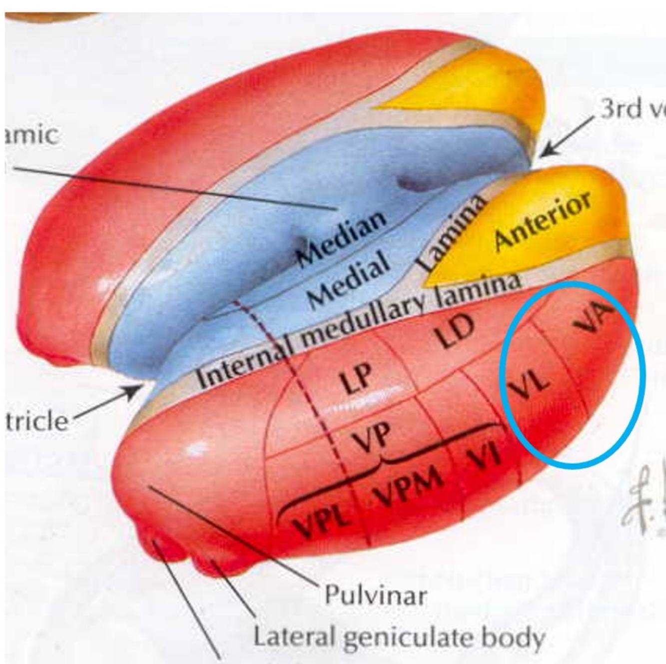
Slide 29 - Section through the caudal midbrain showing the decussation of SCP fibers.



Superior Cerebellar Peduncles decussation

OBJ. # 7

Slide 30 - A diagram of the thalamus showing the motor nuclei: Ventro Lateral and Ventro Anterior where cerebellar fibers terminate. The thalamus will send this information to the motor cortex to influence coordination of movement.



OBJ. # 7

Thalamus

Slide 33 - Ataxia refers to the inability to perform coordinated smooth movements in the absence of paresis, loss of proprioception or movement disorders. However many times these symptoms present together with ataxia.

Cerebellar Lesions

Lack of motor coordination due to cerebellar damage is called ATAXIA

OBJ. # 8

ATAXIA = Inability to perform smooth, coordinated movements that result in irregularity and fragmentation of the normal motor sequence

Lesions to the cerebellum or cerebellar pathways produce different type of abnormalities:

- Incoordination or ataxia
- Intention tremor
- Disorders of equilibrium and gait
- Decreased muscle tone
- Scanning dysarthria
- Stability of eye movements is affected – nystagmus
- Frequently nausea and vomiting are present

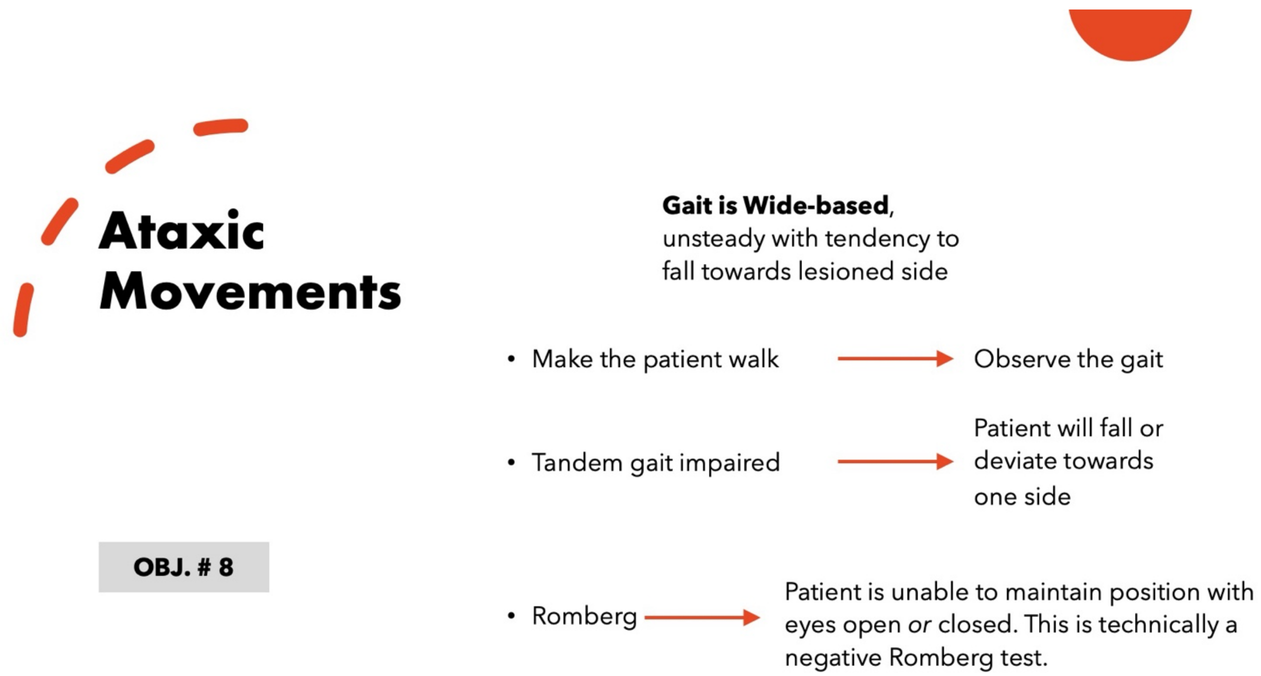
ATAXIC MOVEMENTS (Slides 34, 35)

Ataxic movements include:

- An abnormal trajectory with fragmentation of the movement that has an irregular, wavering path with overshooting and overcorrecting the direction of the movement. This is frequently referred to as **dysmetria, or past pointing** when testing a target-oriented movement. - An abnormal rhythm and timing of movement known as **dysrhythmia.** - Coordination disorders that can also manifest as abnormalities of rapid alternating movements. This is referred to as **dysdiadochokinesia or adiadochokinesia.** - Certain large amplitude **postural tremors** can occur due to cerebellar lesions.

Tests for appendicular ataxia

- Finger-nose-finger test or heel-shin test. Both tests are for dysmetria. - Precision finger tapping or tapping the foot on the floor. Both tests are for dysrhytmia. - Alternating movements such as tapping one hand with palm and dorsum of the other hand. This test for dys- or adiadochokinesia.



Ataxic Movements

Appendicular ataxia

OBJ. # 8

Dysmetria / past pointing
- Finger-nose-finger test
- Heel-shin test

→ Wavering movement with over- or undershooting

Dysrhythmia
- Precision finger tapping
- Tapping on the floor

→ Abnormal timing of movement

Dysdiadochokinesia / Adiadochokinesia

→ Abnormal coordination of Rapid alternating movements

Slide 36 – Cerebellar tremors:

The classic type of tremor associated with the cerebellum is the 'intention' tremor. It is named for the fact that this tremor is most pronounced as one approaches a target. This is an action tremor, which means that it is present with movement and not at rest. You will observe intention tremors when performing the finger-to-nose test with your patients.

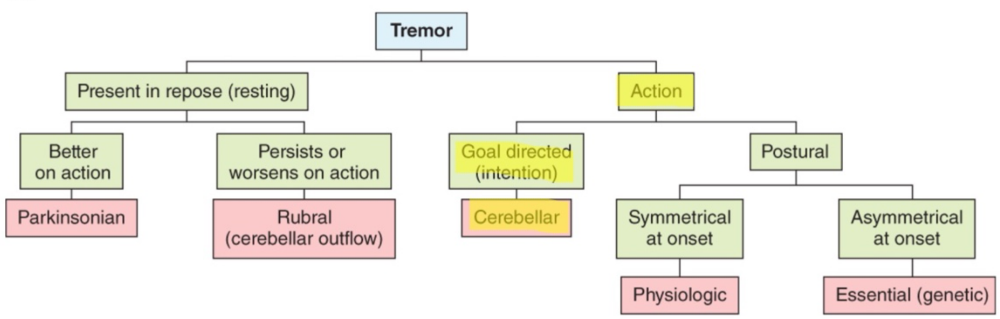
Another type of cerebellar tremor is known as a rubral or cerebellar outflow tremor. This is a coarse tremor which occurs both with action and at rest (mixed.) It is associated with lesions of the superior cerebellar peduncle, midbrain, and posterior thalamus. Despite it's name, the red nucleus need not be involved in the development of this tremor.

Differential Diagnosis of Tremor

OBJ. # 9

There are basically 2 types of tremors:

- Action tremor
- Repose (resting) tremor



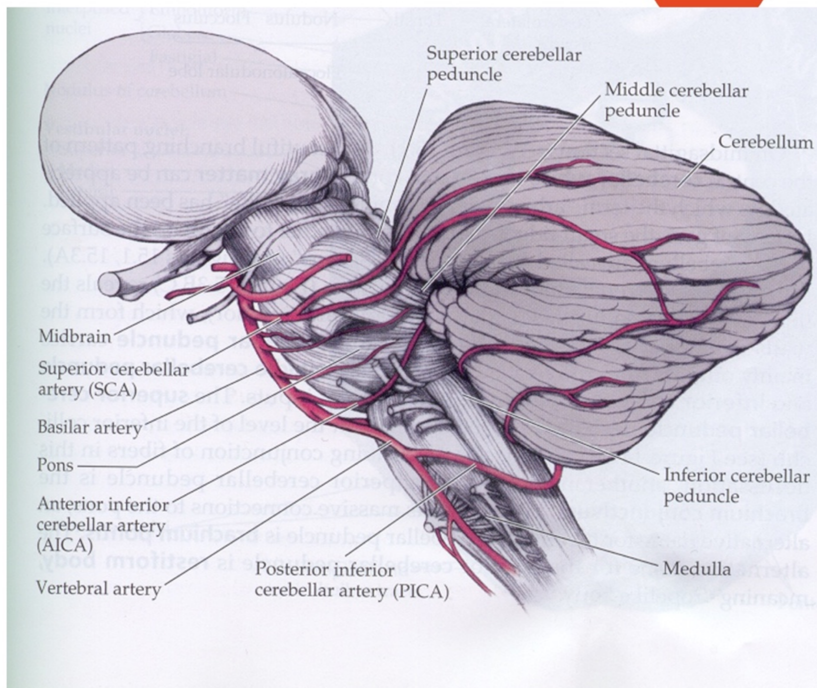
From: Part 2. Cardinal Manifestations of Neurologic Disease
Adams and Victor's Principles of Neurology, 10e, 2014

AccessMedicine
Trusted Content. Instant Answers.

Slide 37-39 - Review of the vascular supply to the cerebellum (See Blumenfeld chapter 15, Cerebellum)

Vascular Supply

OBJ. # 10



Cerebellar Infarcts

OBJ. # 10

3 main arteries that supply the cerebellum:
- Superior cerebellar artery
- Anterior inferior cerebellar artery (AICA)
- Posterior inferior cerebellar artery (PICA)

* Brainstem supply is variable for each of these arteries as some brainstem structures receive more supply from basilar perforating branches

Primary symptoms include:
- Vertigo
- Dizziness
- Nausea and Vomiting
- Gait unsteadiness
- Limb clumbsiness
- Headache
- Dysarthria
- Diplopia

Vascular Supply

OBJ. # 10

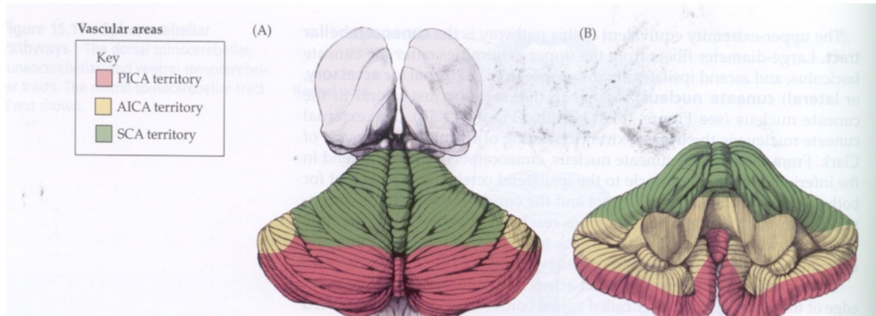


Figure 15.12 Vascular Territories of

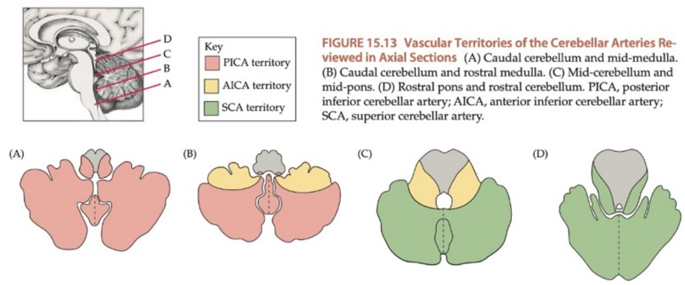


FIGURE 15.13 Vascular Territories of the Cerebellar Arteries Reviewed in Axial Sections (A) Caudal cerebellum and mid-medulla. (B) Caudal cerebellum and rostral medulla. (C) Mid-cerebellum and mid-pons. (D) Rostral pons and rostral cerebellum. PICA, posterior inferior cerebellar artery; AICA, anterior inferior cerebellar artery; SCA, superior cerebellar artery.

Slide 53 - Diagram of the most frequent causes of acute and chronic ataxia

Cerebellar Disorders Etiology

OBJ. # 11

Acute Ataxia

- Toxic
- Ischemic stroke
- Hemorrhagic stroke
- Traumatic hematoma
- Multiple Sclerosis
- Infections / brain abscess
- Para-neoplastic syndrome

Chronic Ataxia

- Cerebellar metastasis: lung and breast carcinomas, melanomas
- Multiple sclerosis
- Chronic ingestion of toxics
- Degenerative disorders
- Genetic ataxias

Acute disorders:

Drug toxicity: The most frequent drug that produces toxicity is alcohol.

Wernicke's encephalopathy is characterized by the triad of ataxia, ophthalmoplegia and confusion. It is more frequent in alcoholics and it is caused by deficiency of thiamine (vitamin B1), so it could occur in any malnourished person. The major sites of pathology are the medial nucleus of the thalamus, the mammillary bodies, the periaqueductal areas in the midbrain and the periventricular areas of the brainstem. Damage to the motor nuclei of CN III, IV and VI produces the ophthalmoplegia. The patient presents with horizontal or combined horizontal and vertical nystagmus. There are also vestibular abnormalities. There is damage to the superior vermis which produces the main symptom: the ataxia, mostly affecting the lower body. The ophthalmoplegia is the first symptom to improve with administration of a high dose of thiamin. The rest of the symptoms start to resolve within a few days. The ataxia persists in 40% of patients, in the cases with full recovery, usually it take several weeks to months for a complete recovery

An amnesic syndrome of variable severity could follow the recovery from Wernicke's syndrome. The major complication is the development of Korsakoff syndrome. It consists of a profound inability to form new memories, resulting in significant loss of short term memory and to a lesser extent long-term memory. They are unaware the memory deficit and they have some memory of past events. Patients are in general apathetic and with important cognitive impairments. It is important to note that **Wernicke's** disease and Korsakoff psychosis are not separate diseases and the transformation of the global confusional state into an amnesic syndrome are successive stages in a single disease process.

Vascular disease: Infarct of the PICA, AICA and SCA are frequent and affect the cerebellar peduncle fibers and so the function of the cerebellum. Each of them will produce a deficit that depends on the artery and the structures affected by the infarct. The lateral medullary syndrome is produced by infarct of the vertebral artery and more frequently PICA and combines both cerebellar and vestibular deficits. Other acute disorder to remember: intracerebellar hemorrhages. Most of them are produced by rupture of small arteries in patients affected with long term hypertension. In general the hemorrhages occur in the deep white matter of the cerebellum and could extend to the fourth ventricle. The onset is sudden and the first symptom would be headache accompanied by nauseas, vomiting, vertigo and ataxia that rapidly evolves to impaired consciousness. Because the hemorrhage could compress the posterior brainstem other symptoms and signs of brainstem involvement could be present.

Among the **chronic disorders** to remember are:

- **Multiple sclerosis** – symptoms are related to demyelination of fibers in the white matter of the cerebellum, cerebellar peduncle fibers and/or brainstem
- **Alcoholic cerebellar degeneration** - This is similar to the Wernick's syndrome and the etiology is the same, but it presents as a chronic form of the disease. It is more common in

men and starts between the ages of 40 and 60 years. The gait ataxia is gradually progressive until it becomes stable. Eighty % of patients develop leg ataxia. There are some distal sensory deficits and hyporreflexia due mostly to plyneuropathy.

- **Spinocerebellar ataxias** represent a group of disorders characterized by slowly progressive cerebellar ataxia that affects gait severely. Symptoms are extremely variable even within a given family. There are no specific treatments for these disorders.
- **Sensory Ataxias –** Among the most frequent causes are: polyneuropathies, vitamin B12 deficiency, tabes dorsalis. These are *not* primary cerebellar disorders
- **Friedreich ataxia** is the most common of the idiopathic degenerative disorders that produce cerebellar ataxia. It begins in childhood, it is transmitted as a recessive autosomal trait and is due to and expanded GAA trinucleotide repeat in chromosome 9. The clinical presentation is characterized by the presence of gait ataxia that evolves in 2 years into appendicular ataxia. Proprioception is affected and some DTR could also be affected. ALS pathways are affected less frequently. During the evolution of the disease upper or lower motor neuron symptoms can appear with + Babinski sign. No treatment is available. Slide 61 is a CT of a child affected with Friedereich Ataxia. The spinal cord has become very thin as the proprioceptive pathways have degenerated.