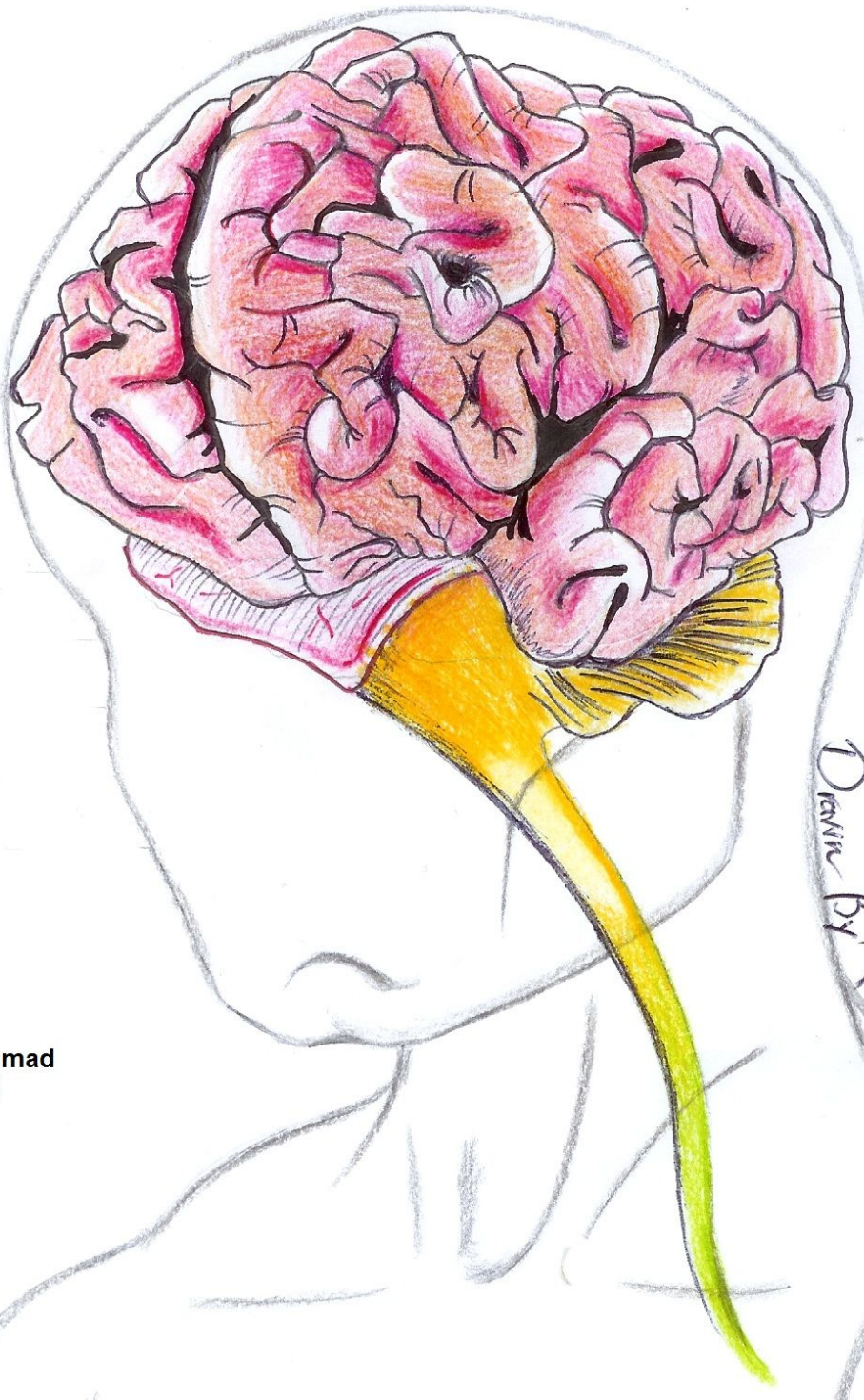
CENTRAL NERVOUS SYSTEM

- ○ Handout
- ★ Sheet
- ○ Slide

- ★ Anatomy
- ○ Physiology
- ○ Pathology
- ○ Biochemistry
- ○ Microbiology
- ○ Pharmacology
- ○ PBL



Drawn By Tariq Bushnaq...

Done By: mohammad olaimat

Dr. Name: Faraj

Lec #: 7

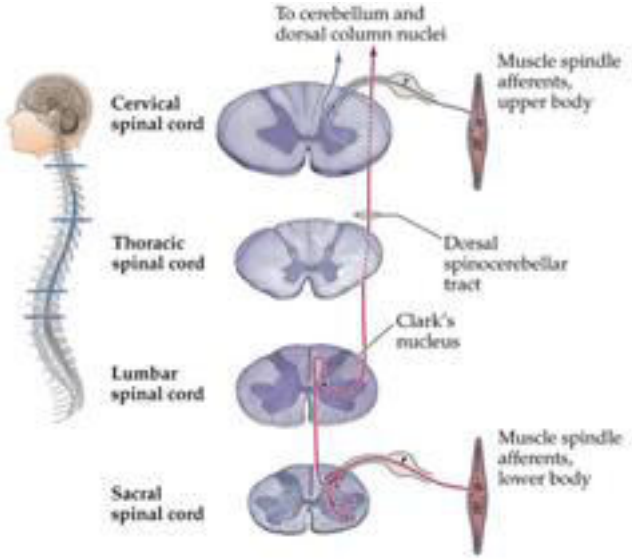
Cerebellum

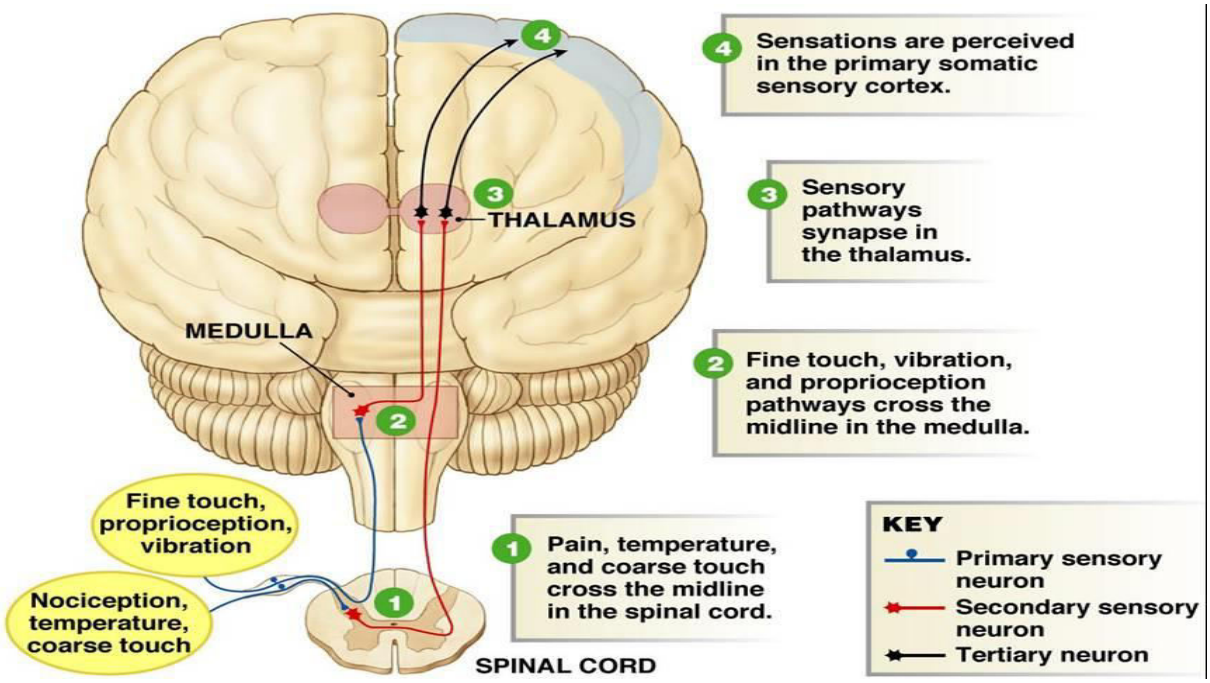
The cerebellum is meant to receive information from muscles, why ? a large part of cerebellum functions to coordinate between different muscle groups, coordination between agonist and antagonist, in order for cerebellum to be able to do this function, it needs a lot of information from the muscle, is the muscle stretched ? is the muscle contracting ?

Bringing information start in receptors, what type of receptors? So we say the receptors for most of these pathways come from **muscle spindle** or **gorgi tendon organ** and sometimes form the skin, from **pressure receptors and touch receptors in skin** and the reason for this is still unknown, the receptors when the cerebellum receives information from the muscle spindle expected, the muscle spindle informs the cerebellum about the condition of the muscle, is it stretched or not, while gorgi tendon organ informs the cerebellum whether the muscle is contacting or not.

Pathways of spino-cerebellum:

Now looking into the **first pathway** of spino-cerebellum, we call it **dorsal or posterior spino-cerebellar tract**, we see the dorsal root of spinal nerve, peripheral process and receptor, the peripheral process will end in muscle spindle, golgi tendon organ as well as pressure and touch receptors of the skin from lower limb and lower trunk. The receptors convert the stimulus, whether it is chemical, thermal or mechanical, into action potential, once there is action potential, this action potential will be transmitted along the dorsal root into the spinal cord; this is what we call “First Order Neuron”.





We have first order neuron or primary sensor neuron, and the second order neuron is located in **nucleus dorsalis of clark's** in the grey matter of segments between **C8-L2**, this dorsal spinocerebellar tract brings information from the **muscle spindle and dermatomes of the lower limb**.

As we know, nerves of lower limb are L4-S3, how these nerves reach the nucleus of the lower limb in L2? The **action potential** which comes from the lower level below L2 ascends in the **posterior column** of the spinal cord,

specifically in **the Gracile tract** reaching L2 then synapses in the nucleus of clark's which is considered as second order neuron, the cells of this nucleus sometimes called **transmission cells**, the **axons** of clark's nucleus then ascend in the **lateral column** of white matter of the spinal cord till they reach the medulla, and enter the cerebellum through the **inferior cerebellar peduncle** and bring with them information of **unconscious proprioception**, (sense of position and sense of movement) which we don't feel them. In order for sense of position to be felt, it should reach thalamus and cortex, so from now on we have to describe to types of proprioception, two types of position sense, **conscious reaching the cortex, unconscious reaching the cerebellum**.

Another pathway is **cuneo-cerebellar tract**, this tract brings the same information of the dorsal spino-cerebellar tract but from the **upper limbs**, its nucleus is **accessory cuneate nucleus** found in the medulla, the fibers will start in the muscle spindle and dermatomes of the upper limb, then they will ascend in **cuneate tract** reaching the cervical region then to medulla reaching their nucleus, after that they will go to the cerebellum through inferior cerebellar peduncle.

These two tracts, dorsal spino-cerebellar tract from the lower limbs and cuneo-cerebellar tract from the upper limbs, bring to the cerebellum the unconscious proprioception which is sense of position and sense of movement that we don't feel it.

Another pathway is called **anterior or ventral spino-cerebellar tract**, its receptors found **only** in the golgi tendon organ, the fibers that come from golgi tendon organ are of **1B type**, these fibers will enter the spinal cord and synapse with the second order neuron which is found in the **layer/laminae 5,6, and 7** of the spinal cord. These laminae are affected by the **interneuron of the flexor reflex**, when the interneuron of the flexor reflex send signals to

the laminae 5,6,and 7, they give them information about everything happening in the muscle. The neurons of laminae 5,6,and 7 send axons along the spinal cord reaching the brainstem specifically midbrain then enter the cerebellum through **superior cerebellar peduncle**, so they have done **double crossing**, **first** crossing in the **spinal cord** and the **second** crossing in the **midbrain**.

What is the significance of this double crossing ?

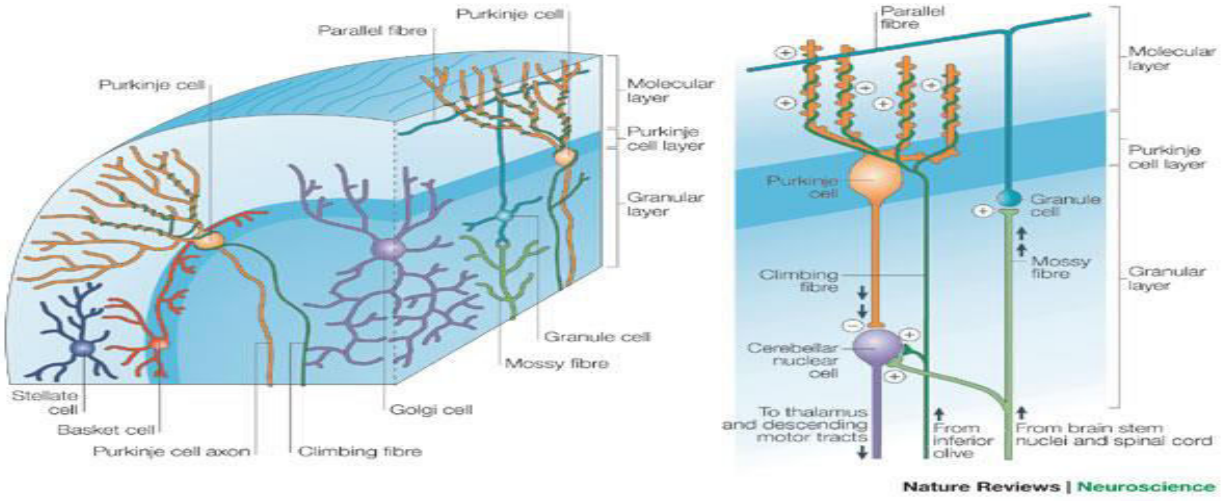
Each **cerebellar hemisphere** will control movement of muscles **on the same side,** in contrast to the **cerebral cortex** which controls movement of the muscles **on the opposite side**, and this what we benefit from the double crossing, it returns from where it begins, right hemisphere controls the right side and left hemisphere controls the left side.

Cerebellar cortex:

It is formed of **three layers**; the most superficial layer called **molecular layer**, the intermediate one known as **purkinje cell layer**, and purkenji cells are most abundant cells in the cerebellar cortex, and the pyramidal cells are the most abundant cells in cerebral cortex, the inner most layer is the **granular cell layer**; here the major neuron is granule cell.

This table is to help you compare layers of the cerebral cortex (neocortex) with layers of the cerebellar cortex.

Cerebral cortex	Cerebellar cortex
molecular	molecular
External granular	
External pyramidal	purkinje
Internal granular	
Internal pyramidal	granular
multiform	



In the molecular layer we have two types of neurons; **stellate and basket cells** and within this layer we have dendrites of two neurons; **dendrites of purkinje** and dendrites of **golgi type 2 cells**, in the first layer we have the axons of the granule cells having a T-shape, and the significance of this is synapse; **axo-dendritic synapse**.

If the action potential reached the granule cells, it will easily reach the purkinje because the axons of granule cells make anastomosis with the dendrites of purkinje. The purkinje layer will send its dendrites to the first layer which will synapse with axons of other neurons mainly the granule cells, and its' axons will enter inside the nuclei, as we know we have **three pairs** of nuclei in the cerebellum; the **dentate nucleus** receiving most of its connections from the **lateral hemispheres**, and the **interposed nuclei** receiving inputs mostly from the **paravermis**, the last pair is the **fastigial nucleus** receiving primarily afferents from the **vermis**.

Inputs of cerebellum:

The pathways we mentioned earlier are inputs, but we have a major input called **cortico-ponto-cerebellar tract**, another input from the vestibula;

vestibulo-cerebellar tract (Juxtarestiform body) and from inferior olive in the medulla called **olivocerebellar tract**.

Most of these inputs enter the cerebellum as mossy fibers except the olivocerebellar tract which enter as climbing fibers, and the difference is that the climbing fibers enter and synapse directly on the purkinje whereas mossy fibers synapse with the granule cells and these cells transmit the signals to purkinje, so in the end the inputs must end in purkinje whether from mossy or climbing fibers.

In the third layer we have what is known as **glomerulus** which is a synaptic nodule, which synapse in granule cells golgi type 2 cells, so through the glomerulus the message will be transmitted very fast from mossy fibers to granule cells and eventually reaching the purkinje.

As the mossy fibers and climbing fibers enter and before reaching the purkinje, they give collaterals which excite the central nucleus and we call this **early excitation**. So what interactions happen here ? the climbing fibers excite the purkinje, the mossy excite the granular which in turn excite the purkinje, stellate, and basket cells. The stellate and basket **inhibit** the purkinje. Golgi type 2 cells get excited from granule cells and they inhibit granule cells, inhibit the cells which caused their excitation. At the end of these interactions the purkinje inhibit the nucleus. So the nucleus will receive early excitation from mossy and climbing fibers and **late inhibition** from purkinje, because of this early excitation and late inhibition the **nucleus remains active** which means there is always outcome from the nucleus, this outcome may go to the cortex or to the reticular formation which will ultimately coordinate between agonist and antagonist, how?

At the beginning of movement, if we want to stimulate the biceps to make a flexion of elbow we have to stimulate the biceps then inhibit the triceps. The output from the cerebellum will excite and support the agonist, after a

period of time when the biceps is flexed; the output will excite and support the antagonist to stop the movement.

We have a test called **finger-nose test**, here we ask the patient to put his finger on tip of the nose, at the beginning of this movement the output from cerebellum will stimulate the biceps, once the finger has touched the nose, the output will stimulate the triceps to stop the movement since both biceps and triceps have opposite actions.

Vestibulo-cerebellum:

The lateral vestibular nucleus is a part of the cerebellum and appears as **it doesn't have nucleus**, it said to be that the nucleus of this part had **migrated to outside**. This part has inputs and outputs, the inputs are **primary and secondary vestibular fibers**, the primary fibers come directly from **the receptors of equilibrium** in the inner ear, the secondary fibers come from the same receptors but synapse in the vestibular nuclei then transmit the message to the cerebellum, how they enter the cerebellum ?

Along the **inferior cerebellar peduncle** as mossy fibers which will synapse with the granule cells and these cells will synapse with purkinje of vestibulo-cerebellum part. Now the output will start from the purkinje cell, and it is supposed to be transmitted to the nucleus inside this part but as we said the nucleus of this part migrated to outside, so the message will be transmitted to outside, so the first output is from the purkinje to the nucleus and the second output is from the nucleus. Now from the lateral vestibular nucleus the output will be transmitted through **lateral vestibulospinal tract** which is a part from **medial motor system** which will influence the alpha and gamma medially so it will affect the **axial and proximal muscles**. Once the output has reached the lateral vestibular nucleus a part of this output will reach other vestibular nuclei either medial, superior, or inferior vestibular nucleus. This pathway called **MLF**, this pathway will transmit the output

from the vestibular nuclei to the nucleus of the **3rd, 4th, and 6th cranial nerves and will coordinate the head movement with eye movement**, if we want to look to the right we will abduct the 6th and adduct the 3rd through medial and lateral rectus; extensor muscles of the eye.

If the MLF pathway has been cut or has been **affected by multiple sclerosis**, the eyes will not move conjugately and by this the patient will suffer from **double vision**, so if the vestibulocerebellum part has been injured or MLF pathway has been cut the patient will have **trunk ataxia and nystagmus** .

What is trunk ataxia? As we said this part takes over control on alpha and gamma which affect the axial muscles, axial muscles are the muscles of vertebral column, so these patients will have **disturbances' in trunk movement**, when standing or sitting he will deviate either to left or right.

What is nystagmus? involuntary movement of the eye, where the eye starts moving rapidly then slows down. This symptom is associated with a lesion of MLF. A lesion of the MLF produces slowed or absent adduction of the ipsilateral eye, usually associated with involuntary jerk eye movements -nystagmus- of the abducting eye, a syndrome called **internuclear ophthalmoplegia**. Because multiple sclerosis causes de-myelination of the axons of CNS, it can cause internuclear ophthalmoplegia when MLF axons get de-myelinated, where it presents as nystagmus and diplopia..

When a patient sees two fingers instead of one (double vision), we will know that he has something wrong in MLF pathway and not in the eyes themselves.

Anterior lobe/ Spino-cerebellum:

Vermis and paravermis are vertical sections whereas anterior lobe, posterior lobe, and folliculonodular lobe are horizontal sections of the cerebellum, so the vermis and paravermis are in anterior lobe, and the inputs of this part are:

1- **spino-cerebellar tract** (dorsal and ventral) from muscle spindle of trunk and limb muscles and golgi tendon organ from the tendons, this tract bring information from muscles about **actual movement**, either the muscle gets contraction and this stimulate the golgi tendon organ or the muscle gets stretched and this stimulate the muscle spindle

2- **Olivo-cerebellar tract** coming from **inferior olive**, and the inferior olive receives information from **cerebral cortex** from area 6 and association cortex, and association cortex which is about thoughts and movements, every movement is preceded by idea which generates from the association cortex. This cortico-olivo-cerebellar tract brings to this part of the cerebellum information about **intended movement**
- الحركة المنوي عملها-

So the spino-cerebellar tract brings to the anterior lobe information about the actual movement and the olivo-cerebellar tract brings information about intended movement. now this part of cerebellum compares **if the actual movement is done according to the plan**, e.g If I want to drink a cup of water the biceps should contract and triceps should be relaxed, now the anterior lobe will compare this actual movement with the plan which mentioned earlier, if the movement was not according to the plan the anterior lobe will interfere and send **correcting signals** ,which are outputs, to the **reticular formation**, the function of correcting signals is to **verify the rate, range, force, and direction of movement,** when these four elements are in their proper state the resulting movement will be accurate.

The reticular formation descends from it the **reticulo-spinal tract**, which is **medial motor system** that affects axial and proximal muscles, now we have reached the Alpha and Gamma.

The output also affects the **red nucleus** which descends from it the **rubro-spinal tract** that affect Alpha and Gamma of distal and a little proximal.

The last output is to **Thalamus**, and from Thalamus to motor cortex which descends from it the **pyramidal tract** that affects mostly distal muscles and a little on proximal.

Three outputs to 1- Reticular formation 2- Red nucleus 3- Thalamus.

By this, the spino-cerebellum regulates the movement of axial muscles, proximal and distal muscles, the axial muscles regulated through the reticulo-spinal tract, and proximal and distal through rubro-spinal tract and **lateral cortico-spinal tract** of pyramidal, and here comes the benefit of the division of motor pathway to medial and lateral; reticulo-spinal medially while pyramidal and rubrospinal laterally.

Spino-cerebellum will regulate actual movement **while it's happening**, same thing goes to vestibulo-cerebellum.

Cerebro-cerebellum/ posterior lobe:

It is the **largest part** of the cerebellum, this part **communicates with cerebral cortex**; it gets inputs from the cortex and its output goes to the cortex, and act **like feed-forward control system**. It receives its' input from wild areas of cerebral cortex; from supplementary motor and premotor(area 6) from primary motor, from somatic sensory area

3,1 and2, individual areas from5 and 7, and the most important and large input from **association cortex**, as we said before association creates ideas about movement, so this part receives **the ideas about movement before it happens and verify the plan before it happens**, in contrast to the previous parts which receive information after it has happened.

These inputs descend in the internal capsule in the brainstem then midbrain reaching pons, where the axons which carry the input synapse with **pontine nuclei**, synapse means end of the tract. Pontine nuclei send other axons which **cross the midline to the other half** and forming the **middle cerebellar peduncle**, so middle cerebellar peduncle is axons of pontine nuclei **of the opposite side**, then middle cerebellar peduncle enters as mossy fibers which will synapse with granule cells that will deliver the message to purkinje, but before it delivers the message it gives collaterals to dentate nucleus.

The output will go from purkinje to dentate, and the final output will exit from dentate nucleus to cerebral cortex.

The input to cerebrocerebellum is through cortico-ponto-cerebellar tract from supplementary motor and premotor area 6, from primary motor, from somatic sensory area 3,1 and2,visual areas, from5 and 7, and the most important and large input from association cortex.

The output will exit from dentate nucleus through **dentato-rubro-thalamo-cortical tract**, from dentate nucleus to red nucleus then to the thalamus and finally to the cortex, this pathway forms the largest part of **superior cerebellar peduncle**.

The pyramidal tract coordinates agonist and antagonist through **interneurons** that can excite the agonist and inhibit the antagonist,

now who is behind all of this? Who tells the pyramidal what to do? **The cerebellum through the cerebro-cerebellum.**

The dentato-rubro-thalamo-cortical tract can be **affected by multiple sclerosis** and this will lead to **the worst cerebellar ataxia** because this tract functions to regulate motor commands before the start of movement, before the execution of command.

If we put an electrode on the posterior lobe it will **show activity 100 millisecond before the onset of movement**, so this part of cerebellum plans for the movement and directs the pyramidal tract.

The vestibulo-crebellum and spino-crebellum receive information about the movement and reply as **feed-back** but the cerebro-cerebellum act as **feed-forward** control system.

The function of cerebro-cerebellum is **learning and storage of the sequential component of skilled movement as well as regulation of ballistic movement** which is a very fast movement e.g moving fingers while typing, or while playing piano. Vestibulo-cerebellum and spinocerebellum regulate the **actual movement** while cerebrocerebellum regulates commands **before the occurrence of movement**. Every complex movement needs a program, needs a plan and this plan comes from the association cortex, and cerebrocerebellum regulates these plans by feed-forward before the occurrence of movement.

Lesions of cerebellum:

Lesions to any part of cerebellum **do not produce paralysis**, but precise and coordinated movements are impossible, and disturbances

in movements known as **ataxia**, and ataxia affects the extrinsic muscles of the eye causing nystagmus, affects muscles of speech that leads to disturbances in speech, and affects muscles of walking that leads to walking disturbances that makes the patient walks like a drunk.

From all of this, we come to conclude that cerebellum acts as a **regulatory system** that modifies motor acts initiated by other regions of the CNS. Some of the cerebellums' functions is **synergy** and coordination between different muscle groups between agonist and antagonist, **asynergia** is the opposite of synergy, another function is **equilibrium** which is done by vestibul-cerebellar tract, and the last function is **regulation of tone**.
Asynergia is loss of coordination results in errors in rate, force, range, and direction of movement. For example if the patient is asked to put his index on the tips of his nose, he might overshoot , i.e he'll put it on his ear.

If a lesion affects the vestibulocerebellum, what will happen?

1-What do we mean by **loss of equilibrium**? Inability to stand upright without support.
2- **Staggering ataxic gait** because there is no coordination between muscles of walking, and there is a tendency to fall towards the side of the lesion. Because there is no coordination between muscles of walking.
3-**nystagmus** which is spontaneous eye movement in which the eyes move slowly in one direction and rapidly in the other- eye jerk-nystagmus reflects asynergia of the extrinsic muscles of the eye.

" Your mind is the greatest weapon, you either control it or let it controls you"
Wait for it...