**Revision of last lecture:**

-The motor system is a complex one

- Motor system includes tracts going to the lower motor neuron. The most important is the voluntary corticospinal tract.

- Non-voluntary tracts are 4 in number.

**Motor system (2):**

Lower motor neurons (their cell bodies are in the spinal cord ) 🡪 give orders directly to muscles. Other tracts give orders from higher levels ( brain ) to lower levels .

Hence, we divide the motor system into :

1) lower motor neurons 🡪 alpha and gamma neurons which give orders directly to the muscles .

2) Upper motor neurons 🡪 descend and control the lower neurons.

-any cut in the spinal cord at any level 🡪 will cause injury or cut in the motor neurons or corticospinaltract (because it is responsible for the voluntary movements).

Depending on the site of the injury and where the cut is found, it could result in:

Monoplegia ,diplegia , hemiplegia , paraplegia , quadriplegia .

-To distinguish between them we depend on:

1) Location of the cut

2) Severity of the cut

3) Number of the affected limbs, and which ones

-problems in the motor system may affect the upper motor tract or the lower motor neurons, we could distinguish them by inspecting the symptoms.

Note: The corticospinal tract is an upper motor neuron. Meaning, that it descends from the brain or the brain stem, passes into the spinal cord and is responsible for the voluntary and involuntary tracts.

-lower motor neurons 🡪 neurons that give orders directly to the muscles and the cell body of these neurons in the spinal cord.

Question: What is the difference between a lesion in an upper motor neuron and a lesion in a lower motor neuron?

\*\* paralysis : means that I can't move -for example my hand- voluntary , so If the upper motor neuron or the lower one is injured 🡪 the result will be paralysis .

\*\* To differentiate between the two injuries :

\_ lower motor neurons give order to the muscle with a base line of action potential and a little bit of muscle tone .

\_ tracts regulate it as they descend, playing a role in the regulation of the tone strength 🡪 either increasing or decreasing it. They also play a role in the regulation of muscle contraction and movement.

\*\* If the injury was in the lower motor neurons, the muscle will not receive any action potential, will not contract and hence be paralyzed. Muscle is wasted and will become flaccid. Also proteins will be degraded and will decrease in number.

\*\* If the injury was in the upper motor tracts, the result will be paralysis as well but with a little bit muscle tone. This is due to the presence of circuits and reflexes in the spinal cord. However they are not under the control of the brain, so paralysis will still occur but with muscle spasm.

Note: Usually the brain and the upper motor neurons DO NOT control reflexes, BUT IF the brain starts controlling the reflexes 🡪 they will decrease .

Hence,

\*\* If the upper motor tract is injured the reflex will be either the same or stronger (usually stronger) … hyperactive deep reflex .

\*\* If the lower motor neuron is injured the reflex will be weaker or there will be no reflex at all … hypoactive deep reflex .

**Babinski sign:**

Reflex usually involves multi-circuits and sometimes in more than one level , these are under the control of brain. If I want to diagnose a patient; I ask him to relax the sole of his foot (here his foot is under the control of brain). If the upper motor neuron is injured the reflex will be different and more exaggerated than the reflex of a normal patient.

\*\* In a normal person, If I stroke the lateral aspect of the sole of foot 🡪 the fingers will curl (this is the reflex when the circuits are under the control of the brain).

\*\* If the upper motor tract is injured, the circuits are no longer under the control of the brain, resulting in a different reflex where the patient will perform extension (extensor planter response; elevation of the big toe and fanning of the other toes), This reflex is the Babinski sign.

 \_Under normal conditions, the spinal cord develops before the brain, so children (from birth till one year of age), will show Babinski sign.

\_ from the age of 9 months to one year 🡪 the upper motor tracts will be developed enough to control the child activities like walking. During this period, his/her reflex will start to change to normal.

\_ after the age of one year 🡪 the child’s reflex should be normal, unless he is injured or shows the babinski sign.

 **Demyelination:**

Recall that alpha motor neurons are the biggest and the most myelinated neurons.

\_ If by any mean the myelin is destroyed; the conduction will be slower. We already know that a myelinated neuron has a faster conduction than an unmyelinated neuron. But how will the conduction be affected if a previously myelinated neuron becomes unmyelinated? It will not only become slower in conduction but will also be inefficient. Why? In a myelinated neuron, the ion channels are far away from each other. Now that the myeline is gone, and the ion channels are still far away from each other hence the neuron will be able to conduct impulses but those are inefficient. For example, if a neuron used to conduct 100/sec it may only conduct about 20/sec.

\_ so any problem in the myelination 🡪 by default there will be a problem in the velocity of conduction and in movement.

\*\* The two most famous diseases are:

1. Multiple sclerosis ( التصلب اللويحي ) : a disease that causes a progressive destruction of myelin sheath that surrounds the axon of a neuron .
2. Amyotrophic lateral sclerosis: a progressive degenerative disease that attacks motor neurons (causing death of these neurons).

\*\* for the two diseases 90% of symptoms are the same ( weakness , paralysis etc .. ) , because both of them affect motor neurons .

\*\* The Dr said "read the two paragraphs; no need for details."

**Regulators:**

\*\* Basal ganglia and cerebellum:

Play an important role in processing and regulating information but without sending orders.

\_ Basal ganglia consist of:

Caudate , putamen , and globus pallidus .

And those involved in the circuit are: substantia nigra and subthalamic nucleus.

\_ Basal ganglia works as a regulator for the motor system (processing), and it helps in initiating and stopping the movement, sometimes it helps in the regulating the sequence of movements.

\*\* There are 4 neurotransmitters for the basal ganglia:

1. Information is sent to the basal ganglia by: glutamate.
2. Calculations and processing is done by: acetylcholine.
3. Calculation is regulated by: dopamine (from substantia nigra).
4. Orders are sent out from the basal ganglia by: GABA

\*\* so when I start moving , our brain starts thinking but before sending orders from the cortex , the basal ganglia will processes them (gives its approval, determines the sequence of the orders, and gives feedback).

\*\* There are 2 disorders involving the basal ganglia:

1. Parkinson disease.
2. Huntington'sdisease.

\*\* Parkinson’s disease:

The cause of this disease is degeneration of dopamine that is released from the substantia nigra.

\_ dopamine in the basal ganglia is responsible for calculating and processing , so if substantia nirga does not send dopamine to the basal ganglia , calculations will be affected , and the motor system or movement will be affected too.

\*\* slide 19 : substantia nigra🡪 the black region in the picture , the left one is for a normal person and the right one is for an abnormal person.

Since the basal ganglia is responsible for the regulation of the initiation and termination, those will be not be regulated properly in case of deficiency in the release of dopamine by the substantia nigra.

Symptoms for degeneration of dopamine include:

1. Tremor
2. Rigidity
3. Bradykinesia

Recall, the motor cortex sends both activating and inhibiting orders (mainly inhibition). If the initiation of a movement couldn’t be properly regulated and calculated, this is an indication that the inhibition and activating orders at rest are imbalanced. Tremor is a symptom of such condition (at rest). Tremor may progress (not only at rest) in late stages.

\*\* when I start moving my hand 🡪 tremor will disappear , but my hand will move slowly , because of the improper regulation ( initiation – termination ) , and as we said before that when the upper motor neurons is injured , muscles will suffer of spasms , and in case of bad regulation ( wrong calculations , wrong feedback ..) from cortex , the second symptom that will be seen on the patient is Rigidity : high reflex and stiffness of the muscle .

\*\* because there is low regulation and wrong calculation , when the patient want to move his hand ,the movement will be slow , and that’s what we call it Bradykinesia .

\_ all these 3 symptoms will progress with time .

\_ neuro-degenerative disease: the death of neurons day after day, and as a result the problem will progress .

\*\* so at the beginning, the patient will suffer from mild tremor , and with time shaking will increase and he will start losing the ability to do certain types of functions , then the rigidity will increase .

Treatment:

1) we give the patient dopamine as a drug

 2) if I couldn’t or dopamine is found in very small amounts and drugs didn’t increase it , we give the patient acetylcholine , because calculations is regulated by acetylcholine

3) surgery: we said that neurons in substantia nigra which should release dopamine are degenerated , so if neurons were 1 million in number , now are only half this value, and hence lesser amount of dopamine is released. To solve this problem I have to strongly activate the half a million neurons left. This is done by stimulating these neurons (forcing the neurons to work) in a process called deep brain stimulation.

The procedure involves placing an electrode (with a battery) in the patient's brain (surgical cure).

\*\* you can watch on youtube videos of patients before and after the stimulation.

\*\*the disease usually happens at old age, neurodegenerative disease involves genetic factors as well as other factors so it is a multi-factorial disorder.

**\*\* Huntington's disease:**

Normally GABA is released from basal ganglia to the cortex, but in this disease, there is degeneration of the output neurons , so the calculations are done well , but orders don’t go to their original destinations , so because GABA is not released 🡪 starting and ending points are not regulated .

 As we said before about dopamine , not all neurons is degenerated but instead of having 1000 neuron , we have 500 , so some orders will be regulated and other orders will not will not have starting and ending point .

\_ the most obvious symptom is involuntary movements:

1. Jerking : involuntary shaking .
2. Chorea : complete involuntary movement of a limb or half of the body .

\*\* You should differentiate between chorea as a symptom of Huntington’s disease and Sydenham chorea which is a different disease affecting children that results from inflammation, infection, and fever attacking the basal ganglia, and as a result neurons will not develop well.

\*\* Huntington's disease:

1. Inherited disorder.
2. Autosomal dominant ( if present , the disease will be transmitted to 50% of population )
3. Males and females are equally affected ( not X-linked disease )
4. At early age before 40

\*\* The disease along with its symptoms will progress with time as a cognitive disorder and will cause dementia (loss of memory ). This is because in the same way that the basal ganglia regulate motor movements, it does so in every other area of the cortex. This explains the fact that at the beginning of the disease the patient will have motor/ movement problem, but eventually the patient will be unable to think reducing the cognitive ability and resulting in dementia. Dementia is most apparent in Huntington’s disease because it evolves at a young age.

 \*\*Cerebellum

Helps us learn skilled movements (how is it done) and perfect them.

By sending an order to move our hand, we assume that this order is correct by 90%. Cerebellum will take this order, save it as being correct by 90% and edit it. This edited movement will be correct by 95%. Another attempt, it will be 96%. By trial and error, the cerebellum will achieve the 100% and will store it until needed. Next time we perform this action, the cortex will send the order to its verifier for verification. After verifying the sent signal with what's saved, the action is performed.

learning happens through the cerebellum.

E,g. If i want to hold an egg, i need to apply enough pressure to hold it and not let it fall but not hard enough to break it. What will give me the precise measurements to hold the egg in the right way is the cerebellum.

These precise measurements are obtained from previous experiences and from the sensory pathways. Sensory pathway will give the information of the pressure applied, [You are providing a pressure of 100].

Actually, the cerebellum takes information from every sensation, literally.

Not only pressure, or somatosensory, but also the motor. If I want to throw an object to someone or catch something thrown at me:

Vision sensation will give the coordinates of its direction, speed and destination after some time.

Cortex will say, "I need to catch this flying object, and in order to do that i need to move my muscles in direction X, speed Y. Inhibition and activation of these muscles are done by specific amounts." Cortex will send this received information for validation and verification (Cerebellum), and then decide if yes, we are going to do it, or no, we are not.

If in the first time it is thrown at me it fell, next time the cerebellum will try to correct the wrong measurements it took last time and correct them. It will continue to do so until I catch the object.

We receive motor sensation in the cortex, then decide the action, send it to the cerebellum for final verification which will send it to the motor unit to perform the action.

Playing a guitar and performing complex things were learnt by the cerebellum.

 Now suppose a normal person knows how to play the guitar and somehow, lost his cerebellum. He will have a disorder called Ataxia.

Ataxia is a general term, a general disorder caused by multiple reasons. It is defined as disturbances of equilibrium of the body and in coordination of movements. One of the causes is cerebellum dysfunction; Cerebellar Ataxia.

Signs and symptoms:

Legs are spread further apart while walking, person leans more than usual. This is due to loss of muscle motor coordination of the legs while walking.

Tremor

Extending the hand to get something, the hand will tremor. This is due to loss of coordination and failure in calculating the right distance away from the hand. This tremor isn’t present at rest, but during movement, this is called Intentional tremor.

Also, this failure of calculation gives dysmetria ( disturbed ability to gauge distances ). If I attempt to reach for an object quickly, my hand will fail to grab the object. Instead, it will reach either in front of or behind the object. A number of attempts may be conducted before successfully grabbing the object.

