Last time we talked about the descending pathways of pain and the ALS. Today we will continue talking about these descending pathways.

Each higher level will control the level under It. In controlling pain we have descending pathways coming from the cortex, hypothalamus, brainstem to decrease , desensitize or to sensitize pain.

1- The first level comes from the **cortex** which is the **corticospinal pathway**. One third of the corticospinal and even the lateral corticospinal tract is from the somatosensory cortex so it helps in movement but also controls the spinal cord level (One of the spinal cord control levels is to sensitize or desensitize the pain)

2- The second level comes from the **hypothalamus**, the hypothalamus doesn't descend directly to the spinal cord most of its interactions with the pain pathway is done through ***locus coeruleus nucleus***, ***raphe nucleus*** and ***precentral grey matter***.

Most of the control is through the brainstem nuclei which descends to the spinal cord, the main brainstem pathway which descends to the spinal cord is the preaqueductal grey matter which is one of the areas that receives painful information, in preaqueductal in grey matter it is the main descending pathway to control and eliminate pain, it has opioid releasing neurons (we will talk about them when we talk about neurotransmitters) these are protein neurons so their axons are short

(protein neurons have short axons why?) because production and control for protein neurotransmitter is found in the cell body and that's why their transport is very slow so usually most of the protein neuron prefer having short axons

that's why it doesn't descend from the grey matter in the mid brain to the spinal cord instead it descends to the raphe nucleus activating it which is serotonin, the serotonin neuron descend to the spinal cord level and they shift back to the upload neurotransmitter neuron to inhibit pain. This is one of the most important descending pathways in controling and inhibiting pain.

P.S. Raphe nucleus produces serotonin

3- The last level is from the **reticular formation** we have a collection of neurons producing norepinephrine and this collection of neurons is found in a place called locus coeruleus .

Reticular formation ascends up and descends down to control the activity of the CNS and the brainstem and the one descending down from the locus coeruleus and norepinephrine neuron helps in controling and eliminating pain.

All these pathways are important in the inhibition of pain or in the control of inhibition of pain. It's like in those who can walk on pins or hot charcoal they actually feel pain but they can control it through these pathways.

- These pathways can be voluntary or involuntary but usually they are involuntary.
- It's our control on the body to block pain when we don't want to feel it.

The Dr showed a diagram about the connections and pain pathways (slide no. 3)

The Dr showed a diagram, showing the preaqueductal grey PAG where it descends and how it inhibits the circuits. (slide no. 4)

The Dr showed another picture of circuits from the lamina side and the circuits which are found in the grey matter of spinal cord, the most important in it is the sensory (the dr. will not ask about the details unless it's required from us in the anatomy). (slide no. 5)

The main control pathways for pain are :

1- **Raphespinal** which comes from periaqueductal grey to serotonin releasing neurons to control descending pathways , it causes activation of some inhibitory neuron and inhibition of some neurons to inhibit the spinothalamic pathway .

2-another control of pain is the **gate pathway**. مرات لما ننجرح او نحس بوجع بأي مكان بنصير نضغط او نحك عمكان الوجع لأنو بخفف الشعور بالألم، ليش بصير هيك؟. because we have the mechanoreceptors which participate in the PCML pathway, before they go up to the PCML pathway they give a collateral branch to deactivate the molar pathways (ALS) in this case we scratch because it's more better, fibers in our way up it will inhibit the ALS pathway, that's why pressure or scratch at site of injury will decrease the feeling of pain.

Through the lamina of the grey matter we have multi neurons and multi connections forming circuits and these circuits will decide which info. is more important and it will go up. The pathways coming to these circuts are:-

1- **DCML pathway**. it will give me inhibition to AMS

2- **control from up to down** that will inhibit some neurons

3- **the neurons themselves** (we know that most of the ALS modalities will synapse in the grey matter before it ascends up and there we have laminea to laminea connection that will control the function of one laminea from the other , because the distribution between nerve 5 receptor or receiving laminae in spinal cord is not equal .

• one of the most important things in this circuit other than the up to down inhibition is the deafferenation pain.

• Resulting from the circuits >>> If I have a cut in the nerve like in case of avulsion in root or amputation in one arm this will ruin the circuits and will also ruin the balance of activation, the brain will stop receiving some of the sensations and the brain will think that these receptors or neurons have higher threshold so the brain will increase their sensitization this is not the only way to increase sensitization, when we have almost small pain and we want to know if it's dangerous or should be ignored the brain at first will increase the sensitization of receptors and neurons receiving these information until the information reaches and the circuits of the spinal cord will decide if it's important or not and then it goes

to the brain. Now what's important for us clinically is when there is a cut in the nerve or avulsions of some routs this circuit will not work properly and the brain will sensitize some of the laminae of the spinal cord so we will have pain without any painful stimuli and no pain when there is painful stimuli.

• The pathways are controlled by their functions so when we have stimulation of the pathway in any place it will emit that modality so if we had activation of the grey matter in the post. horn in the spinal cord these are mainly responsible for pain or ALS modalities which is mainly pain

so that's why the brain when we have amputation in the arm , it will feel pain from the arm and this is called phantom limb its not the only deafferation u will see the most common you will see is avulsion in the routes, cutting some of the spinal nerves. and sometimes we will see it in people with quadriplegia or any other paralysis.

all what we said focuses on the post. horn grey matter in spinal cord the regulation of these neurons to weather fire or not and to send pain up because firing of this neuron to the cortex and even to the thalamus will be felt as pain. the regulation of the neuron (when to fire?) depends on:-

1- what the brain is receiving from the pre synaptic (pain receptors- sensory neurons) **2**- the threshold which depends on what it receives activation or inhibition from the 4 regulatory or descending pathways further more it receives inhibitory from the post. column medial meniscus PCML pathway.

All these will interact to give me either silent neurons and in this case we won't feel pain or active neurons and in this case we receive pain.

so if we have amputation or deafferation to the neurons in these circuits in many cases by sensitization to the upper control the neuron that sends the pain transmission will undergo firing and in this case the patient will feel pain. { all this circuit is ruined so we don't have activation from the ALS pathway, from the spinal cord responsible of ALS modalities so the post-synaptic neurons when they don't recieve activation they will sensitize these receptors on their own, the brain is not recieving info from the neurons so it will cause activation from up to down and there is no inhibition from PCML so all of these will do the function and lately the neuron will fire and transmit pain to the uppercenters you will see this mainly in people with phantom limb who have affirmation in one arm and one leg and in cases of avulsion in roots especially seen in motor accidents .

in this case the patient will feel pain and mostly the control is over the opioids, we give the patient analgesia and even sometimes this doesn't work and we have 2 procedures which are usually for the avulsion or amputation and sometimes they make sth called **post. root entry zone procedure**, *in this case we enter a needle at the site where the post root enters the spinal cord and in this case they usually target lamina 2 and some from lamina 1 and sometimes they apply toxic material like radiopaque to kill the neurons that are found there, in this case we can get balance in the circuit*

because it will decrease the activation of neurons coming from lamina 1 and 2 and the patient stops feeling pain, *so*metimes the material may diffuse more medially and affect the dorsal column pathway which is more medial to lamina 1 and 2. What's more lateral to lamina 1 &2? corticospinal tract.

so sometimes it may diffuse and affect some sensations esp. the post column medial meniscus or the corticospinal.

The second way to control pain sometimes which is less common which controls pain from other sources(continuous or tonic pain sources) other than avulsions and amputations because in this case we need to cut all the pain sensation unlike in the previous way where we only cut one segment so when we perform the post root entry zone we eliminate pain sensation only in one segment but when we want to eliminate pain to a larger area including more than one part of the body we perform **anterolateral cordoctomy** *and here we also insert a needle which is usually an electrically activated needle we insert it from the lateral side to cut or eliminate the area that has the ALS pathway.* عشان هيك في ناس بتكوي الحبل الشوكي

spinocervicothalamic pathway:-

we said we have ALS pathway which transmits some of the modalities which are thermal pain and we have DCML pathway which transmits 2 point discrimination, proprioception and vibration. we have multi-module pathway and multi-synaptic pathway which is the spinocervicothalamic pathway. we have an afferent neuron would enter through the post. root ganglion it will synapse in the lamina which are 4 and 5 unlike ALS which goes to lamina 1 2 3 and the fiber will ascend with DCML in the post. fascicular up to the end of the spinal cord or the lower part of the medulla and there we have the cervical nucleus synapse there continue to the thalamus continue to the cortex, these pathways transmits multi-motor sometimes its responsible for pain when there is trauma to the ALS or recurrence of pain in people with lateral cordoctomy and that's why it's not like the post entry root (post root entry zone success rate is 90-80%)

Sensory pathways to the cerebellum:-

Until now most of the sensory pathways we talked about will ascend through thalamus, hypothalamus and brainstem. The thalamus usually ends in the cortex.

cerebellum has to do a lot with the regulation of motor pathways so it receives information from all parts of the body of all different sensations and the most imprtant. is the somatosensory modalities (mainly proprioception and cutaneous or external stimuli), we have 4 cerebellar tracts that will take the sensation to the cerebellam which are:-

1-Posterior Spinocerebellar Tract/ 2-Cuneocerebellar Tract/ 3-Anterior Spinocerebellar Tract /4-Rostral Spinocerebellar Tract .

case study:- (slide 13)

If we have trauma in the left area (for exp. lesion at C6) what will happen? what's the damage that will occur? which pathway will be affected?

It will interrupt the crossing fibers that's why the fibers of the decussating are the ones affected below C6 (only C7) so the ones above C6 and below C7 are normal ,The patient will have loss of ALS modalities (pain, temp, and crude touch) on one level below C6 which is C7.

1- Loss of dorsal column modalities on the same side(left)

2- loss of two point discrimination, proprioceptin and vibration

3-loss of pain, temp and crud touch on the opposite side(right side)

4-some loss of ALS modalities on the same side because of the decussated axons .

(if the lesion was at T10 it will cause loss of sensation DTML modalities below T10 on the same side, loss of ALS on the other side and on the same side complete loss of sensation)

This disease is a common disease called **syringomyelia**, it can be an enlargement in canal, but when it enlarges and includes the grey matter and affect the motor area it will be called syrnix.

P.S. syringomyelia and syrinx are different names depending on the size of the lesion so if its big and involving the motor it's called syrnix. But sometimes these two diff names indicate diff. origins weather from the central canal or from the spinal cord, but usually these two names are interchangeable.(most common syringomyelia –enlargement to the central canal)

somatotopic representation of ALS . lower >> lateral, upper >> medial. Somatotopic organization is really important during the pathway because its concerned with extramedullary or intramedullary .