CENTRAL NERVOUS SYSTEM

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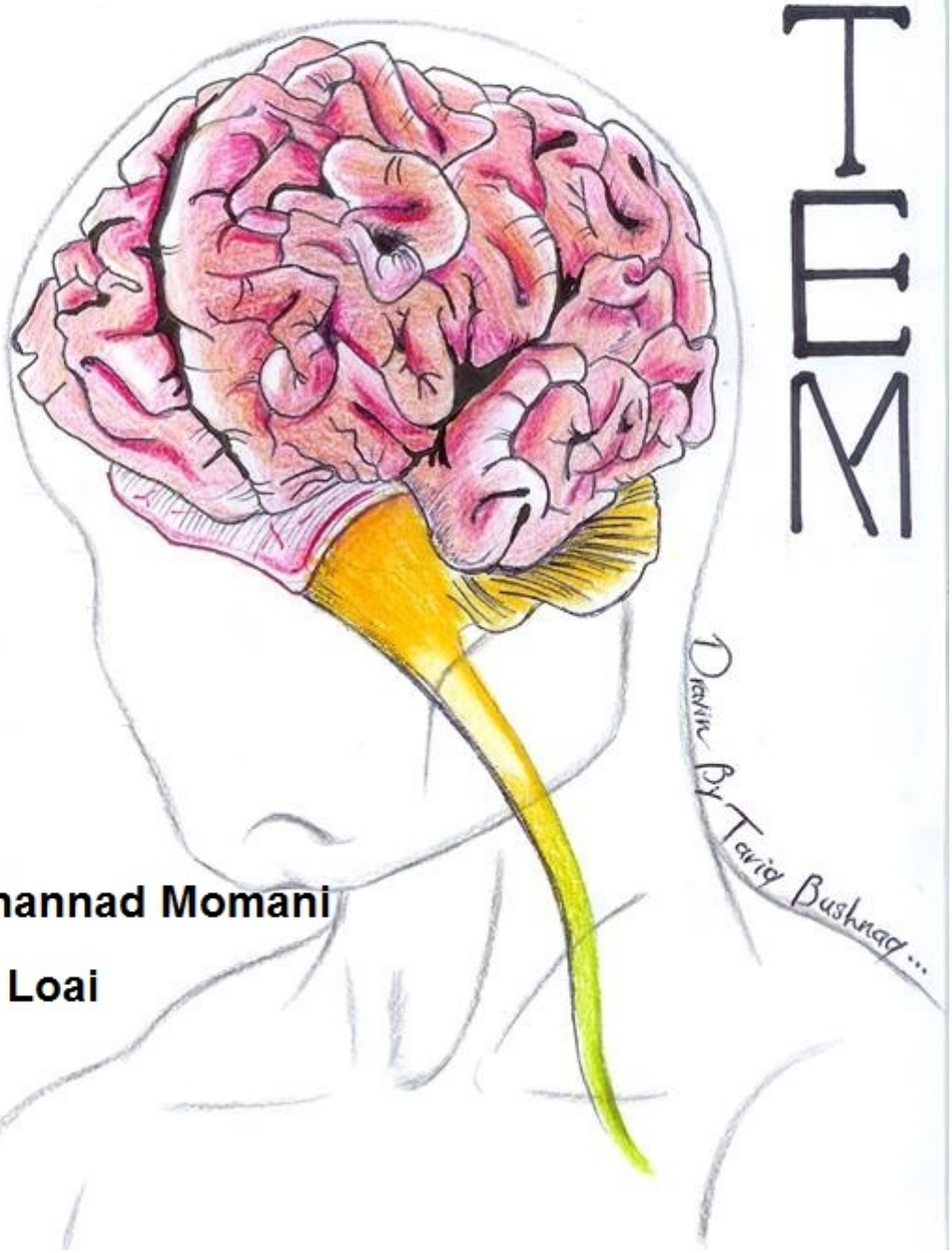

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Lec #: **5**

ANTEROLATERAL PATHWAY

•this sheet was done according to sec1, sec2and some info from pages 241-248

•This sheet needs 3 hours studying, if you finished it in less than that then you are awesome :D

♦Anterolateral pathway:

It's one of the many sensory pathways our body conducts to the cortex, it's very important that it's the one which is responsible for **non-discriminative touch, pain and thermal feelings**. It recognizes various stimuli by receptors which initiate the action potential along the pathway.

But first, let's discuss the pathway in details before discussing its importance.

1) It starts with **receptors** at the base of the dermis and epidermis connected to the **peripheral nervous system**

2) Then it continues to the **spinal cord** and **synapses in the posterior horn of the gray matter**directly upon entry**through the posterior root -**unlike the PCML pathway which doesn't synapse in the spinal cord - and then they'll cross to the other side to reach the anterolateral areain the white matter; from thereit'll continue its pathway upwards.

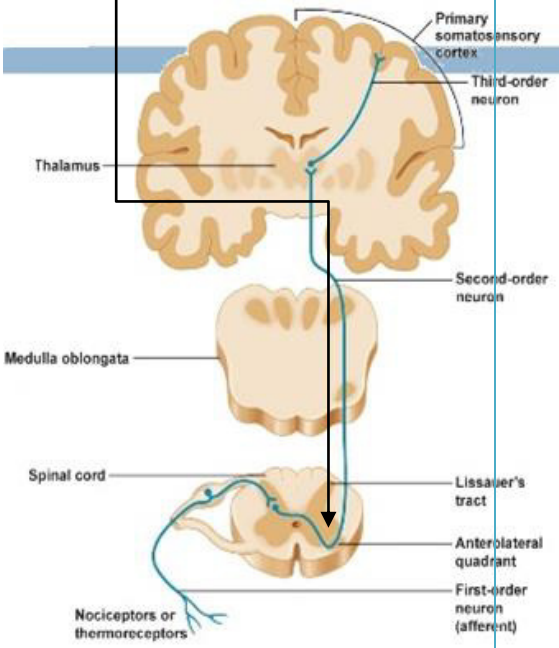
3) It ascends up in the spinal cord until it reaches the **brain stem.**

4) From the brain stem it continues to the **thalamus**, and from the thalamus it gives information to the **cortex**targeting the same somatosensory area, which is also targeted **by the PCML pathway.**

•At the level of the dorsal root ganglia you'll find the cell body of first order neurons.

•At the level of the spinal cord in the gray matter you'll find cell bodies of second order neurons (which are important in the reflex action).

•At the level of the thalamus you'll find cell bodies for third order neurons.



2. Anterolateral pathway

In this lecture we'll focus on pain and injuries.

♦pain

It's just an interpretation of specific information carried from "pain receptors" and processed in the cortex, so we need a receptor and a processing center to feel pain.

•Receptors; they are connected with afferent sensory fibers. They may be chemical, mechanical, (mechanicalwith facilitation of chemicals or thermal stimulation) or simply free nerve endings. So they are mainly chemicals, i.e.no chemical receptors, no pain.

•Chemicals are like; inflammatory mediators, metabolic debris…

•Unlike other somatic sensory receptors, for pain receptors,**adaptation will** make it **easier** for the receptor to be activated by other stimuli!Thishappens by **sensitization;**theyare a second messenger type receptors, so their activation will induce the expression of some genesor increasethe concentration of some proteins,or even change in the structure of receptors. Other type of sensitization is done by lowering the threshold of specific nerves.

Sometimessensitization can be so big that it may affect the surrounding area.

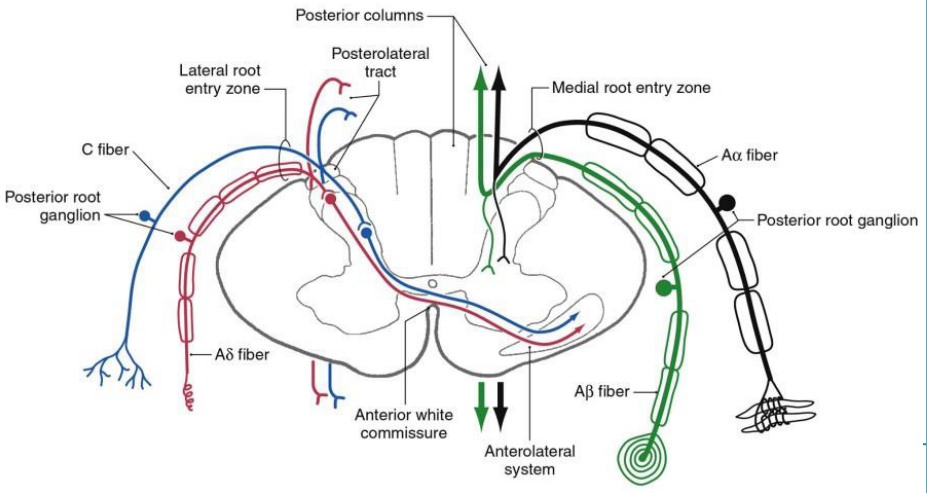
<Tenderness and **hyperalgesia**(which means increased sensitivity to pain) can be explained by this mechanism.>

♦injuries related to the anterolateral pathway

To understand the symptoms, first look at the following pictures and appreciate each part of it, so it'll be easier to know what will happen if any of them got damaged.

Here you can find the dorsal horn, dorsal root and the crossing area,

The anterolateral quadrant; is the area where the fibers continuetheir pathway after synapsing at the dorsal horn.



Dorsal root;which emerge from the spinal cord.

Crossing area, in this area, fibers in the right side will go to the left side and vice versa

- If theinjuredarea is onone side at the dorsal root or horn <before synapsing> the lesion will be ipsilateral
- If we injured the area in the spinal cord at the anterolateral quadrants or in the pathway in the spinal cord, the lesion will be contralateral
- If we injured the crossing area, then the lesionwill happen in both sides <the right & the left>
- If you injured the anterolateral quadrant or the ascending spinal pathway at the cervical levels, all the somatic sensation inferior to that region will be lost.

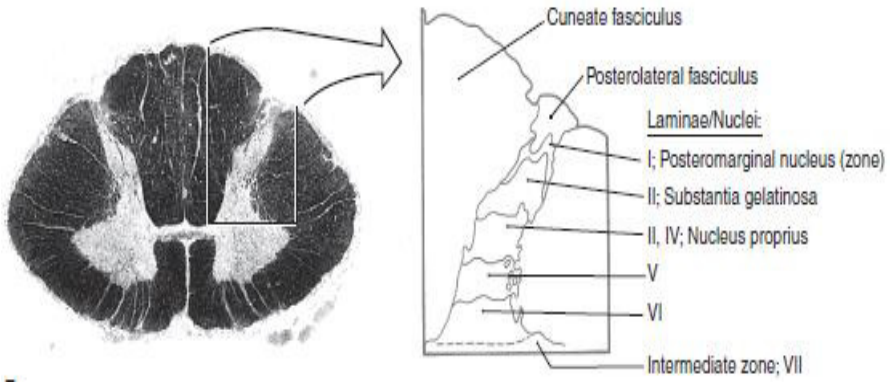
Don't forget to check the slides once available for the MRI pics

♦ **Gray matter** (a closer look)

The gray matter can be divided into10 laminas according to their histological appearance.

ALS modalities synapse mainly with the first 5 laminas. Painstimuli is carried mainly by lamina 1&2 (mainly **2**).

Now, as we took in histo, lamina is a cross section of a continuouscolumn in the spinal cord, so technically the information which isdelivered to lamina 2 will continue its tract upwardsin the column along with the spinal cord.



•So lamina 2, which carries pain information, will deliver said information to the cortex and the thalamus

•Some of these laminas are responsible for reflex action, that's why pain is not transmitted to the cortex instantly (relatively slow); because the spinal cord compensates with some functions like reflexes

•some of these laminas target the emotional centers of the cortex, subcortex and the reticular formation in the brain stem.

That's why the ALS or the spinothalmic pathway can be divided physiologically into; **neospinothalamic**tract (direct) and **paleospinothalamic**tract(indirect).

1)Neospinothalamic tract

Fast pain travels via type Aδ fibers to terminate in the dorsal horn of the spinal cord, where they synapse on dendrites of the **neospinothalamic tract**. The axons of these neurons cross the midline (decussate) **through the anterior white commissure (white matter of spinal cord) and ascend contralaterally along the anterolateral system**.

These fibersterminate on the **ventrobasal complex of the thalamus** and synapse with the **dendrites of the somatosensory cortex**directly through the thalamus.

And since it's going to the cortex; you're using the conscious part of the brain to localize the pain and know what's exactly causing it, and that's why you need Aδfor this job (faster)

2) paleospinothalamic tract

Slow pain is transmitted via slower type C fibers in a **multisynapticway**, to eventually reach the cortex directly or indirectly by going first to thesubcortex and then to the cortex. In the subcortex it may reach the reticular formation in the brainstem, hypothalamus,or a specific area for pain processing called Periaqueductal gray nucleus.

According to the book

> (These s**pinoreticularfibers** terminate in the brainstem reticular formation, which inturn projects to the medial thalamic nuclei. This medially organizedindirect pathway contributes to the perception of dull painsensations as well as to behavioral and motivational changes associatedwith nociceptive stimulation.).

As you can see from above,

> •C fibers connect high functional areas in the brain and thus helping in high functional action like behavior and emotions.
>
> •this pathway connects pain receptors to the cortex and the subcortex so they can not only process and analyze it but also regulate it and control it as we are going to discuss in the next section.

♣Pain transmission,regulation& injuries

In this section we are going to collect all what we've discussed earlier and fill all the missing gaps.

♦Pain transmission

Pain sensations can be carried on by 2 types of fiber bundles, **C type "for slow pain conduction"** and the small myelinated type **A delta** fibers or **Aδ fibers "for fast pain conduction"**

Aδfibers; also help in localizing the pain so you'll know exactly what to answer to "where does it hurt?" unlike type **C**

And as you know pain is not that important, that's why we have small myelinated type.*Correction: not sure about the "not that important" part*

Although the spinal cord is the one which is responsible for processing the pain and reflexes, but still!Every detail should be carried to the cortex to be aware of everything, and this is done by the **Neospinothalamic tract**discussed earlier.

But what is the importance of C unmyelinated fibers? I mean it's not like they can localize the pain now can they? NO!

- C fibers respond to stimuli which have stronger intensities and are the ones to account for the slow, but deeper pain and spread out over an unspecific area.
- <C fibers are considered polymodal because they can react to various stimuli. They react to stimuli that are thermal, or mechanical, or chemical in nature. C fibers respond to all kinds of physiological changes in the body. For example, they can respond to hypoxia, hypoglycemia, hypo-osmolarity, the presence of muscle metabolic products, and even light or sensitive touch>-wiki

But why can't they localize the pain? 2 reasons

- They have a slow response, thus they transmit delayed pain.

•they go through lots and lots of complex connections and synapsis in both the peripheral and the central nervous system, that's why it's hard for them to exactly localize the pain

♦Pain regulation

There is a regulation from parts of thesubcortex; which receive and processemotional stimuliin the brain, they send subcortical descending tracts,and can reduce or even eliminate the pain according to your emotional, conscious or level of activity status, like for example, when girls wear high heels they feel excruciating pain but still can tolerate it for the rest of the day!Because they are feeling happy and pretty wearing them XD

Same applies with males but with no high heels whatsoever, soccer players can be injured many times in the game but they can still go on till the end of it, because of their excitement during the match. Some people train these tracts to stop feeling pain, and that's why some of them can walk on fire for example without feeling a thing! You look at his feet and he has blisters however they feel no pain and can walk on fire.

•This inhibition happens by releasing some inhibitory neurotransmitters to some pain receptors like γ-aminobutyric acid **(GABA)** receptor, a **serotonin**(5-hydroxytryptamine) **receptor**, and a **mu opioid receptor**.

Also bydecreasing the activity of the receptor, or increasing the distance to the threshold.

Morphine drugs work on them as well, so information heading towards thecortex, subcortex and midbrain will be interrupted.

Interesting fact, emotional pain (directly not from peripheral nerves) can sensitize pain receptors and thus transmit actual pain stimulus to the cortex and subcortex

♦Injuries to the anterolateral pathway

Injuries to the **spinal posterior roots** will not only cause loss of sensation, the main complaintfor patients will be**sensory ataxia**

Sensoryataxia(loss of coordination) which is caused by aloss of sensory input to the movement center.So if you asked the patient to touch his nose for example, he'll start moving it in an unorganized way and eventually he may touch his cheeks instead.

But unfortunately, this is not the worst complaint; most patients suffer from**Deafferentation pain**

> -Patients with deafferentation pain usually display varying degrees of sensory loss characterized by disturbances in pain and temperature sensation. In addition to objective sensory loss, many patients also experience abnormal sensory phenomena such as allodynia, hyperalgesia, dysesthesias, and hyperpathia.

But why is that?

Neurons in the gray matter are always active because they have base line firing, after the lesion–when the receptors can't send information to these neurons- the cortex and the subcortex will start missing these signals, so they'll sensitize the

aforementioned cells causing them to be even more active, and causing higher amount of action potential to the cortex. This action potential will be interpreted as pain.Now despite the fact thatpatients can't feel their arm, it will hurt them.

Treating them is done by morphine and opioids, but patientscan develop tolerance, we have to increase dose and this leads to mood swings ☹

♦phantom limb

Phantom limb; is the sensation that an amputated or missing limb is still attached to the body and is moving appropriately with other body parts.

The following info is from wiki:

"Approximately 60 to 80% of individuals with an amputation experience phantom sensations in their amputated limb, and the majority of the sensations are painful. Phantom sensations may also occur after the removal of body parts other than the limbs, e.g. after amputation of the breast, extraction of a tooth (phantom tooth pain) or removal of an eye (phantom eye syndrome)

The missing limb often feels shorter and may feel as if it is in a distorted and painful position. Occasionally, the pain can be made worse by stress, anxiety, and weather changes." -wiki

Why? 2 reasons

- Because the second neurons are still intact and active. Their activation will give you the feeling that your hand is still there; you'll even feel it moving.
- Cortex plasticity: it's a characteristic of the cortex that doesn't exist in other parts of the CNS.

We said before that each part in the cortex has specific function and receives information from specific parts of the body. The cortex can preferentially allocate an area to represent the particular peripheral input sources that are proportionally most used, which leads to a change in shape and function.
-What happens here is that the specific area that was once responsible for the limb before the amputation is now less active or not active at all (no information is reaching this area), so the surrounding areas will try to give some of their work to it in order for it to keep working, as a result, you may hear the patient complaining from severe pain in his missing limb when someone hits him on his face.

♦thalamic syndrome

"Is a condition developed after a thalamic stroke, a stroke causing damage to the thalamus. Ischemic strokes and hemorrhagic strokes can cause lesioning in the thalamus." -wiki

All types of sensation (ALS and PCML) go to the thalamus before reaching the cortex. As you know the thalamus is part of the subcortical level which processes the pain and sensation then sends the processed information to the cortex. In this syndrome, the thalamus is damaged, so the cortex stops receiving any sort of information from the thalamus but the cortex is still active thus causes sensitization of the cells, and in the same principle applied in deafferentation pain a very big pain will result and this pain which results due to a lesion in the thalamus is called **thalamic syndrome**.

From wiki<Most often, thalamic syndrome causes an initial lack of sensation and tingling in the opposite side of the body. Weeks to months later, numbness can develop into severe and chronic pain that is not proportional to an environmental stimulus, called dysaesthesia or allodynia. As initial stroke symptoms, numbness and tingling, dissipate, an imbalance in sensation causes these later syndromes >

♦surgical treatment

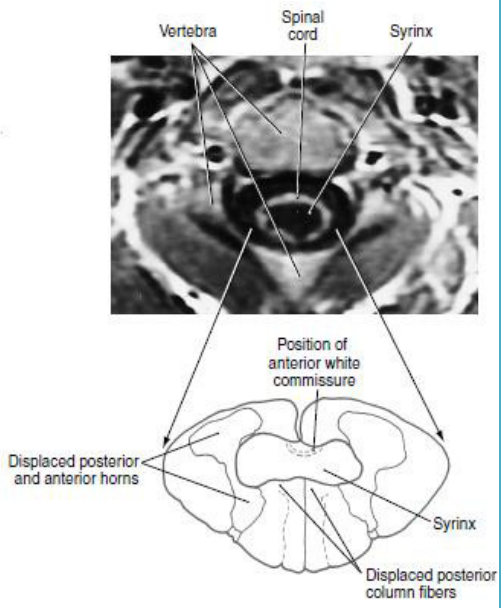
We said that deafferentation pain results from the absence of connection between laminae in the spinal cord thus we have continuous baseline firing. Because of the many side effects of the drugs used in pain management (such as morphine -the control of pain reduces with time-), some invasive procedures have been made to reduce and control the pain. Now these procedures are considered as a last resort treatment, because the patient has nothing more to lose. She/he would accept undergoing these procedures despite the risks. We'll mention 2 procedures:

• **Posterior root entry zone**: we said that the posterior root of spinal nerve will enter the spinal cord to the grey matter mainly to lamina (layer) I and II which are the main layers controlling painful sensation. In this procedure, you simply go to lamina 1&2 and chemically or thermally kill them → no base-line firing and thus the transmitted pain will be reduced. This is an easy, successful procedure but the problem is that the pain may come back because it'll be carried on by other laminas (lamina V). (Layers I, II and V receive most painful stimuli, in this procedure we kill layers I and II but layer V is still active thus sensitization and base-line firing occurs and cells in layer V are the ones responsible for the recurrence of pain.)

• **Anterolateral tractotomy**: a newer, more successful procedure. Surgery can cause damage to the tract itself. It's done chemically rather than thermally but the problem is that it may affect the surrounding areas if leakage of chemical happens. Despite the side effects, but it's okay because the pain will be stopped. This is done by injecting some toxic material in the spinal cord, but careful not to inject more toxins because you may paralyze the patient.

♣Here the doctor was showing us some clinical cases; unfortunately I don't have the slides so I took those pictures from Google and our book.

Case study 1:



This patient has damage at the crossing part within the cervical part of the spinal cord → both sides will be affected → loss of pain, thermal sensation, and crude touch over the shoulders and arms.

* Enlargement, inflammation, or tumor in the canal (or canal wall) → lead to syringomyelia→ which will cause damage of the crossing fibers and the previously mentioned symptoms.

This is called **cape syndrome**. Because the symptoms appear like someone's wearing a cape on his shoulders.

(The following paragraph is from the book but it explains what the doctor was talking about)

"This is Syringomyelia; a condition in which there is cystic cavitation of central regions of the spinal gray matter, may impinge on the anterior white commissure and decussating ALS fibers

•When it is located at the C4 to C5 levels of the spinalcord, this lesion produces bilateral loss of nondiscriminativetactile, nociceptive, and thermal sensations beginning severalsegments below the level where the fibers are interrupted. Thesymptoms present as sensory losses in the configuration of a capedraped over the shoulders and extending down to nipple level."

Somatotopic organization of the anterolateral system:
***In regards to the ALS, the lower most spinal levels (legs) comprise its outer most somatotopic layer, and the upper most spinal levels (arms) comprise the inner aspect.**

- More lateral: lower limb.

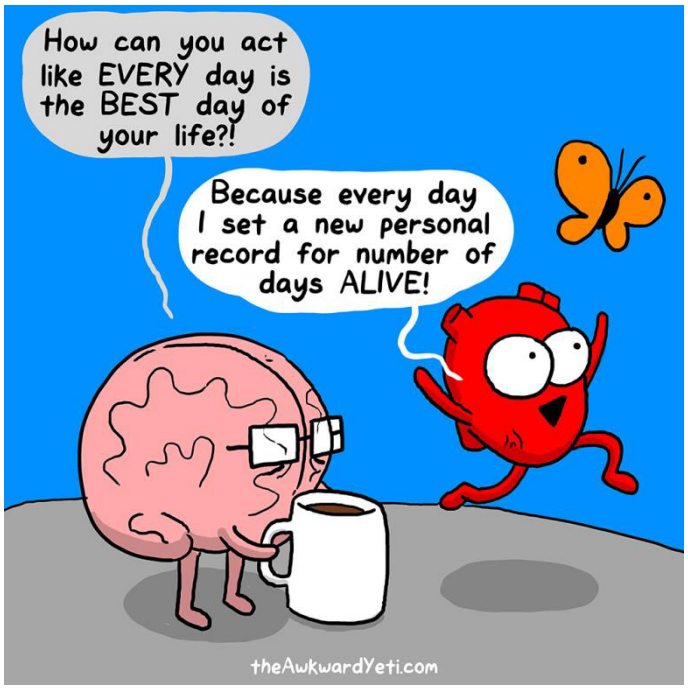
- More medial: upper limb.

Something pressing the spinal cord from lateral to medial will affect the lower limb, while from medial to lateral will affect the upper limb.

•The other clinical case is a repetition from the lecture.

End of the sheet,

Done by MohannedMomani and a special thanks goes to THE ONE AND ONLY TareqHalasehfor giving me his feedback and help in improving the sheet :D



I know we've already recided on what cover to choose, but this is my sheet and I'm gonna use my cover XD :P

University of Jordan - Faculty of Medicine (2013-19)

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- ☐ Biochemistry
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- ☐ Pharmacology
- ☐ Pathology
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☐ Slide ■ Sheet ☐ Handout ☐ Other

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