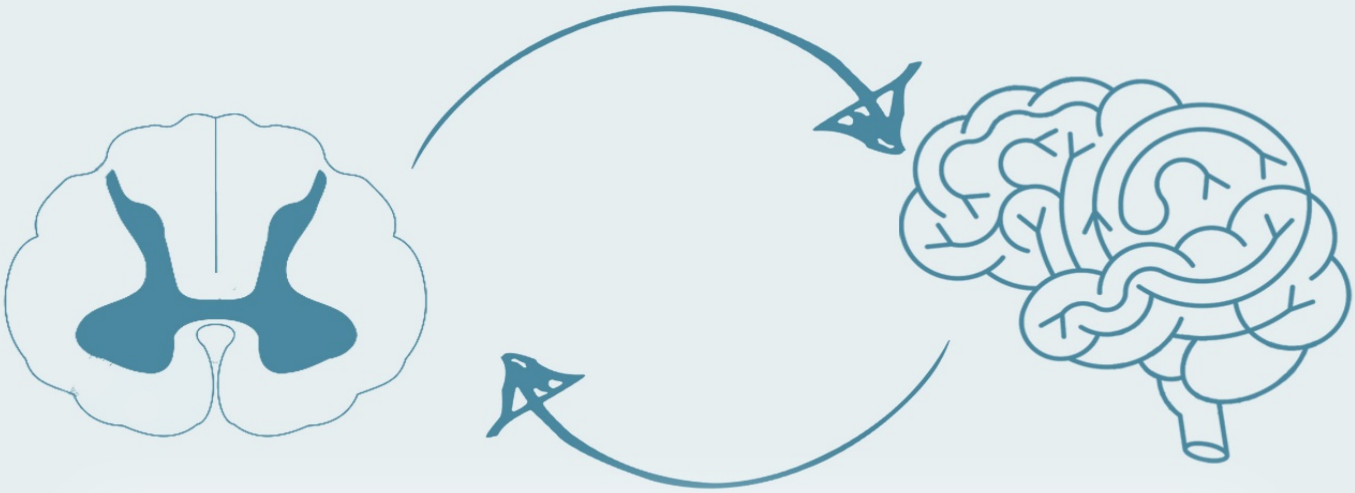


CNS

Anatomy

slides sheets

number 4

Done by Sondos Al Najjar

Correction Dina Dahabreh

Doctor Mohammad Al Salem

Just to know where we are now, in previous lectures we've started talking about sensory tracts that ascend up through the nervous system, you can have a look at this picture "not from the slide" at the end of this sheet, because we'll finish all the sensory tracts and next week we'll start with motor tracts.

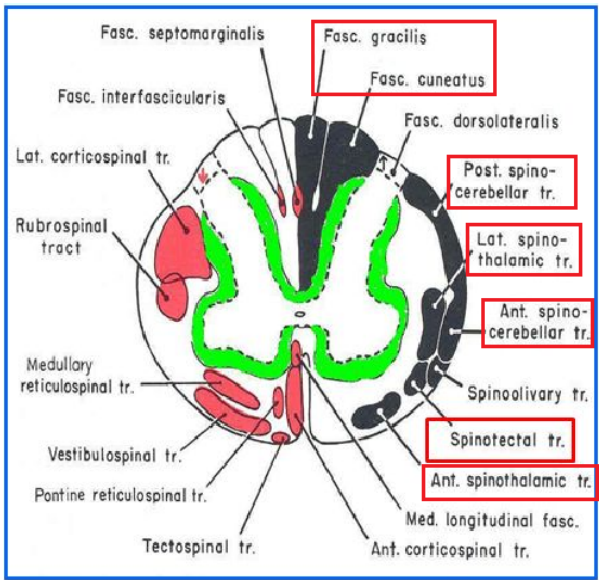
The sensory tracts are:

1- **Posterior white column- Medial leminiscal pathway**
"which is concerned in discriminative touch sensation including vibration and it ends in the primary somatosensory cortex"

2- **Spinothalamic tract**
a- Lateral spinothalamic
**Plus the posterolateral tract of Lissauer
b- Anterior spinothalamic

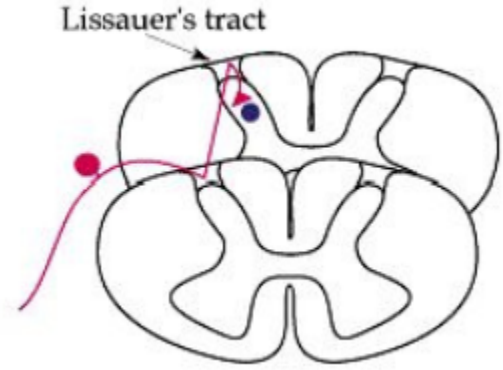
3- **Spinotectal tract**

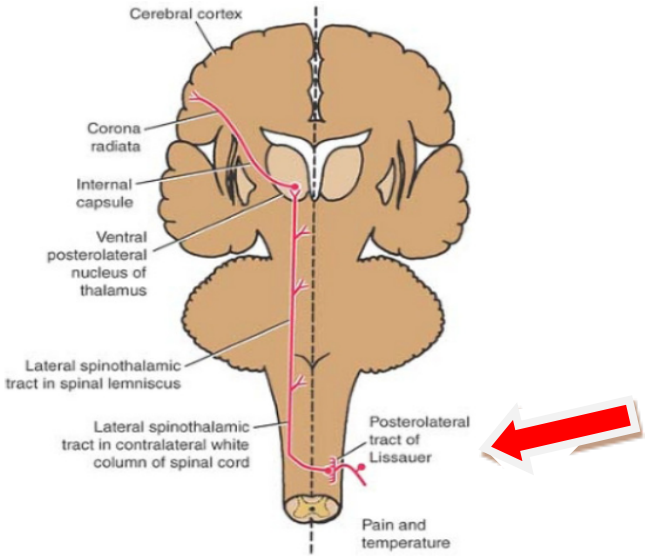
4- **Spinocerebellar tract**
a- Posterior spinocerebellar
b- Anterior spinocerebellar



We finished talking about the first one and parts of the second. We said that the lateral spinothalamic tract transmits pain with its two types (fast and slow) to different terminations. Fibers enter this tract through the dorsal root ganglia and synapse with the 2nd order neuron. When the 1st order neuron fibers enter the spinal cord it's not a must to synapse at the same level, it could synapse with the segment two levels above or two levels below and those fibers that ascend two levels above or descend two levels below create a local tract within the lateral spinothalamic tract which is called **Lissauer's tract "Posterolateral tract of Lissauer"**.

There is huge controversy about this tract in books; in Snell it is indicated as both the ascending and descending fibers while in physiology it is indicated as the ascending fibers only.





- Fast pain is transmitted through A-delta fibers (which are faster than C fibers) and travels the classical pathway (1st order neuron followed by the 2nd and then the 3rd which terminates in the cortex; that's why fast pain is localized.)

- Slow pain has more than one termination and they are the following:

  1- Reticular formation (spinoreticular tract):
  It's the most important one (majority of slow pain fibers), and as its name implies it's related to the reticular formation which is a network of neurons in the core of brain stem. It can be referred to as the conscious mind. So the fibers that ascend up activate the reticular formation and keep you alert of pain.

  2- Cingulate gyrus:
  It is seen from a medial view when a midsagittal section is taken, between the two hemispheres, deep to the longitudinal fissure, and it's a very important part of the limbic system, which is the emotional mind. And as a result of this termination, slow pain has an emotional component.

Pain is defined by the *International Association of the Studies of Pain* as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage."

** Keep in mind "the conditioned place aversion experiment" which is made of 3 compartments; X,Y and Z. X compartment is dark with a rough texture while Z is smooth with bright colors and finally Y is the neutral compartment. We put rats in compartment X and imply pain stimuli to educate them that this compartment is a bad one, opposite to that happens when the same rats are put in compartment Z; they are treated in a good way. They found that after putting the same rats in both X and Z sequentially the rats are now experienced and had the pain experience in compartment X, and when they're put in the neutral Y compartment they will automatically go to compartment Z. If the anterior cingulate gyrus (which is an important part of the limbic lobe) of these rats is removed or injured; the rats' ability to go to the pleasant compartment will be lost and they will now enter both compartments equally. In this case, the rats didn't lose the sensation of pain, only the memory/emotional experience of the pain is lost.
This is the emotional component of pain.

3- Insular gyrus:
It's a hidden part of the cortex located deep to the lateral fissure where you can find frontal and parietal lobes superiorly and temporal lobe inferiorly. It is concerned with the interpretation of pain stimuli from the internal organs of the body and brings about an autonomic response such as tachycardia and vomiting. For example, angina pectoris has an autonomic response to the pain.

- *Don't forget that the previous three terminations are for slow pain which is diffuse and only few fibers from the slow pain reach the cortex. This can explain the ability of feeling the pain even when part of the cortex is removed. You feel the pain at lower centers, this feeling is diffuse and you localize the pain at higher centers "cortex".*

Now we'll talk about the different aspects of pain including the two types of pain, classification of pain according to its origin, referred pain and pain control.

Pain classifications and some differences between them

Fast pain	Slow pain
Sharp, **pricking** "pin prick"	**Dull**, **burning**
A-delta fibers, thicker, more myelinated, fast	**C** fibers the smallest, smaller diameter and unmyelinated; the slowest
Short latency	**Slower onset**
Well localized (They reach the cortex)	**Diffuse** (They terminate in 3 different places)
Short duration	**Long duration**
Less emotional (doesn't reach cingulate gyrus)	**Emotional and autonomic responses**
Mostly from superficial structures (such as the skin mainly)	**Superficial and deep structures** such as the visceral pain (to be mentioned later)
Often named as **spinothalamic** (since it goes to the thalamus then cortex)	**Spinoreticular**
Tract cells = T cells = cells projecting upwards projecting from **lamina 1 and 5** in fast pain	T cells are projecting from **Lamina 1 and 2**
The 3rd order projecting neuron is from the **VPL nucleus** in the thalamus	**VPL** and **interlaminar nucleus**

Notes mentioned by the doctor:

- In the thalamus there is a complex called **Ventrobasal complex** which is composed of two nuclei; **(1) VPL** "ventral posterolateral nucleus" which is responsible for the whole body except head and neck and **(2) VPM** "ventral posteromedial nucleus" which is responsible for the trigeminothalamic tract.
- The thalamus has gray matter with lots of nuclei; these nuclei could be motor, sensory or **interlaminar** which have a connection with the reticular formation.
- Fast pain is good while slow pain is bad.
- Slow pain is not always from the viscera.
- Inflammation of the skin has an emotional component.

Pain according to origin

Pain is classified according to its origin into:

1- **Cutaneous pain** (from skin) and this pain could be fast or slow and transmitted through A-delta and C fibers, respectively.
Example: Skin inflammation

2- **Deep somatic pain** (from muscles, bones, joints and ligaments) and this pain is diffuse (not localized).
Example: Intermittent claudication which is muscle pain during exercise mainly in the muscles of the lower limb especially the calf (e.g. gastrocnemius) caused by peripheral artery disease in diabetic patients. In peripheral artery disease, the blood supply is not enough to remove the metabolites like lactic acid; in this case lactic acid will accumulate causing excitation of the pain. This sign is a very bad one which might progress to gangrene in diabetic patients.
**This pain is relieved at rest.*
**An experiment is made in which the peritoneum is injected with lactic acid and this causes an excitation of pain.*

3- **Visceral pain** (abdominal viscera, thoracic viscera, etc.)
It is poorly localized and is transmitted through C fibers. These C fibers have different types according to the exciting signal; chemoreceptors, baroreceptors, osmoreceptors and stretch receptors. Don't get confused, these fibers are different from those found on the skin, as they (visceral C fibers) are more sensitive towards stretching, chemical damage and ischemia.

Causes of visceral pain:

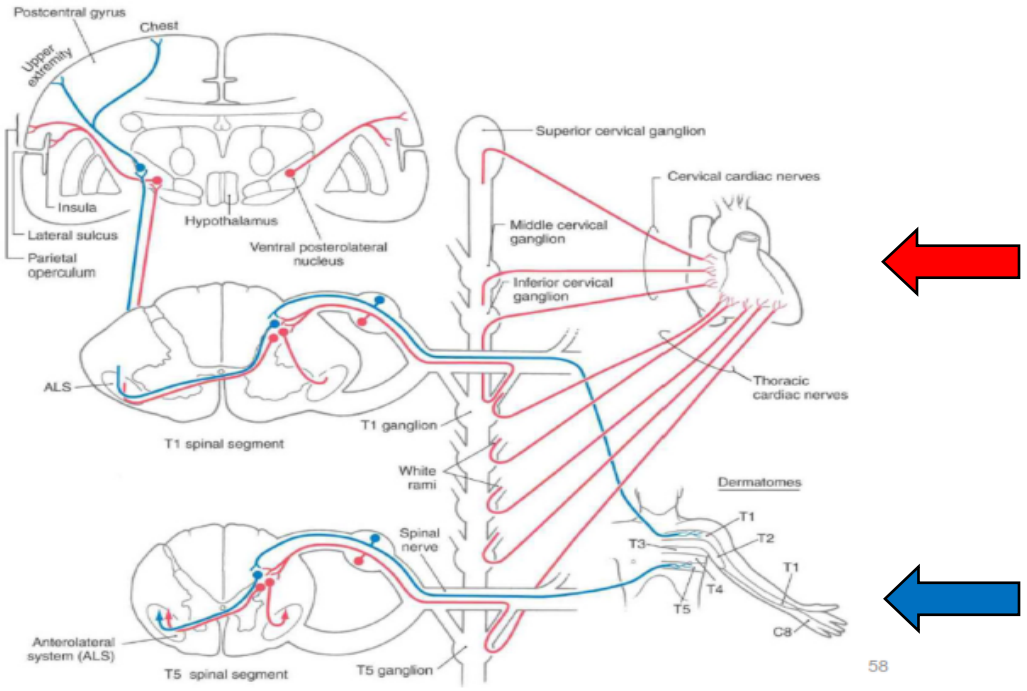
a- Distention of bladder and abdominal viscera (e.g. Irritable Bowel Syndrome IBS which leads to the accumulation of gases and thus visceral pain)
b- Ischemia (e.g. angina pectoris)
c- Spasm which leads to blood vessels compression and accumulation of metabolites
d- Chemical damage (e.g. peptic ulcer or duodenal ulcer which leads to perforation and chemical damage which in turn causes excitation of C fibers and thus visceral pain).

**A cut in the gut doesn't cause pain but in the skin will cause a sharp pain.*

**Visceral pain is often referred (sensed at a different site, far away from the origin of the pain).*

Referred Pain

The mechanism of referred pain // Convergence theory



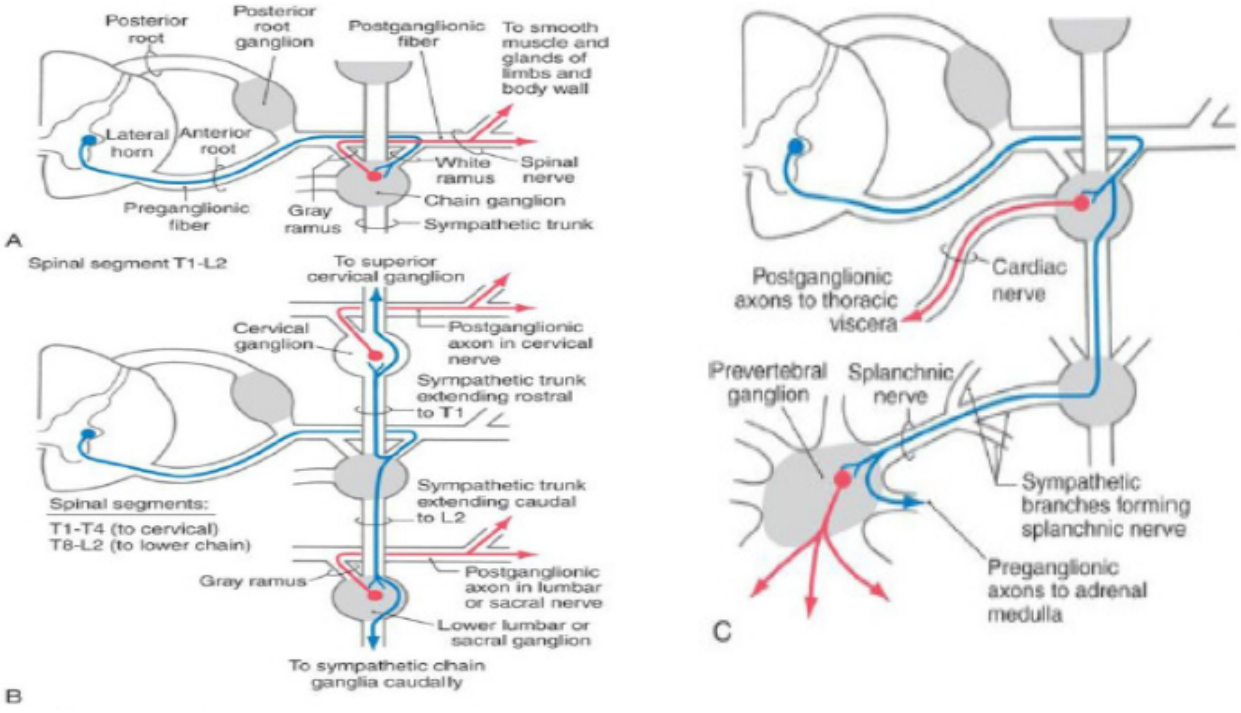
Please look at this picture where the viscera of the heart is seen above (upper red arrow). The C fibers travel to the dorsal root ganglia and synapse in the dorsal horn at a specific segment in the spinal cord. This segment also receives afferent sensory neurons from certain dermatomes (lower blue arrow). It happens that these C fibers and the afferent neurons might synapse with the same 2nd order neuron so the rest of the labelled line will be the same till they reach the cortex. And because visceral pain is very rare, the brain therefore interprets the information coming from visceral receptors as having arisen from receptors on the body surface, since this is where nociceptive stimuli originate more frequently, thus the pain from the viscera (heart for example) is referred to other places (left arm and shoulder in the example).

QUESTION: How did these C fibers reach the spinal cord from the heart in the first place?

They move with the distribution of the autonomic fibers within the same connective tissue component "epineurium" but don't forget that they are not efferent fibers (like sympathetic and parasympathetic), they are afferent fibers entering the spinal cord!

To understand more about the distribution of autonomic nerves see the following question.

QUESTION: Keeping in mind that the dorsal root is purely sensory and ventral root is motor while the sympathetic fibers arise from the lateral horns of T1 to L2, how do the rest of the spinal nerves receive their sympathetic fibers (since the lateral horn is only found from T1 to L2, how do the parotid or submandibular glands receive sympathetic while cranial nerves only contain parasympathetic)?

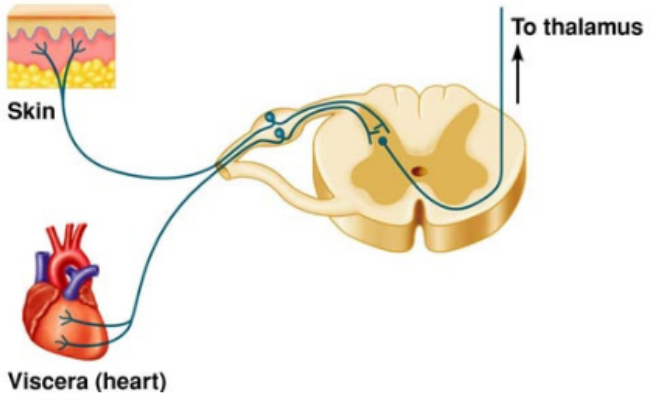


As you can see in picture (A) a fiber leaves from the lateral horn as a preganglionic fiber (Type B fiber/myelinated/white ramus communicans) and enters the sympathetic ganglia/paravertebral ganglia (located in the sympathetic chain). After this, it either synapses there at the same level as in picture (C) or it passes through the ganglia to synapse with higher or lower ganglia, picture (B). The postganglionic fiber is called (gray ramus communicans/unmyelinated/small/type C fiber).

By this way, all the spinal nerves receive sympathetic fibers and are thus called SMS (sensory, motor and sympathetic) and this can also explain how we have three cervical ganglia in order for the submandibular or parotid gland to take sympathetic fibers.

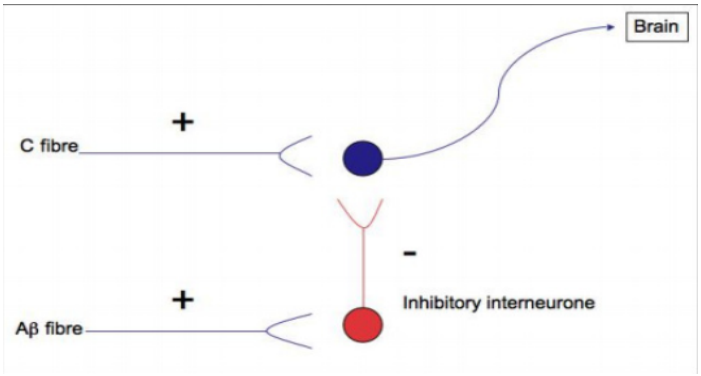
Examples of referred pain:

1- The pain of appendix "appendicitis" is sensed around the umbilicus/ T10 (referred to the umbilicus).
2- Gall bladder problems pain (GB stones for example) is referred to the shoulder. Phrenic nerve originates from C3-C5 and it's considered motor and sensory. Besides phrenic nerve, supraclavicular nerves which are sensory to the shoulder region originate from the same roots, C3-C5.
3- Angina pectoris pain is referred to the left arm and left shoulder. The C fibers from the heart (that have their cell bodies in the dorsal root ganglia) synapse with 2nd order neurons that ascend up until they reach the thalamus then insula where the autonomic response of the pain presents and symptoms like vomiting appear.



Pain control in the central nervous system

1- Gating Theory (Melzack's theory)



The C fibers of pain go and synapse in the dorsal horn and ascend up as 2nd order neurons. Other larger fibers such as A-beta fibers (responsible for touch) are found near them and they synapse with inhibitory interneurons that inhibit the 2nd order neuron of pain system.

So if an A-Beta fiber is stimulated by touch for example, "the gate is closed" inhibiting the pain.

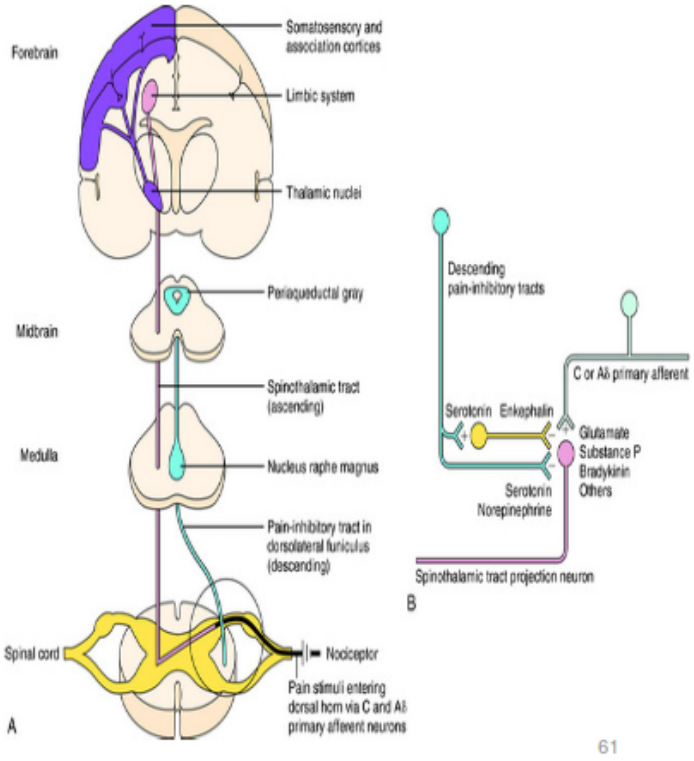
2- Descending control of pain (very important)

It's considered the CNS analgesic system to reduce pain. The spinoreticular fibers activate certain areas named **periaqueductal gray (PAG)**. Then, projecting neurons from PAG descend to the **Nucleus Raphe Magnus (NRM)** in medulla oblongata and activate NRM neurons which (after being activated) release serotonin. Serotonin activates inhibitory neurons in **Substantia Gelatinosa** (Lamina 2 or lamina 2 and 3 together) that secrete endorphins and enkephalins.

Locus Coeruleus is a nucleus near the facial colliculus and it's thought that this nucleus directly inhibits neurons in substantia gelatinosa.

Note 1: The cavity in the midbrain (cerebral aqueduct) connects the 3rd ventricle to the 4th ventricle. And the gray matter surrounding this cavity is called ***periaqueductal gray or central gray matter.***

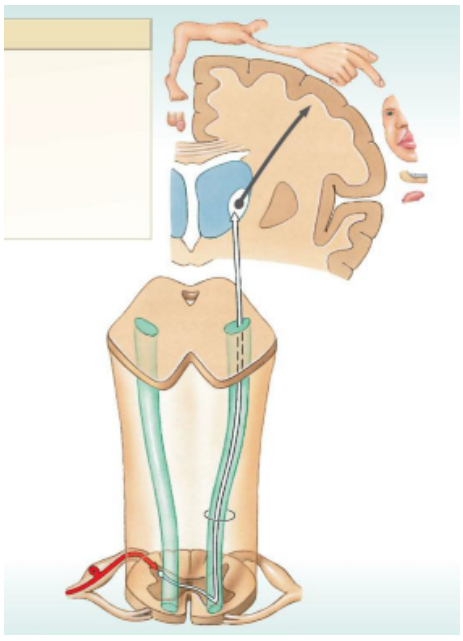
Note 2: Enkephalins and endorphins work on opioid receptors (like morphine which is a pain killer)



By now we've finished the lateral spinothalamic tract with more details about its modality (pain). We'll continue with sensory tracts now.

Anterior spinothalamic tract

The anterior spinothalamic tract is concerned with crude touch "not discriminative" and the pathway for this tract is simple and terminates in thalamic VPL and then the cortex.



Anterior spinothalamic tract with the lateral spinothalamic tract are called together anterolateral system or spinothalamic system. They are combined together in many references as there is huge overlap between both of them, but in our lectures the doctor discussed them individually and asked us to understand that there is always an overlap.

QUESTION: How do fibers ascend up in the nervous system (this is the idea of **lamination**)?

- Remember from the previous lecture that the cell bodies of the posterior white column-medial leminiscal pathway fibers are in the dorsal root ganglia. These fibers enter the posterior column system ipsilaterally (the same side) and they are arranged in a way that the lower fibers (sacral) will find a space and go most medial while the cervical ones will go most lateral. These fibers cross the midline later in the medulla.

- Medial leminiscus is made up of the posterior white column system.

- But fibers in spinothalamic system cross the midline early. First, they synapse at the dorsal horn and cross the midline through the white commissure. So the sacral fibers will be most lateral and the cervical will be most medial.

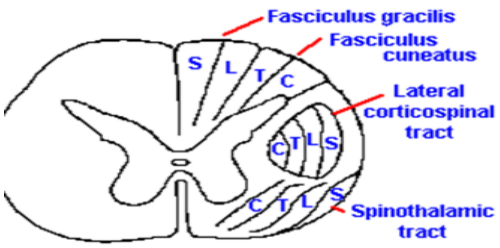
- Spinal leminiscus is made up from the anterior and lateral spinothalamic tract + the Spinotectal tract "will be mentioned at the end of this sheet"

QUESTION: Why do we care a lot about lamination?

Lamination is extremely important in tumors and in understanding their origins and symptoms. For example: in **intramedullary tumors** "tumors from inside" the medial fibers are most affected which are the cervical ones in spinothalamic tract and sacral fibers are least affected (**sacral sparing**).

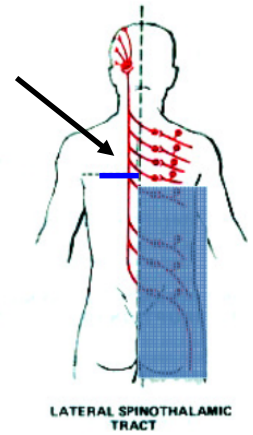
While in **extramedullary tumors** (originating from outside like meningioma), **sacral fibers** are the first to be **affected**.

**sacral sparing means that sacral fibers are least affected; so in this patient perineum is still sensitive (sacral).*



Clinical applications:

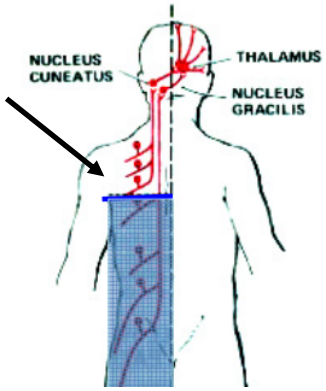
1- **Destruction of the lateral spinothalamic tract.**



A lesion on the left side at the level of T10 will lead to loss of pain and thermal sensation on the contralateral side (because the 2nd order neurons have already crossed the midline) below the level of the lesion (It's sensory).

**If we say the anterolateral spinothalamic we should also include the touch.*

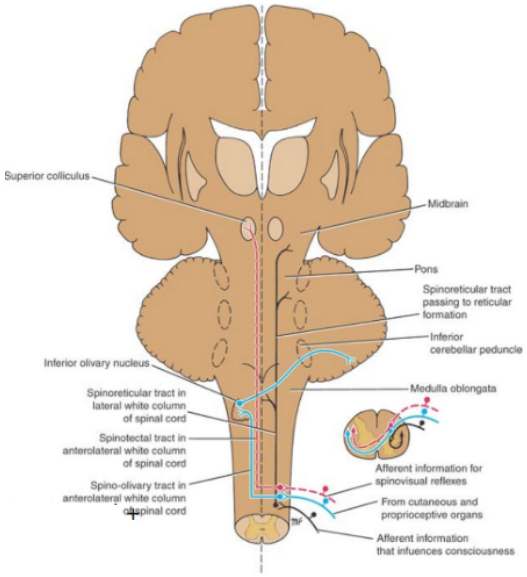
2- **Destruction of Posterior column system (Fasciculus Gracilia and Cuneatus)**



A lesion on the left side at the level of T10 will lead to loss of muscle joint sense, position sense, vibration sense and tactile discrimination on the same side (because the 2nd order neurons cross lately in the medulla) below the level of the lesion (It's sensory).

**It's very rare to find a pure sensory deficit, they are usually both motor and sensory.*

Spinotectal tract



- Brain stem is made of midbrain, pons and medulla
- The anterior part of midbrain is called tegmentum and its posterior part is called tectum
- Tectum is made of 4 masses/balls called **corpora quadrigemina**; *2 superior colliculi (important in visual system) and 2 inferior colliculi (related to auditory system).*
- Fibers/projections from superior colliculi continue to the lateral geniculate nucleus in the thalamus to continue its way to the occipital lobe in the cortex. "Superior brachium"
- Fibers from inferior colliculi continue to the medial geniculate nucleus in the thalamus to continue its way to the temporal lobe in the cortex. "Inferior brachium"

Spinotectal tract reaches the tectum of the midbrain and its main function is the **spinovisual reflex** which is the action of looking towards the stimulus.

If you remember the withdrawal effect which states that when a pin pricks your leg for example, you withdraw it. And also besides this withdrawal action, you look at your leg quickly which is the spinovisual reflex which passed by the superior colliculi.

**Again: in the medulla, the spinal leminiscus is made up from the spinotectal and anterolateral spinothalamic tracts.*

Spinocerebellar tract

As the name implies this tract doesn't reach the cortex, instead it terminates in the cerebellum. This tract can be divided into two parts: Posterior and Anterior.

1- Posterior/dorsal spinocerebellar tract

This tract is responsible for unconscious proprioception such as muscle spindles and joint capsules.
The 1st order neurons -that have their cell bodies in the dorsal root ganglia- enter the dorsal horn and synapse with 2nd order neurons in **lamina 7** which in turn go to cerebellum through inferior cerebellar peduncle to terminate at the cerebellar cortex.
From the root, the fibers ascend ipsilaterally and remain ipsilateral throughout the whole tract, so a lesion in the right side will lead to a problem in the right side. (Opposite to the cerebral tracts)

- Lamina 7 is also called Clarke's nucleus, nucleus dorsalis or posterior thoracic nucleus. *(Different names for the same area.)*

- Lamina 7 can be further divided into:
  a- Intermedio-lateral nucleus which contains the preganglionic fibers of the sympathetic (T1-L2).
  b- Intermedio-medial nucleus (all over the spinal cord) which receives visceral pain.
  c- Clarke's nucleus or dorsalis nucleus which is present at (C8-L2) or (T1-L4). So we can say that this nucleus isn't present below L3 or L4; thus fibers from lower parts must ascend up to reach it.

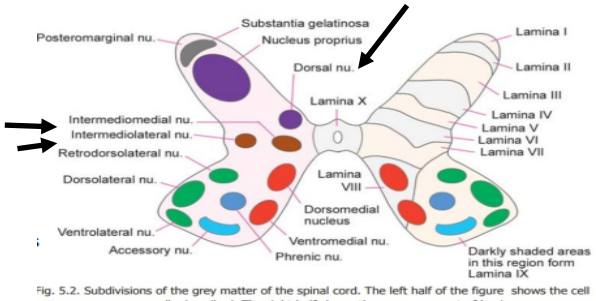


Fig. 5.2. Subdivisions of the grey matter of the spinal cord. The left half of the figure shows the cell groups usually described. The right half shows the newer concept of laminae.

- Cerebellar peduncles are collections of white matter facing the brain stem anteriorly and cerebellum posteriorly. There are three cerebellar peduncles (superior, middle and inferior):
  - Superior peduncle: In relation with midbrain.
  - Middle peduncle: In relation with pons.
  - Inferior peduncle: In relation with medulla oblongata.

- Fibers that enter the cerebellum are either climbing fibers or mossy fibers (the ones that enter through this tract here -> mossy).

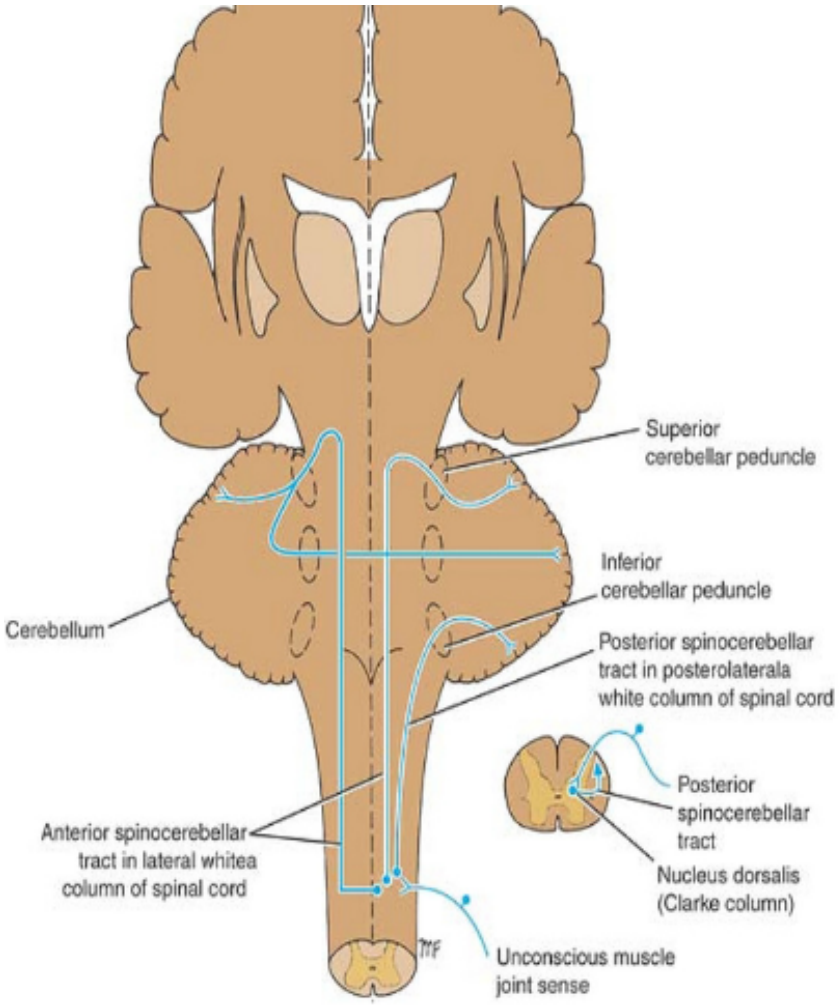
2- Anterior/ventral spinocerebellar tract

The fibers in this tract may follow one of these ways:

☞ **Minority of fibers:**
They follow a pathway very similar to the posterior spinocerebellar tract but they enter through superior cerebellar peduncle.
(The first order neuron enters the dorsal horn and synapses with a 2nd order neuron that leaves to the cerebellum).

☞ **Majority of fibers:**
The 1st order neuron synapses with a 2nd order neuron that ascends up contralaterally after crossing the midline. It then enters the cerebellum through the superior cerebellar peduncle of the opposite side. So the net result will be ipsilateral for all of the cerebellar tracts. (The fibers that crossed at the level of spinal cord cross back again within the cerebellum to return back to their side.)

**Note: they also give small branches to the opposite side (as you can see in the picture below) but mainly for the same side.*



A final small note: please don't skip the pictures as they are really useful.

"No act of kindness, no matter how small, is ever wasted"

GOOD LUCK