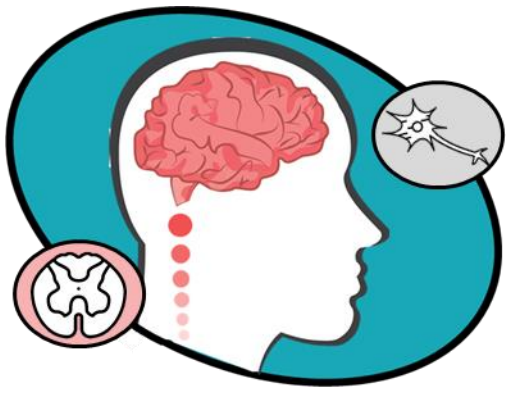

CNS

Anatomy

Sheet Slide

Number

11

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Quick revision:

Posterior White Column-Medial Lemniscal Pathway

- **Modality**:

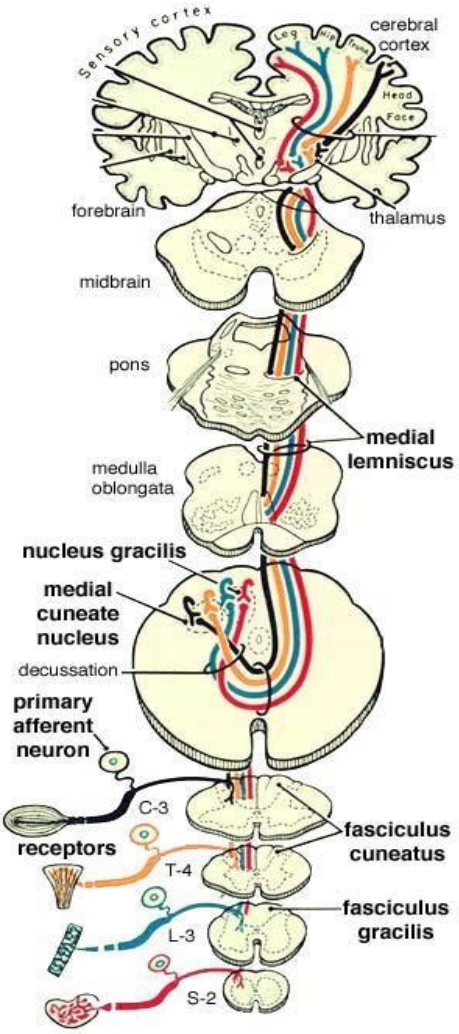
Discriminative (fine) touch and conscious proprioception.

- **Receptors**:

Most receptors expect free nerve endings.

- **1st order neurons:**

Dorsal root ganglion. Fibres will enter the posterior column which can be divided into two bundles: a medial bundle called ***fasciculus gracilis***, and a lateral one called ***fasciculus cuneatus***. Fibers will ascend ipsilaterally to the lower part of medulla oblangata where they synapse with second order neurons.



- **2nd order neurons**:

Dorsal column nuclei(which contain the cell bodies of the 2nd orderneurons). present at the lower border of medulla oblangata and named in a corresponding manner to the bundles: a medial nucleus called ***nucleus gracilis***, and a lateral one called ***nucleus cuneatus***.

Fibers of 2nd order neurons will cross the midline forming arched fibers called ***internal arcuate fibers***. Those fibers ascend, and in their way can be found close to the midline in a cross section forming a leminscus called ***Medial Leminscus***: white matter that ascends to the thalamus to synapse with third order neurons.

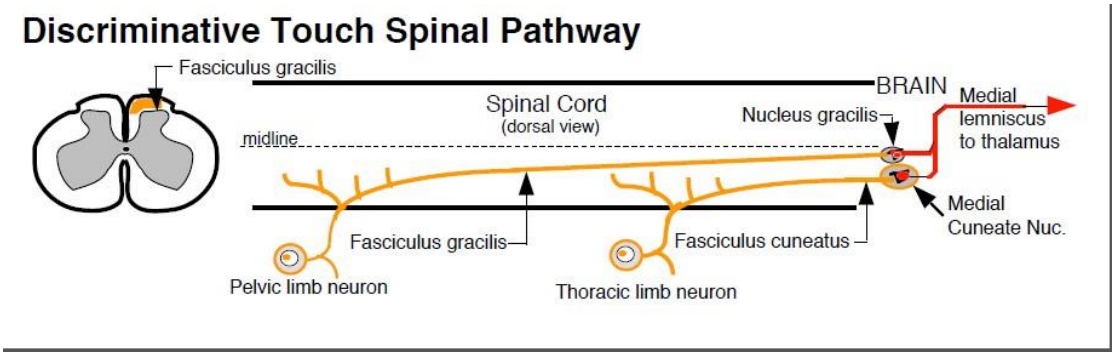
- **3rd order neurons**:

VPL nucleus in the thalamus. Then through the internal capsule (critical point between the thalamus and caudate medially and lentiform laterally), fibers ascend to the cortex.

- **Termination**:

Primary somethetic area (SI).

Fasciculus Gracilis vs fasciculus Cuneatus

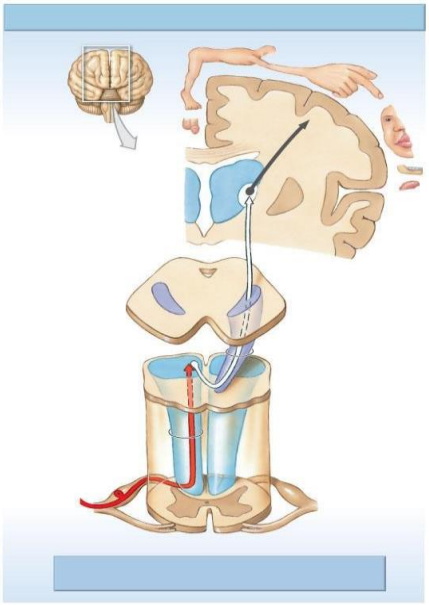


This section shows the spinal cord horizontally, with the lower center (spinal segment) at the left, higher center (brain) on the right and midline of the spinal cord represented as dotted line.

Fibers coming from the **lower** part of the body (pelvic limb for example) will enter the spinal cord, go to the most medial part and form **fasciculus gracilis**.

Fibers from the **upper** part of the body, particularly above the level of T6, occupy the lateral portion(as the medial part is already occupied) of the spinal cord and will together form **fasciculus cuneatus**.

As mentioned before, fibers from both bundles will ascend ipsilaterally reaching the lower part of medulla oblangata, they will then synapse with similarly named nuclei: nucleus gracilis (medially) and nucleus cuneatus (laterally). Fibers then cross the midline and form Medial Lemniscus, which then ascends to thalamus and from there to the cortex.



One last time:

(follow the figure) Fibers of posterior column-medial lemniscal pathway will enter the spinal cord through dorsal root, form fasciculus gracilis and fasciculus cuneatus and ascend ipsilaterally. Reaching lower part of medulla oblangata they will synapse with nucleus gracilis and nucleus cuneatus and cross the midline to form the Medial Lemniscus. Medial lemniscus will ascend to the thalamus, then through

the internal capsule the pathway terminates in the primary somatosensory area(area 3,1,2).

Fibers of the posterior white column:

ELECTROPHYSIOLOGIC CLASSIFICATION OF PERIPHERAL NERVES	CLASSIFICATION OF AFFERENT FIBERS ONLY (CLASS/GROUP)	FIBER DIAMETER (μm)	CONDUCTION VELOCITY (m/s)	RECEPTOR SUPPLIED
Sensory Fiber Type				
Aα	Ia and Ib	13-20	80-120	Primary muscle spindles, Golgi tendon organ
Aβ	II	6-12	35-75	Secondary muscle spindles, skin mechanoreceptors
Aδ	III	1-5	5-30	Skin mechanoreceptors, thermal receptors, and nociceptors
C	IV	0.2-1.5	0.5-2	Skin mechanoreceptors, thermal receptors, and nociceptors
Motor Fiber Type				
Aα	N/A	12-20	72-120	Extrafusal skeletal muscle fibers
Aγ	N/A	2-8	12-48	Intrafusal muscle fibers
B	N/A	1-3	6-18	Preganglionic autonomic fibers
C	N/A	0.2-2	0.5-2	Postganglionic autonomic fibers

The posterior column is responsible for muscle joint sense "conscious proprioception". This system employs mainly ***Aα and Aβ fibers***. Remember Aα is the biggest and the fastest (since it is myelinated), followed by Aβ, Aδ and finally C fibers.

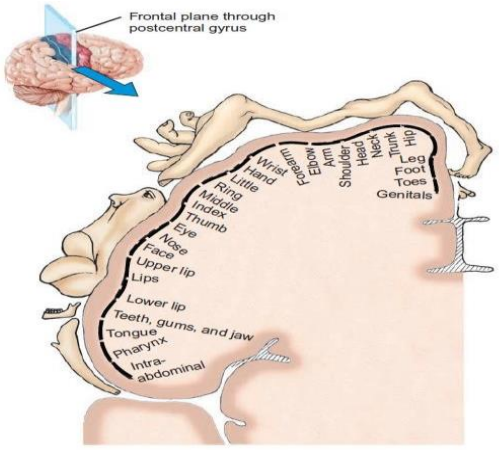
When we discuss the lateral column, we will see that it employs Aδ and C fibers, which are slower and transmit certain types of pain stimuli through thermal (temperature) and nociceptors.

By looking at which fibers each column employs, we can conclude that the posterior column is *faster and more well developed* than the lateral column (and by extension anterolateral column).

On the Homunculus

Sensory homunculus is a diagram that shows the representation of sensory input to the somatosensory cortex from different parts of the body.

Third order neurons from the thalamus will project onto a specific portion of the cortex to be represented on the primary somatosensory area, where the signal is localized and processed.



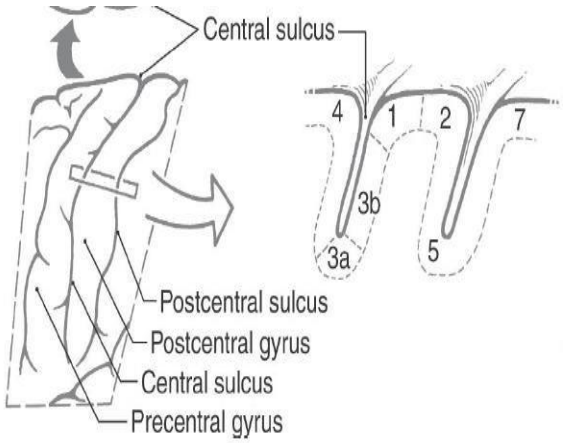
Look at the homunculus, at the region of the paracentral lobule where the foot and the leg are represented. At the lower lateral quadrant we find the head and neck (localization of the signal).

Primary somatosensory cortex (SI)

Anatomically it is the postcentral gyrus. According to Brodmann's classification it is areas 3(a+b).1.2 (anteriorly to posteriorly). This numbering comes as a result of the functional differences between these parts.

Each of these subdivisions represents and (receives signals) different receptors and so different modalities of sensation:

- Area 3a: muscle spindle afferents (mainly).
- Area 2: Golgi tendon organs and joint afferents (mainly).
- Areas 3b and 1: receptors of touch "Merkel cells", pain and temperature.



Notice how the labelled line theory is still applied here.

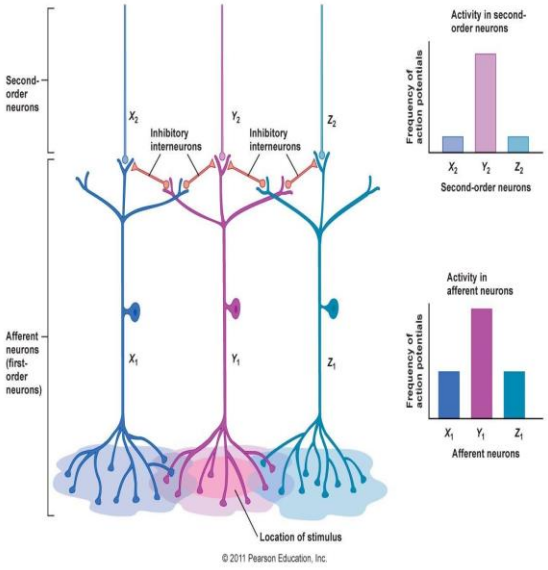
Lateral Inhibition

<u>To facilitate localization and sharpen contrast</u>, lateral inhibition occurs along the neuronal pathways. With lateral inhibition, each activated signal pathway inhibits the pathways next to it by stimulating **inhibitory interneurons** that pass laterally between ascending fibres serving neighbouring receptive fields.

For example: In a class room filled with students, instead of raising their voice (signal), a lecturer would silence students who talk to make his voice louder and clearer. The signal is not actually increased, but other annoying signals were dampened making it *relatively* greater. Same is applied to neurons.

Following this figure, we have first order neurons (X1,Y1,Z1) “primary afferent”, synapsing with second order neurons (X2,Y2,Z2).

Let’s assume Y1, which locates at the site of most intense stimulation, is activated to the greatest extent. And it is Surrounded by receptors that are also stimulated but to a lesser degree (Z1 and X1)(look to the lower left corner). To further sharpen this signal, Y1 will send collateral axons or **inhibitory interneurons** to the other two neurons to inhibit them and reduce their signalling (The most intensely activated receptor pathway halts transmission of impulses in the less intensely stimulated pathways through lateral inhibition. This process facilitates localization of the site of stimulation). (look to the upper left corner)



To further elaborate on this, look at the graph in the upper right corner of the figure and compare it to the one below it:

The activity (frequency of action potential) in Y2 is ***the same*** as the activity in Y1, while the activity in X2 and Z2 is significantly ***reduced*** by the action of the inhibitory interneurons. So, by decreasing the other two signals, we allow Y2 to ***appear*** greater without actually increasing it, resulting in a sharper Y2 signal and better signal resolution.

Lateral inhibition is of a particular importance in the posterior column pathway, since the pathway is responsible for discriminative (fine) touch which employs this principle.

Lateral Spinothalamic Tract

Note: There’s overlap between the lateral and anterior tracts, so it is possible to find them combined into a single anterolateral tract. However, we will be discussing both separately initially to better realize the different modalities of the two, as we find the lateral responsible for

pain and temperature, while the anterior tract responsible for crude touch.

- **Modality**:

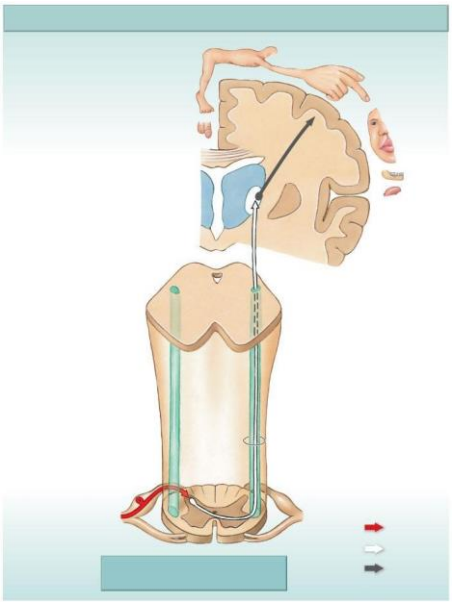
Pain (nociceptors) and temperature (thermoreceptors). There's correlation between the two as sometimes if heat exceeds a certain limit it can become painful.

- **Receptors**:

Free nerve endings. Remember that these receptors were excluded from the posterior column pathway.

- **1st order neurons**:

Dorsal root ganglia (remember it is purely sensory), they enter the spinal cord through the dorsal horn to synapse with second order neurons.



- **2nd order neurons**:

Remember that the dorsal horn is divided into 7 laminae, with 1 being the closest to the tip of the horn. The lateral spinothalamic system employs lamina 1,2 and 5. The need for different laminae instead of one is due to having different types of pain (fast and slow) transmitted in this tract (further discussed as we go).

Second order neurons are found in **substantia gelatinosa**, which is another name for lamina 2 and part of lamina 1. After synapsing with first order, second order neurons will cross the midline and pass the anterior commissure (it's important to know that these fibers cross it to understand the symptoms of spinal cord lesions when they're discussed), then ascend in the lateral white column to reach third order neurons in the thalamus.

Note the difference between the posterior column and lateral tract at this level: first order neurons in the posterior column ascends

ipsilaterally ***before*** synapsing with second order neurons(in the lower part of the medulla), while in the lateral tract first order synapses with second order ***then*** it crosses the midline and ascends.

- **3rd order neurons**:

VPL nucleus in the thalamus. through the internal capsule, third order neurons will project into the cortex.

- **Termination**:

Primary somethetic area (SI) and ***widespread cortical regions!***.

Rexed Laminae

This figure shows the grey matter of the spinal cord. Notice again how the dorsal horn is divided into 7 laminae, with 1 being at the tip. We will focus on laminae 1,2,5 and 7.

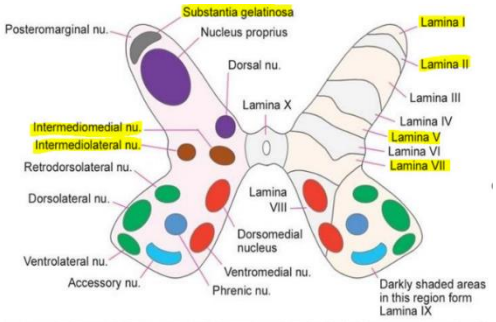


Fig. 5.2. Subdivisions of the grey matter of the spinal cord. The left half of the figure shows the cell groups usually described. The right half shows the newer concept of laminae.

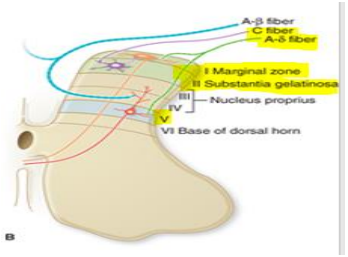
Laminae 1, 2 and 5 all rely information about pain, *crude* touch (as we will study in the anterior pathway in the next lecture) and temperature, and as mentioned before are employed by the lateral tract.

Lamina 7 is related to a type of pain called visceral pain. It is further divided into two nuclei: **intermedio-lateral nucleus**, which contains preganglionic fibers and is present in segments that have a lateral horn(T1-L2) (when the lateral horn is present it is part of lamina 7), and **intermedio-medial nucleus** which is present all over the spinal cord and receives C fibers carrying visceral pain.

Fibers of the lateral tract

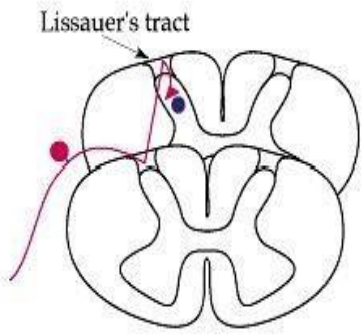
We said before that the lateral tract employs **Aδ and C fibers**, and they carry thermo and nociceptors signals. Each of these fibers will carry a certain type of pain and synapse within a certain lamina.

Aδ (the faster one) transmits **<u>fast pain</u>** and synapses in **laminae 1 and 5**. C fibers (unmyelinated, smallest, and the slowest) carry **<u>slow pain</u>** and synapse in laminae **1 and 2**. Note the figure below.



Posterolateral tract of Lissauer

We know that first order neurons synapse with second order neurons, however this doesn't have to be in the same segment. For example, first order neuronal axons could enter at the level of T2 but ascend and synapse in T1. In this case they will form a local tract behind the tip of the dorsal horn, this local tract is called **Lissauer's trac**t.



Lissauer's tract: a collection of fibers that ascend one or two segments and form a local tract behind the tip of the dorsal horn.

Other terminations of the Lateral Spinothalamic Tract

The lateral tract terminates in the primary somatosensory area where localization takes place, and in *<u>widespread cortical regions</u>*.

But what does that mean?

It means there're other sites of termination for the lateral tract. The reason for this is that the lateral tract transmits pain, and pain itself is a very complex sensory experience with many components.

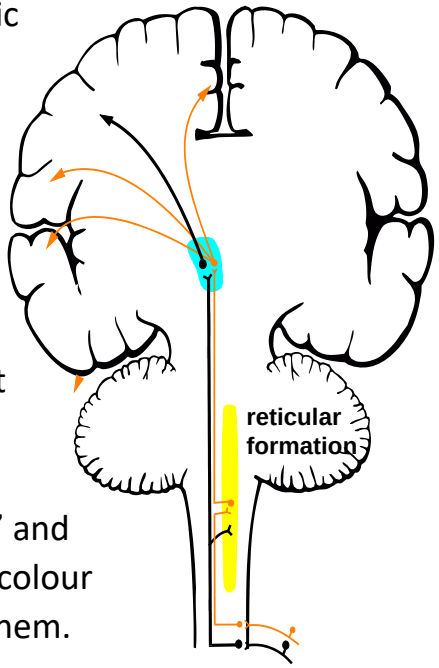
For example, you might find someone who has suffered chronic pain for years suffering from depression as a result of it, this indicates that pain has an ***emotional component***. In fact, according to the international association for the study of pain, which is the biggest association concerned with the research of pain, we define pain as: *<u>the emotional experience related to tissue damage or potential tissue damage</u>*.

In addition, pain also has an ***autonomic component***; we find some types of pain resulting in increased heart rate and sweating.

So, the experience of pain is due to the widespread cortical termination of its components.

These components are spread in different regions:

1- Cingulate gyrus:



Part of Papez circuit in the limbic system. The limbic system is also called *the emotional mind*, since it is responsible for emotions, consolidation and mechanisms of recent memory. Connection to the cingulate gyrus results in the emotional aspect of pain.

This is very important even in animals. In pain research, we can dissect the emotional component of pain in rats in an experiment called: condition-based aversion. In this experiment, we have three rooms: the one in the middle is the "neutral room" and the remaining two, each has a certain texture and colour and the rat will be exposed to different stimuli in them.

When the rat is placed in the right room for example, it will be exposed to a painful stimulus, an electrical shock or a painful injection, while in the left room it won't. After a while, if you place the rat in the neutral room and let it into a room of its choosing, the rat will go to the left and not the right, this is because it came to associate the right room with pain and will avoid it. This is the action of the cingulate gyrus.

If we remove the anterior cingulate gyrus and place the rat in the neutral room again, it may go to the right room. This is because its previous aversion to this room came from the emotional memory of pain associated with it, which was stored in and controlled by the cingulate gyrus that has been removed (no cingulate gyrus, no aversion). Note that pain SENSATION is still intact, if we inject the rat again it will feel pain normally. This indicates that cingulate gyrus has nothing to do with pain sensation itself but with the emotions associated with it.

2- Reticular formation:

Present in the core of the brain stem, it extends from medulla oblangata to the pons then to the midbrain in the median and lateral columns.

During sleep, if a dull sound is made, and despite the tympanic membrane vibrating and the vestibular system functioning normally, you don't wake up. This is because the cortex is "switched off". What switches it off is the reticular formation. The reticular formation is what keeps you aware and so it is called the conscious mind.

In turn, pain switches the reticular formation on and activates it. Ascending fibers of the lateral tract are excitatory to neurons of the reticular formation; when they excite the neurons, you become aware of pain. In addition to keeping you aware of pain, it also reminds you of it. This is why pain can wake you up at night sometimes; it activates the reticular formation which switches the cortex on waking you up from sleep.

Note: the question of whether your pain is waking you up from sleep is common in history taking and is associated with otitis media and toothache.

3- Insular gyrus:

The insula is found deep in the lateral fissure and has two roles: the autonomic response to pain (increasing the heart rate and sweating) and interpretation of visceral sensory information.

Pain classifications: slow vs fast

Fast pain:	Slow pain:
Related to initiation of injury, lasts for a few minutes (knife cut or a needle pinch)	Chronic pain, resulting from inflammatory conditions. A knife cut that get infected with bacteria and has edema, redness, tenderness and swelling. Lasts for 2-3 weeks.
Sharp, pin pricking	Dull, burning
(Aδ) fibers	(C) fibers
Short latency	Slower onset

Well localized (if you have a knife cut you know exactly where the pain is)	Diffused and poorly localized*
Short duration	Long duration
Less emotional	Emotional, autonomic response (chronic pain for years like cancer and osteoarthritis will affect the patient's emotional state more)
Mostly from superficial structures	Superficial (skin with an infection) and deep structures (viscera)
Spinothalamic: "classical" pathway where signal localizes in cortex.	Spinoreticular: named so because of the massive input into the reticular formation. Doesn't exclude it from reaching the cortex
Lamina I and V	Lamina I and II
VPL nucleus	VPL and intraluminal nucleus (for reticular formation)

Note on the table:

The reason why slow pain is diffused and poorly localized is due to the dermatomes involved and the connection between different order neurons in the fibers. When 1 first order neurons synapse with 1 second order neuron and so on, the signal reaching the cortex will be very precise. However, neurons that tend to diverge, where 1 first order neuron synapses with many second order will cause wide representation and stimulation on the cortex, leading the signal to be poorly localized. C fibers which carry slow pain follow this divergence and as a result slow pain is diffuse and poorly localized.

Pain according to origin

- **Cutaneous**: skin
- **Deep somatic**, for example**: intermittent claudication**: muscle pain due to blood supply to them being not enough to get rid of excess metabolites like lactic acid, this leads to their accumulation which results in pain. This is common in diabetic patients, since most of complications they suffer from (nephropathy, retinopathy, neuropathy) are due to problems with blood perfusion(the circulation can't git rid of the lactic acid which in

turn accumulates more and more). It is a bad sign for those patients as it indicates uncontrolled diabetes.

- Visceral: is a type of slow pain, comes from the viscera like those of abdomen and thorax. It is poorly localized and is transmitted via C fibers, as presented within the table.

Mechanisms of visceral pain differ from other types of pain; for example, cutting/slicing the patient's guts would not cause pain, unlike a similar cut in the skin that would. Ischemia, hypoxia and distention on the other hand can cause pain.

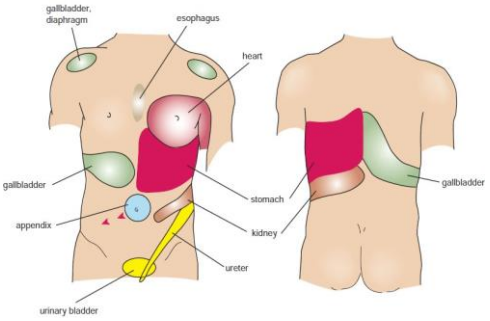
This is due to the C fibers carrying chemoreceptors, baroreceptors, osmoreceptors and stretch receptors. Which are sensitive to ischemia, stretching and chemical damage.

- some causes of visceral pain:
  - Destination of the bladder and abdominal viscera and IBS.
  - Spasm (lead to blood vessels compression and accumulation of metabolites): in the smooth muscle of ureter.
  - Chemical damage: HCl from perforated ulcers in the stomach.

Visceral pain is **often referred, what does that mean?!**.

Referred pain

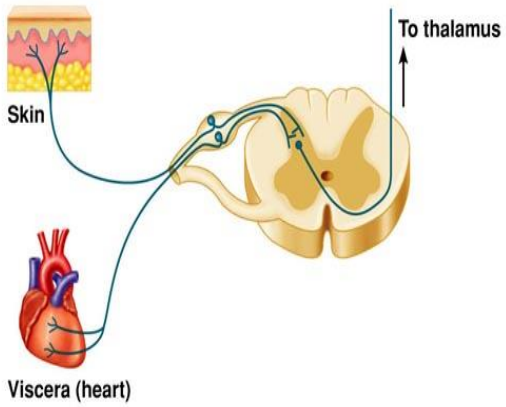
Referred pain is the pain that comes from one place but is felt at another. The most popular example of this is angina pectoris pain; problem is in the myocardium of the heart but is felt in the left arm and shoulder.



<u>Mechanism of referred pain:</u>

As we said, each spinal nerve carries sensory fibers from a particular region on the body surface called a **dermatome.** The body surface can be mapped with multiple dermatomes, each one associated with a different spinal nerve.

These same spinal nerves also carry fibers that branch off to supply internal organs, and sometimes pain originating from one of these organs is “referred” to the corresponding dermatome (surface region) supplied by the same spinal nerve.



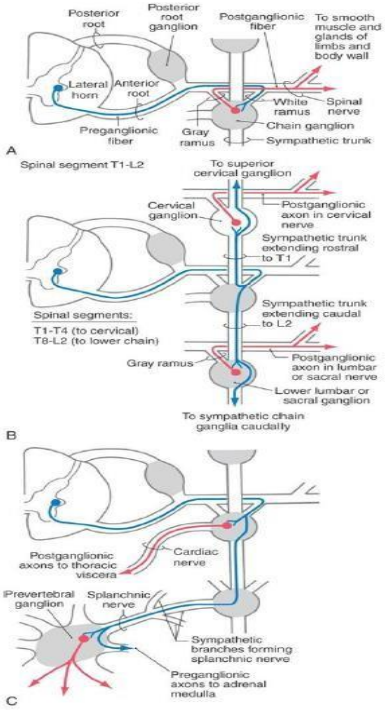
Sensory C fibers coming from the heart enter the spinal cord at the level of T1 (or T2) segment, these fibers then will synapse with second order neurons. This segment happens to be receiving sensory cutaneous fibers from the skin (remember the dermatome map), these fibers will also synapse with the same second order neuron that C fibers synapsed with. When the signal ascends up, the higher perception levels, being more habitual to receiving sensory input from the left arm than from the heart, may interpret the input from the heart as having arisen from the left arm. So, in the case of angina pectoris, it’ll tell you that the pain is from the shoulder, despite it coming from the heart to inform you there’s hypoxia in the myocardium. This is because both fibers activated the same second order neuron.

The location of referred pain is extremely important in clinical practice. One of the more unusual sites is the referred pain of the gallbladder (whose fundus lies on right costal cartilage); it is on the shoulders. The reason for this is the gallbladder is close to the peritoneum, so any irritation in it will also affect it. The peritoneum is supplied by the phrenic nerve (which also gives motor to diaphragm and sensory to pleura). The root values of phrenic nerve are C3, C4 and C5. Supraclavicular nerve that supplys the skin of the shoulders shares some of the phrenic nerve’s root value(C3 & C4).

How did C fibers reach the spinal cord from the heart? To know the answer of this question let's answer the following one before:

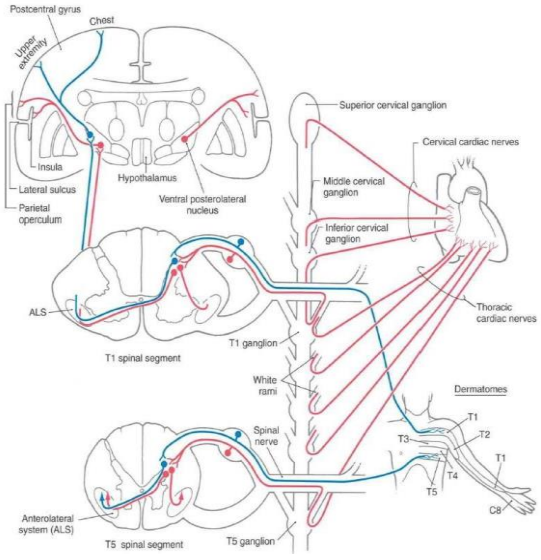
How do the the spinal nerves receive their sympathetic fibers?

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.



Cell bodies of preganglionic fibers are in the lateral horn of the spinal cord. These fibers leave through the **ventral root**, and through the white ramus communicans enter the sympathetic chain where they synapse. Postganglionic fibers exit the sympathetic chain through grey ramus communicans and reach the effector organs (smooth muscle, glands etc).

Know the answer of the first question is: "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(sensory) fibers entering the spinal cord".



So, if you cut the nerve after it leaves the sympathetic chain, you will see postganglionic fibers heading to the effector organ, and in the same place C fibers entering the CNS. These fibers will merely cross and will not influence each other at this level.

In the following figure, blue fibers are cutaneous from the sholuders while red fibers are visceral from the heart. Notice how the visceral fibers are merely crossing along the autonomic fibers. When they enter the CNS, they do so from the ***dorsal root***, further enforcing that they're sensory.

Again, first order neurons from both fibers (blue and red / cutaneous and visceral) will enter at the level of T1 and synapse with the same second order neuron, which then ascends to the cortex leading it to confuse the actual source of the pain.

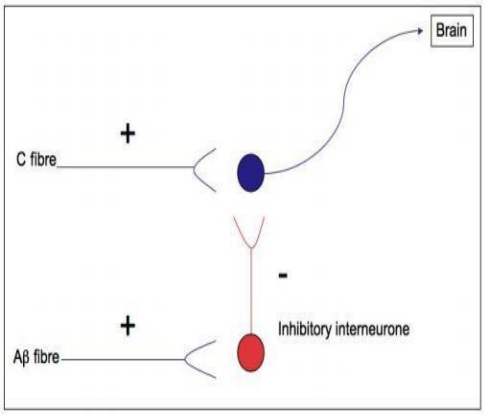
Pain control in the central nervous system

The gating theory

The gate theory of pain asserts that non-painful input(Aβ fibers - which are faster and carry mechanoreceptors, see below) closes the nerve "gates" to painful input(via C fibers), which prevents pain sensation from traveling to the central nervous system. Therefore, stimulation by non-noxious input is able to suppress pain. But how?

The mechanism is as follows:

When first order neurons C fibers are activated, they will activate second order neurons, which in turn will lead to the activation of the cortex and pain sensation.



But when Aβ fibers - which are faster and carry mechanoreceptors - are activated, they will activate **inhibitory interneurons**. These inhibitory interneurons will inhibit second order neurons of the pain pathway, preventing the signal from reaching the cortex and preventing pain sensation.

So, the gate here is actually the Aβ fibers: when they are inactive the gate is “opened”, and pain sensation is transmitted. When they are active inhibitory interneurons are active, which inhibit second order neurons “closing” the gate. No matter how much C fibers are activated, they will find opposition in activating second order neurons by the inhibitory interneurons, this is what “closes” the gate and prevents pain sensation.

The End