CENTRAL NERVOUS SYSTEM

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- ○ Anatomy
- ● Physiology
- ○ Pathology
- ○ Biochemistry
- ○ Microbiology
- ○ Pharmacology
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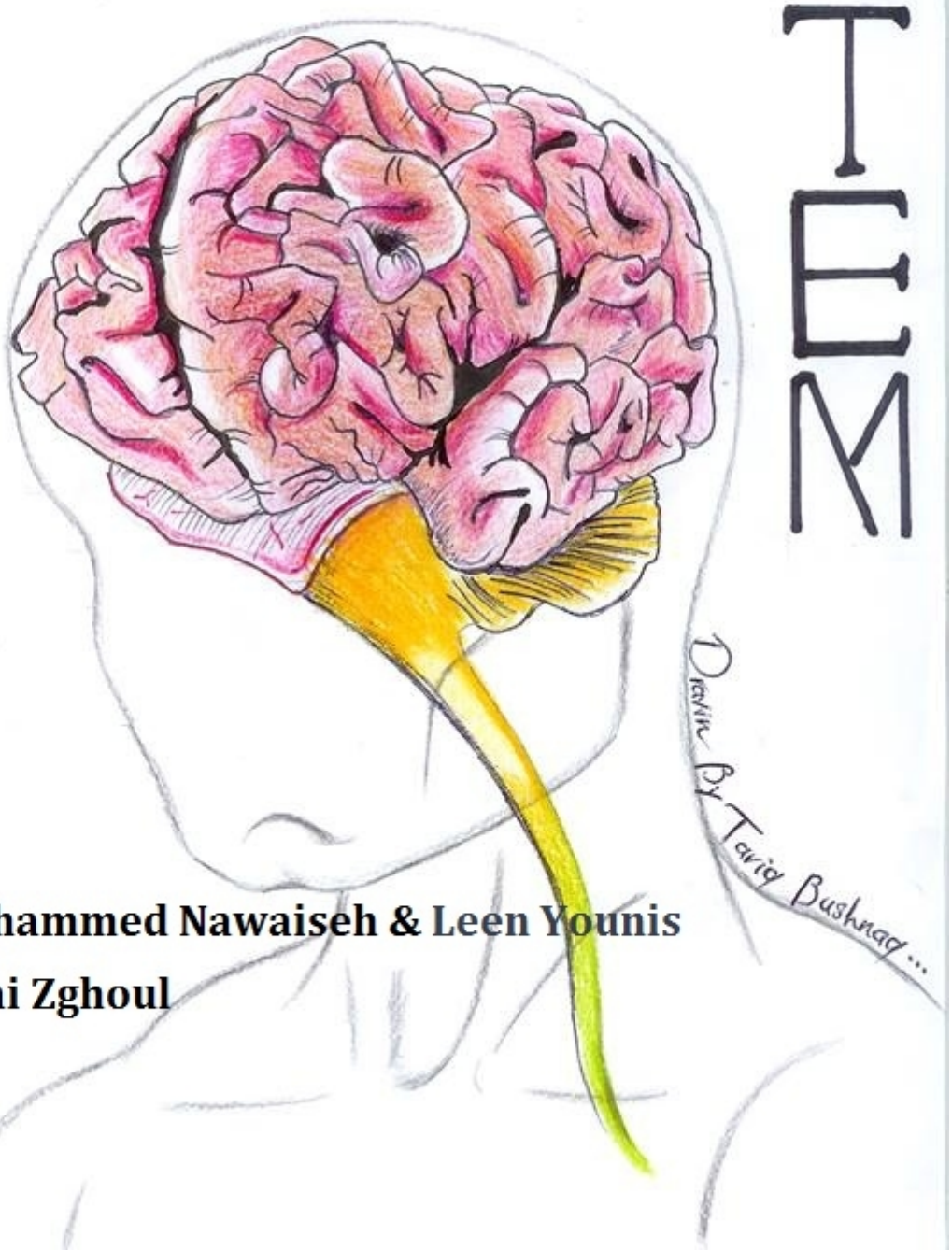

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Lec #: **4**

Physiology of the sensory system

#The DR said that you can study this subject from"Fundamental Neuroscience for Basic and Clinical Applications, Ch 17 {The Somatosensory System I: Tactile Discrimination and Position Sense} + Ch18 {The Somatosensory System II: Nociception, Thermal Sense, and Touch}" or from "guyton, Ch 46+47+48".

I .Discriminative touch

Clinically, there is no such thing called touch; because touch is complex and can't be recognized from pressure, itching or rubbing .So, clinically, it's called discriminative touch (Two -point discrimination).

Fine touch (**Discriminative touch** or **Two-point discrimination**) is a sensory modality which allows a subject to sense and localize touch. In which, if two stimuli were put on the skin at certain distance between them, will the sensory system recognize them as two stimuli and know the distance between them?

The posterior column-medial lemniscus pathway is the pathway responsible for sending of fine touch information to the cerebral cortex of the brain.

The form of touch where localization is not possible is known as **crude touch** (or **non-discriminative touch**) is a sensory modality which allows the subject to sense that something has touched them, without being able to localize where they were touched (contrasting "fine touch"). Its fibers are carried in the spinothalamic tract, unlike the fine touch which is carried in the dorsal column.

Two points discrimination depends mainly on two factors:

1) Receptor density (Number of receptors / area)

The receptive field of a neuron or a receptor is the area in which stimulation leads to response of a particular neuron.

IF the number of the receptors increase or the area decreases, the density will increase → increasing the ability of 2 points discrimination.

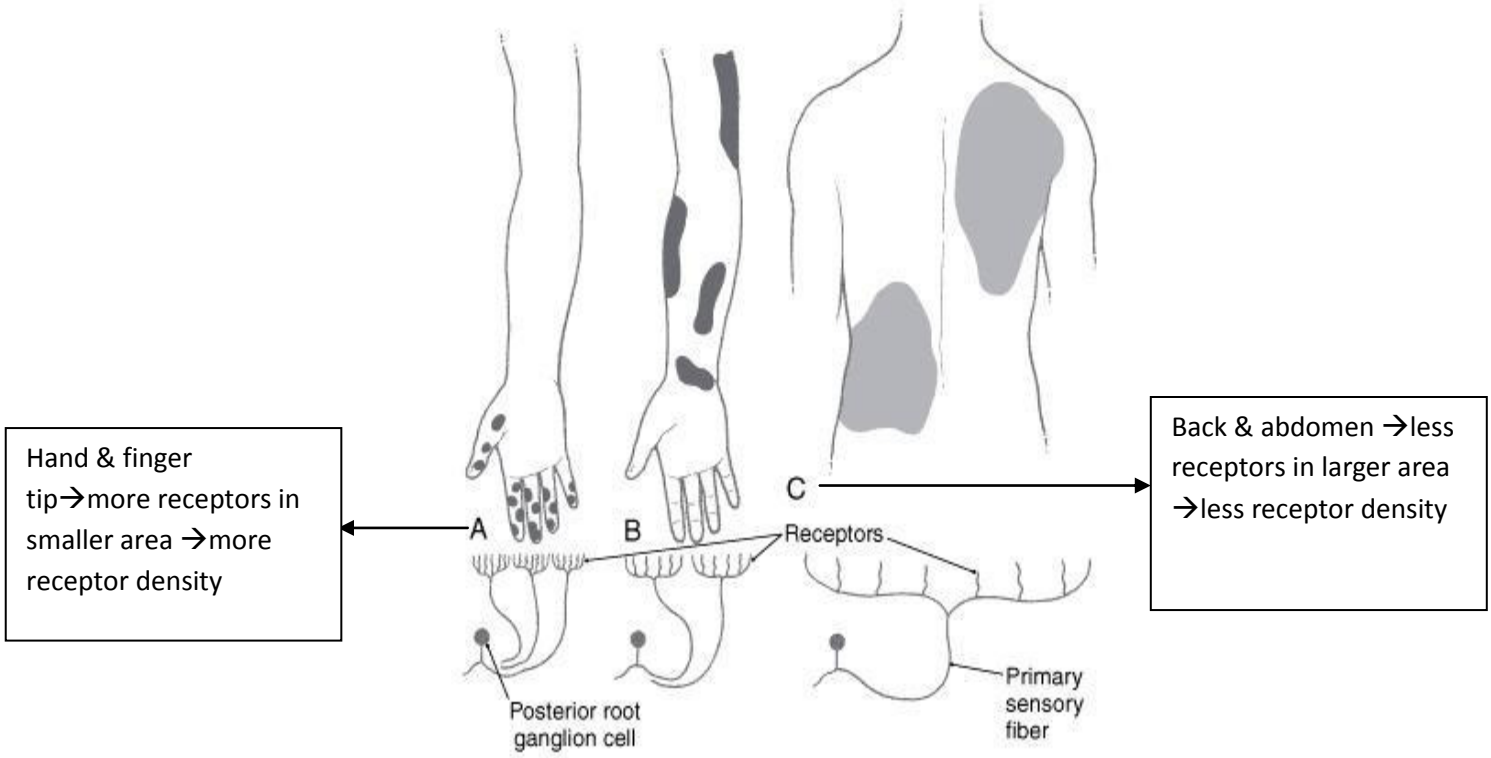
Number of receptors (**Receptor density**) in an area (receptive field) determines the ability for Two points discrimination. The smaller the receptive field, the more accurate the representation.

#If we have a neuron supplying the whole hand , it will be activated wherever we touch the hand , but if we have a neuron restricted to the tip of the finger , it will be only activated in that area. This allows a greater discrimination in sensory inputs. (The accuracy is inversely proportional with the Receptive area for that nerve).

Receptor density; Hand, fingertip and feet (**highest**) →Arms→back and abdomen **(lowest).**

Receptive field; Hand, fingertip and feet (**lowest**) →Arms→back and abdomen **(highest).**

Two-point discrimination; Hand, fingertip and feet (**highest**) →Arms→back and abdomen **(lowest).**



2) Pathway arrangement (design of pathway):

A) Conversion: many neurons make synapse on one neuron that usually goes to the brain.
(Many neurons →One neuron) {**Decrease** Two-point discrimination}

B) Diversion: one neuron synapse with many neurons.
(One neuron → Many neurons) {**Enhance** Two-point discrimination}

#When the pathway is more linear and there is no overlap between receptors (receptors don't affect nearby pathways) → **enhance** Two-point discrimination

#If there is convergence, the signal reaches the brain as one signal and there is no discrimination between the two signals, but if there is no convergence, we can differentiate between the two signals.

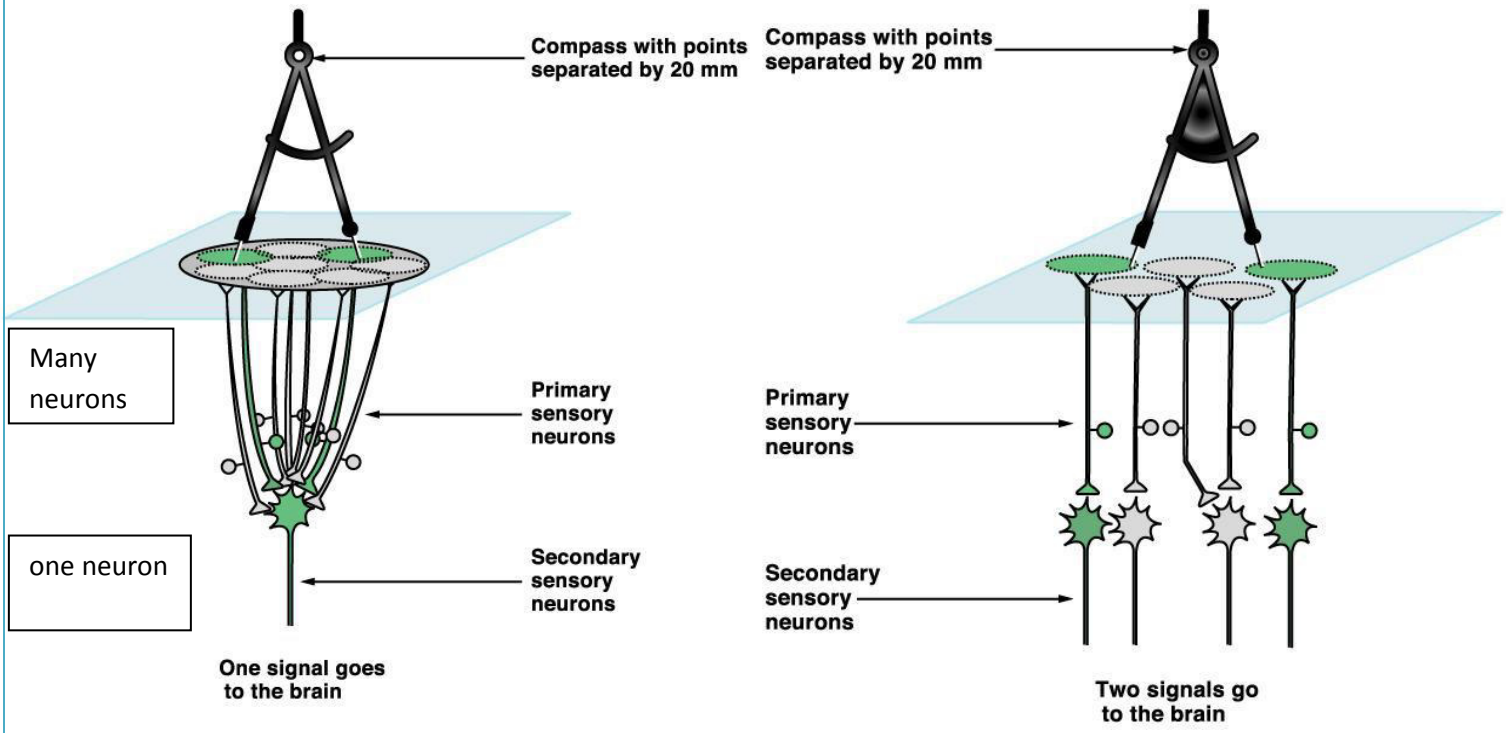
C) Lateral inhibition: This is the process by which neurons inhibits signals from nearby neurons via an intermediate neuron in the CNS. {**Enhance** Two-point discrimination}

Ex: when 2 neurons are activated, but one of them is activated more, it will inhibit the other one.

This enhances the difference between strong signals (at the point of the stimulus) and weaker signals (generated nearby the stimulus), thus the body can pinpoint more exactly where the stimulus is coming from). So, the acuity of two-point discrimination is improved by lateral inhibition.

Conversion (many neurons→one neuron) →one signal goes to the brain →no Two-point discrimination

No Conversion →two signals go to the brain →enhance Two-point discrimination



II .Sensations modalities

There are 6 types of sensations (somato-sensory inputs from the body; muscle, skin and others).

A) Fast and transmitted **by** Posterior Column-Medial lemniscus Pathway **(PCML)**

1) Two-point discrimination and pressure.
2) Vibration.
3) Proprioception (muscle length and tension, joint position and their motion).

B) Slow and transmitted **by** Antero-lateral system **(ALS)** {Spinothalamic pathway}

4) Crud touch (itch & rub)
5) Temperature
6) Pain

#The first three are conducted fast and through the PCML to the cortex and cerebellum because they are critical and important to the brain. The second group (4+5+6) are less important (not critical for the brain), so they are conducted in a slower fashion and through ALS to the spinal cord, brain stem and sub-cortical region of the brain.

III .Somatosensory Pathways

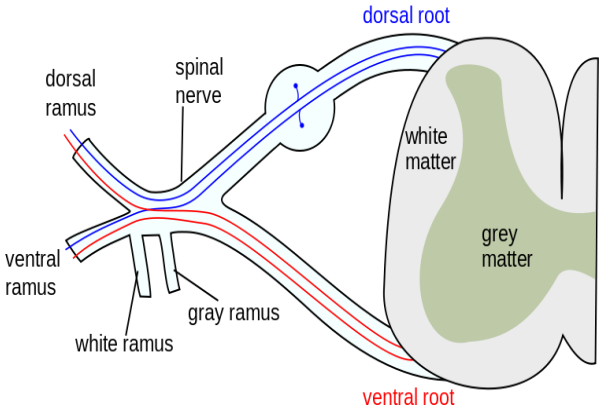
There are two pathways for transmission of somatosensory information to the CNS: the Posterior Column-Medial lemniscus Pathway (**PCML**, dorsal column system) and the anterolateral or spinothalamic system **(ALS).**

As the PCML is the fast pathway and ALS is the slow pathway, so there is a delay in the ALS pathway. Because both of them have 3 neurons (1^{st} ,2^{nd},3^{rd} order neurons), the delay is not due to the synapses between those neurons as they are the same (with respect to their number,#3 neurons and #2 synapses in both pathways). So, the delay in the ALS pathway is because those two pathways have different Nerve Fibers (are classified according to their conduction velocity, which depends on the size of the fibers and the presence or absence of myelination). In the PCML there will be larger diameter and more myelinated fibers →faster conduction. In the ALS, there will be smaller diameter and less myelinated fibers →slower conduction.

The PCML pathway is composed of rapidly conducting, large, myelinated fibers.

A spinal nerve is a mixed nerve, which carries motor, sensory, and autonomic signals (sympathetic) between the spinal cord and the body. Each spinal nerve is formed from the combination of nerve fibers from its **posterior (dorsal)** and **anterior (ventral)** roots. The **posterior** root is the **A**fferent **sensory** root and carries sensory information to the brain. The **anterior** root is the **E**fferent **motor** root and carries motor information from the brain.

Posterior root, **A**fferent, sensory**.**



Anterior root, **E**fferent ,motor**.**

#The nerve fibers in the **posterior** and **anterior** roots are organized in such a way that the larger and more myelinated fibers are on the medial side. And the smaller and less myelinated fibers are more lateral.

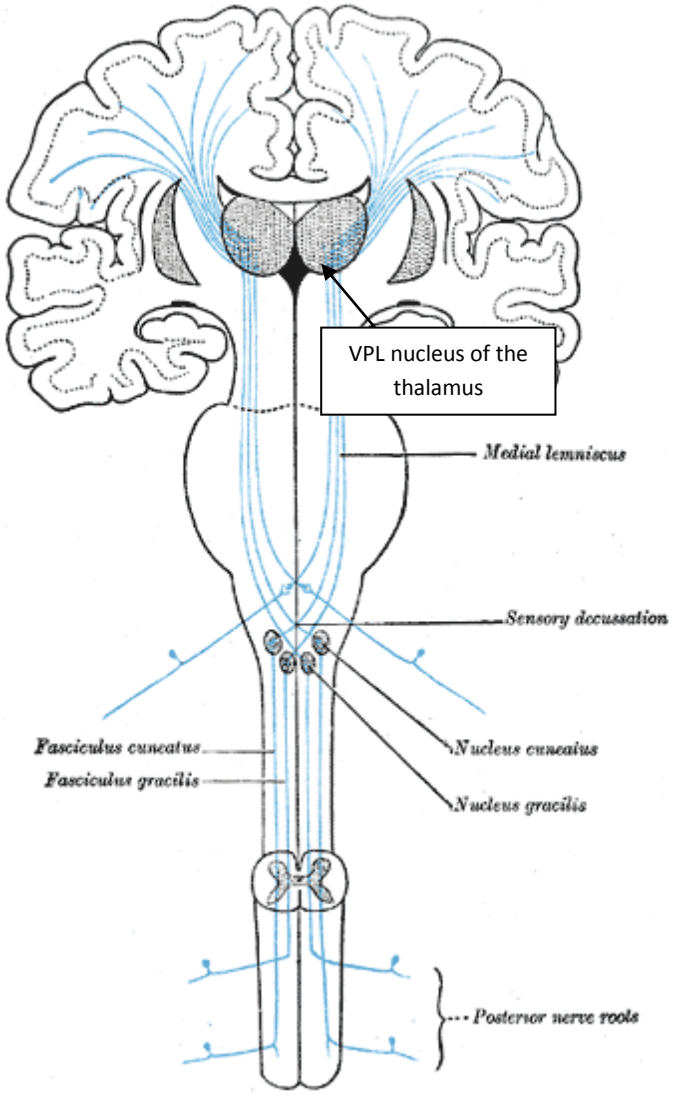
#Clinically; if there is a mass on the;

A) Lateral side →it will affect the smaller and less myelinated fibers →ALS.

B) Medial side→ it will affect the larger and more myelinated fibers→PCML.

1) PCML

This pathway is used for transmitting somatosensory information about Two-point discrimination, pressure, Vibration and Proprioception. It starts at peripheral receptors then it will send information through 1st order neuron to spinal cord {1st order neurons have their cell bodies in the dorsal root ganglion cells}.Then all axons will gather in the posterior column. It will ascend ipsilaterally (same side of the body) to the dorsal (posterior) column nuclei which consists from **nucleus gracilis (lower body)** or **nucleus cuneatus (upper body)** in the medulla of the brain stem. In the medulla, first-order neurons synapse on second-order neurons, which cross the midline. Then, it will ascend to the Thalamus, where they synapse on third-order neurons, then ascend to the cortex.



#The function of synapses between neurons along the pathway is to modulate (regulate, process) the neural signals, in which it will be the site of processing the information conducted in that pathway {The dr. said that you should read more about this point from the book}.

There are synapses in the thalamus, because the thalamus is the site of processing information and any cognitive processing occurs usually in the thalamus.
The thalamus nucleus in which the synapses occur is called VPL (ventral posterior nucleus is the somato-sensory relay nucleus in thalamus of the brain).

2) Anterolateral System {ALS} (not mentioned by the Dr.)

The anterolateral (spinothalamic) system transmits somatosensory information about pain, temperature, and light touch. The anterolateral system consists mainly of group III and group IV fibers. (Recall that group IV fibers have the slowest conduction velocities of all the sensory nerves.) In the anterolateral system, first-order neurons have their cell bodies in the dorsal horn and synapse on thermoreceptors and nociceptors in the skin. The first-order neurons synapse on second order neurons in the spinal cord. In the spinal cord, the second-order neurons cross the midline and ascend to the contralateral thalamus. In the thalamus, second order neurons synapse on third-order neurons, which ascend to the somatosensory cortex.

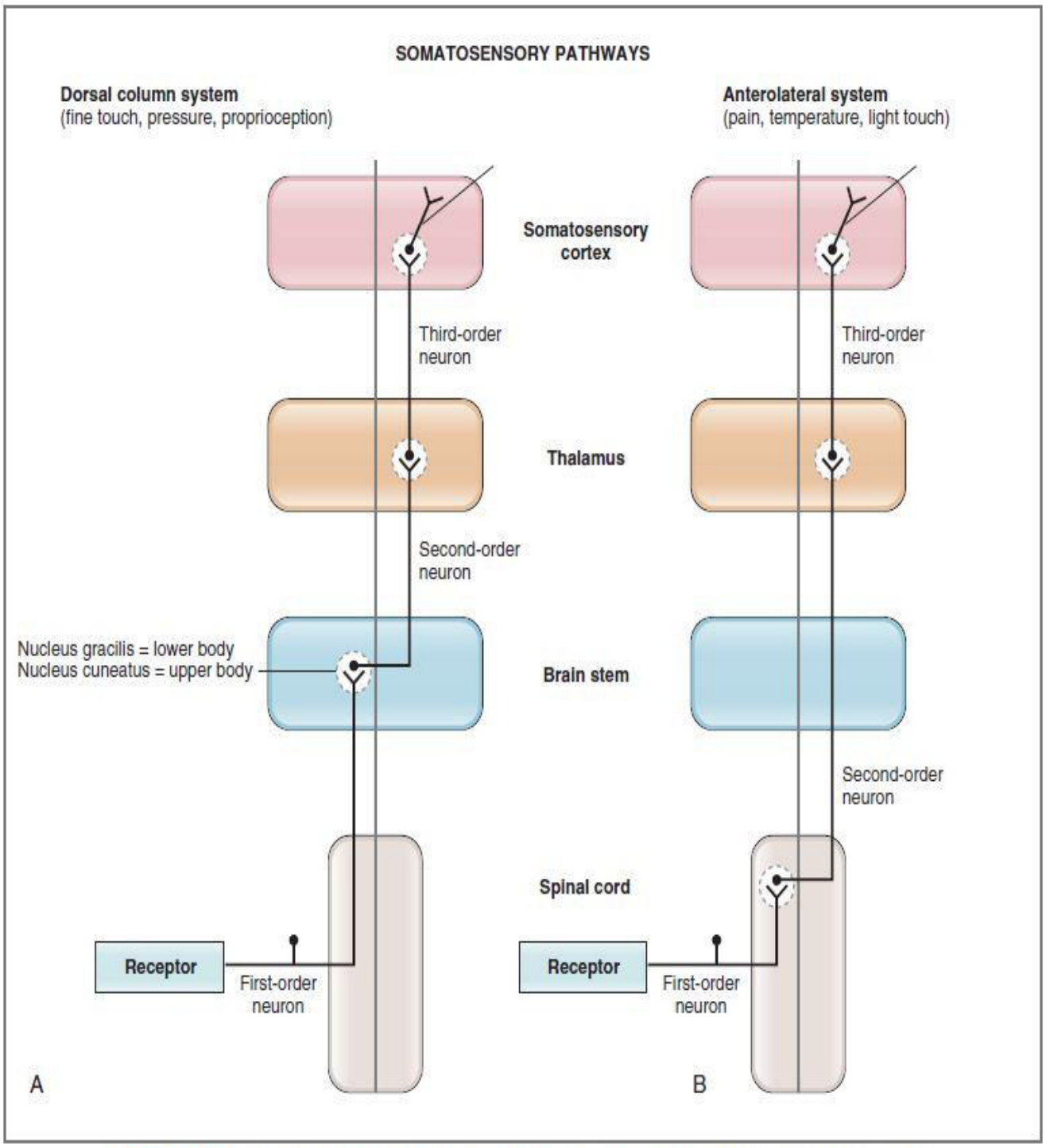


Figure 3–10 Comparison of the dorsal column (A) and the anterolateral (B) somatosensory systems. The dorsal column system crosses the midline in the brain stem. The anterolateral system crosses the midline in the spinal cord.

IV. Somatotopic organization of (PCML)

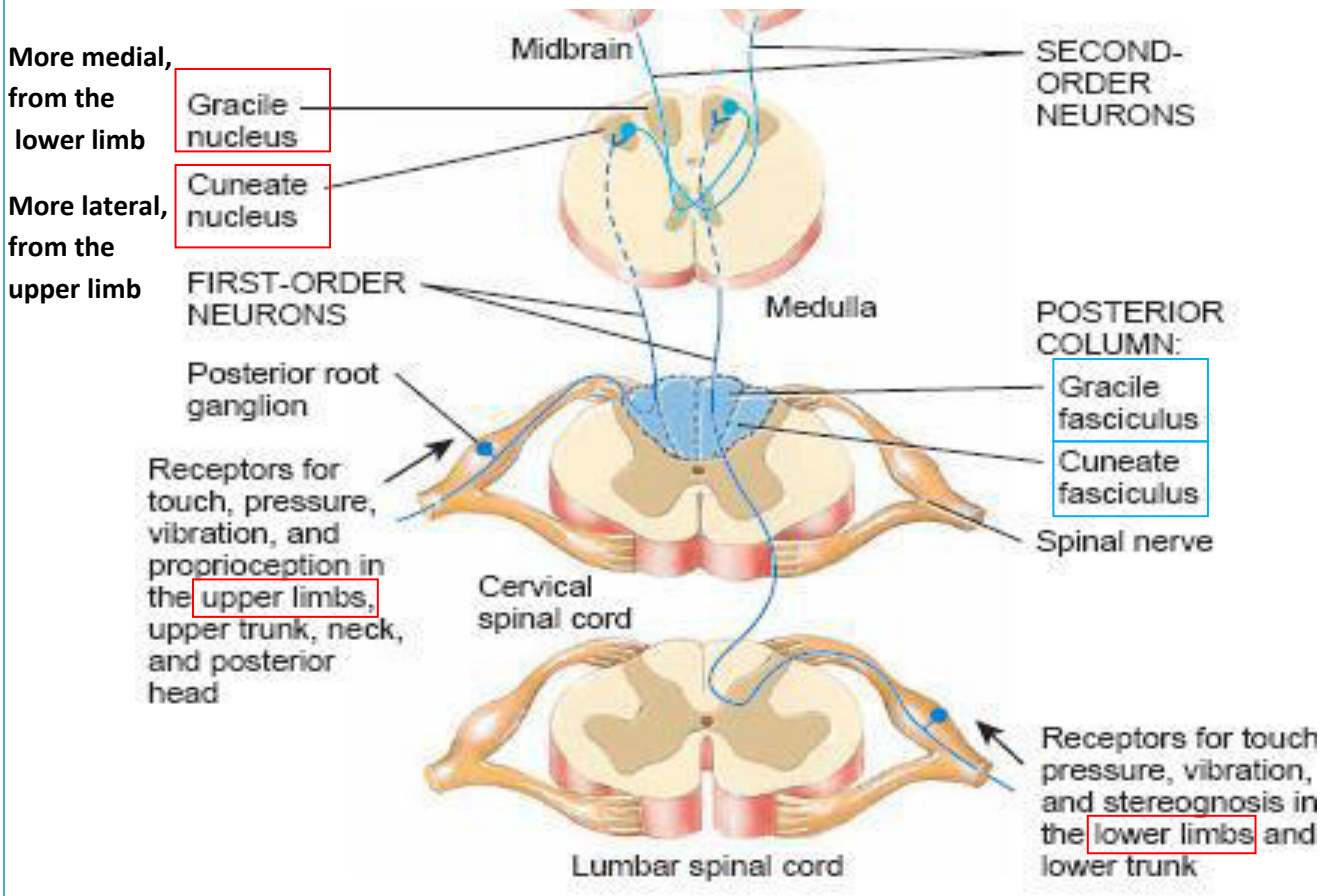
The information will enter the spinal cord one by one, in such a way that the axons will be organized in the spinal cord; the information from the lower limb will enter the spinal cord before the information of the upper limb. And usually, as information enters the spinal cord it will be placed medially.

→Medial structures are from the lower limb. And the more lateral structures are from the upper limb.

*** Medial→nucleus/ fasciculus gracilis *(lower body)***

lateral→ nucleus/ fasciculus cuneatus *(upper body).

#Sensory nerves of lower limbs enter spinal cord before Sensory nerves of upper limbs, so they (nerves of lower limbs) will be located medially.



The SOMATOTOPIC ORGANISATION in the spinal cord:

Information from the **lower limb** will be transferred through the **Gracile fasciculus** (**medially**), and then it will ascend to the medulla to synapse with **gracile nucleus**. Information from the **upper limb** will be transferred through the **cuneate fasciculus** (**laterally**), and then it will ascend to the medulla to synapse with **cuneate nucleus**.
The posterior column nuclei, the gracile and cuneate nuclei, are found in the posterior medulla at the superior end of their respective fasciculi.

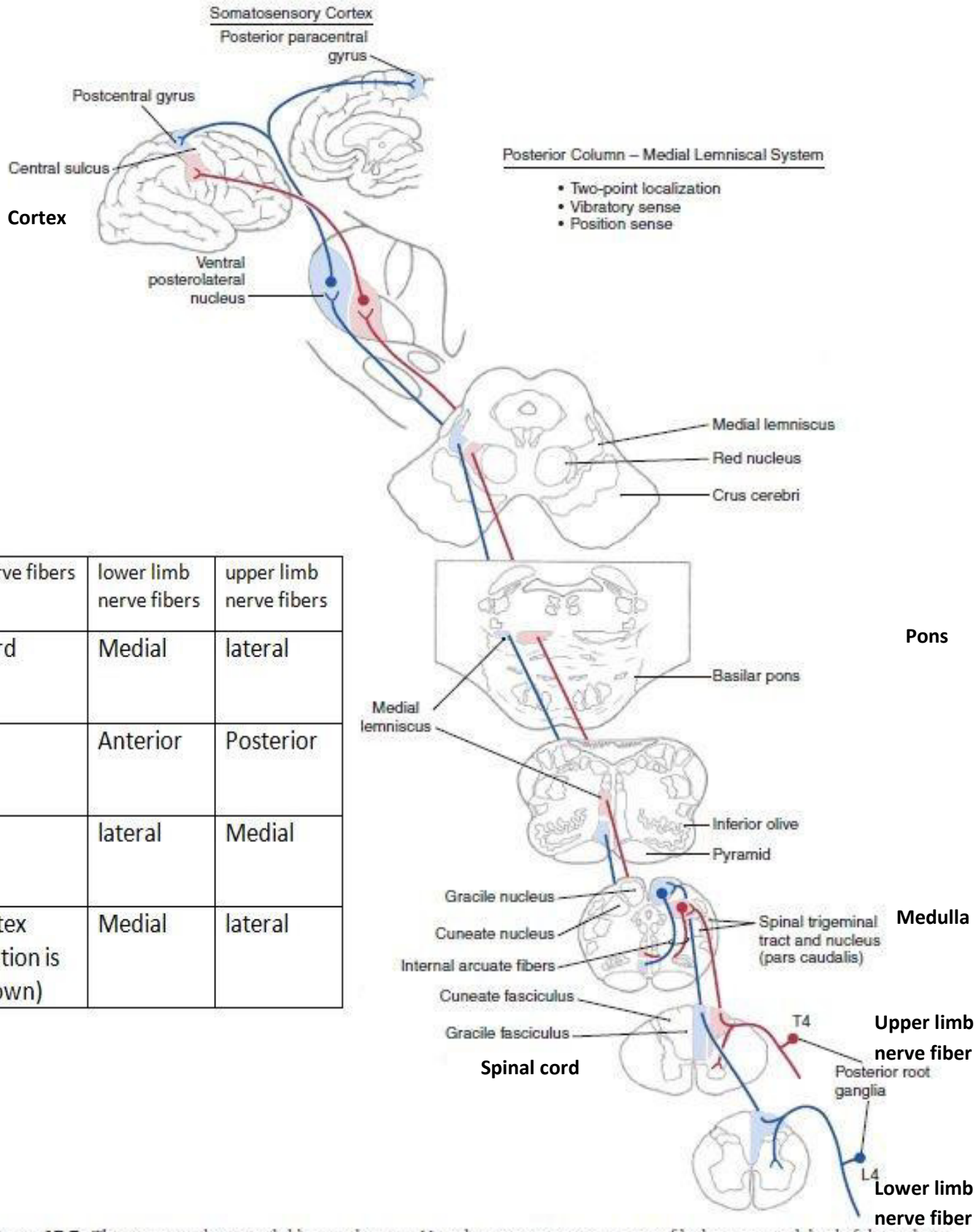
#In lower part of the brain stem (**medulla**), the SOMATOTOPIC ORGANISATION of 2nd order neurons will be: Lower limb Anterior, and upper limb posterior.

After that, shifting and twisting will happen and then, in the **upper pons** they will be straight and horizontal (Lower limb lateral, and upper limb medial) and in the midbrain it will make shifting and twisting again, it will reach the **cortex**, where the body is represented upside down. where the lower limb is medial and upper limp and face is lateral.
#The dr. said that:" where the upper limb is medial and lower limb and face is lateral" which probably is wrong.

#The Somatotopic Organization is important to know; because in MRI pictures or in drawings or in questions, if there is a lesion in certain location in the spinal cord, you should know what is the damaged structure and relate it clinically.

#Spinal cord drawings show the difference between lower part of spinal cord and the cervical sections (upper part).In which the PCML will enlarge in size because the numbers of axons increase.
#Ascending through the levels of spinal cord the thoracic region will be intermediate in size between the cervical and lumbar vertebrae, and the cervical will be like a butterfly.

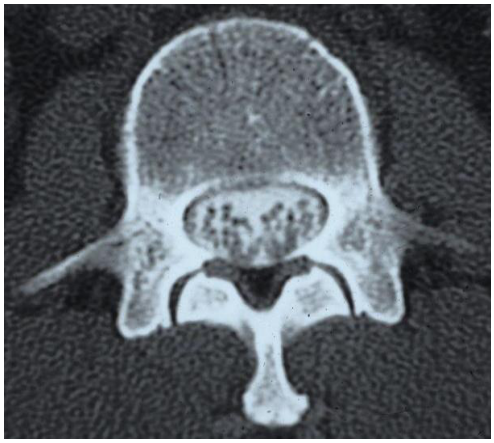
#The spinal cord ends at the lower border of L1(between L1 & L2).So, below L1 spinal cord can't be seen, and lumbar and sacral root will appear instead of spinal cord. This is important for identifying L1 from other lumbar segements.



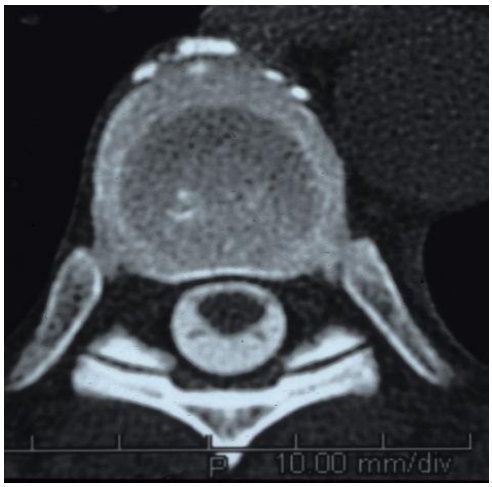
Region\nerve fibers	lower limb nerve fibers	upper limb nerve fibers
Spinal cord	Medial	lateral
medulla	Anterior	Posterior
Pons	lateral	Medial
Brain cortex (organization is upside down)	Medial	lateral

Figure 17-7. The posterior column–medial lemniscal system. Note the somatotopic arrangement of body parts at each level of this pathway.

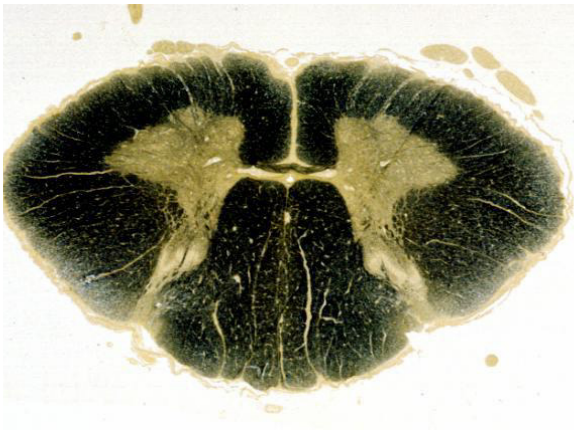
Lumbar level

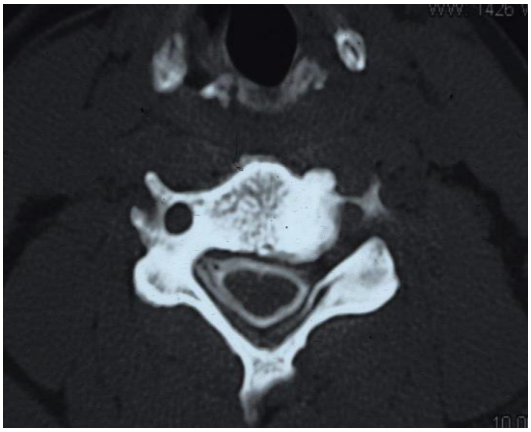


Thoracic level



Cervical level





V. PCML functions & associated lesion symptoms

PCML pathway location could be seen in an MRI, all the way from the cervical region to the brain stem to the cortex. The lower limb, trunk and upper limb are organized in a somatotropic organization.

PCML's function is to transmit two-point stimulation, vibrations and proprioception. This helps with 3 modalities or functions:

- **Sterognosis**: the ability to identify shapes and sizes of structures without looking, using the above mentioned functions. For example, holding a coin without looking at it, you can easily identify it by its size and whether its round or having edges.
- **Graphesthesia**: writing and controlling, depends on all the functions, especially 2 point discrimination.
- **Movement and weight identification**: (to know if an object is heavy or not), depends mainly on proprioception.

If the pathway was damaged at any level→Loss of (2-point discrimination sensation

, Vibration and Proprioception) sensations, then the patient won't be able to identify objects by their shape or size (Asterognosis or sterognosia), as well as agraphesthesia (difficulty recognizing a written number or letter traced on the skin), loss of ability to identify weight (Abarognosis) and sensory ataxia.

Ataxia is a general name that means the inability to coordinate between sensation and motor. Usually parts of our cortex with the help of the cerebellum help coordinate and do movements, so that the input of the sensation guides the output of the target movement. Loss of this coordination is called ataxia, it can be caused by:

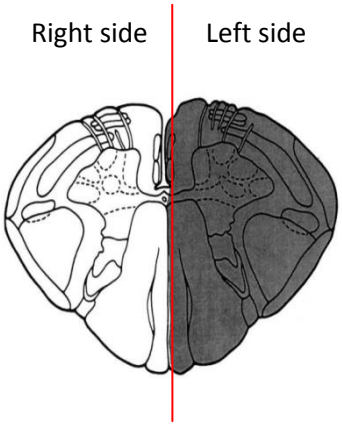
- Damage in the cerebellum, called **cerebellar ataxia.**
- No sensation and therefore no coordination, called **sensory ataxia**.
  If this pathway is damaged, it'll lead to loss of the coordination in the brain. Since the movement in the body requires vibration, 2 point discrimination, touch, pressure and proprioception .Then, if the PCML pathway was lost, there will be some sort of ataxia as there will be no sensation to coordinate with the movement.
- Loss of the connections between areas of the cortex and cerebellum, it's a specific type of ataxia in this case. For example**, ocular ataxia** which is loss of coordination between the movement of the eye and the target. Or the loss of hand coordination.

Since there are other pathways than PCML that deliver proprioception, vibrations and 2 point discrimination to the cerebellum directly from higher cortical levels, there won't be complete ataxia. And the loss of coordination is minimum and it's usually in the distal parts of the limbs more than the trunk. These patients will have normal balance and many body functions are well coordinated, but one of the most prominent symptoms is them stomping hard on the ground during walking to create sensation through the alternative pathways. These ataxic symptoms will increase, if other sensory pathways were eliminated, so if the patient was asked to close their eyes for example (which they would use to help coordinate the movement), that will increase the symptoms of ataxia.

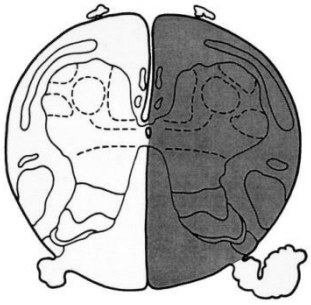
Case studies:

Considering the following MRIs, where the shaded area is the lesion area. How will the patient be affected?

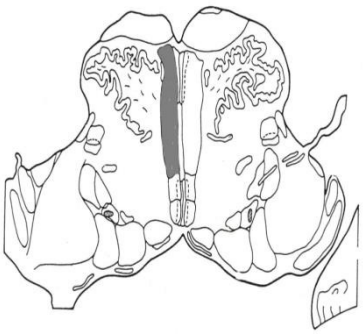
You need to identify the site of the lesion right or left, what sensation is lost, and where the structure is in the body.



This is in cervical part of the spinal cord; the lesion is in the left side, so the patient will lose vibration, 2 point discrimination and proprioception below the cervical area which includes the upper limb, trunk and lower limb. Since no crossing has happened yet (which happens at the lower part of the medulla), these sensations will be lost on the same side (the left one).
The lesion is on left side, before the crossing→loss of sensation will be on the left side.



This is a thoracic/ upper lumber vertebra, so there will be loss of 2 point discrimination, proprioception and vibration on the left side of the lower limb of the patient.
The lesion is on left side, before the crossing→loss of sensation will be on the left side.



This is the upper medulla, lower pons and fibers of the second order neurons (medial lemniscus of the PCML pathway) This lesion is found after crossing, so there will be loss of vibration, proprioception and 2 point discrimination of the upper limb, trunk and lower limb on the contralateral side (left side).
The lesion is on right side, after the crossing→loss of sensation will be on the left side.

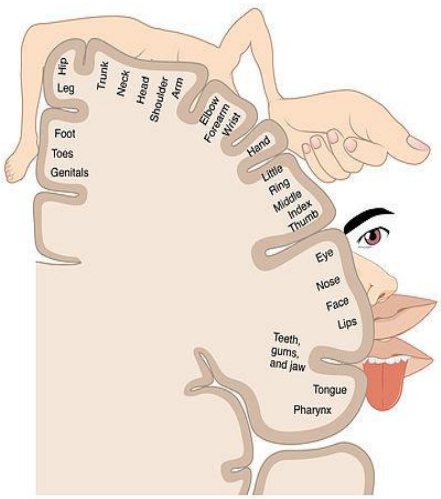
PCML PATHWAY

The first-order neurons reside in dorsal root ganglia and send their axons through the gracile and cuneate fascicule → The first-order axons make contact with second order neurons at the gracile and cuneate nuclei in the medulla → The second-order neurons will cross to the contralateral thalamus→The third order neurons arise from thalamus to the postcentral gyrus in the cortex. Each sensation targets a specific area of cortex, since the cortex's function is processing. So the PCML will go to an area in the cortex that will process the somatosensory sensation.

Each area of the cortex has 3 names:

1. **Physiological name** that is related to its function.
   The area responsible for processing somatosensory information is called somatosensory cortex.
   Area responsible for processing vision is called visual cortex.
   Area responsible for processing hearing is called auditory cortex and so on.
2. **Anatomical name**, that depends on its location in relation to a certain landmark or according to its shape. One of the most important landmarks is the big central salcus. So that, the area that processes the somatosesnory information is called the postcentral gyrus.
3. **Numbers** that were assigned according to histological landmarks. The entire cortex has an almost identical histology regarding the neurons, but they vary in the distribution of layers and certain cells. While studying the cortex, a scientist named **Brodmann** noticed differences between these areas and it's known in the body that the shape follows the function. So that, it means if there are two areas next to each other with different shapes or cells or neuron arrangements, then they both must have different functions. Back then, Brodmann couldn't list all the functions, so he divided the brain into 46 or 48 areas. Later, they discovered that each number or group of numbers have a certain function. Areas 1, 2, 3 are the primary somatosensory cortex.

At the somatosensory (postcentral) area, it'll get distributed there into somatotropical organization. Where the feet are more medial, trunk is at the border and the hand is at the lateral side, while the face is more lateral.



There are disturbances between the size of the organs and the area of the somatosensory cortex. The hand takes about 3 time the area size of the foot or arm despite its small size, that's because they are arranged according to how much processing is needed from that part of the body for sensation and how many neurons are found in the periphery (The accuracy of sensation).

Areas 1, 2, 3 in the cortex are all somatosensory, but there is a slight difference between them because there are 3 modalities and once they reach the cortex, each modality will be processed alone and then the cortex will combine them all for further processing and this is called **Serial point processing**.

If one of these somatosensory areas were eliminated experimentally, there will be a loss of one or more modalities and not all of them. Clinically, they're usually all lost due to vascular causes, tumors, traumas or strokes; because they're all near each other.

The pathway can be further damaged by:

- **Metabolic disorders** like diabetes, where it starts by affecting the long axons which supply the hands and feet (distal parts) before the short axons; since myelination of long axons is lost before the short ones. That'll lead to loss of PCML modalities there and this syndrome is called **stocking glove syndrome**.
#Myelinated neurons aren't lost before the unmyelinated ones, but long neurons are lost before the short ones.

-**Infections** like neurosyphilis, where it damages the posterior columns or nuclei (cuneate and gracilis) or it can affect pathways in the upper cervical part of the spinal cord causing **tabes dorsalis**.

Past paper questions

1) A 29 year old patient was investigated at the neurology clinic, and it was noted that she lacks the 'two point discrimination' ability in her *left hand*. What is the most likely cause of such a presentation?

(a) Fasciculus cuneatus lesion on the right side of the spinal cord at the level of C2.

(b) Dorsal column lesion on the right side of the spinal cord at the level of C5.

(c) Medial lemniscus lesion in the right side of the pons.

(d) Fasciculus gracilis lesion in the right side of the medulla.

(e) Spinothalamic lesion on the right side of the spinal cord.

2) All of the following are true regarding *Tabes Dorsalis* EXCEPT:

(a) Associated with meningoradiculitis and papillary involvement.

(b) Loss of dorsal column modalities of sensation bilaterally.

(c) Ataxic gait only when eyes are closed.

(d) Severe stabbing pain in the lower limbs and abdomen due to involvement of the spinothalamic tract.

(e) Positive Romberg's test due to sensory ataxia.

3) All of the following statements are correct EXCEPT:

(a) Stretch reflex: Monosynaptic reflex. (b) Thalamus: Stereognosis

(c) Muscle contraction: Increases Ia afferent discharge.

(d) Somatic sensory cortex: Tactile discrimination.

(e) Supplementary motor area: Bimanual tasks

4) Which is true about lateral inhibition: Answer → increase localization of pain sensation

1.	2.	3.
c	D	b

شكر خاص لمؤنس البداينة و قصي الشريف .