

The Somatic Sensation from the Body

Required Readings: Blumenfeld Chapter 7, pages 276 – 283 & 288 - 292, the PowerPoint presentation and comments.

LEARNING OBJECTIVES: after studying this chapter, students should be able to:

1. Describe the classification of sensory nerve fibers according to the fiber diameter and conduction velocity.
2. Indicate the sensory modalities transmitted by the DCML pathways and what type of peripheral receptors are involved in this system.
3. Describe the trajectory of the DCML pathway from origin to their termination in the cerebral cortex.
4. Indicate the sensory modalities transmitted by the ALS pathways and the type of peripheral receptors involved in this system.
5. Describe the trajectory of the ALS pathways from origin to their termination in the cerebral cortex.
6. Indicate the location and name of the cortical areas where somatosensory information from the DCML and ALS pathways is processed.
7. Correlate the effects of DCML lesions at all CNS levels with clinical findings.
8. Correlate the effects of ALS fiber damage at all CNS levels with clinical exam findings.
9. Apply your acquired knowledge about the somatic sensation to solve clinical cases using the patient symptoms and signs.

Overview

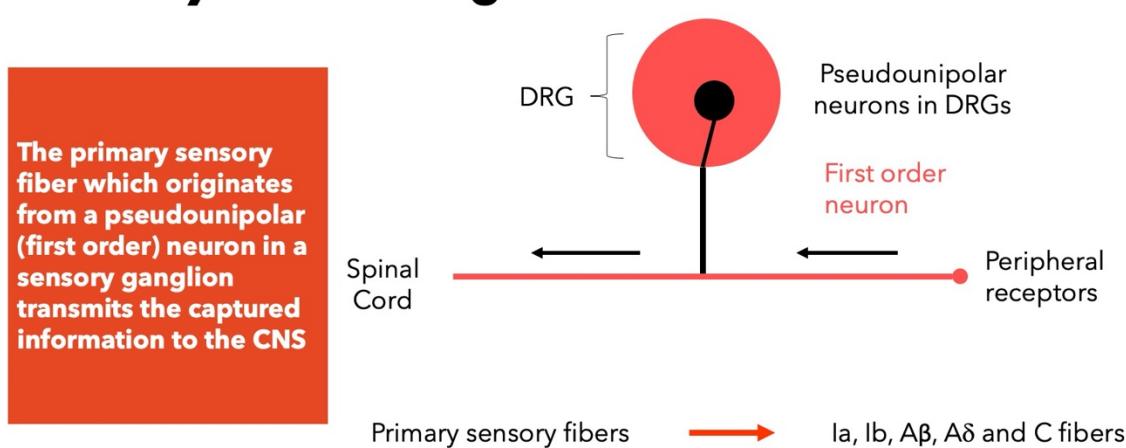
Sensation is the ability to recognize, transduce, encode, and perceive information about our own bodies and/or the world surrounding us. The somatic sensation from the body is transmitted through 2 major pathways: the dorsal column-medial lemniscal pathway (DCML) which transmits light touch, vibration, and proprioception; and the anterolateral system (ALS) which transmits deep touch, noxious (painful), and thermal stimuli. Somatosensory information is transmitted through parallel pathways from the periphery (skin, muscles, soft tissue) to the cerebral cortex in a mostly 3-neuron pathway where the first neuron is always in the peripheral nervous system (Dorsal root ganglion for body sensation) and the second and third are in the central nervous system.

Slides 3 to 6 introduce the study of the sensory systems. Think about these principles as we study sensation and perception, and how a simple group of action potentials can produce such a deep and rich experience in our minds.

Slides 7 and 8 list some general rules which are followed by most sensory systems. It is useful to remember them. Both somatosensory systems from the body follow this general rules.

Slide 9 - Diagram showing the anatomical organization of all sensory fibers. Fibers originate from a pseudounipolar neuron in a sensory ganglion, in this case the DRGs at spinal levels. This pseudounipolar neuron is the first neuron of the pathway. These neurons have one axon which branches out into two different projections: a peripheral projection that contacts the peripheral receptor, in some cases the terminal axon is itself the receptor; the central branch transmits the captured information to the spinal cord; this information enters the cord through the dorsal root to follow different pathways according to the type of information they transmit.

Sensory Fibers Origin



Objective # 1; Slides 10, 11

Two systems are used to classify motor and sensory fibers. These 2 systems are based on conduction velocity, and on the direct measurement of fiber diameter (slide 10). Slide 11 shows the fiber name that we use more frequently to refer to certain motor and sensory axons.



Fiber Size And Velocity

OBJ. # 1

- **A α** fibers - motor fibers innervating skeletal muscle fibers
- **A γ** fibers - motor fibers innervating intrafusal fibers (muscle spindle)
- **B** fibers - preganglionic autonomic fibers
- **C** fibers are non-myelinated
- **I a** fibers - sensory afferents from muscle spindle
- **I b** fibers - sensory afferents from Golgi tendon
- **II** fibers are similar to **A β** - sensory afferents from encapsulated skin or visceral receptors
- **III** fibers are similar to **A δ** fibers - sensory, small myelinated afferent fibers transmitting thermal and nociceptive information
- **IV** fibers are non-myelinated, transmit nociceptive information



OBJ. # 1

Fiber Size And Velocity

There are 2 systems for the classification of nerve fibers:

- Based on conduction velocity
- Based on measured fiber diameter

A, B, C system - based on **conduction velocity**

- **A** fibers are the fastest heavily myelinated sensory and motor fibers. They are subdivided into **A α** , **A β** , **A γ** , **A δ** with **A δ** being the slowest and less myelinated of the A group **C** fibers are non-myelinated
- I, II, III and IV system - measured **fiber diameter**
- I, II and III are myelinated fibers and IV are non-myelinated

Objective # 2; Slide 12

Sensory modalities transmitted by the DCML system: light or discriminative touch or 2-points discrimination, vibration, and the sense of where our body is in the space called proprioception. The peripheral receptors transmitting this type of information are the mechanoreceptors located in the layers of the skin.

The Dorsal Column Medial Lemniscal Pathway

OBJ. # 2

The sensory modalities conveyed by this system are:

- Discriminative touch
 - Vibration
 - Proprioception
- } **FROM THE BODY**

The peripheral receptors involved in this system are:

- Mechanoreceptors - Skin
- Proprioceptors - Muscles and tendons

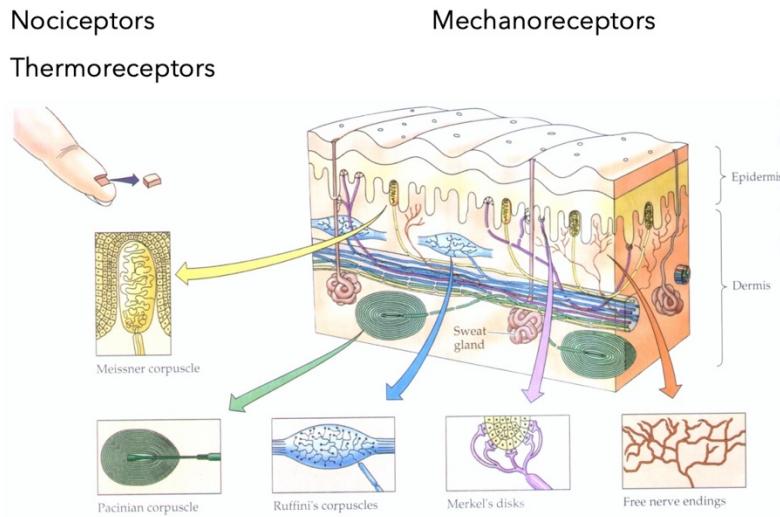


Some sensory receptors are rapidly adapting to the applied stimulus, firing action potentials at the start and at the end of the stimulus, but are silent in between. Other mechanoreceptors are slowly adapting to the presence of a stimulus and continue to fire action potentials for a long time during the presence of the stimulus. Most of these receptors consist of an axon terminal surrounded by a protective capsule, others are not encapsulated and are called free nerve endings. The latter are related to nociceptive stimuli; however, they can also detect touch and pressure. Common examples are the free nerve endings on the cornea of the eye that can detect touch and pressure stimuli.

OBJ. # 2

The Sensory Receptors

All sensory systems originate with the sensation being captured by a peripheral receptor



Objective # 2; Slide 14

The Meissner's corpuscle is an encapsulated receptor. The nerve fiber associated with it is an A β myelinated sensory fiber. These receptors are present in non-hairy skin and are particularly abundant in the fingertips and other areas where they are important for precise discrimination of spatial location of touch sensation. These receptors adapt very rapidly to a given stimulus, they are particularly sensitive to movement of objects over the skin surface and low frequency vibration.

Merkel's discs are mostly found in these same areas of the body although they can be present in hairy skin too. They are in the deeper layer of the epithelium. These cells are contacted by a nerve terminal of the A β type and transmit information related to touch and texture of objects. They transmit an initial strong signal that partially adapts and then a continuing weaker signal that adapts slowly, allowing a person to identify continuous touch of objects against the skin.

Ruffini's endings are in the deep layers of the skin and joint capsules to help signal degrees of joint rotation. They are multibranched encapsulated endings slowly adapting to stimuli. They signal continuous deformation of the tissues such as prolonged touch and pressure signals. Pacinian corpuscles are in the deep hypodermis and facial tissues of the body. They are stimulated by deep local compression of the tissue, and they adapt very rapidly to stimuli. They are particularly good in detecting tissue vibration and rapid changes in the mechanical state of tissues.

Free nerve endings are non-encapsulated receptors and transmit different types of signals. They are always very small type C, unmyelinated fibers. Some of them are very sensitive, rapidly adapting mechanoreceptive free nerve endings that elicit the tickle and itching sensations.

OBJ. # 2

Mechanoreceptors

Cutaneous mechanoreceptors

- Encapsulated or non-encapsulated
- Slowly adapting or rapidly adapting

Encapsulated receptors

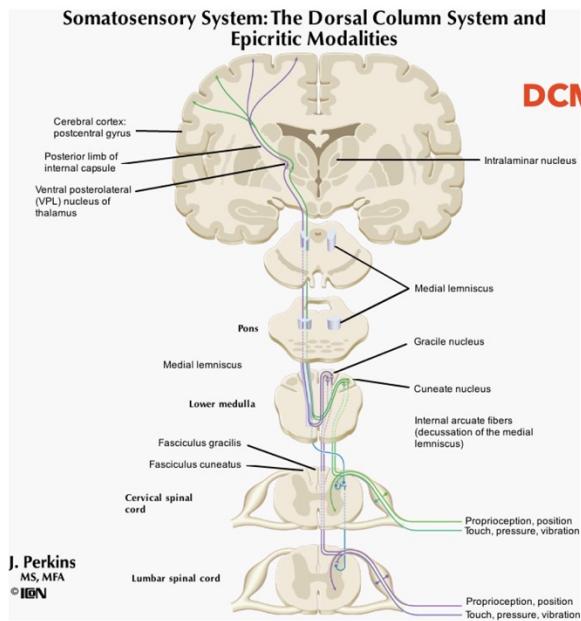
- Pacinian corpuscle (rapidly adapting)
- Ruffinian ending (slowly adapting)
- Meissner corpuscle (rapidly adapting)

Non-encapsulated receptors

- Merkel endings (slowly adapting)
- Some are free nerve endings

Objective # 3; Slide 15

Diagram showing the entire DCML pathway in a longitudinal view. Each receptor sends an axon which through a succession of synaptic steps transmits the somatosensory information to the cerebral cortex where it is processed and perceived.



DCML PATHWAY

OBJ. # 3

- **First Neuron**
Dorsal root ganglion
- **Second Neuron**
Nucleus gracilis + cuneatus
- **Third Neuron**
Thalamus – VPL nucleus

Objective # 4; Slide 16, 17

The anterolateral system is responsible for deep touch or non-discriminative touch, thermal sensation, and nociception which perception is pain. Slide 16 also indicates the 4 main groups of fiber tracts that ascend with ALS and their names. Remember that the first part of the name of a fiber tract always refers to the place where the pathway originates (spinal cord) and the last part of the name refers to the place where the fibers end. So that the spinothalamic tract starts in the spinal cord and terminates in the thalamus and so on.

The peripheral receptors transmitting this type of information are free nerve endings located in the layers of the skin. There are mainly two types of fibers associated with this system: A δ and C fibers. A δ fibers are slightly myelinated and transmit touch, thermal and pain sensation. These fibers are associated with innocuous mechanoreceptor and thermoreceptors and with pain receptors. These fibers transmit the sharp, acute pain that is first felt when damage to tissues occurs. They are part of the spinothalamic fibers that reach the thalamus fast and from the thalamus reach the cortex without making any synapse in the brainstem reticular formation.

The Antero-lateral System

OBJ. # 4

The sensory modalities conveyed by this system are:

- Non discriminative touch
- Thermal sensation
- Nociception - Pain

FROM THE BODY

- The spinothalamic tract
- The spinoreticular tract
- The spinomesencephalic tract
- The spinohypothalamic tract

ALS

Conversely, C fibers are not myelinated and are associated with nociceptors or with polymodal receptors that sense and transmit pain. C fibers transmit the type of dull pain that is lasting, and reaches the thalamus and cortex later than the sharp pain transmitted by A δ fibers.

Pain receptors are free nerve endings widespread in the superficial layers of the skin and internal tissues. They can be excited by 3 types of stimuli: mechanical, thermal, and chemical and they are often coactivated. There are also silent nociceptors found in the viscera which are not normally activated by noxious stimuli. Their activation is thought to be due to secondary hyperalgesia and central sensitization.

Pain signals can be transmitted in two different ways: fast pain and slow pain. The fast pain is elicited by mechanical and thermal stimuli while the slow pain is elicited by the 3 types of stimuli. Chemical substances such as bradykinin, serotonin, histamine etc. are particularly important in stimulating the slow, suffering type of pain that occurs after tissue injury.

The stimuli that activate pain receptors vary in different tissues. For the skin any injury such as cutting, crushing, burning or freezing produces pain. Skeletal muscle pain is caused by ischemia, necrosis, hemorrhage or injection of irritating solutions. Also prolonged contraction which produces ischemia elicits pain in muscles. In joints and ligaments pain is produced by different types of injuries, the most important of which are inflammation of synovial membranes, exposure to hypertonic fluids, and stretching and tearing of ligaments. Pain at visceral levels is produced mostly by distention, inflammation of the mucosa, spasm of the smooth muscle or traction of the mesenteric attachment. Pain receptors adapt very little or not at all. In some cases excitation of pain fibers progressively increases as the stimulus continues. This increased sensitivity of the receptors to prolonged stimulation is called hyperalgesia.



The peripheral receptors of the ALS system

OBJ. # 4

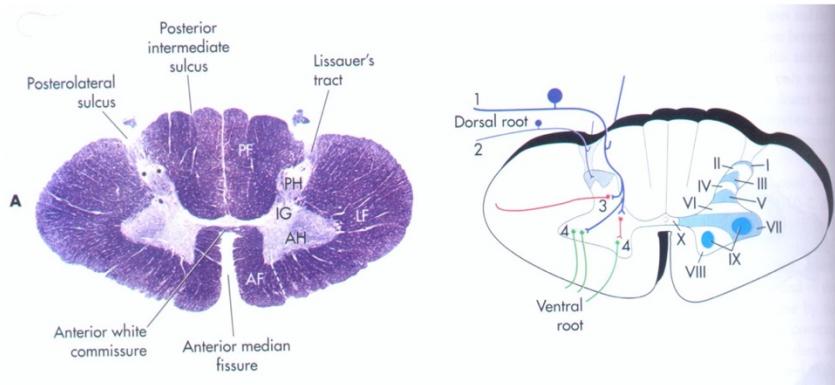
- Most of the peripheral receptors are non-encapsulated terminal axon branches - **free nerve endings**
- Free nerve endings are classified as: **mechanoreceptors, thermoreceptors, chemoreceptors and polymodal nociceptors**
- 2 types of afferent fibers are associated with the transmission of pain: **A- δ thinly myelinated and C fibers non-myelinated**
- Mechanoreceptors transmit innocuous sensation mostly through A- δ fibers
- Thermoreceptors transmit innocuous thermal sensation through A- δ and C fibers
- Nociceptors transmit through A- δ and C fibers

Objective # 5; Slide 18

A diagram of the spinal cord with the central gray matter, dorsal, and ventral horns divided into laminae. In this context, laminae refer to the division of the gray matter into different groups of neurons with different morphologic characteristics and functions. They are like nuclei, in this case columnar nuclei since they expand all the length of the spinal cord. They are named Rexed laminae and are based on the study of the different cell cytoarchitecture in each one of these layers.

Spinal Cord Laminae Of Rexed

OBJ. # 5



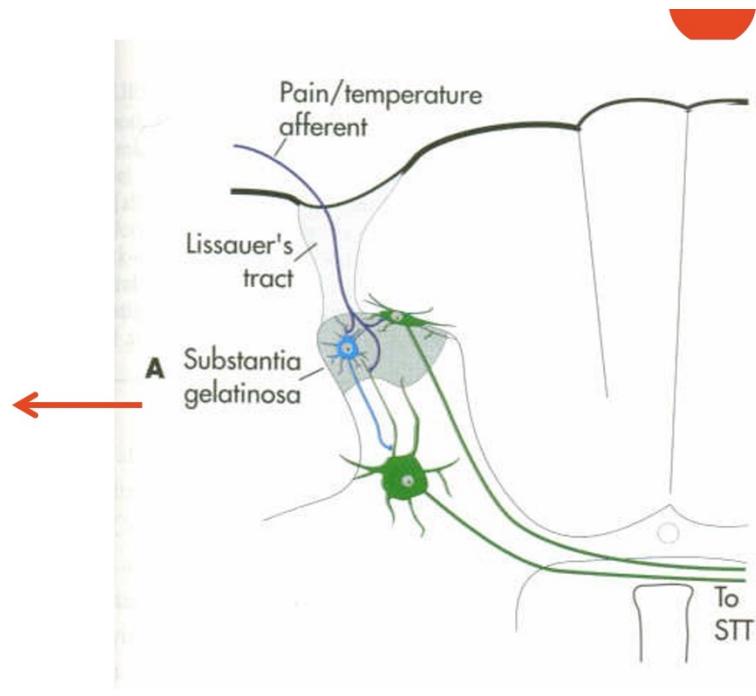
- Primary afferent fiber synapse in dorsal horn with **second order neuron**
- Fibers cross the midline in the anterior white commissure

Objective # 5; Slide 19

The sensory fibers in the ALS system enter the spinal cord at each segmental level with the dorsal root. Once in the spinal cord, the fibers divide in several branches, some of them will ascend or descend one or more segments to reach the second order neurons in those segments. These ascending/descending fibers form the Lissauer's tract in the dorsal spinal cord. Some fibers synapse at the entrance level with sensory neurons located in the dorsal horn laminae.

OBJ. # 5

Neurons in this nucleus are very important in the pathway for internal modulation of pain

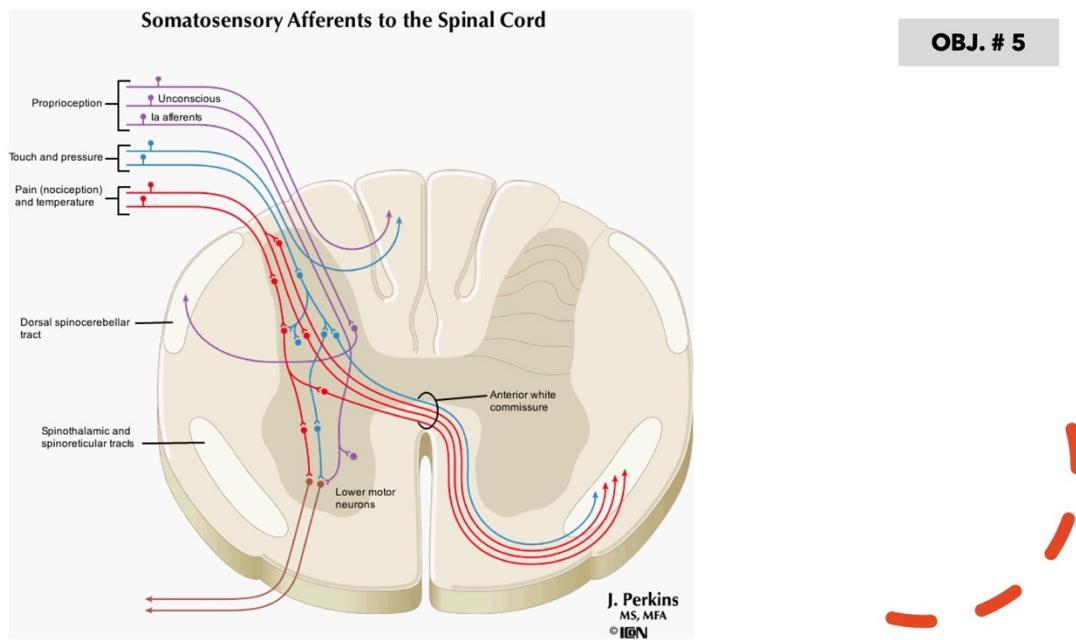


A_δ fibers terminate mostly in lamina I (the marginal zone), the outer part of lamina II (substantia gelatinosa) and lamina V. C fibers terminate mostly in lamina II substantia gelatinosa. The main neurotransmitter used in these synapses is glutamate, but the nerve terminals also release several modulatory neuropeptides such as: substance P, calcitonin-gene related substance (CGRP), and the neurotrophin brain-derived neurotrophic factor (BDNF.) They provide functional plasticity to the synapses and allow for the transmission of particularly intense stimuli. Neurons in laminae I, II and V are the targets of internal descending pain modulating pathways which uses internal morphine-like molecules called endorphins. Endorphins modulate the transmission of pain by spinal cord neurons. In this way transmission of pain stimuli in the spinal cord is influenced by both inhibitory interneurons in the spinal cord and the modulatory projections from the brainstem.

Objective # 5; Slide 20

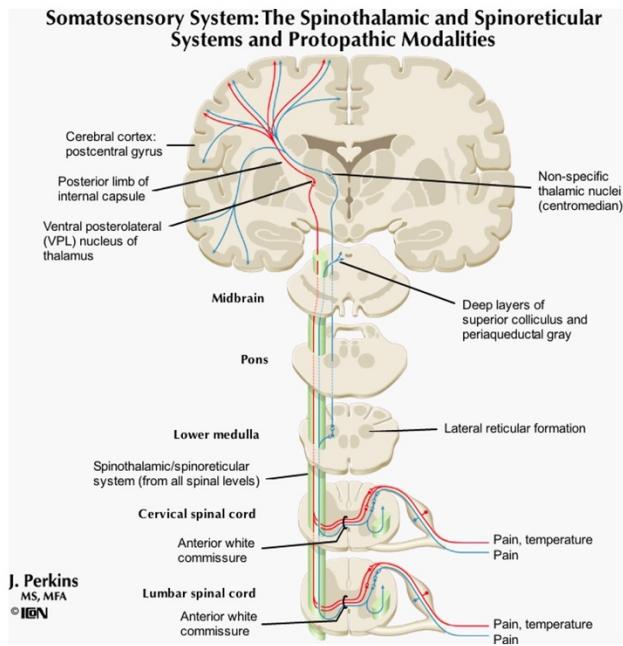
The second order fibers cross the midline through the anterior white commissure to reach the anterolateral funiculus of the spinal cord on the contralateral side. This fiber crossing occurs at every segmental level. Some second order pain fibers project also to the ipsilateral anterolateral funiculus, so they ascend with the ipsilateral ALS system.

You can appreciate the huge number of synaptic contacts occurring in the spinal cord laminae before the spinothalamic and other fiber tracts cross to the contralateral side to form the ALS.



The ALS General Pathway

OBJ. # 5



The entire spinothalamic and Spinoreticular pathways, together with their modalities.

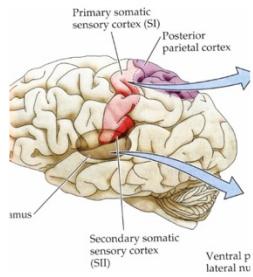
Objective # 6; Slide 22

After the thalamus, the sensory tracts project to three cortical areas for further processing and perception.

OBJ. # 6

Thalamocortical Fibers

Thalamo-cortical fibers from both DCML and ALS systems terminate in 3 cortical areas



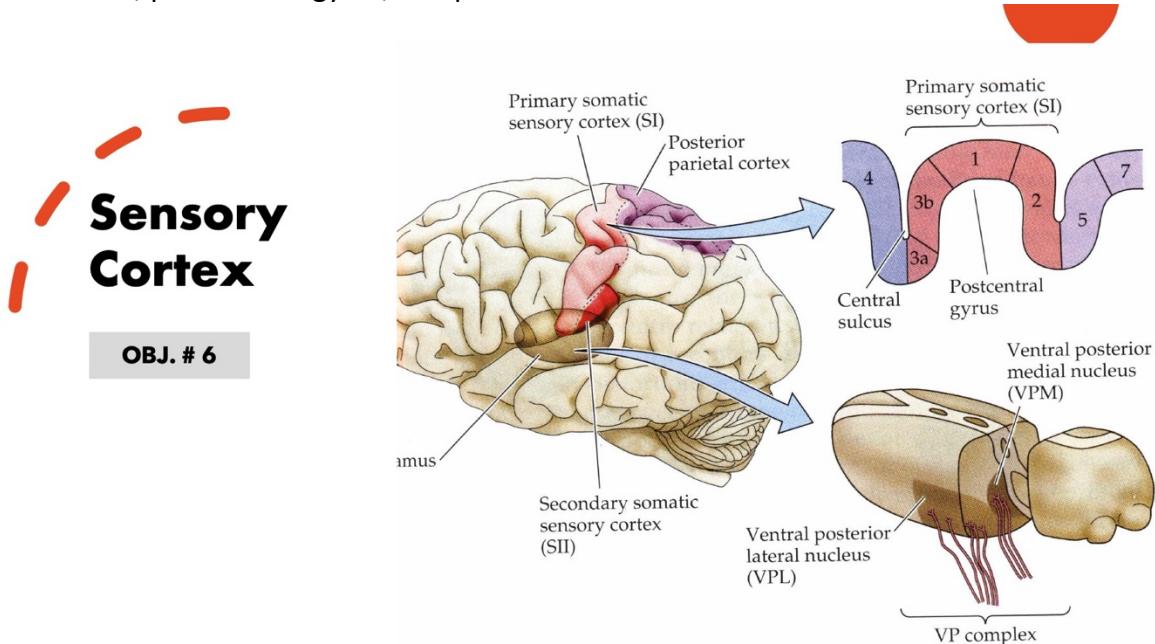
Primary sensory cortex (SI)
Brodmann's 3,2,1

Secondary sensory cortex (SII)

Parietal association cortex,
Brodmann's 5 and 7

Objective # 6; Slide 23

Diagram of a cerebral hemisphere showing the somatosensory (postcentral gyrus) and posterior parietal cortices. You can see the distribution of areas 3a, 3b, 1 and 2 around the central sulcus, post central gyrus, and post central sulcus.



The primary sensory cortex receives information directly from the thalamus. The primary sensory cortex is referred to as S I, or Sensory I (Brodmann's areas 3, 1, 2) and is located in the postcentral gyrus of the parietal lobes. Most of the thalamic fibers from the VPL nucleus reach the primary sensory cortex. Some fibers terminate in the secondary sensory cortex directly. Once the information is processed in the primary cortex, it is transmitted to the secondary somatosensory cortex located posterior to S I in the parietal lobe. The secondary cortex is believed to provide a deeper processing of the sensory perception. However, damage to this region does not tend to produce gross sensory deficits.

After processing in the primary and secondary cortices, the information is sent to the posterior parietal cortex, Brodmann's areas 5 and 7 also called the sensory association area, where it is integrated with other sensory modalities.

There is a division of labor between the different parts of the primary somatosensory cortex. The cortical columns in area 3a, the most anterior area located deep in the central sulcus, respond to muscle, tendon, and joint stretch receptors. These columns project fibers directed to the motor cortex and play a major role in providing feedback for the control of muscle contraction.

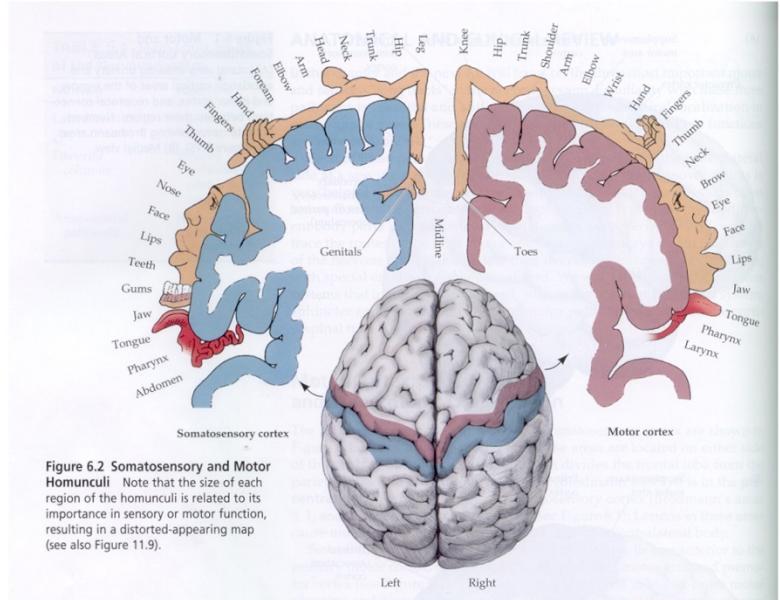
As we move more posterior in the somatosensory cortex, the vertical columns start to respond to other modalities such as deep pressure. In the most posterior portions of the somatosensory cortex the neurons in the vertical columns only respond to stimuli moving across the skin in a particular direction. This represents a more complex level of processing, and it gets even more complex when we move to the association areas in the parietal lobe, areas 5 & 7.

Objective # 6; Slide 24

Somatotopic organization of sensory and motor areas in the cerebral cortex. This organization is referred to as the Homunculus (little man) of Penfield. A somatotopic map is a map of the body represented along the cortical areas dedicated to process a particular modality of information. Somatic sensation for the face and upper limbs is mapped out along the lateral surface of the postcentral gyrus while the lower limbs are mapped out on the medial surface, the paracentral lobule.

OBJ. # 6

Sensory Cortex Somatotopic Organization



Objective # 7; Slides 25, 26

Deficits produced by lesions of the DCML pathway fibers at different levels of the brainstem, spinal cord, and cortical areas. Lesion of the sensory pathways produces symptoms that can be either negative (loss of the sensation) or positives (abnormal sensation, pain.)

Clinical Correlations

OBJ. # 7

- Damage to the **somatosensory cortex** produces:
- Discrete loss of touch, vibration, and proprioception **contralateral** to the side of the lesion. However, a patient can sometimes crudely localize the sensations on a particular hand or leg.
- With cortical damage the patient can lose more sophisticated abilities such as:
 - The ability to judge weights of objects
 - The ability to judge shapes or forms of objects – **astereognosis**
 - The ability to judge texture of materials
- A lesion in the somatosensory association areas (5 & 7) produce:
 - Loss of the ability to recognize objects and forms felt on the opposite side of the body
 - Loss of most of the perception of the patient's own body or body parts on the opposite side – **neglect**

Clinical Correlations

OBJ. # 7

- Damage to DCML pathways, along their ascending trajectory **above decussation**, produces:
 - loss of touch, vibration, and proprioception from the body **contralateral** to the side of the lesion
- Damage to Dorsal Column pathways, in the **spinal cord**, produces the same deficits as above, but on the **same side** of the lesion
- **Positive phenomena:**
 - Paresthesias: tingling, prickling, crawling, burning sensations
 - hyperesthesia: exaggeration of any sensory modality

Objective # 8; Slide 27

The deficits produced by damage to the ALS pathways above and below decussation in the spinal cord. It is important to accurately record, through a thorough neurological exam, the sensory level of deficit in patients with spinal cord lesions to identify the location of the spinal segments or peripheral nerves involved.

Damage to ALS fibers produces negative symptoms when sensation of touch, temperature or nociception is no longer present. Conversely, pain is a positive symptom.

Clinical Correlations

OBJ. # 8

- Damage to the ALS pathways along their ascending trajectory **above decussation**, produces:
 - Loss of thermal, deep touch and pain sensation from the body **contralateral** to the side of the lesion
- Damage to the ALS pathways in the spinal cord produces:
 - loss of thermal, deep touch and pain sensation from the body **contralateral** to the side of the lesion below the lesion level
- Positive phenomenon: **PAIN**
- SENSORY LEVEL = When there is a spinal cord lesion, the sensory deficit level (dermatome) found on the patient's body is helpful to localize the spinal cord **level of damage**

Objective # 8; Slide 28

The perception of pain involves the integration of inputs reaching many cortical areas. Pain signals from the thalamic nuclei are relayed to the primary somatosensory cortex but also to the insular and cingulate cortex.

The cingulate gyrus is part of the limbic system and is thought to be involved in the processing of the emotional states related to the pain experience. The insular cortex processes information about the internal state of the body and visceral structures and through connections with the hypothalamus contributes to the autonomic responses to pain.

Clinical Correlations - Cortical Processing

OBJ. # 8

- With cortical damage, pain is not affected in intensity or quality, but it becomes poorly localized.
- The cortical perception of pain involves several cortical areas.
- Beyond the somatosensory cortex, the insular cortex and cingulate gyrus have a predominant role.
- The insular cortex may be a place where the sensory, affective, and cognitive components of pain are integrated.



Objective # 9; Slides 29, 30

Pathophysiology of PAIN

OBJ. # 9

- Positive symptom of ALS pathways: **PAIN**
- The International Association for the Study of Pain (IASP) defines pain as "an unpleasant sensory and emotional experience which is primarily associated with tissue damage or described in terms of such damage or both"
- FUNCTION OF PAIN:** Alert mechanism to signal that something is wrong. Pain is a perception constructed by the brain and it is not always based on an observable injury
- Pain is produced by tissue injury, inflammation or necrosis
- The injury could be mechanical, chemical or thermal (cold / heat)
- Persistent pain could either be **nociceptive** or **neuropathic** pain
- Central pain** is produced by damage to central pathways, the spinal cord or the thalamic nuclei involved in pain processing



Pathophysiology of PAIN

OBJ. # 9

- Injured cells release intracellular components into the extracellular matrix, amongst them K which depolarizes nociceptors
- Other chemical mediators are also released: hydrogen ions, prostaglandins, leukotrienes, histamine, serotonin, and bradykinin
- These chemical mediators trigger an inflammatory process (See picture in next slide)
- Pain is then perpetuated by inflammation and vasodilatation
- Sensitization of pain receptors leads to **hyperalgesia and allodynia**
- Pain can also be referred from visceral structures to the body surface



Pain has a protective role of alerting the individual that something is wrong. Pain starts when there is tissue injury that produces cell necrosis, ischemia and/or inflammation. Signaling molecules and pro inflammatory mediators are released by injured cells. They include histamine, bradykinins, prostaglandins, leukotrienes together with low pH in cases of ischemia which perpetuate the inflammation and overstimulation of the pain receptors.

Specialized ion channels in the high-threshold nociceptors undergo conformational changes in response to this stimulation. The frequency and duration of the action potentials generated provide the CNS with information related to the onset, intensity, and duration of the stimulus.

In the case of thermal pain, groups of thermal receptors become active and fire action potentials when the temperature is below 5° C or 41° F, or when it is above 45° C or 115° F. High-threshold mechanoreceptors become active with intense mechanical stimuli such as a pinch or a pin-prick.

Over-stimulated pain receptors release from their terminals the peptide substance P into the injured tissues. Substance P is a potent vasodilator, produces mast cells degranulation, is a chemoattractant for leukocytes and increases the production and release of inflammatory mediators such as prostaglandins and bradykinin. Bradykinin is one of the most active pain-producing agents by directly activating A δ and C nociceptors and increasing the synthesis of prostaglandins. All this “neurogenic inflammation” further increases receptor sensitization.

Receptor sensitization leads to hyperalgesia and allodynia. Hyperalgesia refers to an increased sensitivity due to a repetitive exposure to noxious mechanical stimuli which lower the receptor threshold. Patients with hyperalgesia typically report persistent pain in the absence of sensory stimulation.

Allodynia refers to an excessive reaction to all stimuli even to those normally non painful. Patients with allodynia do not feel pain constantly but only when a stimulus that normally will not be painful is applied.

Persistent pain could be subdivided into nociceptive and neuropathic. Nociceptive pain is produced when nociceptors in the skin or soft tissue are activated by a noxious agent or tissue damage and is in general produced by the accompanying inflammatory process. Neuropathic pain is produced by direct injury to nerves in the PNS or nerve fibers in the CNS such as compressions, post-herpetic neuralgia, or phantom limb pain after amputation.

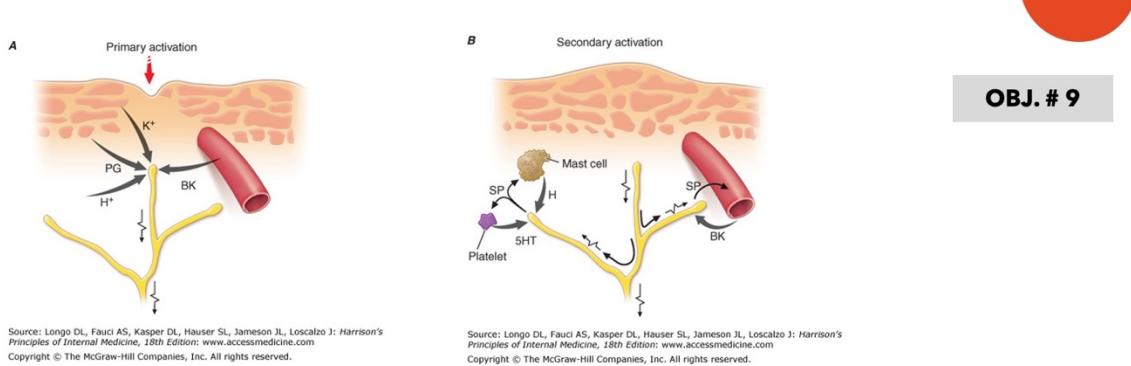
Pain frequently becomes chronic. There are different theories trying to explain the phenomenon of chronic pain. One hypothesis proposes that the injured nerve fibers are capable of spontaneous ectopic activation or that there is some type of ephaptic activation. Ephaptic activation refers to the possibility of nerve-to-nerve cross activation.

When sensory neurons in the dorsal horn of the spinal cord or thalamus have been chronically stimulated by pain signals, they gradually increase their excitability which triggers long-term changes in the responses of those neurons and with time they may be able to spontaneously discharge even in the absence of any sensory stimulus. They may develop a "memory" of the state of the C fiber input. This phenomenon is referred to as central sensitization.

Injury to the spinothalamic tract and its thalamic targets causes in certain situations a severe form of pain named central pain; infarcts of the VPL nucleus of the thalamus can produce this spontaneous pain syndrome. Pain in this situation is not localized

Objective # 9; Slide 31

A diagram showing the complex set of events leading to nociceptor stimulation. Knowledge about the pathophysiology of pain is very important to understand the current therapies used to fight against chronic pain.



Source: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine, 18th Edition*: www.accessmedicine.com
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Events leading to activation, sensitization, and spread of sensitization of primary afferent nociceptor terminals.

- A. Direct activation by intense pressure and consequent cell damage. Cell damage induces lower pH (H^+) and leads to release of potassium (K^+) and to synthesis of prostaglandins (PG) and bradykinin (BK). Prostaglandins increase the sensitivity of the terminal to bradykinin and other pain-producing substances.

- B. Secondary activation. Impulses generated in the stimulated terminal propagate not only to the spinal cord but also into other terminal branches where they induce the release of peptides, including substance P (SP). Substance P causes vasodilation and neurogenic edema with further accumulation of bradykinin (BK). Substance P also causes the release of histamine (H) from mast cells and serotonin (5HT) from platelets.

Objective # 10; Slide 32

The internal mechanisms that modulate pain perception: Pain modulation occurs at different levels of the brain and the spinal cord. One of the places where this modulation becomes more relevant is at the dorsal horn level where pain fibers synapse with second order neuron and projection neurons. The main mechanism for this modulation is the Descending Pain Modulating Pathway.

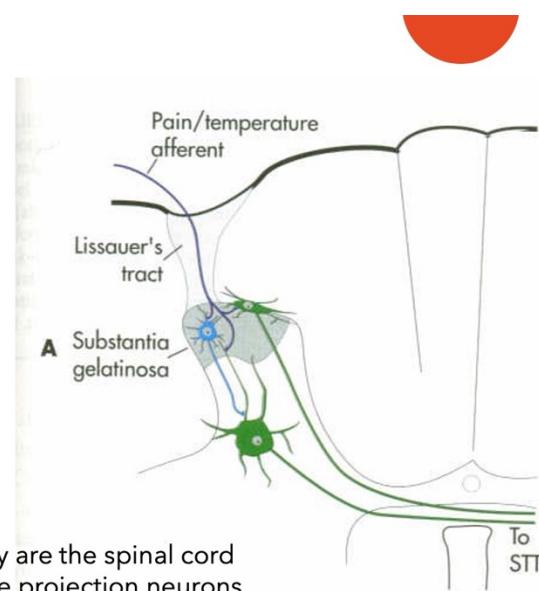
OBJ. # 10

Modulation Of Pain Perception

The body possess intrinsic mechanisms to modulate the transmission of pain.

- The **Descending Pain Modulating Pathway**

The targets of the descending pain pathway are the spinal cord neurons in the substantia gelatinosa and the projection neurons that transmit pain through the spinothalamic tract



Objective # 10; Slide 33

It appears that the central perception of a painful condition depends not only on ascending pathways but also on descending modulating pathways using a variety of neurotransmitters. The major inhibitory group of neurotransmitters in the dorsal horn of the spinal cord is the endogenous opioid peptides: enkephalins, endorphins, dynorphins, and other neurotransmitters such as norepinephrine, serotonin, glycine, and GABA.

The descending analgesia system consists of 3 major components: 1) the periaqueductal areas of the mesencephalon surrounding the aqueduct of Sylvius; 2) the raphe magnus nucleus, a midlinenucleus located in the reticular formation of the lower pons and upper medulla; 3) the nucleus reticularis paragigantocellularis located in the ventral rostral medulla (VRM). From these areas, signals are transmitted down to the spinal cord where they can block pain transmission to the brain.

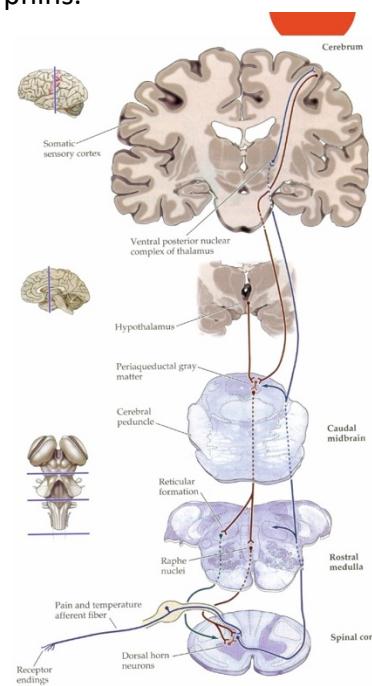
The best characterized descending analgesic pathways involve a projection from the periaqueductal grey (PAG) to the rostral ventral medulla, which in turn project to the dorsal horns of the spinal cord. High levels of endogenous opioid peptides and opioid receptors are found in neurons of the PAG, rostral ventralmedulla, and dorsal horn particularly in lamina I and II.

The discovery of the expression of opioid receptors in the CNS and PNS lead to the definition of major classes of endogenous opioid peptides that interact with specific classes of receptors. The opioid peptides are: enkephalins, β -endorphins and dynorphins.

Modulation Of Pain Perception

OBJ. # 10

- Modulation in the spinal cord through descending modulatory fibers using different neurotransmitters
- Endogenous opioid peptides:
 - Enkephalins
 - Endorphins
 - Dynorphins
 - Norepinephrine
 - Serotonin
 - Glycine
 - GABA



Objective # 10; Slide 34

Diagram showing how modulation of pain can be produced by descending pathways at several spinal cord levels.

Excitatory fibers coming from the rostral ventral medulla, or the raphe nucleus, excite inhibitory interneurons located mostly in the substantia gelatinosa. These inhibitory interneurons when stimulated release enkephalin as neurotransmitter decreasing pain transmission by projection neurons at appropriate dorsal horn levels by acting at the presynaptic terminal

Some norepinephrine containing pathways from the locus coeruleus in the pons and serotonergic pathways from the raphe nucleus in the medulla have been found which are also involved in pain modulation of dorsal horn neurons using mostly the same inhibitory mechanisms.

