Somatosensory System: Pain, heat and cold – anterolateral sensory system Touch, pressure and kinesthesia - the dorsal column system

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Literature: Kandel "Principles of Neuroscience" and Siegel and Sapru "Essential Neuroscience" (Ch15)

General organization of sensory systems

- Our knowledge of the environment around us depends on the information that we receive from peripheral receptors.
- Initial contact with our environment occurs at the sensory receptors, which are specialized neural structures.

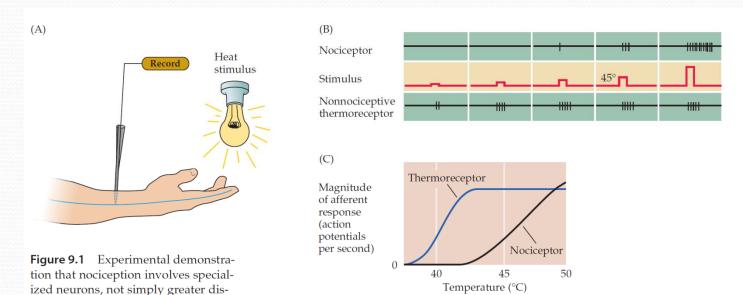
- Receptors –the first-order neuron of the pathway
- the second-order neuron of the pathway
- Thalamus
- Cerebral Cortex
- Interneurons
 – facilitation or inhibition of the signal
- Afferent and efferent pathway
- Convergention of the axons

Pain, heat and cold – anterolateral sensory system

Pain and thermal sensation – anterolateral sensory pathway

- Pain is defined as perception of an unpleasant sensation
- Painful (noxious) stimuli stimulate specialized receptors called **nociceptors**.
- The reception of signals from nociceptors by the central nervous system (CNS) is called **nociception**.
- Thermal sensation are carried via the same pathway as pain sensation. It starts with **thermoreceptors** and is carried by small myelinated Aδ and unmyelinated C fibers.

Nociceptors vs. thermoreceptors



Free nerve endings

charge of the neurons that respond to normal stimulus intensities. (A) Ar-

- Mechanical nociceptors
- Thermal and mechanothermal receptors
- Polymodal receptors

TABLE 15–3 Types of Nociceptors		
Receptor Type	Fiber Group	Sensation
Mechanical	Αδ	Sharp, pricking
Thermal and mechano-thermal	Αδ	Slow burning, cold sharp, pricking
Polymodal	C	Hot, burning sensation, cold, and mechanical stimuli

Nociceptors

- Are activated only when stimulus damages our body
- High treshold
- Low adaptation pain can last for hours or days
- Mechanical nociceptors –activated by mechanical stimuli
- Thermal and mechano-thermal receptors are activated by stimuli that cause slow, burning pain
- Polymodal receptors are activated by mechanical stimuli as well as temperature
 - Cold <10°C
 - Heat >45 °C
 - Acids, alkals
 - Inflamation

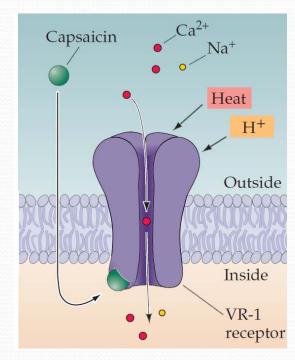
Nociceptors

Sensation of noxious heat: arround 43°C (110°F)

 Same nociceptor also confers sensitivity to capsaicin (ingredient in chili peppers responsible for the tingling and burning sensation produced by spicy foods)

• Vanilloid receptors – sensitive to heat but also to

capsaicin ("hot" food)



Types of the pain

- Superficial sharp, prickling pain: well localized, short-lasting – "first", "fast" pain; conducted via Aδ-fibers
- 2. Superficial burning pain: slower, weak localization, long-lasting (few seconds or minutes), evokes cardio-vascular and respiratory reflexes (tachicardia, tachipnea, deaper breathing) "second" "slower" pain, conducted via C-fibers
- 3. Deep burning, dull, diffuse pain from internal organs, muscles and joints often called "referred pain"

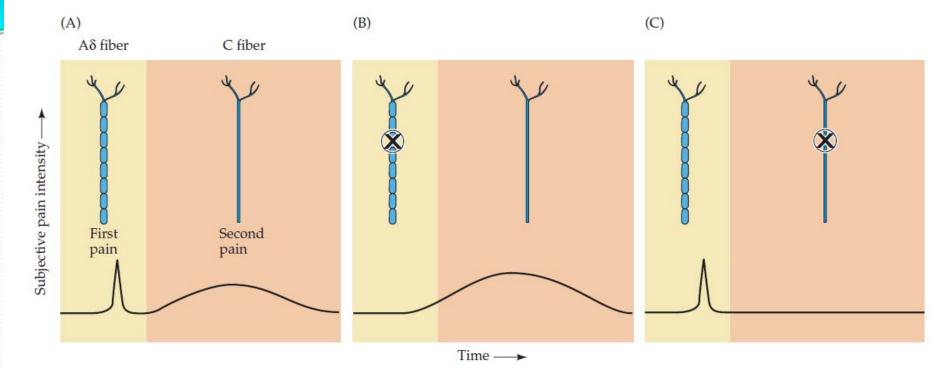


Figure 9.2 Pain can be separated into an early perception of sharp pain and a later sensation that is described as having a duller, burning quality. (A) First and second pain, as these sensations are called, are carried by different axons, as can be shown by (B) the selective blockade of the more rapidly conducting myelinated axons that carry the sensation of first pain, or (C) blockade of the more slowly conducting C fibers that carry the sensation of second pain. (After Fields, 1990.)

Some pain syndromes

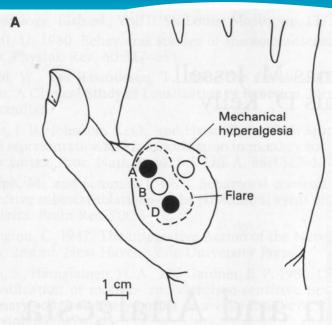
- Hyperalgesia
- Phantom Limb Pain
- Causalgia
- Neuralgia
- Reffered Pain
- Headaches

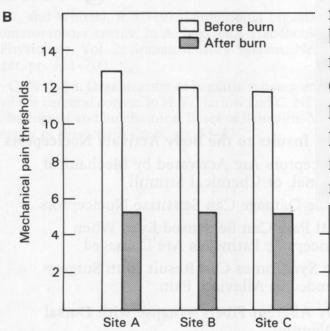
Hyperalgesia enhancement of the sensation of pain

- results from tissue damage and the release of many endogenous chemicals
- These chemicals may activate nociceptors themselves or may sensitize the nociceptors (e.g., lower their threshold)
- prostaglandin E2 is known to sensitize nociceptors
- Aspirin prevents the synthesis of prostaglandins.
- This effect may be responsible for its analgesic effect.
- Other endogenous chemicals that produce hyperalgesia are histamine, substance P, serotonin, and bradykinin.

Tissue injury ATP Prostaglandin Bradykinin Mast cell or 5-HT neutrophil Histamine Blood Substance P vessel Anterolateral system **CGRP** Substance P Dorsal root ganglion cell body Spinal cord

Figure 9.6 Inflammatory response to tissue damage. Substances released by damaged tissues augment the response of nociceptive fibers. In addition, electrical activation of nociceptors causes the release of peptides and neurotransmitters that further contribute to the inflammatory response.





primay hyperalgesia – at the site of injurysecondary hyperalgesia - adjacent to the site of injury

FIGURE 27-1

Burns to the glabrous skin of the hand produce both primary and secondary hyperalgesia to mechanical stimuli but only primary hyperalgesia to heat stimuli. (Reproduced with permission from Raja et al., 1989.)

- A. Mechanical thresholds for pain were recorded at sites A, B, and C before and after burns at sites A and D. The burns consisted of a 53°C stimulus for 30 sec at both sites. The areas of reddening (flare) and mechanical hyperalgesia following the burns in one subject are also shown. In all subjects the area of mechanical hyperalgesia was larger than the area of flare. Mechanical hyperalgesia was present even after the flare disappeared.
- **B.** Mean mechanical thresholds for pain before and after burns for seven subjects. The mechanical threshold for pain was significantly decreased following the burn.

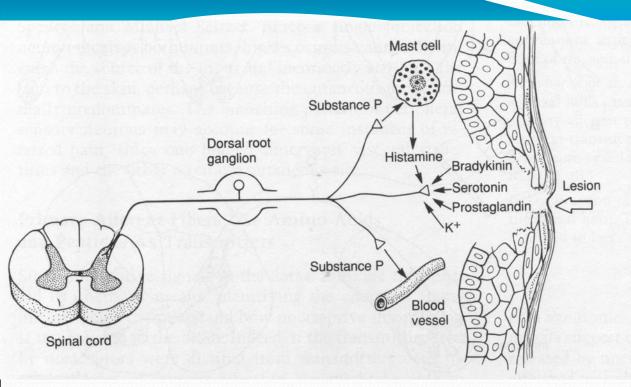


FIGURE 27-2

Chemical mediators can sensitize and sometimes activate the peripheral endings of nociceptors. Injury or tissue damage releases bradykinin (BK) and prostaglandins (PG), both of which activate and sensitize nociceptors. Activation of nociceptors leads to the release of substance P (SP) and other peptides. Substance P acts on mast cells in the vicinity of sensory endings to evoke degranulation and the release of histamine, which directly excites nociceptors. Substance P also produces dilation of peripheral blood vessels, and the resultant edema causes a further liberation of bradykinin. (See Table 27-1 for a list of chemicals that act on nociceptors.) (Adapted from Lembeck and Gamse, 1982, and Fields, 1987.)

Mediators of the inflamatory process sensitise or activate nociceptors:

- •1. Due to injury bradykinin, prostaglandin E2, and K+ are released
- 2. Substace P is than released from the activated nociceptors.
- •3. Histamine is released from mast cells
- •4. Substace P causes vasodilatation
- •5. Local edema evokes further release of bradykinin

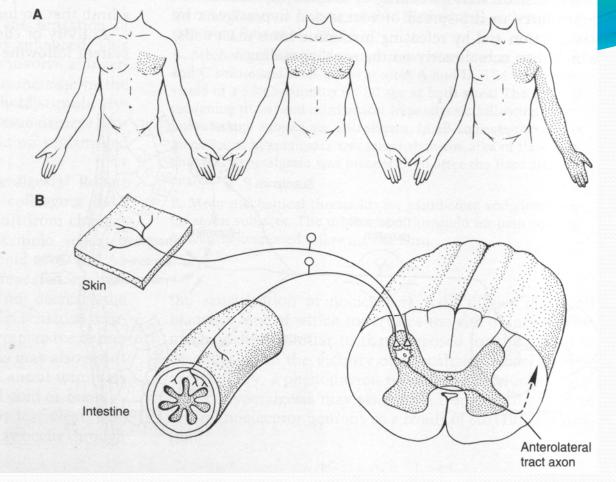
Reffered pain

- Sometimes, pain arising from deep visceral structures is felt at sites on the surface of the body.
- Pain stimuli arising due to myocardial ischemia are felt radiating to the sternum, arms, and wrists.

FIGURE 27-4

Signals from nociceptors in the viscera can be felt as pain elsewhere in the body. The source of the pain can be readily predicted from the site of referred pain.

- **A.** Areas of deep referred pain in myocardial infarction and angina. (From Teodori and Galletti, 1962.)
- B. Convergence of visceral and somatic afferents may account for referred pain. According to this hypothesis, afferent fibers from nociceptors in the viscera and afferents from specific areas of the periphery converge on the same projection neurons in the dorsal horn. The brain has no way of knowing the actual source of the noxious stimulus and mistakenly identifies the sensation with the peripheral structure. (Adapted from Fields, 1987.)



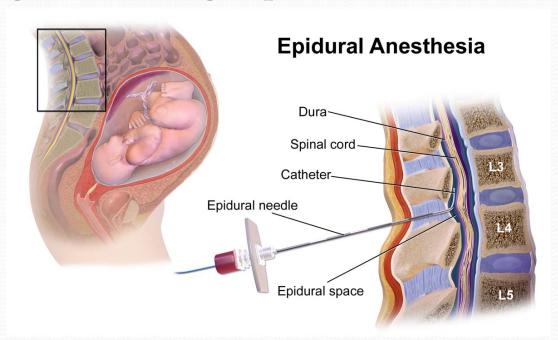
- •sensory pain fibers innervating the heart follow the sympathetic innervation of this organ back to the spinal cord, and their cell bodies are located in thoracic dorsal root ganglia at T1–T5.
- •The neuronal cell bodies supplying the dermatomes of the upper thorax and upper limbs are also located in the same dorsal root ganglia (T1–T5) and synapse on the same second-order neurons in the spinal cord segments (T1–T5) where cardiac sensory pain fibers synapse.

Local anesthesia

- injection of local anesthetic into the vicinity of the nerve blocks action potentials of the nerve (lidocaine)
- 1. Sensation of pain and temperature is diminished(γ motoneuron)
- 2. Sensation of touch, pressure and vibration diminishes afterwards (α-motoneuron)
- Well balanced dose of anesthetic diminishes sensation of pain with preserved sensation of touch, pressure and vibration

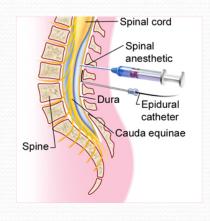
Lidocaine

- bupivacaine, chloroprocaine, lidocaine
- Blocks voltage-gated Na⁺ channels in the cell membrane.
- No depolarization no action potential no exocytosis - no synaptic transmission - anesthesia





SECTION



Central distribution of nociceptive information

- Multidimensional, involving discriminative, affective, and motivational components
- Correspondingly complex, involving multiple areas in the *brainstem*, *thalamus*, and *forebrain*

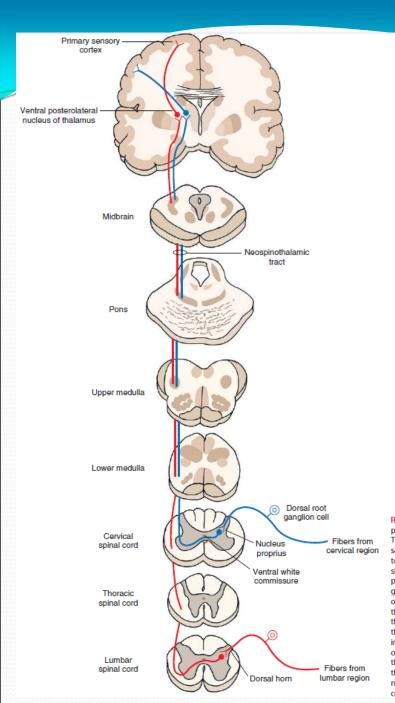
Anatomical Pathways Mediating Pain Sensations From the Body

- The cell bodies of sensory neurons mediating pain are located in the dorsal root ganglia (first-order neurons).
- The central axons (both Aδ and C fibers) of these sensory neurons reach the dorsal horn and branch into ascending and descending collaterals, forming the **dorsolateral tract (fasciculus) of Lissauer.**
- enter the gray matter of the dorsal horn, and synapse on neurons located in laminae I and II (substantia gelatinosa).

- The second-order neurons in laminae IV to VI are collectively called the nucleus proprius (principal sensory nucleus).
- The axons of the principal sensory nucleus, which mediate nociceptive signals, cross to the contralateral side in the *anterior* (*ventral*) *white commissure* of the spinal cord and form the **neospinothalamic tract** in the lateral funiculus.
- posterior nuclei of the thalamus
- primary sensory cortex

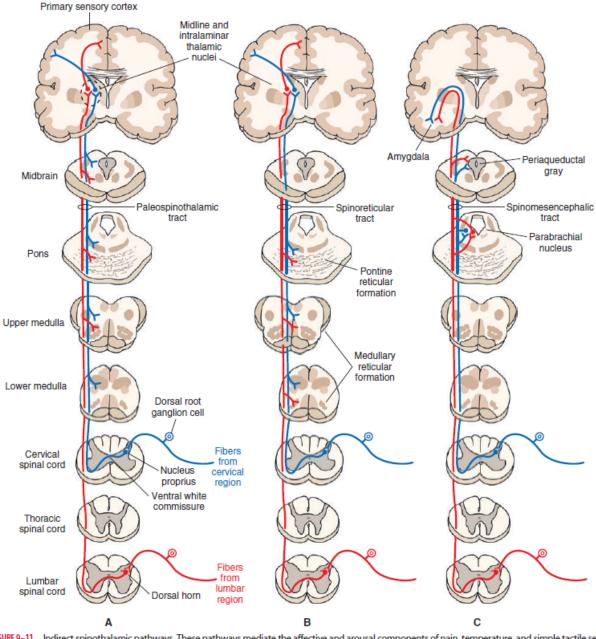
Anatomical pathways

- 1. tractus spinothalamicus lateralis
- tractus spinoreticularis
- 3. tractus spinomesencephalicus
- 4. tractus spinocervicalis
- The neospinothalamic tract



The neospinothalamic tract

FIGURE 9-10 Direct spinothalamic pathway: the neospinothalamic tract. The peripheral processes of these dorsal root ganglion cells end as receptors sensing pain, temperature, and simple tactile sensations. The central processes of these dorsal root ganglion cells synapse with the neurons of the nucleus proprius. The axons of these second-order neurons cross via the anterior white commissure, enter the contralateral white matter, ascend in the lateral funiculus, and synapse on third-order neurons located in the ventral posterolateral nucleus of the thalamus. The axons of third-order neurons project to the primary sensory



A:The paleothalamic tract
B:Spinoreticular tract
C:Spinomesencephalic tract

FIGURE 9–11 Indirect spinothalamic pathways. These pathways mediate the affective and arousal components of pain, temperature, and simple tactile sensations. (A) The ascending axons in the paleothalamic tract synapse in the brainstem reticular formation and neurons in midline and intralaminar thalamic nuclei, which then project diffusely to the cerebral cortex including the cingulate gyrus. (B) In the spinoreticular tract, one group of ascending axons projects to the medullary reticular formation, and the other group projects to the pontine reticular formation. The neurons in the reticular formation then project to neurons located in the midline and intralaminar thalamic nuclei. These thalamic neurons then project to the cerebral cortex. (C) In the spinomesencephalic tract, ascending axons terminate on the periaqueductal gray neurons that, in turn, project to neurons in the amygdala via the parabrachial nuclei.

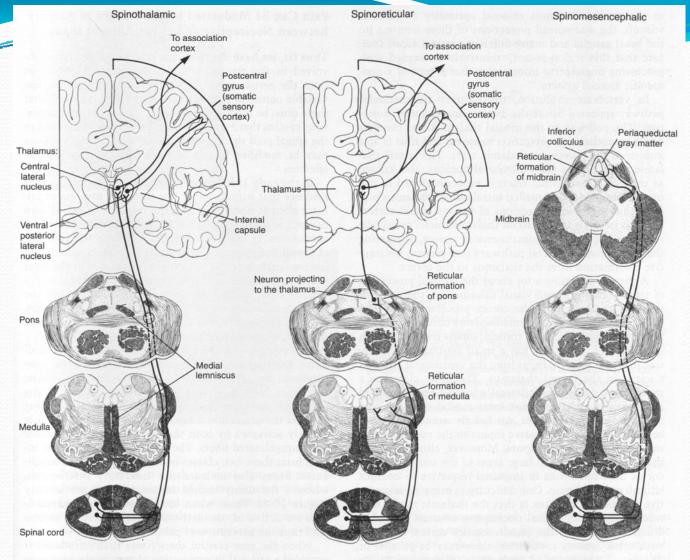
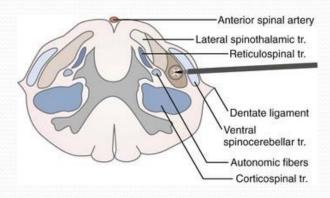


FIGURE 27-7

Three major ascending pathways transmit nociceptive information from the dorsal horn of the spinal cord to higher centers. (Adapted from Willis, 1985.)

- Injury to the neospinothalamic tract in the brainstem or spinal cord results in loss of pain and thermal sensation on the contralateral side below the level of the lesion.
- Elimination of intractable pain by surgically interrupting the spinothalamic tract (**cordotomy**) usually at the level of the spinal cord.



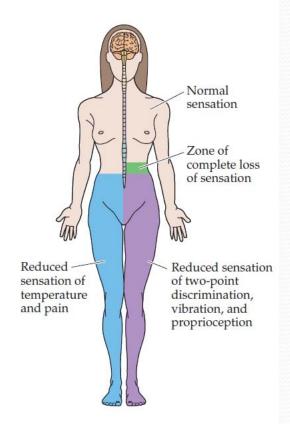
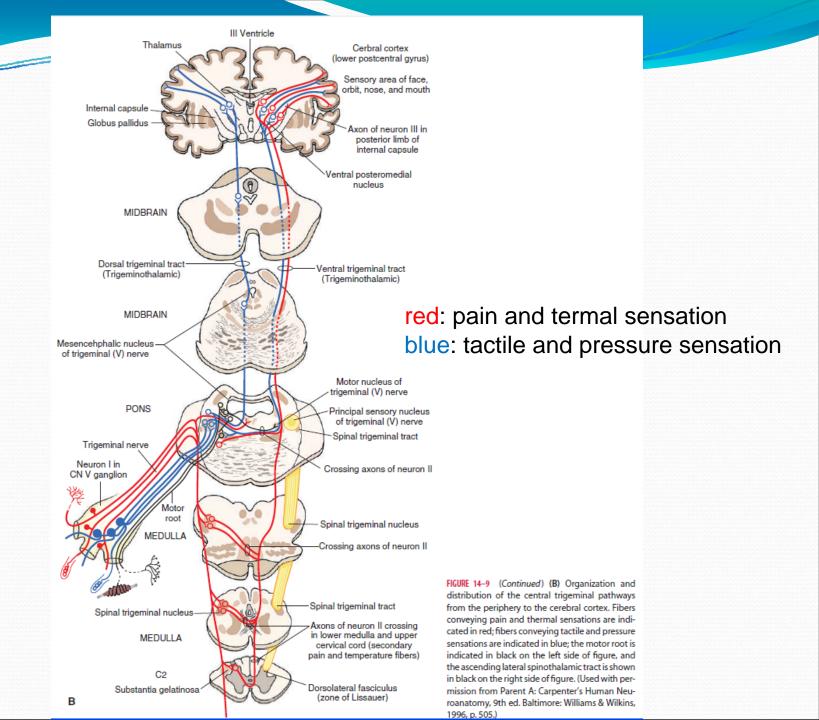
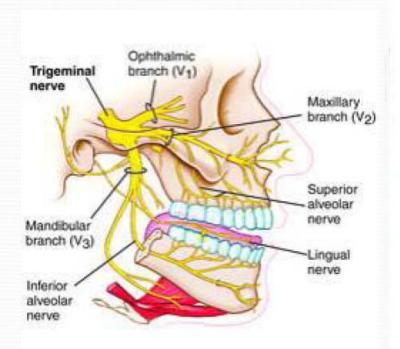


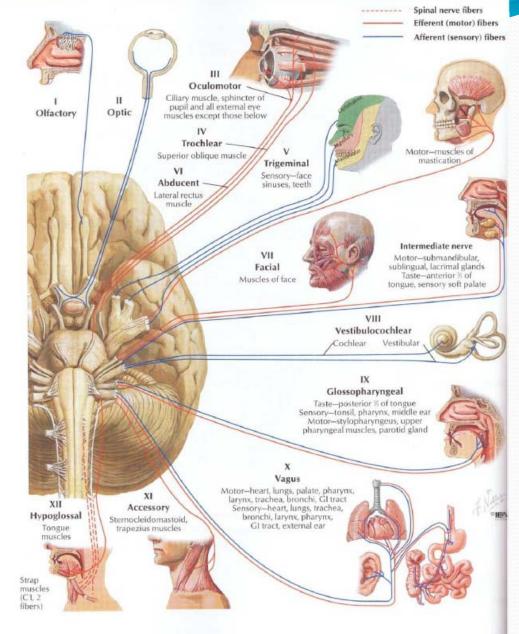
Figure 9.4 Pattern of "dissociated" sensory loss following a spinal cord hemisection at the 10th thoracic level on the left side. This pattern, together with motor weakness on the same side as the lesion, is sometimes referred to as Brown-Séquard syndrome.

Anatomical Pathways Mediating Pain Sensation From the Head and Face

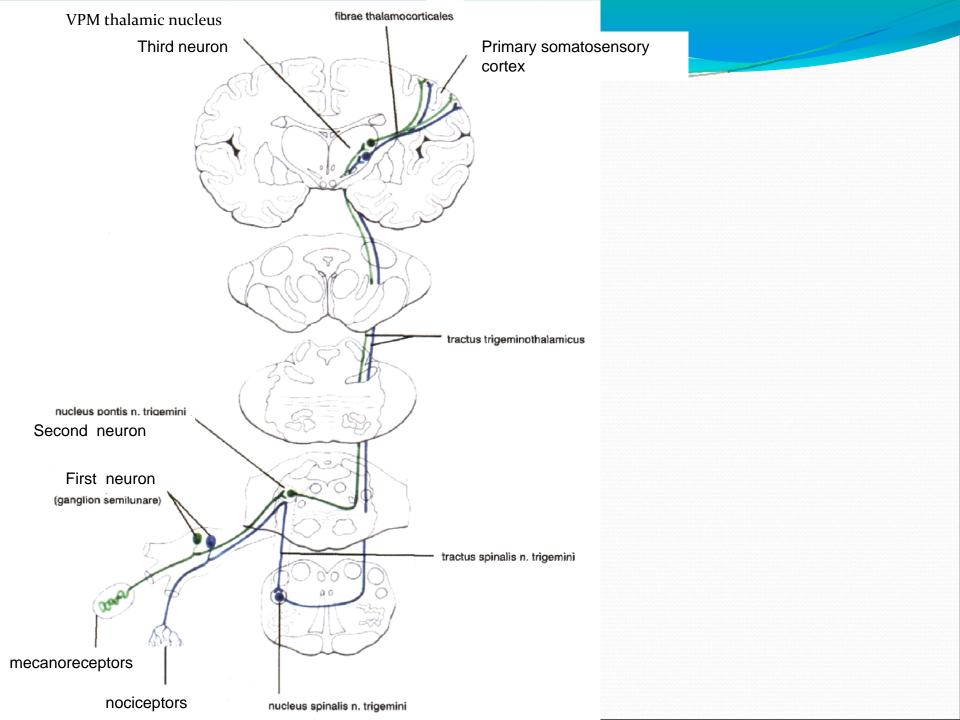
trigeminal thalamic pathways



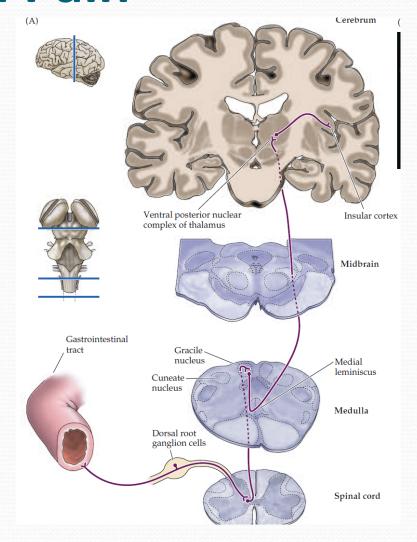


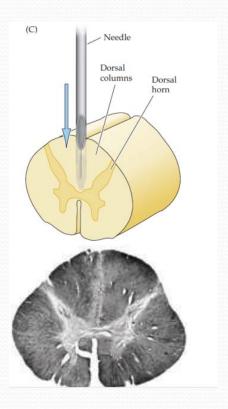


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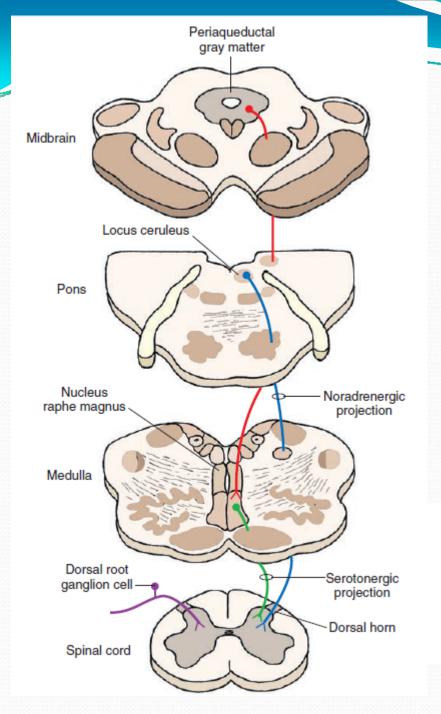
A Dorsal Column Pathway for Visceral Pain





Descending Pathways Modulating Pain Sensory Mechanisms

- Pathway from the Periaqueductal Gray
- Pathway from the Nucleus Raphe Magnus
- Noradrenergic Pathway: Axons of noradrenergic locus ceruleus neurons located in the upper pons



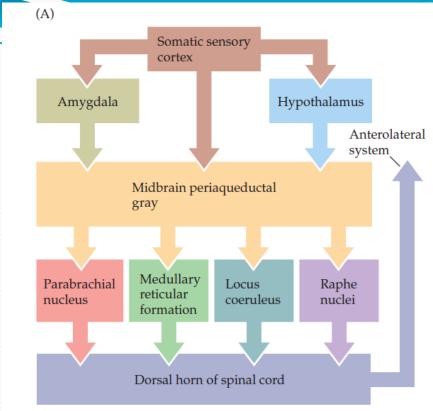


FIGURE 15–3 Descending pathways modulating pain sensory mechanisms. The neurons located in the periaqueductal gray matter of the midbrain project to the serotonergic neurons in the nucleus raphe magnus that is located in the midline of the medulla. Locus ceruleus noradrenergic neurons are located in the upper pons. The axons of serotonergic raphe magnus neurons and noradrenergic locus ceruleus neurons descend to all levels of the spinal cord and synapse on enkephalincontaining interneurons located in the dorsal horn.

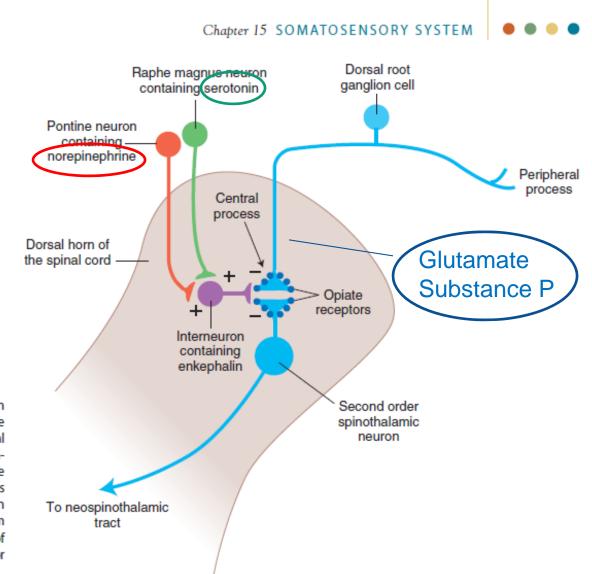
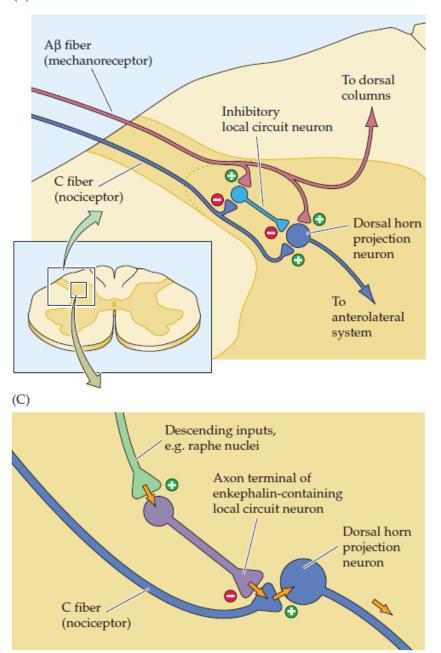


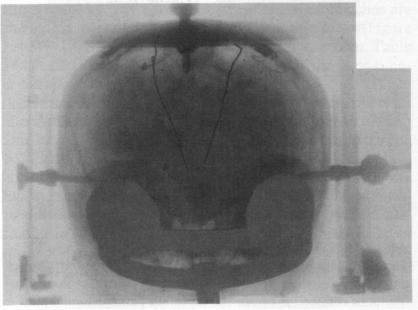
FIGURE 15–4 Neurotransmitters involved in pain pathways. Substance P and glutamate are released in the dorsal horn of the spinal cord in response to peripheral painful stimulus. Descending projections from the nucleus raphe magnus and locus ceruleus activate enkephalinergic interneurons in the dorsal horn. Enkephalin released from these interneurons inhibits the release of substance P and glutamate. (See text for other details.)



Opiate analgetics

- morphine
- Affects central structures of descending pathway
- John Huges i Hans Kosterlitz (USA): there are endogenous opioid peptides in the brain
 - enkephalin
 - endorphin (β-endorphin)
 - dinorphin
- Location of the neurons containing opioid peptides: periaqueductal grisea (PAG), dorsal horn (interneurons)
 Opioid receptors: μ, δ, κ





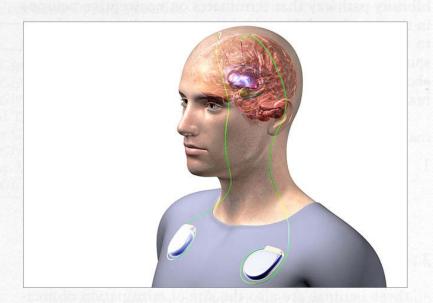


FIGURE 27-9

Stereotaxic method of electrode implantation in a human subject with chronic pain. The **top** radiograph shows a lateral view of a patient's cranium in the stereotaxic frame. Radiopaque medium is used to reveal the ventricular system. The target for placement of the electrodes is lateral to the point where the cerebral aqueduct meets the caudal end of the third ventricle (**arrow**). The **bottom** radiograph, an anterior—posterior view of the same patient, shows the electrodes in place. (Courtesy of J. E. Adams, as shown in Fields, 1987.)

Thermoreceptors

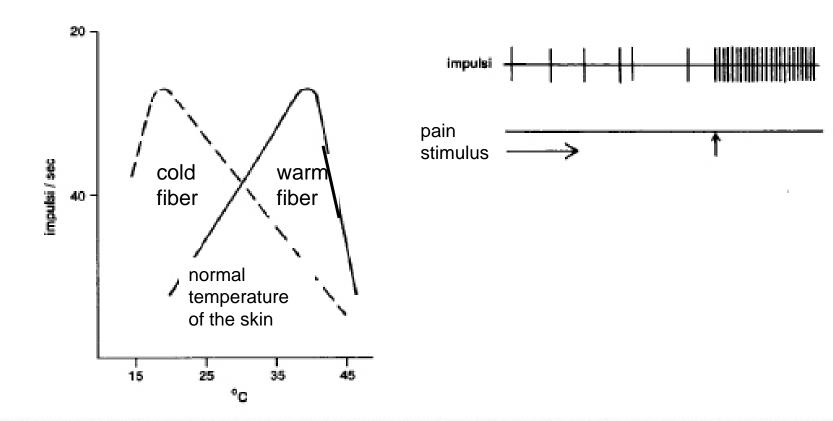
- Perifer skin thermoreceptors
- Enable sensation of heat and cold
- Regulate body temperature
- Static and dynamic
- small <u>changes</u> in temperature (0,1°C)
- Free nerve endings
- Small receptive field (1 mm²)

Termoreceptors for cold

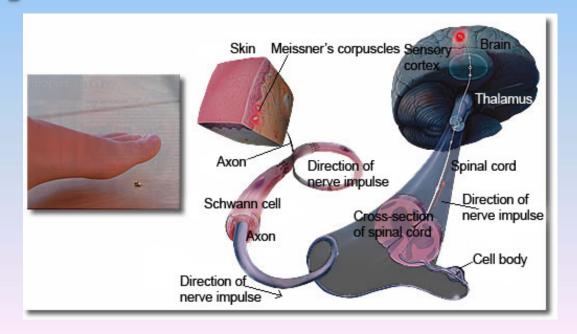
- "cold" Aδ-fibers
- Speed 5-15 m/sec
- Max. activated at 25-27°C
- Worming decreases their activity

Termoreceptors for warm

- "worm" C-fibers
- Low treshold
- Speed <2 m/sec
- Maximally activated at 39-40°C
- If temp>45°C we feel pain –polymodal nociceptors are activated
- Cooling of the skin inactivate "warm" fibers



Touch, pressor and kinesthesia - the dorsal column system



Touch, pressure and kinesthesia - the dorsal column system

- mechanical stimulation of the skin causes different forms of sensation
- Appropriate stimmulus for tactile sensation is mechanical deformation of the skin
- *pressure difference* among two neighbouring skin pieces is very important
- Equaly distributed pressure is not adequate stimulus for tactile sensation.

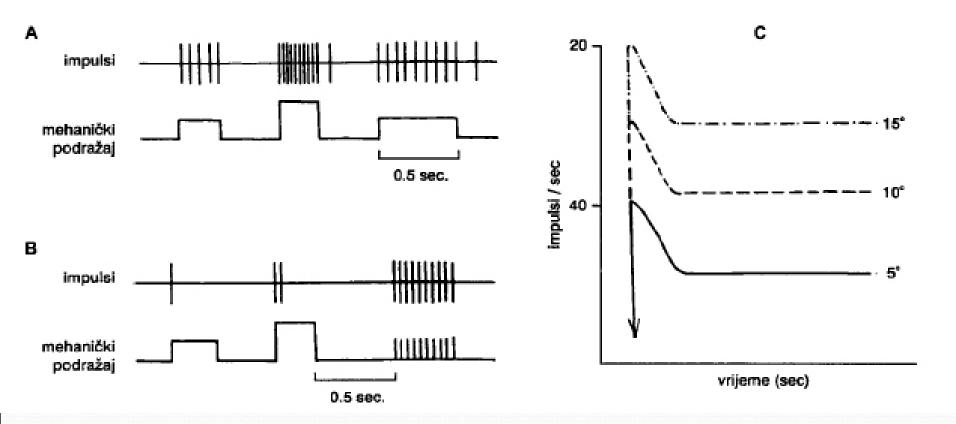
Mechanoreceptors

TONIC

- Respond on PERMANENT pressure to the skin
- Active while the skin is in the new position
- Respond to the speed of skin displacement
- Respond to the direction of the stimulus – better response from the baseline than toward the baseline

PHASIC

- Respond only to CHANGE IN THE POSITION of the skin or hair
- Active through the duration of the movement itself
- Inactive when the skin is in the new position
- Do not respond to the direction of the stimulus
- Have sensibility for high frequency, vibrating stimulus



Four types of cutaneous and subcutaneous mechanoreceptors

- 1. Free nerve endings (A δ -fibers)
- 2. Incapsulated endings (Paccinian, Meissner's, Krause's corpuscles, Ruffini endings)
- 3. Hair follicle receptor
- 4. Merkel disk receptor (group of epiteloid Merkel's cells)

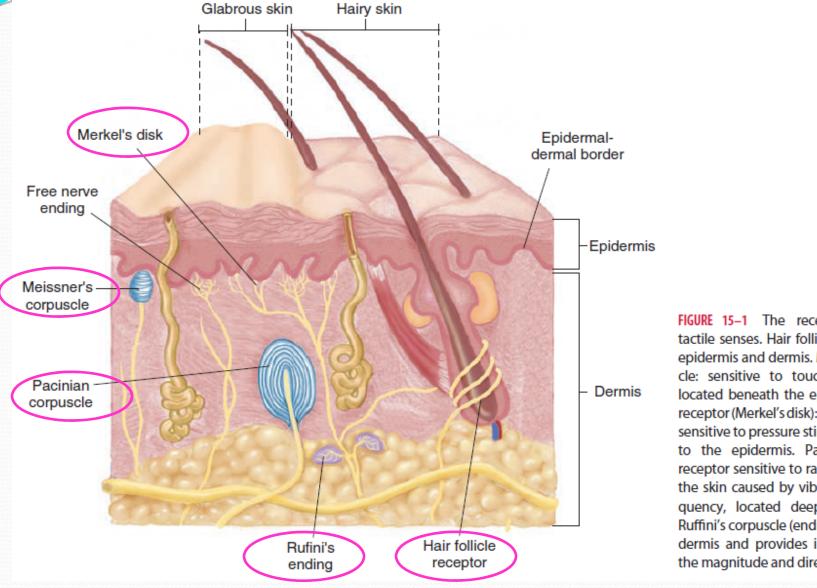


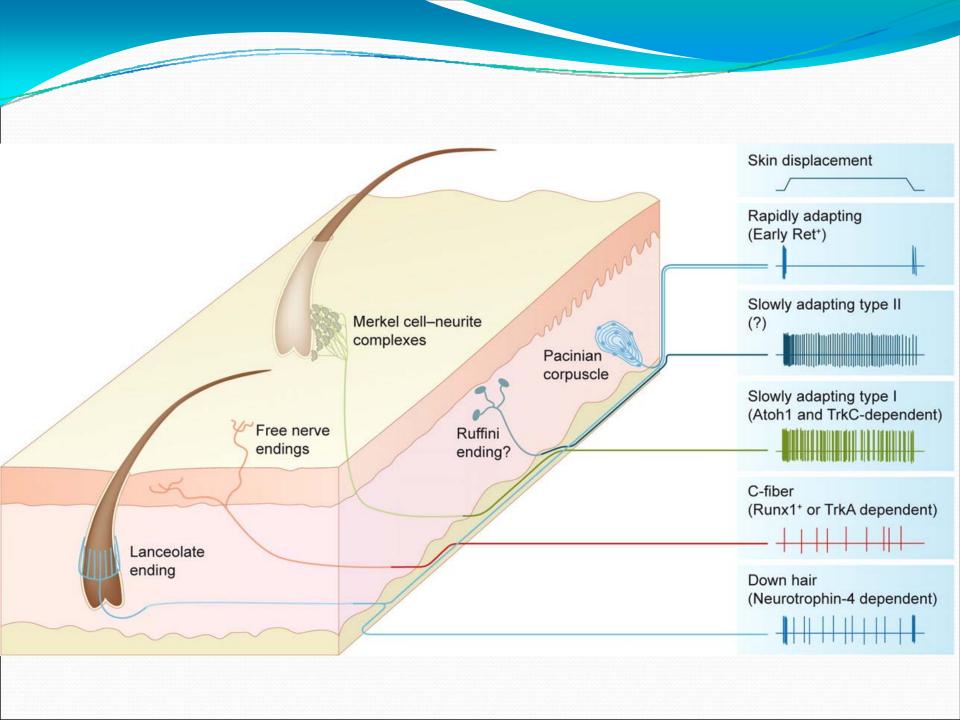
FIGURE 15-1 The receptors mediating tactile senses. Hair follicle: located in the epidermis and dermis. Meissner's corpuscle: sensitive to touch and vibration, located beneath the epidermis. Merkel's receptor (Merkel's disk): mechanoreceptor sensitive to pressure stimuli, located deep to the epidermis. Pacinian corpuscle: receptor sensitive to rapid indentation of the skin caused by vibration of high frequency, located deep in the dermis. Ruffini's corpuscle (ending): located in the dermis and provides information about the magnitude and direction of stretch.

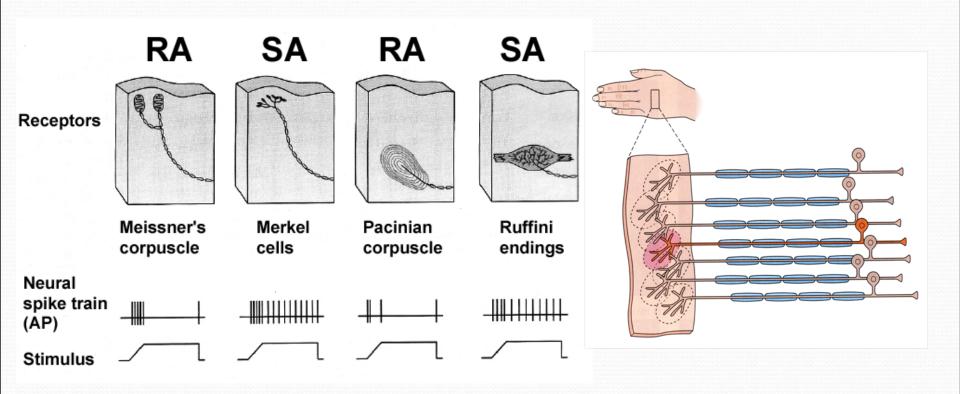
Muscle and skeletal mecahnoreceptors

- Muscle spindle primary
- Muscle spindle secondary
- Golgi tendon organ
- Joint capsule mecahnoreceptors
- Stretch-sensitive free endings

Physiological characteristics

- Adaptation properties
- Sensory treshold
- Rapidly adapting receptors (RA-detectors of speed
 - Active touch, Braill's letter
- Slowly adapting receptors (SA-detectors of the position)
 - Passive touch





Receptive field: Fingers – 2mm, Palm – 10 mm, upper arm- 40mm

	TABLE 15—2 Mechanoreceptors	
Mechanoreceptor Type Receptor	Function	
Cutaneous and subcutaneous: involved in touch, pressure, and vibration	Meissner's corpuscle (low-threshold, rapidly adapting); found in glabrous skin	Touch, vibration below 100 Hz
	Merkel's receptor (low-threshold, slowly adapting); found in glabrous skin	Pressure
	Pacinian corpuscle* (low-threshold, rapidly adapting); found in both hairy and glabrous skin	Rapid indentation of skin, e.g., the se a high frequency vibration (100–400
	Ruffini's corpuscle (low-threshold, slowly adapting); found in both hairy and glabrous skin	Magnitude and direction of stretch
Muscle mechanoreceptors	Muscle spindles	Limb proprioception
	Golgi tendon organ	Limb proprioception
*Pacinian corpuscle is also present in the mesentery.		

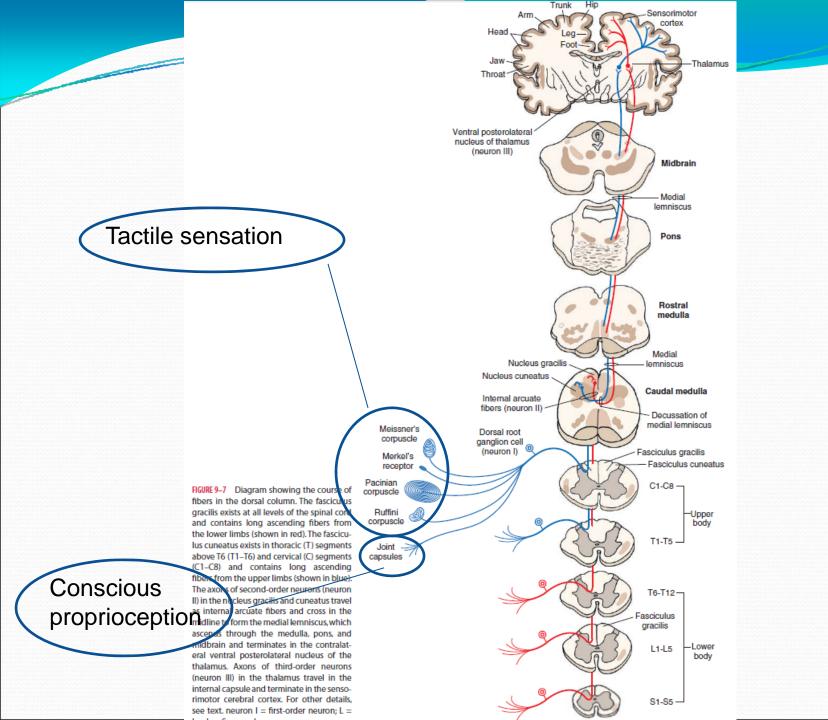
Proprioception

- Awareness of the position and movement of the body parts.
- Conscious proprioception
- proprioceptors respond to mechanical forces generated within the body itself
- receptors located in the joint capsules
 (proprioceptors) provide sensory information to the
 cerebral cortex, which, uses this information to
 generate conscious awareness of kinesthesia (the joint
 position, direction, and velocity of joint movements)

- depend predominantly on joint receptors
- The encapsulated joint receptors are low-threshold mechanoreceptors
- **static aspect of kinesthesia** (i.e., the ability of an individual to judge the **position** of a joint without seeing it and without a movement)
- *dynamic aspect* of kinesthesia (i.e., ability of an individual to perceive the **movement** of a joint and to judge the **direction** and **velocity** of its movement).

Anatomical Pathways

- Tactile sensation and conscious proprioception are mediated by the dorsal column (dorsal or posterior funiculus)-medial lemniscus system
- The cell bodies (1st order neurons) are located in dorsal root ganglia
- tactile sensations (Meissner's, Merkel's, Pacinian, and Ruffini)
- conscious proprioception (receptors located in the joints and joint capsules)



- Nonconsious proprioception
- Muscle spindles and Golgi tendon organs are relayed to the cerebellum rather than to the cerebral cortex.
- Muscle spindles are present in skeletal (flexor as well as extensor) muscles
- arranged parallel to the extrafusal muscle fibers
- Golgi Tendon Organ high-threshold receptors located at the junction of the muscle and tendon.
- arranged in series with the muscle fibers

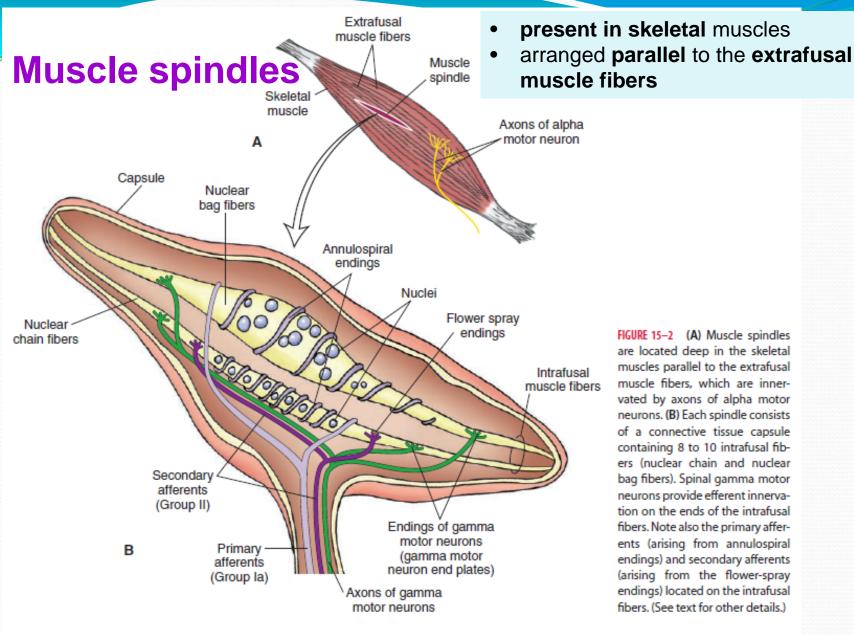
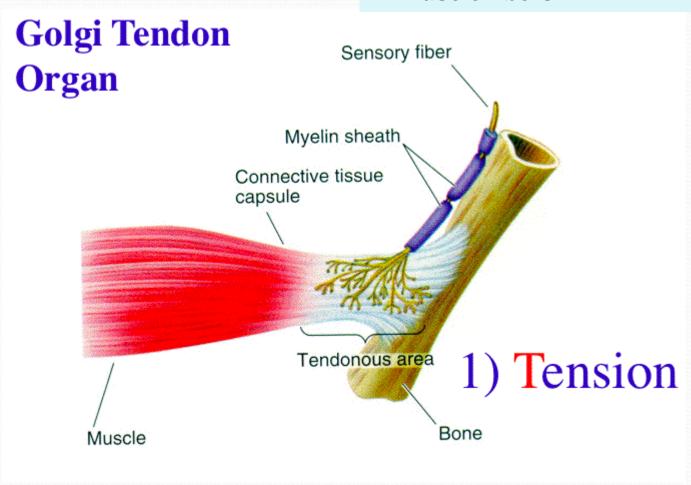


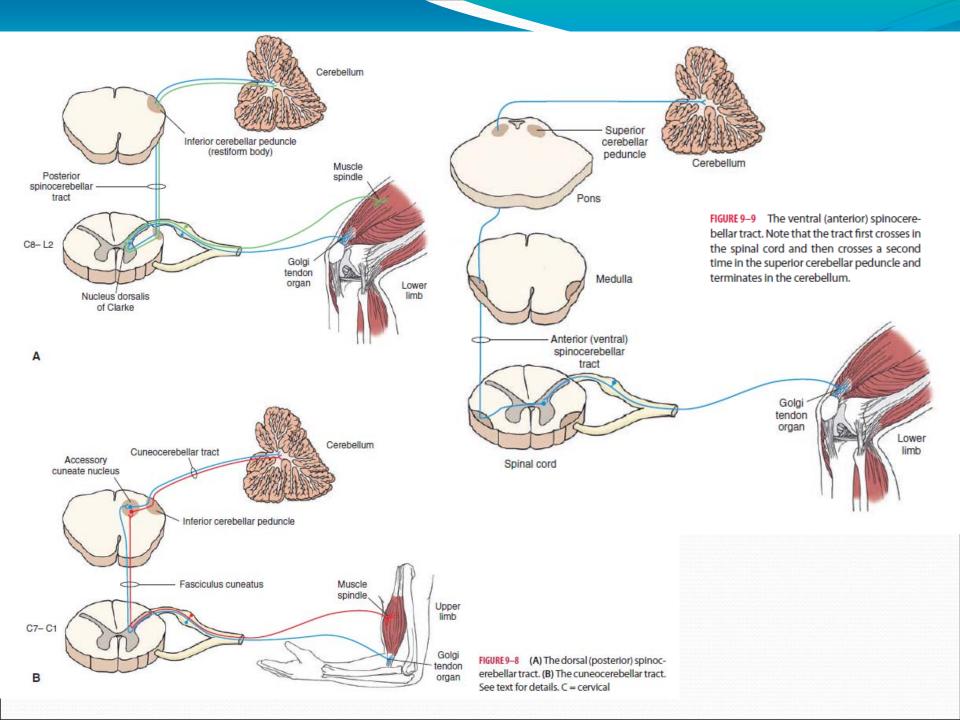
FIGURE 15-2 (A) Muscle spindles are located deep in the skeletal muscles parallel to the extrafusal muscle fibers, which are innervated by axons of alpha motor neurons. (B) Each spindle consists of a connective tissue capsule containing 8 to 10 intrafusal fibers (nuclear chain and nuclear bag fibers). Spinal gamma motor neurons provide efferent innervation on the ends of the intrafusal fibers. Note also the primary afferents (arising from annulospiral endings) and secondary afferents (arising from the flower-spray endings) located on the intrafusal

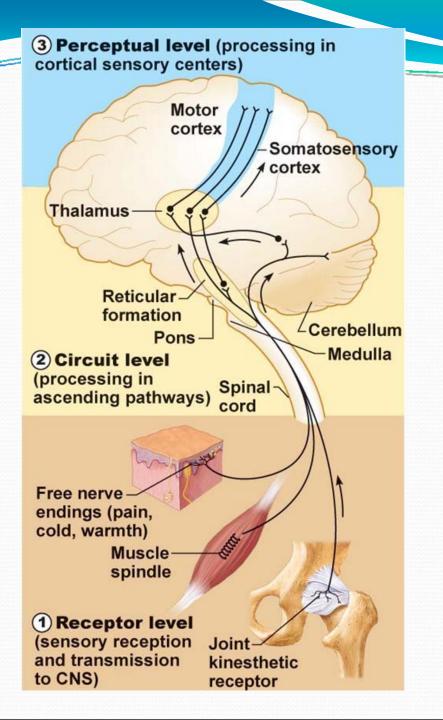
- high-threshold receptors located at the junction of the muscle and tendon.
- arranged in series with the muscle fibers



Anatomical Pathways

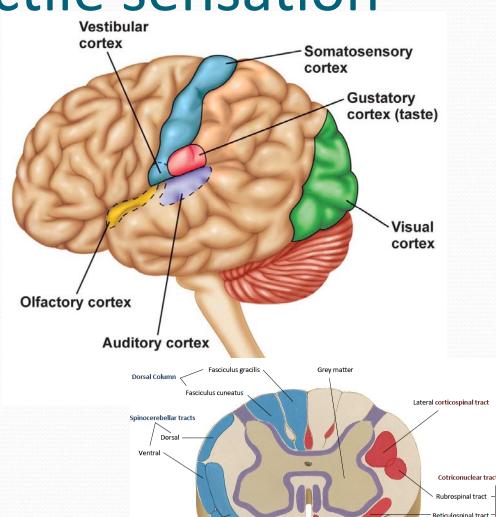
- Posterior (dorsal) spinocerebellar tract
- Anterior (ventral) spinocerebellar tract
- First-order sensory neuron is located in dorsal-rooth ganglia





Pathway for tactile sensation

- FROM BODY:
- 1st order neuron
- 2nd order neuron
- 3rd order neuron
 - dorsal-rooth ganglia
 - Fasciculus gracilis
 - Fasciculus cuneatus
 - Nucleus gracilis and cuneatus
 - Lemniscus medialis
 - Thalamus
 - Cortex



Vestibulospinal tract

Anterolatera

system

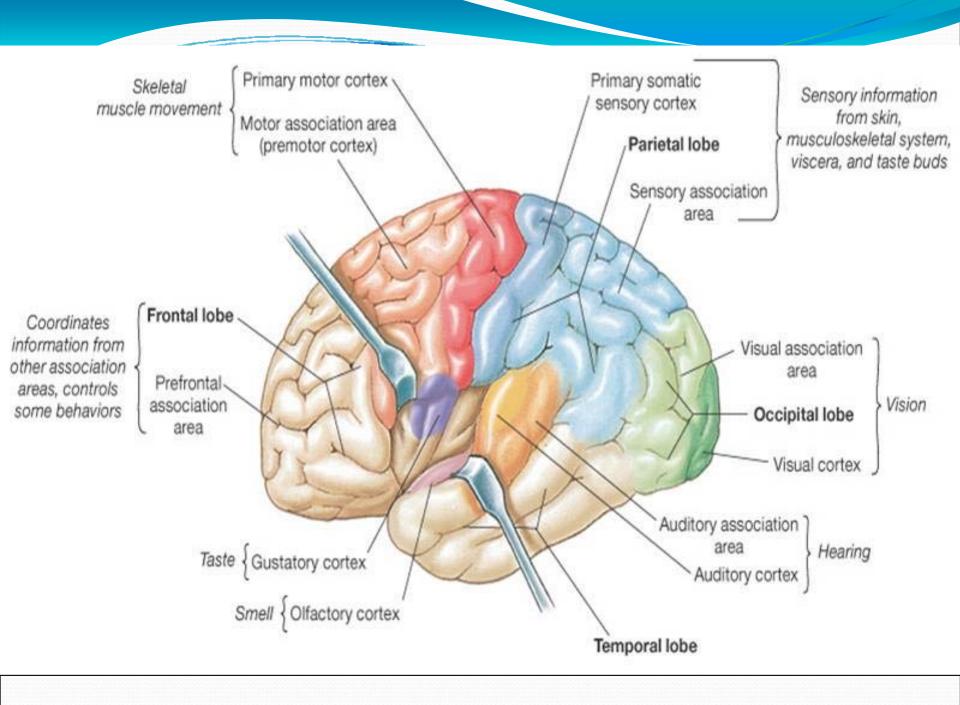
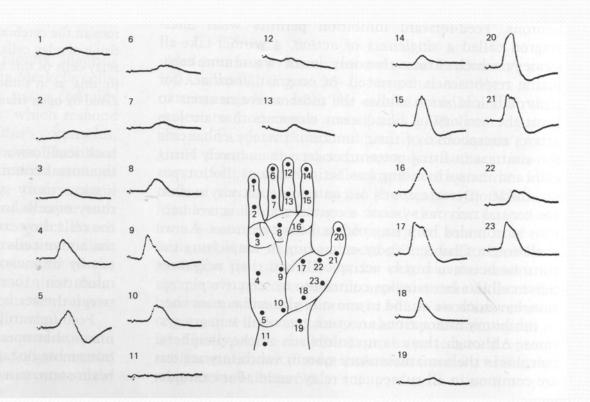


FIGURE 26-3

A map of evoked potentials can be obtained in a monkey from the surface of the left postcentral gyrus of the cerebral cortex by applying stimuli to the body surface on the opposite side. This figure shows the responses of one large group of cells in the left postcentral gyrus to a light tactile stimulus applied to different points on the right palm. These cells respond much more effectively to tactile stimuli applied to the thumb and forefinger (points 15, 16, 17, 20, 21, and 23) than to those applied to the middle or the small finger (points 1, 2, 3, 12, and 13). (Adapted from Marshall, Woolsey, and Bard, 1941.)



Evoked potential – recorded in the left postcentral gyrus by applying light tactile stimuls applied to different points of the right palm. Response is stronger when stimulus is applied to the thumb and forefinger (14-23) and weaker when applied to the middle or the small finger (1-13).

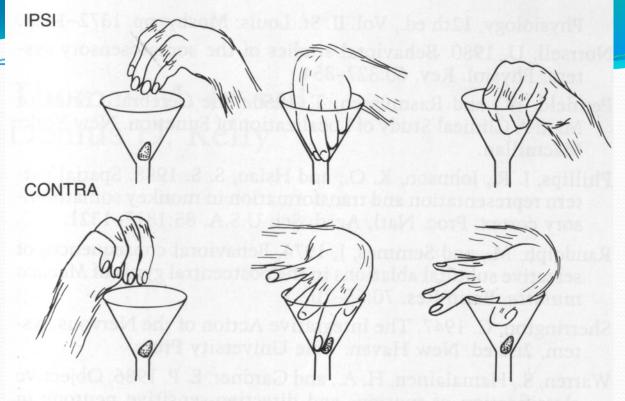
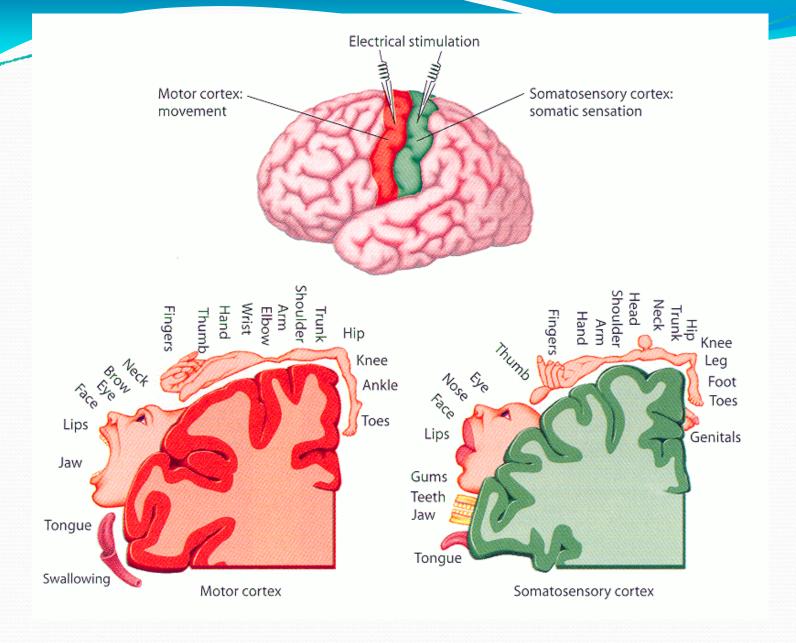
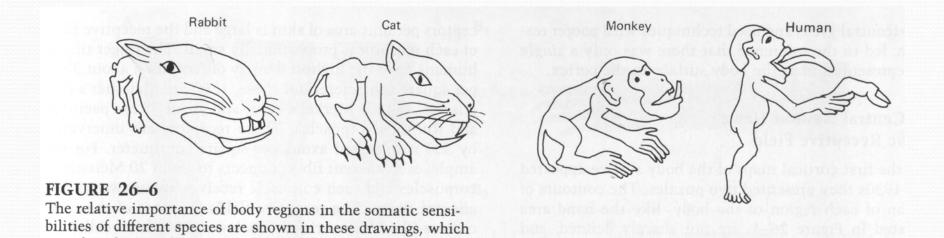


FIGURE 26–15

A monkey's finger coordination is disrupted following the injection of muscimol, a GABA agonist that inhibits synaptic transmission in the somatic sensory cortex. The left hand (ipsi) is able to pick up an apple piece from a funnel. Two hours following the injection of muscimol into Brodmann's area 2 on the left side, the finger coordination of the right hand (contra) is severely disorganized. (Adapted from Hikosaka et al., 1985.)

Brodmann's area 2 sends somatosensory informations to the primarny motor cortex – inhibition of neural activity results in the loss of coordinated fingers movement.





Principles of Neural Science, Kandel, Schwartz, Jessell

cortex.

were based on studies of evoked potentials in the thalamus and

