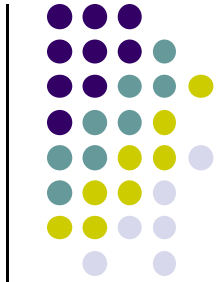
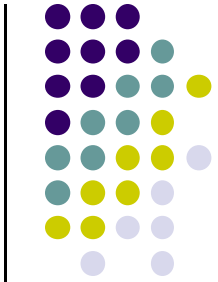


Dr. Mohammad Alsalem, PhD

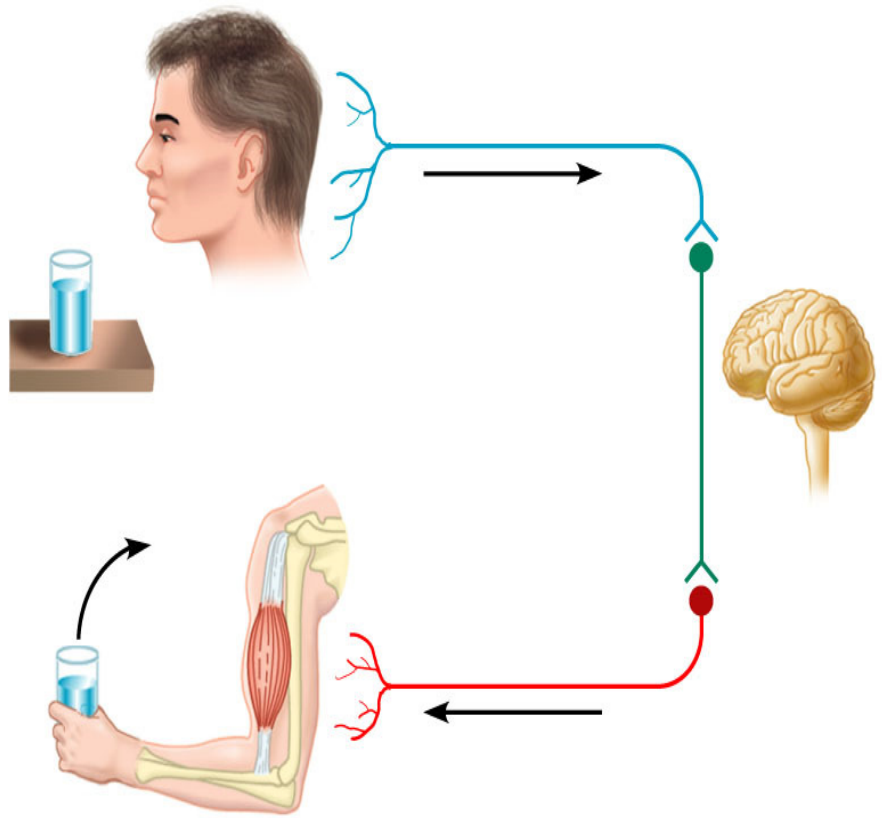
The Nervous System



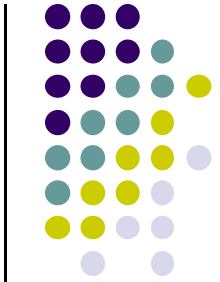
- A network of billions of nerve cells linked together in a highly organized fashion to form the rapid control center of the body.

Basic Functions of the Nervous System

1. Sensation
   - Monitors changes/events occurring in and outside the body. Such changes are known as *stimuli* and the cells that monitor them are *receptors*.
2. Integration
   - The parallel processing and interpretation of sensory information to determine the appropriate response
3. Reaction
   - Motor output.
     - The activation of muscles or glands (typically via the release of neurotransmitters (NTs))

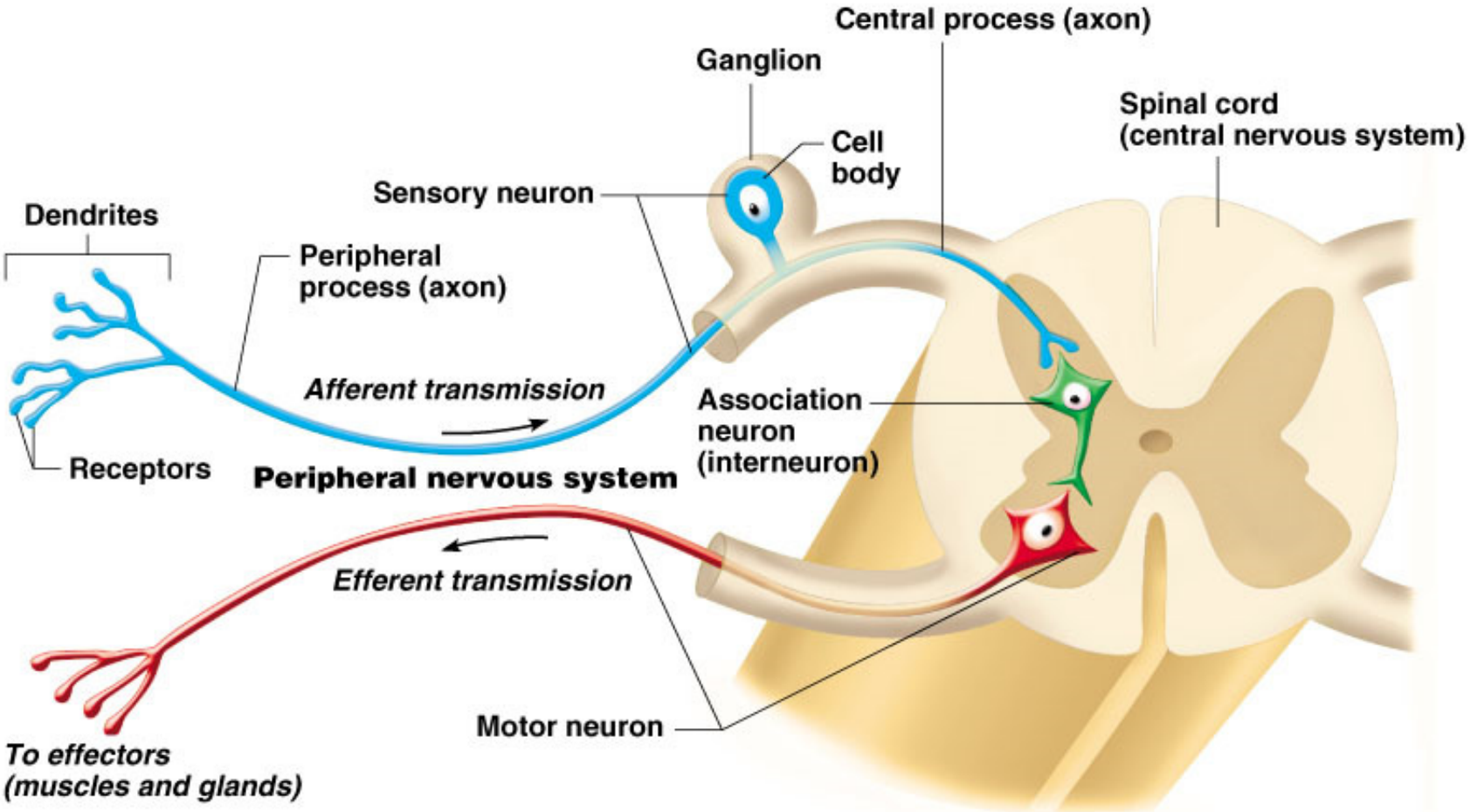


Nervous Tissue



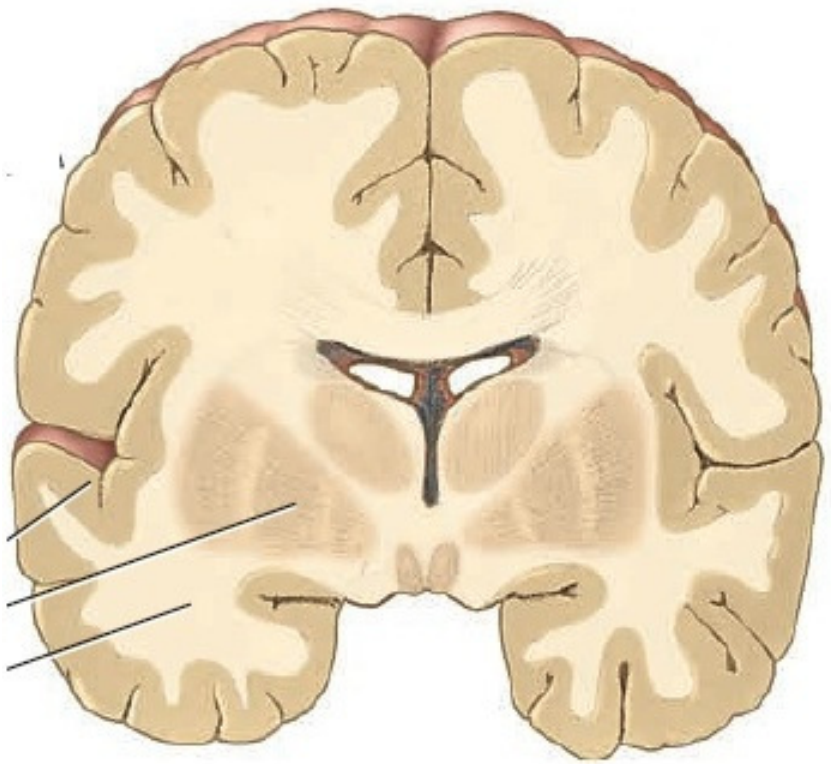
- Highly cellular
- 2 cell types
  1. Neurons
     - Functional, signal conducting cells
     - Do not divide
     - Long lived
     - High metabolic activity
     - Electrically excitable
  2. Neuroglia
     - Support, nourish, and protect neurons
     - Divide
     - Smaller cells but they greatly outnumber neurons by about 5 to 50
     - 6 types of supporting cells: (4 are found in the CNS, and 2 are found in the PNS.

Functional Classification of Neurons

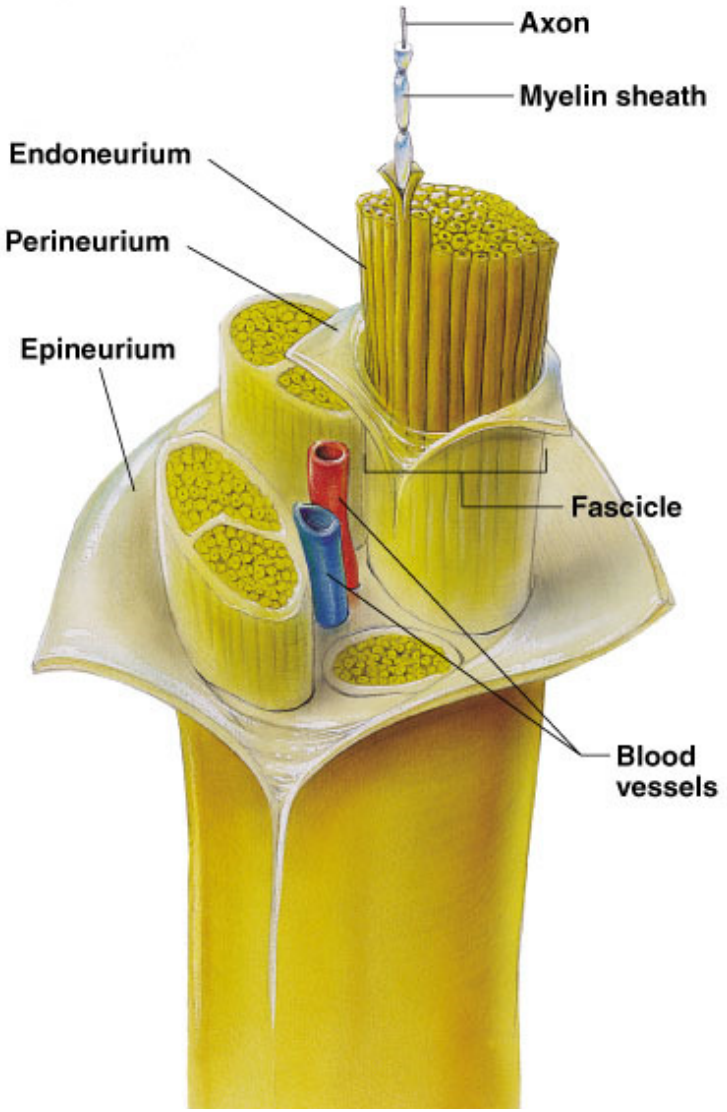


- **White matter:** aggregations of myelinated and unmyelinated axons of many neurons
- **Gray matter:** contains neuronal cell bodies, dendrites, unmyelinated axons, axon terminals, and neuroglia

▪**Nerves**: Bundles of processes in the PNS
▪**Tracts**: Bundles of processes in the CNS (No Connective tissue)
▪**Ganglion**: cluster of nerve cell bodies in PNS
▪**Nucleus**: cluster of nerve cell bodies in CNS (surrounded by white matter)
➢ If not surrounded (Cortex)

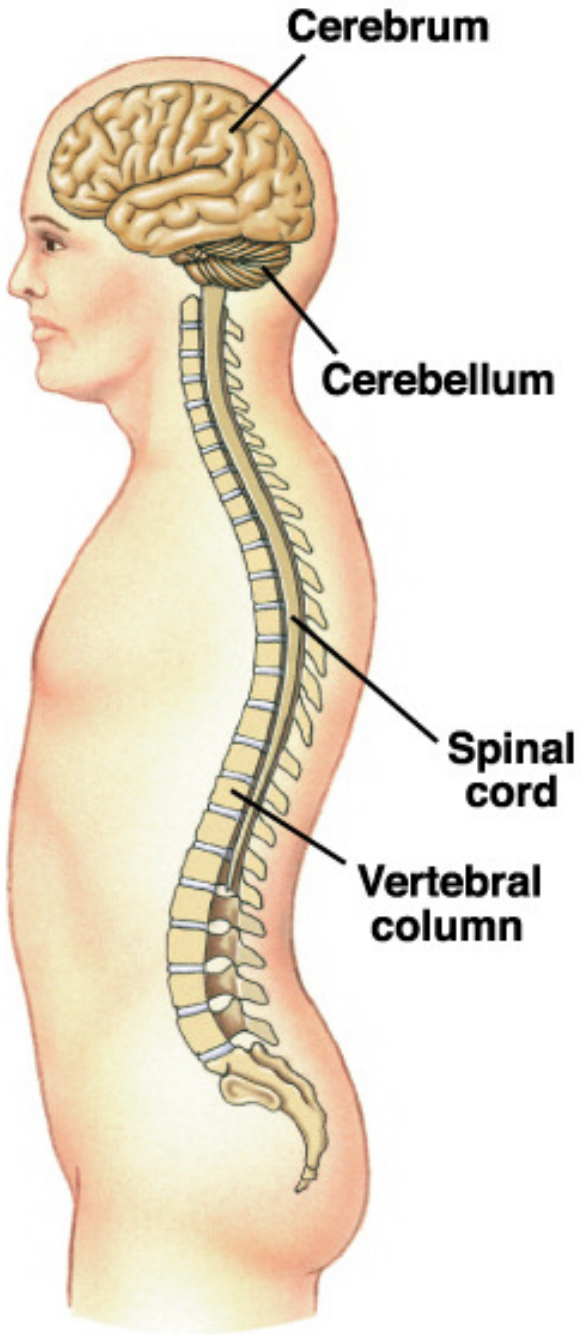


- A bundle of processes in the PNS is a **nerve**.
- Within a nerve, each axon is surrounded by an **endoneurium**
- Groups of fibers are bound together into bundles (fascicles) by a **perineurium**
- All the fascicles of a nerve are enclosed by a **epineurium**



Organization of the Nervous System

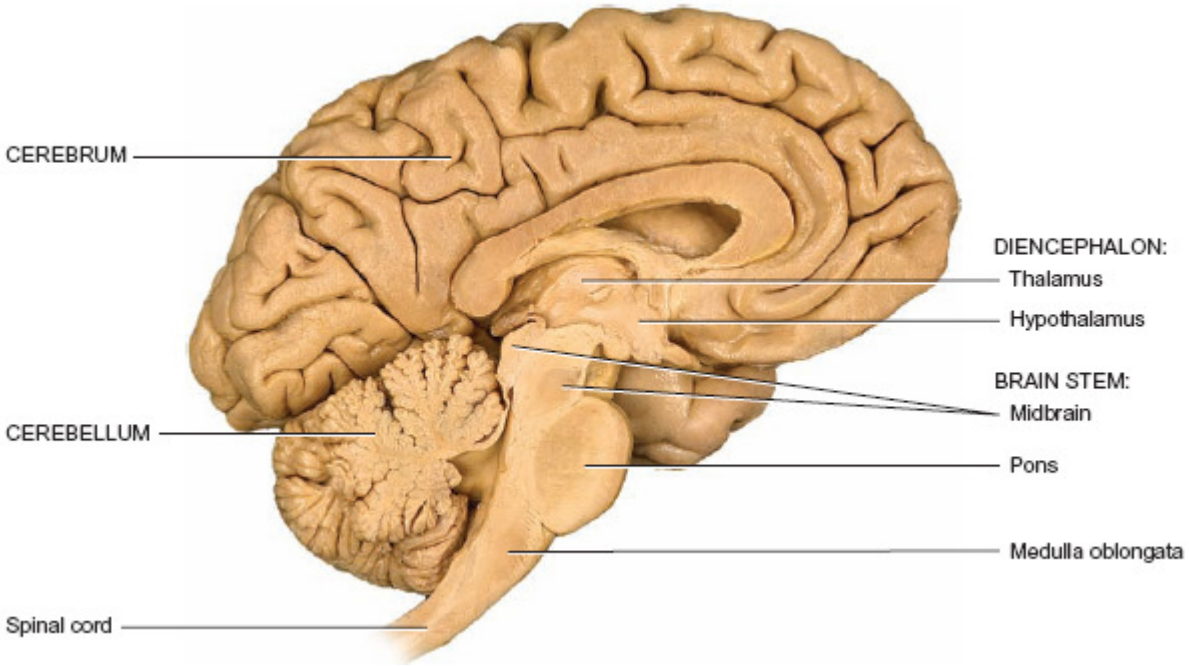
- Anatomical divisions:
  1. Central Nervous System
     - The brain + the spinal cord
       - The center of integration and control
  2. Peripheral Nervous System
     - The nervous system outside of the brain and spinal cord
     - Consists of:
       - 31 Spinal nerves
         - Carry info to and from the spinal cord
       - 12 Cranial nerves
         - Carry info to and from the brain



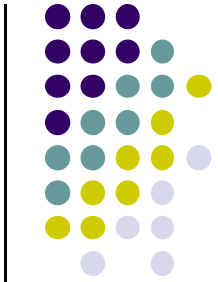
Brain

- **Forebrain**: (Prosencephalon)
  - Cerebrum: (Telencephalon)
  - Diencephalon
    - Thalamus
    - Hypothalamus
    - Epithalamus
    - Subthalamus
- **Midbrain:**

  (Mesencephalon)
- **Hindbrain**: (Rhombencephalon)
  - Pons
  - Medulla oblingata
  - Cerebellum

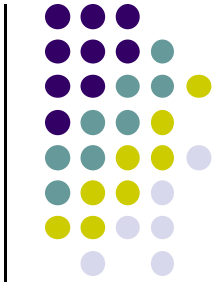


Peripheral Nervous System



- Responsible for communication between the CNS and the rest of the body.
- Can be divided into:
  - Sensory Division
    - Afferent division
      - Conducts impulses from receptors to the CNS
      - Informs the CNS of the state of the body interior and exterior
      - Sensory nerve fibers can be **somatic** (from skin, skeletal muscles or joints) or **visceral** (from organs within the body cavity)
  - Motor Division
    - Efferent division
      - Conducts impulses from CNS to effectors (muscles/glands)
      - Motor nerve fibers

Peripheral Nervous System

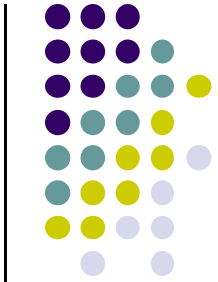


- Somatic nervous system

1) Sensory neurons: (*somatic sensory neurons)*
   - convey information to the CNS from sensory receptors in the skin, skeletal muscles, and joints, and from the receptors for the special senses.

2) Motor neurons: (*somatic motor neurons)*
   - VOLUNTARY
   - conduct impulses from the CNS to skeletal muscles

Peripheral Nervous System



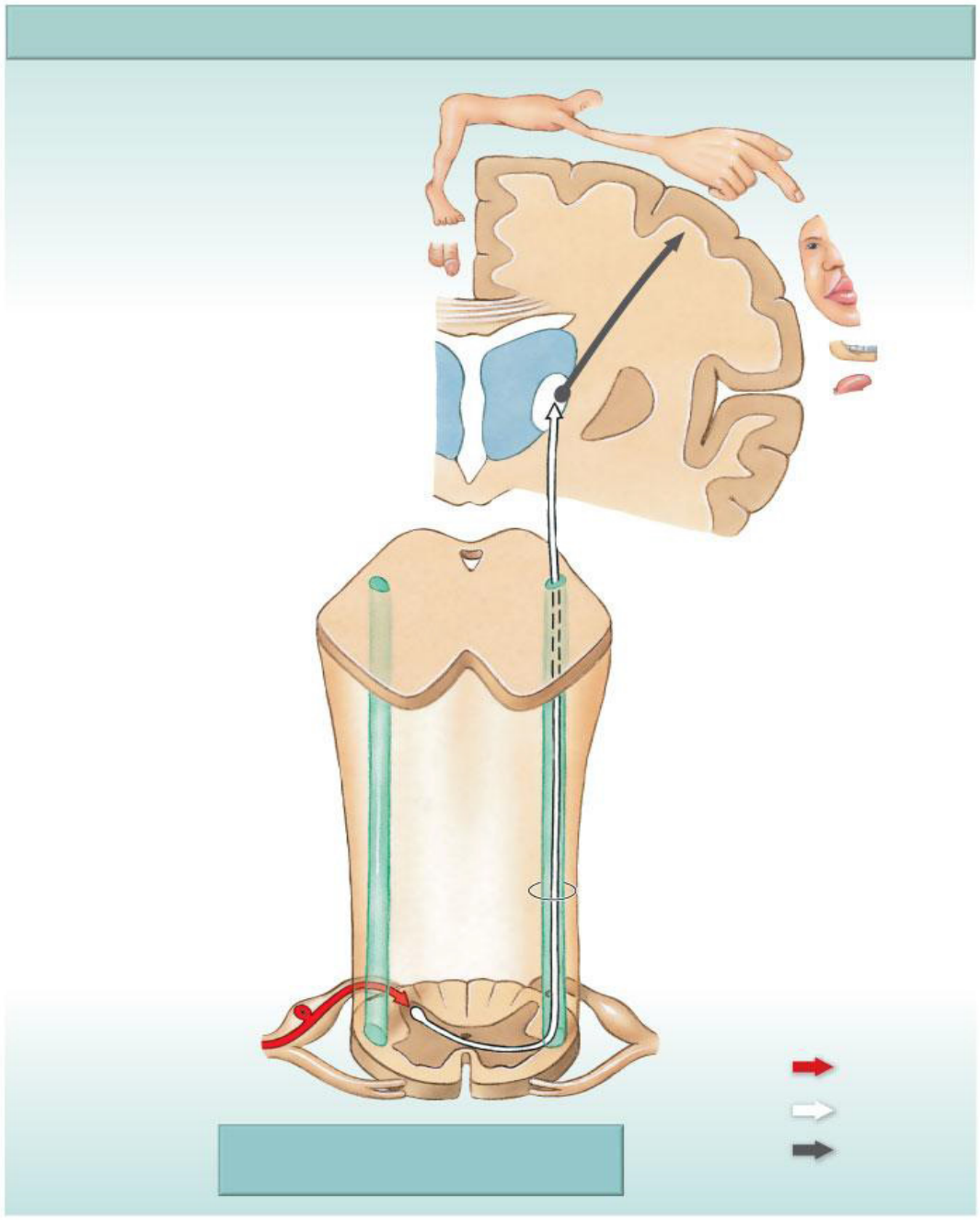
- Autonomic nervous system

1) Sensory neurons: Autonomic (visceral) sensory neurons

convey information to the CNS from autonomic sensory receptors, located primarily in the visceral organs (smooth muscle organs in the thorax, abdomen,and pelvis)

2) Motor neurons: Autonomic motor neurons

- INVOLUNTARY (generally)
- Conducts impulses from the CNS to smooth muscle, cardiac muscle, and glands.



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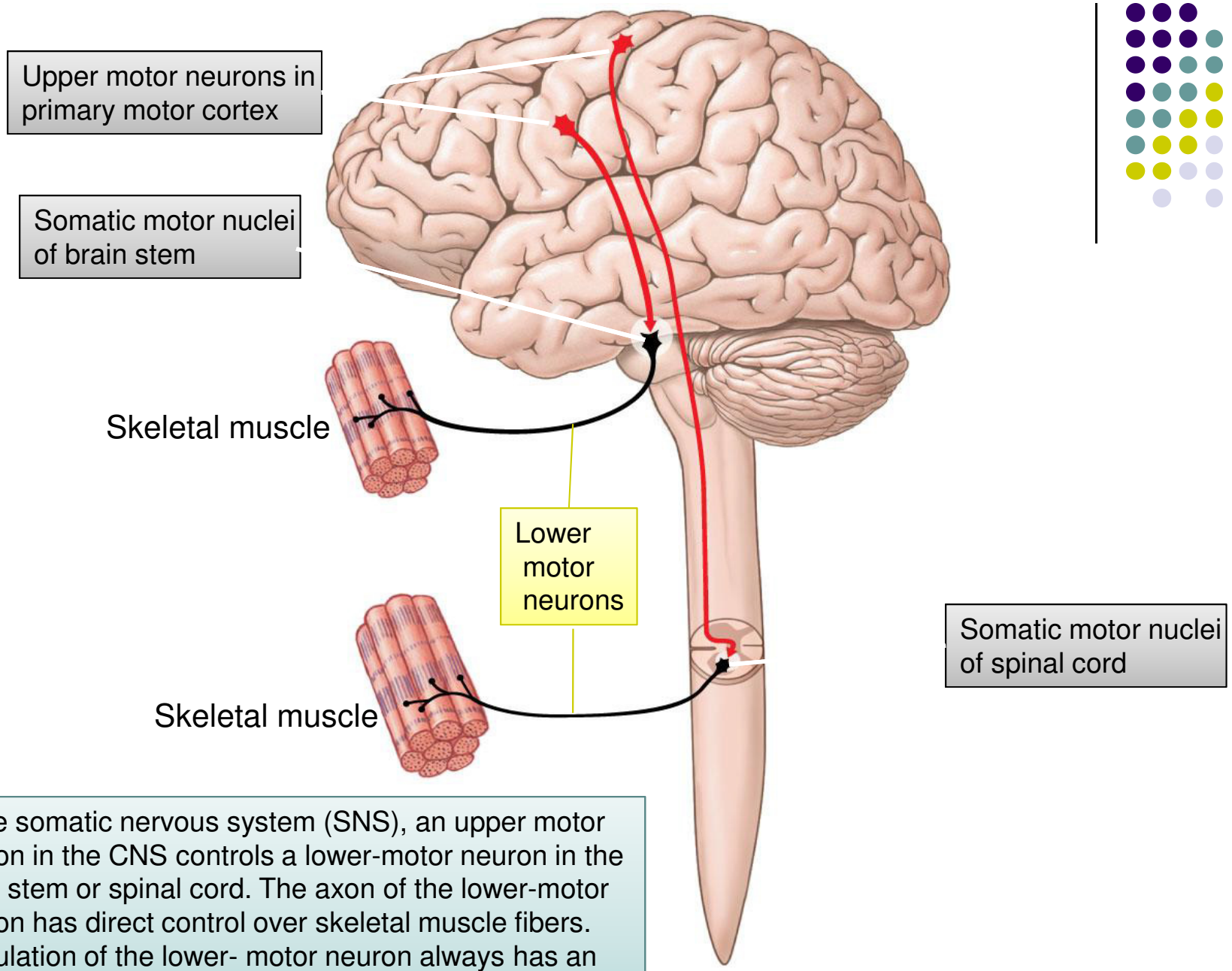
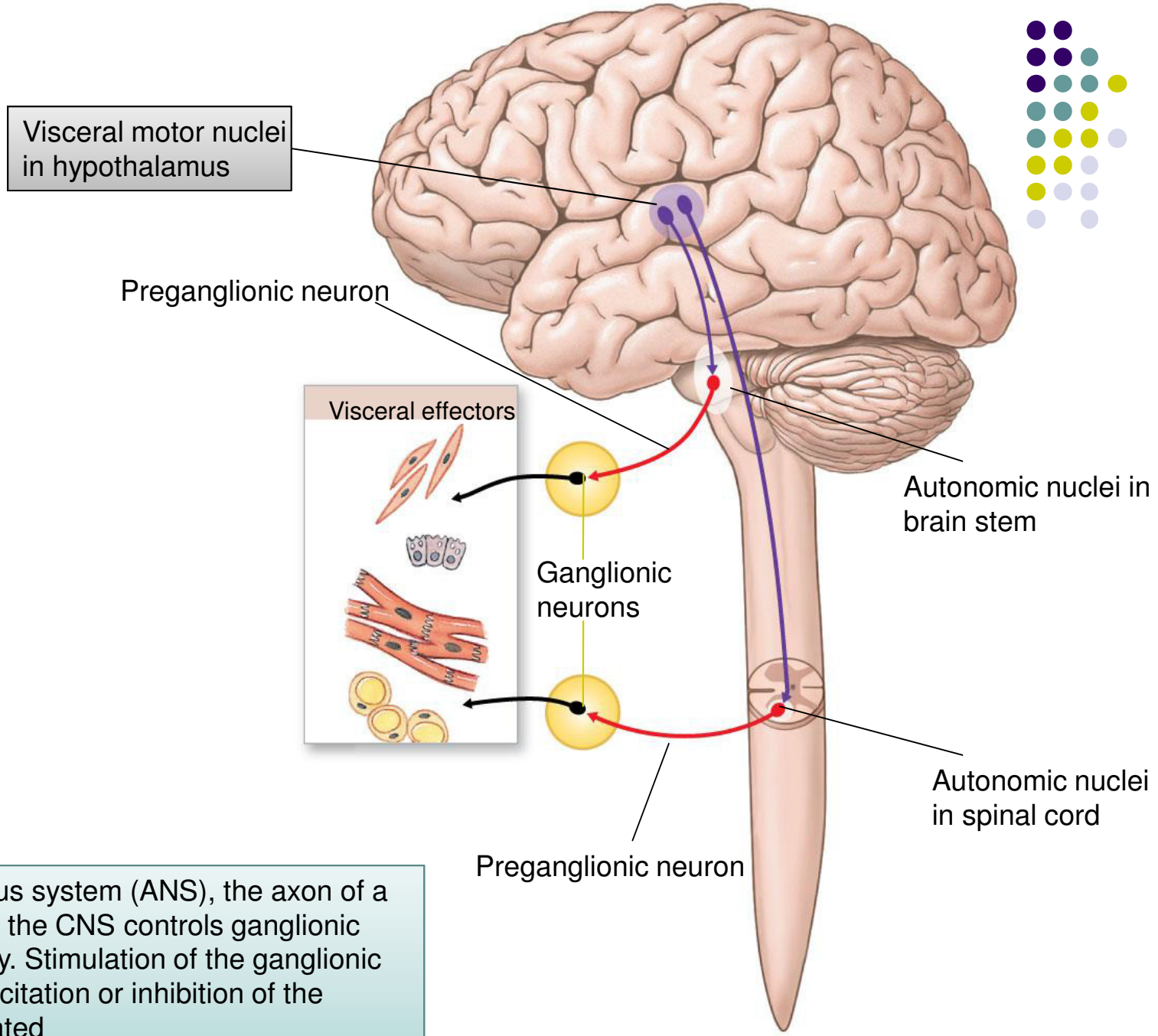


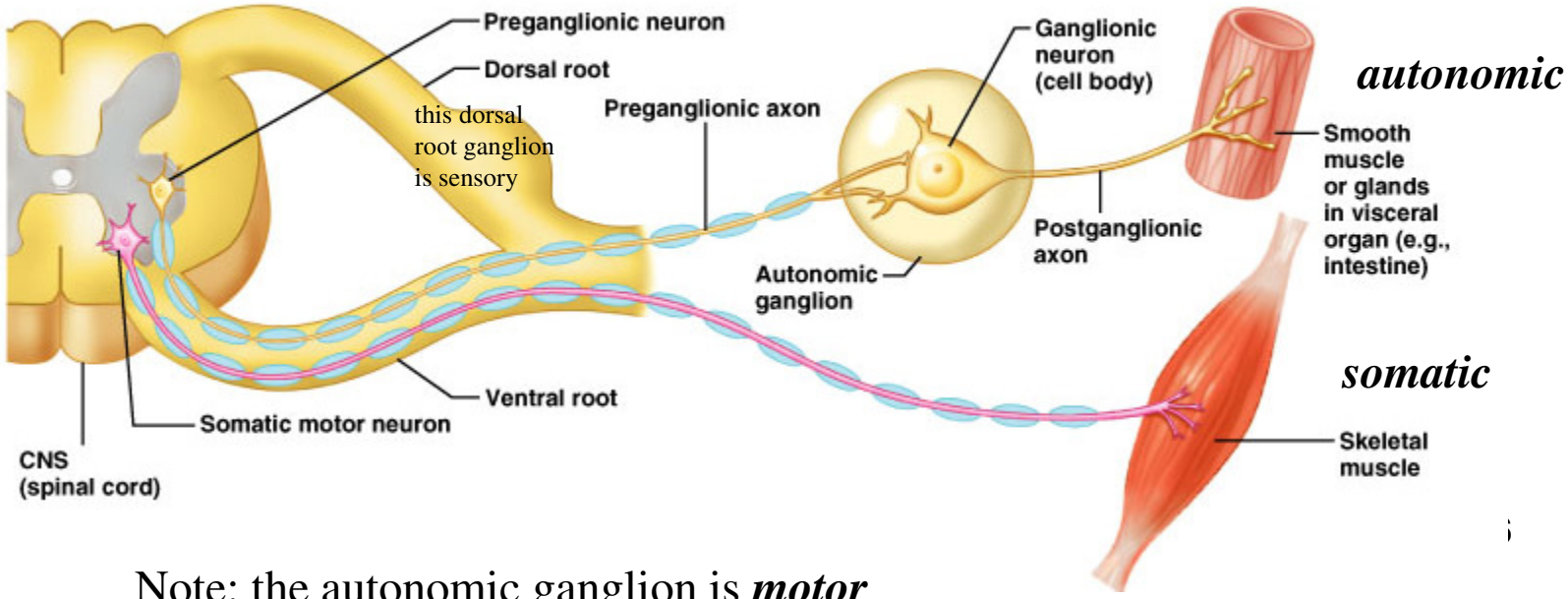
In the somatic nervous system (SNS), an upper motor neuron in the CNS controls a lower-motor neuron in the brain stem or spinal cord. The axon of the lower-motor neuron has direct control over skeletal muscle fibers. Stimulation of the lower- motor neuron always has an excitatory effect on the skeletal muscle fibers.



In the autonomic nervous system (ANS), the axon of a preganglionic neuron in the CNS controls ganglionic neurons in the periphery. Stimulation of the ganglionic neurons may lead to excitation or inhibition of the visceral effector innervated

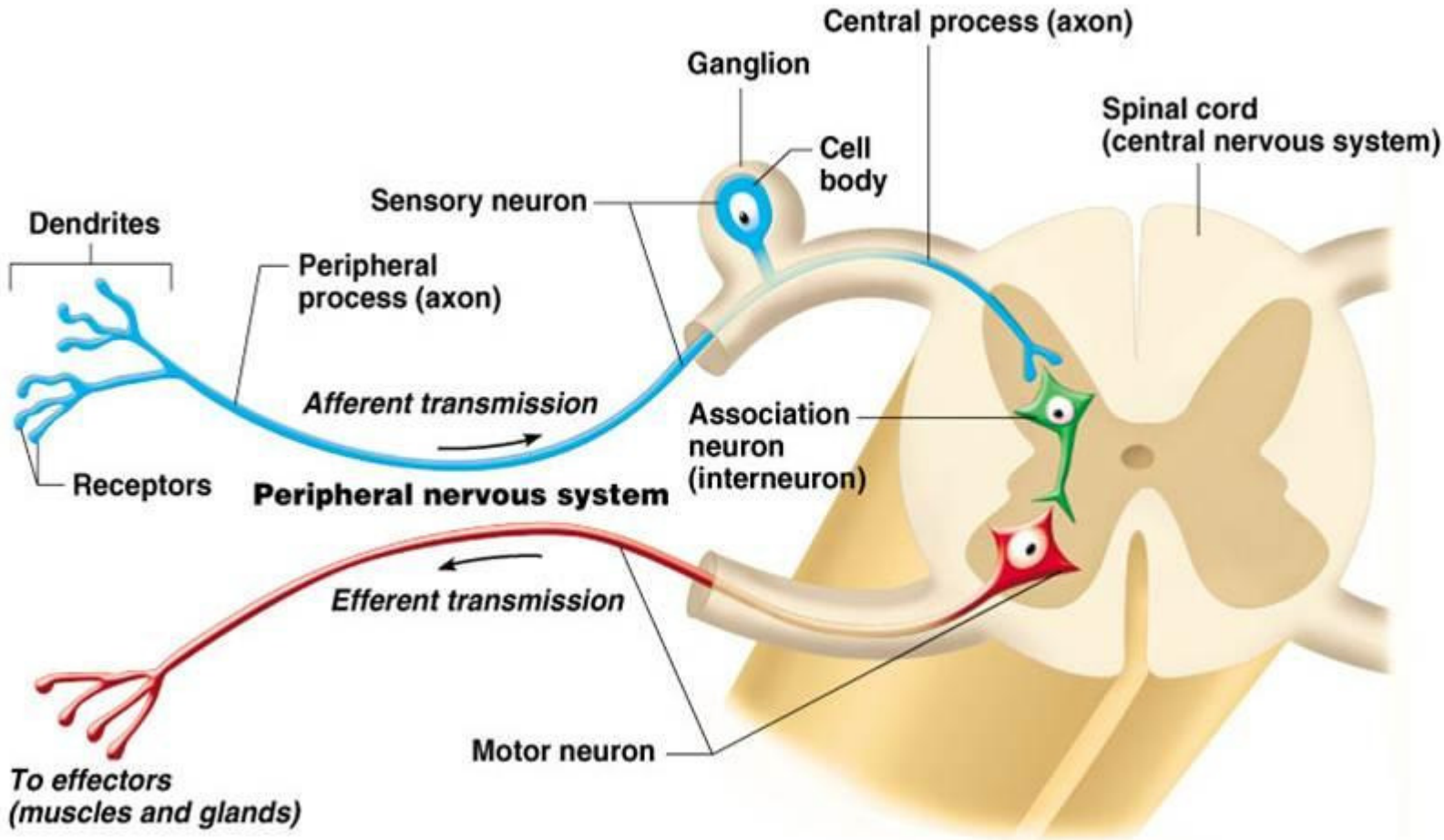
- Axon of 1st (*preganglionic*) neuron leaves CNS to synapse with the 2nd (*ganglionic*) neuron
- Axon of 2nd (*postganglionic*) neuron extends to the organ it serves

Diagram contrasts somatic (lower) and autonomic:



Note: the autonomic ganglion is ***motor***

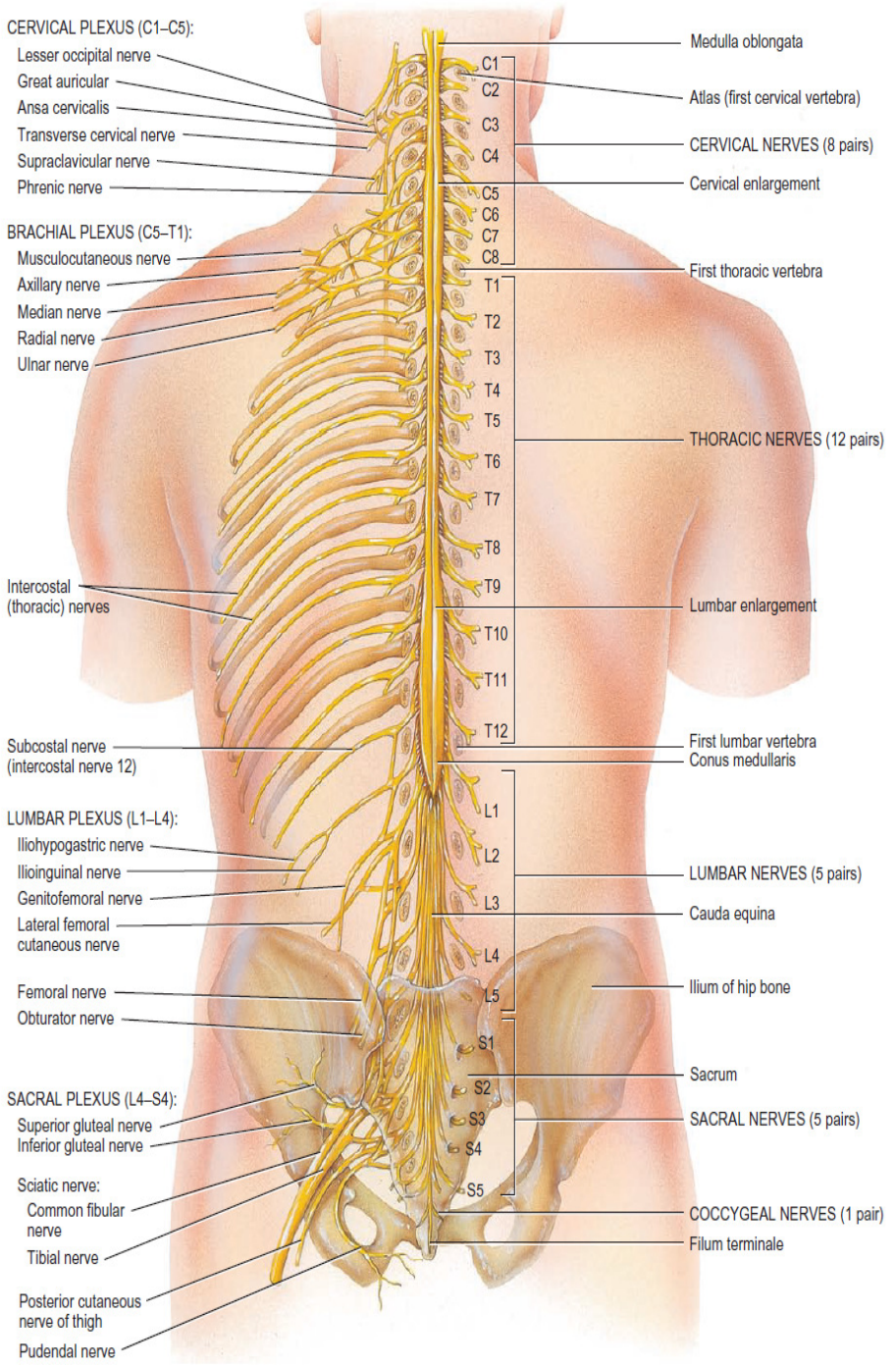
Sensory ganglion



Ganglion cells in dorsal root ganglia do not receive synapses

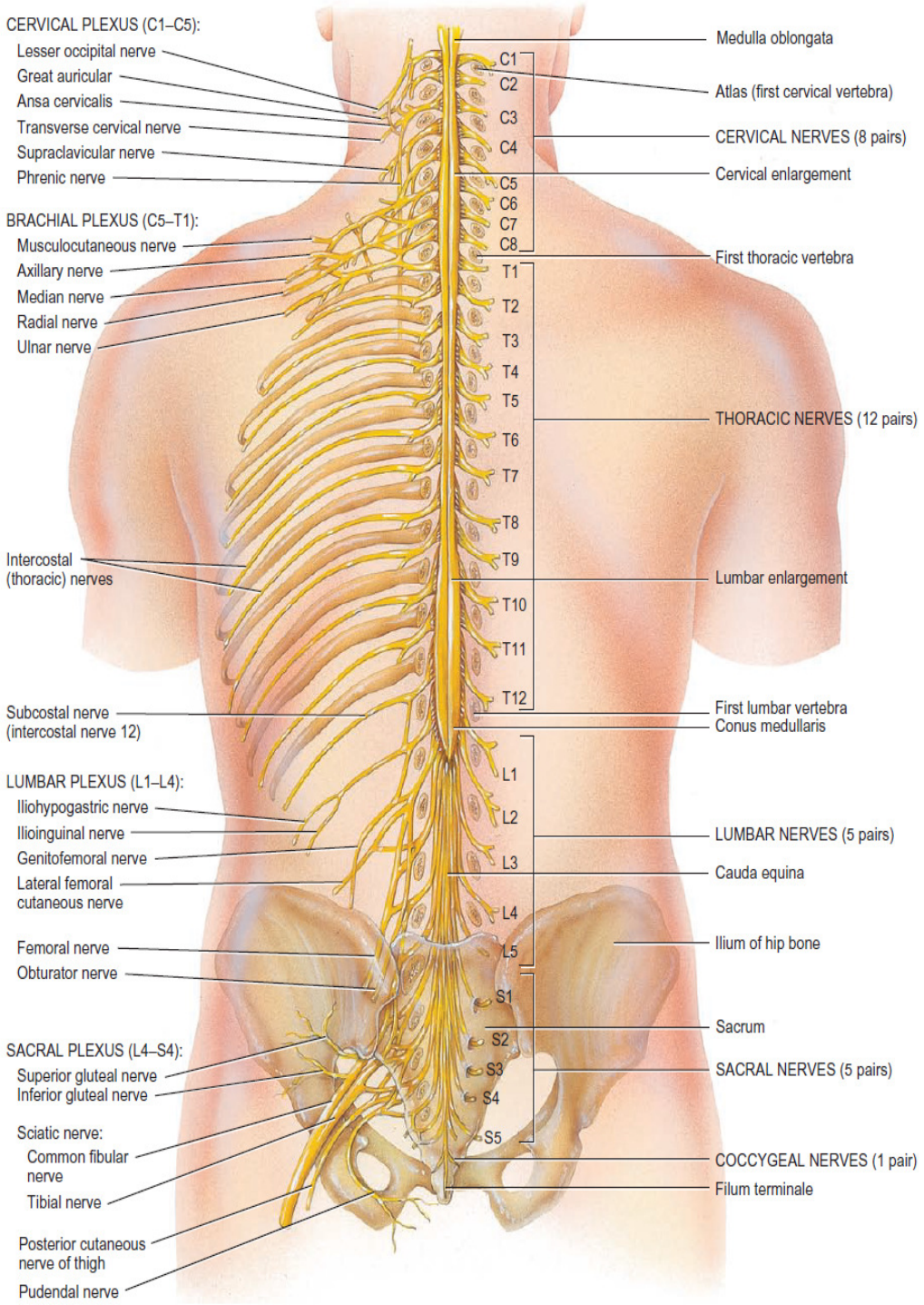
External anatomy of Spinal Cord

- Runs through the vertebral canal
- Extends from foramen magnum to second lumbar vertebra
- Regions
  - Cervical (8)
  - Thoracic (12)
  - Lumbar (5)
  - Sacral (5)
  - Coccygeal (1)
- Gives rise to (31) pairs of spinal nerves
  - All are *mixed* nerves
- Not uniform in diameter
  - Cervical enlargement: supplies upper limbs
  - Lumbar enlargement: supplies lower limbs



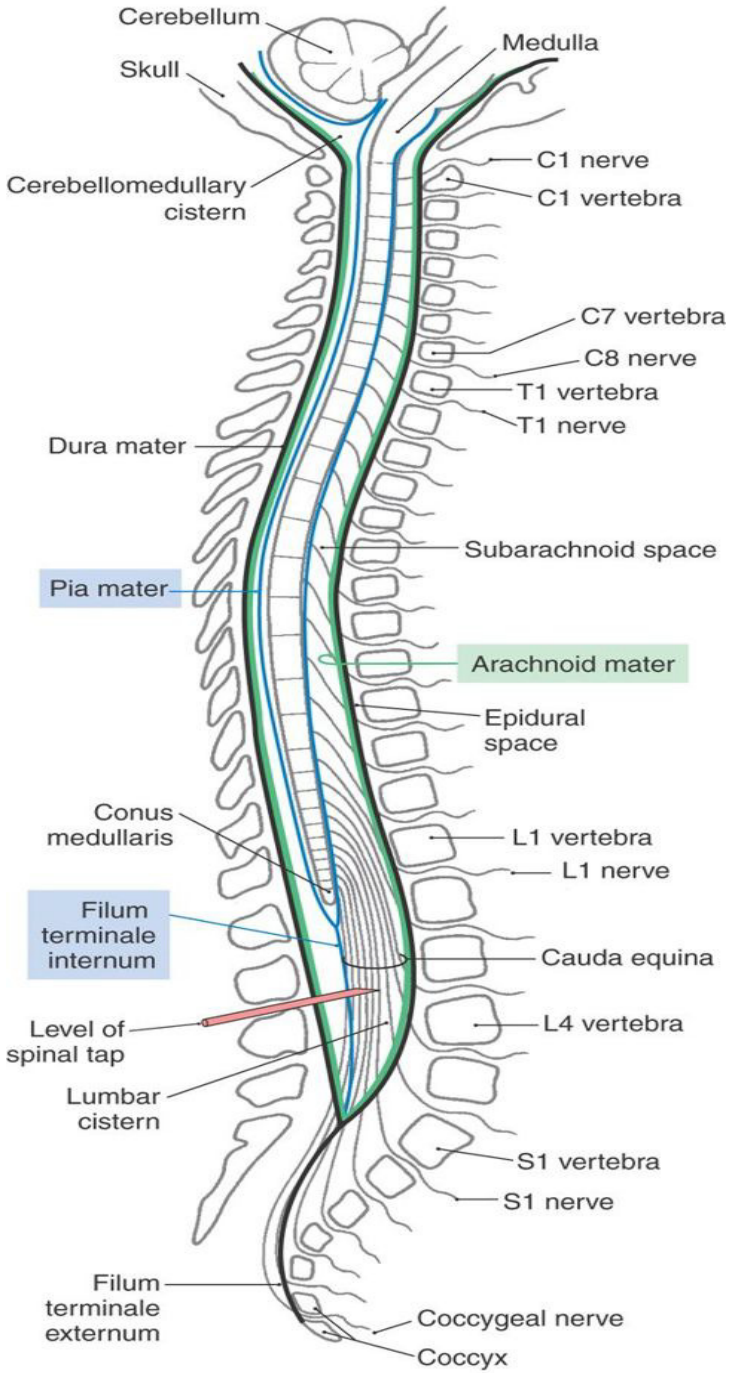
External anatomy of Spinal Cord

- Flattened slightly anteriorly and posteriorly
- length of the adult spinal cord ranges from 42 to 45 cm
- Conus medullaris- tapered inferior end (conical structure)
  - Ends between L1 and L2
- Cauda equina - origin of spinal nerves extending inferiorly from conus medullaris.



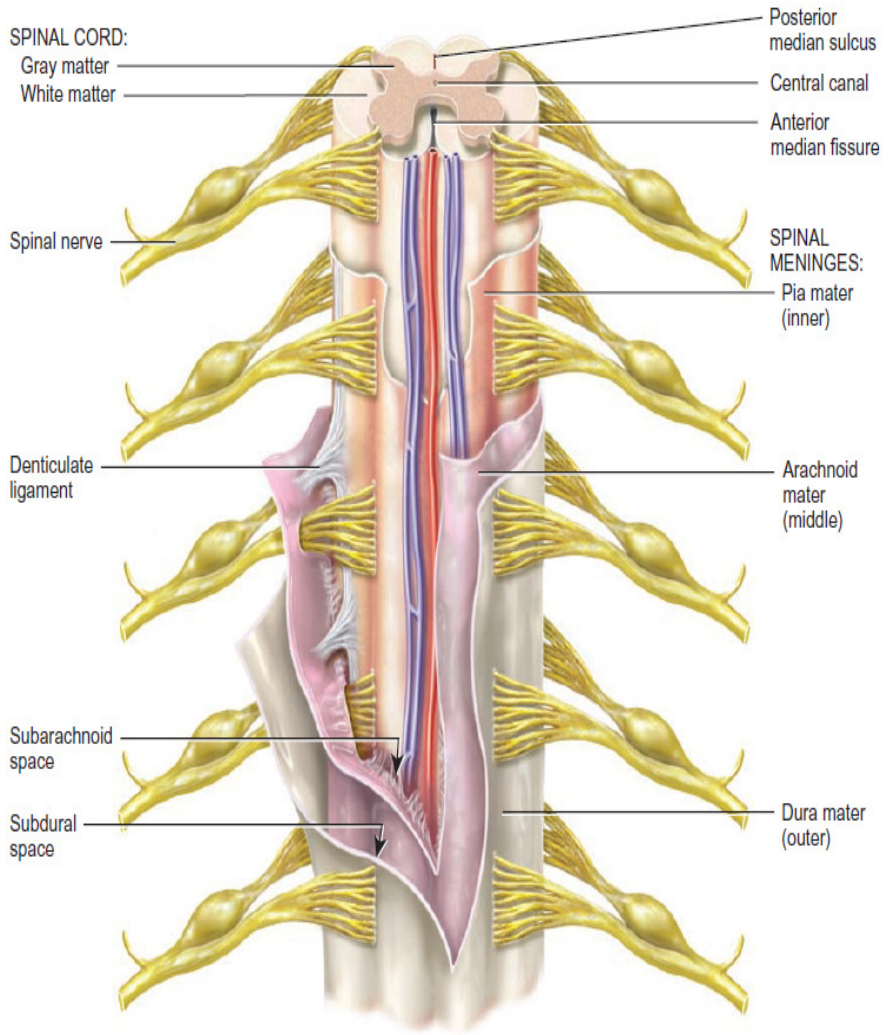
Meninges

- Connective tissue membranes
  - **Dura mater:**
  - Outermost layer; continuous with epineurium of the spinal nerves
  - Dense irregular connective tissue
  - from the level of the foramen magnum to S2
  - Closed caudal end is anchored to the coccyx by the **filum terminale externum**
  - **Arachnoid mater**:
  - Thin web arrangement of delicate collagen and some elastic fibers.
  - Adheres to the inner surface of the dura mater



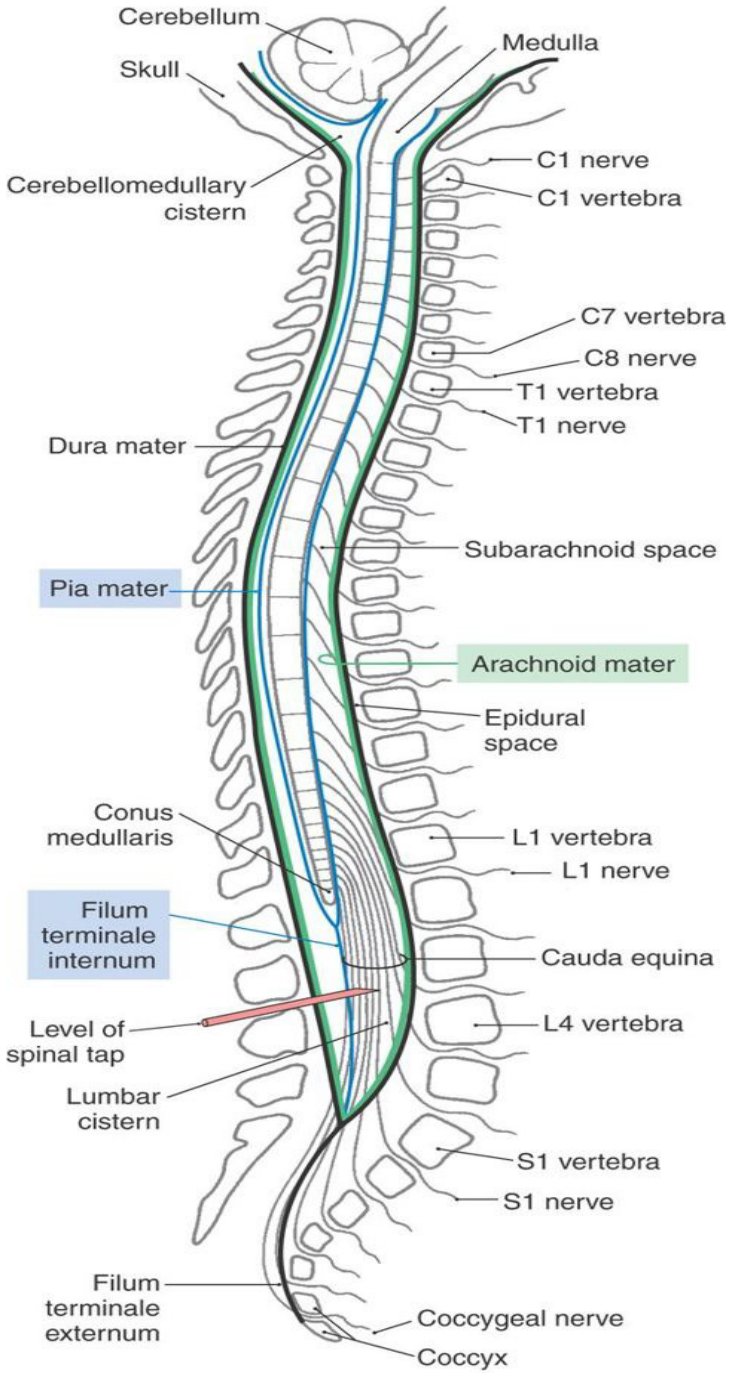
Meninges

- Connective tissue membranes
- Pia mater:
  - Bound tightly to surface
  - Thin transparent connective tissue layer that adheres to the surface o the spinal cord and brain
  - Forms the filum terminale
    - anchors spinal cord to coccyx
  - Forms the denticulate ligaments that attach the spinal cord to the arachnoid mater and inner surface of the dura mater



Spaces

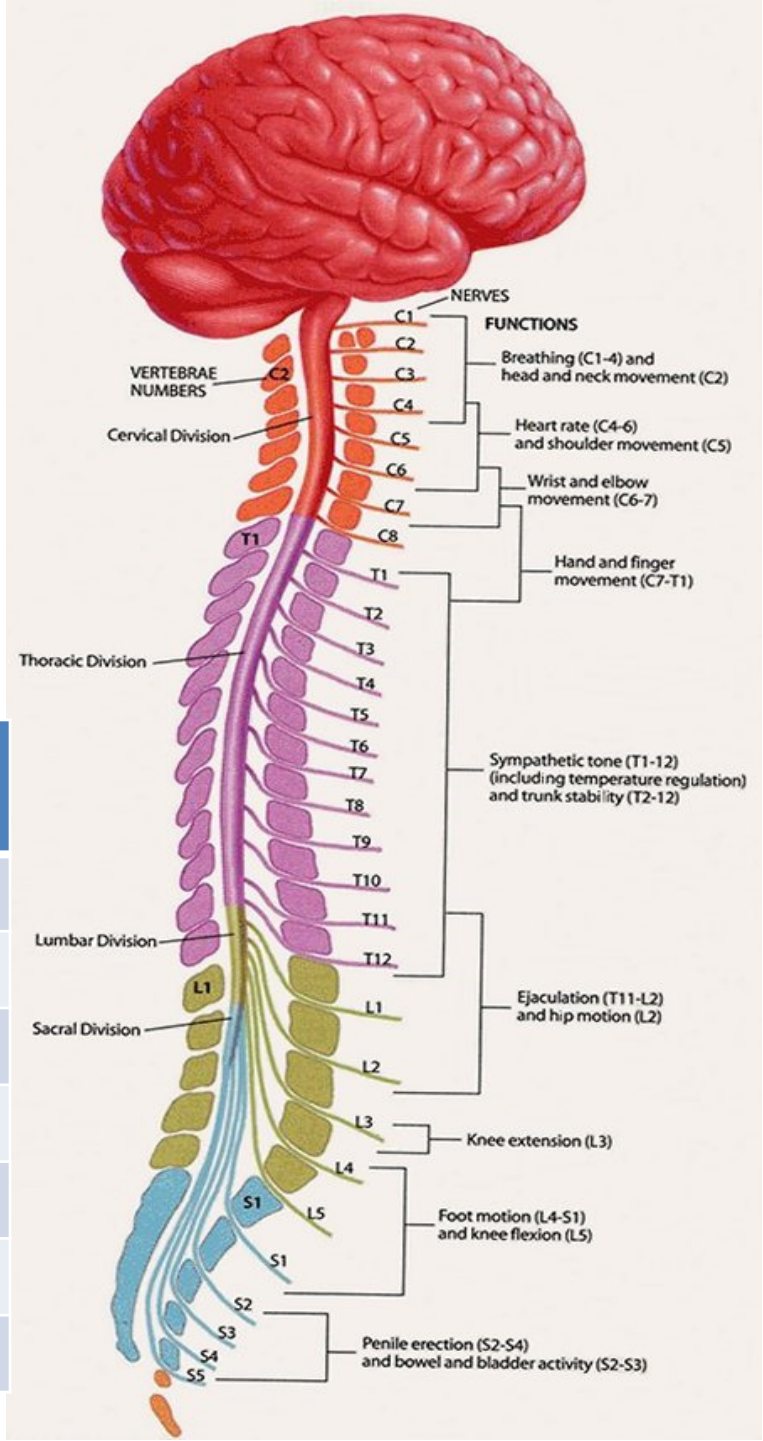
- **Epidural**: space between the dura mater and the wall of the vertebral canal.
  - Anesthestics injected here
  - Fat-fill
- **Subdural space**: serous fluid
- **Subarachnoid**: between pia and arachnoid
  - Filled with CSF
  - Lumbar puncture
  - supracristal line
  - L3-L4



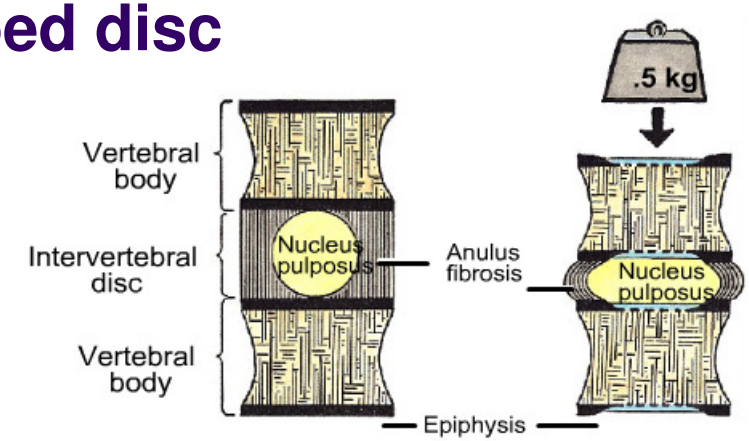
Spinal cord segment

- The segments of the spinal cord are not in line with the corresponded vertebrae and the difference increases as we go downward.
- The roots increase in length as you go downward.
- Every spinal nerve emerges from the spinal column through the intervertebral foramen under its corresponding vertebra
- first 7 cervical nerves pass above their corresponding vertebrae

Spinous process	spinal cord segment
C7	C8
T3	T5
T9	T12
T10	L1-2
T11	L3-4
T12	L5
L1	S1-end



Herniated Disc/ ruptured disc/ slipped disc

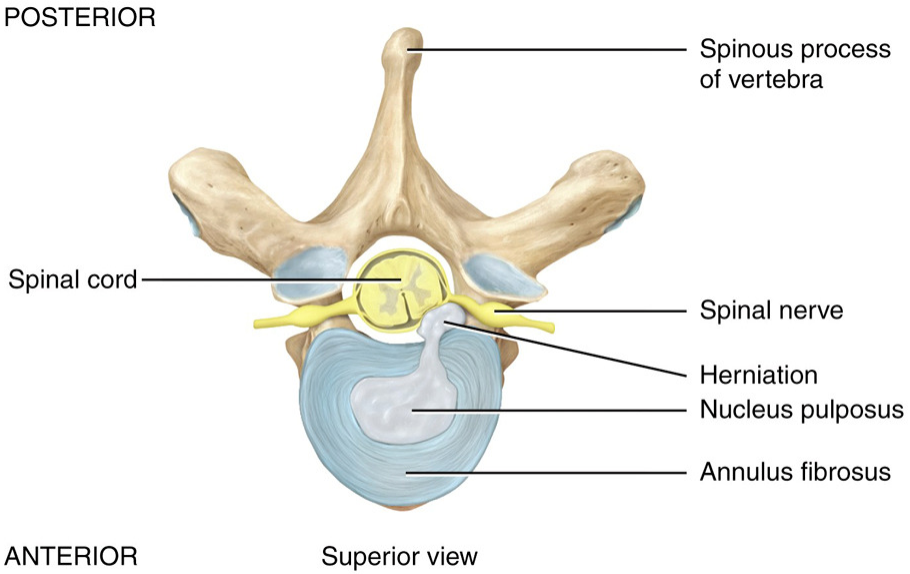


protrusion (leakage) of the gelatinous nucleus pulposus through the anulus fibrosus of IV disc

Posterolateral direction:

Thinner annulus fibrosus

95% in L4/L5 or L5/S1



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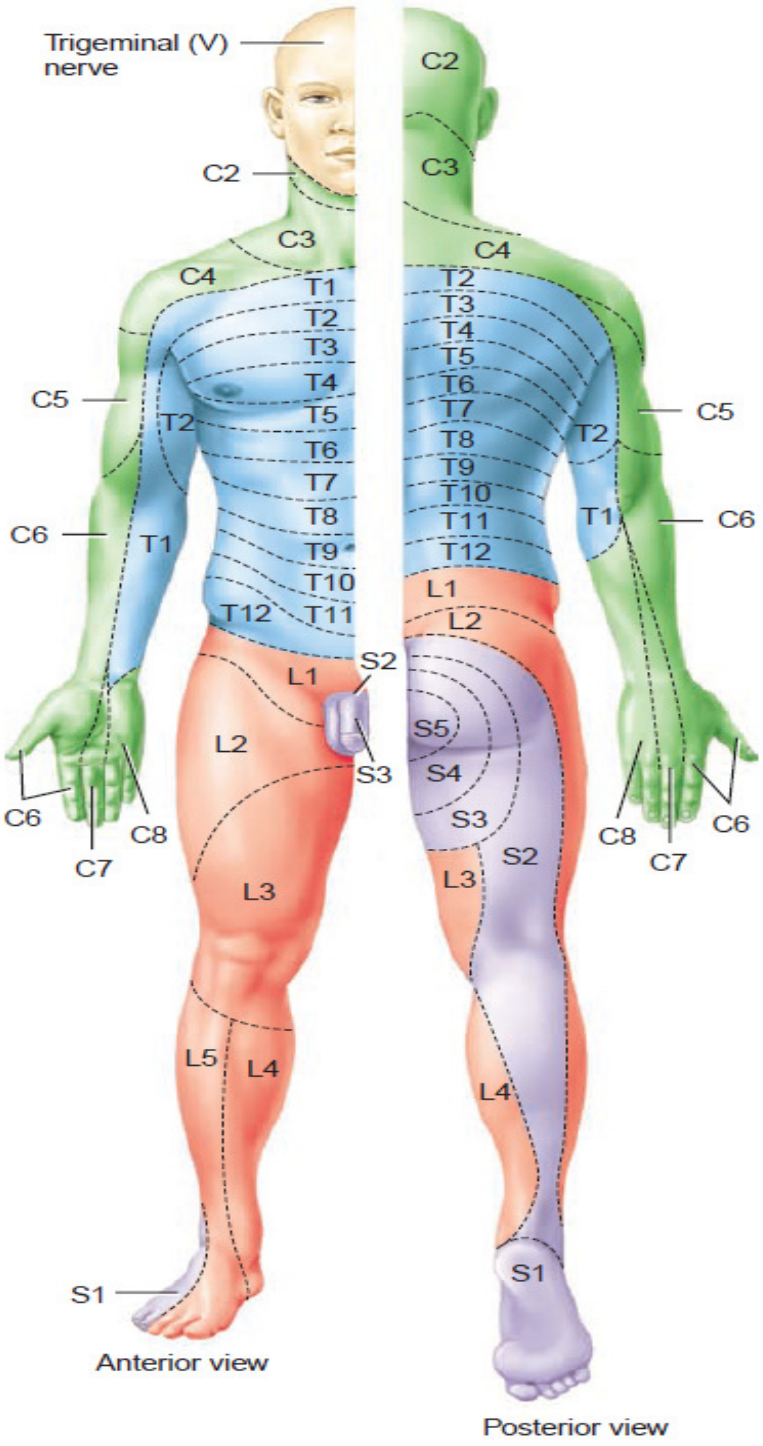
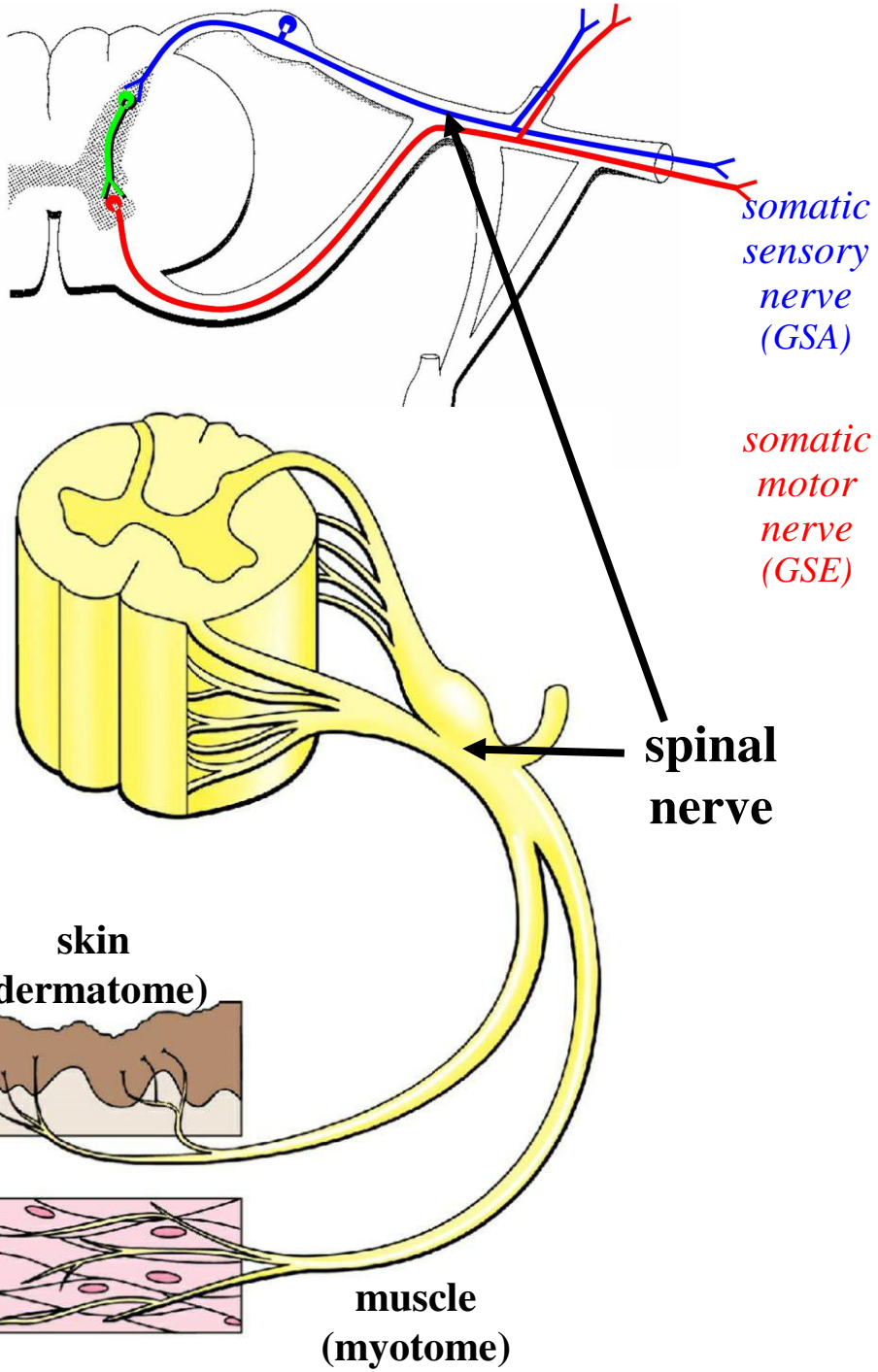

Trigeminal (V) nerve
C2
C3
C4
C5
C6
C7
C8
T1
T2
T3
T4
T5
T6
T7
T8
T9
T10
T11
T12
L1
L2
L3
L4
L5
S1
S2
S3
S4
S5
Anterior view
Posterior view

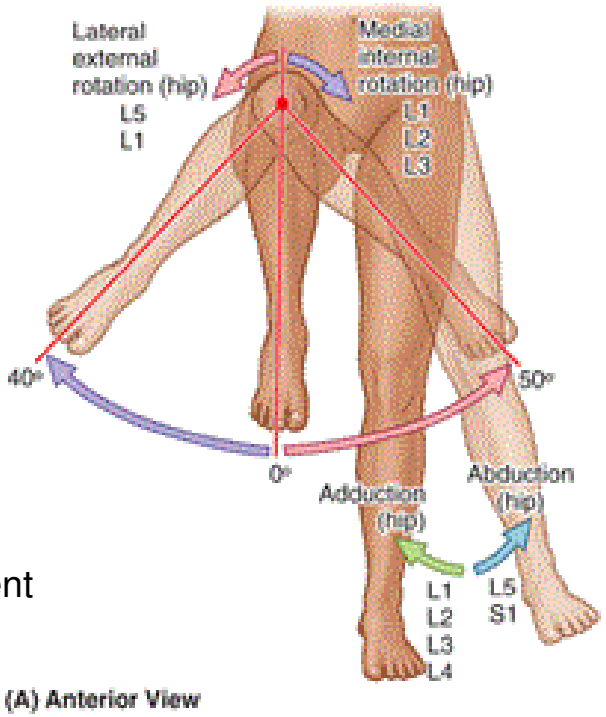

somatic sensory nerve (GSA)
somatic motor nerve (GSE)
spinal nerve
skin (dermatome)
muscle (myotome)

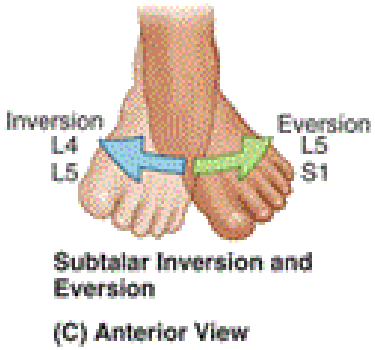
Common lumbar disc problems

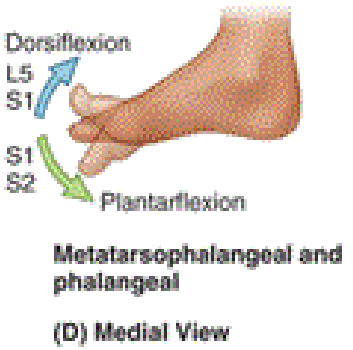
Disc	Root	Percentage	Motor weakness	Sensory changes	Reflex affected
L3-L4	L4	3-10%	Knee extension (Quadriceps femoris	Anteriomedial leg (saphenous)	Knee jerk
L4-L5	L5	40-45%	Big toe dorsifelxion (EHL) and TA	Big toe , anteriolateral leg (Common P)	Hamstring jerk
L5-S1	S1	45-50%	Foot planter flextion (Gastrocnemius)	Lateral border of foot (sural)	Ankle jerk

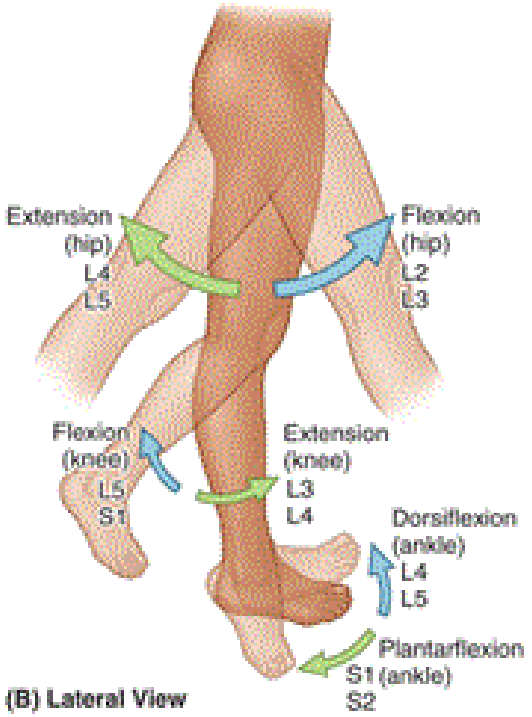
Important myotomes of lower limb

- **Test L5**: by asking the patient to stand on his heels
- **Test S1**: by asking the patient to stand on his tiptoes



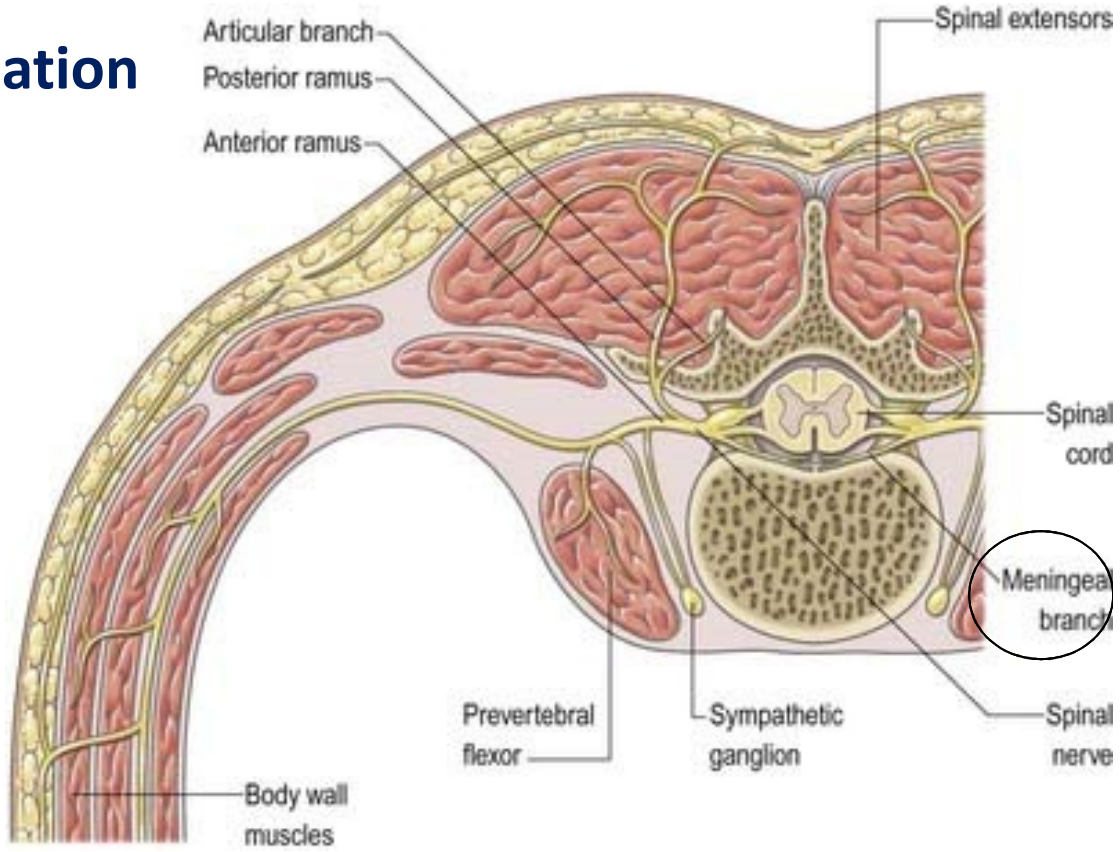


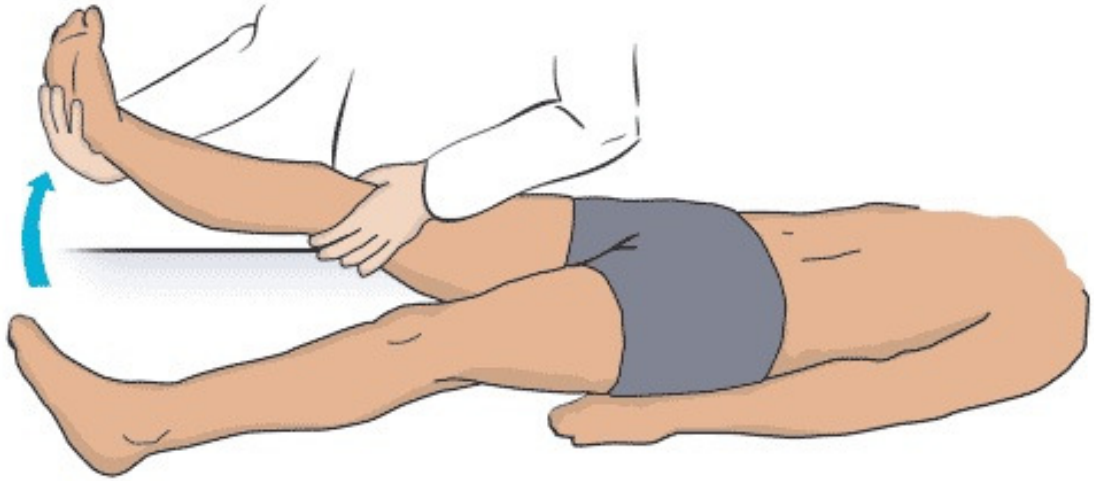




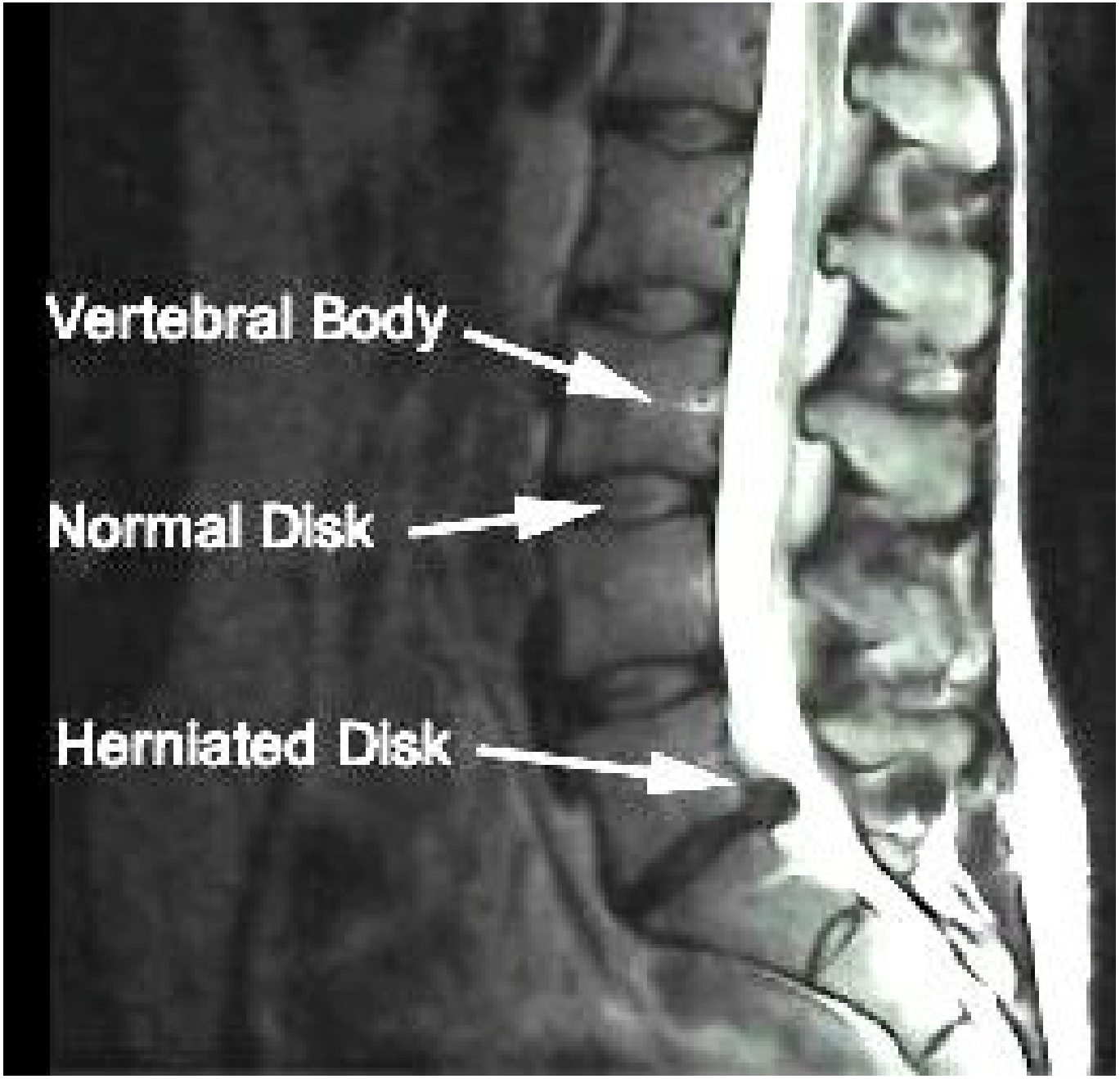
Major symptoms of disc herniation

- **Low back pain**: radiating to the gluteal region, the back of the thigh and back of the leg
- spinal nerve gives a meningeal branch bring sensation from the dura matter
- Dura matter is sensitive to stretch
- Pain is diffused due to overlapping dermatomes
- **Straight Leg Raise Test (SLR)**





- MRI is commonly used to aid in making the diagnosis of a herniated disc



Cross Section of Spinal Cord

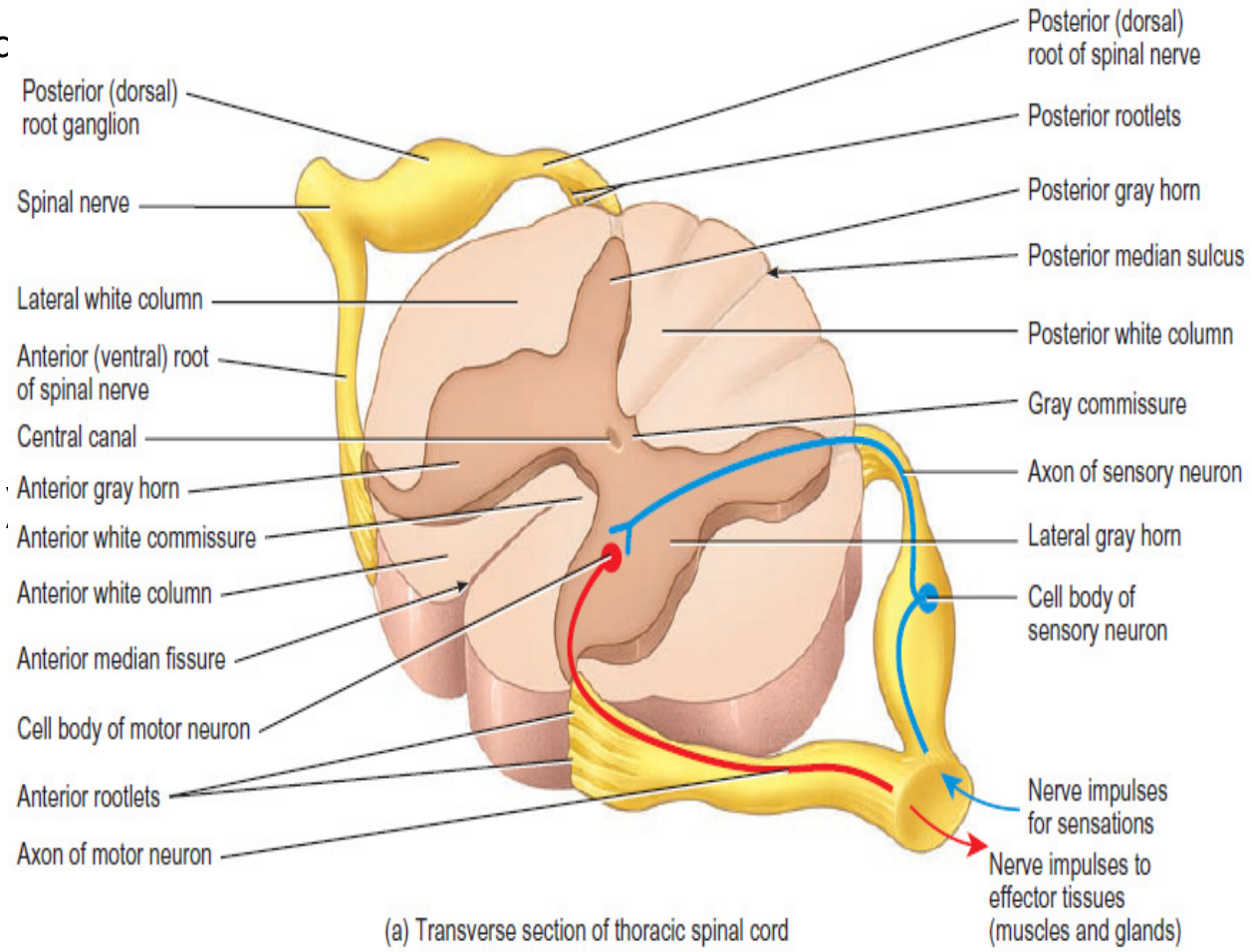
- Anterior median fissure:

wide groove on the Anterior aspec

- posterior median sulcus:

Narrow groove on the posterior aspect

- Gray matter: neuron cell bodies, dendrites, axons
  - Divided into *horns*
  - **Posterior** (dorsal) horn (cell body of sensory N
  - **Anterior** (ventral) horn (cell body of motor N to skeletal M)
  - **Lateral** horn (cell body of motor N to cardiac M, smooth M, glands)



(a) Transverse section of thoracic spinal cord

Cross Section of Spinal Cord

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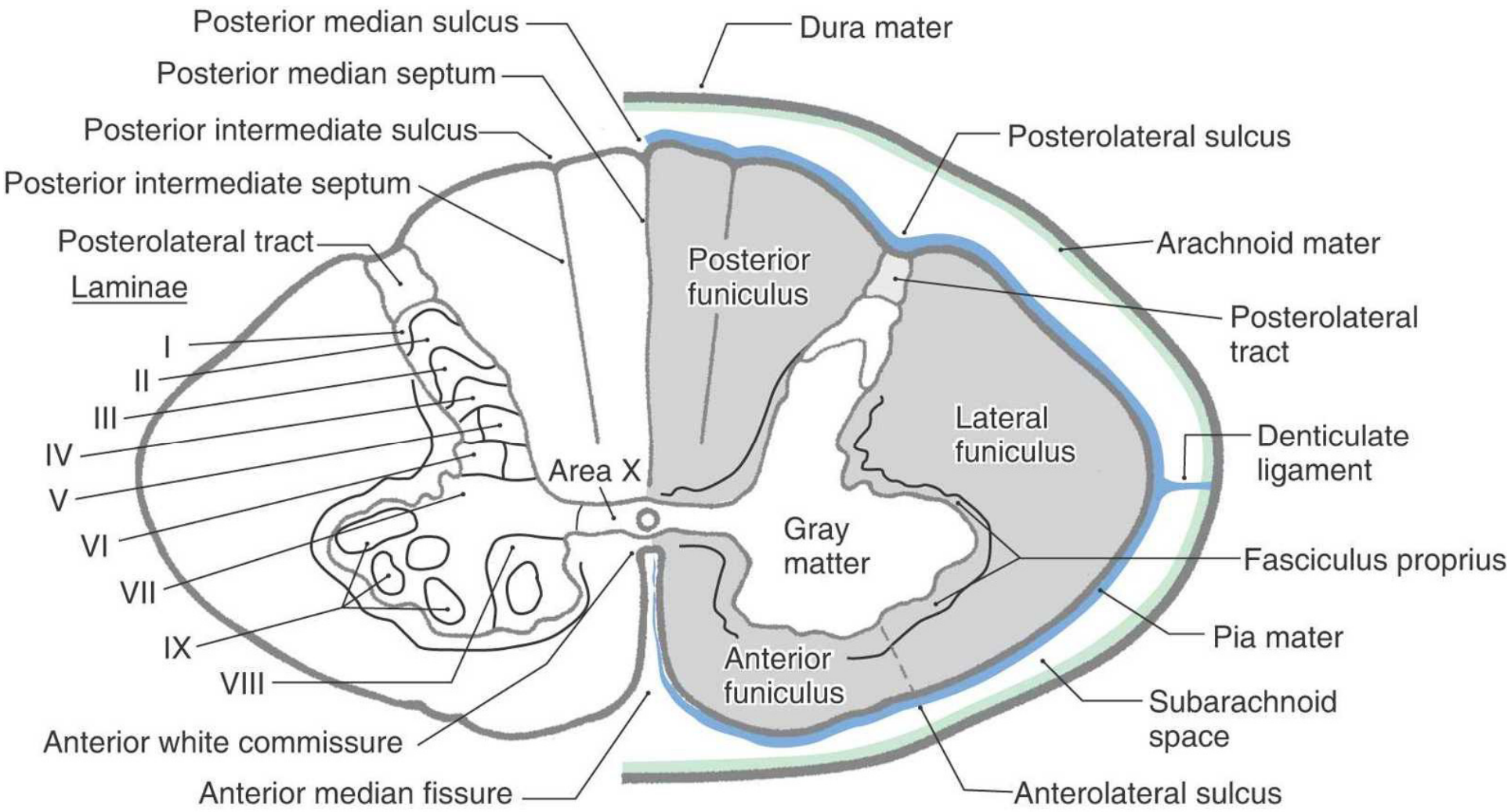
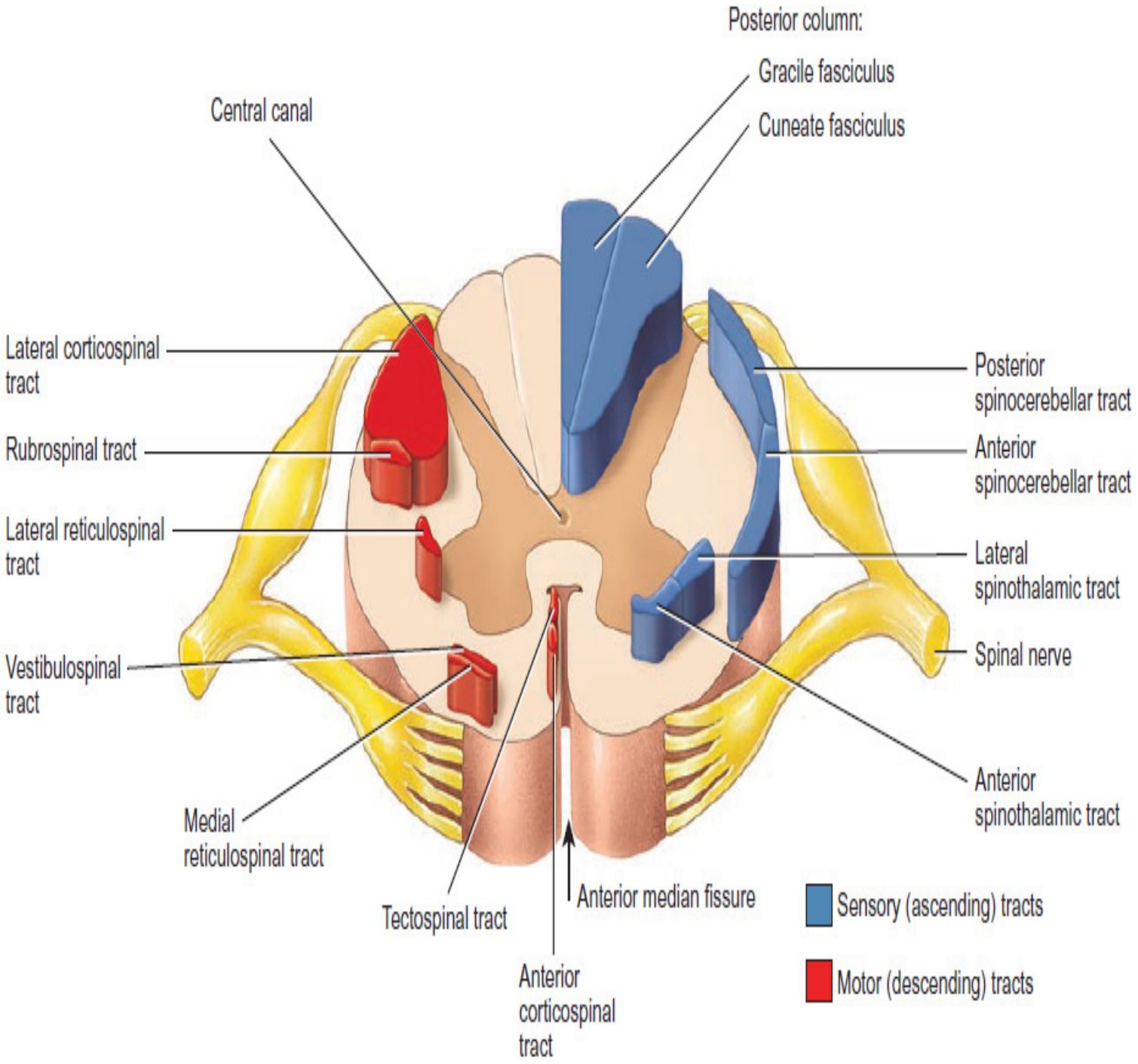
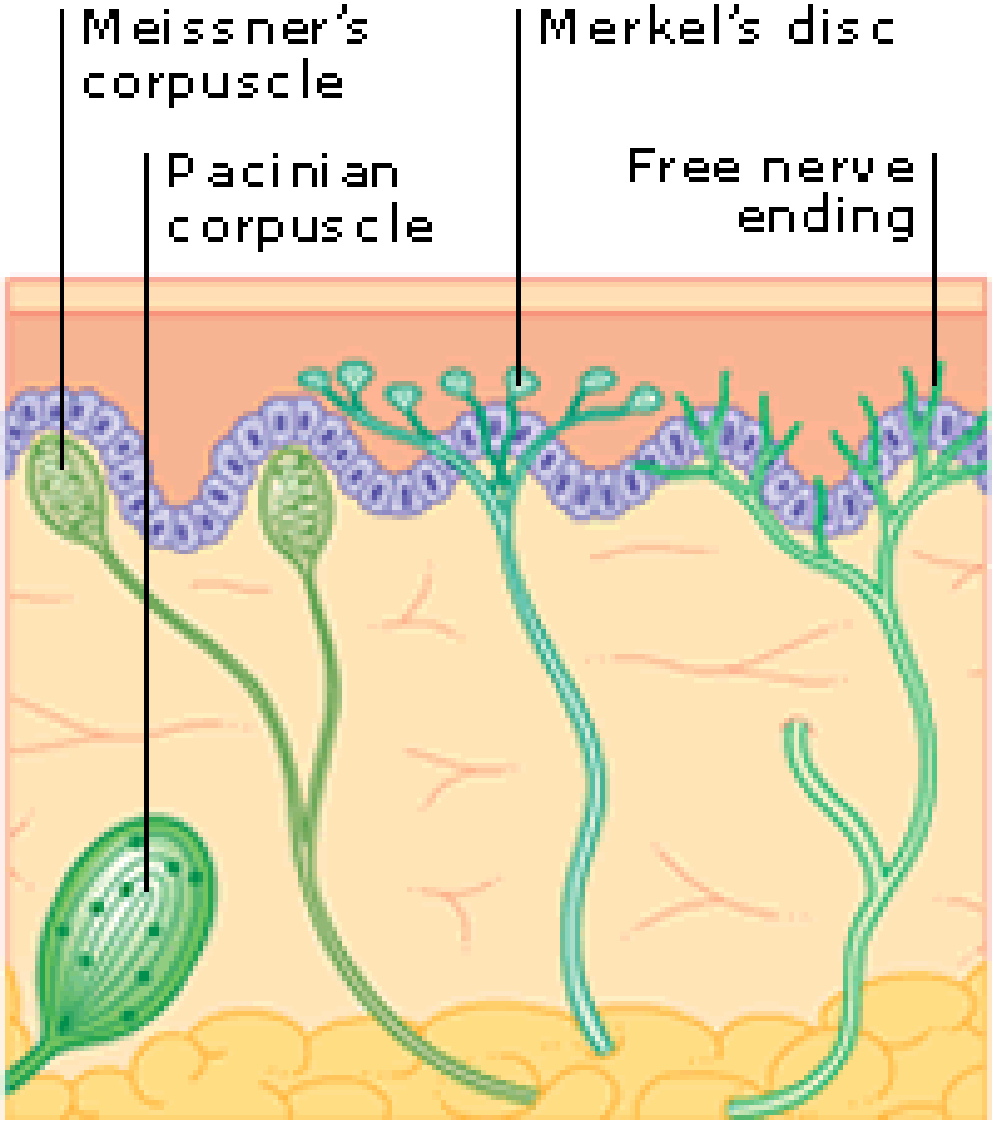



Posterior column:
Gracile fasciculus
Cuneate fasciculus
Central canal
Lateral corticospinal tract
Rubrospinal tract
Lateral reticulospinal tract
Vestibulospinal tract
Medial reticulospinal tract
Tectospinal tract
Anterior median fissure
Anterior corticospinal tract
Posterior spinocerebellar tract
Anterior spinocerebellar tract
Lateral spinothalamic tract
Spinal nerve
Anterior spinothalamic tract
Sensory (ascending) tracts
Motor (descending) tracts

❑ Mechanoreceptors

- **Meissner's corpuscle**
  - Respond to touch, pressure and low frequency vibration (low frequency)
  - rapidly adapting
- **Merkel's disc (Tactile Disc)**
  - Discriminative touch
  - Slowly adapting
- **End organ of Ruffini**
  - sensitive to skin stretch
  - Slowly adapting
- **Pacinian corpuscles**
  - Vibrations (high frequency)
  - rapidly adapting

➢**Rapidly adapting**: signals fade away after stimulus exposure
➢**Slow adaptation:** signals is transmitted as long as the stimulus is present



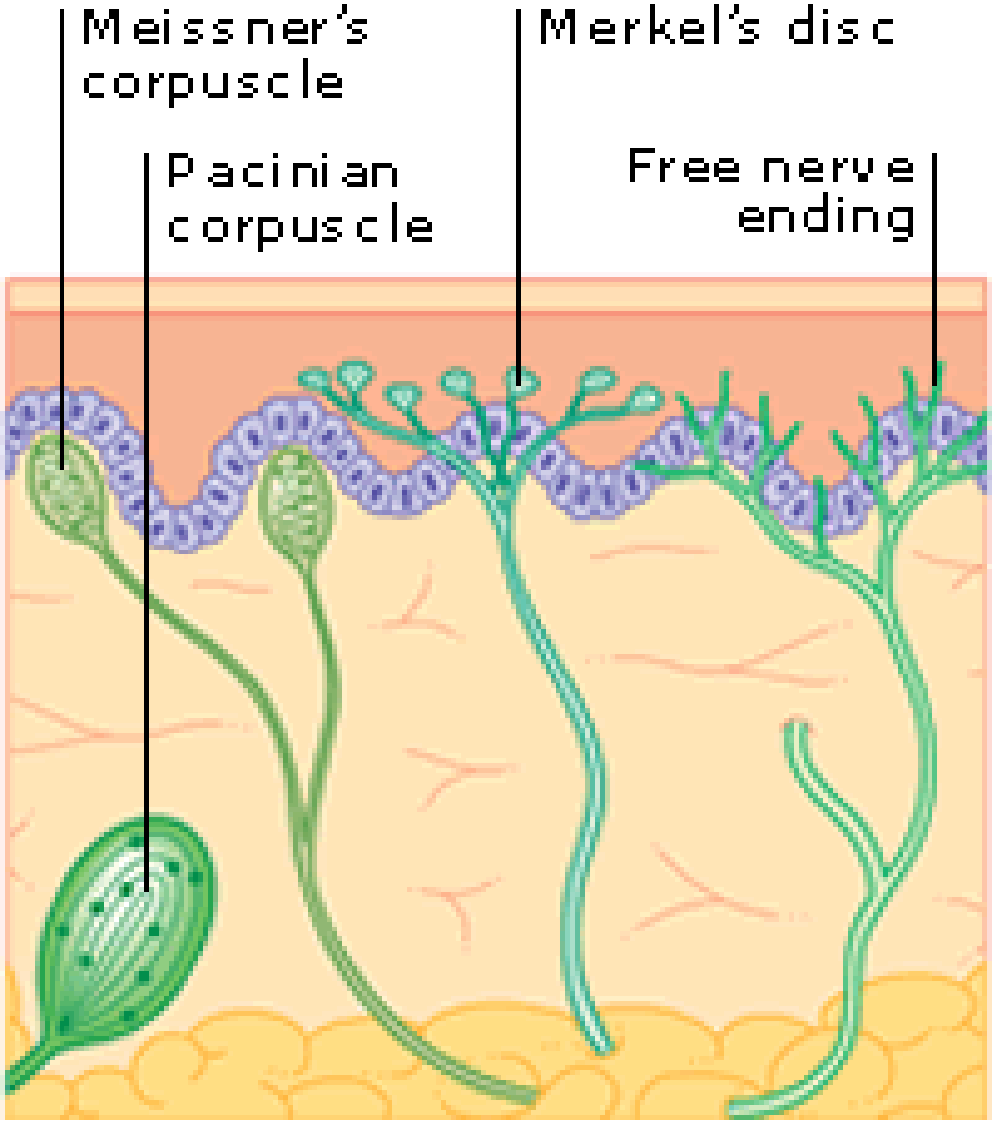
Adaptation of receptors occurs when a receptor is continuously stimulated. Many receptors become less sensitive with continued stimuli. Rapidly adapting receptors are best at detecting **rapidly changing signals**, while slowly adapting receptors are capable of detecting **a long, continuous signal**

❑ Thermoreceptors

- ❖ Free nerve endings
- ❖ Detect change in temperature
- ❖ TRP channels

❑ Nociceptors

- ❖ Free nerve endings
- ❖ Detect damage (pain receptors)
- ❖ Multimodal

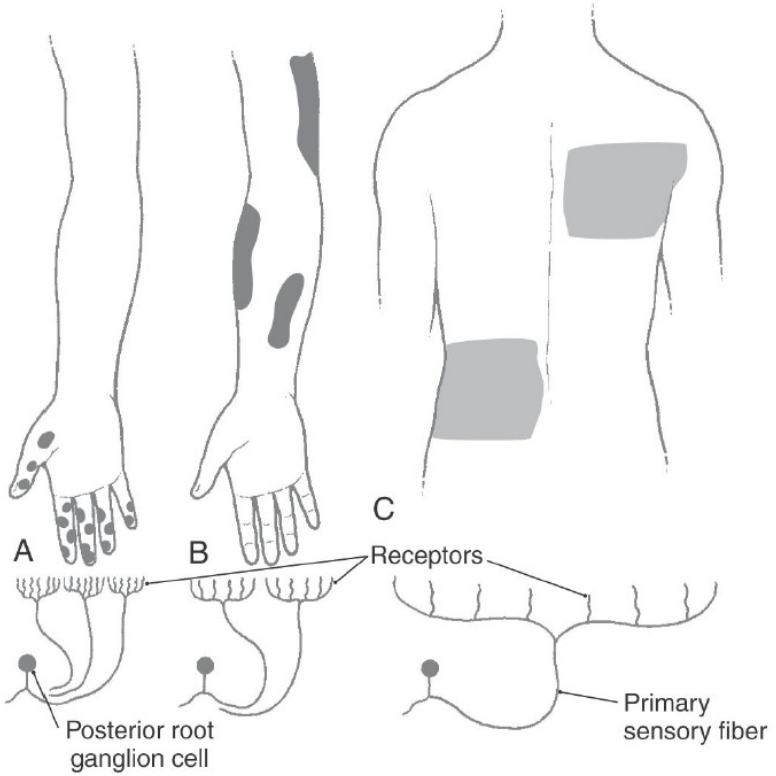


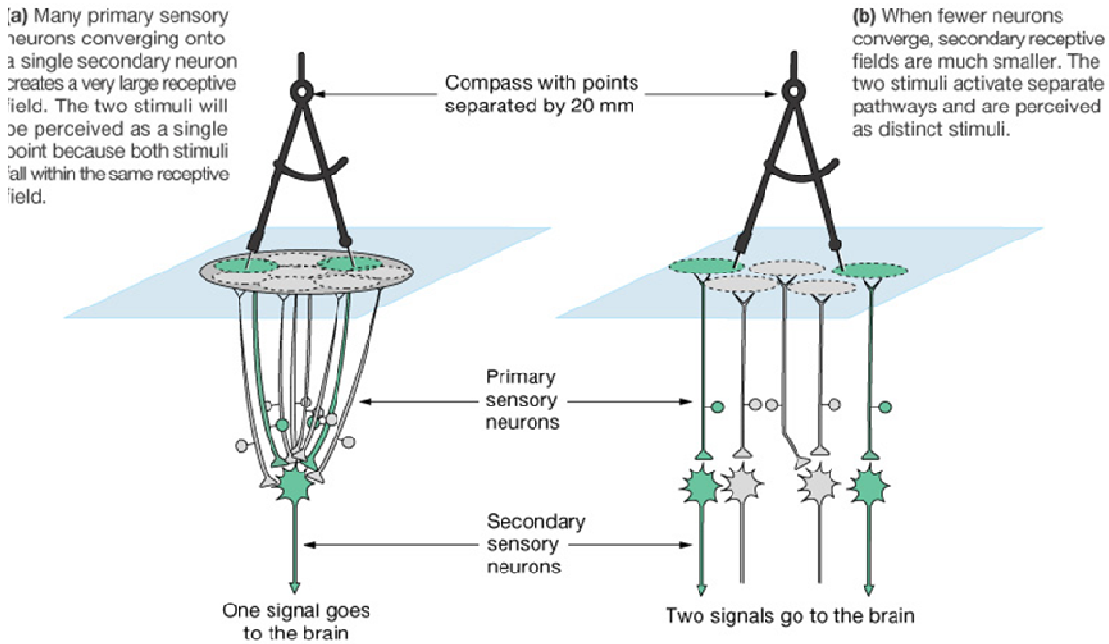
Adaptation of receptors occurs when a receptor is continuously stimulated. Many receptors become less sensitive with continued stimuli. Rapidly adapting receptors are best at detecting rapidly changing signals, while slowly adapting receptors are capable of detecting a long, continuous signal

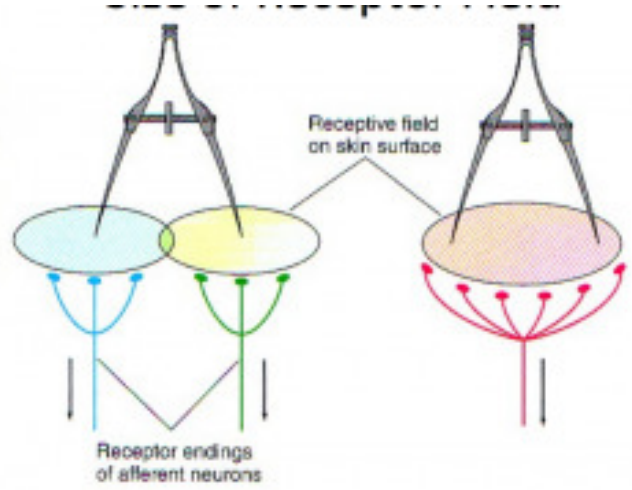
ELECTROPHYSIOLOGIC CLASSIFICATION OF PERIPHERAL NERVES	CLASSIFICATION OF AFFERENT FIBERS ONLY (CLASS/GROUP)	FIBER DIAMETER (μm)	CONDUCTION VELOCITY (m/s)	RECEPTOR SUPPLIED
Sensory Fiber Type				
Aα	Ia and Ib	13-20	80-120	Primary muscle spindles, Golgi tendon organ
Aβ	II	6-12	35-75	Secondary muscle spindles,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

❑ Receptive field

- ➢ Every receptor receives sensation from a certain area of the skin, (**receptive field)**
- The greater the density of receptors, the smaller the receptive fields of individual afferent fibers
- The smaller the receptive field the greater is the acuity or the discriminative touch







Labelled line theory

- individual receptors preferentially transduce information about an **adequate stimulus**
- individual primary afferent fibres carry information from a single type of receptor

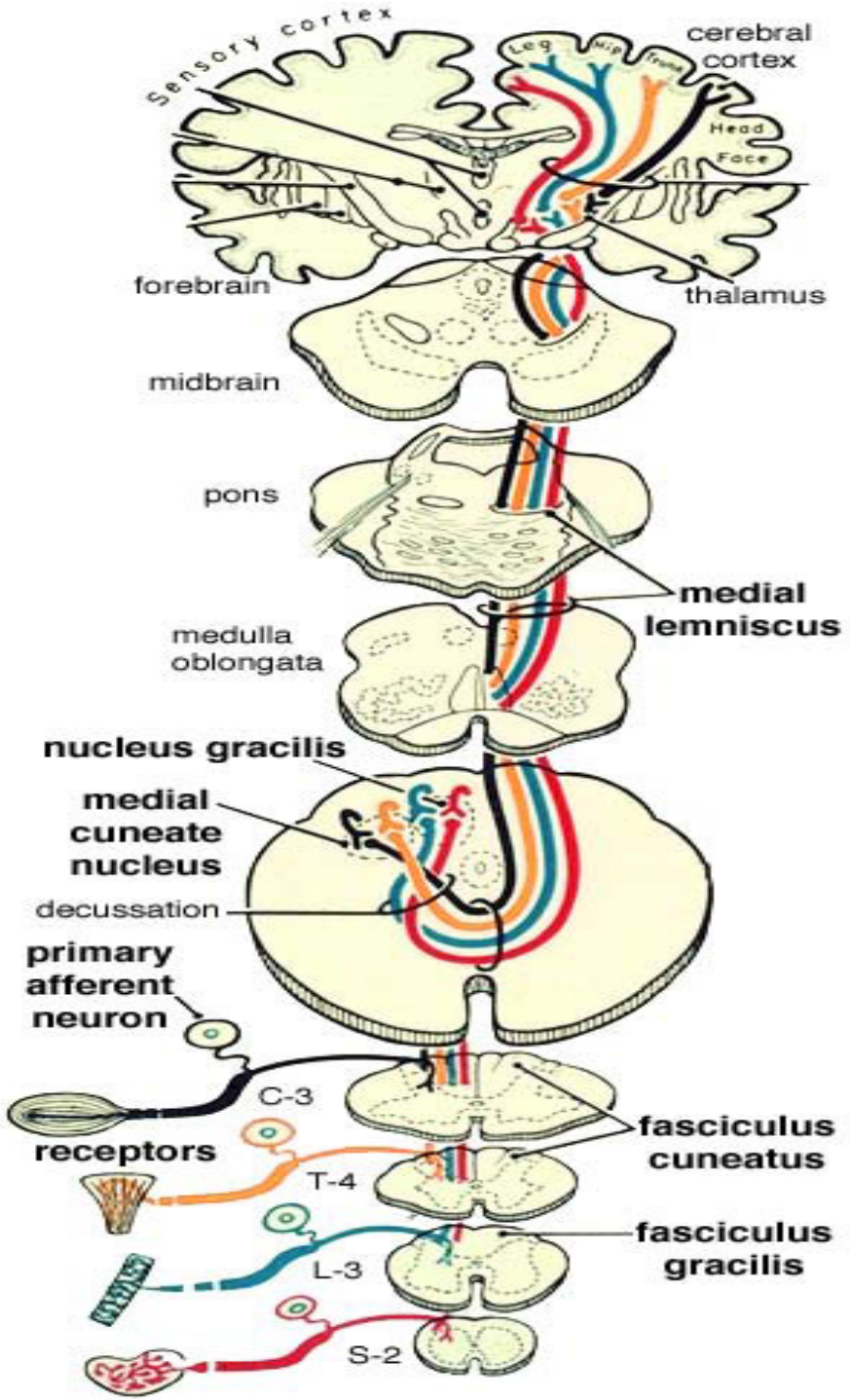
- **Conclusion:**
- pathways carrying sensory information centrally are therefore also specific, forming a "labelled line" regarding a particular stimulus

  - **Note: The adequate stimulus is the amount and type of energy required to stimulate a specific sensory organ**

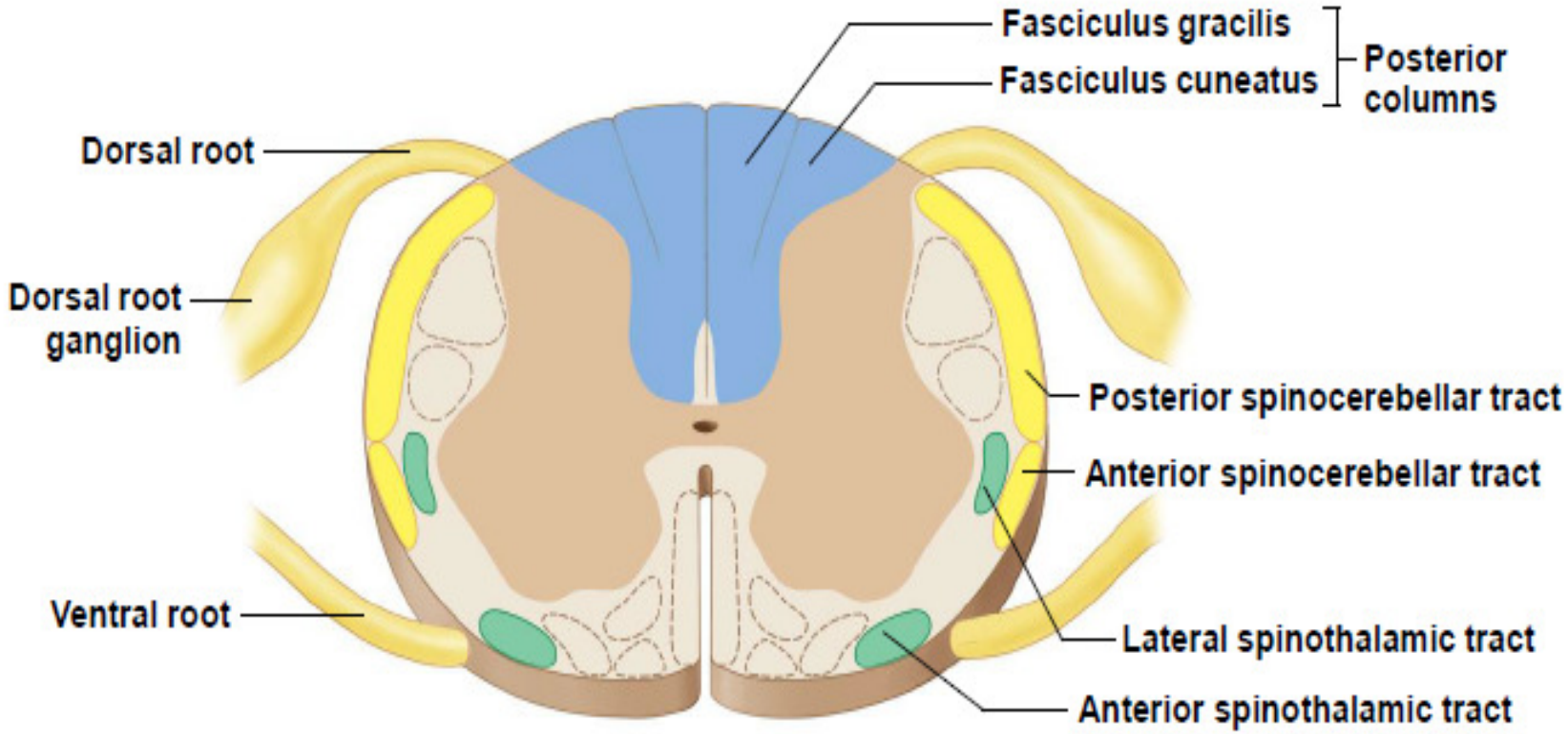
- **Sensation:**
  - Modality
  - Locality
  - Intensity

Posterior White Column-Medial Lemniscal Pathway

- Modality: Discriminative Touch Sensation (include Vibration) and Conscious Proprioception
- Receptor: Most receptors except free nerve endings
- Ist Neuron: Dorsal Root Ganglion
- 2nd Neuron: Dorsal Column Nuclei (Nucleus Gracilis and Cuneatus)
  ---Internal Arcuate Fiber - Lemniscal Decussation
  ---Medial Lemniscus
- 3rd Neuron: Thalamus (VPL) Internal Capsule ----- Corona Radiata
- Termination: Primary Somesthetic Area (S I)



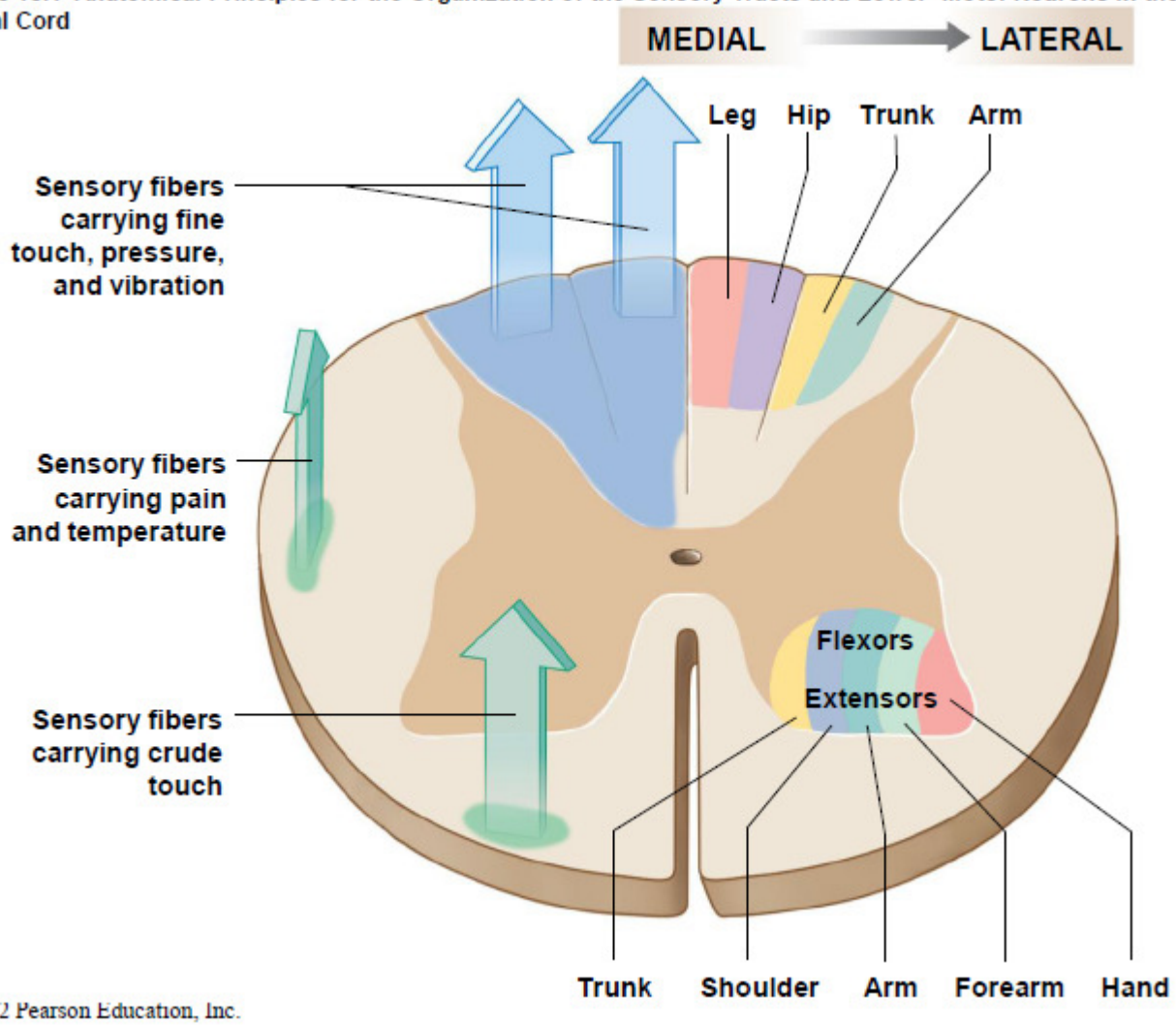
Posterior White Column-Medial Lemniscal Pathway



Discriminative touch, vibratory sense, and conscious muscle-joint sense

- **Posterior Column tract consists of:**
- **Fasciculus gracilis**
- Transmits information coming from areas inferior to T6
- **Fasciculus cuneatus**
- Transmits information coming from areas superior to T6

Figure 15.1 Anatomical Principles for the Organization of the Sensory Tracts and Lower–Motor Neurons in the Spinal Cord



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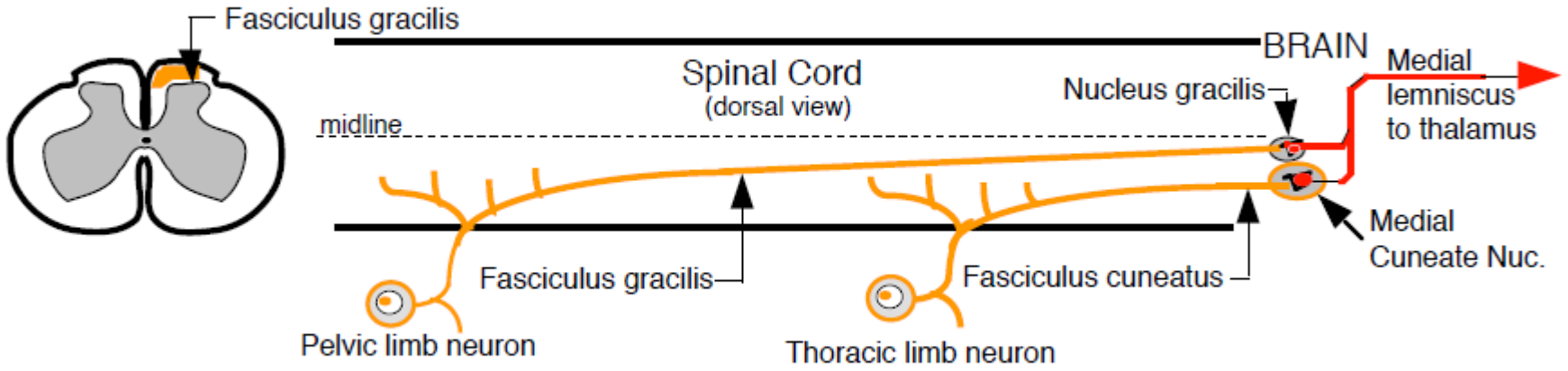
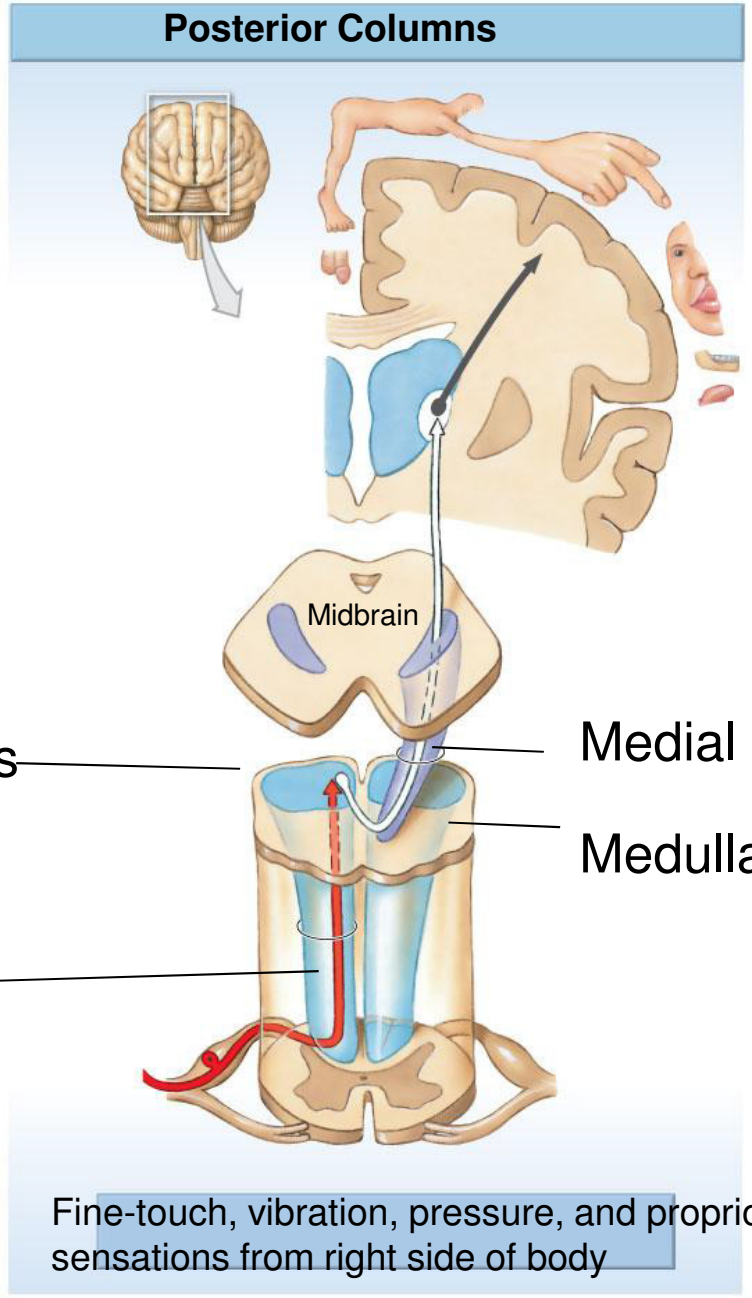
Discriminative Touch Spinal Pathway




Posterior Columns
Midbrain
Nucleus gracilis
nucleus cuneatus
Medial lemniscus
Medulla oblongata
Fasciculus cuneatus
fasciculus gracilis
Fine-touch, vibration, pressure, and proprioception sensations from right side of body
a

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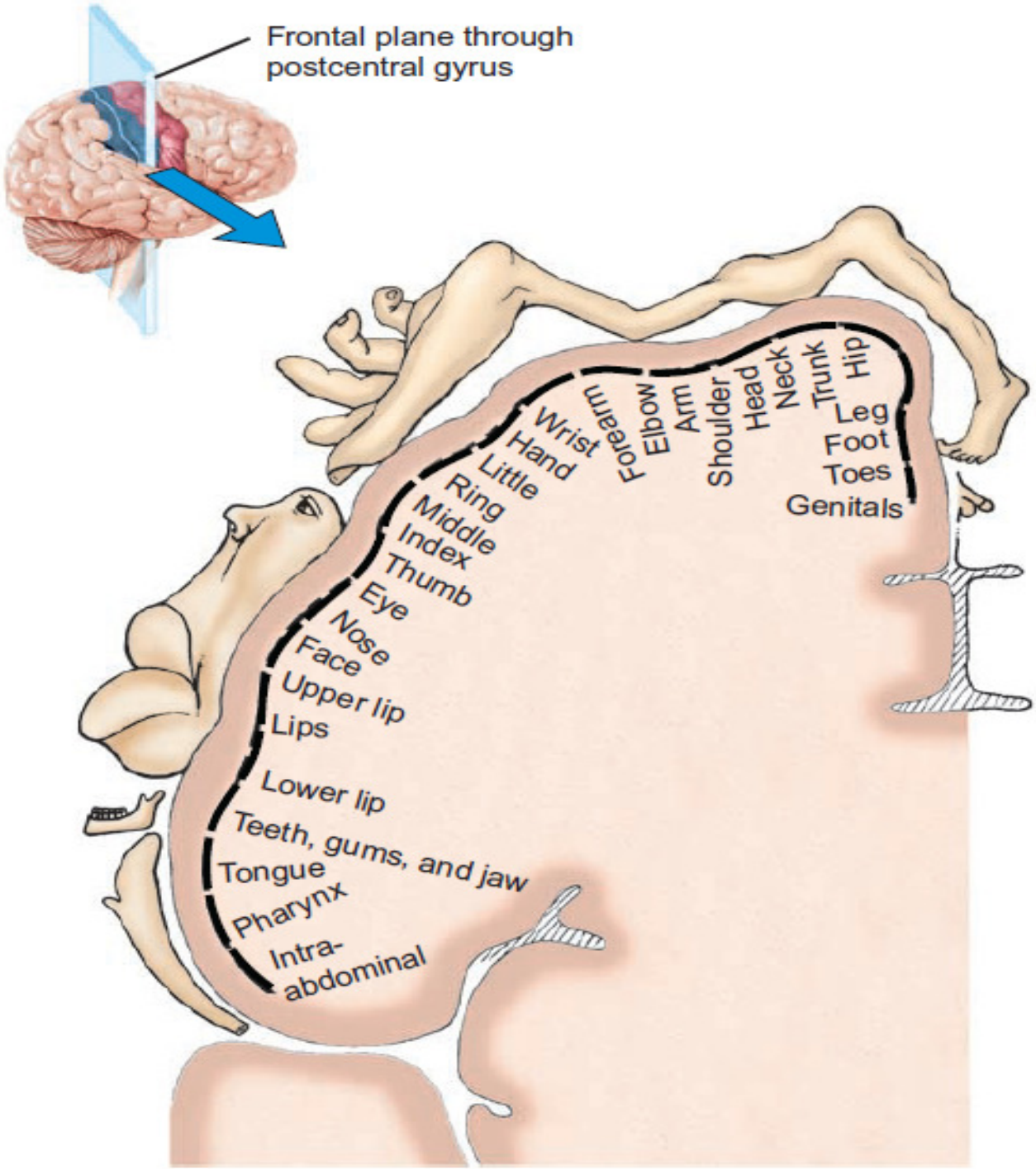
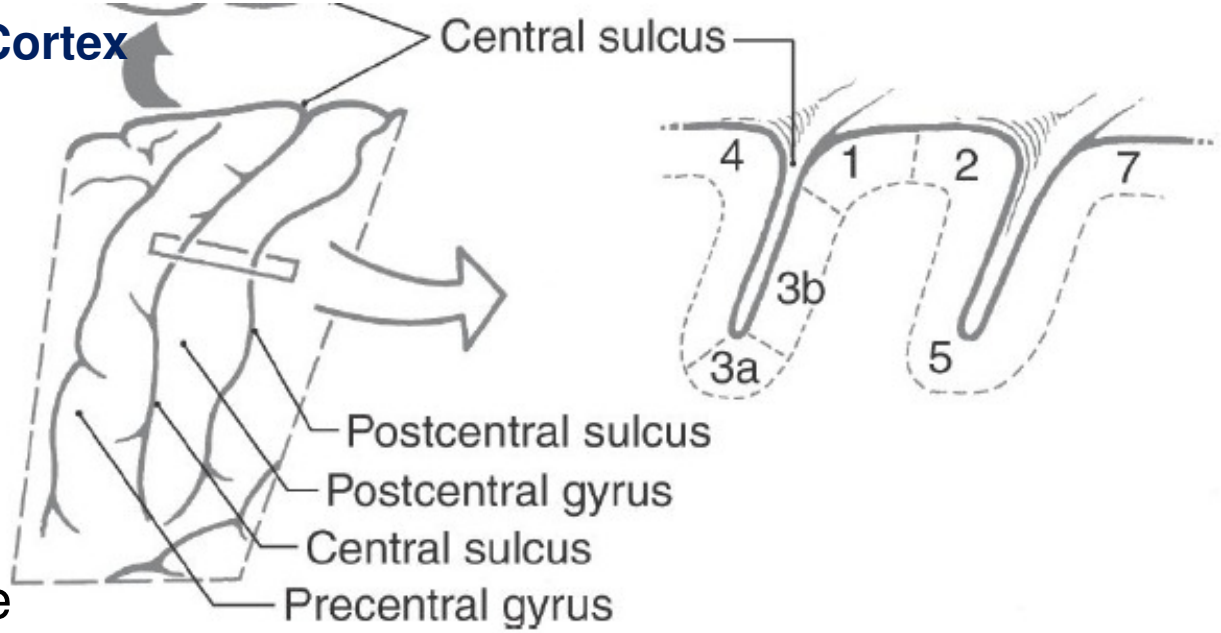

Frontal plane through
postcentral gyrus
Wrist
Hand
Little
Ring
Middle
Index
Thumb
Eye
Nose
Face
Upper lip
Lips
Lower lip
Teeth, gums, and jaw
Tongue
Pharynx
Intra-
abdominal
Forearm
Elbow
Arm
Shoulder
Head
Neck
Trunk
Hip
Leg
Foot
Toes
Genitals

Primary Somatosensory (SI) Cortex

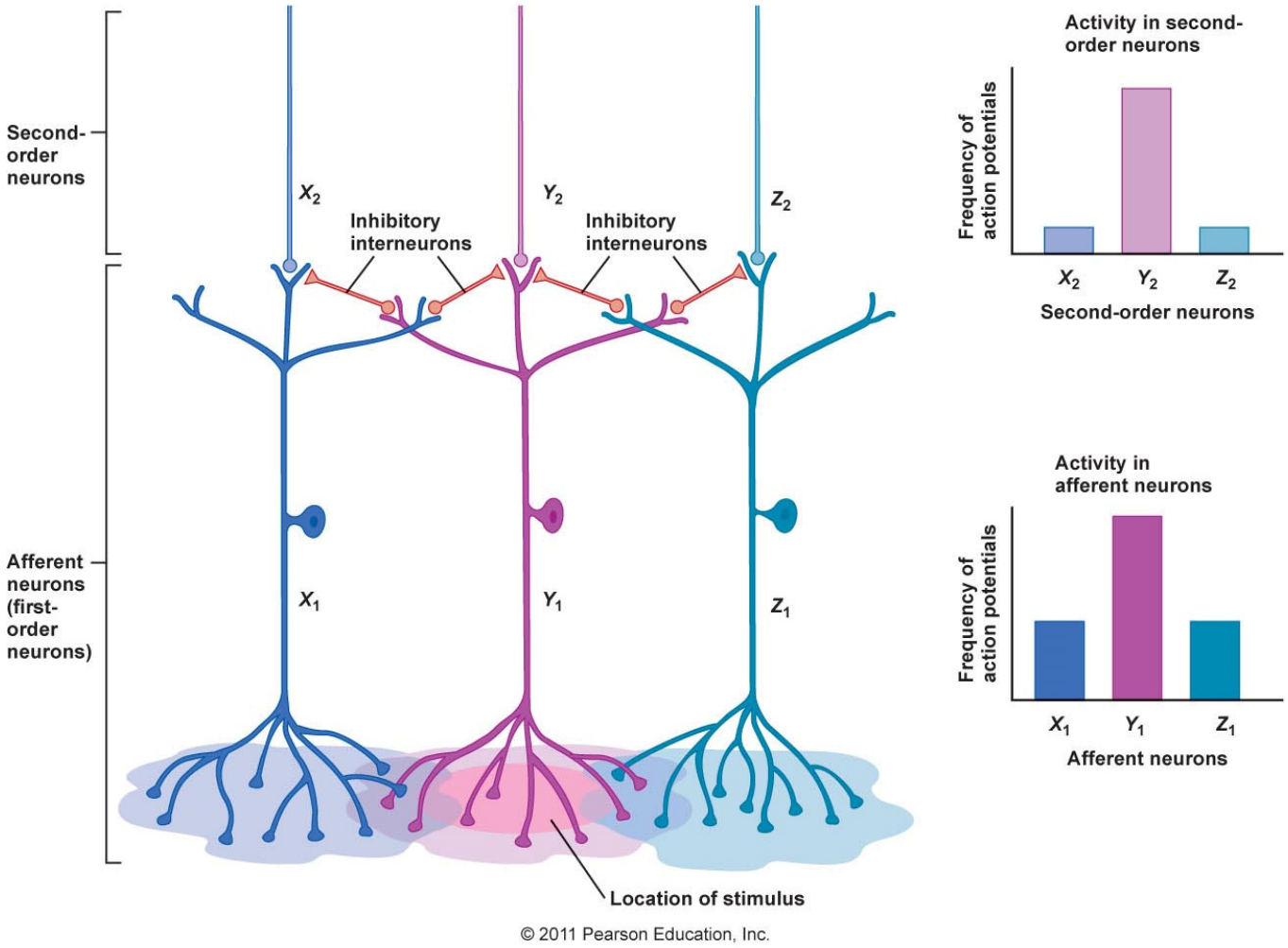
- Axons from third-order thalamic neurons terminate in the **primary somatosensory (SI)cortex**
- subdivided into four distinct areas; from anterior to posterior, these are **Brodmann areas 3a, 3b, 1, and 2**



- **Area 3a:** muscle spindle afferents (mainly)
- **Area 2:** Golgi tendon organs, and joint afferents (mainly).
- **Areas 3b and 1:** They receive cutaneous afferents from receptors such as Meissner corpuscles and Merkel cells). also receive input from cutaneous receptors that transmit pain and temperature

Lateral inhibition

- The receptor at the site of most intense stimulation is activated to the greatest extent. Surrounding receptors are also stimulated but to a lesser degree
- The most intensely activated receptor pathway halts transmission of impulses in the less intensely stimulated pathways through lateral inhibition



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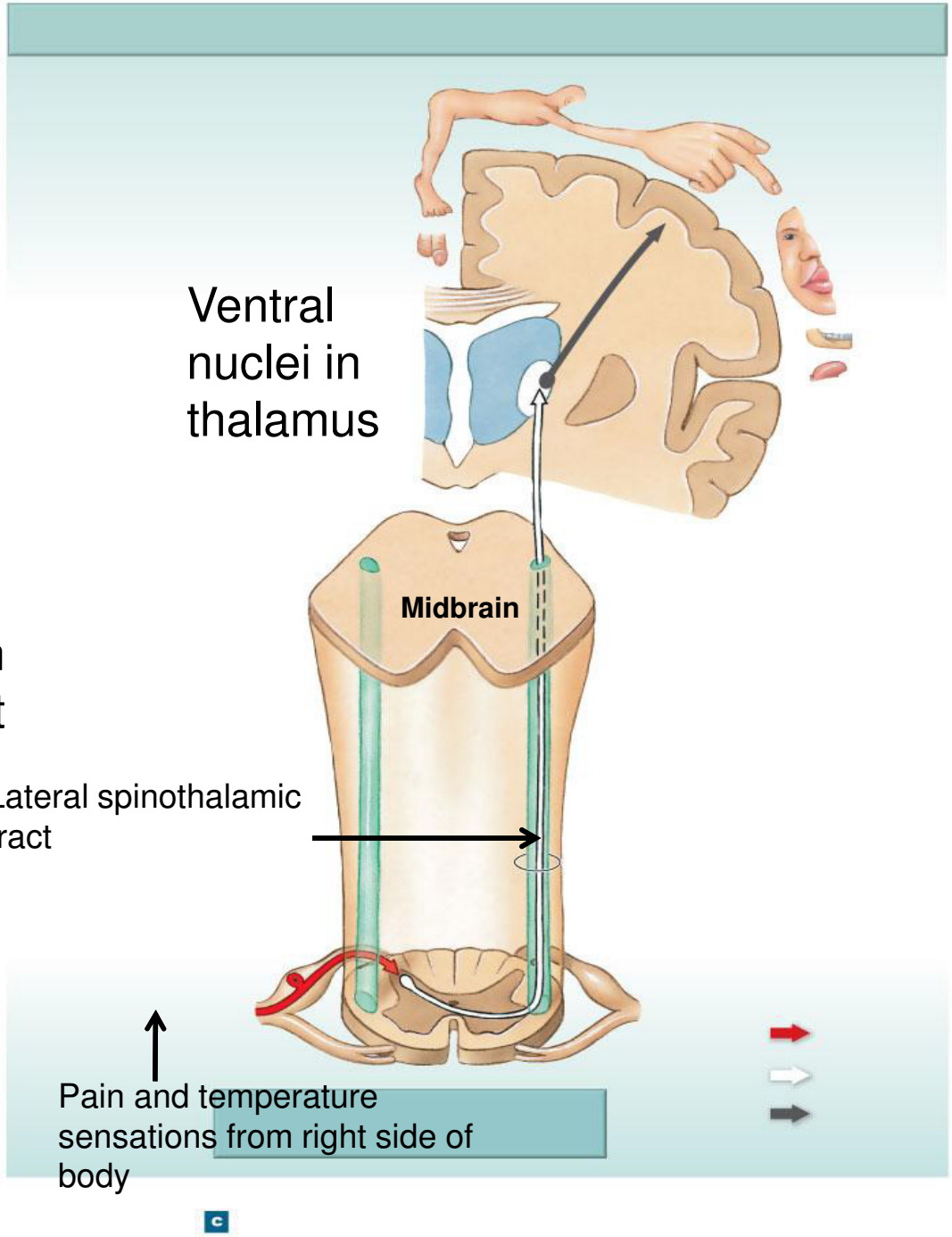
- This process facilitates the localization of the site of stimulation

lateral spinothalamic tract

- Modality: pain and temperature
- Receptors: free nerve endings
- 1st Neuron: Dorsal root ganglia
- 2nd Neuron: the posterior gray column (substantia gelatinosa) The axons of 2nd order neurons cross obliquely to the opposite side in the anterior gray and white commissures , ascending in the contralateral white column as the lateral spinothalamic tract
- 3rd Neuron: Thalamus (VPL) Internal Capsule ----- Corona Radiata
- Termination: Primary Somesthetic Area (S I) and Widespread Cortical Region



Rexed laminae

- **Lamina 1** relay information related to pain and temperature
- **Lamina 2:** relay information related to pain and temperature **(pain modulation)**
- **Lamina 3 and 4:** nucleus proprius; these laminae have many interneurons

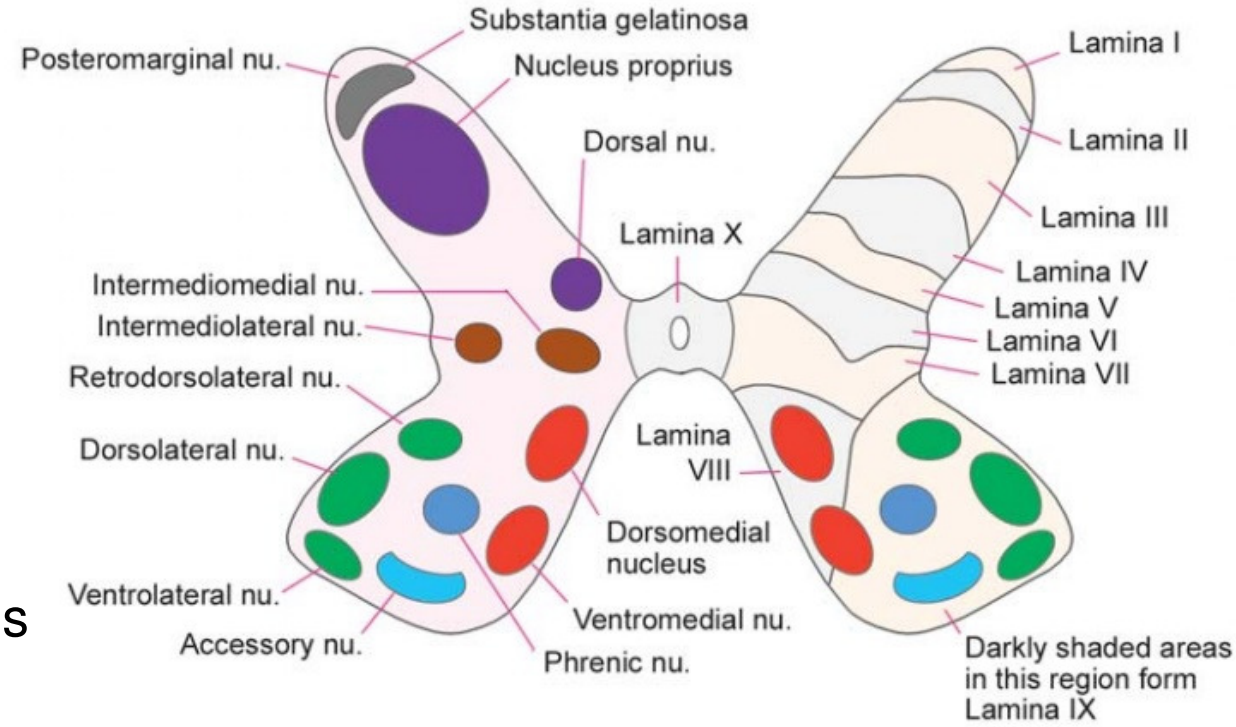
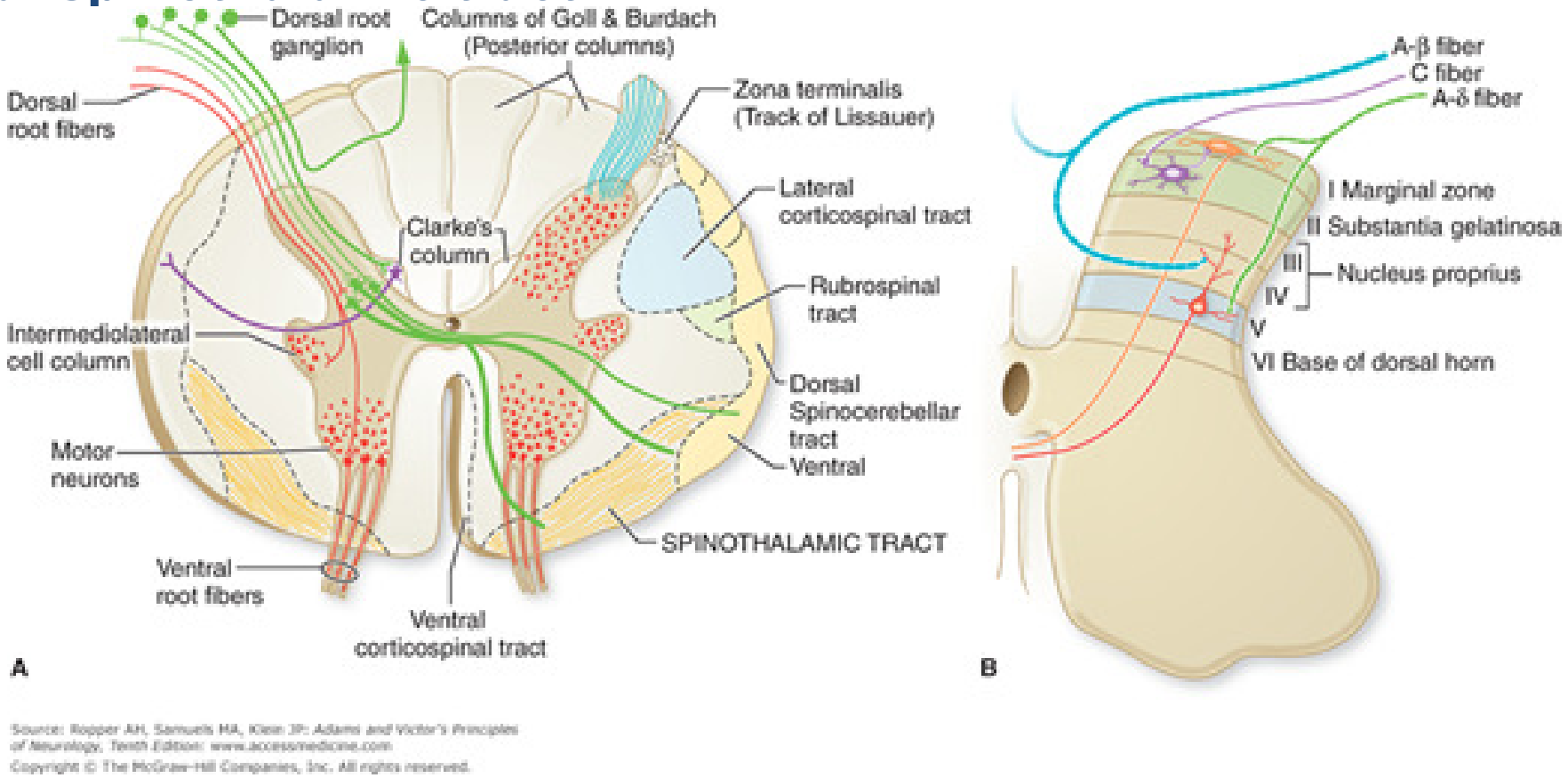


Fig. 5.2. Subdivisions of the grey matter of the spinal cord. The left half of the figure shows the cell groups usually described. The right half shows the newer concept of laminae.

- **Lamina 5:** relay information related to pain and temperature
- **Lamina 6:** presents only at the cervical and lumbar enlargements and receives proprioception
- **Lamina 7: Intermedio-lateral** nucleus, contains preganglionic fibers of sympathetic (T1 -L2). **Intermedio-medial nucleus** ,all over the spinal cord, receive visceral pain. **Dorsal nucleus of Clark's** presents at (C8 – L2 or T1-L4) , relay center for **unconscious proprioception**

lateral spinothalamic tract



Source: Ropper AH, Samuels MA, Klein JP: *Adams and Victor's Principles of Neurology*, Tenth Edition: www.accessmedicine.com
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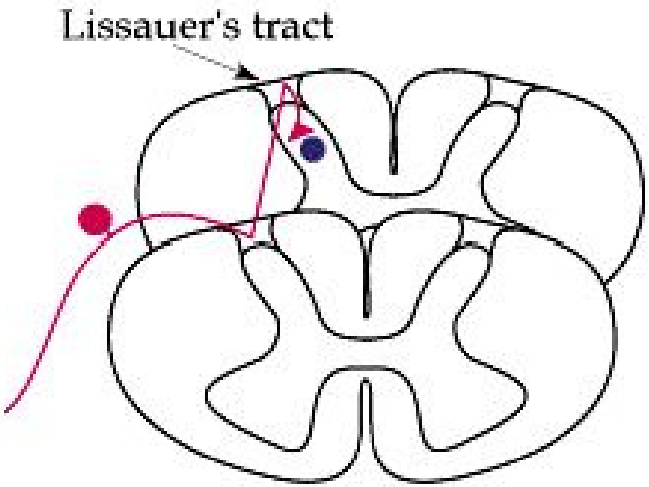
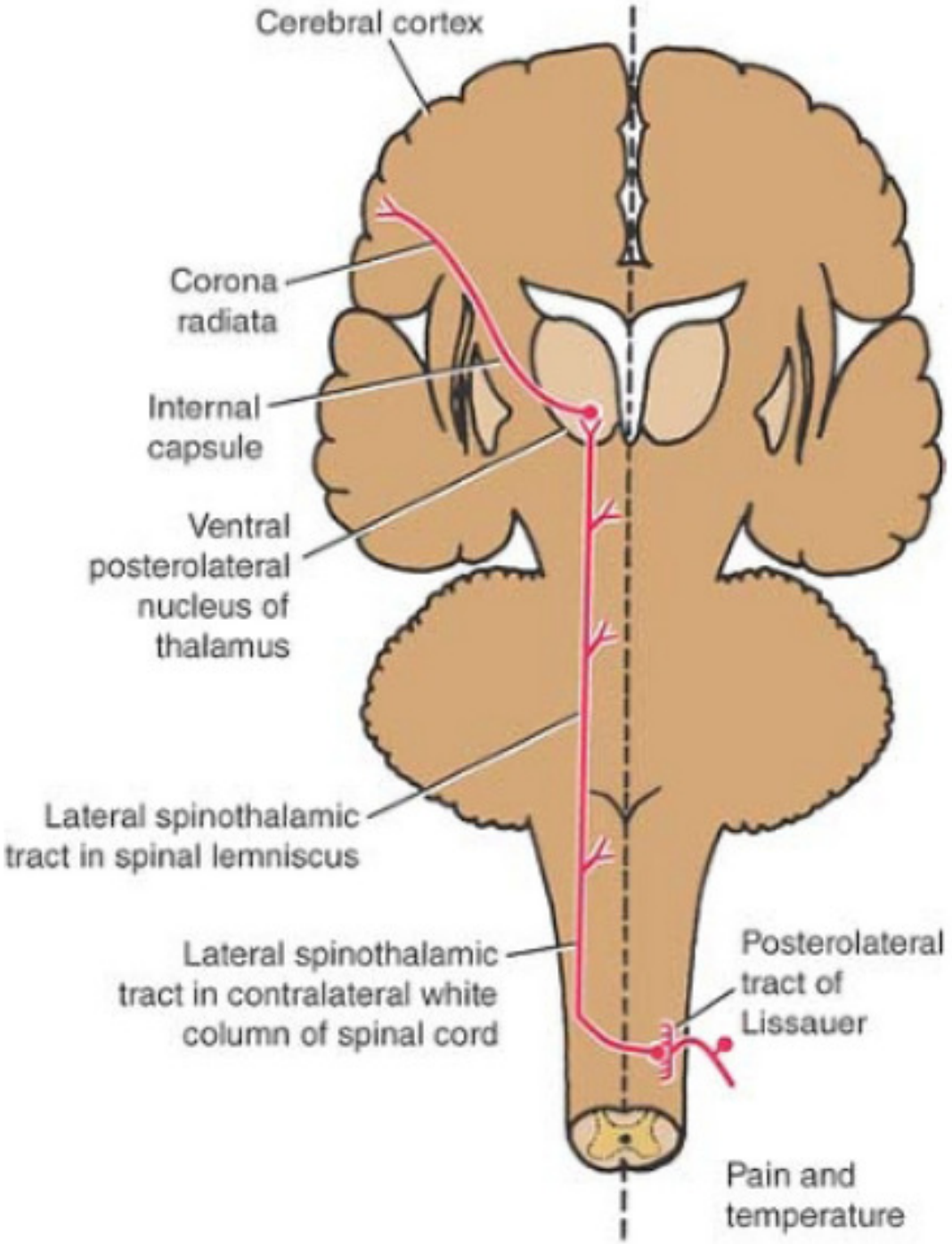
- Lamina 1+ 5: the spinothalamic tract ascend which transmit pain, temperature and touch. (A delta fibers)
- Lamina 1+ 2: the spinothalamic tract ascend (C fibers).

Posterolateral tract of Lissauer

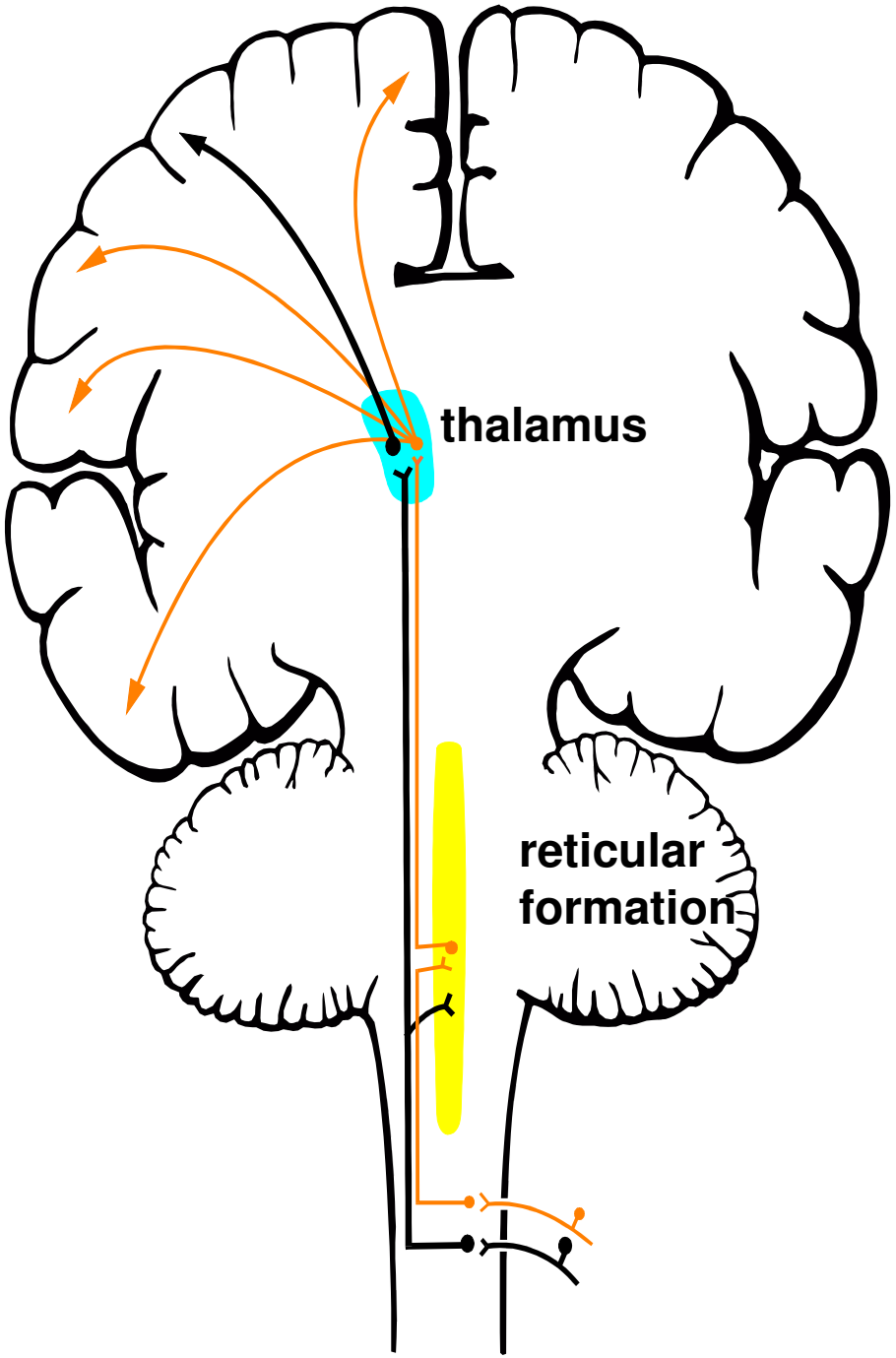
- located between the posterior white column and the lateral white column





Other Terminations of the Lateral Spinothalamic Tract

- **Reticular formation**: (majority of the slow pain fibers) individual becomes aware of the pain
- **Cingulate gyrus:** interpretation of the emotional aspect of pain
- **Insular gyrus:** concerned with the interpretation of pain stimuli from the internal organs of the body and brings about an autonomic response



Pain classifications slow and fast

Fast Pain	Slow Pain
Sharp, pricking	Dull, burning
(Aδ) fiber	(C) fiber
Short latency	Slower onset
Well localized	Diffuse
Short duration	Long duration
Less emotional	Emotional, autonomic response
Mostly from superficial structures	Superficial & deep structures
Spinothalamic	Spinoreticular
lamina I & V	lamina I & II
VPL nucleus	VPL & intraluminar nucleus

Pain According to origin

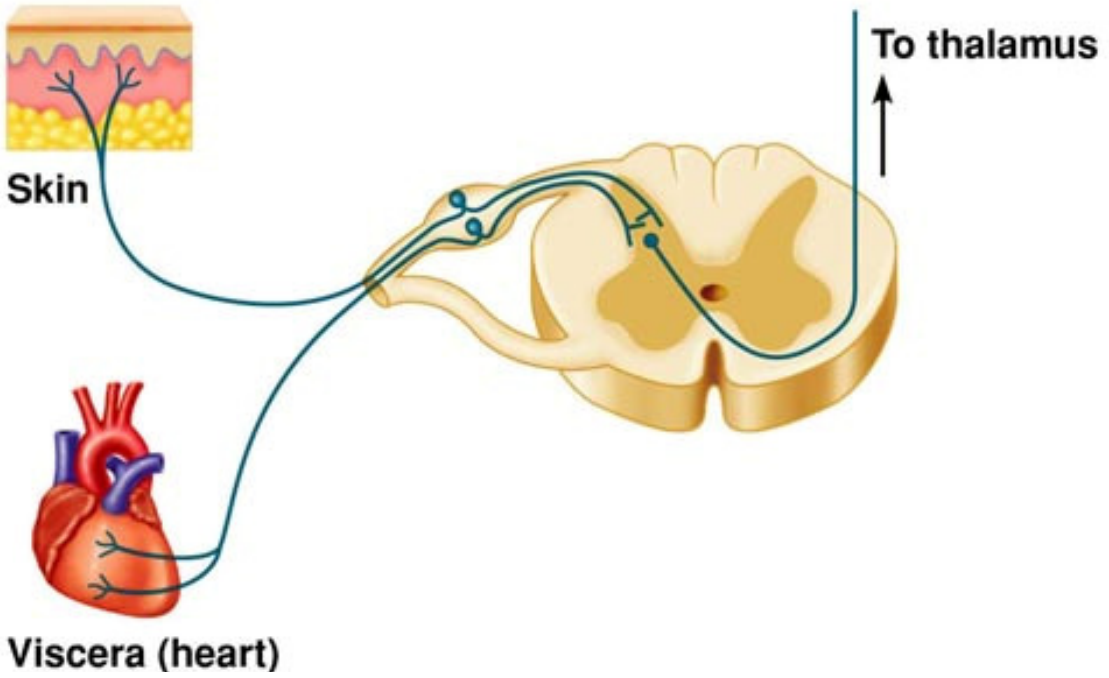
- **Cutaneous:** skin
- **Deep somatic:** muscles , bones , joints & ligaments , dull diffuse
  - **Intermittent claudication**: muscle pain which occurs during exercise classically in the calf muscles due to peripheral artery disease (blood supply is not enough to remove the metabolites esp. lactic acid)
- **Visceral:** poorly localized & transmitted via C fibers
  - Chemoreceptors, baroreceptors, osmoreceptors, and stretch receptors
  - Sensitive to ischemia, stretching, and chemical damage
  - **Often referred**

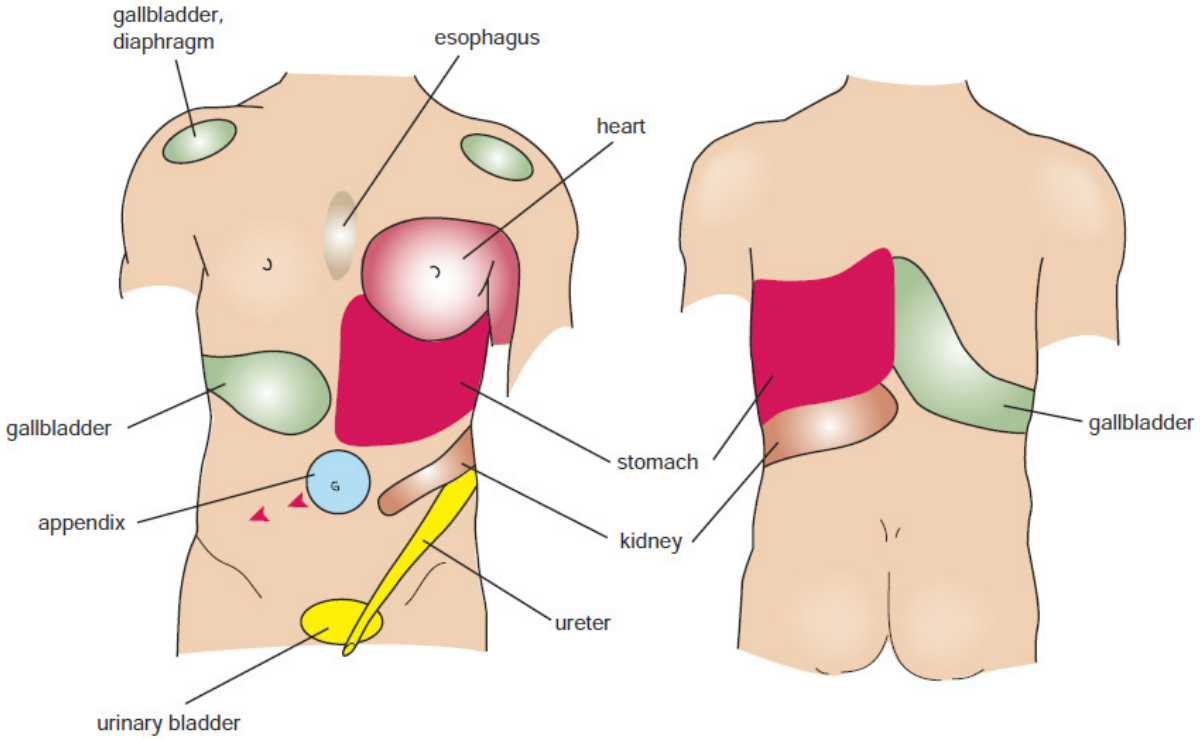
- **Cuases of visceral pain**
  - Distention of bladder and abdominal viscera
  - Ischemia
  - Spasm: leads to blood vessels compressions and accumulation of metabolites.
  - Chemical damage :HCl from perforated ulcer

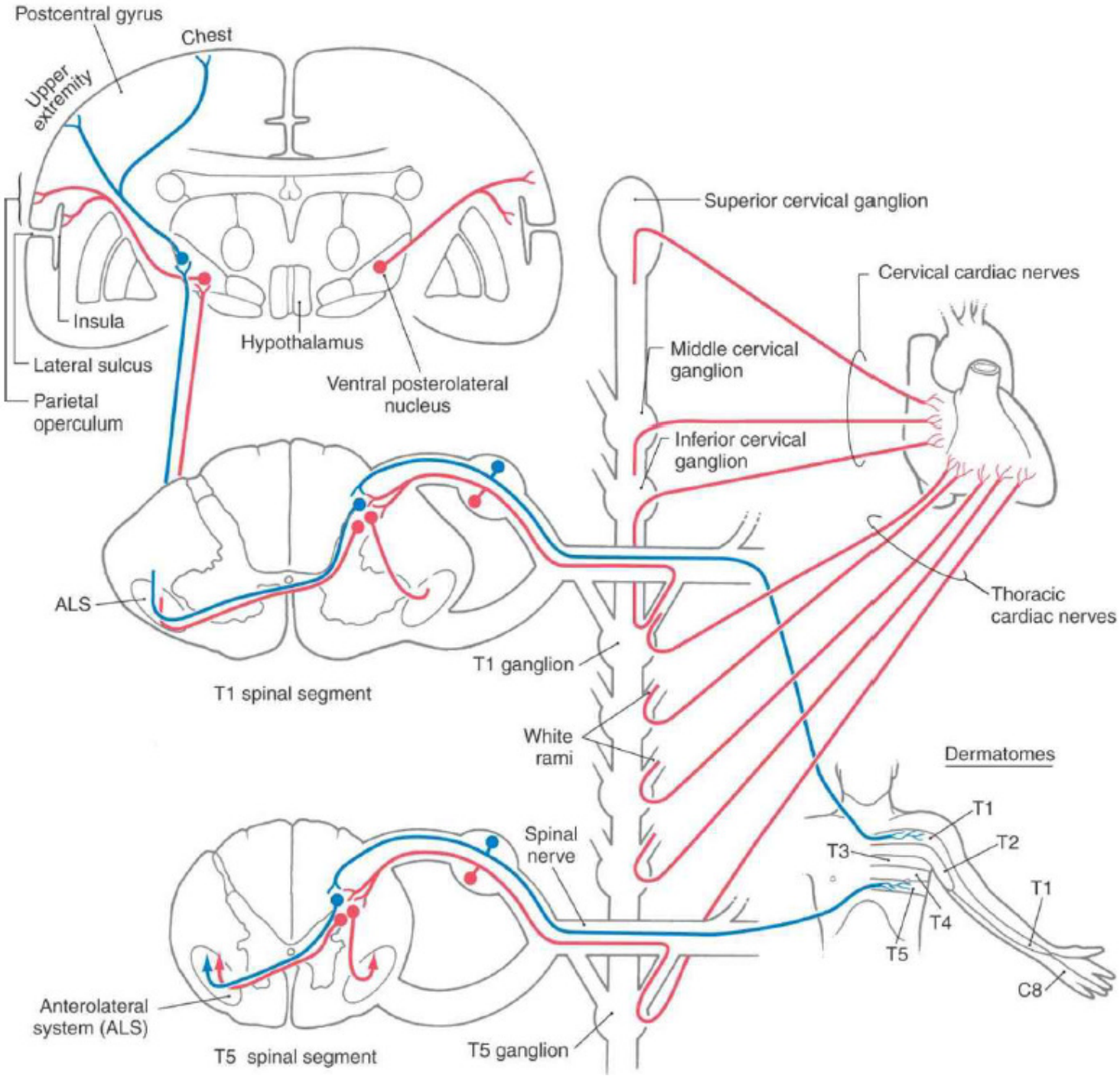
Referred pain mechanism

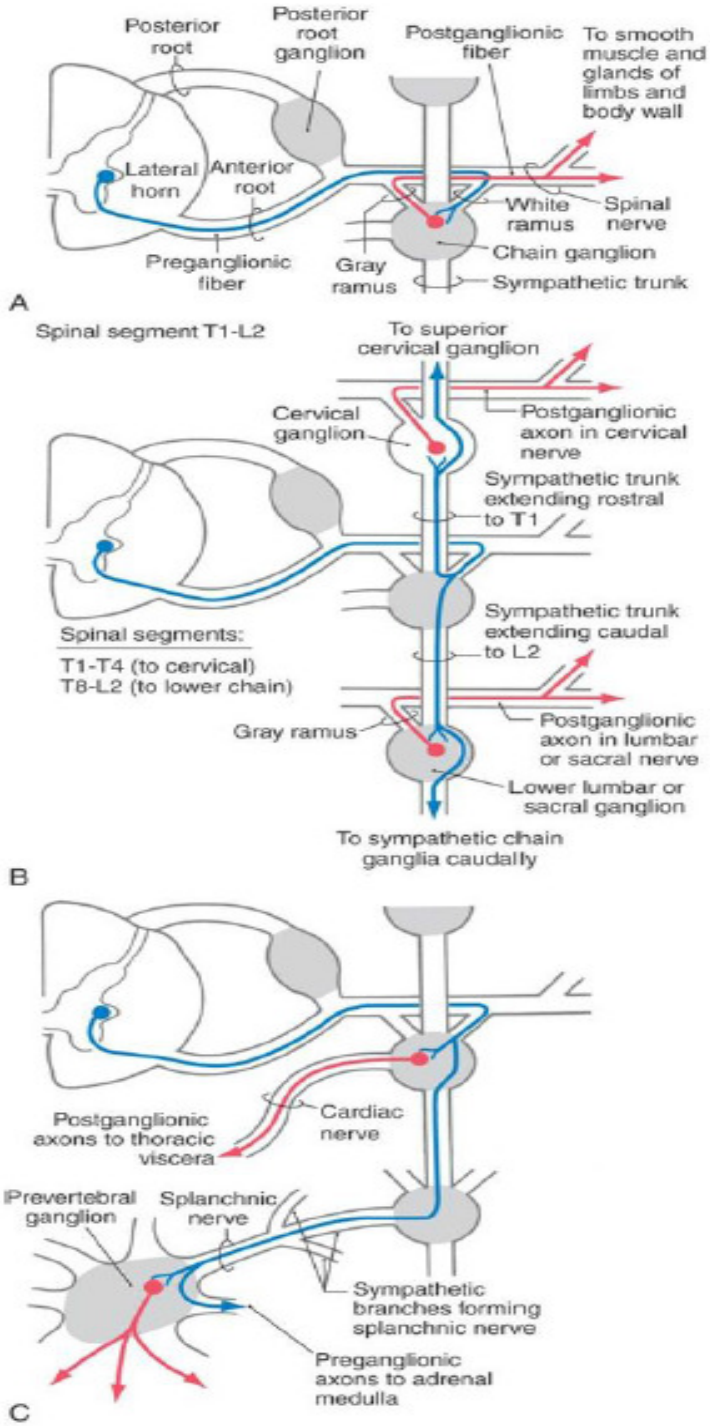
convergence theory

- Referred pain is presumed to occur because the information from multiple nociceptor afferents converges onto individual spinothalamic tract neurons
- The brain therefore interprets the information coming from visceral receptors as having arisen from receptors on the body surface, since this is where nociceptive stimuli originate more frequently

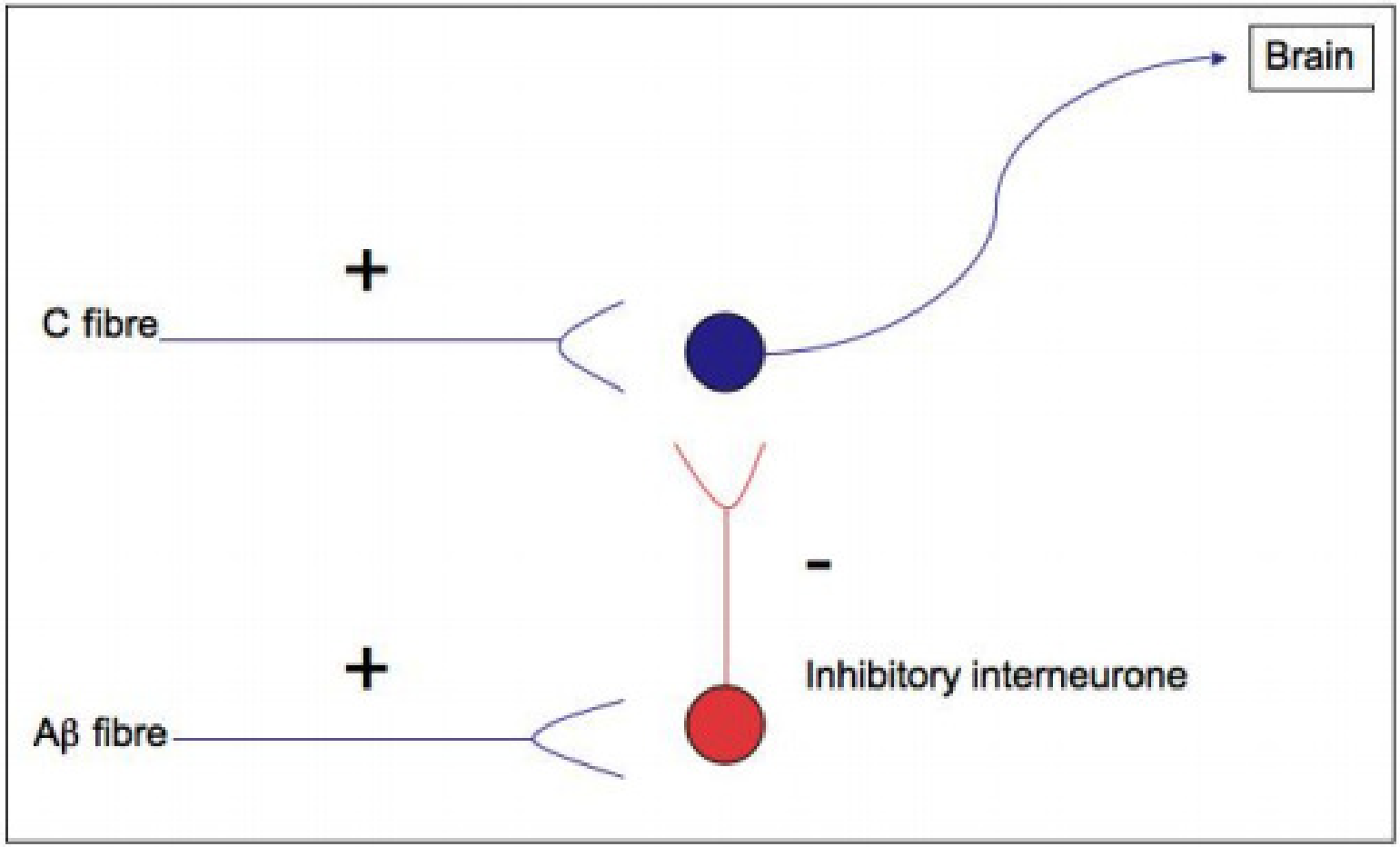





Postcentral gyrus
Chest
Upper extremity
Insula
Lateral sulcus
Parietal operculum
Hypothalamus
Ventral posterolateral nucleus
Superior cervical ganglion
Cervical cardiac nerves
Middle cervical ganglion
Inferior cervical ganglion
Thoracic cardiac nerves
ALS
T1 spinal segment
T1 ganglion
White rami
Dermatomes
T1
T2
T3
T4
T5
C8
Spinal nerve
Anterolateral system (ALS)
T5 spinal segment
T5 ganglion


Posterior root
Posterior root ganglion
Postganglionic fiber
To smooth muscle and glands of limbs and body wall
Lateral horn
Anterior root
White ramus
Spinal nerve
Chain ganglion
Preganglionic fiber
Gray ramus
Sympathetic trunk
A
Spinal segment T1-L2
To superior cervical ganglion
Cervical ganglion
Postganglionic axon in cervical nerve
Sympathetic trunk extending rostral to T1
Sympathetic trunk extending caudal to L2
Spinal segments:
T1-T4 (to cervical)
T8-L2 (to lower chain)
Gray ramus
Postganglionic axon in lumbar or sacral nerve
Lower lumbar or sacral ganglion
To sympathetic chain ganglia caudally
B
Postganglionic axons to thoracic viscera
Cardiac nerve
Prevertebral ganglion
Splanchnic nerve
Sympathetic branches forming splanchnic nerve
Preganglionic axons to adrenal medulla
C

Pain Control in the Central Nervous System
The Gating Theory



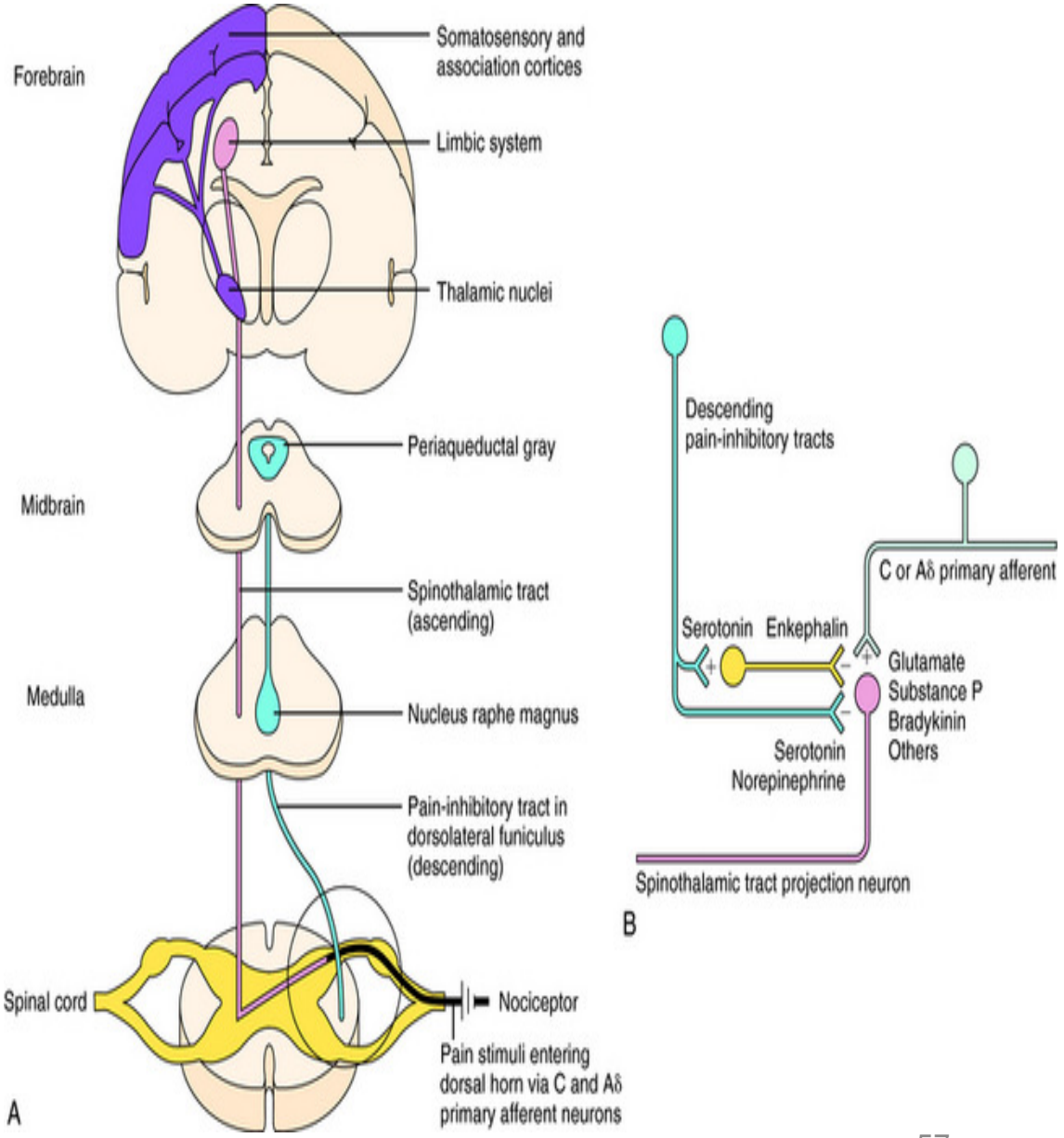
- At the site where the pain fiber enters the central nervous system, inhibition could occur by means of connector neurons excited by large, myelinated afferent fibers carrying information of nonpainful touch and pressure

Pain Control in the Central Nervous System

Descending control of pain

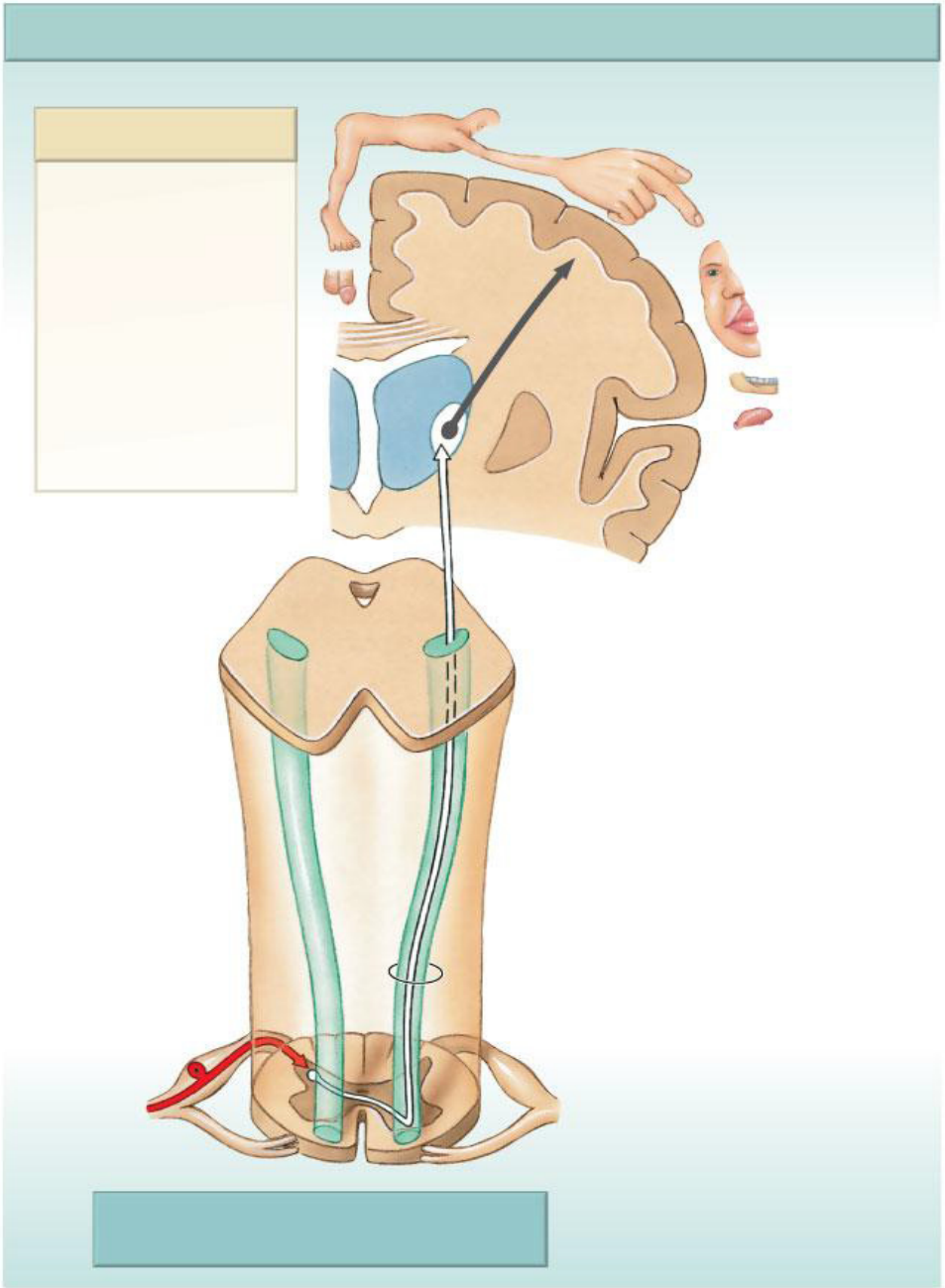
- Spinoreticular fibers stimulates **periaqueductal gray** (**PAG)**
- Exitatory neurons of PAG projects to Nucleus raphe magnus (NRM)
- (NRM) neurons produces serotonin which activates inhibitory neurons that secretes **enkephalins and the endorphins** (morphinelike actions) in substantia gelatinosa

❑ **Locus coeruleus** (in Pons), thought to directly inhibit substantia gelatinosa neurons



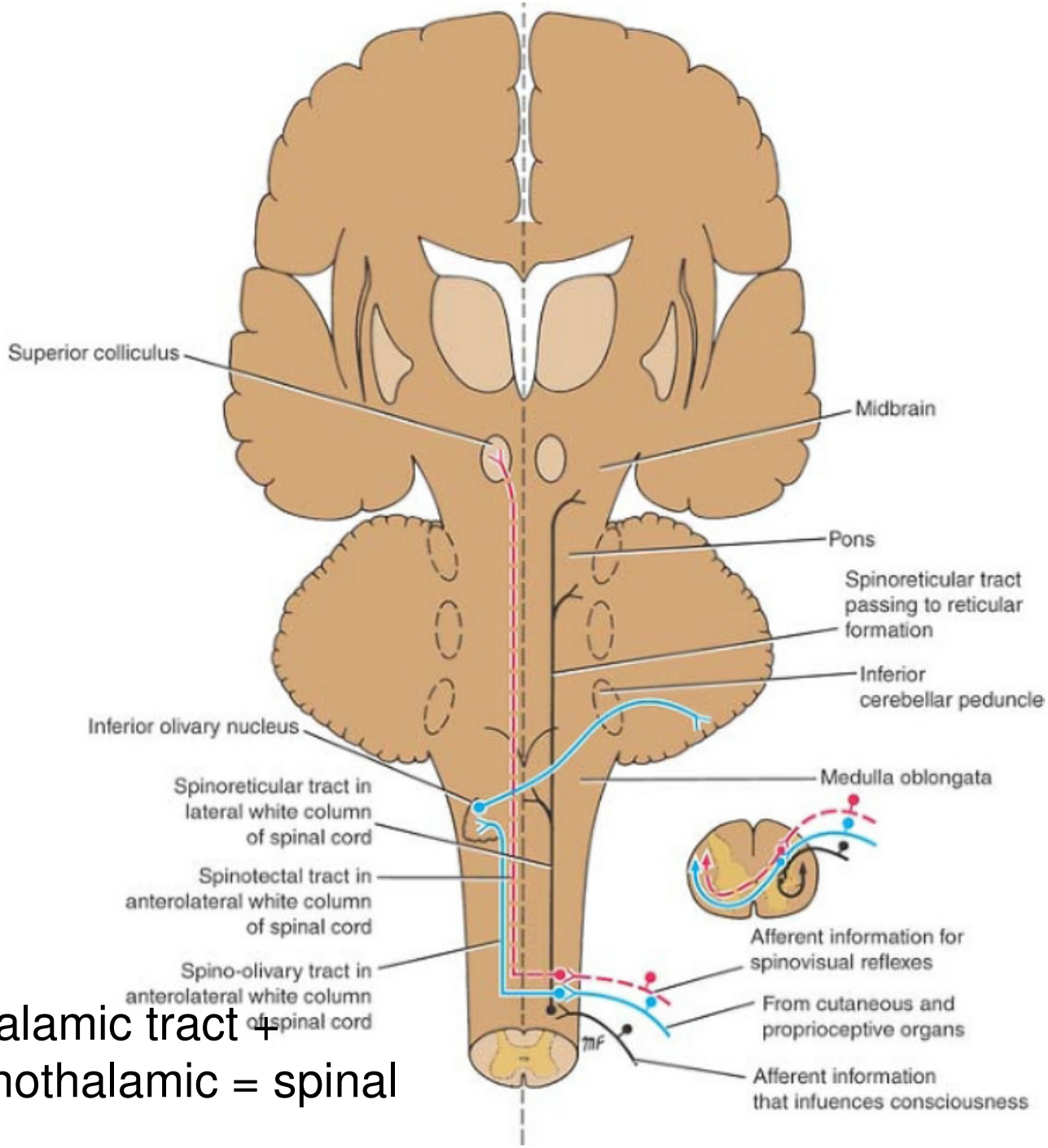
Anterior spinothalamic tract

- Modality: crude touch and pressure
- Receptors: free nerve endings
- 1st Neuron: Dorsal root ganglia
- 2nd Neuron: the posterior gray column **(nucleus proprius)** The axons of 2nd order neurons cross obliquely to the opposite side in the anterior gray and white commissures , ascending in the contralateral white column as the Anterior spinothalamic tract
- 3rd Neuron: Thalamus (VPL) Internal Capsule ----- Corona Radiata
- Termination: Primary Somesthetic Area (S I)



Spinotectal Tract

- ascend in the anterolateral white column lying close to the lateral spinothalamic tract
- Terminate: superior colliculus
- Provides afferent information for spinovisual reflexes

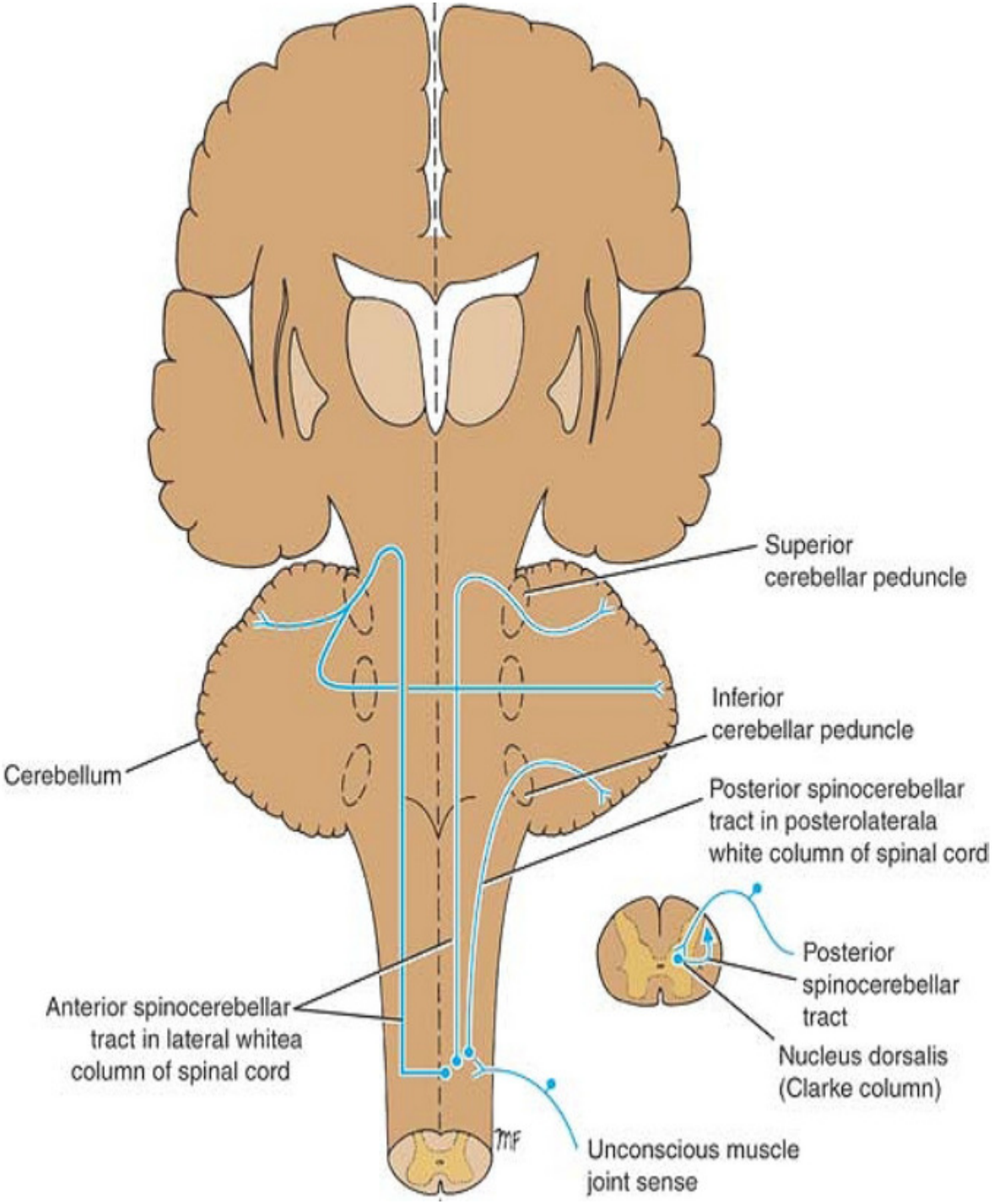


In Medulla: ant spinothalamic tract + spinotectal + lateral spinothalamic = spinal leminiscus

Posterior spinocerebellar

- muscle and joint sensation
- 1st order neuron axons terminate at the base of post gray column (nucleus dorsalis or **Clarks nucleus**)
- the axons of 2nd order neurons enter posterolateral part of the lateral white matter on the **same side**
- ascend as the posterior spinocerebellar tract to medulla oblongata
- Terminates in cerebellar cortex (through inferior cerebellar peduncle)

➢ *note: axons of lower lumbar and sacral spinal nerves ascend in the posterior white column until they reach L3 or L4 segments where they synapse with nucleus dorsalis*



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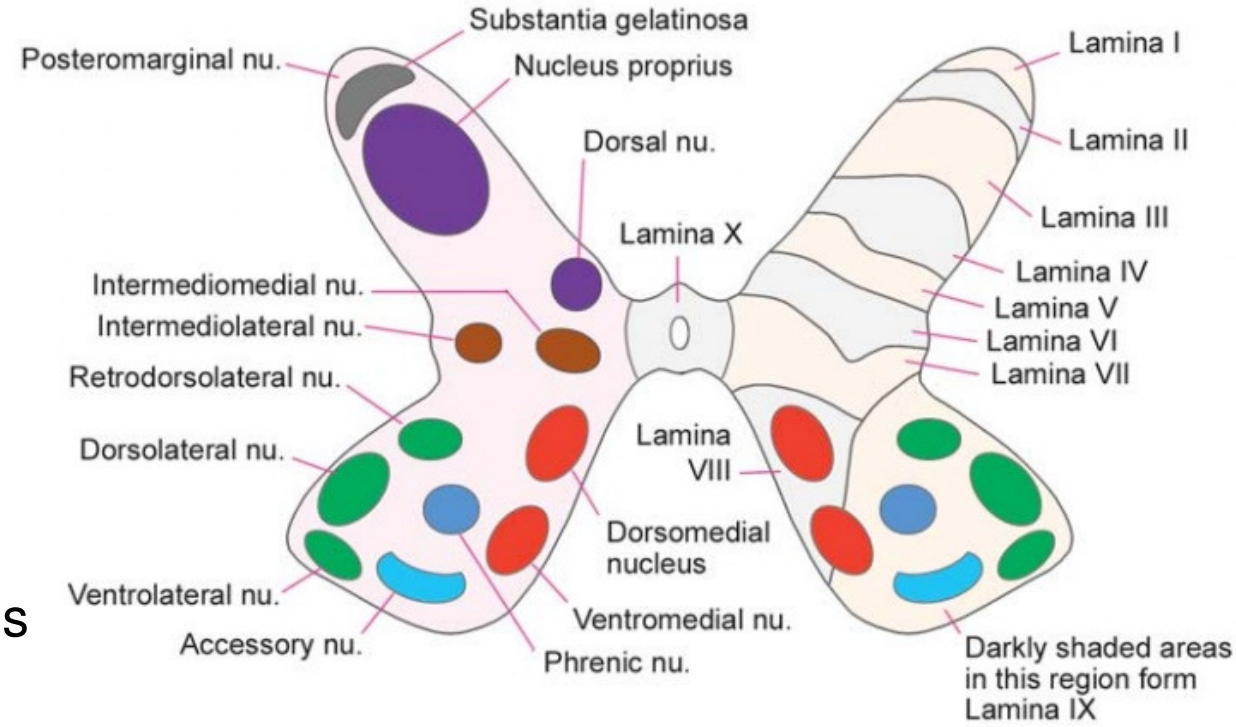

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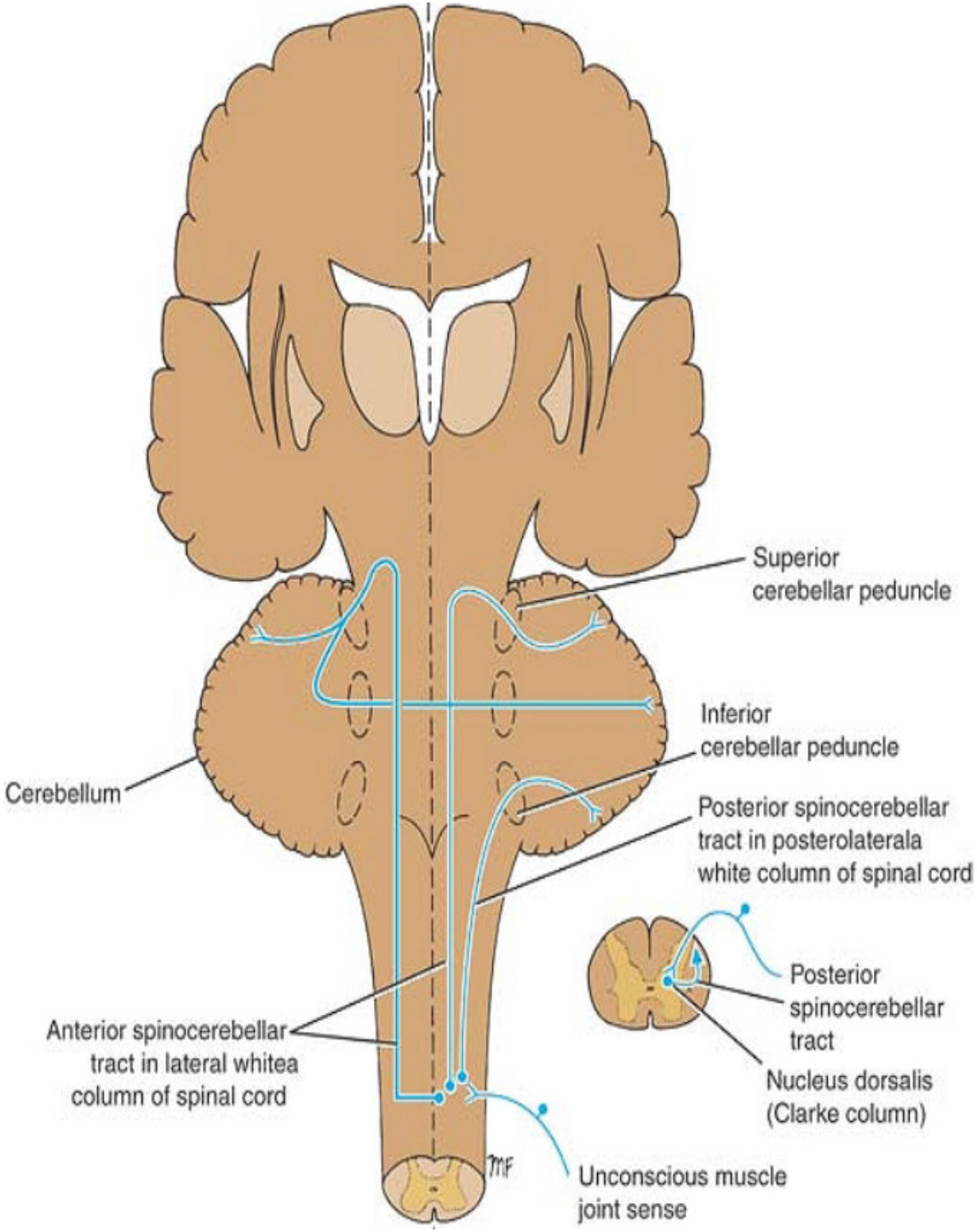
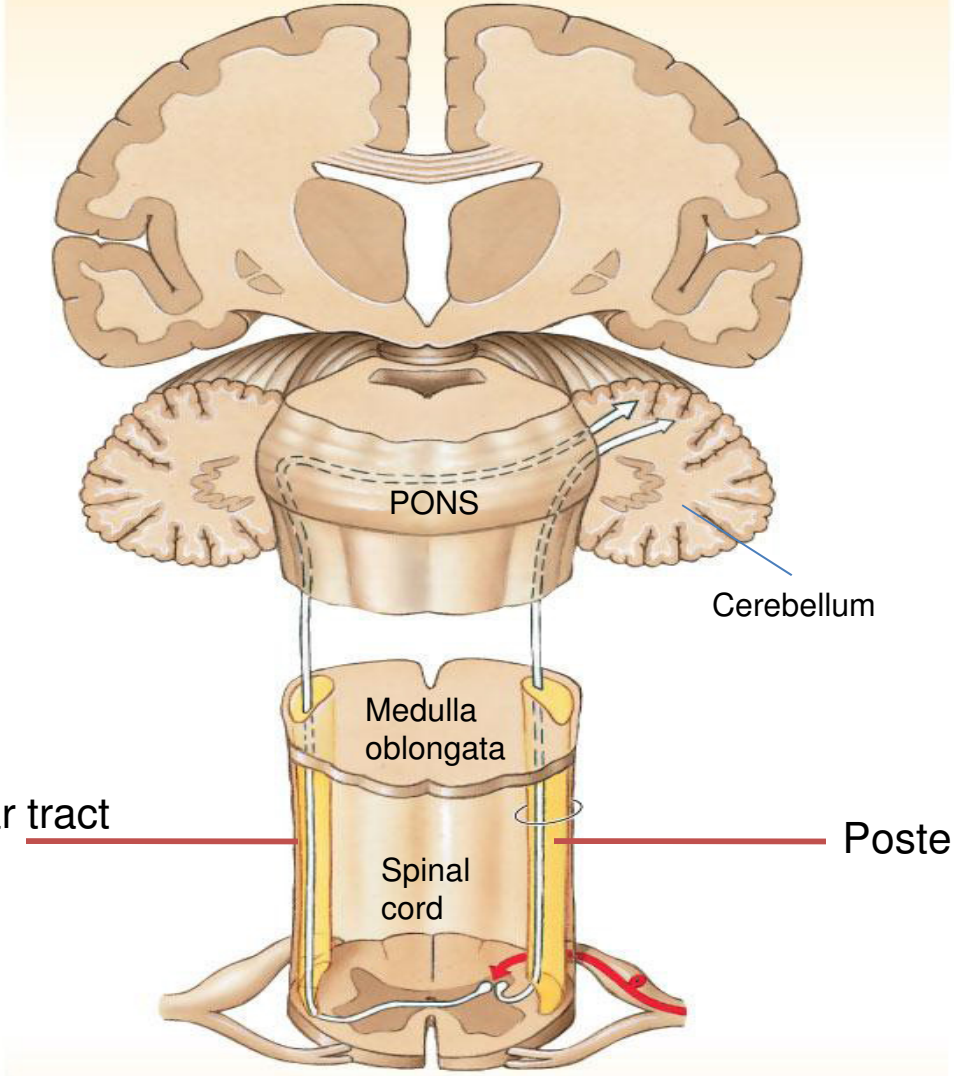
Anterior spinocerebellar tract

- muscle and joint sensation
- 1st order neuron axons terminate at the base of post gray column (nucleus dorsalis)
- the majority of axons of 2nd order neurons cross to opposite side and ascend as anterior spinocerebellar tract in the contralateral white column
  - ➢ *the minority of axons ascend as anterior spinocerebellar tract in the lateral white column Of the same side*
- ascend as anterior spinocerebellar tract to medulla oblongata and pons
- Terminates in cerebellar cortex (through superior cerebellar peduncle)
  - ➢ *the fibers that **crossed over** in spinal cord **cross back** within cerebellum*



Spinocerebellar Tracts



Anterior spinocerebellar tract

Posterior spinocerebellar tract

Proprioceptive input from Golgi tendon organs,
muscle spindles, and joint capsules

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