

Physiology of Pain (Essay/ Short essay)

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Pain- Definition

- Unpleasant sensory and emotional experience associated with potential tissue injury or damage.

Types of nociceptive stimuli or Noxious stimuli

- Mechanical
 - Spasm of smooth muscle
 - Stretch of meninges or blood vessels
 - Obstruction
- Chemical
 - Inflammation
 - Infection
 - Injury
- Thermal

Chemicals released at the site of injury which can induce pain

- Bradykinin
- Histamine
- 5HT
- K
- ATP
- Substance P

Classification of Nociceptors

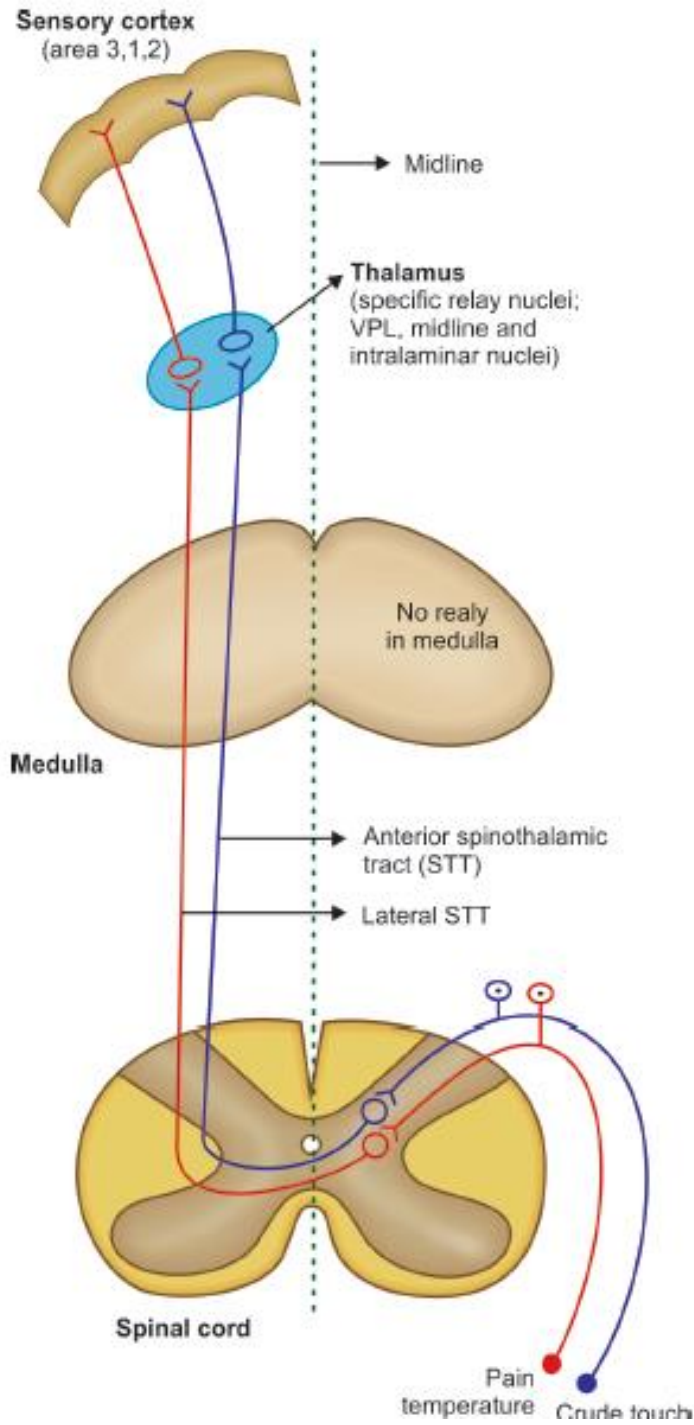
- A δ Monomodal –respond only to mechanical not to chemical or thermal
- Type C polymodal respond to mechanical, thermal and chemical stimuli
- Other thermal nociceptors
 - CMR1
 - VR1-Stimulated by temperature greater than 43degree Celsius and also stimulated by capsaicin, a type of vanillin
 - VRL1- They are stimulated by temperature greater than 50 degree Celsius
 - All are TRP family of ion channels
 - Ion channel triggered by binding with PIP2

Pain pathways

- By lateral spinothalamic tract (carry temperature and itching also)
- Two types
- Paleospinothalamic pathway- for slow pain
- Neospinothalamic tract- for fast pain

Neospinothalamic pathway

- Carry fast pain
- A δ fiber



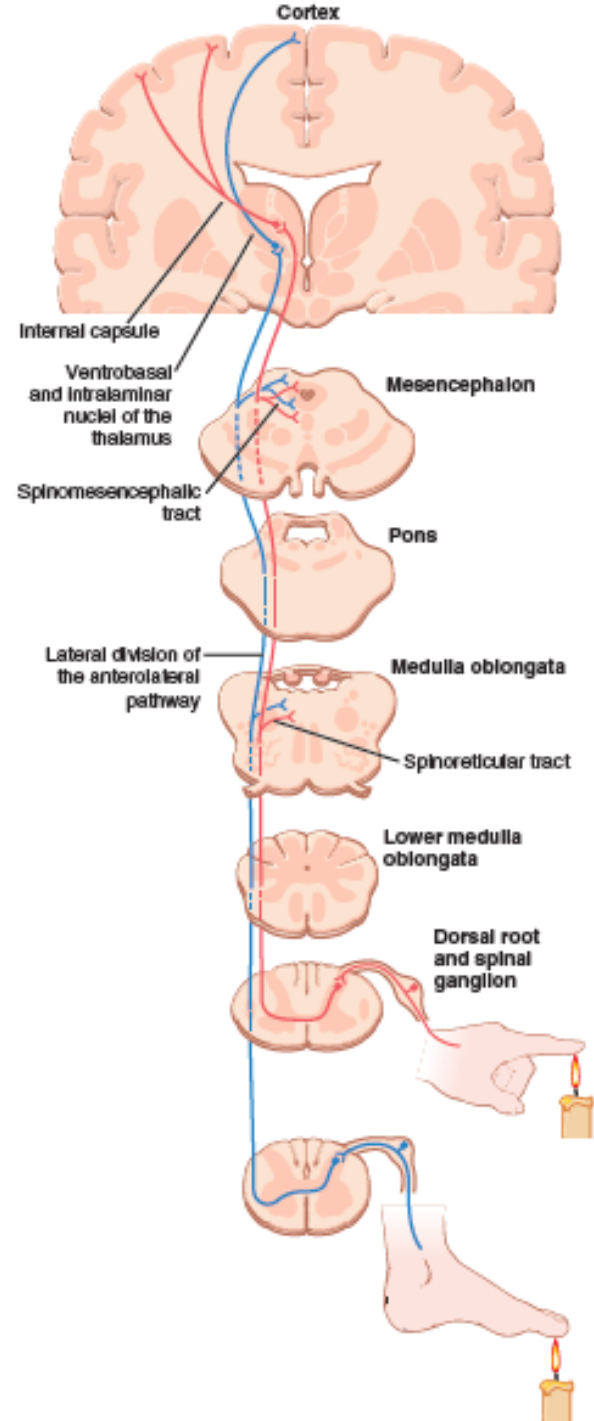


Figure 17-12 The corticospinal tract (afferent and efferent pathways).

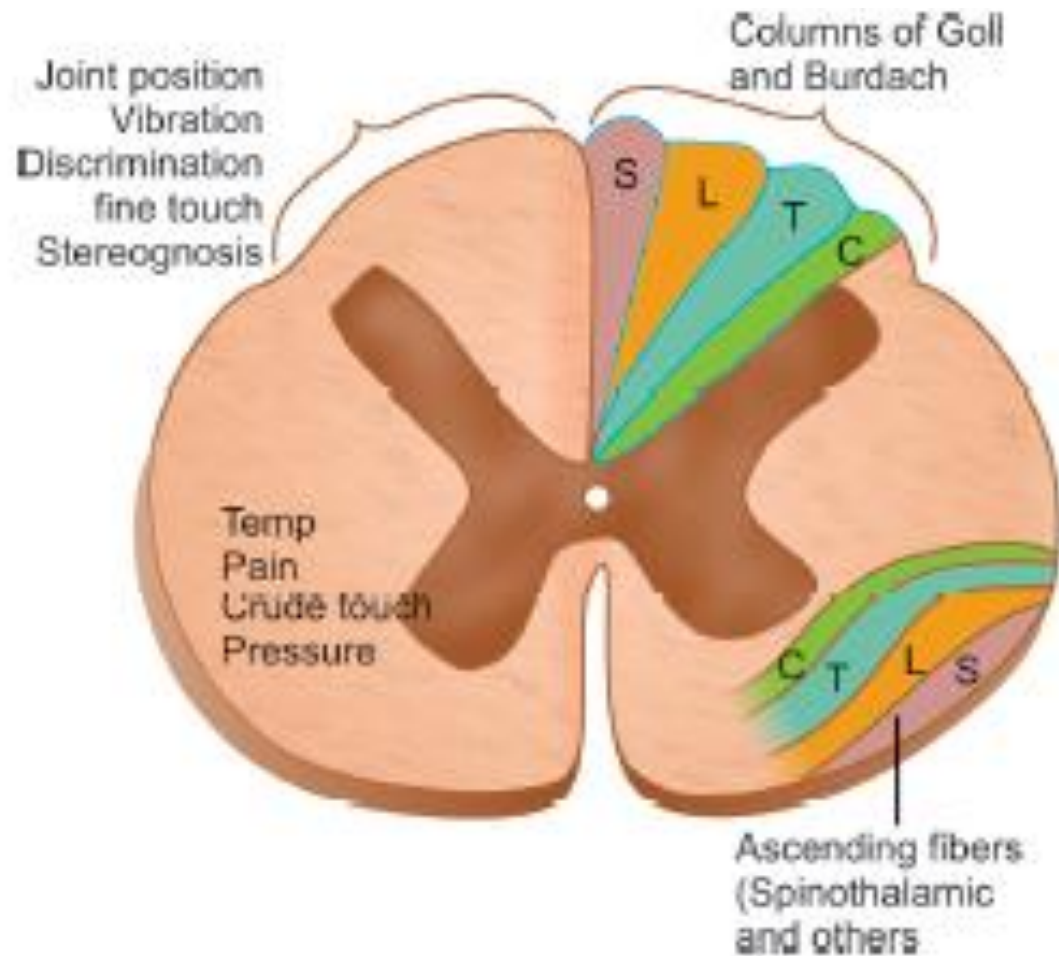
First order neuron

- Start from nociceptors and thermoceptors
- Fiber enters spinal cord through dorsal root and cell bodies are present in DRG
- Terminate in the laminae I and laminae V of the dorsal horn

Second order neuron

- Cell bodies of these neurons are present in the dorsal horn of spinal cord
- Axon cross the midline and ascend up in the opposite side of lateral funiculus to reach lateral nuclear group of thalamus (VPL nucleus) via lateral spinothalamic tract
- Topographic organisation
- Fibers from lower body parts are placed laterally and upper medially in the lateral funiculus
- Fibers from sacral segment is placed laterally and from cervical region is placed medially

Topographic organization of ascending fibers in spinal cord



Third order neuron

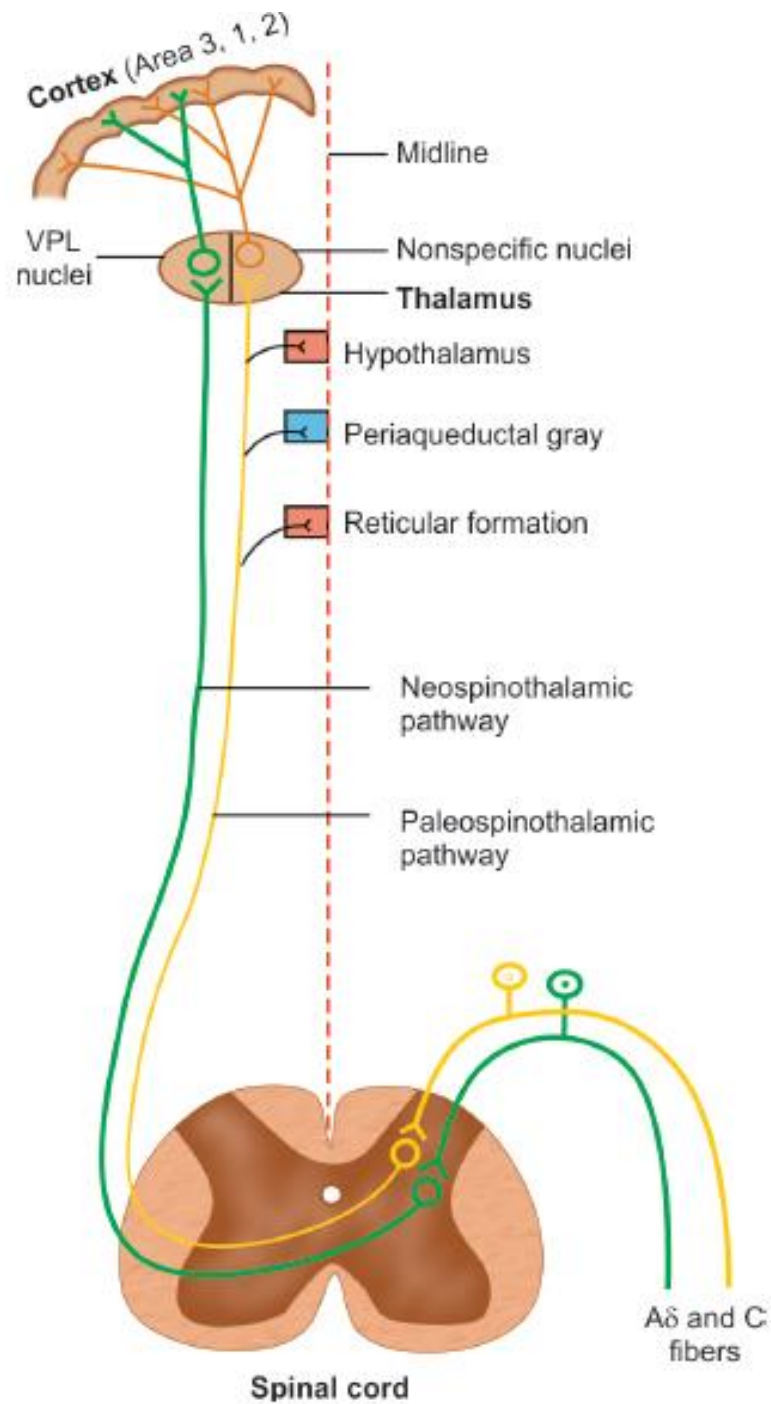
- Originate from thalamic nuclei
- Project to post central gyrus (sensory cortex)

Special features

- Localization of pain
- Detect quality and intensity of pain

Paleospinothalamic pathway

- Oldest pathway
- Carry slow pain sensation
- Mostly C fibers



First order neuron

- Start from nociceptors and thermoceptors
- Fiber enters spinal cord through dorsal root and cell bodies are present in DRG
- Terminate in the laminae II (Substantia gelatinosa of Rolando) of the dorsal horn

Second order neuron

- Cell bodies of these neurons are present in the dorsal horn of spinal cord
- Axon cross the midline and ascend up in the opposite side of lateral funiculus to reach thalamus (medial nuclear group- midline and intralaminar group)
- Fibers are placed medially in the spinothalamic tract

- On the way to thalamus fiber project to three major nuclear groups forming three subsystems
 1. At the level of medulla- collaterals from second order neurons project to reticular formation- spinoreticulothalamic pathway
 2. Fibers project to midbrain nuclei like midbrain reticular formation, parabrachial nuclei, periaqueductal gray (spinomesencephalic fibers)
 3. Fibers project to hypothalamus- spinohypothalamic fiber system

Third order neurons

- Starts from medial nuclear group of thalamus
- Project to different areas of cortex including limbic cortical areas

Special features

- Non specific projection
- Poorly localised
- Due to projection to reticular formation- slow pain keeps a person awake
- Evokes emotional experience- due to projection to limbic system
- Mediates autonomic responses- due to hypothalamic connections
- Mediates motivational- affect component of pain

Classification of Pain

- Mode of transmission
 - Slow pain
 - Fast pain
- Depending on the site of pain
 - Superficial pain
 - Deep pain
- Clinical classification
 - Somatic pain
 - Visceral pain
 - Referred pain

	Slow pain	Fast pain
Definition	Felt after a gap	Felt immediately
Transmitted by	C Fibers	A δ Fibers
Myelination	Non myelinated	Myelinated
Tract	Paleospinothalamic tract	Neospinothalamic tract
Collaterals to Reticular formation	More	Less
Relay station	Relay in the Intralaminar and midline nuclei of Thalamus	Relay inn the VPL nuclear complex of Thalamus
Cortical representation	Poor	Good
Localization	Poor	Good
Neurotransmitter	Substance P	Glutamate

Superficial pain

- Pain elicited in superficial structures like skin and subcutaneous tissue
- Fast pain
- Localized

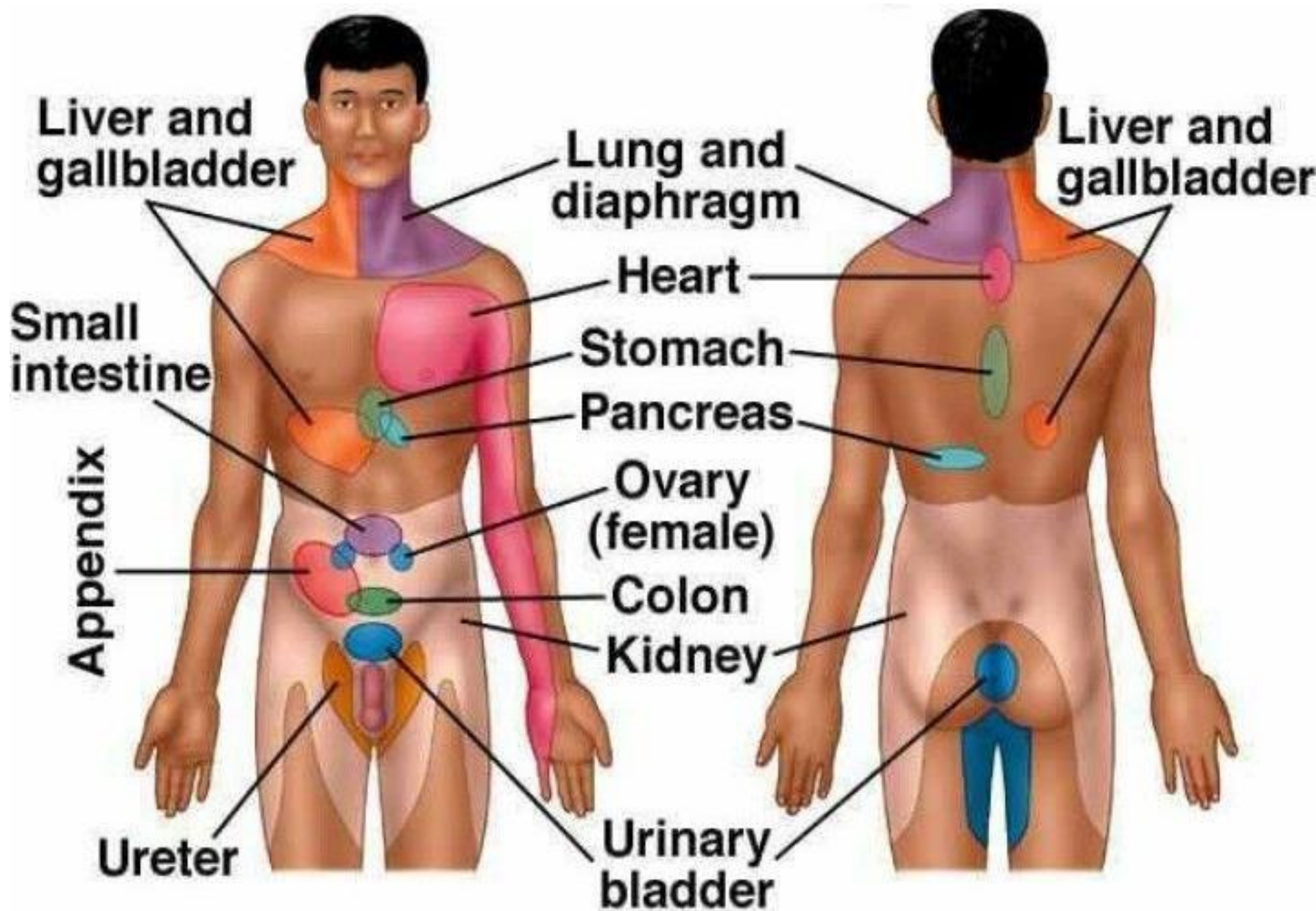
Deep pain

- Pain from deep structures like muscle tendon bones periosteum etc
- Accompanied by contraction of surrounding muscles
- Muscle contraction cause ischemia and result in the release of substance P which induces pain
- Poorly localized dull aching type- due to deficiency of A δ fibers and less number of receptors in deep structures

	Somatic pain	Visceral pain
Definition	Pain from somatic structure	Pain from viscera
Nerve carrying the sensation	Carried by somatic nerve	Carried by autonomic nerves
Autonomic features	Not associated with autonomic features	Associated with autonomic features
Localization	Well localized	Poorly localized
Referred	Not referred	Radiate to other structures
Guarding	Absent	Present (Associated with superficial muscle contraction)
Smooth muscle involvement	Not involved	Caused by spasm of smooth muscles and distention of viscera

Referred pain (Short essay/ Write briefly)

- Pain taking origin from a viscera is being felt as if it comes from a somatic structure which is not having any anatomic contact with the viscera
- Cardiac pain is referred to medial aspect of the left upper limb.
- Pain from appendix is felt around the umbilicus first and then it is felt from the right iliac fossa
- Pain from the last molar tooth is felt from the middle ear
- Pain from the sub diaphragmatic structure like gall bladder is felt from the tip of the right shoulder



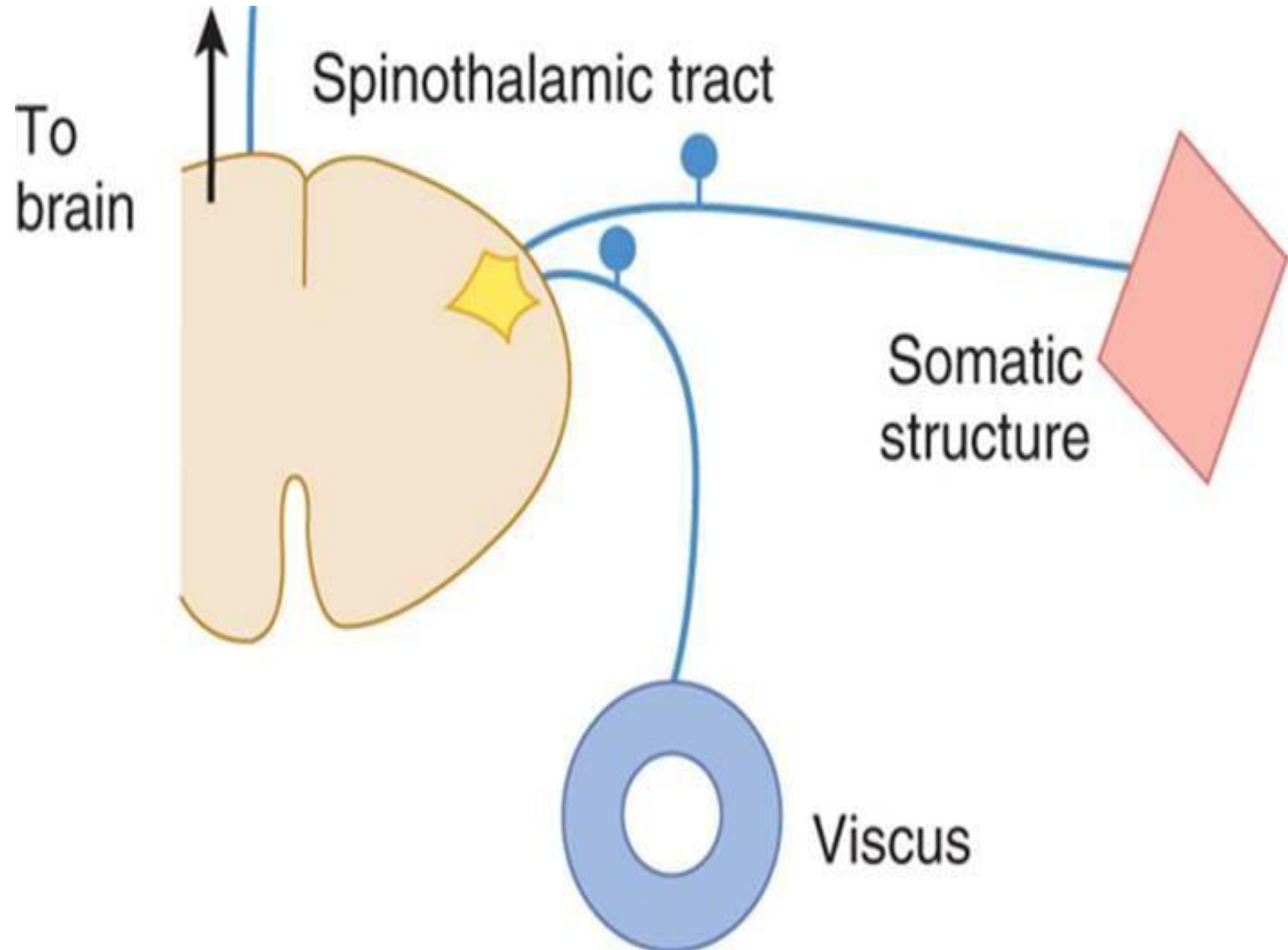
Theories of referred pain

1. Dermatomal theory
2. Convergence theory
3. Facilitation theory
4. Theory of experience

1. Dermatomal theory

- Visceral pain is usually referred to a structure that develops from same embryonic segment (dermatome)
- Heart and inner aspect of arm develop from same dermatome

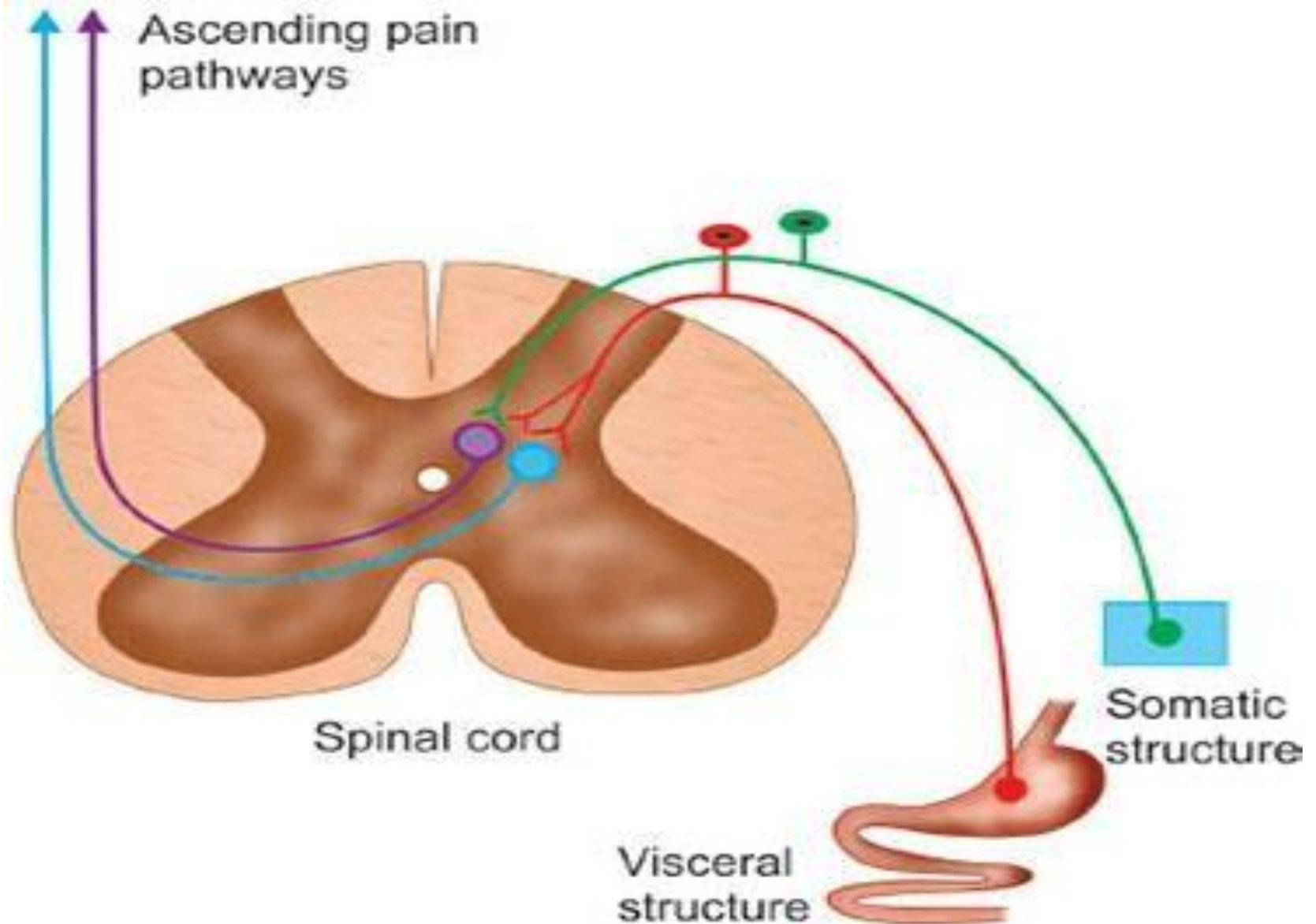
2. Convergence theory



2. Convergence theory

- The first order neurons of both viscera and somatic structure converge on the second order neuron in the spinal grey matter and ascend in spinothalamic tract
- Cortex cannot differentiate the site of origin of pain sensation as ascending fibers projecting to cortex from both structures are same (law of projection)
- Pain is perceived as if it comes from the somatic structure also, from where the first order neuron is converging

3. Facilitation theory



- Collaterals arising from visceral afferent fibers project to the spinothalamic neurons that receive afferents from somatic structures
- Pain sensation from somatic structure is facilitated by activity in the visceral afferents
- Minor activity in the somatic afferent can cause pain

4. Experience theory

- Pain instead of being felt at its usual site may be referred to some other structure or area in which the patient had experience of pain earlier
- Pain from inflamed viscera usually refer to midline but in patients with previous history of surgery, pain is referred to surgical scar

Endogenous pain control mechanism/ Endogenous analgesic systems (Short essay)

1. Descending pain modulating/ inhibiting system
2. Endogenous opioid system
3. Gate control theory of pain
4. Stress induced analgesia

1. Descending pain modulating system

(Write briefly)

- Raphespinal serotonergic pathway
- Ceruleospinal Norepinephrinergic pathway

Raphespinal serotonergic pathway

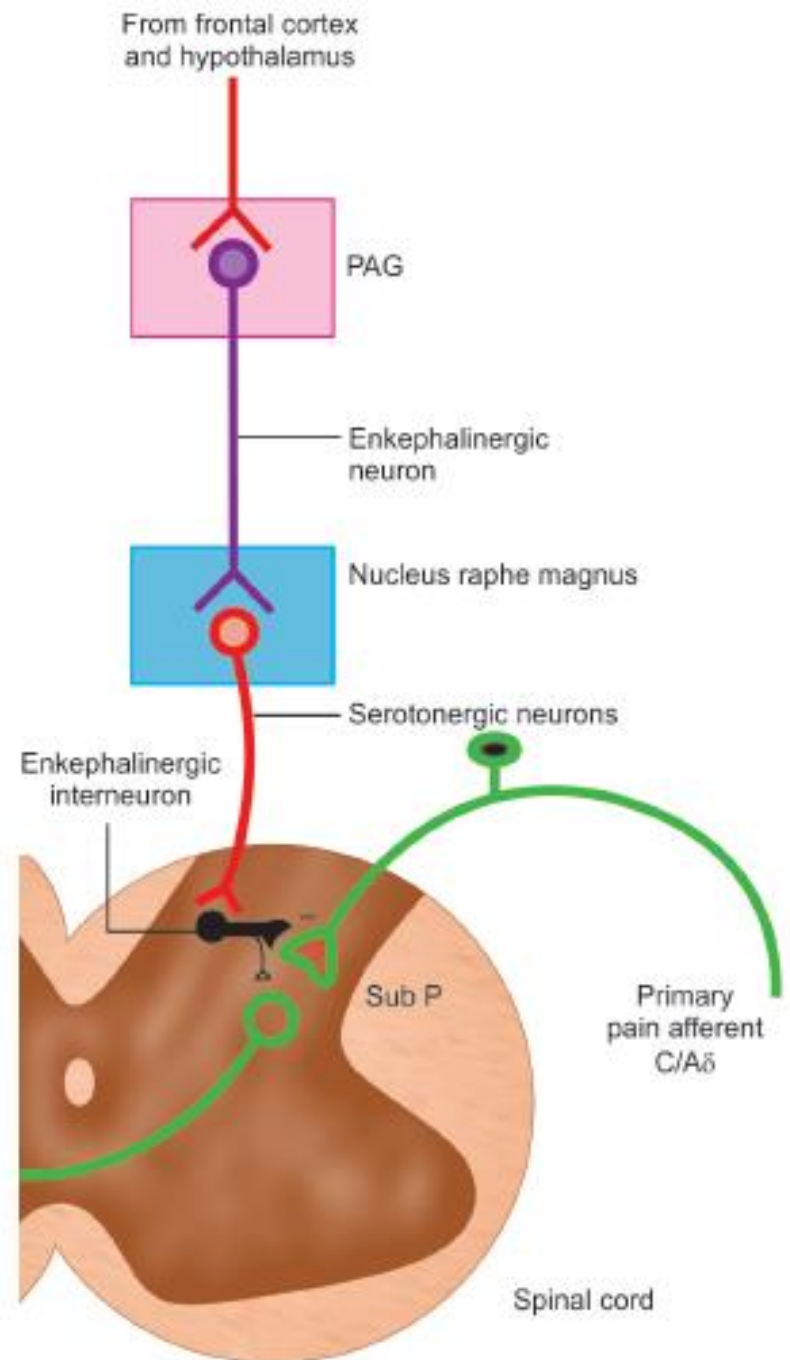


Fig. 120.7: Endogenous neural analgesia system.

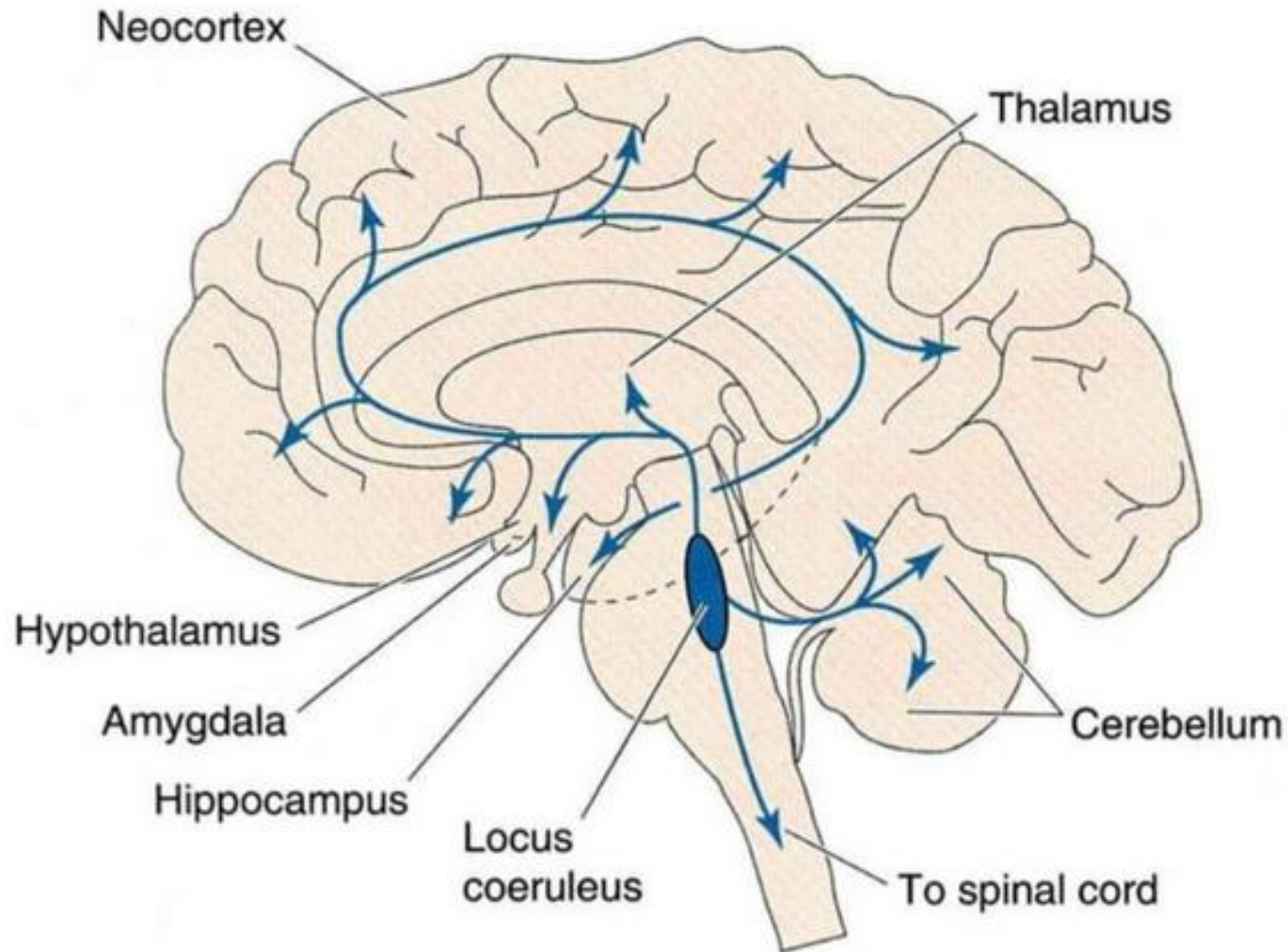
Raphespinal serotonergic pathway

- **Origin**- frontal cortex and hypothalamus and project to periaqueductal region of midbrain
- **Course**- from PAG to nucleus raphe magnus in the medulla (Neurotransmitter- enkephalin)
- From raphe nucleus to spinal cord via raphespinal pathway (Neurotransmitter- serotonin)
- **Termination**- on inhibitory interneuron in laminae I, II, V of spinal cord

Function

- Inhibitory interneuron releases enkephalin
- Enkephalin inhibits the release of Substance P from presynaptic ending
- Thus inhibit transmission of impulse in pain pathway
- Pathway is activated by prolonged pain
- Fibers from ascending pain pathway terminate on PAG and raphe nucleus and activate the descending analgesic pathway
- Autoinhibition of pain

Cerulospinal norephrinephrnergic pathway



Cerulospinal norepinephrinergetic pathway

- **Origin**

- ✓ From nucleus locus ceruleus and nucleus subceruleus of pons

- **Course**

- ✓ Descend down ipsilaterally in the spinal cord to terminate on interneurons in dorsal horn

- **Function**

- ✓ Contains norepinephrine
- ✓ Inhibitory to nociceptive afferents

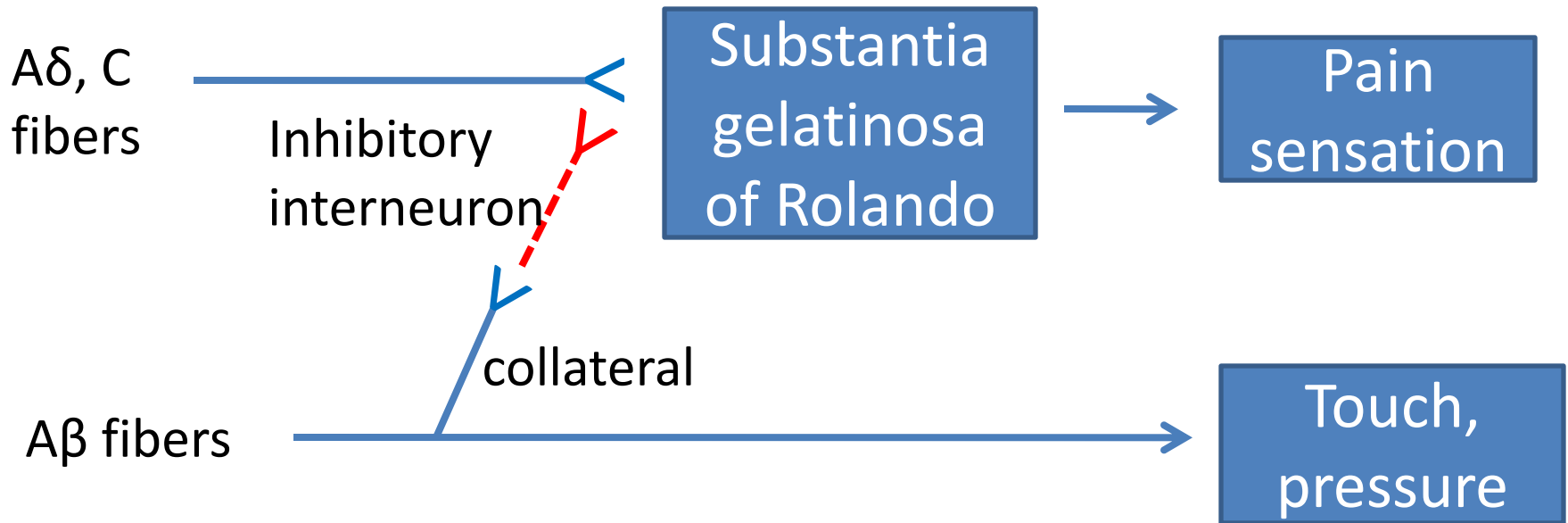
2. Endogenous opioid systems

- Morphine is an endogenous analgesic peptide
- Act on opiate receptors
- Binding to opiate receptor decreases nociceptive synaptic excitability
- 3 major classes of receptors- μ, δ, κ
- Morphine – potent agonist of μ
- Produces pre and postsynaptic inhibition
- Increases potassium conductance in post synaptic membrane and inhibit release of Substance P in presynaptic membrane

Endorphin

- Endogenous morphine like substance
- Important endorphins are enkephalin, β -endorphin, γ -endorphin, dynorphin
- Act on endorphin receptors present in spinal cord, PAG of midbrain, raphe nucleus
- Produces post synaptic inhibition by opening of K channels

3. Gate control theory of pain (Write briefly)



Gate control theory of pain

- Collaterals from large myelinated afferent fibers (touch- $A\beta$ fibers) can presynaptically inhibit $A\delta$ and C fibers of pain in the dorsal horn of spinal cord
- Large afferent fibers of touch acts as a gate in the spinal cord in the transmission of pain impulses

Applied aspect

- Application of pain balm relieves pain
(Physiological basis)
 - Gate control theory
- Acupuncture and acupressure produces analgesia
 - by release of endogenous opioids and gate control theory of pain

4. Stress induced analgesia

- During stress, reaction to pain is suppressed
- By both opioid and non opioid mechanism
- By activation of descending analgesic system and opioid analgesic
- Soldiers wont feel pain in battle field

Applied

- Hyperalgesia-
- Hypoalgesia-
- Analgesia-
- Hyperpathia
 - defect in perception, increased reaction to pain stimuli
- Allodynia-

Causalgia

- Burning pain following traumatic peripheral nerve injury
- Persist even after complete recovery
- Accompanied by hyperalgesia and allodynia
- Sympathetic fiber is responsible
- Relieved by sympathectomy or adrenergic blockers

Neuropathic pain/ Neuralgia

- Due to injury to the nerve
- Eg: trigeminal neuralgia due to herpes zoster infection
- Diabetic neuropathy

Itch

- Unpleasant sensation that evokes the sensation to scratch
- By mechanical or chemical stimuli
- Bile salt, histamine, kinins produces itching
- Itch receptors- ending of unmyelinated C fibers
- Pathway- lateral spinothalamic tract