Lateral spinothalamic tract

- Carries pain & temperature
- Receptors: thermoreceptors & nociceptors

- **Thermoreceptors :** cold- $A\delta$ & C fibres
  warmth- C fibres

- **Nociceptors :** $A\delta$ & C fibres

Thermal sensation

- Can be graded
- Cold: freezing cold, cold or cool

- Heat : warm, hot, burning hot

Thermoreceptors

- Cold receptors: A^{δ} & C fibres
- Warmth receptors: C fibres
- Pain receptors : stimulated by freezing cold & burning hot

- Cold & warm receptors are located just under the skin at discrete spots called cold sensitive & heat sensitive spots
- 4-10 times as many cold sensitive spots as heat sensitive spots
- More no. of receptors are present at finger tip & lips & less on trunk
- Temperature of subcutaneous tissue determine the response as the receptors are located there

Response of thermoreceptors at different temperatures

- 10-15^{0}C - pain fibres stimulated by cold
- 15-29^{0}C - cold fibres stimulated
- 30-45^{0}C - warm fibres stimulated
- >45^{0}C - pain fibres stimulated by heat

Vanilloid receptors

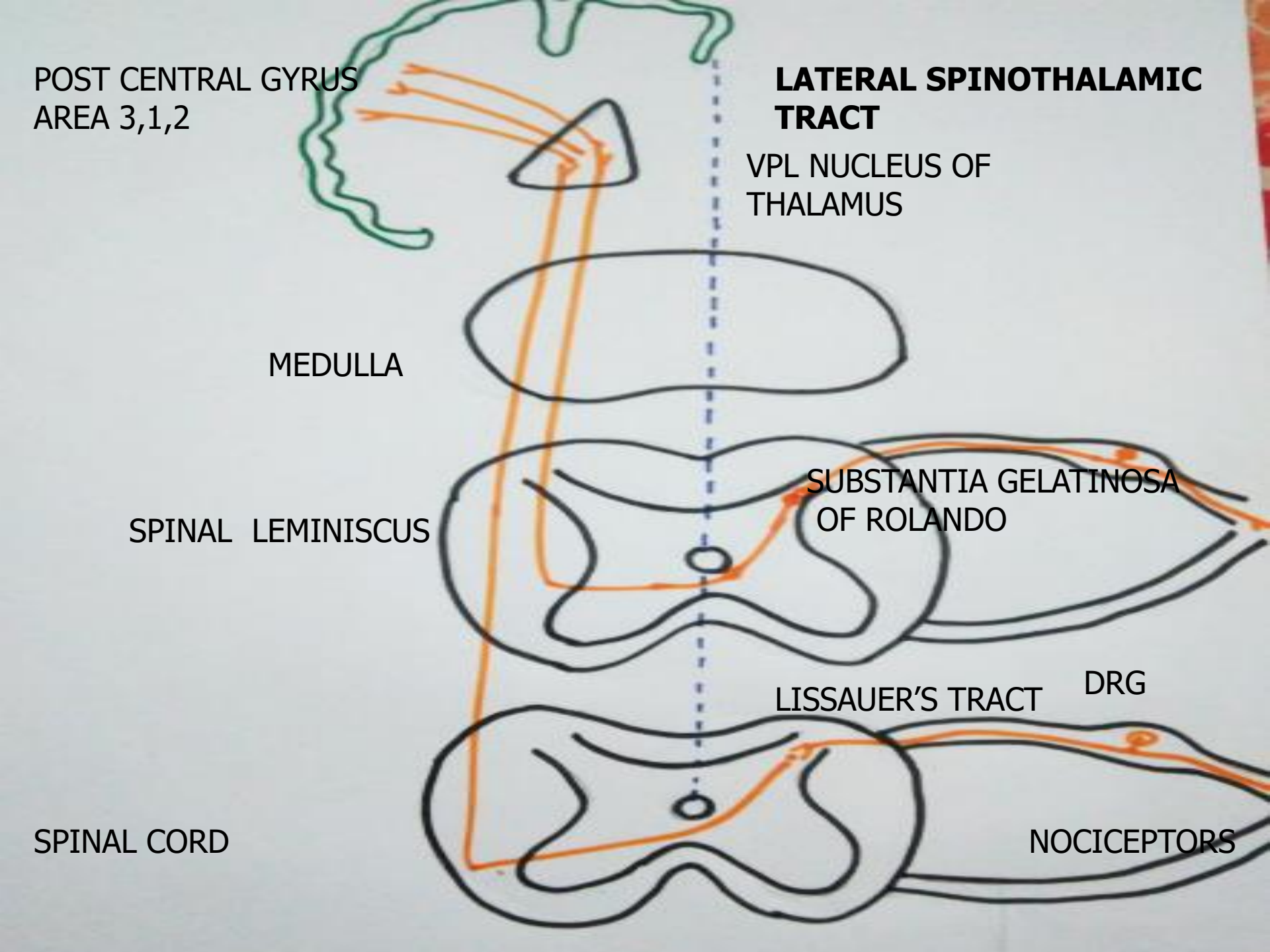
- Respond to noxious heat
- Vanillins are a group of compounds including Capsaicin that cause pain
- **VR I** : receptors respond not only to capsaicin but also to protons & temperature > 43^0C
- **VRL I** : respond to temperature > 50^0C & not to capsaicin
- Isolated from C fibre ending
- **Cold menthol sensitive receptor I (CMR I):**
- Receptors for moderate cold

Mechanism of stimulation of thermal receptors

- Cold & warmth receptors are stimulated by changes in their metabolic rate
- Temperature alters the rate of intracellular chemical reactions > 2 fold for each 10^0C change

Lateral spinothalamic tract

- 1st order neuron-DRG
- Central process reach spinal cord via posterior nerve root
- The tract ascends or descends a short distance between tip of posterior horn & periphery of cord before ending in cells of Substantia gelatinosa of Rolando
- This short tract is called **Lissauer's tract**


POST CENTRAL GYRUS
AREA 3,1,2
LATERAL SPINOTHALAMIC TRACT
VPL NUCLEUS OF THALAMUS
MEDULLA
SUBSTANTIA GELATINOSA OF ROLANDO
SPINAL LEMINISCUS
DRG
LISSAUER'S TRACT
SPINAL CORD
NOCICEPTORS

- A^{δ} fibres synapse with neurons in lamina I & V of spinal cord
- C fibres synapse with neurons in lamina I & II (Substantia gelatinosa of Rolando)of dorsal horn
- 2^{nd} order neurons arise from dorsal horn & cross to opposite side in anterior commisure
- Temperature carrying fibres take an oblique course where as the pain fibres cross to opposite side in same segment
- Then it reaches lateral funiculus & ascend as lateral spinothalamic tract

- Cervical fibres are placed medially & sacral fibres lie lateral most
- In the brain stem lateral spinothalamic tract ascends close to ventral spinothalamic tract – spinal leminiscus or spinal fillet
- Fibres end in reticular area of brain & posteroventral nucleus of thalamus
- 3rd order neurons from thalamus convey sensation to post central gyrus (sensory area 3, 1, 2)
- Some fibres end in insular cortex also

Pain

- Defined as an unpleasant sensory & emotional experience associated with actual or potential tissue damage (by International association for study of pain IASP)
- Sherrington called pain as a physical adjunct to an imperative protective reflex

- Painful stimulus initiate potent withdrawl & avoidance responses
- Pain has a built in unpleasant affect
- Helps to prevent further tissue damage by conditioned experience
- Disadvantageous in conditions like malignancy where it ↑ suffering
- Absence of pain → further tissue injury & deformity eg. Leprosy, syringomyelia

Classification of pain:

General classification :

Physiological: fast pain & slow pain

Pathological :inflammatory & neuropathic pain

Classification based on site of origin :

Somatic :

- superficial – from cutaneous & subcutaneous tissue
- Deep : from muscle, joint & bone

Visceral : from internal organs

Differences

Superficial pain

- Involves skin & subcutaneous tissue
- Sharp in character
- Localised
- Numerous receptors
- Richly innervated by Aδ fibres
- Usually does not radiate
- Asso. with withdrawl movements, ↑HR, BP, RR

Deep / visceral pain

- Involves muscle & hollow viscera
- Dull in character
- Diffuse poorly localised
- Less no. of receptors
- Less Aδ fibres, C fibres mainly
- Both local & radiate to distant site
- Asso with faintness, nausea, sweating, ↓BP & HR

Types of physiological pain

Fast pain:

- Also called first pain/ sharp pain / pricking pain/ electric pain
- Felt soon after the noxious stimulus
- Felt as sharp localised sensation due to the activity in Aδ fibres

- **Slow pain:**
- Also called second pain as it follows fast pain
- Other terms: slow burning pain,aching pain, nauseous pain
- Felt as dull, intense diffuse pain with unpleasant feeling due to activity in C fibres
- Usually associated with tissue destruction

Comparison between fast and slow pain

Fast pain	Slow pain
1. Small myelinated A delta fiber – carry fast pain.	1. Small unmyelinated C fiber carry slow pain.
2. Neurotransmitter at spinal cord is glutamate.	2.Neurotransmitter at spinal cord is substance P.
3. Less in number compared to c fibers.	3. More in number than A delta fibers
4. Respond to mechanical Stimulus	4. Respond to chemical, thermal, mechanical stimuli
5.Most sensitive to pressure hence mechano receptors	5.Most sensitive to local anaesthetic & chemical agents
6.Less associated with emotional component	6. More association with emotiona component
7.Good localisation present	7.Poor localisation
8.Sensitivity to electrical stimulus is more	8.Less sensitive to electrical stimul

Quality of pain

- Pricking
- Burning
- Tearing
- Colicky
- Cutting
- Stabbing
- Crushing
- aching

Receptors for pain

- Free unmyelinated nerve endings of $A\delta$ & C vanilloid receptors
- **More in:**
- superficial layers of skin & mucous membrane
- internal tissues like periostium, parietal pleura, peritoneum, pericardium, arterial wall, joint surfaces, falx cerebri, tentorium
- Less in : viscera & deeper tissues

Stimuli that excite nociceptors

- Thermal : >45^{0}C
- Strong electric current
- Mechanical stimuli:↑ pressure & stretch
- Chemical stimuli: bradykinin, histamine, serotonin, K, acetyl choline, proteolitic enzymes, lactic acid, adenine, Lewis P factor
- Ischemia : → muscle spasm→release of chemical mediators

Characteristics of pain

- Threshold stimuli causes pain
- Subthreshold stimulus causes no pain
- ↑in intensity of stimulus →↑pain sensation
- Distraction of mind ↑ pain threshold
- Severe excitement & emotion can abolish pain
- Pain fibres are slowly adapting or tonic receptors

- Superficial pain is better localised than slow pain
- Visceral pain is referred to other areas overlying the tissues
- Pain initiates strong withdrawl & avoidance responses
- Connections with cingulate gyrus of limbic system causes association of pain with emotions
- Reaction to pain varies from person to person & from time to time
- Depends on intensity of stimulus, pain perception & rate of tissue damage

Ischemic pain

- When blood flow to a tissue is blocked→ pain in few minutes
- When blood flow to muscle is occluded muscle contraction causes pain due to accumulation of Lewis P factor
- This factor is washed off or metabolised when blood flow is restored
- This releives pain

- P factor may be K+
- Eg: **intermittent claudication:**
- in occlusive vascular disease there is calf muscle pain on walking a short distance
- It dissappears at rest
- **In angina pectoris**: substernal pain due to myocardial ischemia
- Accumulation of P factor in muscle
- Pain releived by rest as this ↓ oxygen requirement & ↑ blood supply to remove the P factor

Pain pathways

- Dual pathway

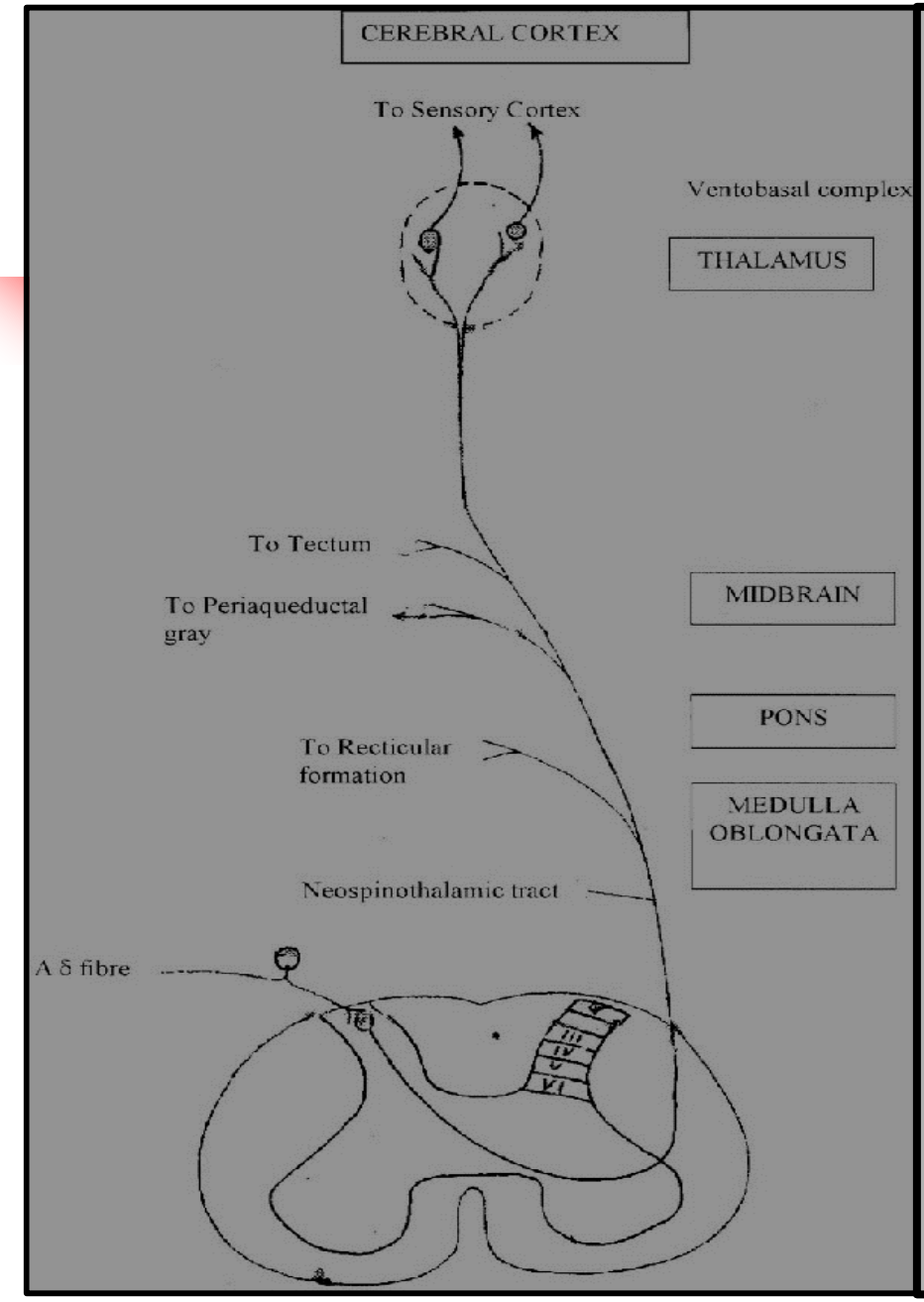
Receptors:

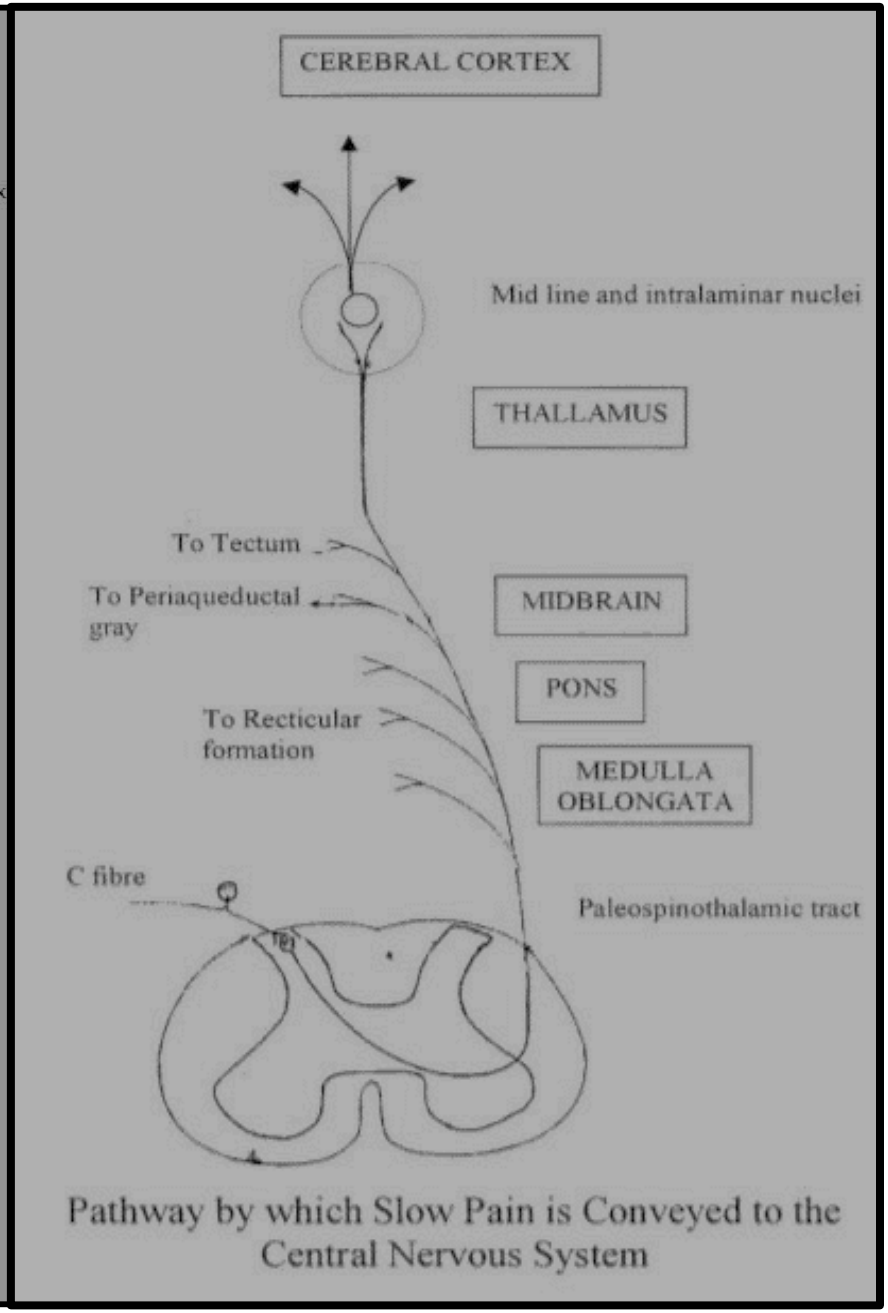
- Fast pain: Aδ fibres Slow pain: C fibres
- 1st order neuron is in DRG
- Fibres ascend or descend a short distance before synapsing in spinal cord forming **Lissauer's tract**
- Aδ fibres end mainly in lamina I & V of dorsal horn
- C fibres end in neurons in lamina I & II of dorsal horn (substantia gelatinosa of Rolando)

- After entering spinal cord pain signals take 2 pathways:
- Neospinothalamic pathway
- Paleospinothalamic pathway

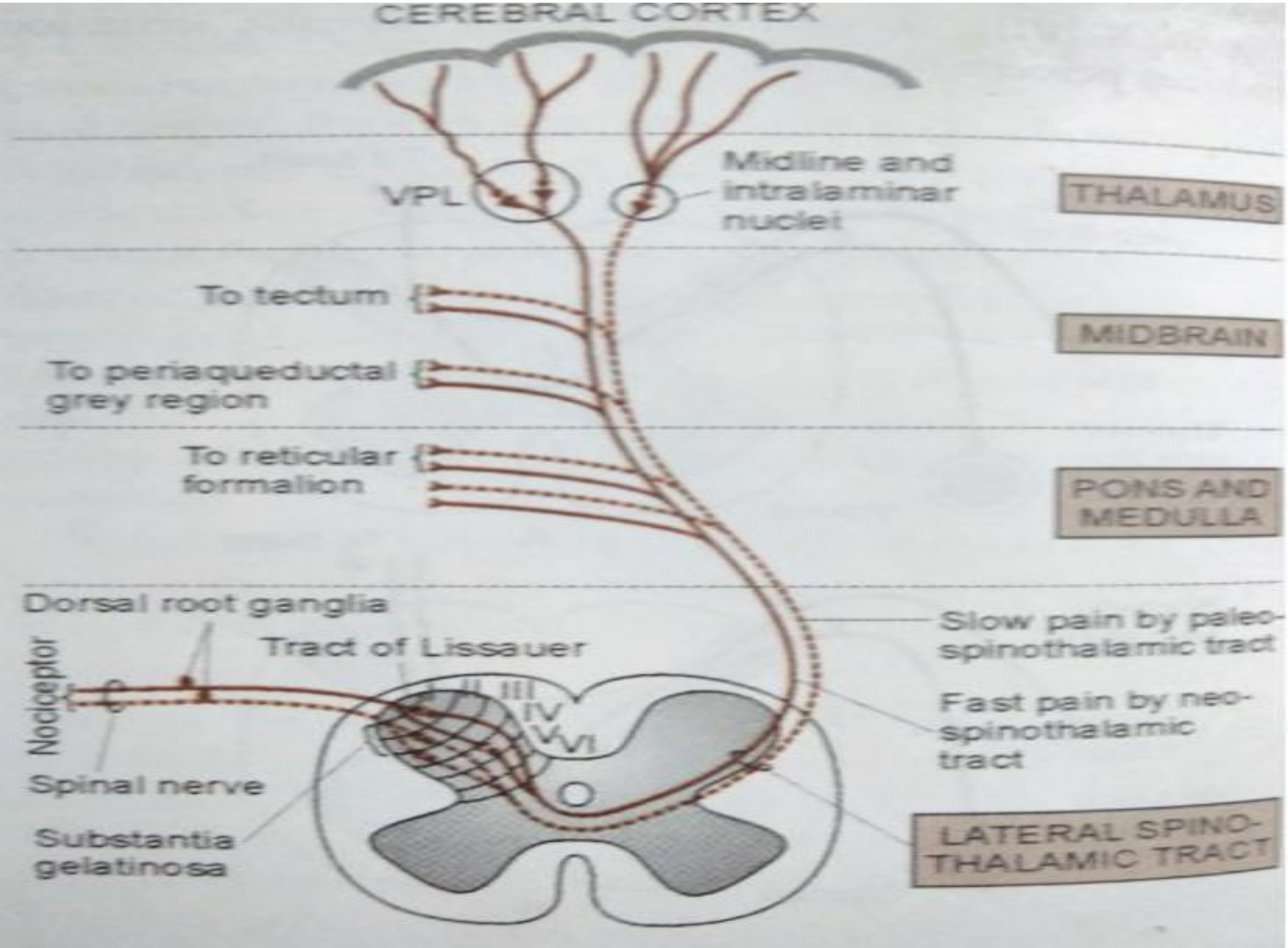
Neospinothalamic pathway

- Aδ fibres carrying fast pain synapse in lamina I & V of spinal cord
- 2nd order fibres after crossing ascend in anterolateral column
- Some fibres end in reticular area of brain stem
- Most fibres pass to thalamus –ventrobasal complex & posterior nucleus
- Sensations are then carried to somatosensory area 3,1,2



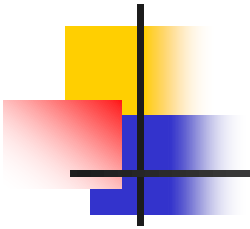


Pathway by which Slow Pain is Conveyed to the Central Nervous System


CEREBRAL CORTEX
VPL
Midline and intralaminar nuclei
THALAMUS
To tectum
To periaqueductal grey region
MIDBRAIN
To reticular formalion
PONS AND MEDULLA
Dorsal root ganglia
Nociceptor
Tract of Lissauer
Spinal nerve
Substantia gelatinosa
II
III
IV
V
VI
Slow pain by paleo-spinothalamic tract
Fast pain by neo-spinothalamic tract
LATERAL SPINO-THALAMIC TRACT

Paleospinothalamic pathway

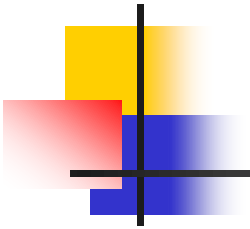
- They end in lamina I & II
- 2nd order neurons cross to opposite side & ascend in anterolateral column
- ¼- 1/10 of this fibres pass to thalamus→ cerebral cortex
- Rest of the fibres end in one of 3 different areas



1. reticular nuclei of medulla, pons & midbrain

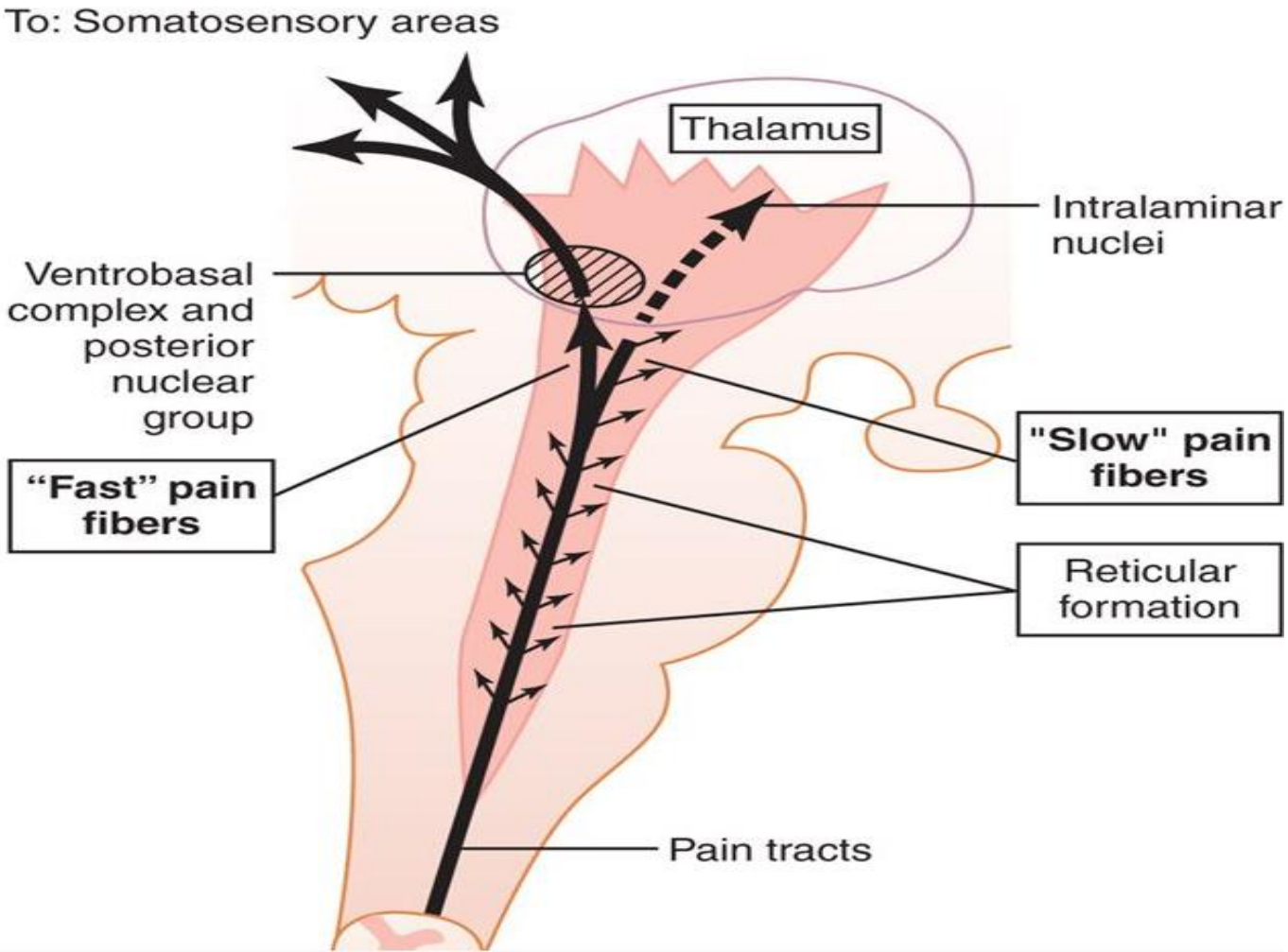
2. Tectal area of mesencephalon

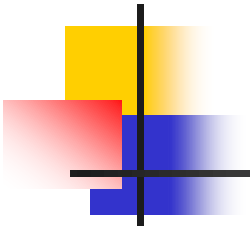
3. Periaqueductal grey surrounding the aqueduct of Sylvius



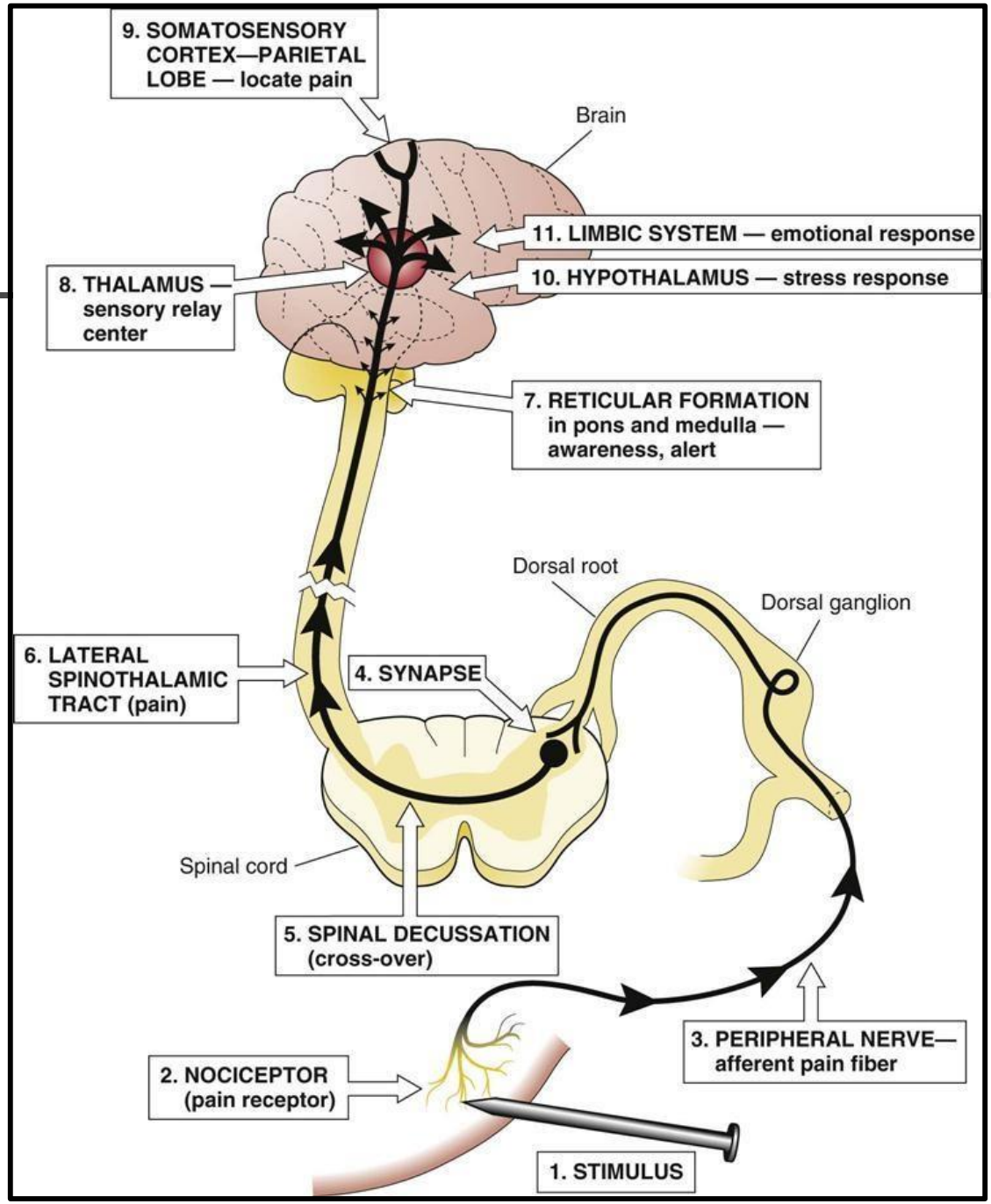
- From brain stem pain areas impulses are conveyed to :
- intralaminar & ventrolateral nucleus of thalamus
- portions of hypothalamus &
- basal regions of brain

Termination of pain pathways





- Lower centres are concerned with the feeling of suffering type of pain (motivational affect component of pain)
- Reticular areas of brain stem & intralaminar nucleus of thalamus have very strong arousal effect on brain
- This explains why a person in severe pain is wide awake


9. SOMATOSENSORY CORTEX—PARIETAL LOBE — locate pain
Brain
11. LIMBIC SYSTEM — emotional response
10. HYPOTHALAMUS — stress response
8. THALAMUS — sensory relay center
7. RETICULAR FORMATION in pons and medulla — awareness, alert
Dorsal root
Dorsal ganglion
6. LATERAL SPINOTHALAMIC TRACT (pain)
4. SYNAPSE
Spinal cord
5. SPINAL DECUSSATION (cross-over)
3. PERIPHERAL NERVE— afferent pain fiber
2. NOCICEPTOR (pain receptor)
1. STIMULUS

Neurotransmitters

- At Aδ nerve ending the NT secreted is glutamate (excitatory)
- At C fibre ending the glutamate & substance P (slowly released) are secreted

Characteristics of Transmission in the Anterolateral Pathway

- The anterolateral system is a cruder type of transmission system than the dorsal column-medial lemniscal system.
- The velocities of transmission are only one-third to one-half of those in the dorsal column-medial lemniscal system, ranging between 8 and 40 m/sec.
- The degree of spatial localization of signals is poor.
- The gradations of intensities are also far less accurate.
- The ability to transmit rapidly changing or rapidly repetitive signals is poor.

Sensation transmitted through anterolateral system - Anterior and lateral spinothalamic tract

1. Pain
2. Temperature.
3. Tickle.
4. Itch.
5. Sexual sensation
6. crude touch and pressure.

Visceral pain

- Pain originating from visceral structures.
- Severe, poorly localised .
- Associated with autonomic symptoms like nausea, vomiting, ↓BP & HR
- Often radiates & is referred to other areas
- There are no proprioceptors & only few pain , temperature & touch receptors

Stimuli for visceral pain

- Distension of hollow viscera
- Ischemia
- Spasm of smooth muscle
- Traction on mesentry
- Inflammation eg: appendicitis, cholecystitis
- Visceral pain causes spasm of adjacent skeletal muscle (guarding)
- vasodilation→pain eg) in meningeal vessels→head ache

Stretching or distension

Stretching or **distension** of the organ, particularly hollow cavities like the gastrointestinal tract.

1. These organs can stretch, often significantly compared to its smallest size, but will lead to pain if over distended.
2. Pain develops if the distended organ compresses surrounding organs, nerves, blood vessels and other structures.
3. Distension may also collapse the blood vessels supplying the organs thereby starving the tissue of oxygenated blood and further contributing to tissue damage (ischemia) and pain.

Ischemia

Ischemia lead to damage of tissue associated with an interruption in its blood supply.

Disruption of the oxygen supply causes accumulation of the metabolites & may cause inflammation or directly irritate nerve endings.

Cramping

- **Cramping** is due to spasm of the smooth muscle within an organ.
- Pain associated with spasm may be due to compression of the nerve endings itself or disruption of the blood supply thereby leading to ischemic pain.

Chemical injury

- **Chemical injury** is more often associated with the gastrointestinal tract and its digestive enzymes.
- If these enzymes leaks out of the gut, it can cause significant damage to the tissue.
- Visceral pain may also arise in other hollow organs if noxious substances are delivered to the site, either by ingestion, injection or through other invasive procedures.

Mechanical injury

- **Mechanical injury** rarely arises in an organ without first penetrating the outer layers and thereby eliciting somatic and/or parietal pain.
- It may happen with calculi (stones), malignancies that invade surrounding tissue and other disturbances in growth and structure but this usually arises internally.

Guarding

When inflamation of viscera involves peritoneum reflex spasm of related muscle occurs. This is called guarding.

Guarding is a protective reflex .

It helps to protect underlying inflamed viscera from unintentional injuries.

Insensitive viscera

- Liver parenchyma
- Lung alveoli

Pathway for visceral pain

- Visceral afferents reach CNS via sympathetic & parasympathetic pathways
- They travel along same pathways as somatic sensation in spinothalamic tract → thalamic radiations
- Cortical receiving areas are intermixed with somatic receiving areas

Pain from the viscera is frequently localized to two surface areas of the body at the same time because of the dual transmission of pain through

1.The referred visceral pathway.

2.The direct parietal pathway.

Pain from the viscera is frequently localized to two surface areas of the body at the same time because of the dual transmission of pain through

1.The referred visceral pathway.

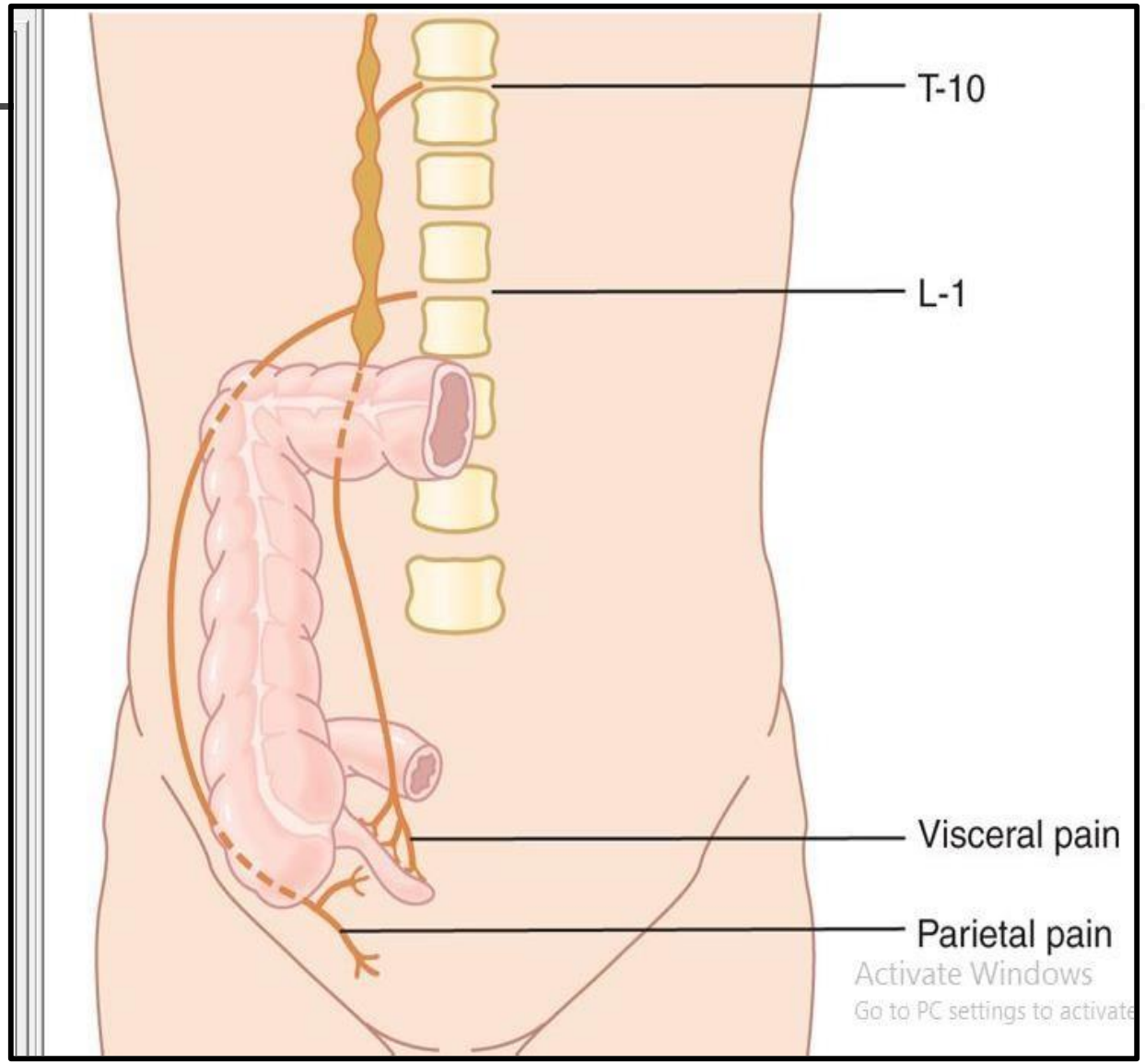
Pain impulses pass first from the appendix through visceral pain fibers located within sympathetic nerve bundles, and then into the spinal cord at about T-10 or T-11; & is referred to an area around the umbilicus and is of the aching, cramping type. .

2.The direct parietal pathway.

Pain impulses originating in the parietal peritoneum where the inflamed appendix touches or is adherent to the abdominal wall cause pain of the sharp type directly over the irritated peritoneum in the right lower quadrant of the abdomen.

- When a disease affects a viscus, the disease process often spreads to the parietal peritoneum, pleura, or pericardium.
- These parietal surfaces are supplied with extensive pain innervation from the peripheral spinal nerves.
- Therefore, pain from the parietal wall overlying a viscus is frequently sharp and well localized
- Example : A knife incision through the *parietal* peritoneum is painful, whereas a similar cut through the visceral peritoneum or through a gut wall is not painful.

Figure shows dual transmission from an inflamed appendix



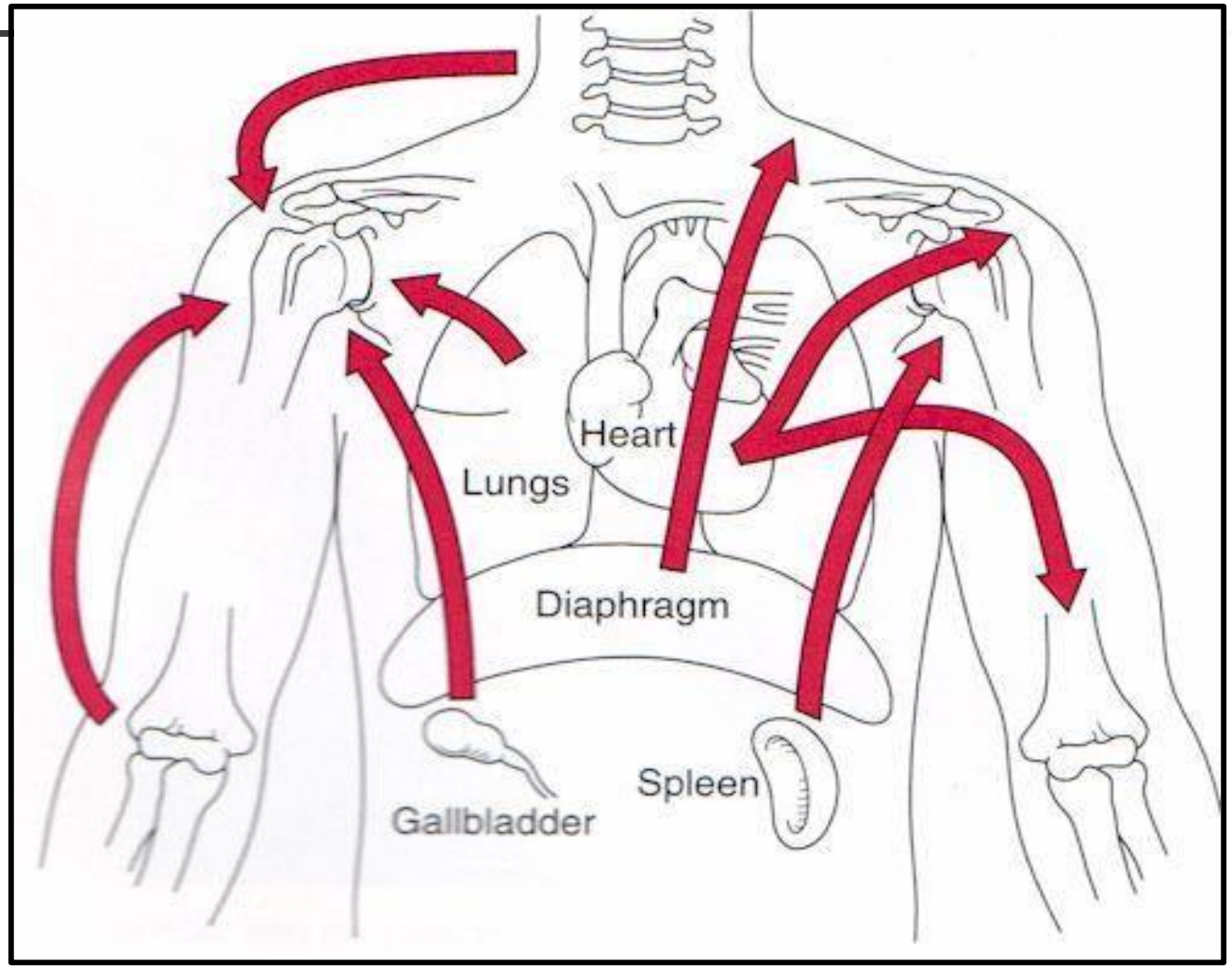
Referred pain

- Irritation of a visceral organ produces pain that is felt not at that site but in some somatic structure that may be considerable distance away

- Knowledge of referred pain aids in diagnosis of visceral disease

Visceral pain	Site of referral
Cardiac pain	Inner aspect of left arm
	Unusual sites: abdominal pain , pain in neck & back
Appendicitis	Umbilicus
Diaphragmatic pain	Shoulder tip
Ureteric pain	Testicles
Maxillary sinus	Nearby teeth

Referred pain



Dermatomal rule

- When pain is referred it is usually to a structure that developed from the same embryonic segment or dermatome as the structure in which the pain originates
- Eg. Heart & arm have same dermatomal origin
- Testicles have migrated with its nerve supply from primitive urogenital ridge from which kidney & ureter develop
- Hence ureteric pain is referred to testes

cause of referred pain

- main cause of referred pain appear to be plasticity in CNS with convergence of visceral & peripheral nerve fibres in same second order neuron of spinal cord that project to brain

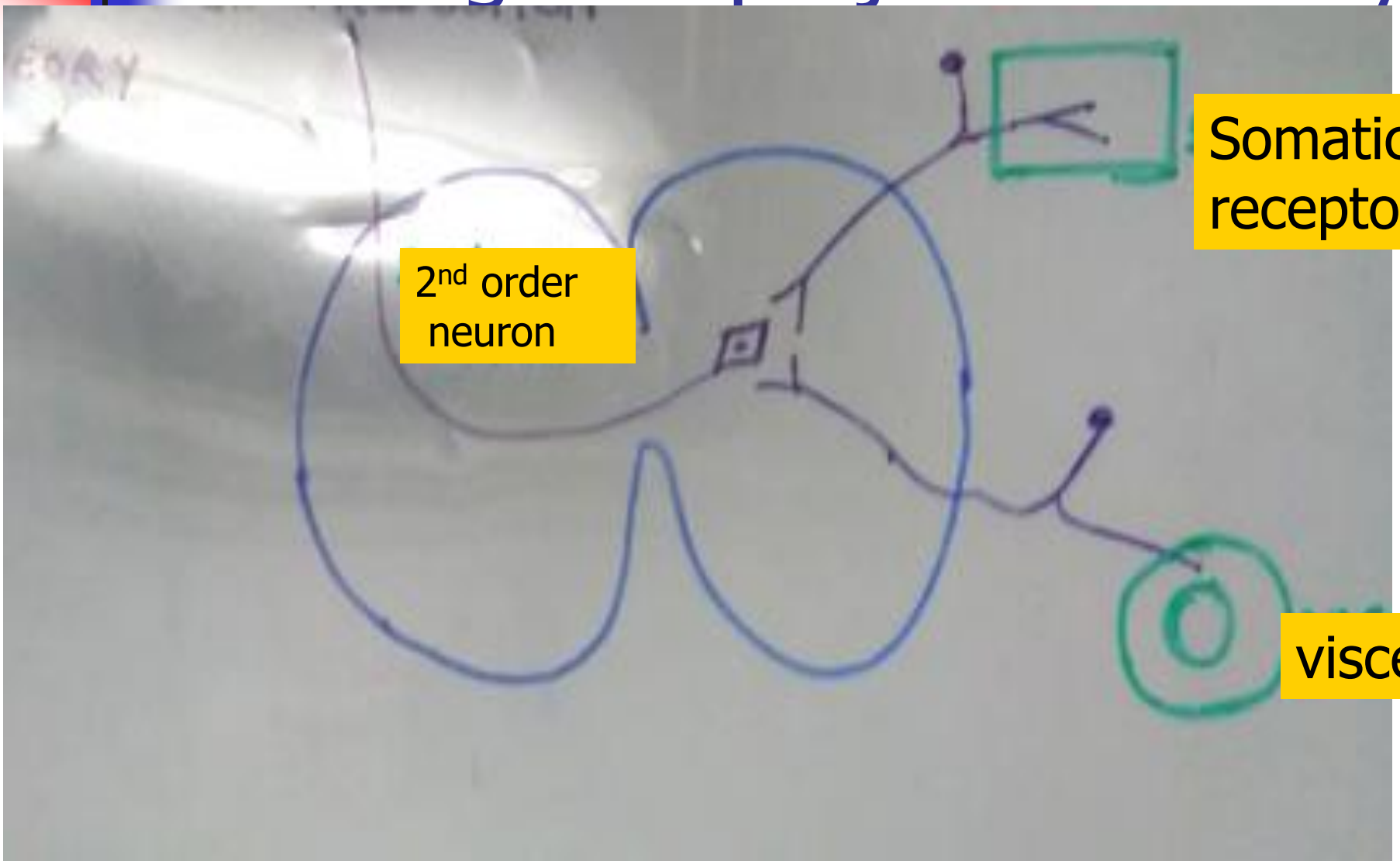
Theories of referred pain

- Convergence projection theory
- Facilitation theory

Convergence projection theory

- Convergence of somatic & visceral pain fibres occur on same 2nd order neuron that project to brain
- As somatic pathway is more frequently stimulated pain arising from visceral organ will be interpreted by brain as that arising from somatic structure

Convergence projection theory

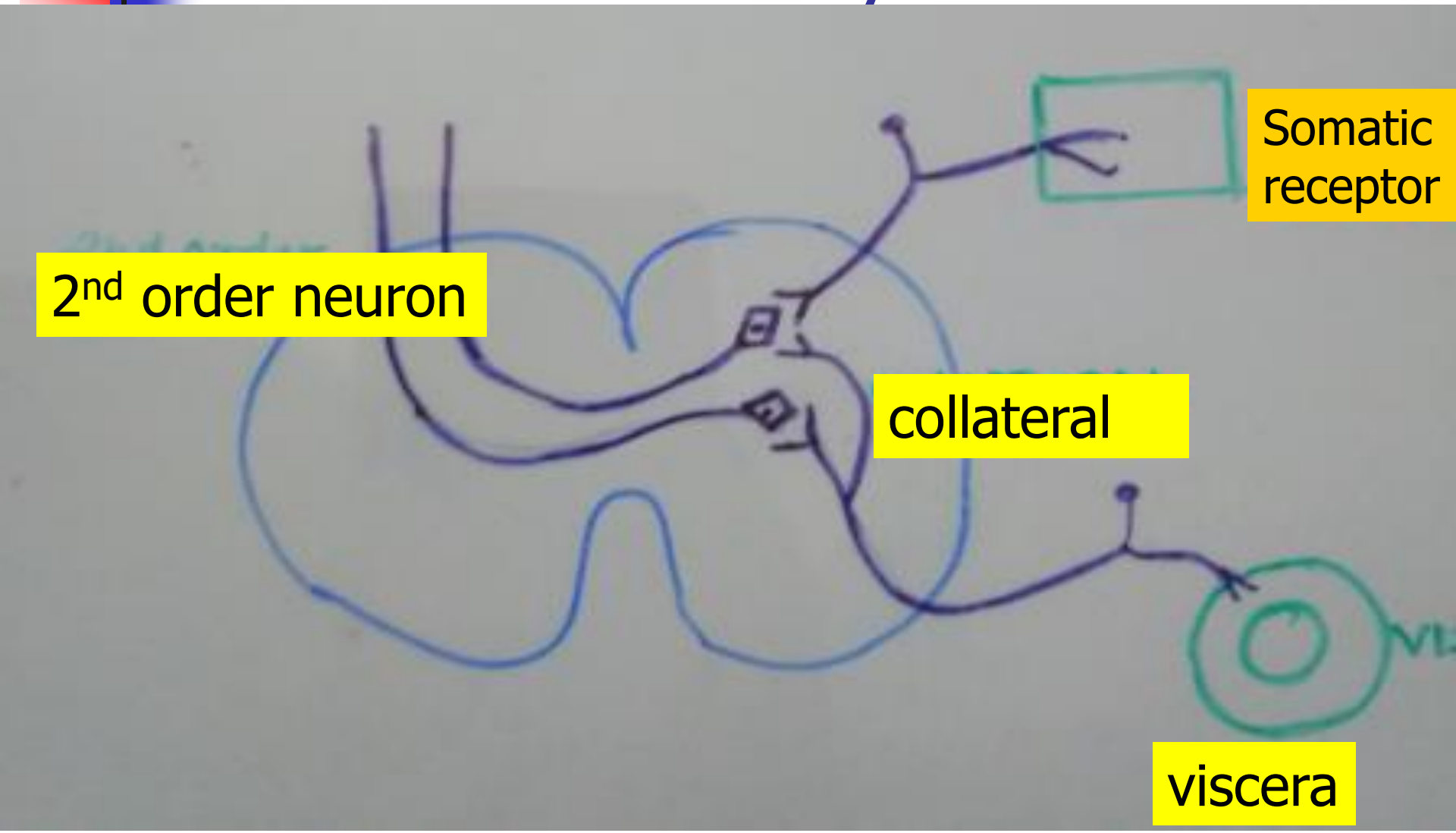


Facilitation theory

- Fibres in visceral organs give collaterals to neurons of pain pathway from cutaneous region
- So 2nd order neurons of cutaneous pain pathway comes in the subliminal fringe zone of visceral afferent pathway
- Prolonged visceral stimulation therefore causes activation of fibres from somatic structures due to subliminal fringe effect

- Minimal activity in somatic pain pathway which in normal cases dies out in spinal cord is facilitated & causes strong pain

Facilitation theory



- Previous experience play a role in referred pain
- In abdominal diseases pain is referred to midline of abdomen
- If patient had a previous abdominal surgery the pain is referred to region of scar