Neuro-Block: Lecture 6

جامعة الملك سعود
King Saud University

Physiology of Pain

By Laiche Djouhri, PhD

Associate Professor

Dept. of Physiology

Email: ldjouhri@ksu.edu.sa Ext:71044

Week1 Lecture 6

Chapter 48

(Guyton & Hall)

Somatic Sensations: Pain, headache and Thermal Sensations

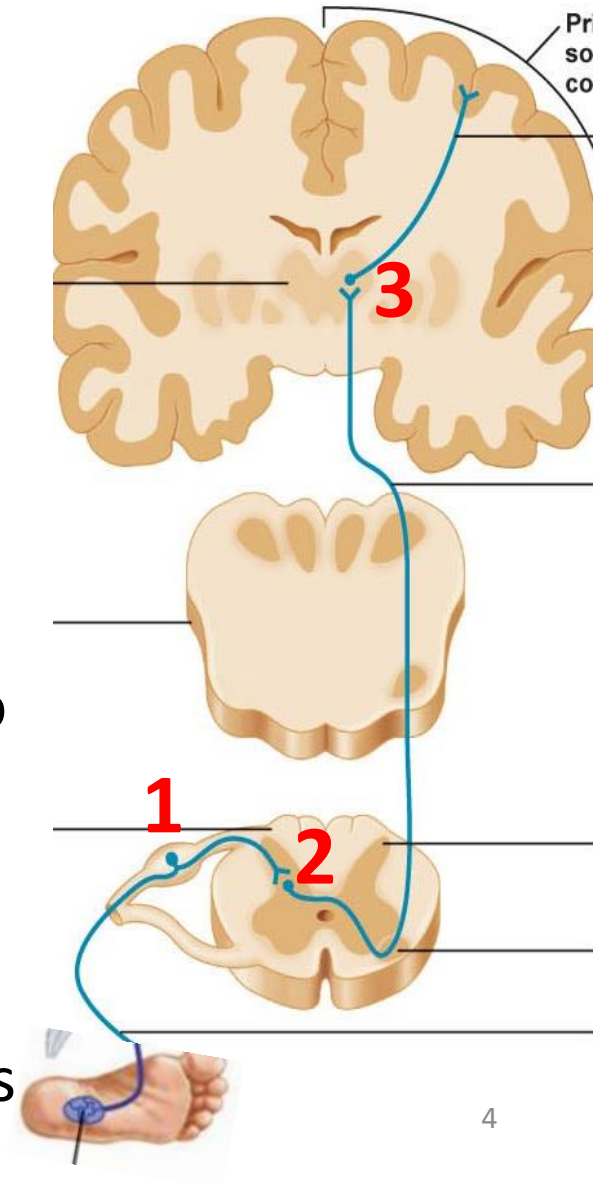
Objectives

By the end of this session students are expected to:

- Differentiate between pain & nociception
- Describe the types of nerve fibres and receptor types that mediate pain
- Describe different types of pain and pain pathways
- Describe the role of thalamus and cerebral cortex in pain perception

Definitions-1

- **Primary sensory (afferent) neurons:** first-order neurons in the sensory system responsible for transmitting sensory information from the periphery to the CNS
- **Sensory receptors:** are specialized peripheral endings of primary afferent neurons.
- **Noxious stimulus:** any stimulus (mechanical, chemical or thermal) that produces tissue damage or threatens to do so (**≠ innocuous**).
- **Nociceptors (*pain receptors*):** primary afferent receptors that respond selectively to noxious stimuli.
- **Polymodal nociceptors:** respond to various noxious stimuli.

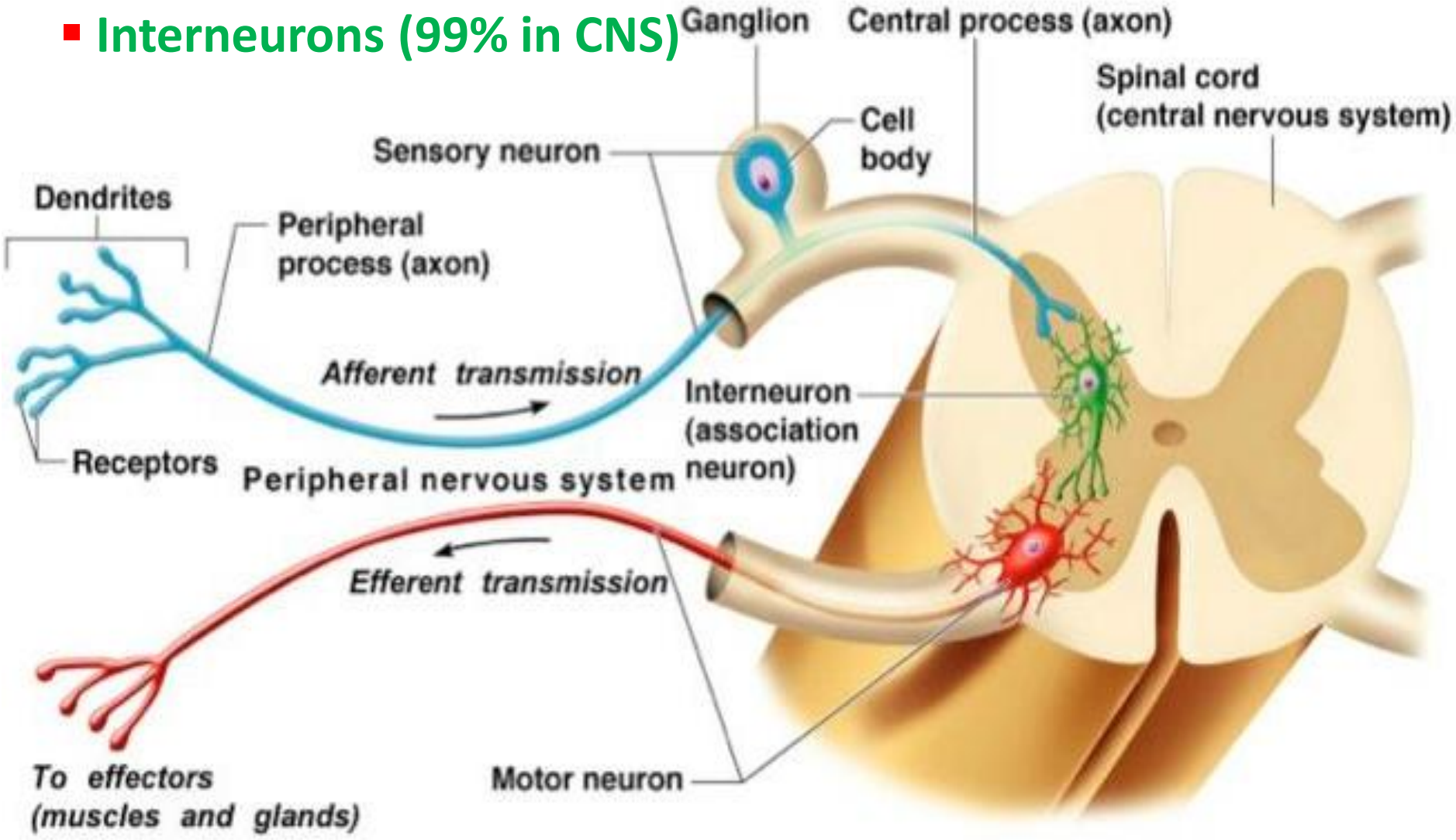


Definitions-2

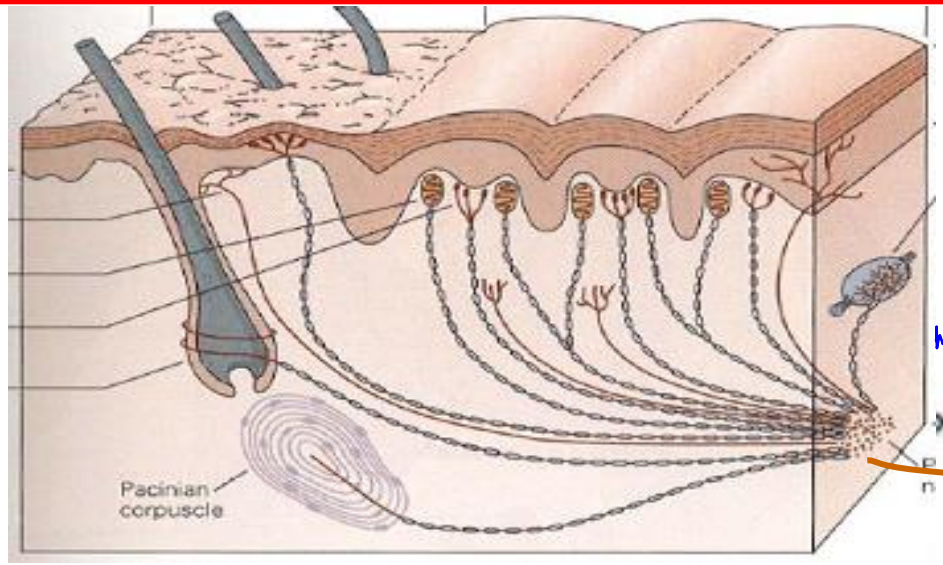
- **Adequate stimulus:** the form of energy to which a specific receptor is most sensitive
- **Somatic pain** – pain originating from skin, joints, muscles, and other deep tissues
- **Visceral pain** – pain originating from the internal organs
- **Allodynia** – pain caused by a stimulus that is not normally painful (e.g. touch)
- **Hyperalgesia** – an increased sensitivity to a stimulus that is normally painful.
- **Spontaneous pain:** stimulus independent pain (ongoing pain)

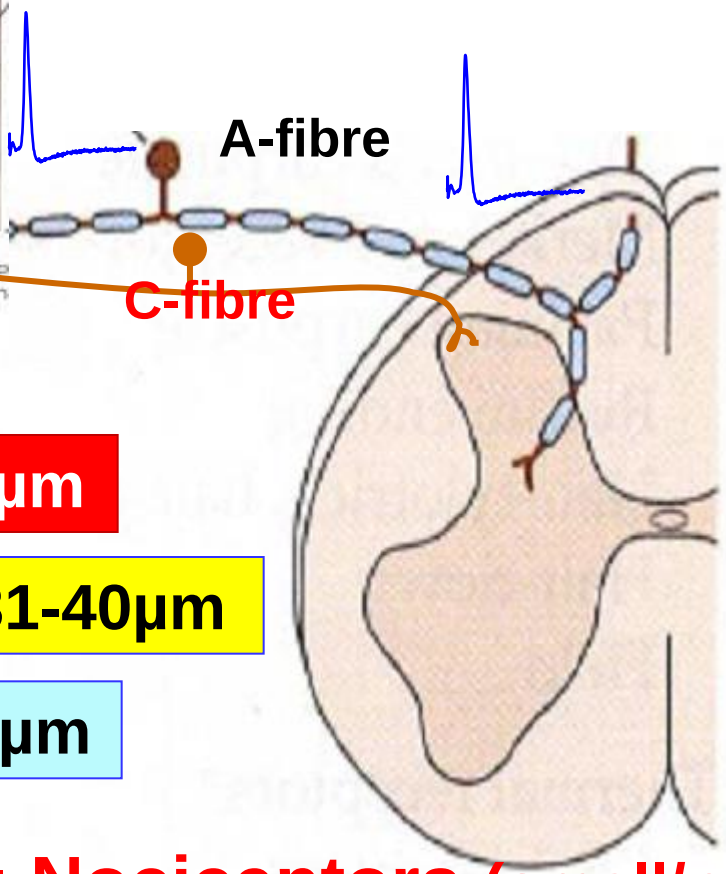
Afferent & Efferent Neurons

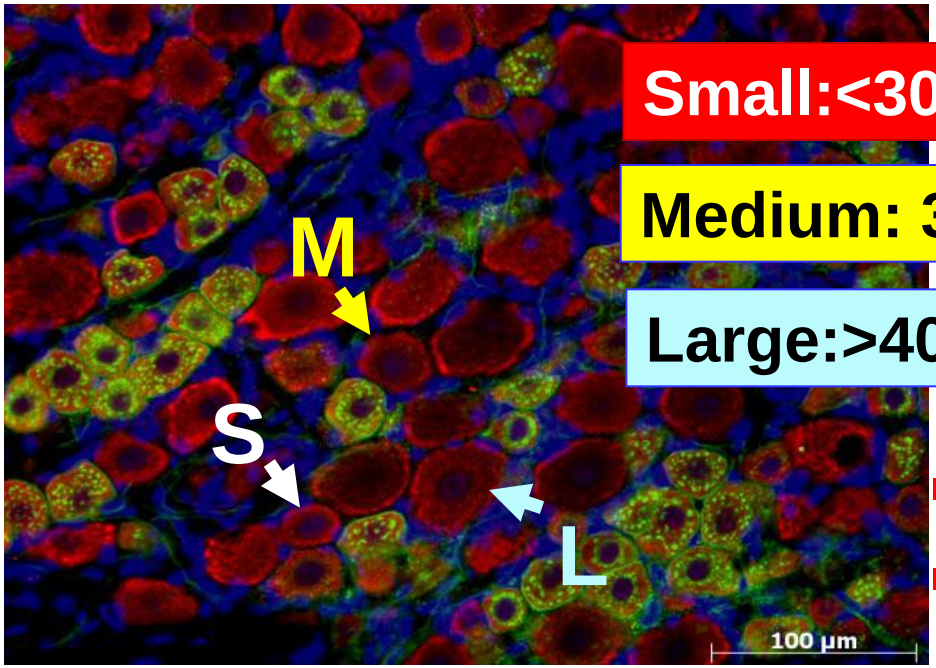
- Sensory neurons (Afferent neurons)
- Motor neurons (Efferent neurons)
- Interneurons (99% in CNS)



Afferent Neurons & Receptors







Small:<30µm

Medium: 31-40µm

Large:>40µm

- **Nociceptors (small/medium)**
- **Non-nociceptors (large)**

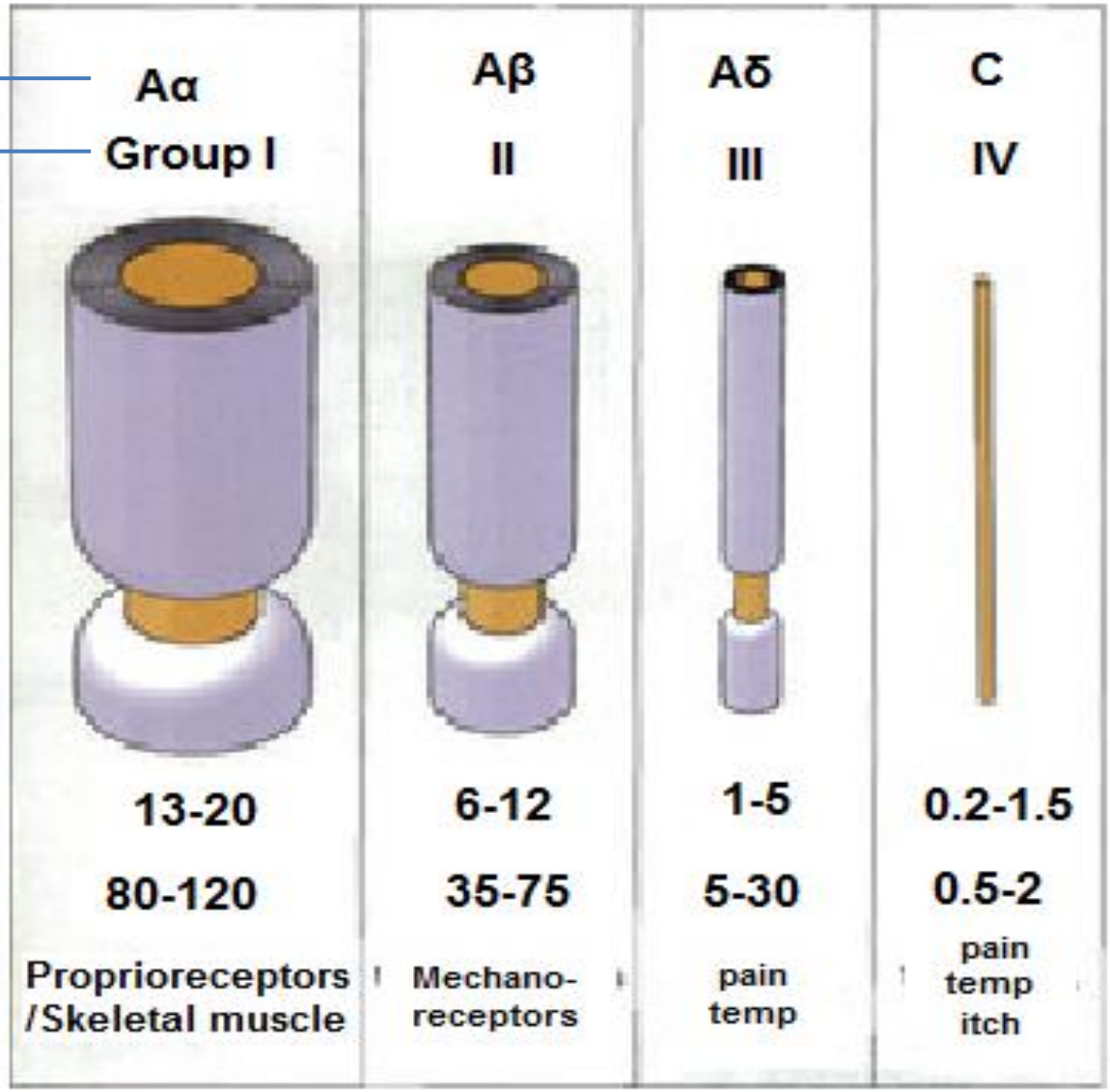
Classification of Nerve fibers

Skin & other tissue ←

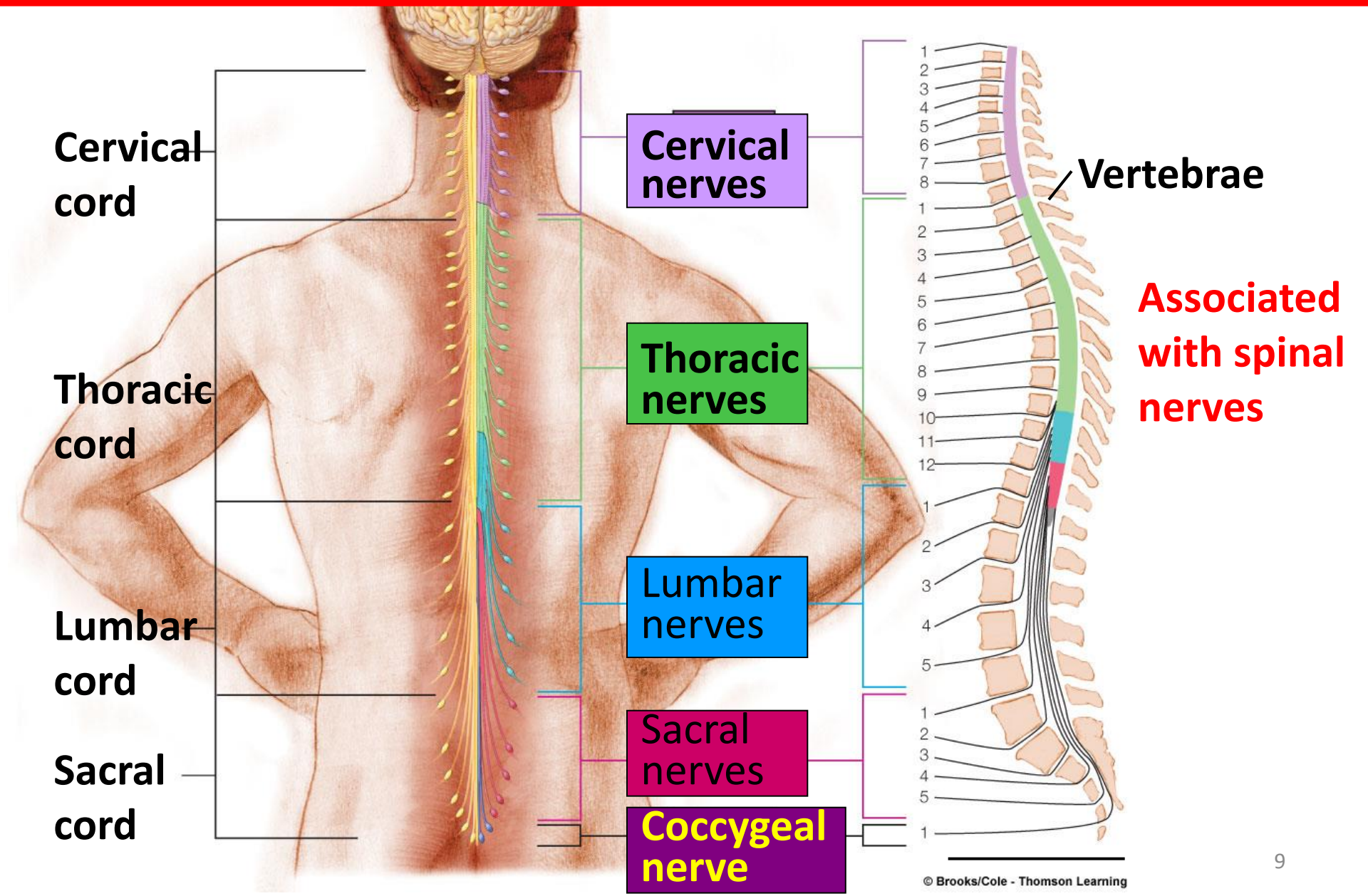
Skeletal muscle tissue ←

Types of nerve fibers:

- **Myelinated (A-fiber)**
  - **Aα** (thickly myelinated)
  - **Aβ** (intermediate m.)
  - **Aδ** (thinly myelinated)
- **Unmyelinated (C-fiber)**

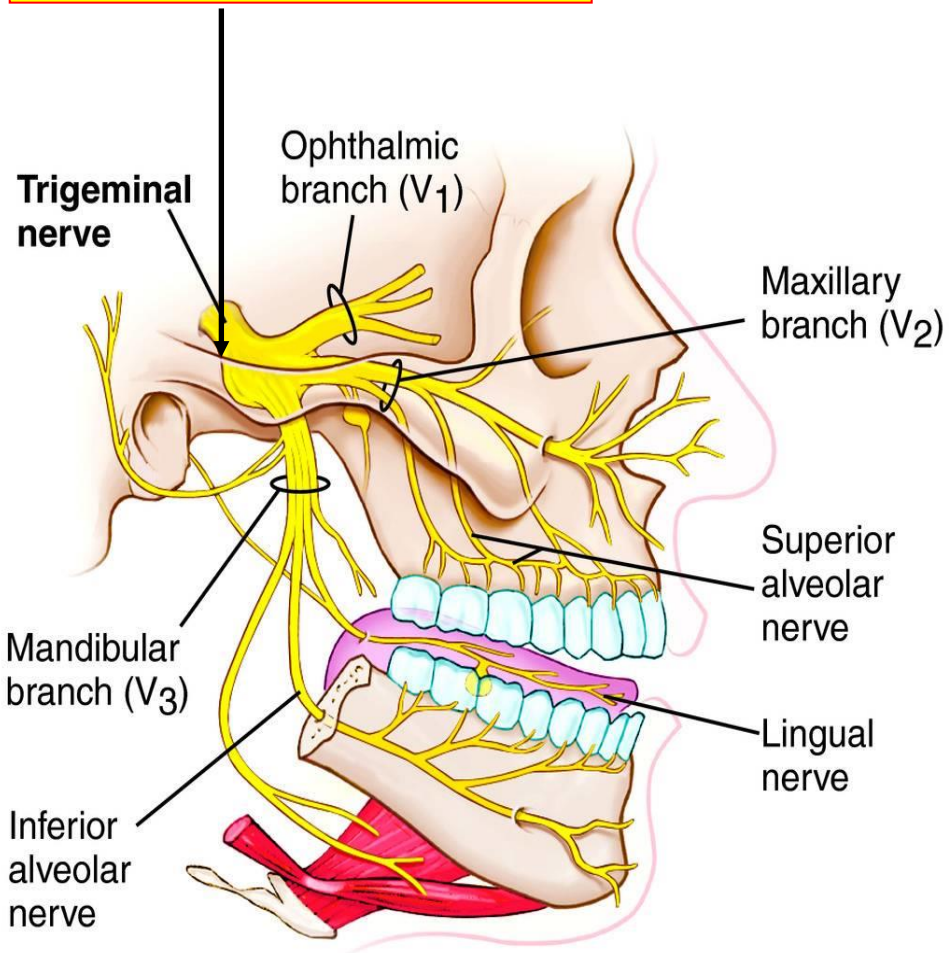


Primary Afferent Neurons: Where are They?



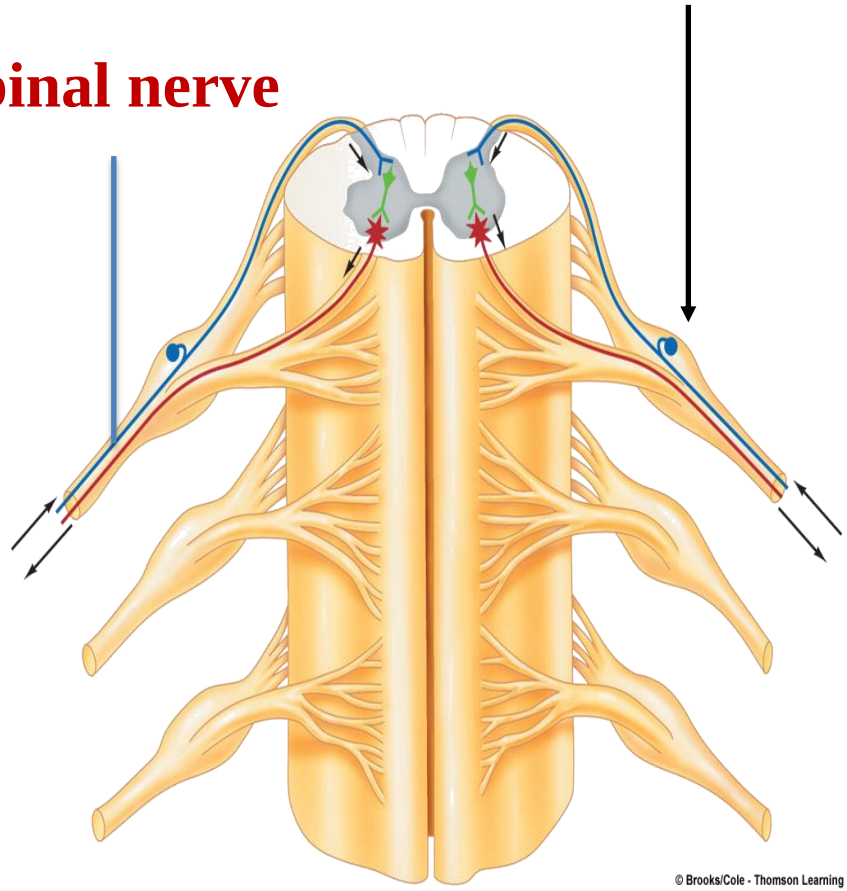
Afferent (Sensory) Neurons: Where are They?

Trigeminal Ganglion



Cranial nerves = 12

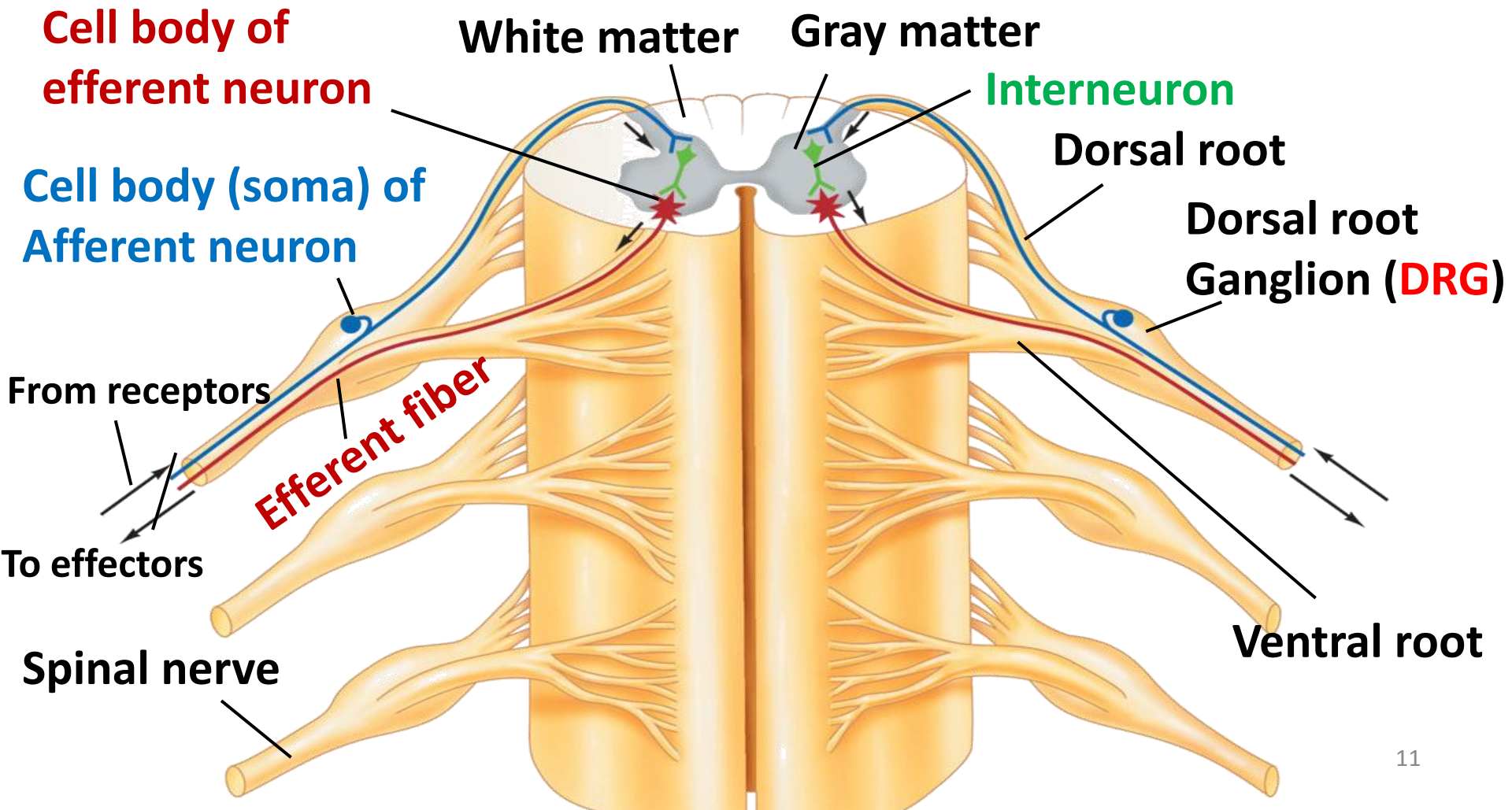
Dorsal root Ganglion



Spinal nerves =31

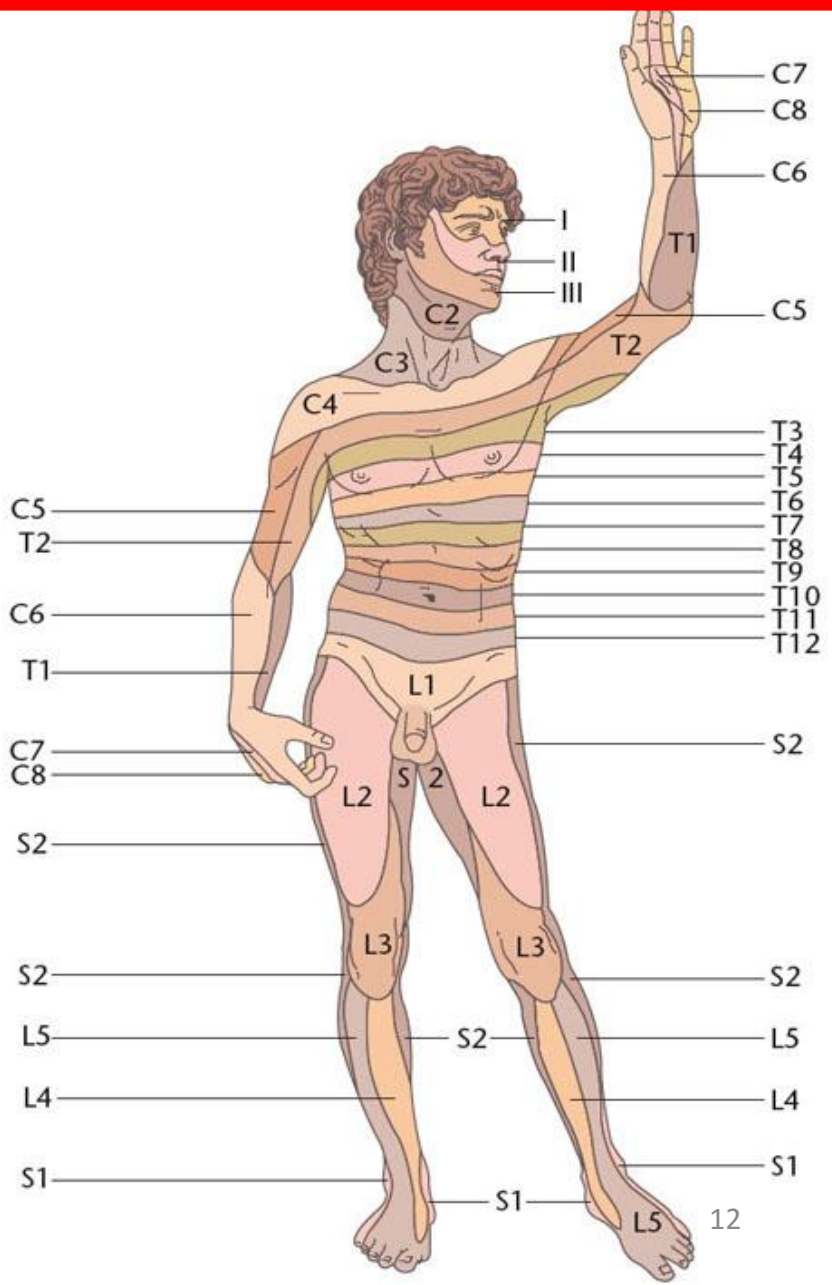
What is a Spinal Nerve?

Is a mixed nerve: somatic (sensory and motor) and visceral (autonomic nerve fibers).



What is a Dermatome?

- Each spinal nerve supplies a dermatome
- **Dermatome** (derma, "skin", tome, "cut up")
- **Dermatome**: skin area innervated by a single spinal nerve
- **Dermatomal map:** is an important diagnostic tool for determining site of spinal cord injury



Pain Receptors `Nociceptors`?

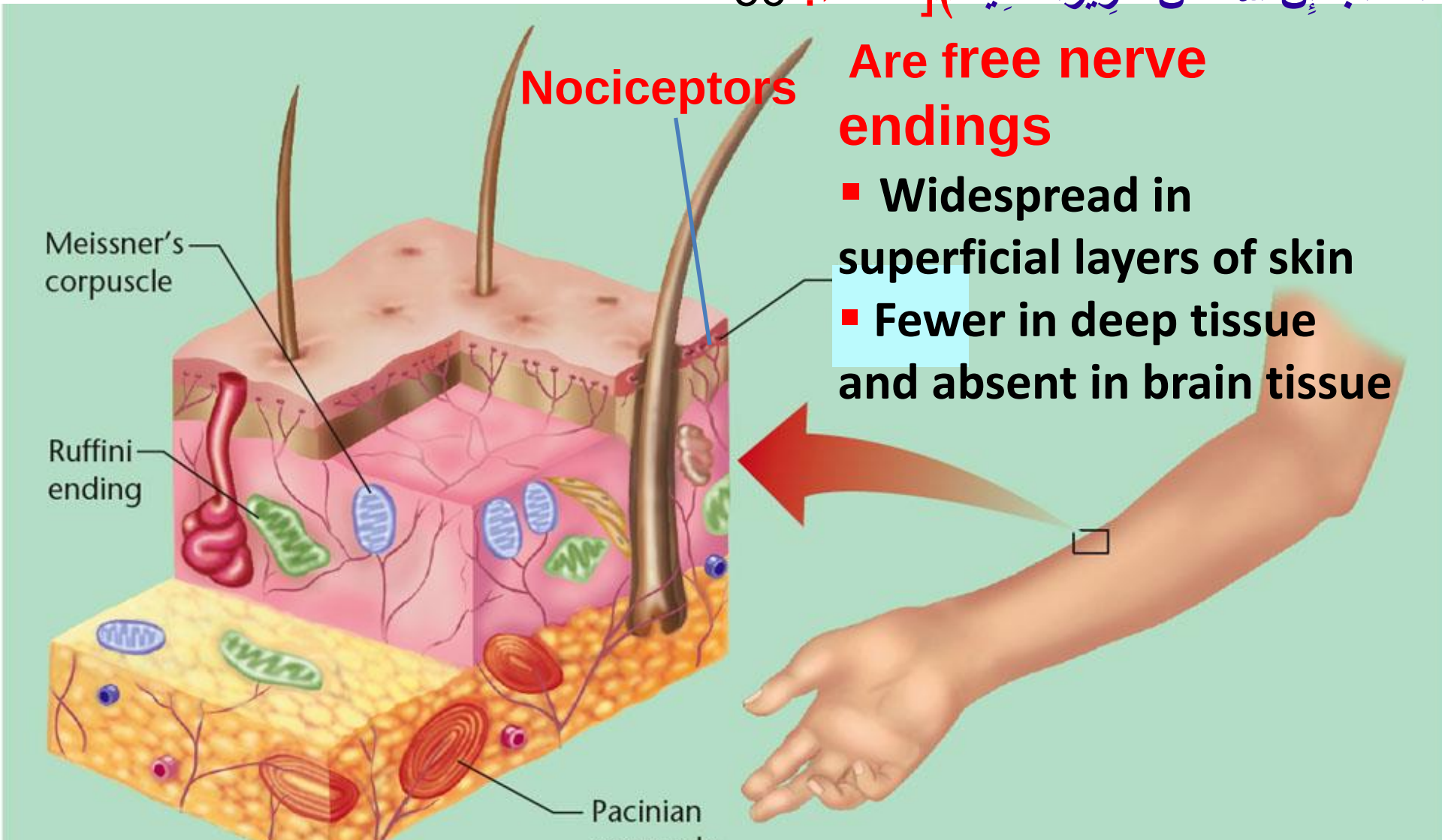
*" are special receptors that respond only to **noxious** stimuli and generate nerve impulses which the brain interprets as "pain". **Sherrington 1906***

- They are specific (have adequate stimulus) in that pain is not produced by **overstimulation** of other receptors.
- Heat pain threshold **> 43 °C**
- Do not adapt (or very little) to repetitive stimulation (**can be sensitized by various agents, eg. prostaglandins**)

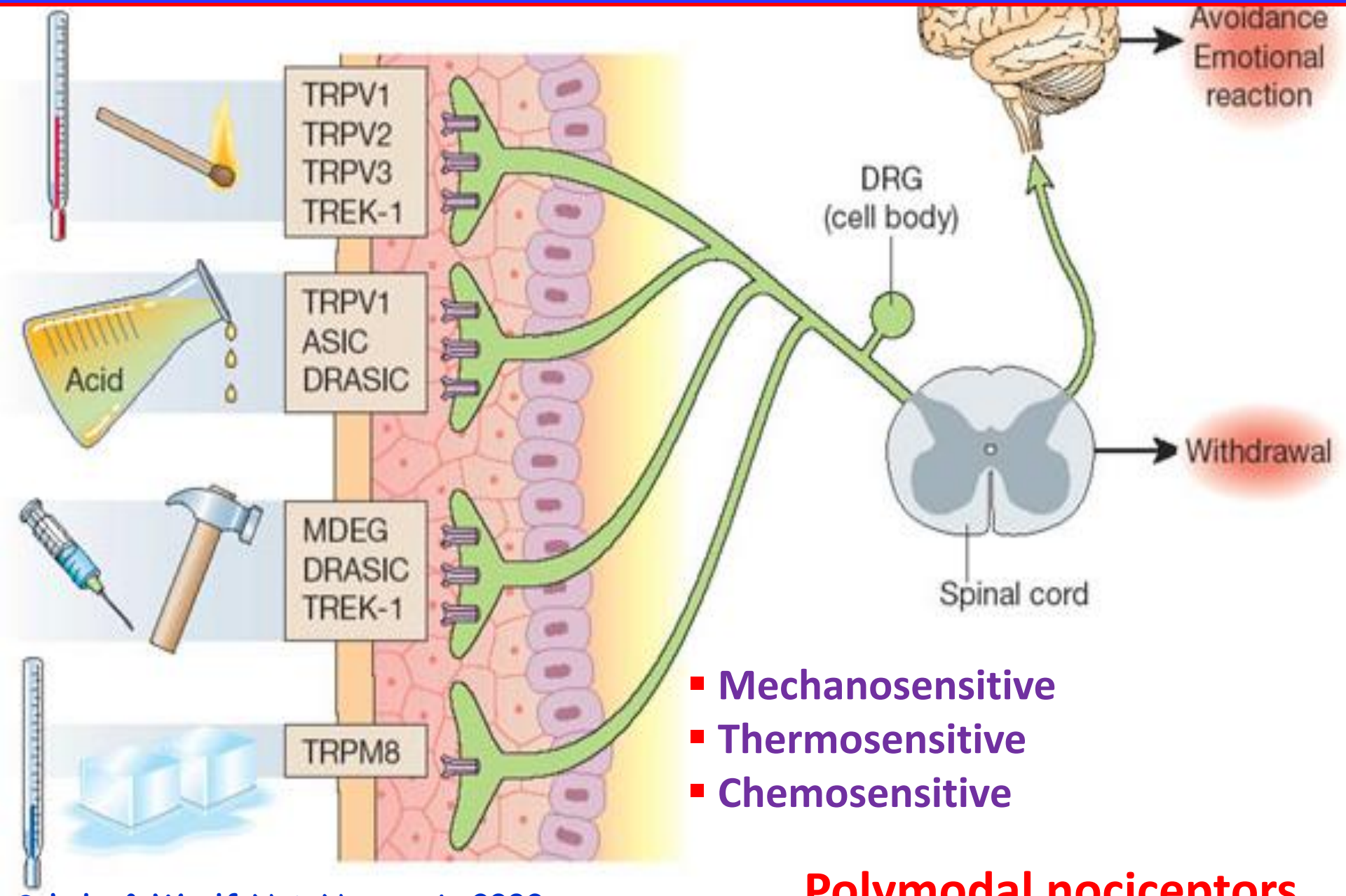
Sir Charles Scott Sherrington (1857-1952)

Distribution of Pain Receptors (Nociceptors)

﴿إِنَّ الَّذِينَ كَفَرُواْ بِآيَاتِنَا سَوْفَ نُصْلِيهِمْ نَاراً كُلَّمَا نَضِجَتْ جُلُودُهُمْ بَدَّلْنَاهُمْ جُلُوداً غَيْرَهَا لِيَذُوقُواْ الْعَذَابَ إِنَّ اللّهَ كَانَ عَزِيزاً حَكِيماً﴾[النساء: 56



Types of Nociceptors

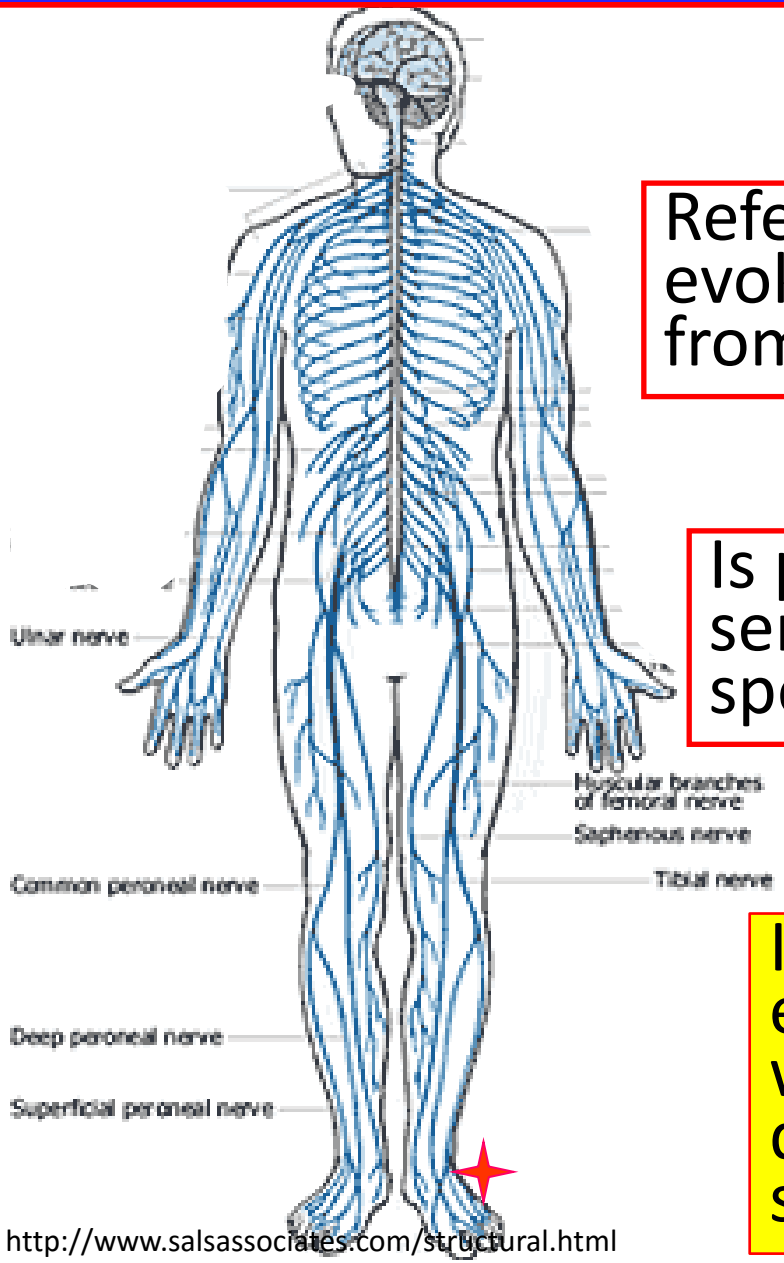


- Mechanosensitive
- Thermosensitive
- Chemosensitive

Polymodal nociceptors

Scholz & Woolf Nat. Neurosci. **2002**

Pain & Nociception-1



http://www.salsassociates.com/structural.html

What is nociception?

Refers to the transmission of signals evoked by activation of nociceptors from periphery to the CNS.

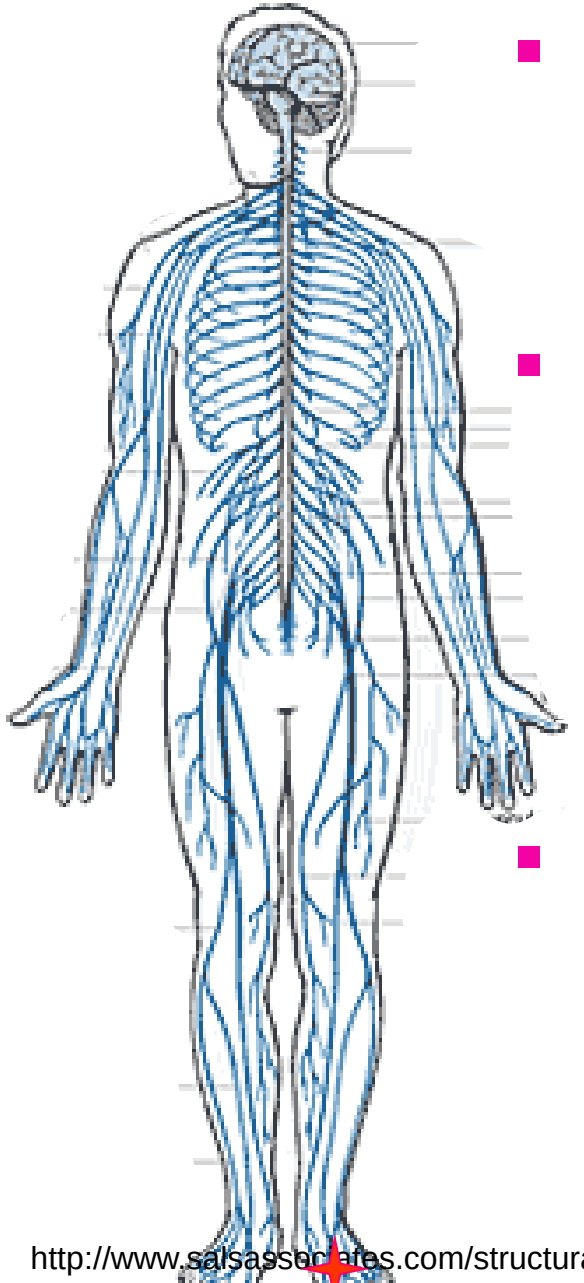
What is pain?

Is perception of unpleasant sensation that originates from a specific body region.

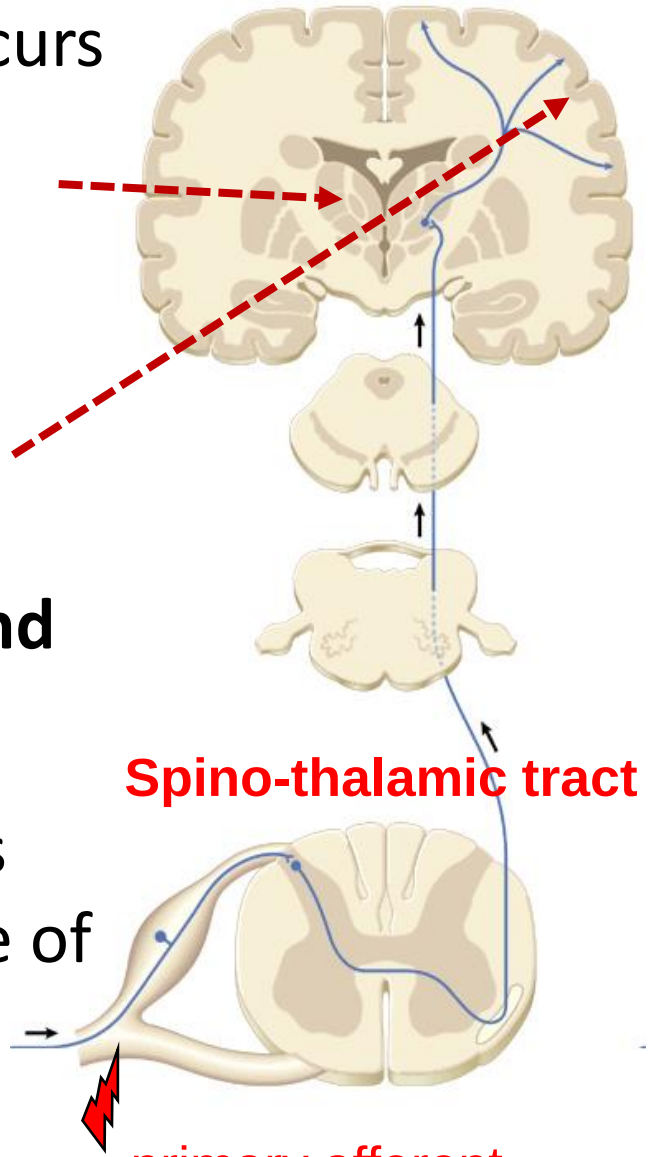
Formal definition

Is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage (**IASP**)

Pain & Nociception-2



- **Pain perception** occurs at the level of the **thalamus**
- The somatosensory cerebral cortex determines pain **intensity/quality and locates its source**
- Stimulus intensity is encoded by the rate of action potentials



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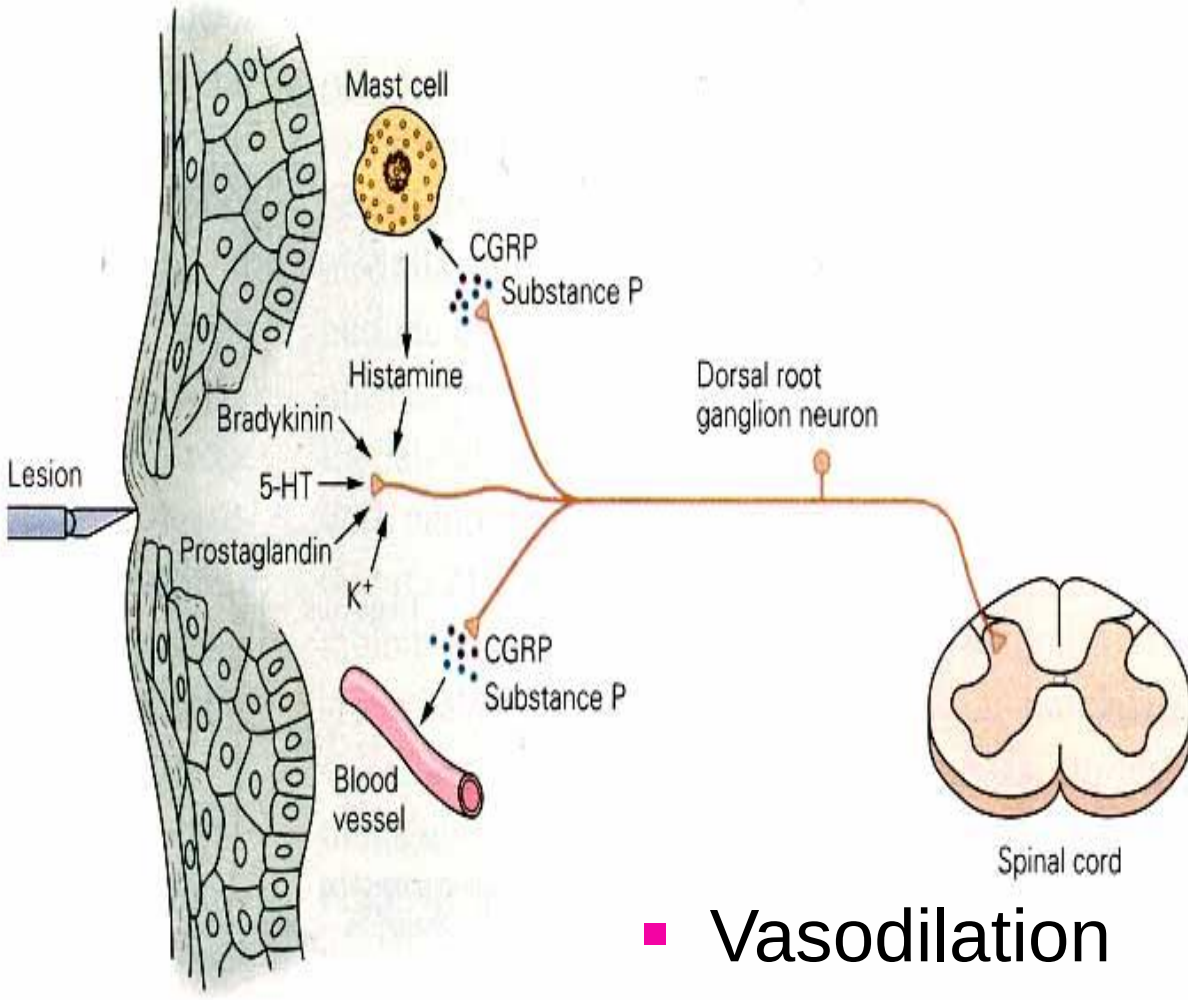
Pain Mediators After Tissue damage



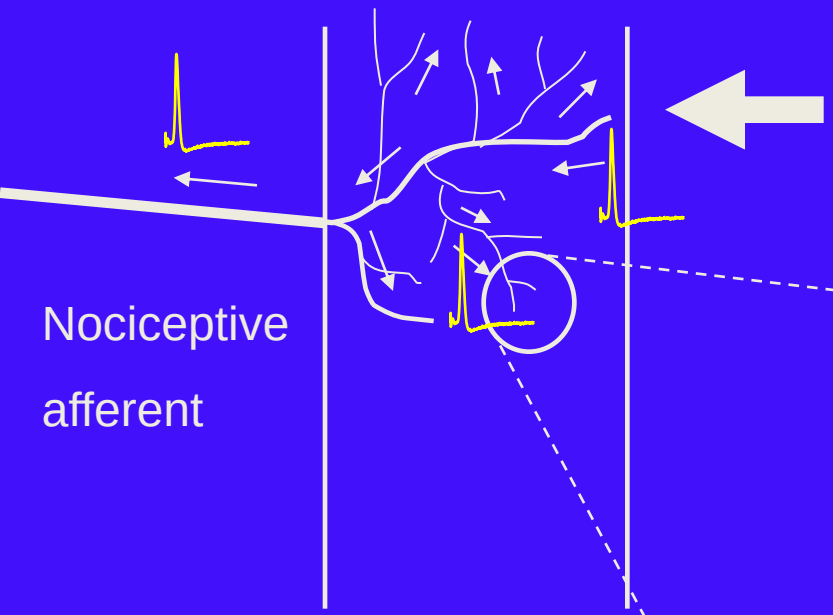
- Nociceptive neurons release peptides e.g. substance P, and **CGRP (Calcitonin gene related peptide)** which stimulate mast cells and blood vessels

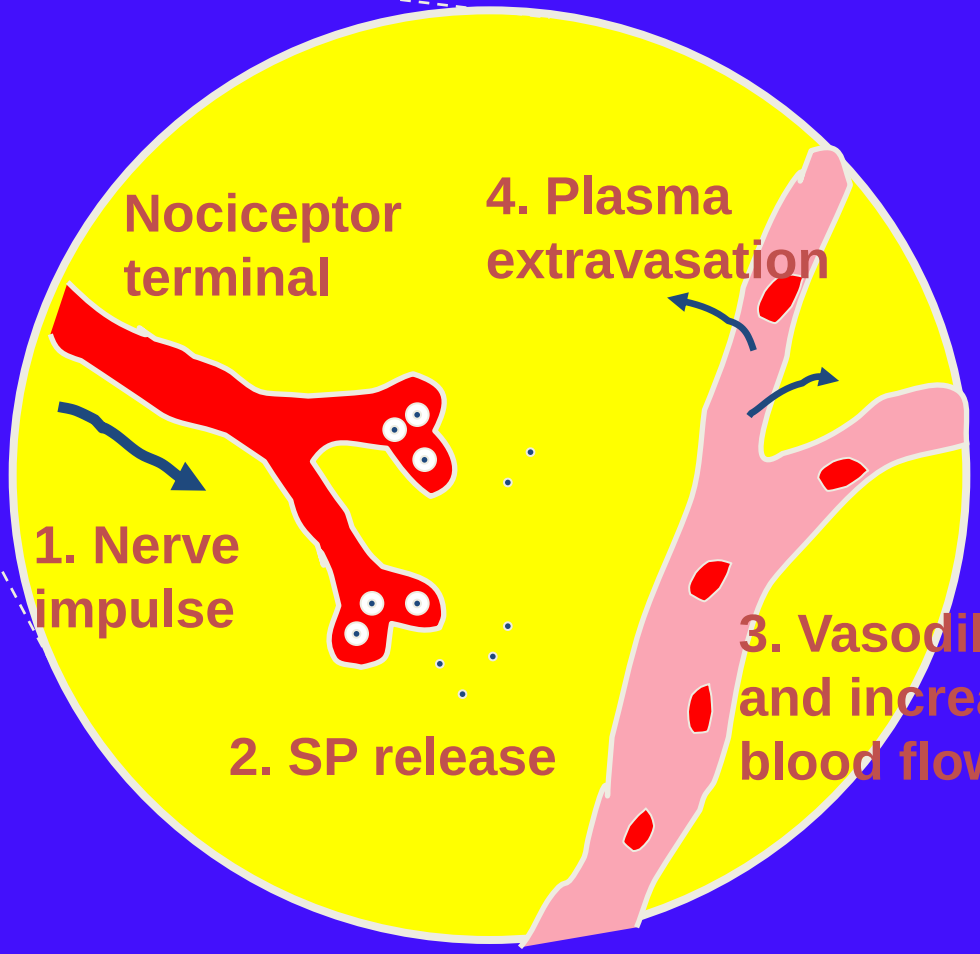
(via **axon reflex**)

- Vasodilation
- Extravasation

Efferent Function of Nociceptors

Axon Reflex





- **Many nociceptors have Afferent as well as Efferent actions**

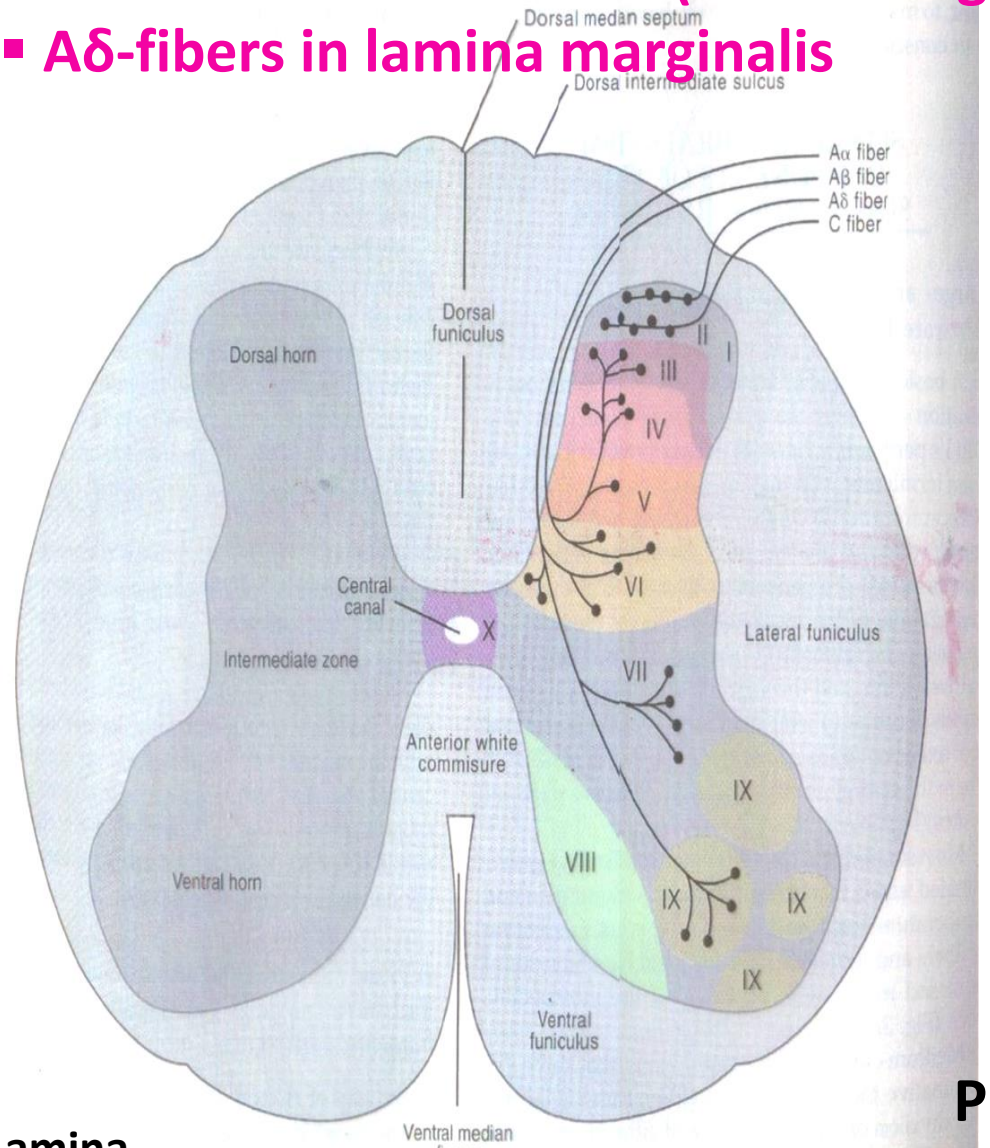
Reproduced from Berne & Levy, 1993

Significance of Pain: Why do we feel pain?

- It is a protective mechanism that make us aware that tissue damage is occurring or is about to occur
  - Avoid noxious stimuli
  - Remove body parts from danger
  - Promote healing by preventing further damage
- Storage of painful experiences in memory helps us to avoid potentially harmful event in the future
- The sensation of pain may be accompanied by behavioural responses (withdrawal, defense) as well as emotional responses (crying or fear).

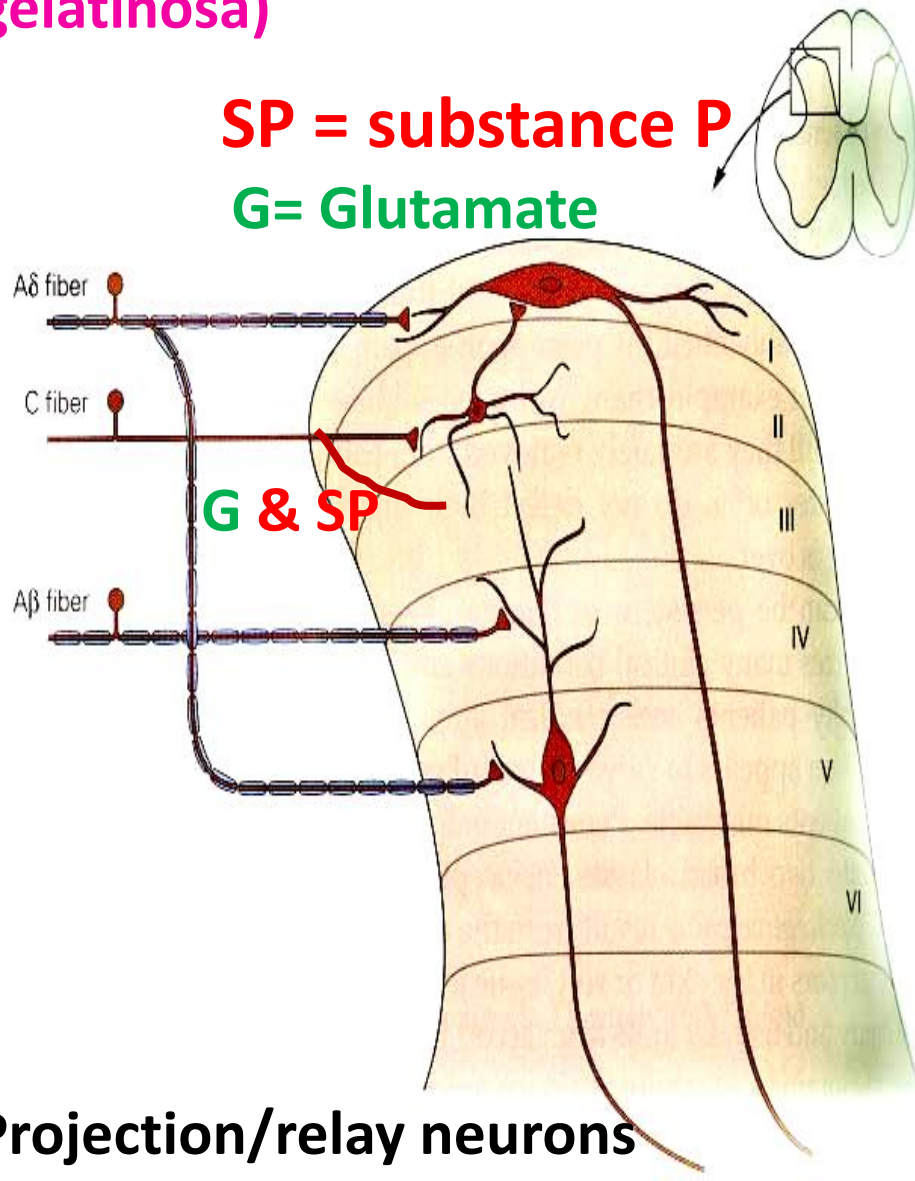
Nociceptive Input to the Spinal Cord

- C-fibers in laminae II-III (subtantia gelatinosa)
- Aδ-fibers in lamina marginalis



SP = substance P

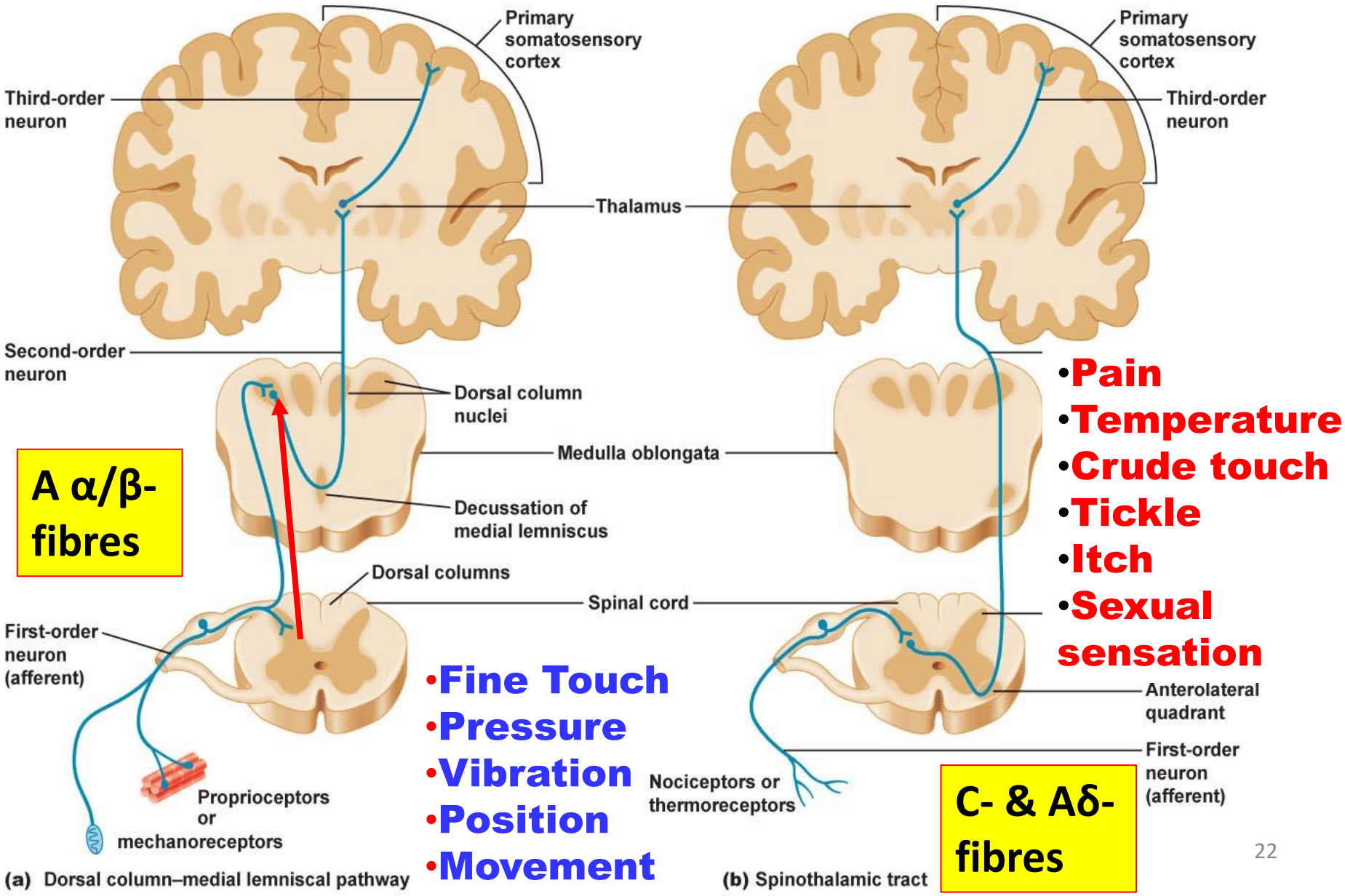
G= Glutamate



Projection/relay neurons

Lamina

Nociceptive vs Non-nociceptive Pathways



A α/β-fibres

- **Fine Touch**
- **Pressure**
- **Vibration**
- **Position**
- **Movement**

- **Pain**
- **Temperature**
- **Crude touch**
- **Tickle**
- **Itch**
- **Sexual sensation**

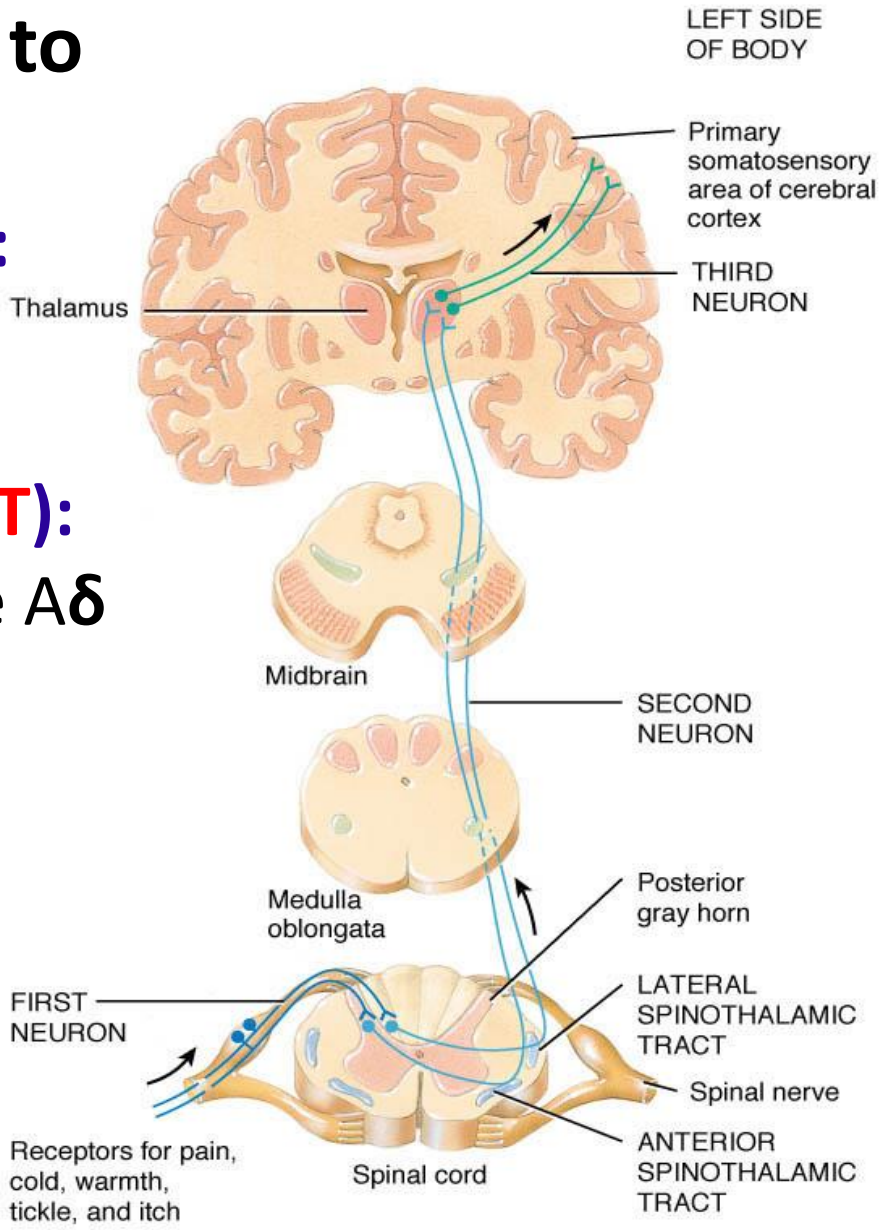
C- & Aδ-fibres

Dual Pain Pathways

Pain signals take 2 pathways to the brain:

- **Neospinothalamic (lateral STT):**
  - Fast pain (**Aδ-type**)
  - Thermal pain (acute type)
- **Paleospinothalamic (ventral STT):**
  - Slow pain (**C-type**) plus some A**δ**
  - Crude touch & pressure
  - Itch & tickle
  - Sexual sensations

Separation between the 2 pathways is no longer so clearly identified!!



Where Do Fibers of lateral & Ventral STT terminate?

- **Most pain fibers of lateral STT (**L-STT) pass all the way to thalamus:
  - Ventrobasal complex
  - Posterior nuclear group

- **Only few pain fibers of ventral STT pass** all the way to thalamus: they project to
  - Brain stem reticular formation

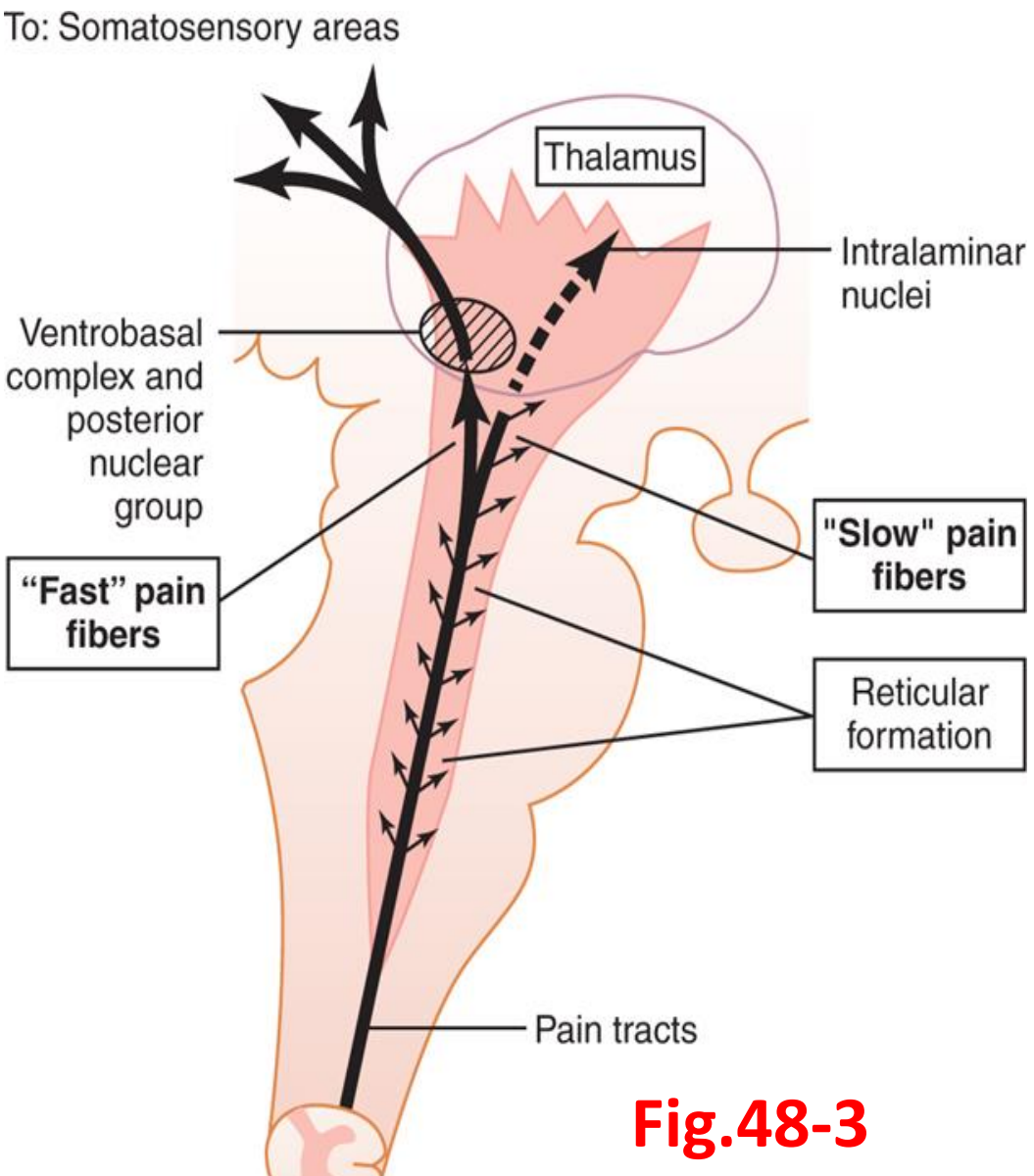
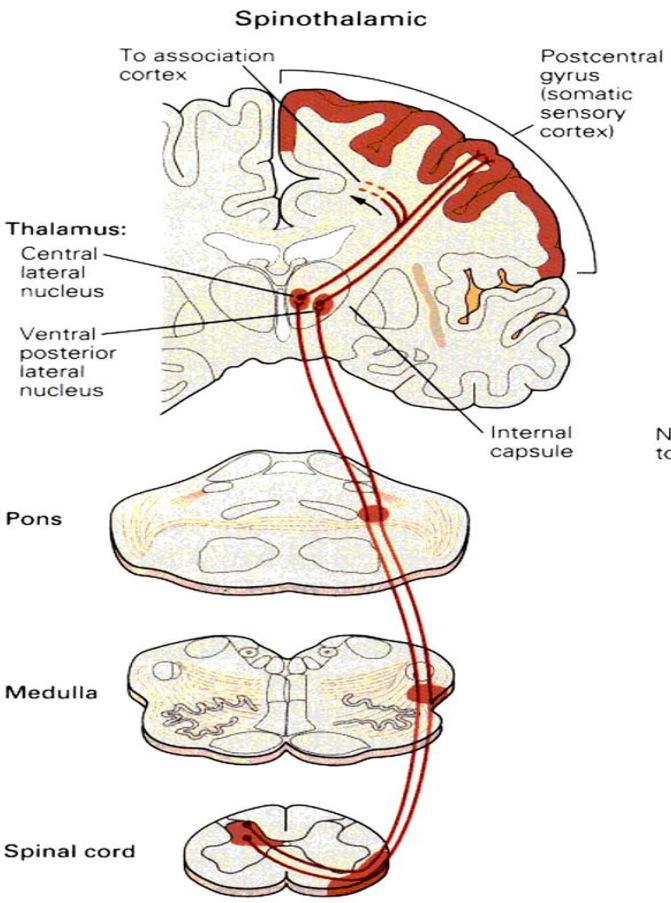
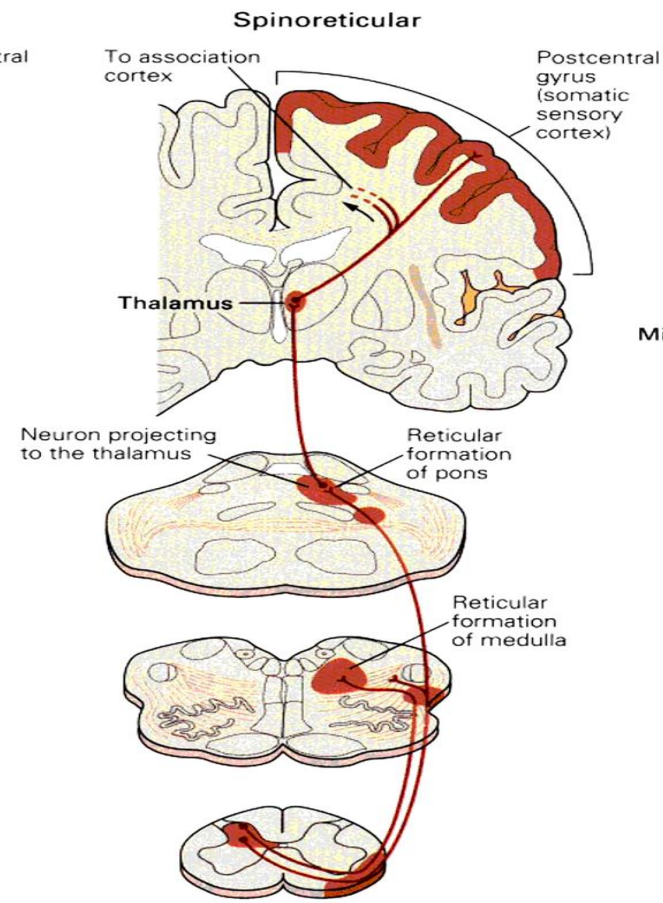
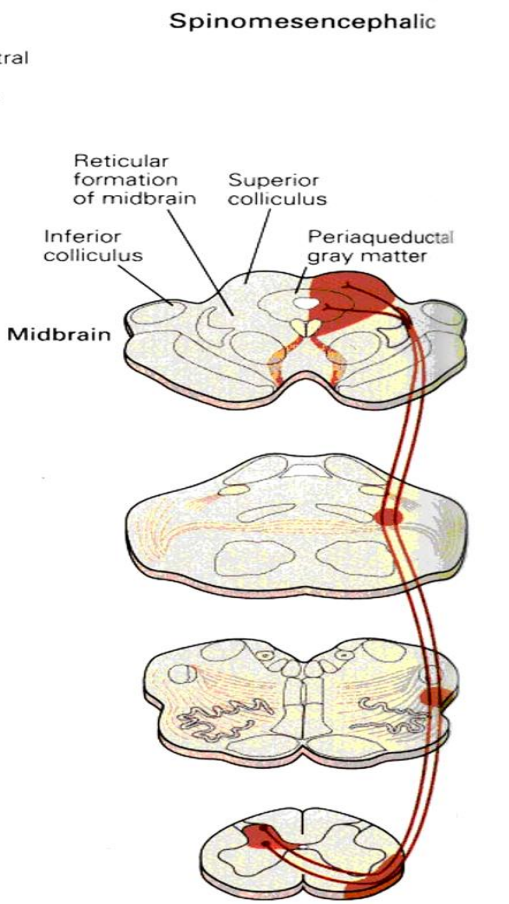


Fig.48-3

Other Ascending Pain Pathways







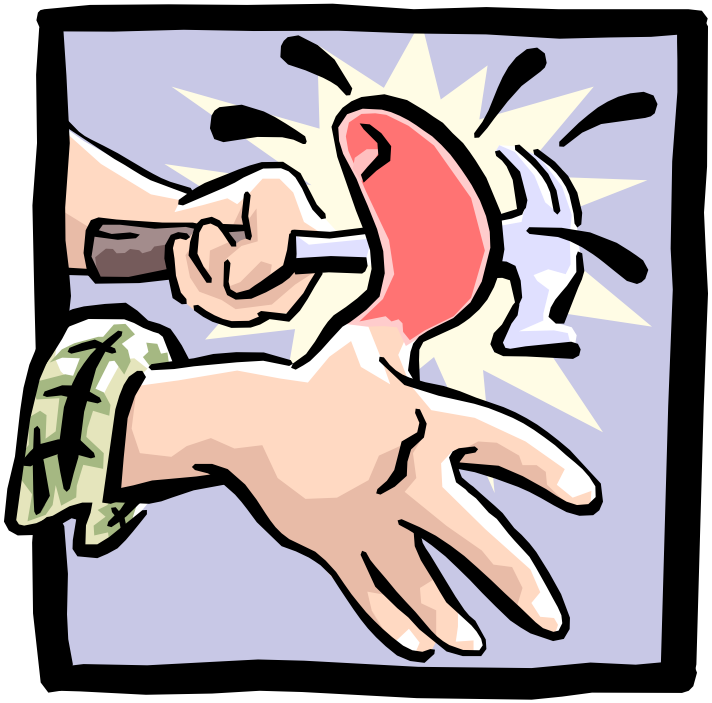
Spinothalamic **Spinoreticular** **Spinomesencephalic**

Pain pathways that provide different brain regions with information for processing different aspects of pain

Types and Qualities of Pain

Question

What are the qualities/types of pain you feel when you injure "cut" yourself ?



Types and Qualities of Pain

- Fast/Sharp (1st) pain vs slow diffuse (2nd) pain

Phenomenon of double-pain

Fast pain

- Sharp, intense, pricking, begins without delay (felt within **0.1 sec**)
- Associated with reflex withdrawal
- Usually somatic not visceral
- Easily localized and is mediated by **Aδ-fiber nociceptors (also Aβ)**

Slow pain

- Burning, aching, throbbing "unbearable" after ~ **1 sec or more**
- Associated with tissue destruction
- Can occur in skin or any internal organ/tissue
- Poorly localized and is mediated by **C-fiber nociceptors** (misery)

Acute "Physiologic" & Chronic "Pathologic" Pain

Normal acute pain 'good': protective role

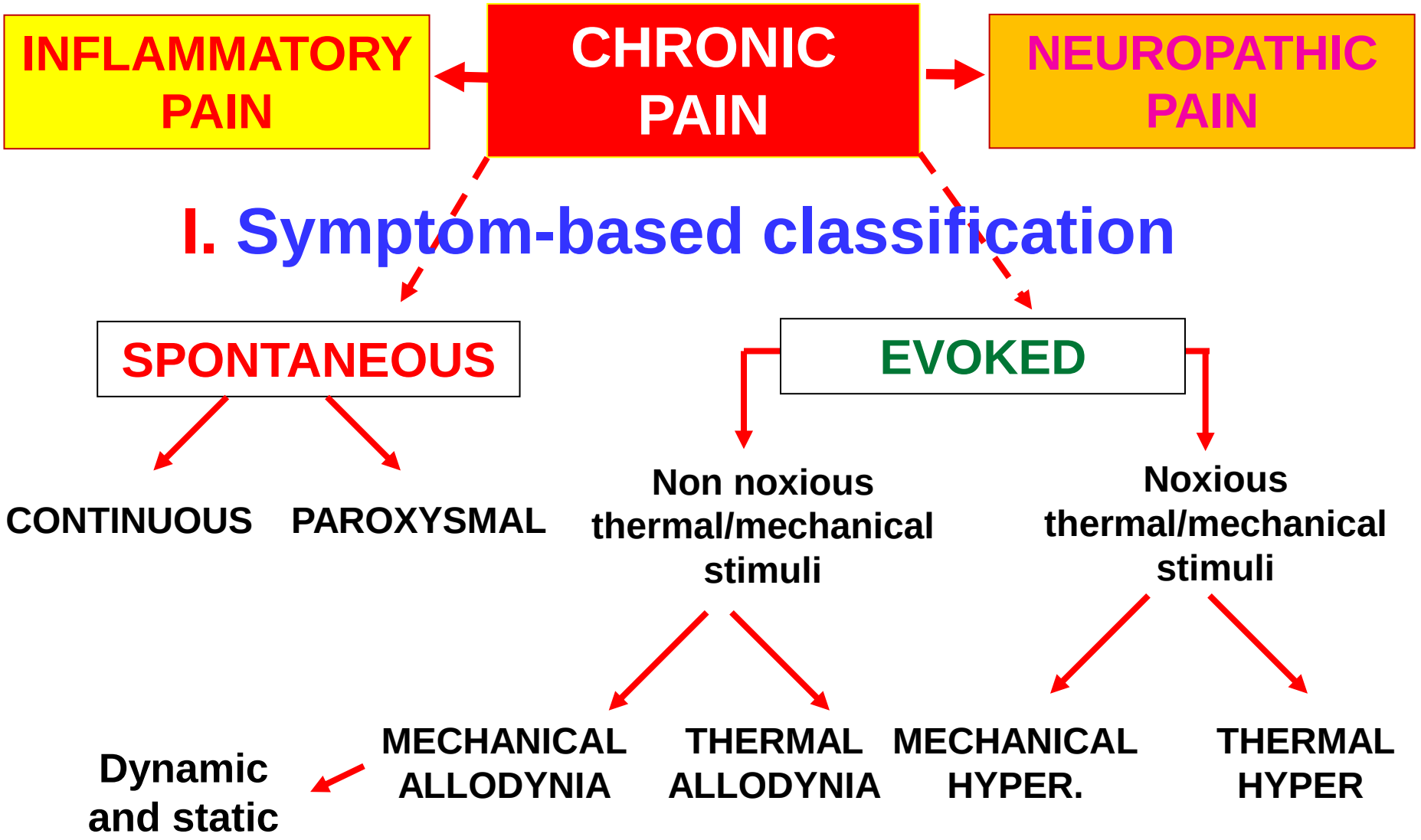
- Cause is known and pain resolves spontaneously
- Somatic pain (bones, joints, muscles)
- Visceral pain (internal organs, e.g. stomach).
- Activation of nociceptors
- **Responsive to common analgesics**

Chronic pain 'bad' no useful function

- Cause often unknown
- Duration >6 months, can last for years or life time
- Affects **~ 20%** of population world wide
- **Inflammatory** (tissue injury) **pain** & **neuropathic** (nerve injury) **pain**
- Abnormal/spontaneous impulse generation in afferent axons.
- **Often resistant to common analgesics**

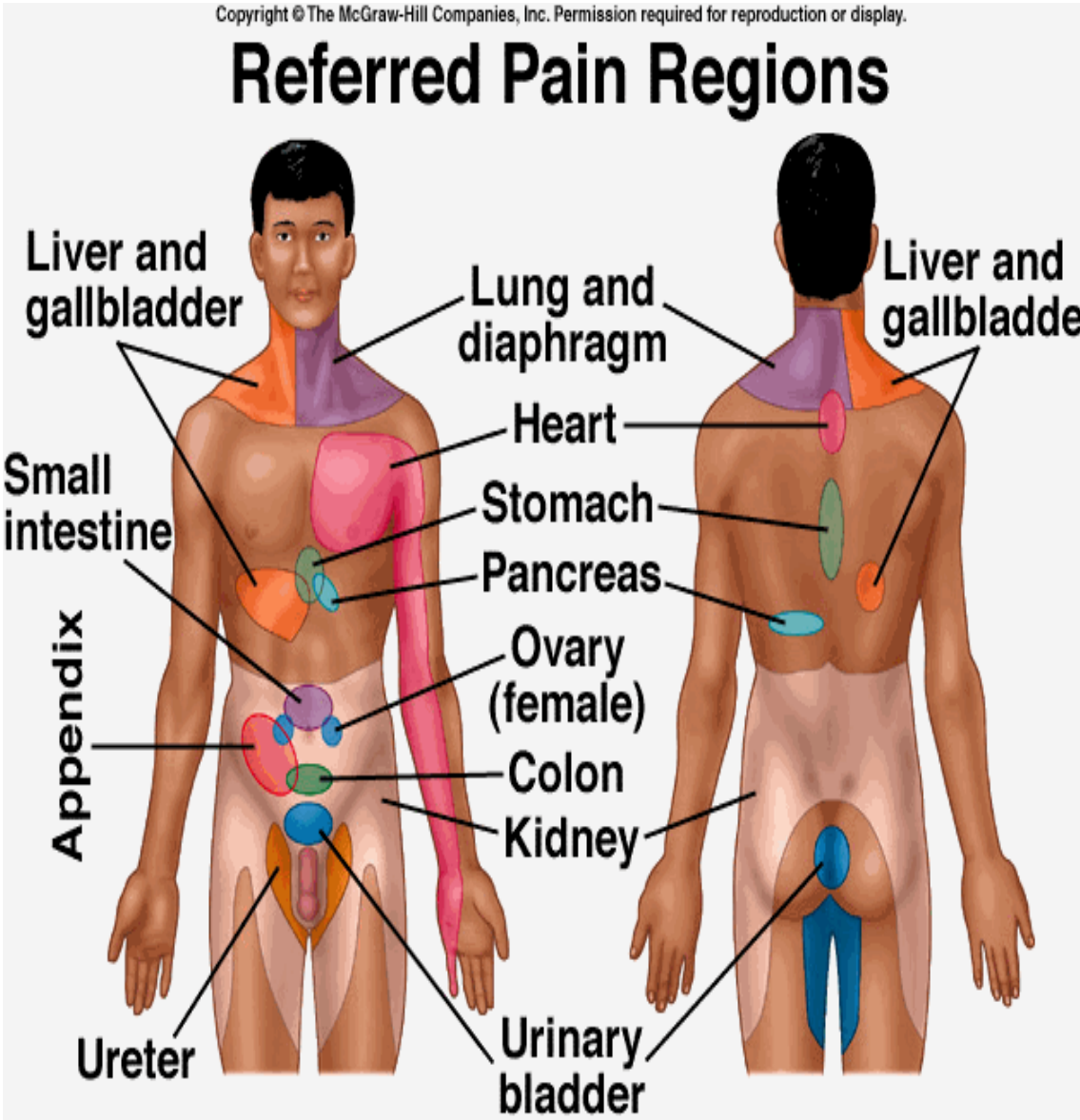
Classification of Chronic Pain

II. Cause-based classification



Referred Pain

- Visceral pain that is felt at a somatic structure that can be far away from the origin site
- Poorly localized and **is not identical in all people:**
  - **In some people** heart pain can be referred to right (not left) arm or neck



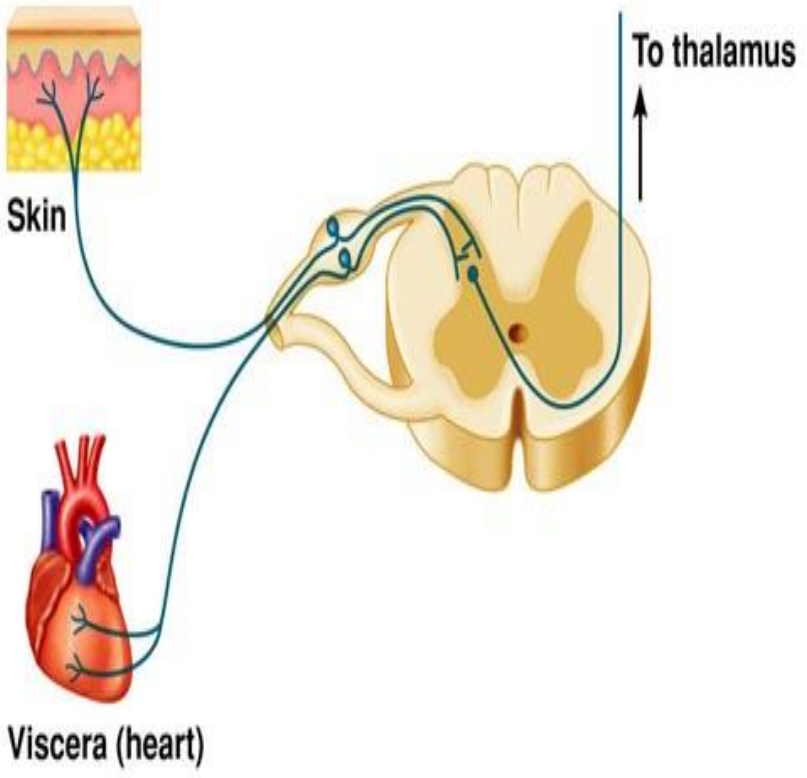
Basis of Referred Pain

- **Convergence theory:**

Referred pain is presumed to be due to converge of cutaneous and visceral nociceptors onto the same spinothalamic tract (STT) neurons

- **Facilitation theory:**

Pain fibers from a visceral organ decrease the threshold of STT neurons, increasing their excitability



The brain interprets the information coming from visceral nociceptors as having arisen from cutaneous nociceptors, because this is where nociceptive stimuli originate more frequently


Thank You
Any Questions
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