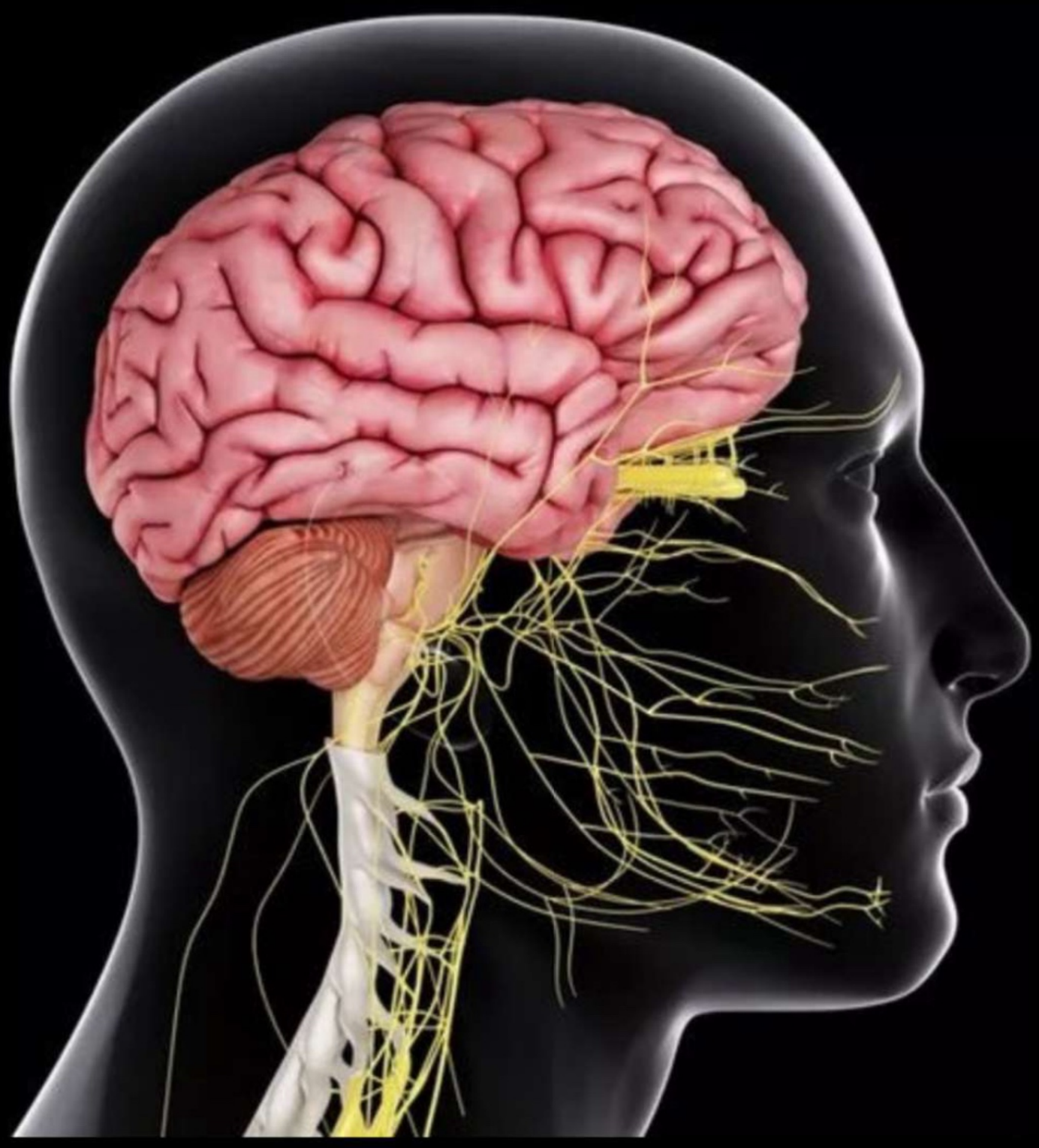
ناجي : سكة

الدعثور : سكة
وسرح

النادي الطبي

CENTRAL NERVOUS SYSTEM



SUBJECT : physiology

LEC NO. : 3

DONE BY : Nehaya & Jana

وَقُل رَّبِّ زِدْنِي عِلْمًا

Slow pain & crude Temp (slow قديم) paleo

localized
fast pain & first Temp (new fast جديد) neo

cortical

Subcortical

Reticular fav. (neurons في in BM core)

nonspecific n. (thalamus)

⇓

arousal

Spinothalmic مراجعة من elect 2

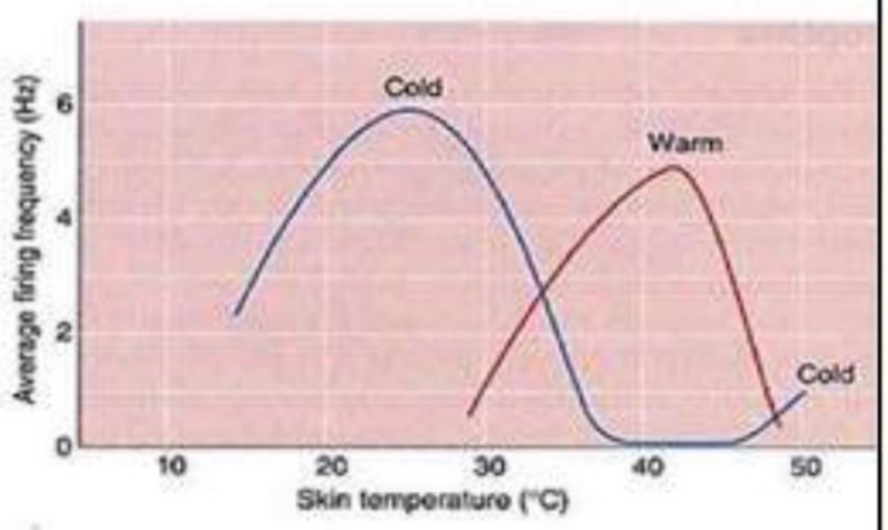
lateral
- pain
- Temp.
- sexual sensation

anterior
- touch
- tickle
- itch

Thermoceptive Sensation

Characters of thermal receptors

- Have a small receptive field and widely separated.
- * Cold R. are 10 times more numerous than warm R. عدد
- Cold R. * adapt more slowly than warm. (يشفر بالوصول signals للدماغ)



Thermoreceptors are stimulated chemically by changing the metabolic rate

in extreme Temp there is pain activation (WHY): Both pain & Temp are located in lateral white column (spinothalm So they're close ↓

⊕ Temp = ⊕ pain
↓
extremes *

- There are 2 types of thermoreceptors (1) Internal thermoreceptors located in the anterior hypothalamus for detection of the head temperature (2) External thermoreceptors: These include cold and warmth receptors and also certain pain receptors that are stimulated only by extreme degrees of heat and cold (leading to the freezing cold and burning hot sensations). These receptors are located under the epithelial layer of the skin, and there are discrete cold and warmth sensitive spots (with thermally insensitive areas in between), and the cold spots are 4-10 times more in number.

من المحاضرة الاولى:

Thermo is moderetly adapting

- THE WARMTH RECEPTORS are special free nerve endings that transmit warmth sensation along with type C afferent nerve fibers.
- THE COLD RECEPTORS: They are free nerve endings transmitting cold sensation along type C and type A- delta nerve fibers (لسرعه لانه اخطر البرد)

The thermosensitive pain receptors are brought into action below 10o C and above 45oC. pain امتداد الطيف لل Temp من

كن نعرف إذا بارد أو سخن من حرارة الجلد المحسوس باد Thermoreceptors على ال skin & SC ليه؟ ↓
برد : جلدي بارد (لانه دلل على ماهو سخن = فقد حرارة)

* ليه؟ Receptors البرد أخطر = (VC = لا يصلو دم

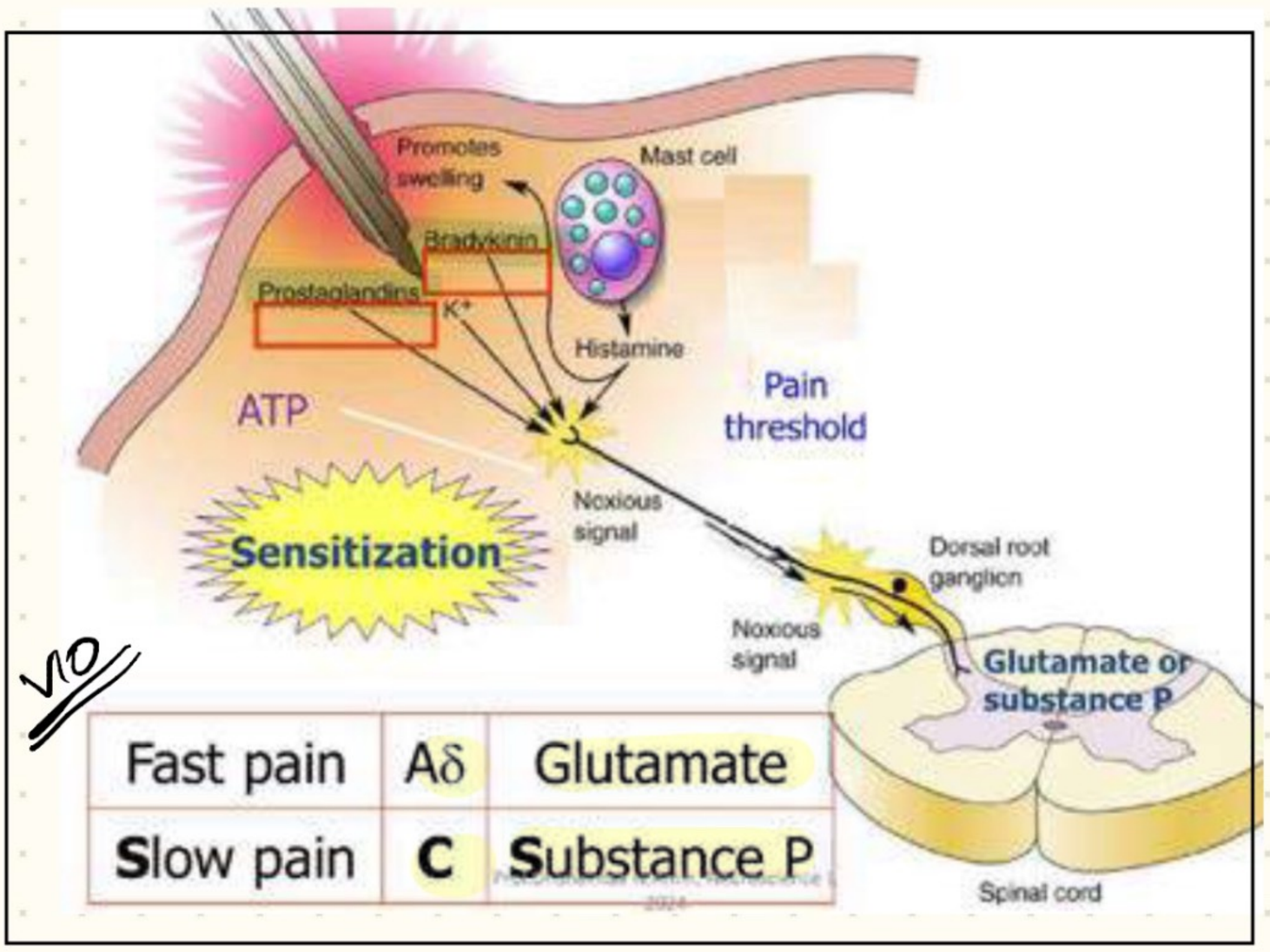
- **Stimulation of the thermoreceptors i**s stimulated chemically by changes in their metabolic rates produced by the thermal stimuli.
- **Adaptation of the cutaneous thermoreceptors:** These receptors are moderately adapting, and the warmth receptors adapt more rapidly than the cold receptors.
- **Central pathway of thermal sensations:** the lateral spinothalamic tract.

- **Testing thermal sensations**: This is carried out by touching the skin with the end of a metal tube that is electrically heated in a controlled manner, and the subject with closed eyes is asked to differentiate between various temperatures. Test tubes containing hot and cold water at different temperatures can also be used

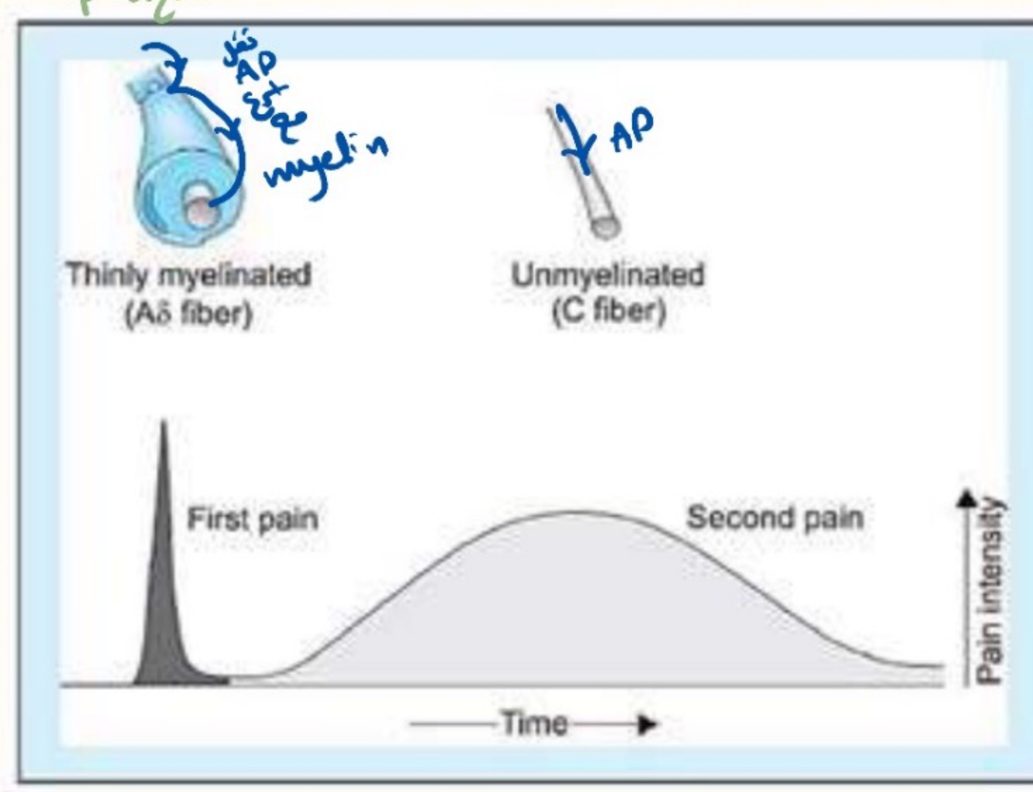
Pain

Nociceptors

- Free nerve endings, slowly (non) adapting to prolonged stimulation
- 4 types:
  a. Mechanical pain receptors.
  b. Thermal pain receptors.
  C. Chemical pain receptors.
  d. Polymodal pain receptors



Fast pain	Aδ	Glutamate
Slow pain	**C**	**S**ubstance P



PAIN SENSATION

- Pain is a specific unpleasant sensation, but its adequate stimulus is not specific (produced by any noxious stimulus, whether mechanical, thermal or chemical. It has a protective function and is almost non-adapting
- **Pain receptors (the nociceptors)** are specific naked free nerve endings. They are more abundant in the skin than in the deep tissues and viscera, and they are stimulated mainly chemically by substances released from damaged tissue, especially bradykinin and certain proteolytic enzymes
- Actually, nociceptors are ion channel, which are called Transient Receptor Potential channel (TRP).

- All TRP channels are gated by temperature and various chemical ligands, but different types respond to different temperature ranges and have different activation thresholds. At least six types of TRP receptors have been identified in sensory neurons.
- **Fast and slow pain**: According to its site, pain may be classified into cutaneous, deep, and visceral pain. However, it is more frequently divided into fast and slow types.

To remember
ناجي : الاسبل
regenerated بتكون
- free (unencapsulated)
- C/γ afferent
less (السرعة)

تذكروا من pathо
general
pain by • BK
mediators • PG
• His b.

neo : γ
مستو بستقبله اد
مستو ما يستقبله اد cortex
cortex المحترم

Types of pain

Fast pain	Slow pain
Felt within 0.1 sec	Felt within 1 sec or more
Short duration	May be prolonged
Well localized	Poorly localized
Mechanical or thermal	All types of receptors
Usually in skin, rare in deep tissues	Skin, deep tissues & viscera

Fast pain	Slow pain
Carried by Aδ, blocked by pressure	Carried by C, blocked by local anaesthetics
Aδ release Glutamate	C release Substance P
Transmitted by Neo-spinothalamic T	Transmitted by Paleospinothalamic T
Its fibers end in sensory cortex	End in RF → Non-specific thalamic nuclei → whole cortex

	FAST PAIN	SLOW PAIN
Site (origin)	Almost only in the skin	Skin. deep tissues and viscera
Stimulus	Mainly the mechanical and thermal noxious stimuli	Mechanical, thermal, and chemical. noxious stimuli
Quality	Pricking (sharp or acute)	Burning (aching or chronic)
Perception	0.1 second after stimulation	second or more after stimulation
Duration	Less than one second	Many seconds to a few minutes
Localization	Well-localized	Diffuse (poorly-localized)
Afferent nerve	Type A-delta nerve fibers which release glutamate	Type C nerve fibers which release substance P
Carrying tract	Neospinothalamic tract	Paleospinothalamic tract
Centre in CNS	Cerebral cortex	Reticular formation & thalamus

Central perception of pain sensation

- Pain sensation is transmitted to the higher centers by the lateral spinothalamic tract, which consists of 2 parts

(l) ***Palaeospinothalamic tract*** transmits slow pain and terminates subcortically, especially at the reticular formation and the intralaminar thalamic nuclei.

(2) ***Neospinothalamic tract:***transmits fast pain, and its fibers relay first in the ventrobasal complex of the thalamus, then finally terminate at the cortical somatic sensory areas

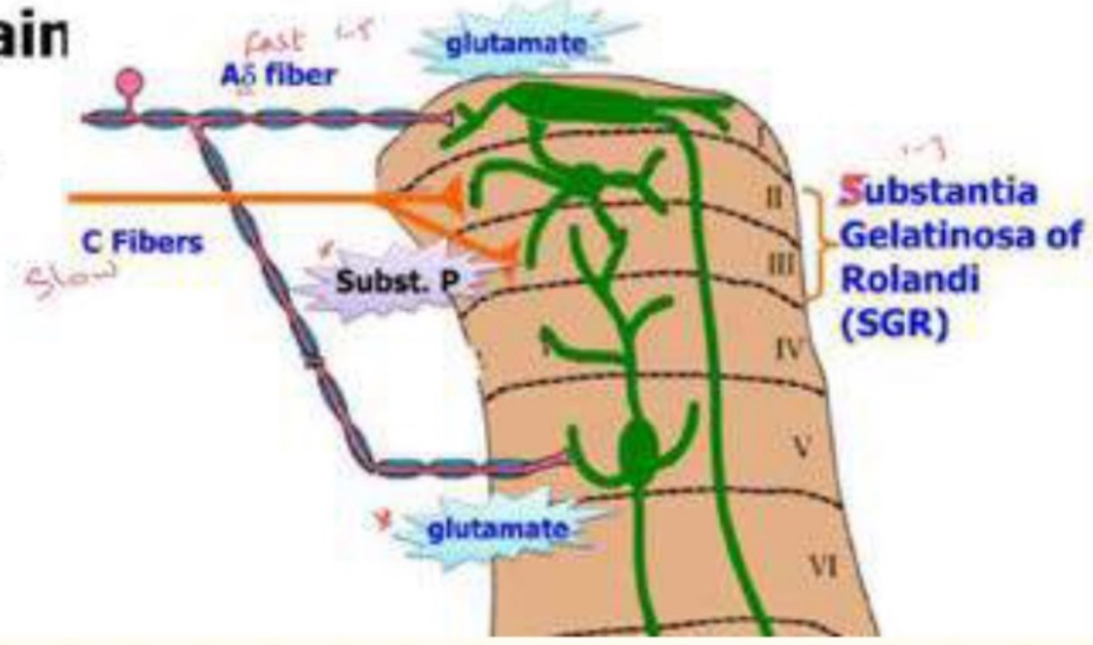
"الله هو
الي يحافظ
عليا مش احنا
الي بنحافظ
على نفسنا"

- Removal of the cortical somatic sensory areas does not abolish the perception of both types of pain. This indicates that pain is generally perceived mainly at a subcortical level (in the thalamus, reticular formation, and other lower centers). However, the cortical centers are essential for interpreting the quality and locality of pain.

قلنا الـ لا عددهم
اقل الأغلب ⇐
مش معناه ما بيستقبله
subcortical = cortex

Roles of the cortex in pain perception are ?

1. **Localization of pain.**
2. **Discrimination of pain**
3. **Modulation of pain.**



Distribution of pain receptors

pain insensitive ⇓

Widely distributed	Less distributed	Absent
Sup. Layers of skin (1) Periosteum (2) Arterial walls (3) Joint surface (4) Flax & tentorium of cranial cavity (5)	Deep tissues & Viscera	Liver (1) Parenchyma (2) Lung alveoli (3) Brain tissue (4)

less receptors in viscera

5. visceral الأغشية
pleural/peritoneal/pericardial

CUTANEOUS PAIN:

- This may be fast, well-localized, pricking, or slow, diffuse burning pain. It is not referred to and is tested by either pricking the skin with a pin or heating the subject's skin and recording the temperature at which pain occurs.

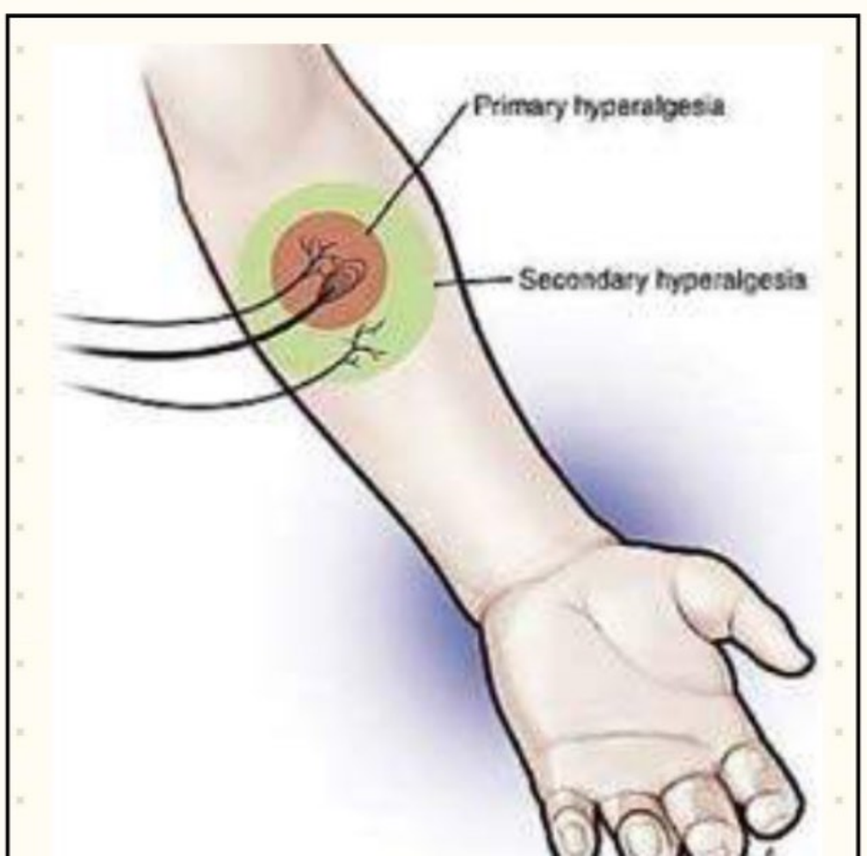
CUTANEOUS HYPERALGESIA

- : This is pathological hypersensitivity to pain. It is of 2 types:

(I) ***Primary hyperalgesia:*** This occurs in the injured skin area and the surrounding area of flare V.D.), in which the pain threshold is lowered so that non-noxious stimuli become painful). It is due to sensitization of the pain receptors by some substances released from the damaged tissues (histamine, kinins, K, certain enzymes, or prostaglandins). It has also been suggested to be due to the release of substance P from nerve endings due to a local axon reflex through antidromic impulses, which sensitizes the pain nerve endings and produces V.D. (i.e. flare), the triple response

- (2) ***Secondary hyperalgesia:*** This occurs in the healthy skin area beyond primary hyperalgesia. The pain threshold is not lowered in this area but is normal or even elevated. However, the pain aroused from such an area is prolonged and exaggerated. This is explained by the convergence facilitation mechanism, which occurs as follows: The central neurons are facilitated by impulses discharged from the area of injury, and afferent fibers from the area of secondary hyperalgesia converge on the facilitated neurons. Thus the pain aroused in this area becomes exaggerated.

- ** Secondary hyperalgesia can occur in the absence of primary hyperalgesia if there is central facilitation of sensory transmission. This occurs in certain thalamic and spinal cord lesions



DEEP PAIN:

2

- This originates from muscles, joints, periosteum. It initiates reflex contraction of near muscles Deep pain may result from trauma to the deep structures, bone fractures, and inflammation, arthritis inflammation of joints) and muscle ischemia.

ISCHEMIC PAIN

- This occurs due to either a severe muscle spasm cramp) or occlusive vascular disease. A certain metabolite known as the Lewis P factor causes pain if it accumulates in the muscle. At rest, muscle ischemia causes the liberation of a small amount of this factor (due to damage of some muscle fibers) that can often be washed off, so pain is absent during rest. However on performing an exercise, the P factor is formed in larger amounts that accumulate in the muscle (due to the impaired blood flow), leading to pain Thus, ischemic pain appears only after a latent period from the start of exercise. Examples of this pain are (a) Angina pectoris and (b) Intermittent claudication (severe pain in the muscles of the lower limbs during walking that commonly occurs as a result of vascular occlusive disease).

VISCERAL PAIN

3

- Pain is almost the only sensation produced from the viscera (since there are only a few thermal and touch receptors and no proprioceptors in the viscera). Most viscera contain only a few pain receptors, so localized damage does not cause significant pain. However, generalized damage causes significant pain. Also, if a viscus is inflamed, minor stimuli may cause severe pain, a type of primary hyperalgesia. Some viscera are pain insensitive, e.g., the liver tissue, lung alveoli, the visceral layers of the peritoneum, pleura, and pericardium (but the parietal layers of these membranes are very painful).

- *Characters of visceral pain*: It is frequently referred to specific areas in the skin. It is often associated with sweating, nausea, parasympathetic effects (e.g., bradycardia and hypotension), and some somatic effects, e.g., contraction of the near abdominal muscles (known as guarding rigidity).

REFERRED (RADIATING) PAIN

- This pain is felt away from its original site. It is most common with visceral pain (deep pain may be referred, but cutaneous pain is not referred). The structure in which pain originates and the structure to which pain is referred develop from the same embryonic segment, and frequently they are far away from each other due to the migration of the various organs during development

same root بغذيهم

visceral pain
: receptors are widely seperated
حتى يحصل ⊕ عالي لازم ⊕ عدد receptors كبير

EXAMPLES OF REFERRED PAIN

(1) Pain of an inflamed gall bladder is transmitted by afferent phrenic nerve fibers, so it is usually referred to the tip of the right shoulder.

(2) Cardiac pain is usually referred to the left shoulder and inner side of the left arm (less frequently to the right shoulder or the epigastrium).

(جهة القلب LT)

(3) Pain from the kidneys and ureters is referred to the testicular region.

(4) Pain of appendicitis is referred to the umbilical region.

Radiated vs. Refferred

Radiated: الألم في مكان المشكلة والمكان الآخر

Refferred: الألم في مكان آخر غير مكان المشكلة
* MI
* GB

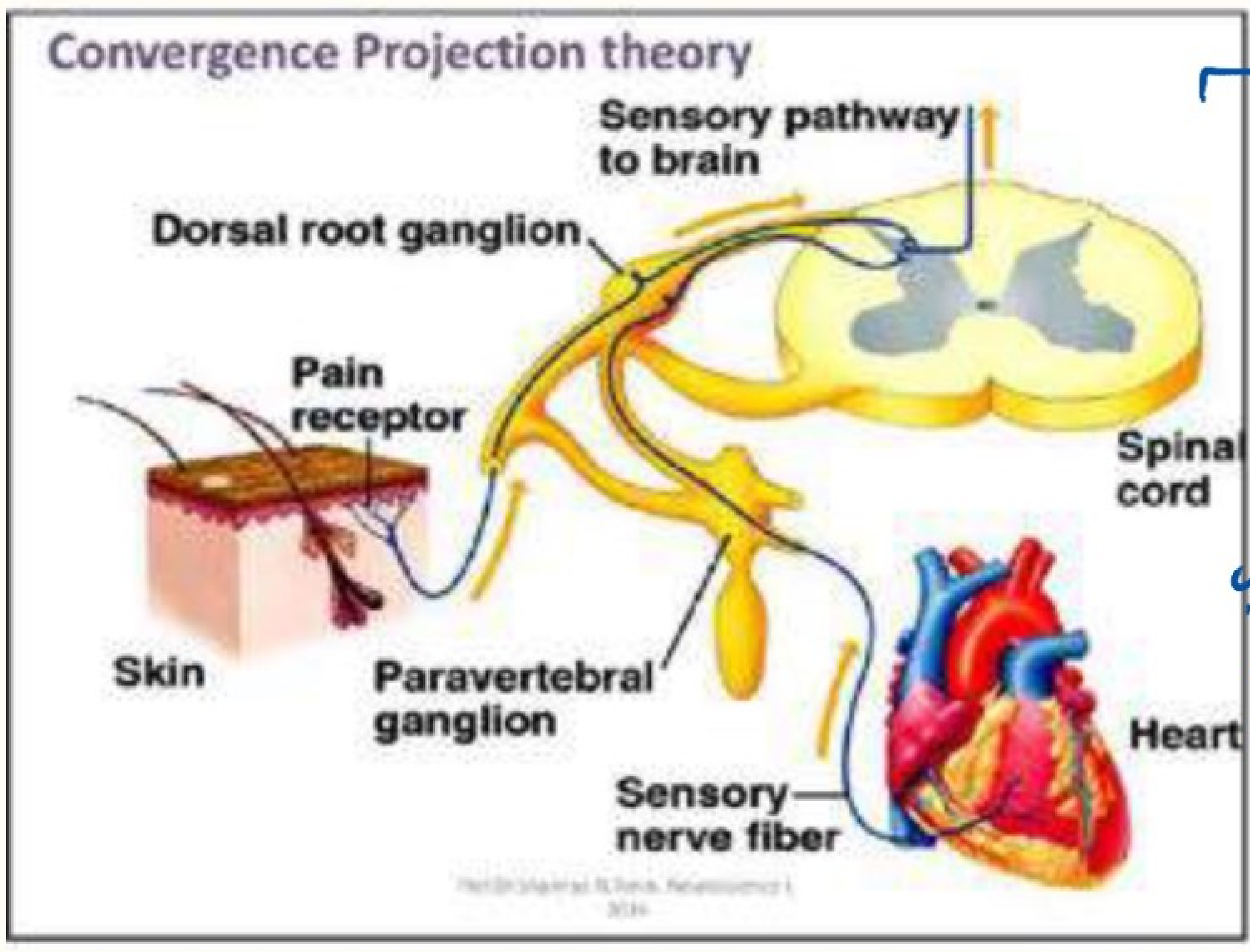
not only visceral
الـ refferal عكس
← بضل الـ autonomic / somatic sensations
autonomic → Nausea & vomit
somatic → muscle cont.
↓
عند فحص الـ abdomen
حالة التهاب المرارة: الـ abd wall هيكون متحجر لانه في referred muscles واصل الـ contraction وعامله

- MECHANISM OF REFERRED PAIN:

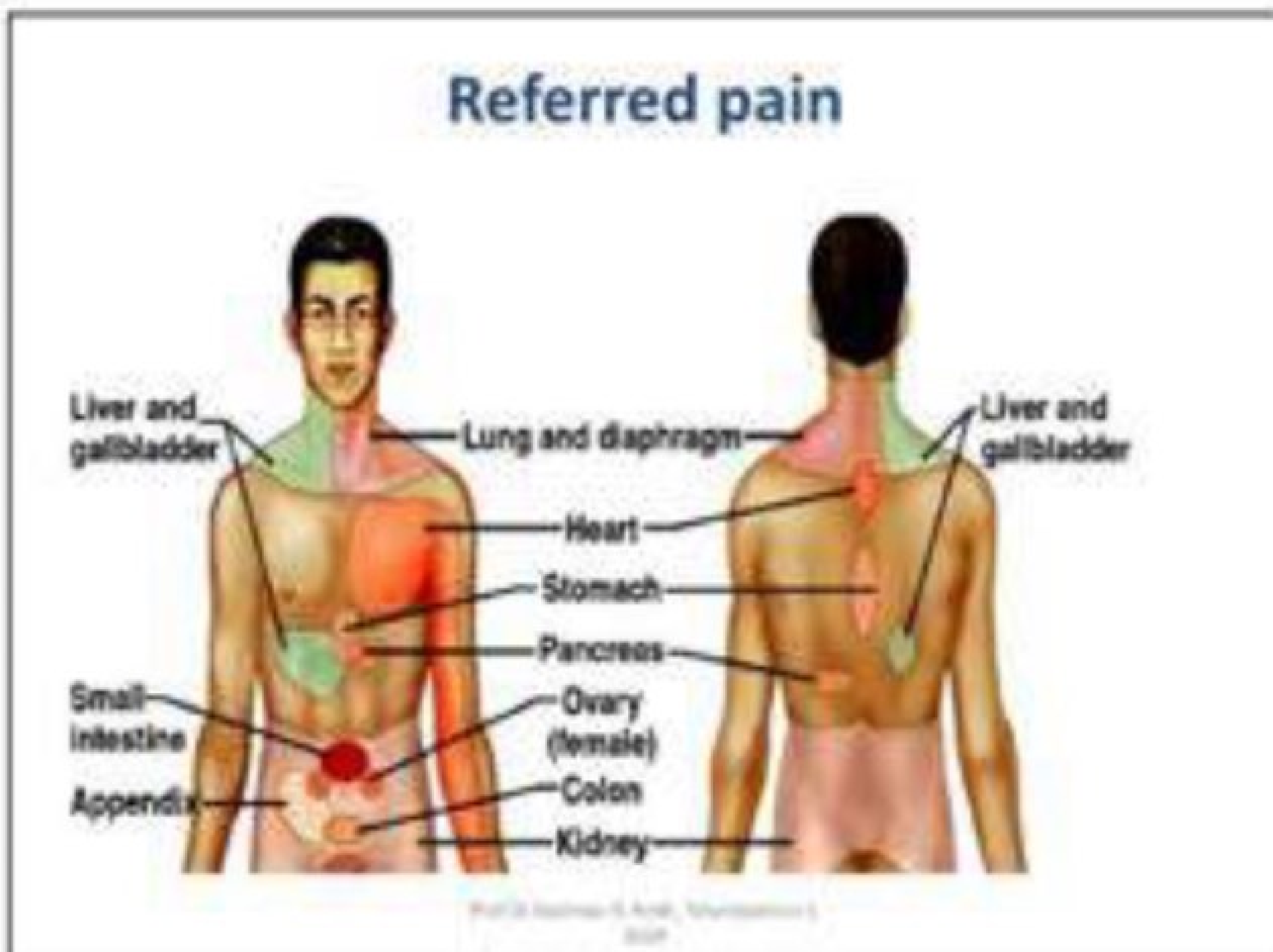
The main cause of referred pain is the convergence of peripheral and visceral pain fibers on the same spinothalamic neurons that project to the high centers in the brain (in addition to plasticity in the CNS). It is explained by the convergence projection mechanism as follows: Pain stimuli from a diseased viscus excite the spinothalamic neurons at a certain segment of the spinal cord, which then discharges to the brain. However, pain is projected to the somatic area from which the sensory nerves enter the same spinal segment. Normally, the brain does not receive signals from the viscera, and it is even unaware of their existence.

(الا)

* الم skin & viscera بلتقات
→ converge in the same (SGR)
بيصلات لنفس الـ cortical area
↓
project pain to skin
لانها متعودة دايما بيجي الـ stimuli منها



→ هاي الـ theory
فكرتها انه جسمك متعود الالم غالبا من الـ skin
مش قلبك زي المدرس لو صار مشكلة بشي بالمتاعب
يلي دايما بتعمل مشاكل مش بالعادي (skin)
(قلب) فبحس بالام متلا shoulders
لانه هيك عقلي ترجمه
+ skin فيه الـ receptors اكثر



Headache

Pain referred to the surface of the head from deep structures.

I. Headache of intracranial origin

- **The brain is insensitive to pain**
- **Pain receptors are found only in :**
  - Venous sinuses
  - Dura
  - Dural arteries
  - Tentorium

I. Causes of intracranial H.

Meningeal causes	Non Meningeal intracranial causes
1. Meningitis	1.Hypertension
2. Brain tumour	2.Drop of intracranial pressure
3. Alcohol	3.Migraine ☆
4. Trauma	
5. Constipation	

II. Causes of extracranial H.

1. Muscular spasm
2. Inflammation of nasal sinuses
3. Errors of refraction ☆☆
4. Otitis media
5. Toothache
6. Systemic disorders
7. Trigeminal neuralgia

☆ vessels spasms → VD → H.

☆☆ إجهاد عضلات العين = H.

HEADACHE

- This is a painful sensation at the head that is referred from other structures, and its causes are either intracranial or extracranial in origin.
- **(A) Intracranial causes of headache**
- The intracranial pain-sensitive structures include (a) The venous sinuses (b) The blood vessels of the meninges, especially the middle meningeal artery (c) The dura at the base of the brain (d) The tentorium cerebelli. Irritation of the supra-tentorial pain-sensitive structures initiates signals transmitted by the trigeminal nerve (leading to frontal headache). In contrast, irritation of the infra-tentorial structures initiates signals transmitted by the second cervical nerve (leading to occipital headache).

mostly **(B) Extracranial causes of headache**

- (1) Eye diseases e.g., glaucoma (due to rise of the intraocular pressure) and hypermetropia (due to persistent contraction of the ciliary muscle), which cause retro-orbital or peri-orbital headache.
- (2) Teeth diseases associated with toothache.
- (3) Sinusitis The headache may be retro-orbital or in the forehead (in case or the frontal sinus) or in the face (in case of the maxillary sinus).
- (4) Otitis media and otitis externa.
- (5) Prolonged emotions and tension (psychogenic headache) partly due to spasm of the muscles attached to the scalp and occiput.

The brain tissue itself is insensitive, and the commonest causes of intracranial headache include the following :

(1) Meningeal irritation by inflammation (= meningitis), tumours, alcohol, and constipation by toxic products absorbed from the colon (although some authors believe that constipation headache is due to rectal distention).

(2) Lowering of CSF pressure: Removal of only about 20 ml of the CSF by a lumbar puncture needle causes severe headaches, especially in the upright position due to stretching and distortion of the various dural surfaces.

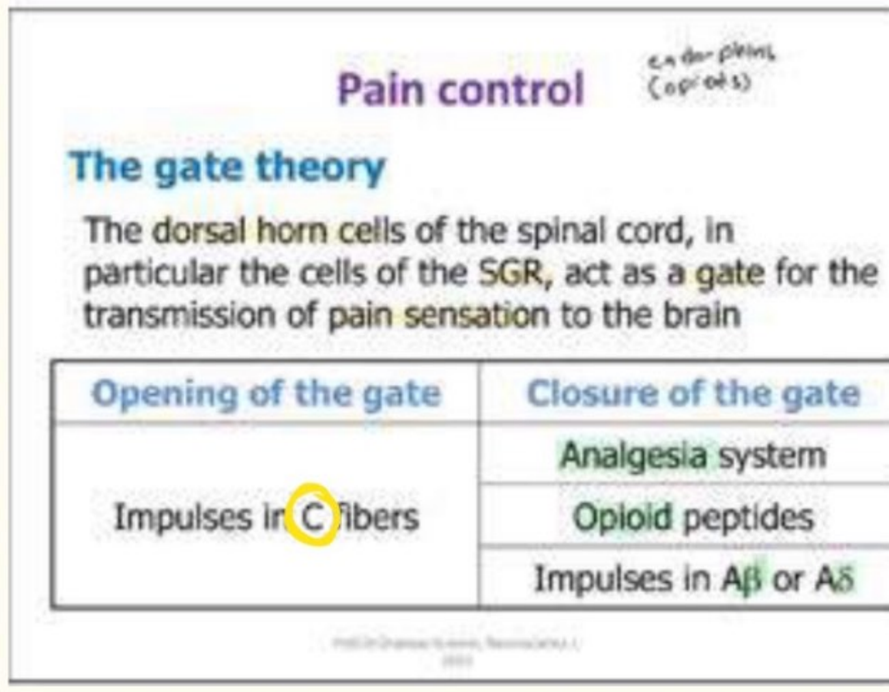
(3) Distention of the intracranial arteries, e.g., fevers, hypertension (which causes throbbing headache), and migraine. The latter has a genetic tendency, and it occurs more in females ♀ commonly following prolonged tension or emotions. These conditions lead to reflex V.C. of the cerebral arteries, which results in ischemia, followed by intense V.D. that causes the headache.

بتعب العضلة

معروفة prodroma
↓blood = ↑metabolite
aura
migraine
episode

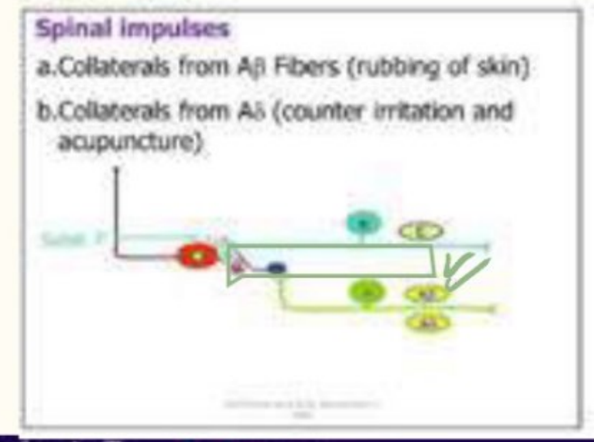
THE PAIN CONTROL ANALGESIA SYSTEM

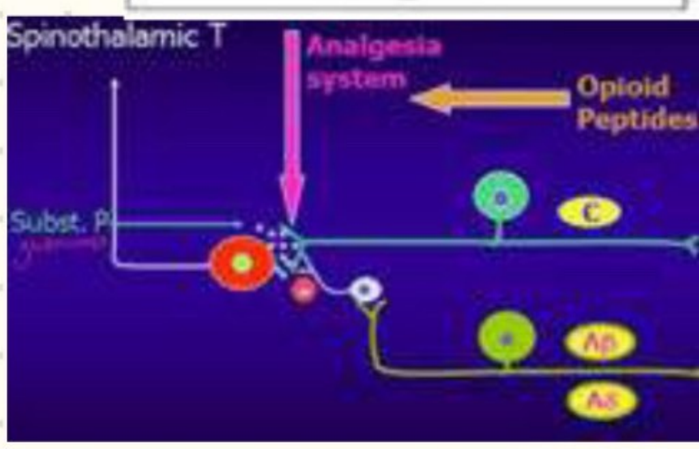
- This is a specific system that blocks pain transmission in the CNS (Its major constituents include the following:
- 1. The periventricular nuclei in the hypothalamus.
- 2. The periaqueductal gray area (PAG) in the midbrain and upper pons.
- 3. The raphe Magnus nucleus (RMN) in the lower pons and upper medulla.
- 4. pain inhibitory complex (PIC) in the spinal cord's dorsal horns.Certain cortical areas are also involved in the pain analgesia system (especially the limbic association areas), and the principal mediators in this system are the opioid peptides (see next)



THE OPIOID PEPTIDES

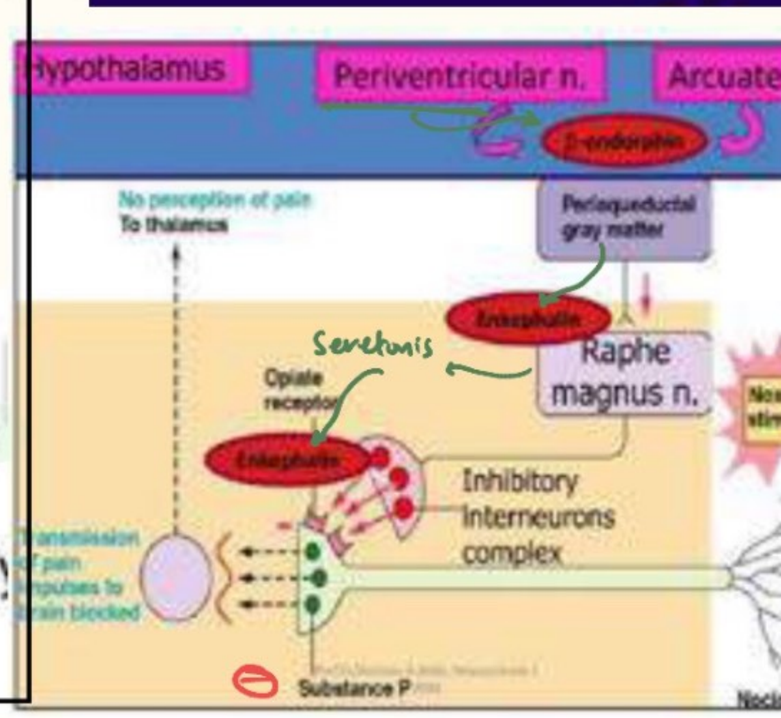
- These are morphine-like neurotransmitters naturally formed in the body (so they are called the own body's morphine). Morphine (the active substance in opium) is a potent analgesic substance that produces its effect by binding to specific opiate receptors in the nervous system. Similarly, opioid peptides are analgesic substances that act by binding to opiate receptors. The most important opioid peptides include the following:
- (1) Enkephalins : These are 2 types, met- enkephalins and leuenkephalin.
- (2) Endorphins: There are several types, the commonest of which is beta-endorphin.
- (3) Dynorphins are normally present in minute amounts in the CNS





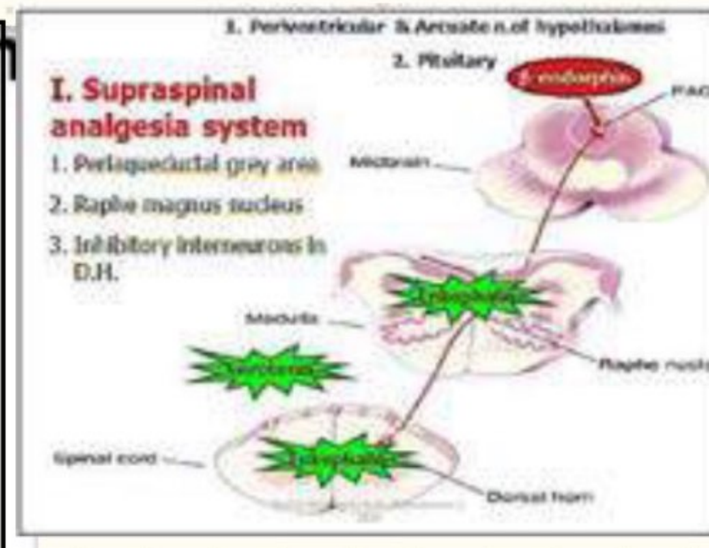
- **The opiate receptors**

These are 5 types, and they are especially present in the analgesia system and on the central endings of the pain- conducting nerve fibers at the dorsal horns. They can be stimulated both exogenously (by morphine) and endogenously (by the opioid peptides).



Mechanism of pain control by the analgesia system

- **The Gating Theory:** Ronald Melzak and Patrick Wall proposed this theory in 1960.The hypothesis focused on the interaction of neurons in the dorsal horn of the spinal cord (Lamina I to IV).The analgesia system produces its effect by stimulating the Pain Inhibitory complex (PIC). The PIC consists of short enkephalinergic neurons that terminate on the central endings of the pain-conducting afferent nerves. The released enkephalin is believed to cause both presynaptic and postsynaptic inhibition of incoming type C and type Aδ pain fibers where they synapse in the dorsal horns



- Pain inhibition by this mechanism occurs through the following 2 pathways:

(A)Peripheral pathway of pain inhibition (spinal inhibition): Collaterals from the thick A-beta nerve fibers that transmit mechanoreceptive sensations directly stimulate the PIC. This explains how pain is relieved by counterirritants, mechanical stimuli (e.g. skin rubbing), and acupuncture (see below). Depending on such a mechanism, severe pain can be relieved by electrical stimulation of the thick sensory nerve fibers.

- ***(B)Central pathway of pain inhibition (supraspinal inhibition):*** Excitation of the hypothalamic periventricular nuclei or certain cortical areas depresses pain as follows:
  - (I) The nerve fibers from the hypothalamic or the cortical areas release beta-endorphins, which stimulate the PAG.
  - (2) The PAG projects enkephalinergic neurons (i.e. neurons that release enkephalin) that stimulate the raphe Magnus nucleus (RMN).
  - (3) The RMN projects serotonergic neurons (i.e., neurons that release serotonin) that block pain signals by activating the PIC.
- It is also probable that the analgesia system can inhibit pain transmission at other points than the PIC, especially at the thalamic intralaminar nuclei and the reticular nuclei in the brain stem.

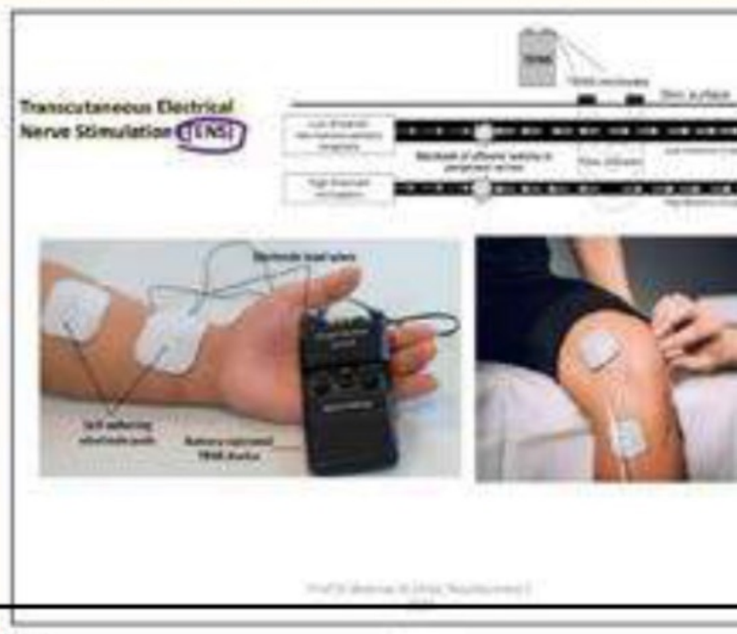
Stress analgesia: Certain stress conditions are associated with analgesia e.g. during the stress of a battle, severely-wounded soldiers frequently feel no pain till the battle is over. Such analgesia is produced by impulses discharged from the cerebral cortex and hypothalamus, which excite the central pathway of pain inhibition (see above)

- **Acupuncture**: Acupuncture relieves pain by activating the peripheral pathway of pain inhibition and psychogenic excitation of the central pathway. Both mechanisms lead to stimulation of the PIC in the dorsal horns of the spinal cord, which blocks pain transmission by releasing enkephalins (see above)

وأن ليس للإنسان إلا ما سعى

Transcutaneous electrical nerve stimulation (TENS) activates a complex neuronal network to result in a reduction in pain. At frequencies and intensities used clinically, TENS activates large-diameter afferent fibers.

A-beta & delta

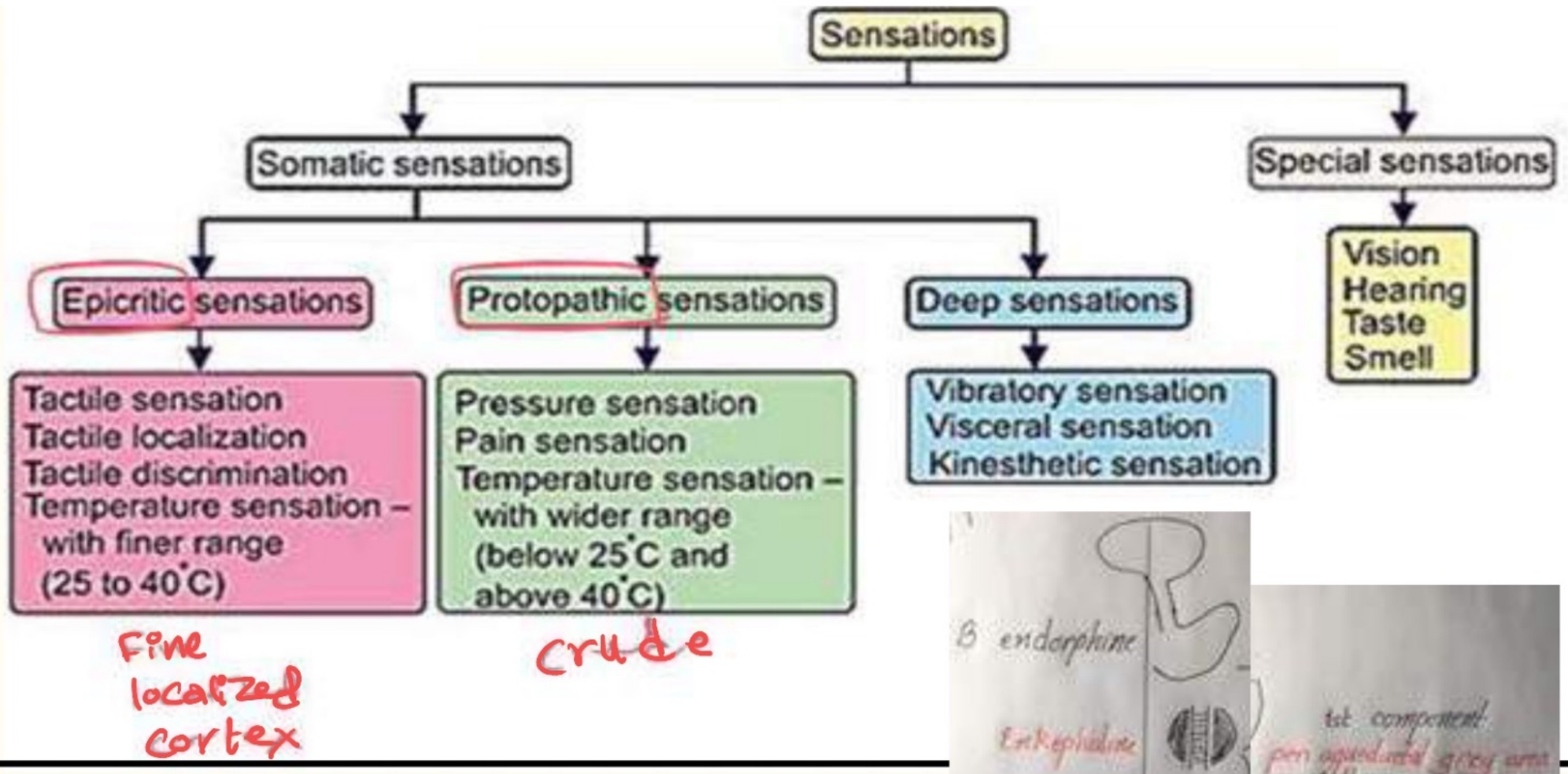


mild
peripheral ⊕ = ⊕ß fibers = محفزات كهربائية خفيفة توضع باليد

الرد ← lateral inhibition (inhibitory complex 2nd order neuron)

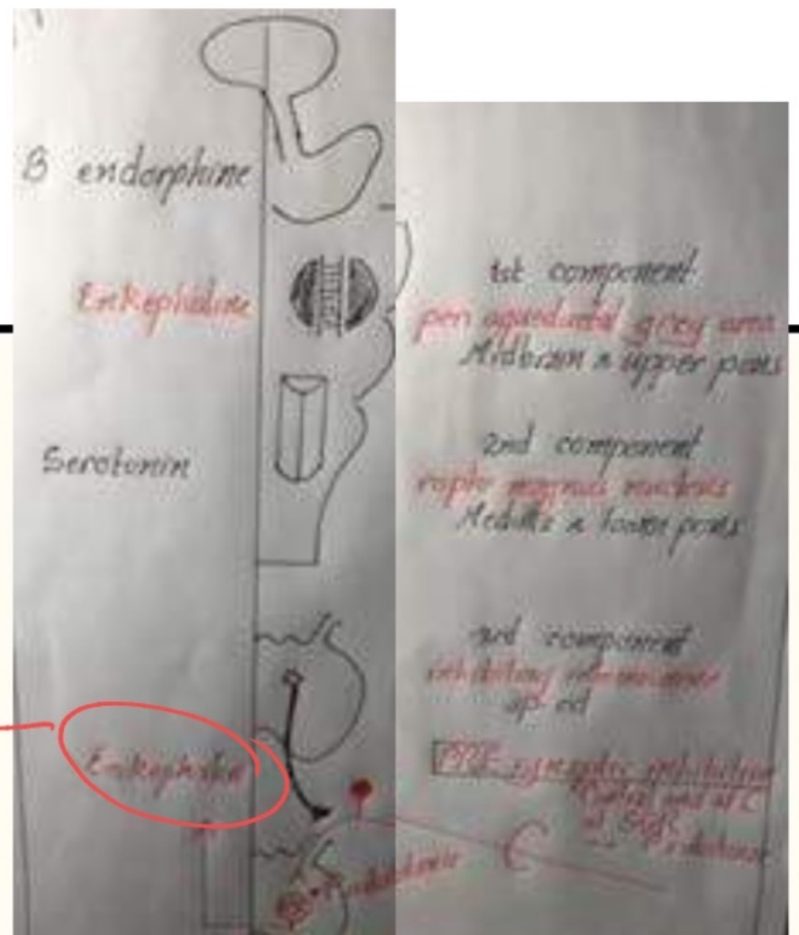
PROTOPATHIC AND EPICRITIC SENSATIONS

- 1) **Protopathic (primitive) sensations**: These are crude sensations that are perceived at a subcortical level (mainly at the thalamus). They include gross movements ("joints, crude pain and tactile sensations and extremes of temperature.
- (2) **Epicritic (cortical) sensations:** These are fine sensations perceived in the cortical sensory areas, e.g. tactile Localization and discrimination, stereognosis, and fine grades of temperature. These sensations are well localized.



Fine localized cortex

crude



الوصيلة النخاعية ← supraspinal