



## 30<sup>th</sup> Lecture

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## Pain Modulation

**PHYSIOLOGY TEAM – 430**

This Lecture is done by:

Al-Waleed Al-Johar

## Pain Modulation

- **Introduction:**

- Pain modulation means pain perception variability which is influenced by endogenous and exogenous mechanism

- **Pain variability:**

- Pain varies from person to another, it is controlled by three factors, they are:

1) Spinal Modulation

2) Supraspinal Modulation

3) Opioid Neurotransmitters Modulation

### 1) Spinal Modulation (Gate Mechanism):

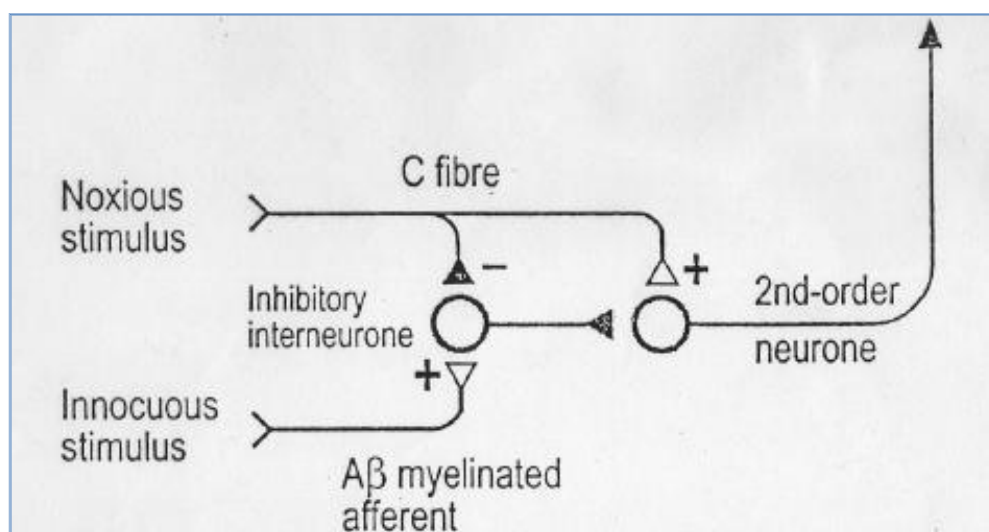
- When we feel pain → We rub its site → Stimulation of A $\beta$  fibers → stimulation of interneuron → it inhibits 2<sup>nd</sup> order neurons of C fibers → Pain goes away

- Further Explanation:

When we feel pain we rub it, while rubbing we are stimulating the A $\beta$  fibers, these fibers stimulate an interneuron that is located between C & A $\beta$  fibers, and that interneuron will inhibit the 2<sup>nd</sup> order neuron of C fibers "which are responsible for slow pain transmission"

**Note:**

A $\beta$  fibers are only effective against C fibers but not A $\delta$ , because A $\delta$  fibers are so fast that they transmit pain before you have a chance to rub



## 2) Supraspinal Control:

- It means pain modulation from higher control
- Ascending fibers (From SC to Thalamus) → Pain Stimulation
- Descending fibers (From Cortex and Thalamus to SC) → Pain Inhibition
- Descending fibers pathway:  
Cortex → Midbrain (Periaqueductal Gray Matter) → Medulla (Nucleus Raphe Magnus) → Dorsal horn of SC

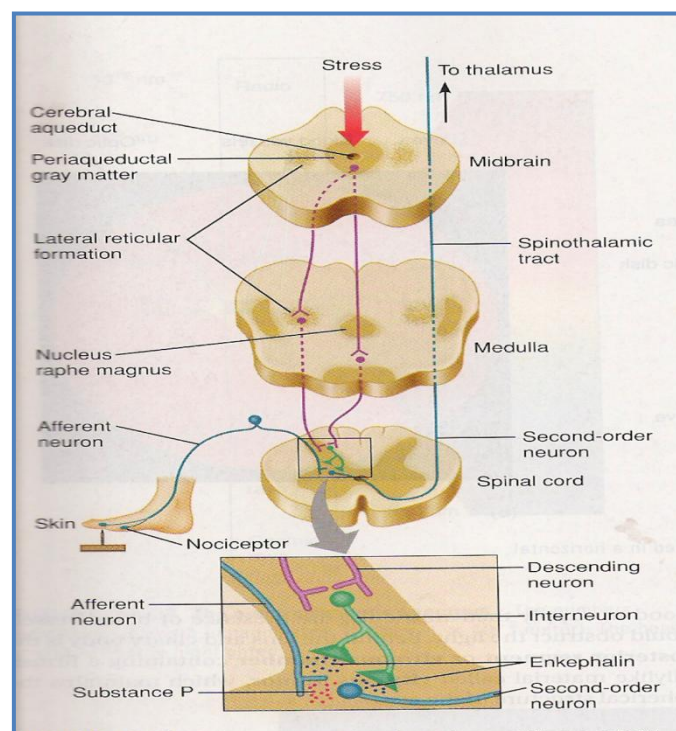
## 3) Opioid Receptor Modulation:

- There are secretions of pain inhibitors at the level of the Mid Brain, Medulla and Dorsal horn of SC
- Mainly Endorphin + Enkephalin are released to relief pain, they are morphine like substances
- **Enkephalin is released mainly in PAG of Midbrain and Dorsal Horn of SC**
- **Serotonin is released mainly in Raphe Magnus of Medulla**
- Enkephalin works via inhibition of Substance-P Pre & Post synaptically

**Remember !** (this is a note to help you link everything together)

Substance-P is the pain transmitter in C Fibers, and we said C fibers are the ones that are inhibited in pain modulation not A $\delta$ , if we want to inhibit A $\delta$  we have to inhibit Glutamate. but we can't because it's fast

- If there's a lot of pain, we inject morphine (Mechanism of morphine action is well discussed in Pharmacology )

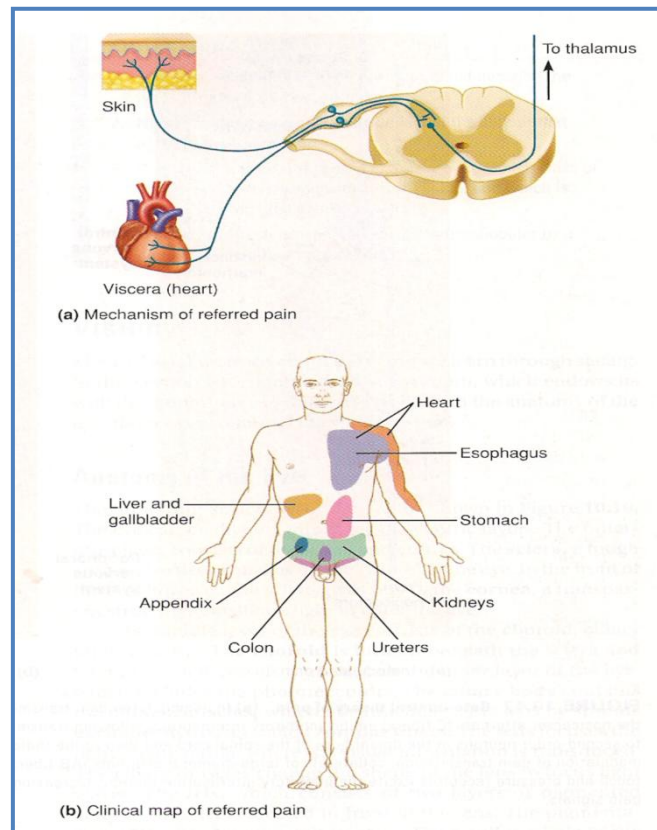


- **Referred pain:**

- The problem is in one organ but pain is referred to another place

- **Theory of referred pain: Convergence theory:**

The organ which is causing the pain, and the place where the referred pain is felt, both synapse at the same level of SC. The brain always think that pain comes from the skin, and rarely comes from visceral organs, so when an organ produces pain the brain will always think that it's the skin because it is used to receive pain from there



- **Sites of referred pain:**

Organ	Site of referred pain
Meninges	Back of head and neck
Heart	Central chest, arms (usually left), neck, occasionally abdomen
Trachea, Esophagus	Behind sternum
Diaphragm	Shoulder tip
Stomach, Duodenum	Upper abdomen, epigastrium
Small bowel, Pancreas	Around umbilicus
Large bowel, Bladder	Lower abdomen, above pubic bone



- **Visceral pain:**

- It is the same as the referred pain
- No pain receptors inside the intestine wall, they are located in the mesentery
- Pathway of Visceral pain:  
Aδ Fibers carry pain and goes with the Autonomic Nervous System (Through the vessels) → SC → Lateral Spinothalamic Tract → Thalamus → Somatosensory cortex
- Associated with nausea and autonomic disturbance (Because it's accompanied with the ANS)
- It is poorly localized
- It is often referred to another part of the body
- Cutting and crushing are not painful when applied to viscera (Because there are no pain receptors)
- Pain is caused by distension, ischemia and inflammation (Because it will then involve other parts which are rich in pain receptors)

- **Chronic pain (Refractory pain, Neuropathy pain):**

- Very hard to treat
- Two good examples:

- ✓ **Post Herpetic Neuralgia:**

After being cured from Chicken Pox during childhood, the virus will hide in the dorsal root ganglion. Years later, after growth, this virus will rise again and attack the nerves (Because it was hidden there), mainly will damage the intercostal nerves, luckily the person will be cured from this attack, but later, he will develop SEVERE pain again which is VERY HARD to treat or cure

- ✓ **Diabetic Neuropathy:**

In Diabetes Mellitus, patients will have segmental demyelination and sensory sensation disturbance, this will result in burning pain in the periphery

- **Phantom pain:**

- It is not real
- Patients who removed an organ from their body for any reason, will have pain in that organ !
- For example, someone removed his leg, he will complain from a pain in his big toe! (Not real)
- This pain usually goes away after 2-4 weeks

- **Stress induced anesthesia:**

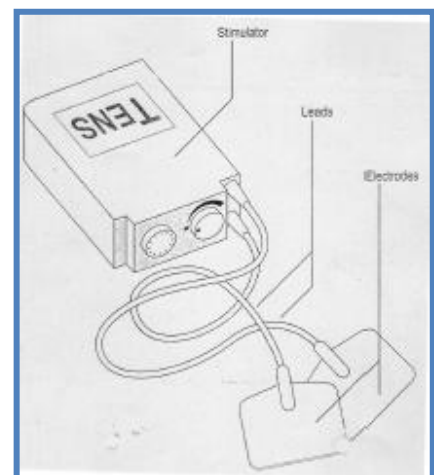
- It means not feeling the pain while being under stress
- It is caused by the release of Endorphin and other substances
- For example, When you just had a car accident, and suppose your knee hit something, you will not feel the pain until things cool down. Because you were under stress which gave an anesthetic effect on the pain

- **Important terms to remember:**

- **Hyperalgesia:** Severe pain (if someone had a hemisection in T3, he will develop pain in T2)
- **Allodynia:** Pain caused by any other sensation (e.g. Touch), and it is neither caused by A $\delta$  nor C fibers
- **Muscular pain:** Less blood flow in the muscles (Ischemia), it happens when you suddenly play football when you're not ready for it
- **Causalgia:** Burning pain which involves the nerves
- **Thalamic Syndrome:** Obstruction of arterial blood flow to the thalamus which causes SEVERE pain (Logically, person should lose pain sensation, but what happens is the opposite, the mechanism is not known)

- **Sites & Mechanism of Pain Relief:**

I	Block production of inflammatory mediators e.g. aspirin; nonsteroidal anti-inflammatories
II	Sectioning of peripheral nerves rarely relieves pain as most chronic pain syndromes are in part due to re-organisation of central nociceptive pathways and sensory processing
III	Sympathectomy can be useful, especially in cases of reflex sympathetic dystrophy.
IV	Manipulation of endogenous opioid network using exogenously administered opioid-like drugs.
V	Electrical stimulation of the dorsal columns can alleviate pain originating below site of stimulation.
V'	Selective activation of large diameter afferent fibres by transcutaneous electrical nerve stimulation.
VII	Stimulation of brainstem sites, or administration of drugs which can modify serotonergic or noradrenergic synapses (e.g. antidepressants)



This device plays the role of the Rubbing, it is implanted in patients who suffer from chronic pain, therefore A $\beta$  will be released all the time and patient will be relieved