MODULATION OF PAIN

The gate theory of pain

Special neurons located in the gray matter of the spinal cord **(Substantia Gelatinosa)**

From the gate through which pain impulses must pass to reach brain

Three variable control this gate

- A Delta fibers (fast pain)

- C fibers(slow pain)

- A Beta fibers (light touch)

This gate has the ability to block the signals from the A delta and C fibers preventing them from reaching the brain

Gate opened or closed by 3 factors

1. activity or stimulation of the pain fibers –opens the gate
2. activity in other sensory nerves –close the gate
3. messages from the brain concentrating on the pain or trying not to think about it

Impulses coming along **type C pain fibers** cause the release of substance P from these fibers and tend to **open the gate**

While impulses coming **along Aβ fibers** tend to keep **the gate closed** by process of presynaptic inhibition of C fibers and postsynaptic inhibition of secondary neurons in dorsal horn

- If impulses in the C and A delta fibers are stronger than the A beta fibers the gate opens

- If impulses in the A beta fibers are stronger than the C and A delta fibers the gate closes

(A delta fibers are always stronger)

The gate theory explains the pain relief by skin rubbing, shaking the painful part transcutaneous electrical stimulation all supposed to stimulate mechanoreceptors that activate neurons of dorsal column ,collateral relieve pain

The gate is under control of higher centers

Specialized nerve impulses arise in the brain itself and travel down the spinal cord to influence the gate

This is called the **central control trigger** and it can send both inhibitory and excitatory signals

The inhibitory neurons make a pain blocking agent called **enkephalin**

Enkephalin : is an opiate substance similar to heroin which can **block substance P** which is release from C fibers and this keeps the gate closed

The opioid peptides

These are morphine like substances naturally present in body

They are natural analgesic substances that act by binding to opiate receptors in analgesic system and dorsal horn of spinal cord on central ending pain conducing fibers

They are present in high concentration in

1. the spinal dorsal horn

2.medulla

3. hypothalamus

4.peripherally

Three classes of opioid peptides

1- **Endorphine**
basal hypothalamus proopiomelanocortin is the precursor for β ENDβ

2- **Enkephalins**
dorsal horn ,raphe magnus and globus ballidus.

3- **Dynorphins**
Hypothalamus, PAG(periaqueductal grey area),reticular formation, dorsal horn

Opioid antagonist Naloxone

Use to reverse opioid overdose

Displace receptors bound opioids

Good for overcoming respiratory and CVS depression

The pain control analgesic system

This is specific system that blocks pain transmission in CNS

its **major constituents are:**

1. perventricular nucleus in hypothalamus near third ventricle

2. periaqueductal grey area in mid brain

3. raph magnum nucleus in upper medulla

Pain inhibitory complex (PIC) in dorsal horn of spinal cord is consisted of multiple short encephalinergic neurons that terminate on central ending of pain conducting afferent fibers

When these neurons are stimulated , the released encephalin cause pre &postsynaptic inhibition of pain transmission

i.e it prevents the release of substance p from pain nerve endings

Analgesia occurs as follows

1. periaqueductal grey area receives neuronal inputs from thalamus , hypothalamus and cerebral cortex .

2. periaqueductal grey area projects neurons containing aspartate & glutamate that stimulate raph magnus N

3. raph magnum nucleus projects serotoninergic neurons ,this in addition to noradrenergic neurons projects from adjacent medulla to dorsal horn .
They block pain signals by activating PIC

Some important definitions

Chronic pain

- Chronic pain can be considered as bad pain because it persist long after injury and is often refractory to pain killers.
- Chronic pain caused by nerve injury is called neuropathic pain

Neuropathic pain

- Caused by the damage to peripheral nerve (adrenalin release by sympathetic discharge)
- The distal cut end develops a scar tissue forming rounded ball (neuroma) which is sensitive to pressure.
- Repeated activation causes continuous pain.
- Examples are like, post herpetic neuralgia and diabetic neuropathy.

Phantom pain

- Pain felt in an amputated part long after amputation was done.
- Many explanations are given to explain this phenomenon.

Stress induced analgesia

- It's a well known phenomenon seen when the soldier is wounded in battle field but feels no pain until the battle is over. The cause is not known may be it is similar to Gate control hypothesis

Terms frequently used

Hyperalgesia: Excessive Pain

Allodynia: Pain caused by any other sensation

e.g. touch will cause pain.

Muscular Pain: Less blood flow in the muscles (ischemia).

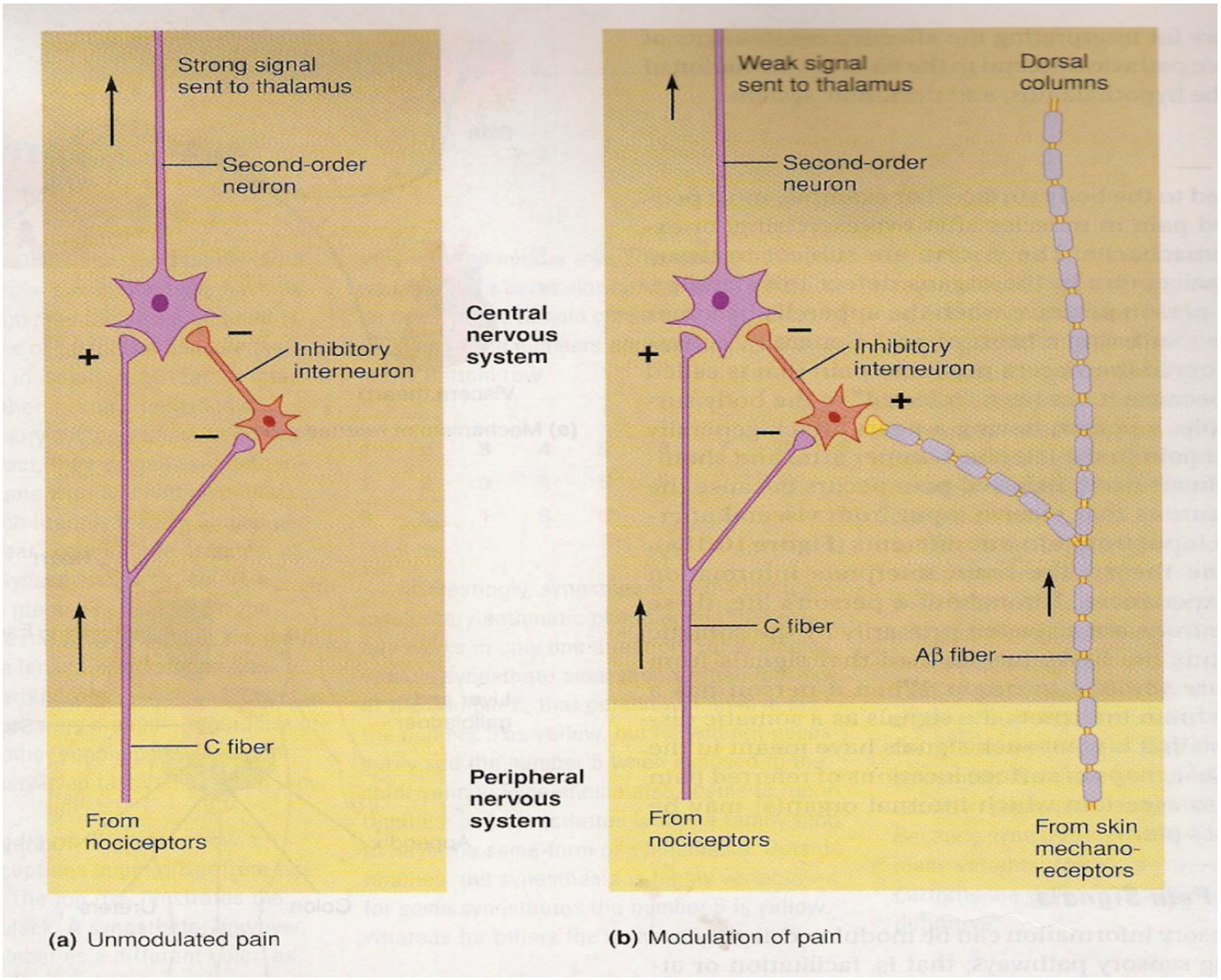
Stress analgesia: Mild degree of pain is not felt if the other part of the body has excessive pain.

Causalgia: Burning pain.

- Thalamic Syndrome

Obstruction of the thalmogeniculate branch of the posterior cerebral artery Affects posterior thalamic nuclei.

. Prolonged severe pain



(a) Unmodulated pain (b) Modulation of pain

Summary

Nociceptors

- Nociceptors are free endings of C fibres (80%) and Aδ nerve fibres (20%).
- Nociceptors are high-threshold receptors.
- Aδ fibres produce sharp well-localized pain, C fibres produce dull aching poorly localized pain.
- Inflammatory mediators, including prostaglandins and leukotrienes, increase the sensitivity to pain.
- Nociceptor axon reflexes release substance P which degranulates mast cells.

Done By:

Ghada Al Mutairi