



بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

السلام عليكم ورحمة الله وبركاته



Pain Modulation

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Learning Objectives

● *Describe the pain suppression analgesic system:-*

● *Spinal modulation (Gate theory of pain control)
Supra spinal modulation (Special analgesic system)*

● *Pain modulation by opioid neurotransmitters*

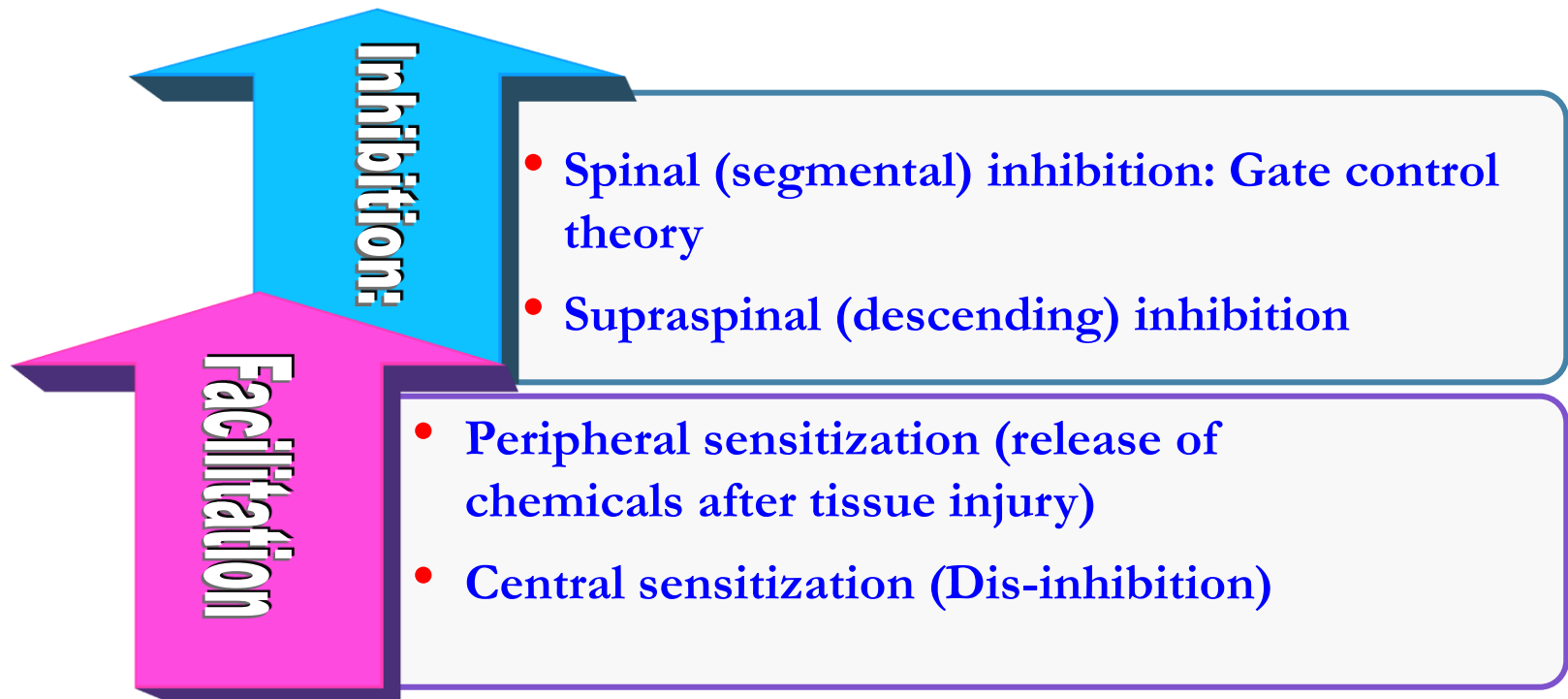
● *Appreciate that pain can also be facilitated*

● *Know the sites & mechanism of pain relief*

What is Pain Modulation

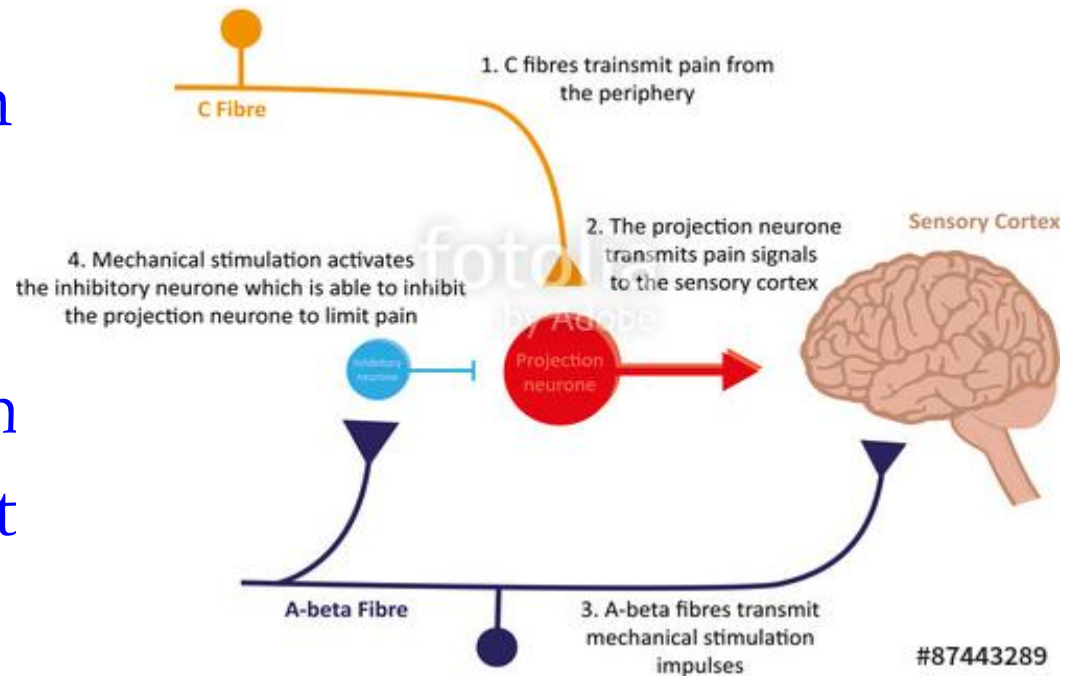
❖ It means pain perception variability (the degree to which a person reacts to pain)

i.e. A decrease or an increase in the sensation of pain caused by inhibition or facilitation of pain signals

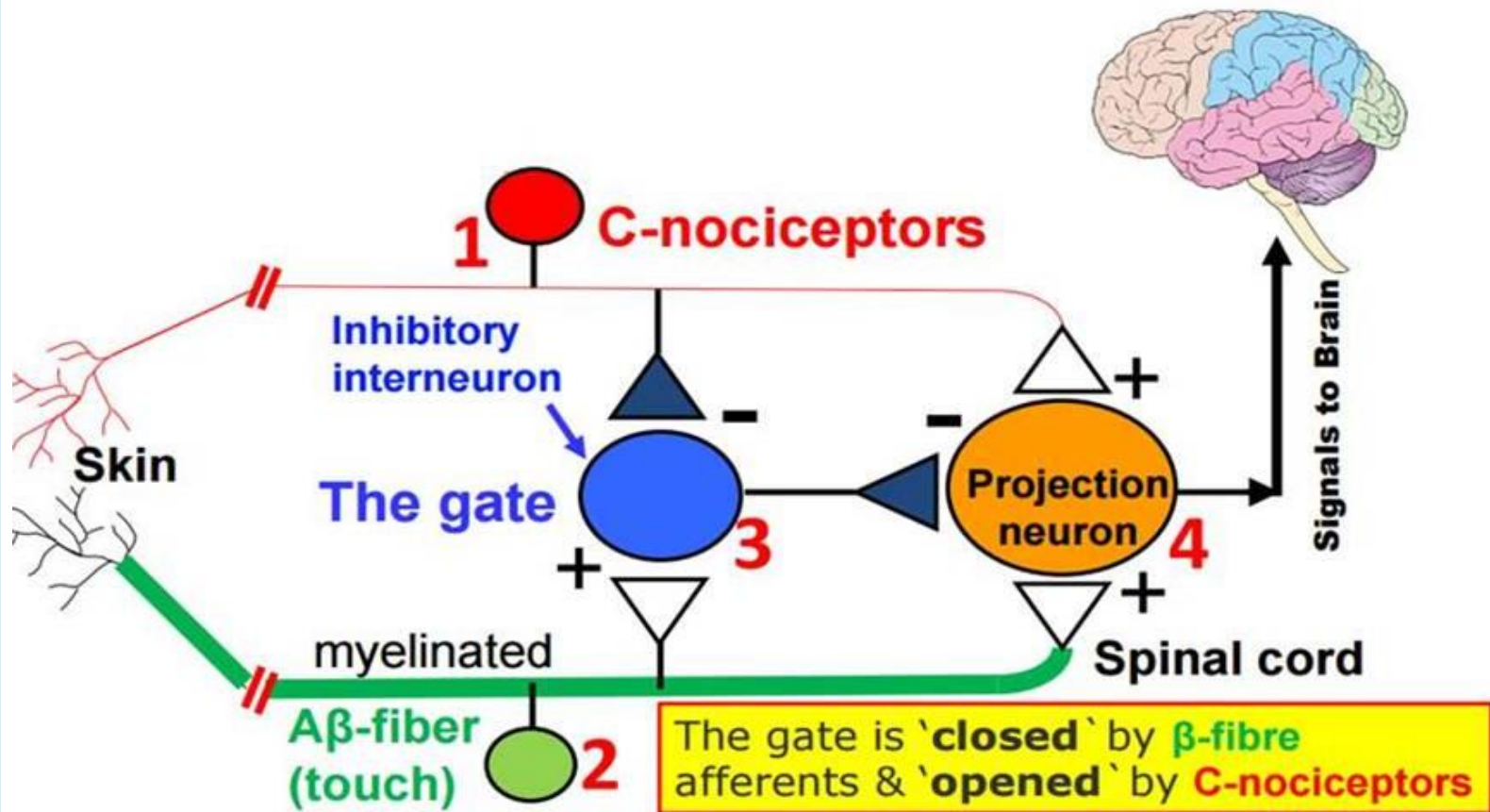
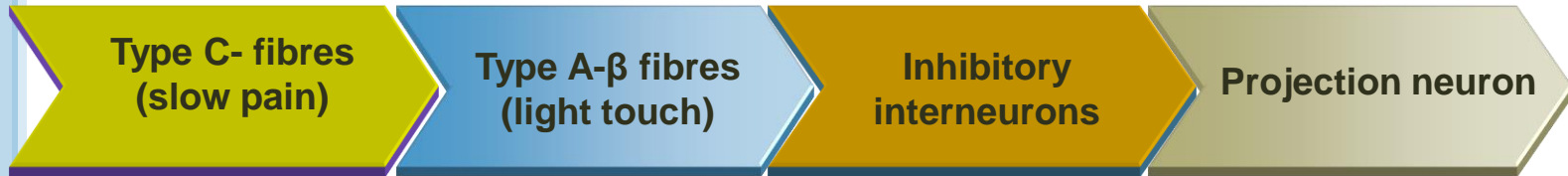


The gate theory of pain control

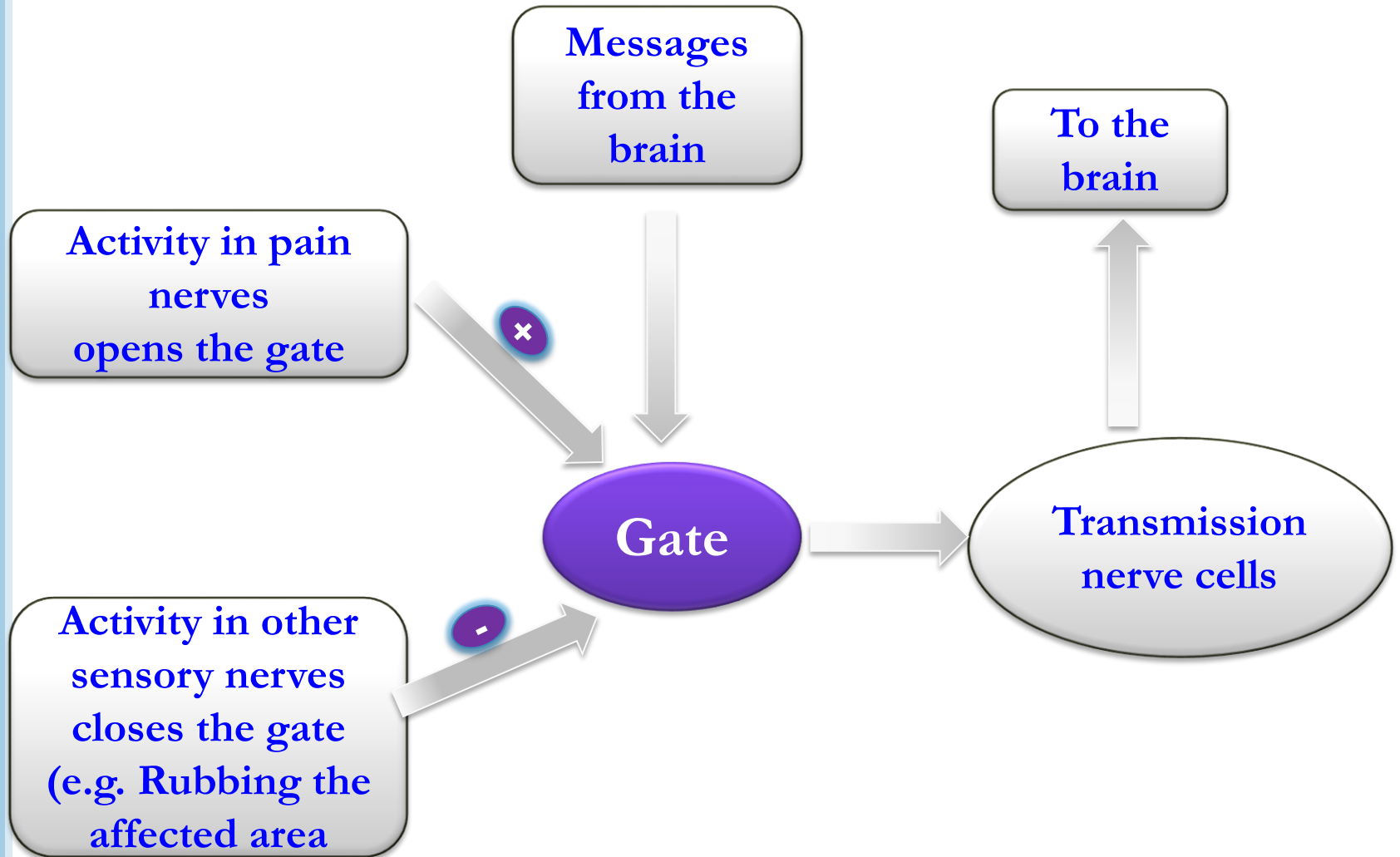
Special neurons in the the dorsal horn of spinal cord (SGR) form the gate through which pain impulses must pass to reach brain.



Four variables control this gate:

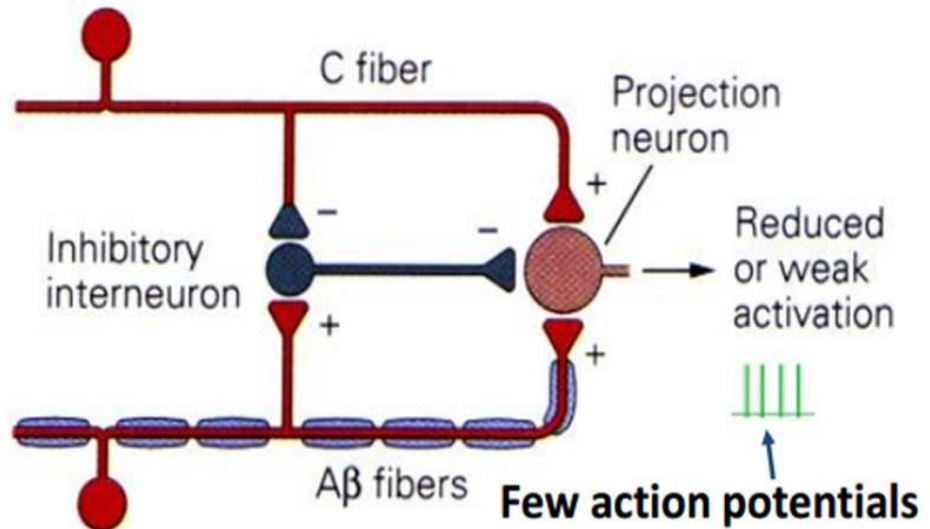
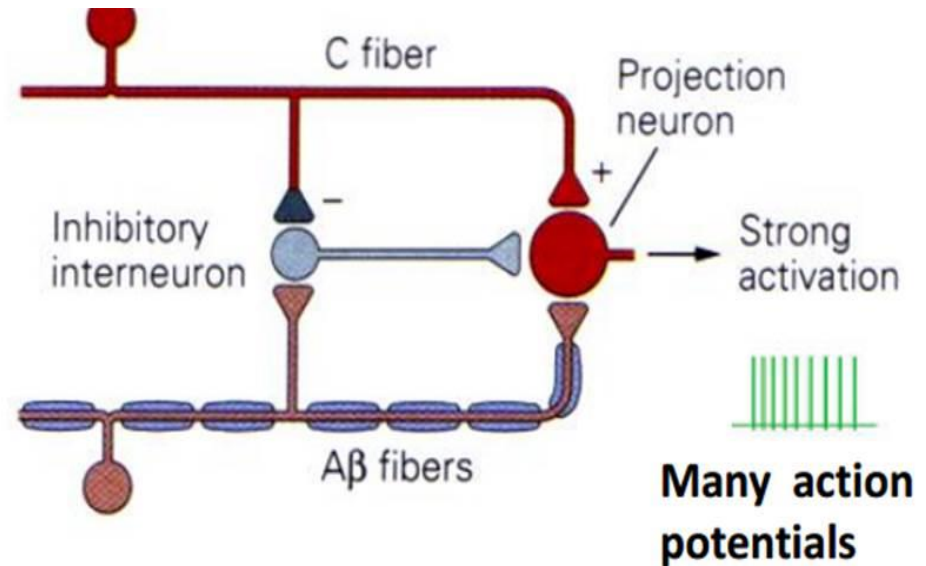


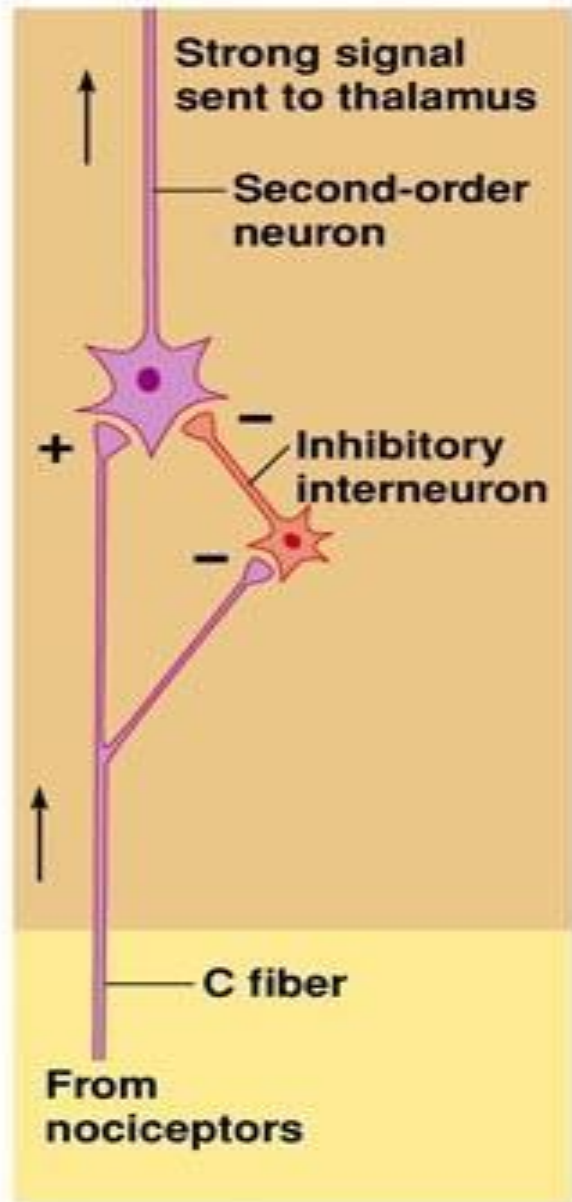
Gate opened or closed by 3 factors:



The gate theory of pain control (Cont.)

- Projection neuron receives input from both C-fibers and A β fibers.
- Impulses coming along type C pain fibers cause the release of substance P from these fibers and inhibits the inhibitory interneuron (open the gate).
- While impulses coming along A β fibers tend to keep the gate closed by activating the inhibitory interneuron.

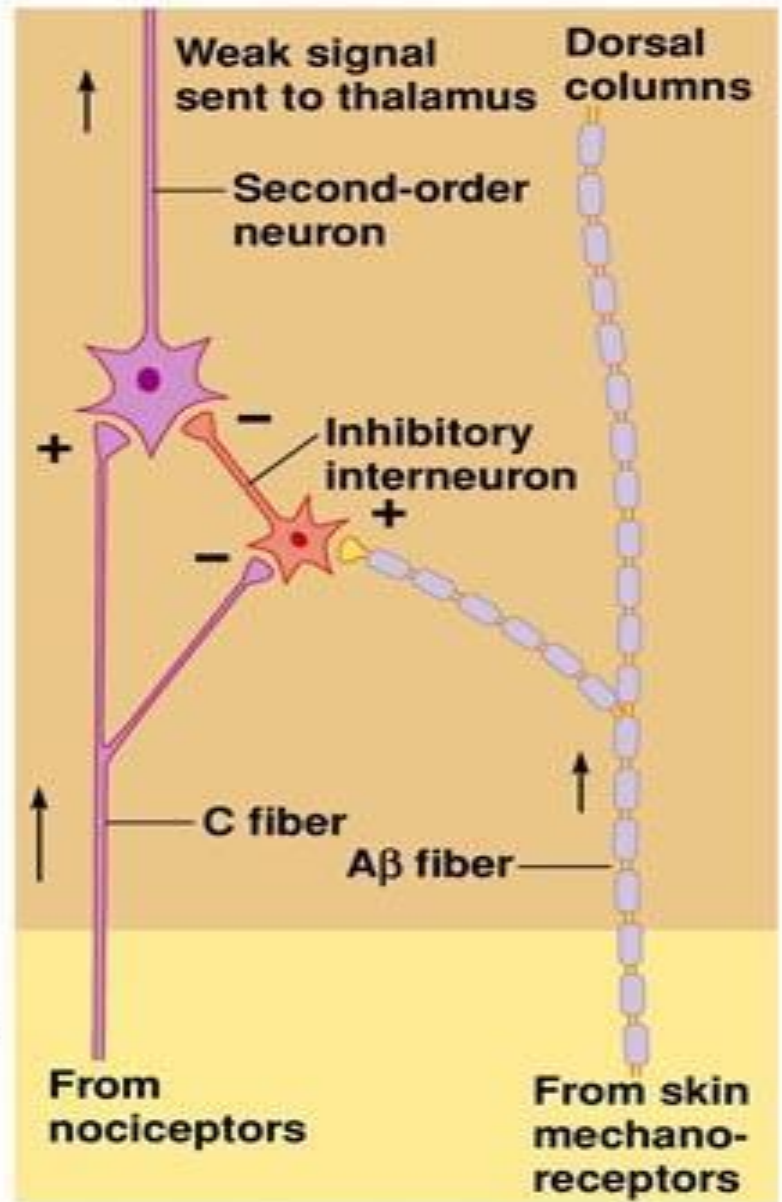




(a) Unmodulated pain

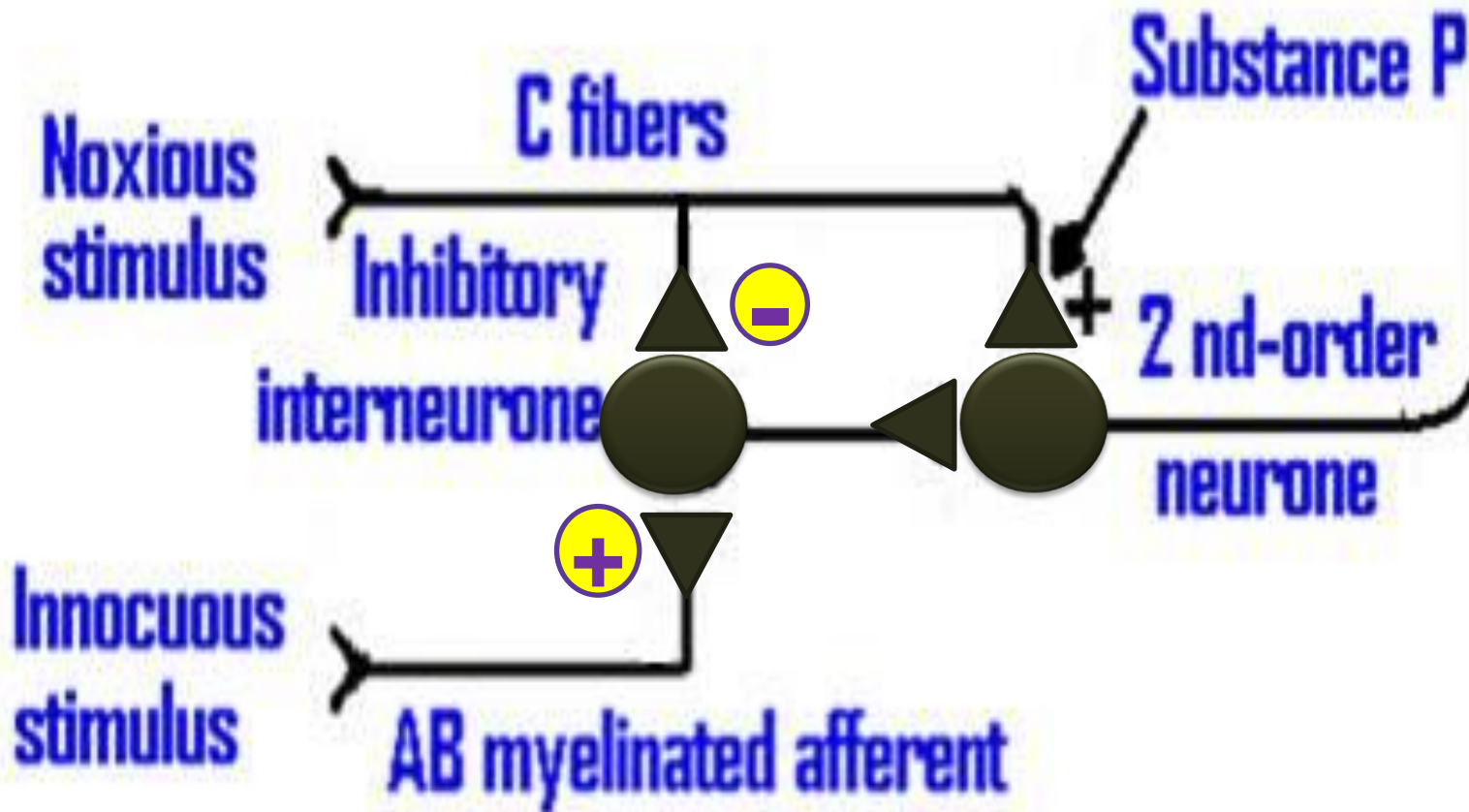
Central nervous system

Peripheral nervous system



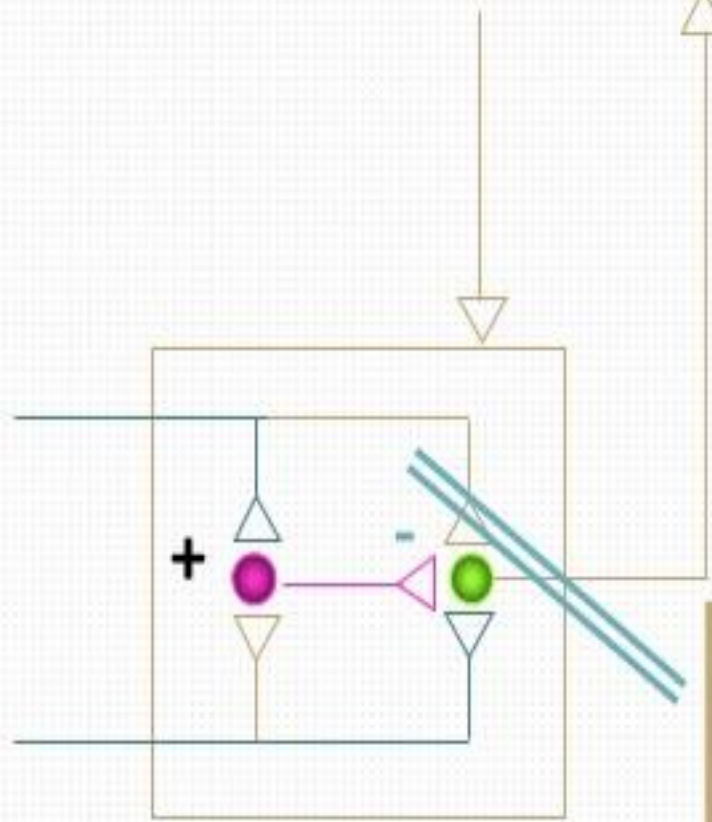
(b) Modulation of pain

How non-painful (innocuous) stimulus can reduce transmission of a noxious stimulus?



Gating of pain

Gate control theory



pain is
not felt



gate is
closed

When pain and touch fibres are stimulated together, gate will be closed & pain is not felt

Central Nervous System

A β fibers

C fibers

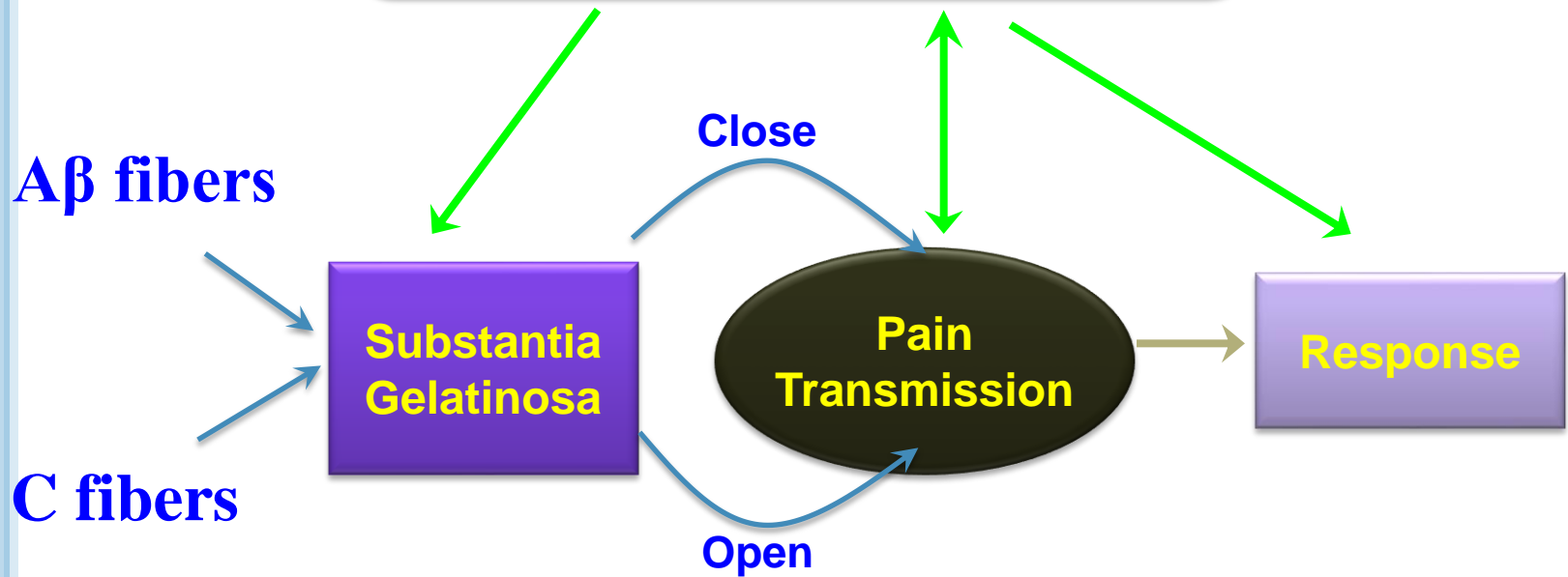
Substantia
Gelatinosa

Close

Open

Pain
Transmission

Response



- The gate theory explains the pain relief by:
 - Skin rubbing
 - Shaking the painful part
 - Trans Cutaneous Electrical Nerve Stimulation (TENS)
 - Acupuncture
- All are supposed to stimulate mechanoreceptors that activate neurons of dorsal column, the collaterals relieve pain.



What is the Central Control Trigger

- Specialised nerve impulses arise in the brain itself and travel down the spinal cord to influence the gate.

- It can send both inhibitory and excitatory messages to the gate sensitising it to either C or A- β fibres.

- The inhibitory neurons make a pain blocking agent called enkephalin.

- Enkephalin is an opiate substance which can block substance P, the neurotransmitter from the C fibers, and this keeps the gate closed.

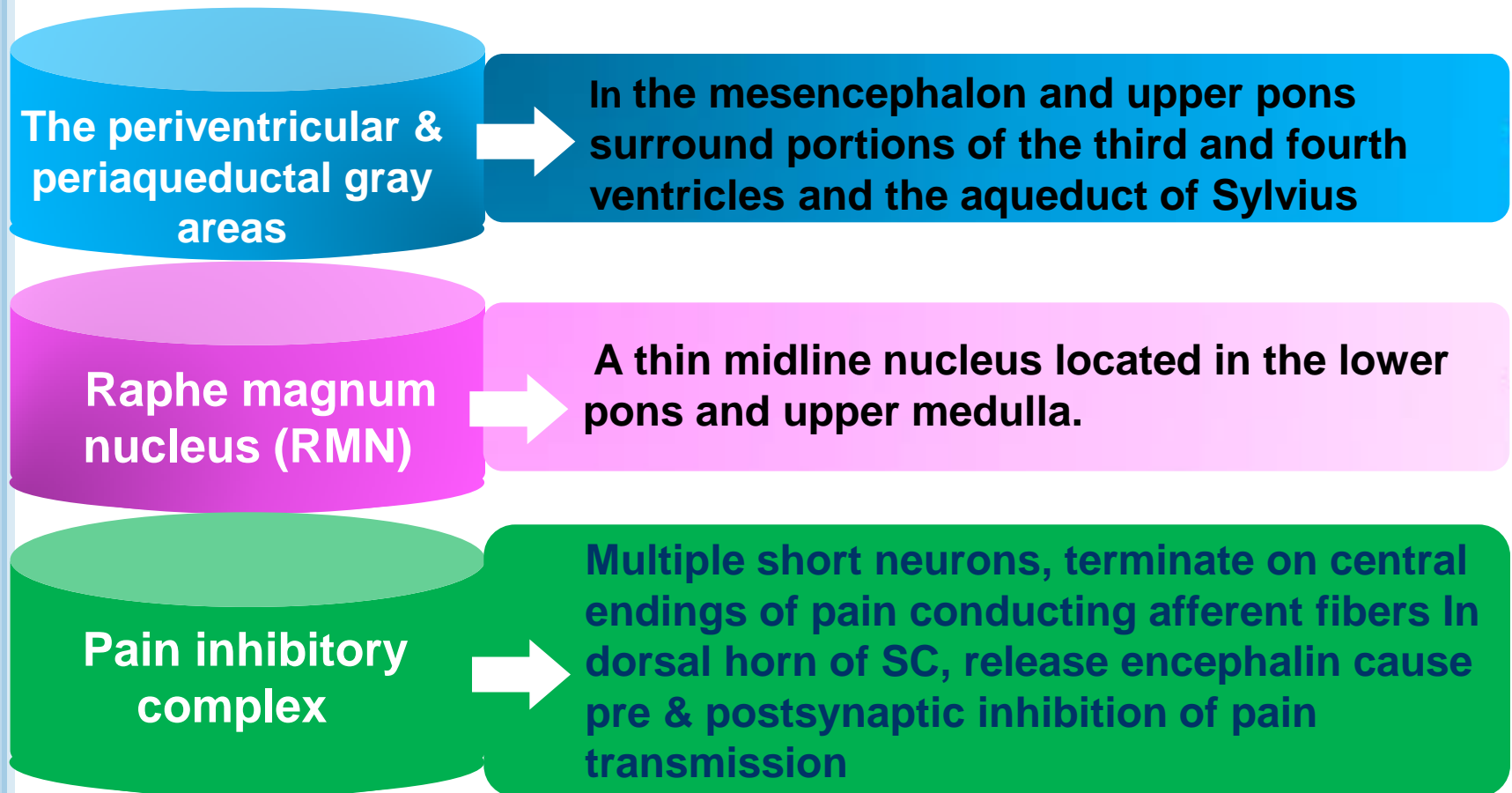
Conditions that open or close the gate

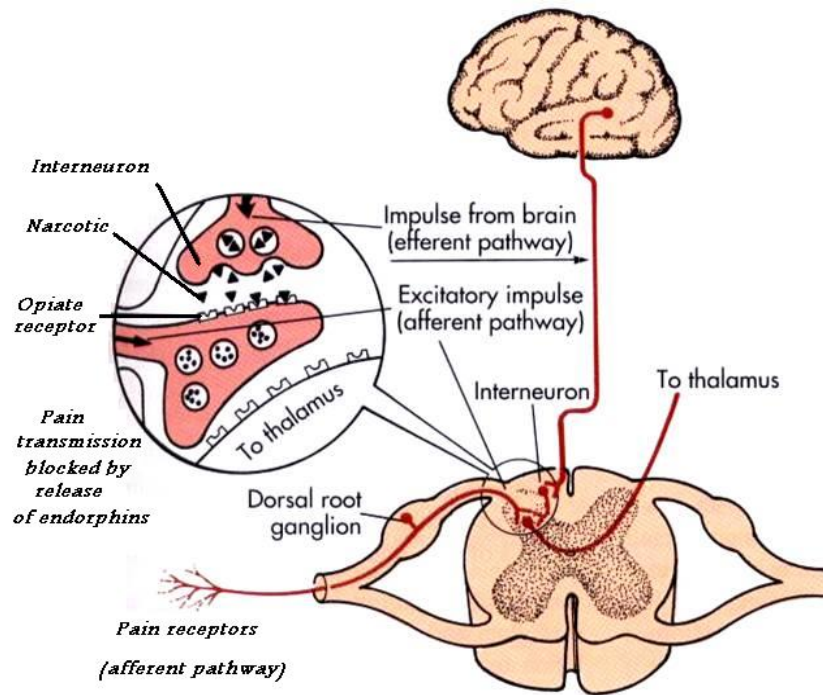
	<i>Conditions that open the gate</i>	<i>Conditions that close the gate</i>
<i>Physical conditions</i>	<ul style="list-style-type: none">▪ <i>Extent of the injury</i>▪ <i>Inappropriate activity level</i>	<ul style="list-style-type: none">▪ <i>Medication</i>▪ <i>Counter stimulation, e.g. massage</i>
<i>Emotional conditions</i>	<ul style="list-style-type: none">▪ <i>Anxiety or worry</i>▪ <i>Tension</i>▪ <i>Depression</i>	<ul style="list-style-type: none">▪ <i>Positive emotions</i>▪ <i>Relaxation</i>▪ <i>Rest</i>
<i>Mental conditions</i>	<ul style="list-style-type: none">▪ <i>Focusing on the pain</i>▪ <i>Boredom</i>	<ul style="list-style-type: none">▪ <i>Intense concentration or distraction</i>▪ <i>Involvement and interest in life activities</i>

Supra spinal modulation

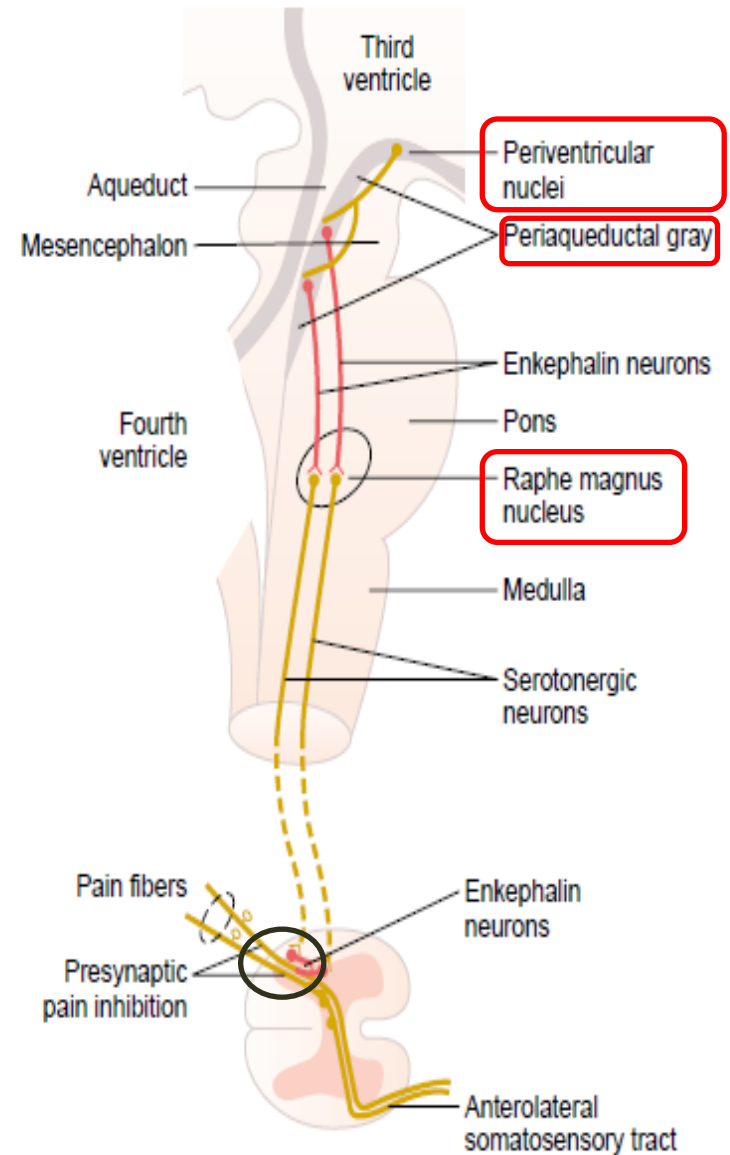
(Special pain control analgesic system)

This is a specific system that blocks pain transmission in CNS. Its major constituents are:





Pain inhibitory complex



Analgesia system of the brain and spinal cord, showing (1) inhibition of incoming pain signals at the cord level and (2) presence of *enkephalin-secreting neurons* that suppress pain signals in both the cord and the brain stem.

Analgesia occurs as follows:



Enkephalin neurons from PAG and periventricular areas send signals to RMN



RMN projects serotonergic neurons to dorsal horn.

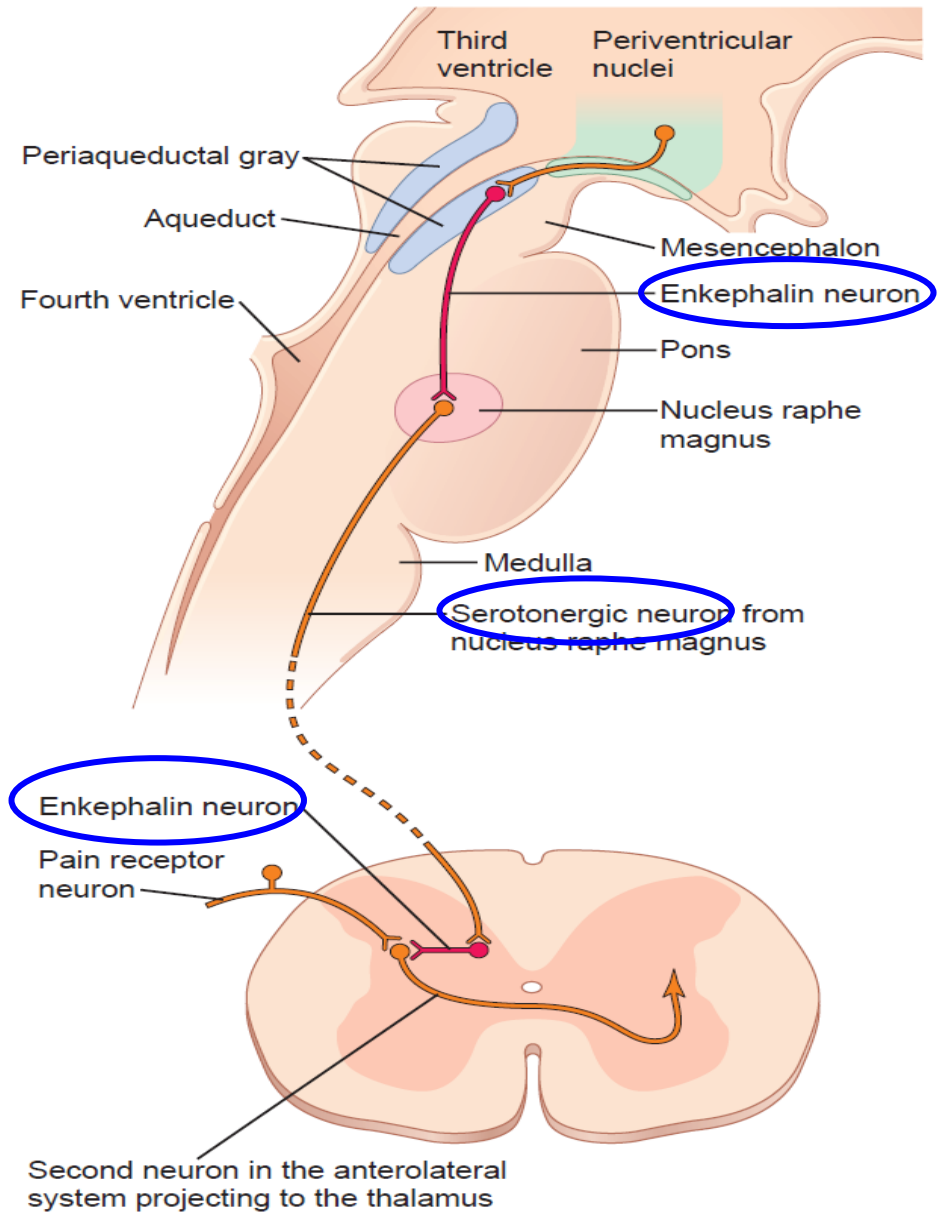


Serotonergic neurons act on local neurons (PIC) at dorsal horn to release enkephalin



At this point, the analgesia signals can block the pain before it is relayed to the brain

Pain Suppression ("Analgesia") System in the Brain and Spinal Cord

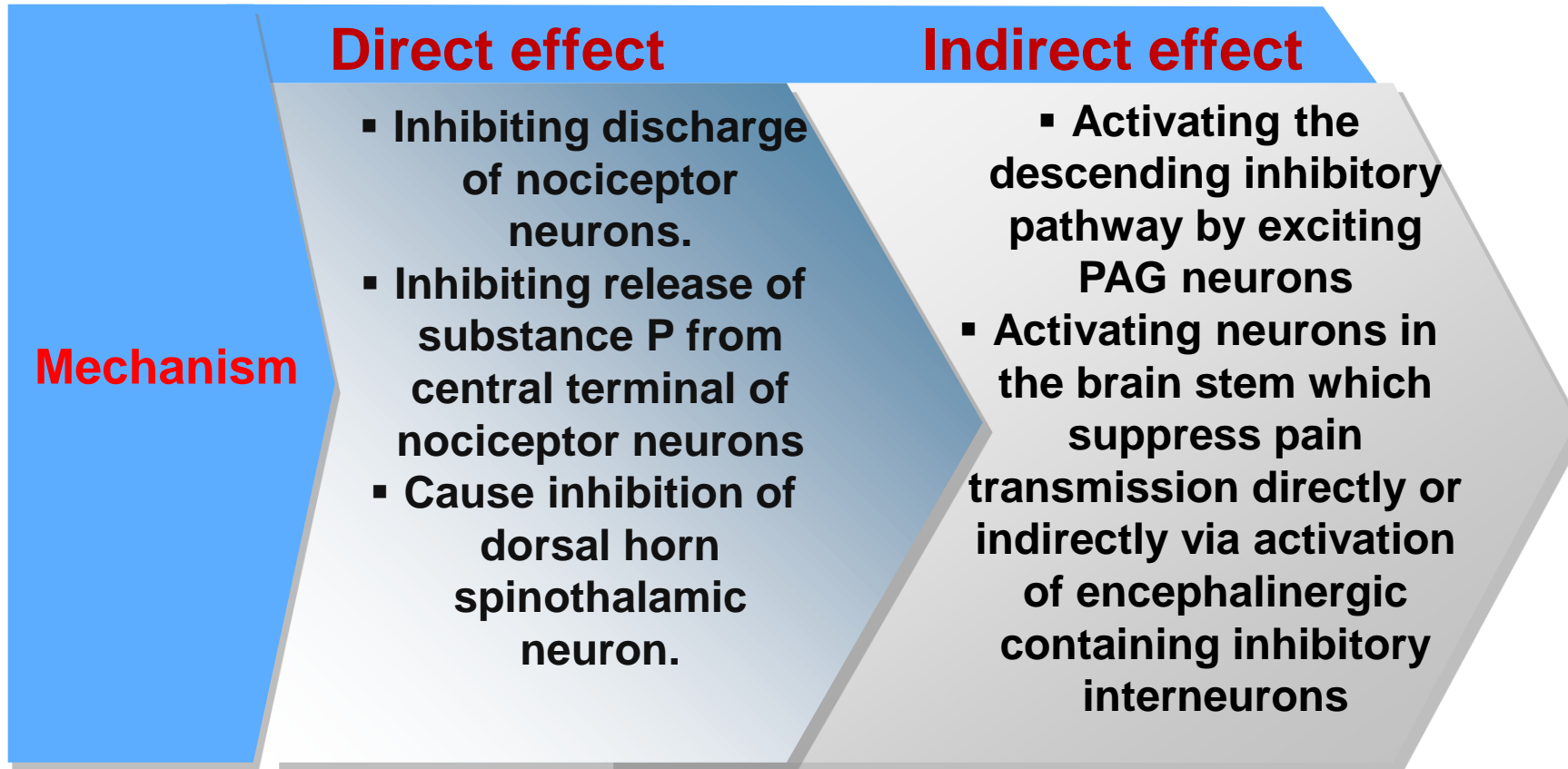


Opioid Peptides and Pain Modulation

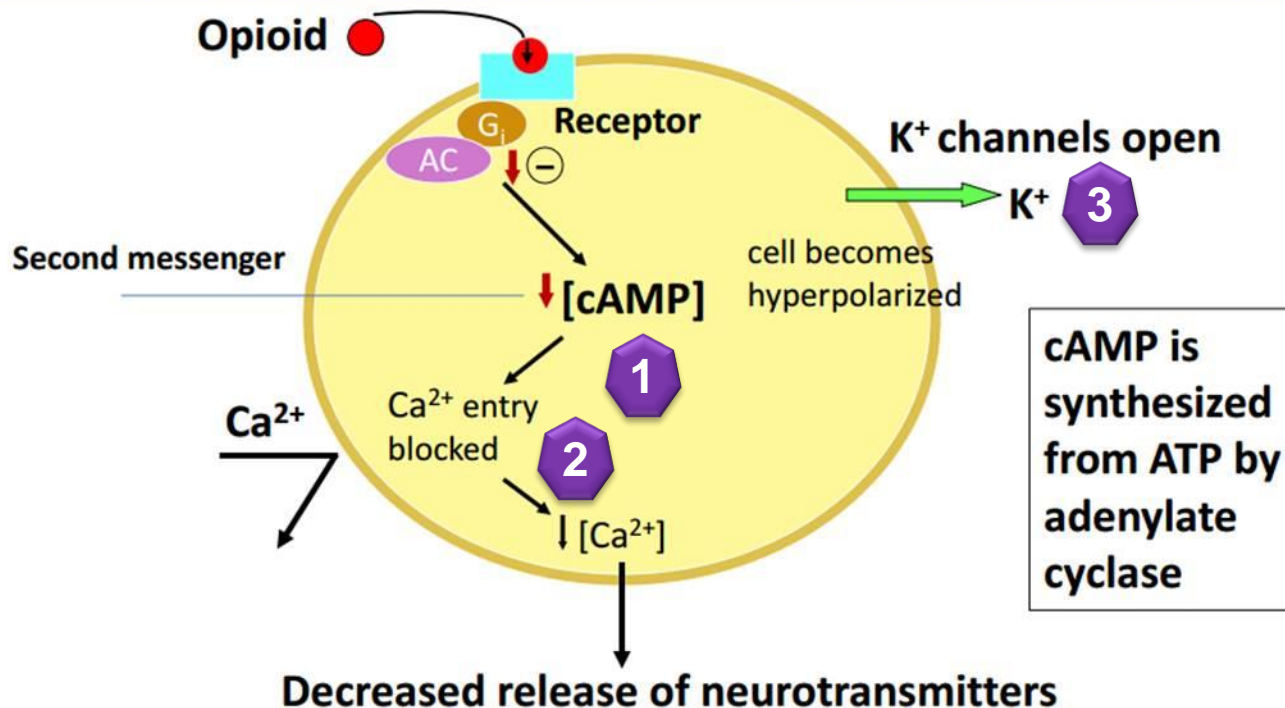
- They are natural analgesic substances (morphine-like substances) present in body.
- They act by binding to opiate receptors in analgesic system and dorsal horn of SC on central ending of pain conducting pain fibers.
- E.g. endorphin, enkephalin, dynorphin, endogenous morphine.

Mechanism of actions of Opioid peptides on pain transmission

They exerts their analgesic effects by acting at various sites in peripheral & CNS

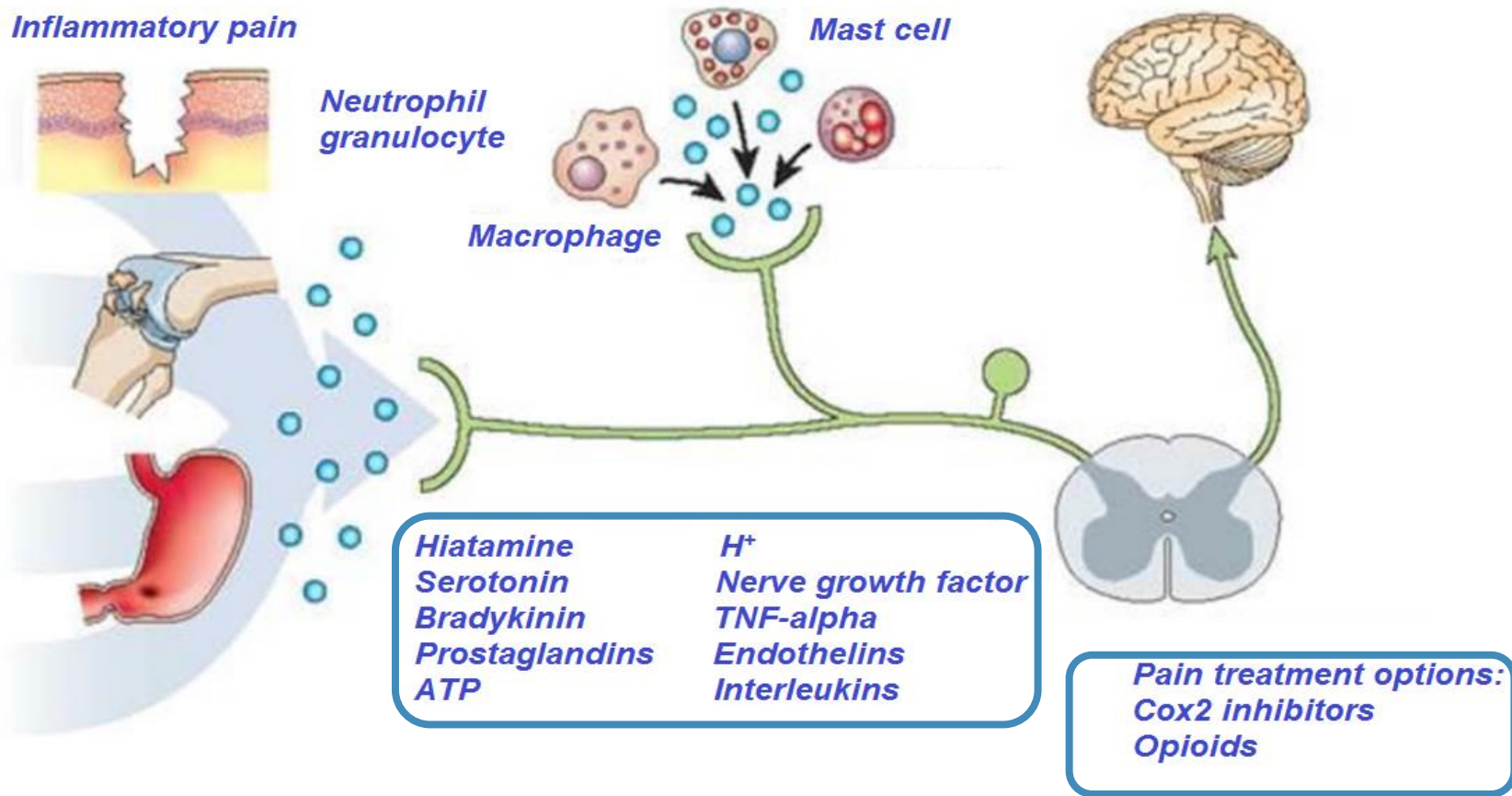


Cellular actions of Opioid peptides



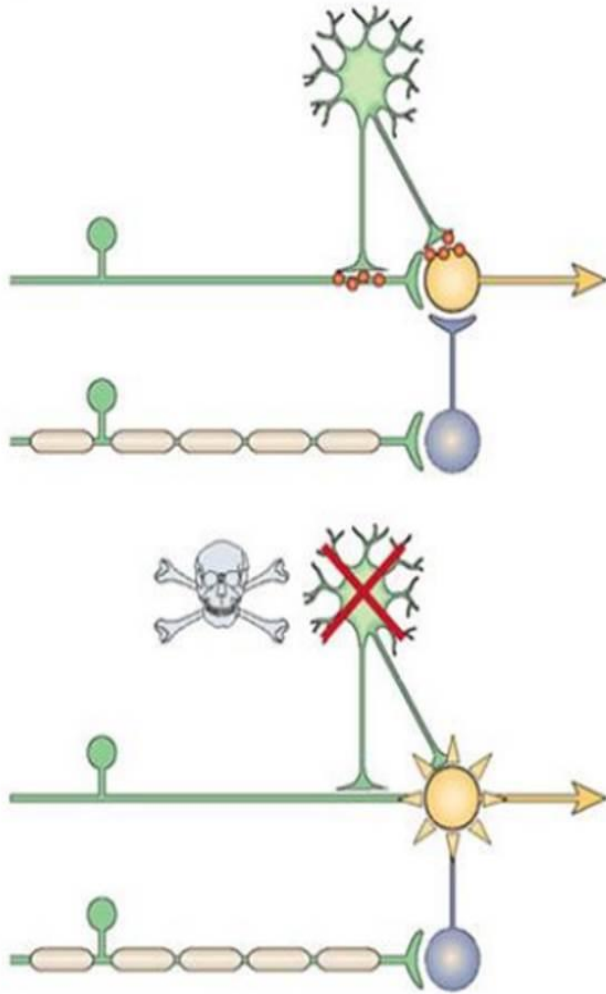
- Reduction of cAMP synthesis by inhibiting Adenyl cyclase
- Inhibition of transmitter release by inhibiting opening of Ca⁺⁺ channels
- Hyperpolarization by facilitating opening of voltage gated K⁺ channels

Pain Facilitation: Peripheral Sensitization



- Inflammatory mediators can directly activate nociceptors or cause their sensitization (decrease threshold as prostaglandins)

Pain Facilitation: Dis-inhibition



- Pain transmission is controlled by inhibitory interneurons
- Loss of these inhibitory interneurons after excessive release of glutamate results in increased excitability of projection neurons and thus enhanced pain sensation

Terms frequently used

Hyperalgesia

Excessive Pain (e.g due to sun burn)

Muscular Pain

Less blood flow in the muscles (ischemia)

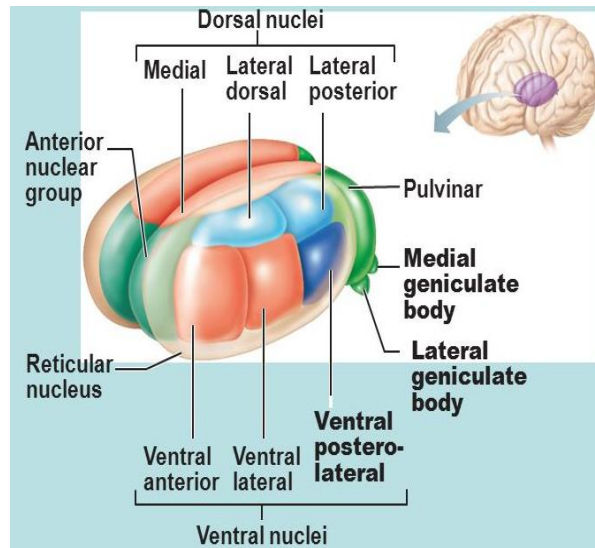
Allodynia

Pain caused by any other sensation e.g. touch

Causalgia

Burning pain

Thalamic Syndrome



- It is a neurological condition that results from a brain stroke affecting the thalamus.
- Cause: Obstruction of the thalamogeniculate branch of the posterior cerebral artery.
- Affects posterior thalamic nuclei
- Causes prolonged severe pain.

*Trigeminal
neuralgia*



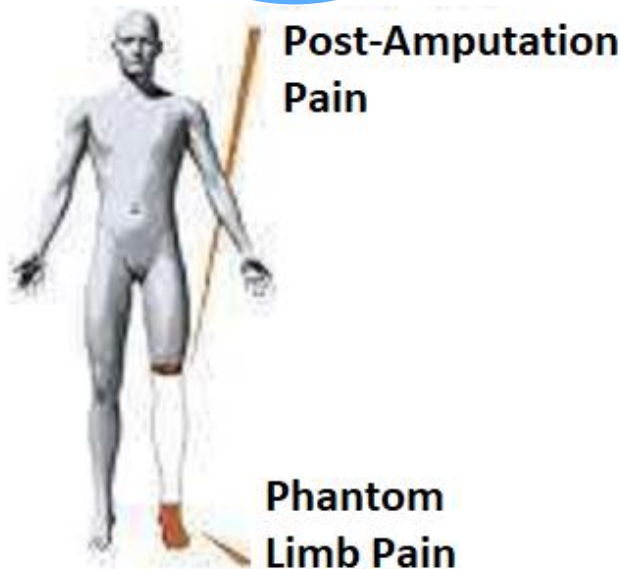
- It is excruciating intermittent pain by stimulation of trigger area in the face.
- e.g. Washing of face, combing hair, blast of air on face.
- It results from compression of trigeminal nerve root by blood vessels.

Stress induced analgesia



- Pain suppression response that occurs during or following exposure to a stressful or fearful stimulus.
- 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.

*Phantom
pain
sensations*



Impression of pressure and pain that an individual experiences relating to a limb or an organ that is not physically part of the body. Our brain can reorganize at the ventral posterior thalamic nucleus if sensory input is cut off even after that part is amputated

Neuropathic pain (NP)

- Pain caused by a primary lesion or dysfunction in the nervous system.
- Classification:
 - Central NP-Damage of CNS
 - Peripheral NP- Damage to PNS
- Resistant to the current analgesic therapy.
- Can persist for years.
- Clinical symptoms: Hyperalgesia, allodyni and spontaneous pain
- Examples: post herpetic neuralgia, diabetic neuropathy and after chemotherapy.



Mechanism of pain relief

Block production of inflammatory mediators .e.g. Aspirin & nonsteroidal anti-inflammatories.

Exogenously administration of opioid like drugs.

Sympathectomy can be useful.

Electrical stimulation of the dorsal column.

Selective activation of large diameter afferent fibers by transcutaneous electrical nerve stimulation.

Stimulation of brainstem sites or administration of drugs which can modify serotonergic or adrenergic neurons e.g. antidepressants.

Thank You!

