Pain Modulation

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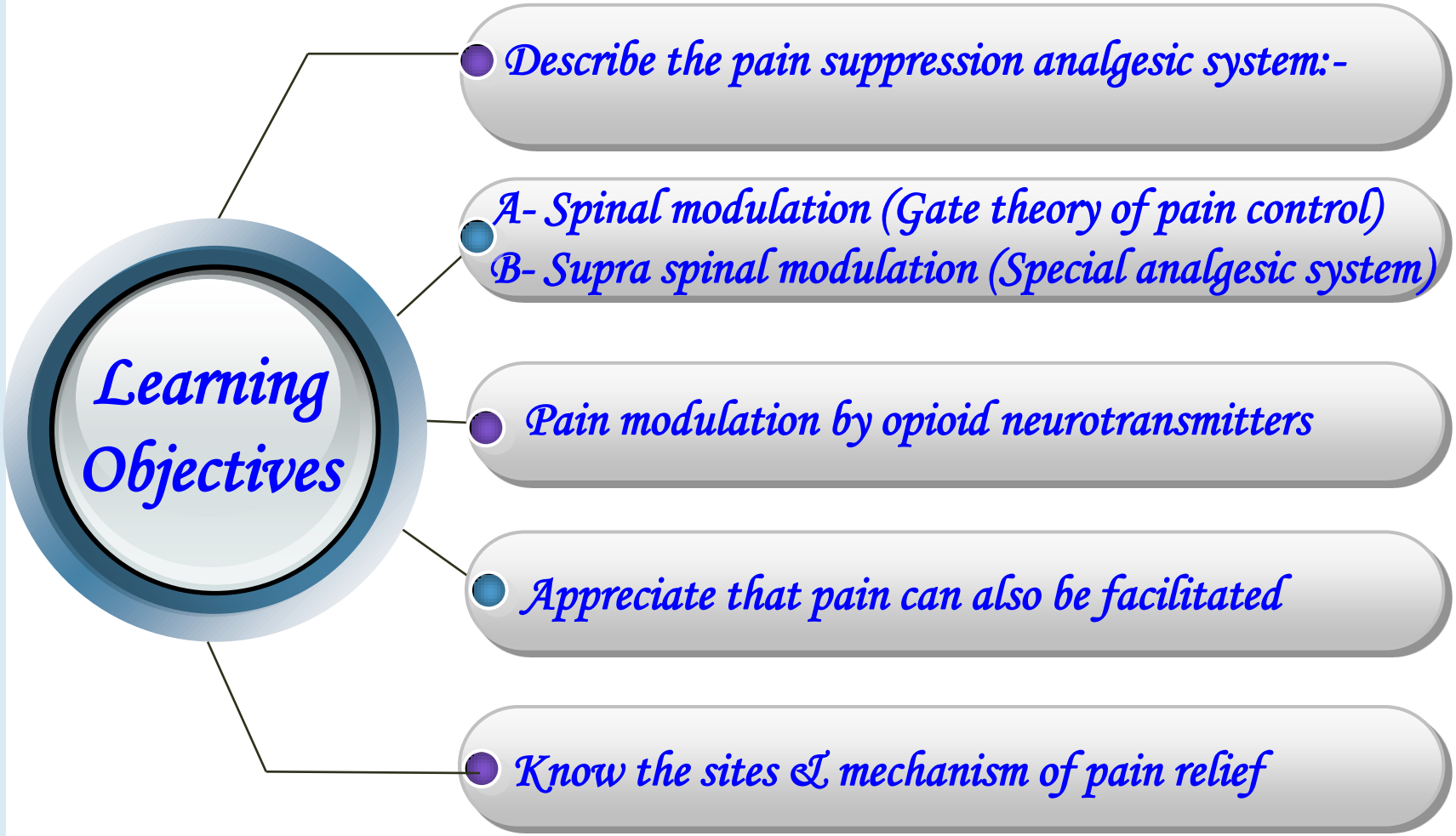
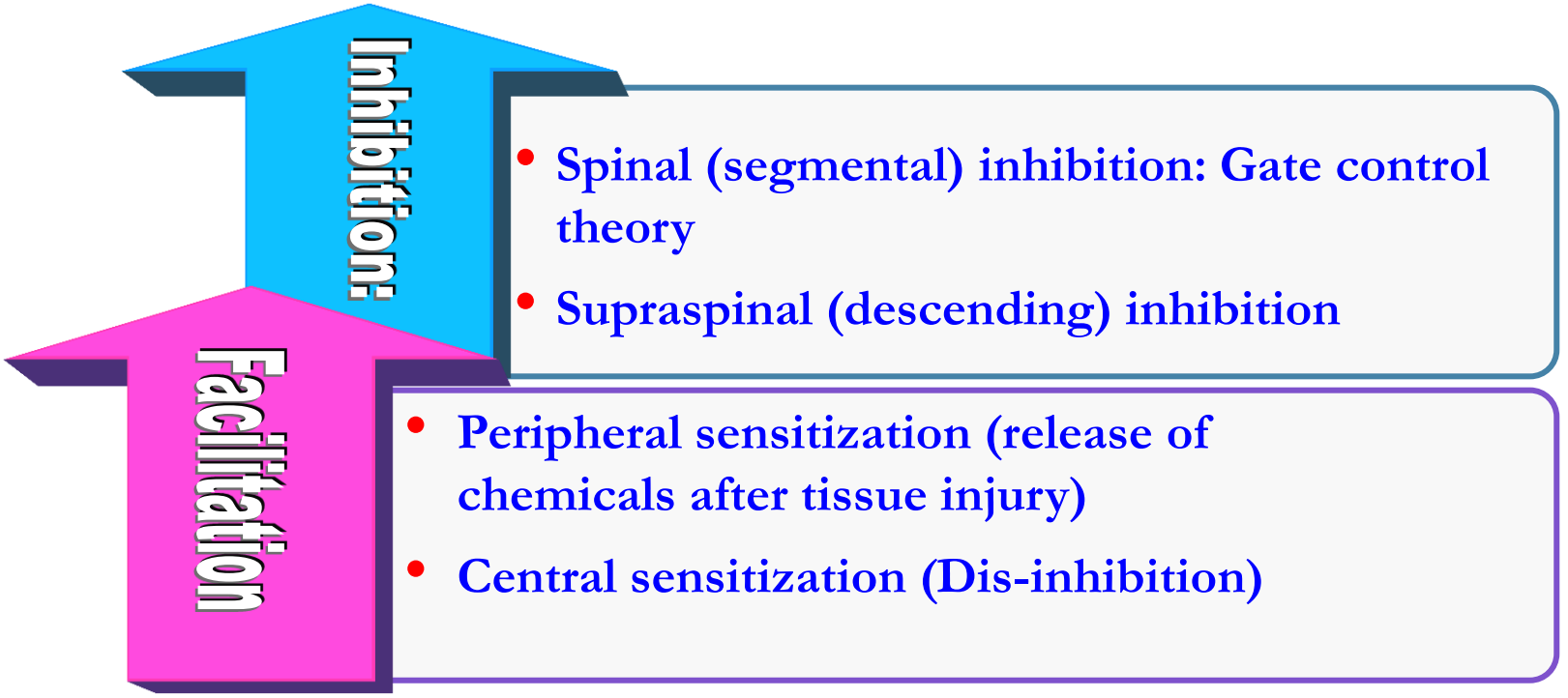

Learning Objectives
Describe the pain suppression analgesic system:-
A- Spinal modulation (Gate theory of pain control)
B- Supra spinal modulation (Special analgesic system)
Pain modulation by opioid neurotransmitters
Appreciate that pain can also be facilitated
Know the sites & mechanism of pain relief

What is Pain Modulation

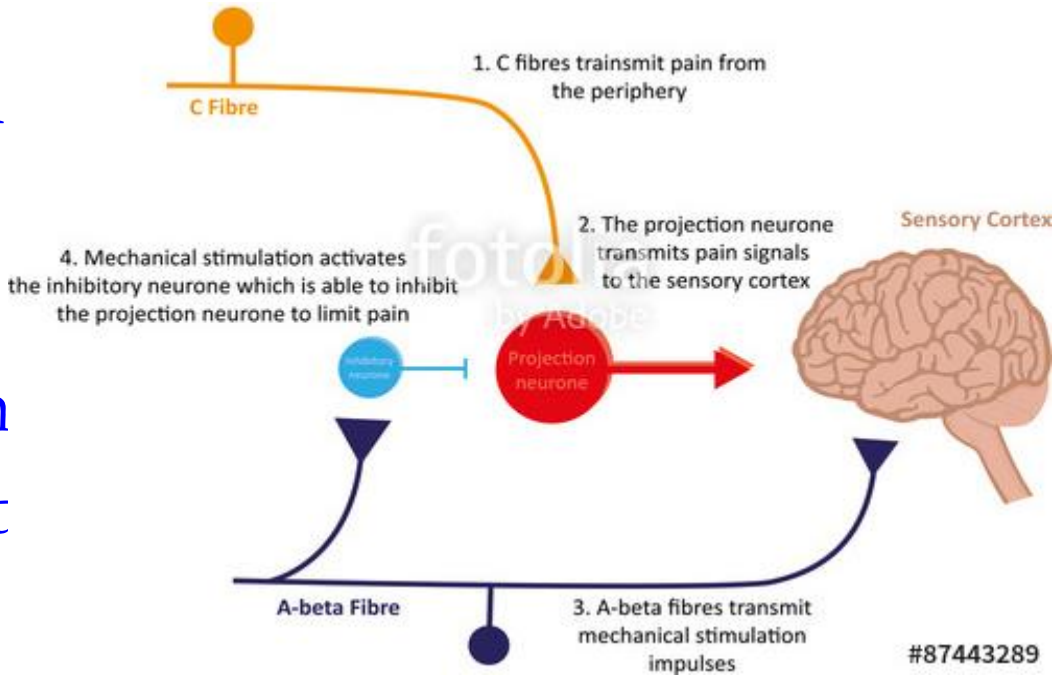
- It means pain perception variability (the degree to which a person reacts to pain)

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



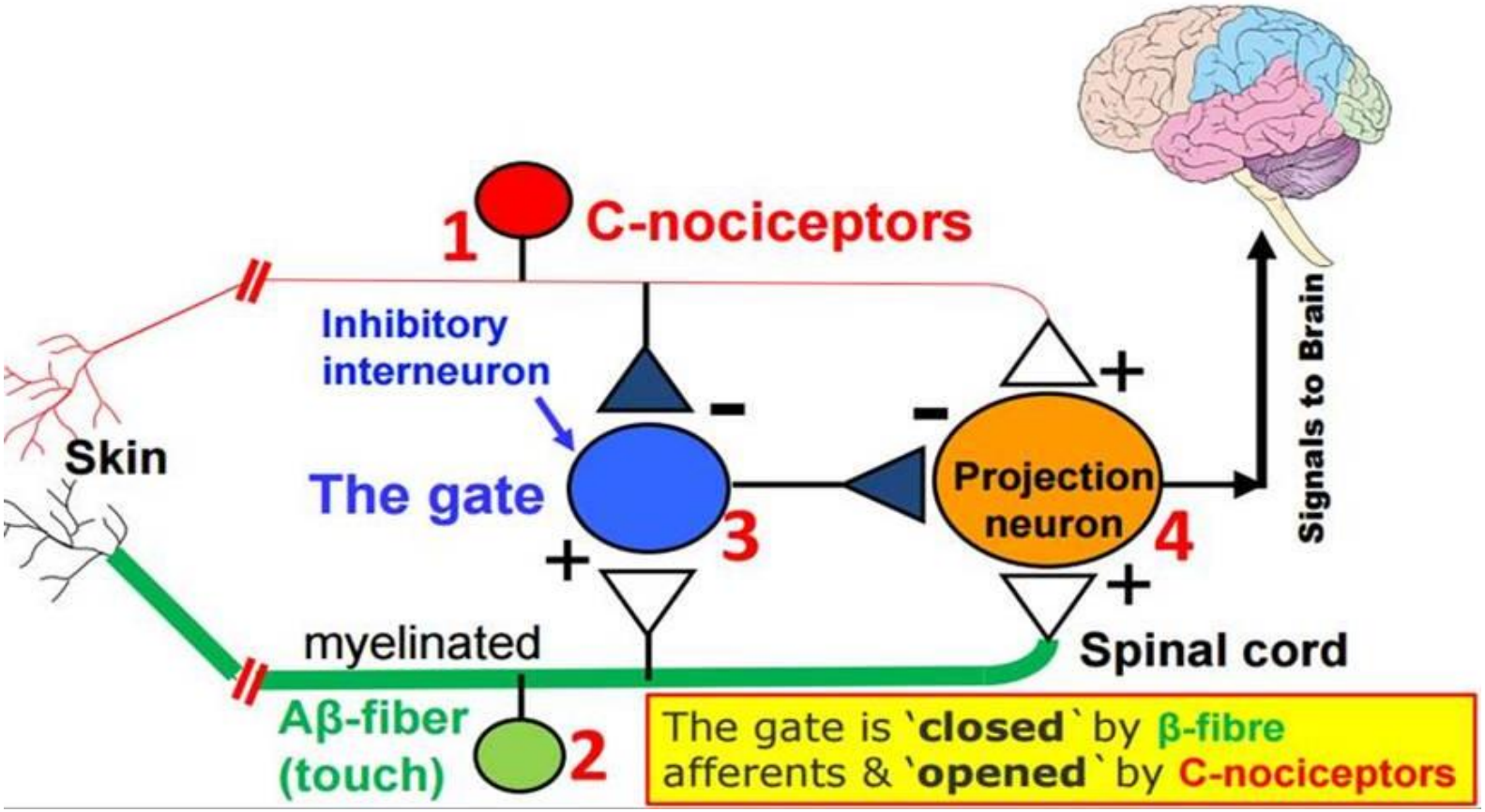
The gate theory of pain control

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

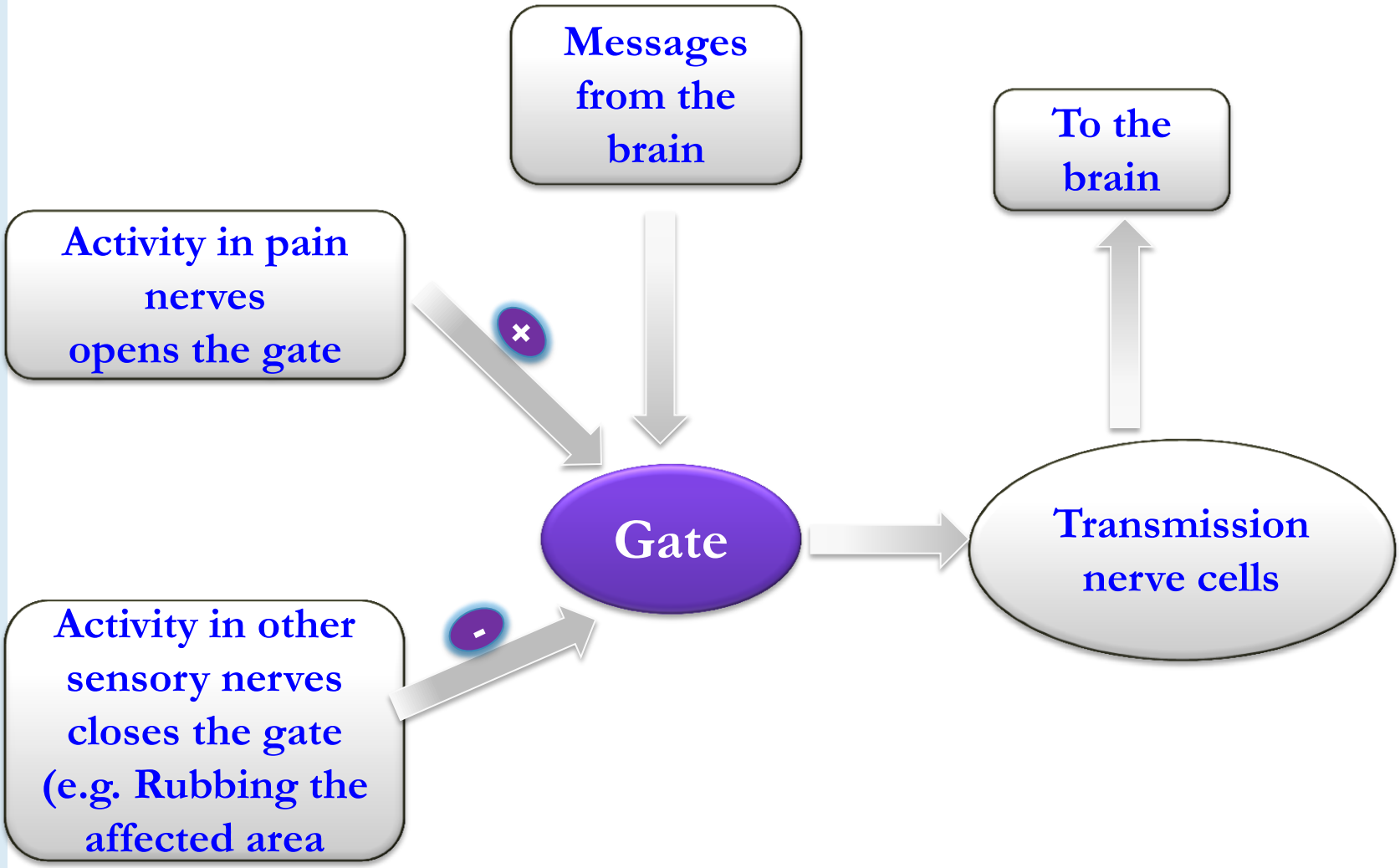


Four variables control this gate:

Type C- fibers (slow pain) → Type A-β fibers (light touch) → Inhibitory interneurons → Projection neuron

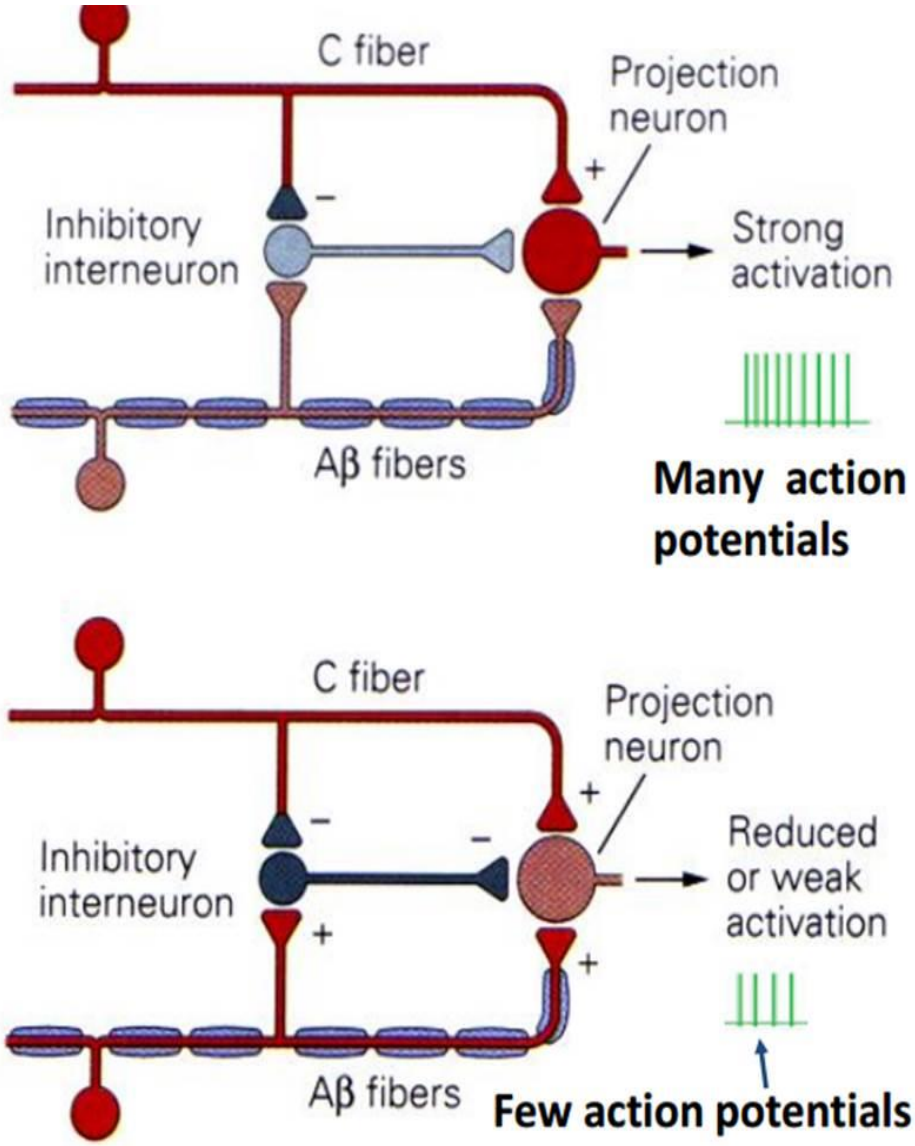


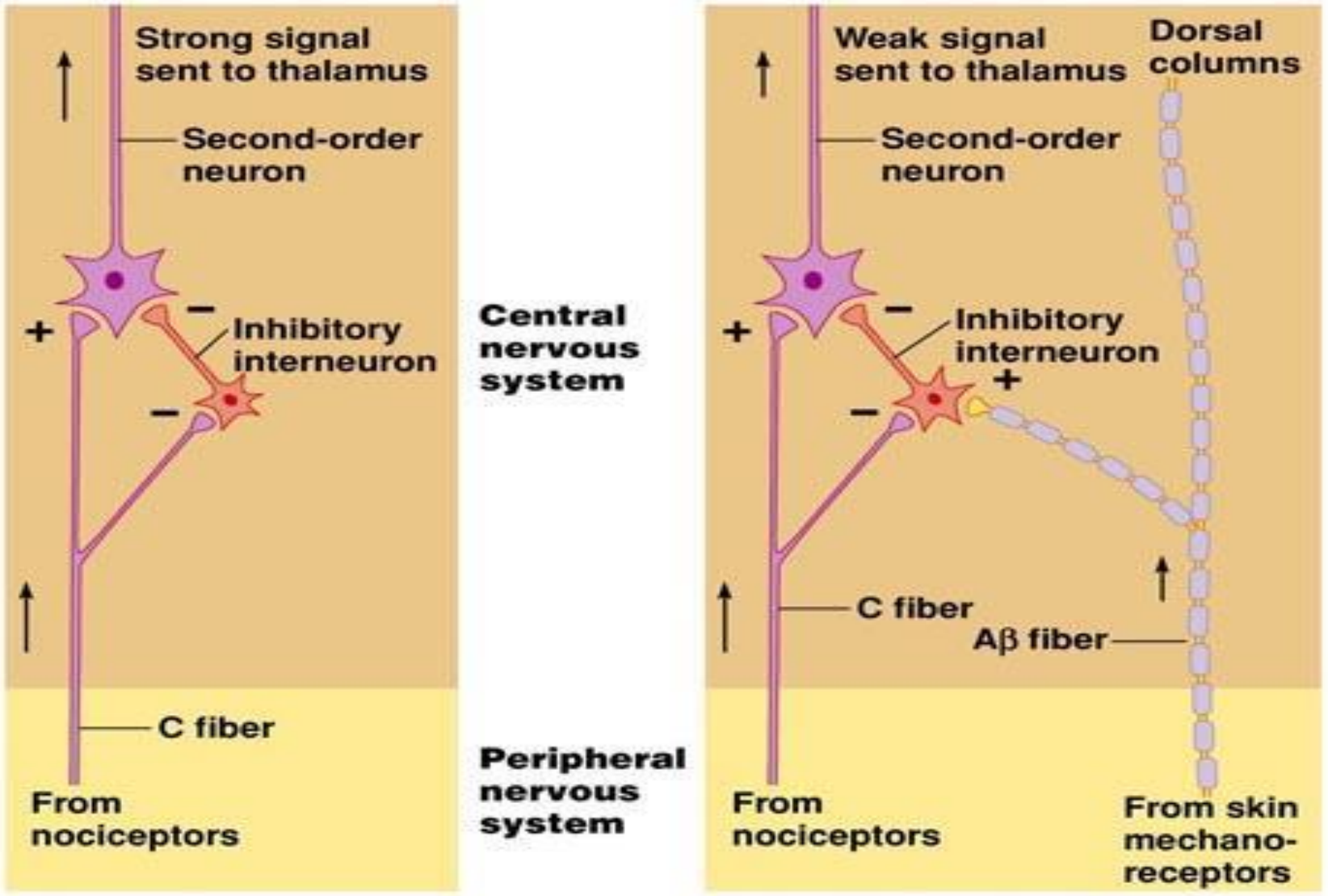
Gate opened or closed by 3 factors:



The gate theory of pain control (Cont.)

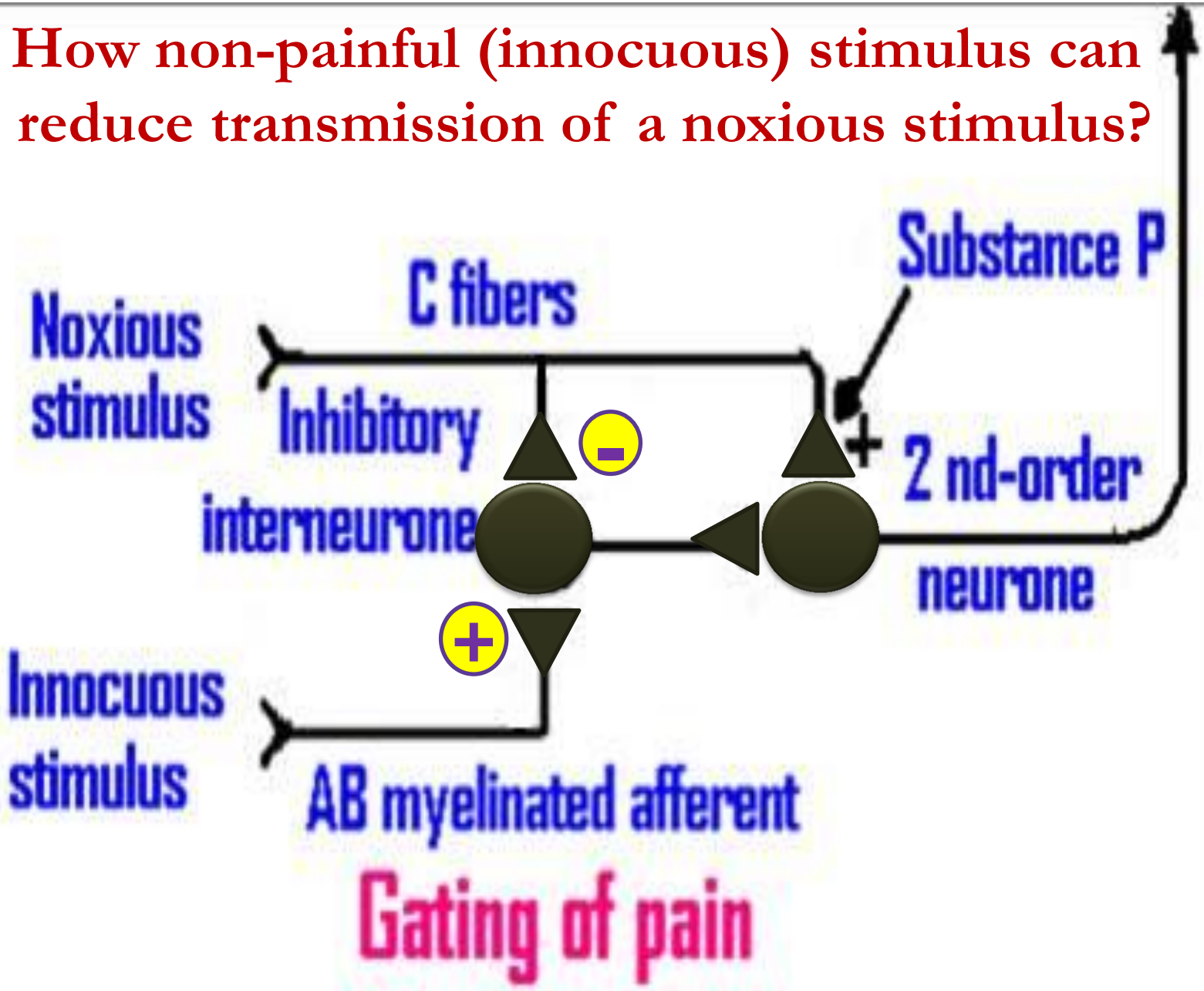
- Projection neuron receiv input from both C-fibers and Aβ fibers.
- Impulses coming along type C pain fibers cause the release of **"substanc P"** from these fibers and inhibits the inhibitory interneuron (open the gate).
- While impulses coming along Aβ fibers tend to keep the gate closed by activating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



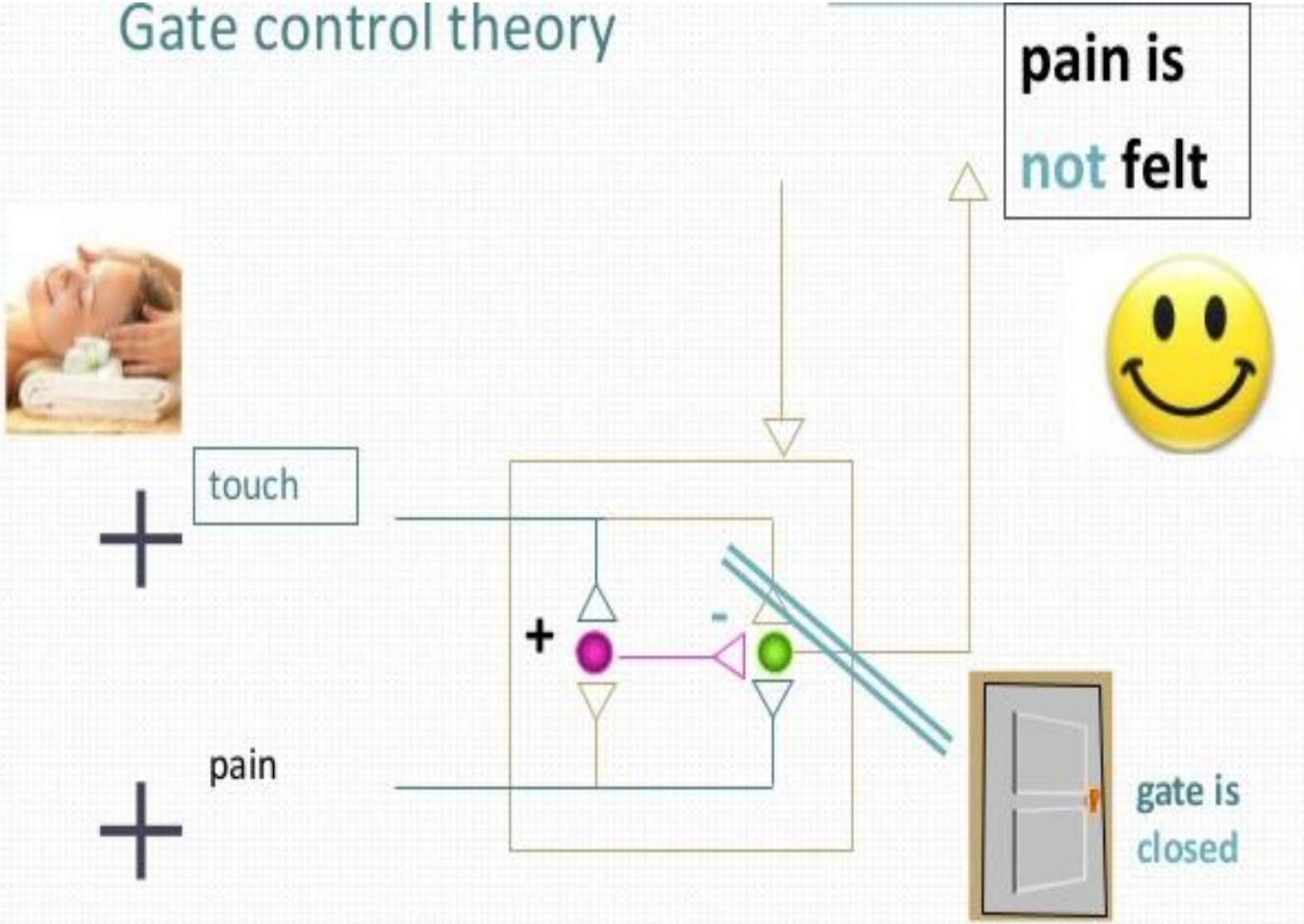


(a) Unmodulated pain (b) Modulation of pain

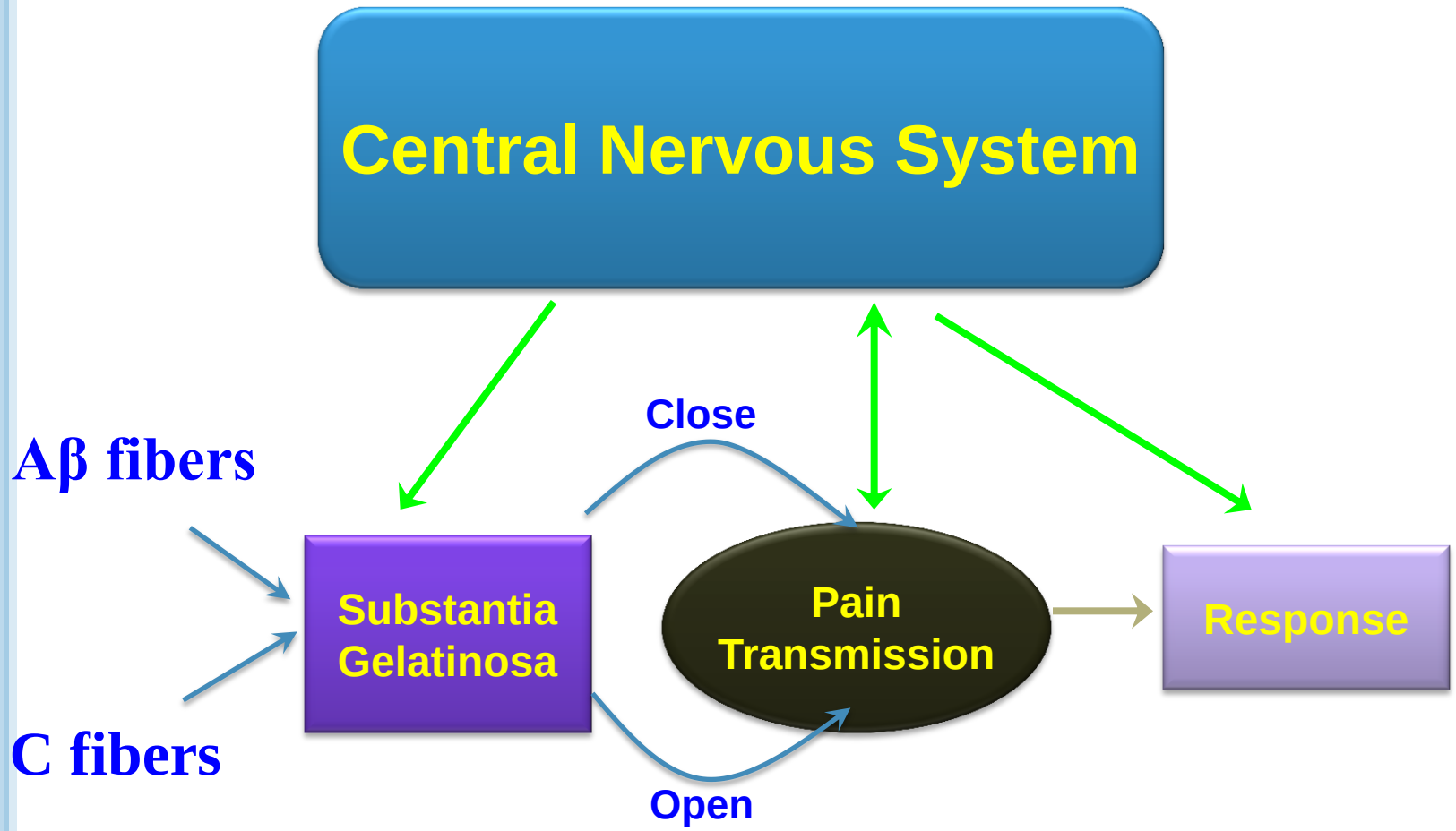
How non-painful (innocuous) stimulus can reduce transmission of a noxious stimulus?



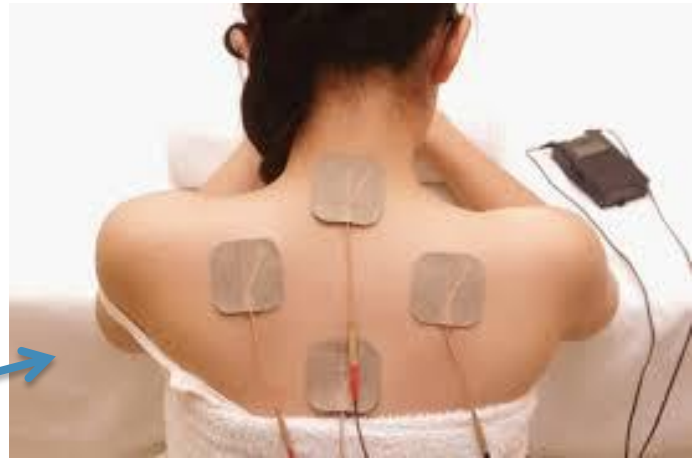
Gate control theory



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


Central Nervous System
Close
Aβ fibers
Substantia Gelatinosa
Pain Transmission
Response
C fibers
Open

- 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

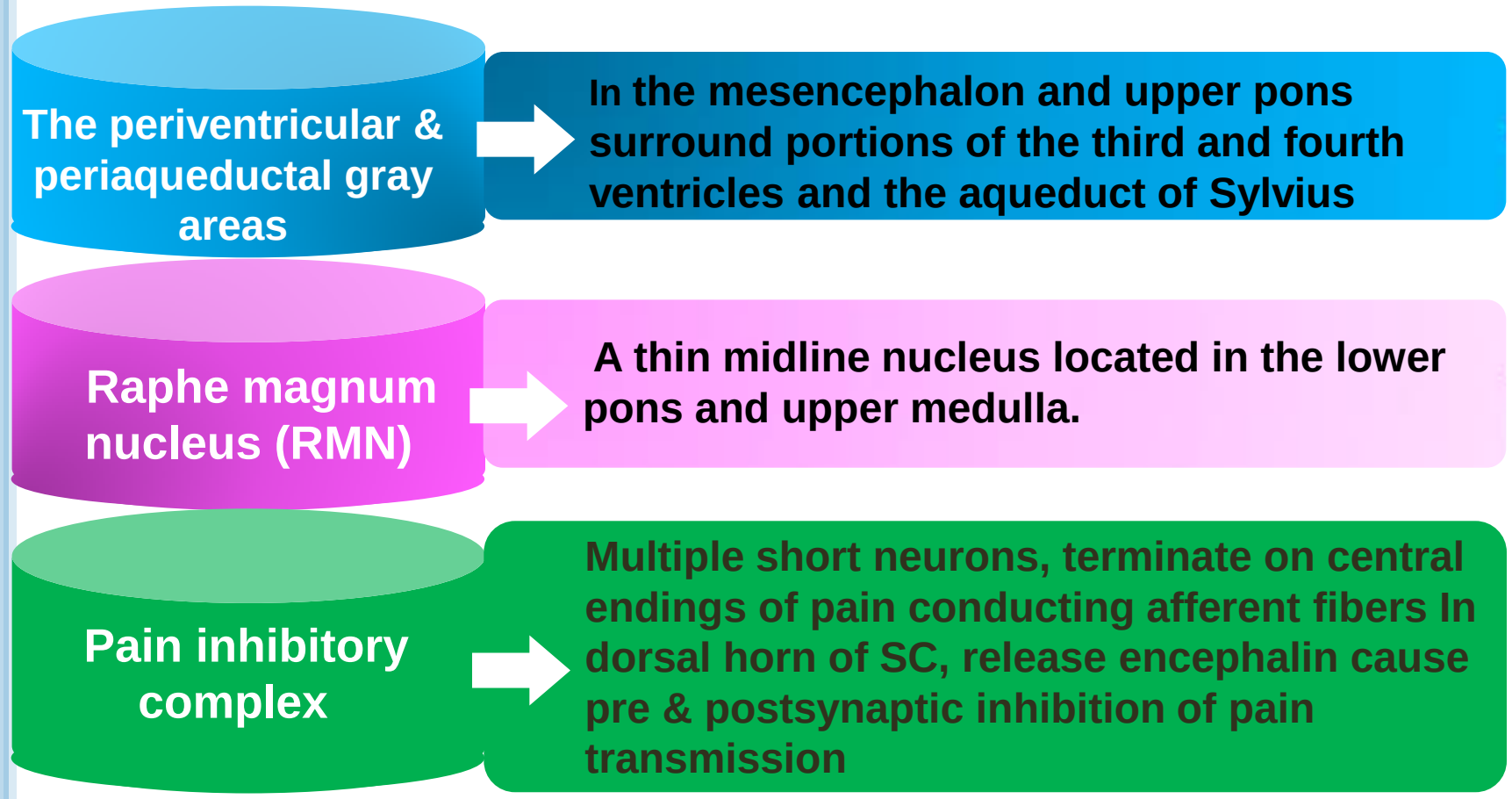
- Specialised nerve impulses arise in the brain itself and travel down the spinal cord to influence the gate.
- It can send both inhibitory and excitatory messages to the gate sensitising it to either C or A-β fibres.
- The inhibitory neurons make a pain blocking agent called encephalin.
- Encephalin is an opiate substance which can block the neurotransmitter from the C fibers (substance P), and this keeps the gate closed.

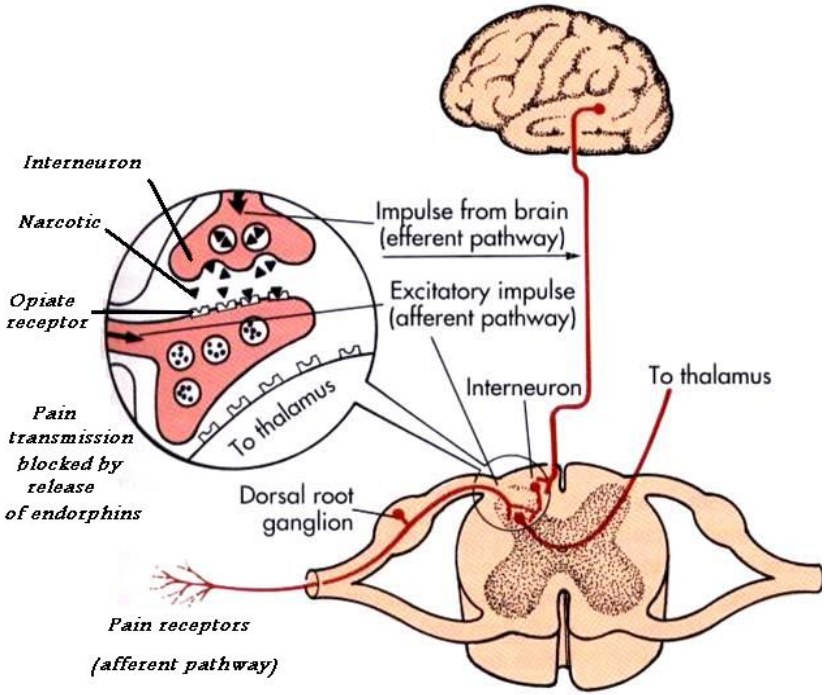
Conditions that open or close the gate

	Conditions that open the gate	Conditions that close the gate
Physical conditions	▪ Extent of the injury ▪ Inappropriate activity level	▪ Medication ▪ Counter stimulation, e.g. massage
Emotional conditions	▪ Anxiety or worry ▪ Tension ▪ Depression	▪ Positive emotions ▪ Relaxation ▪ Rest
Mental conditions	▪ Focusing on the pain ▪ Boredom	▪ Intense concentration or distraction ▪ Involvement and interest in life activities

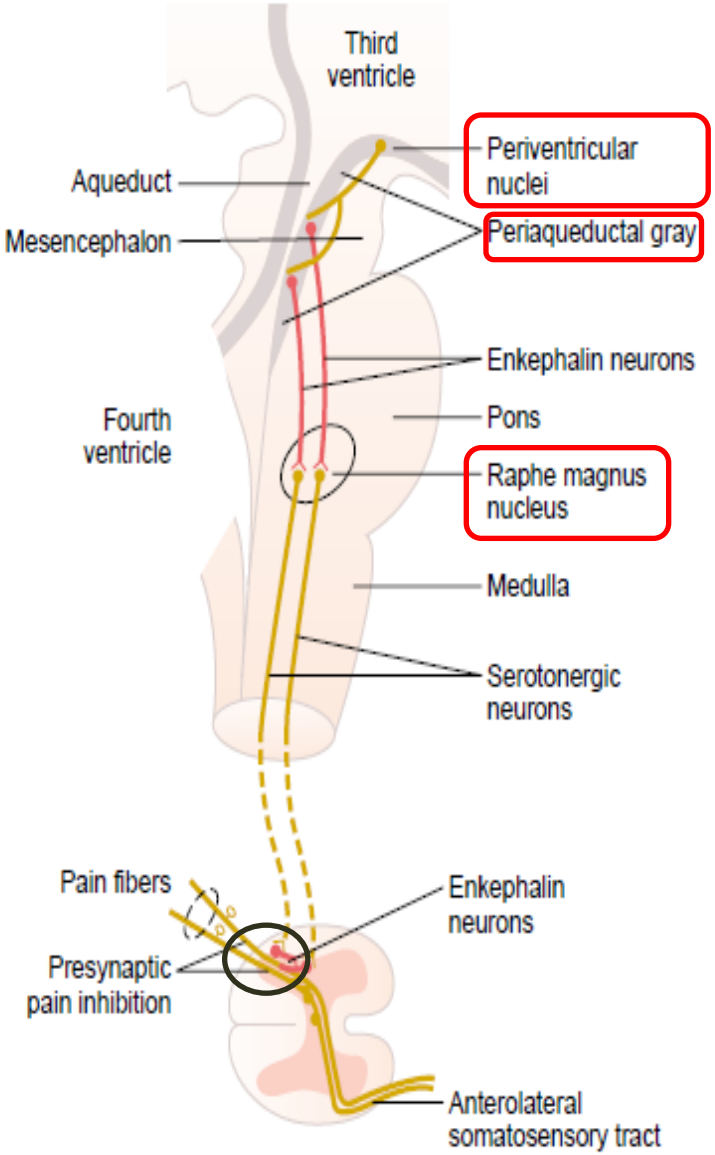
Supra spinal modulation
(Special pain control analgesic system)

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



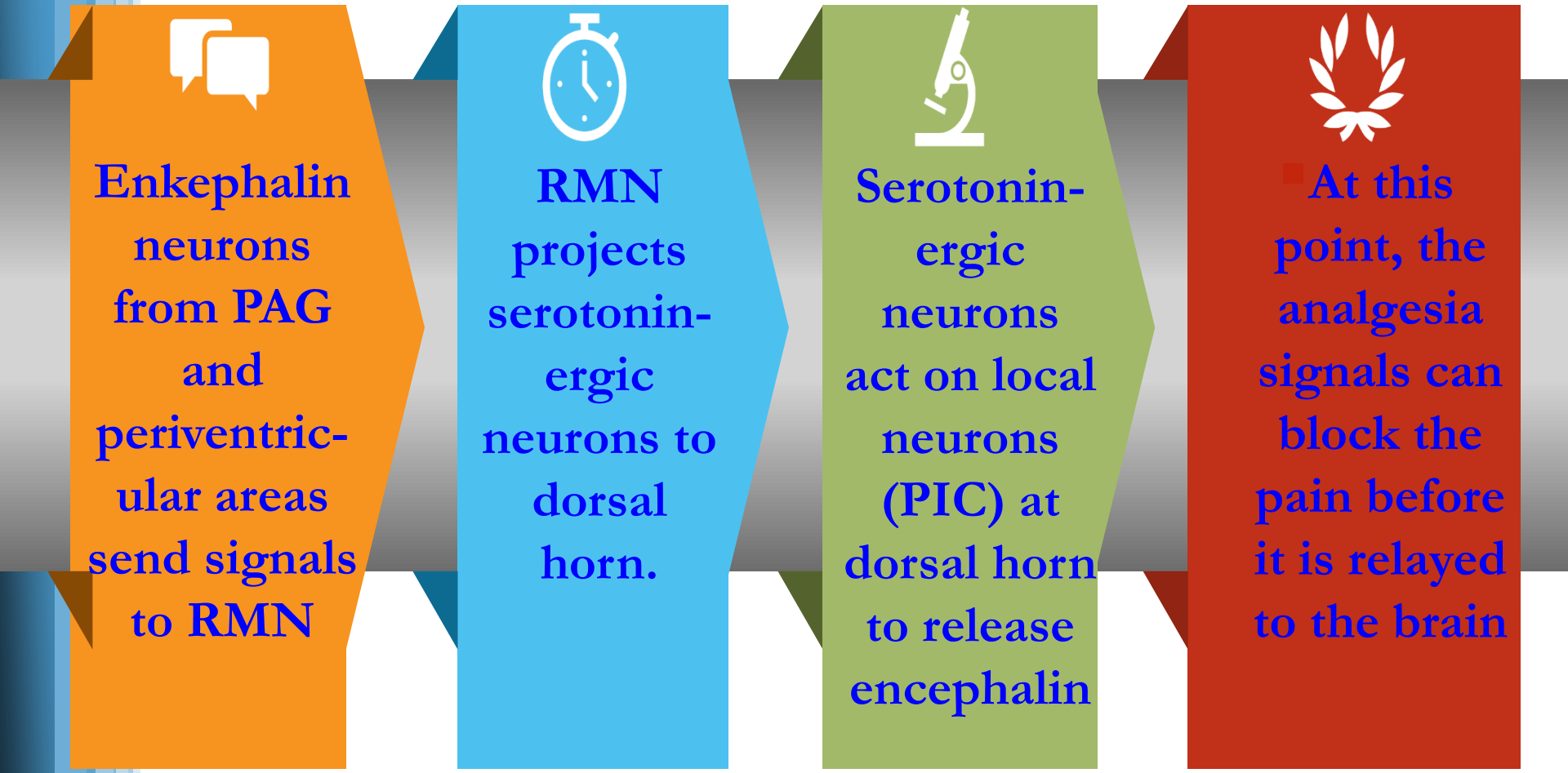


Pain inhibitory complex

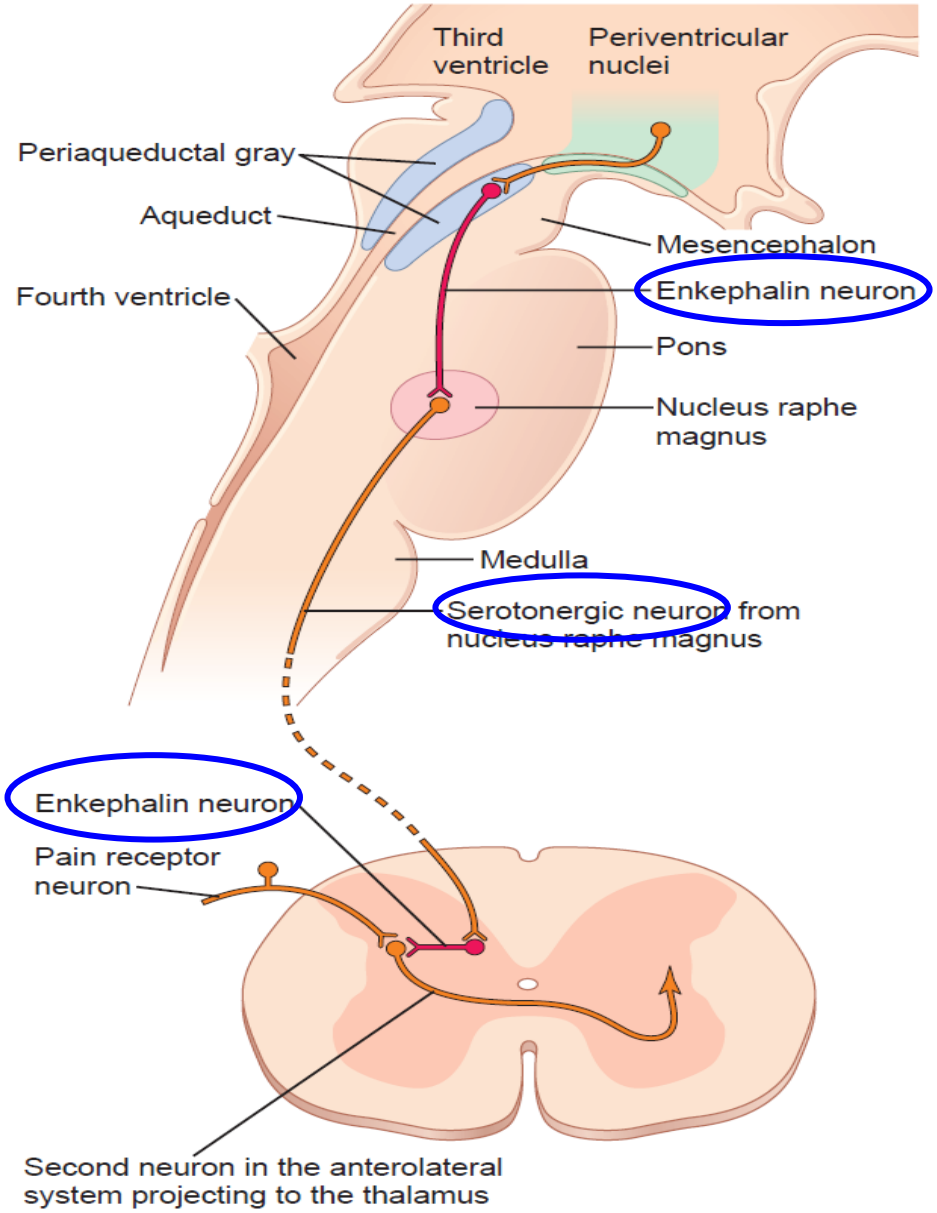


Analgesia system of the brain and spinal cord, showing (1) inhibition of incoming pain signals at the cord level and (2) presence of *enkephalin-secreting neurons* that suppress pain signals in both the cord and the brain stem.

Analgesia occurs as follows:



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, encephalin, 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

Mechanism

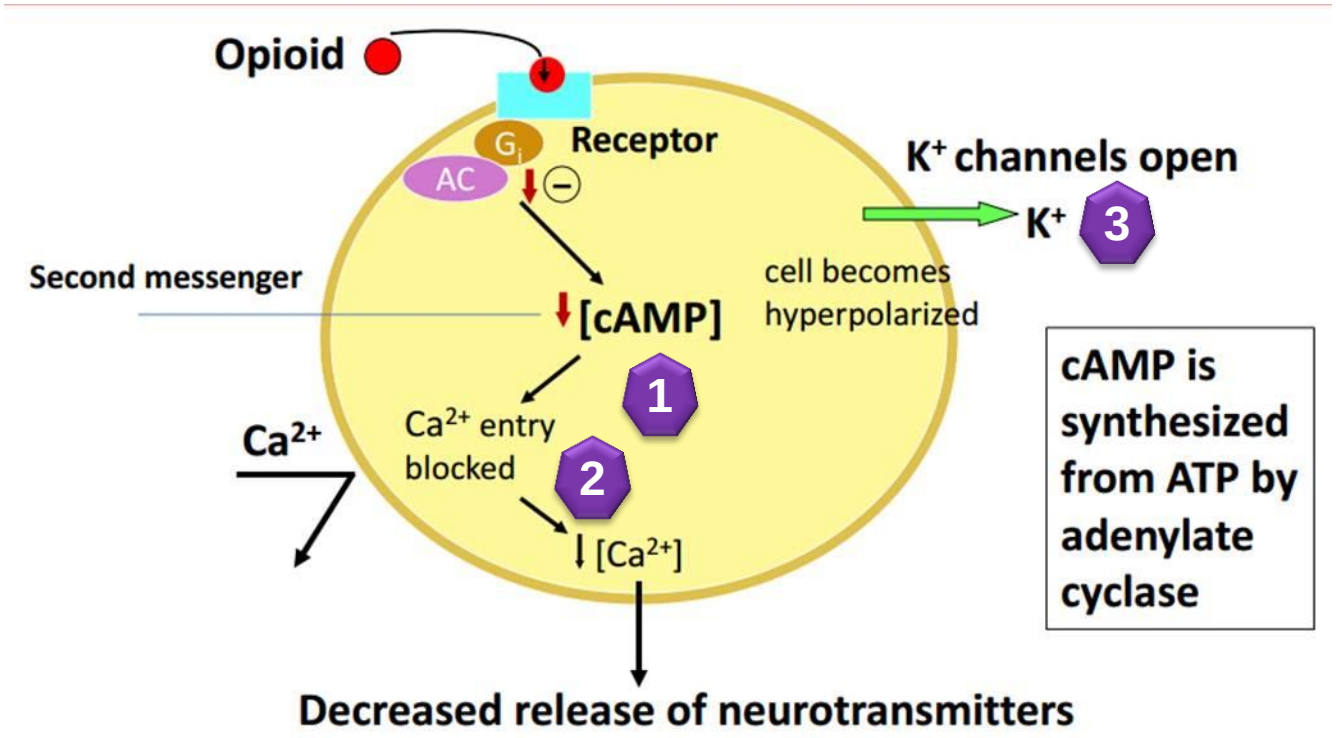
Direct effect

- Inhibiting discharge of nociceptor neurons.
- Inhibiting release of substance P from central terminal of nociceptor neurons
- Cause inhibition of dorsal horn spinothalamic neuron.

Indirect effect

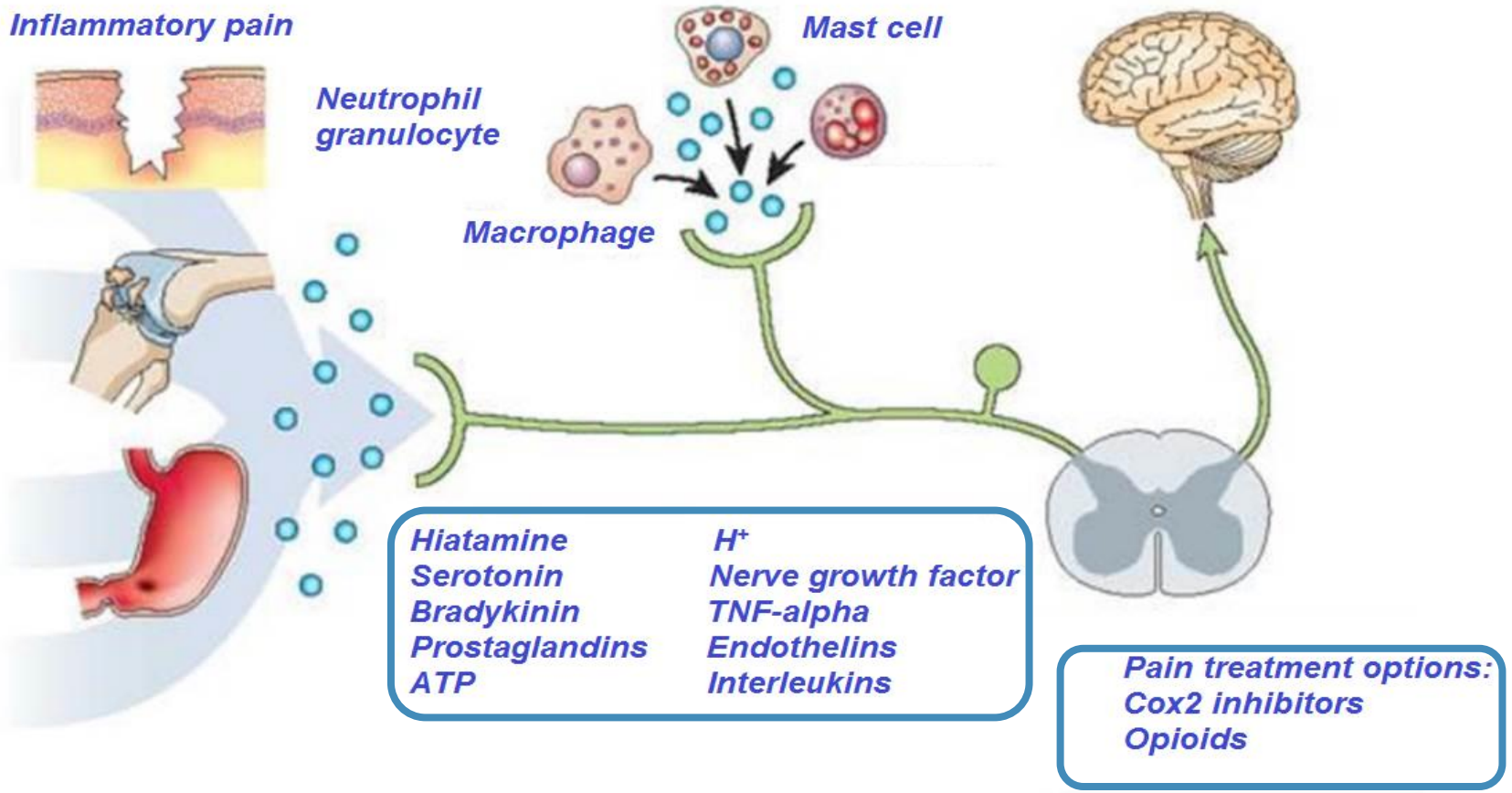
- Activating the descending inhibitory pathway by exciting PAG neurons
- Activating neurons in the brain stem which suppress pain transmission directly or indirectly via activation of encephalinergic containing inhibitory interneurons

Cellular actions of Opioid peptides



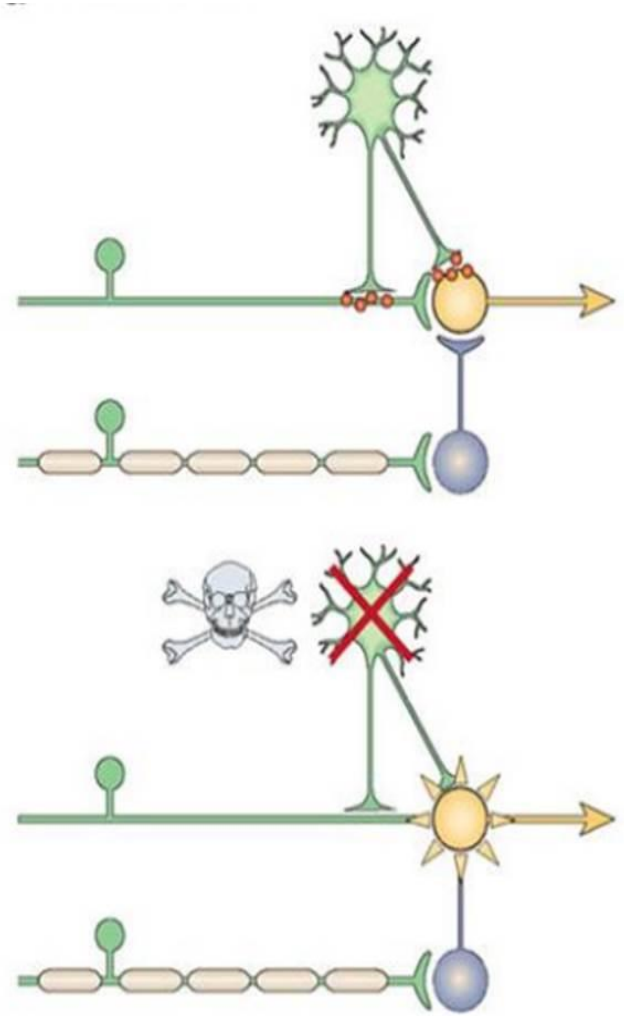
- Reduction of cAMP synthesis by inhibiting Adenyl cyclase
- Inhibition of transmitter release by inhibiting opening of Ca^{++} channels
- Hyperpolarization by facilitating opening of voltage gated K^+ channels

Pain Facilitation: Peripheral Sensitization



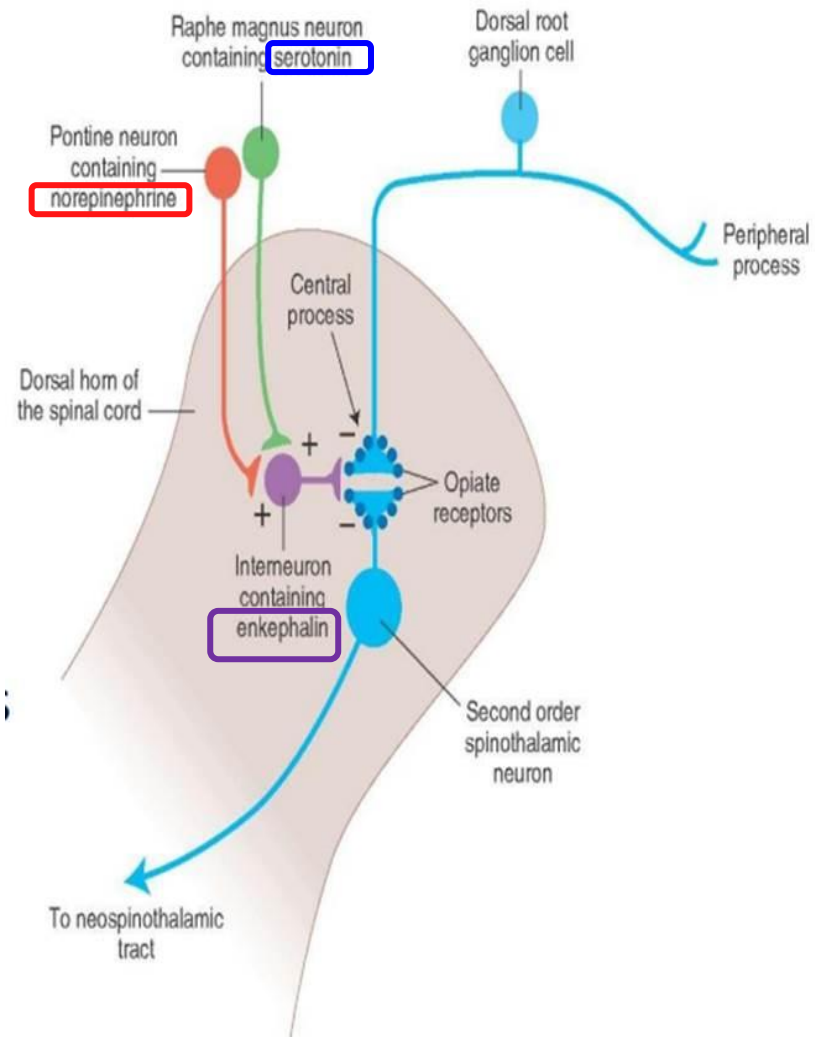
- Inflammatory mediators can directly activate nociceptors or cause their sensitization (decrease threshold as prostaglandins)

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

Neurotransmitters for Pain Modulation



- Serotonin
- Noradrenaline
- Encephalin

- The serotonergic and noradrenergic neurons are crucial in the supraspinal modulation
- Destroying these neurons with neurotoxins blocks the their analgesic actions

Terms frequently used

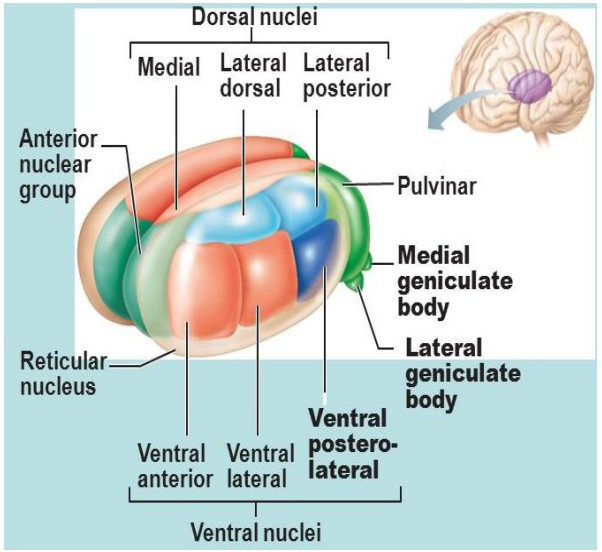
Hyperalgesia
Excessive Pain (e.g due to sun burn)

Allodynia
Pain caused by any other sensation e.g. touch

Muscular Pain
Less blood flow in the muscles (ischemia)

Causalgia
Burning pain

Thalamic Syndrome



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

Trigeminal neuralgia

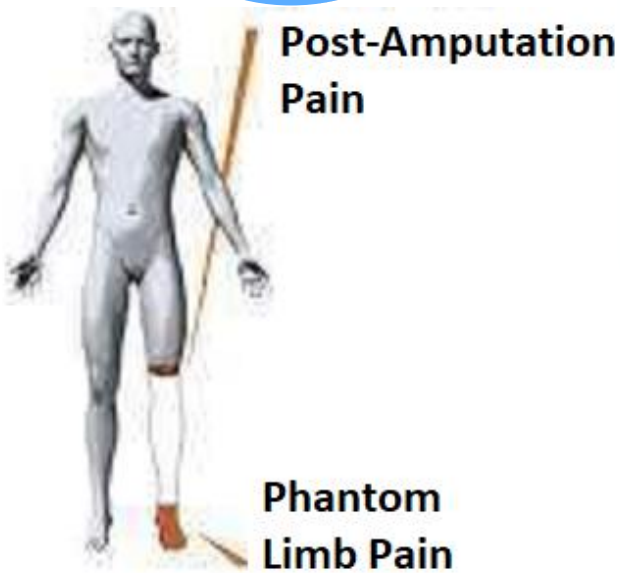
- It is excruciating intermittent pain by stimulation of trigger area in the face.
- e.g. Washing of face, combing hair, blast of air on face.
- It results from compression of trigeminal nerve root by blood vessels.

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.

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 serotoninergic or adrenergic neurons e.g. antidepressants.

Thank You!