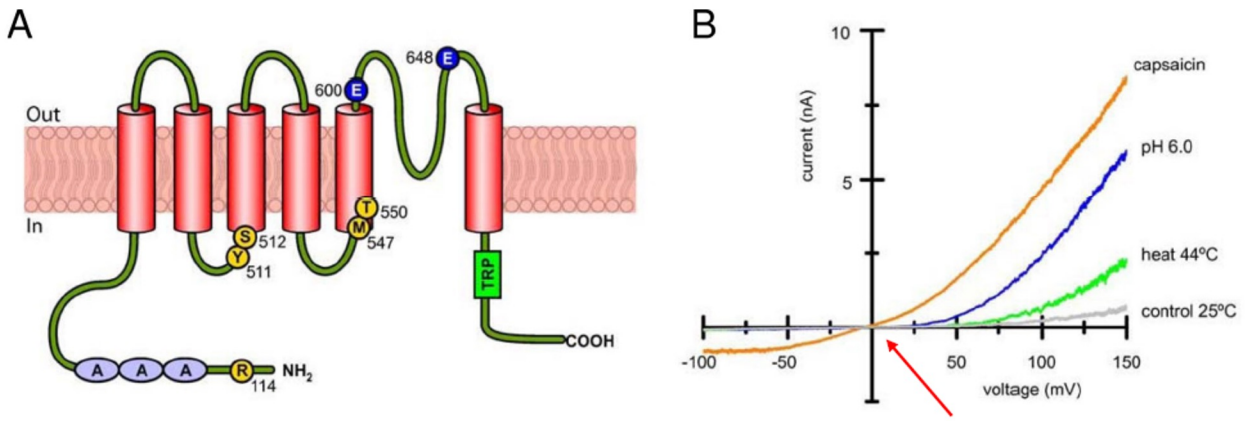
Pain – Exercise solutions

1) Nociceptive system: Explain the primary sensory transduction process in a free nerve ending of a nociceptive sensory neuron. Which ion channel (name?) is involved in this process and what is its ion permeability? Name three types of stimuli which can, in principle, activate a nociceptor.

TRP channels: A large group of non-selective cation channels activated by different chemical and physical signals



Subfamilies:
TRP-C
TRP-V
TRP-M
TRP-A
TRP-N
…

-Many activated by pathways downstream of PL-C (e.g. Diacylglycerol)
-Many activated in a mechanosensitive way
-Also activated by heat, cold, irritants

Note: E_{rev} = 0 mV
=> non-selective cation channels!

Belmonte & Viana, *Mol. Pain* 2008

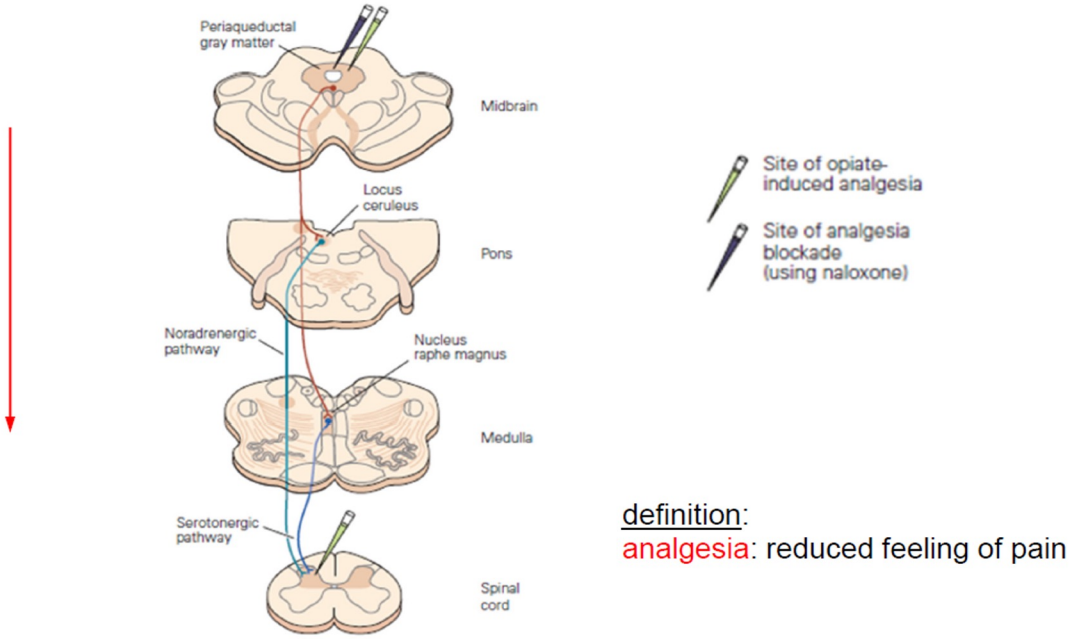
Transient receptor potential channel (TRP channel)

Non-selective cation channel

Capsaicin
Low pH value (H^+)
Heat

2) Explain the analgetic action of **morphine**, and where in the central nervous system it acts. During operations (e.g. a cesarean), morphine is often applied intrathecally (injected into the spinal cord of the corresponding level). Explain what is a possible advantage of this "local" application of morphine as compared to, for example, oral application.

Reduced pain sensation (= analgesia) after
1) Stimulation or 2) local infusion of opiates in i) periaqueductal grey (PAG)
and ii) local infusion of opiates in dorsal horn:

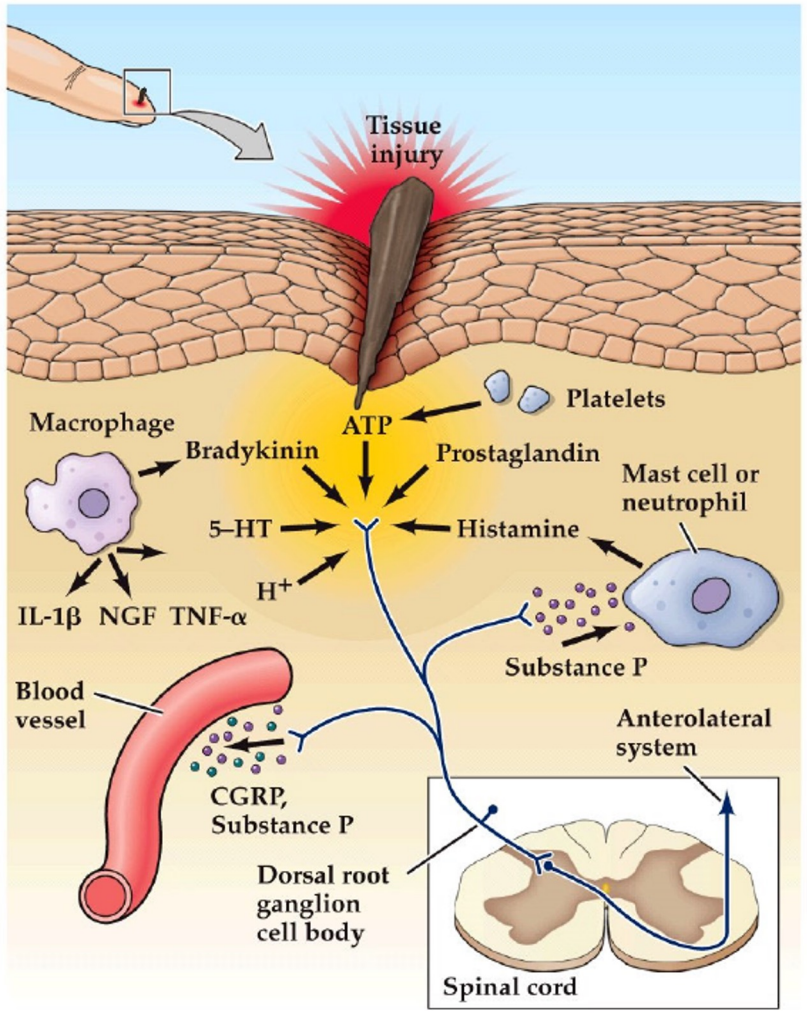


definition:
analgesia: reduced feeling of pain

1.Direct Action at Pain Site: Intrathecal administration delivers morphine directly to the spinal cord, the primary site for processing pain signals. This allows for a more direct and potent pain relief.
2.Reduced Systemic Side Effects: Since the morphine is applied locally, less of the drug circulates through the bloodstream. This reduces systemic side effects such as nausea, vomiting, and constipation, which are common with oral or intravenous administration.
3.Lower Doses Required: The direct application allows for lower doses of morphine to be effective, reducing the risk of opioid-related side effects and dependencies.
4.Rapid Onset of Action: Intrathecal administration provides a quicker onset of analgesia compared to oral routes, which is particularly beneficial in a surgical setting where immediate pain relief is necessary.
5.Prolonged Duration of Action: When administered intrathecally, morphine can have a longer duration of action, providing sustained pain relief during and after surgery.

3) What is the general mechanism behind peripheral sensitization? How is it different from central sensitization?

Inflammatory response to tissue damage



Sensitization:
hyperalgesia (increased pain Perception)
in the area of injury

1) Peripheral sensitization:

"Inflammatory soup"
Bradykinin
ATP, H^+
histamin
Prostaglandins (synth. by COX)

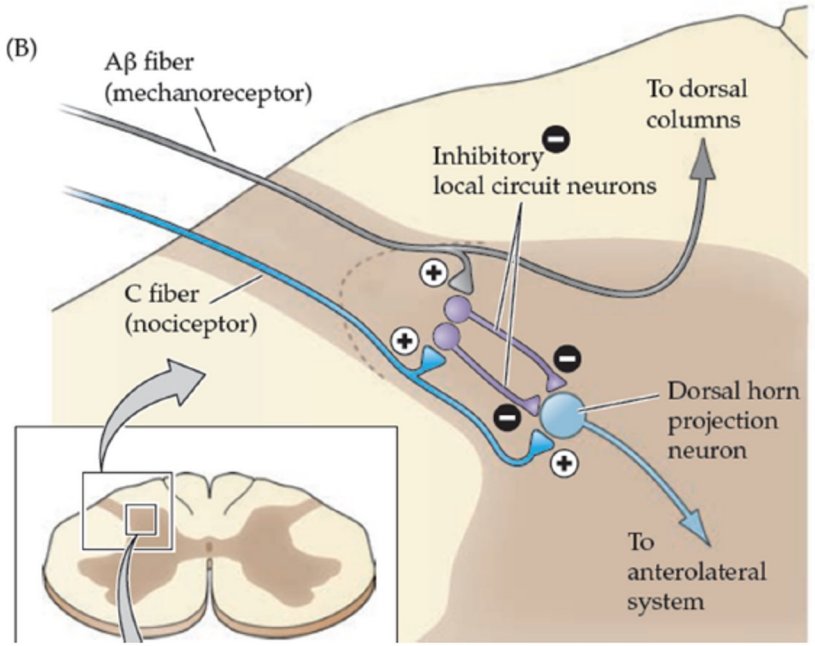
2) Central sensitization

Spinal cord dorsal horn

Purves Fig. 10.7

4) Why does “rubbing” diminish the subjective feeling of pain?

Gate theory of pain: Activation of mechanoreceptors modulates nociceptive processing in spinal cord dorsal horn



- **Aβ, and C-fibers** (carrying nociceptive info) synapse in dorsal horn
- Aβ fibers (mechanosensation) pass through dorsal horn (see Unit 4)
- **but**, in dorsal horn, Aβ fibers make **collateral** synapses on local inhibitory interneurons
- *the latter* inhibit dorsal horn projection neurons of the nociceptive system

=> "rubbing" diminishes subjective feeling of pain

Purves Fig. 10.8 B

5) “Chronic pain is long standing pain that persists beyond the usual recovery period or occurs along with a chronic health condition, such as arthritis.” What do you think are the physiological and cellular basis of chronic pain? [speculative]

1.Peripheral Sensitization: In chronic pain, peripheral nerves (nerves outside the brain and spinal cord) can become sensitized. This means that the threshold for activating these nerve endings is lowered, so they may respond to stimuli that wouldn't normally be painful (like light touch). This sensitization is often due to changes in ion channels on nerve cells or the release of inflammatory substances that make the nerves more sensitive.

2.Central Sensitization: This is a key feature in chronic pain. It occurs in the spinal cord and brain and represents an enhancement of the signaling and processing of pain. Nerve cells in the spinal cord become more excitable and can amplify pain signals before they reach the brain. There's also reduced effectiveness of the body's natural pain control mechanisms. This can lead to a phenomenon known as "wind-up," where repetitive stimulation leads to progressively increasing responses in the central nervous system, making the pain experience more intense and long-lasting.

3.Neuroplastic Changes: Chronic pain is associated with neuroplasticity, where the nervous system undergoes structural and functional changes. This includes changes in how pain signals are processed in the brain and can lead to the pain being maintained even in the absence of the original cause. For instance, in conditions like phantom limb pain, the brain continues to receive pain signals from nerves that originally innervated the now-missing limb.