Pain Pathophysiology

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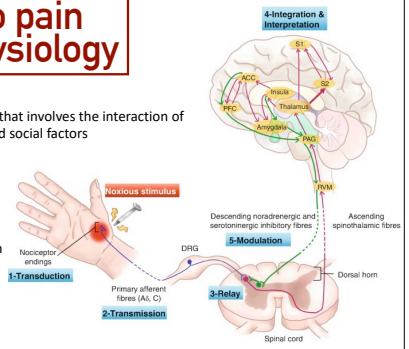
Intro to pain pathophysiology

Pain is a complex process that involves the interaction of biological, psycological and social factors

Pain pathophysiology

- describes the process that lead to pain experience
- involves the transmission of pain signals from the site injury to the brain
- determine brain response to the signals



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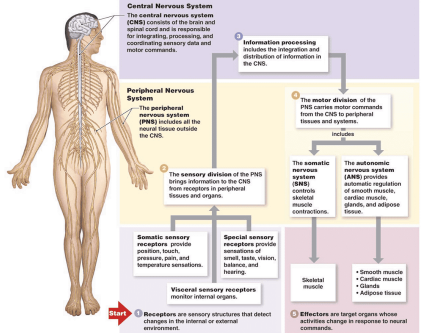
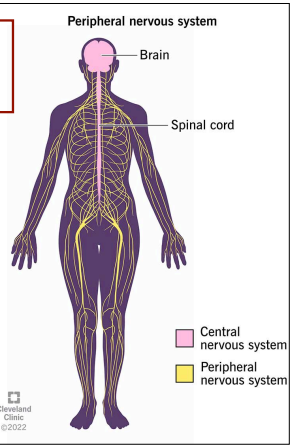
Nervous System



The pain pathways

Steps from the moment a noxious stimulus is detected to the perception of pain:

- the peripheral pathway
- the central pathway



The somatic nervous system

- Part of the peripheral nervous system —>controls voluntary movements and sensations
- Made of **sensory neurons:** from the body receptors to the CNS and **motor neurons** that transmit commands from the CNS to the muscles.
- SN: Detecting different stimuli (touch, temperature, pain, and proprioception)
- MN: activate the skeletal muscles and control contraction (body to move and maintain posture)
- SNS: under **conscious control** (influenced by external factors, such as learning, training, and motivation)

The somatic nervous system

- Damage: A motor and sensory impairments, such as paralysis, weakness, numbness, or loss of coordination.
- Disorders affecting the somatic nervous system can also **lead to involuntary movements, such as tremors or spasms, or abnormal sensations, such as phantom limb pain.**

The autonomic nervous system

- A part of the **peripheral nervous** system regulates the **body's internal environment**, including **organs, glands, and blood vessels**.
- It operates **automatically and involuntarily**
- responsible for **maintaining homeostasis**
- Divided in: the **sympathetic nervous system** and the **parasympathetic nervous system**.

The autonomic nervous system

- The **sympathetic nervous system** prepares for **action and stress** (increase heart rate, blood pressure, and respiration, and by diverting blood flow from non-essential organs to the skeletal muscles)
- The **parasympathetic nervous system** promotes **relaxation and recovery** (slowing down heart rate…)
- ANS also includes the **enteric nervous system**, which regulates the digestive system's motility and secretion independently of the central nervous system.
- Dysfunction: hypertension, cardiovascular disease, digestive problems, or sweating disorders.
- Treatments: include lifestyle modifications, medications, or specialized therapies, such as biofeedback or exercise training.

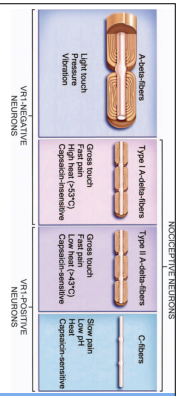
Peripheral pathway

Begins when a **noxious stimulus**, such as a cut, burn, or injury, activates **specialized sensory receptors** called **nociceptors**.

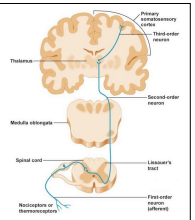
These nociceptors are located throughout the body in **skin, muscle, and internal organs**

Once the nociceptors are activated, they generate an **electrical signal** that travels along nerve fibers, called **afferent fibers**, towards the **spinal cord**.

Two types of afferent fibers:
- A-delta fibers: responsible for sharp, localized pain
- C fibers: responsible for dull, throbbing pain



A-delta fibers



Type of nerve fiber that are responsible for the transmission of fast, sharp, well-localized pain signals.

- **large diameter, myelinated, which allows for rapid transmission of signals**

Noxious stimulus, activates the nociceptors located in the skin, A-delta fibers are responsible for **transmitting the pain signal to the spinal cord and then to the brain**

The activation of A-delta fibers results in the **perception of fast, sharp pain that is well-localized** to the area of the body where the stimulus was applied.

A-delta fibers are considered a fast pain pathway, as they transmit pain signals quickly to the brain.

They are responsible for the initial stages of pain perception, and the activation is responsible for the **"first pain"** sensation that is **experienced immediately after a noxious stimulus**.

A-delta fibers

Understanding the role of A-delta fibers in pain perception brings to effective treatments for pain management:

- **Developing targeted pain medications** (drugs that block the transmission of pain signals in A-delta fibers, such as local anesthetics, can be used to provide targeted pain relief)
- **Developing non-pharmacological pain management techniques**: (development of non-pharmacological pain management technique transcutaneous electrical nerve stimulation (TENS)
- **Developing personalized pain management strategies:** (differentiate those who experience chronic, diffuse pain may benefit more from treatments that target other types of nerve fibers)

C fibers

Unlike A-delta fibers, C fibers are **unmyelinated** and have a **smaller diameter**, (transmit pain signals more slowly than A-delta fibers)

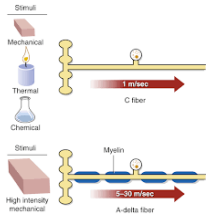
are responsible for the transmission of slow, dull, and poorly localized pain signals

The activation of C fibers results in the perception of slow, dull, and poorly localized pain that is often described as aching, burning, or throbbing.

considered a slow pain pathway

responsible for the later stages of pain perception, and their activation is responsible for the "second pain" sensation that is experienced after the initial sharp pain sensation

C fibers

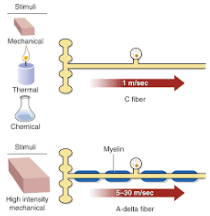


Understanding the role of C fibers in pain perception is important for developing effective treatments for pain management.

For example, medications that target C fibers, such as opioids, can be used to provide relief for **slow, dull, and poorly localized pain**.

However, **these medications are associated with a risk of addiction** and other side effects, which underscores the importance of understanding the underlying mechanisms of pain perception to develop safer and more effective treatments.

C fibers



Because C fibers are responsible for transmitting **slow, dull, and poorly localized pain signals**, medications that target C fibers can be used to provide relief for this type of pain.

Medications that targets C fibers is **opioids.**

- binding to opioid receptors, on the surface of C fibers in the spinal cord, which blocks the transmission of pain signals to the brain.
- Opioids are they are associated with a risk of addiction, tolerance, and other side effects.

C fibers

Other medications are :

- Nonsteroidal anti-inflammatory drugs (NSAIDs) (ibuprofen and aspirin) which work by **inhibiting the production of prostaglandins** that are involved in the **inflammatory response that can activate C fibers.**
- Antidepressants and anticonvulsants are also sometimes used to treat chronic pain by blocking the transmission of pain signals in the spinal cord.

Understanding the role: inform the development of **combination therapies**

Medications targeted on **both A-delta fibers and C fibers** may be more effective at providing relief for both fast, sharp pain and slow, dull pain than medications that only target one type of fiber.

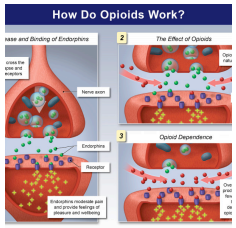
How opioids works?

Binding to opioid receptors located on the surface of these nerve fibers in the spinal cord.
Block the transmission of pain signals from C fibers to the brain, thereby reducing the perception of pain.

There are three main types of opioid receptors: **μ, δ, and k**

μ receptors are the **most abundant** and responsible for the **analgesic effects** of opioids. Binding to **μ** receptors on C fibers in the spinal cord, they activate a cascade of intracellular events that ultimately inhibit the release of neurotransmitters involved in pain transmission.

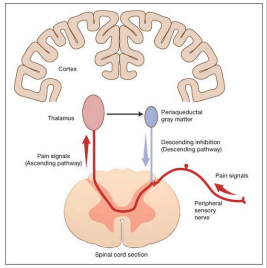
How opioids works?



Opioids also bind to mu receptors in other areas of the nervous system:
- Brainstem
- Limbic system

- Range of side effects (respiratory depression, sedation, nausea, and constipation).
- The binding in the brain make it responsible for their **addictive properties**, as it can result in feelings of euphoria and reward
- The most commonly used opioids, such as morphine, fentanyl, and oxycodone, primarily target the **μ receptor**

How antidepressant works?



- **Serotonin reuptake inhibitor** (SSRI)
- **Serotonin-norepinephrine reuptake inhibitor** (SNRI)

Effective in the treatment of chronic pain conditions, including pain associated with fiber C nerve fibers.

The exact mechanism how work on fiber C nerve fibers **is not completely understood**, but it is believed to **involve the modulation of certain neurotransmitters (**serotonin and norepinephrine)

Central pathway

The central pathway begins in the **spinal cord**, where the **afferent** fibers carrying pain signals synapse with **second-order neurons**.

Delivered to the **brainstem** and transmitted to the **thalamus (relay station)**, (receiving sensory information from the spinal cord and sending it to brain)

Transmitted to the **somatosensory cortex**, for processing sensory information.

The **modulatory pathway** is a series of descending pathways that run from the brainstem to the spinal cord.

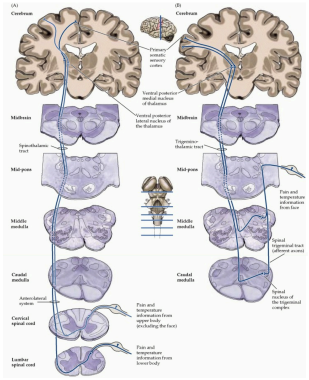
These **pathways release neurotransmitters**, such as serotonin, norepinephrine, and endorphins, that act to either enhance or inhibit the transmission of pain signals.

Central pathway

The **descending pathway** is responsible for the **inhibition of pain signals** and involves the **release of neurotransmitters** from the brainstem that act **on the dorsal horn of the spinal cord.**

The neurotransmitters involved in the descending pathway include **serotonin, norepinephrine, and dopamine.**

Also several other factors that can modulate the perception of pain, i.e.cognitive and emotional factors (anxiety and depression can increase the perception of pain, while distraction and relaxation can decrease the perception of pain)



The spino-talamic tract

- A pathway in the nervous system that carries information about pain, temperature, and crude touch from the body to the brain.
- Starts in the sensory receptors (skin, muscles, and internal organs)
- Sends information to the **spinal cord** through small nerve fibers called A-delta and C fibers.

second-order neurons (cross the midline) ascend to the brainstem and thalamus.

terminates in the **somatosensory cortex**, which is responsible for processing the sensations of touch, temperature, and pain.

The spino-talamic tract

Damage cause various forms of pain, such as **burning, shooting, or stabbing pain**, and may result in **hypersensitivity** to stimuli.

Central pain syndromes, such as those seen in patients with spinal cord injury or stroke, are often related to the spinothalamic tract's dysfunction.

The trigemino-talamic tract

- A pathway in the nervous system that carries information about pain, temperature, and touch from the face to the brain.
- Starts in the sensory receptors located in the **face, such as the skin, mucous membranes, and teeth**, and sends information to the **trigeminal ganglion**.
- transmitted through the **trigeminal nerve to the brainstem,** where it synapses with second-order neurons.

cross the midline of the brainstem and ascend to the **thalamus** (primary relay center for sensory information in the brain)

The trigemino-talamic tract

- Terminates in the **somatosensory cortex** (touch, temperature, and pain are processed)
- Damage result in **facial pain**, such as trigeminal neuralgia, which is characterized by sudden, severe, and shooting pain in the face.
- Disorders affecting the trigeminothalamic tract can also lead to **abnormal facial sensations, such as tingling, numbness, or hypersensitivity to touch.**

Modulatory pathways

The modulatory pathway regulates sensory and motor functions

- originate **in the brainstem through the spinal cord**, where modulate the transmission of sensory and motor signals.
- **serotonin, norepinephrine, and dopamine**
- primary function is to regulate **pain sensation**

Activated to **reduce the transmission of pain signals** from the site of injury to the brain.

Help to **reduce the sensation of pain** and promote healing.

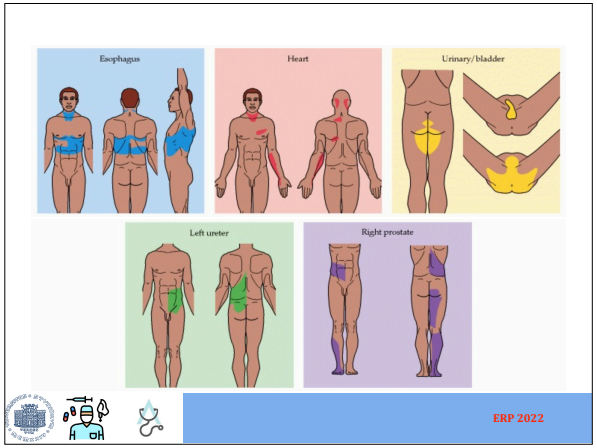
Plays a role in **motor control**, helping to regulate movement and coordination

Disorders of Modulatory pathways

Have significant impacts on sensory and motor function.

Dysfunction can lead to **chronic pain, movement disorders**, and other neurological conditions.

Understanding the role of the modulatory pathway is therefore critical for the diagnosis and treatment of these conditions.


Esophagus
Heart
Urinary/bladder
Left ureter
Right prostate
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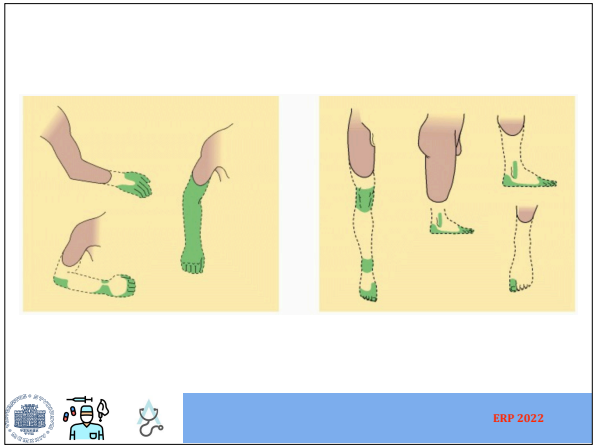
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