PAIN RESPONSE

(CHAPTER 32)

QUESTION 1

Describe the four stages of pain processing.

transduction

↓

transmission

↓

perception

↓

modulation

Transduction is the **creation** of an electrical pain signal in the free nerve endings of a **nociceptor**.

A noxious stimulus (heat, cold, mechanical pain) creates a **graded potiential** which, if intense enough, will trigger an **action potential**, leading to...

Transmission, in which the action potential travels down the length of the nerve, entering the spinal cord and then traveling upward to the brain.

Once it arrives in the brain...

Perception occurs, in which the brain actually perceives or feels the sensation of pain.

After the signal is received and processed in the brain...

The final step, **modulation**, kicks in.

The brain sends a signal **back down** the spine, causing the release of endogenous opioids which inhibit the pain signal at synapses **in the spinal cord**.

QUESTION 2

Why are these stages useful?

Understanding the four stages of pain processing is useful because they present us with the possible avenues of pain **treatment** and **prevention**.

You can:

- Block the signal from being created (at the source)
- Intercept or block the signal during transmission
- Alter the perception of the signal in the brain

(We'll go into more depth on this with question 24.)

QUESTION 3

Describe the mechanism of action of non-steroidal anti-inflammatory drugs (NSAIDs) in relief from pain.

Prostaglandins are a type of chemical produced throuhout the body which play a vital role in the body's inflammatory response, producing pain, swelling, and vasodilation.

They contribute to pain **transduction** by altering the membrane potential of nociceptors.

Prostaglandins are produced by a pair of enzymes known as **cyclooxygenases** (COX-1 and COX-2,) which create them from the precursor **arachidonic acid**.

NSAIDs block the action of one or both of these COX enzymes, reducing the body's ability to produce prostaglandins.

(Most NSAIDs block both, but a few, such as celecoxib (Celebrex) block only COX-2. You'll talk about this more in pharm.)

QUESTION 4

Describe the two types of pain fibers. What types of pain do they subserve?

Two types of nerve fibers involved in pain response:

Aδ (A-delta) fibers are **thicker**, **myelinated** neurons, meaning **low resistance** and **super fast** transmission.

C fibers are **thinner** and **unmyelinated**, meaning the action potential travels **much more slowly**.

Myelinated **Aδ fibers** enable **immediate response** to a stimulus by triggering quickly and getting the signal to the brain **as fast as possible**.

They are usually associated with a sharp, stinging or burning sensation.

Unmyelinated **C fibers**, which are much more numerous, provide a **low, ongoing response** to a persistent stimulus.

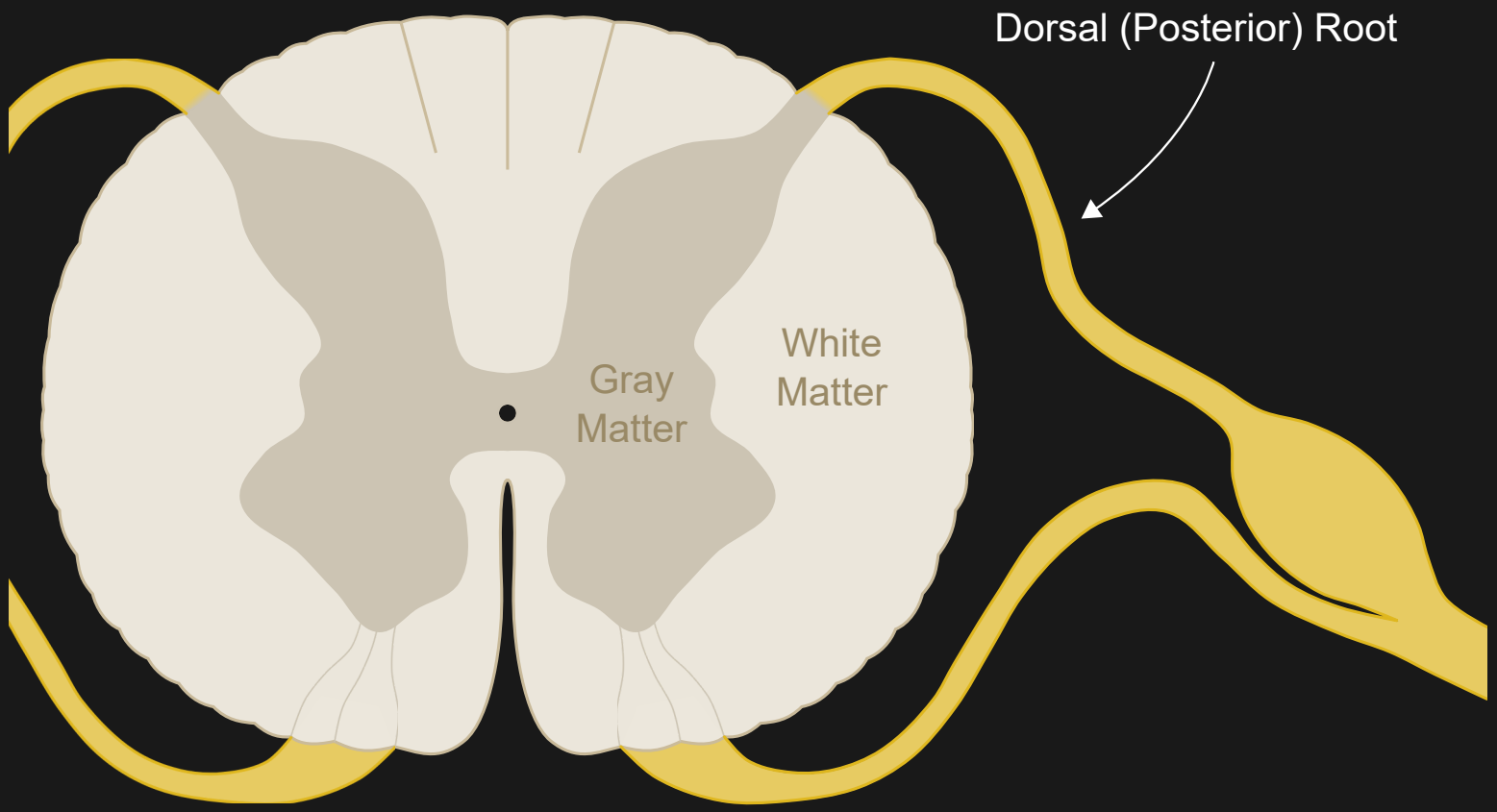
They are usually associated with a dull, ongoing soreness or aching sensation.

Example: When you get an injection, your Aδ fibers transmit the immediate "ouch." Your C fibers are the dull, sore sensation that lingers afterward.

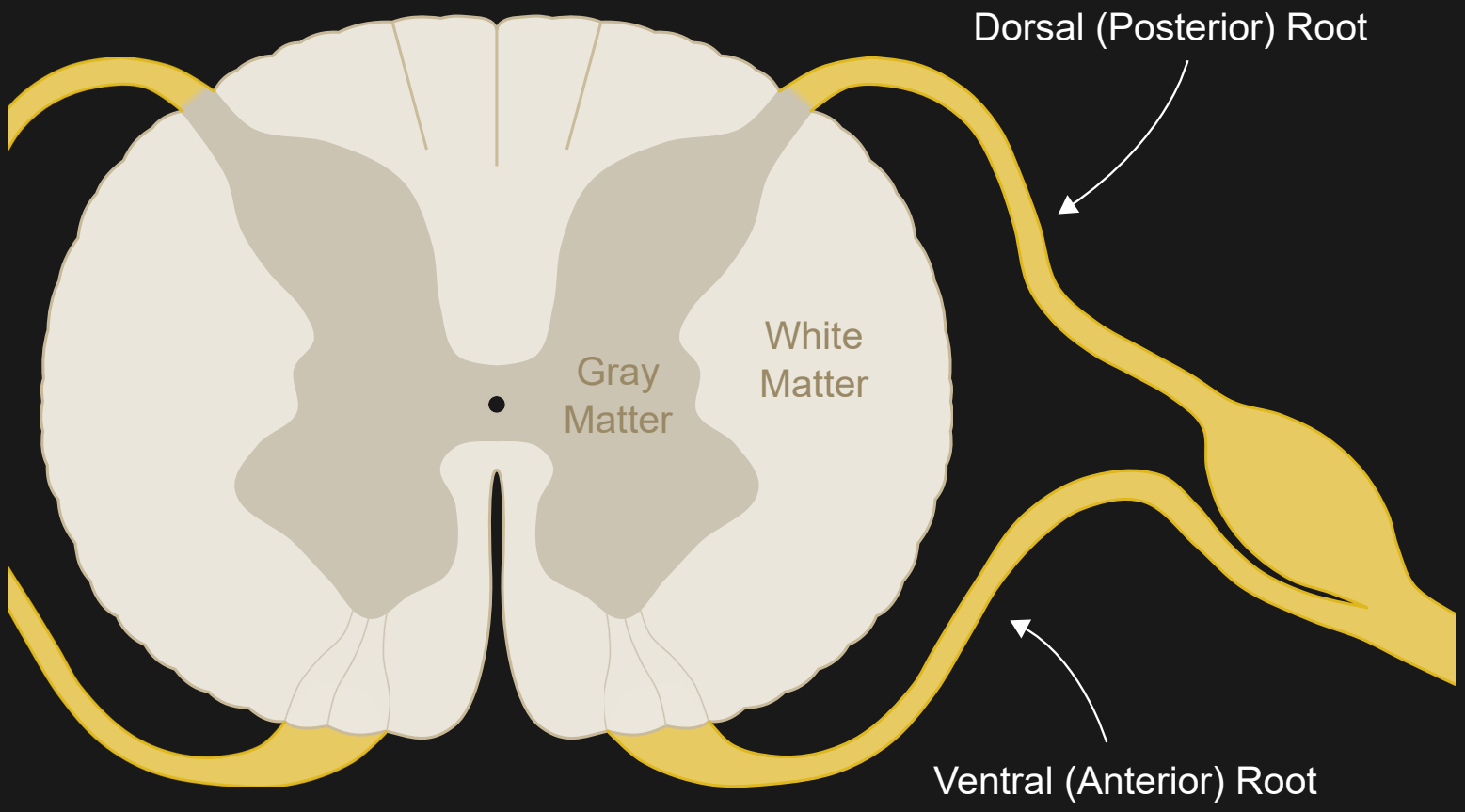
QUESTION 5

Where do the pain fibers enter the spinal cord? What is the major neurotransmitter released by pain fibers?

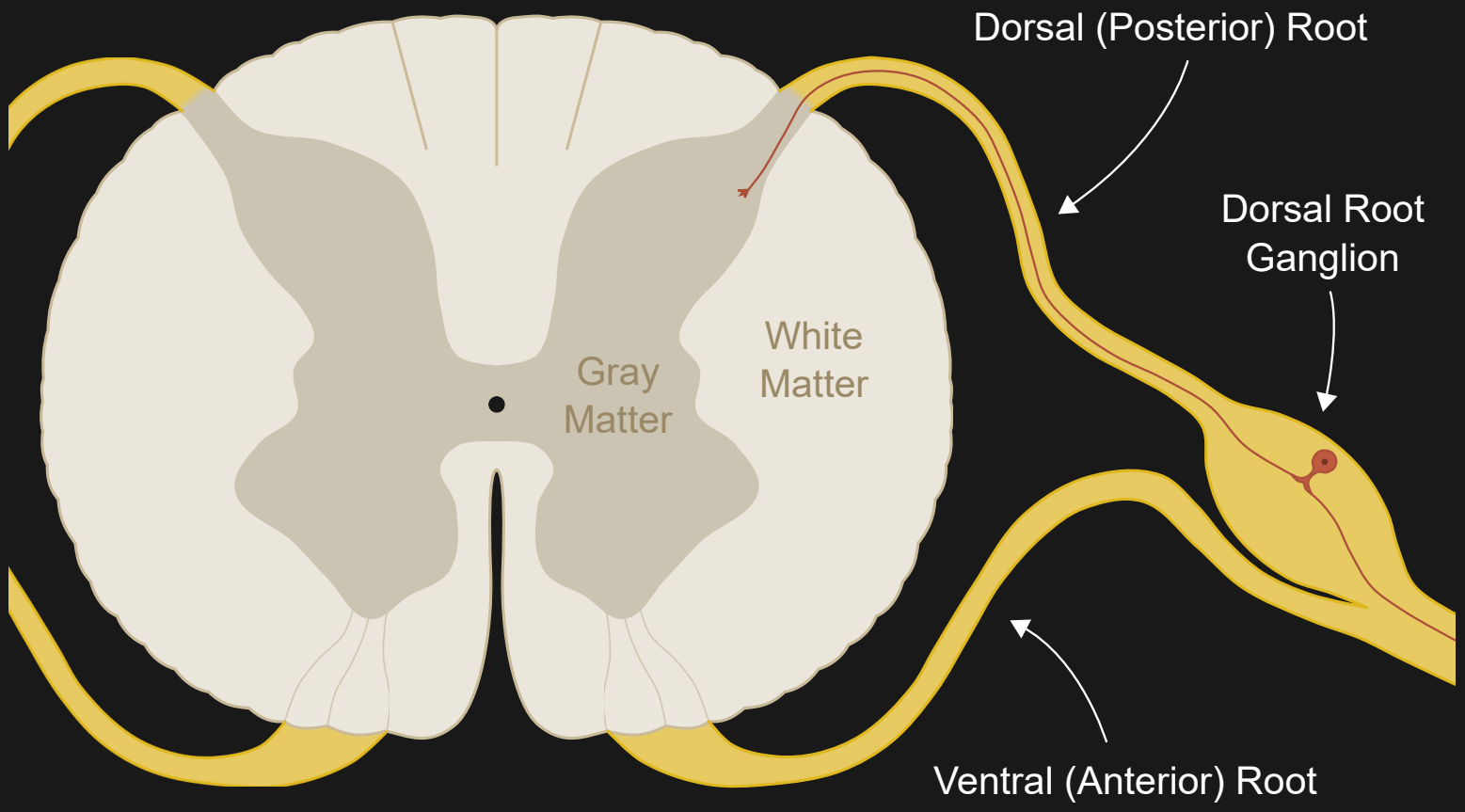
First, let's review some A&P...



Remember that sensory (afferent) nerves enter through the **dorsal root**...



and motor (efferent) nerves exit through the **ventral root**.



Nociceptors are **pseudo-unipolar neurons** in the **dorsal root ganglia**.

Pain signals originate from **free nerve endings** at the end of the nociceptor's dendrite, and travel along the dendrite towards the CNS.

They then follow the axon through the **dorsal (posterior) root** and enter the gray matter of the spinal cord.

The major **excitatory** neurotransmitter of sensory nerves (including nociceptors) is **glutamate**.

Many other neurotransmitters are involved in pain tranmission, both excitatory (e.g. Substance P, CGRP) and inhibitory (e.g. γ-aminobutyric acid/GABA.)

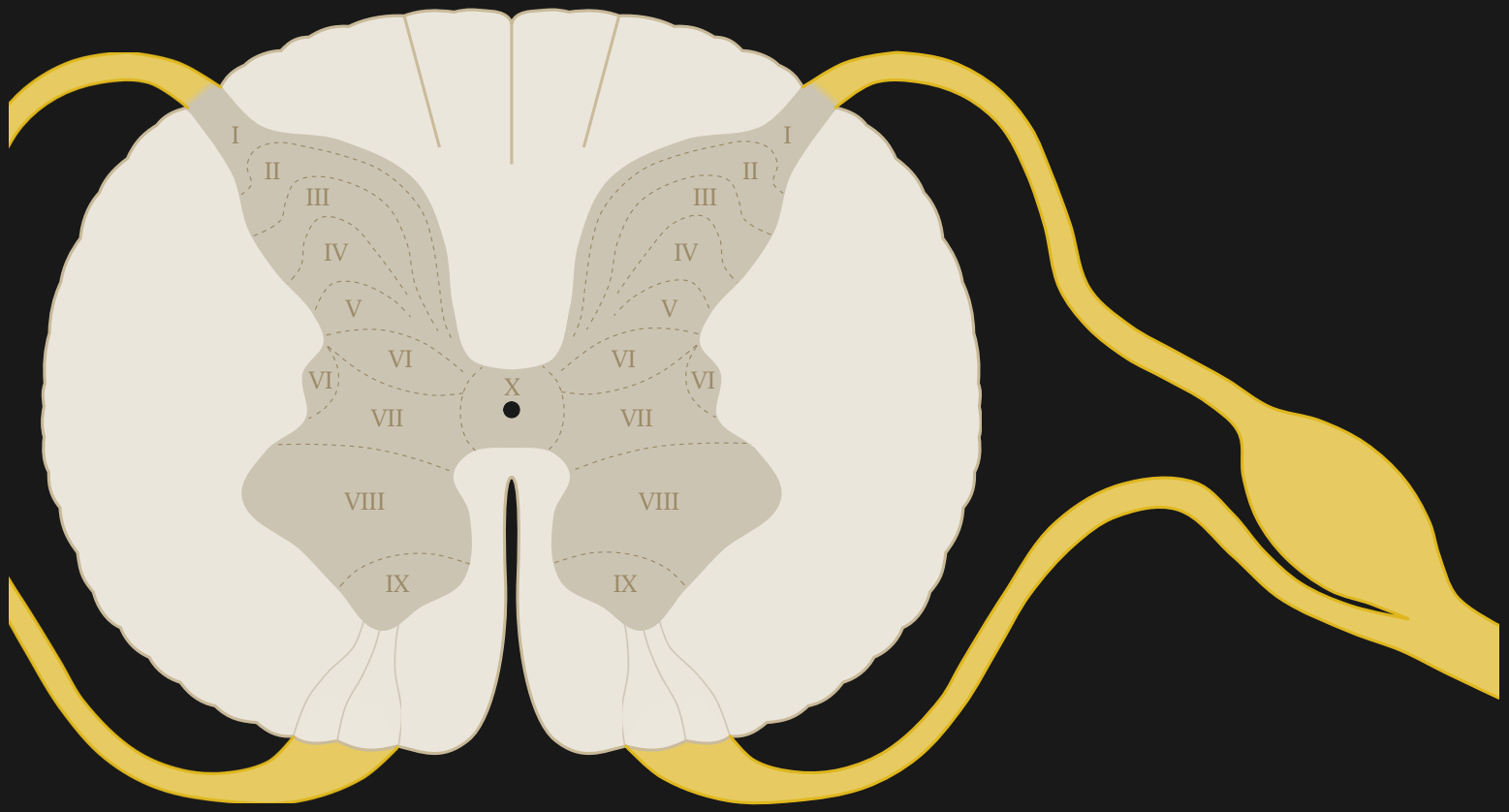
One thing to know about glutamate:

Repeated, long-term exposure of C fibers to glutamate can cause them to become **more sensitive**, leading to chronic pain **even after the stimulus is removed**.

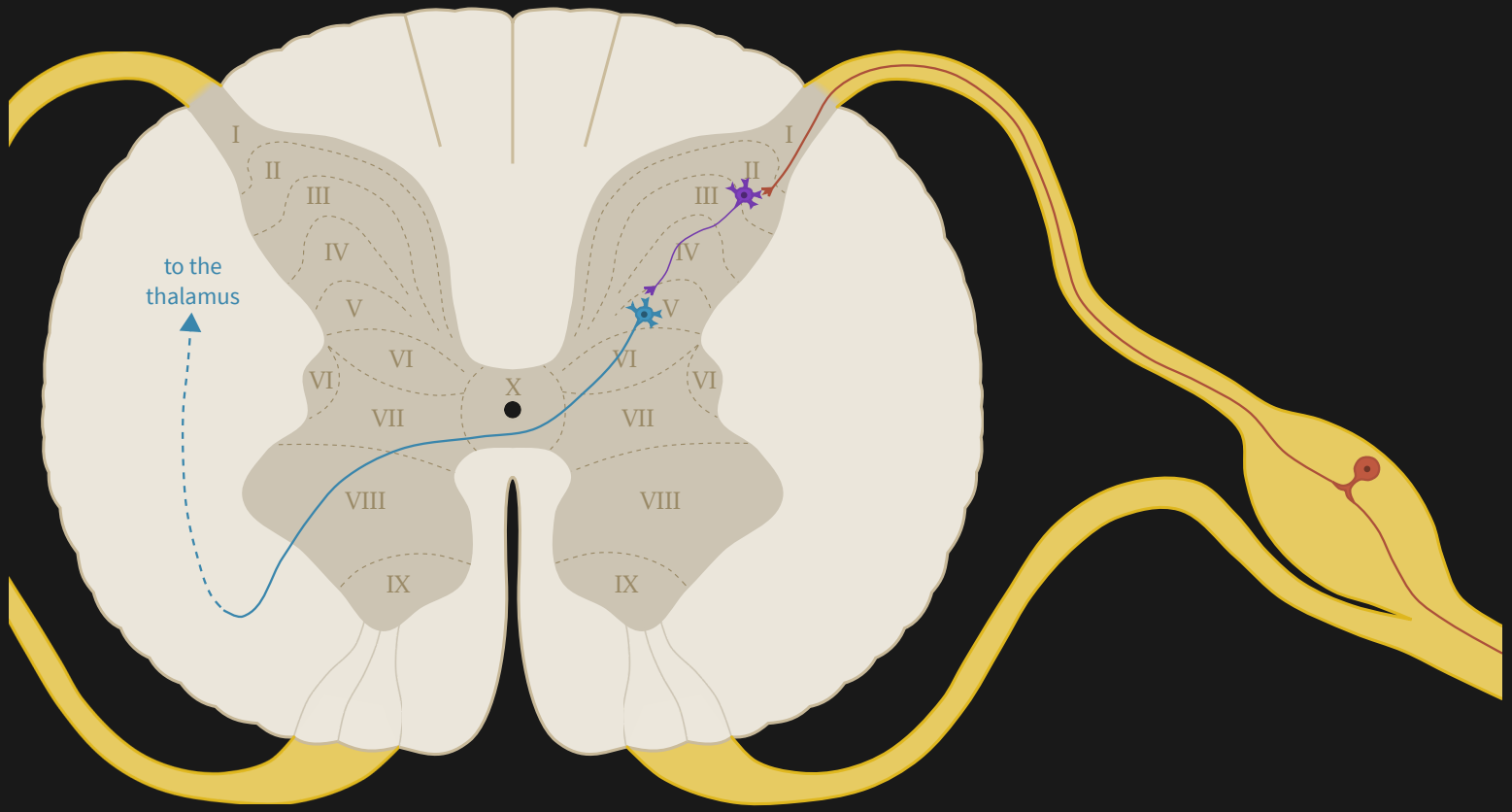
This condition is referred to as **central sensitization** or the "**wind-up phenomenon**."

QUESTION 6

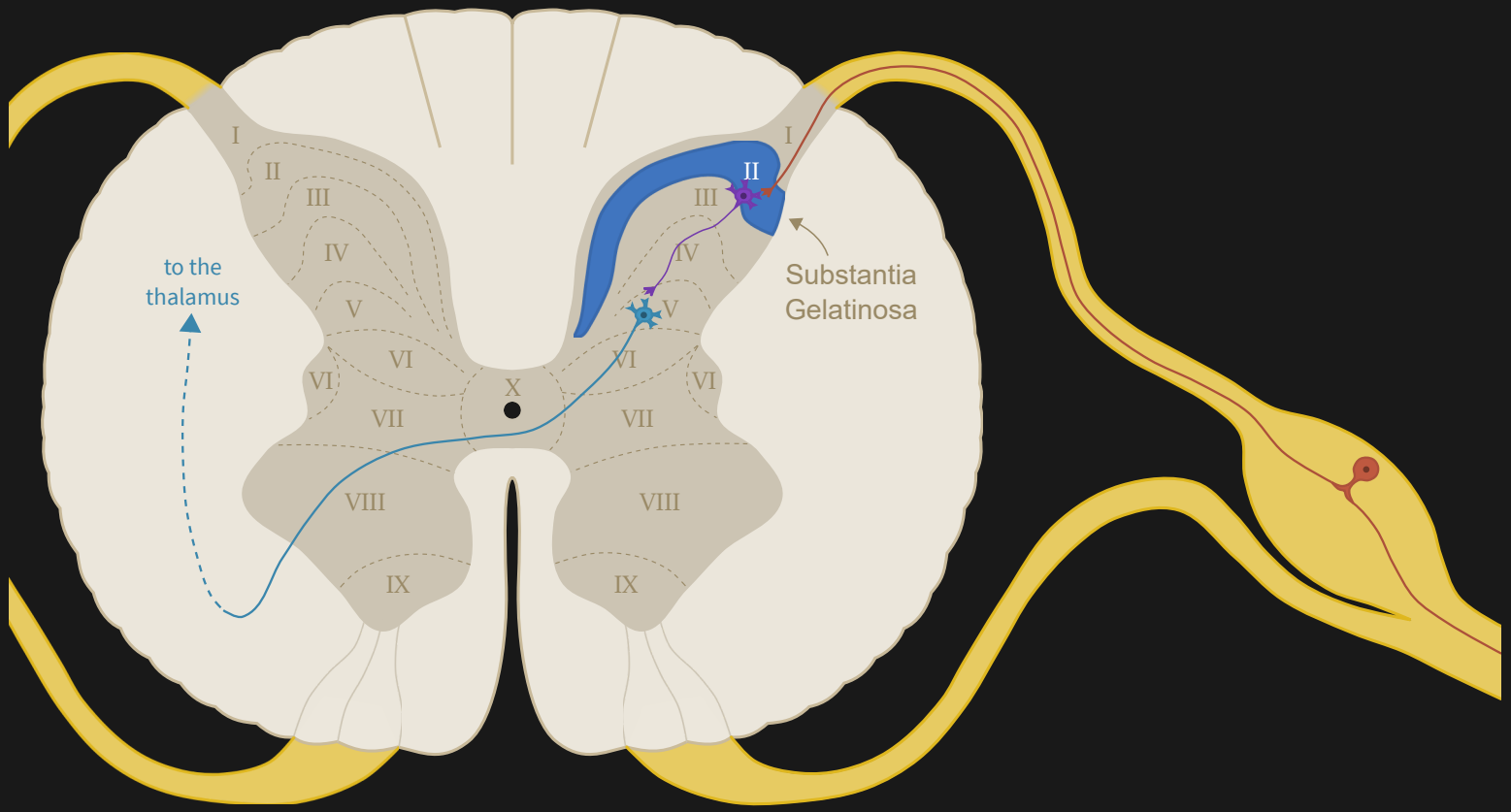
Which area of the spinal cord can enhance or inhibit pain?



The gray matter of the spinal cord is divided into 10 areas called **laminae**.



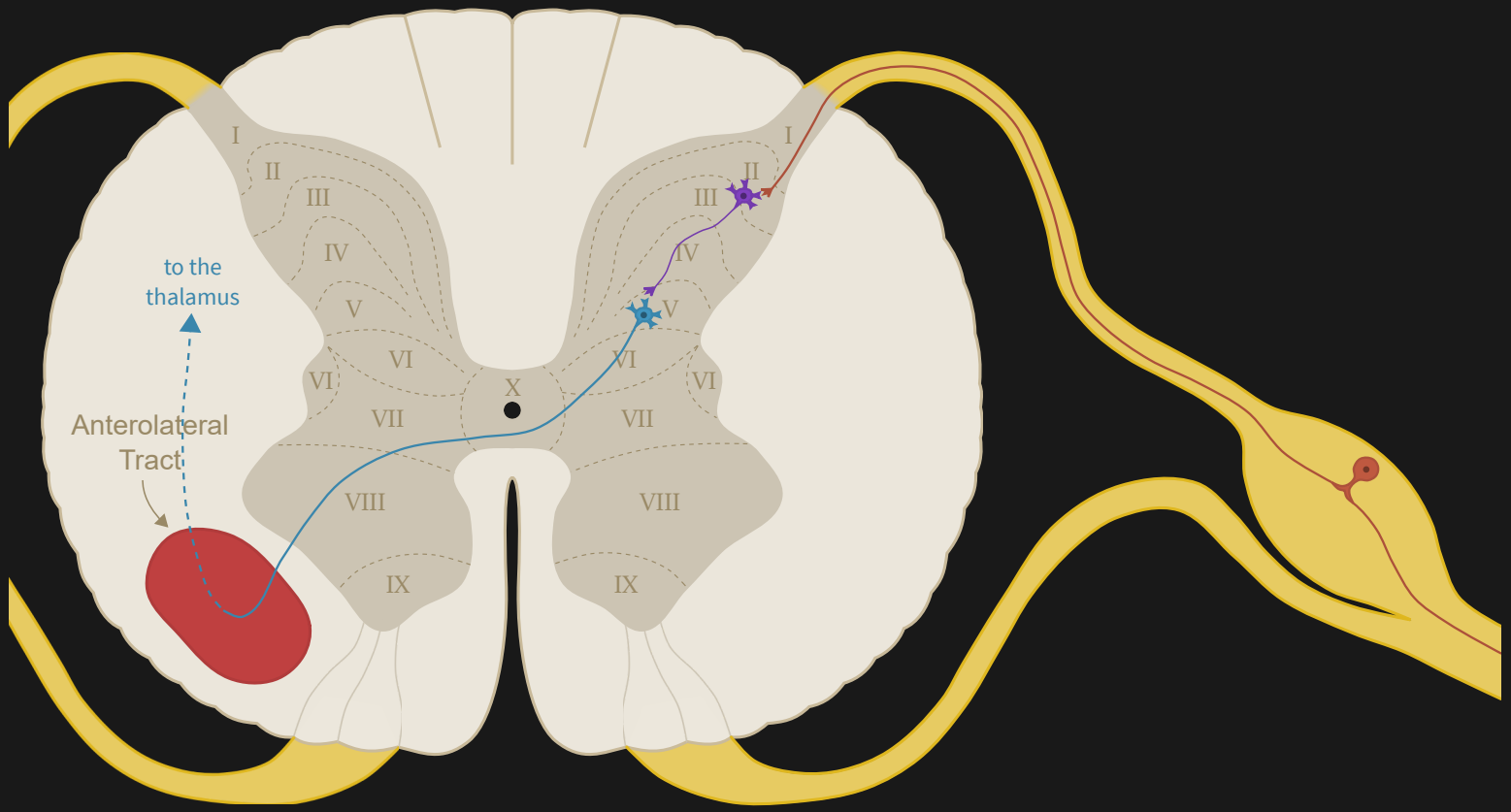
Nociceptors synapse with second-order neurons and interneurons in laminae I, II, and V.



Pain modulation primarily occurs in lamina II, the **substantia gelatinosa**.

QUESTION 7

Describe the difference between the neospinothamalic and paleospinothalamic tracts.



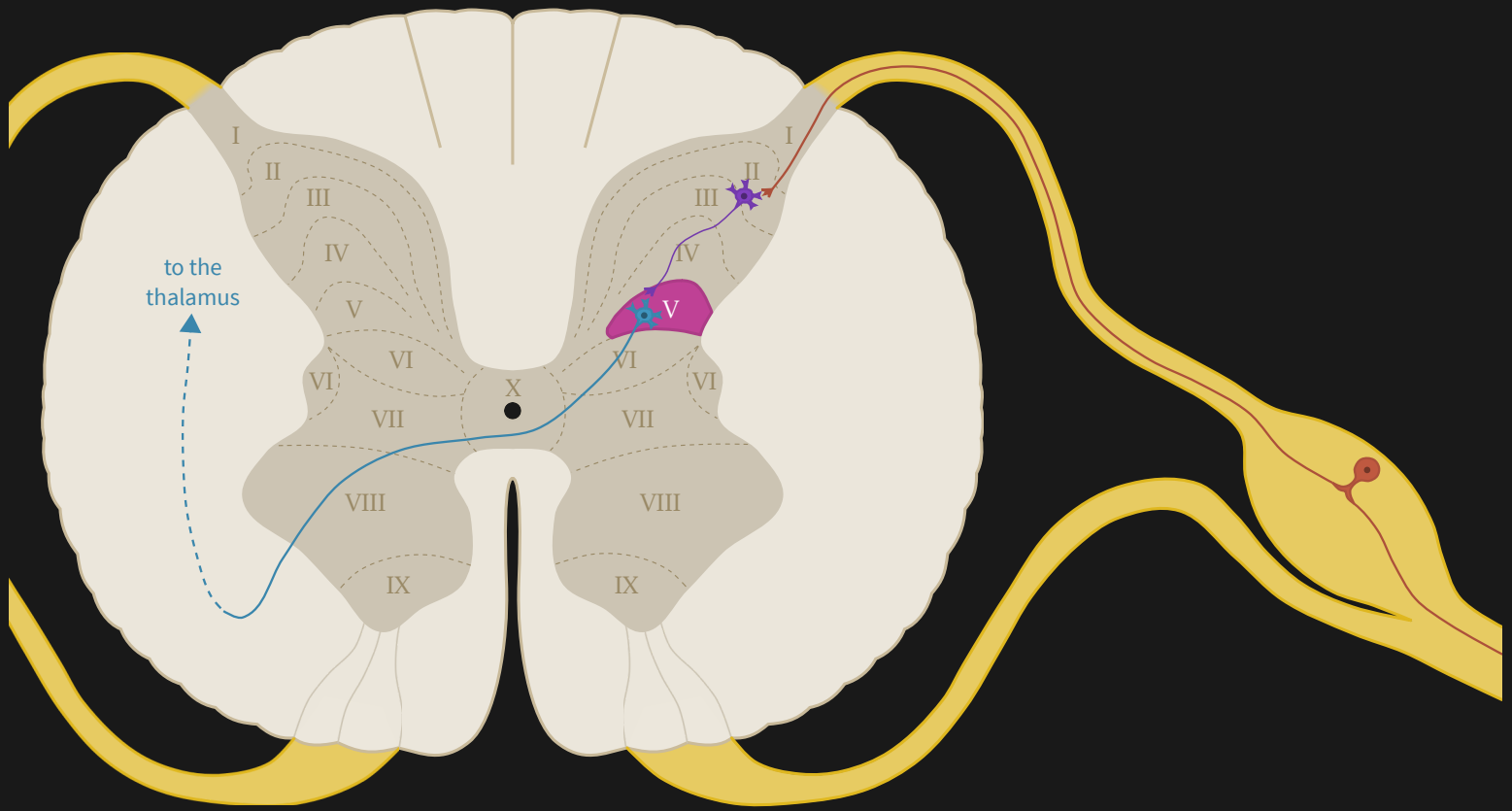
Both **spinothalamic tracts** are found in the **anterolateral white column**.

The **neospinothamalic** division carries signals from **Aδ** (fast) fibers towards the cerebral cortex, synapsing again in the thalamus.

The **paleospinothalamic** division carries signals from **C** (slow) fibers to various destinations in the midbrain.

QUESTION 8

Which lamina of the spinal cord dorsal horn gray matter is involved in referred pain?



Referred pain originates in lamina V. Why does referred pain occur?

Neurons synapsing in lamina V have "**wide dynamic range**," meaning they transmit a wide range of visceral and somatic sensory signals.

This can lead to neurons getting cross-wired and visceral pain being interpreted as somatic pain.

QUESTION 9

At what level of the brain is pain interpreted?

The sensation and quality of pain are interpreted in the **primary sensory cortex**. Remember that this is the final destination of the **neospinothalamic tract**.

In contrast, the **midbrain** controls only the conscious awareness of pain, not interpretation.

QUESTION 10

Dermatomal maps help which function in pain?

Dermatomal maps provide a layout of which areas of the body are innervated by neurons from each level of the spinal column.

This is useful for determining the source of **neuropathic** pain.

If you determine where it **feels** like the pain is coming from, you can determine which nerves are involved.

QUESTION 11

Distinguish between pain tolerance and pain expression.

pain tolerance - how much pain you can **internally** handle

(How much pain does it take before it becomes unbearable and you seek relief?)

pain expression - how do you externally display or communicate your pain to others?

Both of these vary widely from person to person, and pain expression also has a strong **cultural aspect**.

QUESTION 12

Describe presynaptic inhibition of pain. Which neurotransmitter is involved?

Presynaptic inhibition occurs when a **first-order neuron** is prevented from transmitting its signals to a second-order neuron or interneuron.

Opioids such as β-endorphin and enkephalins play a role, as does the neurotransmitter γ-aminobutyric acid (GABA.)

QUESTION 13

Describe the gate control theory of pain relief.

Thick **Aβ fibers** linked to **touch** receptors can **take priority** over Aδ/C pain signals when stimulated.

Gate control theory states that pain can be reduced by providing an additional, non-noxious stimulus to trigger Aβ fibers and cut off pain transmission.

QUESTION 14

What are the names of the endogenous and exogenous opioids?

First, what *are* endogenous and exogenous opioids?

endogenous opioids – opioids produced **internally** by the body

exogenous opioids – **external** opioids introduced to the body, e.g. as drug therapy

Examples:

endogenous opioids – endorphins, enkephalins

(endorphins = "endogenous morphine")

exogenous opioids – morphine, codeine, hydrocodone, methadone, etc.

QUESTION 15

Which of the opioid receptors provide analgesia?

There are four types of opioid receptors in the CNS:

- μ (mu) ← ☆
- κ (kappa) ← ☆
- σ (sigma)
- δ (delta)

μ (mu) and **κ (kappa)** are the two involved in pain modulation.

QUESTION 16

Pain is classified according to three criteria. What are they?

duration – is it **acute** or **chronic**?

source – neuropathic, ischemic, somatic, visceral, etc.

location – where is the pain being experienced?

QUESTION 17

What is fibromyalgia? Describe it.

A chronic disease characterized by **widespread musculoskeletal pain** and **extreme tenderness** at specific areas of the body.

Allodynia, which we'll talk about in a second, is a typical symptom of fibromyalgia.

QUESTION 18

How does cancer cause pain?

There are many mechanisms, any of which can be considered "cancer-related" pain. They can include:

- Infiltration of organs by cancerous growth
- Pressure on nerves from a tumor (neuropathic)
- Pain secondary to cancer treatment (iatrogenic)

QUESTION 19

How is neuropathic pain different from tissue injury pain?

Most (somatic/visceral) pain signals **damage to tissues**.

In **neuropathic pain**, the **nerve itself** is the source of the pain, rather than responding to an external stimulus.

Neuropathic pain often has a shooting/burning quality and radiates along the path of the nerve.

Examples include:

sciatica – neuropathy due to impingement of sciatic nerve

trigeminal neuralgia – facial neuropathy due to demyelination of trigeminal nerve

diabetic neuropathy – neuropathy due to poor circulation to peripheral nerves

QUESTION 20

Define allodynia and hyperalgesia.

állos (other)

odúnē (pain)

ALLODYNIA

"a **painful** response to a typically **non-painful** stimulus"

hupér (over)

algéō (to feel pain)

HYPERALGESIA

"an **exaggerated** or **prolonged** response to a painful stimulus"

Remember one common source of allodynia: **fibromyalgia**.

QUESTION 21

Describe diabetic neuropathy. How are the senses changed?

Chronically elevated blood glucose causes damage to peripheral blood vessels, resulting in **ischemia** of peripheral nerves (usually in legs and feet.)

This can result in both motor changes such as weakness, and sensory changes (numbness, tingling, and pain.)

QUESTION 22

Describe referred pain, post-herpetic neuralgia, and ischemic pain.

referred pain – "cross-wiring" between visceral and somatic pain neurons results in visceral pain being interpreted as somatic

(Remember the role of lamina V in this process.)

post-herpetic neuralgia – a common sequela of **shingles** in which chronic pain persists long after the initial infection has cleared

ischemic pain – acute pain due to insufficient blood flow (and thus insufficient oxygen) to tissues

(An associated term is **claudication**, ischemic pain—often in the legs—which goes away with rest.)

QUESTION 23

What are some differences in pain therapy in the young and the elderly?

Pain in the very young can be harder to diagnose and treatment is sometimes lacking.

Insufficient treatment can lead to long-term changes in the CNS.

Elderly patients can also experience pain that goes inadequately treated.

QUESTION 24

Describe the three points of pain management. Give examples.

1. **blocking transduction or transmission**
    - NSAIDs
    - local infiltration/nerve block

2. **blocking/modulating pain at the spinal cord**
    - Transcutaneous Electrical Nerve Stimulation (TENS)
    - Epidural anesthesia

3. **altering perception of pain in the brain**
    - Opioid analgesics
    - Non-pharmacologic techniques (breathing, relaxation techniques, etc.)