Episode 76: Pain Pathways

On this episode: Dr. Jed Wolpaw and Dr. Mark Bicket

In this episode, episode 76, I welcome <u>Dr. Mark Bicket</u> to the show to discuss pain pathways. We shape this one around some great board style questions that Mark put together.

Prime Yourself!

Hyperlinks to related question.

Which sensory information is transmitted via Type C primary afferent fibers?
What is the concept of modulation?
What is the main pathway for nociceptive input into the brain?
What in the dorsal horn of the spinal cord is related to pain pathways?
What is the definition of pain transduction?
What is the definition of central sensitization?
Which fibers transmit information about pain via the sensory afferent neurons?
To which Rexed lamina in the spinal cord do most nociceptive neurons send signals?
What are some common anatomical targets in the trunk/abdomen?
What is the relationship between pain and age?

Which of the following types of sensory information is transmitted via Type C primary afferent fibers?

- a) Sharp pain
- b) Burning pain
- c) Cold
- d) A and B
- e) All of the above

Answer:

Choice B. Type C afferent fibers do not contain specialized nerve endings. Their smaller diameter and lack of myelination transmit signal more slowly. Type C fibers are slow to come on, like burning pain. This is in contrast to myelinated A δ fibers, which have nodes of Ranvier that transmit signals through faster saltatory conduction. Sharp pain comes on fast!

Speed of transmission related to myelination and diameter.

When you take multiple choice tests – you can narrow down without knowing anything. In this example, a pain test probably doesn't ask about cold, so eliminate C and E.

Which of the following illustrates the concept of modulation?

- a) Noxious stimulus converted into action potential propagated by neurotransmitters
- b) A peripheral noxious stimulus transmitted to thalamus via spinal cord
- c) Peripheral noxious stimulus processed in limbic system where it elicits an emotional response
- d) Noxious stimulus modified by excitatory and inhibitory inputs

Answer:

Choice D. <u>Modulation</u> is defined as a noxious stimulus that is modified inhibitory and excitatory inputs, or in other words, a signal that is changed by neural input. For example, your hand is hurting but you're your younger brother punches you. Now your hand doesn't hurt as much.

Each of these answer choices relate to the critical pain pathways.

Choice A refers to <u>transduction</u> which is one of the first elements of the pain pathway. A stimulus outside the body, such as a sharp toothpick or a feather, is a mechanical action that evokes an action potential communicated via neurotransmitters (commonly norepinephrine, GABA, glutamate) in the pain transmission pathway.

Choice B refers to a signal that made its way to the spinal cord and then ascends up to the brain in the region of the thalamus. The signal being transmitted from the spinal cord to the thalamus, is known as <u>transmission</u>.

Choice C refers to <u>perception</u> that processes a physical or emotional response in the brain. Functional MRI scans shows activity in the brain and in certain regions of the limbic systems that bring about an emotional response. For example, you are upset by the pain you have. You are perceiving what is happening in the pain pathways.

In humans, what is the main pathway for nociceptive input into the brain?

- a) Corticospinal tract
- b) Spinothalamic tract
- c) Spinocerebellar tract
- d) Limbic system
- e) Rubrospinal tract

Answer:

Choice B. The spinothalamic tract starts at the spinal cord and ascends to the thalamus.

It's important to understand all the tracts. These tracts typically tell you where it starts and ends, so it helps to break it down.

Choice A refers to the tract from the cerebral cortex and descends down to the spinal cord. This tract is responsible for voluntary motor control.

Choice C refers to the tract from the spinal cord and ascends to the cerebellum, which is involved in balance, coordination, and processing movements.

Choice D refers to the system related to emotions, which is involved in the pain pathway but after the signal has reached the brain.

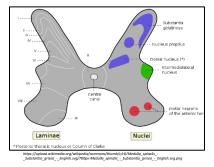
Choice E refers to the descending motor tract that helps with voluntary movement, not pain. The inhibitory pain pathway typically involves areas such as the periaqueductal grey space, or rostral/ventral/medial medulla.

Which of the following is true about the dorsal horn of the spinal cord?

- a) Cells from lamina 1 and 2 project to the hypothalamus
- b) Neurons from spinothalamic tract synapse first to lamina 2
- c) Lamina 2 is found in thoracic segment of spinal cord only
- d) Discharge from lamina 1 decreases as noxious stimulus increases
- e) Wide dynamic range neurons are predominantly located in lamina 2

Answer:

Choice B. Neurons from spinothalamic tract synapse first in lamina 2. The cross-section of a spinal cord is oval shape, sort of like an 'X'. The top portion is typically posterior, bottom is anterior. Different neurons synapse at different locations of the spinal cord. Pain fibers typically synapse in laminae 1,2, and 5. A δ and C fibers typically come into these laminae. Substantia gelatinosa is generalized as the same area as laminae 1,2, and ~5. This is the first synapse, or the "first order neuron", which ascends and crosses over or "decussate" into the thalamus.



Choice A is incorrect because the pain pathway projects into the thalamus. It's not "spinohypothalamic" tract :

Choice C uses the word "only", which should send of alarms! Be certain with these absolutes. Lamina 2 is not exclusive.

Choice D is incorrect because noxious stimulus increases discharge from laminae 1 (2, and 5).

Choice E refers to an important part of pain transmission but is not predominantly in lamina 2. The wide dynamic range neurons are found deeper like lamina 4 or 5 and beyond.

Which of the following is the definition of pain transduction?

- a) Point at which sufficient pain transmitting stimulation has reached the brain
- b) Conversion of chemical information into electrical impulses that move towards the spinal cord
- c) Conscious experience of discomfort when pain threshold reached
- d) Phase at which stimuli from the periphery move toward the brain

Answer:

Choice B. This is the definition of <u>transduction</u>.

Choice A refers to the pain <u>threshold</u>, or the threshold at which you can feel pain. Example: Dr. Wolpaw microwaves soup which he then picks up because he feels he can carry it to the table. Halfway to the table, his fingers start to burn and he wants to drop the bowl. This is because the pain threshold has been reached! (He'll start using potholders too..)

Choice C refers to <u>perception</u>, which occurs with higher order processes such as consciousness. In other words, the experience of discomfort when pain threshold reached at a conscious level.

Choice D is the definition of <u>transmission</u>.

You are describing neuronal plasticity and spinal modulation to patient at the pain clinic. Which phenomena is associated with central sensitization?

- a. Gate control of pain theory
- b. Low threshold stimulation
- c. Aβ fiber inhibition
- d. Wind-up
- e. Depletion of substance P of sensory nerves

Answer:

Choice D. Applying a painful stimulus, waiting a few seconds, then repeating it again and again should feel the same amount of pain on a healthy individual after each exposure. However, with <u>wind-up</u>, the level of pain increases with each stimulus. Lab studies have shown that painful stimulus applied to damaged nerve (nociceptor activated state). These two stimulations couple so that the rate and amplitude increased successively when put close together. Think of it as "winding-up" with every extra stimulus the amount of response to that nerve is going up. This relates to <u>central sensitization</u>, where the issue is with the nerve and how it processes pain in an aberrant way. Nerves activated in an aberrant state will have its threshold for pain altered. It passes on more signals to pain, such as with hyperalgesia or allodynia.

Choice A refers to the theory first proposed in 1965 by Drs. Melzack and Wahl. If you stimulate the skin via A δ fibers, it can inhibit processing of pain through C fibers, almost like closing the gate of C fibers. This eventually led to the discovery of spinal cord stimulation. We now know that it's more dynamic than this and recognize that the theory has some limitations. Using the previous example of modulation, where your hand hurts less after your younger brother punches you, is an application of the gate control theory of pain.

Choice B refers to applications like the Transcutaneous Electrical Nerve Stimulation (TENS) device, which provide some stimulation like $A\delta$ fibers but not much.

Choice C is similar to gate control of theory where $A\beta$ fibers are activated to block C fibers. This is not related to central sensitization as $A\beta$ fibers are involved with general touch. These myelinated fibers faster than $A\delta$. For example, when Dr. Wolpaw is hit by a baseball on the arm, then rubs it lightly (to be sensed as touch vs as pain when getting punched the arm by brother).

Choice E is incorrect because substance P is an excitatory neurotransmitter along the whole pain transmission pathway.

Which of the following statements are incorrect about sensory afferent neurons?

- a. Order of conduction velocity is $A\beta > A\delta > C$
- b. Sensory axons regularly have spontaneous firing activity
- c. Aß terminals have specialized nerve endings
- d. Glutamate is an excitatory amino acid released in the superficial dorsal horn

Answer:

Choice A. Think of it as if you're filing these letters. A $\underline{\beta}$ comes before A $\underline{\delta}$ before C!

Choice B is incorrect. When you check in normal state, they are quiet. This has been shown in animal models and perceived to be true in humans as well. The axons do spontaneously fire when injured, but most cases will slowly resolve over time. This is a marker for nerve injury.

Choice C refers to the $A\beta$ specialized nerve endings such as Merkel and Pacinian corpuscles.

Choice D: The other excitatory amino acids include substance P and aspartate. Inhibitory amino acids include GABA and glycine.

To which Rexed lamina in the spinal cord do most nociceptive neurons send signals?

- a. 1, 2, 3
- b. 1, 2, 5
- c. 4,6
- d. 7
- e. 4

Answer:

Choice B. See <u>earlier question</u>. Substantia gelatinosa is mostly 1, 2. C fibers \rightarrow 1, 2. A δ fibers \rightarrow 2, 5.

A patient presents with visceral pelvic pain secondary to radiation therapy for rectal cancer. Which of following intervention will relieve the pain?

- a. Celiac plexus block
- b. Lumbar sympathetic block
- c. Bilateral pudendal nerve block
- d. Superior hypogastric plexus block

Answer:

Choice D. The superior hypogastric plexus sits in front of the vertebral body where the pain pathway from the hepatic flexure of colon to rectum go through. This would include the abdominal and rectal viscera.

Choice A would be appropriate for a patient with pancreatic cancer. The celiac plexus covers the distal stomach to hepatic flexure of colon. This block can help with side effects of opioid medications.

Choice B would be appropriate for patients with sympathetically mediated pain, eg complex regional pain syndrome, vasoconstriction, and even peripheral vascular disease.

Choice C would be appropriate for patients with pudendal neuralgia, which is more superficial and in a pudendal nerve distribution (from external genitalia + skin around anus + perineum). This differs from the pain from rectal cancer.

Patient returns to clinic to undergo the procedure. Radiology technician asks you what anatomical target you have for the block. What is your response?

- a. L2
- b. L3
- c. L4
- d. L5
- e. Sacral hiatus

Answer:

Choice D. The superior hypogastric block targets the plexus on the anterior surface of L5. The approach is typically taken posteriorly, and under fluoroscopy, CT or other radiologic guidance.

Choice B would be for a lumbar sympathetic block. The chain lateral to L3 is the best answer, although practitioners have approached superior of L2 and inferior to L4.

The celiac plexus block is directed towards L1.

Choice E are typically targeted for performing caudal epidural injections on pediatric patients or adults who need lysis of epidural adhesions.

When performing a celiac plexus block, what are some potential complications? Hitting the aorta (although there is a transaortic approach) or vena cava. Now thinking about other anatomy in the area: L1 – where the diaphragm can be located, so potential pneumothorax. The kidneys are also in that area; L3 – more vascular structures; L5 – iliac crests can be in the way, but also colon and rectum.

Which of the following is true regarding pain and age?

- a. Pain threshold increases with age
- b. Pain tolerance increases with age
- c. Different regions of body (head, foot) demonstrate similar changes in pain thresholds due to age
- d. Different pain modalities (heat, pressure) demonstrate similar changes in pain tolerance in older adults

Answer:

Choice A. The pain threshold, or the level at which pain is perceived, increases with age. In other words, a younger individual is more "sensitive" to pain. For example, young daughters won't get in the bathtub because it's hot to them, but warm to Dr. Wolpaw.

Choice B can be explained be one form of the "ice bucket challenge" where you shove your hand in an ice bucket and see how long you can hold it there. *How long you can sustain a stimulus that is painful*? A younger individual generally has greater pain tolerance, so the threshold decreases with age.

Choice C is incorrect because more sensitive areas have more innervation, which have greater change over time. Hands and finger tips are more sensitive, and thus undergo more change over time, than less sensitive areas such as the scalp.

As age \uparrow , pain threshold \uparrow while pain tolerance \downarrow

Choice D is incorrect because modality have different profiles in how they change.

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