

Lecture 16 - Pain and Analgesia -- MacDermott

1. Different kinds of pain:
 - Acute
 - Inflammatory
 - Neuropathic
2. To understand the pharmacology of pain, you must know the anatomy and physiology of the system.
 - Peripheral nociceptors
 - Dorsal horn – major center for integration of afferent and efferent signaling
 - Ascending pathway
 - Descending pathway
3. What is unique to the nociceptors and temperature detecting peripheral neurons?
 - Signal transduction proteins
 - Nociceptor-specific Na⁺ channels
 - Afferent fiber conduction and pain
 - Nociceptive inputs go to lamina I, II and V in the dorsal horn
4. Sensitization in the pain pathway results in hyperalgesia (hypersensitivity to a noxious stimulus) and allodynia (pain that results from a non-noxious stimulus).
 - Peripheral sensitization
 - skin and viscera
 - Central sensitization
 - dorsal horn
 - higher centers
5. Peripheral sensitization – injury to the local tissue or to the nerve fibers themselves releases many factors that excite peripheral nociceptors. The nociceptors themselves may change properties such as changes in expression of voltage gated sodium channels.
6. Synaptic transmission in the dorsal horn
 - Sensory fibers sensitive to pain and temperature synapse with dorsal horn neurons in lamina I, II, and V, releasing glutamate and excitatory peptides.
 - Local excitatory interneurons also release glutamate as the fast transmitter, some also release co-transmitters such as peptides with slower excitatory action.
 - Local inhibitory interneurons release GABA and glycine as fast transmitters, some also release co-transmitters such as enkephalins.
 - Descending inputs synapse with projection neurons, interneurons, and terminals of nociceptors.
7. The spinal cord dorsal horn has a heterogeneous cell population including:
 - projection neurons, especially lamina I
 - excitatory interneurons
 - inhibitory interneurons
8. Central sensitization associated with some forms of hyperalgesia and allodynia are associated with cellular and molecular changes in the superficial dorsal horn.
9. Ascending thermal and nociceptive pathway
10. Descending Pathway – regulation of nociception
 - Multiple levels of control

Reciprocal connections

Include excitatory and inhibitory projections to the dorsal horn

11. Opioids are important regulators of nociceptive signaling and they act at many levels of the nervous system:

primary afferents

dorsal horn neurons

higher centers

Relevant reading: Chapter 24 in “Principles”