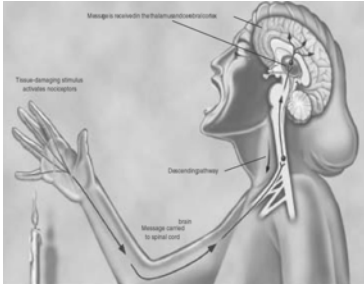


Basic mechanisms of pain

PAIN

- an unpleasant sensory and emotional experience associated with actual or potential tissue damage.
- has a dedicated neural pathway
- individual and subjective
- more than a symptom



DIFFERENT KINDS OF PAIN:

- Acute
- Inflammatory
- Neuropathic

Amy MacDermott, PhD Department of Physiology and Cellular Biophysics and the Center for Neurobiology and Behavior.

Fig from Brain Awareness – SFN 2003

To understand the pharmacology of pain, you must know the anatomy and physiology of the system.

1. Peripheral nociceptors
2. Dorsal horn – major center for integration of afferent and efferent signaling
3. Ascending pathway
4. Descending pathway

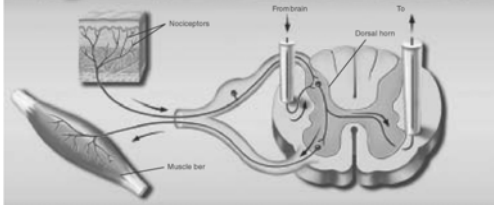
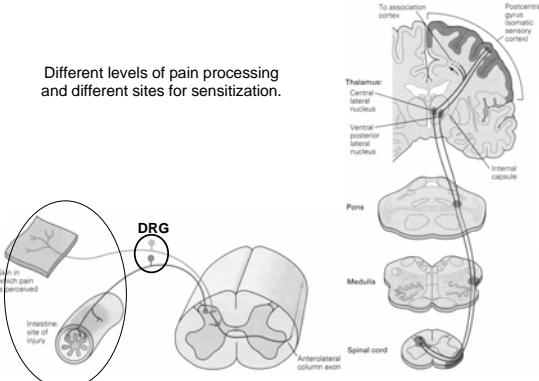


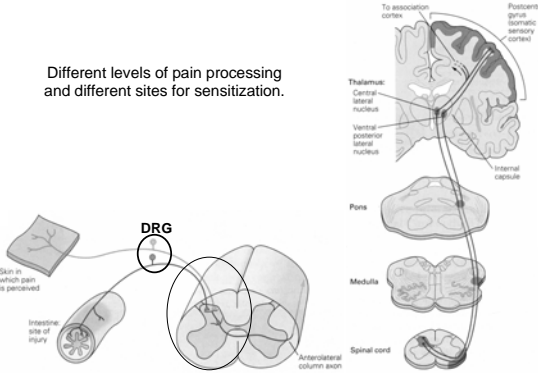
Fig from Brain Awareness – SFN 2003

Different levels of pain processing and different sites for sensitization.



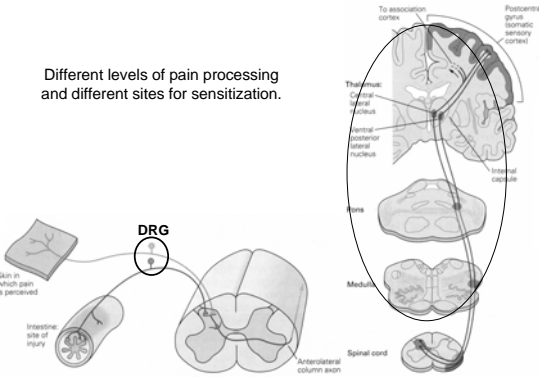
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Different levels of pain processing and different sites for sensitization.



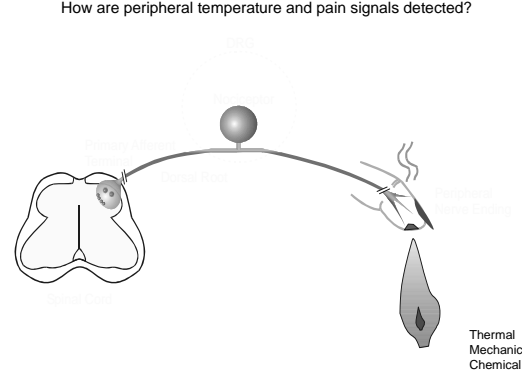
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Different levels of pain processing and different sites for sensitization.

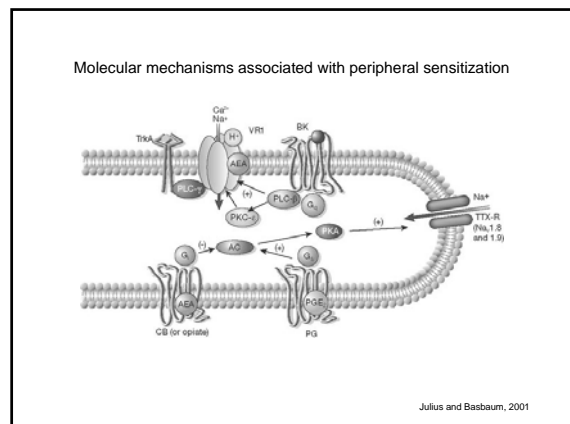
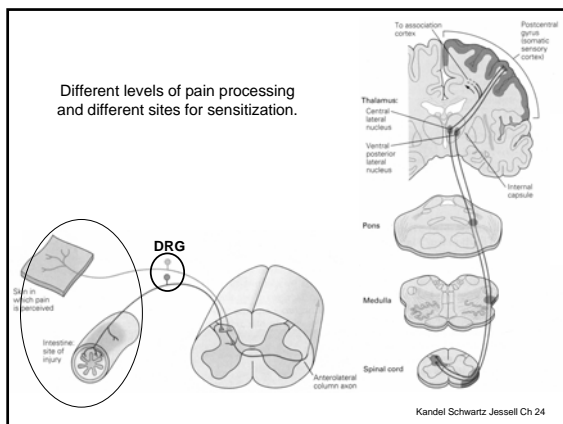
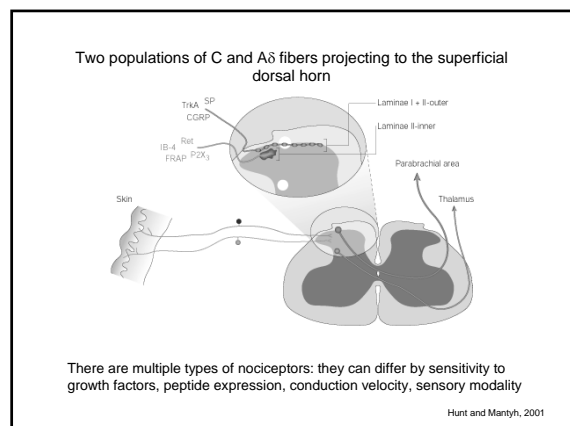
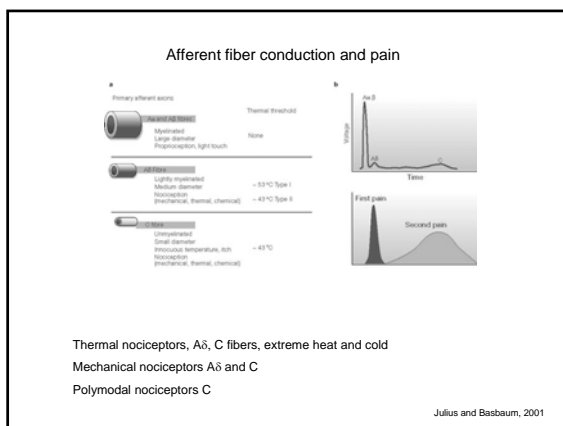
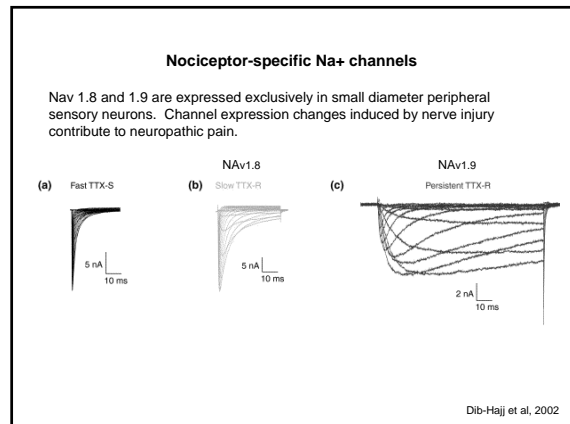
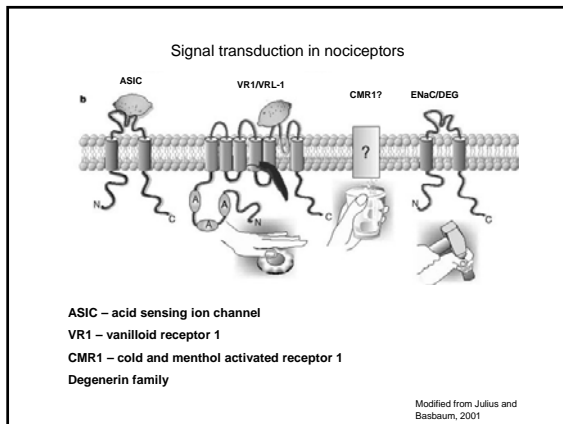


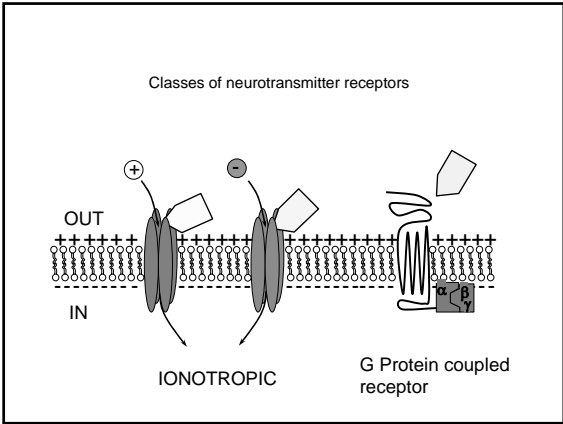
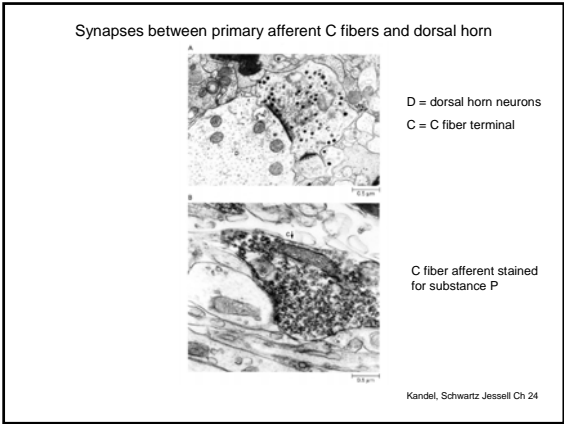
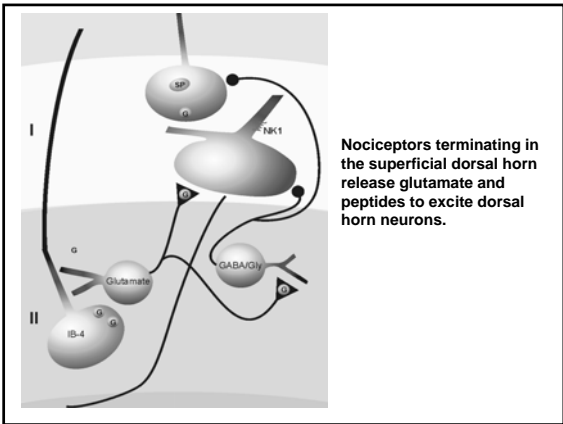
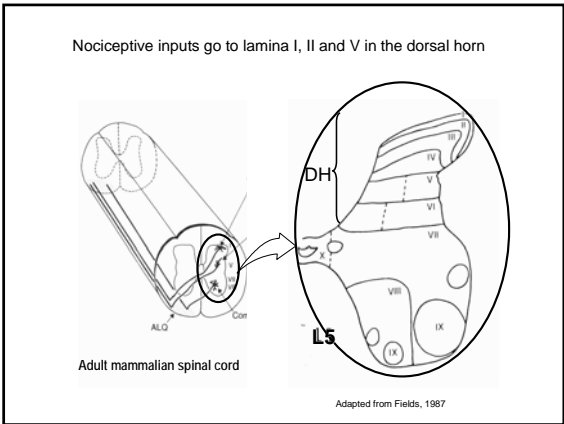
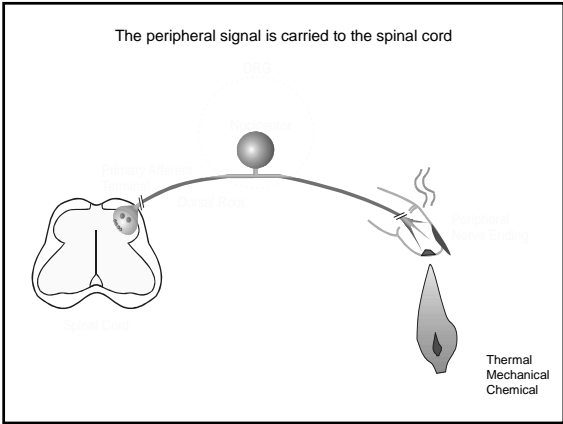
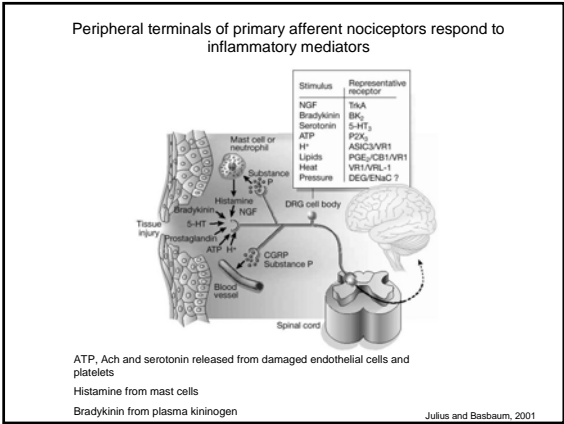
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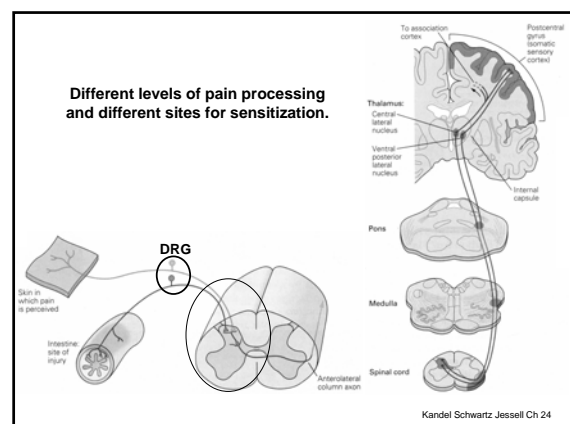
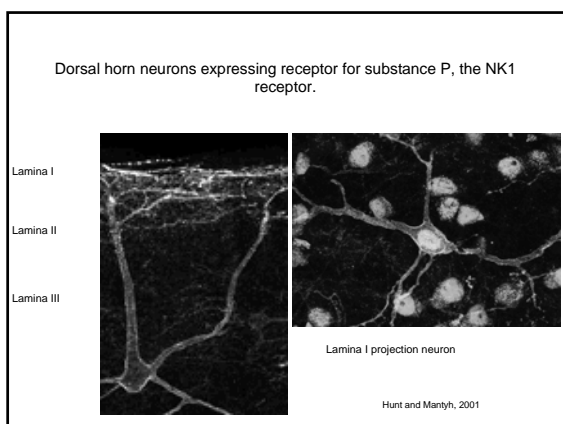
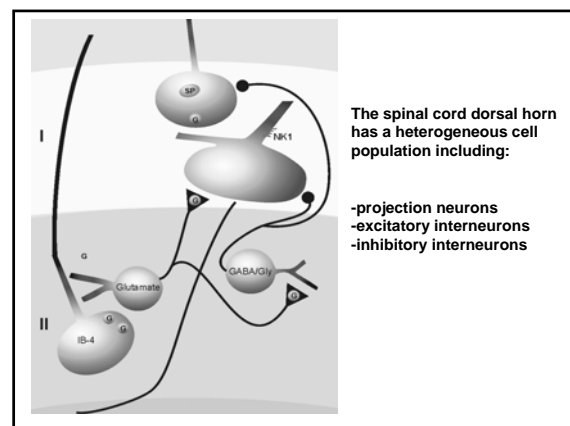
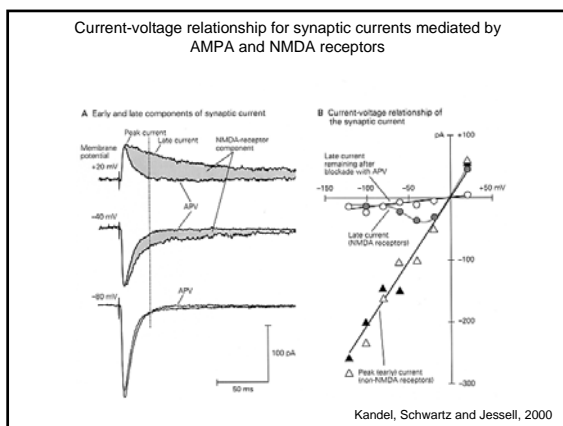
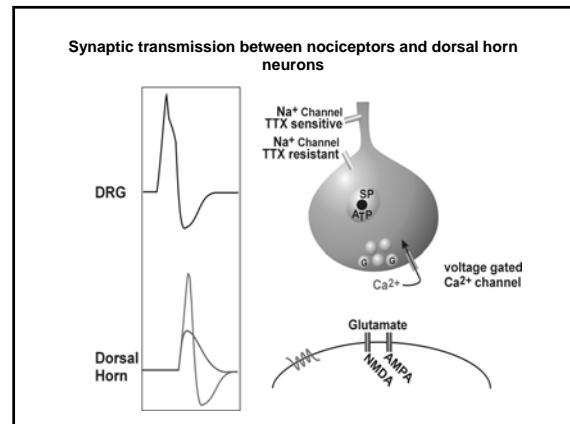
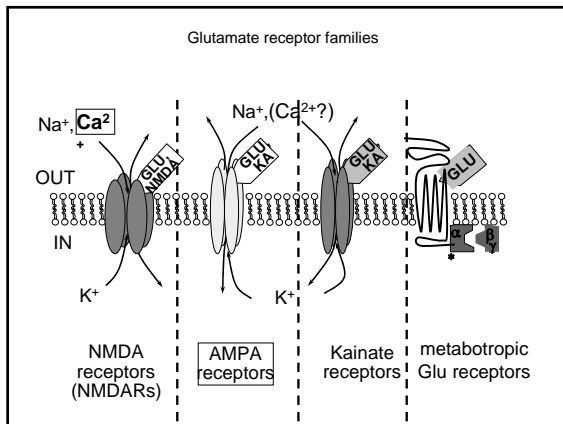
How are peripheral temperature and pain signals detected?

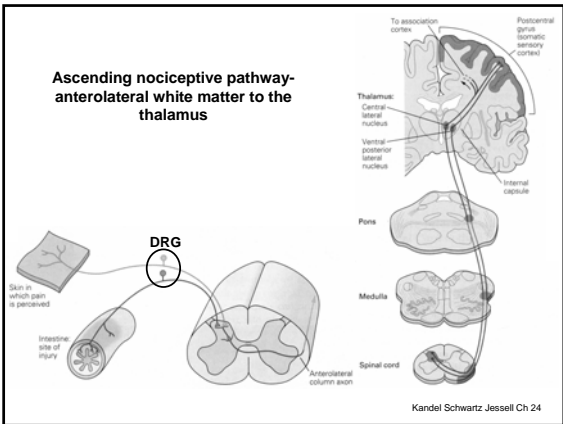
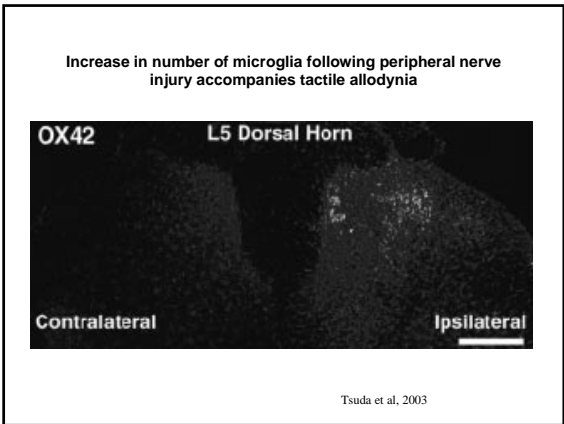
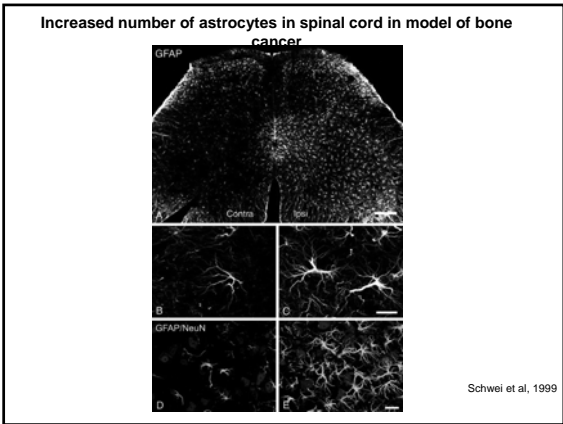
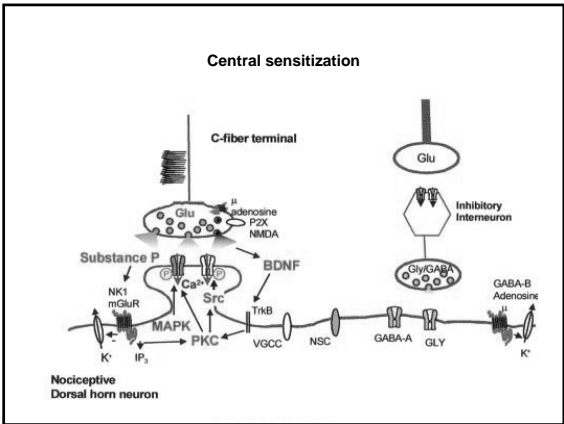
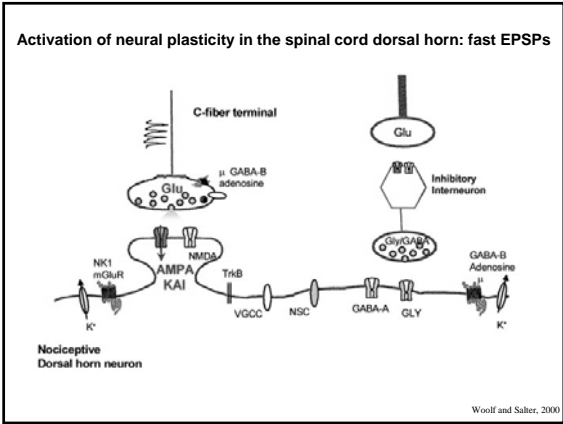
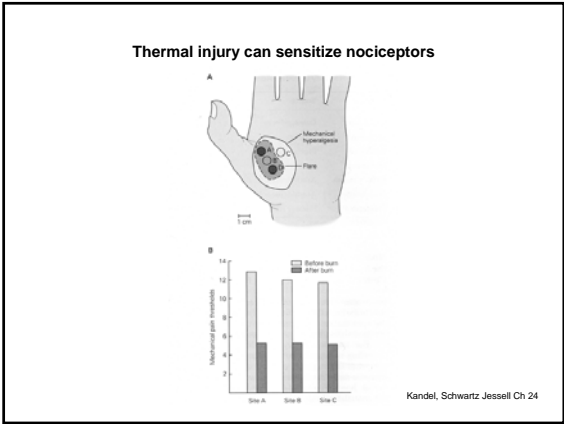


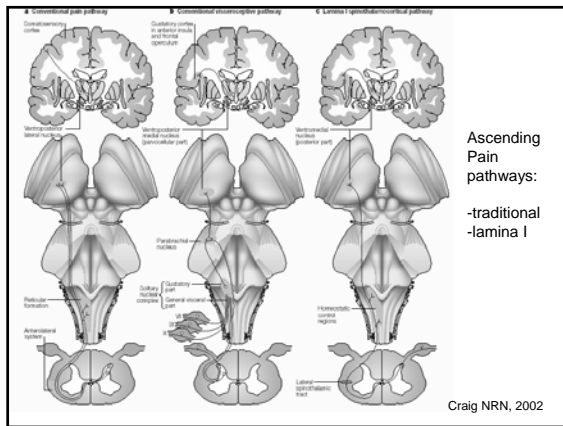
Thermal
Mechanical
Chemical





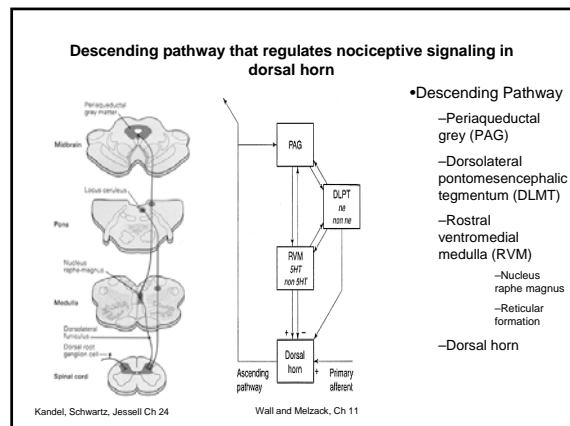
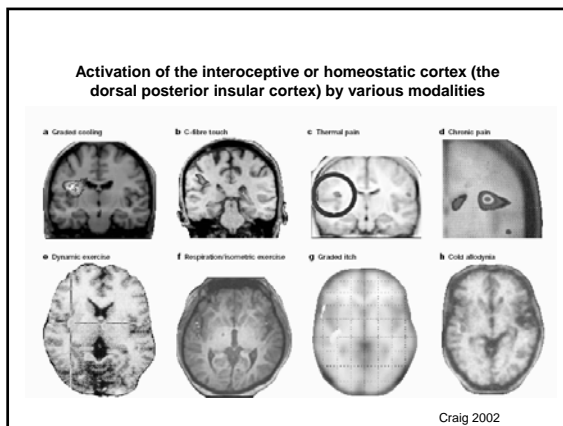






The thermal-grill illusion of pain
 -burning pain with innocuous warm (40°) and cool (20°) bars.

Demonstrates central inhibition of a polymodal C nociceptive sensory channel by innocuous thermosensory activity.



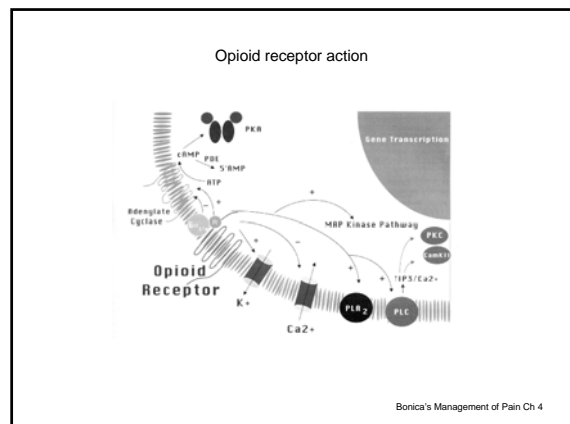
Opioid receptors – 3 gene families

μ opioid receptor – activated by morphine, β endorphin and enkephalins

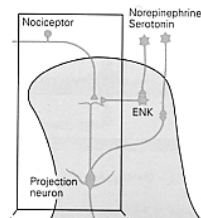
κ opioid receptor activated by dynorphin

δ opioid receptors activated by enkephalins and β endorphin

Bonica's Management of Pain Ch 4

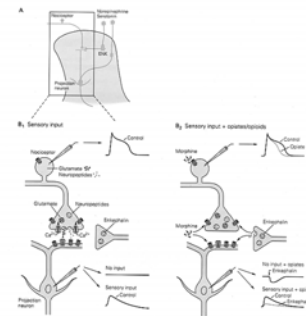


Opioids are important regulators of nociceptive signaling

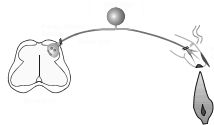


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Local circuit interneurons



Kandel, Schwartz Jessell Ch 24



Summary:

- There are multiple types of nociceptors: they can differ by sensitivity to growth factors, peptide expression, conduction velocity, sensory modality
- All nociceptors release glutamate thus glutamate receptors are potential targets for pain management
- Sensitization occurs peripherally and centrally
- Dorsal horn neurons project to multiple higher levels in the brain, notably the parabrachial nucleus, the thalamus and the insular cortex and receive descending input, directly or indirectly, from all of those same areas
- There are good targets for pain management on peripheral and central terminals of nociceptors as well as through regulation of inhibition in the dorsal horn