Pain

- An unpleasant sensory and emotional experience associated with actual or potential tissue damage
    - It is an experience so not necessarily a sensation
    - Motivational-affective dimension: unpleasant feeling associated with pain so it evokes an emotional and sensory experience and even an ANS response
    - It could be considered a protective mechanism or cause a change in behaviour if the pain is chronic
    - It is subjective (different thresholds) and learned (about responses to potentially damaging stimuli and even overcome some)

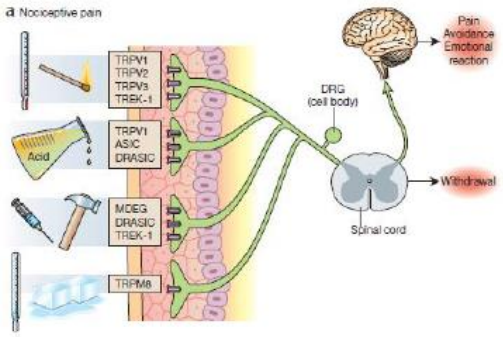
Nociception

- The neural process of encoding noxious stimuli
    - Involves activation of cells throughout the entire nervous system
    - Nociceptors are cells that are physiologically activated by noxious stimuli
    - Pain sensation/experience is not necessarily implied; e.g. anaesthetised, not perceived because areas of perception are blocked but all of the encoding of the noxious stimuli/activity of the cells is still occurring so there is nociception without pain

Different types of pain

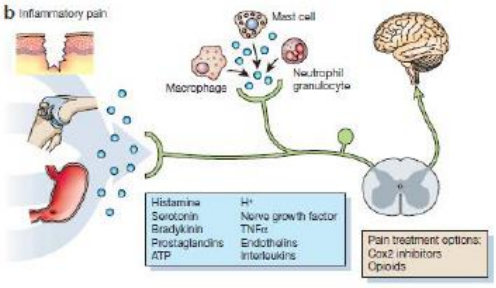
Nociceptive pain

- Pain that arises from arises from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors
- It is a warning, protective pain; subsequent signalling resulting in the experience of pain, avoidance and withdrawal Different noxious stimuli can activate specific receptors and/or ion channels on peripheral nociceptors leading to transduction
- It is very acute, like a pinch, burn, cold etc.



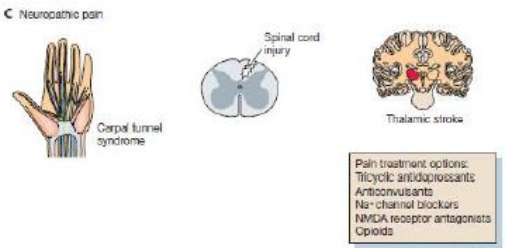
Inflammatory pain

- Pain that is driven by inflammation; e.g. due to tissue damage, the mediators are products of certain inflammatory cells like mast cells/granulocytes/macrophages etc.
- Some inflammatory mediators directly activate peripheral nociceptors to produce pain
- Others produce change in sensitivity of peripheral nociceptors to noxious stimuli



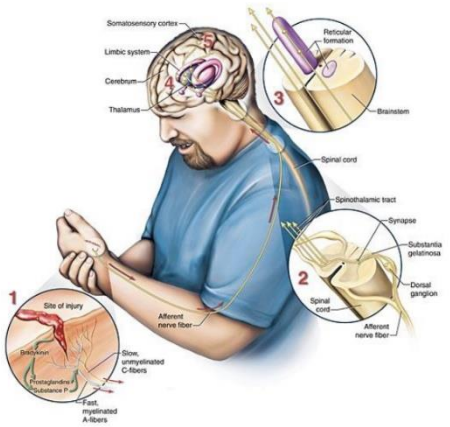
Neuropathic pain

- Pain caused by a lesion or disease of the somatosensory nervous system
- It is a result to the nerves of the peripheral or central nervous system that causes permanent changes in circuit sensitivity and CNS connections
    - The last two present for much longer than nociceptive pain

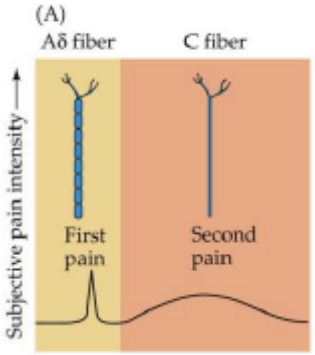


Pain signalling and nociception

- Nociceptors: are very fast peripheral neurons which transduce noxious stimuli into electrical potentials and take information to the CNS; it travels into the spinal cord via the dorsal root ganglion and synapses with a second neuron which travels up to the brain (the other cell is in the trigeminal ganglion
- Pain perception occurs in the cerebrum after the signal has passed through the brain stem (reticular formation), thalamus and before being processed in the cerebrum then the somatosensory cortex
- Descending modulation of pain signalling can suppress pain
- Nociceptors transduce noxious stimuli into APs:
    - They usually respond to high threshold stimulation (e.g. >45 degrees etc.) unlike the light touch of mechanoreceptors
    - Increased firing indicates higher intensity of noxious stimulus
    - Conduct slowly relative to low threshold sensory neurons

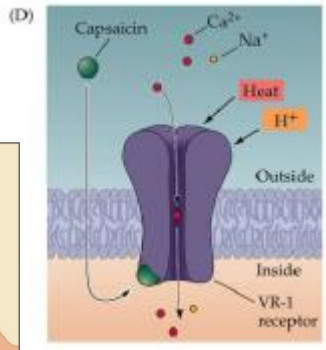


- Nociceptors are usally descried as having unspecialised, free nerve endings and can be classified according to their conduction properties which are much slower than the thickly myelinated mechanoreceptors:
    - A(delta)-fibre axons:
        - Thinkly myelinated
        - Conduction velocities 5-30 m/s
        - Fast (sharp) pain
    - C-fibre axons
        - Unmyelinated
        - Conduction velocities <2m/s
        - Slow, burning pain



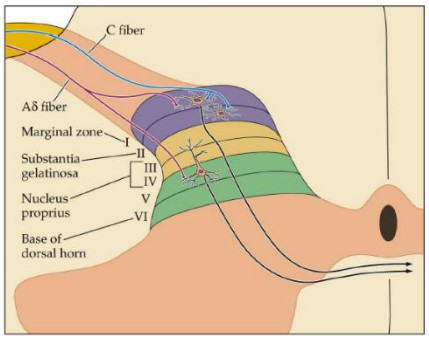
Modality specificity

- Nociceptors are also classified by their modality (i.e. the sensory stimulus that activates them
    - Mechanical receptors are stimulated by mechanical stimuli like cutting, crushing, pinching
    - Thermal nociceptors respond to noxious temperature
    - Polymodal nociceptors: respond to combinations of the above, and/or chemicals or inflammatory mediators
- Specific combinations of ion channels or receptors may be involved in the transduction for each and if identified, it may enable pain modulation of the 6 different types of nociceptors found in the DRG using RNA transcriptome analyses
- TRPV1 is polymodal – noxious heat, acids and capsaicin; it is an ion channel allowing the passage of Ca2+
    - Polymodal neurons in the cornea express TPRV1; increasing temperature or concentration of capsaicin increases impulses

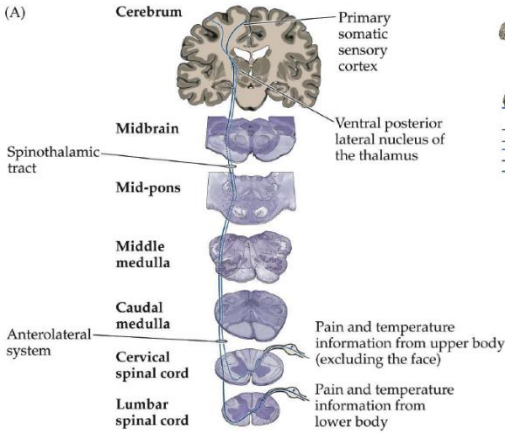


The dorsal horn synapse

- Second order neurons originate in different lamina (they have "lamina specificity") and ascend towards the brain
- Interneurons communicate between the lamina and contribute to processing
    - A(d) fibres synapse in the base of the dorsal horn
    - C fibres synapse at the marginal zone

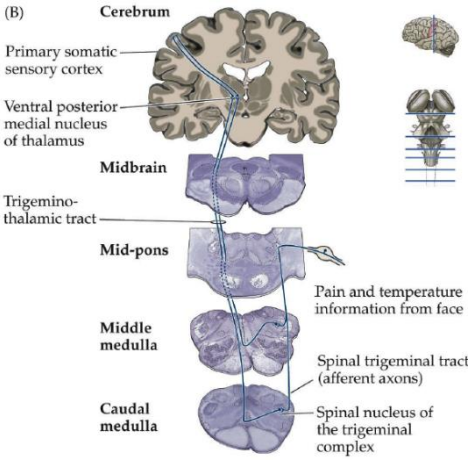


Ascending pathways for discriminative aspects of pain/temperature (of somatic tissues) for the body



- Entering at any given level at the dorsal horn, it then crosses over at that level and ascends contralaterally in the white matter tracts (in the anterolateral system); some synapse in brain stem nuclei, others in cortices of the brain
    - No longer performed, but in cases of chronic pain, a lesion could be created in the anterolateral system to remove this pain
- It travels in the spinothalamic tract in the midbrain, synapses in the ventral posterior lateral nucleus of the thalamus than mostly in the primary somatosensory cortex

Ascending pathways for discriminative aspects of pain/temperature (of somatic tissues) for the face and head



- These nerves must synapse in the trigeminal complex before ascending the trigemino-thalamic tract to the ventral posterior MEDIAL nucleus of thalamus and then to the cortex