

General Notes

## Molecular Mechanisms of Nociception

Extended nociceptor activity can hypersensitize the NS

- >Meaning; more receptors=more binding= more triggering
- >Allodynia
- >Fibromyalgia

Pain is beneficial; Generates protective responses

>CIPA

Genetic mutation where afferent fails to transmit nociceptor facts

\*TrkA mediates nerve growth factor (NGF)

## Neurogenic inflammation

Stimulated by:

Peptides, lipids, neurotransmitters, heat, acidity, pressure and depolarizes the nociceptor to transmit signal to brain or spinal cord

Ex) ATP is released during tissue damage (bladder distends when full and it becomes painful to hold urine)

Neutrophils release histamine – NGF facilitates axon growth and regeneration, protects against death and damage of cells, promotes angiogenesis, regulates Schwann cell

Glutamate dumps to postsynaptic receptors

>AMPA; permits sodium

>NMDA; permits sodium and calcium; Ca<sup>+</sup> can effect gene expression

Prostaglandins

>Account for DOMS, hangovers

>NSAIDs inhibit CoX, thus inhibit prostaglandins... reducing pain

Cortisol injections block the release of AEA (PLA2)

Bradykinins; directly stimulated primary sensory neurons and provoking the release of substance P (pain). Bronchoconstrictor (asthma)

A-delta (Mostly superficial, stimulated by thermal or mechanical)

>Myelinated, responsible for sharp pain

C (Mostly deep, stimulated by thermal, mechanical or chemical)

>Unmyelinated, responsible for dull, slow, generalized pain

A-alpha and A-beta

>Proprioception

>Faster and stronger (thicker myelinated)

>Result of holding your wrist when you hurt it—overtakes sensation

In regard to the reflex arc and pain;

Let's say you touch a hot surface, the nociceptors in your fingertips begin to fire with an influx of calcium, glutamate is transferred to post synaptic neurons and the message begins to travel down both A-delta and C fibers. A-delta is a thickly myelinated neuron, thus transmitting the message quicker through the afferent pathway, to the dorsal horn to the interneuron where a withdrawal message is transmitted through the ventral horn to the efferent pathway to instruct the muscles to pull away. Meanwhile, the slower C-fibers follow a similar pathway, but instead ascended via the spino-thalamic tract to the medulla, midbrain and cerebrum, back down the descending pathway with instruction of sensation.