Basic Pain Anatomy and Physiology

George D. Comerci, Jr., MD, FACP, AAPM-Diplomate
Professor of Internal Medicine
Objectives
At the end of this session the participant will:

1. Review basic definitions related to the discussion of pain
2. Describe the function of a nociceptor
3. Describe basic pain pathways in the CNS
4. Discuss mechanisms of pain inhibition and facilitation
Basic Definitions

- **Pain:**
  - an unpleasant sensory and emotional experience associated with actual or potential tissue damage

- **Chronic Pain:**
  - pain that continues beyond the expected time of tissue healing
Basic Definitions

➢ Somatic Pain:
  • Pain associated with thermal, chemical or mechanical stimuli-(producing tissue damage)

➢ Neuropathic Pain:
  • pain that arises as a direct consequence of damage to the somatosensory nervous system

➢ Existential Pain:
  ▪ pain that occurs upon questioning and doubting the value of one’s ongoing existence as a living, sentient being -gc
The Nociceptor

- A transducer...converts one form of energy to another
- Specialized neuron that responds to mechanical, thermal and/or chemical stimuli
Types of Sensory Neurons

- **C fiber**: non-myelinated
- **A-delta fiber**: lightly myelinated
- **A-beta**: thickly myelinated (light touch/ proprioceptive)
Cross Section Peripheral Nerve
(Dept of Physiol. Univ. of Sydney)
The Nociceptor (Nature. 2001)

http://www.nature.com/nature/journal/v413/n6852/fig_tab/413203a0_F3.html#figure-title
The Nociceptor (J Clin. Invest. 2010)
Nociceptor Function

- **Stimulus transduction**
  - The receptor (gate) is triggered to open by a noxious stimulus causing sodium to enter the cell and an electrical “spike” to occur

- **Action Potential Generation**
  - The “spike”, if strong enough, causes the nerve to depolarize by means of a flood of sodium entering the cell
Nociceptor Function

- **Action Potential Propagation:**
  - The wave of sodium entry/depolarization rushes down the length of the neuron towards the presynaptic membrane

- **Transmitter Release**
  - At the presynaptic membrane, the wave of depolarization causes packets of neurotransmitters to be released into the synaptic space
The Nociceptor

Important neurotransmitters

- Calcitonin Gene related peptide
- Substance P
- Glutamate
- Aspartate
- Many more.....
The Nociceptor (J Clin. Invest. 2010)
The Synapse

- The junction of the nociceptor with the 2nd order (spinal) neuron
- Second order neuron relays information to the *supraspinal* structures of the brain
- The synapse of the nociceptor with the spinal neuron occurs in the *Laminae of Rexed*
Laminae (J Am Acad Ortho Surg. 2012)

Inputs

- Descending (Inhibition & excitation)
  - PAG / Raphe / LC / reticulospinal / corticospinal

- Intrinsic interneurons
- Primary afferent
  - Aδ fiber
    - high t/h mechanical/thermal/chemical polymodal/cold
    - D-hair
  - C-fiber
    - high t/h mechanical/thermal/chemical polymodal/silent warm
  - Aβ fiber
    - low t/h mechanical

Outputs

- Spinothalamic
- Postsynaptic dorsal column
- Spinocervical
- Spinocerebellar
- Spinomesencephalic
- Spino-recticular

Dorsal horn connections

Projection

Local circuit

Intersegmental

To ventral horn
Pain Pathways from the Spine to the Brain

- **Spinoreticular Tract:**
  - Spinal neurons that synapse in the *Periaqueductal Gray* and *Nucleus Raphe Magnus*-[role in descending pain modulation]
  - Spinal neurons to the medial thalamus-[role in memory and affective components of pain]
Pain Pathways from the Spine to the Brain

- Spinothalamic Tract:
  - spinal neurons that synapse in the Ventroposterolateral (VPL) thalamus-[role in pain localization-below the head]

- (Trigeminothalamic Tract):
  - spinal neurons that synapse in the VPL lateral thalamus-[role in pain localization-face and head]
Spinal Pathways
The Thalamus

- Ventroposterolateral (VPL) Nucleus:
  - Synapse with neurons going to somatosensory cortex with the role of localization of pain

- Medial (Centromedian) Nucleus
  - Synapse with neurons in the limbic system
Spinothalamic Pathways
The Thalamus

- Functions not only as a “switching station” but also has an important role in certain chronic pain conditions

- Storage of memory recall of the sensory and affective components of pain that is long past
  - These may be kept “at bay” by inhibitory neurons
  - *Thalamic Syndrome*
Pain and the Cerebral Cortex

- Somatosensory Cortex
- Secondary Somatosensory Cortex
- Anterior Cingulate Cortex
- Insular Cortex

Pain Localization

Pain Experience
Modulation of Nociceptive Input

Endogenous Excitatory Mechanisms

• Amplification of nociceptor firing
• Amplification of secondary neuron firing (NMDA)
• Amplification of descending facilitory neurons
Modulation of Nociceptive Input

- **Endogenous Inhibitory Mechanisms**
  
  **Nociceptor**
  - Inhibition of nociceptor firing (NSAIDS, anesthetics/antiepileptic drugs)

  **Spinal**
  - Inhibition of secondary neuron firing (GABA)
Modulation of Nociceptive Input

**Brainstem**
- Amplification of descending inhibitory neurons from the periaqueductal gray (TCAs/NSRIs)

**Cortex**
- Cognitive manipulations (distraction, hypnosis, expectation)
Risk Factors for the development of chronic pain

- Gender and Sex
- Age
- Efficacy of Endogenous pain modulation
- Genetics
- Environmental Factors
- Psychologic Factors
Summary

We’ve discussed:
- Nociception
- Pain pathways in the CNS
- Facilitatory and Inhibitory Factors