

## INTRODUCTION

### A. Pain Vocabulary

<i>-algnesia</i>	refers to pain
<i>hyperalgesia</i>	increased sensitivity to pain
<i>hypoalgesia</i>	decrease of pain sensitivity
<i>analgesia</i>	loss of or decrease in pain sensation
<i>neuralgia</i>	pain that follows the course of a nerve or is related to a nerve (e.g. trigeminal neuralgia)
<i>causalgia</i>	burning pain associated with previous tissue injury (sympathetic dystrophy)
<i>allodynia</i>	pain induced by an ordinarily non-painful stimulus
<i>hyperpathia</i>	combination of hyperalgesia and allodynia
<i>algesiometer</i>	device for generating quantitative pain stimulus
<i>dolorimeter</i>	device for generating quantitative pain stimulus

### B. Special Aspects of Pain

Pain is a somatic sensation with many properties in common with other somatic sensations. However, pain has some unique aspects, among which are the following:

1. Wide variety of adequate stimuli
2. Subject to sensitization and self-reinforcement
3. Referred pain localization errors
4. Modulation or gating
5. Sensitization
6. Reflexes

## PAIN MODALITY and ADEQUATE STIMULI

### A. Distinct Modality (not extreme stimulation of other modalities)

1. Pain intensity can be reduced while other sensory modalities are maintained (analgesia without anesthesia)
2. Distinct afferent endings and pathways
  - a. endings innervated by small axons: A- $\delta$  or C
  - b. characteristics of endings
    - 1) free nerve endings
    - 2) widely distributed in throughout the body (skin, muscles, bones, joints, viscera, blood vessels)
    - 3) high threshold
    - 4) some respond to specific types of energy, others are polymodal (can be excited by several types of stimuli)

PAIN MODALITY and ADEQUATE STIMULI

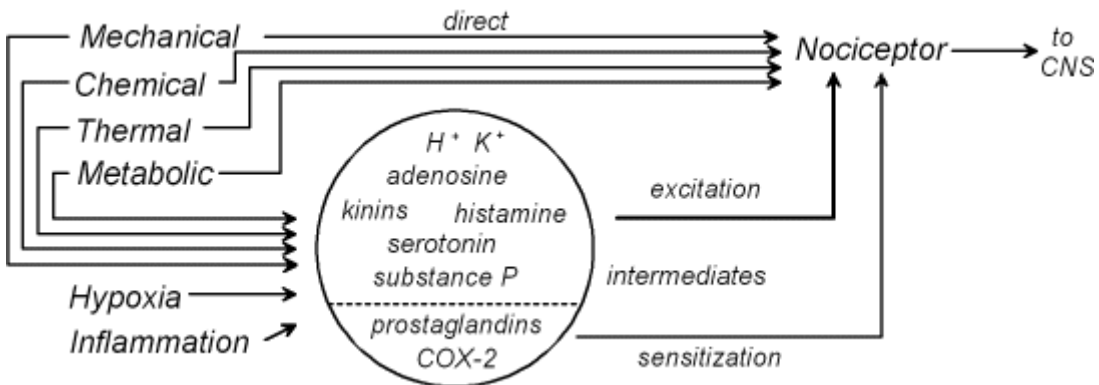
B. Adequate stimulus: many

1. mechanical (tissue distortion)
2. thermal (Temperature > 45C, also cold)
3. caustic chemicals
4. inflammation
5. endogenous mediators (e.g. histamine, kinins)
6. metabolic byproducts (e.g. H<sup>+</sup>, K<sup>+</sup>)
7. hypoxia; usually due to ischemia (e.g. angina, claudication)
8. osmotic and/or electrolyte imbalance
9. capsaicin

Common characteristic of stimuli: Noxious (damaging or potentially damaging to tissue)

Thus, pain endings are termed "nociceptors"

C. Stimulus-Response Mechanisms



1. When stimulated, pain endings can release the neurotransmitter/vasodilator substance P
2. Note positive feedback: nociceptor activation ⇔ inflammation; results in nociceptor sensitization
3. Note effect of nociceptor stimulation on local blood flow increase (axon reflex, red flare)

D. Submodalities

1. Major submodality classification

	<u>Axons</u>	<u>Conduction velocity</u>	<u>Quality</u>
Sharp	A-δ (1-5 μm)	"fast" (6-30 m/sec)	sharp, pricking
Dull	C-fiber (0.2-1.5 μm)	"slow" (0.5-2 m/sec)	dull, aching, burning

2. Other submodalities may be due to

- a. mixture of inputs from the various types of nociceptive endings
- b. simultaneous excitation of other modalities

## PAIN LOCALIZATION

### A. Acuity of Localization

1. Generally poorly localized, due to
  - a. low density of peripheral endings
  - b. wide receptive fields
  - c. much convergence (summation) in ascending pathways
  - d. coarse topographic representation in CNS
2. Acuity depends on
  - a. fiber type: A- $\delta$  (better), C-fiber (worse)
  - b. location: superficial (better), deep & visceral (worse)
  - c. simultaneous stimulation of other modalities (better)

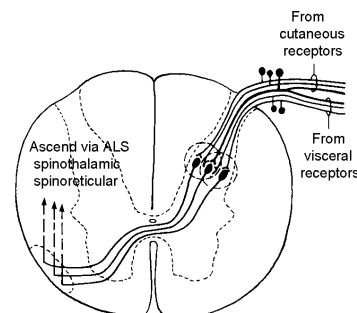
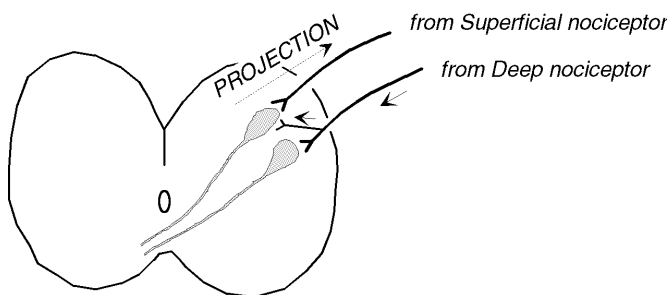
### C. Errors in Pain Localization

1. Projection, as in other sensory modalities (e.g. pinched dorsal root, carpal tunnel syndrome/repetitive stress injury, phantom limb)
2. Referred pain: pain originating at nociceptors at one site in the body (usually deep/visceral) is sensed as originating at another site (usually superficial); examples

left arm pain in heart attack: pain often referred to left arm due to cardiac hypoxia

headache (some types): pain referred to head surface from sinus irritation or pain endings in cerebral blood vessels

- a. Pain is often referred to superficial regions sharing the same dorsal root as the deep/visceral site from which the pain actually originated
- b. Pain can be referred and correctly localized simultaneously
- c. Theories of the basis of referred pain
  - 1) Convergence-Projection: afferents from cutaneous pain endings and deep/visceral pain endings converge on the same neuron somewhere along the ascending CNS pathway. When the deep/visceral pain endings are stimulated, sensation is projected back to the cutaneous endings. Also, deep pain may facilitate transmission of normally subliminal pain from peripheral receptors.



- 2) Learning theory: pain is projected to body regions previously associated with pain

## PAIN INTENSITY

### A. Intensity Evaluation

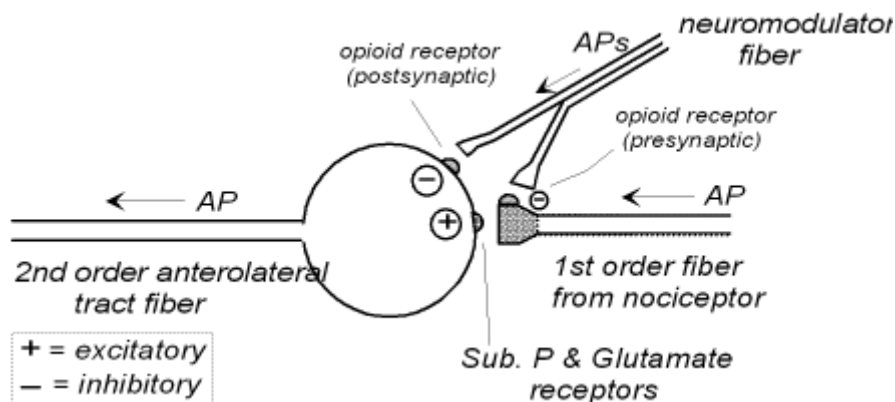
1. 0 (no pain) to 10 (maximum pain) subjective scale
2. Face scale for children

### B. Afferent Input

1. Strength of stimulus at individual nociceptors (firing frequency)
2. Recruitment (summation important, particularly for dull pain)

### C. Modulation (gating)

1. Define: reduced synaptic excitability of nociceptive pathway neurons due to release of inhibitory neuromodulator



Note: major mechanism: presynaptic inhibition

Note: compared to neurotransmitters, neuromodulators are longer acting and change synaptic excitability rather than directly activating postsynaptic cell

### 2. Neuromodulators and receptors

- a. agonists: opioid peptides -- endorphins, enkephalins, dynorphin
- b. receptors: opioid receptors

Example: Spinal perfusion with morphine for intractable pain of cancer

PAIN INTENSITY (continued)

D. Modulation Pathways

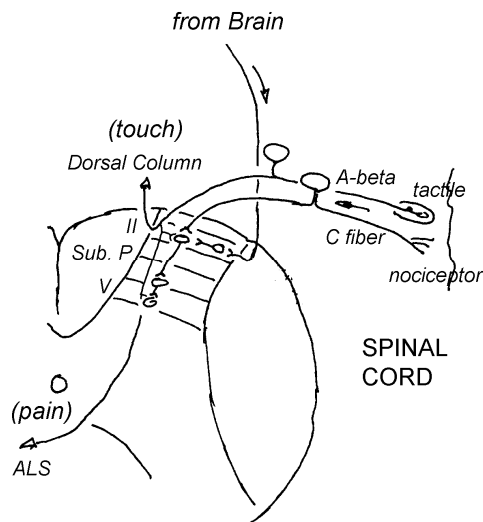
1. Peripheral

- a. mediated by excitation of primary somatosensory large diameter axons ( $A\alpha$ ,  $A\beta$ )
- b. action: inhibit synaptic transmission in nociceptive pathway

Examples: TENS (Transcutaneous Electrical Nerve Stimulation)

2. Central Modulation: descending system

- a. originate in neurons whose cell bodies are in the midbrain
- b. descend through the brainstem and spinal cord
- c. descending neurons eventually terminate on synapses mediating pain transmission and reduce synaptic excitability (neuromodulator opioid peptide)
- e. originating neurons in the brain receive input from the cerebral cortex, hypothalamus, and the ascending sensory neurons
- d. the descending system can be activated by certain opioid peptides



Example: Stress-induced analgesia

E. Sensitization and Adaptation

- 1. Most nociceptors are either nonadapting or only slowly adapting
- 2. Sensitization
  - a. Define: increased response at a given stimulus level (hyperalgesia) or response in the absence of a noxious stimulus (allodynia)
  - b. Peripheral Sensitization: increased sensitivity of the primary afferent nociceptor; e.g. inflammation mediators, peripheral feedback from Substance P
  - c. Central Sensitization: increased or spontaneous synaptic excitation on the nociceptive pathway

## PAIN-INDUCED REFLEXES

### A. Superficial Pain

1. flexion-withdrawal
2. tachycardia
3. hypertension
4. general sympathetic activation

### B. Deep-Visceral Pain

1. contraction of overlying muscles
2. bradycardia
3. hypotension (can lead to shock)
4. nausea

## ACUTE AND CHRONIC PAIN IN BODY FUNCTION

### A. Acute Pain: can have useful role

1. Protective (reflex, etc.)
2. Alerting
3. Avoidance
4. Learning and motivation (reinforcement)

### B. Chronic Pain: generally no useful role; pathological; possible contributors

1. Continued noxious stimulus
2. Increased sensitivity of pain pathway, so that subthreshold or mild noxious stimuli (hyperalgesia) or non-noxious stimuli (allodynia) lead to maintained pain; possible contributors:
  - a. increased nociceptive ending sensitivity (e.g. positive feedback in inflammation; effect of nerve injury)
  - b. increased synaptic excitability (up regulation of receptors)
  - c. individual differences; inherent sensitivity to painful stimuli and associated affect