PAIN, ITCH AND TICKLE SENSATIONS

Rodolfo T. Rafael, M.D.

Introduction

• Primary afferent neurons have their cell bodies in the dorsal root ganglia or equivalent in cranial nerves.
• They enter the spinal cord or brain stem and make polysynaptic reflex connections to motor neurons at many levels as well as connections that relay impulses to the cerebral cortex.
Dorsal horns are divided into laminas I-VI

DORSAL HORN LAMINAS

Figure 7-1. Schematic representation of the terminations of the 3 types of primary afferent neurons in the various layers of the dorsal horn of the spinal cord. (Modified from Salt TH, Hill RE: Neurotransmitter candidates of somatosensory primary afferent fibers. Neuroscience 1983;10:1033.)
Name and describe the importance of Lamina I

Posteromarginal nucleus - lamina I

– Important in sensory processing for pain and temperature
Name and describe the importance of Lamina II

Substantia gelatinosa - lamina II

– receives sensory input and integrates it with input from lamina I.
Name and describe the importance of Lamina III and IV

Nucleus proprius - lamina III and IV

- Integrates sensory input with descending modulatory input from brain and brainstem.
Name and describe the importance of 3 types of primary afferent fibers

• Large myelinated A β fibers
  – transmit impulses generated by mechanical stimuli.

• Small myelinated A δ fibers
  – some transmit impulses from cold receptors
  – nociceptors that mediate fast pain
  – some transmit impulses from mechanoceptors

• Small unmyelinated C fibers
  – Concerned with pain and temperature
  – Few transmit impulses from
Comparative properties of primary afferent fibres

<table>
<thead>
<tr>
<th>Fibre class</th>
<th>Threshold</th>
<th>Main transmitters</th>
<th>Main Receptor activated</th>
<th>Laminar location</th>
<th>Target spinal cord neurons</th>
<th>Normal Sensation</th>
<th>Pathological Sensation</th>
</tr>
</thead>
<tbody>
<tr>
<td>C Ad</td>
<td>High</td>
<td>Peptides EAA</td>
<td>NMDA, AMPA, mGlu</td>
<td>I-II, V</td>
<td>NS WDR</td>
<td>Slow pain</td>
<td>Fast pain Alodynia</td>
</tr>
<tr>
<td>Ab</td>
<td>Low</td>
<td>EAA</td>
<td>AMPA</td>
<td>III-VI</td>
<td>LT WDR</td>
<td>Touch Vibration</td>
<td>Pressure Mechanical alodynia</td>
</tr>
</tbody>
</table>

Key: EAA = Excitatory amino acids; NS = Nociceptive specific; LT = Low Threshold; WDR = wide dynamic range; NK = neurokinin (peptide) receptor; NMDA, AMPA, mGlu are different types of glutamate receptors

Pathways to the Cerebral Cortex

- Dorsal column or Lemniscal System
  - fibers mediating fine touch and proprioception \( \rightarrow \) dorsal column \( \rightarrow \) medulla \( \rightarrow \) gracile and cuneate nuclei
  - second order neuron \( \rightarrow \) medial lemniscus \( \rightarrow \) ventral posterior nucleus (thalamus)

- Anterolateral System
  - touch, temp, and pain fibers \( \rightarrow \) dorsal horn \( \rightarrow \) axons cross the midline \( \rightarrow \) ascend in the anterolateral quadrant of the Spinal cord

Figure 7-8: Touch, pain, and temperature pathways from the trunk and limbs. The anterolateral system both and lateral spinothalamic and related ascending tracts also project to the mesencephalic and thamic thalamus and the nonspecific thalamic nuclei.
Cortical Representation

Figure 7.3. Major spinal pathways. The solid lines on the right represent the line of incision in performing an anterolateral rhizotomy. Note the termination of the tract. S1, sacral; L, lumbar; T, thoracic.

Figure 7.4. Brain areas concerned with somatic sensation, and some of the cortical receiving areas for other sensory modalities in the human brain. The numbers are those of Bogen's cortical areas. The auditory (acoustic) area is actually located in the sylvian fissure on the top of the superior temporal gyrus and is not normally visible.
PAIN

• Mainly a protective mechanism for the body
  – It occurs whenever any tissues are being damaged
  – It causes the individual to react to remove the pain stimulus.

• Sense organs for pain are the naked nerve endings found in almost every tissue of the body.
Definition

- Pain is one of mankind’s oldest and most dreaded fears.
- To the neuroscientist
  - pain is a sensory phenomenon registered on perception
- To the psychologist
  - it may be a learned or conditioned behaviour
- To the doctor
  - it is a warning sign to be decoded for diagnosis and treatment

International Association for the Study of Pain

- “an unpleasant sensory or emotional experience that is associated with actual or potential tissue damaging stimuli”.
Pain are transmitted to the CNS by 2 fiber system:

- Small myelinated A δ fibers
- Unmyelinated C fibers

Small Myelinated A δ fibers

- elicited by either mechanical or thermal pain
- 2-5 μm in diameter
- conduct at rates of 12-30m/s (6-30m/s)
- ends in the dorsal horn
- terminate primarily on neurons in laminas I and V
- glutamate is the neurotransmitter substance secreted in the spinal cord.
  - One of the most widely used excitatory transmitter in the CNS
Unmyelinated C fibers

- elicited by chemical or by persisting thermal and mechanical stimuli
- 0.4-1.2 μm in diameter
- found in the lateral division of the dorsal roots and are often called DORSAL ROOT C Fibers
- conduct at the low rate of 0.5-2 m/s
- ends in the dorsal horn
- terminate on neurons in laminas I and II
  - Guyton Lamina II and III
- Substance P the probable neurotransmitter

Two kinds of Pain

- **Fast or sharp pain, pricking pain, acute pain, electric pain**
  - A painful stimulus causes a “bright” sharp, localized sensation
  - pain is felt within about 0.1 second after a pain stimulus is applied
  - not felt in most of the deeper tissues of the body
  - can be elicited by mechanical and thermal
  - A δ pain fibers

- **Slow or slow burning pain, aching pain, throbbing pain, nauseous pain, chronic pain.**
  - Dull, intense, diffuse and unpleasant feeling
  - Begins only after 1 sec or more and then increases slowly over many seconds and sometimes even minutes
  - Usually associated with tissue destruction
  - Can occur both in the skin and in almost any deep tissue or organ
  - Can be elicited by mechanical, thermal, and chemical
  - C pain fibers
PAIN RECEPTORS AND THEIR STIMULATION

• All Pain Receptors are free nerve endings
  – Widespread in the superficial layers of the skin as well as in certain internal tissues such as periosteum, the arterial walls, the joint surfaces, and the falx and tentorium of the cranial vault

THREE TYPES OF STIMULI EXCITE PAIN RECEPTORS

• Mechanical

• Thermal
  – Average person first begin to perceive pain when the skin is heated above 45°C
  • This is temp at which the tissues begin to be damaged by heat; indeed, the tissues are eventually destroyed
  – Pain resulting from heat is closely correlated with the ability of heat to damage the tissues.

• Chemical
  – Bradykinin, serotonin, histamine, potassium ions, acids, acetylcholine, and proteolytic enzymes
  – Especially important in stimulating the slow, suffering type of pain that occurs after tissue injury.
Subcortical Perception

- there is evidence that sensory stimuli are perceived in the absence of the cerebral cortex, and this is especially true with PAIN.

- The cortical receiving areas are apparently concerned with the discriminative, exact, and meaningful interpretation of pain, but perception alone does not require the cortex.

- Pain was called by Sherrington the “physical adjunct of an imperative protective reflex”
  - Stimuli that are painful generally initiate potent withdrawal and avoidance responses.
  - Unique among the senses coz associated with strong emotional component
  - Information transmitted via the special senses may secondarily evoke pleasant or unpleasant emotions, but pain alone has a “built-in” unpleasant affect.
  - Present evidence indicates that this affective response depends upon connections of the pain pathways in the thalamus.
    - Damage to the thalamus may be associated with a peculiar overreaction to painful stimuli known as the thalamic syndrome
Deep Pain

- Poorly localized
- Nauseating
- Associated with sweating and changes in blood pressure

Adequate Stimulus

- Pain receptors are specific, and pain is not produced by overstimulation of other receptors
- Adequate Stimulus for pain receptors is not as specific as that for others, because they can be stimulated by a variety of strong stimuli
Muscle pain

• If a muscle contracts rhythmically in the presence of an adequate blood supply, pain does not usually result.
• If occluded, contraction soon causes pain. **WHY?**
  – Accumulation of large amounts of lactic acid in the tissues as a consequence of the anaerobic metabolism that occurs during ischemia.
• Muscle with a normal blood supply is made to contract continuously without periods of relaxation → ache
  – compresses the blood vessels supplying the muscle.
  – Release during contraction a chemical agent (Lewis “P factor”).

Muscle Spasm

• Common cause of pain and it is the basis of many clinical pain syndrome
• Pain produce partially from the direct effect of muscle spasm in stimulating mechanosensitive pain receptors
• Pain also results from the indirect effect of muscle spasm to compress the blood vessels and cause ISCHEMIA.
• Increase the rate of metabolism in the muscle tissue at the same time, thus making the relative ischemia even greater, creating ideal conditions for release of chemical pain-inducing substances
Hyperalgesia

- In pathologic conditions, the sensitivity of the pain receptors is altered.
- **There are 2 important types of alteration**
  - Primary Hyperalgesia
  - Secondary Hyperalgesia

Primary Hyperalgesia

- seen in the area surrounding an inflamed or injured area
- the threshold for pain is lowered so that trivial stimuli cause pain
- Seen around the area of the flare
- The region of vasodilation around the injury
- Flare in surrounding undamaged tissue is due to substance \( P \) liberated by antidromic impulses in primary afferent fibers
- Pain are due to substances liberated from injured cells
Secondary Hyperalgesia

- the threshold for pain is actually elevated
- the pain produced is unpleasant, prolonged and severe.
- The area from which this response is obtained extends well beyond the site of injury
- The condition does not last as long as primary hyperalgesia
- Due to central facilitation by impulses from the injured area → spinal, thalamic or cortical level → unpleasant pain

Somatic

- Somatic Sensory Pathways
  - relay information from somatic receptors to the primary somatosensory area in the cerebral cortex and to the cerebellum.
  - The pathways to the cerebral cortex are composed of thousands of sets of three neurons:
    - First-order-neuron
    - Second-order-neuron
    - Third-order neuron
- Somatic sensory impulses entering the spinal cord ascend to the cerebral cortex by two general pathways:
  - The posterior column-medial lemniscus pathway
  - Anterolateral (spinotinalamic) pathways
The pathways to the cerebral cortex are composed of three neurons:

- **First-order-neuron**
  - Conduct impulses from the somatic receptors into either the brain stem or spinal cord.
  - From the face, mouth, teeth and eyes, somatic sensory impulses propagate along cranial nerves into the brain stem.
  - From the neck, body, and posterior aspect of the head, somatic sensory impulses propagate along spinal nerves into the spinal cord.

- **Second-order-neuron**
  - Conduct impulses from the spinal cord and brain stem to the thalamus.

- **Third-order neuron**
  - Conduct impulses from the thalamus to the primary somatosensory area of the cortex (postcentral gyrus) where conscious perception of the sensations results.
Visceral Pain

- poorly localized
- unpleasant
- associated with nausea and autonomic symptoms
- often radiates to other areas

Visceral Pain

- Afferent mechanisms play a major role in homeostatic adjustment
- No proprioceptors
- Afferent fibers reach the central nervous system via **sympathetic and parasympathetic pathways**. Their cell bodies are located in the dorsal roots and the homologous cranial nerve ganglia.
- Visceral afferent
  - Facial, Glossopharyngeal, Vagus nerves
  - Thoracic and Upper lumbar dorsal roots
  - Sacral roots
  - Eye in the trigeminal nerve
- In the CNS Visceral sensation travels along the same pathways as somatic sensation in the spinothalamic tracts and thalamic radiations, and the cortical receiving areas for visceral sensation are intermixed with the somatic receiving areas in the postcentral gyri.
Causes of True Visceral Pain

- **Ischemia**
  - Because of the formation of acidic metabolic end products or tissue-degenerative products, such as bradykinin, proteolytic enzymes, or others that stimulate the pain nerve endings
- **Chemical Stimuli**
  - Damaging substances leak from the GI tract into the peritoneal cavity.
- **Spasm of a hollow Viscus**
  - Spasm of the gut, the gallbladder, a bile duct, the ureter, or any hollow viscus
    - cause pain possibly by mechanical stimulation of the pain endings
    - cause might be diminished blood flow to the muscle combined with increased metabolic need of the muscle for nutrients.
    - Spastic viscus occurs in the form of cramps, the pain increasing to a high degree of severity and then subsiding, this process continuing rhythmically once every few minutes. The rhythmical cycles result from rhythmical contraction of smooth muscle. Ex. Gastroenteritis, constipation, mensturation, parturition, gallbladder disease, or ureteral obstruction
- **Overdistention of a Hollow Viscus**
  - Overfilling of a hollow viscus because of overstretch of the tissues.
  - It can also collapse the blood vessels that encircle the viscus or that pass into its wall, thus perhaps promoting ischemic pain.
Insensitive Viscera

- Parenchyma of the liver
- Alveoli of the lungs

Stimulation of Pain Fibers in the Viscera

- Few pain receptors in the viscera
- Poorly localized
- Receptors in the walls of the hollow viscera are especially sensitive to distention of the organs
- When a viscus is inflamed or hyperemic, MINOR stimuli cause severe pain
- Traction on the mesentery
Muscle Spasm and Rigidity

- Initiates reflex contraction of nearby skeletal muscle
- Reflex spasm is usually in the abdominal wall and makes the abdominal wall rigid
- The spasm protects the underlying inflamed structures from inadvertent trauma “guarding”
- Classic signs of inflammation in an abdominal viscus
  - Pain
  - Tenderness
  - Autonomic changes (hypotension, sweating)

Referred Pain

- **Pain** in a part of his/her body that is considerably remote from the tissues causing pain
- **Pain** is usually initiated in one of the visceral organs and referred to an area on the body surface.
- **Important** in clinical diagnosis
- **Mechanism**
  - Branches of visceral pain fibers are shown to synapse in the spinal cord with some of the second-order neurons that receive pain fibers from the skin. When the visceral pain fibers are stimulated, pain signals from the viscera are then conducted through at least some of the same neurons that conduct pain signals from the skin, and the persons has the feeling that the sensations originate in the skin itself.
  - Irritation of a viscus frequently produces pain which is felt not in the viscus but in some somatic structure that may be a considerable distance away.
- Deep somatic pain may also be referred
- Superficial pain is not referred
Dermatomal Rule

- When pain is referred, it is usually to a structure that developed from the same embryonic segment or dermatome as the structure in which the pain originates (called Dermatomal Rule)
- Example→the heart and the arm have the same segmental origin, the testicle has migrated with its nerve supply from the primitive urogenital ridge from which the kidney and ureter also developed.
Role of Experience

• Although pain originating in an inflamed abdominal viscus is usually referred to the midline, in patients who have had previous abdominal surgery the pain of abdominal disease is frequently referred to their surgical scars.

Itch and Tickle

• is transmitted by small type C, unmyelinated fiber
ITCH

• Itch spots can be identified on the skin by careful mapping
  – Produce by mild stimulation
  – The distribution of itch and pain are different
    • Low-frequency stimulation of pain fibers produces pain not itch
    • High-frequency stimulation of itch spots on the skin may merely increase the intensity of the itching without producing pain
    • These observations indicate that C fiber system responsible for itching is not the same as that responsible for pain.
  – Itching is annoying
  – Pain is unpleasant
  – Itching can be produced by chemical agents
    • Histamine produces intense itching, and injuries cause its liberation in the skin.
    • Kinins cause severe itching

Tickling

• Tickling sensation is usually regarded as pleasurable
  – Free nerve endings and lamellated corpuscles are thought to mediate the tickle sensation
  – Why the tickle sensation chiefly arises only when someone else touches you?
    • Still a mystery.
Thank You For not Listening