Pain Physiology in the Chronic Pelvic Pain Context

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No relevant financial relationships in the past twelve months by presenter or spouse/partner.
Presentation Outline

1. Definitions
2. Why bother? Scope of the problem
3. Types of pain
4. Pain pathways
5. The neuro pathologic response to pain
6. Conclusions
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Pain

An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.

It is a complex collection of multiple, learned perceptions that change over time and that motivate individuals to circumstance appropriate self-protective action.


Berkley KJ. Neuroscience, FSU. 2005
Chronic Pelvic Pain

• Non-malignant
• Non cyclic pain*
• >3mo duration*
• Localizes
  – Anatomic pelvis
  – Anterior abdominal wall at or below the umbilicus
  – Lumbosacral back
  – Buttocks
• Sufficient severity to cause functional disability or lead to medical care.
• Related negative cognitive, behavioral and social consequences.

A lack of physical findings does not negate the significance of a patient’s pain.

Normal examination results do not preclude the possibility of finding pelvic pathology. It is more likely that patients are poorly evaluated and not that the physical examination is normal.

Chronic Pelvic Pain Syndrome

- CPP
- Impaired usual function
- Signs of depression
- Pain out of proportion to pathology
- Unresponsive to usual therapy
- Altered family roles

ACOG Patients educational pamphlet AP 129. Chronic pelvic pain. Washington DC 1989
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• 20 - 30% of all ObGyn Office visits
• 15 - 20% of all ER ObGyn Visits
• 20 - 40% of all Gyn Laparoscopies
• Up to 61% undiagnosed - untreated

• 41% never seek consultations
• 31% with symptom related anxiety (compared with 7% without CPP)
• 50% had also urinary symptoms and/or functional bowel disease

Zondervan KT, Yudkin PI et al. The community prevalence of chronic pelvic pain in women and associated illness behaviour. Brit J Gen Practice 2001;541
• Up to 75% of Gyn medical disability in the United States
• 80% of patient’s are unsatisfactorily managed
• Only 15% of physicians surveyed said they “enjoyed” caring for CPP patients

Zondervan KT, Yudkin PL et al. The community prevalence of chronic pelvic pain in women and associated illness behaviour. Brit J Gen Practice 2001;541
Quality of Life

- Inability to exercise 81%
- Difficulty sleeping 79%
- Lack of enjoyment of leisure 67%
- Inability to perform chores 65%
- Interference with socializing 65%
- Difficulty walking 59%
- Interference with sexuality 54%
- Difficulty concentrating 49%
- Inability to work 41%

Cost

- Medical cost
  U$ 1.2 billion/year

- Productivity loss
  U$ 15 billion/year

Association of professors of gynecology and Obstetrics: monography January 2000
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Pain Source

- Nociceptive
  - Somatic Pain
  - Visceral Pain
- Non nociceptive
  - Neuropathic Pain

Mixed Pain

- Acute Pain
- Chronic Pain

Pain Duration

References:
Nociceptive pain arises from the stimulation of specific pain receptors.
Somatic Pain

– Caused by the activation of pain receptors
  • Body surface
  • Musculoskeletal tissues
– Usually aggravated by activity and relieved by rest
– Receptors respond to stimuli released from damaged cells
  • Heat
  • Cold
  • Vibration
  • Stretch
  • Chemical
Visceral Pain

– Caused by damaged or injured internal organs or abdominal muscles (spasm)
– Caused by the activation of pain receptors in the chest, abdomen or pelvic areas
– Vague and not well localized
– Usually described as pressure-like, deep squeezing, dull or diffuse
– Referred pain


Non Nociceptive Pain

arises from within the peripheral and central nervous system
Neuropathic Pain

• Caused by injury or malfunction to the spinal cord and peripheral nerves
• Typically a burning, tingling, shooting, stinging, or "pins and needles" sensation
• Also complain of a stabbing, piercing, cutting, and drilling pain
• Usually occurs days, weeks or months after the injury
• Tends to occur in waves of frequency and intensity
• Is diffuse and occurs at the level or below the level of injury

Acute Pain

• Typically is produced by sudden injury

• Accompanied by physical signs

• Tends to resolve as the injury or disease does
Chronic Pain

- 3-6 mo duration
- Persistent pain
- In many cases no physical cause can be found
- Is a disorder in itself rather than being the symptom of a disease process
- Repeated pain from an acute injury changes the nervous system responses

[Diagrams of network patterns]

References:
- Wall and Melzack’s Textbook of Pain, Churchill Livingstone: 5th edition 2005
Acute vs. Chronic Pain

• Acute Pain
  *Symptom* of tissue damage and an underlying disease

• Chronic Pain
  Pain becomes a *disease*

«Some individuals who have acute pain can be caught in a vicious cycle that leads to chronic pain and disability»

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Pain is a direct or indirect consequence of several diseases. However patients with moderate to severe pain are often under-treated in both developing and developed countries(…)

It is important to recognize that pain is a problem in its own right, not “just” an indicator of an underlying disease or damage process, but one which extracts a great toll on individuals and society. Alleviation of pain itself, as a symptom, should be a therapeutic target. In order to improve the quality of life, the objective should be to avoid any unpleasant perception with an approach based on the right communication between the care giver and the patient.
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Descartes “Tubules”

• 3 components
  – **First order neurone**
    • cell body in dorsal root ganglion
    • Transmits pain from a peripheral receptor
  – **Second-order neurone**
    • Dorsal horn of the spinal cord
    • Axon crosses the midline
    • Ascend in the spinothalamic tract to the thalamus
  – **Third-order neurone**
    • Projects to the postcentral gyrus (via the internal capsule)
    • Generate periferical response

• The progression of pain research has been hindered by the dominating view that pain is a purely nociceptive phenomenon

• Now we know is much more complex (even more for the chronic pain)
  – Peripheral receptors
  – Neural pathways
  – Spinal Cord mechanisms & long tracts
  – Brainstem, thalamus, cortex & other areas
  – Descending pathways

Initial connections

Local interconnections

Ascending pathways

Neospinothalamic tract
Spino-reticulo-diencephalic pathway

Spinal cord

Gate Control

Perception of Pain
In cerebral cortex

Sensory and motor cortex areas
Premotor cortex

*Pre Frontal cortex*
Other parts of the parietal cortex
Cingulate cortex
Insula
Occipital cortex

Descending modulation

First pain
(pain only nociceptors)

Second pain
(polimodal nociceptors)

Peripheral receptors

A delta fibres
C fibres
Brain regions involved in pain processing

Somatosensory Cortex

Prefrontal Cortex

Insular Cortex

Thalamus

Anterior Cingulate Cortex (ACC) / Locus coeruleus

Anatomy of Pain **Overlaps** Anatomy of Emotion

Common areas of activation in pain studies (PET and MRI)

- **Anterior Cingulate Cortex (ACC) / Locus coeruleus**
  - Cognitive functions and reasoning
    - Reward Anticipation
    - Decision Making
    - Empathy
    - Emotion
  - Integrates emotional stimuli with attentional functions
- **Prefrontal cortex**
  - Perform and accomplish
  - Working memory
  - Decision making
  - Planning and judgment
- **Insular Cortex**
  - Processes convergent information to produce emotionally relevant context for sensory experience
- **Somatosensory Cortex**
- **Thalamus (and Amygdala)**
  - Processing
  - Memory of emotional reactions

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• Pain mechanisms in patients with chronic pain

  – Altered **Pain processing**
  – **Cross – Talk**
  – **Convergence and Hiperalgesia**
    • Visceral – somatic
    • Visceral - visceral
  – Dorsal horn **neuroplasticity**
  – **Centralization**
  – Neurogenic inflammation / Antidromic transmission
  – Visceral “**Silent”** Afferents
Altered Pain-Processing

Severe, unrelieved pain for more than 24 hr

Excessive and prolonged stimulation of N-methyl-D-aspartate (NMDA) receptors

Plastic neuropathic change at dorsal horn receptor cell

Produces hyperexcitable neurons, alldynia and hyperalgesia

Repeat Stimulation of Nociceptive Neurons

- Changes Nerve Fibers
  - Lowers Threshold
  - Peripheral Sensitization
    - Exaggerated Transmission Response
      - Recruits higher and Lower Neurons
        - Self-Sustaining Activation

References:


Spinal Windup
Neuronal plasticity

Barrage of painful stimuli to dorsal horn

Decrease threshold or loss of inhibition (allodynia)

Expansion of receptive fields

Permanent biochemical change

Exaggerated reflex output with end-organ dysfunction

Up regulation of sensory processing

Cross-talk

The very strong electrical signals originated in poorly isolated (or poorly myelinated) nerves produce de novo electrical signals on adjacent afferent nerve fibers that are not involved in the painful stimuli.


Visceral somatic convergence

- Only 2 to 7% of all afferent fibers of each dorsal root ganglion are visceral
- The interneurons in the dorsal horn are greatly influenced by somatic fibers
- So
  - The somatic pain is referred as visceral pain (specially in the abdominal wall)
  - The visceral pain is diffuse and poorly located
- Visceral muscular reflex and induced myalgia - PFTM


Visceral-somatic hiperalgesia

Referred neurogenic inflammation

- BPS/IC + vulvodinia
- IBS + abdominal trigger points

Brumovsky PR, Gebhart GF. Visceral organ cross-sensitization - an integrated perspective. Auton Neurosci 2010;153(1-2):106
Visceral - visceral hiperalgesia

- BPS/IC + IBS

- Endometriosis + BPS/IC

- Hernias + PCS


Dorsal horn neuroplasticity

• Nociceptive stimuli modulation in patients with CPP (highly subjective)
  – Primary hiperalgesia

• Afferent pathways remodeling - dorsal horn

• Downstream influences from supraspinal sites
  – Secondary hiperalgesia and allodynia
    • Hiperalgesia far from the original painful site
Central sensitization

- Enhanced nociceptive synaptic transmission within the spinal cord following persistent pain states
  - Dissociation of pain
  - Perception from a noxious stimulus or injury
  - Expansion of hyperalgesia beyond the site of injury
  - Extra-dermatomal hypersensitivity across other somatic and visceral structures

- Despite removal of original (primary pain generator) “insult” pain persists (30-50%)
- The dorsal horn is still hyper excitable with spontaneous activity.
- Phantom limb
- Spinal memory
- Reorganization of somatosensory cortex
- “A chance to cut is NOT a chance to cure”

Neuro-inflammation by antidromic transmission

- Release of neuropeptides at the terminus of afferent nerves
  - Substance P
  - CRGP
  - Neurokinin A
  - Neurokinin B

- Resulting in tissue reaction
  - Reddening (vasodilation)
  - Edema (plasma extravasation)
  - Hyperalgesia

- Non neuropathic refered pain
  - Dyspareunia and PCS

Visceral “Silent” Afferents

• Thinly or unmyelinated – easily damaged locally

• 30% to 80% visceral afferents are silent

• Silent afferents become active with prolonged stimuli

• Silent afferents play major role in tissue sensitization

• Many more interneuronal synapses

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In summary

- Pain itself can be the disease
- Sometimes the normal responses to pain create **new pain generators**
  - Look for the original insult – if still present
  - Treat **all** sources of pain and dysfunction
  - “Turn down the pain”
- Avoid inducing further wind-up in patients with **pre-existing up-regulation**
If you only have a hammer, it’s tempting to treat everything as if it were a nail.

- Abraham Maslow

(1.908 – 1.970)