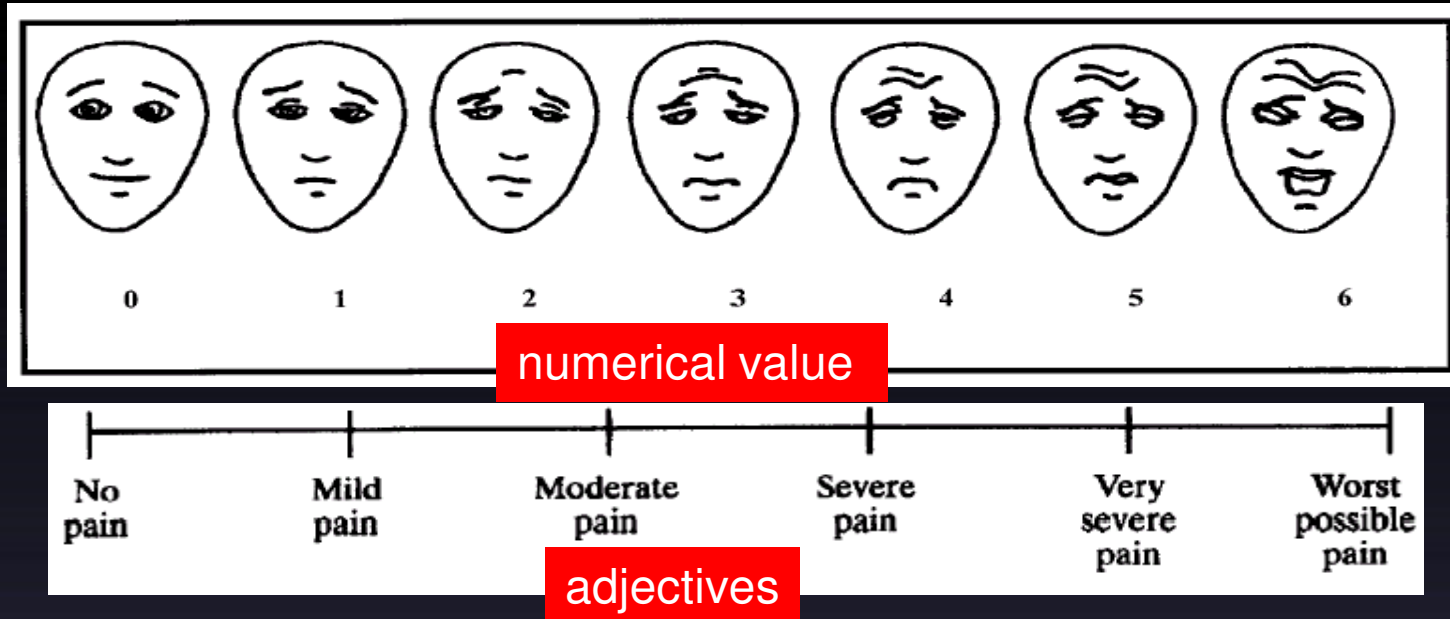


PAIN MODULATION



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OBJECTIVES

At the end of this lecture you should be able to describe:

- **Nociceptors, Referred Pain, radiating pain**
- **“Gating” of Pain**
- **Pain Suppression (“Analgesia”) System in the Brain and Spinal Cord**
- **Transcutaneous Electrical Nerve Stimulation (TENS)**
- **Transcranial Direct Current Stimulation (tDCS)**
- **Applied aspects of pain**

Nociceptive & Neuropathic Pain

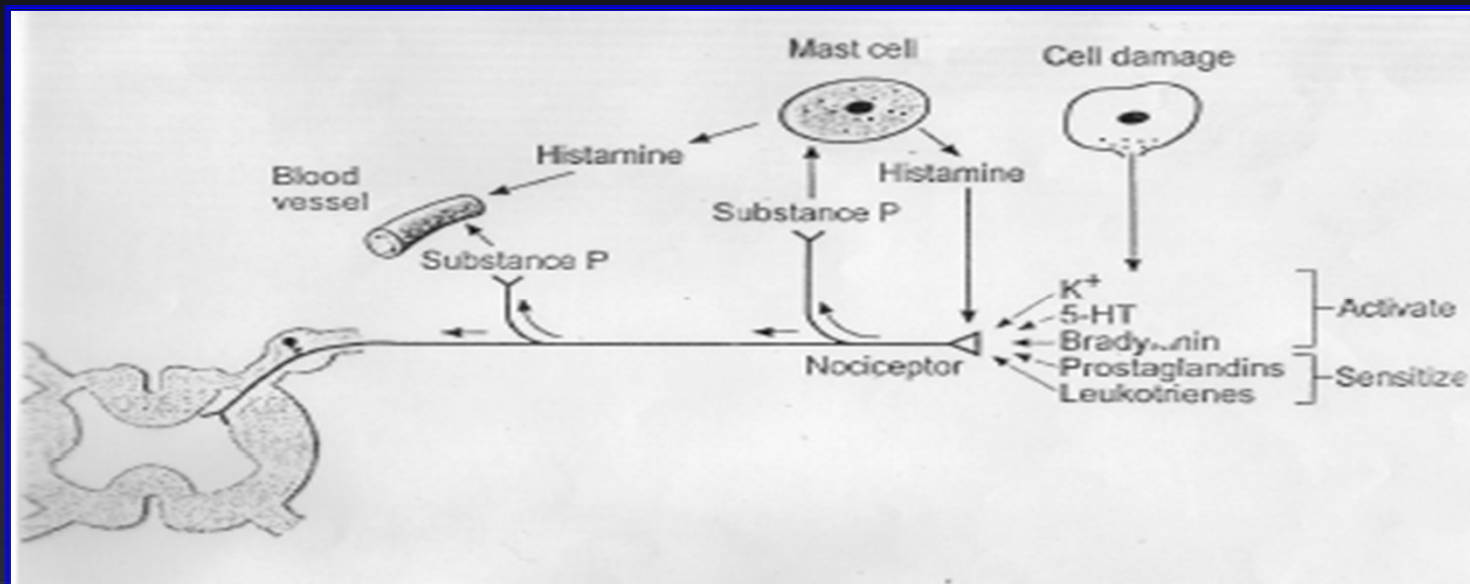
- **Nociceptive pain** is detected by specialized transducers connected to A-delta and C-fibers (stimuli from somatic and visceral structures)
- **Neuropathic pain** damage to nerves (trigeminal neuralgia, postherpetic pain, diabetic neuropathy)

4 Basic Processes

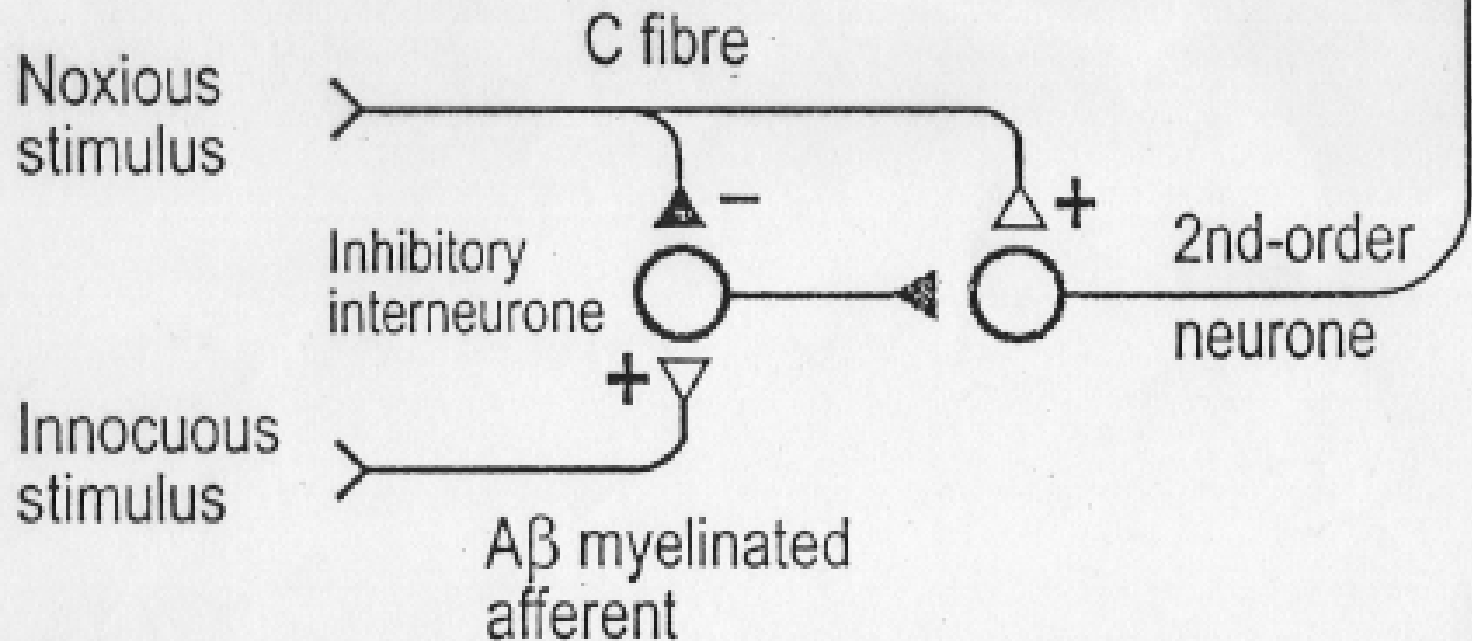
1. **Transduction**—nociceptors free nerve endings
2. **Transmission**
3. **Perception of Pain**-At cortical Level
4. **Modulation of Pain**, Changing or inhibiting pain impulses in the descending tract (brain → spinal cord) [norepinephrine and serotonin]

Chemical agents that produce pain

- **Nociceptors are activated by:** Bradykinin, serotonin, Histamine, K^+ ion, Acids, acetyl choline, & proteolytic enzymes.
- **Nociceptors are sensitized by:** Prostaglandins & substance P



A MODEL OF "GATING" OF PAIN



Implies a non-painful stimulus can block the transmission of a noxious stimulus. Is based on the premise that the gate, located in the dorsal horn of the spinal cord, modulates the afferent nerve impulses.

1. A-Delta fibres (sharp pain)
2. C fibres (dull pain)
3. A-Beta fibres that carry messages of light touch

Conditions that open or close the gate

	Conditions that open the gate	Conditions that close the gate
Physical conditions	Extent of the injury	Medication
	Inappropriate activity level	Counterstimulation, eg massage
Emotional Conditions	Anxiety or worry	Positive emotions
	Tension	Relaxation
	Depression	Rest
Mental conditions	Focusing on the pain	Intense concentration or distraction
	Boredom	Involvement and interest in life activities

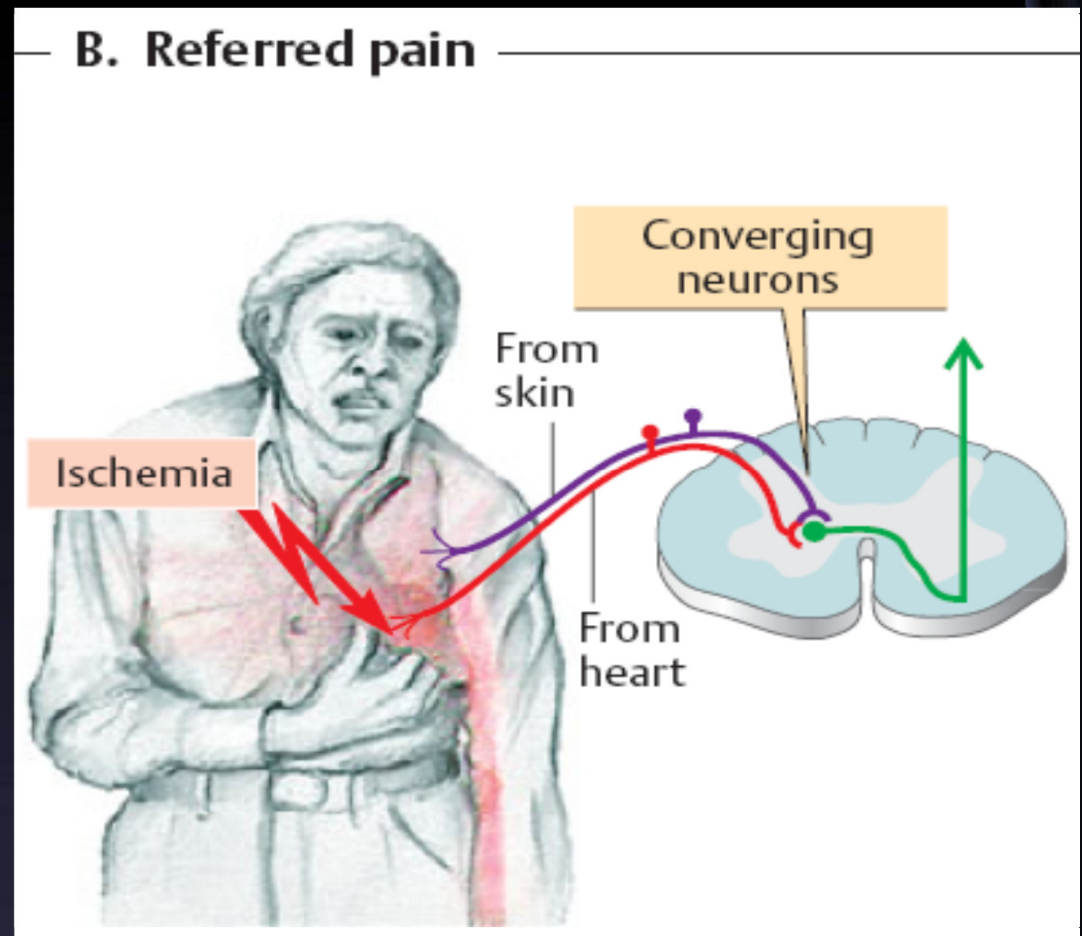
REFERRED PAIN

- Pain that is not felt in the diseased structure itself, but at another place in the body far away from the site of origin.
- Visceral and deep somatic pain are often referred, but superficial pain is not.
- Mechanism of referred pain
 - Convergence of peripheral & visceral pain on the same second order neuron that project to brain
 - Facilitation theory: Impulses from diseased viscus pass through afferents which give collaterals to ST neurons receiving pain fibers from skin dermatomes

REFERRED PAIN

Convergence

Branches of visceral pain fibers synapse in the spinal cord on the same second-order neurons that receive pain signals from the skin



REFERRED PAIN

When visceral pain is referred to the surface of the body, the person generally localizes it in the dermatomal segment from which the visceral organ originated in the embryo, not necessarily where the visceral organ now lies.

- Cardiac pain is referred to the jaw, left shoulder & inner side of left arm.
- Pain of appendicitis is referred to periumbilical region.
- Pain from the ureter is referred to testicular region

Dermatomal rule

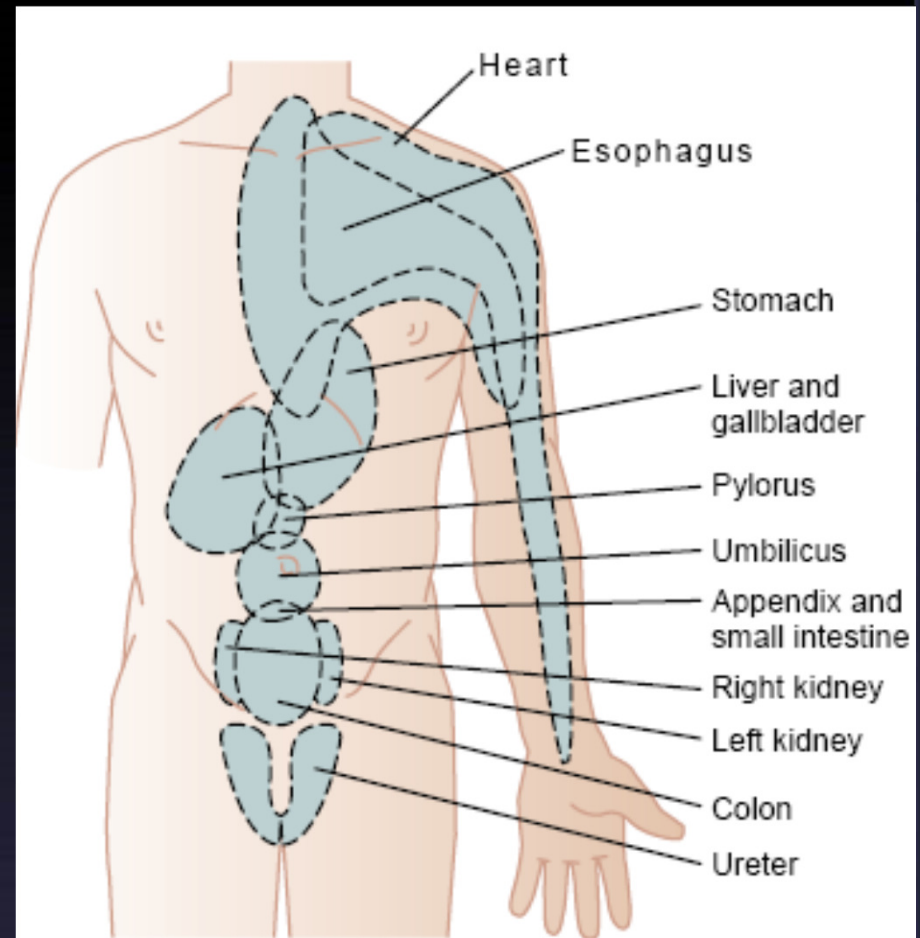
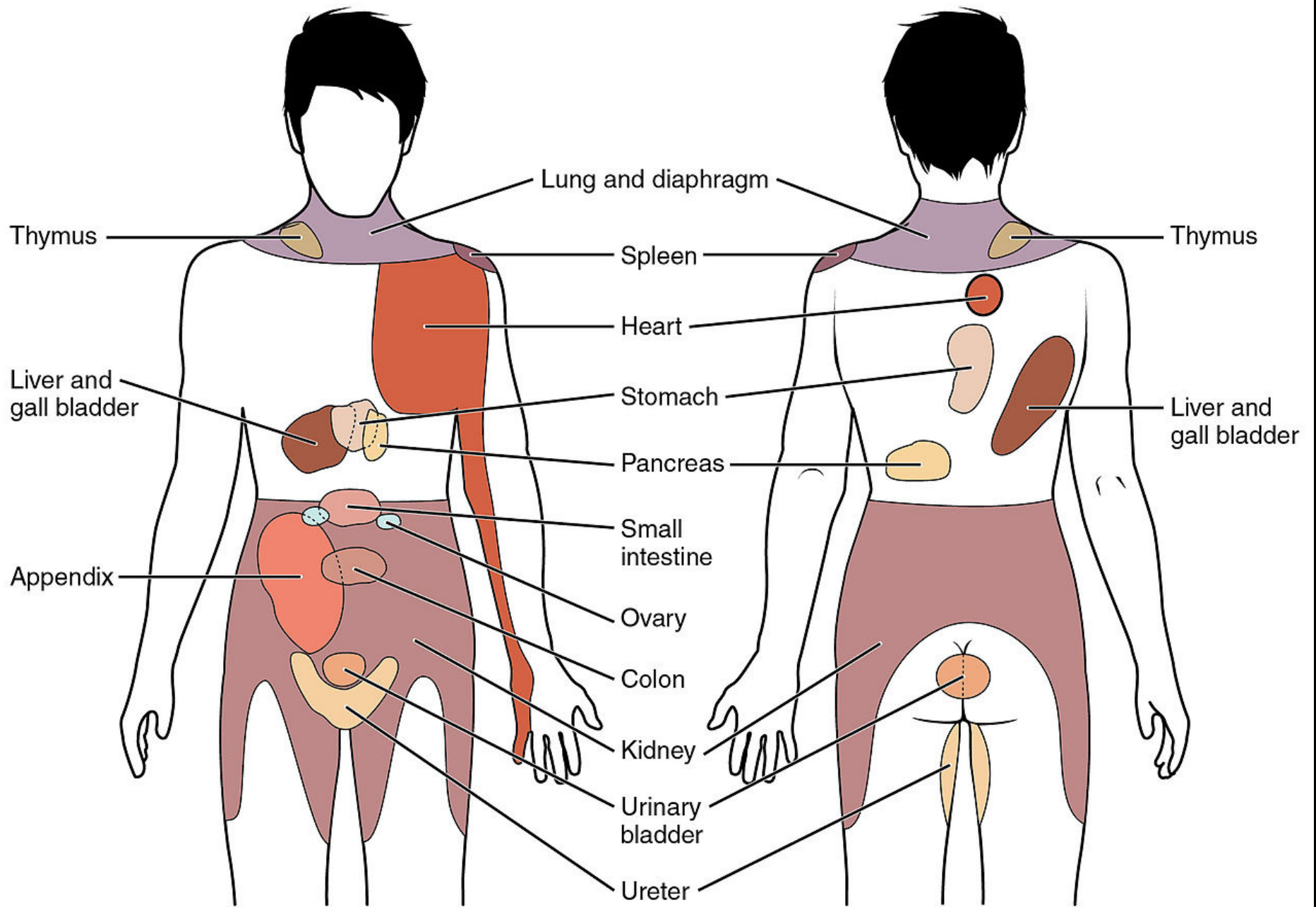


Figure 48-6

Surface areas of referred pain from different visceral organs.



REFERRED PAIN

Localization of Visceral Pain “Visceral” and the “Parietal” Pain Transmission Pathways

When pain migrates/referred
from its original site of
localization it called
RADIATING PAIN

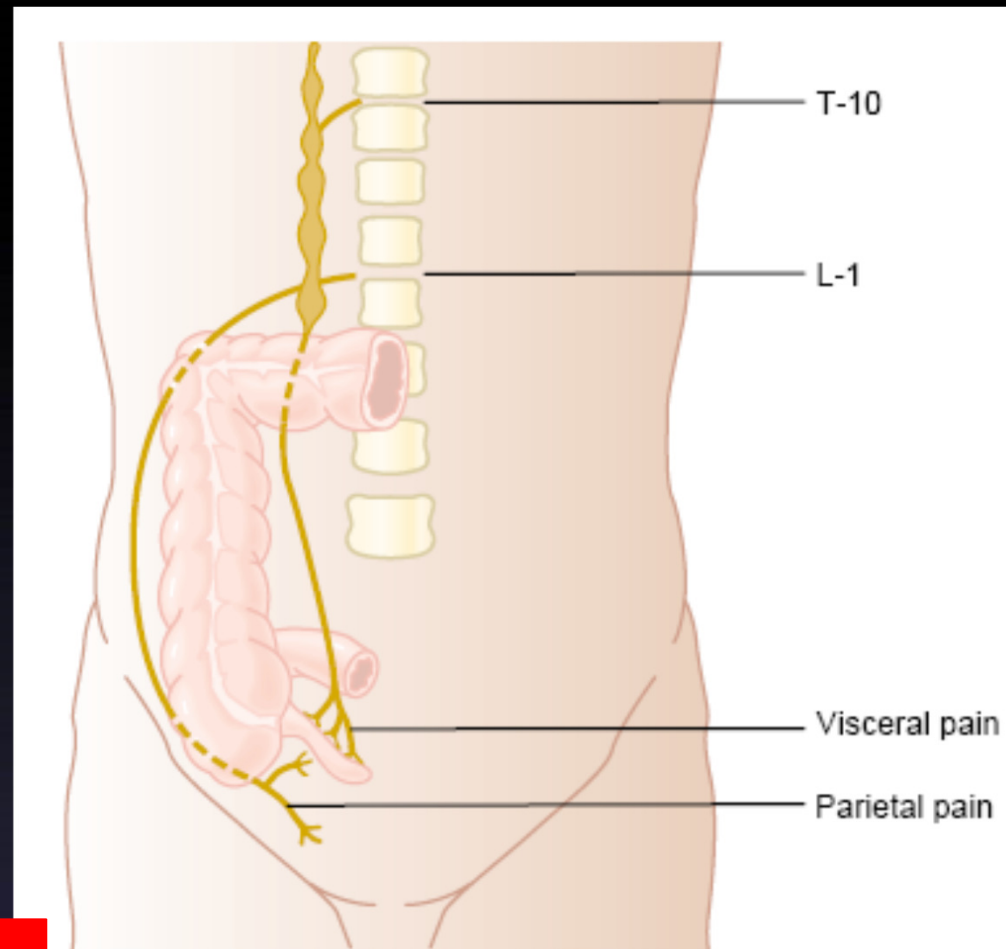


Figure 48-7

Visceral and parietal transmission of pain signals from the appendix.

CHARACTERISTICS OF VISCERAL PAIN

- Gradual Onset
- Poorly localized
- Associated with nausea and autonomic disturbance
- Often referred
- Cutting, crushing are not painful when applied to viscera
- Pain is caused by distension, ischemia and inflammation
- Accompanying autonomic symptoms of nausea and diaphoresis are common

Visceral Pain sensations are carried by unmyelinated C-fibers Travel with autonomic (sympathetic) afferents
Gen Visceral Afferent

Spinal cord
(Dorsal Horn)
Lat. spinothalamic tract

Thalamus

Somatosensory Cortex

The brain tissues themselves are almost totally insensitive to pain.

Tugging on the venous sinuses around the brain, damaging the tentorium, or stretching the dura at the base of the brain can cause intense pain that is recognized as headache. Also, almost any type of traumatizing, crushing, or stretching stimulus to the blood vessels of the meninges can cause headache.

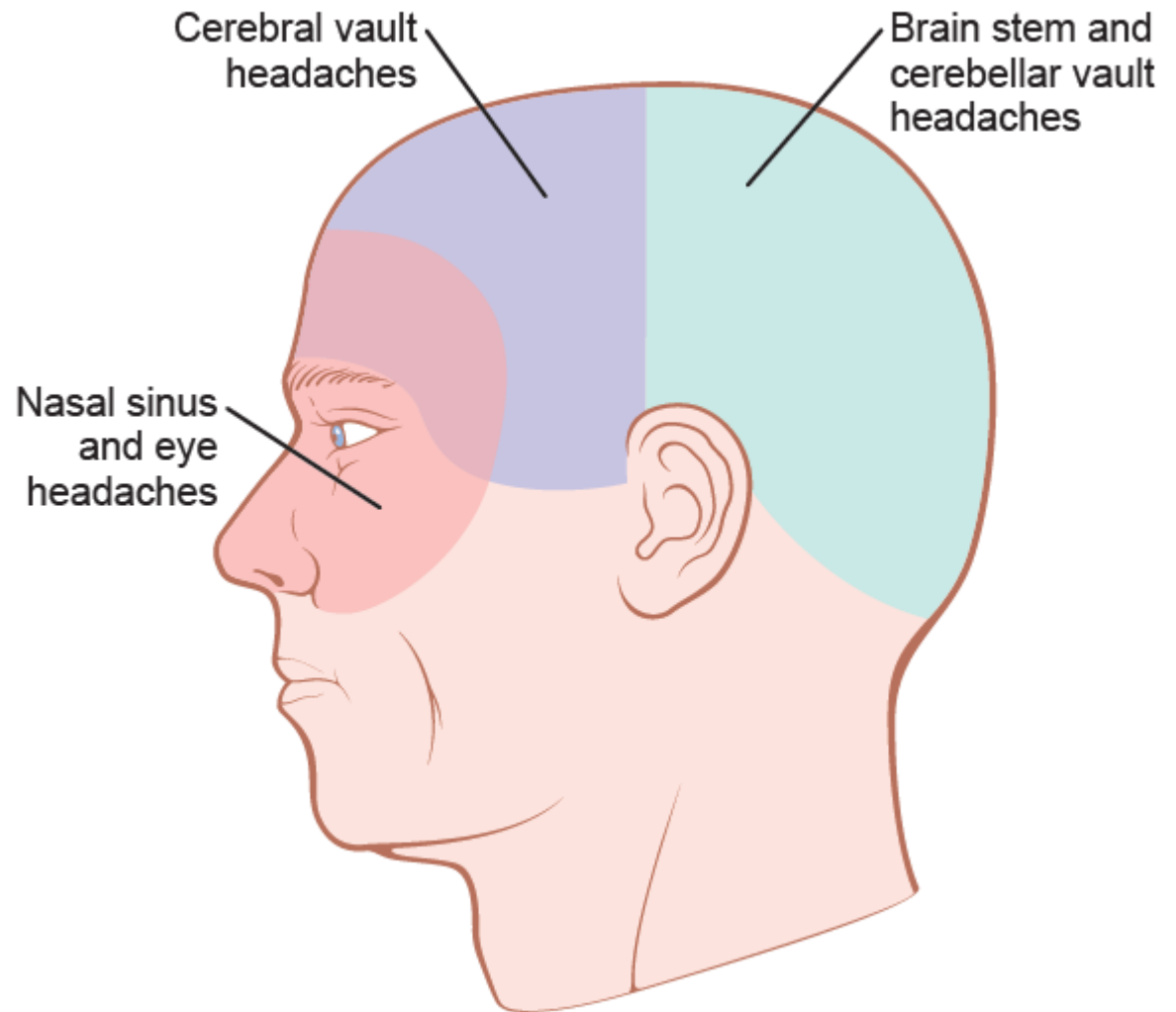


Figure 49-9. Areas of headache resulting from different causes.

أَخْبَرَنَا أَحْمَدُ بْنُ جَعْفَرِ بْنِ حَمْدَانَ ، ثنا بِشْرُ بْنُ مُوسَى ، ثنا أَبُو عَبْدِ الرَّحْمَنِ الْمُقْرِيُّ ثنا سَعِيدُ بْنُ أَبِي أَيُّوبَ 3 ، ثنا مُحَمَّدُ بْنُ عَجْلَانَ ، عَنِ الْقَعْقَاعِ بْنِ حَكِيمٍ ، عَنِ أَبِي صَالِحٍ ، عَنِ أَبِي هُرَيْرَةَ ، عَنِ رَسُولِ اللَّهِ صَلَّى اللَّهُ عَلَيْهِ وَسَلَّمَ ، أَنَّهُ قَالَ :

" الشَّهِيدُ لَا يَجِدُ أَلَمَ الْقَتْلِ ، إِلَّا كَمَا يَجِدُ أَلَمَ الْقَرْصَةِ "

(الشَّهِيدُ لَا يَجِدُ أَلَمَ الْقَتْلِ إِلَّا كَمَا يَجِدُ
أَحْدَكُمْ أَلَمَ مَسِ الْقَرْصَةِ)

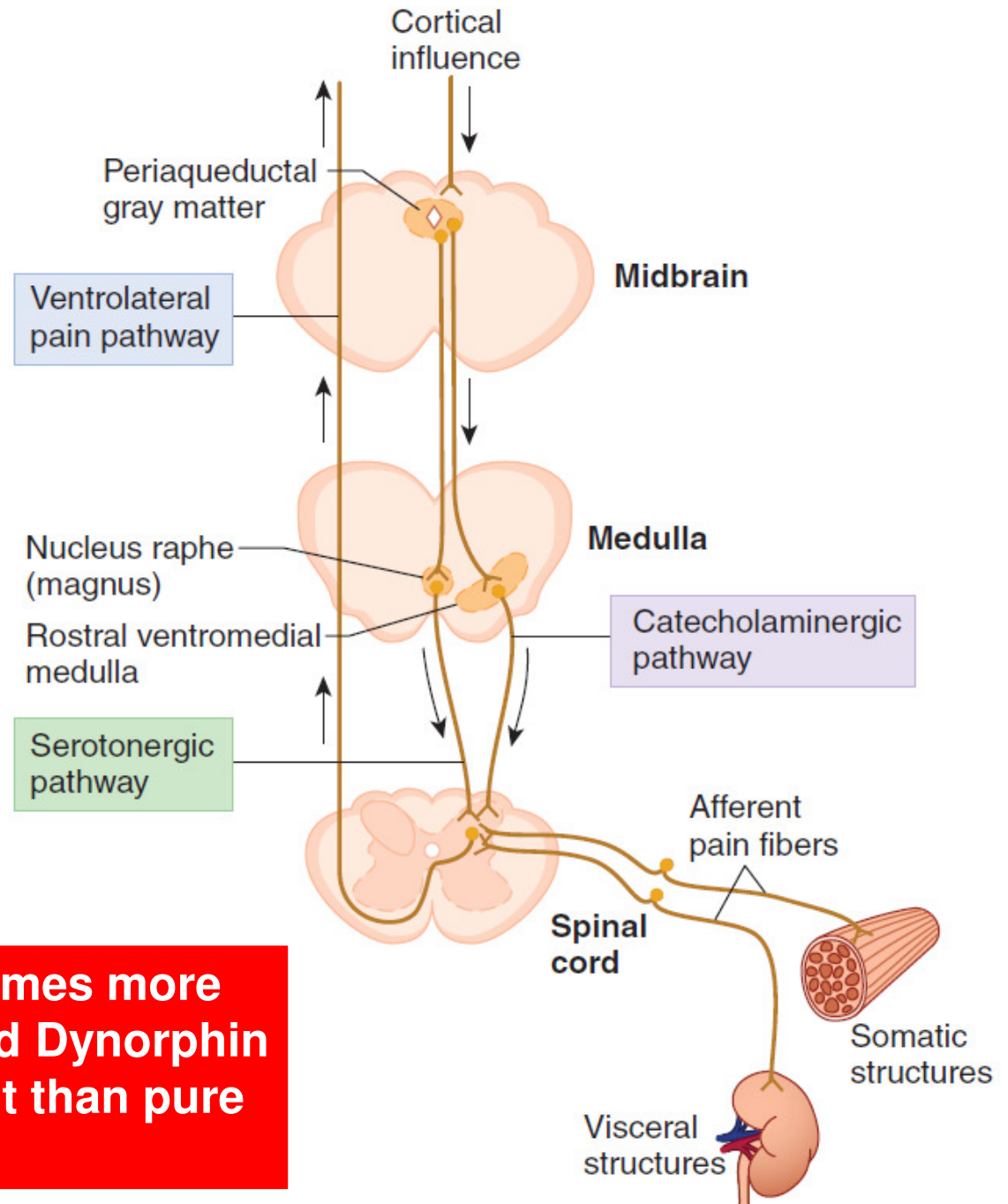
ابن ماجه

Pain Suppression ("Analgesia") System in the Brain and Spinal Cord

Ascending Pain
Pathway

Descending
Analgesic
Pathway

Beta Endorphin is 50 times more
potent than morphine and Dynorphin
is 200 times more potent than pure
morphine



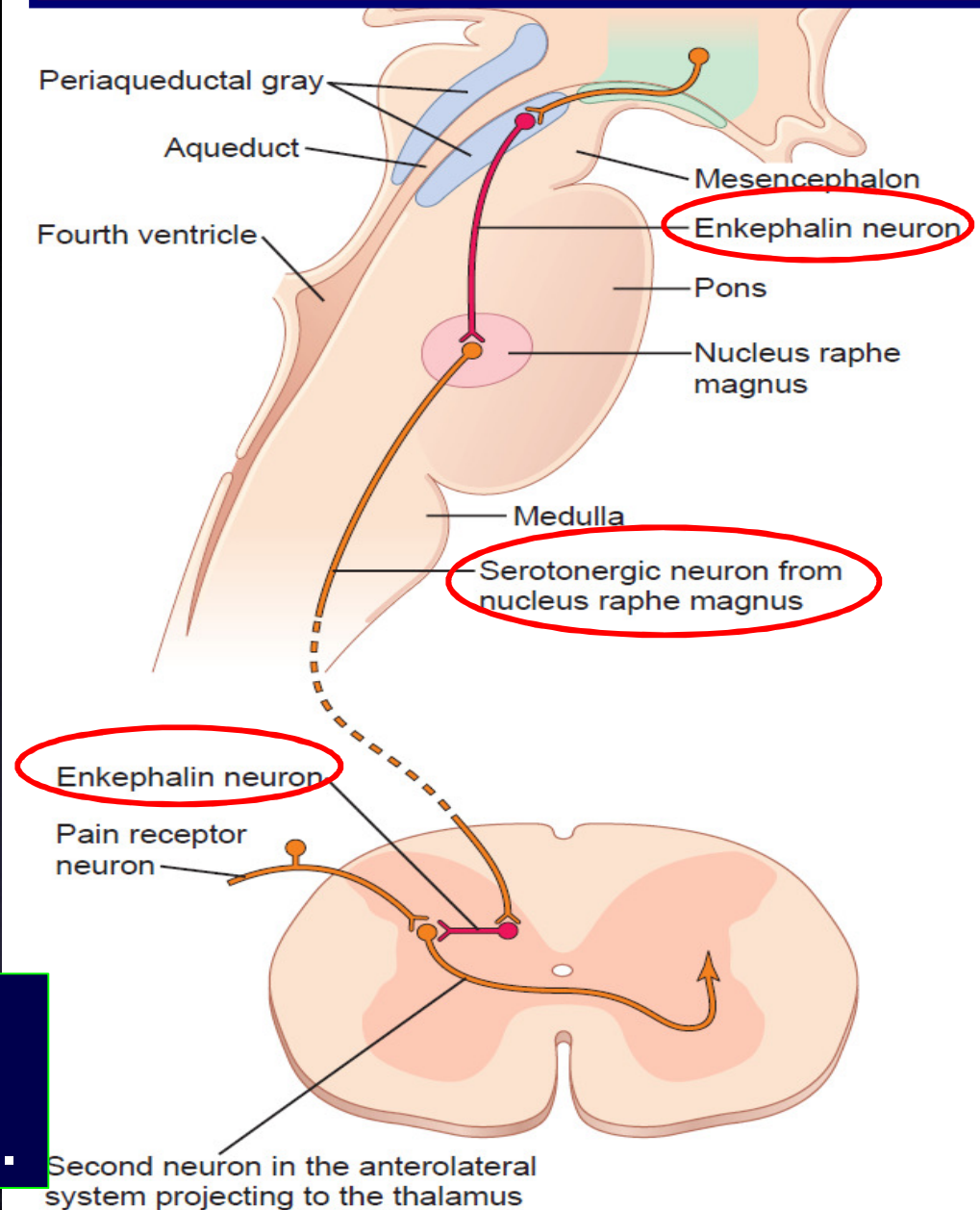
(1) **Enkephalin Neurons** from **periaqueductal gray and periventricular** areas of the **mesencephalon and upper pons** send signals to

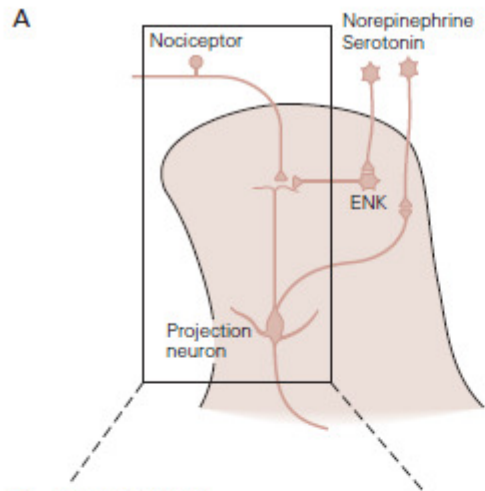
(2) **Raphe magnus** nucleus, in the lower pons and upper medulla. From these nuclei, second-order N go down the dorsolateral columns in the spinal cord & secrete **Serotonin** which act on **local neurons to secrete Enkephalin**

(3) a **pain inhibitory complex** in the dorsal of spinal cord

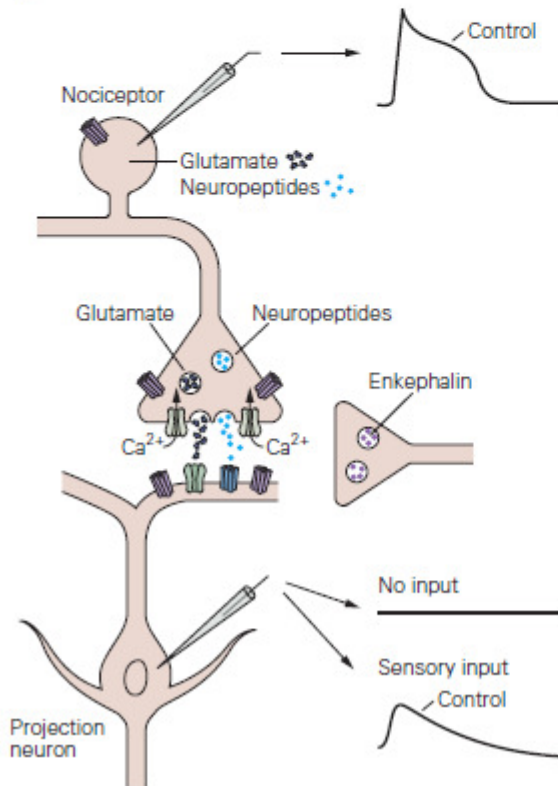
At this point, the analgesia signals can block the pain before it is relayed to the brain.

Pain Suppression (“Analgesia”) System in the Brain and Spinal Cord

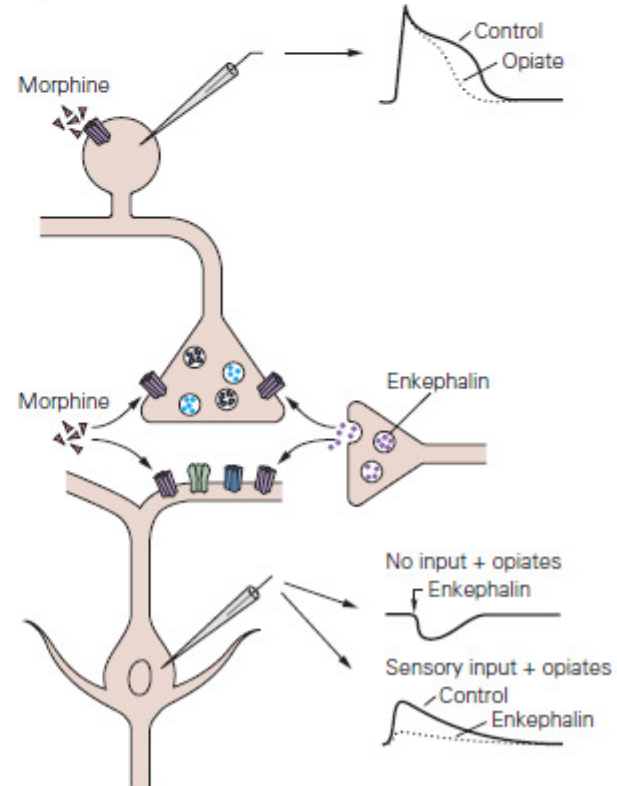




B₁ Sensory input



B₂ Sensory input + opiates/opioids

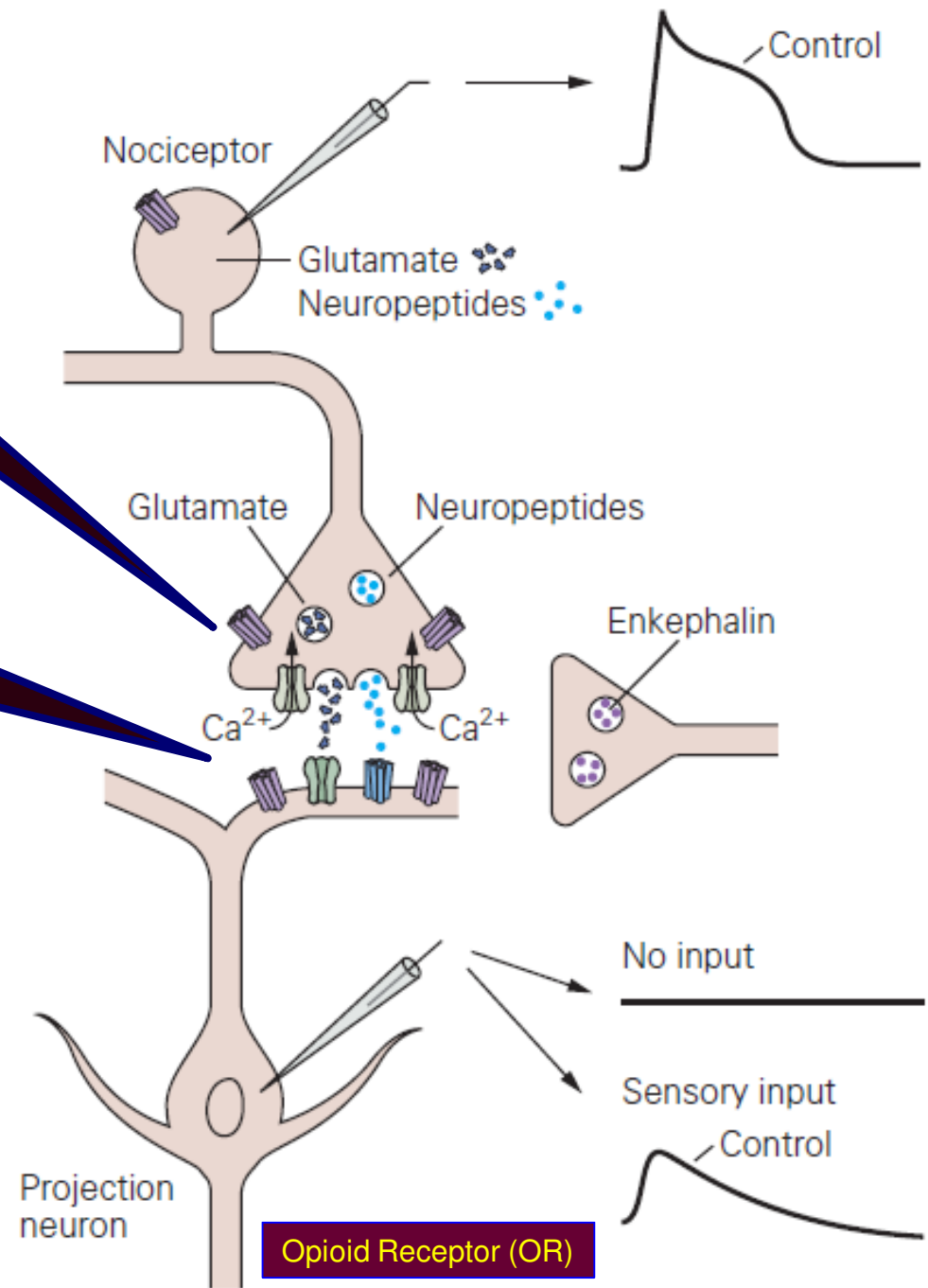


Activation of the presynaptic OR leads to a decrease in Ca^{2+} influx, resulting in a decrease in release of glutamate and substance P.

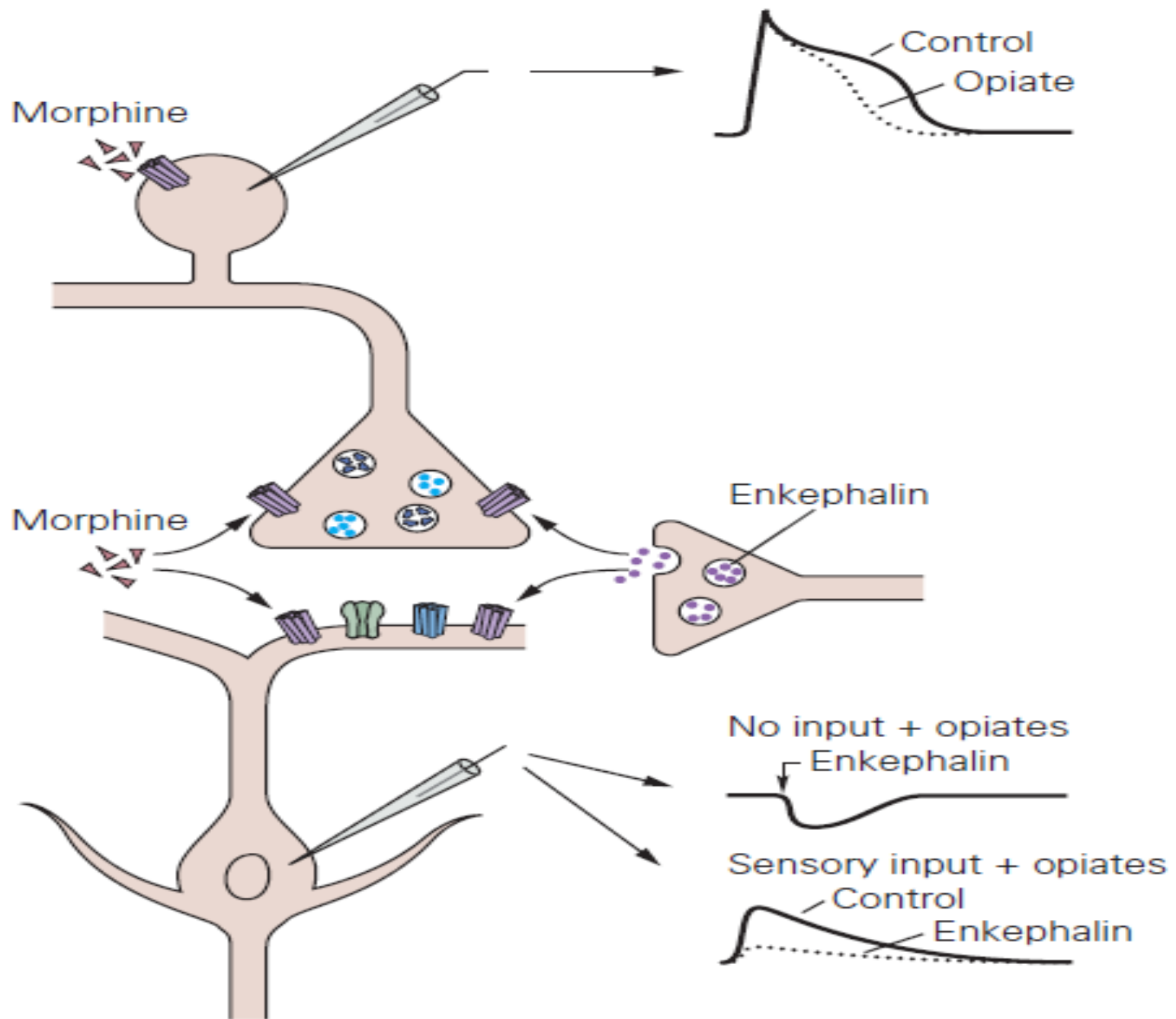
Activation of the postsynaptic OR hyperpolarizes the dorsal horn interneuron by causing an increase in K^{+} conductance.

- \downarrow duration of the EPSP in the dorsal horn neuron.
- Activation of OR on dorsal root ganglia cell bodies also contributes to reduced transmission from nociceptive afferents.

B_1 Sensory input

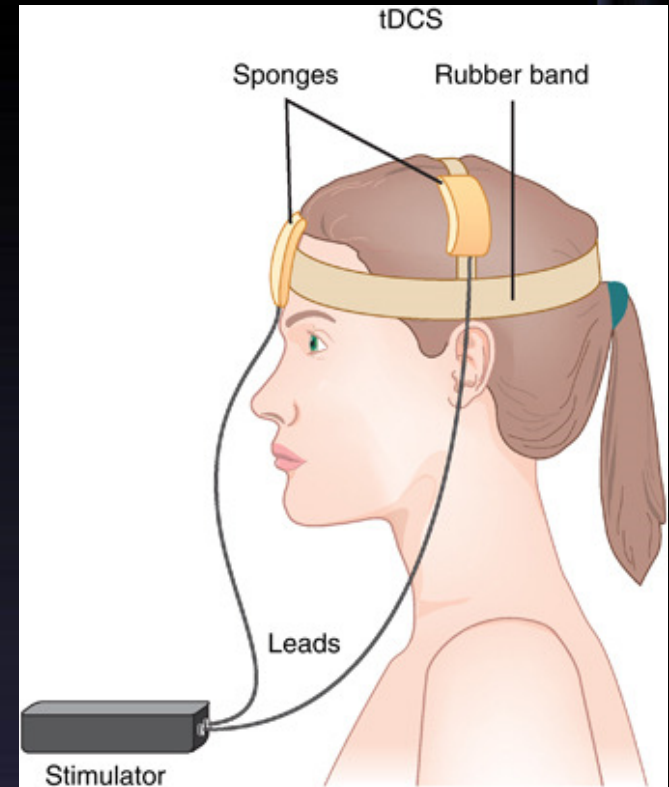


B₂ Sensory input + opiates/opioids



TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS)

- It is a non-invasive procedure in which a device sends a small Direct Current (DC) across electrodes in the areas of interest on the scalp to modulate brain function.
- This current flow can increase or decrease the neuronal excitability in the specific area being stimulated, based on which type of stimulation.
- When the current passes from the anode to the cathode, it may increase the activity of the brain at the anode site and decrease the activity of the brain near the cathode site.



TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS)

- The gate-control mechanism of pain modulation and serves as the rationale behind the use of transcutaneous electrical nerve stimulation (TENS) for pain relief.
- TENS uses electrodes to activate $A\alpha$ and $A\beta$ fibers in the vicinity of the injury. **TENS** stimulates sensory nerves to block pain signals, stimulate endorphin production to help normalize sympathetic function.



INTERFERENTIAL STIMULATION

Interferential Stimulation differs from TENS because it allows a **deeper penetration** by using two frequencies of the tissue with more comfort (compliance) and increased circulation.

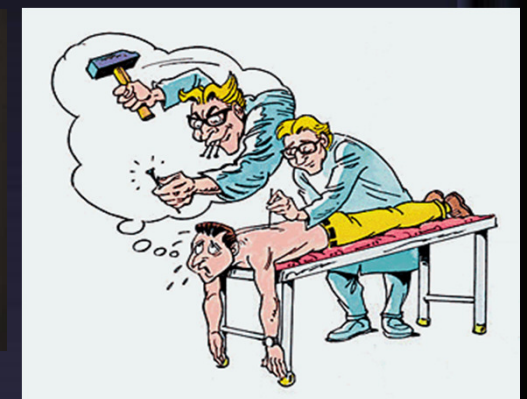
Stimulate parasympathetic nerve fibers for increased blood flow.



Inhibition of Pain Transmission by Tactile Sensory Signals

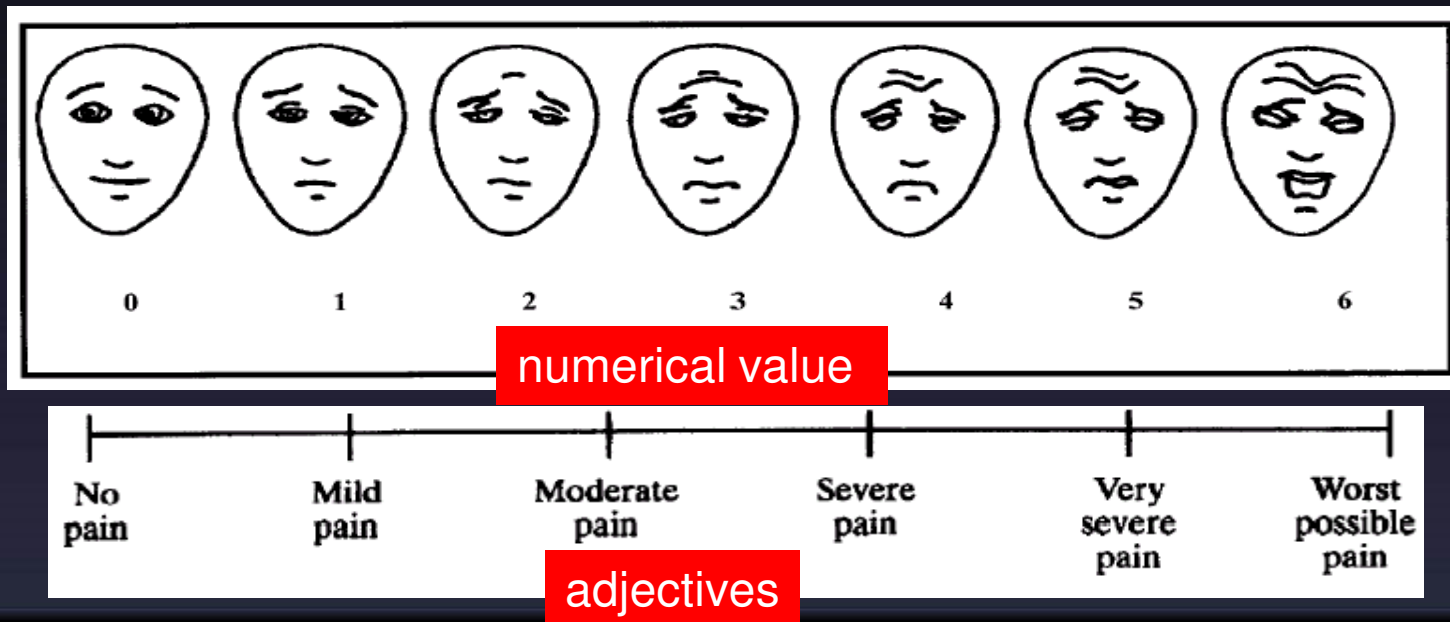
- Stimulation of large type A β sensory fibers from peripheral tactile receptors depress transmission of pain signals from the same body area by lateral inhibition in the spinal cord
- The simultaneous physical and psychogenic excitation of the central analgesia system is the basis of pain relief by **ACUPUNCTURE**.

The analgesic effect of electroacupuncture may involve the release of endogenous opioids and activation of descending pain modulatory pathway.



PAIN SCALES

- Visual Analog Scale
- Locate area of pain on a picture
- **McGill pain questionnaire**
 - Evaluate sensory, evaluative, & affective components of pain
 - 20 subcategories, 78 words



Mc Gill-Melzack PAIN QUESTIONNAIRE

Patient's name _____ Age _____
 File No. _____ Date _____

Clinical category (e.g. cardiac, neurological, etc.): _____

Diagnosis: _____

Analgesic (if already administered):

1. Type _____
2. Dosage _____
3. Time given in relation to this test _____

Patient's intelligence: circle number that represents best estimate
 1 (low) 2 3 4 5 (high)

This questionnaire has been designed to tell us more about your pain. Four major questions we ask are:

1. Where is your pain?
2. What does it feel like?
3. How does it change with time?
4. How strong is it?

It is important that you tell us how your pain feels now. Please follow the instructions at the beginning of each part.

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Part 2. What Does Your Pain Feel Like?

Some of the words below describe your present pain. Circle ONLY those words that best describe it. Leave out any category that is not suitable. Use only a single word in each appropriate category--the one that applies best.

- | | | | |
|--|---|--|--|
| 1
Flickering
Quivering
Pulsing
Throbbing
Beating
Pounding

5
Pinching
Pressing
Gnawing
Cramping
Crushing

9
Dull
Sore
Hurting
Aching
Heavy

13
Fearful
Frightful
Terrifying | 2
Jumping
Flashing
Shooting

6
Tugging
Pulling
Wrenching

10
Tender
Taut
Rasping
Splitting

14
Punishing
Cruel
Viscious
Killing

18
Tight
Numb
Drawing
Squeezing
Tearing | 3
Pricking
Boring
Drilling
Stabbing
Lancinating

7
Hot
Burning
Scalding
Searing

11
Tiring
Exhausting

15
Wretched
Blinding

19
Cool
Cold
Freezing | 4
Sharp
Cutting
Lacerating

8
Tingling
Itch
Smarting
Stinging

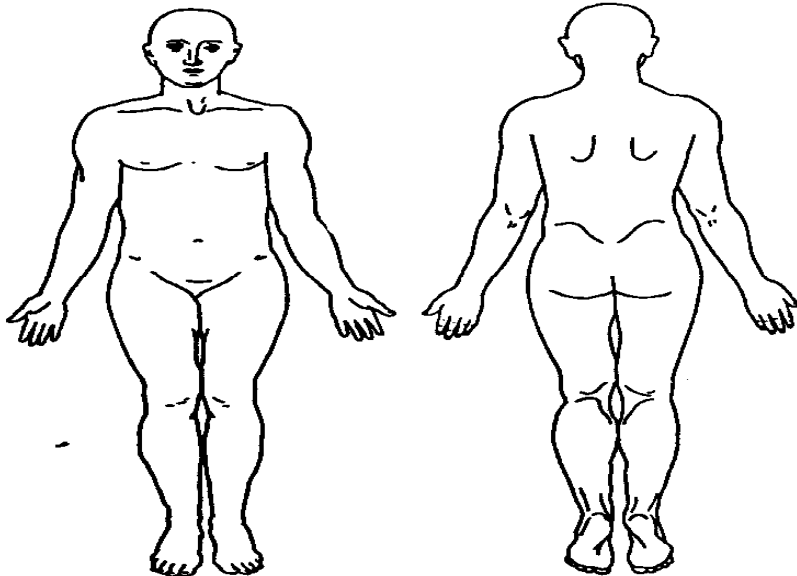
12
Sickening
Suffocating

16
Annoying
Troublesome
Miserable
Intense
Unbearable

20
Nagging
Nauseating
Agonizing
Dreadful
Torturing |
|--|---|--|--|

Part 1. Where is your Pain?

Please mark, on the drawings below, the areas where you feel pain. Put E if external, or I if internal, near the areas which you mark. Put EI if both external and internal.



Part 3. How Does Your Pain Change With Time?

1. Which word or words would you use to describe the pattern of your pain?

- | | | |
|---------------------------------------|---|--------------------------------------|
| 1
Continuous
Steady
Constant | 2
Rhythmic
Periodic
Intermittent | 3
Brief
Momentary
Transient |
|---------------------------------------|---|--------------------------------------|

2. What kind of things relieve your pain?

3. What kind of things increase your pain?

Part 4. How Strong Is Your Pain?

People agree that the following 5 word represent pain in increasing intensity. They are:

- | | | | | |
|-----------|--------------------|------------------|---------------|-------------------|
| 1
Mild | 2
Discomforting | 3
Distressing | 4
Horrible | 5
Excruciating |
|-----------|--------------------|------------------|---------------|-------------------|

To answer each question below, write the number of the most appropriate word in the space beside the question.

1. Which word describes your pain right now? _____
2. Which word describes it at its worst? _____
3. Which word describes it when it is least? _____
4. Which word describes the worst toothache you ever had? _____
5. Which word describes the worst headache you ever had? _____
6. Which word describes the worst stomach-ache you ever had? _____

Applied

1. What will happen if sensory area S1 is removed?

Ans. persons ability to interpret the quality of pain & precise location of pain will be affected.

2. Why patient with chronic pain syndrome have difficulty in sleeping?

Ans. Paleospinothalamic pathway sends information to reticular formation and thalamic nuclei which are part of brain activating / alerting system, therefore chronic pain syndrome causes difficulty in sleep.

Placebo Effect

- **Placebo** stems from the Latin word for “I shall please”
 - Used to describe pain reduction obtained from a mechanism other than those related to the physiological effects of the tx.
 - Linked to psychological mechanisms
- All Treatments TM have some degree of placebo effect
 - Most studies involving TM involving the use of a sham TM (ultrasound set at the intensity of 0) and an actual treatment have shown ↓ levels of pain in each group.

Congenital Analgesia

Congenital insensitivity to pain (CIP), also known as congenital analgesia, is one or more rare conditions in which a person cannot feel (and has never felt) physical pain due to gene mutation

- A well-known case of congenital insensitivity to pain is a girl referred to as **'Miss C'** who was a student at McGill university in Montreal in the 1950s.
- She was normal in every way, except that she could not feel pain. When she was a child she had bitten off the tip of her tongue and had suffered third-degree burns by kneeling on a radiator.
- She did not feel any pain when she was given strong electric shocks or when exposed to very hot and very cold water. When these stimuli were presented to her she showed no change in heart rate, blood pressure or respiration.
- She died at the age of 29 as a result of her condition, because she damaged her knees, hips and spine.

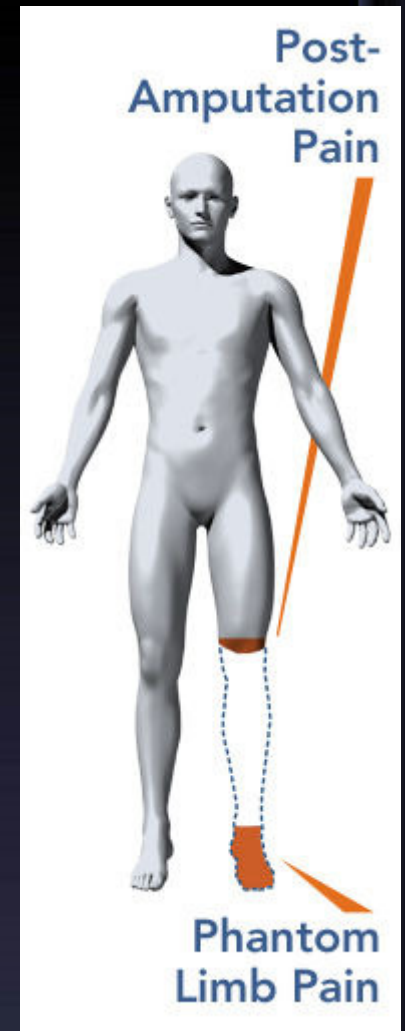
Fibromyalgia: Pain Without Injury

- **The occurrence of body-wide pain in the absence of tissue damage, as in fibromyalgia, interferes with all aspects of a person's life and undermines their credibility.**
- **The problem is that normal activities can be exhausting, sleep is disturbed, the ability to concentrate is impaired, gastrointestinal function is often abnormal, persistent headaches are common, and the unrelenting pain that no one can see is often detrimental to their personal and professional lives--as it creates a "credibility gap."**

Phantom limb pain

- Phantom limbs give impression of pressure and pain
- Even if phantom limb is experienced as spatially detached from the body, it is still felt to belong to the patient.
- Paraplegic people experience phantom limbs. They can even experience continually cycling legs.
- It is the emotional and motivational systems that cause the phantom limb experience.

Our brain can reorganize if sensory input is cut off at the ventral posterior thalamic nucleus even after that part is amputated



TERMS FREQUENTLY USED

- **Hyperalgesia:** Increased sensitivity to Pain
- **Allodynia:** A person feels pain from stimuli that don't normally cause pain due to central sensitization. For example, lightly touching your skin or brushing your hair might feel painful.
 - clinical feature of many painful conditions, such as neuropathies, complex regional pain syndrome, postherpetic neuralgia, fibromyalgia, and migraine
 - Muscular Pain: Less blood flow in the muscles (ischemia).
- **Stress analgesia:** Mild degree of pain is not felt if the other part of the body has excessive pain.
- **Causalgia:** It is chronic burning pain condition seen after the section (damage, cutting) of a nerve Triggered by a simple stimulus e.g. breeze or vibration.
- **Neuralgia** - sharp pain along a nerve pathway (eg; Trigeminal N)
- **Thalamic Syndrome:** Obstruction of the thalamogeniculate branch of the posterior cerebral artery Affects posterior thalamic nuclei. Patient suffers from prolonged severe pain with variable quality (Dejerine Roussy Syndrome)

This acquired tolerance is different from addiction

Opiate Tolerance

receptor desensitization
compensatory adaptations in neuronal circuit
learning mechanisms

Physical Dependence

compensatory adaptations in neuronal circuit

Drug Withdrawal

removal of opiate unmasks compensatory adaptations

Drug Addiction Psychological addiction is extremely rare during treatment of pain

- This acquired tolerance is different from addiction, which refers to a psychological craving.
- Psychological addiction rarely occurs when morphine is used to treat chronic pain, provided the patient does not have a history of drug abuse.