Pain

- It is unpleasant sensation and emotional experience
- It is a subjective feeling (it differ from one individual to another)
- It is a primitive response to injury (all living creatures have the feeling of pain)

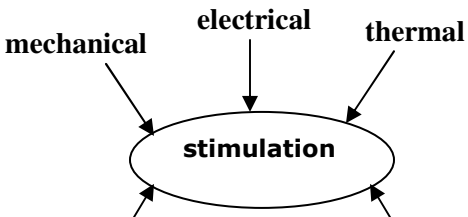
⌖ Outline of study:

- ♣ Receptors
- ♣ Peripheral nerve pathway
- ♣ Inside the spinal Cord
- ♣ central pathway
- ♣ cortex

♣ Receptors:

- nociceptores (obnoxious , unpleasant stimuli) is the pain receptor, which are free nerve endings , remember that they are slow adapting

mechanism of stimulation:



Sensitizers

- Tissue damage will induce the release of substance such as :
  a. *Prostaglandin*
  b. *Leukotriene*
     ✓ *From arachidonic acid*

♣ *These substances are known as sensitizers*
♣ *Sensitization occurs between stimulation & generation of AP .*
♣ *Pain is reduced by blocking of prostaglandin (aspirin) .*

Activators

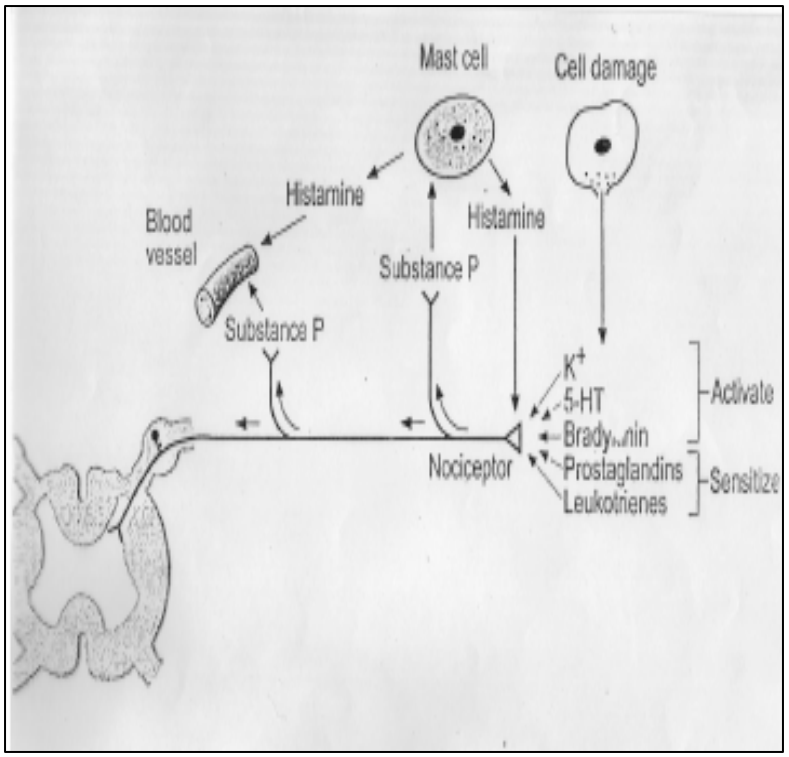
- Through: K+
  a. *Serotonin-5-HT*
  b. *Bradykinin*

♣ *These substances known as activators*

☑ Sensitizers & activators are produced from damaged tissue as a result of inflammation and act on 1st order neuron , after that the 1st order neuron will release substance P → this substance will act on mast cell to release histamine → which will act on receptor and will cause dilation of blood vessels.

☑ Sensitizers well lead to decrease threshold of pain & will facilitate stimulation.

☑ Sensitizers & activators are indirect stimuli because they come from tissue near the pain receptors.



♣ Peripheral nerve pathway :

- these nerve fibers are :
  - **Aδ** : Thin medulated "myline " fibers (carrying *fast* pain)
  - **C** : Thin Unmylinated fibers (carry *slow* stimulus)

    ⇒ The neurotransmitter in *Aδ* is *(glutamate)* but in *C* it is *(P-substance)*
  - N.B : **Aβ** carries Touch stimulus , but if it is stimulated with *strong* frequency , this fiber will carries pain stimulus , and this is known as (Polymodal Fiber)

    ⇒ the neurotransmitter in *polymodal* fibers is *(P-substance)*

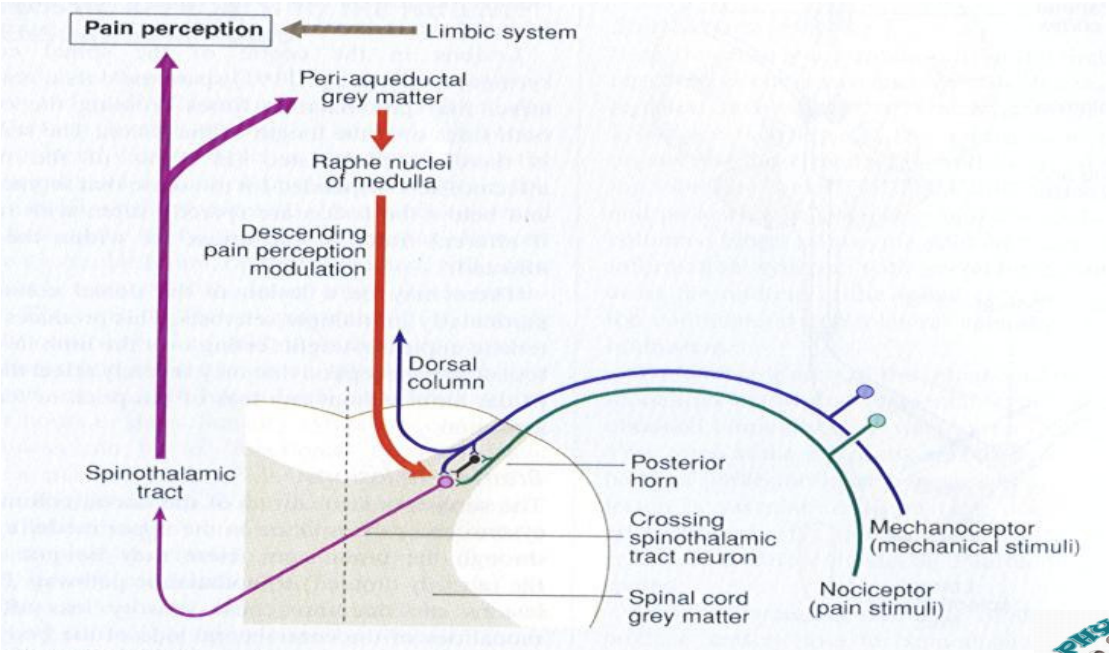
    ► After that the nerve will go to the spinal cord

♣ Inside the spinal cord up to the cortex :

- The nerve fibers enter the spinal cord through the dorsal horn
- The dorsal horn is divided into several layers called Redox layers
- They are 5 layers:
  - ✓ *Aδ* is recived in the <u>first layer</u> , coming from skin
  - ✓ *C* is recived in the <u>2nd layer</u> which is known as (Substantic gelatinnosa of Rolando)
  - ✓ *Polymodal Aβ* is In the <u>5th layer</u>

N.B :

- ► for the second order neuron they are received by dorsal horn then they cross infront & behind the central canal to pass up in the anterolateral tract of the opposite side.
- ► then to the thalamus
- ► N.B : **thalamus is the higher center for pain** , cortex is important to localize the site of pain , but it is not essential for reception of pain



So , as we said pain is unpleasant sensation and *emotional*

✓ We discussed that the unpleasant sensation is carried by the Aδ and C fibers in the Lateral spinothalmic tract

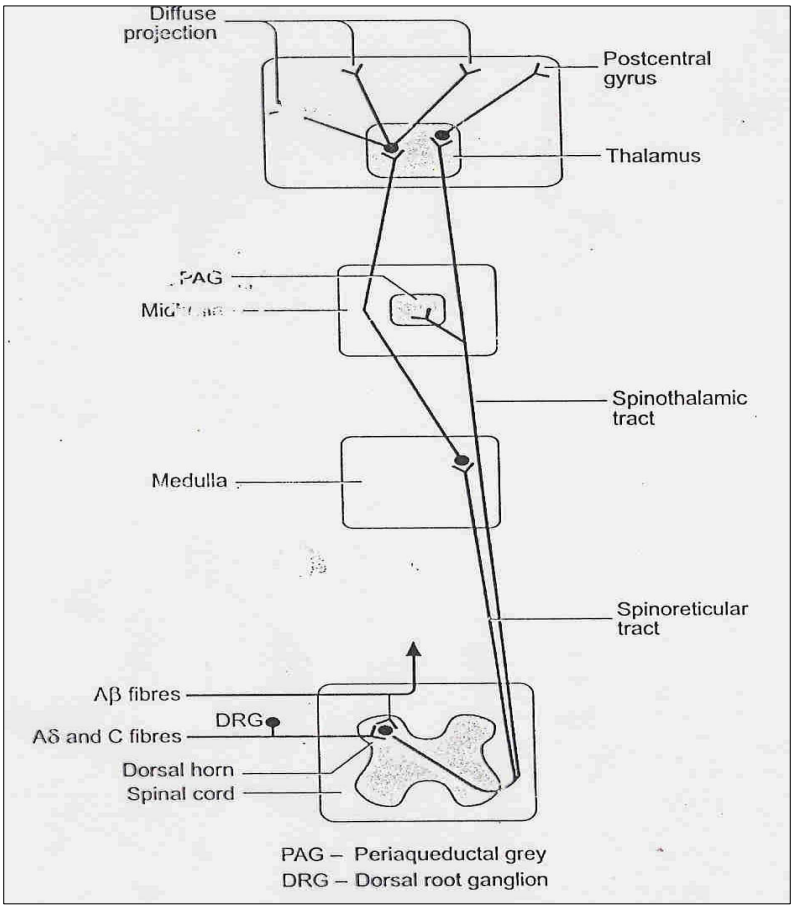
► So, **how is emoitinal sensation carried then** ?????

⌖ *emotional part of the pain:*

- carried by spinoreticular tract (medially).
  - Spinoreticular tract ends at all level of reticular formation in Medulla and pons which also keeps you awake.Then they go to Thalamus Then to cortex.

✓ **Highest center for emotion is gyrus cinguily in Cortex.**

✓ The Leteral spinothalamic and the Spinoreticular tract are the asending tracts



Pain Pathway:

1-causing :by lateral spinothalamic and spinoreticular which ascending.(discussed)

2-Decreasing:analgesic pathway which descending.

Descending analgesic Pathway:

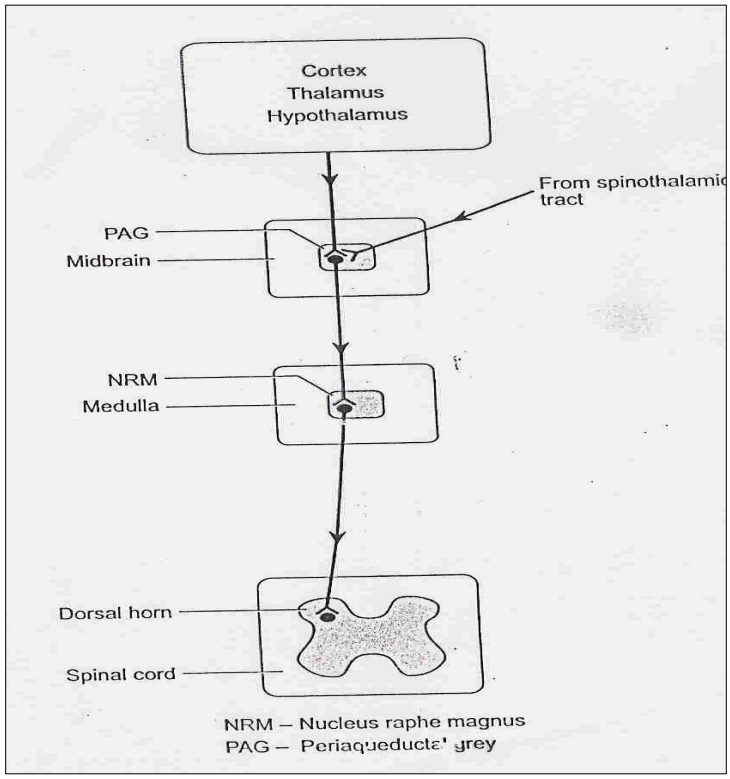
- In the midbrain there is peri-aquedutal gray matter (PAG) which is present around aqudauct of Sylvins

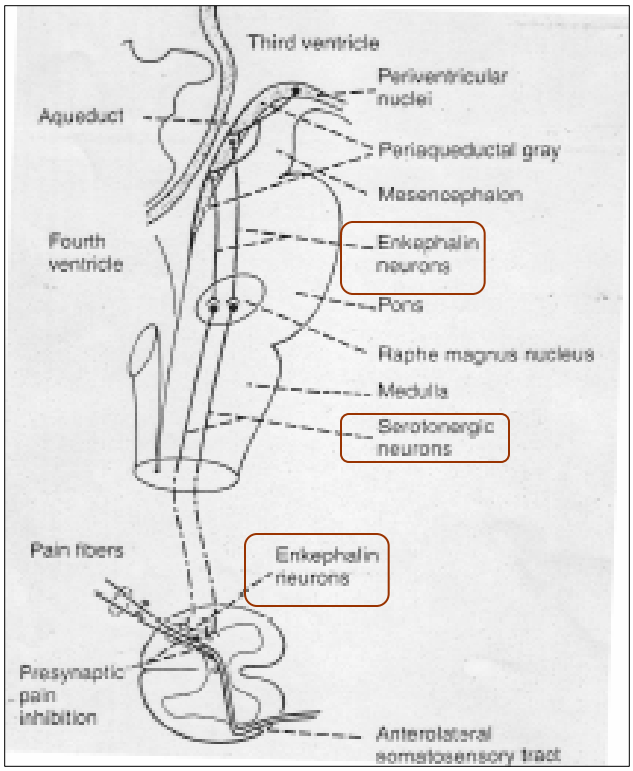
  - ✓ This area recive neural input from Cortex ,Hypothalamus and thalamus ….

  - ✓ PAG projects neurons that stimulate raphe magnus in the medulla , Then from the medulla to the doral horn

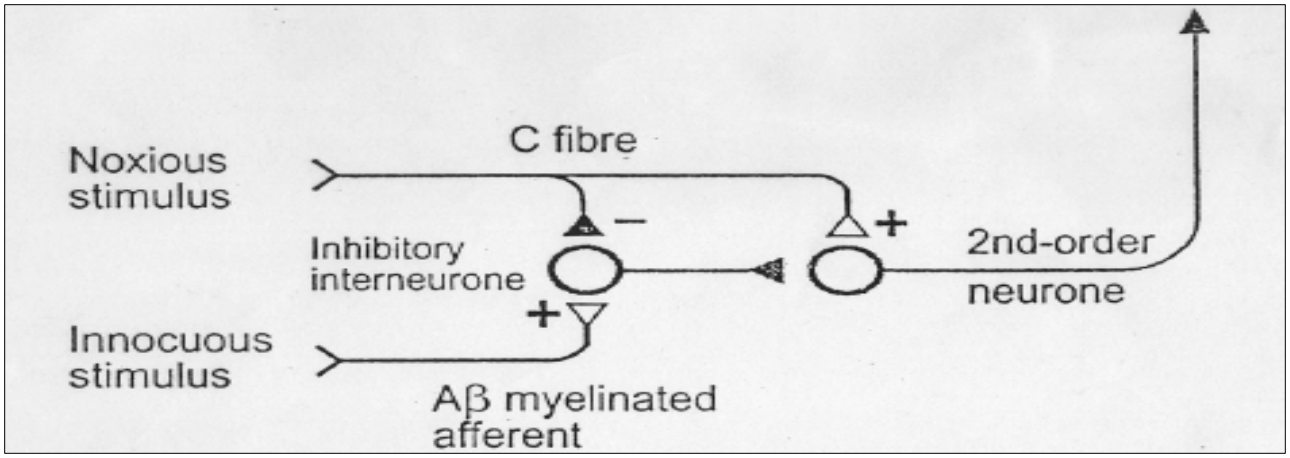
  - ✓ Then the three interneural connect which works as ANALGESIC TRACT

- The upper part of this pathway is serotogenic.
- The areas of the upper part have morphine receptor .
- The lower part of this pathway has Encephalin





► Gate Mechanism of Pain:



- This theory assumes that the Dorsal horn of the spinal cord form the gate through which pain impulses must pass to reach the brain.

  - ✓ Impulses coming along type C pain fibers cause the release of substance P from theses fibers and open the gate

  - ✓ While impulses coming along Aβ fibers close the gate by process of pre-synaptic inhibition of C fibers and post synaptic inhibition of 2ry neurons in dorsal horn

✓ This is seen when you have a pain let`s say in your hand and normally we will rule our skin to relieve the pain .

Classification of pain

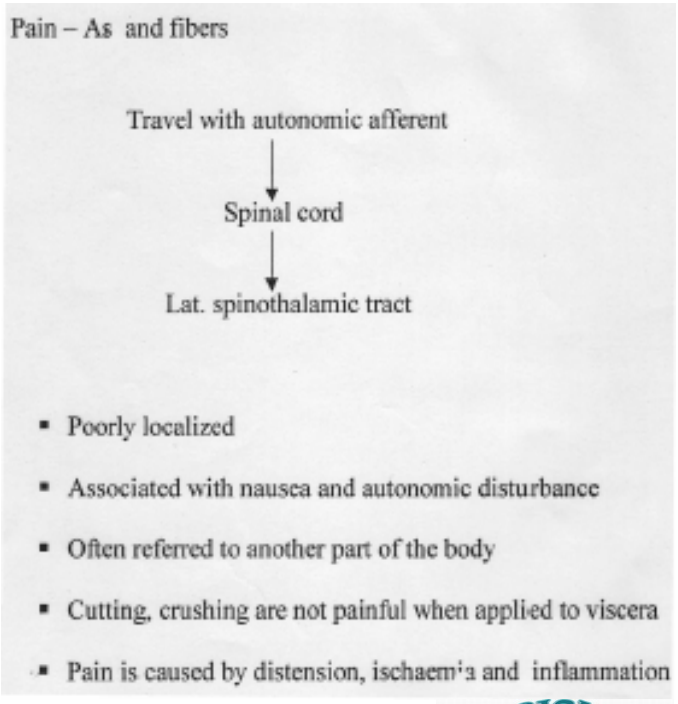
Sensation	PAIN		
Quality	Somatic		Visceral
Character	Superficial	Deep	
Time-course	Initial or delayed	Initial or delayed	
Origin	Skin	Bone, joints, muscles	
Conditions	Pinching Pricking Cutting Burning	Cramps Arthritis Rheumatism	Ulcers Appendicitis Angina Migraine Renal colic

- By two ways First :

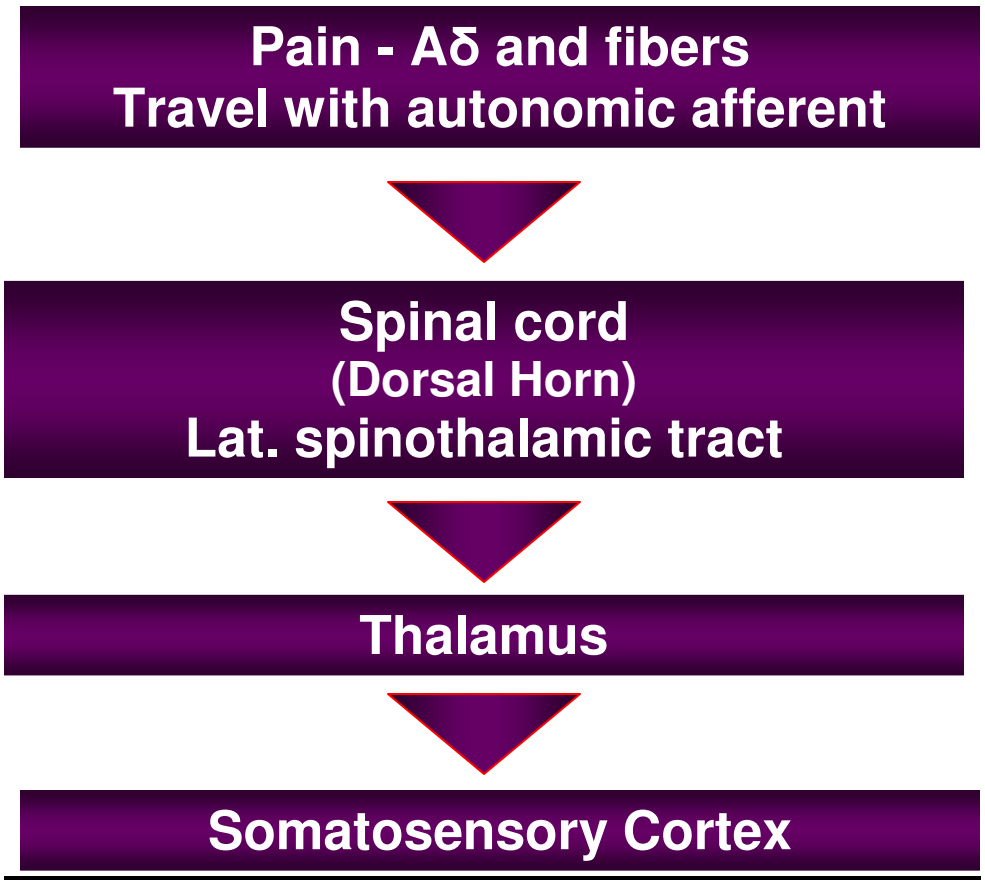
Visceral pain :

- Visceral afferent fibers travel with the autonomic nervous system fibers by joining the dorsal horn at the spinal cord.

- There is no pain sensations in the viscera, but the pain occur due to visceral wall distention



VISCERAL PAIN PATHWAY



2nd way of classification of pain

Fast pain	Slow pain
Aδ fibers	C fibers
20% of pain receptors	80% of pain receptors
Well localized	Poor localization
Glutamate is the NT	Substance P is the NT
Its usually superficial	Occurs in skin, deep tissue and viscera
	Intensity increase with time

Referred pain

- Pain referred to a place other than the initial place of pian.
- Physiologists proposed two theories regarding the cause of it:
    - The dermatomal theory: dermatomes receive pain stimuli from a specific location and the pain is sensed in another location supplied by the same dermatome due to the brain thinking that the latter one is the original pain location.

The convergence theory: afferent fibers from different locations converge in the same place in the spinal cord. Note that this is a weak theory.

Referral of pain from the internal organs

Organ	Site of reffered pain
• Meninges	Back of head and neck
• Heart	Central chest arms (usually left), neck, occasionally abdomen.
• Trachea	Behind sternum
• Diaphragm	Shoulder tip
• Oesophagus	Behind sternum
• Stomach, duodenum	Upper abdomen, epigastrium
• Small bowel, pancreas	Around umbilicus
• Large bowel, bladder	Lower abdomen above pubic bone

Some medical terms and concepts

- *Analgeric*: loss of pain sensation
- *Analgesic*: pain killing drug
- *Anesthesia*: drug used to lose pain sensation temporarily / condition in which all pain sensations is lost.
- *Hyperalgesia*: extreme sensitivity of pain. It has two main types:
  - ✓ Primary: initial injury pain.
  - ✓ Secondary: pain from inflammation following the initial injury.
- *Allodynia*: pain sensation due to reasons other than pain receptors stimulation.(for example, a person with allodynia may perceive light pressure or the movement of clothes over the skin as painful, whereas a healthy individual will not feel pain)
- *Causalgia*: burning pain due to nerve damage (neuropathic pain)
- *Headaches*: annoying pain caused by meningeal distention and dilatation of blood vessels in the brein.
- *Thalamic Syndrome :* Obstruction of the thalmogeniculate branch of the posterior cerebral artery Affects posterior thalamic nuclei.
  - ✓ Prolonged severe pain.

REVISION

Summary

Nociceptors

- Nociceptors are free endings of C fibres (80%) and Aδ nerve fibres (20%).
- Nociceptors are high-threshold receptors.
- Aδ fibres produce sharp well-localized pain, C fibres produce dull aching poorly localized pain.
- Inflammatory mediators, including prostaglandins and leukotrienes, increase the sensitivity to pain.
- Nociceptor axon reflexes release substance P which degranulates mast cells.

I	Block production of inflammatory mediators e.g. aspirin; nonsteroidal anti-inflammatories
II	Sectioning of peripheral nerves rarely relieves pain as most chronic pain syndromes are in part due to re-organisation of central nociceptive pathways and sensory processing
III	Sympathectomy can be useful, especially in cases of reflex sympathetic dystrophy.
IV	Manipulation of endogenous opioid network using exogenously administered opioid-like drugs.
V	Electrical stimulation of the dorsal columns can alleviate pain originating below site of stimulation.
VI	Selective activation of large diameter afferent fibres by transcutaneous electrical nerve stimulation.
VII	Stimulation of brainstem sites, or administration of drugs which can modify serotoninergic or noradrenergic synapses (e.g. antidepressants)