



# Pain Modulation



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- Important
- Further Explanation

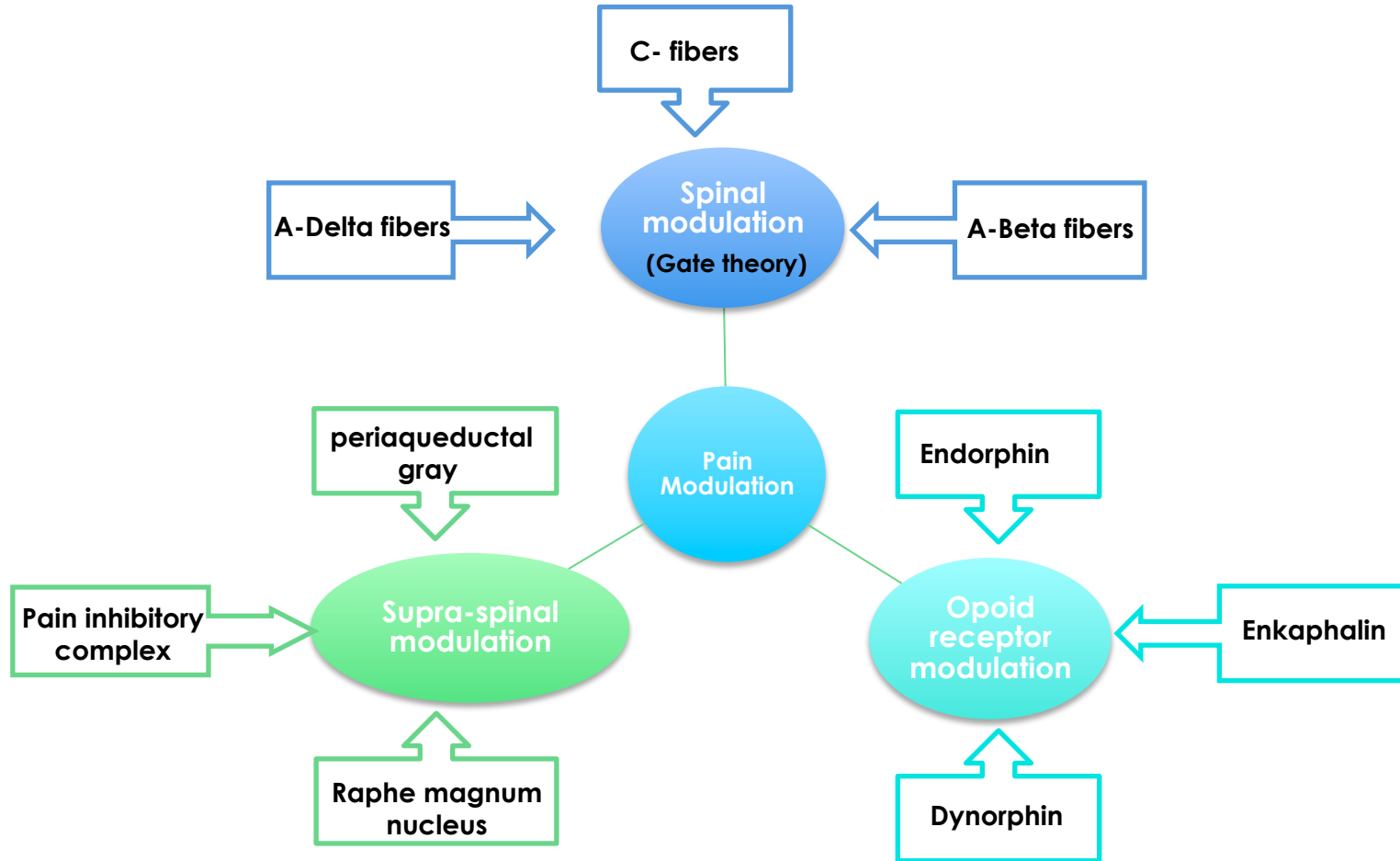
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# Pain Modulation

✧ its pain perception variability  
(the degree to which a person reacts to pain)

✧ Pain modulation is influenced by:

- Endogenous mechanism
- Exogenous mechanism

A decrease or an increase in the sensation of pain caused by inhibition or facilitation of pain signal.

## **FACILITATION:**

- 1-Peripheral sensitization  
(release of chemicals after tissue injury)
- 2-Central sensitization (Dis-inhibition)

## **INHIBITION:**

nociceptive input can be inhibited by:

1- Spinal (segmental) inhibition: Gate control theory

2-Supraspinal modulation (Special pain control analgesic system) :

- **Role of periaqueductal grey (PAG) matter.**
- **Role of Nucleus Raphe Magnus (NRM)**

3-pain Modulation By Opioid Neurotransmitters As:  
Endorphin, Enkephalin, Dynorphin.

# Gate theory of pain control

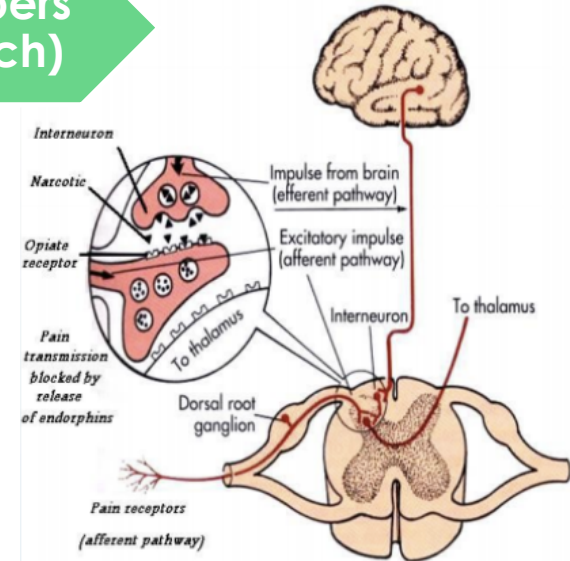
Special neurons in the dorsal horn of spinal cord (SGR)<sup>1</sup> form the gate through which pain impulses must pass to reach brain, this gate has the ability to block the signals from the **A-delta** and **C fibers** preventing them from reaching the brain.

## Controlled by:



## Gate opened or closed by 3 factors:

1. Activity in the pain fibers → opens the gate.
2. Activity in other sensory nerves → closes the gate.
3. Messages from the brain.

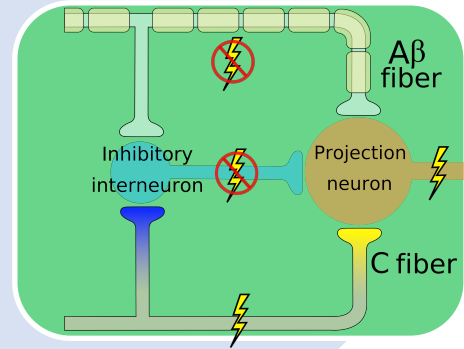


1: Substantia Gelatinosa of Rolando

# Gate theory of pain control

Impulses coming along type C pain fibers cause the release of substance P from these fibers and tend to **open** the gate.

While impulses coming along  $A\beta$  fibers tend to keep the gate closed by process of presynaptic inhibition of C fibers and postsynaptic inhibition of secondary neurons in dorsal horn.



- The gate will **open** if  $\longrightarrow$  the impulses in C & A-delta fibers stronger than the A-beta fibers .
- The gate will **close** if  $\longrightarrow$  the impulses in A-beta fibers stronger than C & A-delta fibers .
- A-delta fibres are always **stronger**.

# Gate theory of pain control

- ✧ Specialized nerve impulses arise in the brain itself and travel down the spinal cord to influence the gate. This is called the **central control trigger** and it can send both inhibitory and excitatory messages to the gate sensitizing it to either C or A- $\beta$  fibers.
- ✧ The inhibitory neurons make a pain blocking agent called enkephalin. **Enkephalin** is an opiate substance similar to heroin which can block Substance P, the neurotransmitter from the C fibres and this keeps the gate closed.

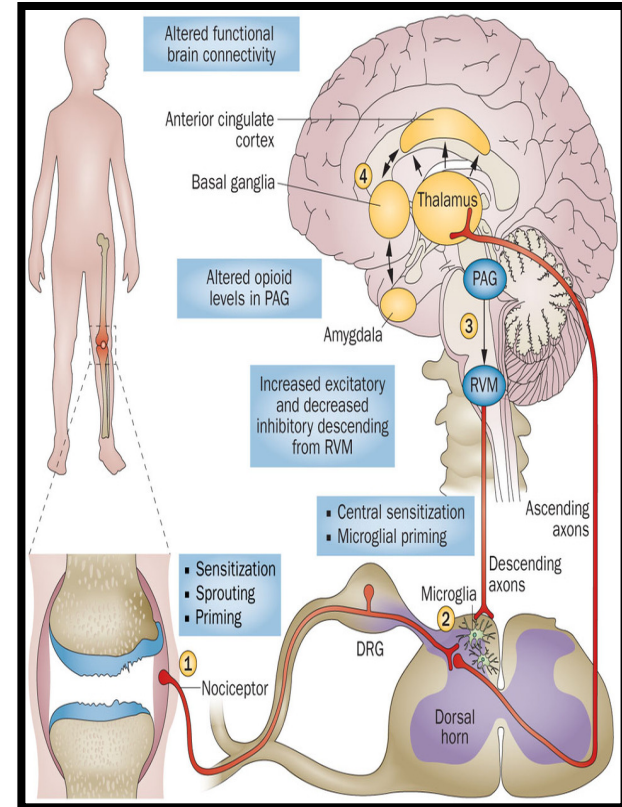
The gate theory explains the pain relief by skin rubbing, shaking the painful part, acupuncture & trans Cutaneous electrical Nerve stimulation (TENS)  
All are supposed to stimulate mechanoreceptors that activate neurons of dorsal column, the collaterals relieve pain.

# Supra spinal modulation (Special pain control analgesic system)

❖ This is a specific system that blocks pain transmission in CNS.

❖ It consist of :

- The periaqueductal gray and periventricular areas.
- Raph magnum nucleus.
- Pain inhibitory complex .



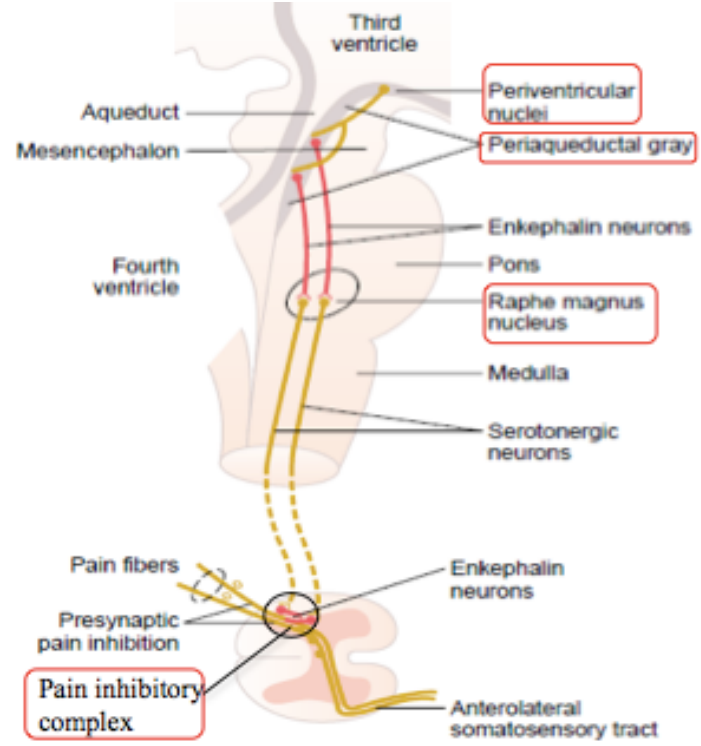


**-The periaqueductal gray and periventricular areas** of the mesencephalon and upper pons .  
 surround the aqueduct of Sylvius (periaqueductal) and portions of the third and fourth ventricles(periventricular) .

\*aqueduct of Sylvius is a narrow channel in the mesencephalon that connects the third and fourth ventricles.

- **Raph magnum nucleus**, a thin midline nucleus located in the lower pons and upper medulla, and the **nucleus reticularis paragigantocellularis**, located laterally in the medulla.

**-Pain inhibitory complex**  
 in dorsal horn of SC.



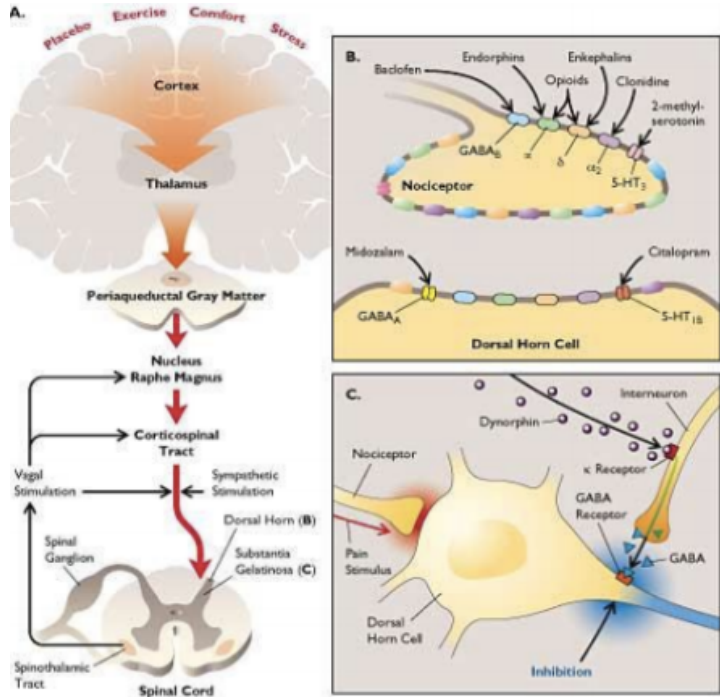
- ✧ It consists of multiple short encephalinergetic neurons that terminate on central endings of pain conducting afferent fibers.
- ✧ When stimulated, encephalin release.
- ✧ Enkephalin cause pre & postsynaptic inhibition of pain transmission.

# Analgesia occurs as follows:

The thalamus, hypothalamus and cerebral cortex send neuronal signals to the Periaqueductal grey area .

PAG projects neurons containing aspartate & glutamate that stimulate raph magnus nucleus (RMN)

RMN projects serotonergic neurons, this in addition to noradrenergic neurons project from adjacent medulla to dorsal horn They block pain signals by activating PIC

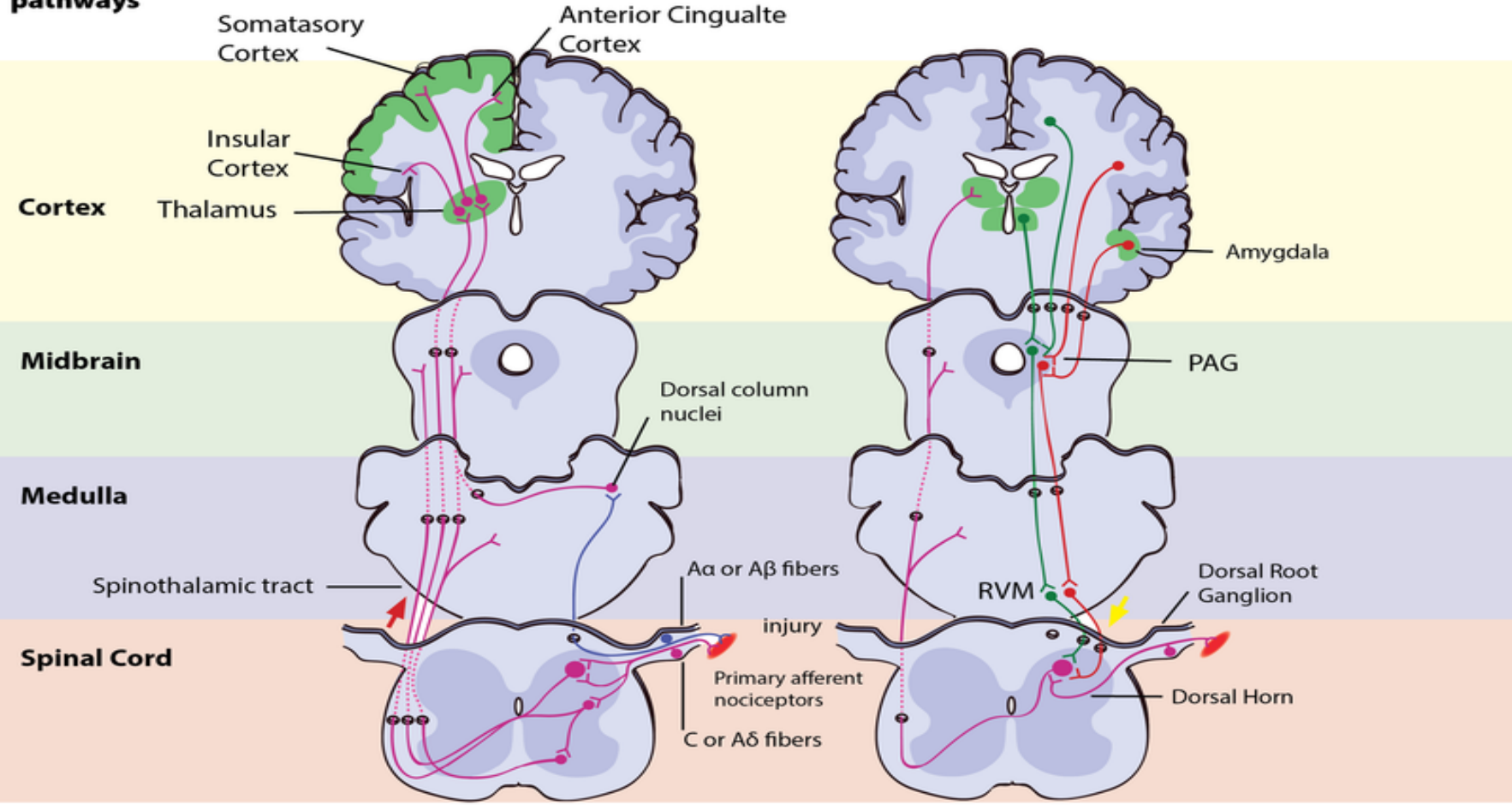


PIC: pain inhibitory complex

# Pain processing pathways

## a Ascending

## b Descending



# Opioid receptor modulation

- ❖ Opioid peptides are morphine-like substances present in body.
- ❖ They are natural analgesic substances that act by binding to opiate receptors in analgesic system and dorsal horn of SC on central ending of pain conducting pain fibers.

## Mechanism of opioid neurotransmitter action:

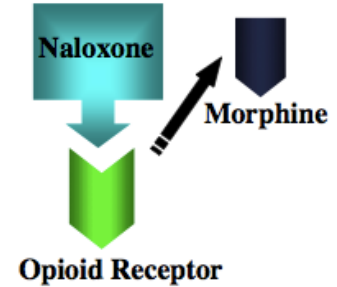
Endorphin	Neurons using endorphin or enkaphalin are found in PAG where they inhibit GABAergic interneurons that normally suppress the anti-nociceptor neurons
Enkephalin	It is used by interneurons in lamina II responsible for inhibiting the lamina – I nociceptor-specific spinothalamic neurons
Dynorphin	In hypothalamus, PAG, reticular formation, and dorsal horn.
Endogenous morphin	In terminals forming synapses with neuron having $\mu$ -opioid receptors in pain modulating pathways.

# Opioid Antagonist: Naloxone

Used to reverse opioid overdose .

Displaces receptor-bound opioids .

Good for overcoming respiratory and CV depression .



## Terms frequently used in abnormalities of pain sensation

**Hyperalgesia:** Excessive pain (e.g due to sun burn).

**Allodynia :**Pain caused by any other sensation e.g. touch will cause pain.

**Muscular Pain:** Less blood flow in the muscles (ischemia).

**Causalgia :**Burning pain.

**Phantom pain:**Pain felt in an amputated part long after amputation was done.

“because the area will still be presented in the brain”

## Stress induced analgesia

- ✧ Is the minimal level of pain perceived when a person is exposed to extreme physical trauma.
- ✧ In this situation, person forgets about its injuries and just run for saving his life .
- ✧ It's a well known phenomenon seen when the soldier is wounded in battle field but feels no pain until the battle is over. The cause is not known may be it is similar to Gate control hypothesis.

## Thalamic Syndrome

## Trigeminal neuralgia

Obstruction of the thalamogeniculate branch of the posterior cerebral artery “which supply posterior thalamic nuclei”

It is excruciating intermittent pain by stimulation of trigger area in the face e.g. Washing of face, combing hair, blast of air on face

Affects posterior thalamic nuclei

It results from compression of trigeminal nerve root by blood vessels

as a result: Prolonged severe pain.

### Chronic pain

Chronic pain can be considered as bad pain because it persist long after injury and is often refractory to pain killers.

Chronic pain caused by nerve injury is called neuropathic pain.

### neuropathic pain

- Caused by the damage to peripheral nerve.
- The distal cut end develops a scar tissue forming rounded ball (neuroma) which is sensitive to pressure.
- Repeated activation causes continuous pain.
- Examples: post herpetic neuralgia and diabetic neuropathy.

# Sites and mechanism of pain relief

- Block production of inflammatory mediators.e.g. Aspirin & nonsteroidal antiinflammatories.
  - Sympathectomy can be useful.
  - Exogenously administration of opioid like drugs.
- Electrical stimulation of the dorsal column can alleviate pain originating below site of stimulation.
- Selective activation of large diameter afferent fibers by transcutaneous electrical nerve stimulation.
- Stimulation of brainstem sites or administration of drugs which can modify serotonergic or adrenergic neurons e.g. antidepressants.

**1- impulses coming along type C pain fibers will:**

- A. Close the gate.
- B. Open the gate.
- C. A&B
- D. None

**2- Gait theory is:**

- A. Spinal modulation of pain input
- B. Opioid receptor modulation
- C. Supraspinal modulation
- D. None

**3- an opioid neurotransmitter that inhibit GABAergic interneurons that normally suppress the antinociceptor neurons:**

- A. dynorphin.
- B. endorphin.
- C. morphin.
- D. enkephalin.

**4-pain felt in an amputated part long after amputation was done:**

- A. Phantom pain.
- B. allodynia.
- C. causalgia.
- D. Muscular pain.

**5-neurons projecting from PAG contain:**

- A. aspartate.
- B. adrenaline.
- C. glutamate.
- D. Both A and C.

**6-thin midline nucleus located in the lower pons and upper medulla:**

- A. Red nucleus.
- B. Raph magnum nucleus.
- C. Nucleus reticularis paragigantocellularis.
- D. Both B and C.

- 1. B
- 2. A
- 3. B
- 4. A
- 5. D
- 6. B



### 1- Pain modulation is influenced by?

- . Endogenous and Exogenous mechanisms.

### 2- What are the processes that A $\beta$ fibers using to keep the gate closed?

- . 1- presynaptic inhibition of C fibers.
- 2- postsynaptic inhibition of secondary neurons in dorsal horn.

### 3- What is the central control trigger?

- . It is a specialized nerve impulses arise in the brain itself and travel down the spinal cord to influence the gate.

### 4-what are the major constituents of the supra spinal modulating system?

- .1) The periaqueductal gray and periventricular areas.
- 2) Raph magnum nucleus and the nucleus reticularis paragigantocellularis.
- 3) Pain inhibitory complex .

### 5-what is trigeminal neuralgia?

- . It is excruciating intermittent pain by stimulation of trigger area in the face.

THANK YOU FOR CHECKING OUR WORK!

# BEST OF LUCK

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