

The Art and Science of Pain Management

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The pain systems :

The neural circuits that are responsible for pain and the reactions to pain, can be termed the *pain system*.

1. peripheral neurons with a set of peripheral receptive elements, the nociceptors.
2. numerous central neuronal relay pathways
3. sets of integrative neurons that impose excitatory or inhibitory influences on nociceptive information at numerous levels of the neuraxis
4. perception

fastbl

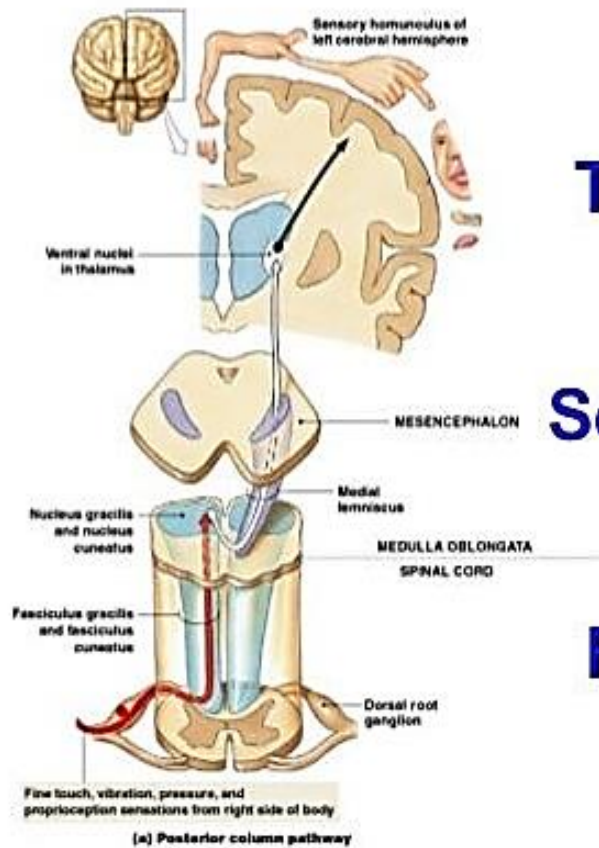
Nociceptors transmit information to **second-order** neurons located in the spinal cord or brainstem level innervated

- ✓ the lumbar spinal cord for leg input
- ✓ the thoracic spinal cord for stomach lining input
- ✓ the trigeminal spinal nucleus for face input
- ✓ cervical spinal cord to hands

✓ Nociceptive signals are then transmitted by **projection neurons** of the pain system to integration sites in the brainstem.

A **primary integration site** for sensory information is the **thalamus**, but numerous other brainstem and higher brain structures are participants in the integrative neuronal circuits responding to pain.

Organization of Sensory Pathways

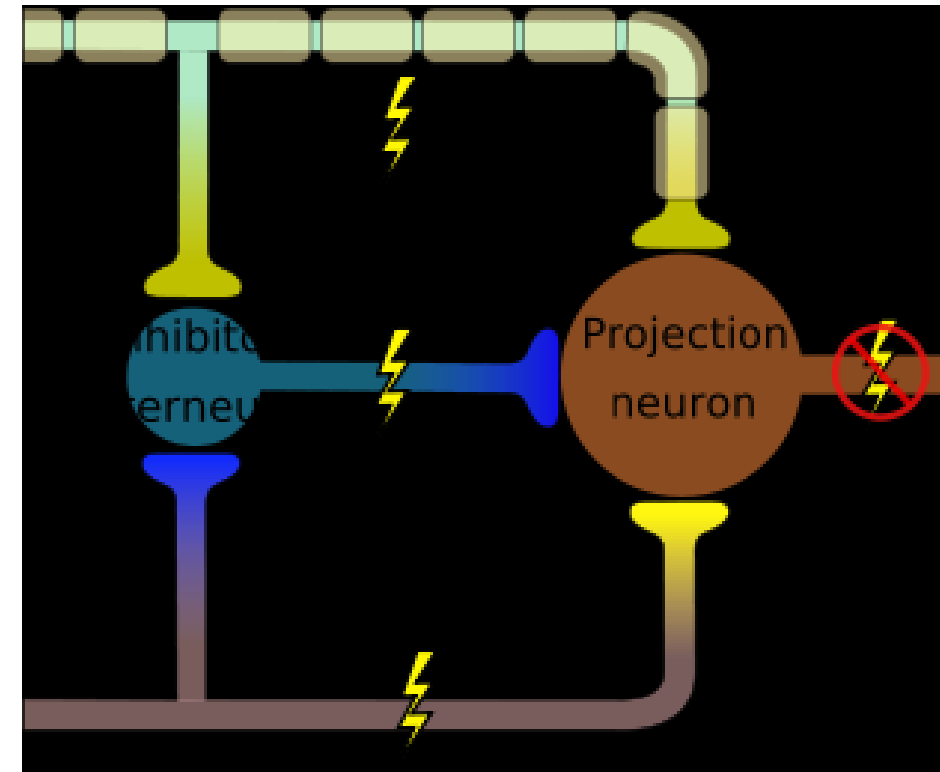


Third-Order Neuron



Second-Order Neuron

First-Order Neuron



Coordinated pain reactions

Including :

protective somatic and autonomic reflexes,

endocrine actions,

emotional responses, LIMBIC SYSTEM!

learning

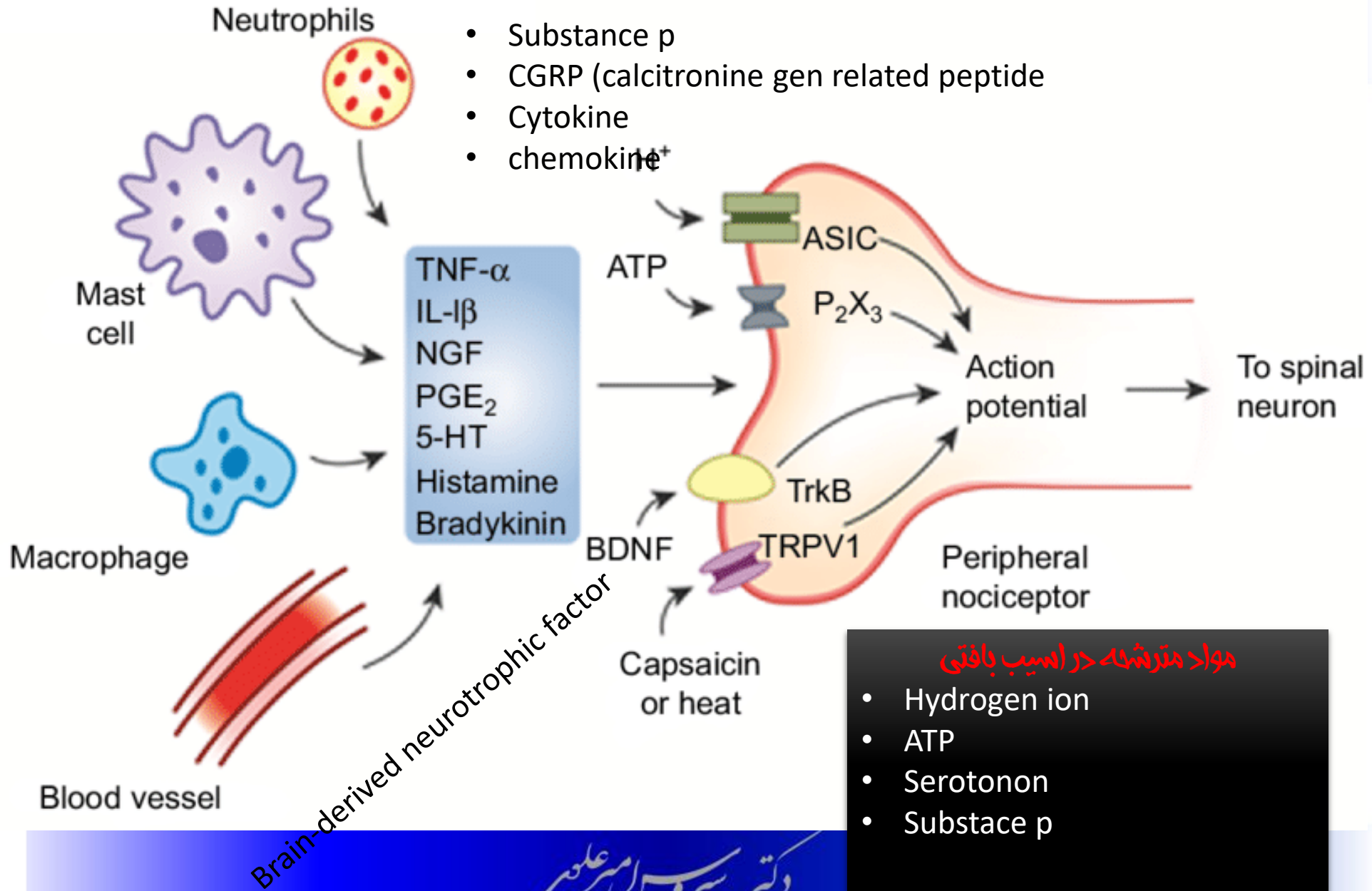
memory about the event,

cortical awareness of pain. RETICULAR SYSTEM!

the Brain negative or positive feedback :

- reduces or accentuates pain and pain reactions.
Negative feedback to the spinal cord circuitry is mediated by descending pathways that are often called the:
“**endogenous analgesia system.**”

The mechanism and pathways responsible for accentuation of pain and pain reactions,
referred to as **central sensitization** or facilitation.



PERIPHERAL SENSITIZATION

Tissue Damage

Inflammation

Sympathetic
Terminals

SENSITIZING 'SOUP'

Hydrogen Ions

Histamine

Purines

Leucotrienes

Noradrenaline

Potassium Ions

Cytokines

Nerve Growth Factor

Bradykinin

Prostaglandins

5-HT

Neuropeptides

Transduction
Sensitivity

High Threshold Nociceptor

A δ - C

Low Threshold 'Nociceptor'

Mechanisms of Pain: Neuroplasticity

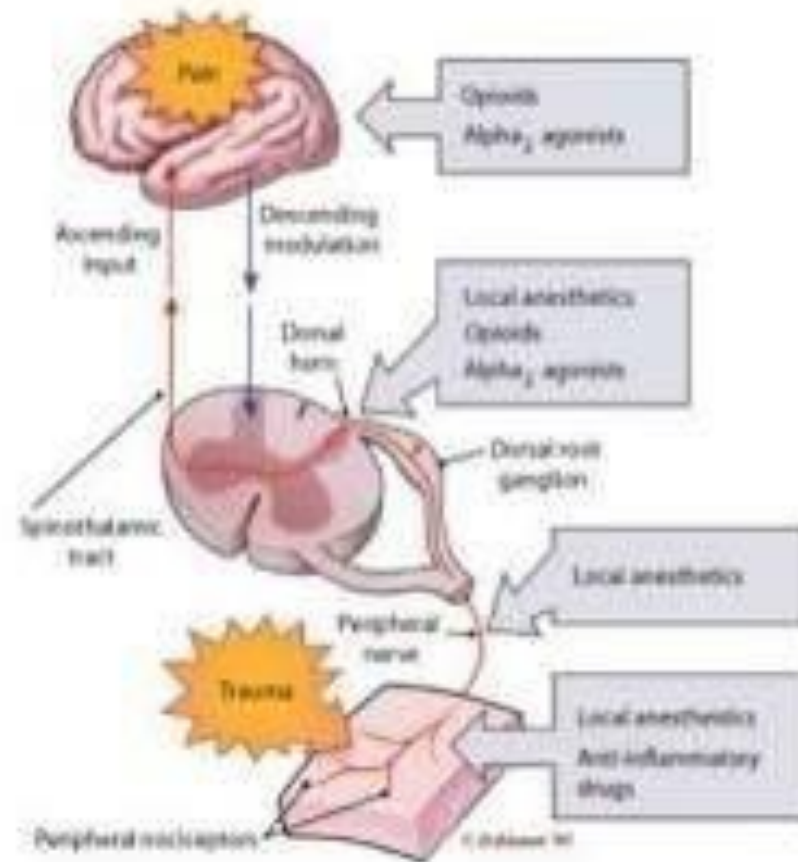
How does a Chronic Pain State Develop?

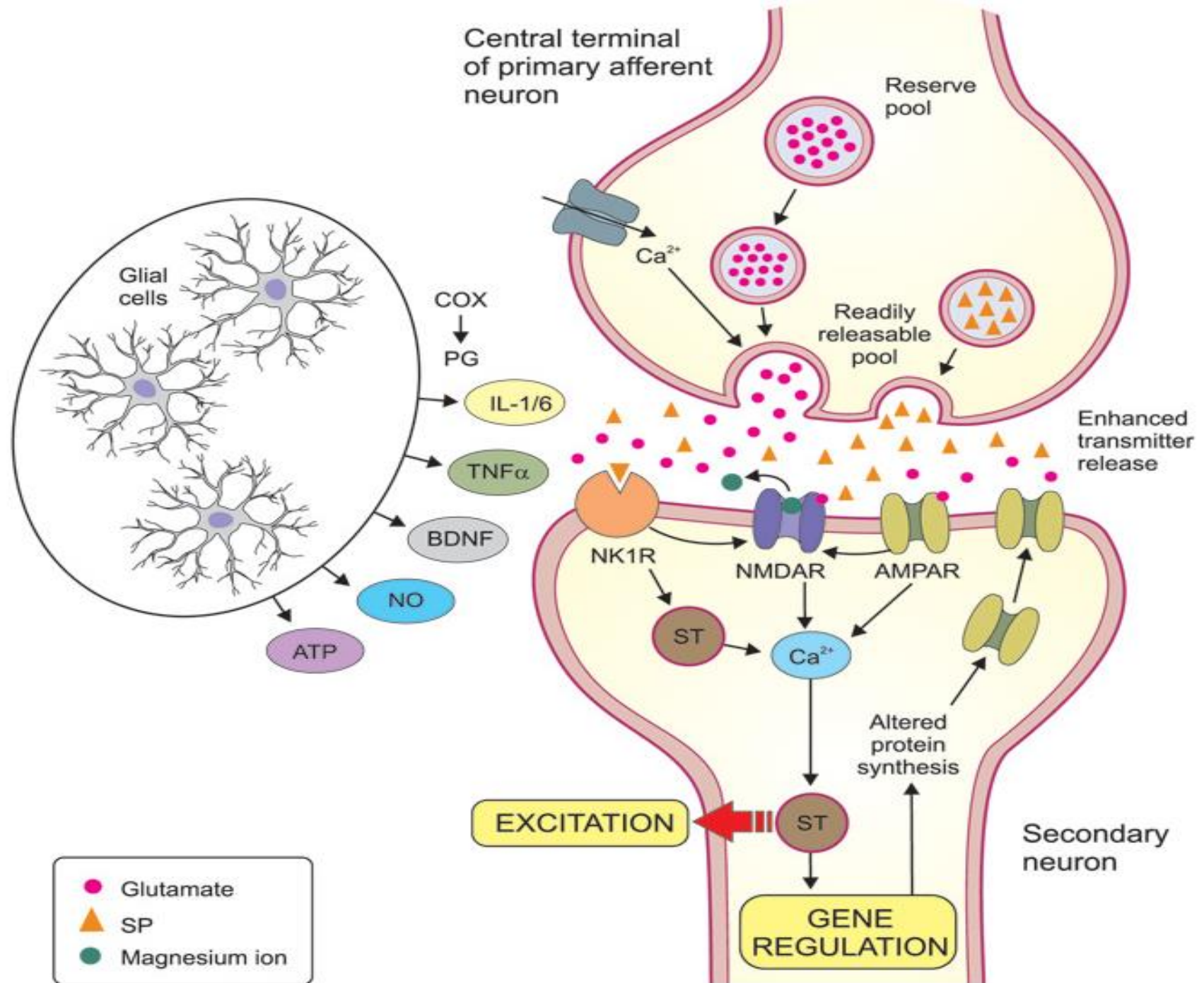
- **Peripheral Sensitization**

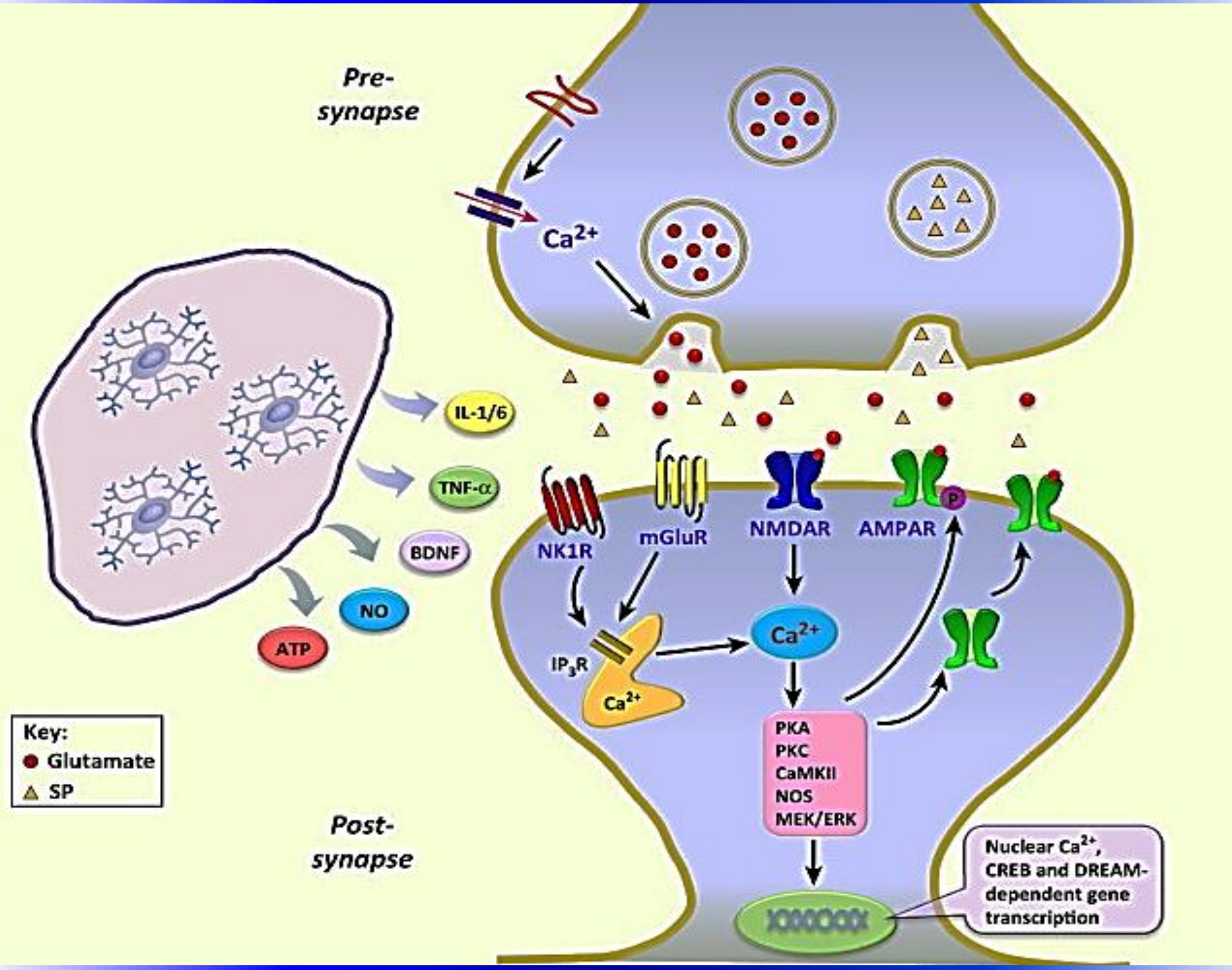
- Injury causes release of "sensitizing soup"
- Reduction in threshold and increase response of nociceptors

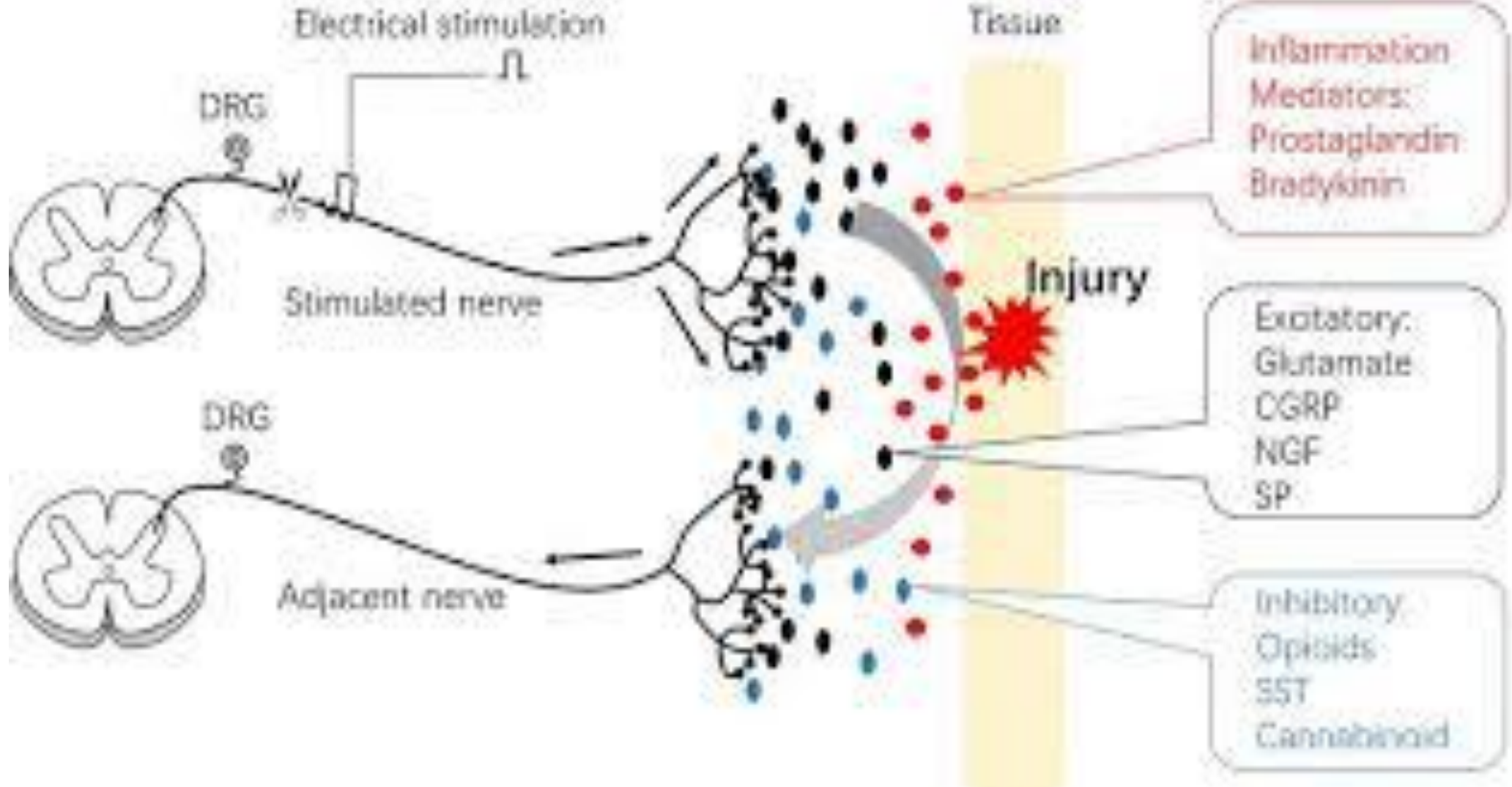
- **Central Sensitization**

- Membrane excitability, synaptic recruitment and decreased inhibition
- Uncoupling of pain from peripheral stimuli









central sensitization

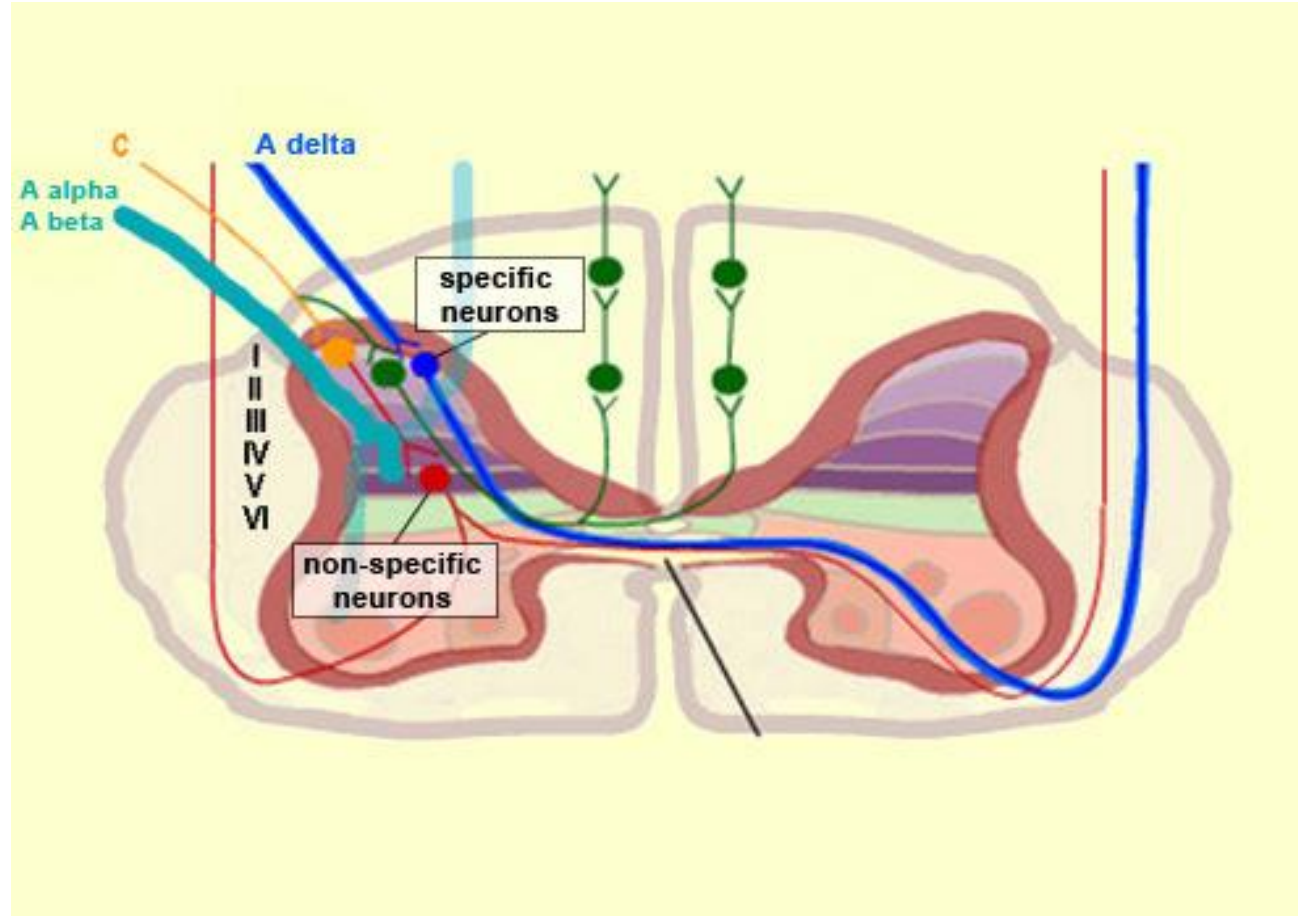
Increased responsiveness at all levels of the pain system, including :

1. the peripheral nociceptors,
2. spinal cord,
3. brainstem,
4. higher centers.

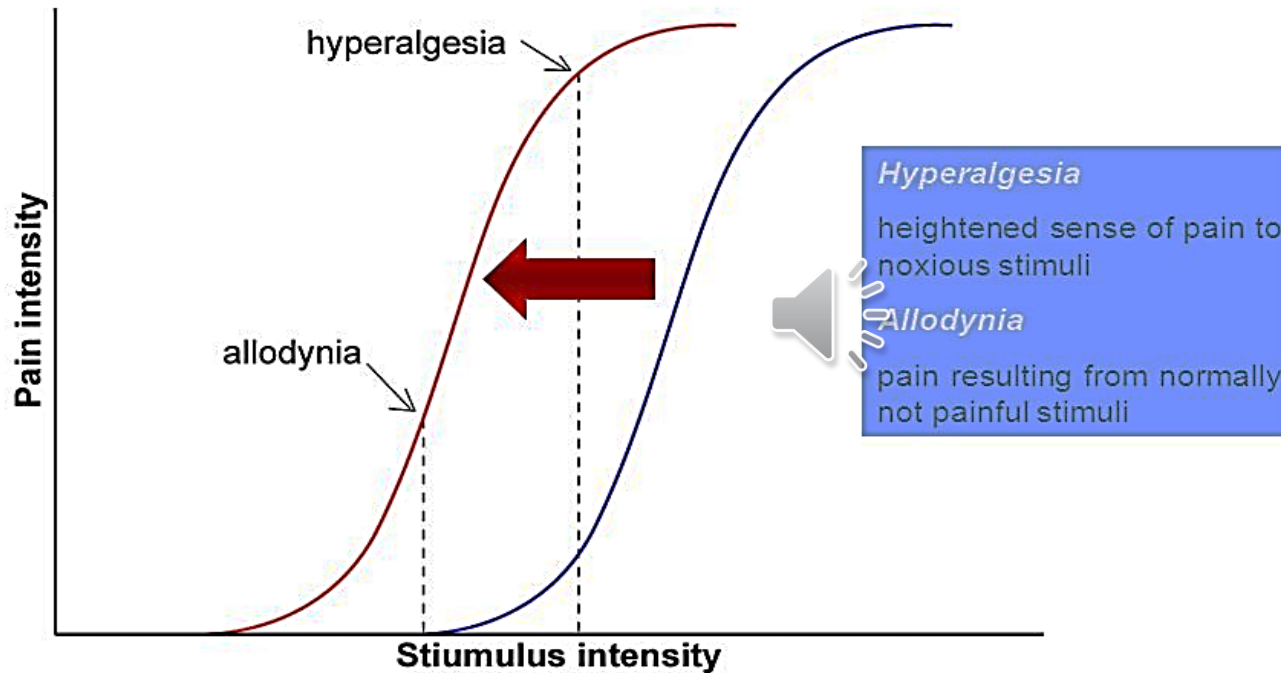


The net effect of the positive and negative alterations in circuitry leads to the perceptual experience of “pain.”

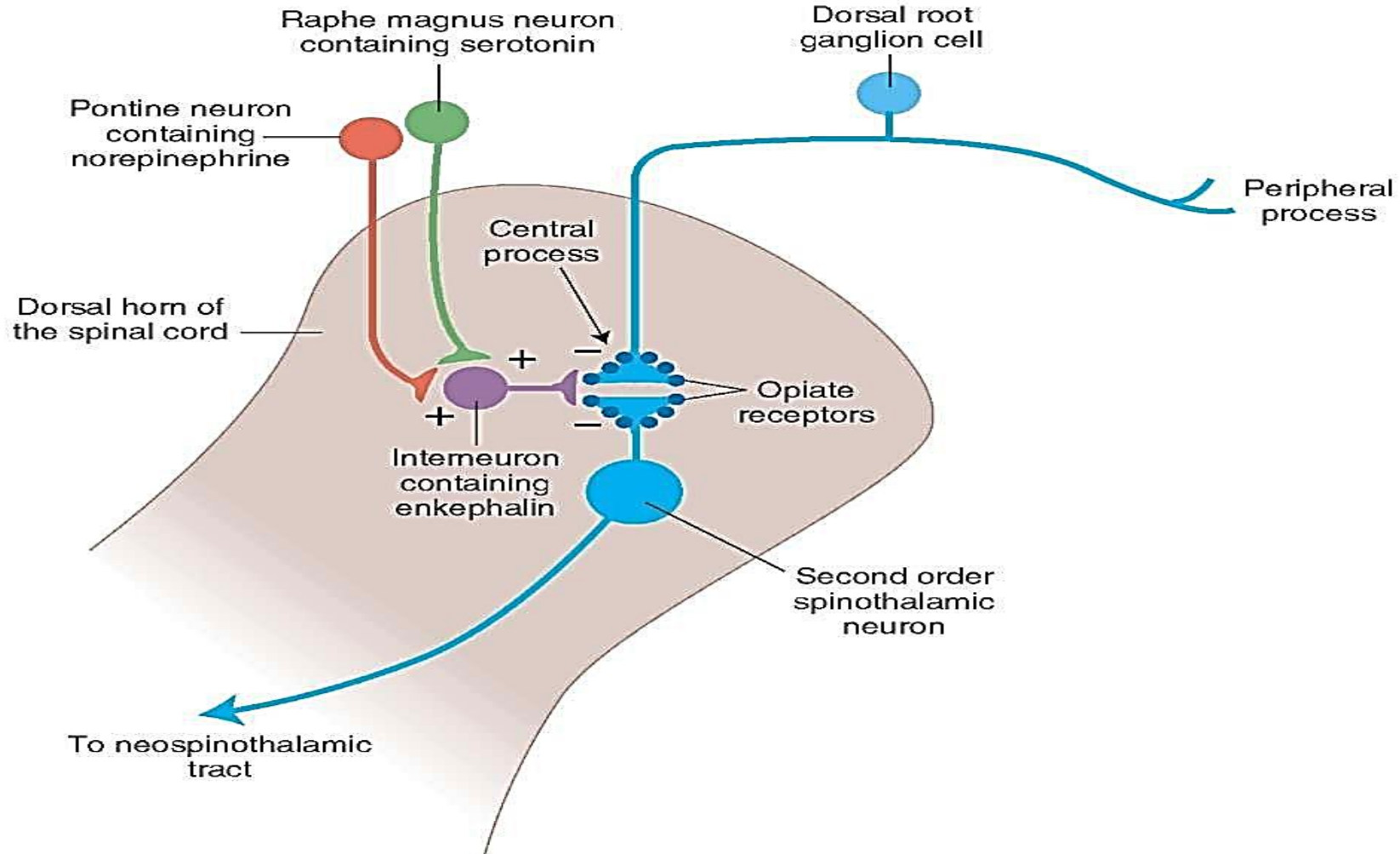
SPINAL CORD TERMINATIONS



Sensitization: A Common Mechanism



- Increased excitability of nociceptive neurons
- Changes in gene expression





GABAergic

GABA interneurons are uniquely qualified to provide
the “presynaptic” inhibition of nociceptive input

Other inhibitory neurons in the dorsal horn contain **dynorphin and glycine**.

Interestingly, neurons in lamina II, the substantia gelatinosa, do not respond to release of SP since they lack neurokinin 1 (NK1 or SP) receptors.⁸³

SP terminal endings are located on nociceptive projection cells in both lamina I and the deep dorsal horn, including lamina I cells with NK1 receptors that rapidly internalize the receptors on nociceptive stimulation.

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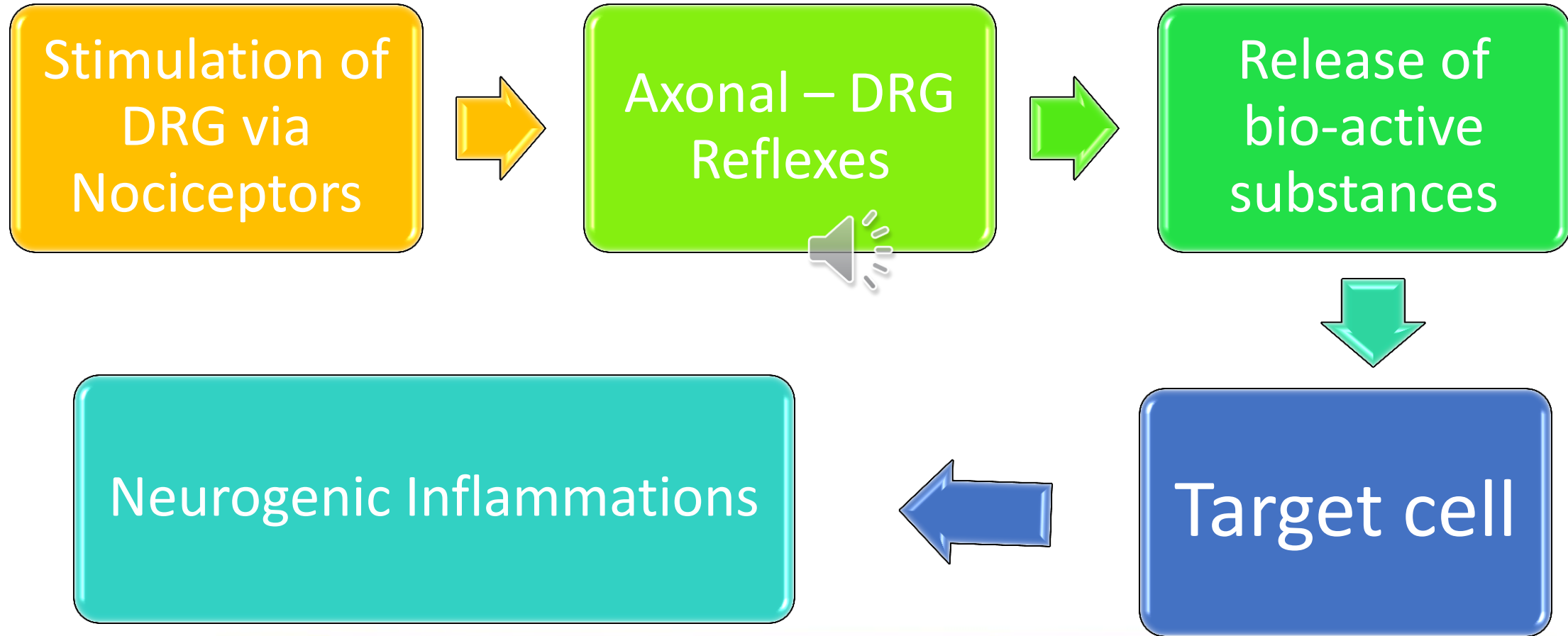
In the case of **intense or prolonged nociceptive stimulation**, the same anatomic arrangement of the dorsal horn circuitry providing “presynaptic inhibition” by GABA interneurons can override the inhibition and result in sensitization.

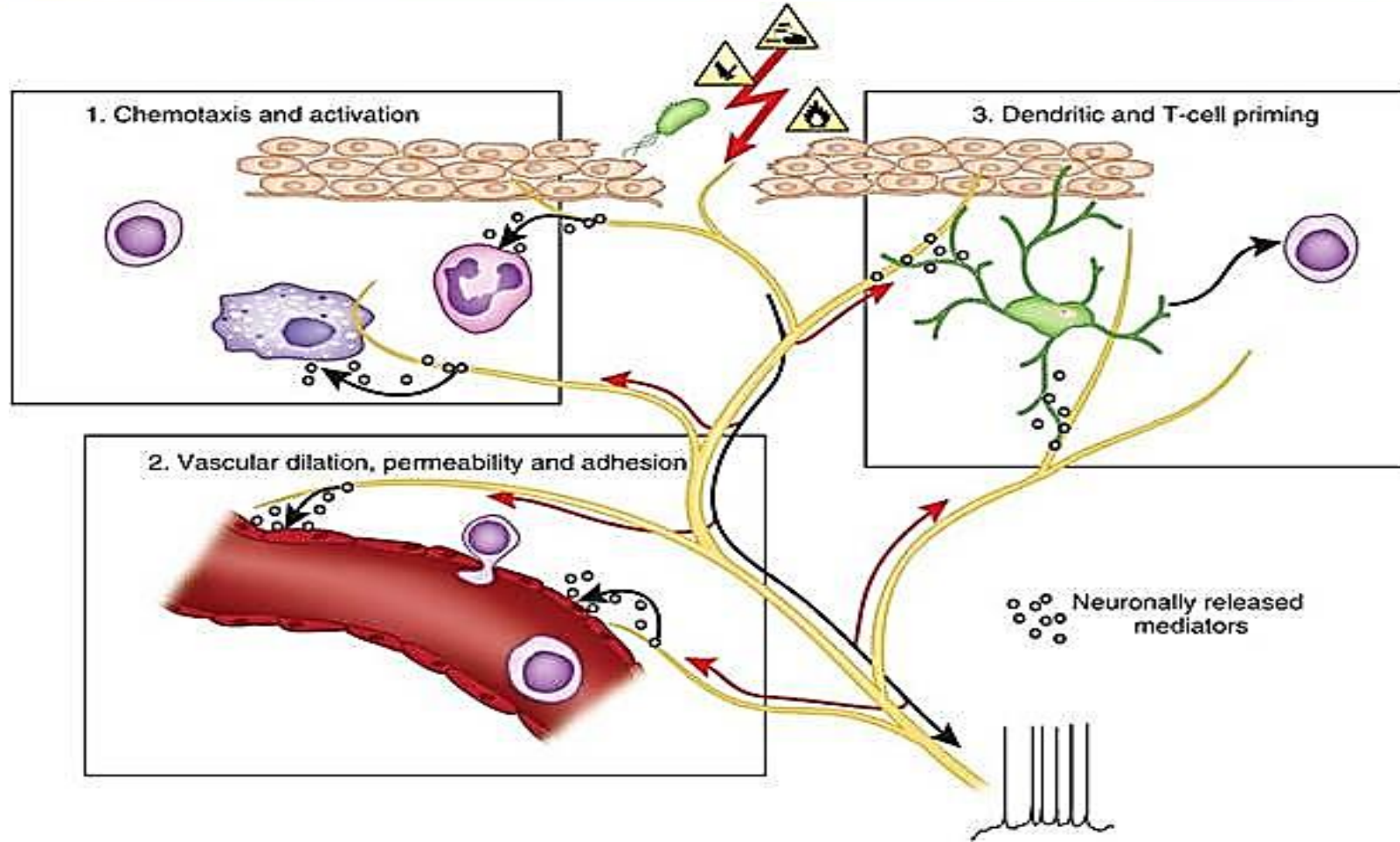
Prolonged membrane hyperpolarization evokes a secondary role of GABA_B receptors that changes their role from inhibition to excitation by altering the membrane conductance of central primary afferent terminals.

This results in diminished presynaptic inhibition and depolarization of the afferent nerve terminal endings themselves, which generates an action potential that travels back out the afferent nerve toward the periphery

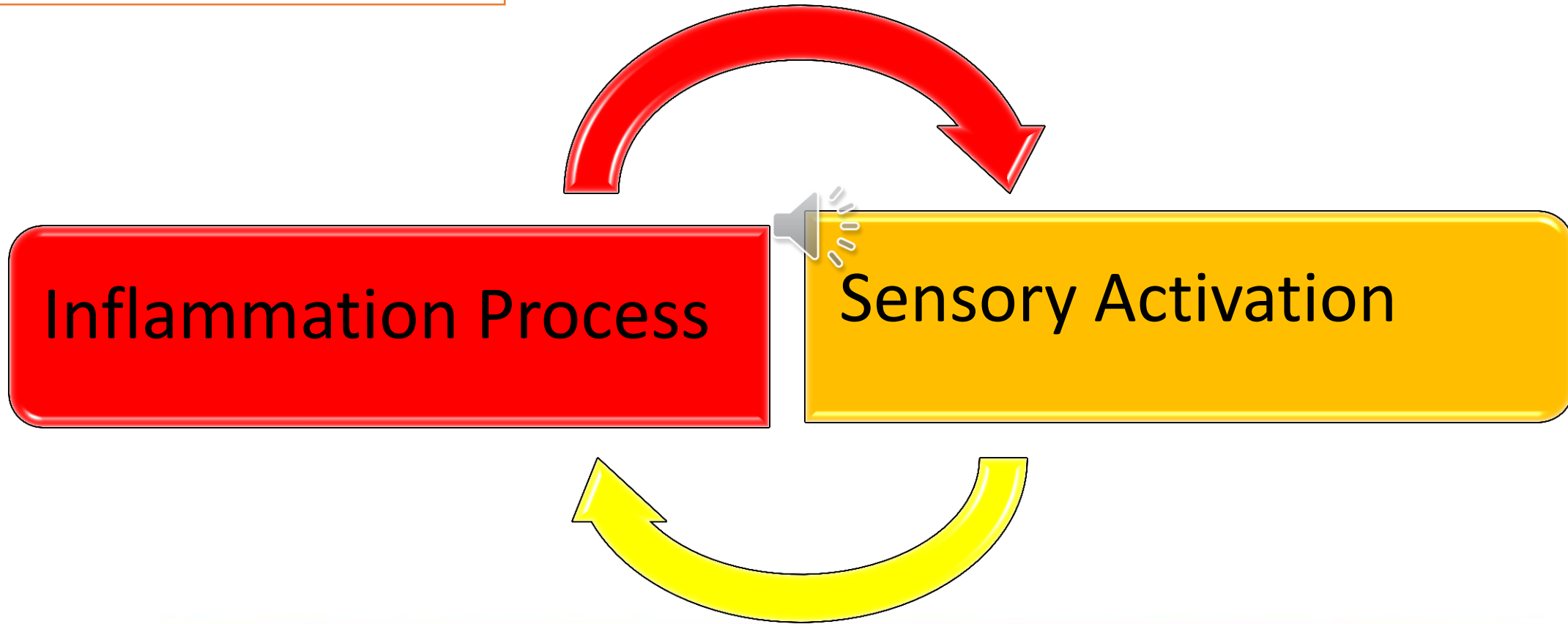
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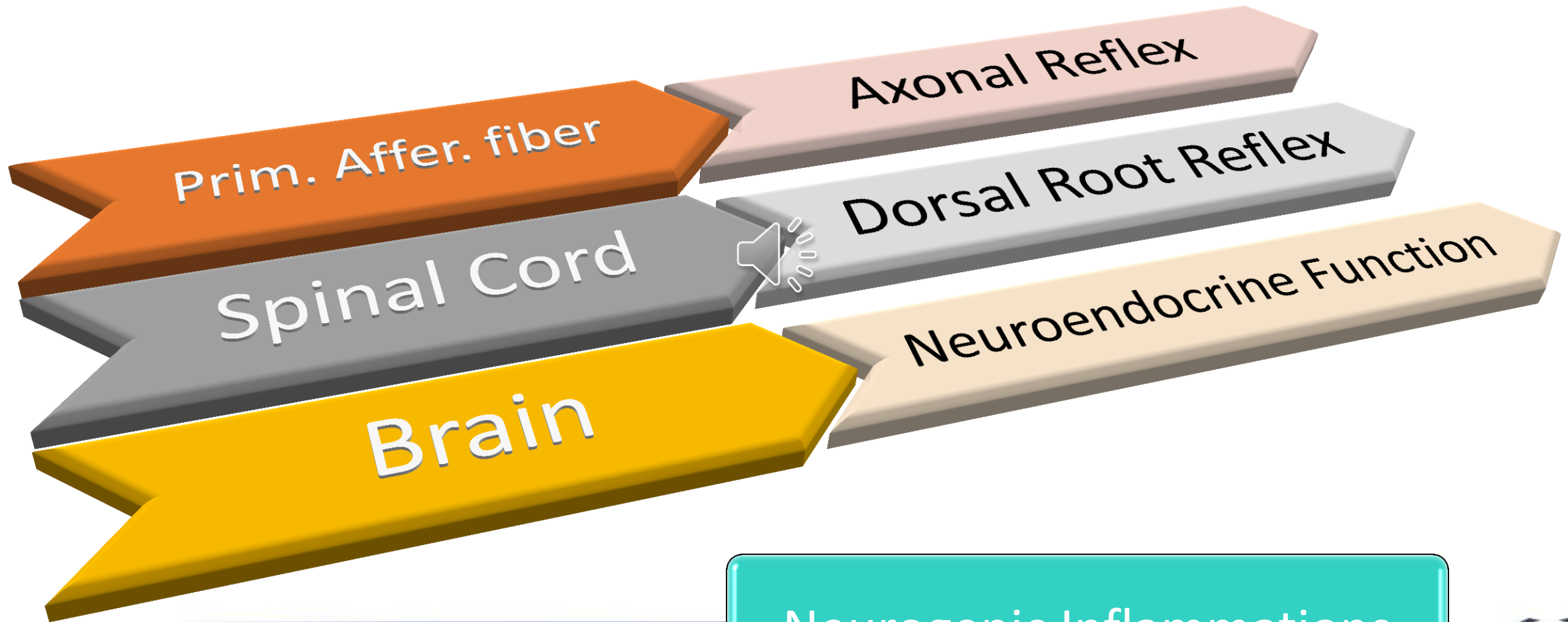






Bi-directional Relationship





Neurogenic Inflammations