

# NITROMEDICINE TEAM



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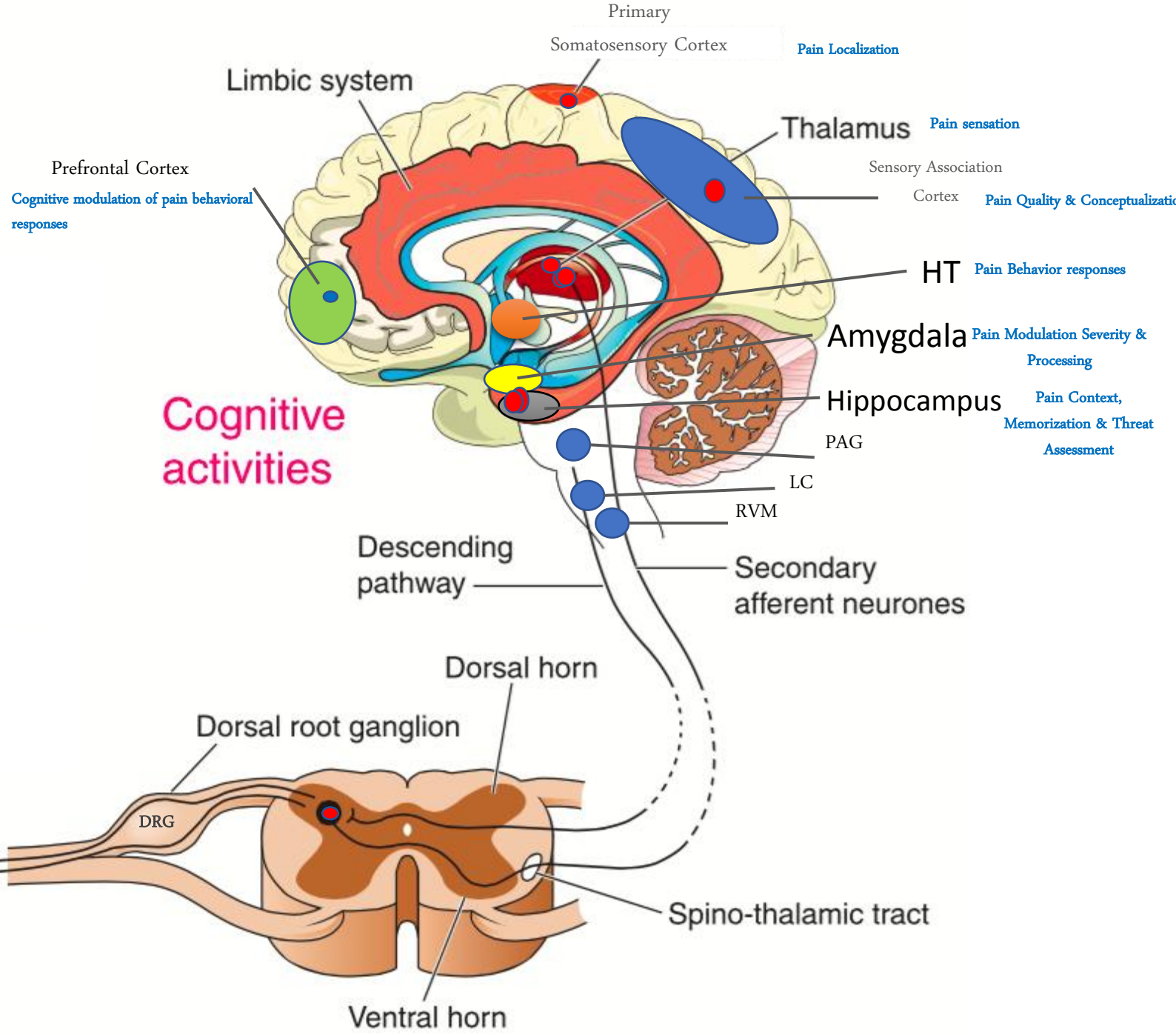
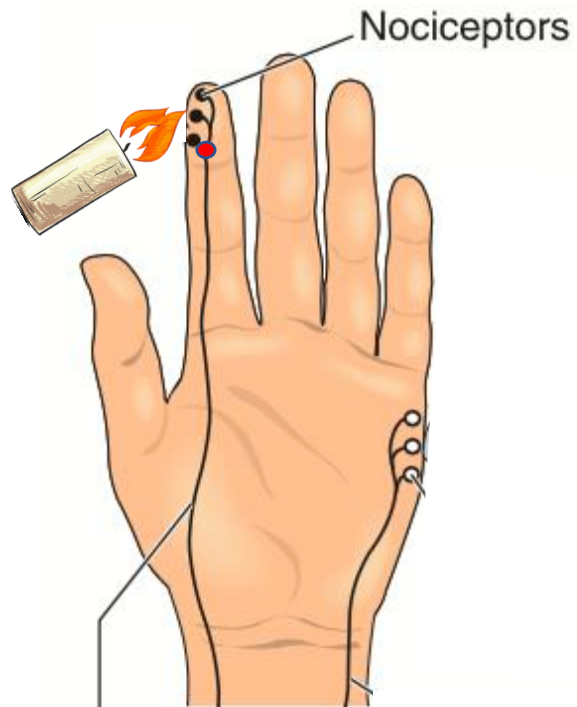
# CENTRAL PAIN VS PERIPHERAL PAIN GENERATORS

**Central Pain Generator** is Neuropathic pain that happens when the central nervous system doesn't process pain signals properly

**Peripheral Pain Generator** is Nociceptive pain that is not part of the nervous system and caused by inflammation or injury such OA, RA, Burn, fracture, etc

**About 20 percent of patients with OA who have had their knee or hip replaced continue to have chronic pain. The pain has likely become centralized—it is no longer caused by the inflammation or injury. Now the pain is driven by dysfunction in the central nervous system (CNS).**

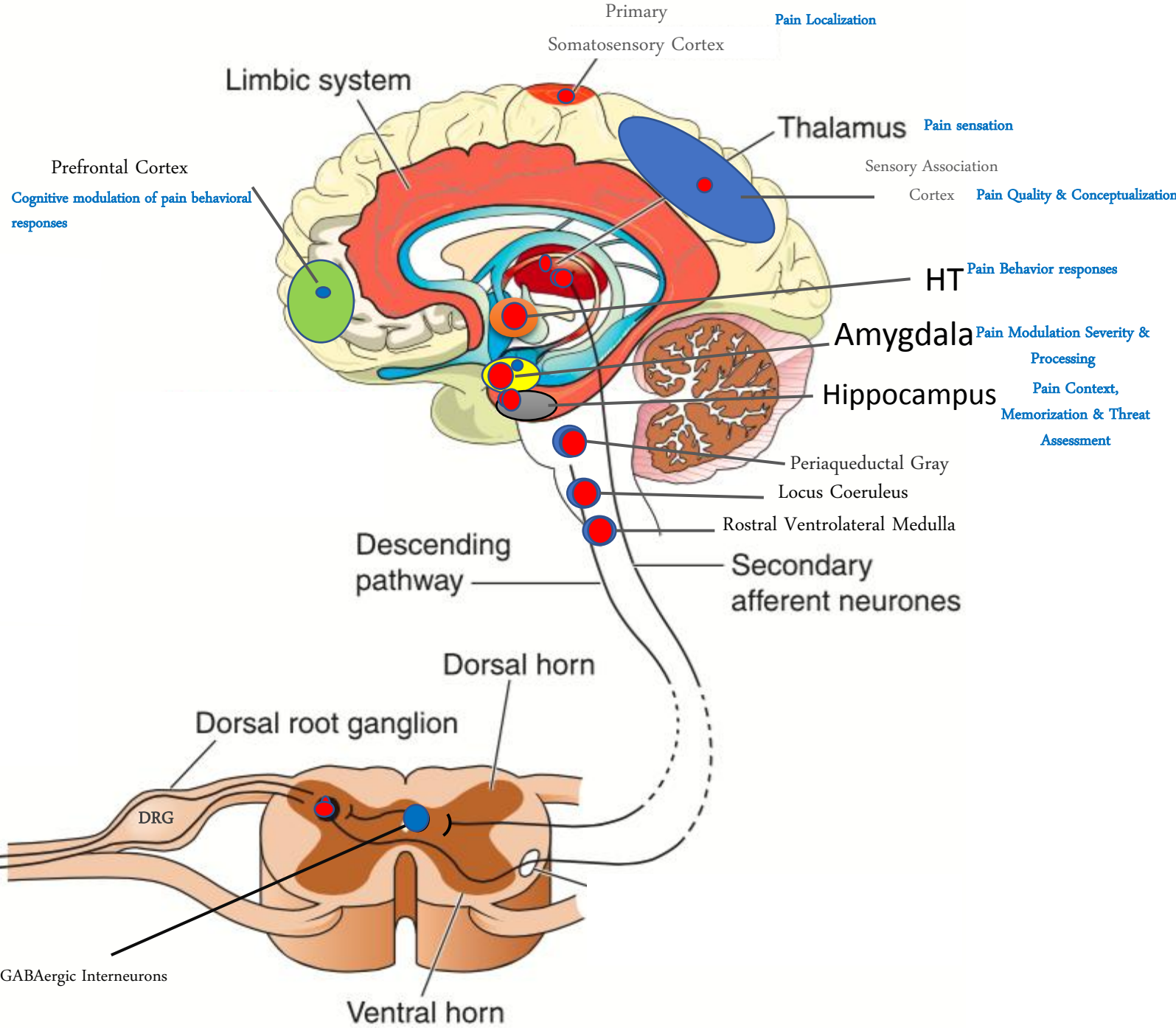
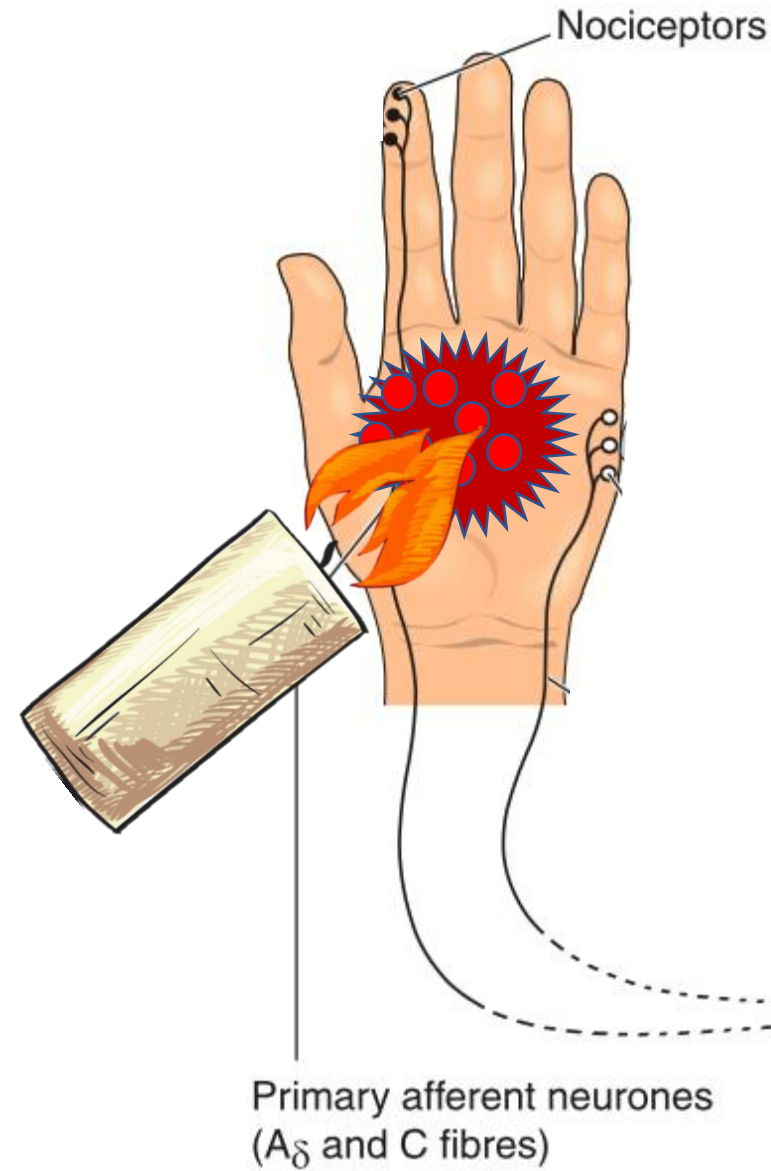
# Noxious stimulus



# Cognitive activities

● STIMULATION      ● INHIBITORY

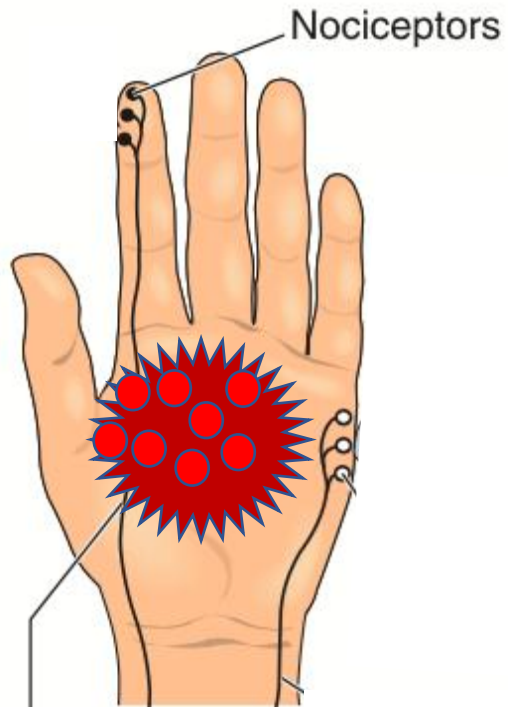
# Noxious stimulus



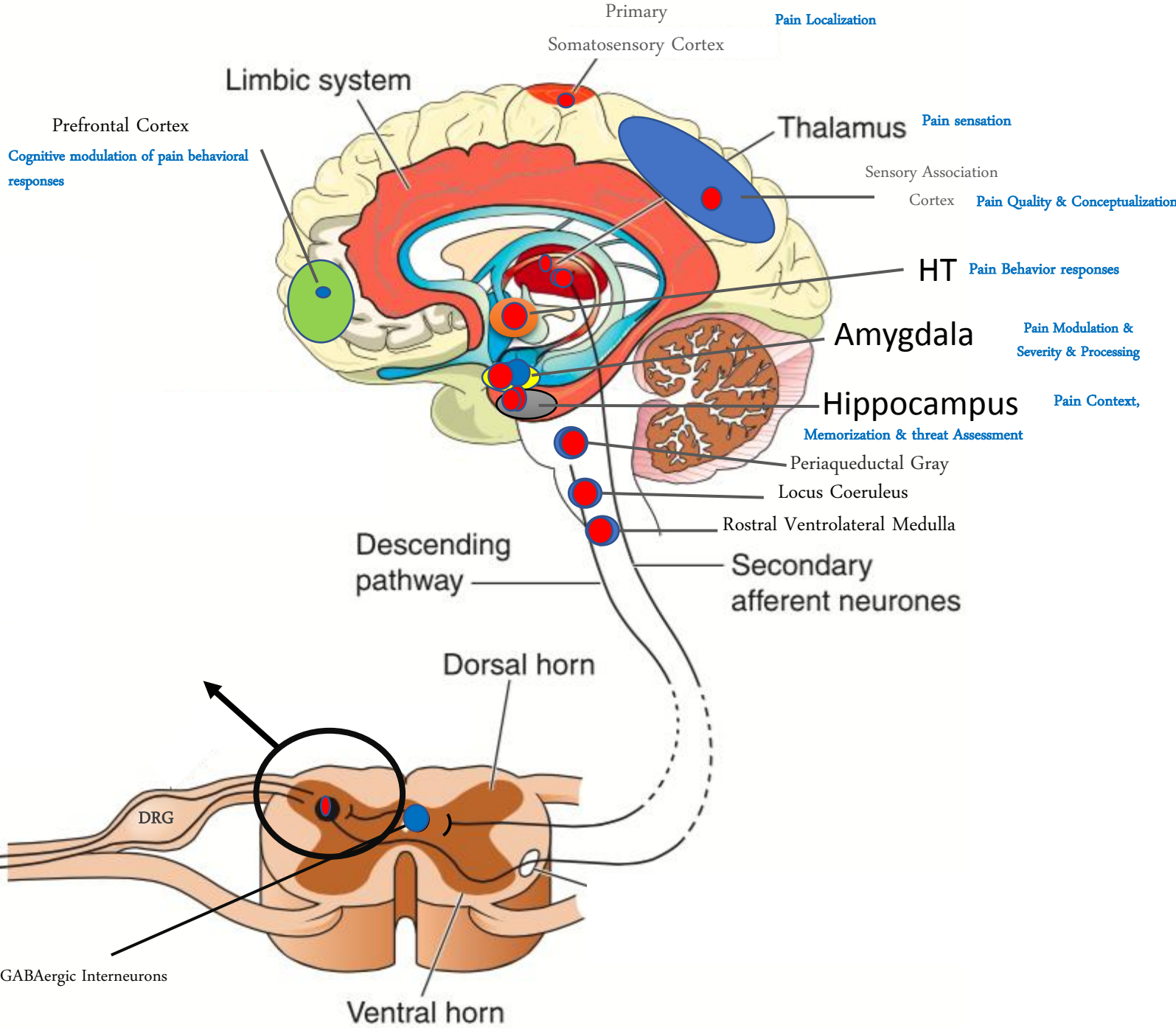
● STIMULATION

● INHIBITORY

# Noxious stimulus

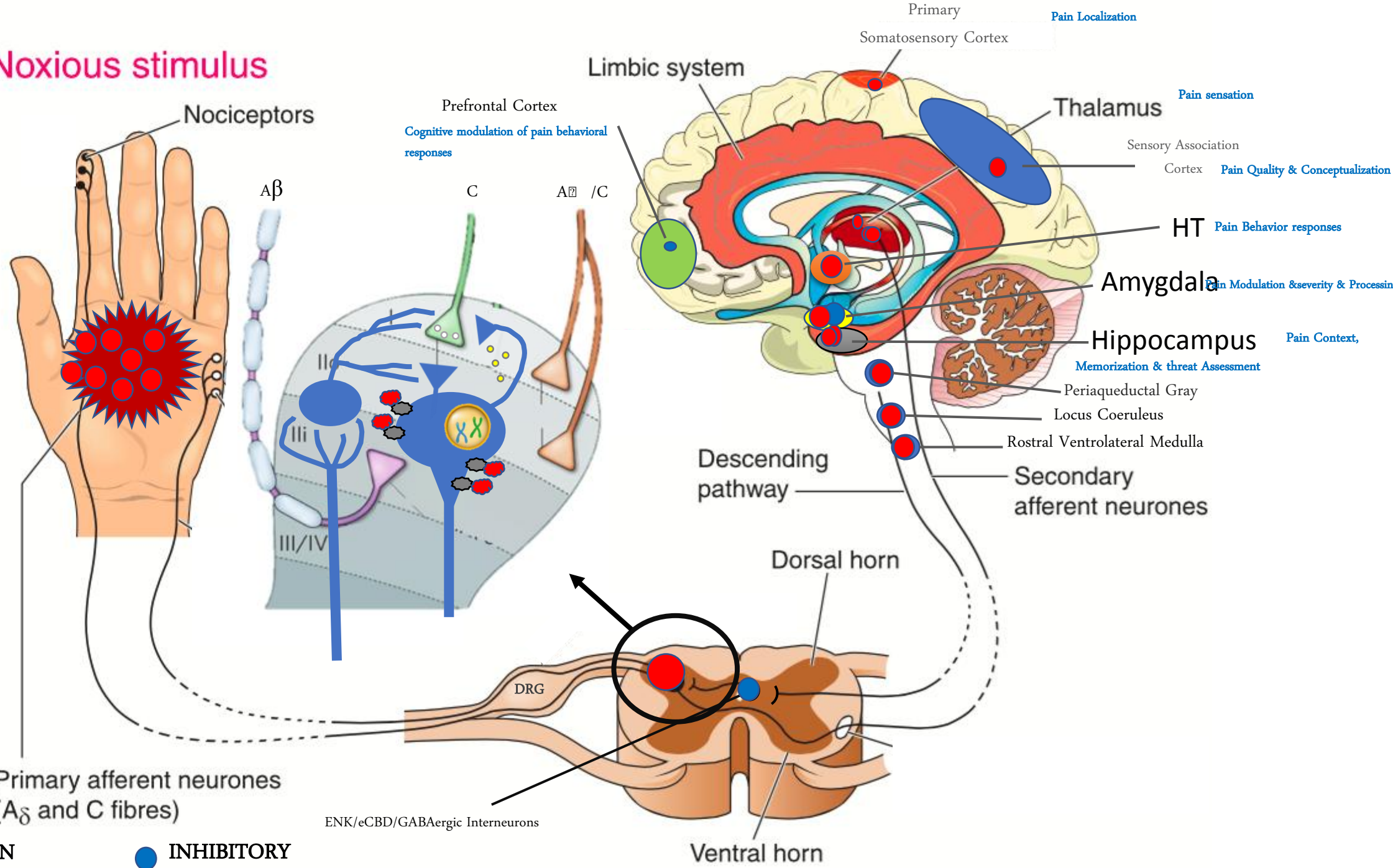


Primary afferent neurones (A $\delta$  and C fibres)



● STIMULATION      ● INHIBITORY

# Noxious stimulus



● STIMULATION

● INHIBITORY

ENK/eCBD/GABAergic Interneurons

DRG

Dorsal horn

Ventral horn

Descending pathway

Secondary afferent neurones

Rostral Ventrolateral Medulla

Locus Coeruleus

Periaqueductal Gray

Hippocampus

Amygdala

HT

Sensory Association Cortex

Pain sensation

Thalamus

Primary Somatosensory Cortex

Pain Localization

Limbic system

Prefrontal Cortex  
Cognitive modulation of pain behavioral responses

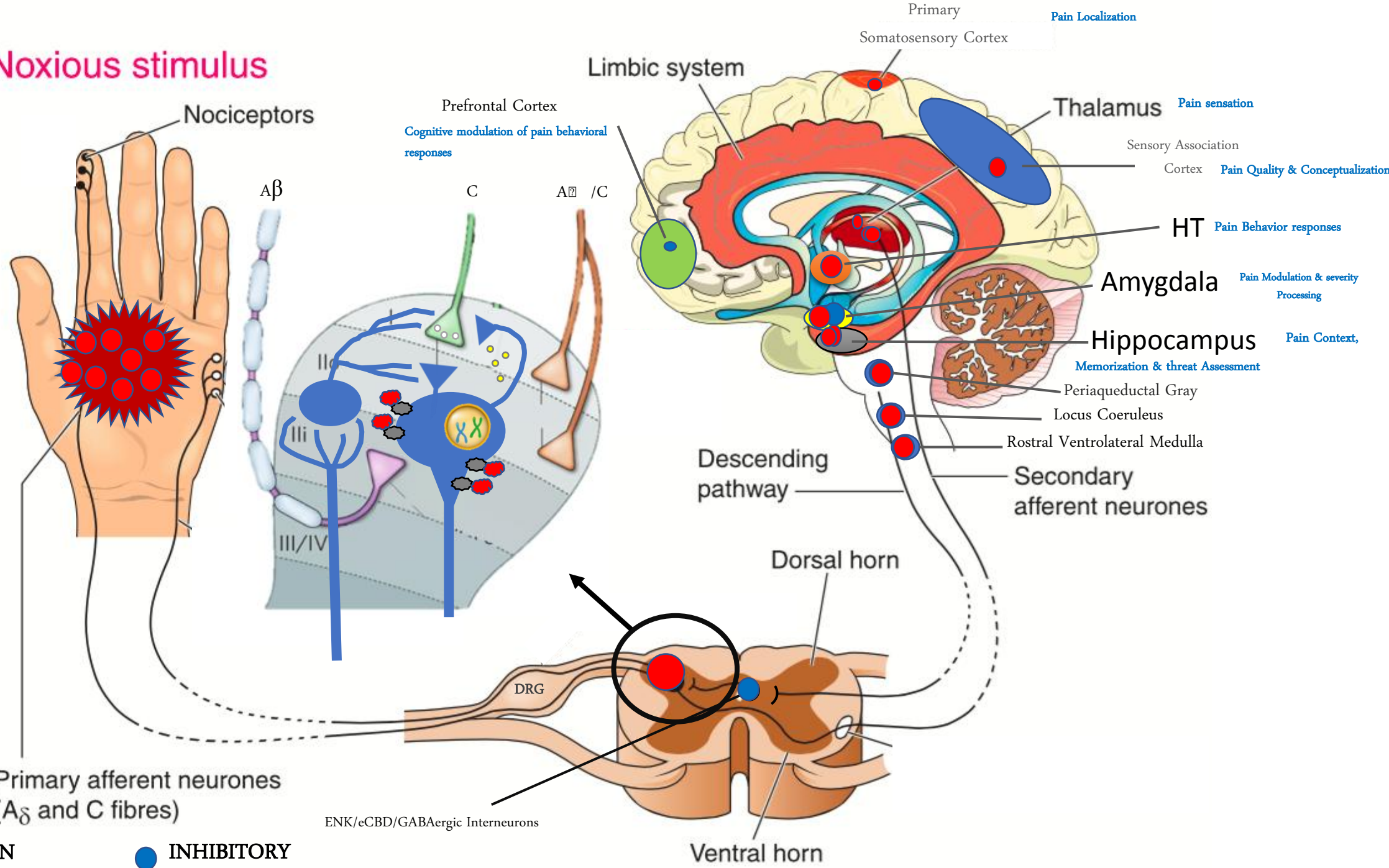
A $\delta$  /C

C

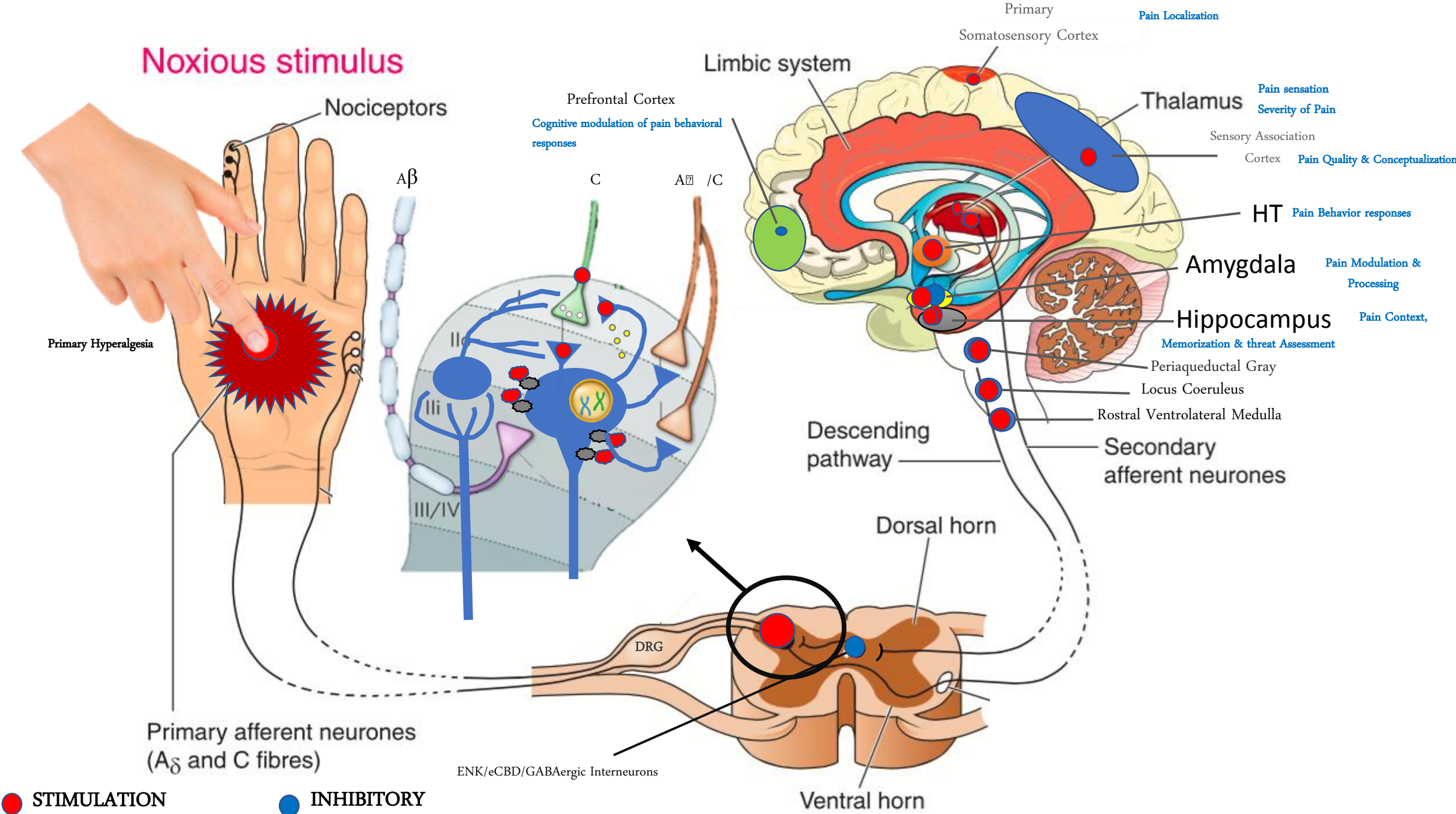
A $\beta$

Nociceptors

# Noxious stimulus

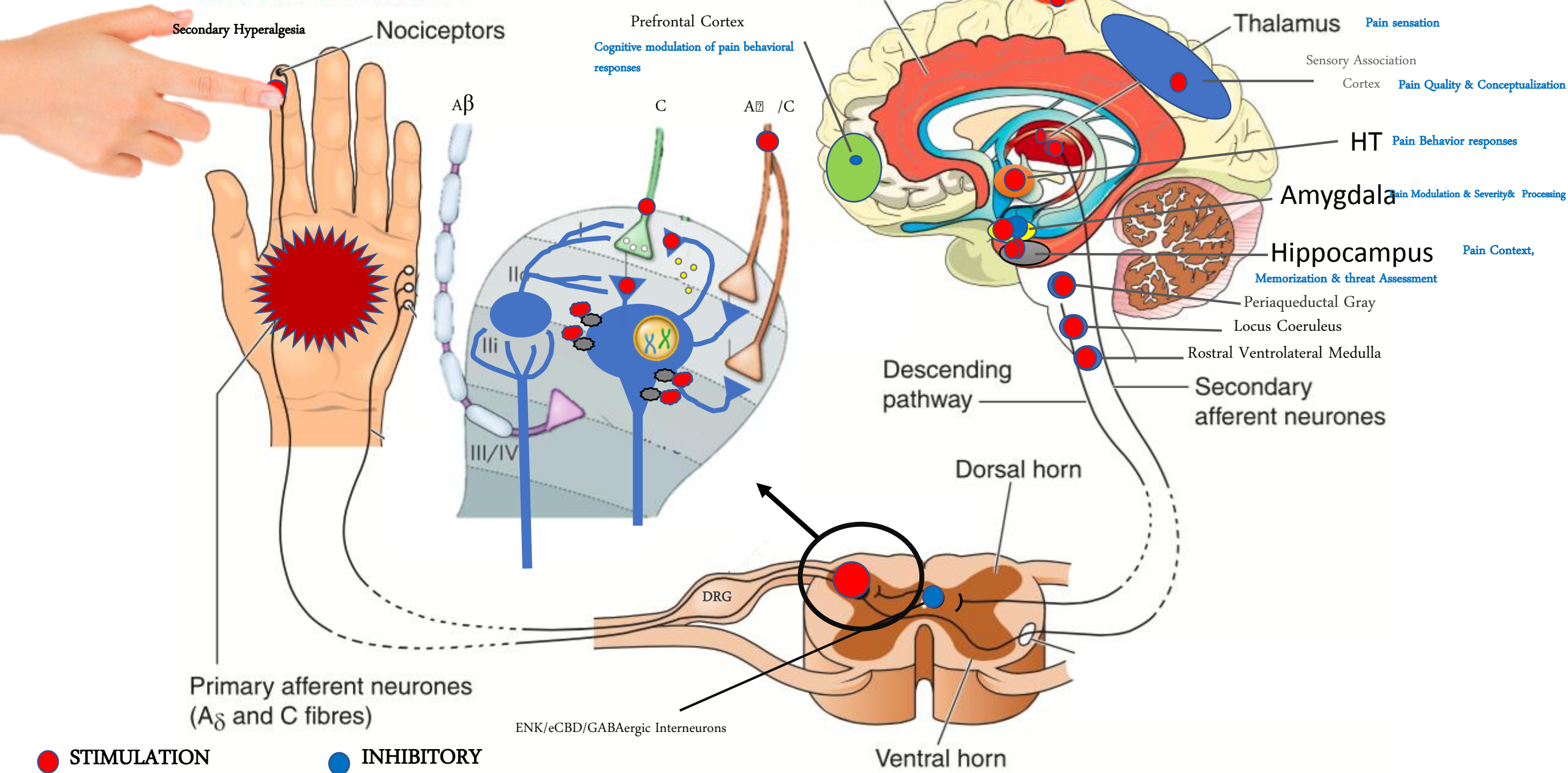


# Noxious stimulus

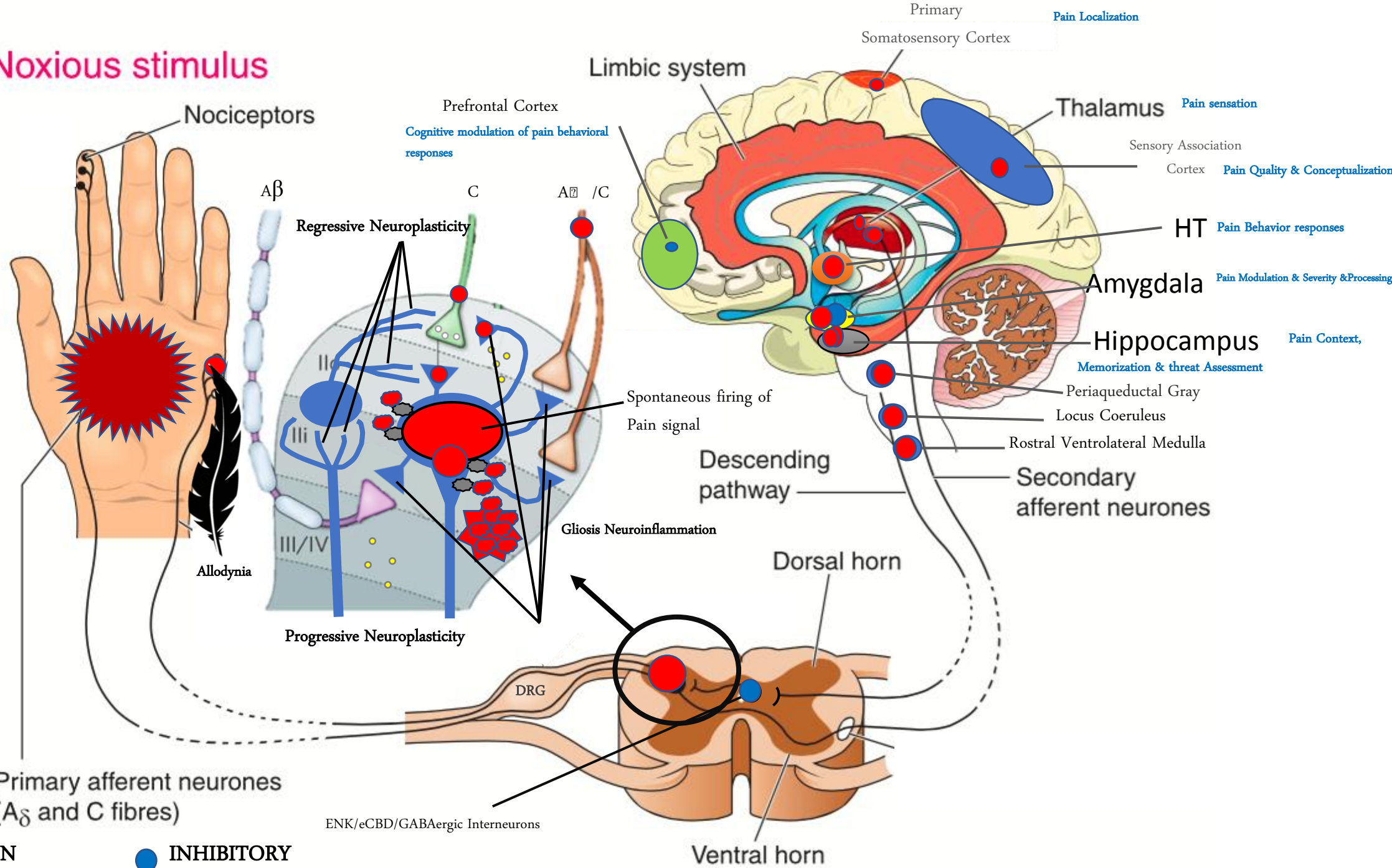




# Noxious stimulus



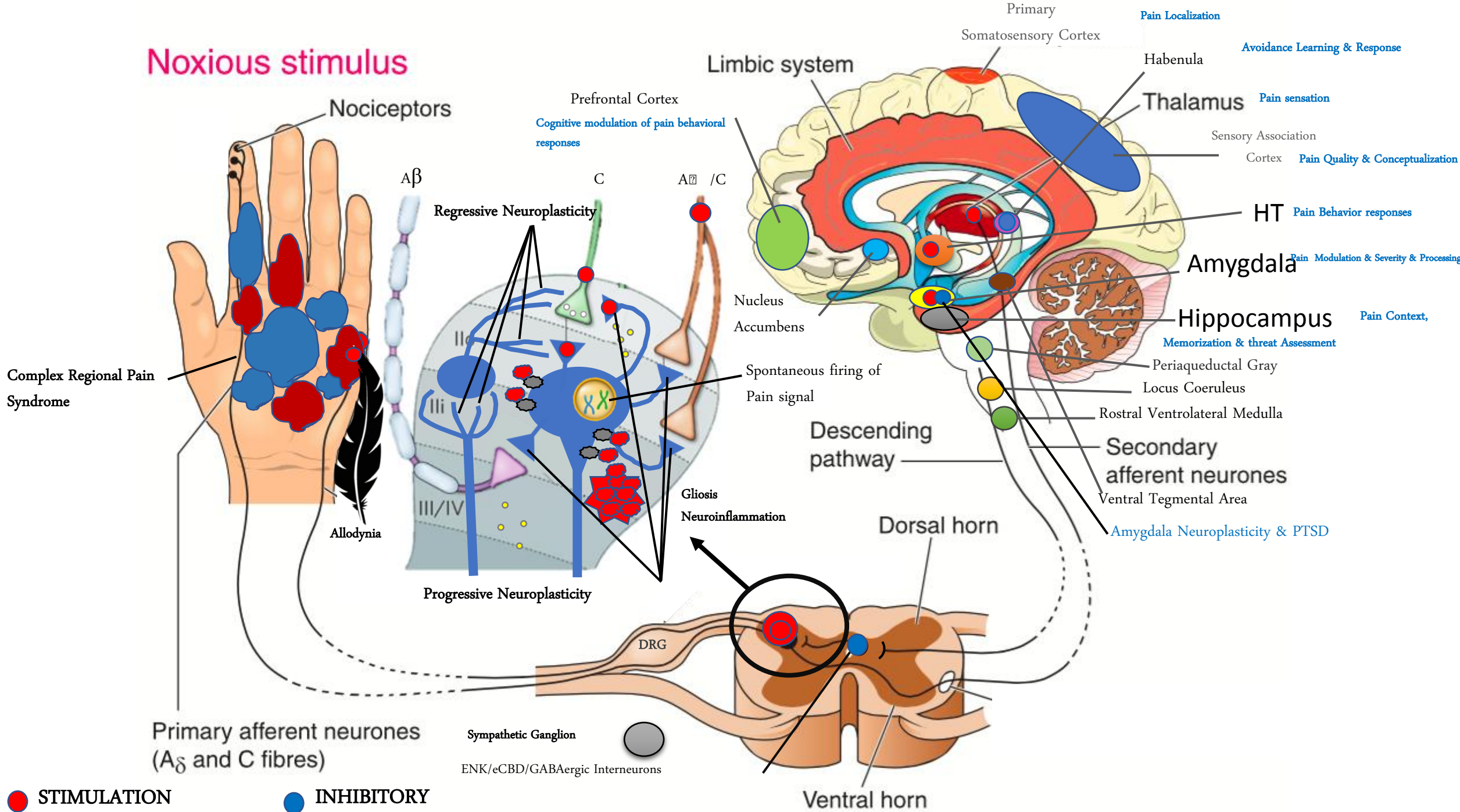
# Noxious stimulus



● STIMULATION

● INHIBITORY

# Noxious stimulus



- = Opioid Receptor
- = CB Receptor
- = K<sup>+</sup> Channel
- = Noradrenaline Reuptake Receptor
- = Serotonin Reuptake Receptor

= NMDA Receptor

= Opioid

= CBD & THC

= TCA

= SSRI

= GBP/KET

= NSAID

= Steroid

= B12

= Curcumin

= ALA

= Exosomes

A $\beta$

C

A $\delta$ /C

# Regressive Neuroplasticity

Photo Medicine

Mitochondrial Dysfunction

Hyperpolarization & Analgesia

Receptor Desensitization & Addiction

Increased Opioid Receptor Sensitization & Treat Addiction

CAT/SOD

COX/LOX

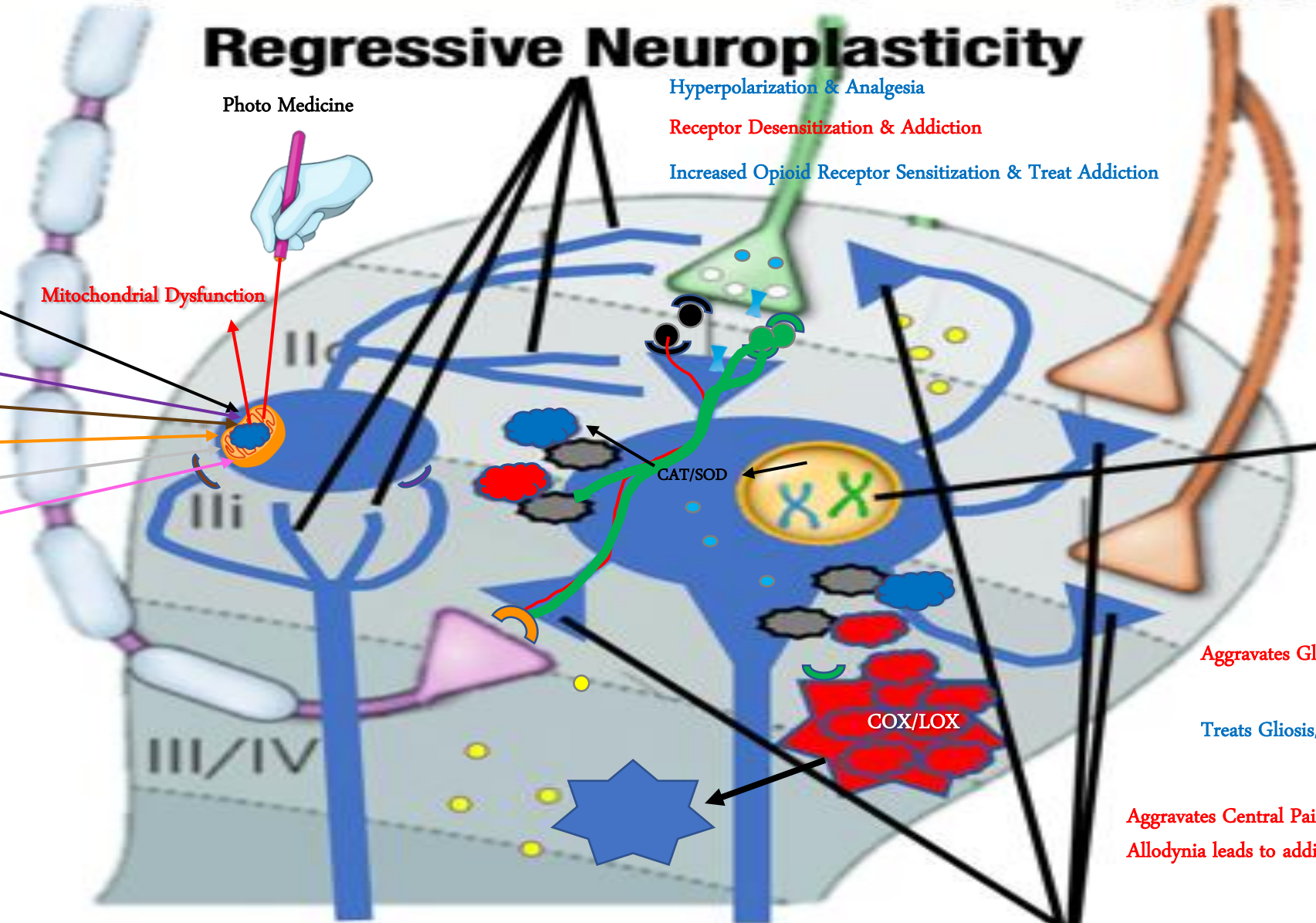
Aggravates Gliosis/ Neuroinflammation

Treats Gliosis/ Neuroinflammation

Aggravates Central Pain Sensitization, Hyperalgesia & Allodynia leads to addiction

Treats Central Pain Sensitization, Hyperalgesia, Allodynia & Addiction

# Progressive Neuroplasticity



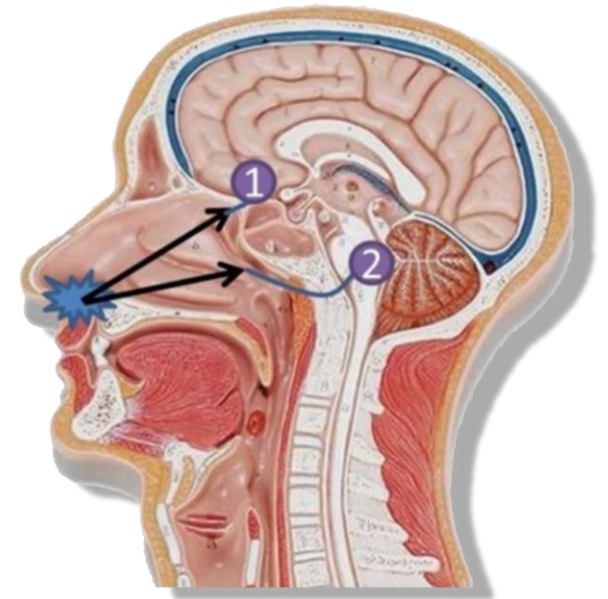
# CBD's Effect in the Brain

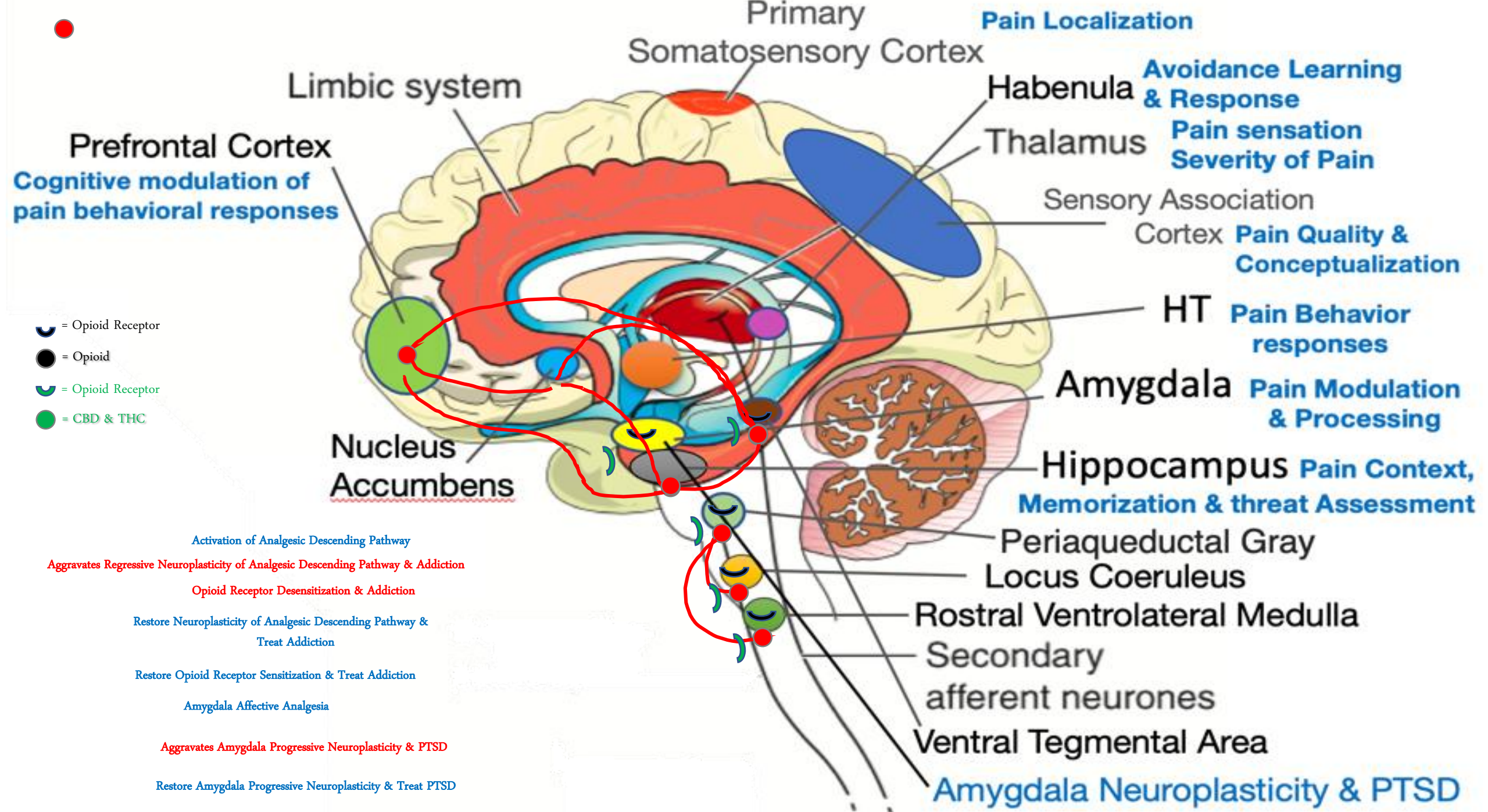
- Blocks the NMDA receptor
- Reduces free radical generators
- Prevents Ca<sup>+</sup> influx
- Stops the activation of the NOX enzyme
- Restore Opioid Receptor Sensitization & treats addiction

## What is the delivery of choice for CBD?

Neuroprotective drugs are proven to be exceptionally difficult to activate due to the blood-brain barrier.

- **Intranasal**
  - Transport CBD directly to the brain
  - Olfactory thru the cribriform plate and Trigeminal nerves.
- **Water-soluble CBD**
  - Enhances the bioavailability creating an absorption process superior to any other form of delivery.
- **Methylcobalamin B12**
  - creates an even greater absorption to the brain.
  - blocks the NDA receptors





Primary Somatosensory Cortex

Pain Localization

Limbic system

Avoidance Learning & Response

Habenula

Pain sensation Severity of Pain

Thalamus

Prefrontal Cortex  
Cognitive modulation of pain behavioral responses

Sensory Association Cortex

Pain Quality & Conceptualization

- ☪ = Opioid Receptor
- = Opioid
- ☪ = Opioid Receptor
- = CBD & THC

HT

Pain Behavior responses

Amygdala

Pain Modulation & Processing

Nucleus Accumbens

Hippocampus  
Pain Context, Memorization & threat Assessment

Periaqueductal Gray

Locus Coeruleus

Rostral Ventrolateral Medulla

Secondary afferent neurones

Ventral Tegmental Area

Amygdala Neuroplasticity & PTSD

Activation of Analgesic Descending Pathway

Aggravates Regressive Neuroplasticity of Analgesic Descending Pathway & Addiction

Opioid Receptor Desensitization & Addiction

Restore Neuroplasticity of Analgesic Descending Pathway & Treat Addiction

Restore Opioid Receptor Sensitization & Treat Addiction

Amygdala Affective Analgesia

Aggravates Amygdala Progressive Neuroplasticity & PTSD

Restore Amygdala Progressive Neuroplasticity & Treat PTSD

# Somatomotor Cortex

Primary Somatosensory Cortex

Pain Localization

Limbic system

Avoidance Learning & Response

Habenula

Pain sensation  
Severity of Pain

Thalamus

Sensory Association Cortex

Pain Quality & Conceptualization

Prefrontal Cortex

Cognitive modulation of pain behavioral responses

HT

Pain Behavior responses

☪ = Opioid Receptor

● = Opioid

☪ = Opioid Receptor

● = CBD & THC

Amygdala

Pain Modulation & Processing

Nucleus Accumbens

Hippocampus Pain Context, Memorization & threat Assessment

Opioid Rewarding Responses, Euphoria, & Addiction

Opioid Receptor Desensitization & Addiction

Opioid Withdraw Dysphoria & Addiction

Inhibition of Opioid Withdraw dysphoria & Treat Addiction

Restored Opioid Receptor Sensitization & Treat Addiction

Other Therapies

Cognitive-Behavioral Therapy, Meditation & Biofeedback

Transcranial & intranasal Photo Therapy

Periaqueductal Gray

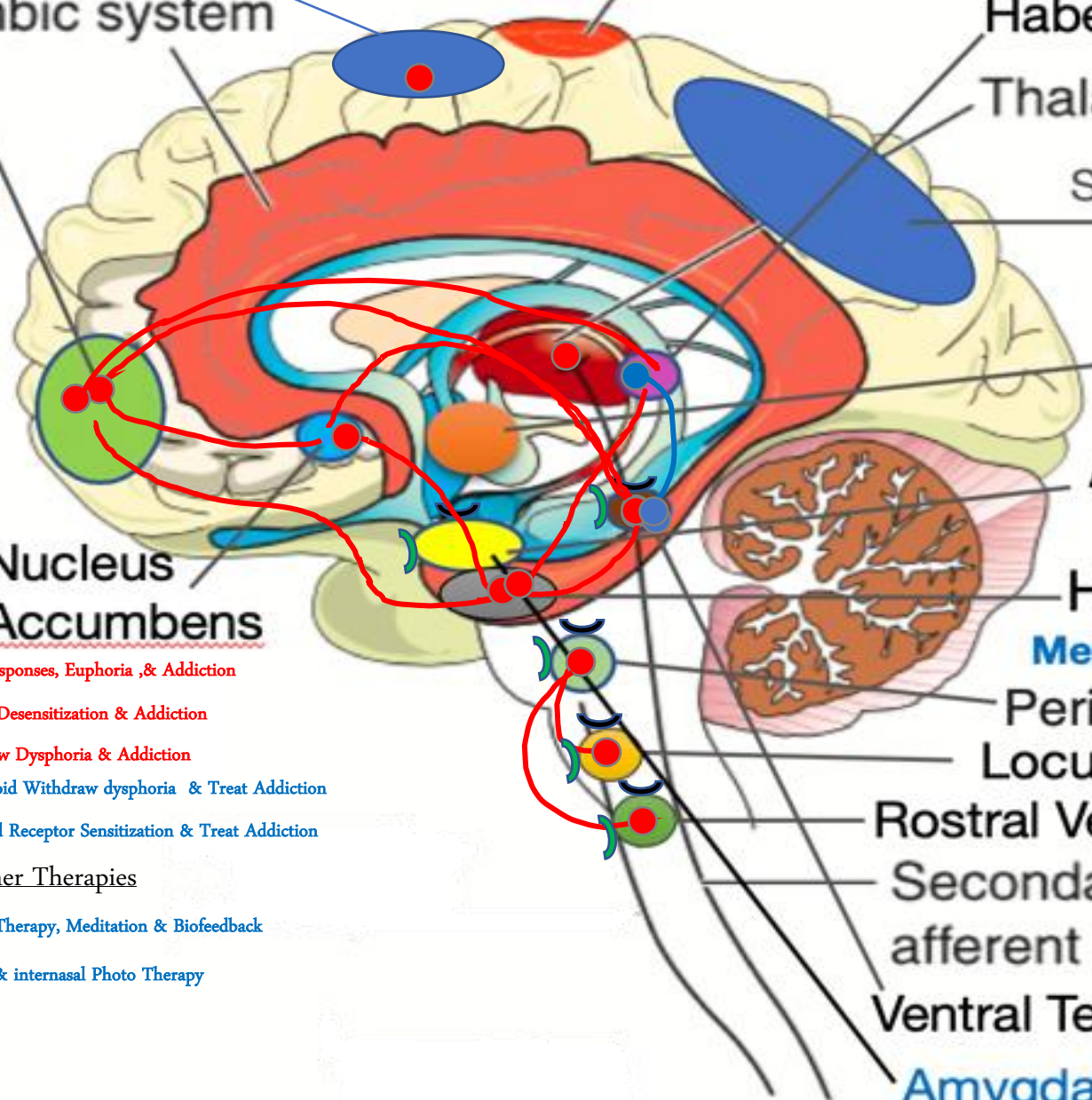
Locus Coeruleus

Rostral Ventrolateral Medulla

Secondary afferent neurones

Ventral Tegmental Area

Amygdala Neuroplasticity & PTSD



# Patient With Complex Regional Pain Syndrome



A 42 -year-old man presented to my office with a history of left arm pain and swelling for a duration of 5 years. The patient twisted his left arm at work while drilling a hole in the ground. He was diagnosed with ulnar nerve entrapment and underwent a complicated ulnar nerve dislocation surgery which progressed into left upper limb CRPS and he received series of unsuccessful left cervical ganglion steroid injection blocks.

The Patient suffered five years of constant and sever left upper limb swelling, deep aching pain, allodynia, hyperalgesia and discoloration and he was on the highest dose of narcotics without relief. He lost his job, disabled and sustained a harsh economic and social life.

After 6 months of series blue, infrared and red photobiomodulation therapies on his left arm and left cervical sympathetic ganglions along with application of topical Nitrocompounding medications, the patient recovered from his pain, weaned from narcotics , returned back to his work and he was able preform his normal daily activities.