OUCH!!
What is a Pain?

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Who am I??

- Graduated from Iowa State University College of Veterinary Medicine in 1992
- General practice for 13 years (variety of stuff)
- Internship and residency at Iowa State University College of Veterinary Medicine 2005 – 2009
- Mississippi State University College of Veterinary Medicine as Service Chief of Anesthesiology from 2009 – 2016.
- Michigan State University College of Veterinary Medicine Staff Supervisor and Service Chief 2016 – 2022
- Currently Associate Professor Anesthesiology at Oregon State University College of Veterinary Medicine

Goals of this discussion

1. Physiology of normal pain
2. Concepts and misconceptions of analgesia and anesthesia
3. Pathophysiology of abnormal pain
4. Preventive analgesia for the veterinary practitioner

AAA

- Analgesia
  - Absents of pain
  - Absents of nociception?
- Analgesics
  - Modality that helps decrease pain
  - Modality that helps decrease the process of nociception

- Anesthesia
  - Loss of all afferent sensory input locally, regionally, or generally.

In Vet Med we tend to confuse general anesthesia with analgesia

Pain Vs. Nociception

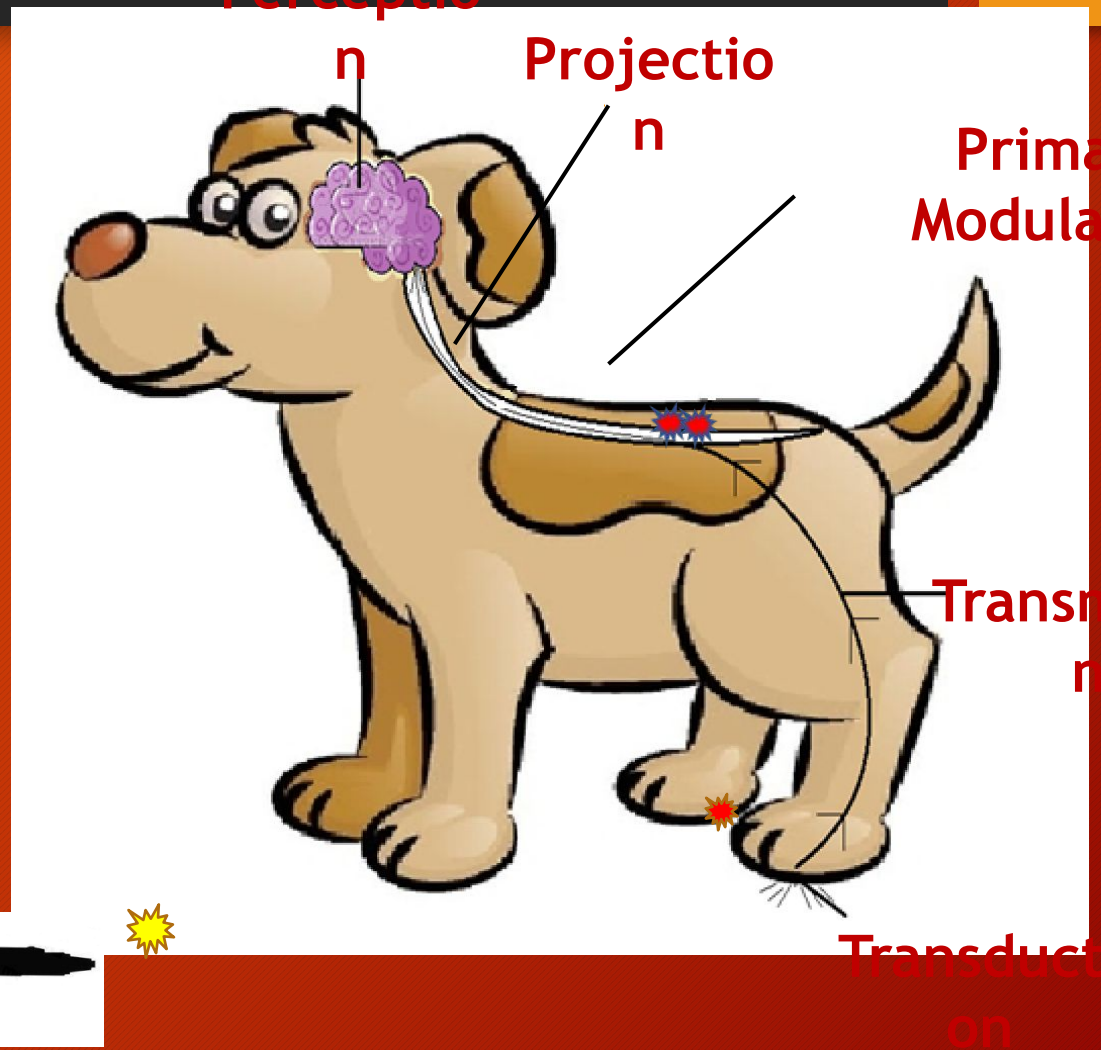
- Pain
  - “an unpleasant **sensory** and **emotional** experience associated with **actual or potential** tissue damage or described in terms of such damage.”
  - Somatosensory + emotional/behavioral response to nociception.
  - Tends to be over emphasized, which is a good/bad thing…
- Nociception
  - The neurophysiological process whereby noxious mechanical, chemical, or thermal stimuli are transduced into electrical signals (action potentials) by high-threshold nociceptors. These action potentials follow a series of pathways that ultimately end in the brain
  - Tends to be under emphasized which is a bad thing…

Five physiological steps of nociception

1. Transduction
2. Transmission
3. Primary modulation/segmental modulation
4. Projection
5. Perception/suprasegmental modulation

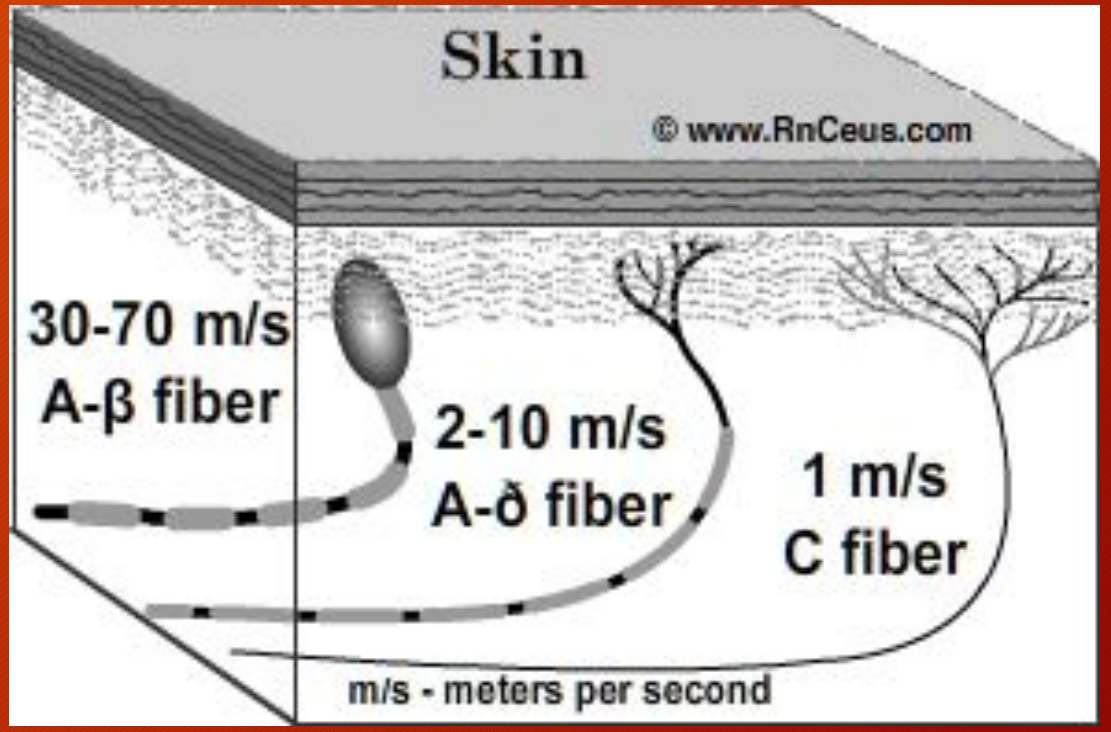
Process of nociception

- Transduction
  - Aβ, Aδ, c-Fibers, silent,
- Transmission
  - Dorsal horn, CNS
- Primary (segmental) modulation
  - Segmental reflexes
- Projection
- Perception (supra-seg modulation)
  - Conscious (pain, memory, emotions avoidance)
  - Unconscious (ANS, PAG)
- Humans/animals



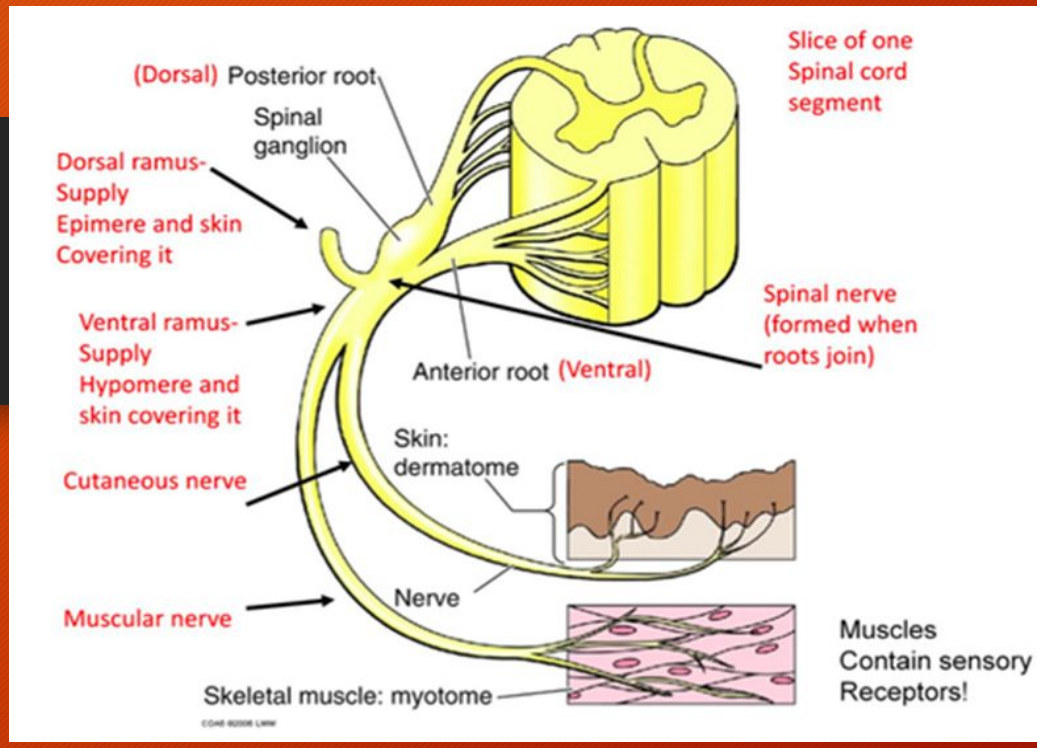
Transduction

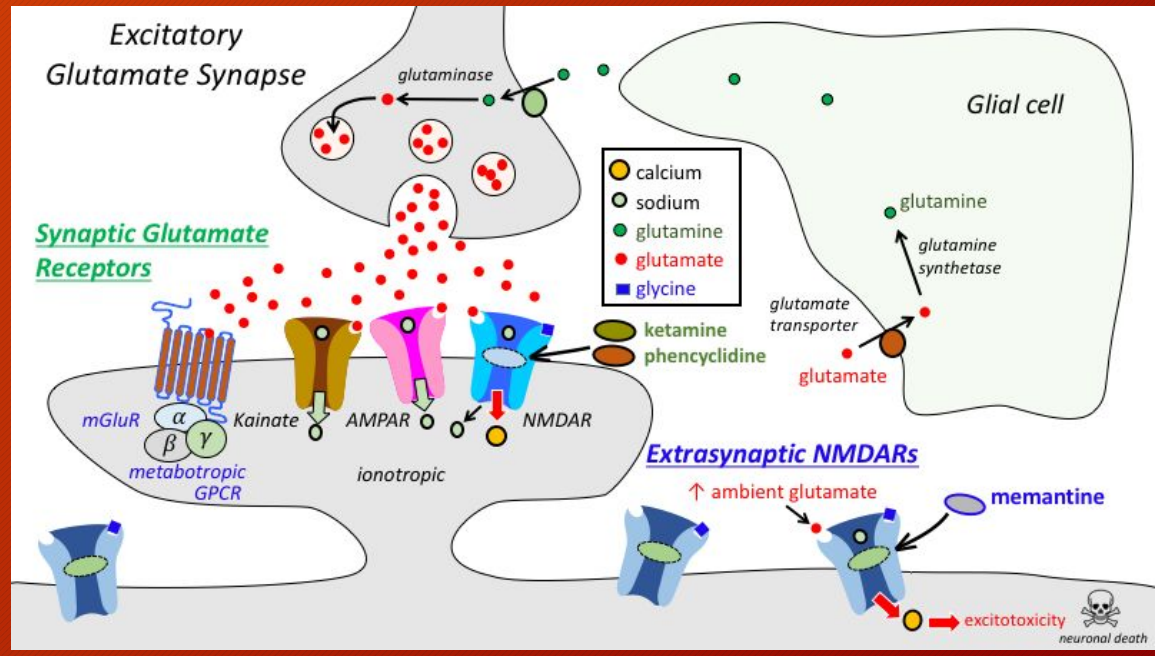
- Many subclasses of nociceptors with mechanical versions being the most prominent but least understood.
- A-δ fibers
  - Myelinated, thin
  - Rapid, quick noxious sensory
- C-fibers
  - Unmyelinated, very thin
  - Throbbing, slow noxious sensory
- Silent fibers
  - Inactive C-fibers
- A- β fibers
  - Tactile sensory
  - Can be recruited -> C-fibers



Transmission

- Nerve supplying the dermatome
- Dorsal root ganglion
- Dorsal horn spinal cord
- Glutamate – AMPA receptor
  - Protective, healthy nociception
- Glutamate – NMDA receptor
- Substance P – NK1 receptor
  - Windup or central nociception

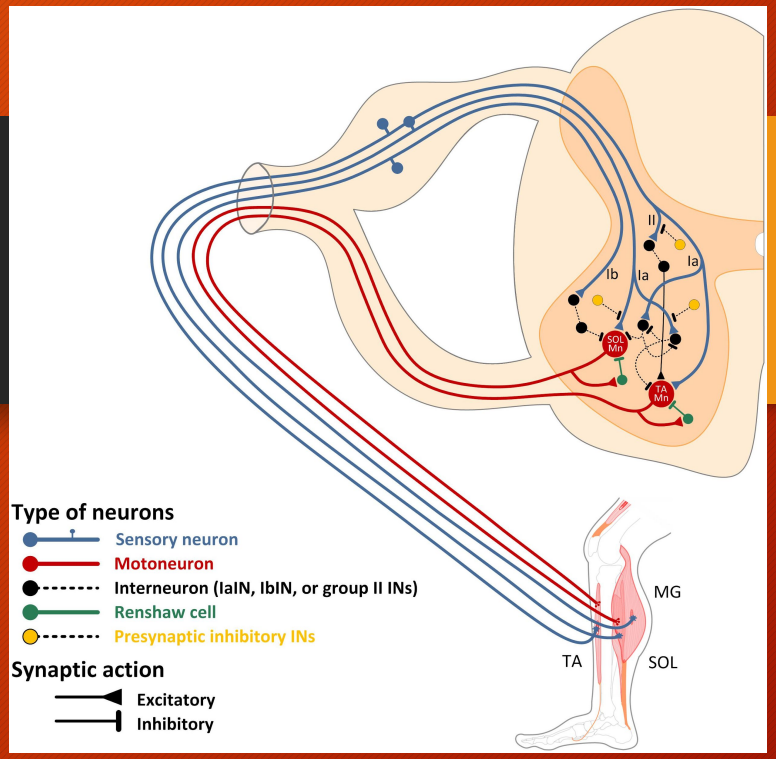


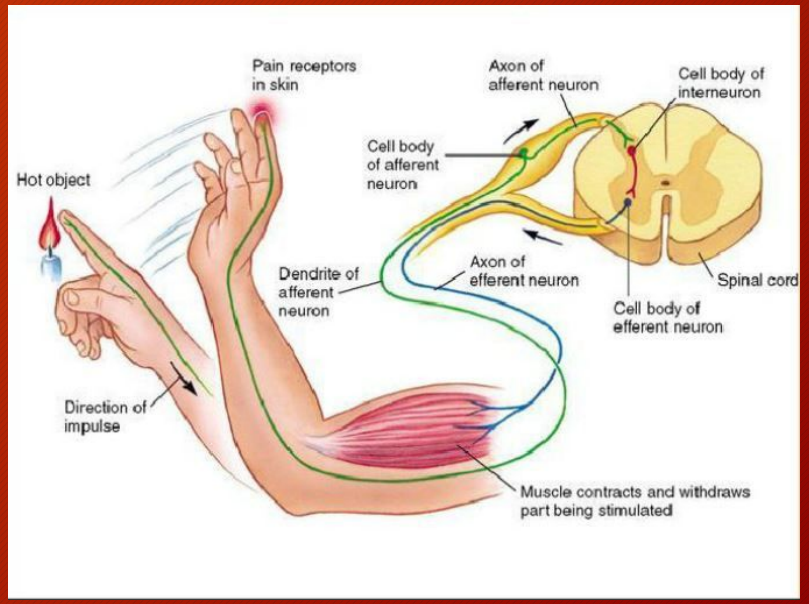


Primary/segmental modulation

- Spinal reflex
  - Withdrawal reflex
- Interneuron
  - Sensory processing
  - Inhibition
- Interneuron
  - Segmental/gate processes
- Most noxious afferent -> lamina II
  - Lamina I also but excitatory
  - Proprioception too
- NGF plays a role in central excitatory
- WDR fiber (conversion neurons) muti-receptive -> lamina IV -> RAS/thalamus
- Primary processing is spinal with control

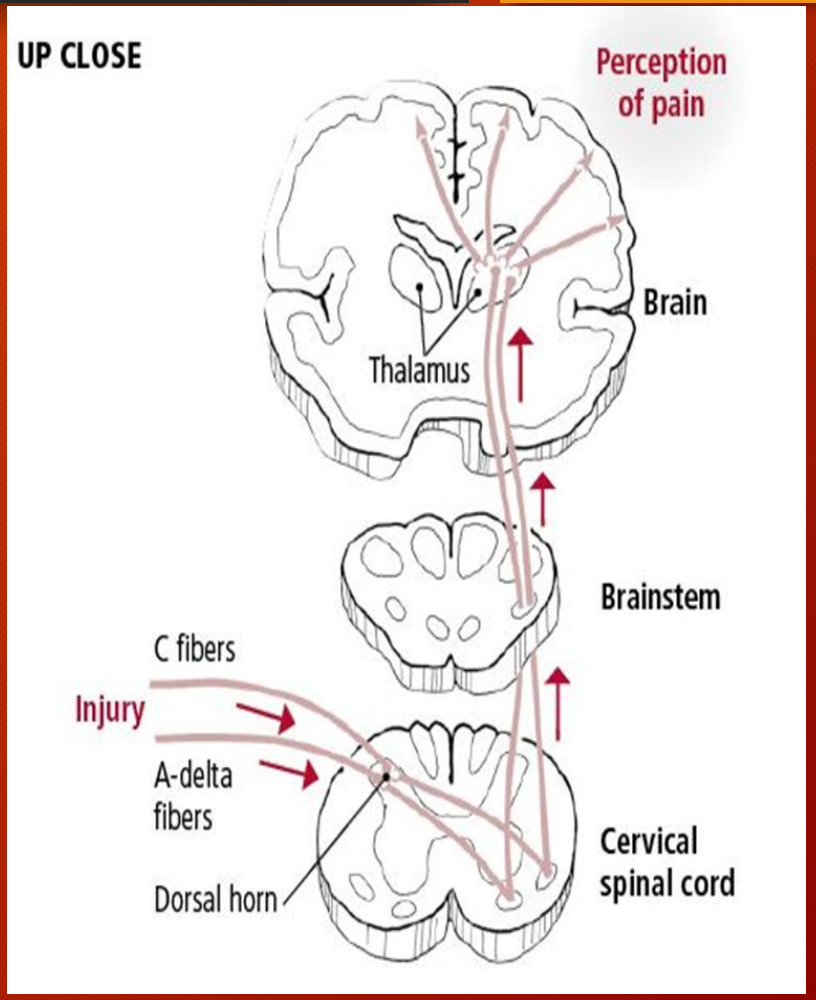
NGF!!



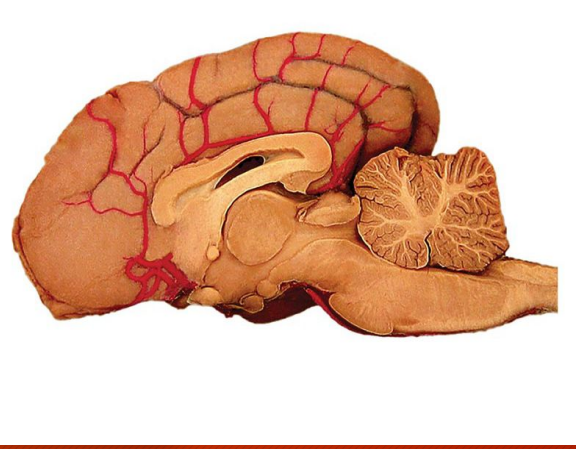


Projection

- Spinal tracts
  - Processed sensory info to brain
- Two primary tracts for nociception
  - Spinothalamic tract
    - Sensory discriminative
  - Spinoreticulothalamic/spinobulbar tract
    - Sensory indiscriminate
- Descending pain modulation
  - PAG
  - Rostral Ventral Medulla (RVM)



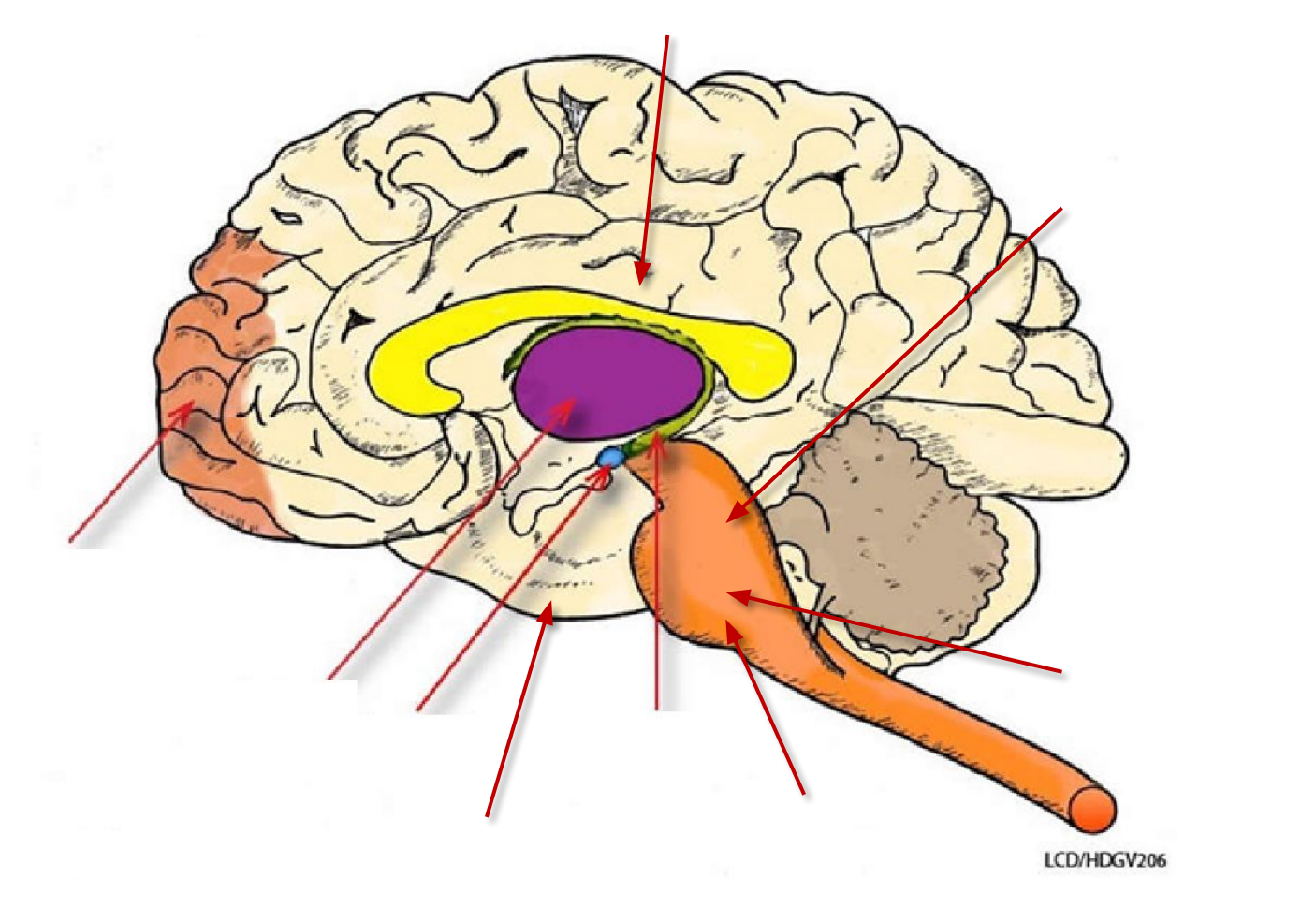
Supra-segmental modulation, perception



- Conscious components
  - Pain
  - Memory
  - Emotions
  - Avoidence
- Consciousness does not exist during GA
  - Pain not exist during GA
  - What about the rest of nociception?

- Unconscious component
  - Autonomic
    - PNS
    - SNS
  - Neurochemical
    - Norepinephrine
    - Serotonin
  - Pain modulation
    - PAG (-> release norepi, serotonin, endocannabinoids)
    - RVM (final say)

Perception



- Cortex
  - Perception
- Thalamus
  - Integration
- Cingulate gyrus
  - Behavior, Emotions
- Periaqueductal gray
  - Modulation
- Locus coeruleus
  - Arousal, vigilance
- Reticular formation
  - Antinociception, integration
- Hippocampus
  - Memory
- Hypothalamus
  - ANS
- Amygdala
  - Fear, anxiety

Temporal Classification of Pain

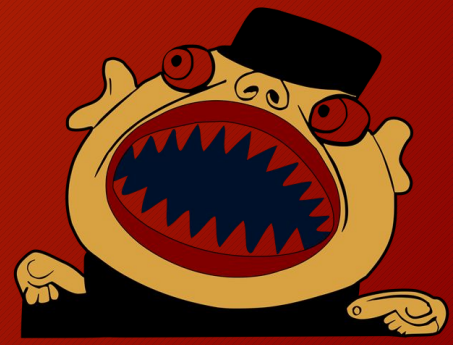
- Acute
  - Hours to days
  - Pain that follows injury, disappears w/ healing
  - Self-limiting
- Chronic
  - Weeks to months
  - Pain that persists beyond normal healing time when non-malignant in origin
  - Chronic pain is NOT long-standing acute pain!!

"Chronic pain is acute pain that was ineffectively treated…"

When good pain goes bad

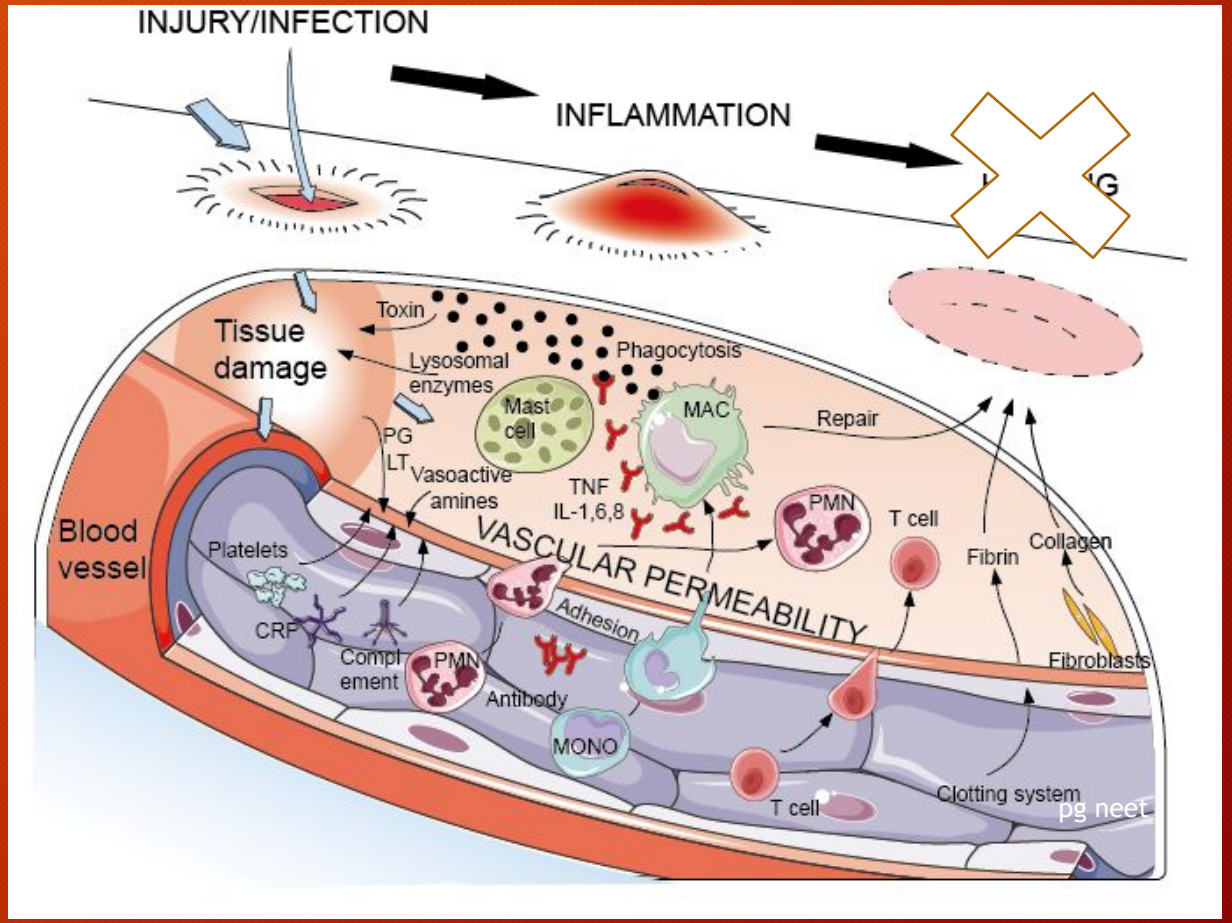
- Hypersensitization
- Peripheral sensitization/wind-up
- Central sensitization/wind-up
- Allodynia
  - Peripheral
  - Central

- Three major pathophysiological process occur that help magnify the process of nociception both peripheral and central.
  - Loss of inhibitory complexes
  - Recruitment
  - Neuroplasticity



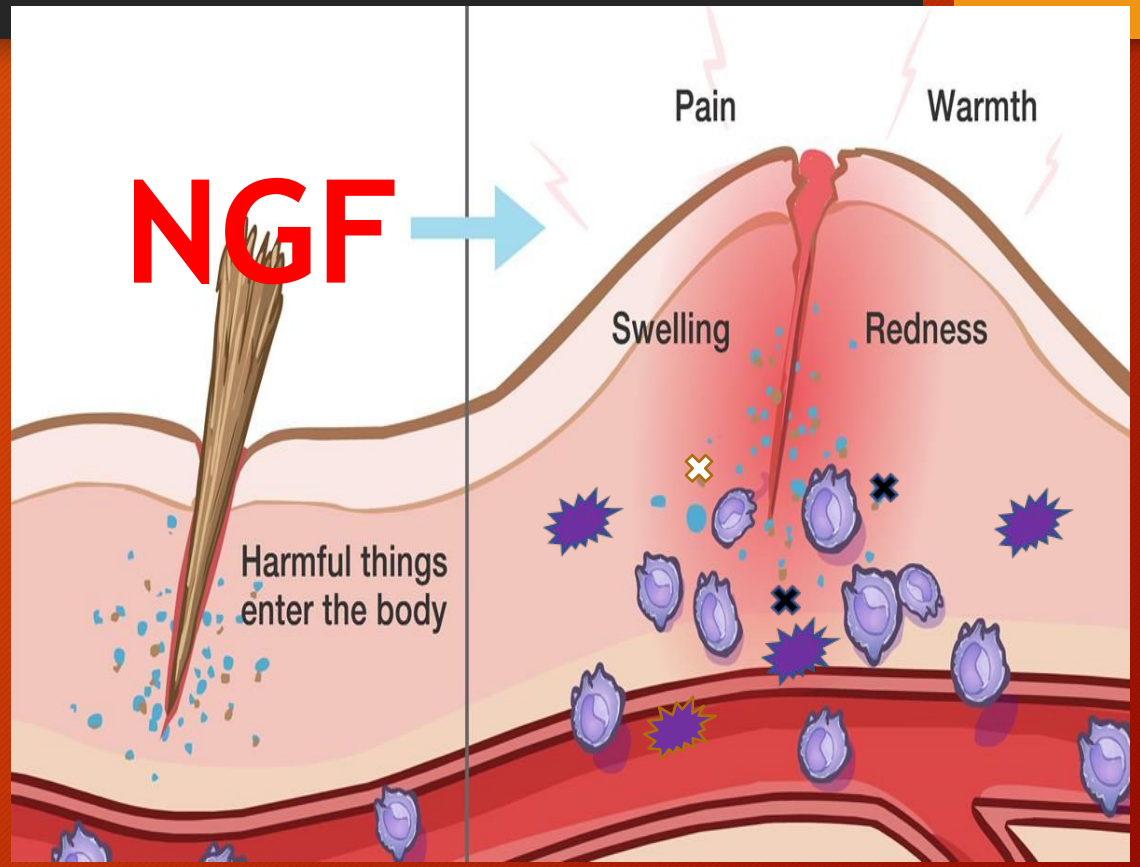
Peripheral sensitization/wind-up

- Inflammatory processes
  - Under physiological conditions inflammation tends to be self-limiting and not insidious to the body.
  - Eventually -> repair
  - Anti-inflammatory modalities help this process
  - With extreme forms of inflammation, inflammation that is not well managed, the inflammation becomes self-generating.
  - Self-generating inflammation leads to a state of hypersensitization
  - Repair is delayed
  - Peripheral hypersensitivity/allodynia



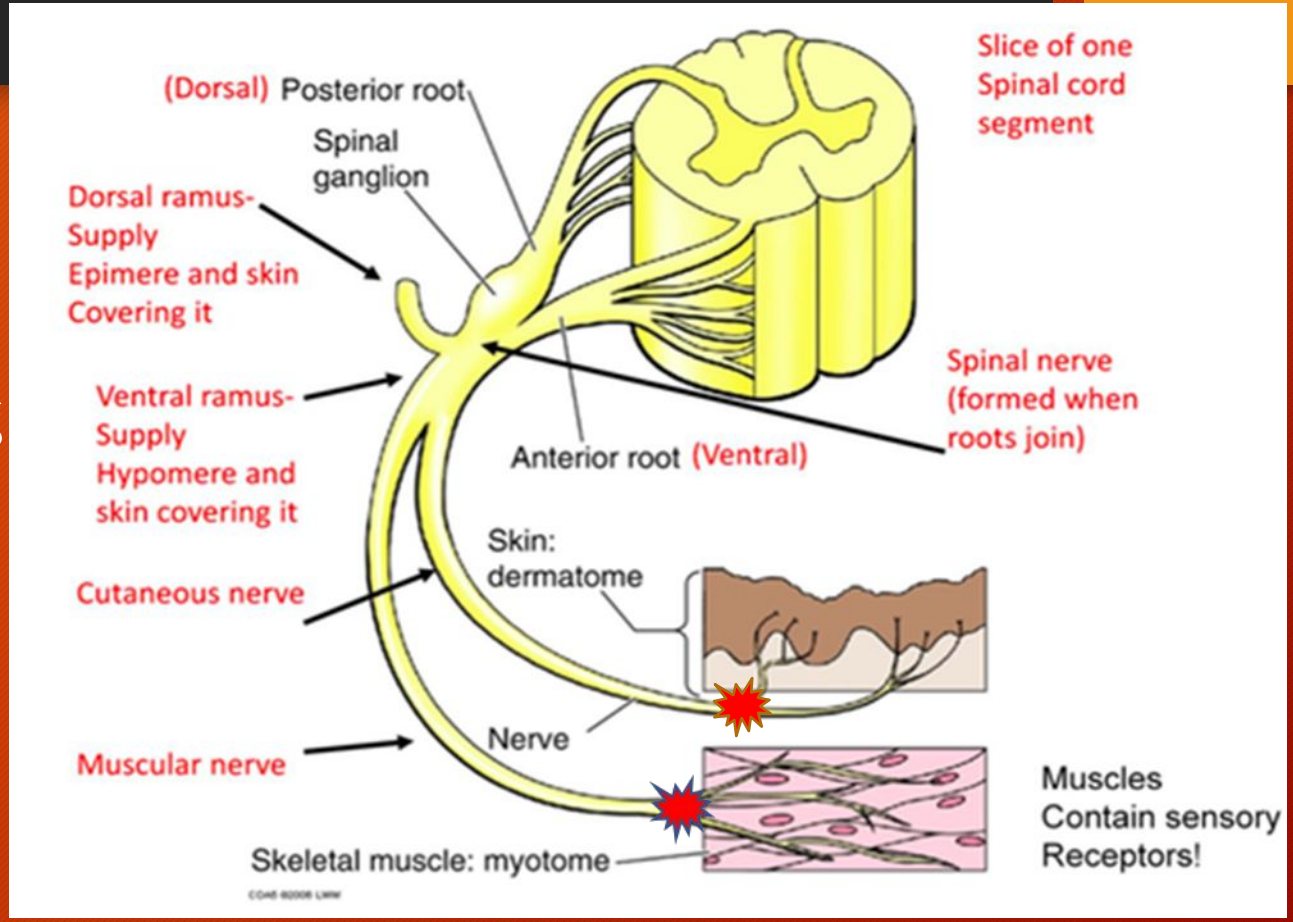
Peripheral sensitization/wind-up

- Loss of inhibitory complexes
  - Mediators that help regulate inflammation are overwhelmed
- Recruitment
  - Increase numbers of pro-inflammatory complexes, cells, etc.
- Neuroplasticity
  - Aß nociceptors -> c-nociceptors fibers
  - Silent fibers -> c-nociceptor fibers
- Peripheral NGF plays significant role



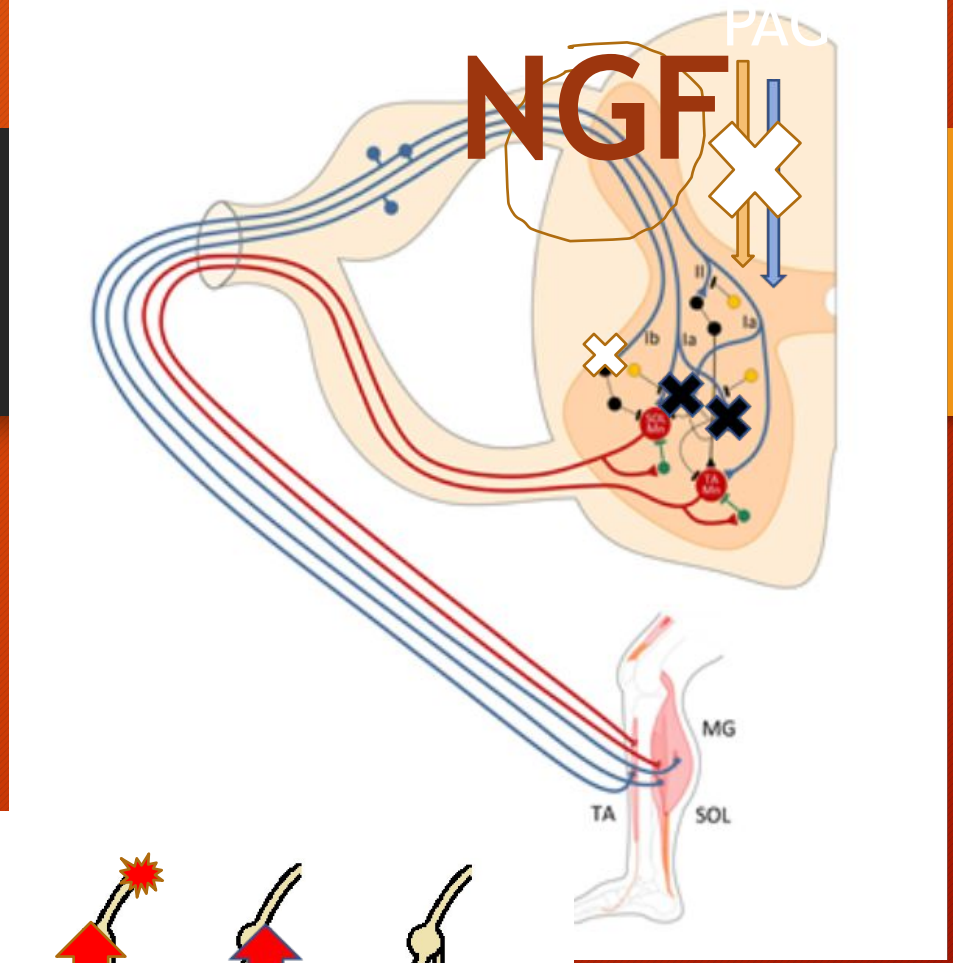
Central sensitization/wind-up

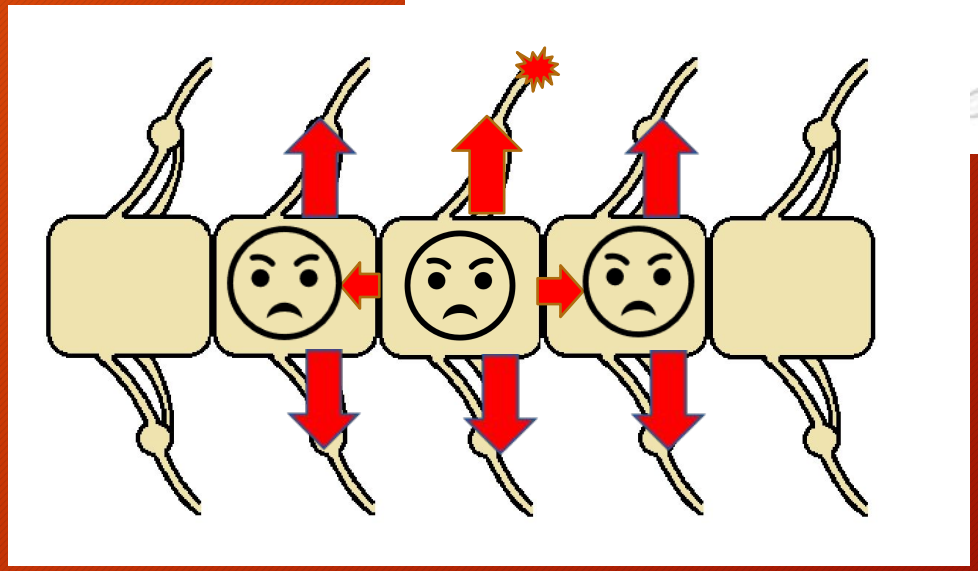
- Peripheral sensitization increases the frequency and degree of afferent noxious impulses delivered by c-nociceptor fibers bombarding dorsal horn of spinal cord.
- Neuropathic injury
  - Does not necessarily require peripheral sensitization



Central sensitization/wind-up

- Neuroplasticity
  - Glutamate-AMPA switch to Glutamate/Subst P-NMDA/NK1.
  - Inhibitory interneurons switch to enhancing.
  - Central NGF enhances this transition
- Loss of inhibition
  - Loss of inhibitory interneurons
  - PAG zone decreases inhibition
- Recruitment
  - Primary spinal cord segment recruit adjacent spinal segments -> hypersensitized





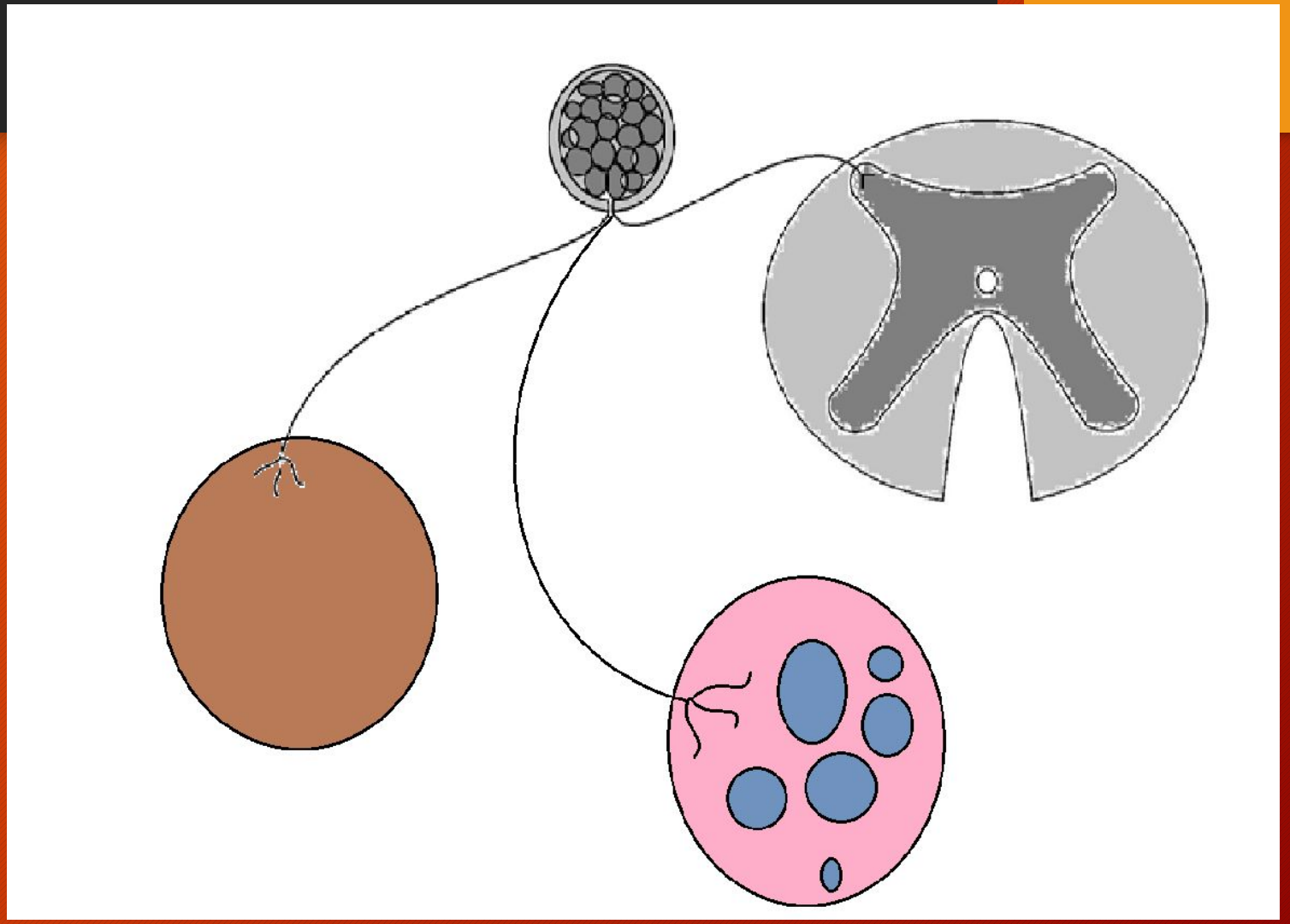
What happens if…?

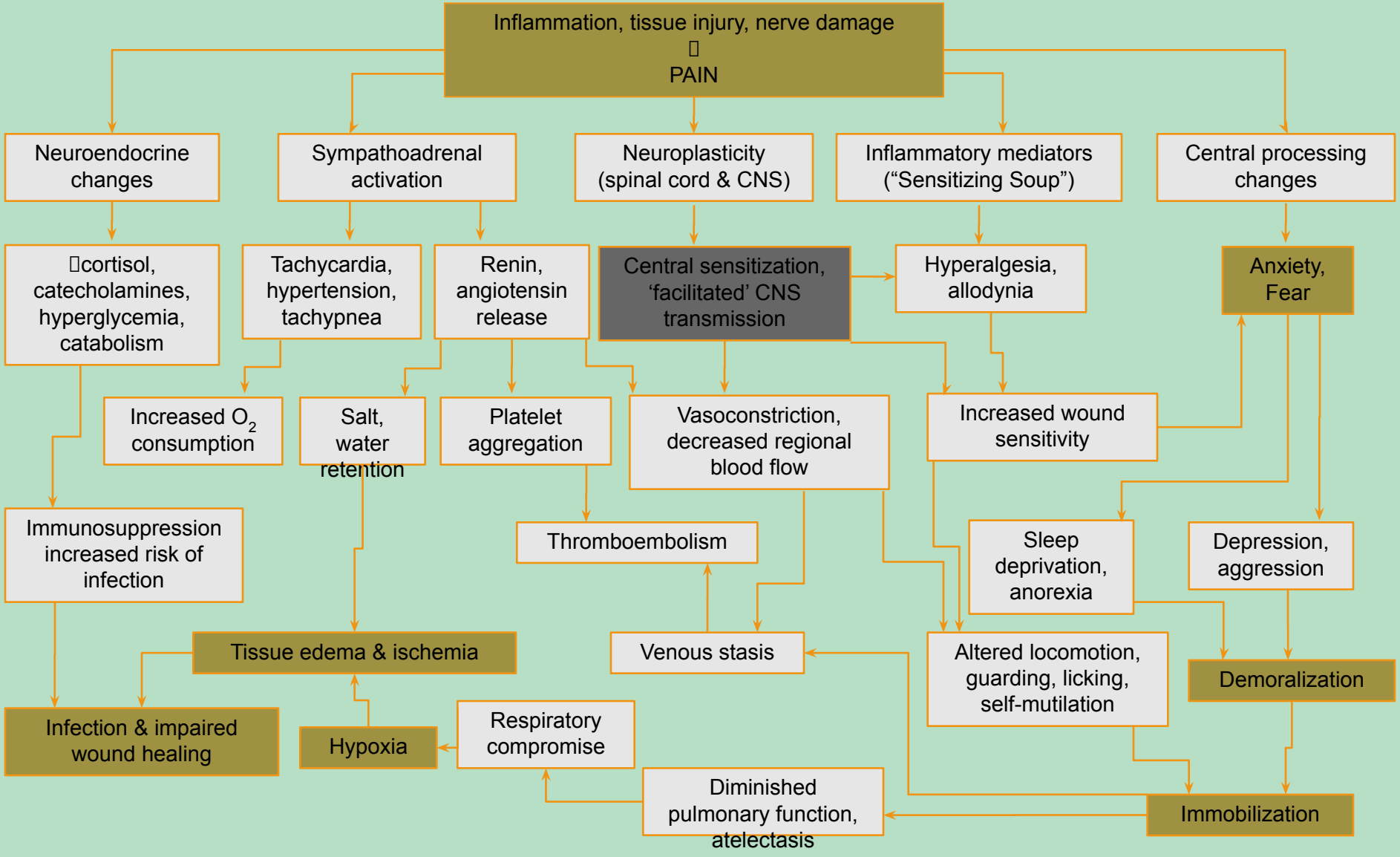
- Peripheral Wind-up
  - Injury
  - Inflammatory soup
  - Silent nociceptors
  - Conversion Aß fibers
  - NGF
  - Hyperalgesia
- AMPA-Glutamate
- NMDA-glutamate

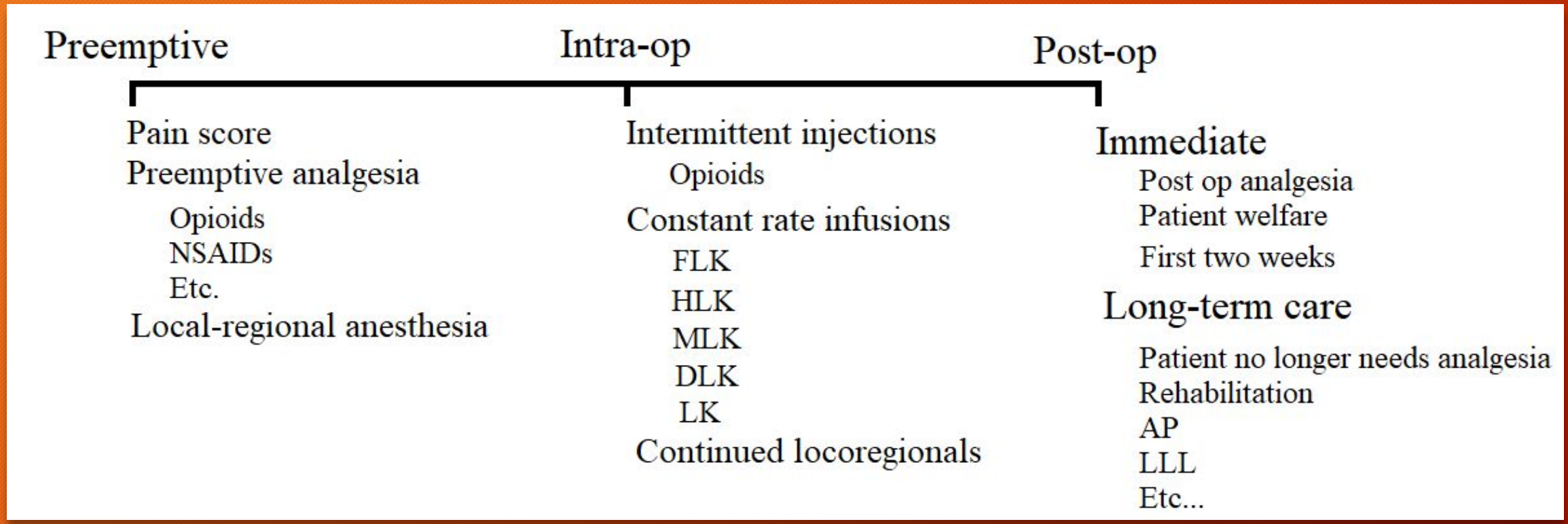
- Central Wind-up
  - Subst-P – NK1
  - NGF
  - Loss of inhibition
  - Multi-segmental allodynia
- Neuropathic nociception

Maladaptive/chronic/windup

- Peripheral wind-up
- Centralized wind-up
- Chronic pain
- Somatovisceral reflexes
- Viscerosomatic reflexes
- Maladaptive/dysfunctional pain
  - QOL
  - Debilitating




Inflammation, tissue injury, nerve damage
PAIN
Neuroendocrine changes
Sympathoadrenal activation
Neuroplasticity (spinal cord & CNS)
Inflammatory mediators ("Sensitizing Soup")
Central processing changes
cortisol, catecholamines, hyperglycemia, catabolism
Tachycardia, hypertension, tachypnea
Renin, angiotensin release
Central sensitization, 'facilitated' CNS transmission
Hyperalgesia, allodynia
Anxiety, Fear
Increased O_2 consumption
Salt, water retention
Platelet aggregation
Vasoconstriction, decreased regional blood flow
Increased wound sensitivity
Immunosuppression increased risk of infection
Thromboembolism
Sleep deprivation, anorexia
Depression, aggression
Tissue edema & ischemia
Venous stasis
Altered locomotion, guarding, licking, self-mutilation
Demoralization
Infection & impaired wound healing
Hypoxia
Respiratory compromise
Diminished pulmonary function, atelectasis
Immobilization

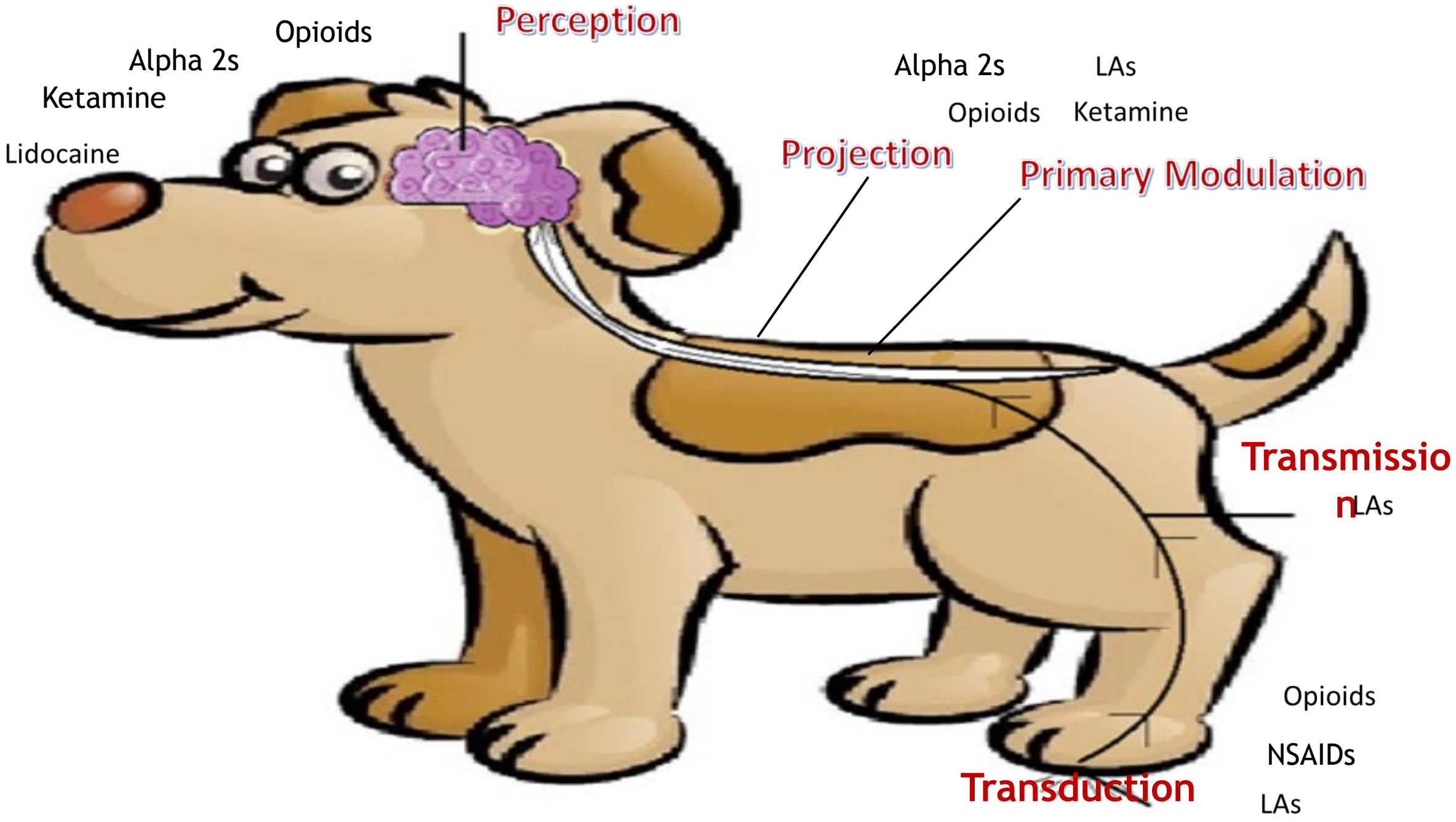


Preventive analgesia

Multimodal Analgesia

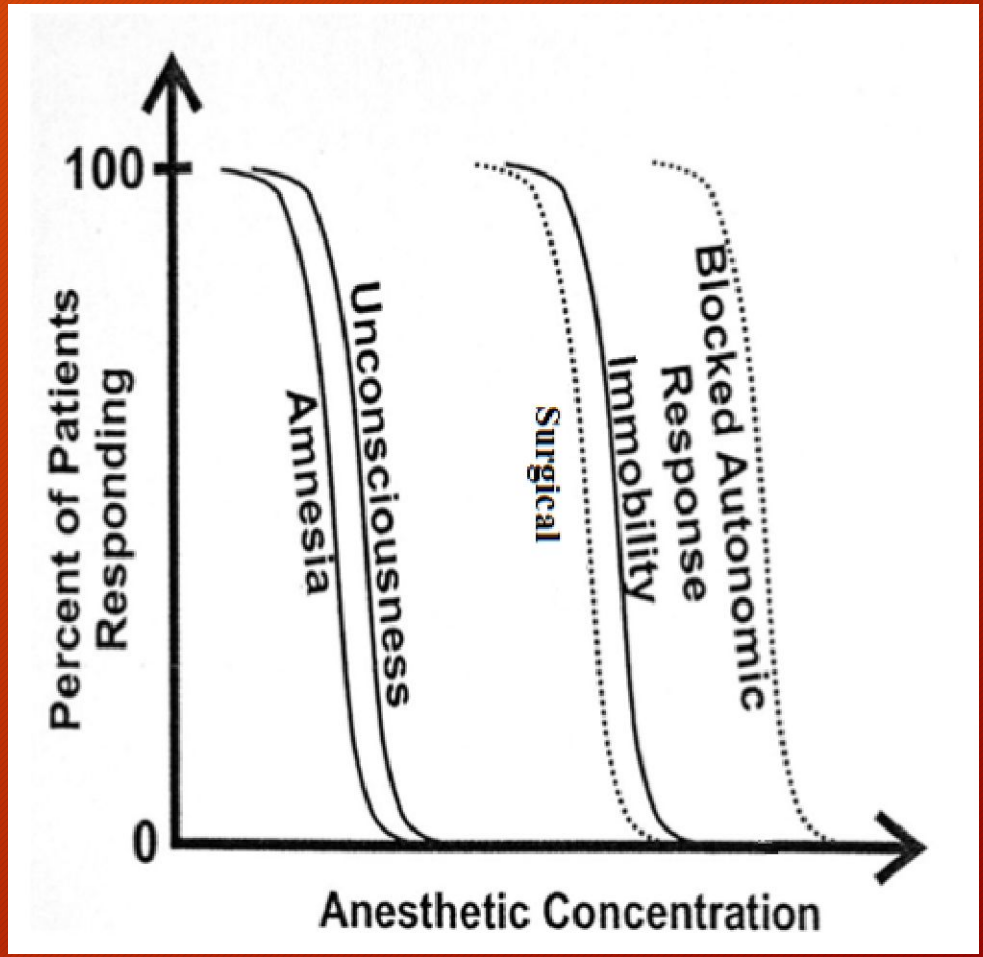
Pain management: Pharmacological

- Opioids
  - Inhibit glutamate release at dorsal horn of SC
  - Effects in brain; decrease symp tone
- Alpha 2 agonists
  - Like opioids
  - Profound effects in brain
  - Muscle relaxation
- NMDA antagonists
  - Dorsal horn SC
  - Some effect the brain (ketamine)
  - Includes amantadine
- Local anesthetics
  - Fast Na+ channel blocking drugs
  - Local and regional anesthesia
- NSAIDs
  - COX inhibitors
  - Peripheral inflammation
- Misc
  - Benzodiazepines
    - NOT analgesics
    - Muscle relaxation
  - Gabapentin
  - Maropitant


Perception
Opioids
Alpha 2s
Ketamine
Lidocaine
Alpha 2s
LAs
Opioids
Ketamine
Projection
Primary Modulation
Transmission
LAs
Opioids
NSAIDs
LAs
Transduction

MAC…..the reality!!!

- Degree of stimulus
  - MAC awake
  - MAC for intubation
  - MAC no movement
  - MAC-BAR
  - MAC-BAR = MAC-NM?
- Iso > 2%
- Sevo > 2.5%



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Questions & Discussion