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PRESBYTERIAN COLLEGE
SCHOOL of PHARMACY

THE PAIN SOCIETY OF THE CAROLINAS

Central Sensitization

Pathophysiology of Chronic Pain

International Association for the Study of Pain®

PAIN

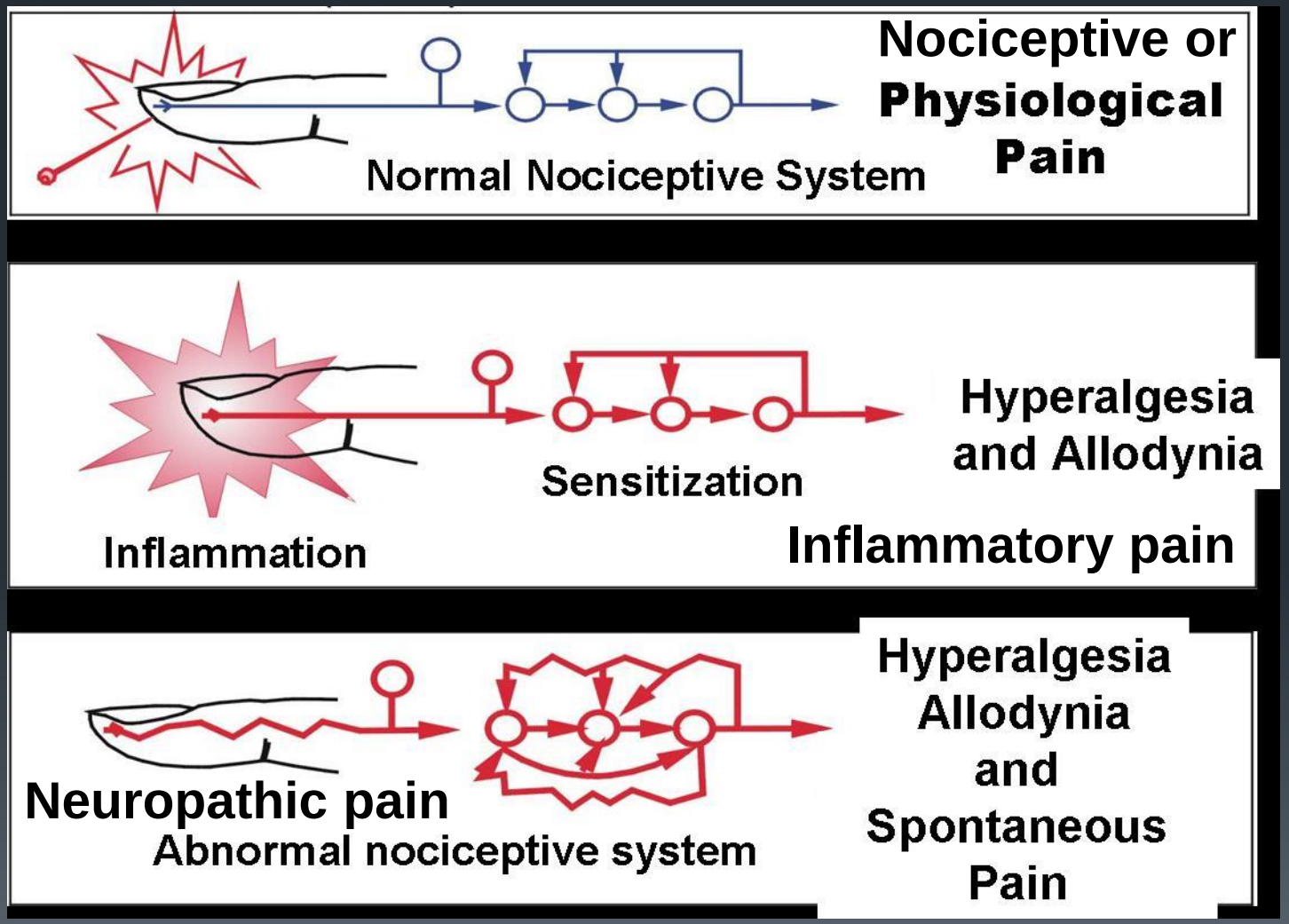
An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage

NOCICEPTION

The activity produced in the nervous system by potentially tissue-damaging stimuli (activation of nociceptors)

Types of Pain

Types of Pain



Cervero y Laird en 1991

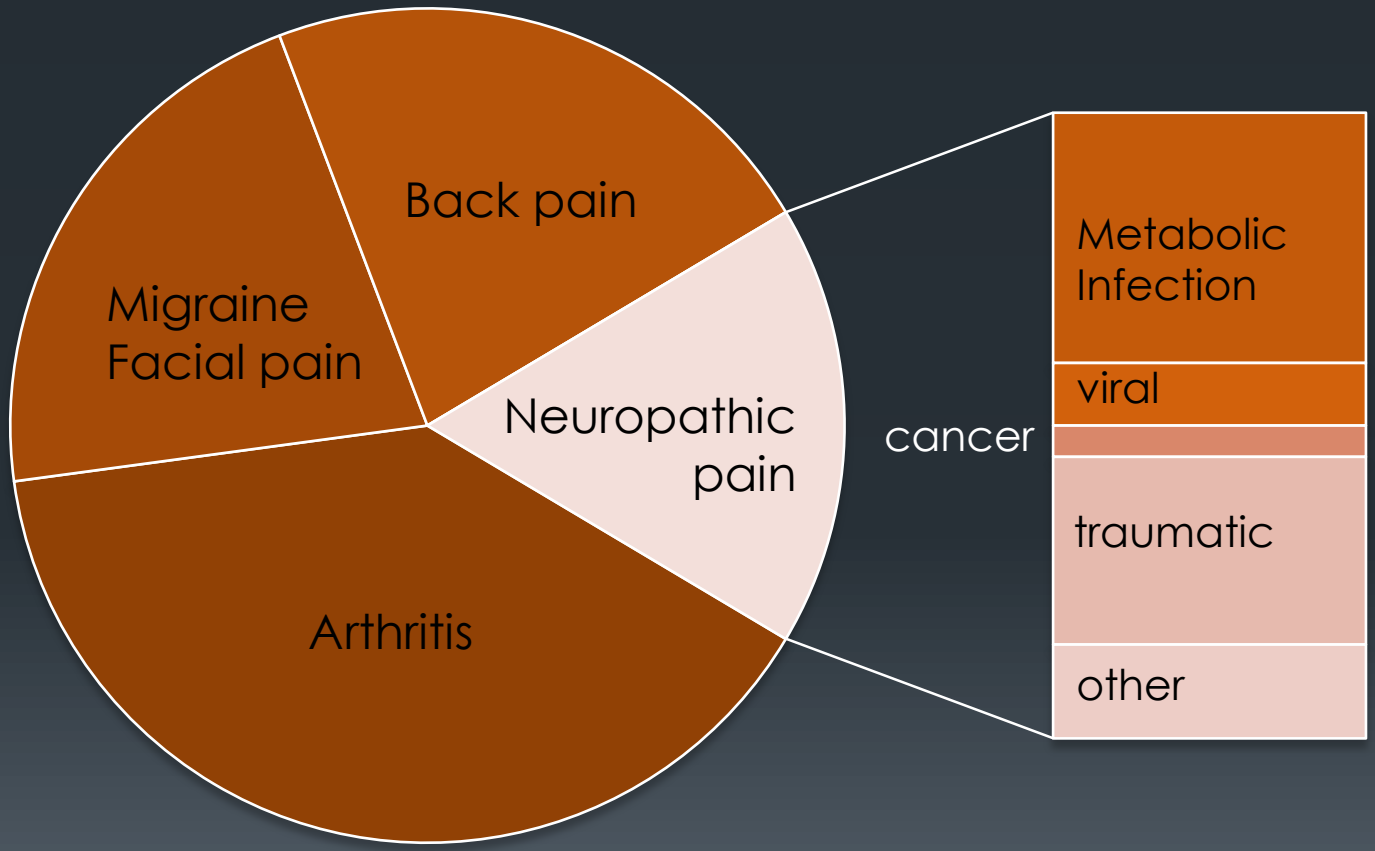
Acute Pain vs. Chronic Pain

- Signals tissue Injury
- Cause usually obvious
- Rest / Immobilize
- Disappears with Treatment
- Opioids effective usually
- No secondary gains
- Adrenergic – Fight or Flight / anxiety

- Serves no useful function
- Cause is often unclear
- **Involves central sensitization**
- Often unresponsive to many forms treatment
- Opioids: Effective?
- Secondary gains?
- Learned behaviors
- Vegetative signs - depression

Chronic Pain

116 million Americans (25% of population)



Diabetes
Alcohol

Post-herpetic neuralgia, HIV/AIDS

Tumor pain
Chemotherapy

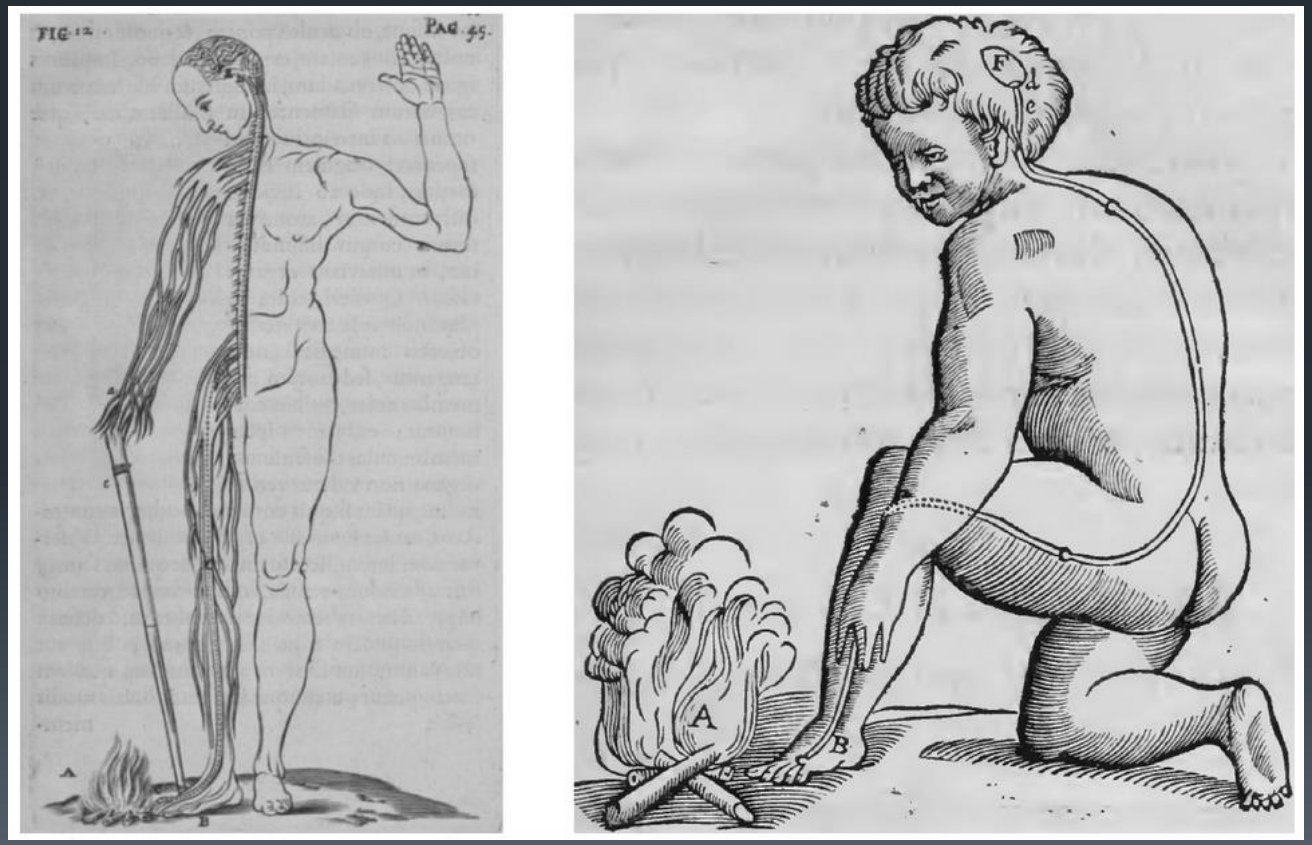
Nerve entrapment
CRPS
Spinal cord injury
Phantom limb pain

Post-stroke
MS, GB
Trigeminal neuralgia

Annually $560-635 billion in direct and in-direct costs

The Nociceptive Pathways

Descartes first described a "nociceptive pathway" in 1664



From René Descartes. L'homme.

The Nociceptive Pathways

- Peripheral sites:

  Nociceptors (free nerve endings)

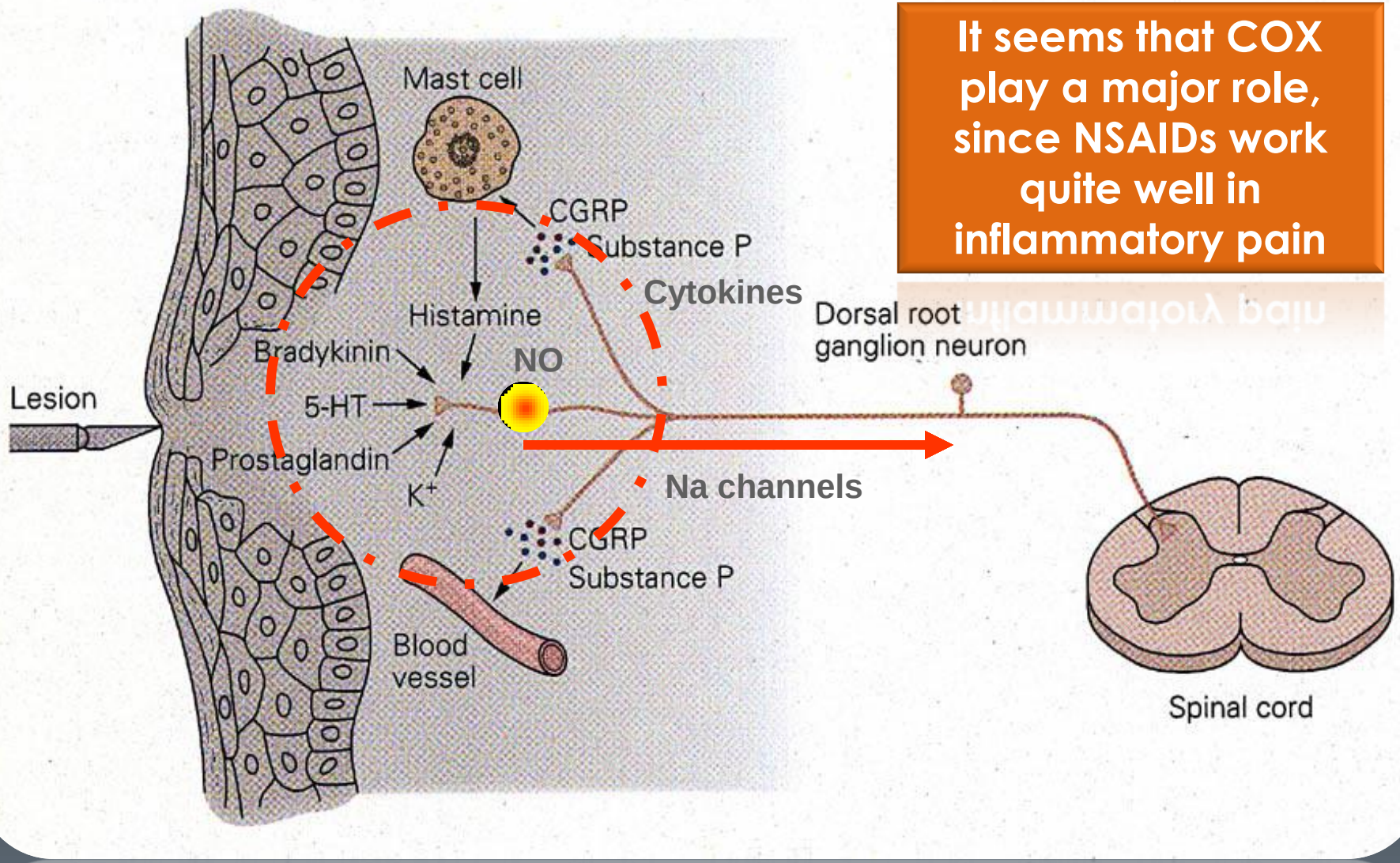
- Spinal Cord:

  The “Gate” of pain control

- Supraspinal (Brain):

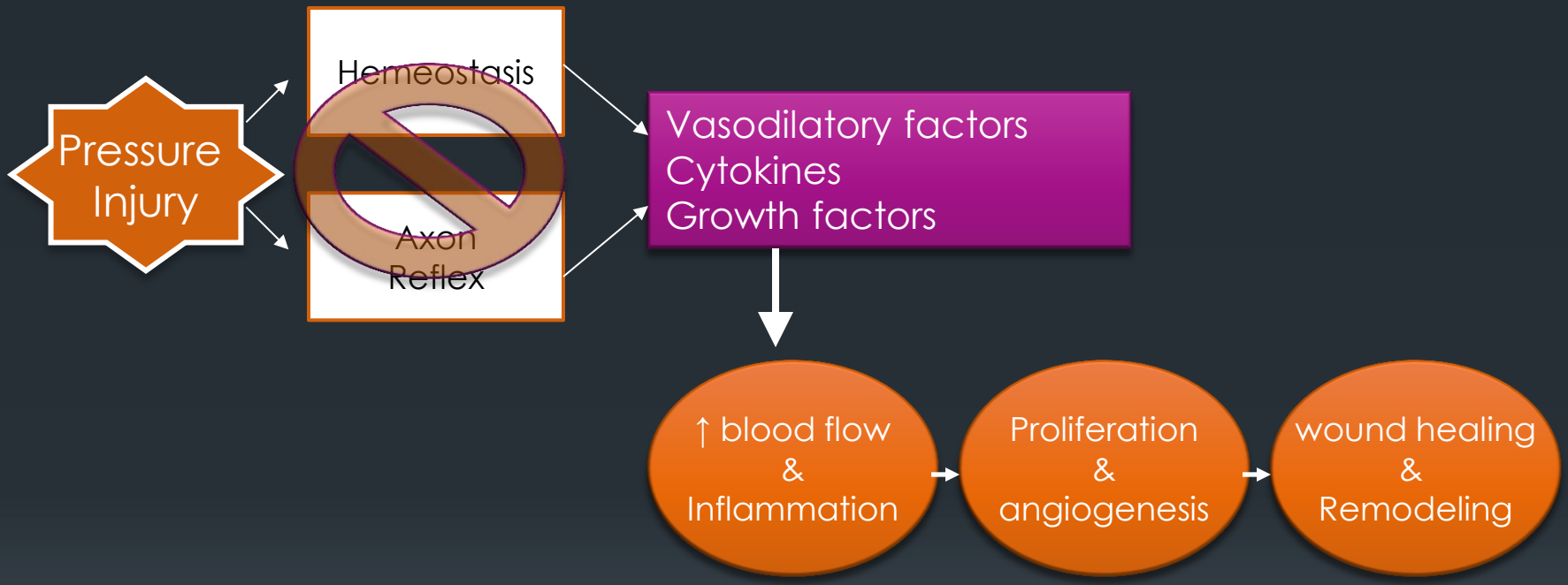
  Perception, previous experience, stress, emotions, etc.

The Periphery



Neurogenic inflammation

- Initiation of Wound Healing

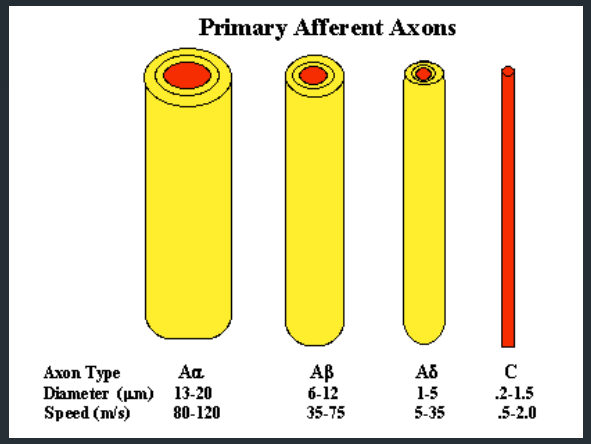


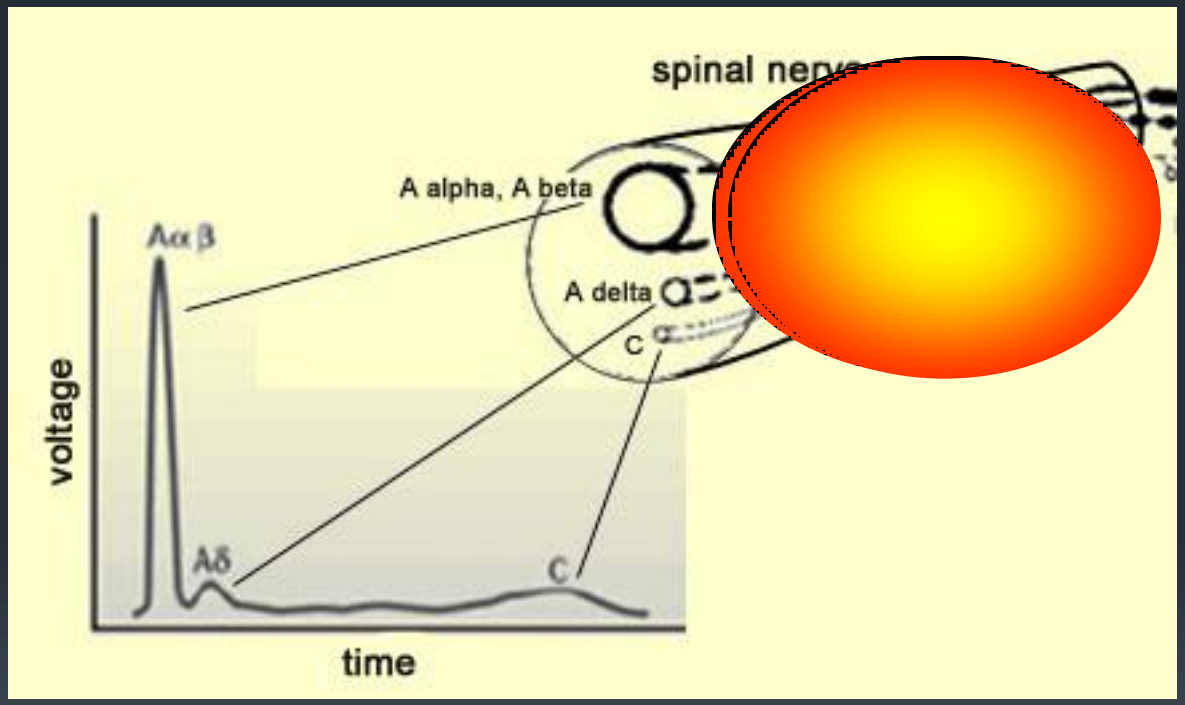
- On-going pain (peripheral sensitization) prevents re-injury

dysfunction → Neuropathy (100% of ulcers)

The Periphery

Peripheral nerve fiber



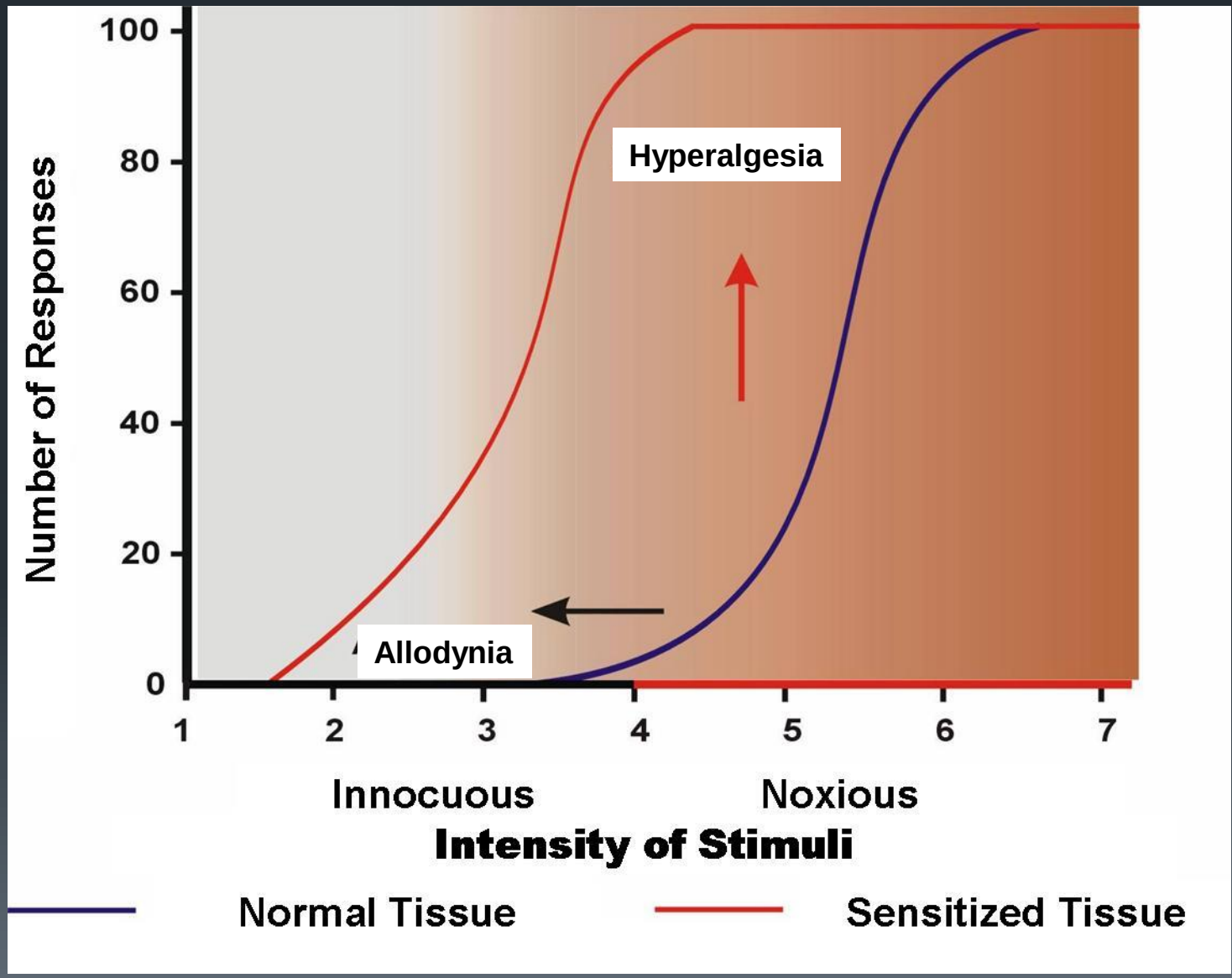


Do not respond to painful stimulation, but just to innocuous stimulation

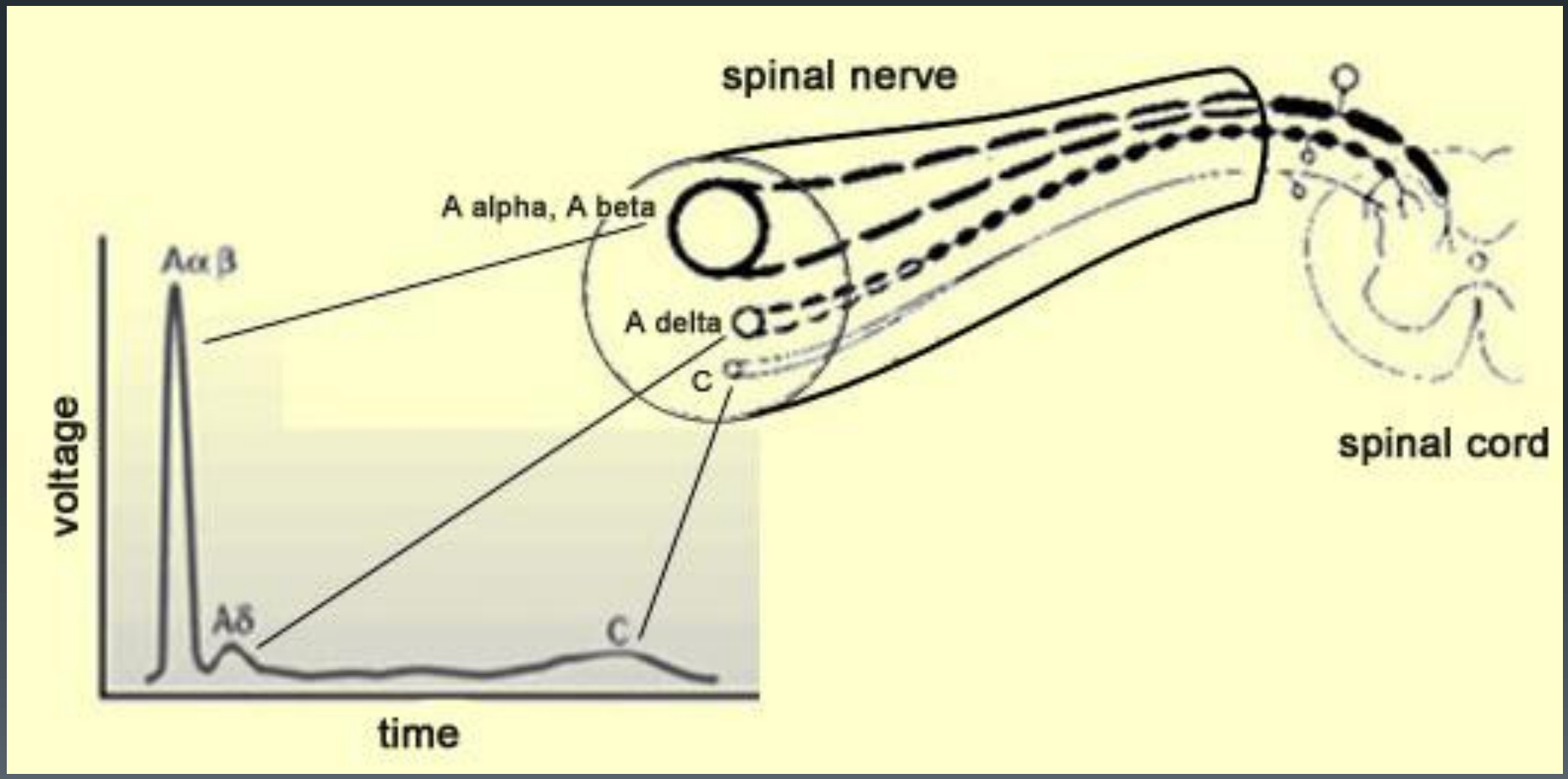
When active, they reduce pain sensation

Respond to painful stimulation → Now they respond to innocuous stimulation

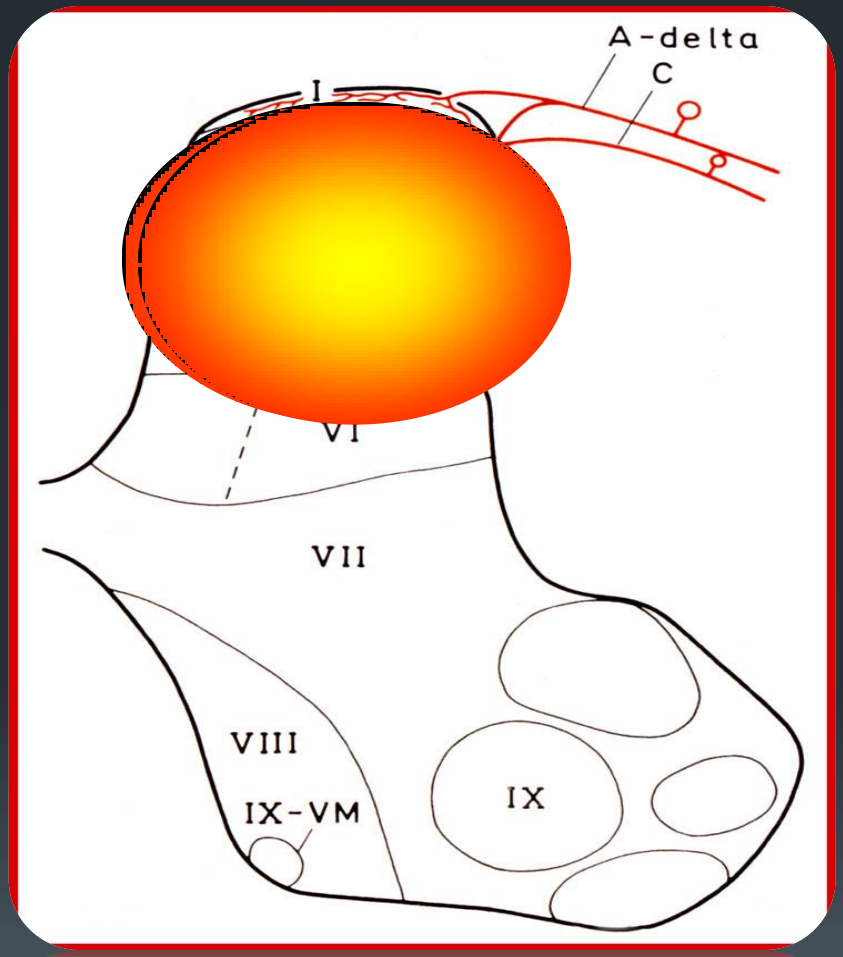
The Periphery



The Periphery

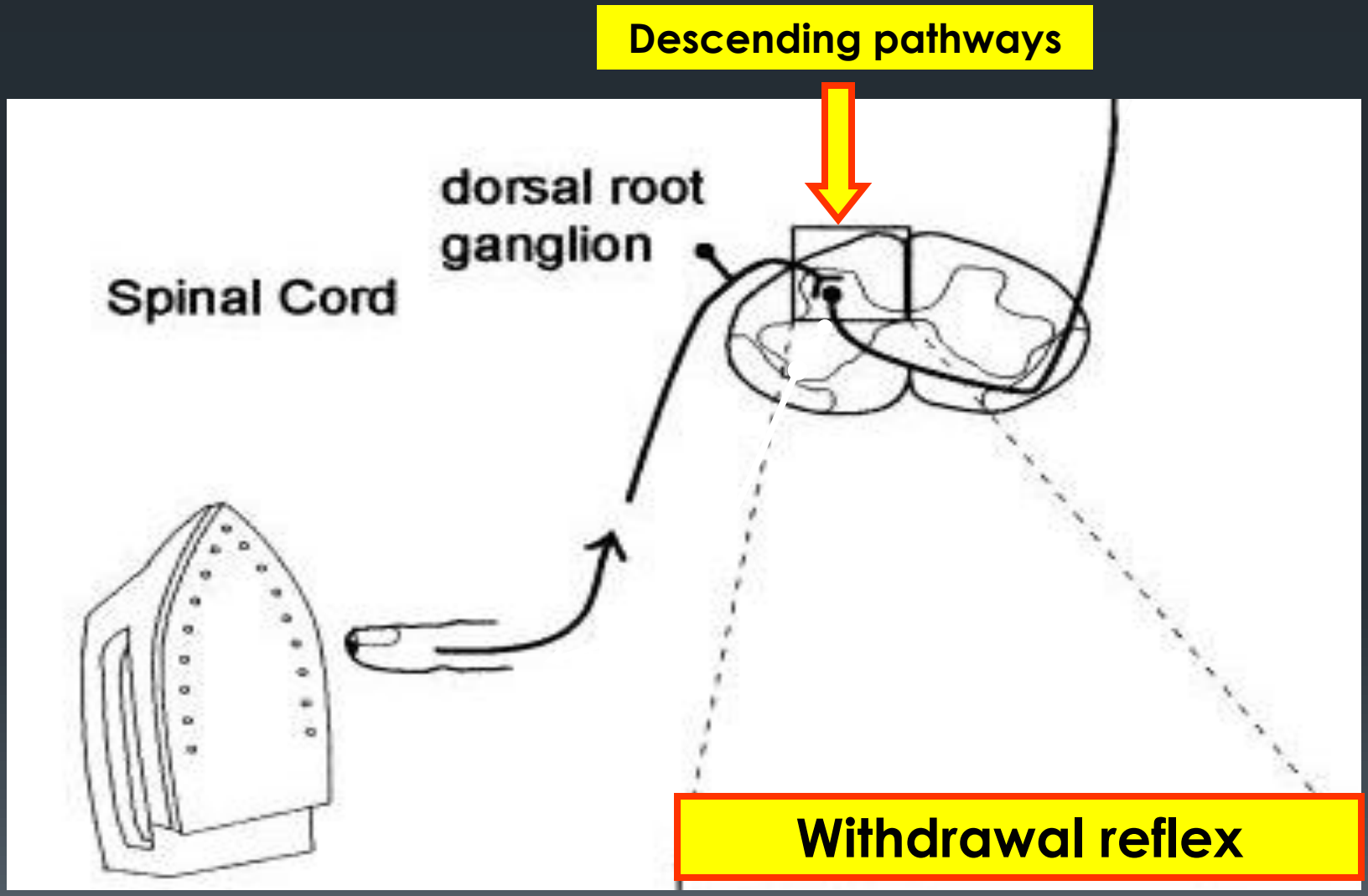


The Spinal Cord



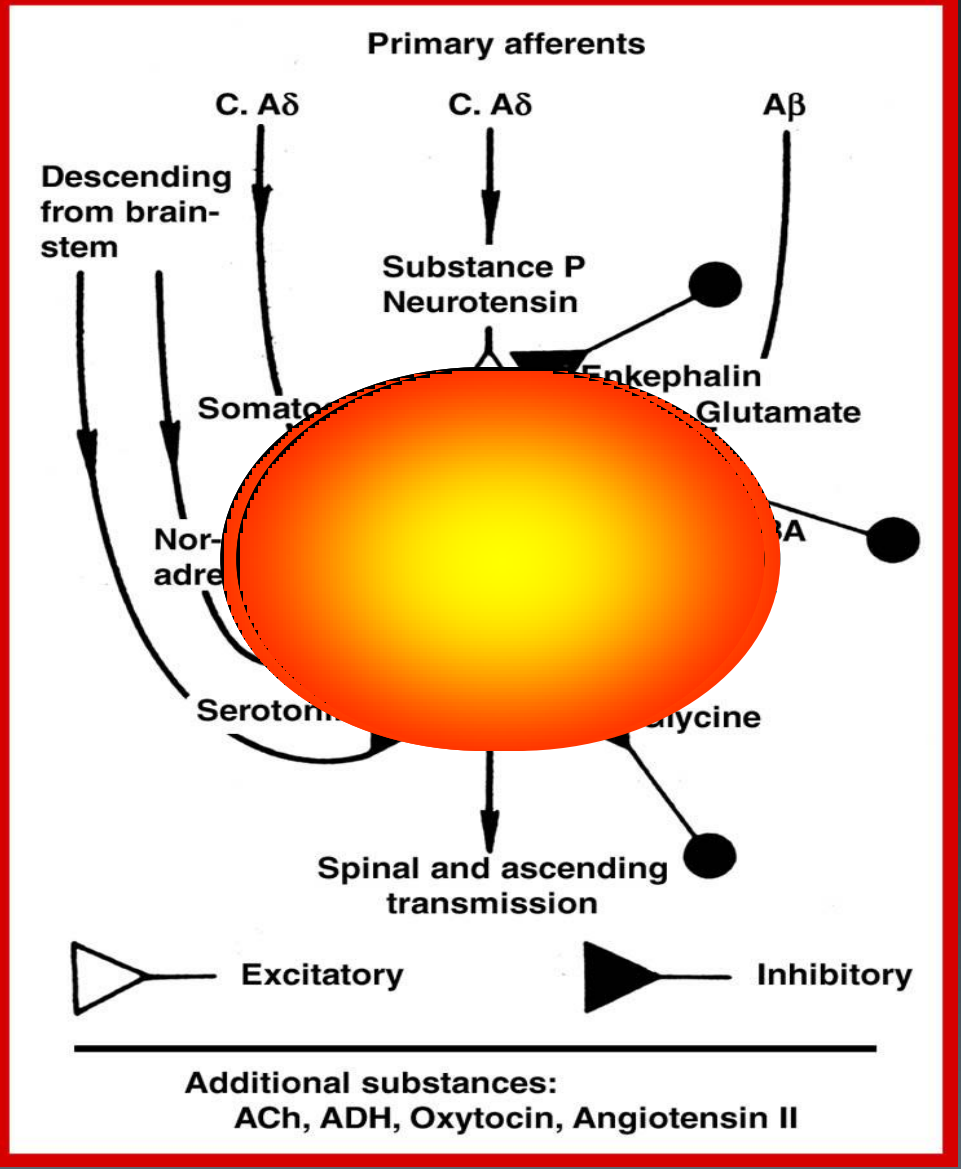
http://youtu.be/5g2crxb-PJs

The Spinal Cord



Modified from: Cheryl L. Stucky, Michael S. Gold, and Xu Zhang
Proc Natl Acad Sci U S A. 2001 October 9; 98(21): 11845–11846

The Spinal Cord



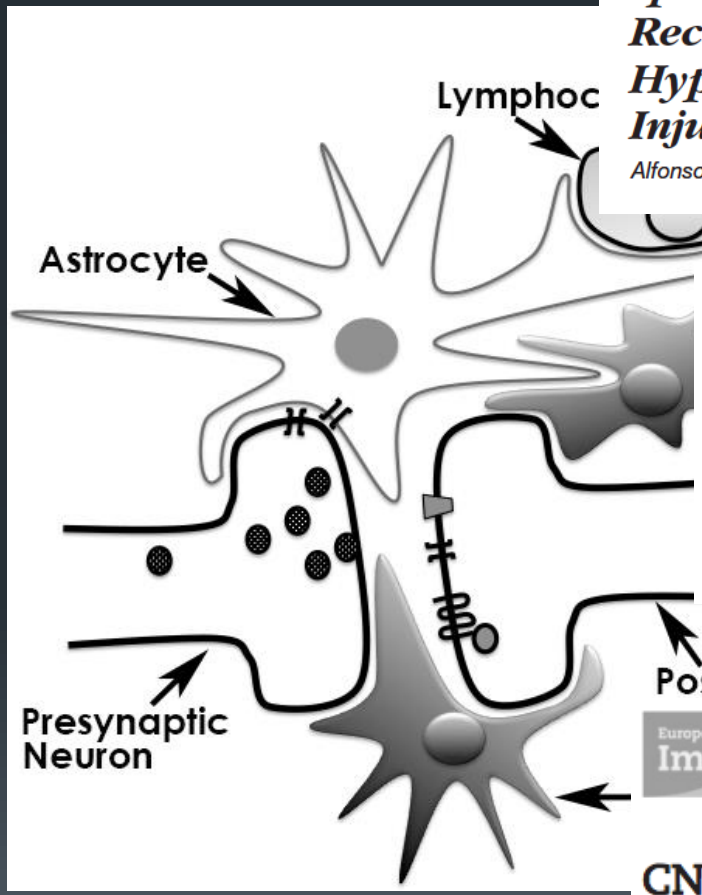
This is a key anatomical place in which central sensitization takes place due to an extended or intense barrage from the periphery

- NMDA receptors
- Voltage-gated Ca channels (a2δ subunit)
- NE
- 5-HT

No major role in CNS

•COX-2 or NK1 recep

The Spinal Cord



Anesthesiology 2008; 108:722–34

Spinal Microglial and Perivascular Cell Cannabinoid Receptor Type 2 Activation Reduces Behavioral Hypersensitivity without Tolerance after Peripheral Nerve Injury

Alfonso Romero-Sandoval, M.D., Ph.D., Nancy Nutile-McMenemy,† Joyce A. DeLeo, Ph.D.‡*

OPEN ACCESS Freely available online

PLoS one

Evidence for a Role of Endocannabinoids, Astrocytes and p38 Phosphorylation in the Resolution of Postoperative Pain

Matthew S. Alkaitis[1,2], Carlos Solorzano[3], Russell P. Landry[1,4], Daniele Piomelli[3], Joyce A. DeLeo[1,4,5], E. Alfonso Romero-Sandoval[1,4,5]*

European Journal of Immunology

CNS-infiltrating CD4⁺ T lymphocytes contribute to murine spinal nerve transection-induced neuropathic pain

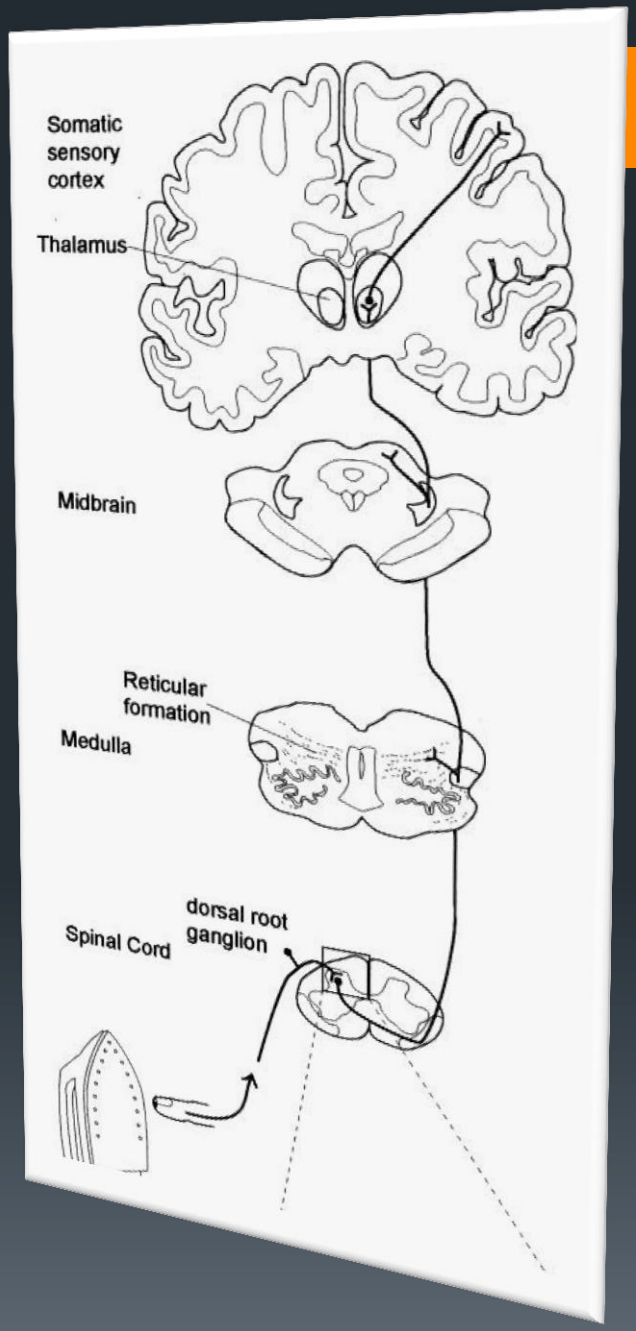
Ling Cao[1] and Joyce A. DeLeo[1,2]

The Brain

Spinothalamic tract

Spinomesencephalic tract

Spinoreticular tract



Cheryl L. Stucky, Michael S. Gold, and Xu Zhang
Proc Natl Acad Sci U S A. 2001 October 9; 98(21): 11845–11846

The Brain

Psychological factors

Psychological factors rarely cause pain but these factors may trigger or exacerbate a pain episode, help maintain the pain disorder, and contribute to the distress and disability experienced with chronic pain disorders

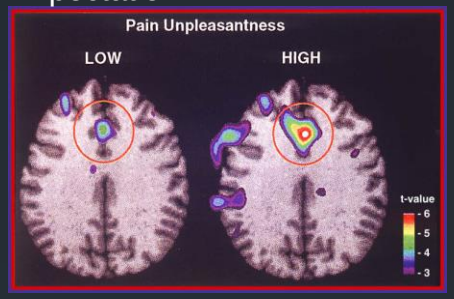
The stimulus does not determine the experience to be considered as painful

The Brain

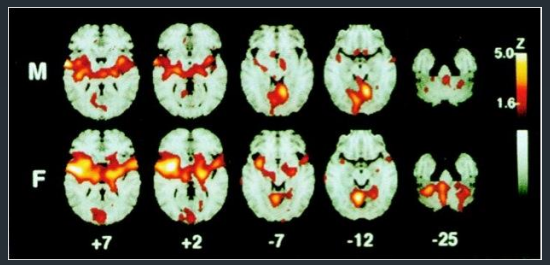
Psychological factors

- Expectation
- Attention
- Gender
- Mood
- Stress

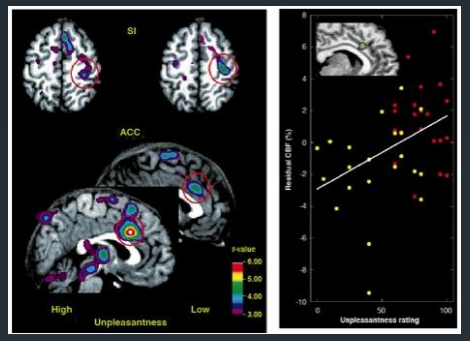
Expectation



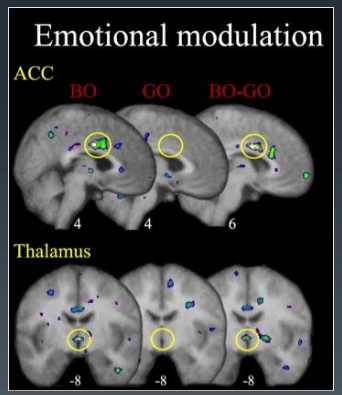
Gender



Attention

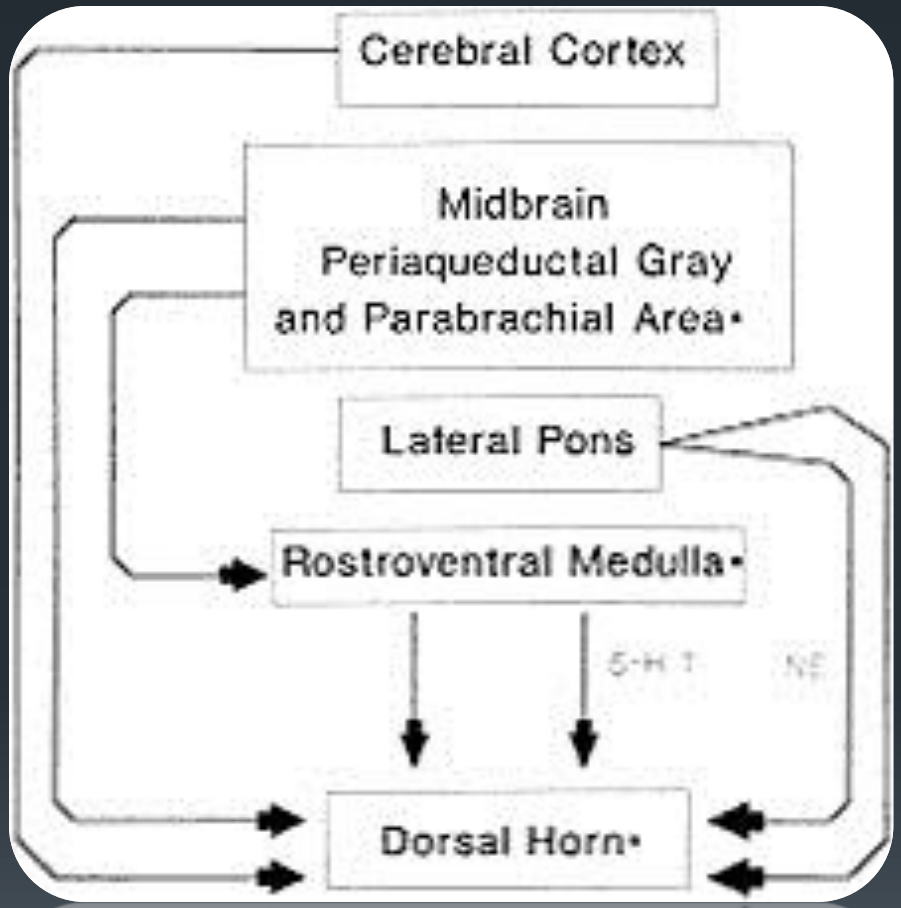


Hypnosis changed unpleasantness without changing pain intensity



Mood

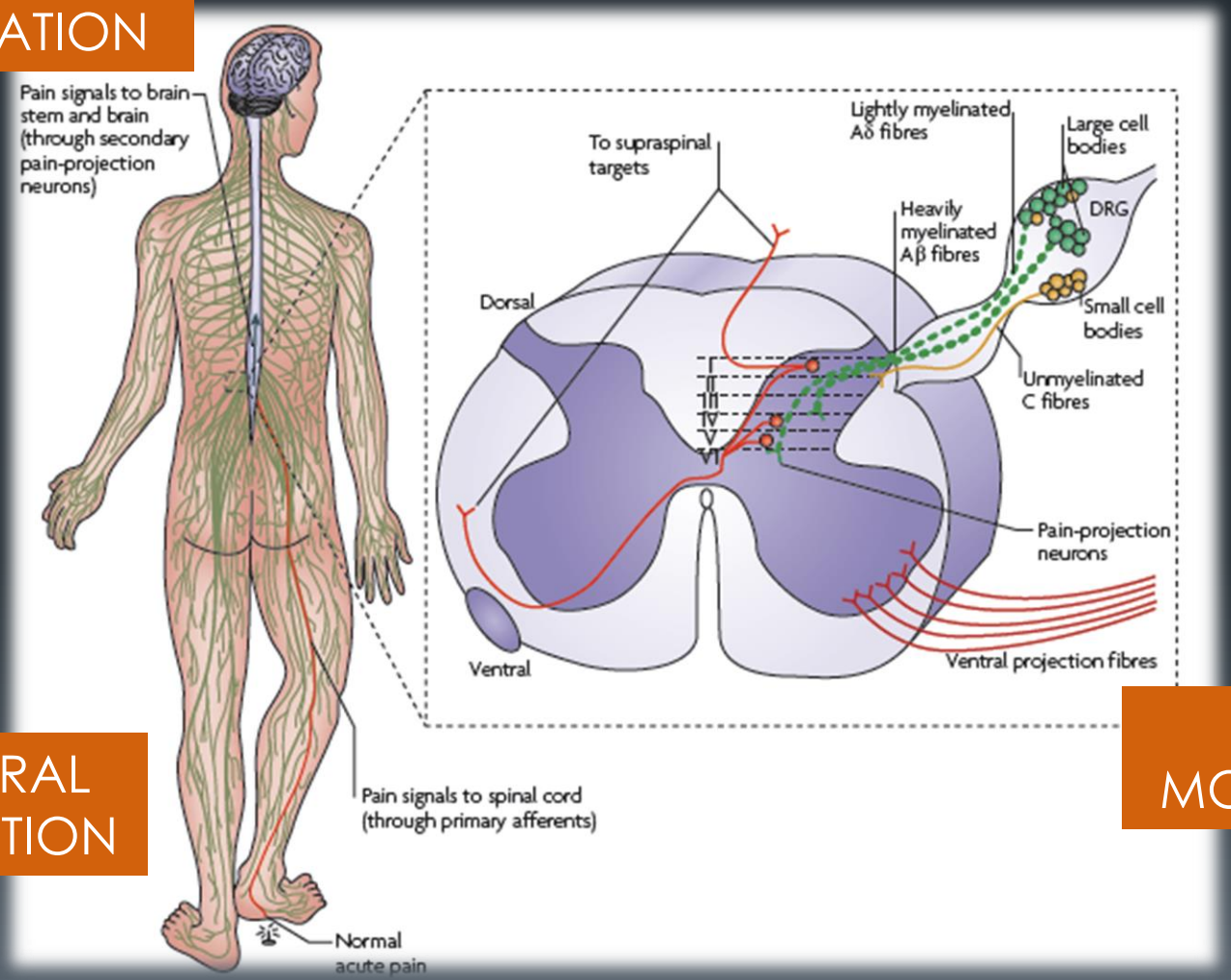
Back to the Spinal Cord



Recognition and Alleviation of Pain and Distress in Laboratory Animals (1992) Institute for Laboratory Animal Research.

Areas of Pain Processing

SUPRASPINAL MODULATION



PERIPHERAL MODULATION

SPINAL MODULATION