

# Acute Postoperative pain Management

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Fellowship of pain medicine



**➤ PAIN?**

**➤ CENTRAL SENSITIZATION?**

**➤ STRESS RESPONSE?**

# Neurogenic Inflammation → Peripheral Sensitization

## Axon Reflex Arc

Stimulus	Representative receptor
NGF	TrkA
Bradykinin	BK <sub>2</sub>
Serotonin	5-HT <sub>3</sub>
ATP	P2X <sub>3</sub>
H <sup>+</sup>	ASIC3/VR1
Lipids	PGE <sub>2</sub> /CB1/VR1
Heat	VR1/VRL-1
Pressure	DEG/ENaC ?

⚡ Inflammation:

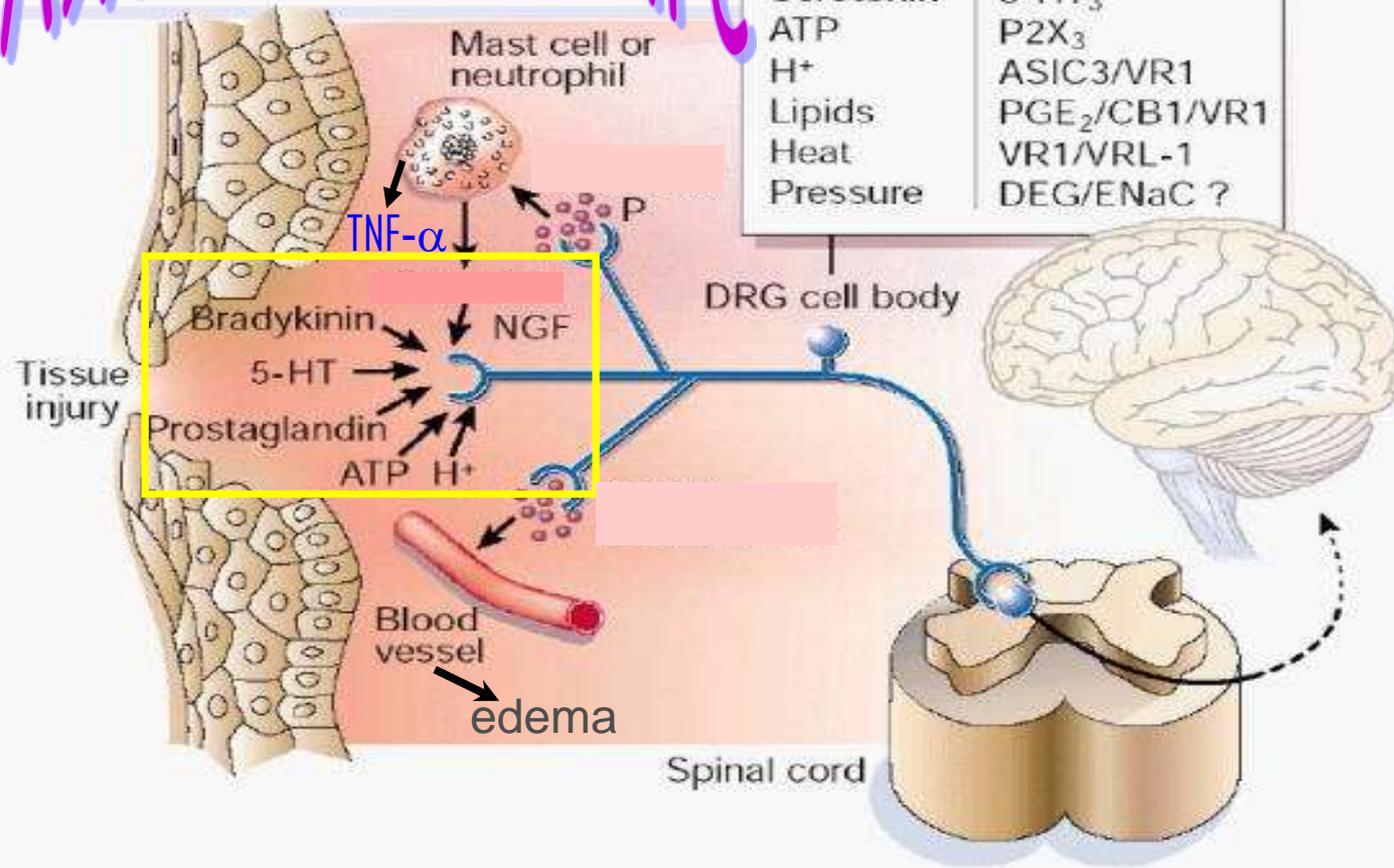
🎵 Heat

🎵 Redness

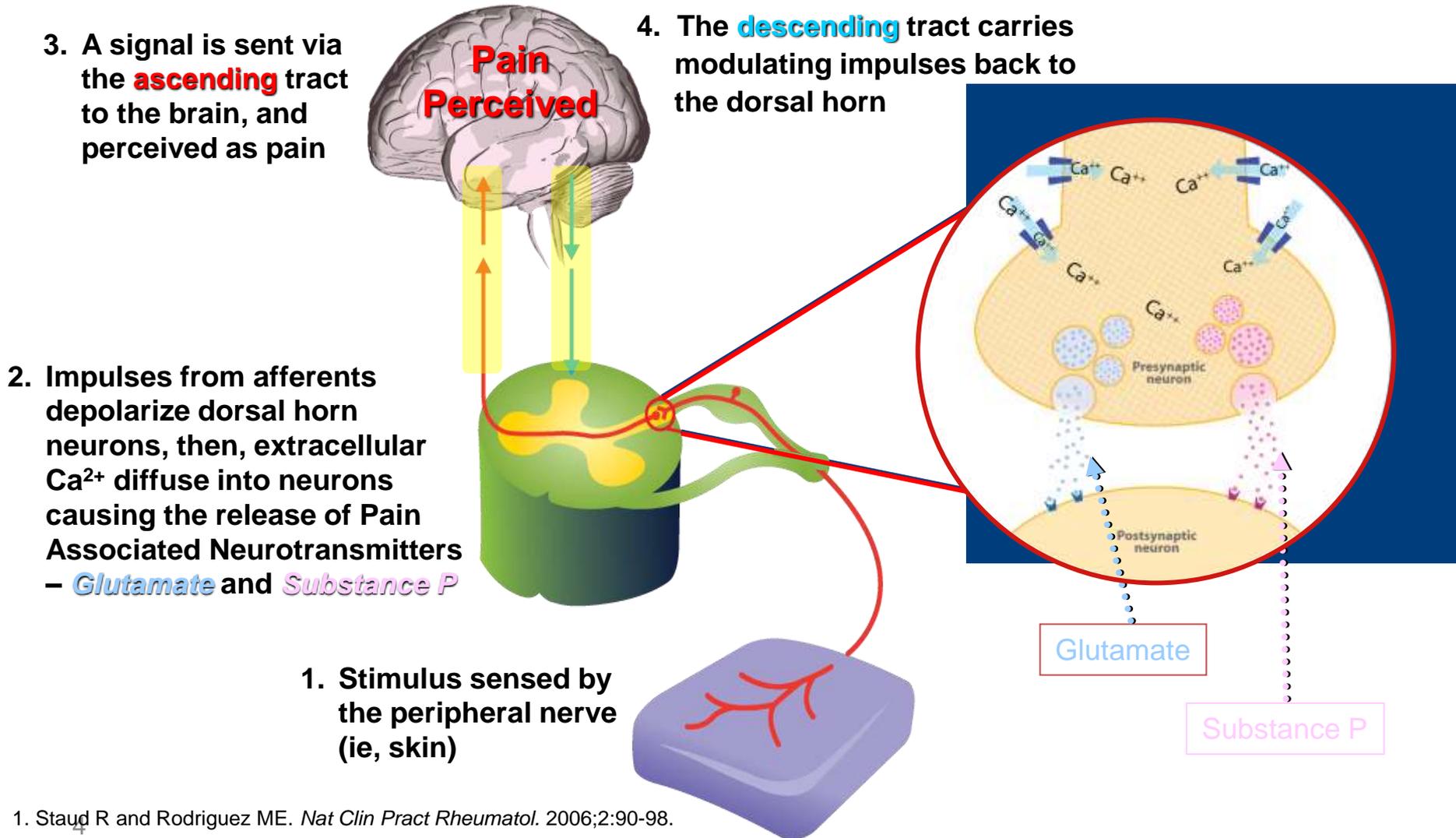
🎵 swelling

⚡ Can be produced by application of Substance P

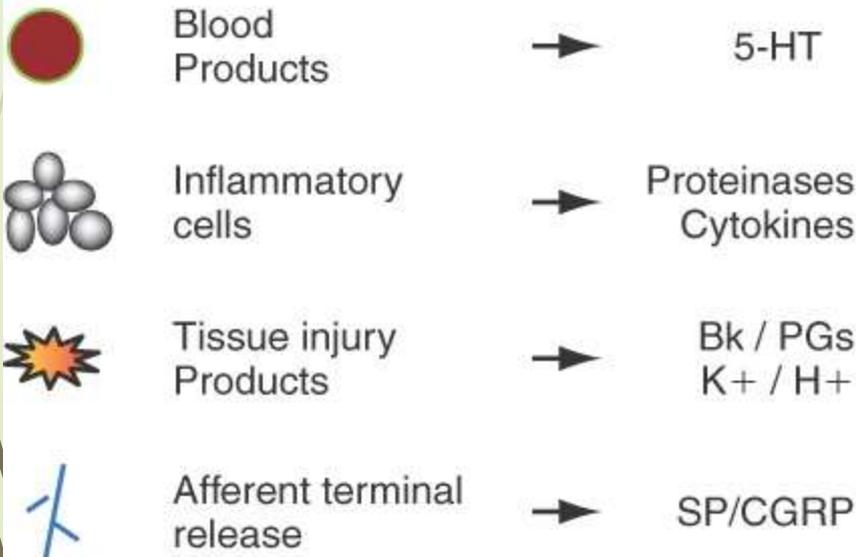
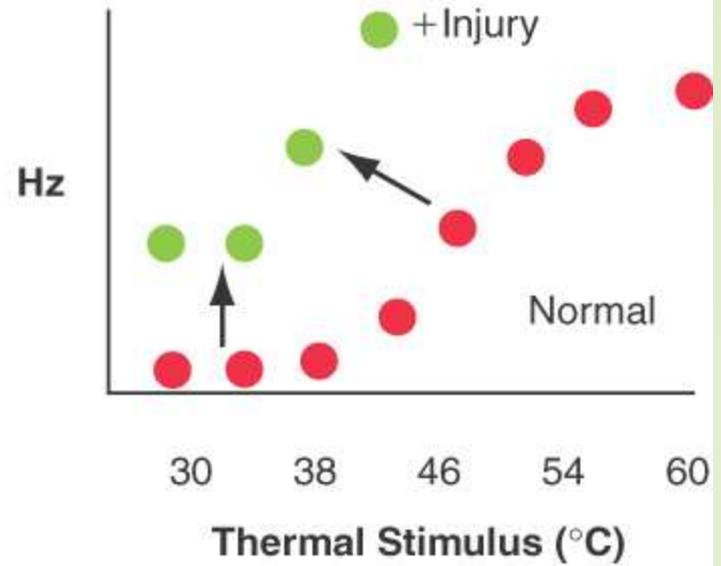
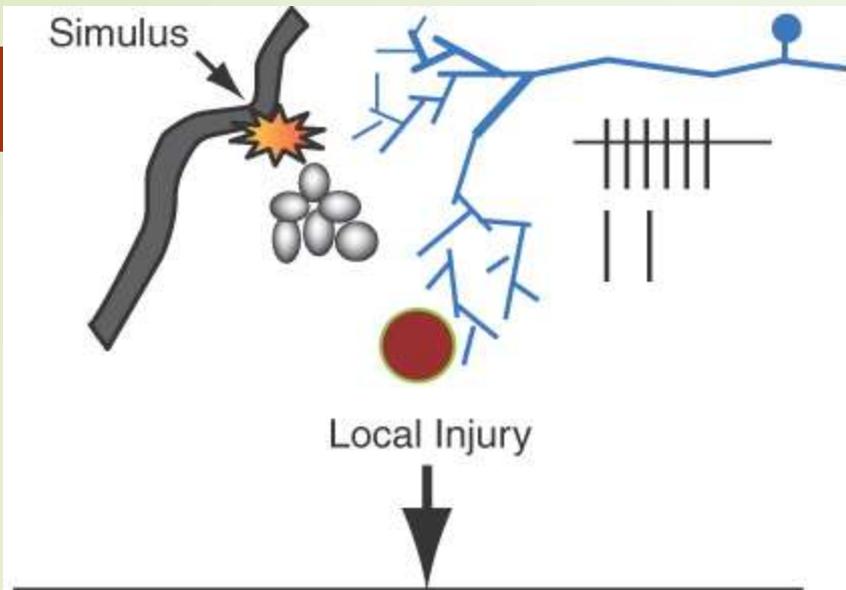
⚡ Antagonists of Substance P block neurogenic inflammation



# The Normal Pain Processing Pathway



1. Staud R and Rodriguez ME. *Nat Clin Pract Rheumatol*. 2006;2:90-98.  
2. Gottschalk A and Smith DS. *Am Fam Physician*. 2001;63:1979-1984.



→

**Spontaneous Activity**

**Sensitization of Terminal**

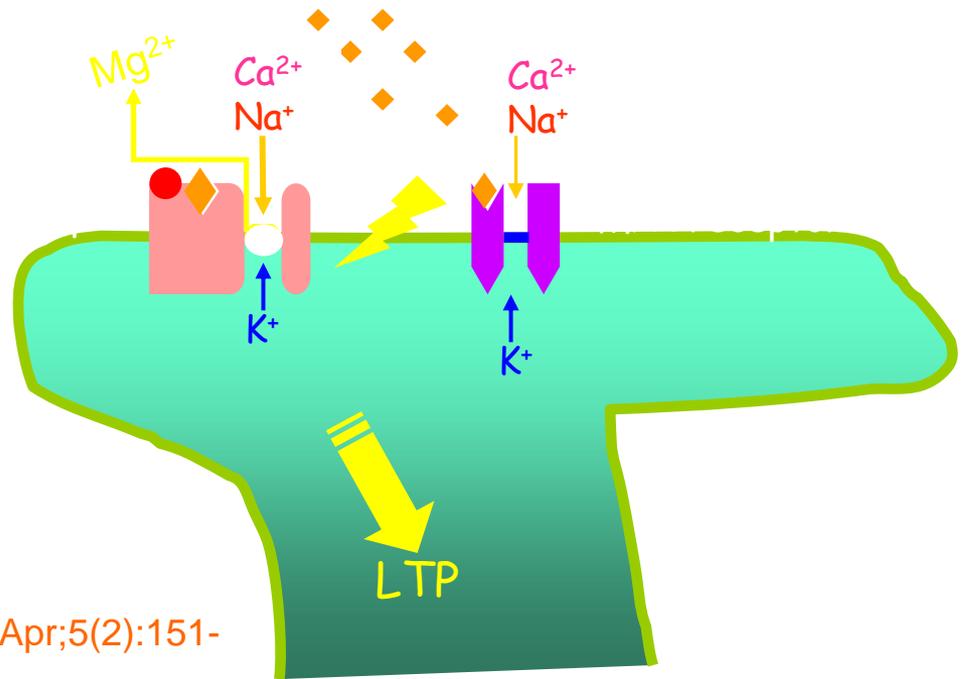
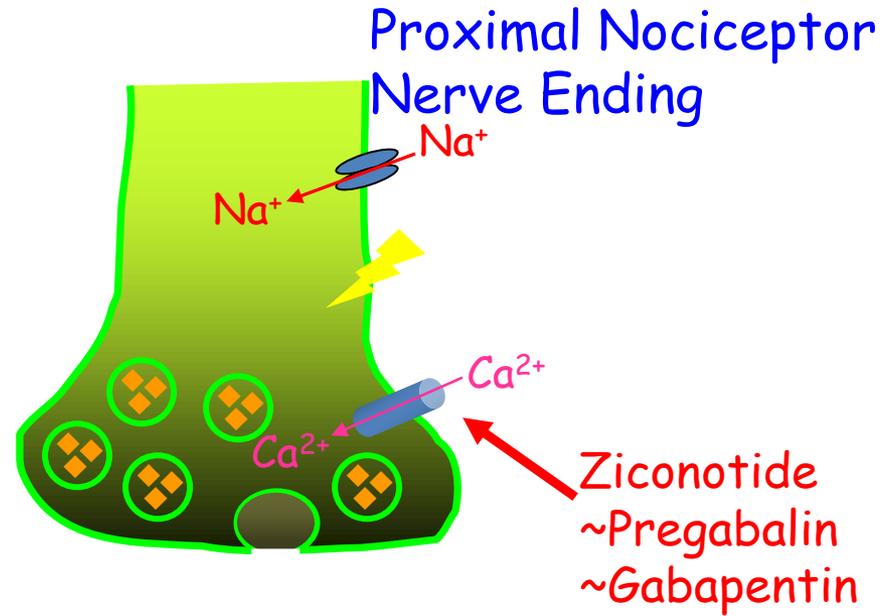
# Central Sensitization

(major excitatory neurotransmitter)

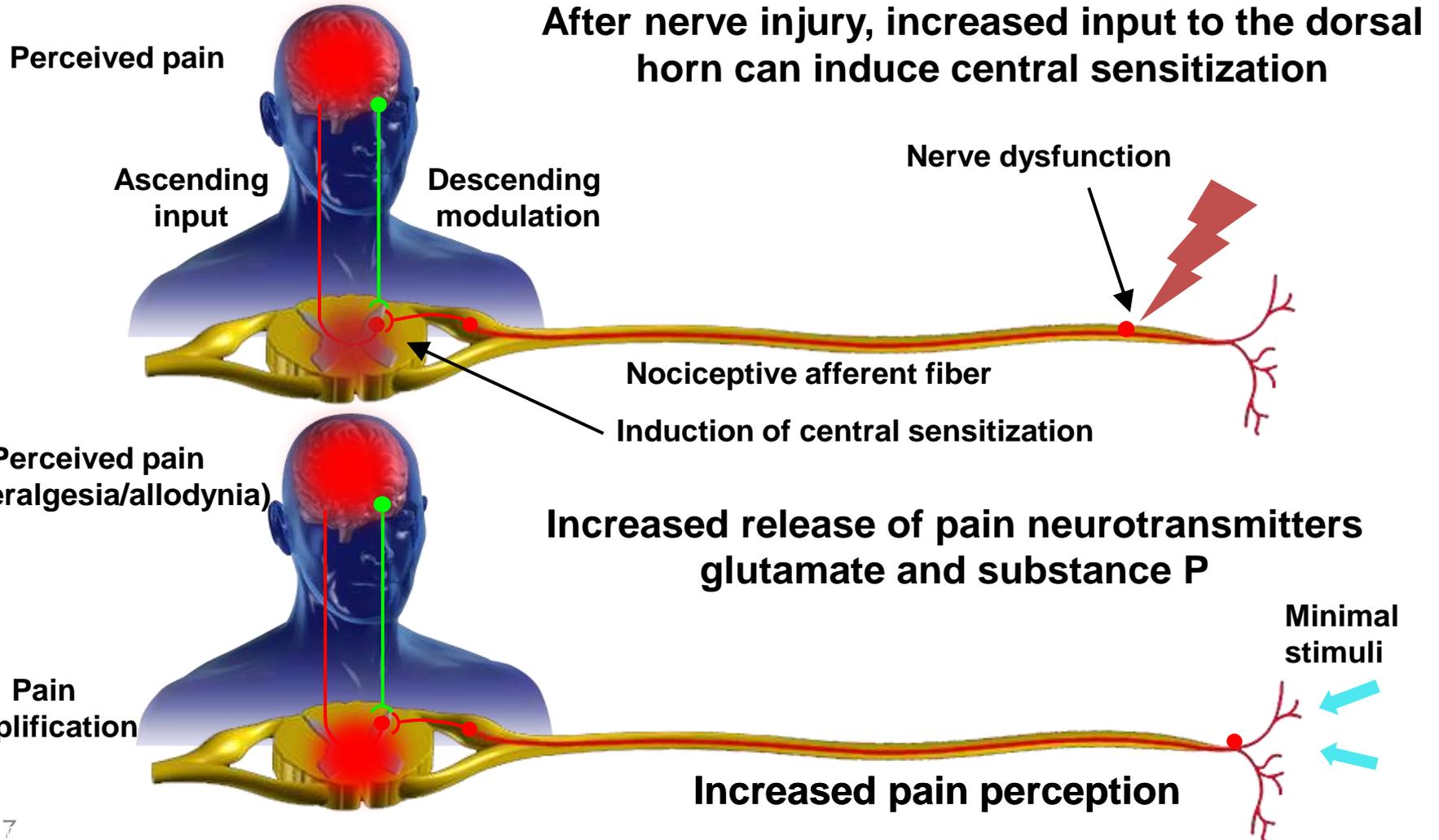
◆ Glutamate

● Glycine

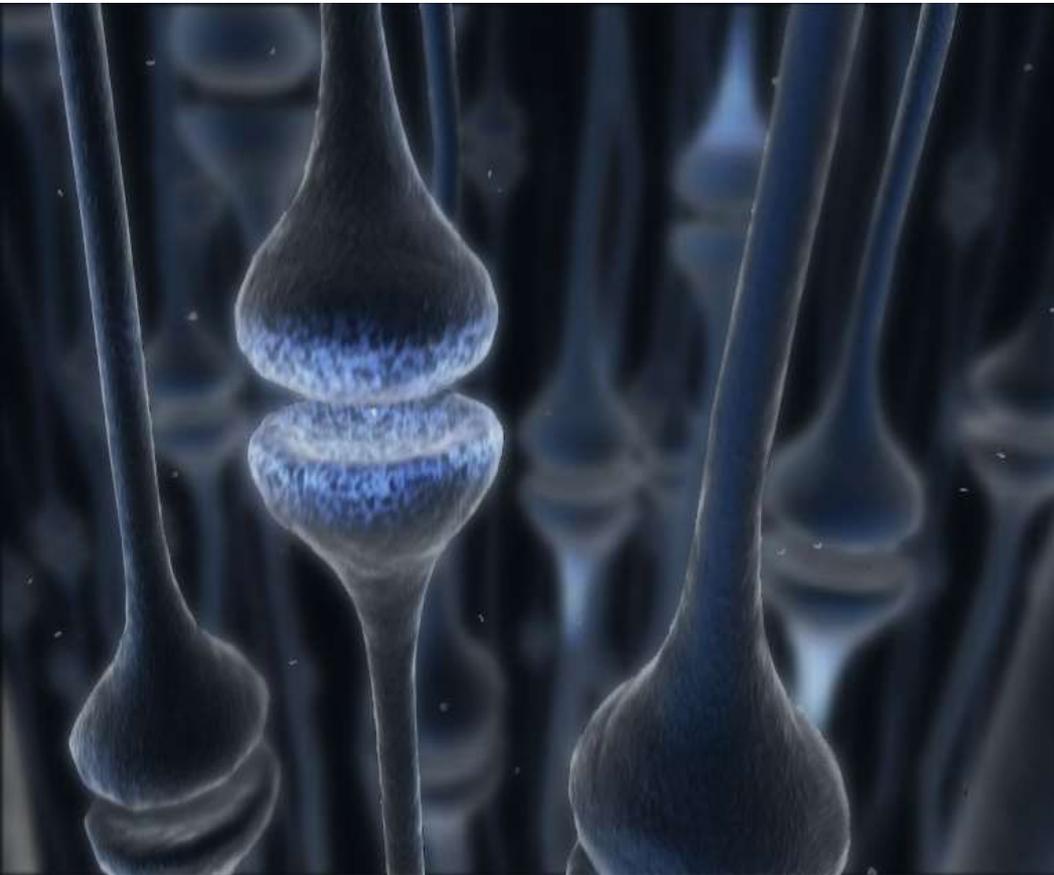
Nociceptor synapse  
in dorsal horn



# Central Sensitization Produces Abnormal Pain Signaling

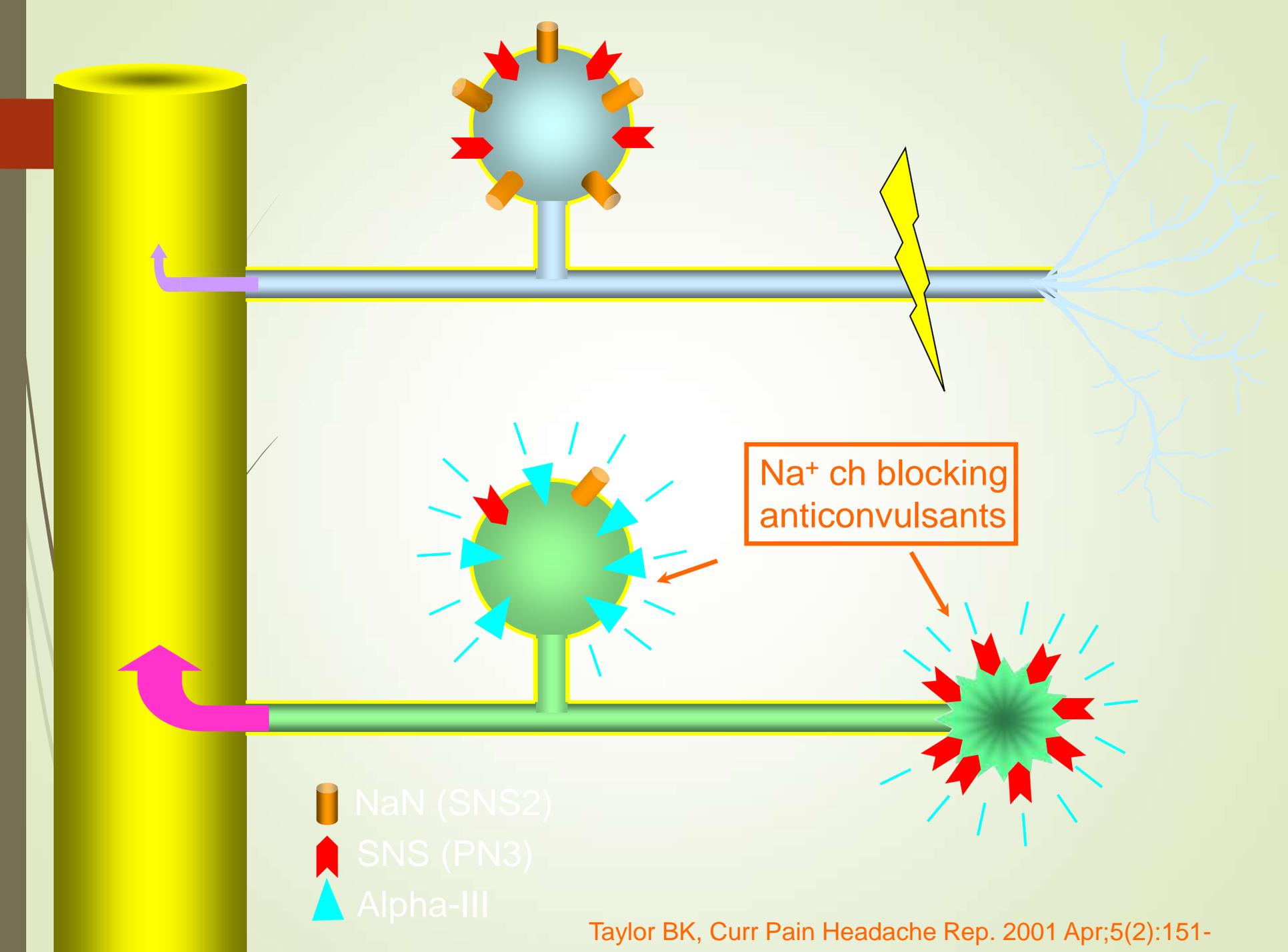


# Hyperexcitation



⚡ At the synapse level, sensitized primary afferent sensory fibers decrease the threshold for activation of nociceptor neurons which become hyperexcitable and transmit frequent action potentials

- 
- Opioids phenyl pyridines (M,P,T)
  - NSAID
  - Ketamine
  - Acetaminophen
  - TCA
  - Anticonvulsants



# Hyperexcitability

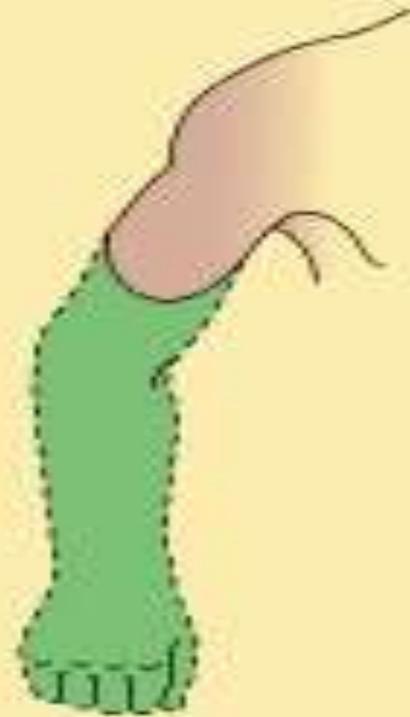
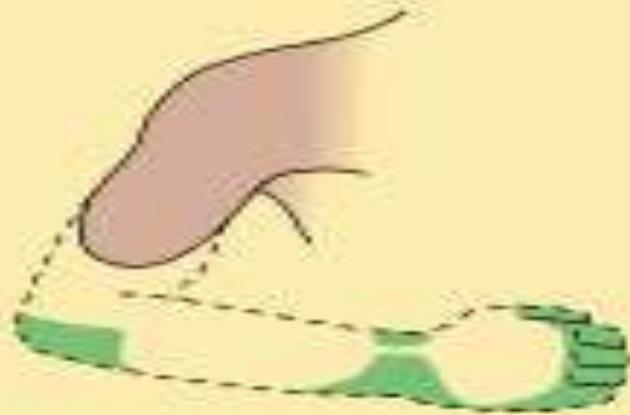
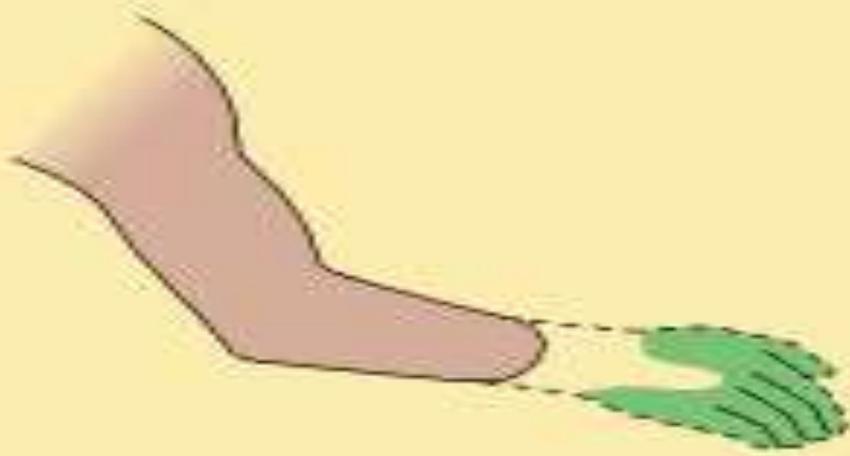


- The focus of **excitability in the damaged sensory fibers** causes
- the stimulation of the higher centers to perceive **spontaneous pain** (e.g. phantom pain, sciatica)

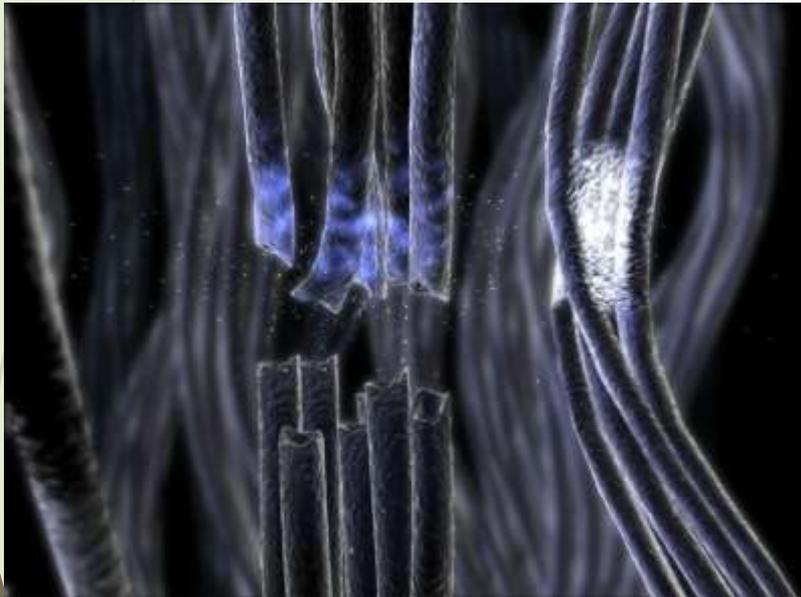
Millan MJ. *Progress in Neurobiology* 1999;57:1–164.

Suzuki R and Dickenson AH. *Neuroreport* 2000;11:R17–21.

Waxman S. *Pain* 1999;6:S133–140.



# Cross Talk



- ***Ephaptic (non synaptic) transmission:***
- Complete severance of peripheral afferent sensory fibers results in hyperexcitability of damaged nerves and transmission of action potentials along adjacent, undamaged unstimulated sensory fibers, or cross talk



# Acute effects of post operative Pain

- Noxious stimuli → neuronal sensitization → of **new genes expression** within **1 h**



# REFLEX Response

- Increased skeletal **muscle tone**
  - Inhibition of **phrenic nerve** function
  - Decreased **GI motility**
- 



# DECREASE PHERENIC ACTIVITY

- ▶ **upper abdomen and thoracic surgery**

→ **Deep breathing and cough**



## Neuroendocrine **Stress Response**

- **hypothalamic – pituitary-  
adrenocortical**
  - **Increase** sympathetic tone
- 

- 
- **Cortisol      Adrenocorticotrophic**  
**Antidiuretic      Glucagon**  
**Aldosteron      Renin-angiotensin**
  - **Decreased** secretion of  
**anabolic** hormones



# The effects

- Na and water retention
- Blood Glucose
- FFA
- Ketone bodies
- Lactate

→Catabolic state

- 
- ▶ **stress response is proportional to:**

**surgical trauma**

**type of anesthesia**

# postoperative hypercoagulability

➡ SR →

**Increase:** Procoagulants ,  
platelet reactivity , plasma  
viscosity

**Decrease:** Natural anticoagulant,  
fibrinolysis

➡ DVT

Graft failure

Ischemia



# SR

- **Immunosuppression**
- **Hyperglycemia (wound healing)**
- **Sym: myocardial ischemia**
- **Delay in GI motility and ileus**



# Treatment

Traditional approaches

## Reactive pain management

- Ineffective:
- **nurses**
- **treatment after pain**
- **under medicated**

- 
- 
- Healthcare providers : **underestimate** the amount of pain
  - **Misunderstanding**
  - Patients may be reluctant to complain or voluntarily ask for analgesics



# Proactive pain management

- treatment **before** pain occurs
- **continuous** peripheral or epidural infusion  
Very effective
- High tech / Equipment dependent



# Intravenous analgesia

- **Continues infusion**
  - **Intermittent IV bolus**
  - **Continues + demand dose**
  - **PCA**
- 

# High thoracic Epidural Analgesia

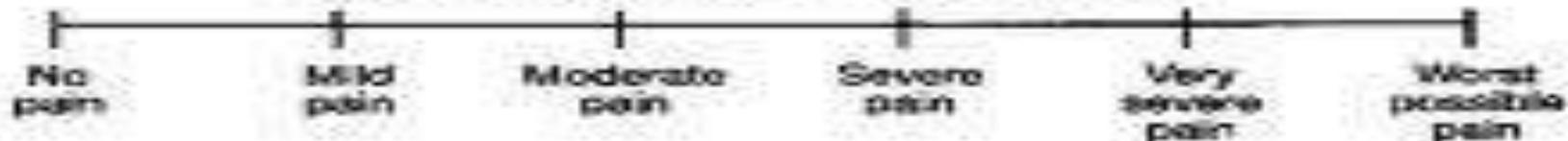
- Provide analgesia superior to that with systemic analgesic
- Early extubation
- Reduced dose of other analgesics and their complications
- Attenuating the stress response and hypercoagulability



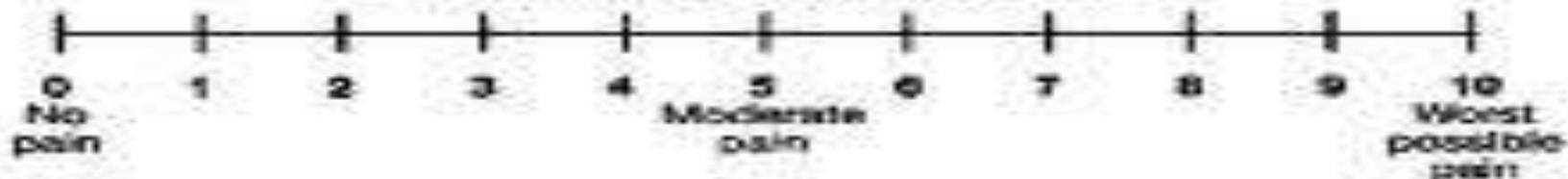
**► Favorable redistribution of  
coronary blood flow**



### Simple Descriptive Pain Intensity Scale<sup>1</sup>



### 0-10 Numeric Pain Intensity Scale<sup>1</sup>



### Visual Analog Scale (VAS)<sup>2</sup>



<sup>1</sup>If used as a graphic rating scale, a 10-cm baseline is recommended.  
<sup>2</sup>A 10-cm baseline is recommended for VAS scales.



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Cochrane Database of Systematic Reviews | Review - Intervention

# Pregabalin for neuropathic pain in adults

Sheena Derry, Rae Frances Bell, Sebastian Straube, Philip J Wiffen, Dominic Aldington, R Andrew Moore

Authors' declarations of interest

Version published: 23 January 2019 | Version history

<https://doi.org/10.1002/14651858.CD007076.pub3>

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## Abstract

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## Background

This review updates part of an earlier Cochrane Review titled "Pregabalin for acute and chronic pain in adults", and considers only neuropathic pain (pain from damage to nervous tissue). Antiepileptic drugs have long been used in pain management. Pregabalin

## Contents

Abstract

PICOs

Plain language summary

Authors' conclusions

Summary of findings

Background

Objectives

- 
- Daily oral doses of 300-600mg
  - For painful diabetic neuropathy and PHN
  - Evidence for other type of neuropathic pain is very limited
  - Appears not to be effective for HIV associated painful peripheral neuropathy
  - Important benefit effects on sleep deprivation, fatigue and depression

# Oral non-steroidal anti-inflammatory drugs versus other oral analgesic agents for acute soft tissue injury

✉ Peter Jones, Rain Lamdin, Stuart R Dalziel Authors' declarations of interest

Version published: 12 August 2020 [Version history](#)

<https://doi.org/10.1002/14651858.CD007789.pub3>

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## Abstract

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## Background

Acute soft tissue injuries are common and costly. The best drug treatment for such injuries is not certain, although non-steroidal



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ENG

6

- 
- **NSAIDS and paracetamol** : no difference in analgesia
  - **NSAIDS** : small increase in GI adverse events
  
  - **NSAIDS and opioids**: no difference in analgesia
  - **NSAIDS** : fewer GI and neurologic adverse effects

# Perioperative intravenous ketamine for acute postoperative pain in adults

Elina CV Brinck, Elina Tiippana, Michael Heesen, Rae Frances Bell, Sebastian Straube, R Andrew Moore, Vesa Kontinen | Authors' declarations of interest

Version published: 20 December 2018 | Version history

<https://doi.org/10.1002/14651858.CD012033.pub4>

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## Abstract

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## Background

Inadequate pain management after surgery increases the risk of postoperative complications and may predispose for chronic postsurgical pain. Perioperative ketamine may enhance conventional analgesics in the acute postoperative setting.

## Objectives

To evaluate the efficacy and safety of perioperative intravenous ketamine in adult patients when used for the treatment or prevention of acute pain following general anaesthesia.

## Search methods

We searched CENTRAL, MEDLINE and Embase to July 2018 and three trials registers (metaRegister of controlled trials, ClinicalTrials.gov and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP)) together with reference checking, citation searching and contact with study authors to identify additional studies.

## Selection criteria

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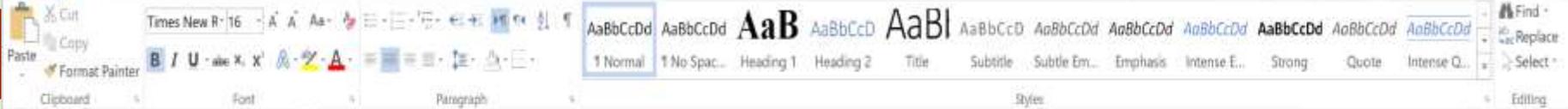
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[Cochrane Clinical Answers\(1\)](#)

- 
- 
- Racemic ketamine bolus doses were predominantly **0.25 mg to 1 mg/kg**, and infusions 2 to 5  $\mu\text{g}/\text{kg}/\text{minute}$  (**0.12-0.3 mg/ kg /h**)
  - Perioperative intravenous ketamine reduced postoperative opioid consumption over 24 hours by 8 mg morphine equivalents
  - Overall, 187/3614 (5%) participants receiving ketamine and 122/2924 (4%) receiving control treatment experienced an adverse event

- 
- 
- reduces postoperative analgesic consumption and pain intensity.
  - Results were consistent in different operation types or timing of ketamine administration



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Archives of Anesthesiology and Critical Care (Winter 2022); 0(0): 00-00.

Available online at <http://aacc.tums.ac.ir>



## Section Article

# The effect of analgesia induced by continuous IV administration of ketamine and morphine and paracetamol in hospitalized patients in north-eastern Iran

***Mokarram Mehrdad<sup>1</sup>, Sedaghat Alireza<sup>2</sup>, Lotfalizadeh Nasibeh<sup>3</sup>, Ziaee Maliheh<sup>\*4</sup>, Morrovatdar Negar<sup>5</sup>, Bicheranloee Soheila<sup>6</sup>***

*1: Department of Anesthesiology and critical care medicine, Emam Reza Hospital, Mashhad University of medical Science*

*2: Anesthesia department, Mashhad University of medical science*

*3: Anesthesia department, Mashhad University of medical science*

*4\*: corresponding author:*

*MD, Community Medicine Specialist, Assistant Professor of Community Medicine, Department of Community Medicine, School of Medicine, Social Determinants of Health Research Center, Gonabad University of Medical Sciences, Gonabad, Iran*

- 
- 
- The primary dose of morphine was **0.01 mg/kg/h** history of opioid consumption and physical dependence: **0.02 mg/kg/h**. The starting dose for the prevention of opioid tolerance increased by 30% every week.
  - Paracetamol: **15 mg/kg every 6 h**, this dose was reduced to 30% after **three days** of initiation of the treatment to prevent liver toxicity and was discontinued after one week
  - Continuous IV infusion for Ketamine was **0.15 mg/kg/hr**. Continuous IV infusion of ketamine and morphine was performed by 100cc silicone pump.

- 
- 
- ▶ Continuous IV infusion for Ketamine was **0.15 mg/kg/hr**. Continuous IV infusion of ketamine and morphine was performed by 100cc silicone pump.
  - ▶ **Results:** The mean NRS was significantly reduced in the first visit after the intervention (three hours later) ( $8.5 \pm 1.04$  vs.  $3.9 \pm 1.74$ ;  $p < 0.001$ ) and this decrease was observed in NRS in continuous observations ( $P > 0.001$ )