

**Universidade Federal de Juiz de Fora**  
Instituto de Ciências Biológicas  
Departamento de Farmacologia





**Dor Mecanismos e Manejo**  
**Roteiro da aula**

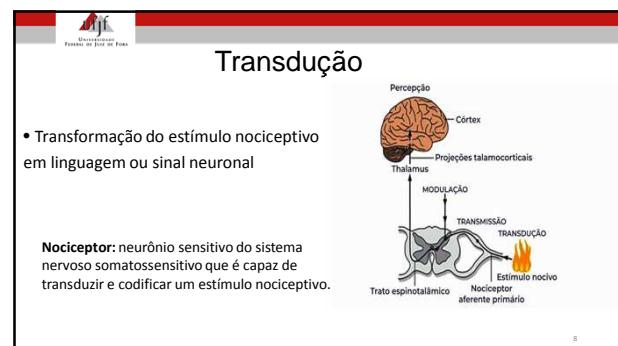
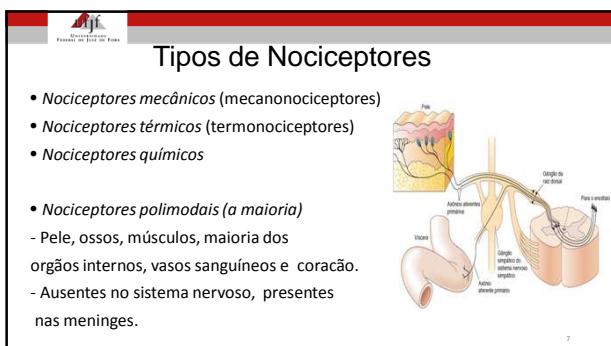
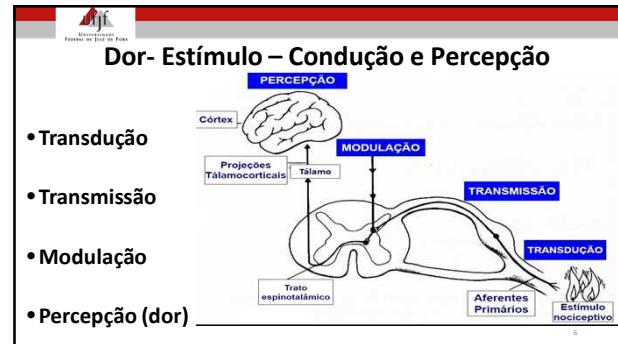
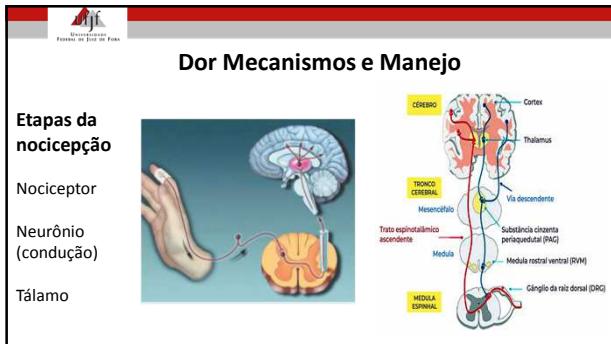
- Dor e mecanismos
- Fisiopatogenia
- Circuitos da dor
- Sensibilização periférica e central
- Aspectos básicos para o manejo da dor de acordo com a patogenia
- Mensagem final – pontos importantes

The diagram illustrates the sequence of events in pain perception across different brain regions:

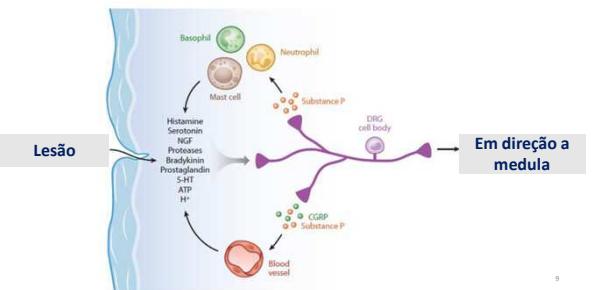
- Periphery:** Nerve fibers from the hand enter the spinal cord via the dorsal root.
- Spinal Cord:** The fibers are labeled as **Fibra A-delta** (conduction velocity ~10-20 m/s) and **Fibra C** (conduction velocity ~0.5-2 m/s). The **Intercônditilo** (intercostal) nerve is also shown.
- Spinothalamic Tract:** Fibers from the dorsal root ganglion ascend through the posterior column and cross in the **Côrto dorsal (intercônditilo)** to reach the **Via ascendente**.
- Medulla:** The tract continues through the **Medula** to the **Trato neopontâstico** and **Trato paleopontâstico**.
- Reticular Formation:** The tract passes through the **Formação reticular**.
- Hipófise:** The **Núcleo talâmico intrínseco** receives input from the tract.
- Thalamus:** The tract continues to the **Núcleo talâmico extrínseco**, specifically the **área pretálâmica**.
- Cerebral Cortex:** The **Côrto somatosensorial** receives the signal.
- Higher Processing:** The **Área de hipófise pré-frontal** and **Lobo temporal (espinhana, ferida)** are involved in the emotional and cognitive aspects of pain.
- Reflex Pathway:** The diagram shows a reflex arc involving the **Gânglio da raiz dorsal** and the **Côrto dorsal (intercônditilo)**.

The figure is divided into three main sections:

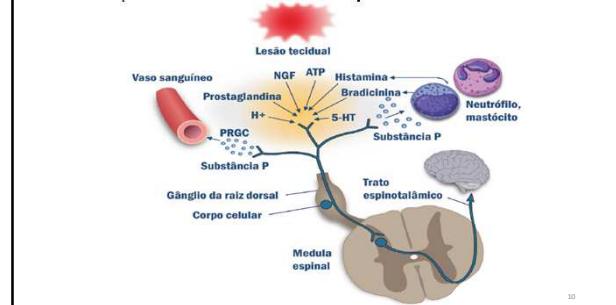
- Nociceptiva**: Shows a cross-section of the spinal cord with labels for "INJÚRIA TISSULAR", "MASTOCITOS OU NEUROFIBRAS", "Neurofibroma", "Célula mastoide", "Célula ganglionar", "Célula de Schwann", and "Sensação". It also shows the "CORPO ESPINAL" and "SISTEMA SIMPATICO".
- Neuropática**: Shows a diagram of the "Spinal cord injury" with a yellow spinal column and a brain with a black lesion area. Below it are two images: one of a brain with a lesion labeled "Stroke" and another of a hand labeled "Postherpetic neuralgia".
- Nociplástica**: Shows a diagram of the "Peripheral vascular disease, diabetes" with a yellow spinal column and a leg with a lesion. It also shows a diagram of the "Fibromyalgia" with a yellow spinal column and a torso with red dots. The final diagram shows the "Bladder pain syndrome" with a yellow spinal column and a bladder with a red lesion.



### Mediadores da Dor



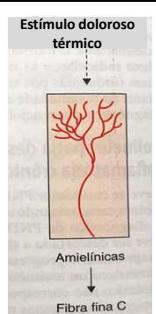
### Liberação de Mediadores Após Lesão Tecidual



### Aferente Primário

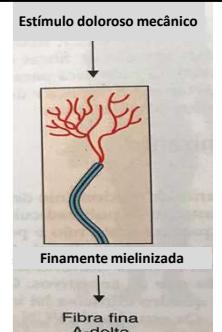
#### Fibras C

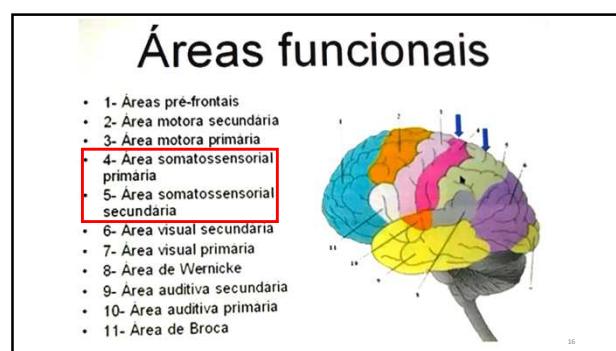
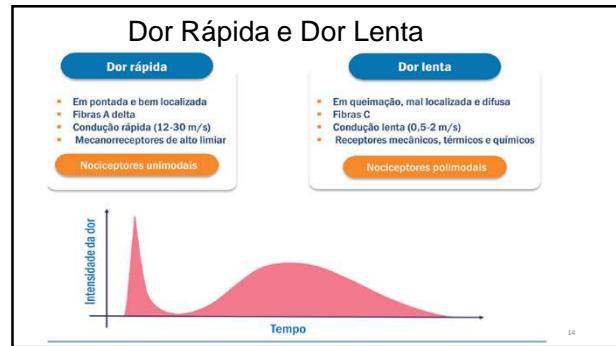
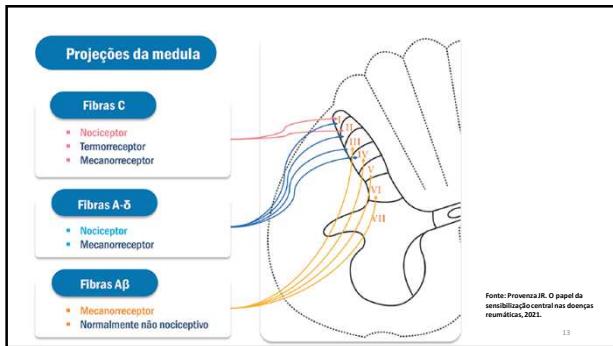
- Não mielinizadas
- Pequeno diâmetro
- Baixa velocidade de condução
- Neurônios polimodais (térmico, químico e mecânico)

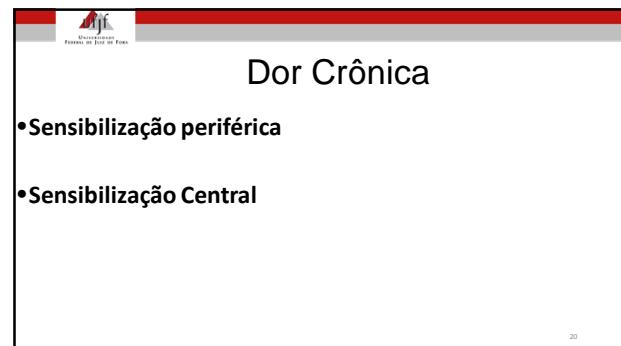
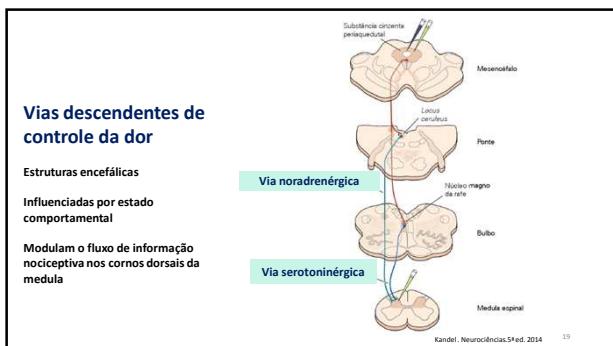
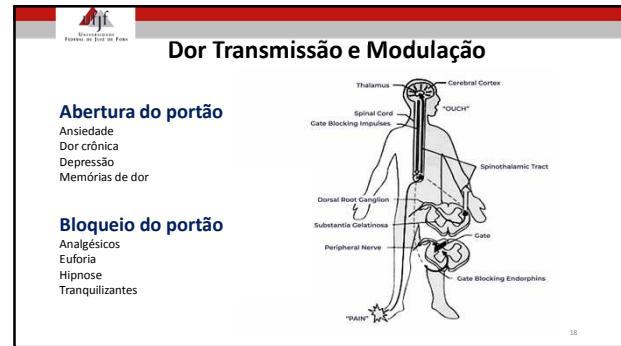
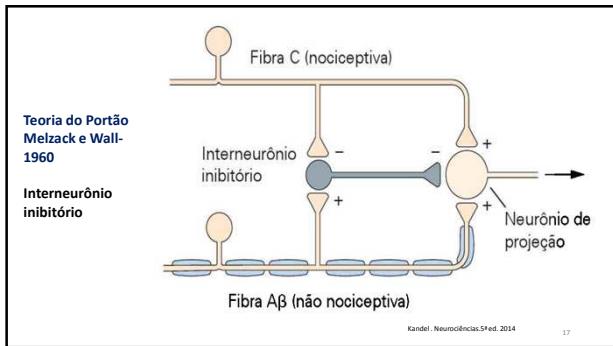


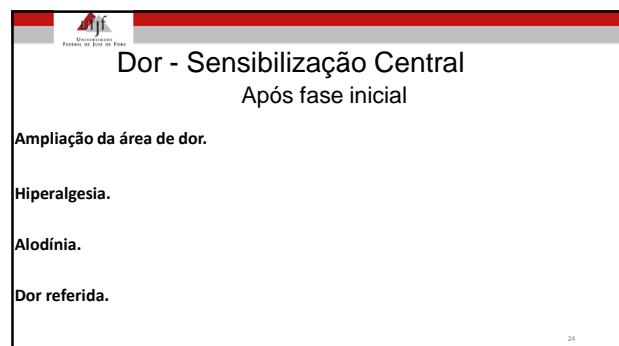
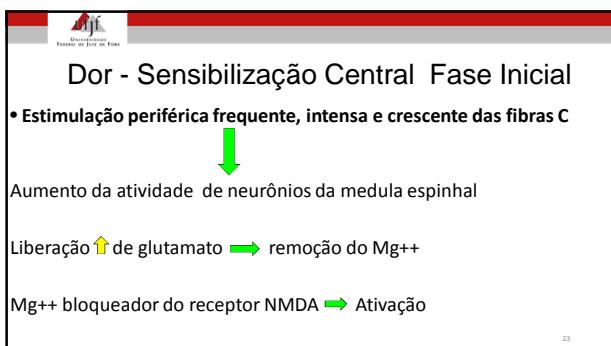
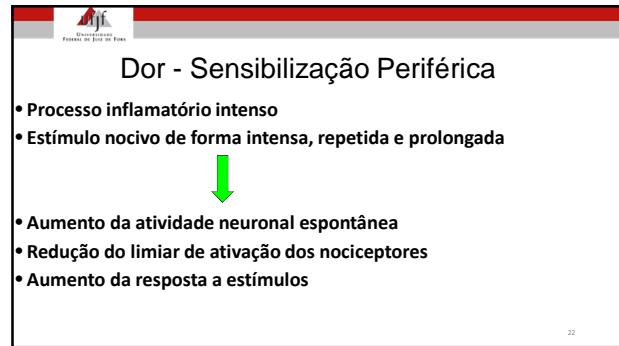
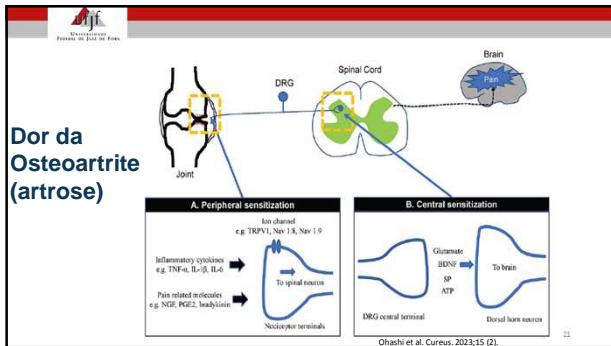
### Aferente Primário

- Fibras Aδ
- Mielinizadas
- Diâmetro médio
- Velocidade de condução rápida









**Dor - Sensibilização Central**  
Após fase inicial

Intensa ativação de receptores e a maior liberação de neurotransmissores

Envolvimento de fibras nervosas adjacentes que estavam adormecidas e que passam a participar deste processo nociceptivo → Denomina neuroplasticidade

Explica a amplificação da área dolorosa além da lesão inicial

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**Manejo da Dor**

**Condição para um manejo adequado**

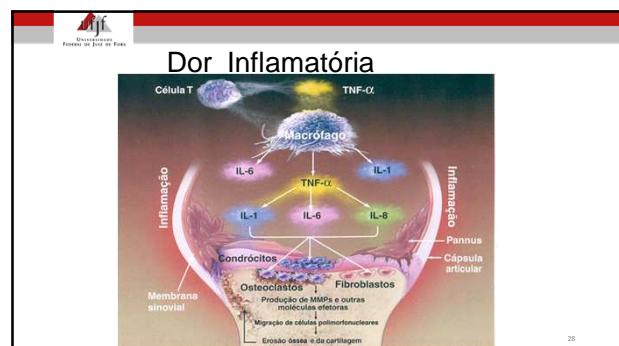
Fundamental tentar responder a pergunta:  
Qual o processo que gerou a dor?

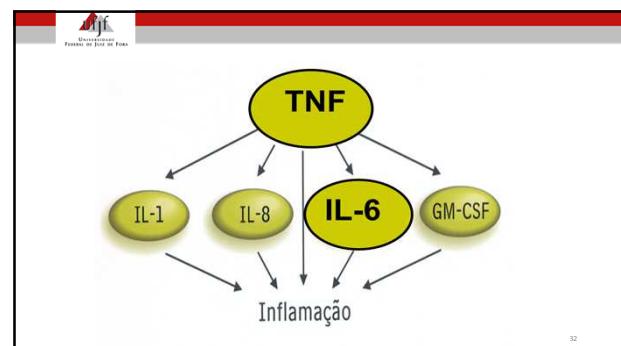
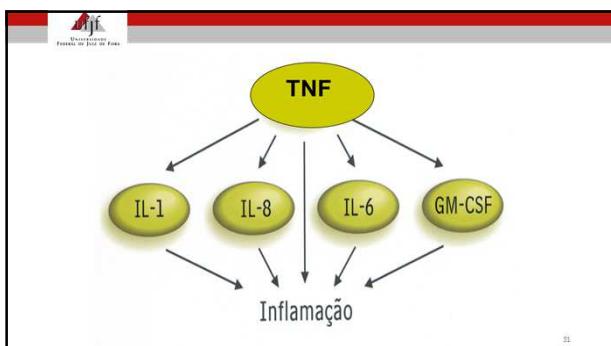
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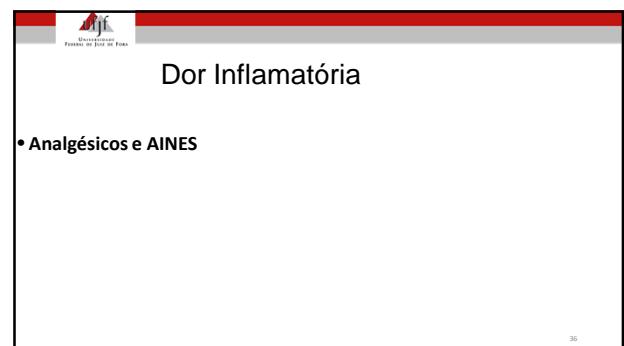
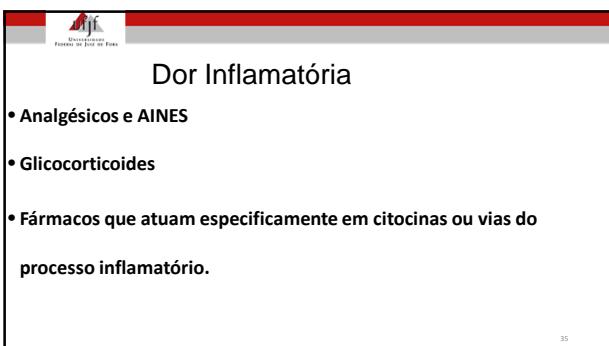
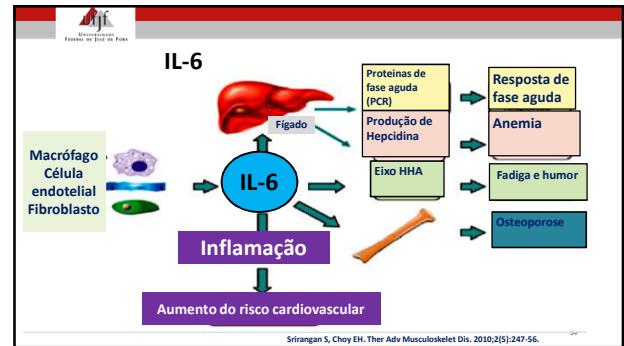
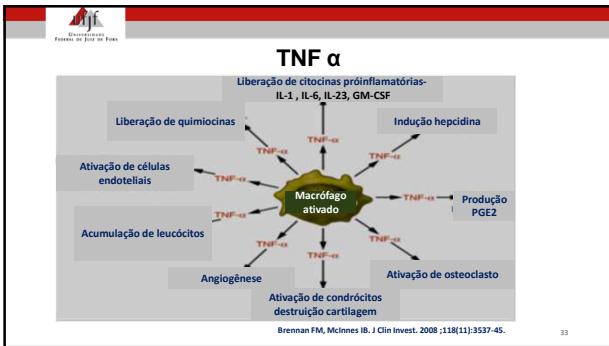
**Tratamento Farmacológico da Dor**

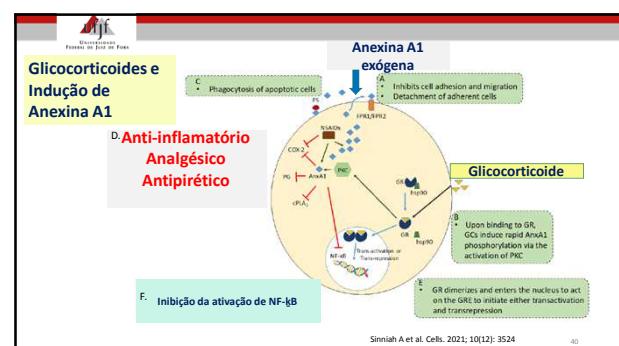
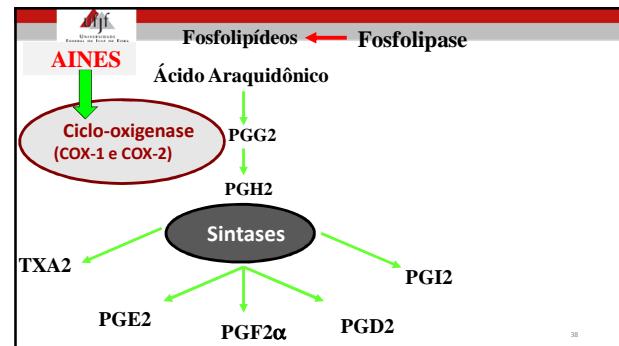
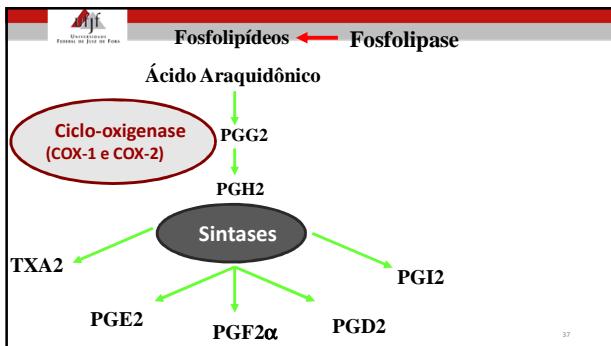
- Analgésicos e AINES
- Opioides
- Antidepressivos
- Anticonvulsivantes (antiepilepticos)

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**Fármacos Biológicos**

- Alvos específicos

Citocinas

TNF

IL-6

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**Dor Nociceptiva**

- Opioides

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**Dor Nociceptiva**

- Analgesia
- Aliviam o sofrimento alterando o componente emocional da experiência dolorosa

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**Opioides Endógenos**

**Encefalinas** - Distribuição ampla por todo o SNC

**Endorfinas** - Hipotálamo, núcleo do trato solitário e lobo anterior da hipófise

**Dinorfinas** - Hipotálamo, células superiores do lobo da hipófise

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**Receptores Opioides**

**Mu( $\mu$ ) - Kappa( $\kappa$ ) - Delta( $\delta$ )**

$\mu 1 \rightarrow$  analgesia supramedular, miosis, euforia

$\mu 2 \rightarrow$  analgesia medular, depressão respiratória, redução do trânsito intestinal

Estrutura do receptor opioide

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**Opioides e Analgesia - receptores  $\mu$**

PAG- região periaquedatal cinza  
RVM – medula rostroventral  
A-âmigdala  
Cl-côrtex insular  
H-hipotálamo

Expressão de receptores  $\mu$

Córtex  
Mesencéfalo  
Medula  
Medula espinal

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**Opioides - Classificação**

<b>Opioides Fracos</b>	<b>Opioides Fortes</b>
Codeina	Morfina
Tramadol	Oxicodona
	Metadona
	Fentanil

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**Dor Neuropática e Nociplástica**

**Fármacos Adjuvantes**

- Antidepressivos
- Anticonvulsivantes

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**Dor Neuropática e Nociplástica**

**Antidepressivos**

Independe do efeito antidepressivo

↑ Noradrenalina e serotonina SNC

Reforço de vias inibitórias

Diniz URL et. al. Molecules. 2019; 6:24(24):4469.  
J Clin Pharmacol 2012;52:6-17

**Dor Neuropática e Nociplástica**

**Anticonvulsivantes (antiepilepticos)**

Gabapentina

Pregabalina

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**Gabapentina / Pregabalina – Mecanismo de Ação**

Limita entrada de Ca++ nos neurônios

- inibe liberação de Glutamato, Noradrenalina e substância P
- Aumenta expressão cerebral da descarboxilase do ácido glutâmico (GAD) enzima que sintetiza GABA

Adaptado de Wilfleld, 2010.

**Mensagem Final – Pontos Importantes**

- A complexidade de todo o processamento do estímulo, surgimento e manutenção da dor.
- A dificuldade de intervenção precisa no circuito da dor e nos mediadores envolvidos.
- A necessidade da busca constante no mecanismo de dor e sua individualização.
- A busca de fármacos eficazes e que sejam bem tolerados.

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