

# Kivun fysiologiaa

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anestesiologian erikoislääkäri

kivunhoidon erityispätevyys

dosentti / KYS, anestesiologian ja tehohoidon klinikka

tutkija / KY, farmakologian ja toksikologian laitos

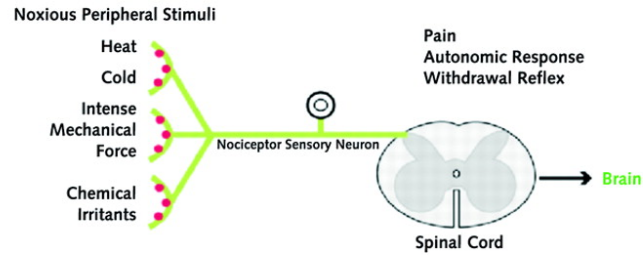
# Kivun syy on joko kudosisvaurio tai hermovaurio, ei esimerkiksi ikä

- Kudosisvauriokipu
  - viskeraalinen tai somaattinen
    - reagoi yleensä hyvin hoitoihin
- Hermovauriokipu
  - perifeerinen tai sentraalinen
    - vaste hoidoille ei aina yhtä ennustettava

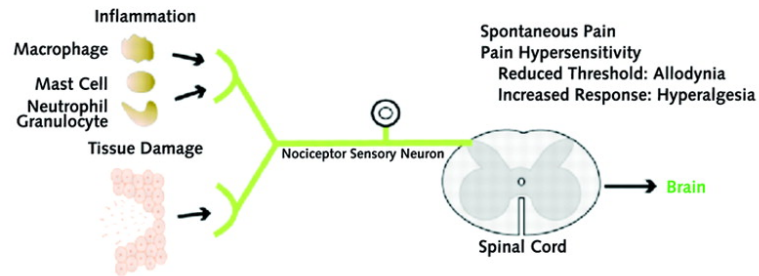
# Kivun fysiologiaa

## Kivun tyypit

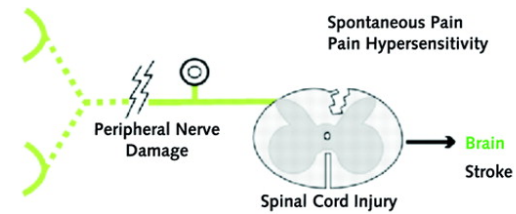
### A. Nociceptive Pain



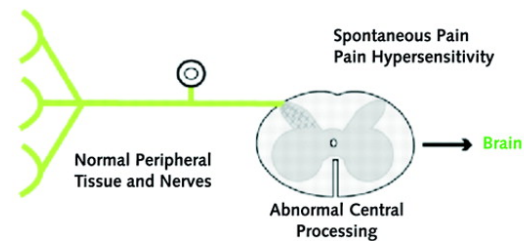
### B. Inflammatory Pain



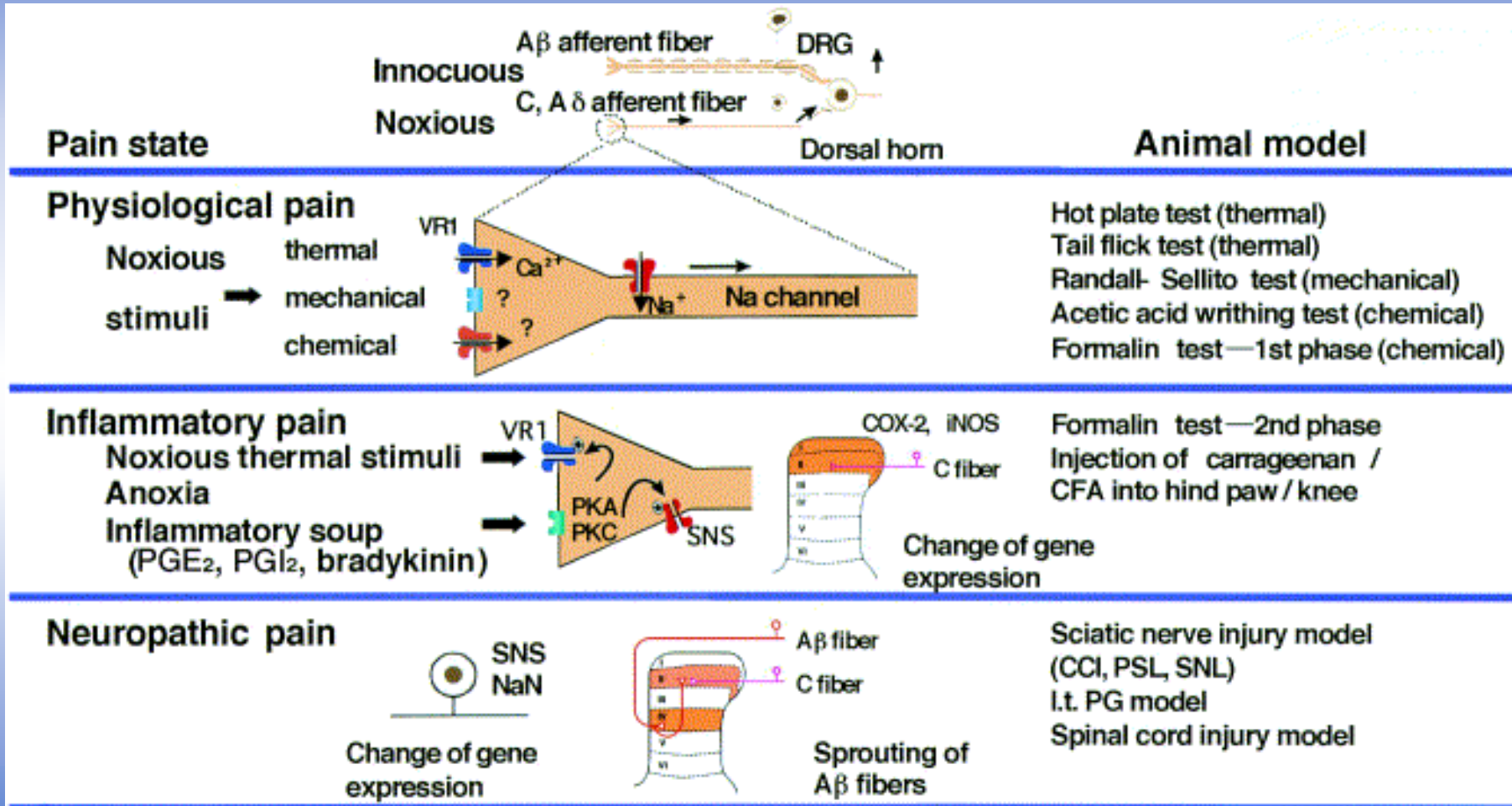
### C. Neuropathic Pain



### D. Functional Pain

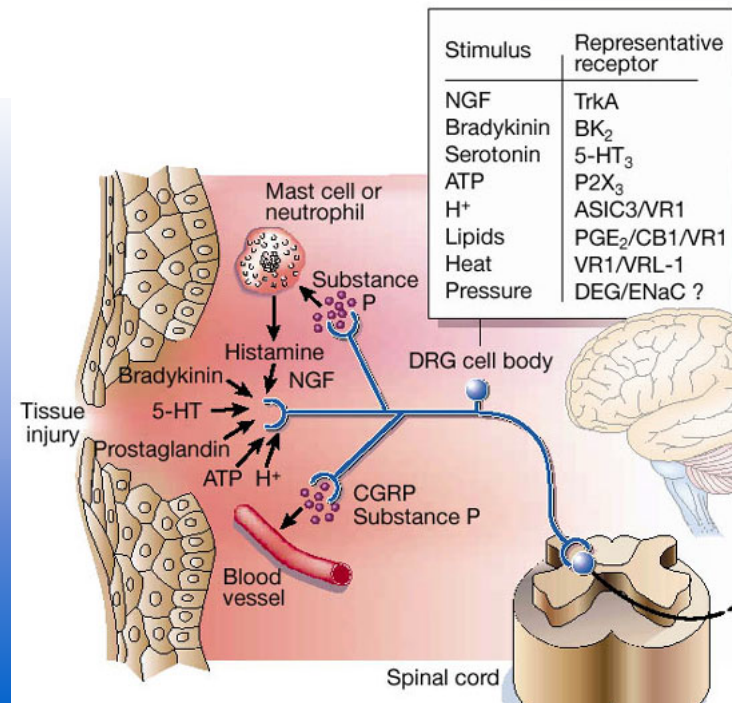


# Kivun fysiologiaa

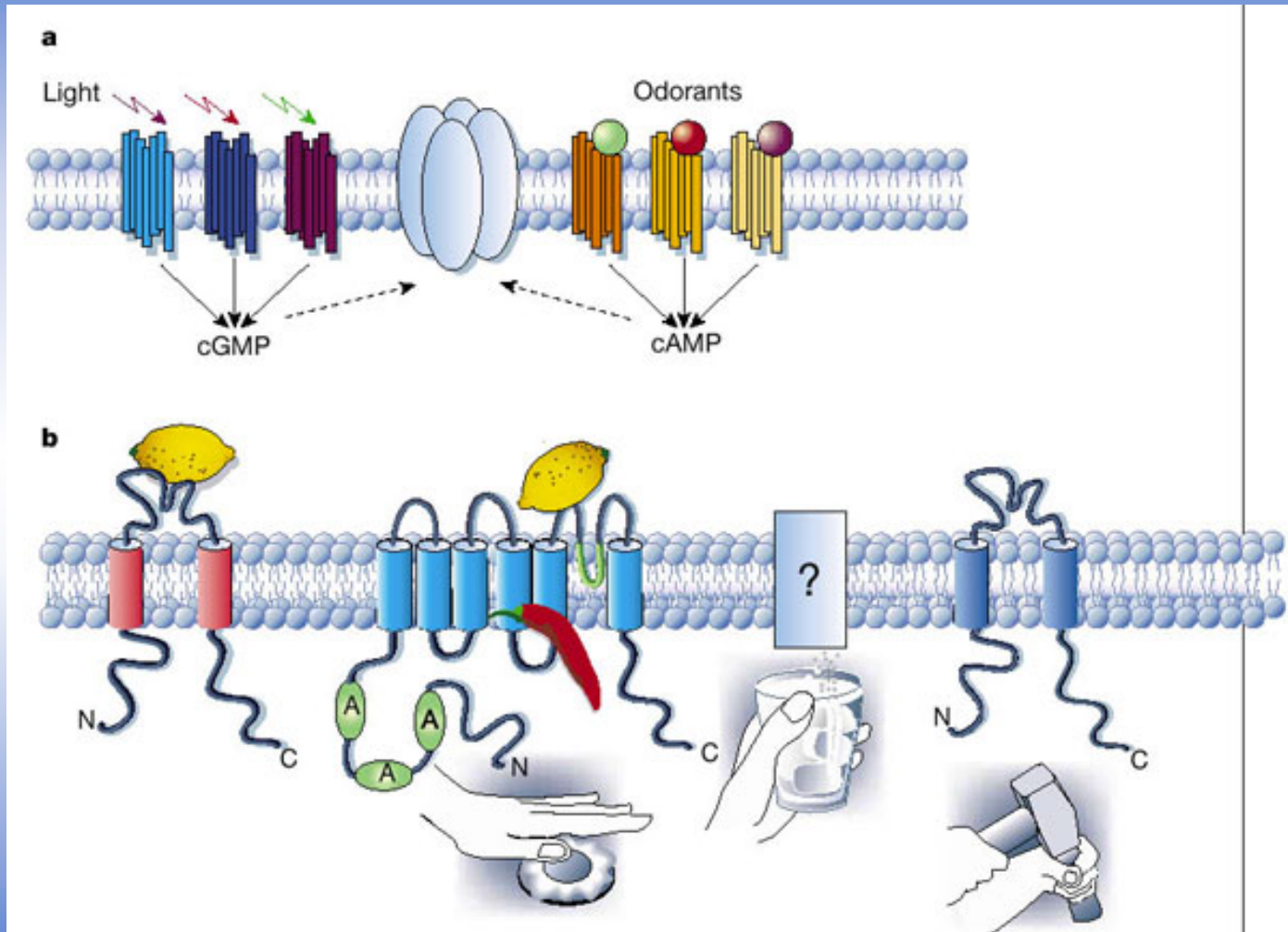


## Nosiceptors

- Peripheral receptors for pain, free nerve endings
- Nociceptors include receptors which are sensitive to painful mechanical stimuli, extreme heat or cold, and chemical stimuli.

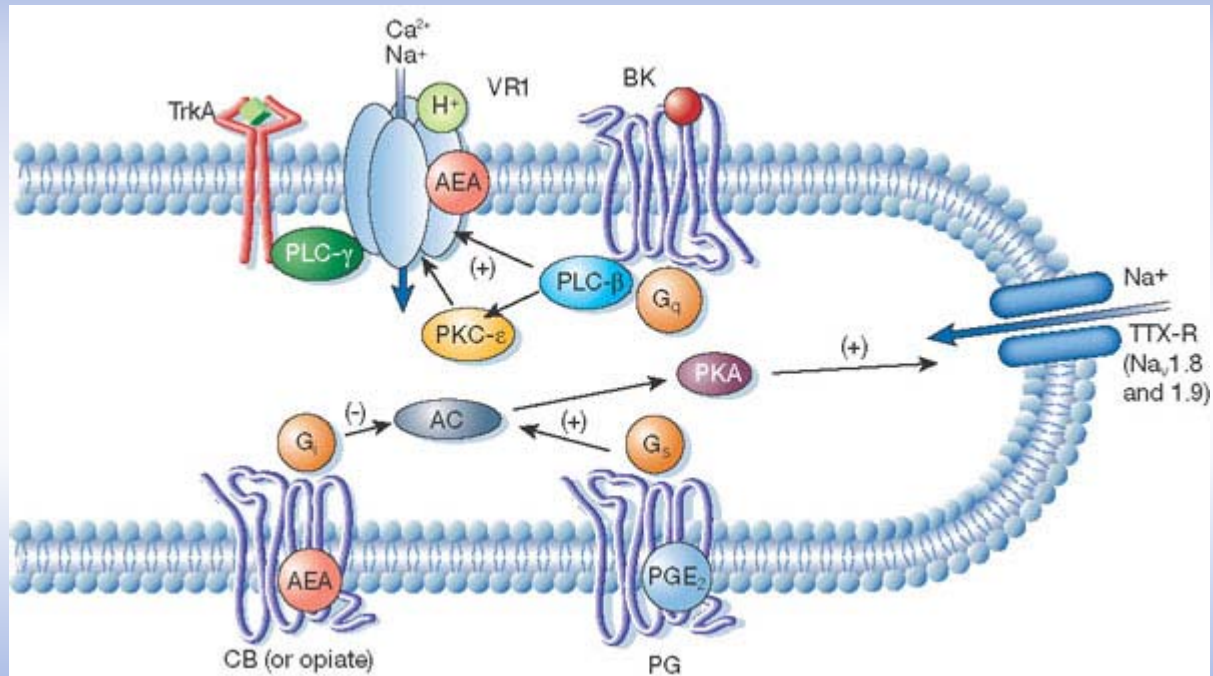


# Kivun fysiologiaa



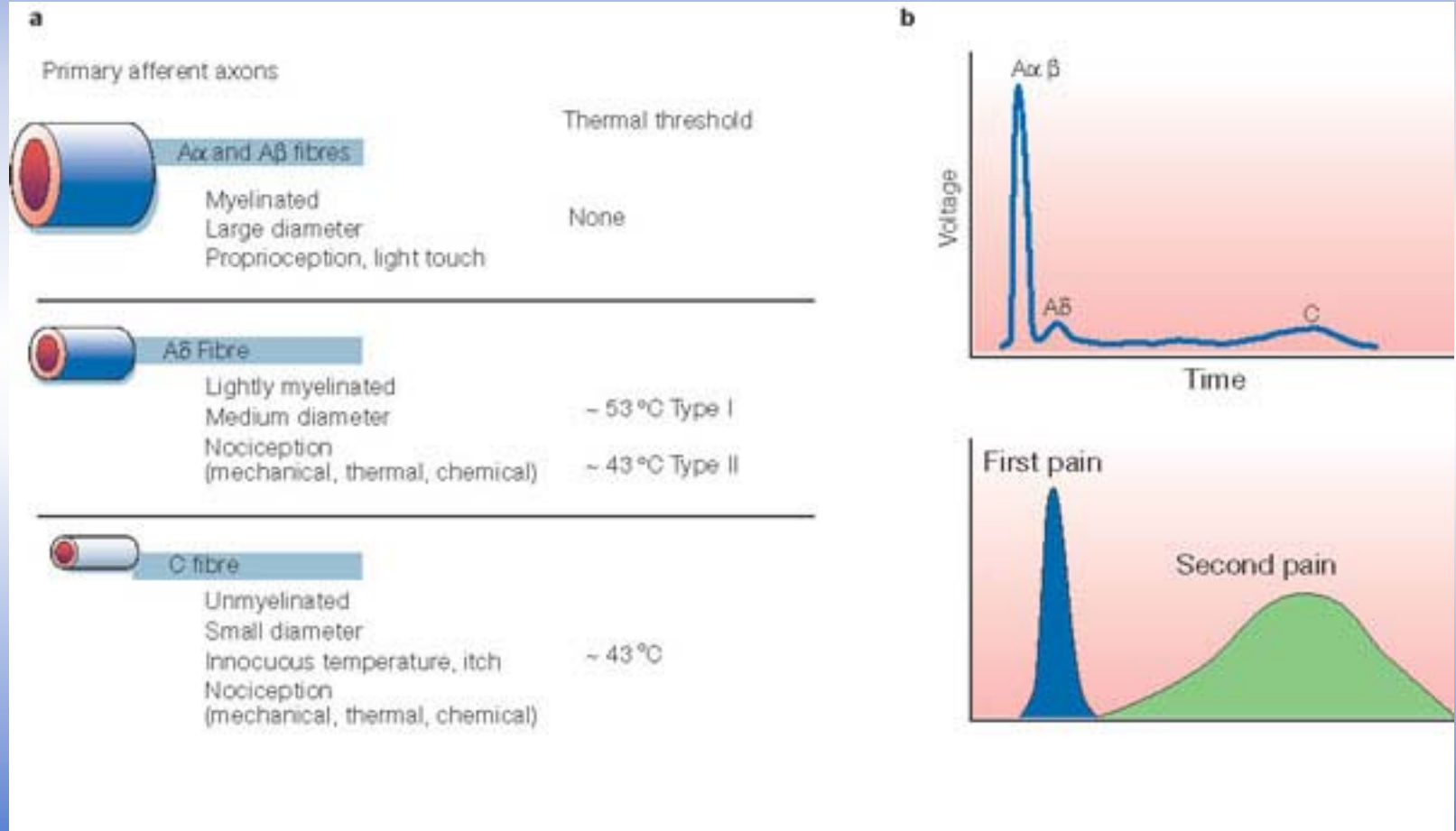
- Polymodal nociceptors use a greater diversity of signal-transduction mechanisms to detect physiological stimuli than do primary sensory neurons in other systems.

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When nociceptors are exposed to products of injury and inflammation, their excitability is altered by a variety of intracellular signalling pathways.

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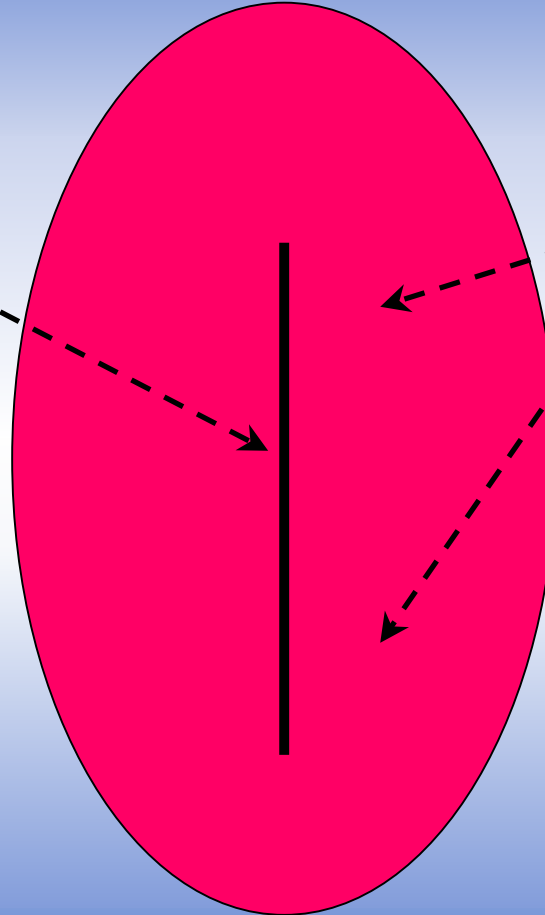




# Kivun fysiologiaa

## Ensi kipu

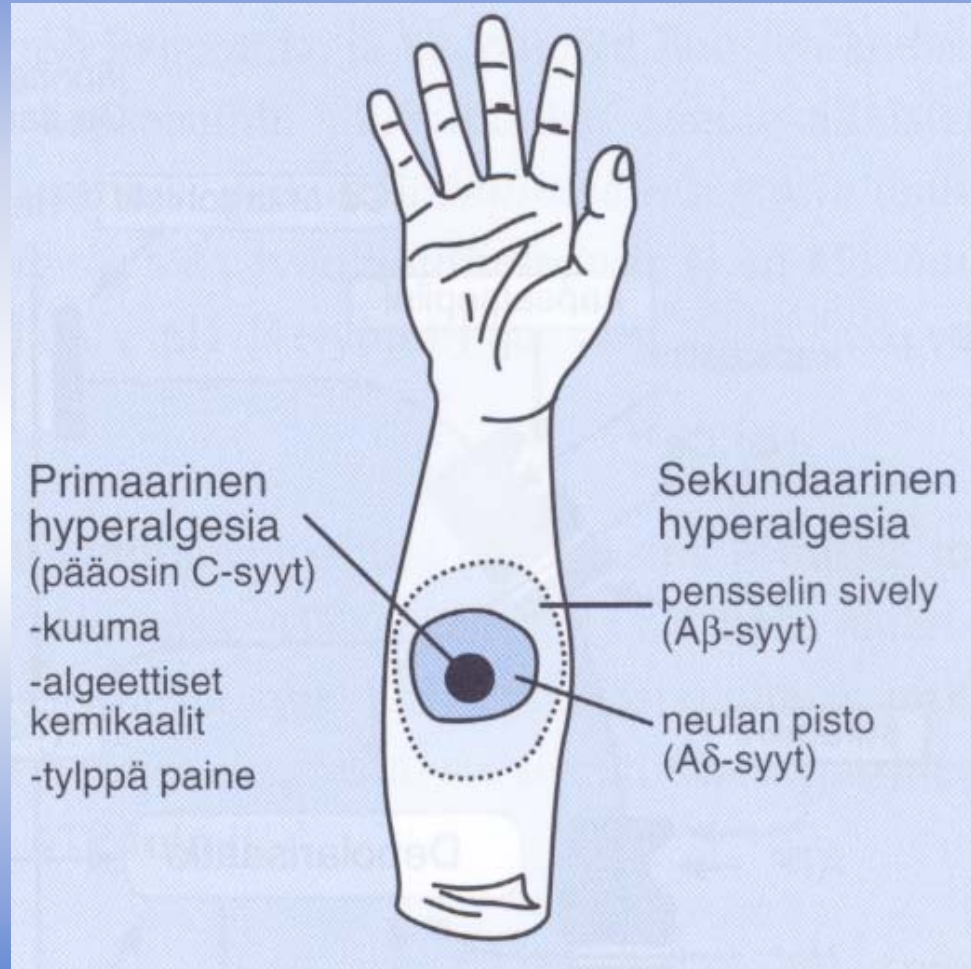
Lyhyt, terävä,  
hyvin paikallistuva



## Myöhempi kipu

Tylppä, huonommin  
paikantuva, pidempi-  
kestoinen

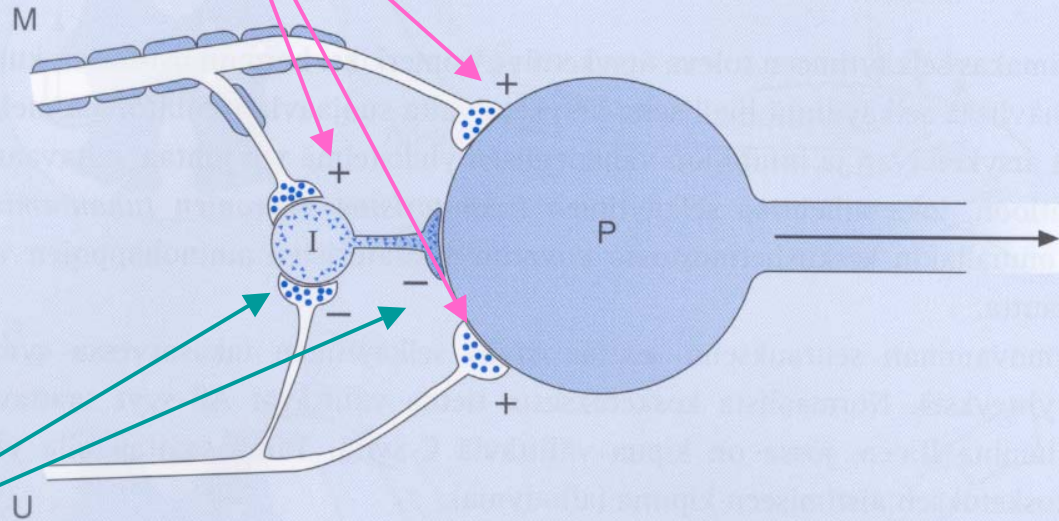
# Kivun fysiologiaa



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Aktivaatio

M = myeliinitupellinen hermosyy  
U = myeliinitupeton hermosyy  
I = inhibitorinen interneuroni  
P = projektioneuroni



Inhibitio

afferentit impulssit	vaikutus I-neuroniin	vaikutus P-neuroniin	P-neuronin aktiivisuus
M	+	+	0
U	-	+	++
M+U	0	+	+

Porttikontrolliteoria

The neurobiology of infant pain: Development of excitatory and inhibitory neurotransmission in the spinal dorsal horn. RAPM 2004

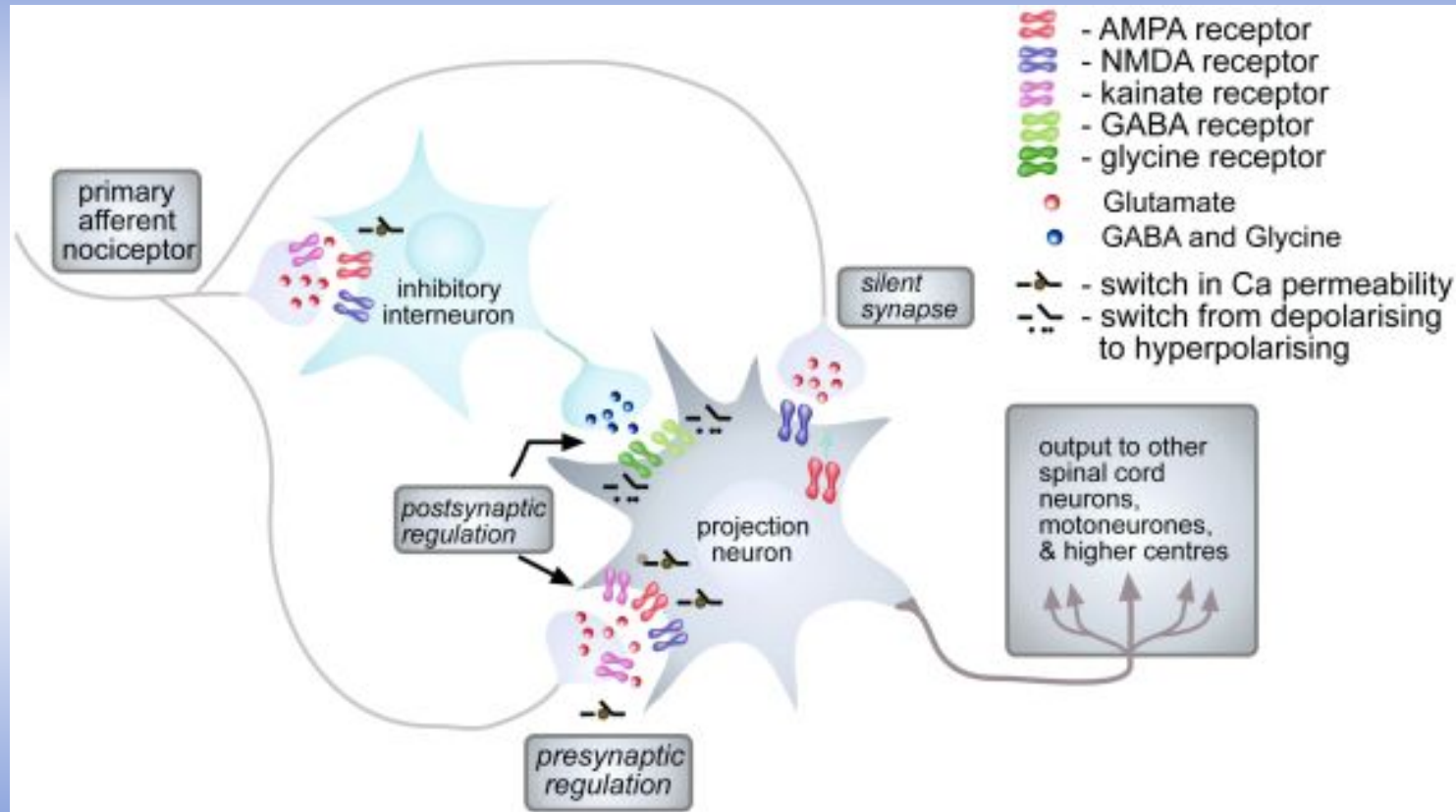
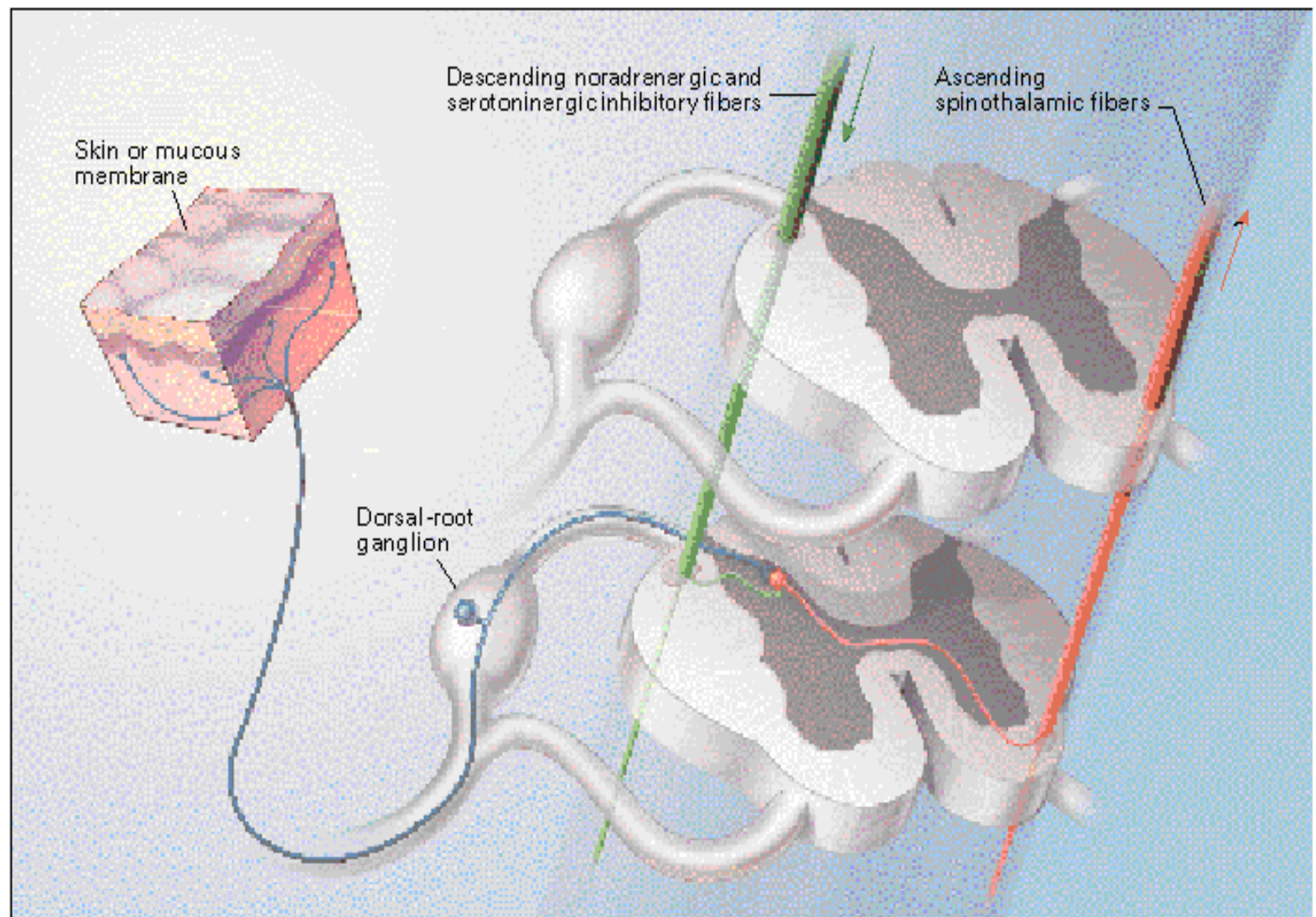
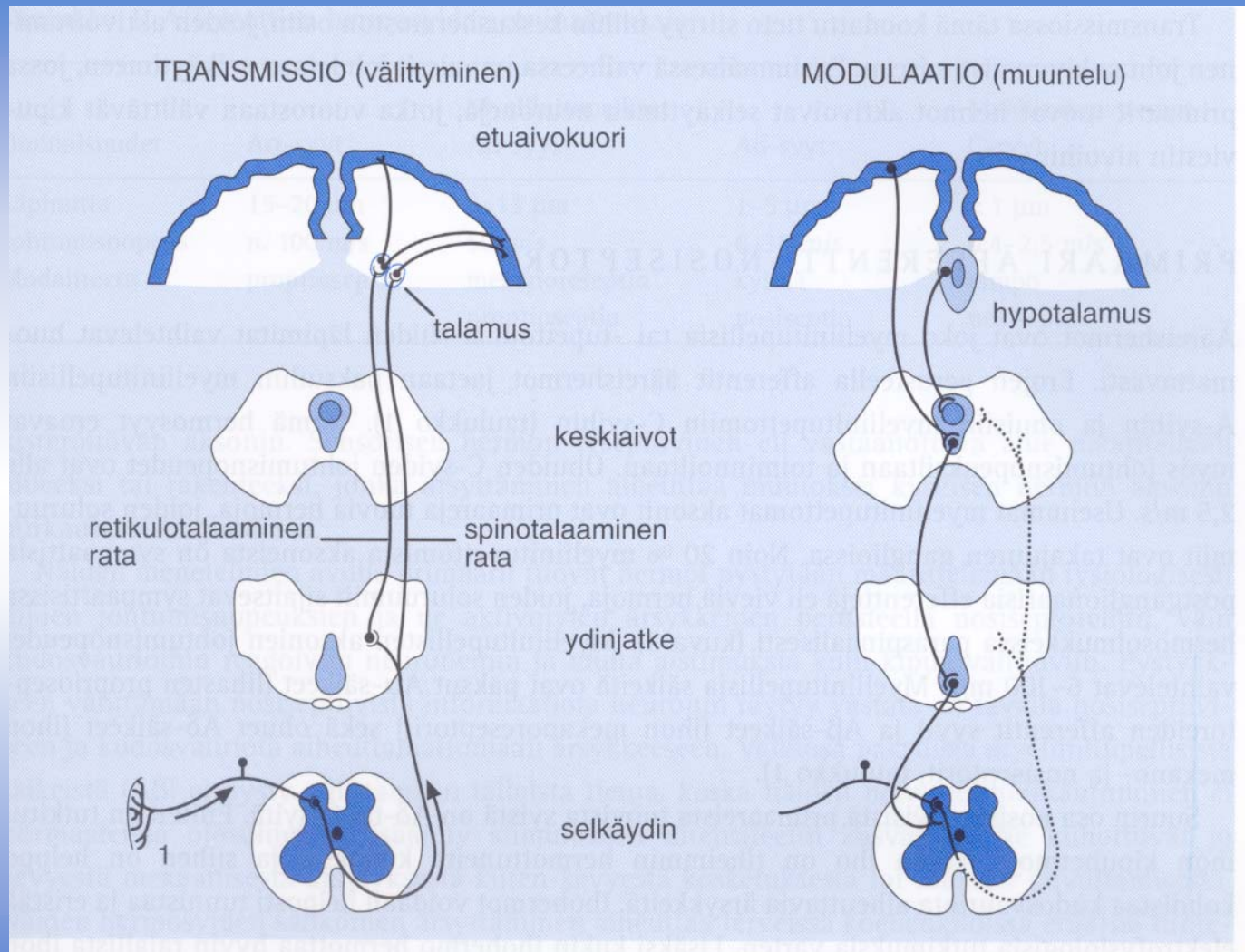


Diagram illustrating the synaptic basis for altered neurotransmission in the dorsal horn over the postnatal period.



Normaali kipuradan toiminta  
Kost and Straus 1996

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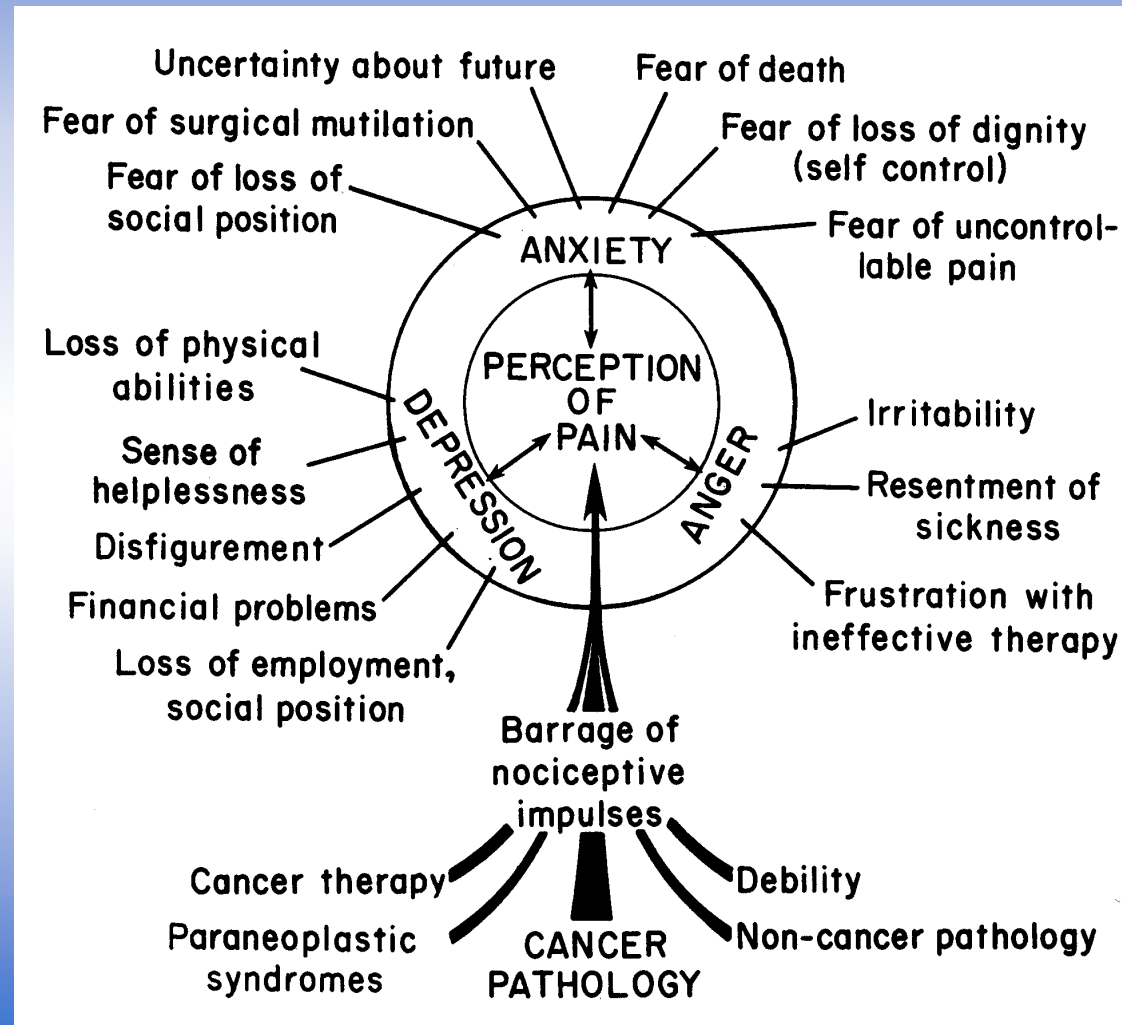


Kipujärjestelmän aktivaatio, välittyminen, muuntelu ja kokeminen

# Kivun fysiologiaa

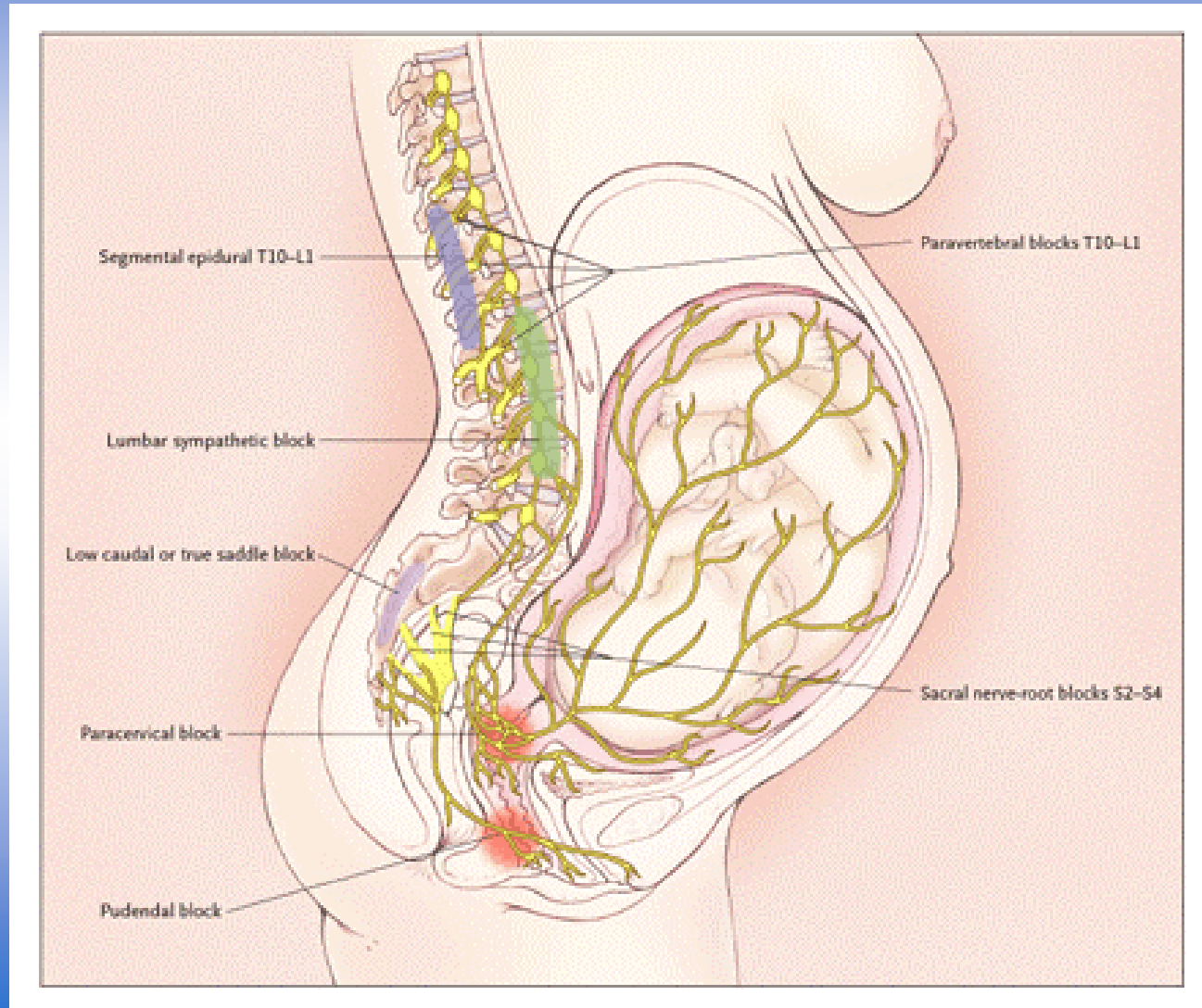
- *Perception* is influenced by myriad factors, including age, gender, culture, and individual history.
- *Suffering* is the result of how pain is interpreted.

# Kivun fysiologiaa





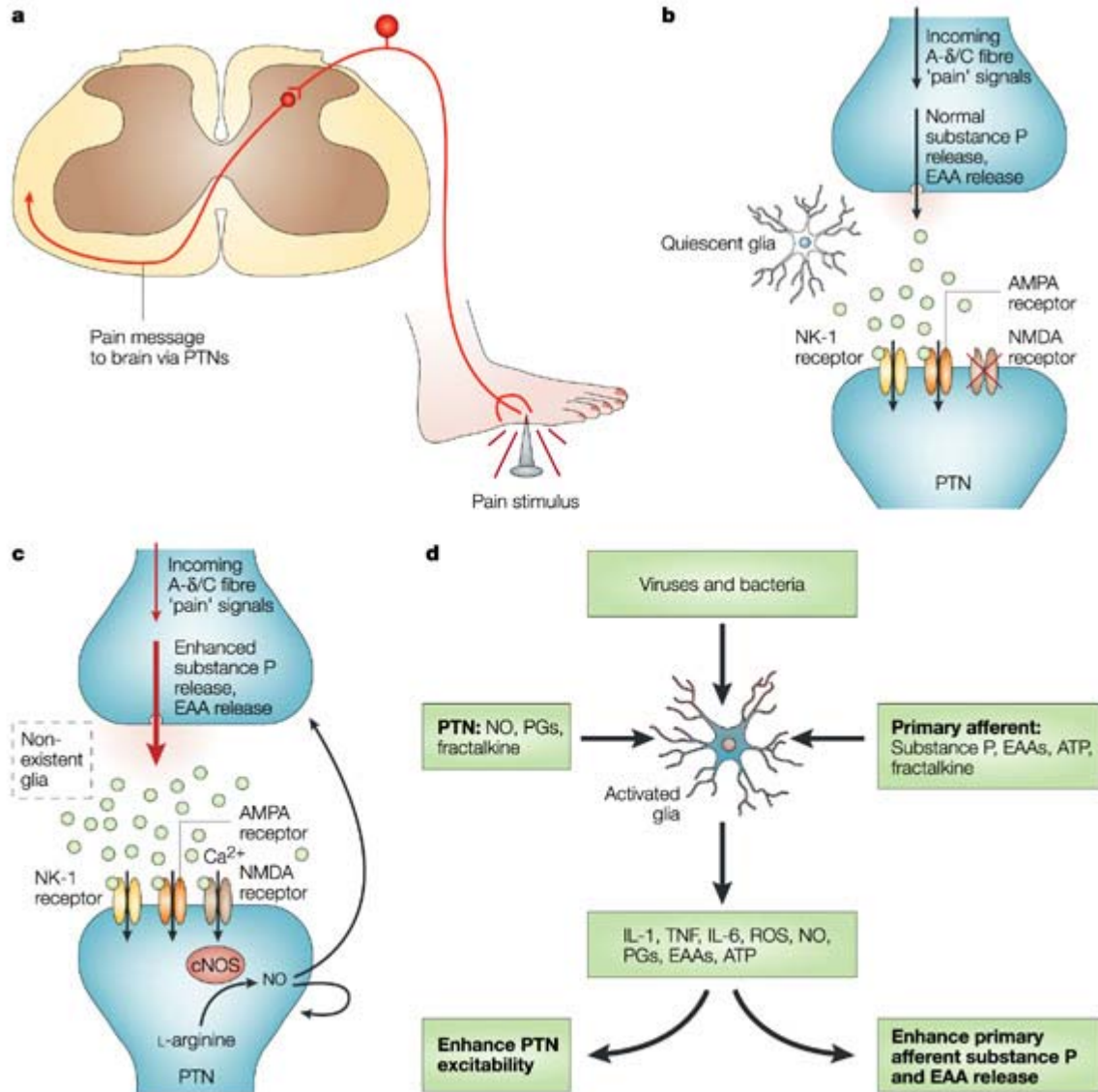
# Kivun fysiologiaa





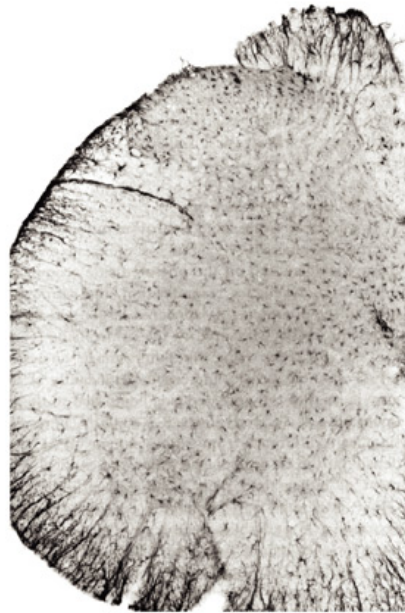
- Allodynia
  - Normaalisti kivuton stimulaatio aiheuttaa kipua.
- Hyperalgesia
  - Kivuliaat ärsykkeet aistitaan tavanomaista voimakkaammin.

# Kivun fysiologiaa

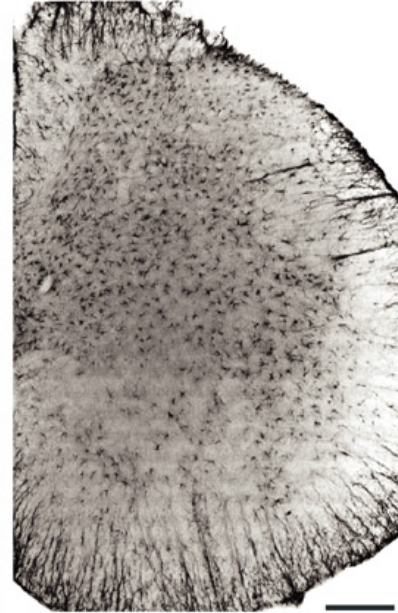


# Kivun fysiologiaa

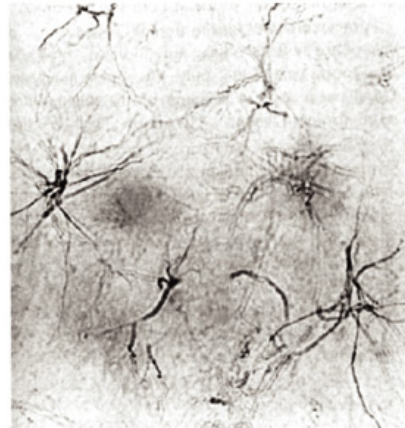
**a** Intact side



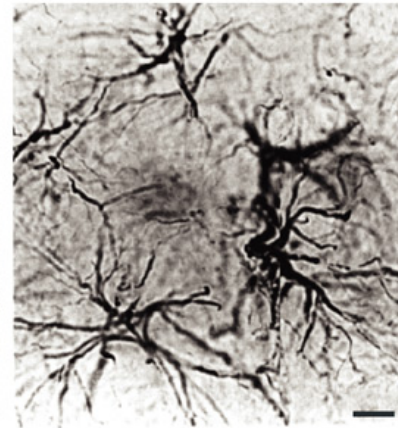
**b** Nerve-damaged side



**c** Intact side

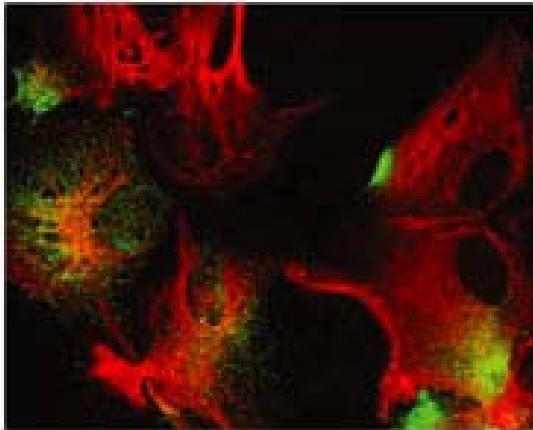


**d** Nerve-damaged side

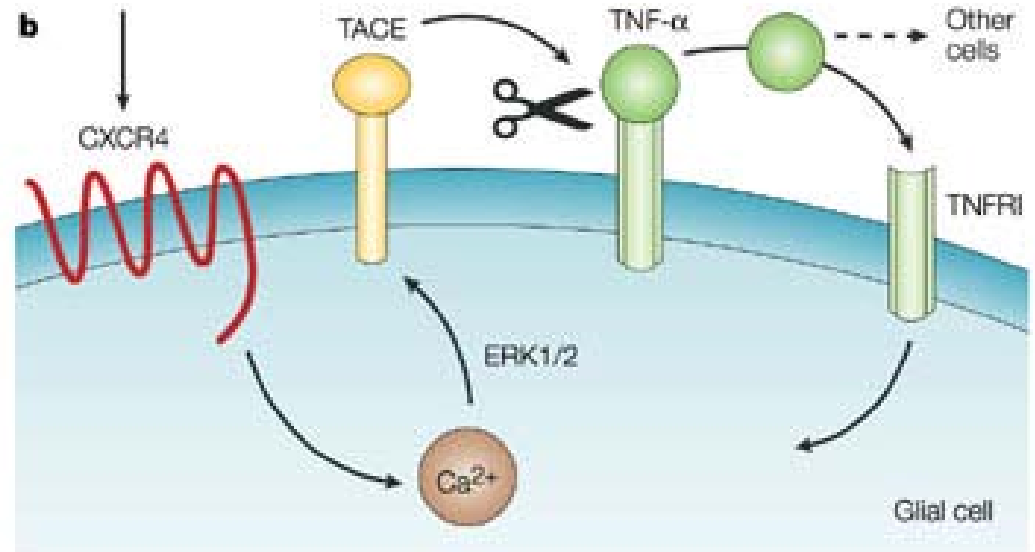


# Kivun fysiologiaa

**a**



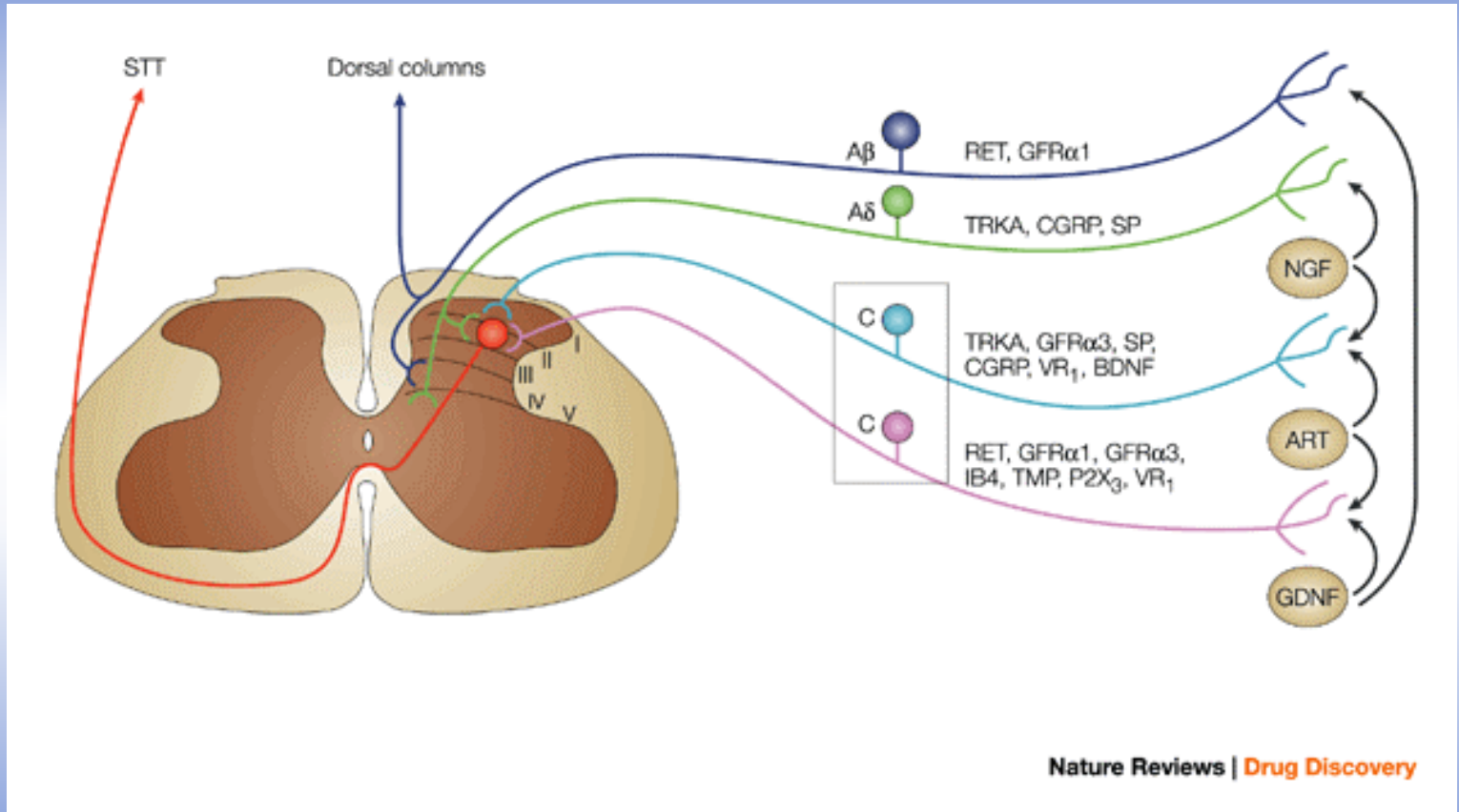
**b**



Nature Reviews | Drug Discovery

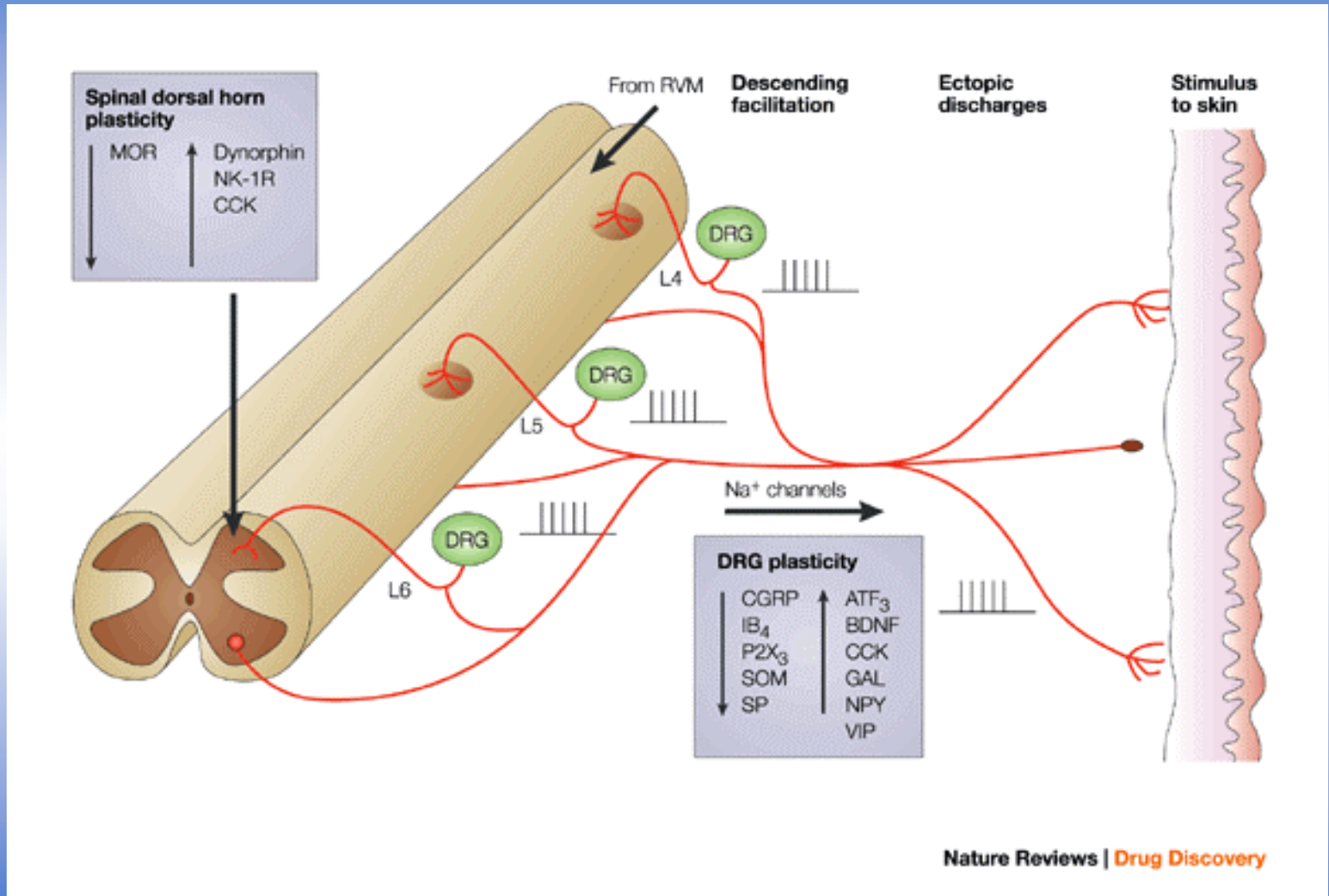
Constitutive expression and rapid release of tumour-necrosis factor (TNF)

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Subclasses of dorsal root ganglia neurons and sensory input to the spinal cord.

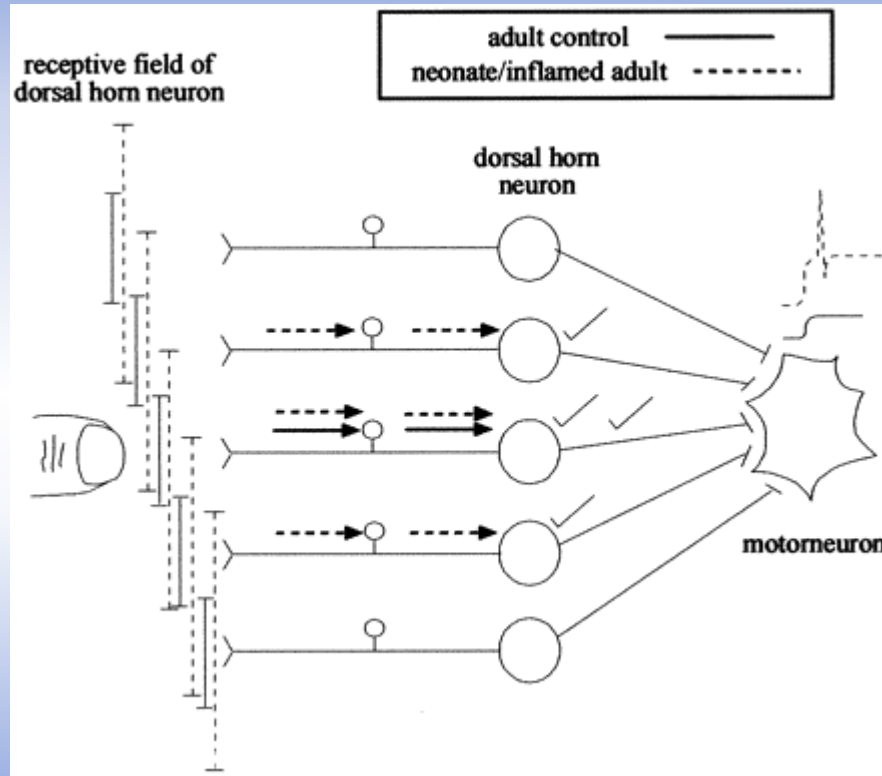
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Cellular mechanisms of neuropathic pain.

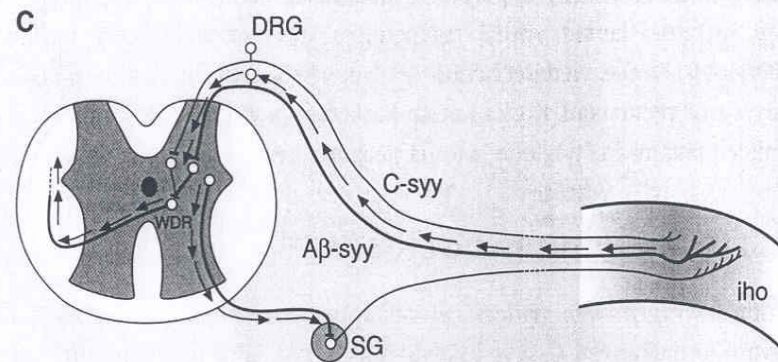
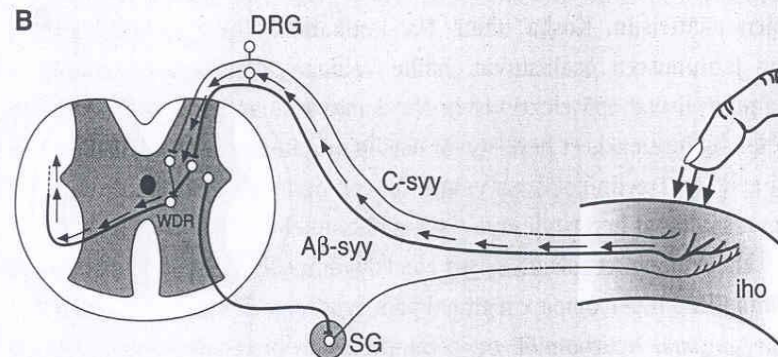
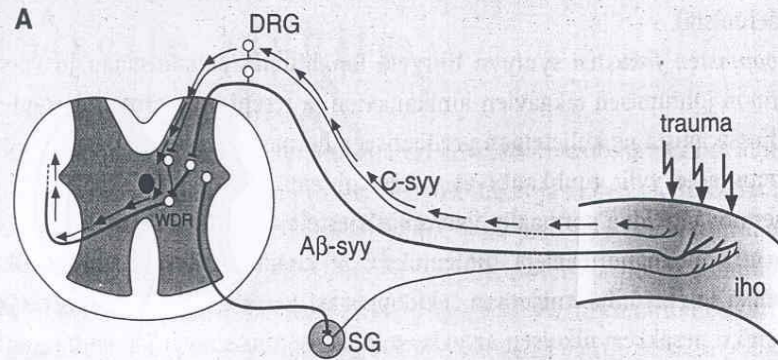


Age-dependent effects of peripheral inflammation on the electrophysiological properties of neonatal rat dorsal horn neurons. J Neurophysiol. 2002



Schematic representation of how large receptive fields can result in lower thresholds. given stimulus may well activate neurons in the spinal cord dorsal horn but the resultant input to motor neurons may be subthreshold in terms of evoking the

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WDR = "wide dynamic range" -neuronit  
SG = sympaattinen ganglio

## Neuropaattinen kipu on luultua yleisempää



**Neuropaattinen kipu**

**Seka-  
muotoinen kipu**

**Nosiseptiivinen kipu**

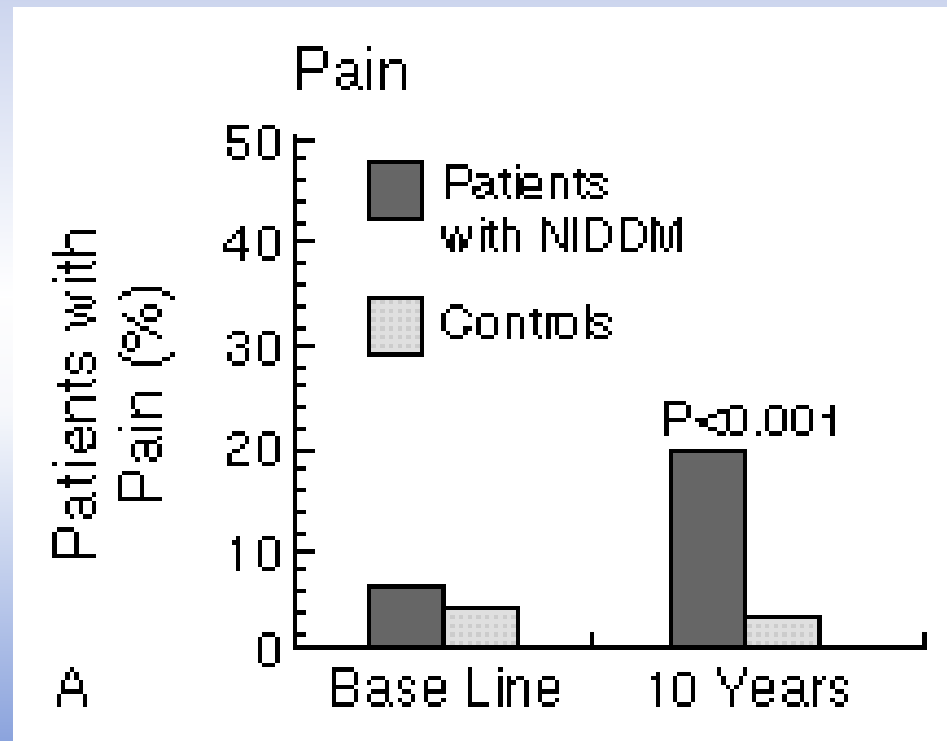
### Tyypillisiä oireita:

- Polttava
- Tuikkiva
- Kihelmöivä
- Pistelevä
- Lisääntynyt herkkyys kosketukselle tai lämpötilalle

### Tyypillisiä oireita:

- Särky
- Jomotus
- Terävä kipu

# Diabetes ja hermokivut



Partanen J, et al. N Engl J Med 1995

# Kivun fysiologiaa

Table 1 | **Causes and sub-types of neuropathic pain**

<b>Class</b>	<b>Sub-type of neuropathic pain</b>
Traumatic mechanical injury	Entrapment neuropathy Nerve transection Causalgia Spinal cord injury Post-surgical pain Phantom limb pain Scar formation
Metabolic or nutritional	Alcoholic neuropathy Pellagra Beriberi Burning feet syndrome
Viral	Post-herpetic neuralgia HIV/AIDS pain
Neurotoxicity	Vincristine Cisplatin Taxol Thallium Arsenic Radiation therapy
Disease (non-viral)	Diabetes Malignancies Multiple sclerosis Trigeminal neuralgia Guillain-Barre syndrome Fabry's disease Tangier disease Vasculitic/angiopathic Amyloid Idiopathic
Ischaemia	Thalamic syndrome Post-stroke pain
Neurotransmitter function	Complex regional pain syndrome

- PERIFEERINEN HERKISTYMINEN

# • PERIFERINEN HERKISTYMINEN

Kudosvaurio

Inflammaatio

Sympaattisen hermot

HERKISTÄVÄ "SEOS"

Vety ionit  
Adrenaliini  
Bradykiniini

Histamiini  
Kalium ionit  
Prostaglandiinit

Puriinit  
Sytokiinit  
5-HT

Leukotrieenit  
Hermon kasvutekijä  
Neuropeptidit

Nosiseptoreiden  
herkistyminen

Korkean ärsytyskynnyksen  
nosiseptorit

Alhaisen ärsytyskynnyksen  
nosiseptorit

- KESKUSHERMOSTON  
HERKISTYMINEN



- KESKUSHERMOSTON HERKISTYMINEN

Nosiseptoreiden ärsytys



Ärsytyksestä riippuva  
takasarven neuronien  
lisääntynyt herkkyys



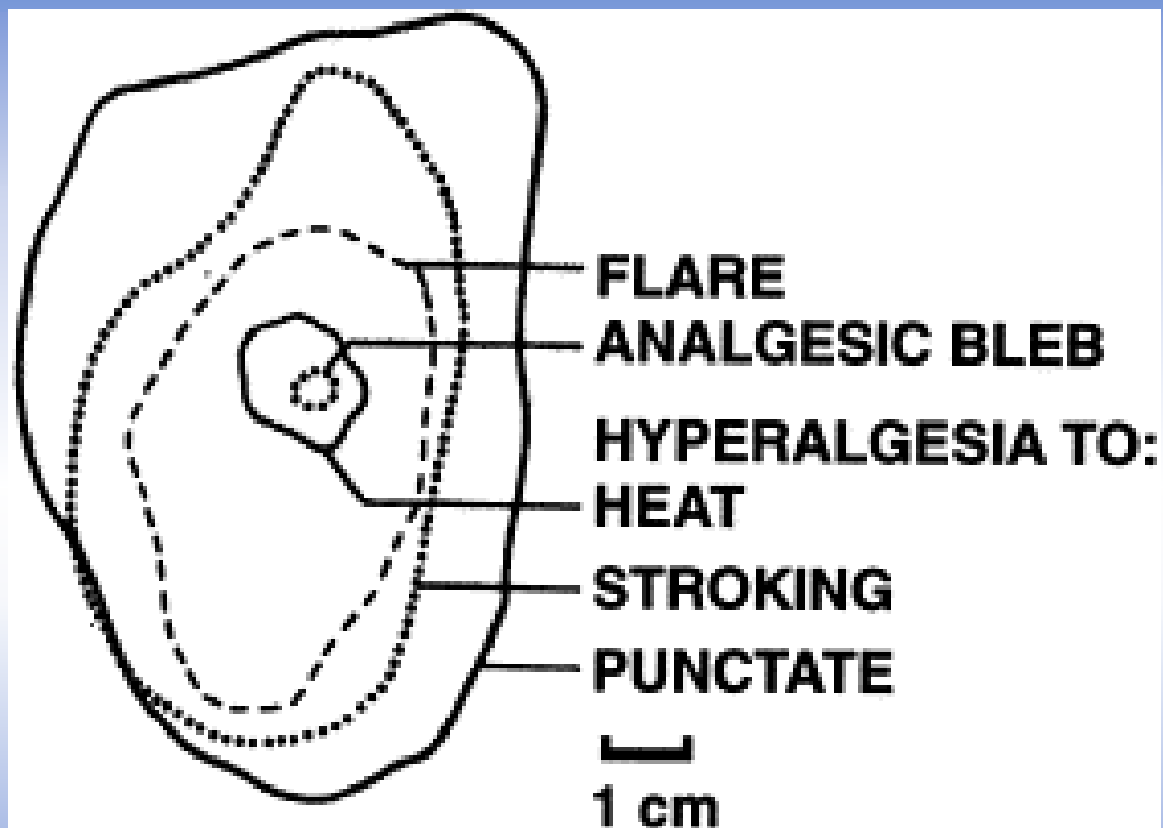
Herkistynyt vaste



KIPU  
Mekaaninen allodynia

Alhaisen ärsytyskynnyksen  
mekanoreseptorit  
(A- $\beta$  hermot)





- Keskushermoston herkistyminen

# Lumettako vain ? Eija Kalso

## Duodecim 2002; 118:1733-4

- PET-kameralla todettu että lume (NaCl) ja opioidi (remifentaniili) aktivoi osittain samat hermoverkot ja lumeesta hyvän analgesian saavien kivut lievittyvät opioideillakin tehokkaasti
- ”Lume aktivoi kognitiivisten vihjeiden avustamana hermoverkoston, jossa endogeeninen opioidijärjestelmä välittää kivunlievityksen”