

Neurobiologie van Pijn

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Definitie van pijn

Pijn is een onplezierige, sensorische en emotionele ervaring die gepaard gaat met feitelijke of mogelijke weefselbeschadiging of die beschreven wordt in termen van een dergelijke beschadiging.

IASP 1979

Definitions of Pain

- **PAIN**

“An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.”¹

- Alternative proposals:

- *“Pain is a distressing experience associated with actual or potential tissue damage, with sensory, emotional, cognitive and social components.”*²
- *“An aversive sensory and emotional experience typically caused by, or resembling that caused by, actual or potential tissue injury.”*³

- **CHRONIC PAIN**

“Persistent or recurrent pain lasting longer than 3 months”

1. IASP 1994 & 2008. Williams AC, Craig KD. Updating the definition of pain. *Pain*. 2016;157(11):2420-33. proposed by the IASP Definition of Pain Taskforce Aug 2019.4. Treede R-D, et al. et al. *Pain*. 2019;160:19–27

ICD-11 adopted !

MG30 Chronic pain

Persistent or recurrent pain lasting longer than 3 months

MG30.0 Chronic primary pain

MG30.1 Chronic cancer related pain

MG30.2 Chronic postsurgical or post traumatic pain

MG30.3 Chronic secondary musculoskeletal pain

MG30.4 Chronic secondary visceral pain

MG30.5 Chronic neuropathic pain

MG30.6 Chronic secondary headache or orofacial pain

MG30.Y Other specified chronic pain

MG30.Z Chronic pain, unspecified

MG31 Acute pain

MG3Z Pain, unspecified



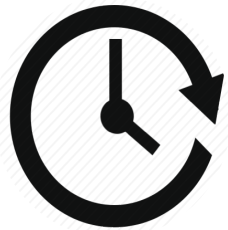
World Health Assembly Update, 25 May 2019

25 May 2019 | News release | Geneva

International Statistical Classification of Diseases and Related Health Problems (ICD-11)

Member states agreed today to adopt the eleventh revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-11), to come into effect on 1 January 2022.

Classificatie van pijn



Duur

Acuut
Chronisch



Mechanisme

Nociceptief / Inflammatoir
Neuropathisch
Nociplastisch
Gemengd



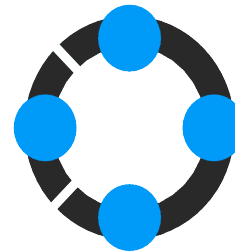
Intensiteit

Mild
Matig
Ernstig



Aandoeningen

Kanker
Niet-kanker



andere

Achtergrondpijn
Doorbraakpijn

Nociceptie (pijnzin)

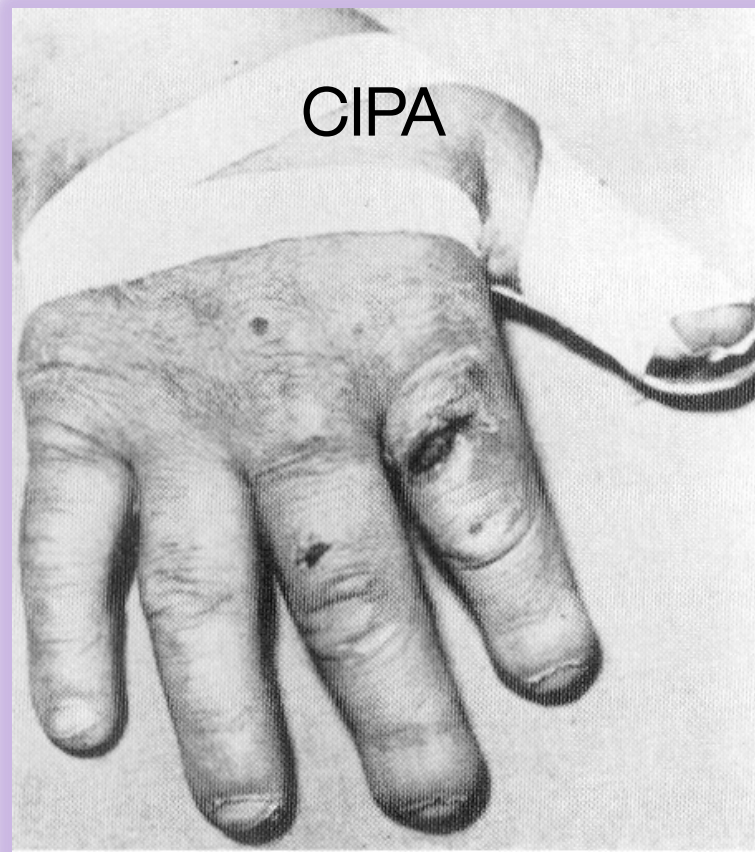
...het vermogen van een organisme om weefselbeschadiging of dreigende weefselbeschadiging waar te nemen

IASP: Het neurale proces van codering van (potentieel) schadelijke stimuli.

- *Gevolgen van deze codering*
 - *autonoom (vb. verhoogde bloeddruk)*
 - *gedragmatig (vb. terugtrekken of meer complex pijngedrag).*
 - *Pijnervaring is niet noodzakelijk.*



Pijn als beschermend mechanisme

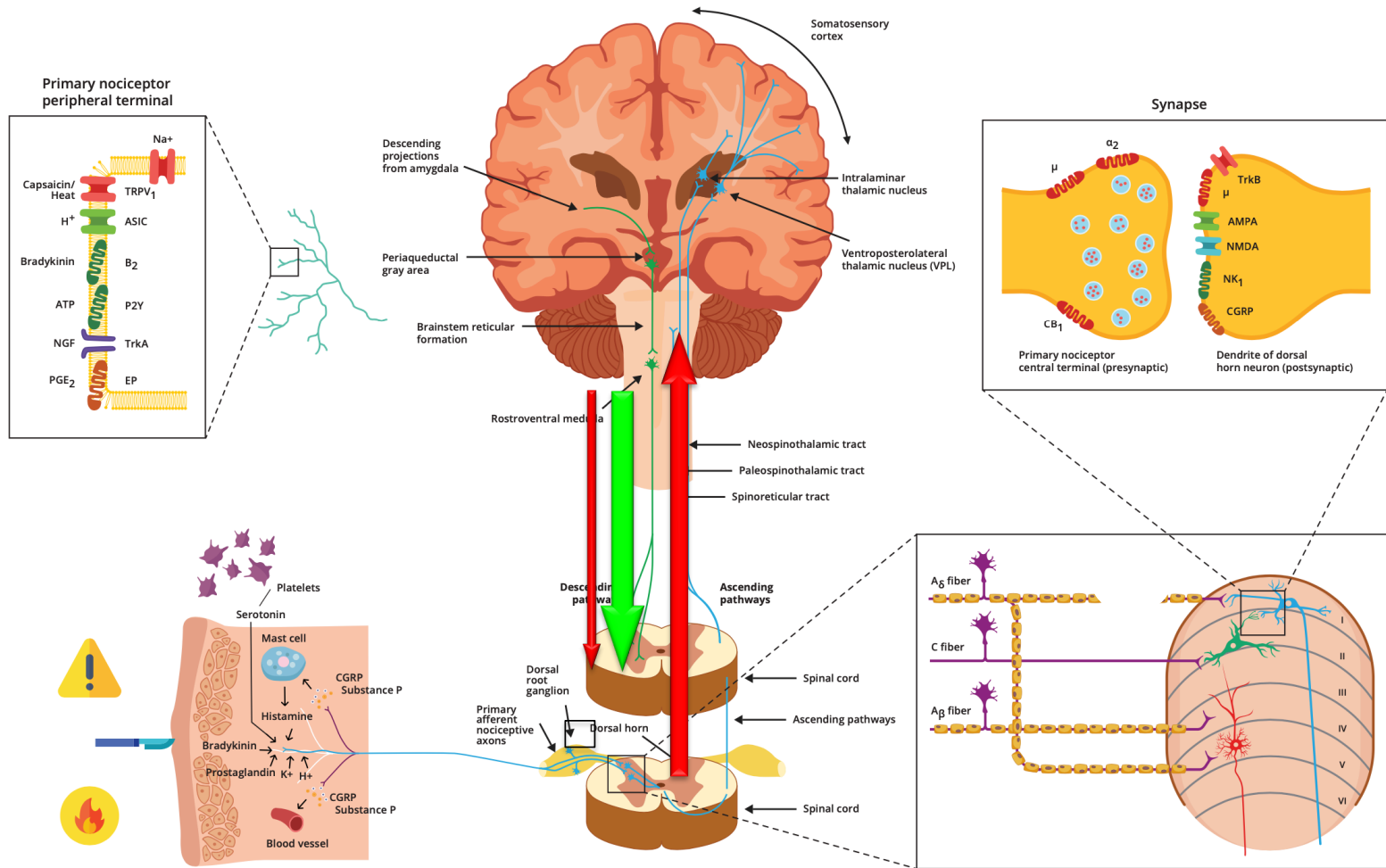


Pijn is een biopsychosociaal fenomeen



Neurobiologie van pijn

- Transductie
- Transmissie
- Modulatie
- Perceptie



Graphic composed by the author

Neurofarmacologie

- **Transductie**

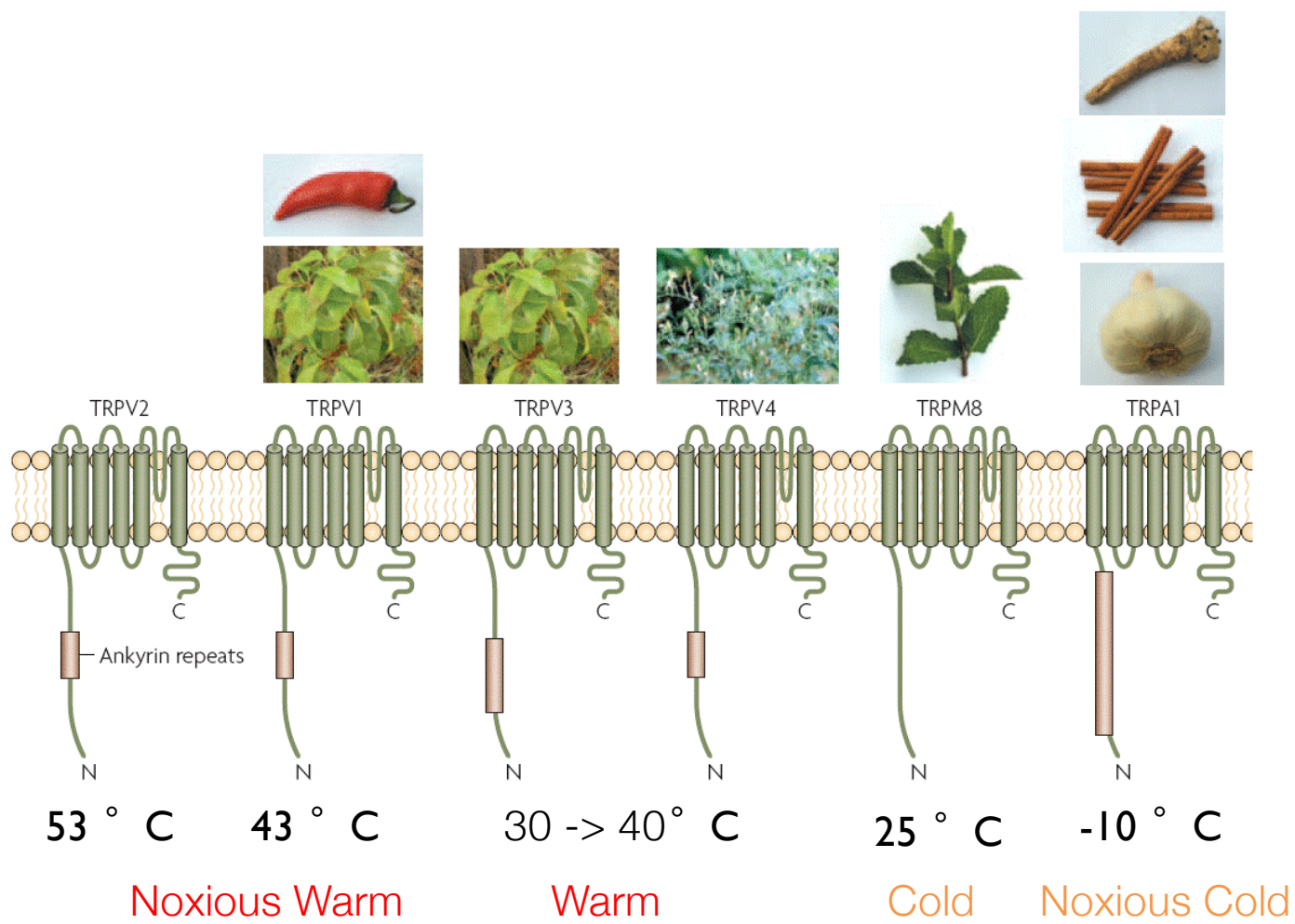
- Temperatuur Warmte: TRPV1, TRPV2, TRPV3, TRPV4, P2X3
- Temperatuur Koude: TRPM8, TRPA1
- Mediatoren bij weefselschade : P2X3, P2Y, Bradykinine B1/2, 5-HT3 en andere 5-HT
- Mechanoreceptoren: TRPV4, TRPC/V/P
- Inflammatoire mediators en targets: H⁺, PG, NGF, IL-1, TNF, Ligand en Spanningsafhankelijke kanalen (bv. TRPV1, NaV1.9, NaV1.7 en NaV1.8)

- **Transmissie**

- NaV1.7, NaV1.8, NaV1.9, NaV1.1, NaV1.2, NaV1.6

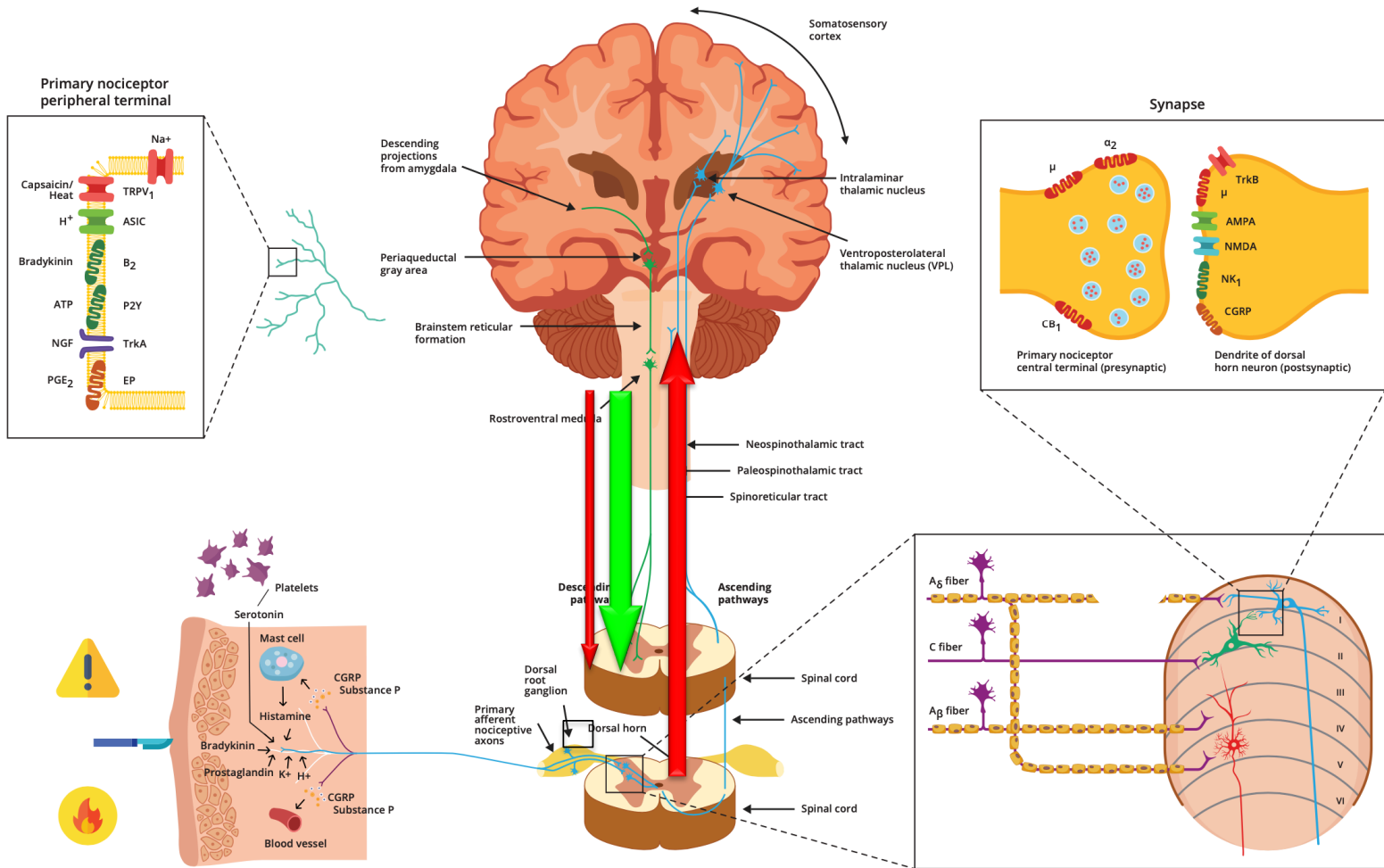
- **Modulatie**

- Excitatorisch: Glutamaat, ATP, Neuropeptiden, BDNF
- Inhibitorisch: Glycine, MOR, CB1/CB2 GABA
- Microglia activatie: ATP via P2X4, P2X7, CCL, BDNF, Fractaline



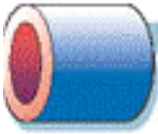


Neurobiologie van pijn

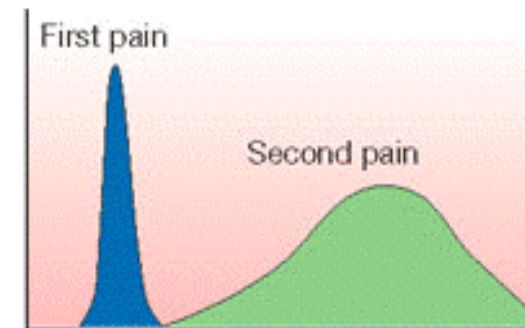
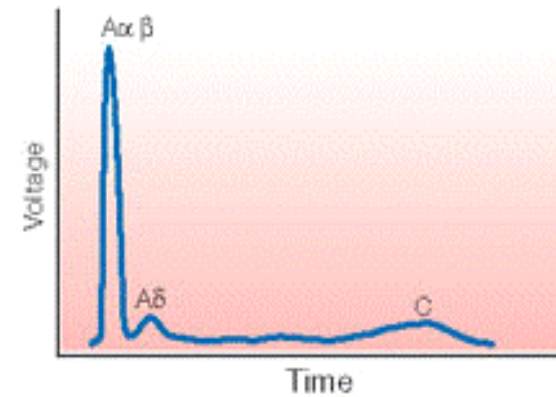
- Transductie
- Transmissie
- Modulatie
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Graphic composed by the author

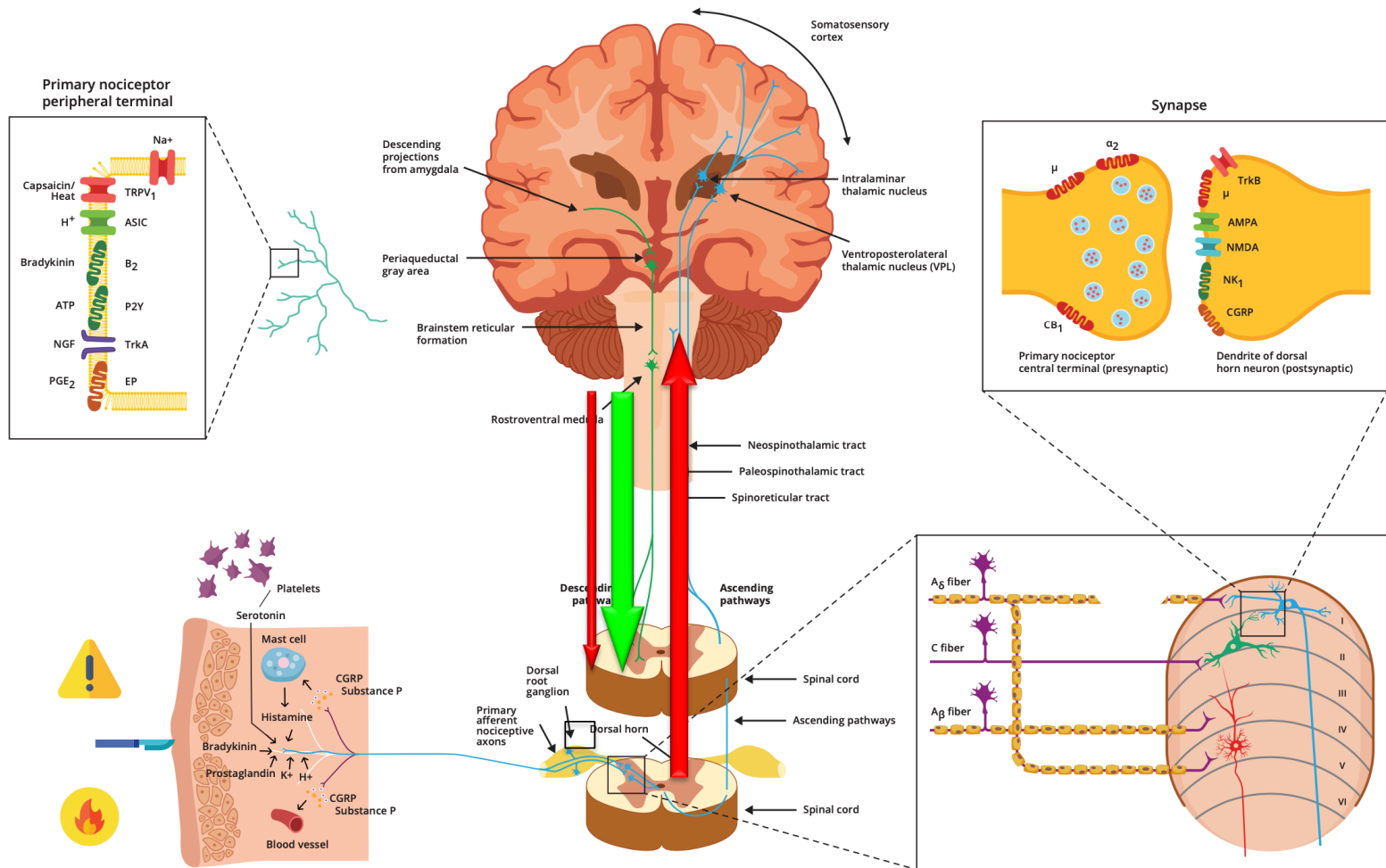
Primary afferent axons

Primary afferent axons		Thermal threshold
 <p>Aα and Aβ fibres</p> <p>Myelinated Large diameter Proprioception, light touch</p>		None
 <p>Aδ Fibre</p> <p>Lightly myelinated Medium diameter Nociception (mechanical, thermal, chemical)</p>	<p>~ 53°C Type I</p> <p>~ 43°C Type II</p>	
 <p>C fibre</p> <p>Unmyelinated Small diameter Innocuous temperature, itch Nociception (mechanical, thermal, chemical)</p>		~ 43°C

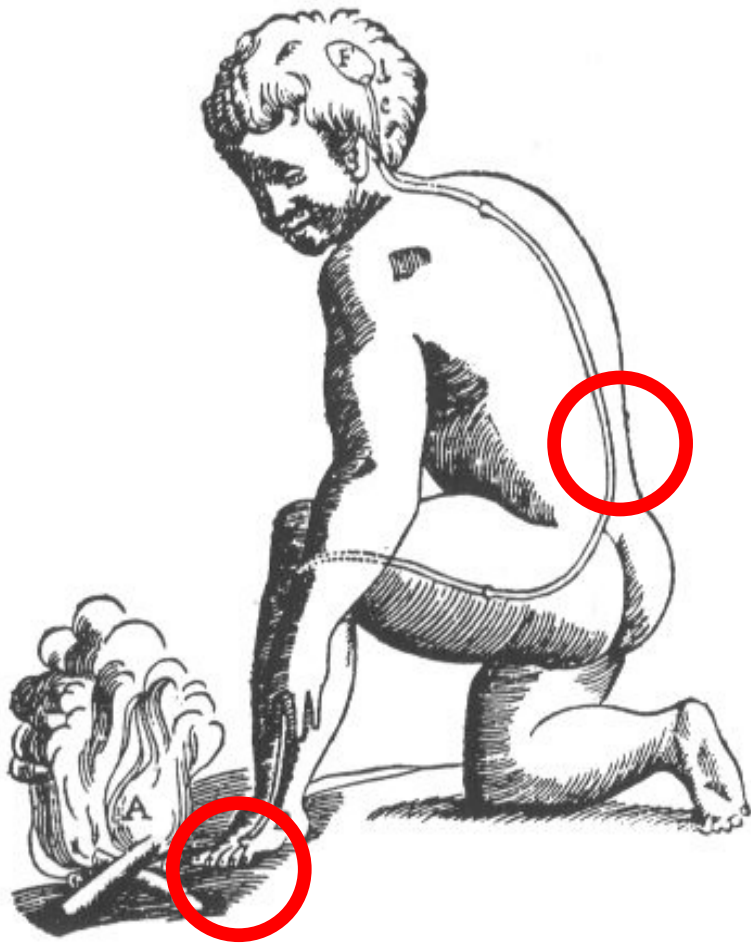


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Graphic composed by the author



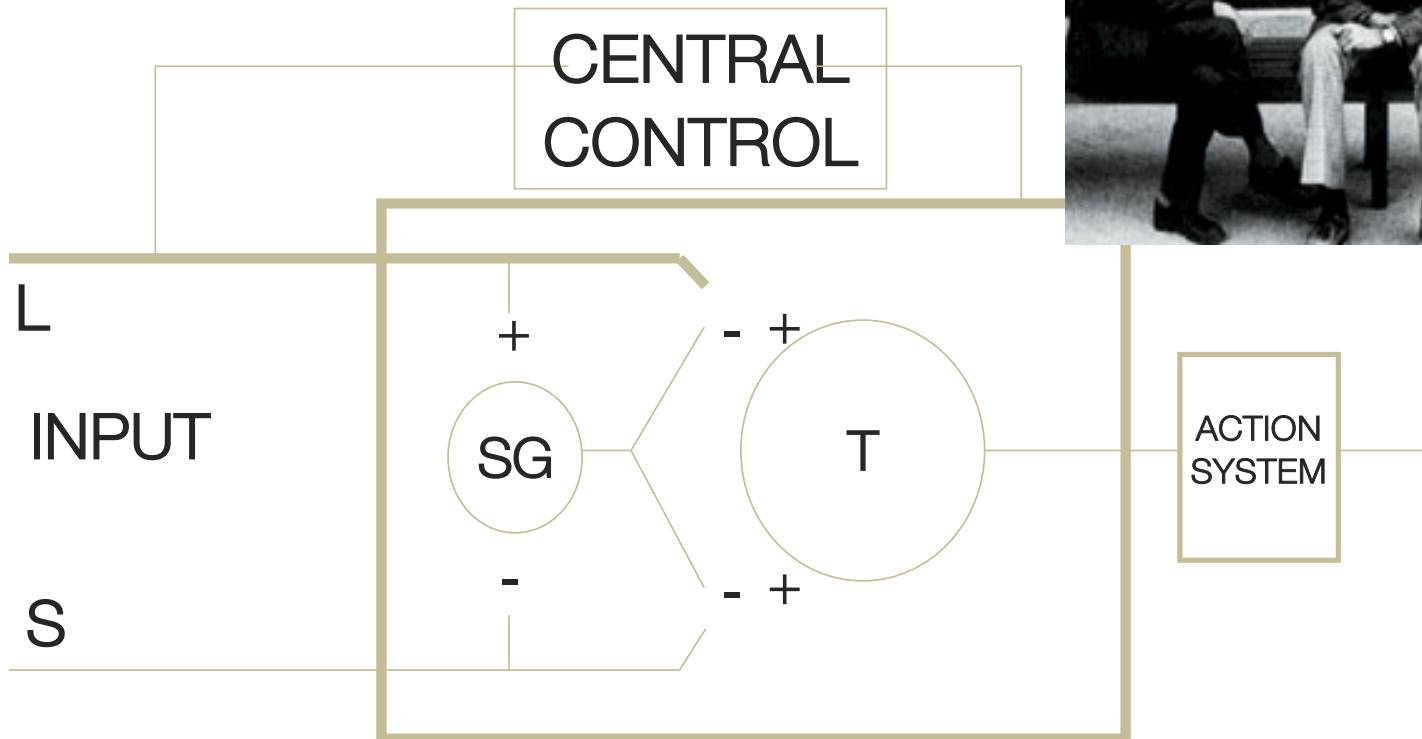
**Filter in het
ruggenmerg**

**Sensoren
Voelers, metertjes**



“Gate Control Theory”

Melzack en Wall 1965

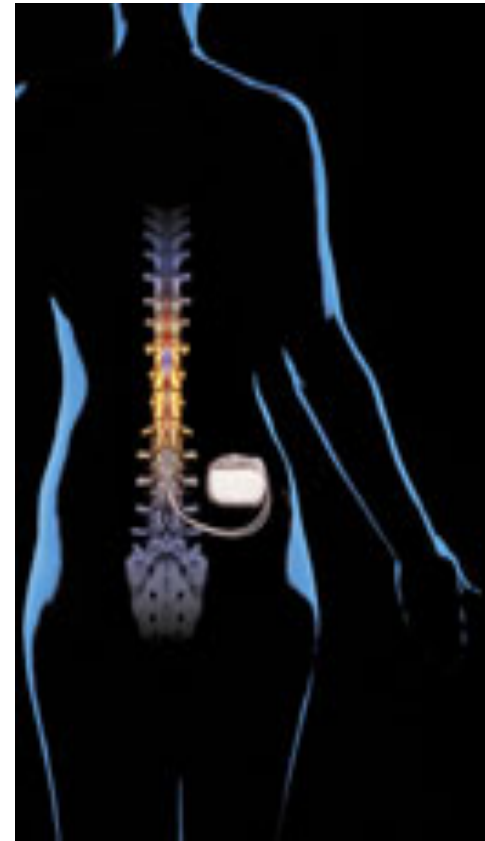
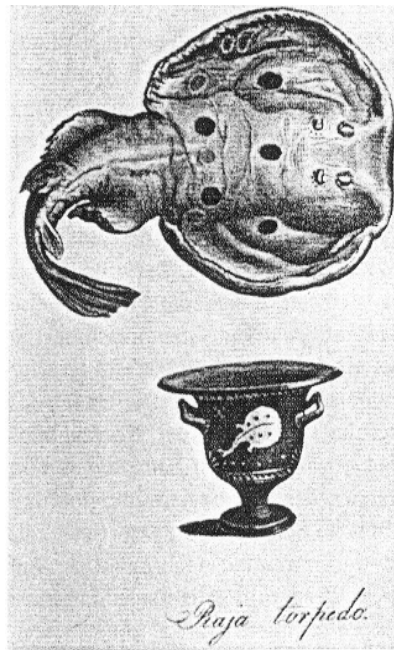
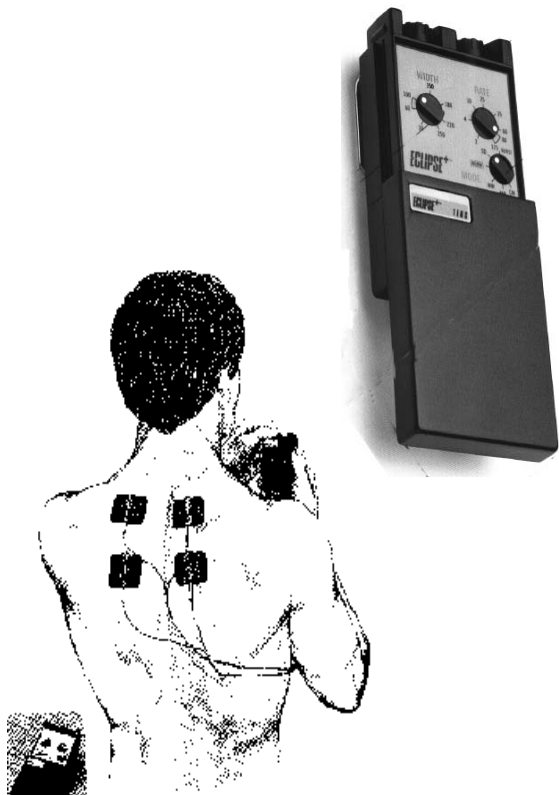


De Poorttheorie

- Aangename prikkels kunnen pijnpoorten sluiten.
- De hersenen kunnen ook pijnpoorten sluiten.

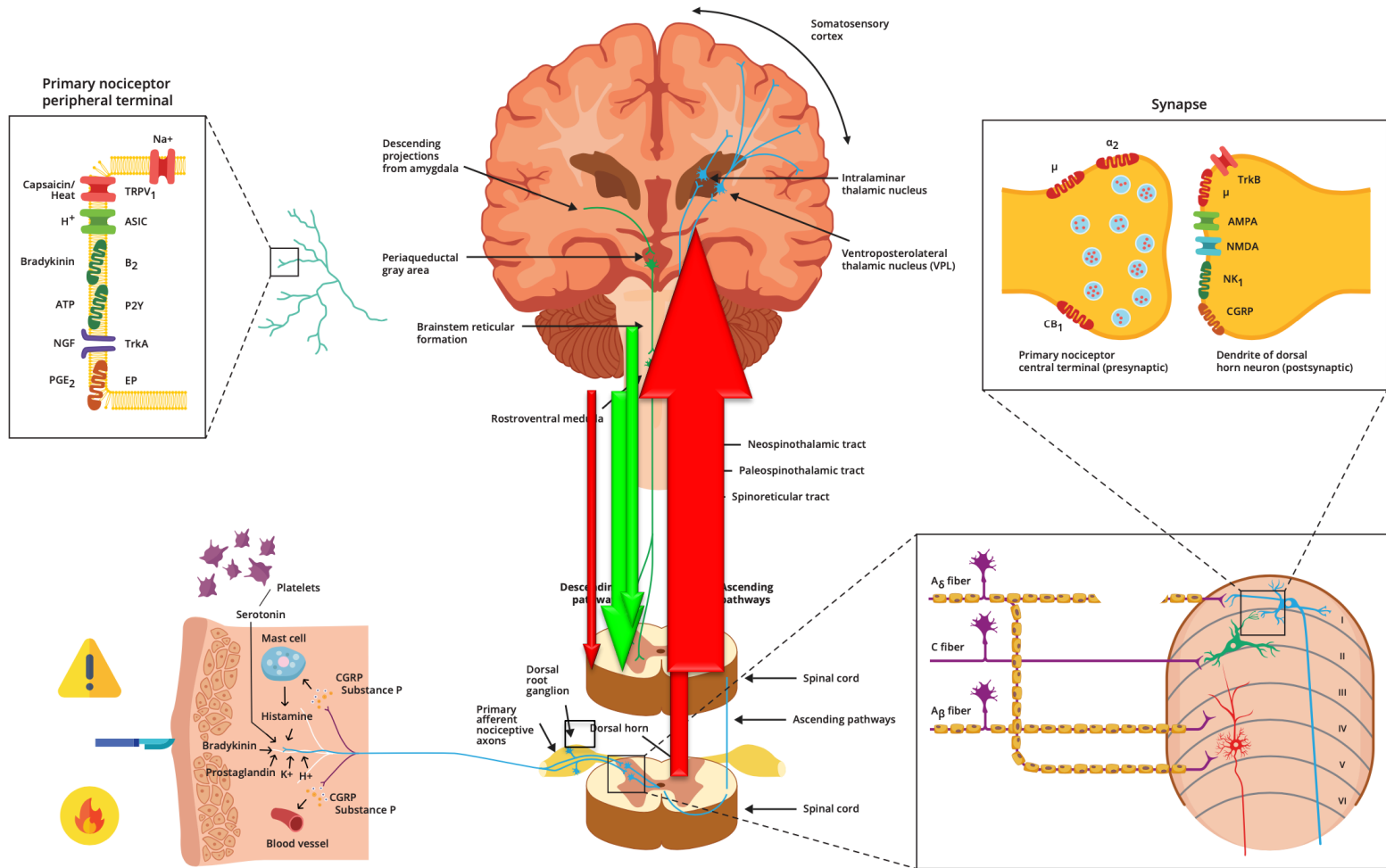


TENS & neurostimulation (SCS)

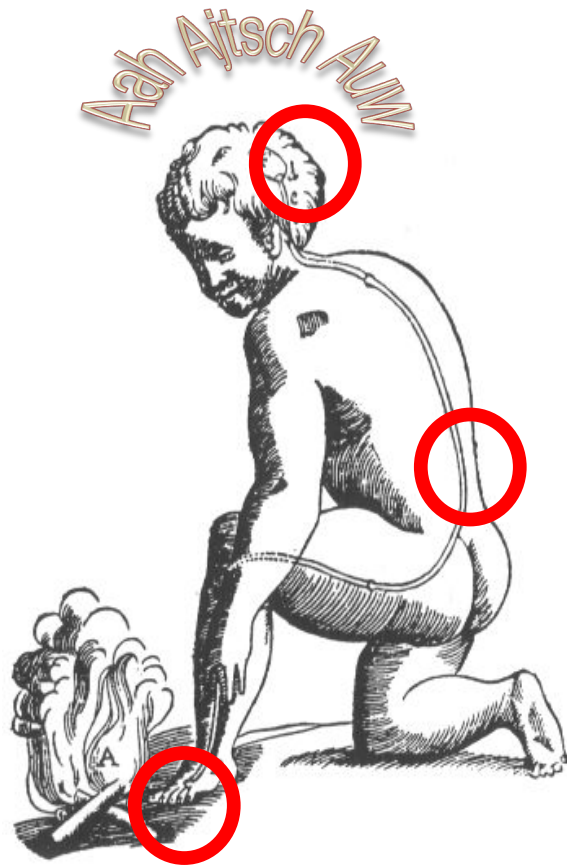


Neurobiologie van pijn

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Graphic composed by the author



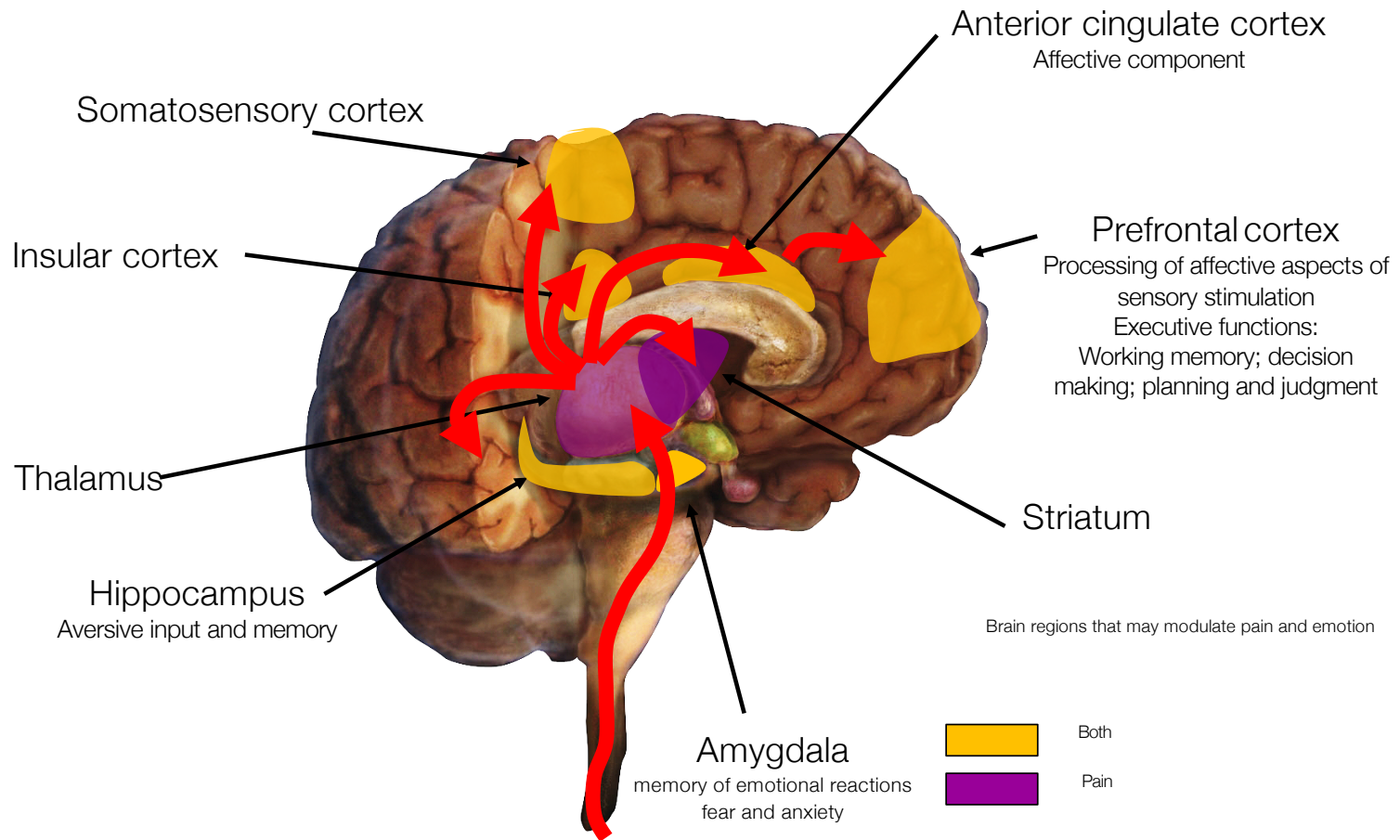
Pijnervaring

Centrale verwerking

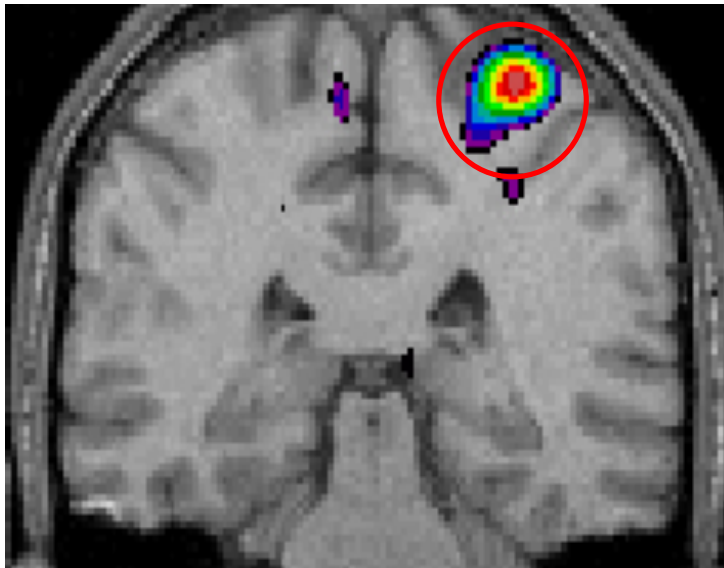
Spinale integratie

Perifere nociceptie

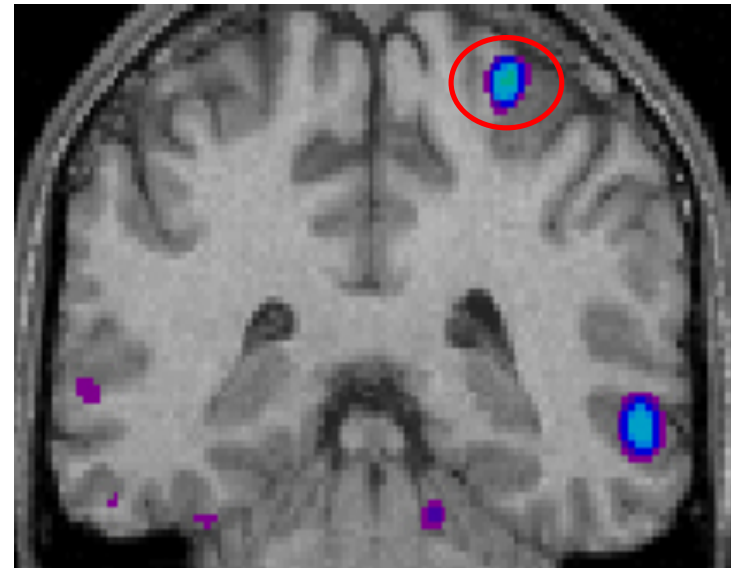
Pijn en Emotie



Modulatie van pijn door aandacht



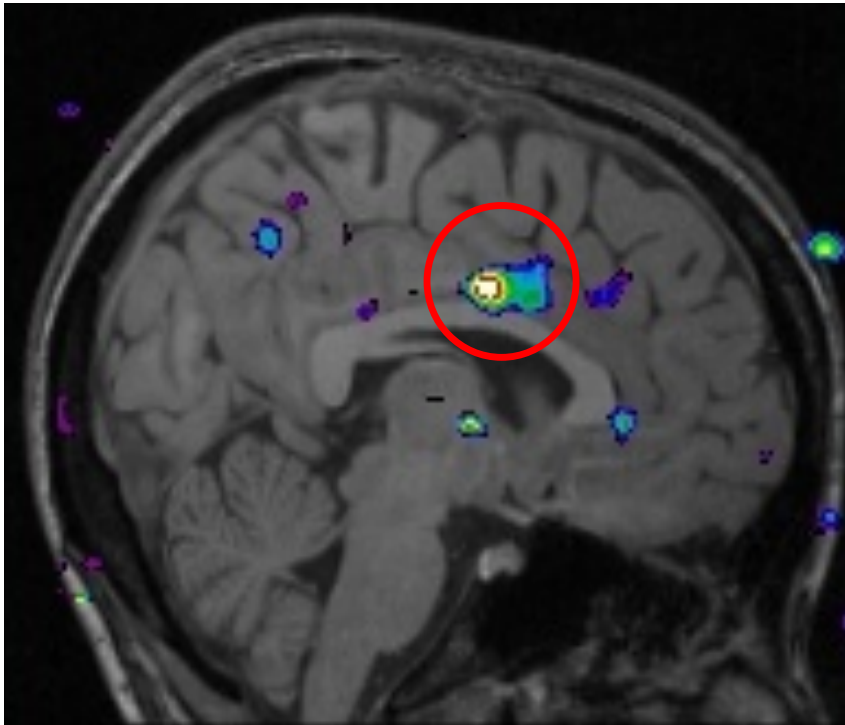
Aandacht naar pijn



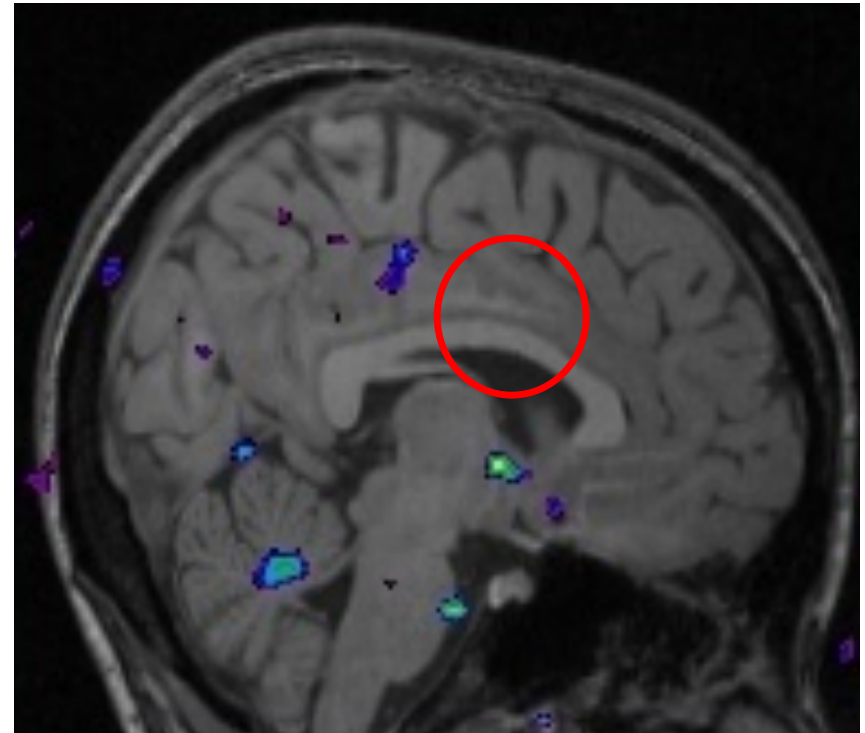
Aandacht naar
geluidstonen

Adapted from Bushnell et al. Proc Natl Acad Sci USA 1999;96(14):7705-09.

Modulatie van pijn door stemming



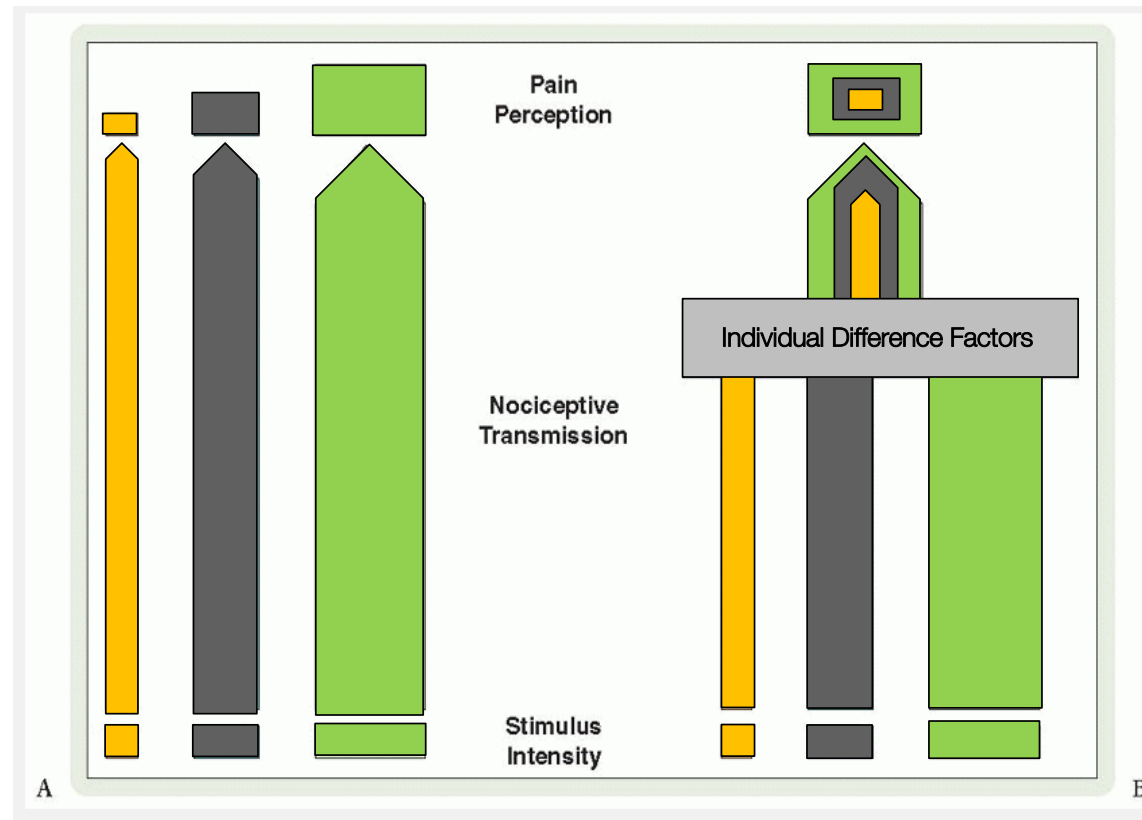
Slechte stemming + pijn



Goede stemming + pijn

Adapted from Villemure et al. J Neurosci 2009;29(3):705-15.

Zwakke associatie tussen stimulus en pijnlijke ervaring



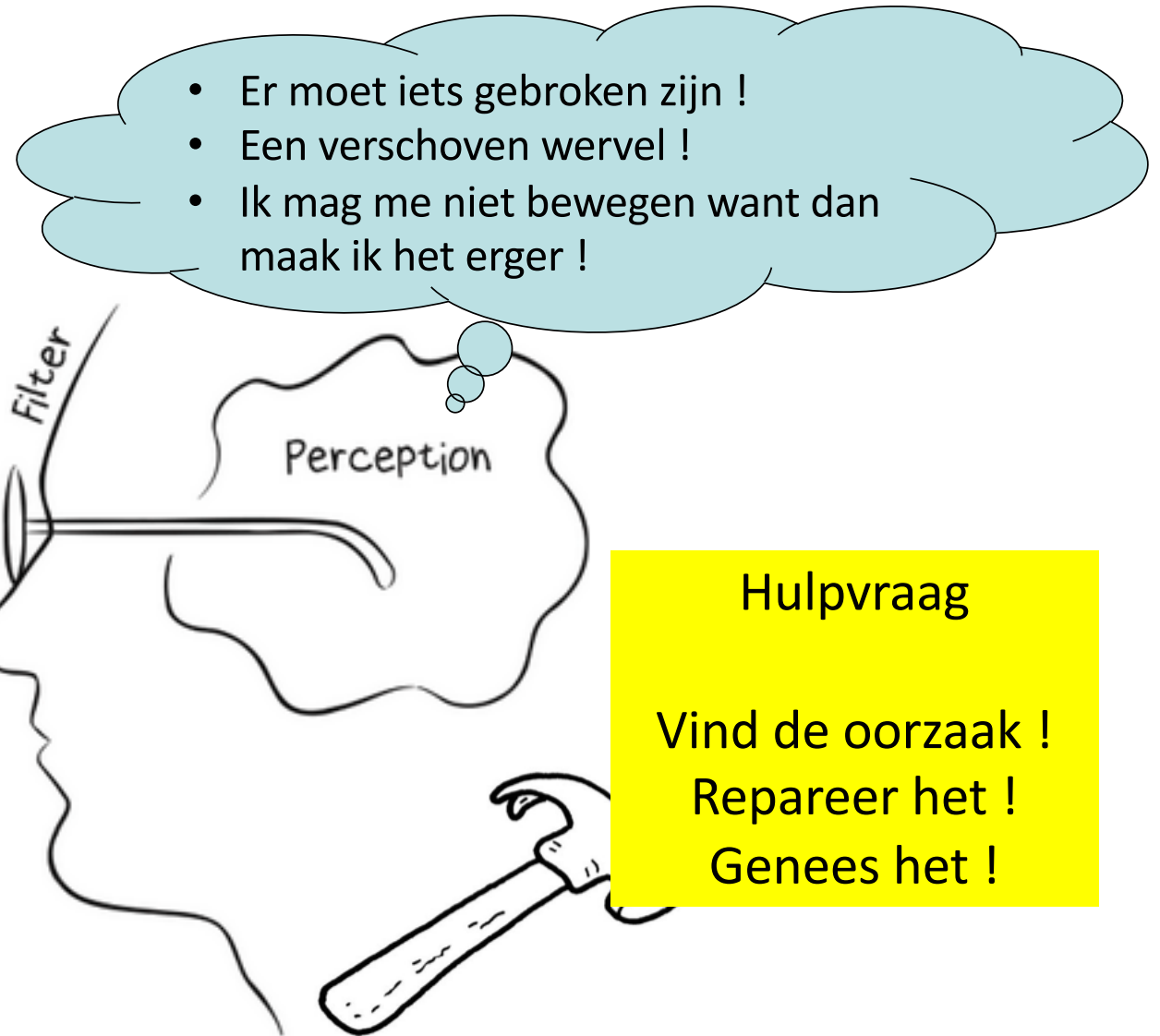
Fillingim R. in *Bonica's Management of Pain*, Eds. Fishman SM, et al. Lippincott Williams & Wilkins: Philadelphia; 2010.

De patiënt

Rugpijn

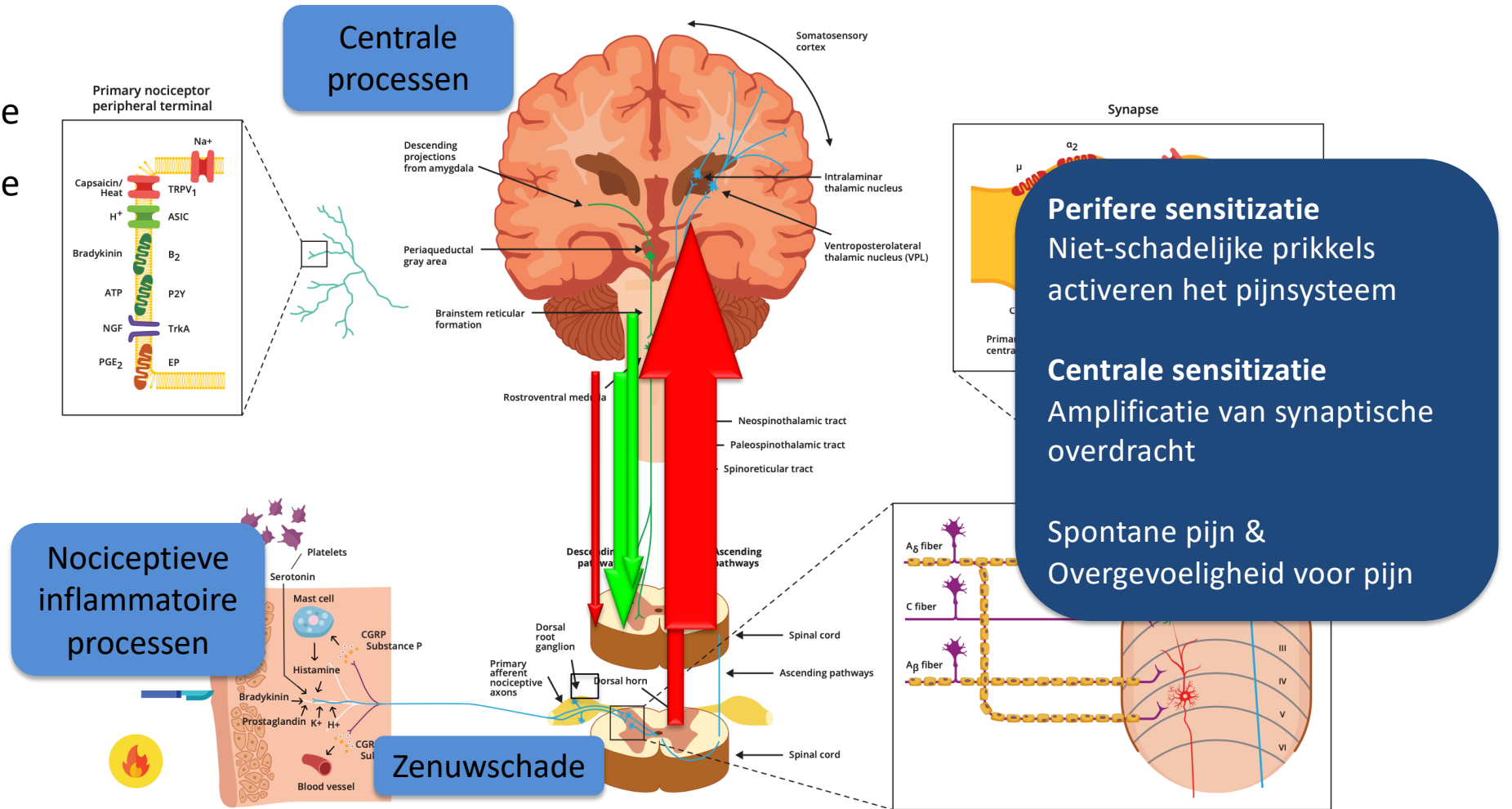


Information →



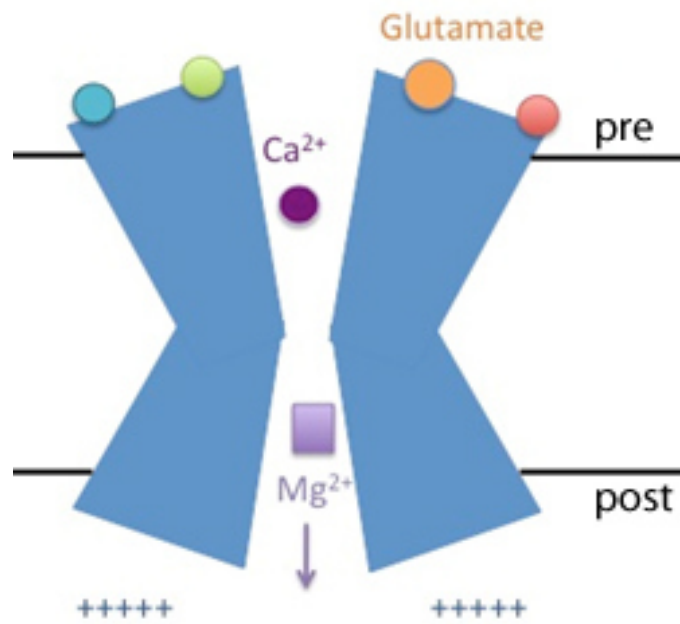
Transitie van acute naar chronische pijn: maladaptieve neuroplasticiteit

- Transductie
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Graphic composed by the author

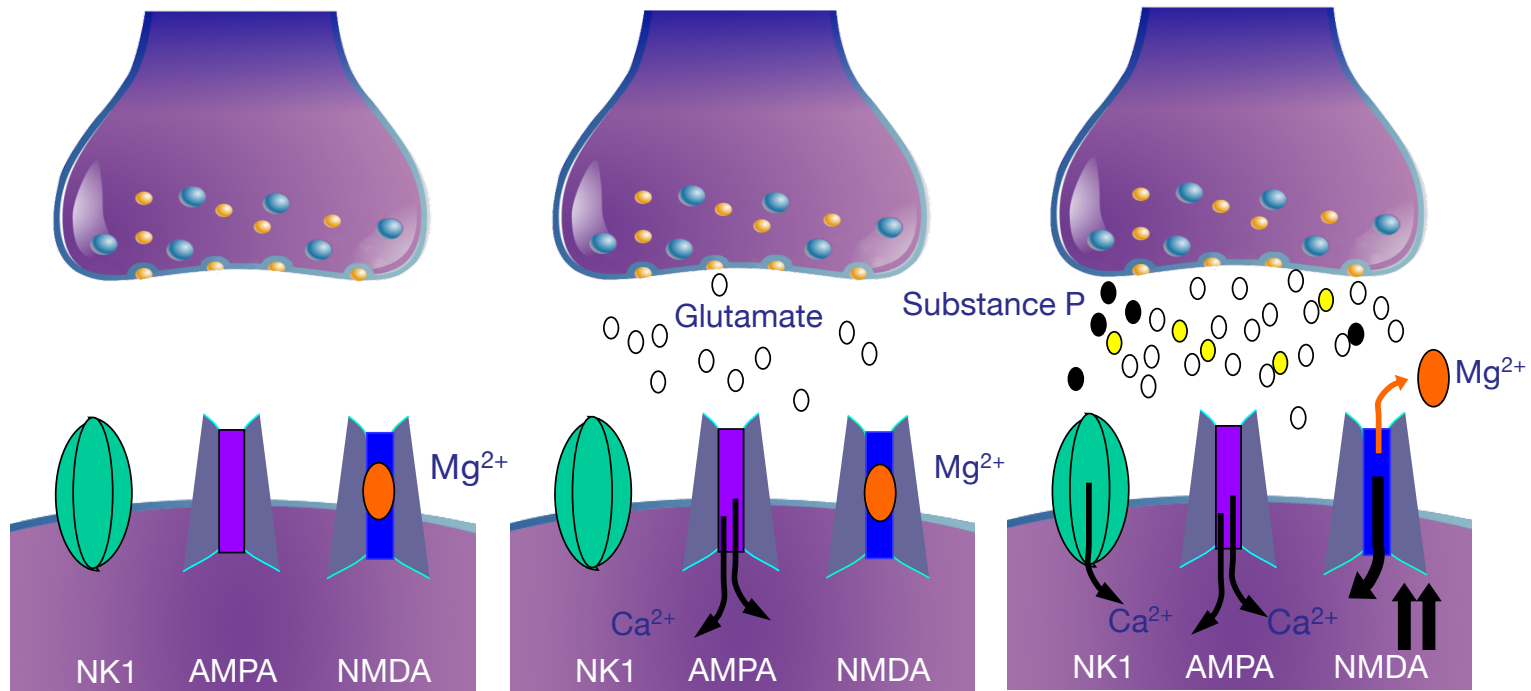
NMDA Receptor



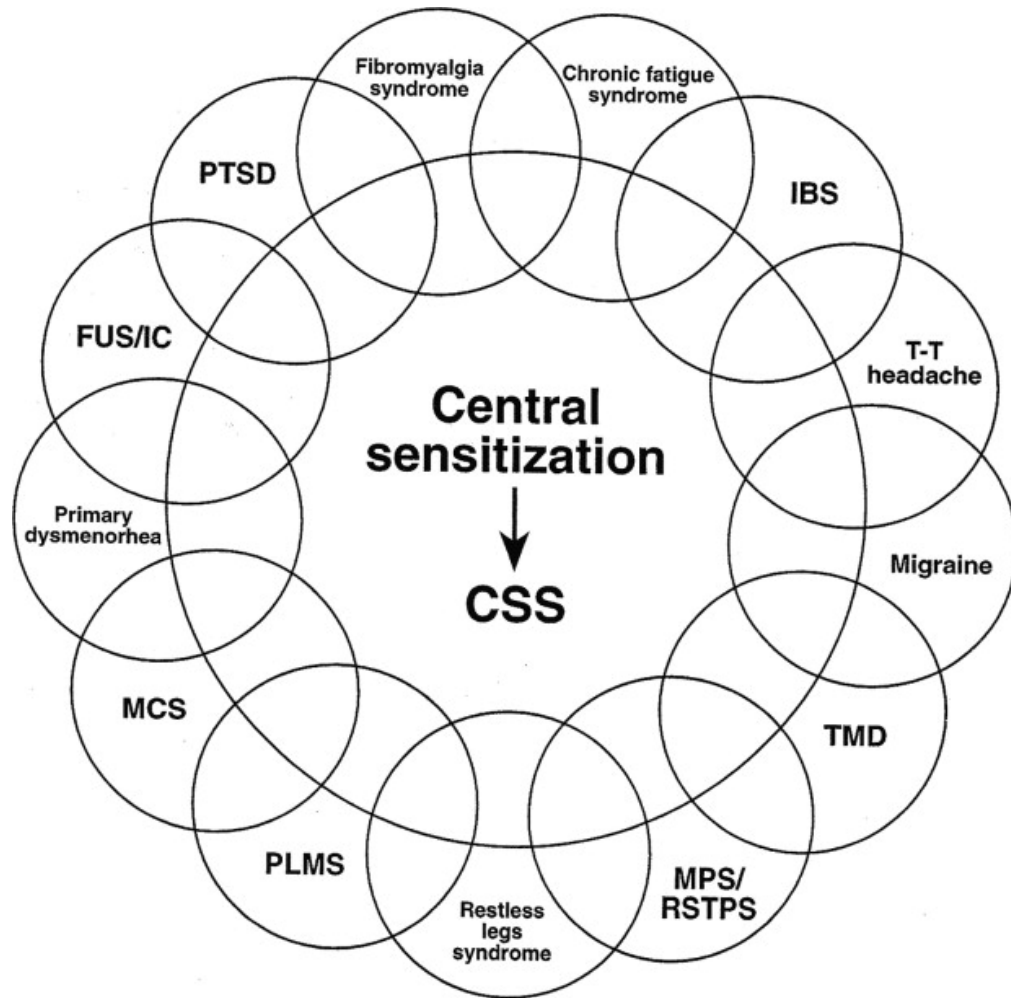
Presynaptic glutamate + postsynaptic depolarization → Mg^{2+} block displaced, Ca^{2+} enters cell



Neuroplasticity in Spinal Cord Processing: Wind-up and Long-term Potentiation



AMPA=Alpha-amino-3-hydroxyl-5-methyl-4-isoxazolepropionic acid; Mg^{2+} =Magnesium block;
NK-1=Neurokinin-1 receptor; NMDA=N-methyl-D-aspartic acid.

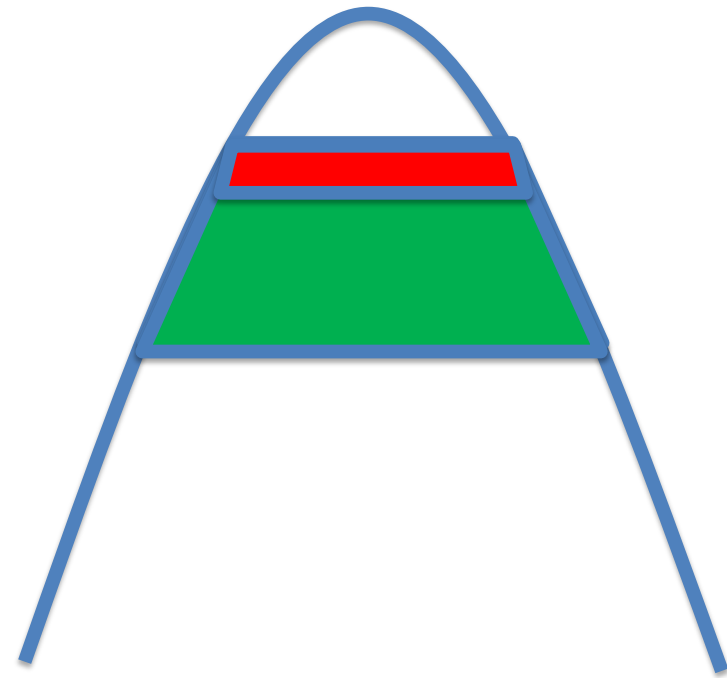
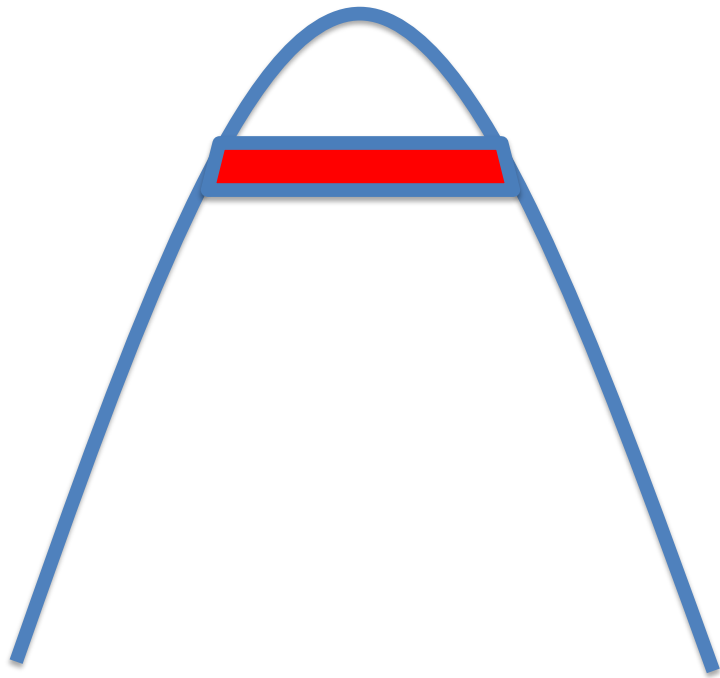


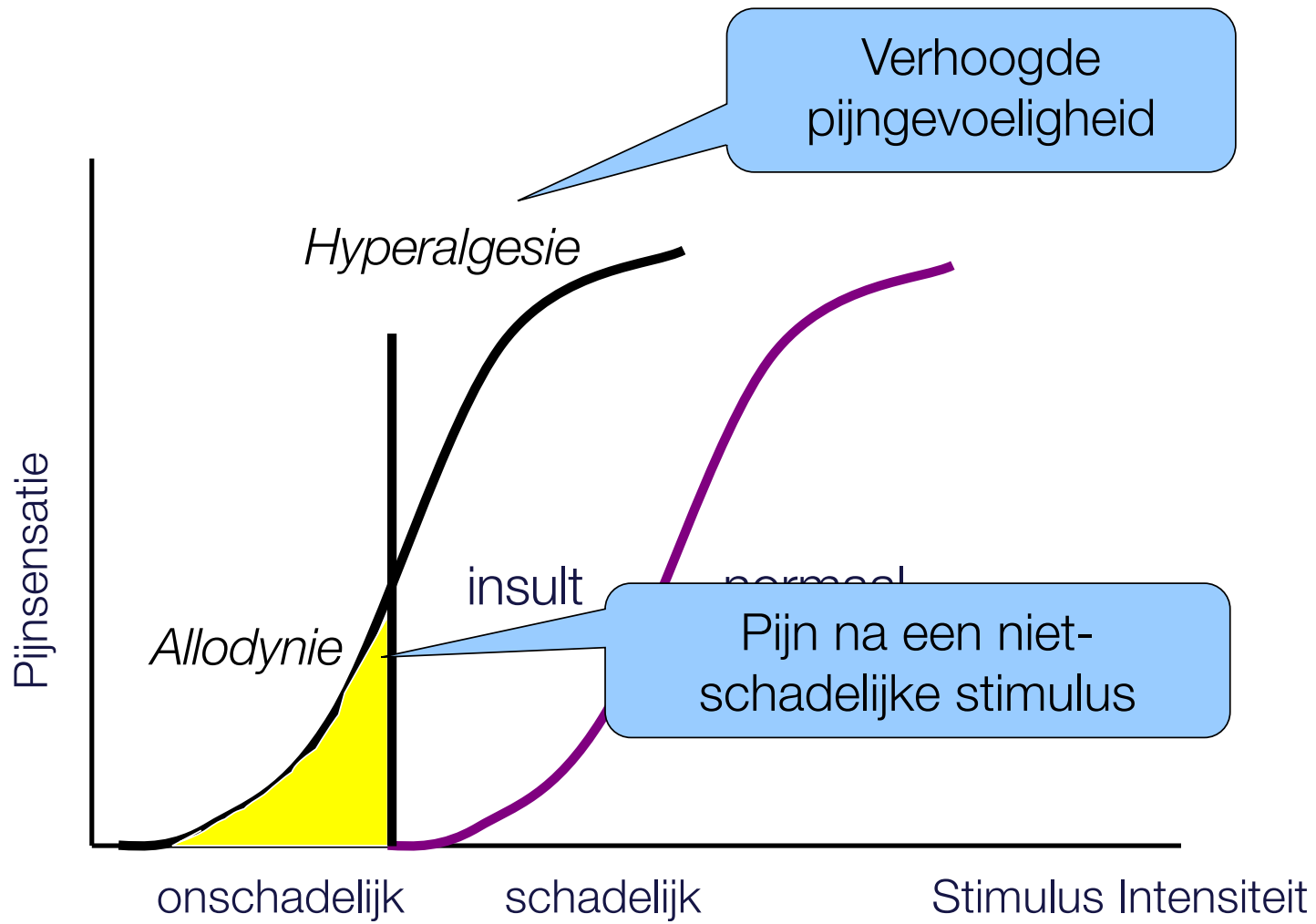
Centrale Sensitatie & Pijn

Central Sensitivity Syndromes (CSS)

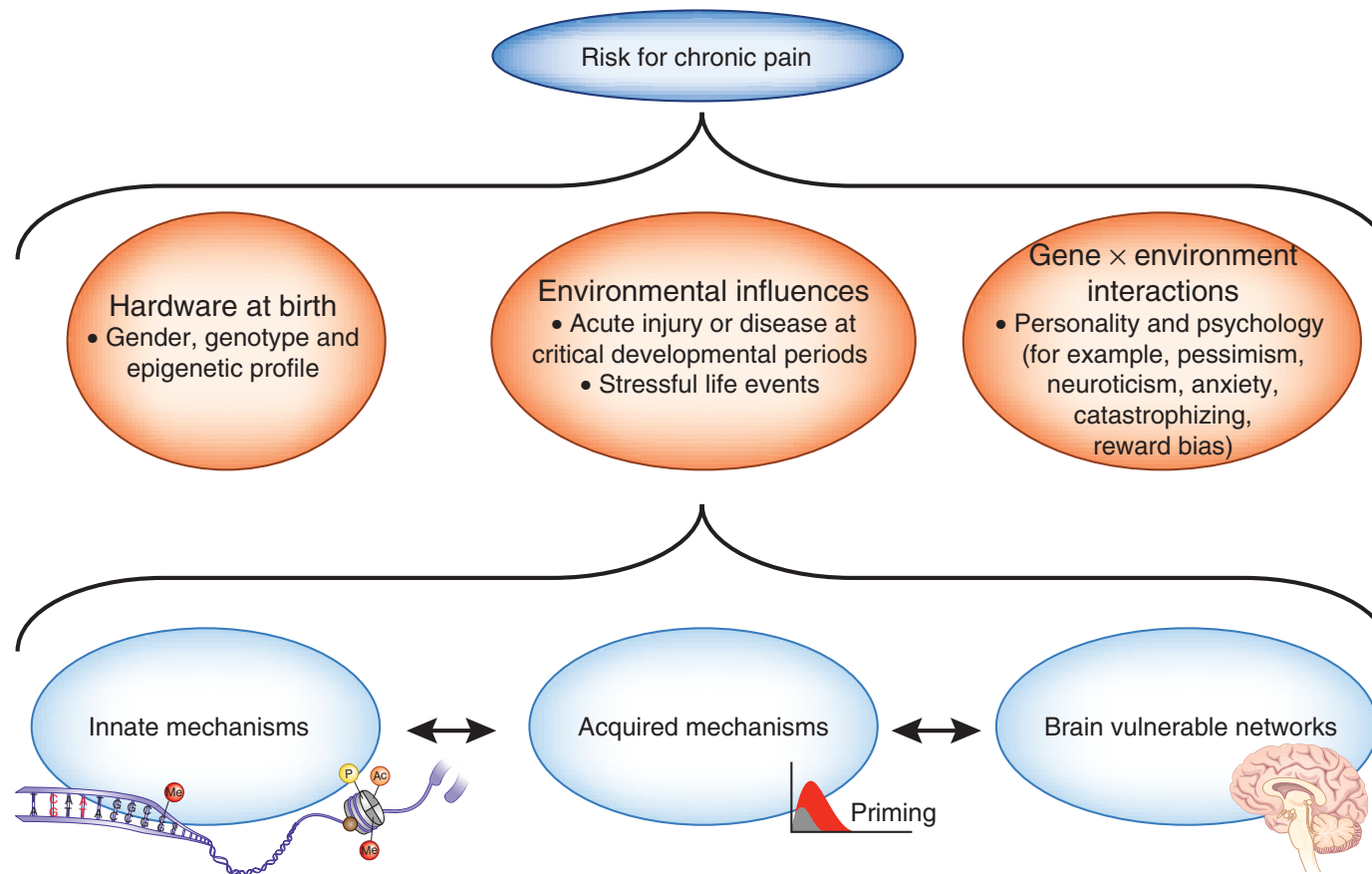
- **Centrale sensitatie**
 - Amplificatie van neurale signaalprocessen in het centraal zenuwstelsel dat overgevoeligheid voor pijn uitlokt.
 - Betekent niet dat de pijn niet reëel is, of ingebeeld, enkel dat de pijn niet geactiveerd wordt door schadelijke stimuli.
- **Hyperalgesie** = hevigere pijnreactie op schadelijke stimuli
- **Allodynie** = pijnlijke reactie op onschadelijke stimuli

Overbeschermd !





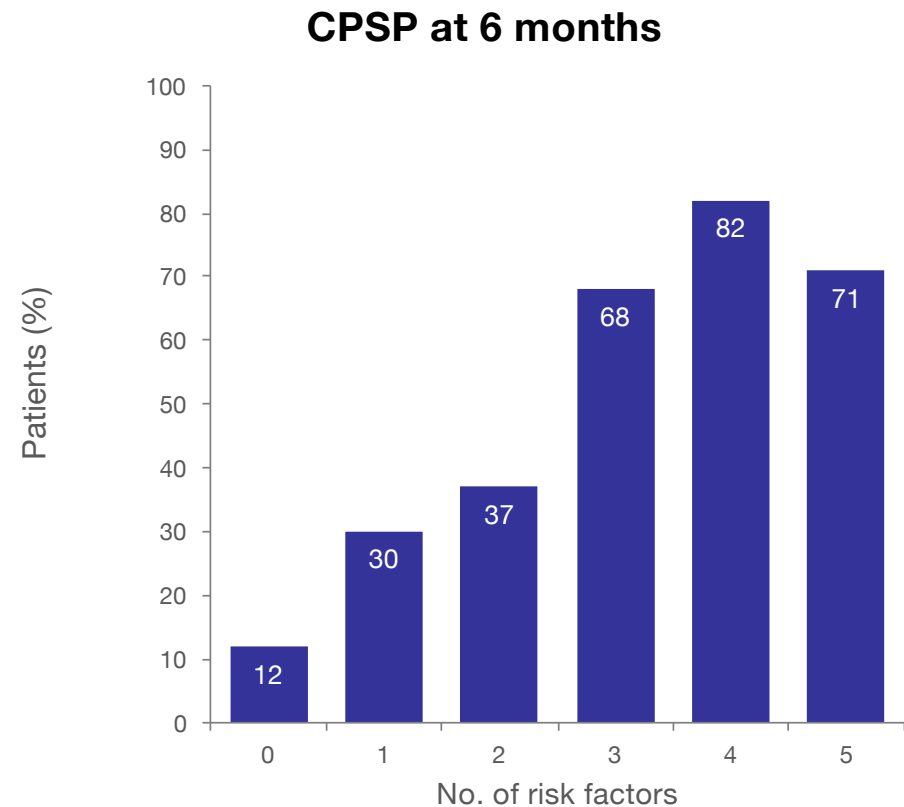
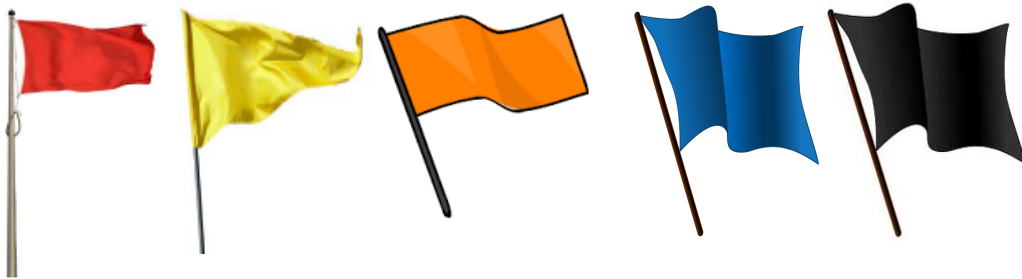
Vulnerability and resilience toward developing chronic pain



Risicofactoren voor persisterende postoperatieve pijn

6 domeinen

- Genetisch
- Demografisch
- Psychosociaal
- Pijn
- Klinisch
- Chirurgisch



Klinische pijnsyndromen



Nociceptief

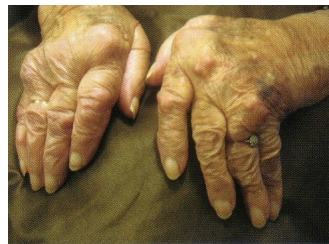
Inflammatoir

Neuropathisch

Nociplastisch



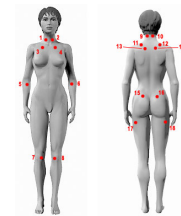
Schadelijke stimuli



Ontsteking
Perifere pathologie



Laesie of ziekte in het
somasensorisch systeem perifeer
of centraal



Geen schadelijke stimuli
Geen ontsteking
Geen zenuw schade
Geen perifere pathologie

Beschermend

Heling / Herstel / Pathologisch

Pathologisch

Pathologisch

Hoge drempel

Lage drempel

Nociplastic Pain

The descriptor is primarily intended for patients suffering from chronic pain conditions characterized by **evidence of altered nociceptive processing**, such as those currently labelled as:

- Fibromyalgia
- CRPS
- Nonspecific chronic low-back pain
- Irritable bowel syndrome
- Other “functional” visceral pain disorders

In addition, patients suffering initially from nociceptive pain, such as osteoarthritis, may develop alterations in nociceptive processing manifested as altered descending pain inhibition, accompanied by spread of hypersensitivity.

Translation of central sensitization to the clinic

- Higher pain intensity
- More widespread referred pain
- Occasionally hyperesthesia and allodynia
- Poor relation between pain and radiographic evidence
- Typical comorbidity of chronic pain
 - Fatigue
 - Sleep disturbance
 - Cognitive disturbance

POSITION PAPER

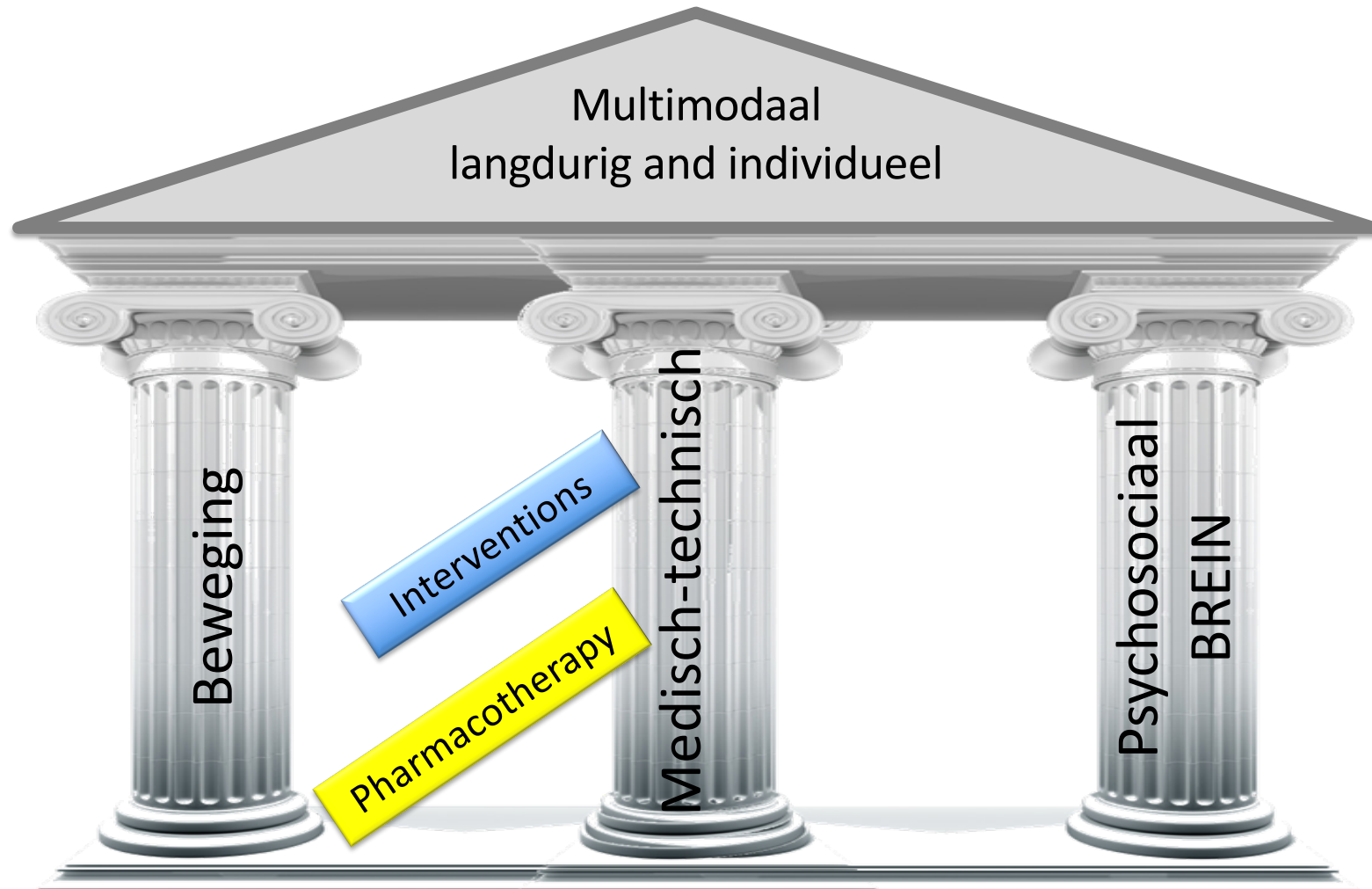
EJP
European Journal of Pain

Assessment and manifestation of central sensitisation across different chronic pain conditions

L. Arendt-Nielsen¹, B. Morlion², S. Perrot³, A. Dahan⁴, A. Dickenson⁵, H.G. Kress⁶, C. Wells⁷,
D. Bouhassira⁸, A. Mohr Drewes⁹

Arendt-Nielsen L, et al. Eur J Pain 2018;22:216–41.

Controle strategieën: werkbaar of niet-werkbaar?



Adapted from Morlion B. . Nat. Rev. Neurol. 462-473 (2013)