# La coscienza del dolore fisico

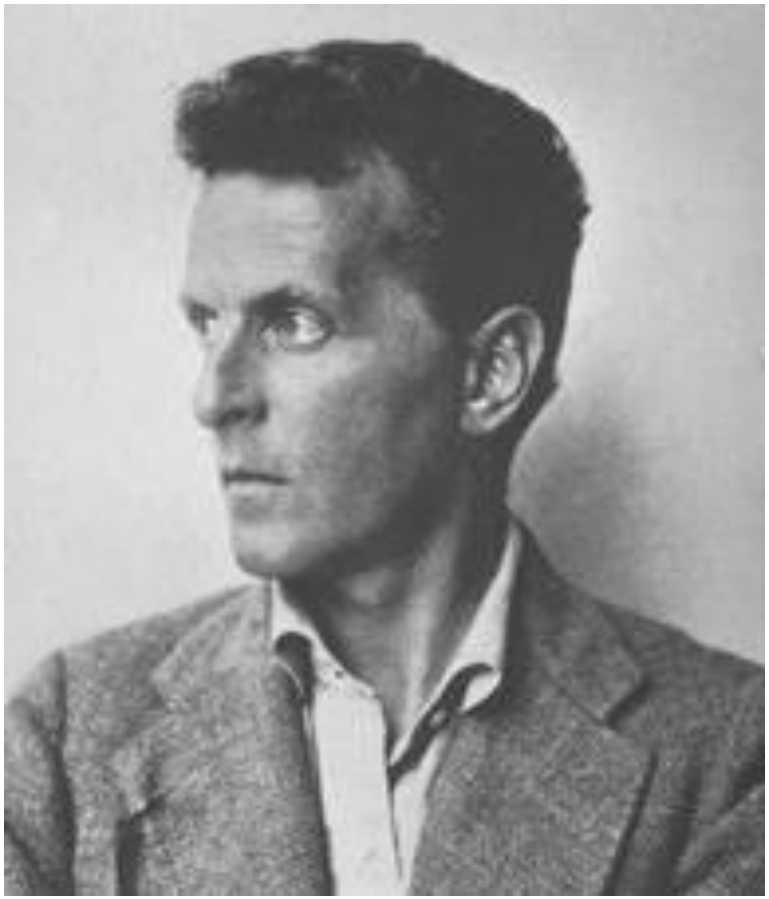
- *Il dolore è il prodotto emergente di vari sistemi simultanei d'attività cerebrale associato a sensazioni emozioni e cognizioni*

**Oxford Companion to Consciousness 2009**

- *Il dolore è un'esperienza sensoriale ed emotiva sgradevole che si manifesta in modi diversi, associata al danno attuale o imminente di una parte del corpo, descritta nei termini della lesione che lo provoca.*

**Associazione Internazionale per lo studio del dolore**

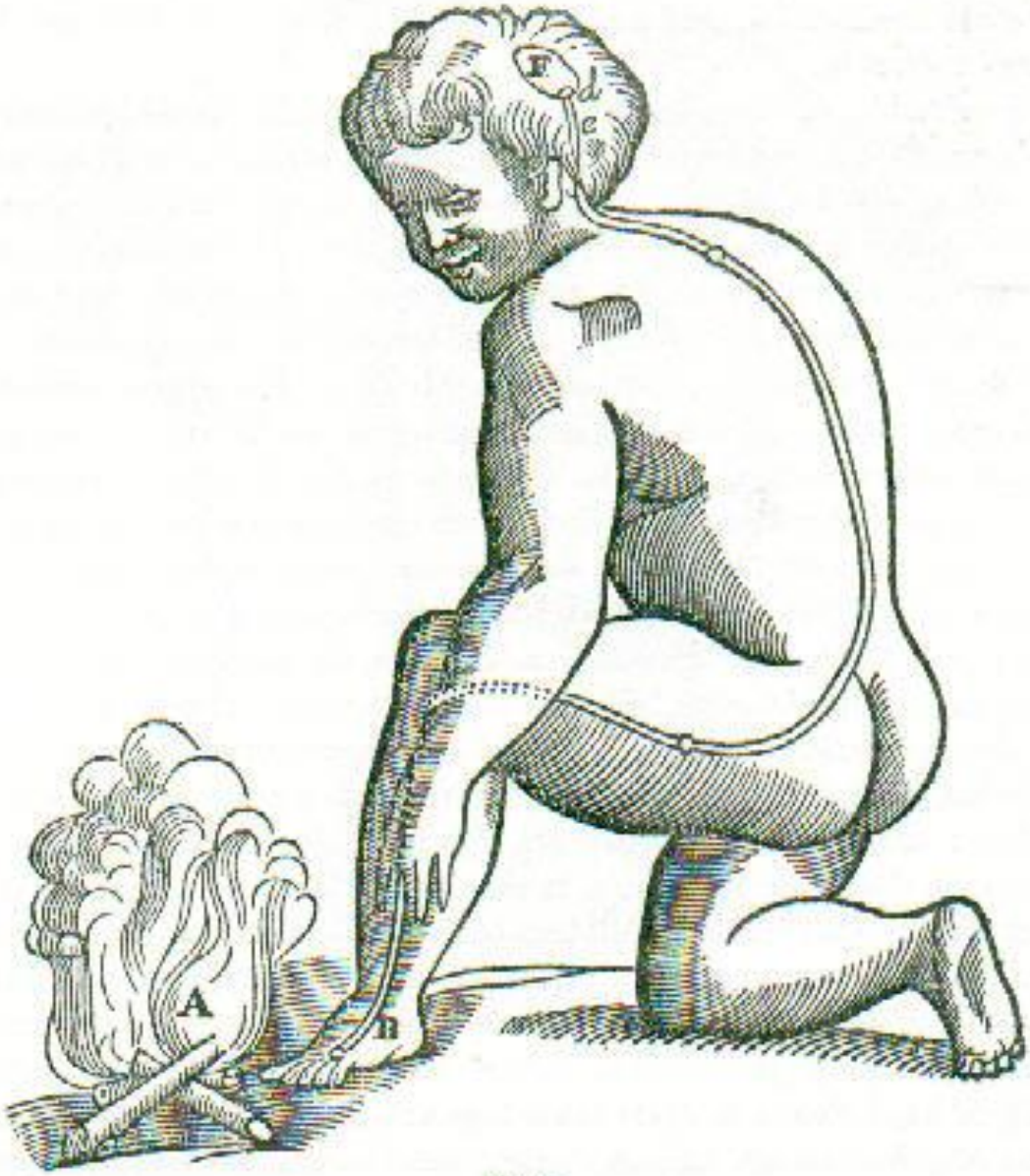
# Ludwig Wittgenstein

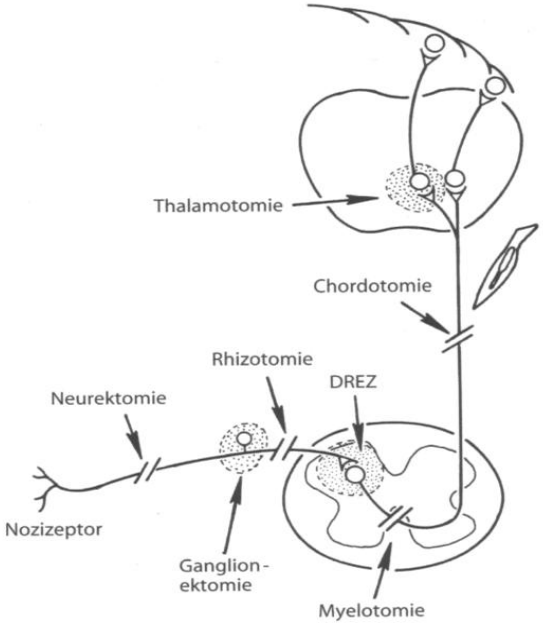


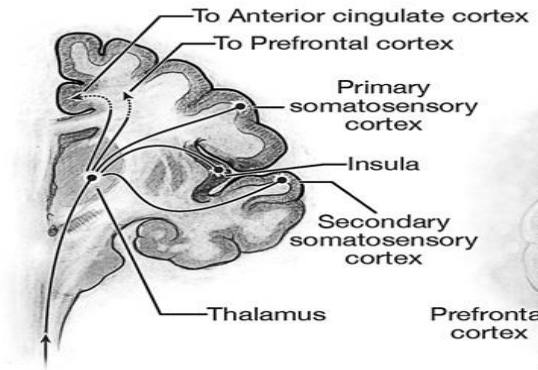
- **“Una persona che non ha mai avuto dolori riuscirebbe a capire il significato della parola dolore? […] Ciascuno dice di sé stesso di co-noscere esclusiva-mente i suoi dolori.”**

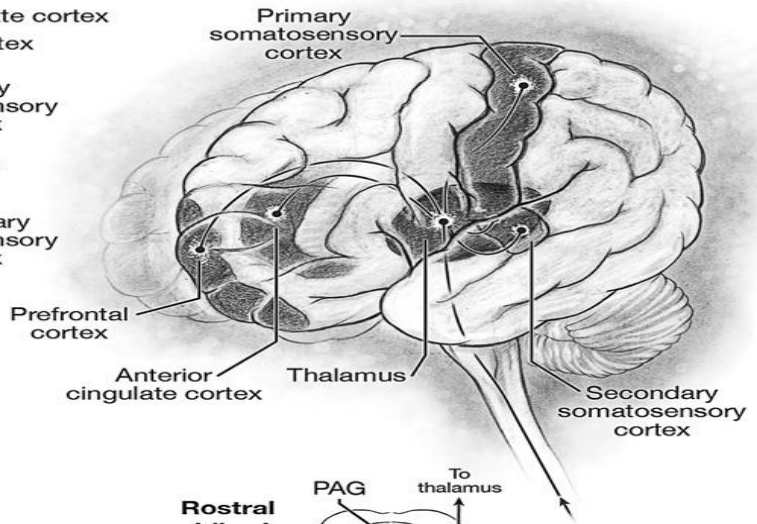
- ***Philosophische Unter-suchungen* Suhrkamp Frankfurt a/M 2001**

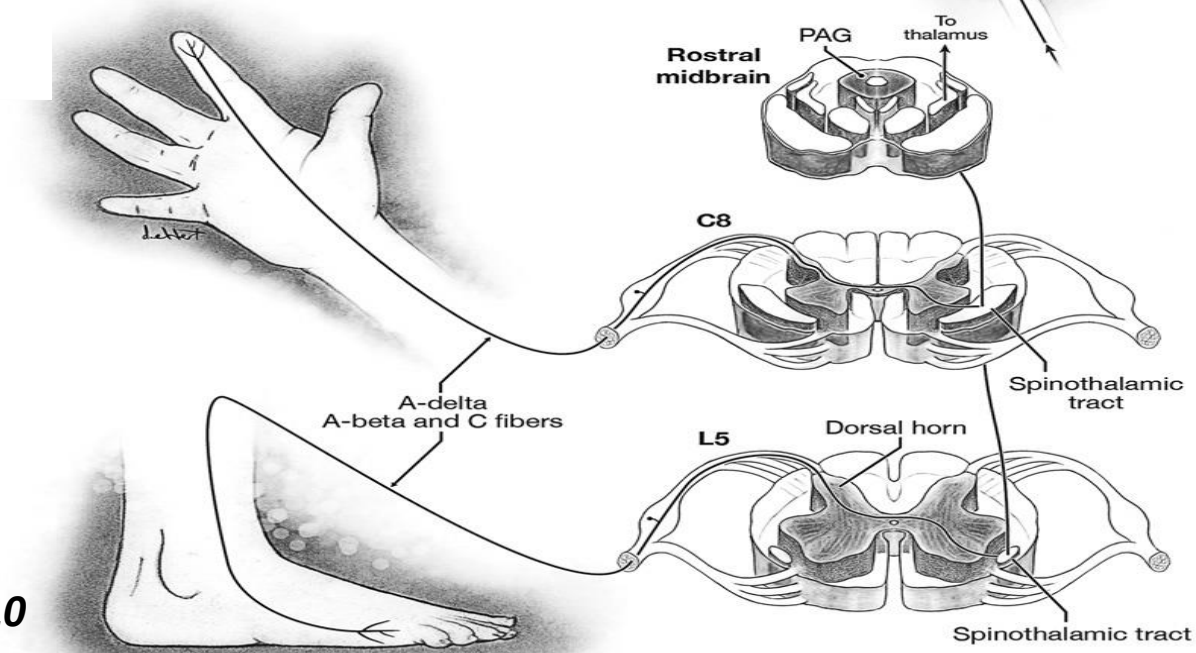
# L'HOMME
DE
RENÉ DESCARTES






***J. of Pain***
***11, 2-12,2010***

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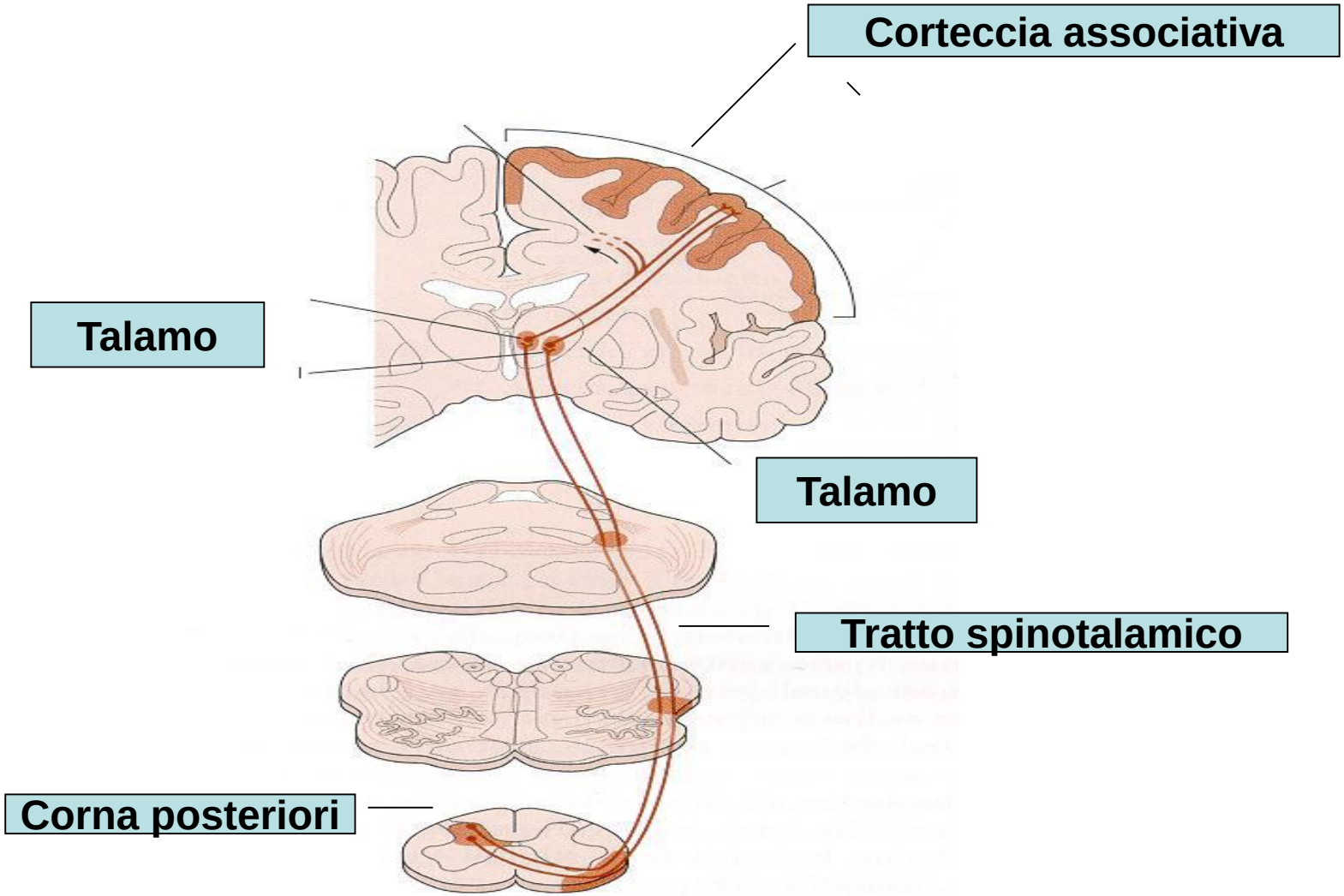
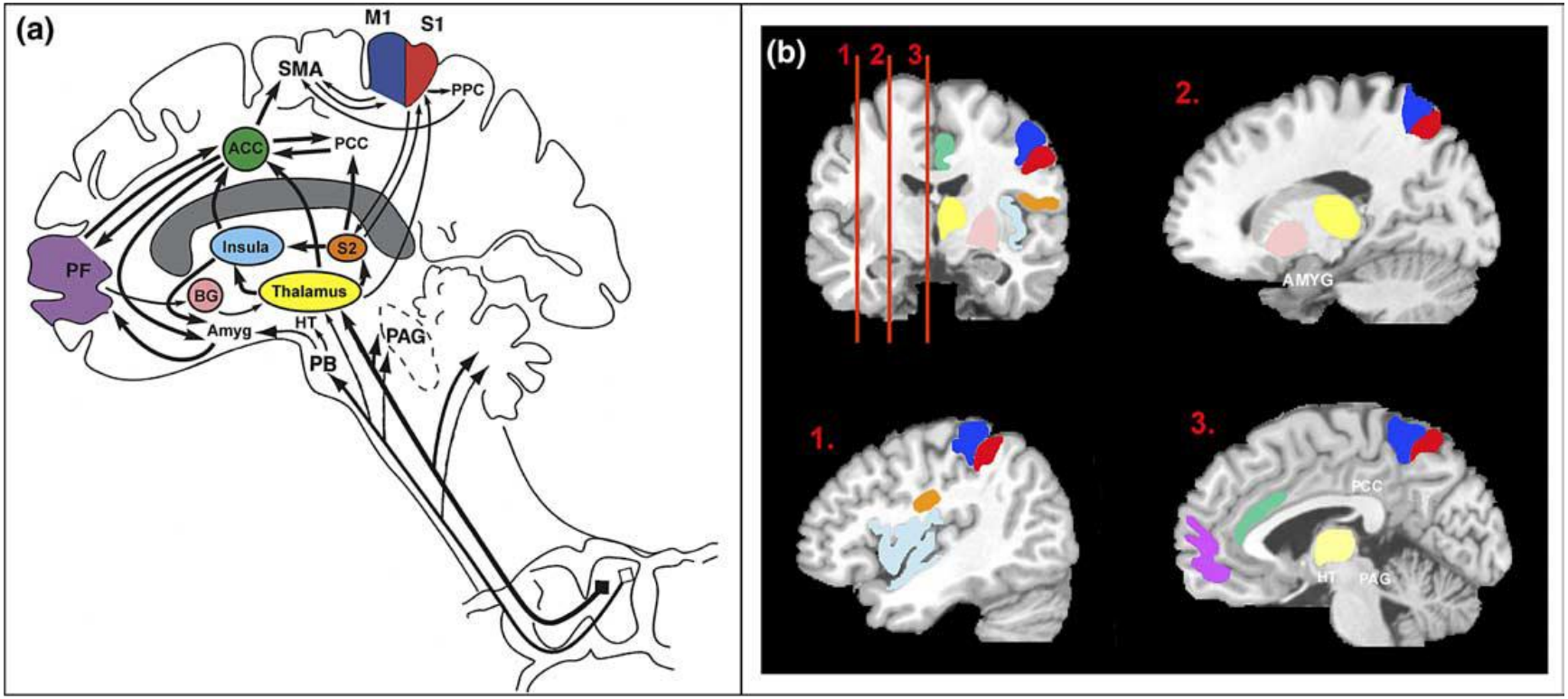
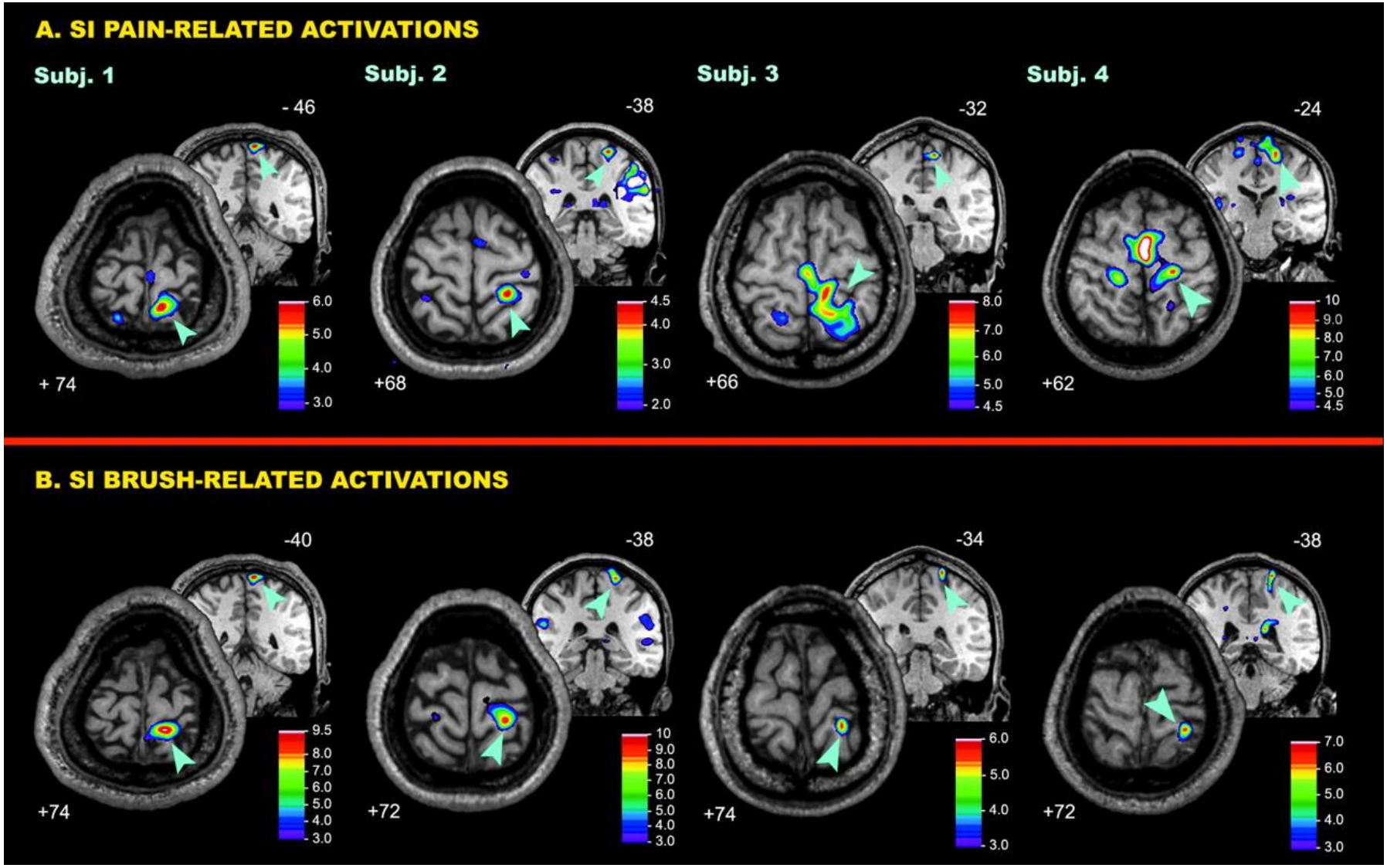

Corteccia associativa
Talamo
Talamo
Tratto spinotalamico
Corna posteriori

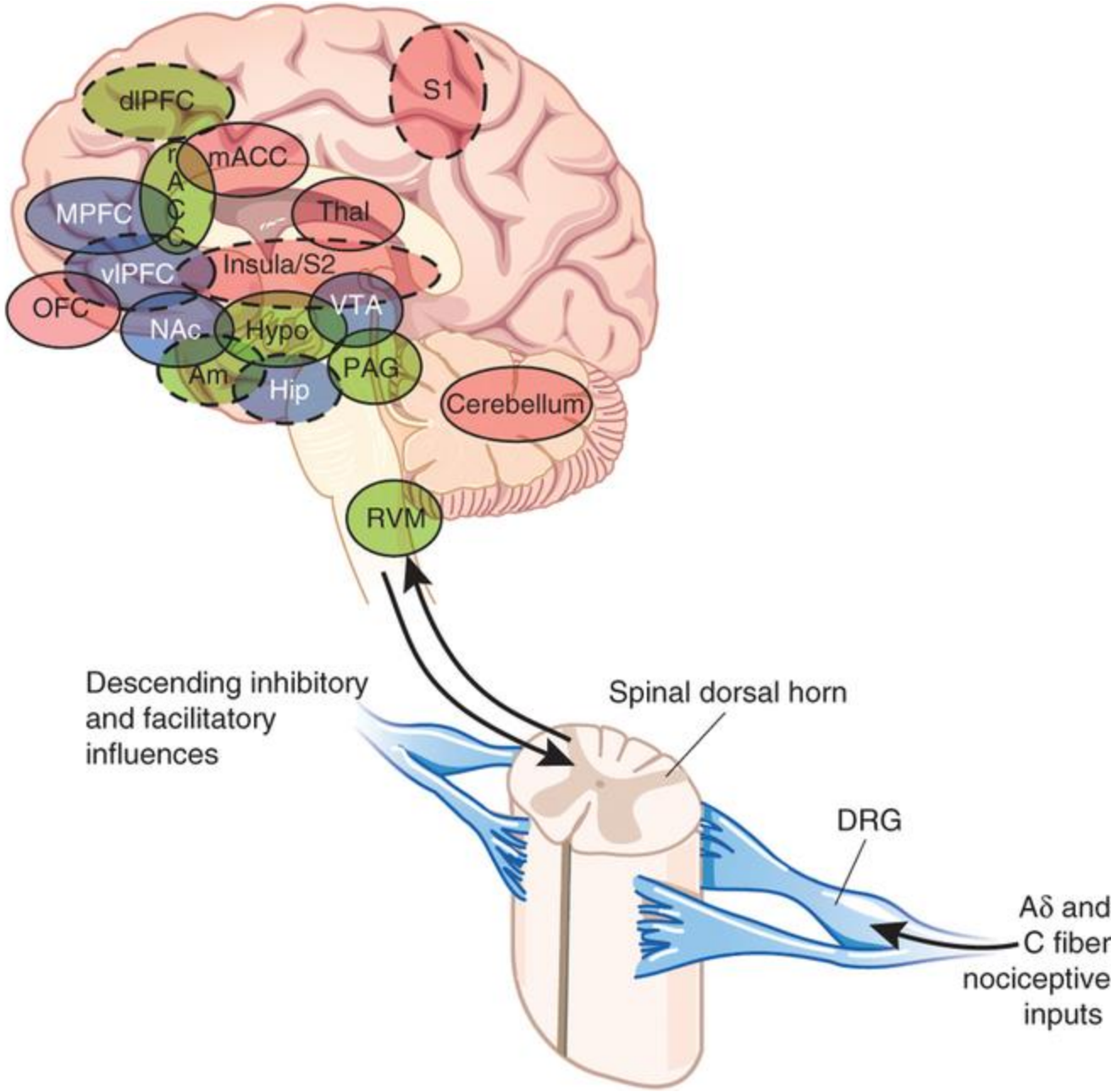



**Aree del dolore acuto-subacuto: S1 e S2; ACC, insula, aree prefrontali (memoria), talamo e gangli della base, cervelletto**

***European Journal of Pain 9, 463-484,2005;***
***The J. of Pain 11,2-12,2010***

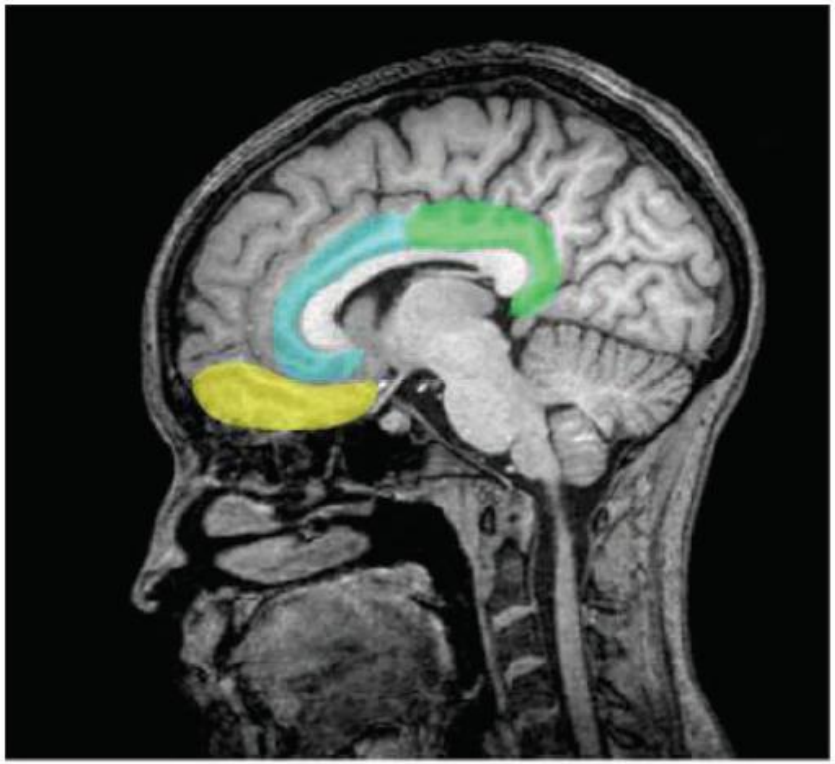



*J. Chen et al. J. Neurophysiology 88, 464-474, 2002*




***F. Denk et al. Nature Neuroscience 17, 192-200,2014***

# Regioni cerebrali delle emozioni



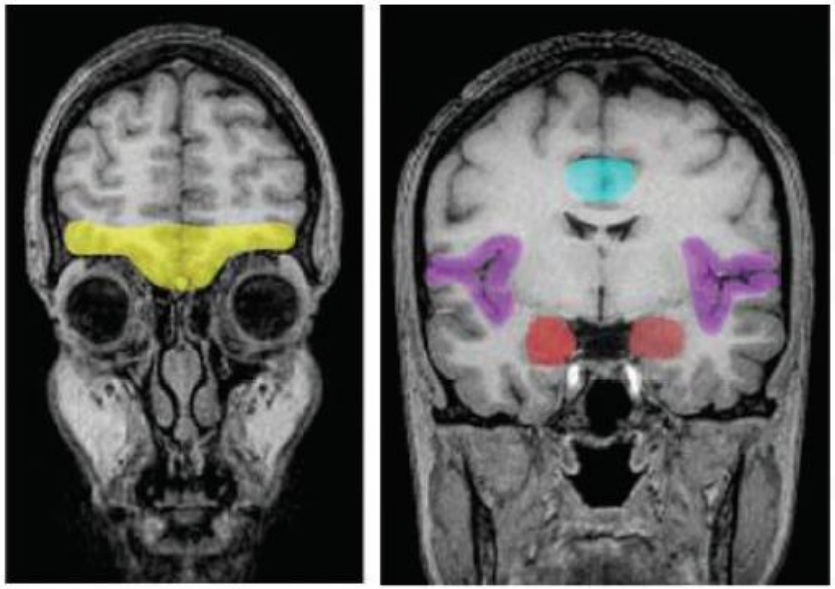


**Fig. 2.** Brain regions implicated in emotional experience include orbitofrontal cortex (yellow), insular cortex (purple), and anterior (blue) and posterior (green) cingulate cortices. The amygdala (red) is involved in linking perception with automatic emotional responses and memory.

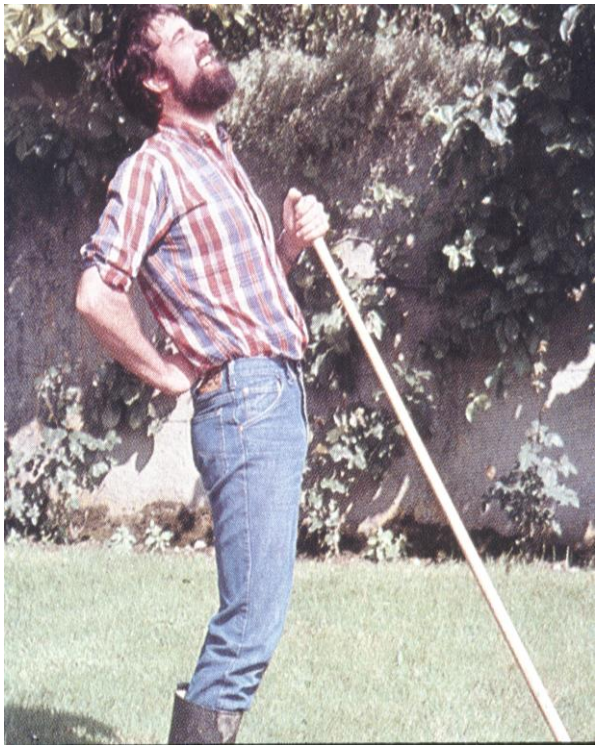
# Dolore

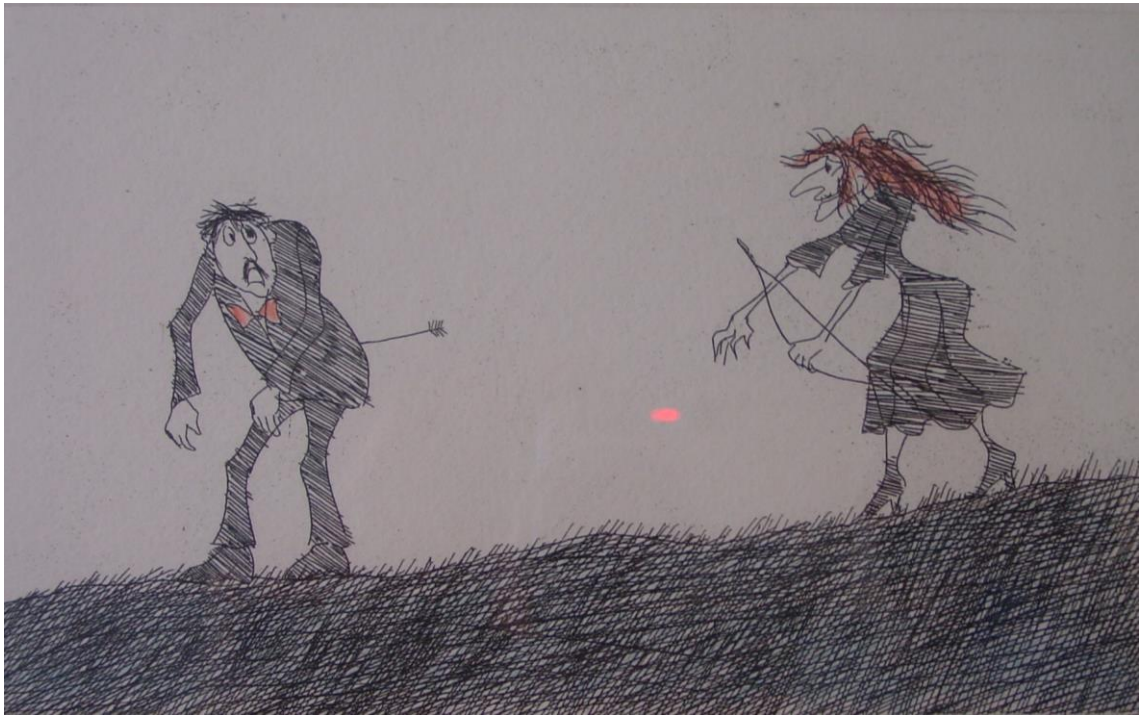
- ***Sindrome* del dolore:**
- **Dolore acuto fino a 7 gg [nocicezione]**
- **Dolore subacuto  da 7 gg a 3 mesi**

- **Dolore come *malattia*:**
- **Dolore cronico (20% della popolaz.adulta)**
- **Dolore neuropatico**
- **Dolore centrale postinfarto cerebrale**

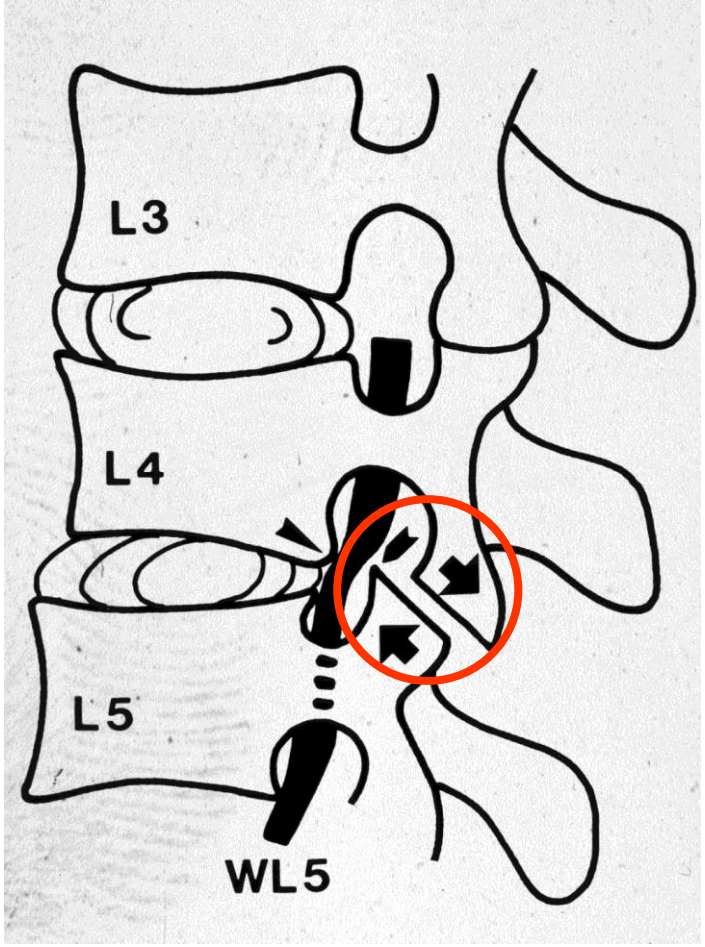
- **Prurito**

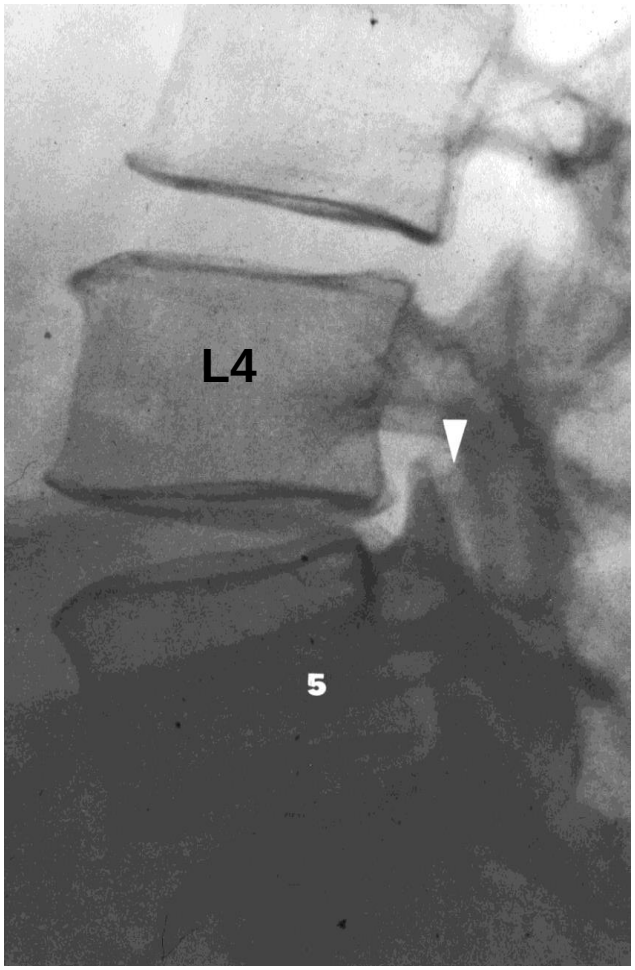
# Lombaggine acuta
# *„Colpo della strega“*



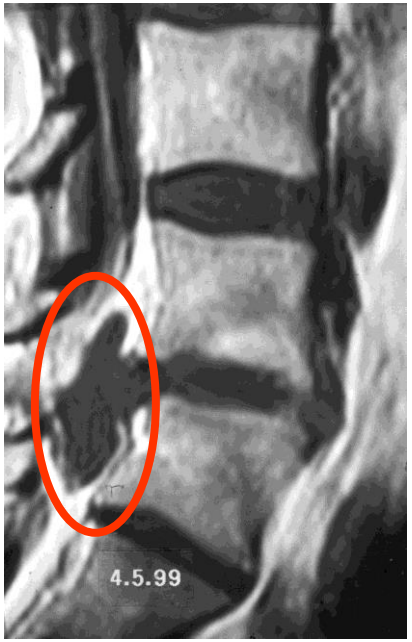


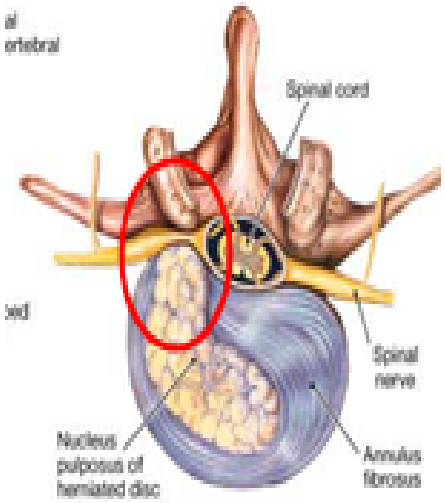
# „Colpo della strega“

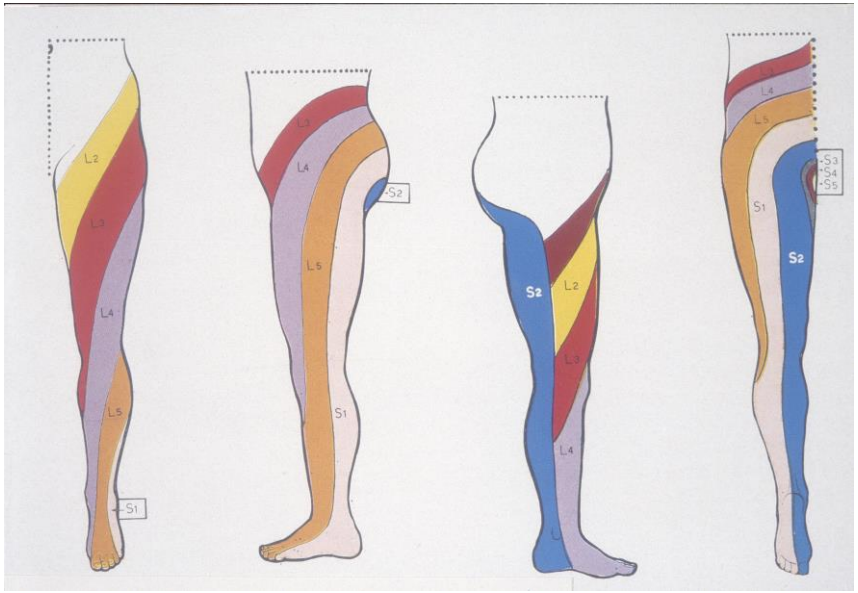


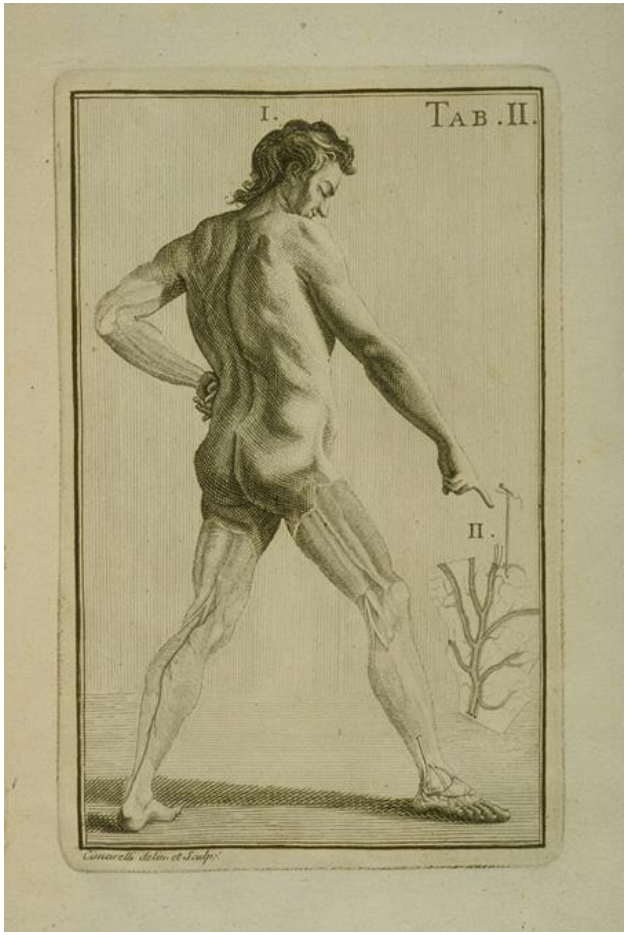



# Ernia del disco lombare



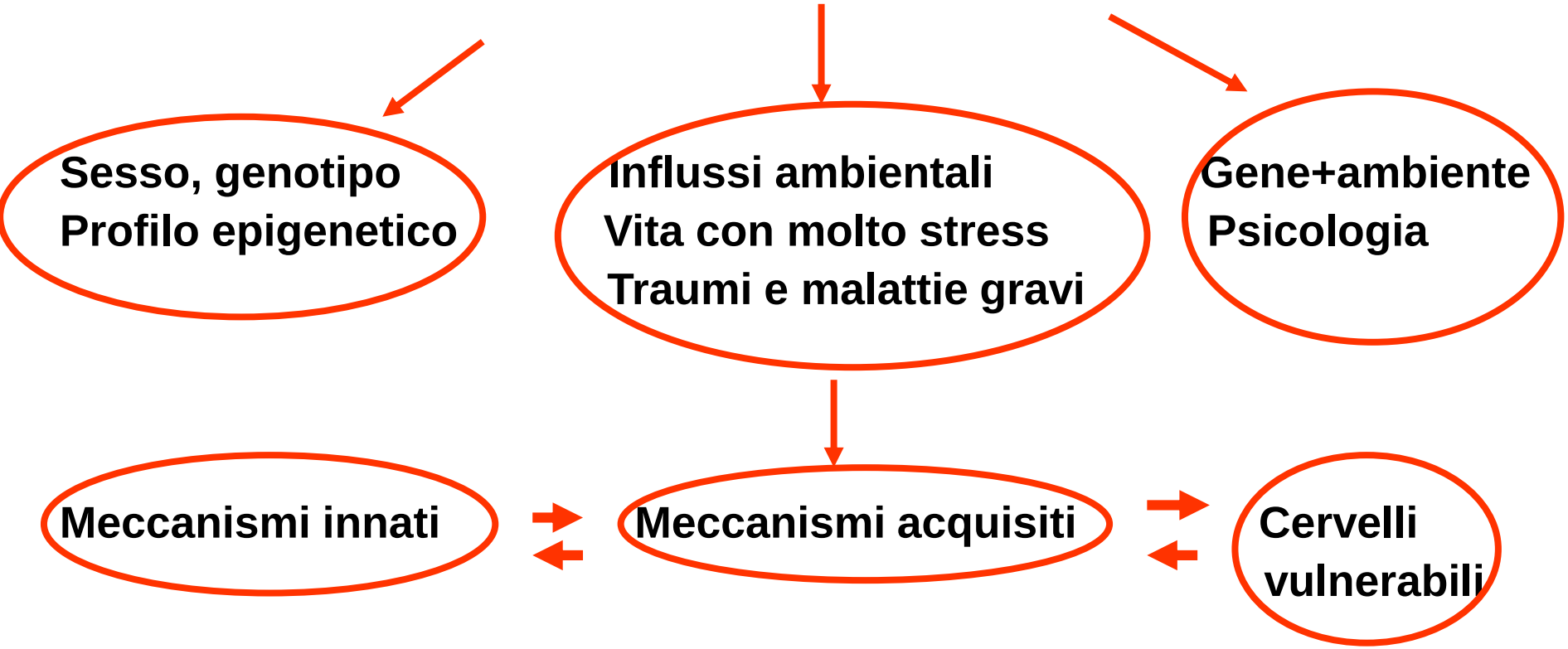



# Dolore cronico

- **Dolore continuo, a lungo e forte**
- **Alterazioni delle strutture nel midollo, nella corteccia, in aree subcorticali**
- **Produzione di proteine a livello periferico, midollare e centrale con alterazione della chimica cerebrale**
- **Plasticità delle sinapsi**

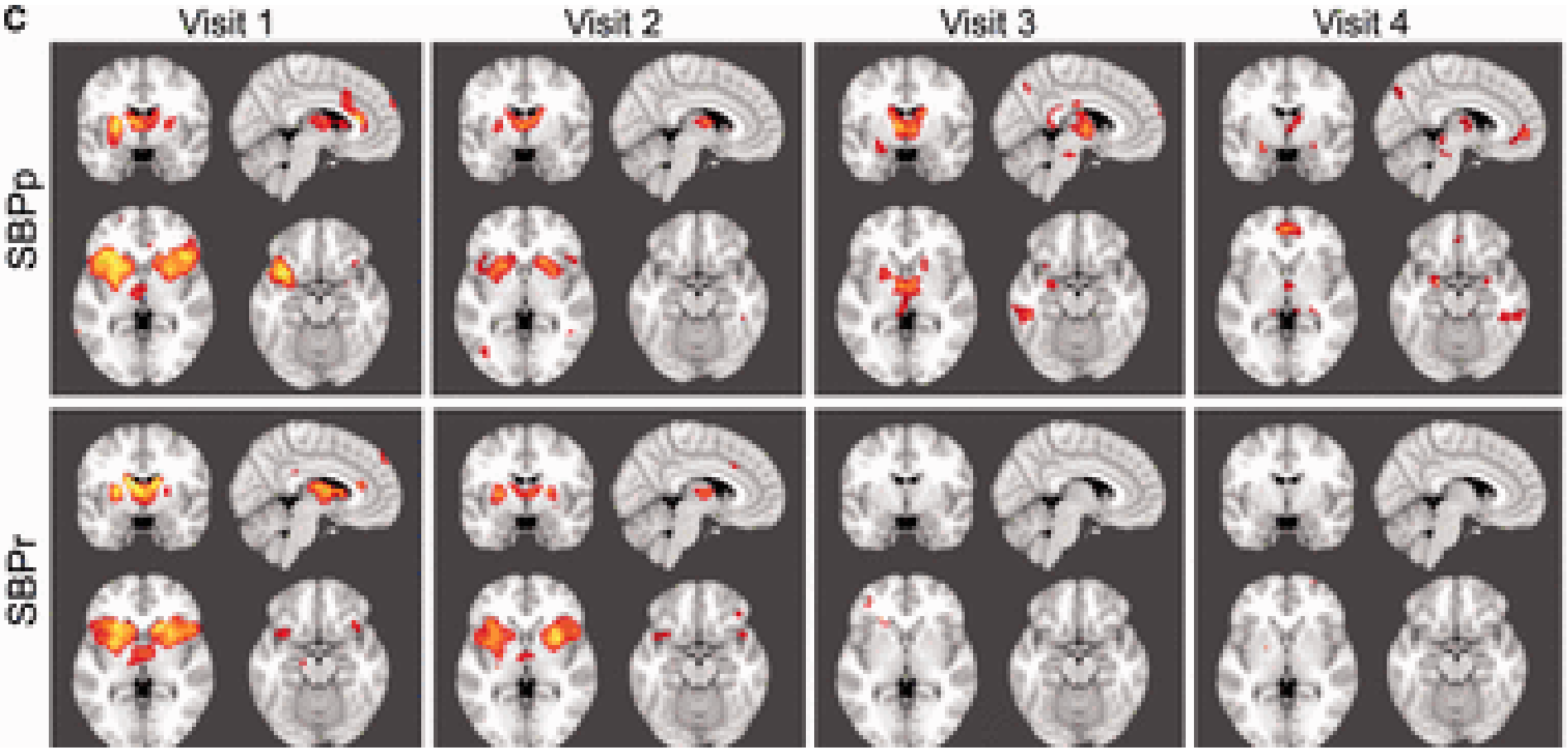
| Nature-Neuro-science 17, 192-200, 2014 | | Chronic Pain | Incidence (%) |
|---|---|---|---|
| . | | | |
| Diabetes | 15,692 | Total incidence of neuropathy | 48 |
| | | Painful neuropathy | 34 |
| Postsurg. pain | 159,000 | Amputation | 30–50 |
| | 479,000 | Breast surgery | 20–30 |
| | Unknown | Thoracotomy | 30–40 |
| | 609,000 | Inguinal hernia repair | 10% |
| | 598,000 | Bypass surgery | 30–50 |
| | 220,000 | Caesarean section | 10 |
| Lower back pain | 448 | Pain 5 years after first presentation: prospective study | 36.9 |
| | 180 | Pain 12 months after initial consultation: prospective study | 34 |
| Neck pain | 5,277 | Incidence of chronic neck pain in cohort of patients reporting at least one episode of acute neck pain | 18 |

# Rischio del dolore cronico




**I fattori di rischio sono a livello molecolare, cellulare e di rete**

F. Denk et al. Nature Neuroscience 17,192-200,2014

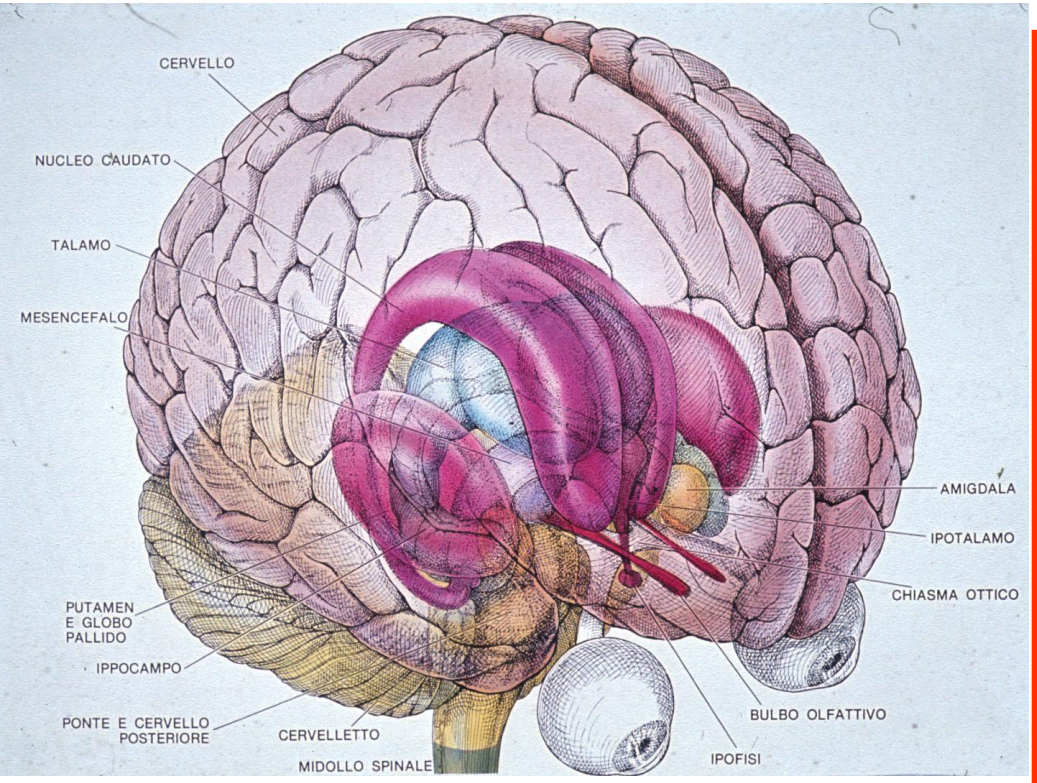



**9 sett.** **16 sett.** **39 sett.** **54 sett.**

**J.A. Hashmi et al.**

***Brain 136, 2751-2768, 2013***

# Variazioni morfologiche del cervello nel dolore cronico

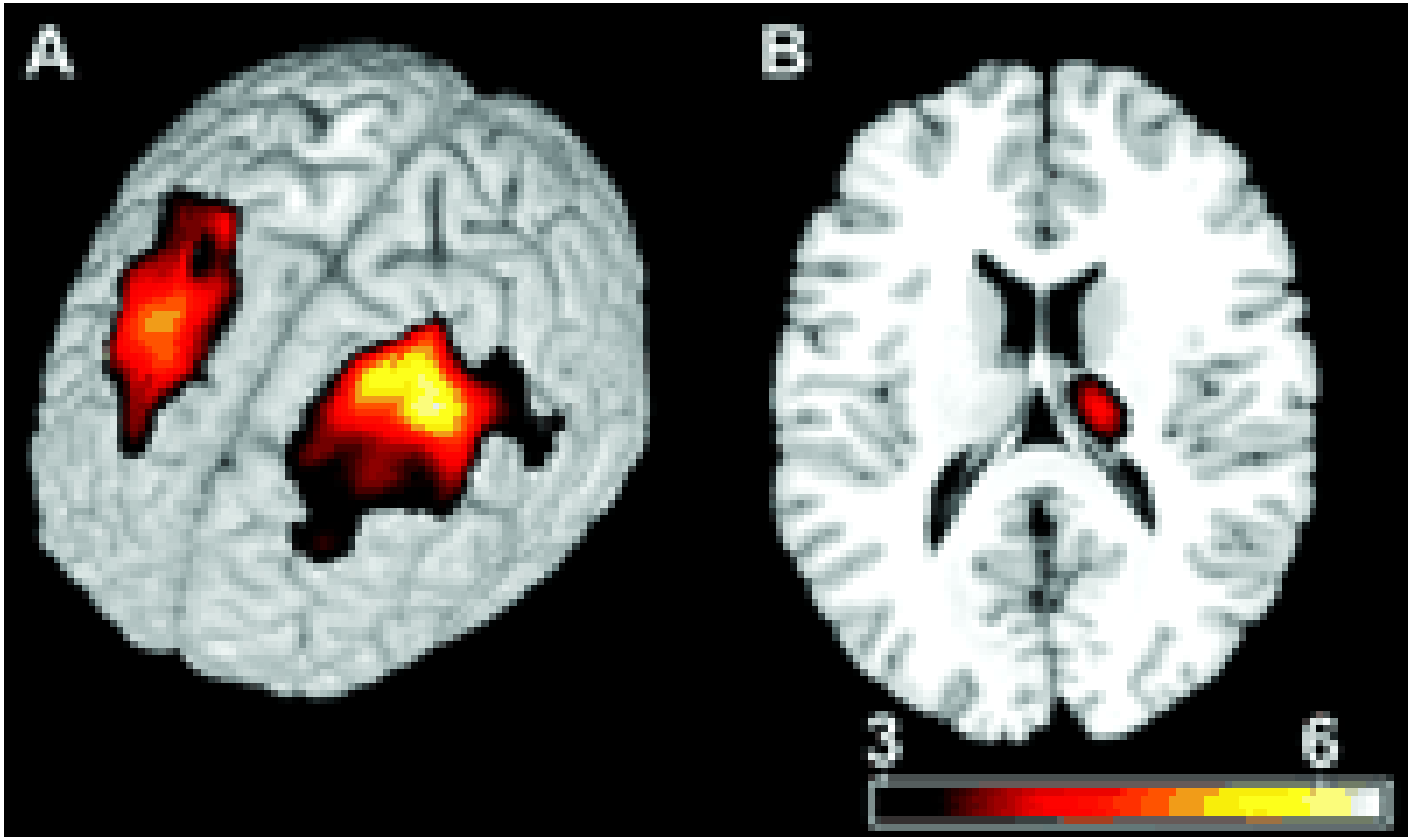



- **Corteccia: diminuzione del volume (5.4%) e della densità (5.9%) della sostanza grigia, specie della parte laterale della corteccia prefrontale (modulaz. discendente)**
- **Ipotrofia del talamo, specie a sn**
- **Neurochimica:**

  **++ glutammato**

  **--- sensibilità agli oppiodi**

**J.Neuroscience 24, 10410-10415,2004**
**Brain 136, 2751-2768,2013**
**Nature Neuroscience 17, 192-200,2014**




**A.V. Apkarian et al.**
**J. Neuroscience 24, 10410-10415,2004**

# Dolore Neuropatico

- **Lesioni dei nervi periferici, dei rami del plesso, delle radici, del midollo, lesioni cerebrali.**

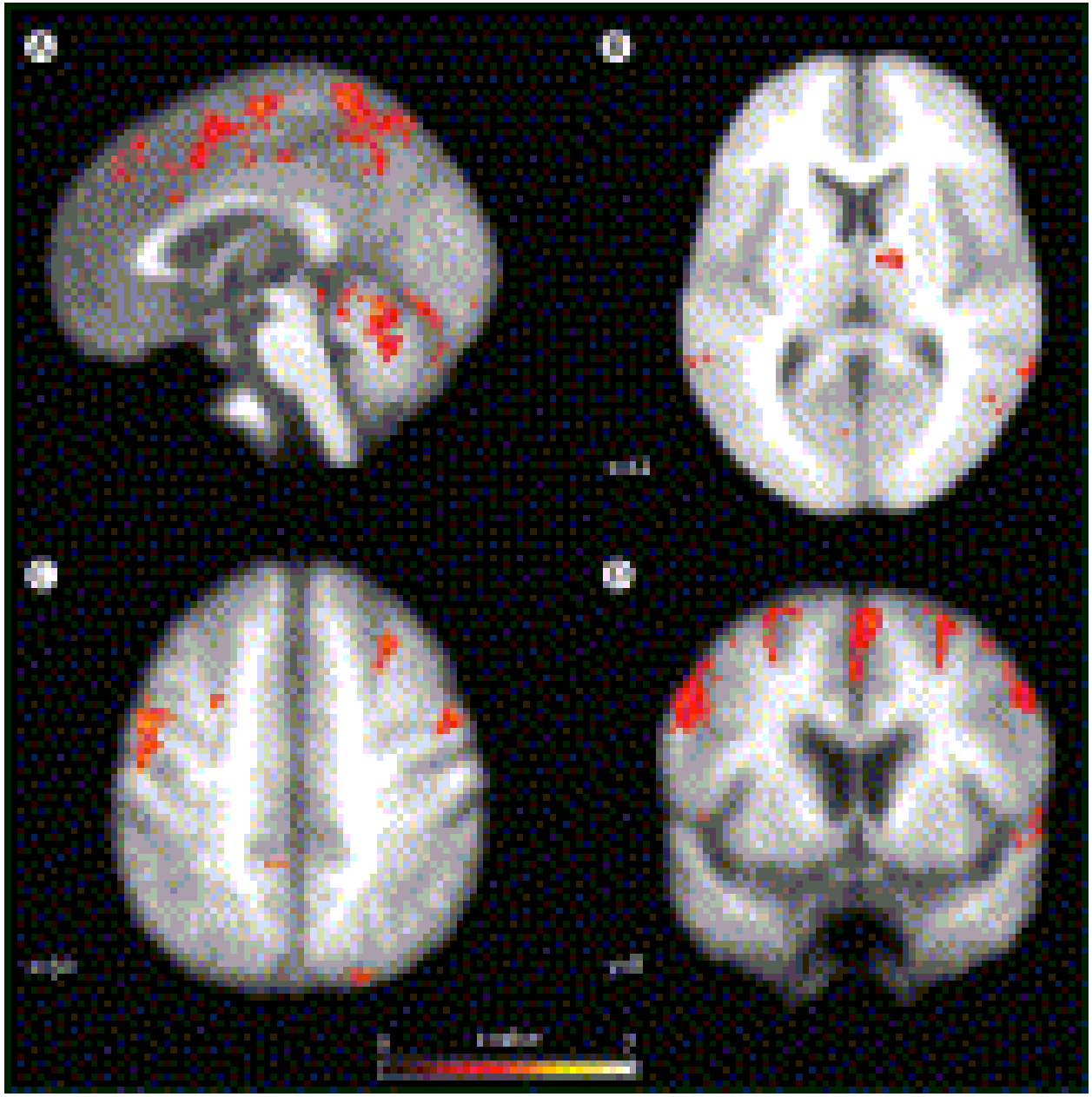
  **** Traumi, polineuropatie, infiammazioni, compressioni acute e croniche***

# Dolore centrale dopo infarto cerebrale (talamo, insula, cort. cingolata, corteccia prefront.)

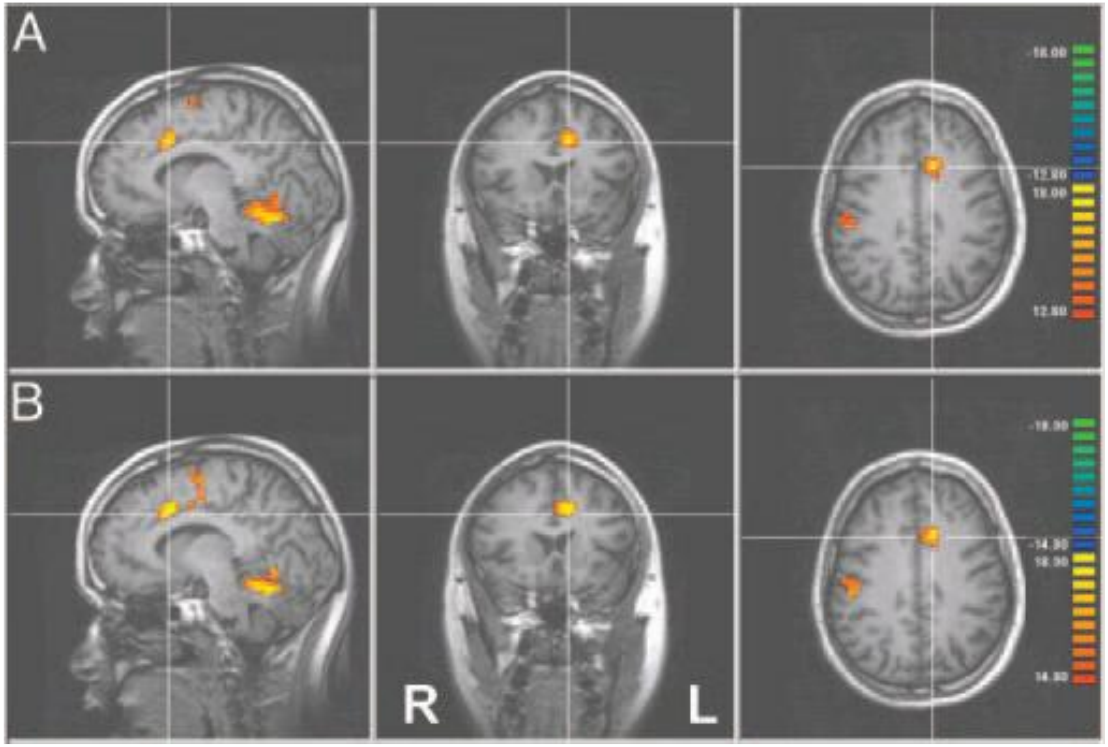
- **Inizio dopo 3 mesi fino a 1 anno (anche dopo ripresa funzionale e regressione parziale del deficit)**
- **Dolore continuo, sordo e teso, d‘intensità fluttuante nell‘emicorpo colpito, talora risparmio della faccia**
- **Dolore urente , pressorio, da schiacciamento, fluttuante e poi continuo, con iperalgesia e allodinia**
- **Sviluppo più o meno lento, profondo, cupo, pulsante**
- **Talora aggravato dal movimento e dallo sforzo**
- **Deficit: ridotta precisione motoria, dismetria, emianopsia, deficit della sensibilità di posizione, tremore intenzionale, movimenti atetosici, emiparesi spastica, atassia della marcia**

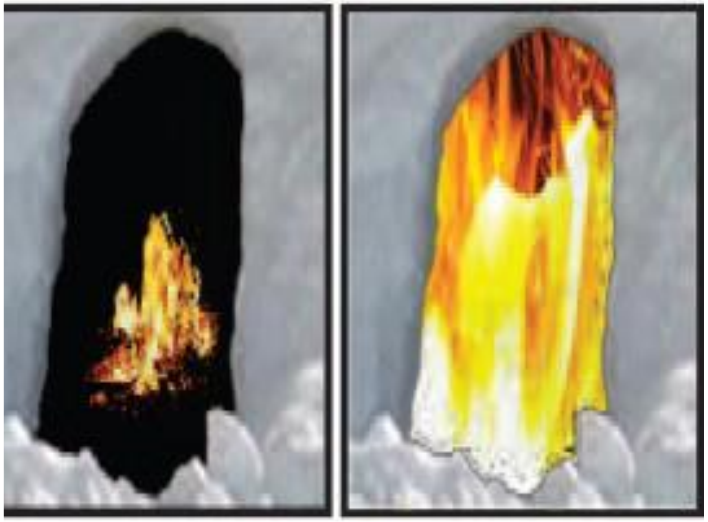
**F. Villoch et al. *Pain* 108, 213-220,2004**

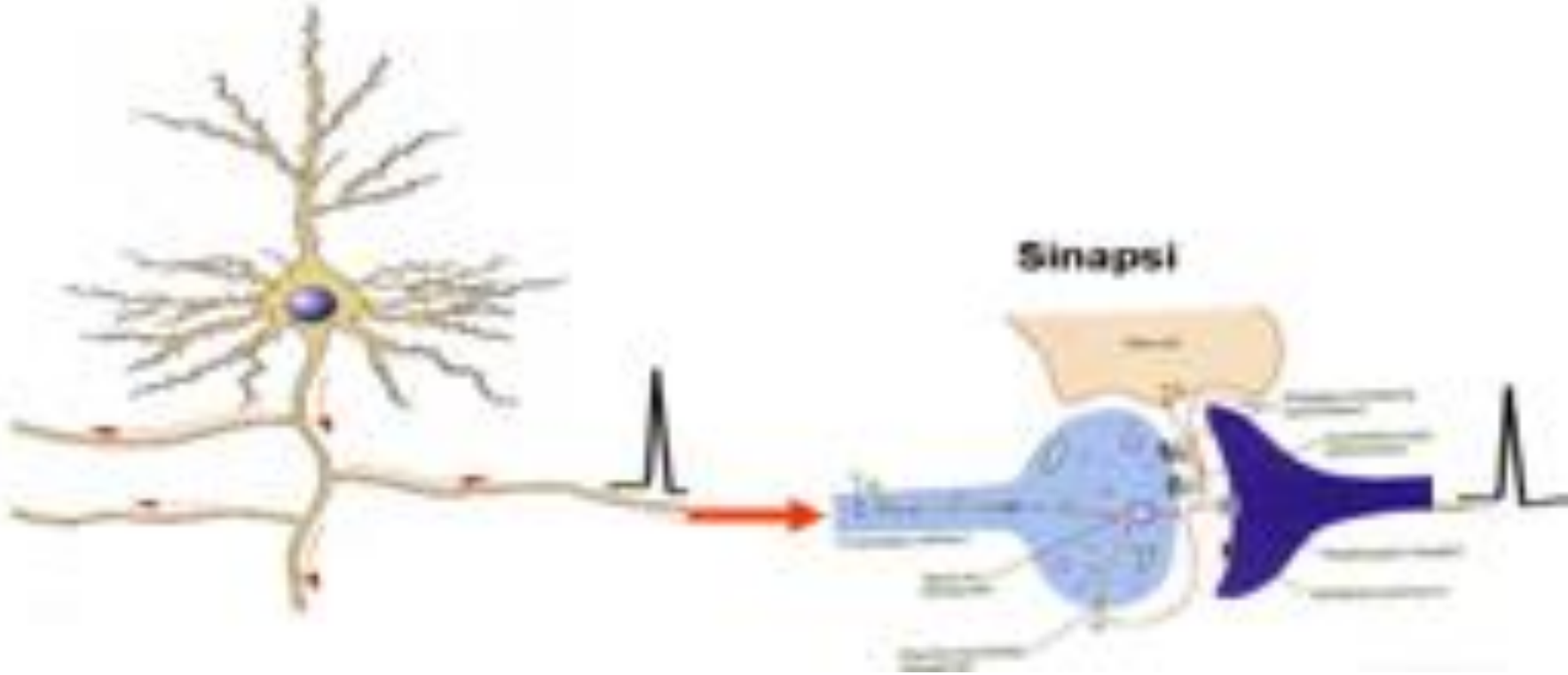
**AA.VV. Pain assessment in elderly adults with dementia (Alzheimer)**
**Lancet Neurology 13, 1216-1267,2014**



**R.C. de Charms et al.**
**Control over brain activation and pain learned by using real-time functional MRI**
***PNAS 102, 18626-18631,2005***





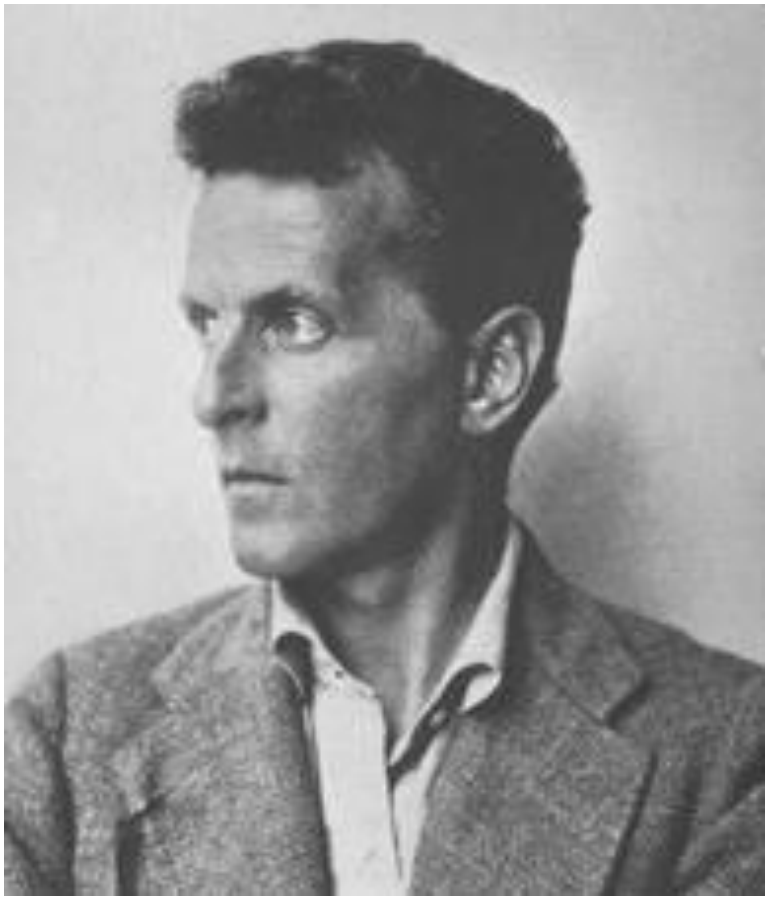

**86 miliardi**
**cellule della glia: 4-6 vv tanto**

**86 miliardi x 5.000**

# Prurito

- Puntura d‘insetto, malattie della pelle, nelle vicinanze di una ferita, in malattie interne (itterizia)
- Stimolaz. nervosa da parte dell‘istamina
- Anche se forte, non è mai dolore
- Resistente ai più potenti antidolorifici
- Grattarsi porta sollievo perché il dolore così provocato attenua il prurito.

# Ludwig Wittgenstein

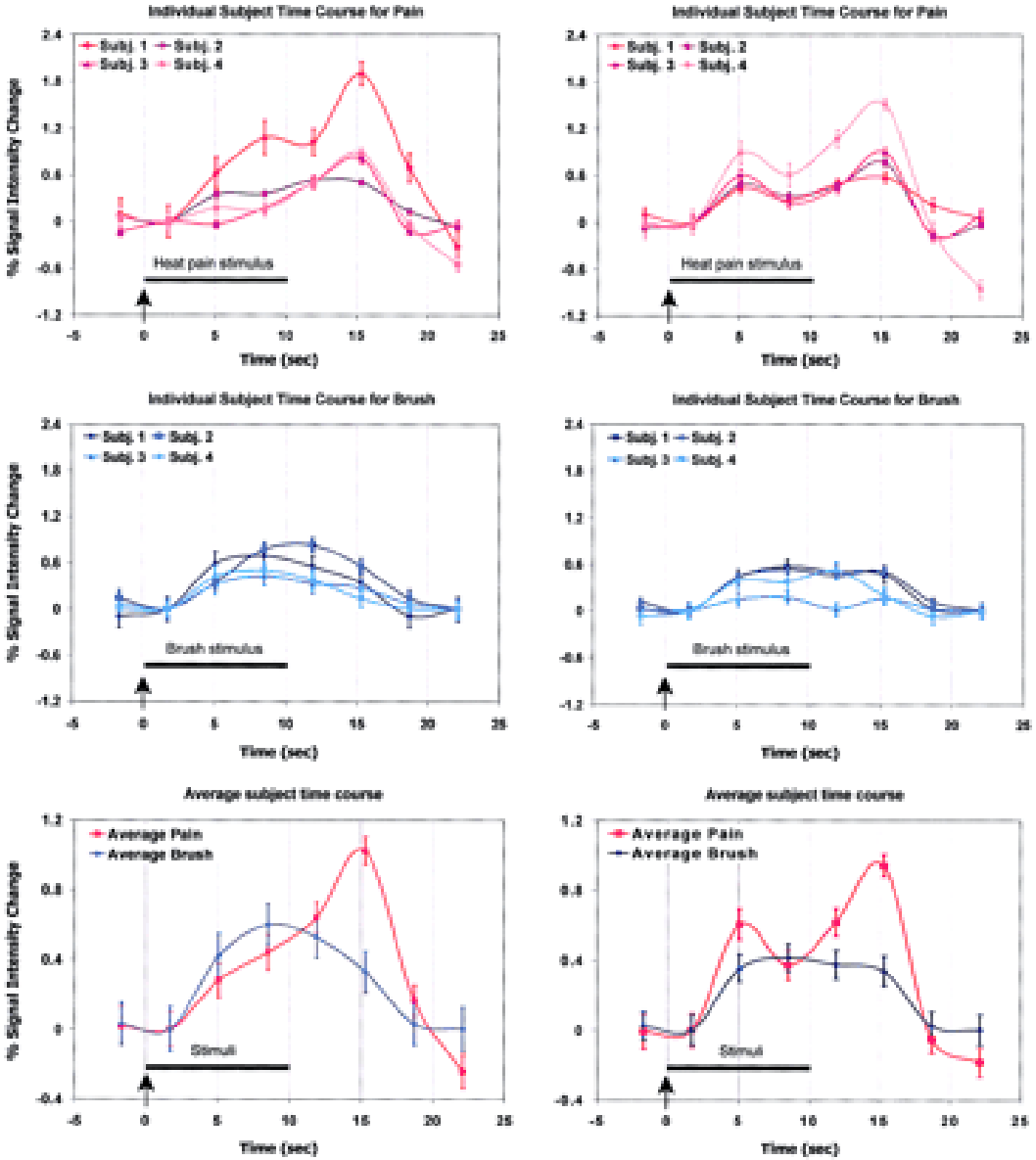


- **“Una persona che non ha mai avuto dolori riuscirebbe a capire il significato della parola dolore? […] Ciascuno dice di sé stesso di co-noscere esclusiva-mente i suoi dolori.”**

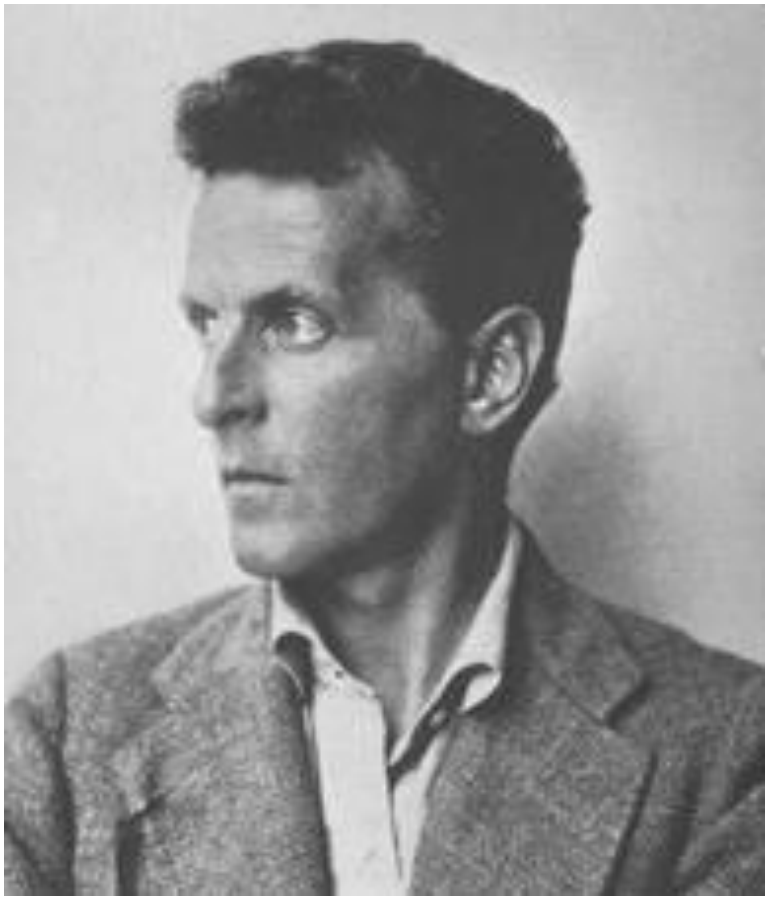
- ***Philosophische Unter-suchungen* Suhrkamp Frankfurt a/M 2001**

A SI pain- & brush-related activity time course

B SII pain- & brush-related activity time course



# L. Wittgenstein



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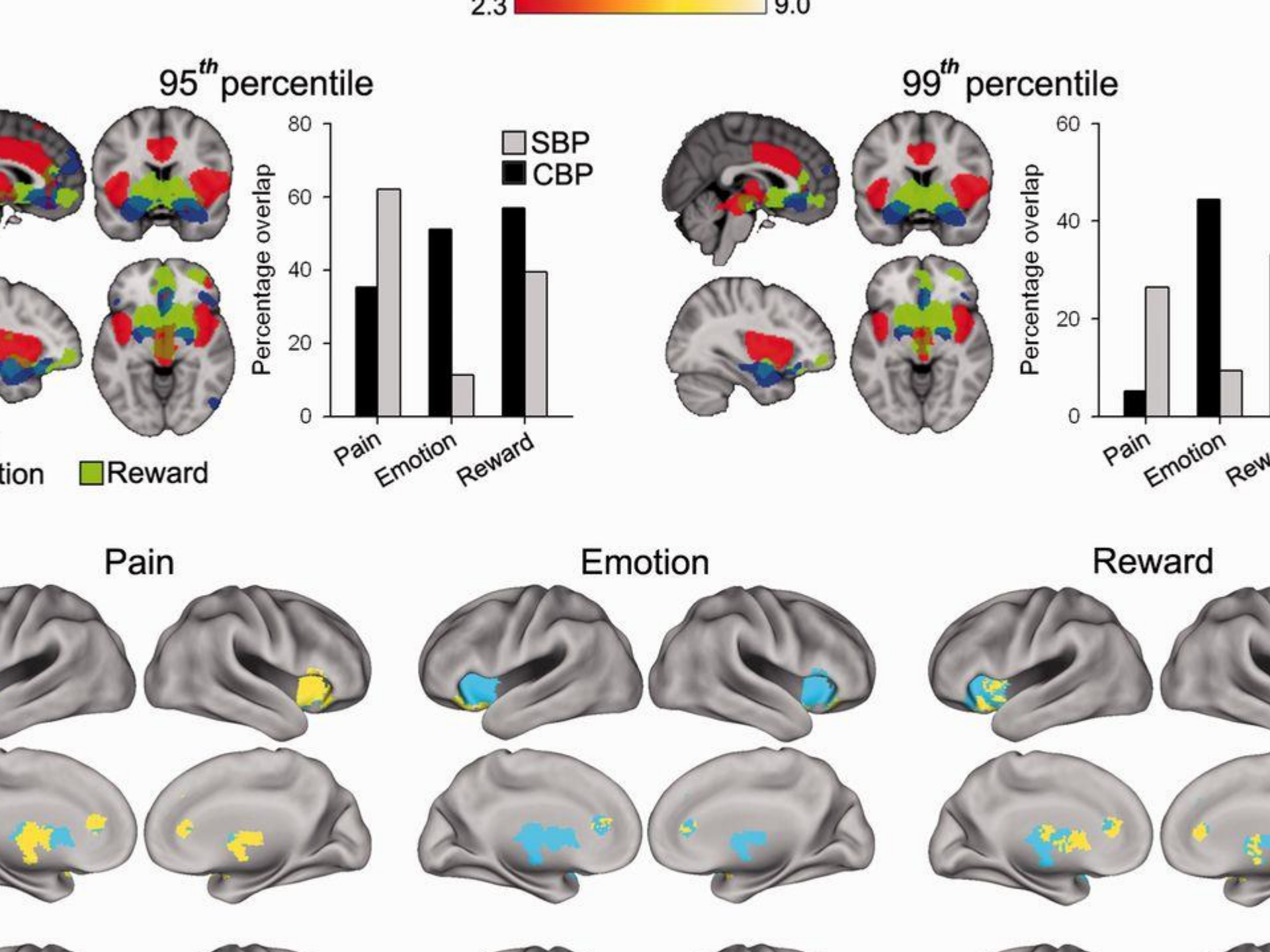
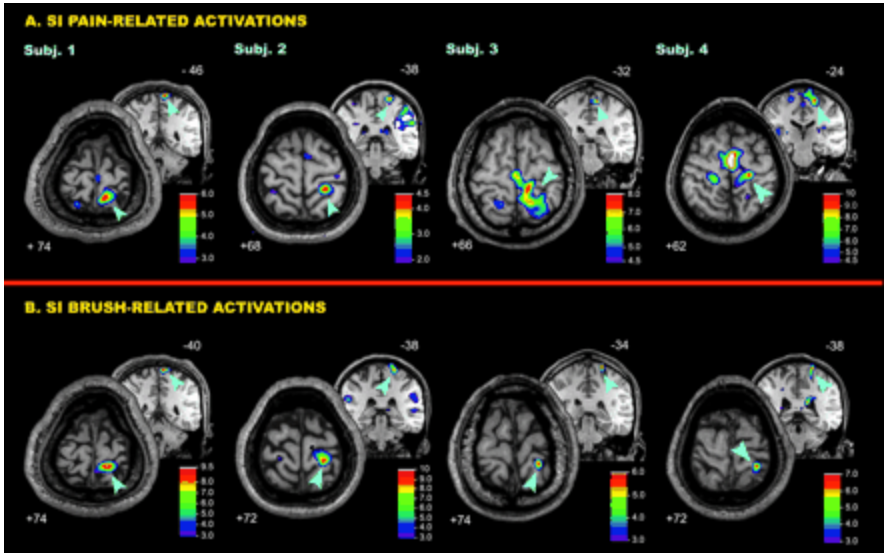
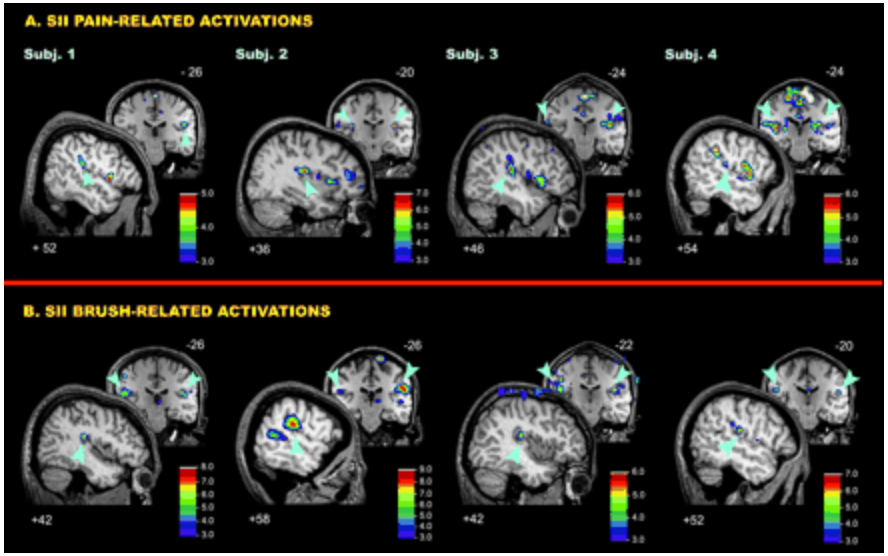
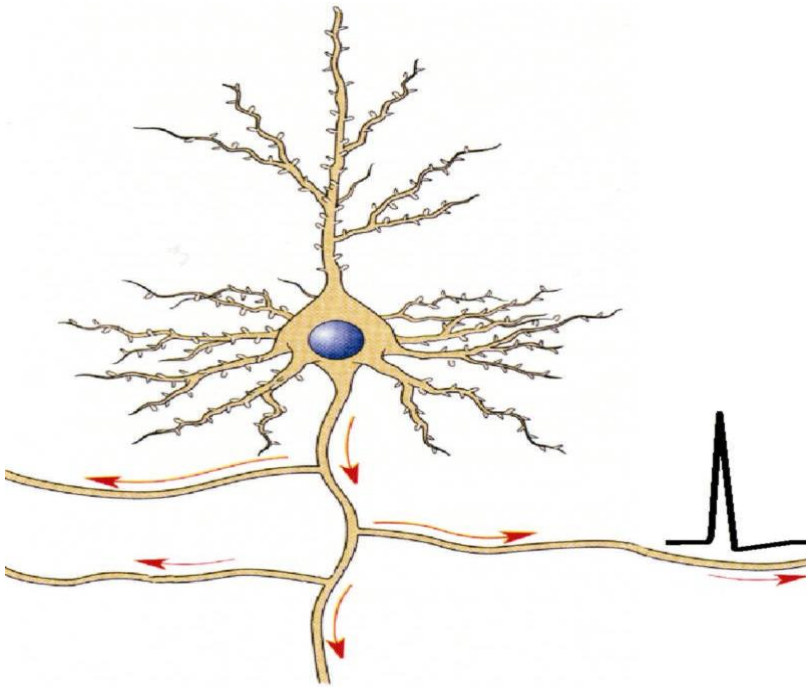

2.3
9.0
95th percentile
99th percentile
SBP
CBP
Percentage overlap
80
60
40
20
0
Pain
Emotion
Reward
tion
Rew
Pain
Emotion
Reward

48Klinische Beobachtungen zur Schmerzchronifizierung

- Ungenügend behandelte starke oder längerdauernde Schmerzen sensibilisieren das Nervensystem, es bleibt oft eine Hyperalgesie
- Viele Schmerzpatienten hatten (früh-)kindliche Schmerzerfahrungen, z.B. durch körperliche Strafe, invasive Therapie
- Durch wirksame perioperative Schmerzbehandlungsinkt das Risiko für spätere chronische Schmerzen
- Lokal-und Spinalanästhesie bereits vor einer Amputation reduziert das Risiko für Phantomschmerzen
- Bei Gürtelrosewird durch frühzeitige Schmerzbehandlung und Neuroprotektion das Risiko für eine chronische Neuralgie verringert
- Durch intensive Trainingstherapie (GRIP) wird Chronifizierung von Rückenschmerzen mit dem Risiko der Frühberentung unterbrochen

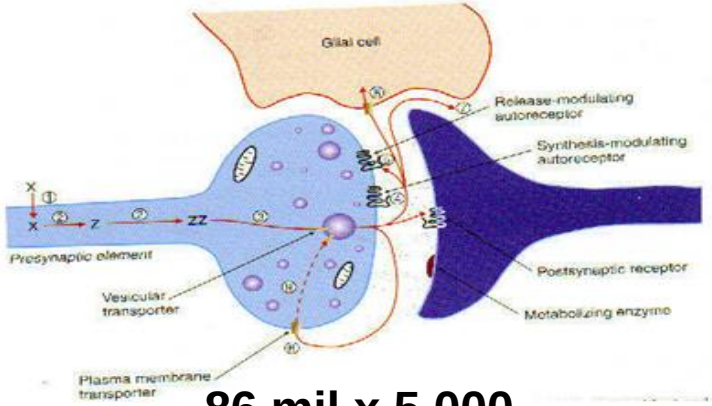

A. SI PAIN-RELATED ACTIVATIONS
Subj. 1
Subj. 2
Subj. 3
Subj. 4
-46
-38
-32
-24
+74
+68
+66
+62
B. SI BRUSH-RELATED ACTIVATIONS
-40
-38
-34
-38
+74
+72
+74
+72


A. SII PAIN-RELATED ACTIVATIONS
Subj. 1
Subj. 2
Subj. 3
Subj. 4
B. SII BRUSH-RELATED ACTIVATIONS

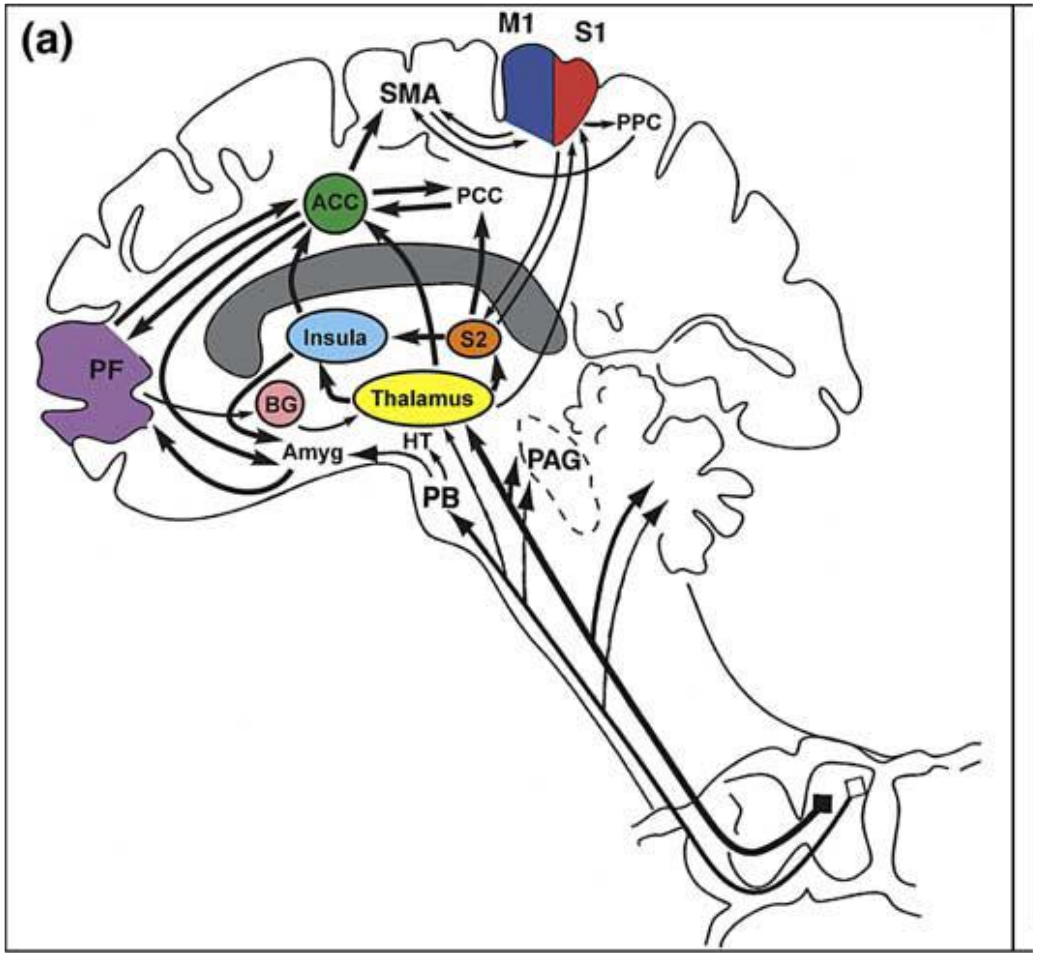


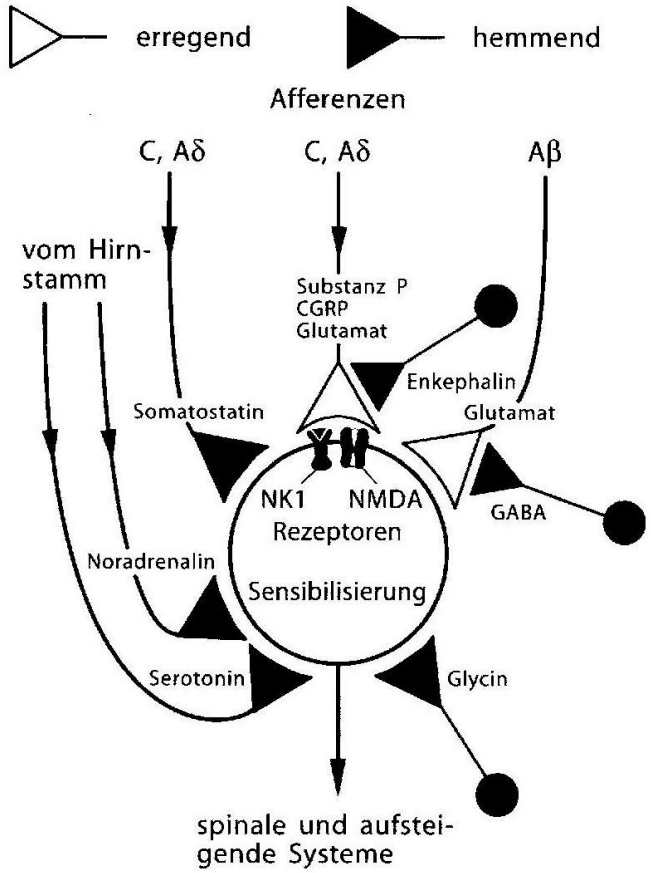
86 miliardi

## Sinapsi




86 mil.x 5.000


(a)
M1
S1
SMA
PPC
ACC
PCC
Insula
S2
PF
BG
Thalamus
Amyg
HT
PAG
PB

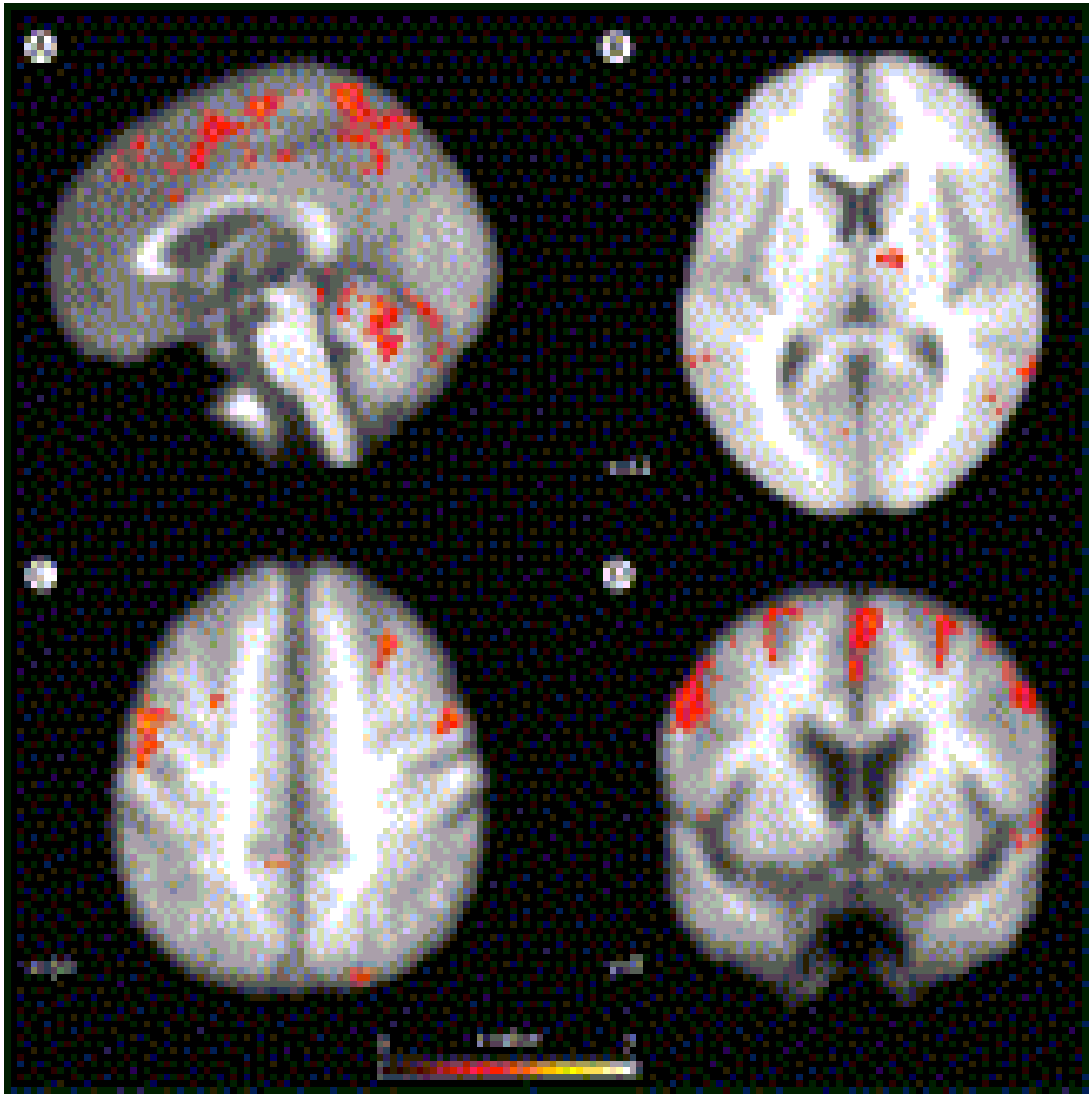


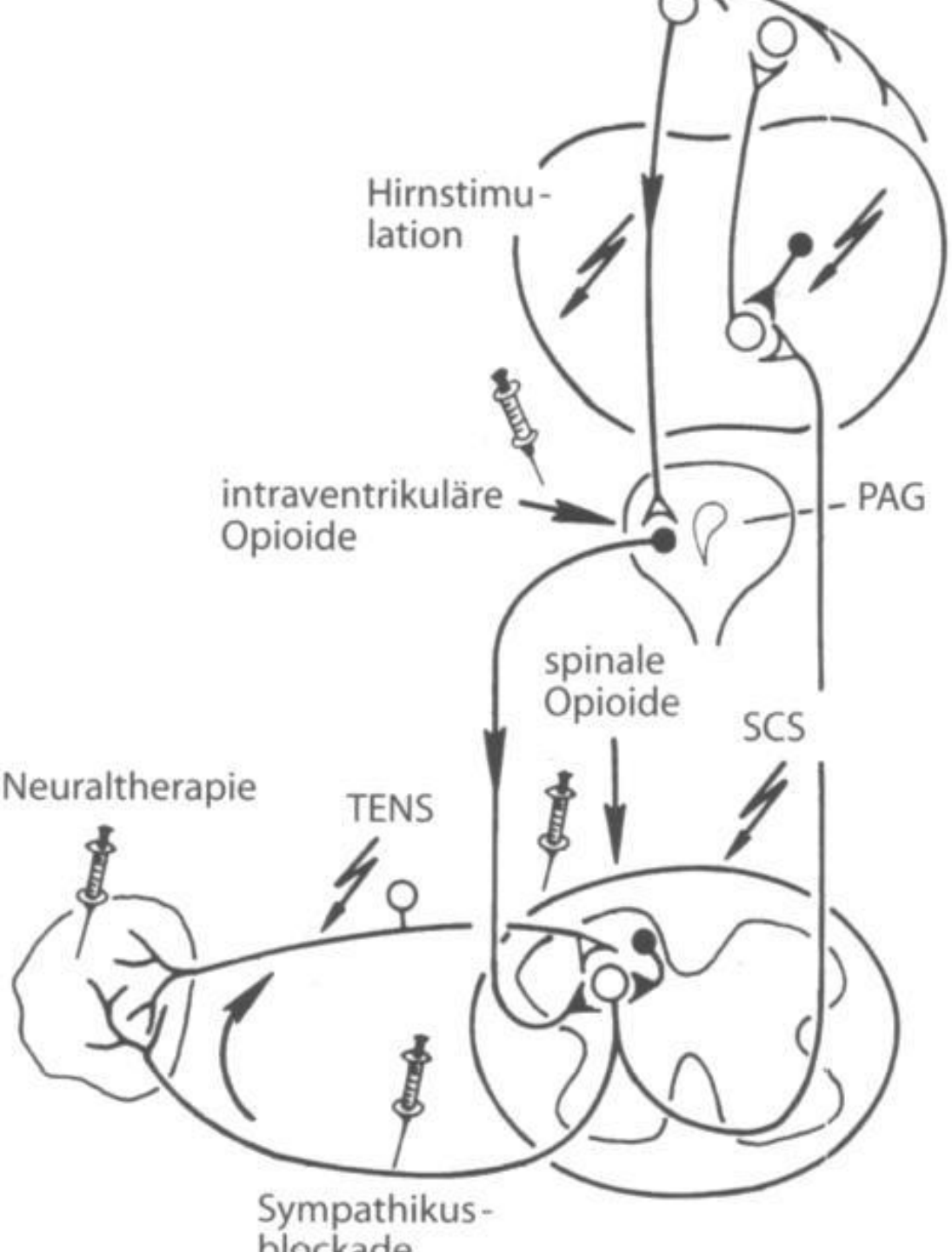

- Das Hinterhorn-Neuronim Rückenmark --Eingangsfilter des Schmerzsystems
- •Balance von Erregung und Hemmung
- •Schmerzmodulation durch segmentale und deszen-dierende Hemmung
- •Sensibilisierung erregender Synapsen
- •Schwächung hemmender Systeme
- •Allodynie durch Aß-Input
- •Langdauernde Plastizität

# Cronicificazione del dolore

- Dolore continuo, a lungo e forte
- Alterazioni delle strutture nel midollo, nella corteccia, in aree subcorticali
- Produzione di proteine a livello periferico, midollare e centrale
- Plasticità delle sinapsi

**AA.VV. Pain assessment in elderly adults with dementia (Alzheimer) Lancet Neurology 13, 1216-1267,2014**




Hirnstimu-
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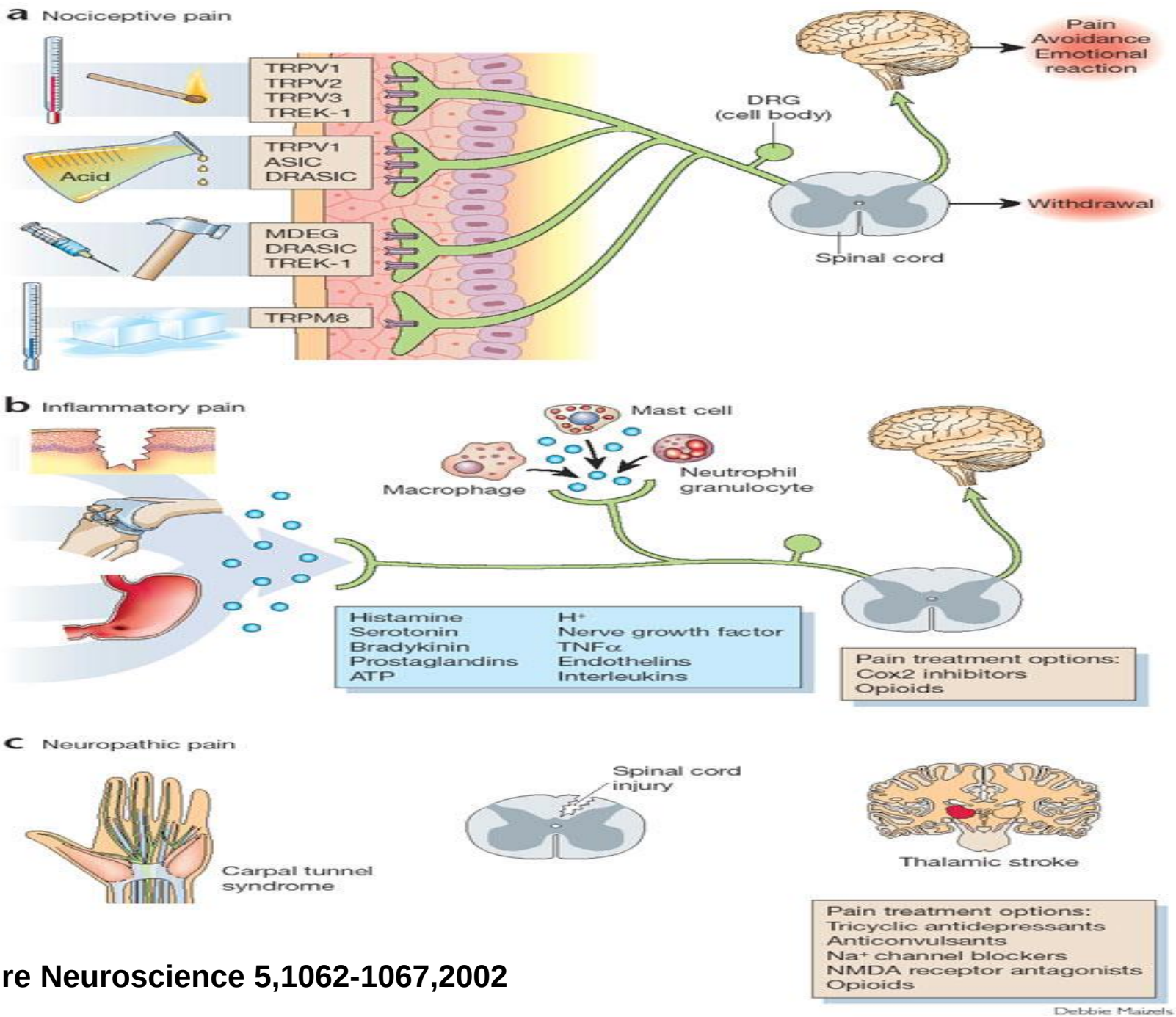
intraventrikuläre
Opioide
PAG
spinale
Opioide
SCS
Neuraltherapie
TENS
Sympathikus-




**Nature Neuroscience 5,1062-1067,2002**

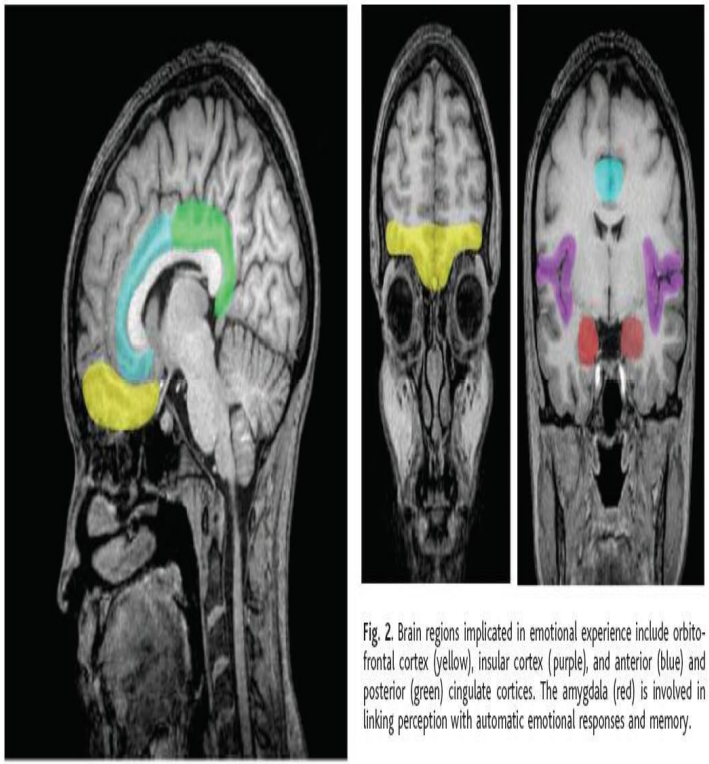
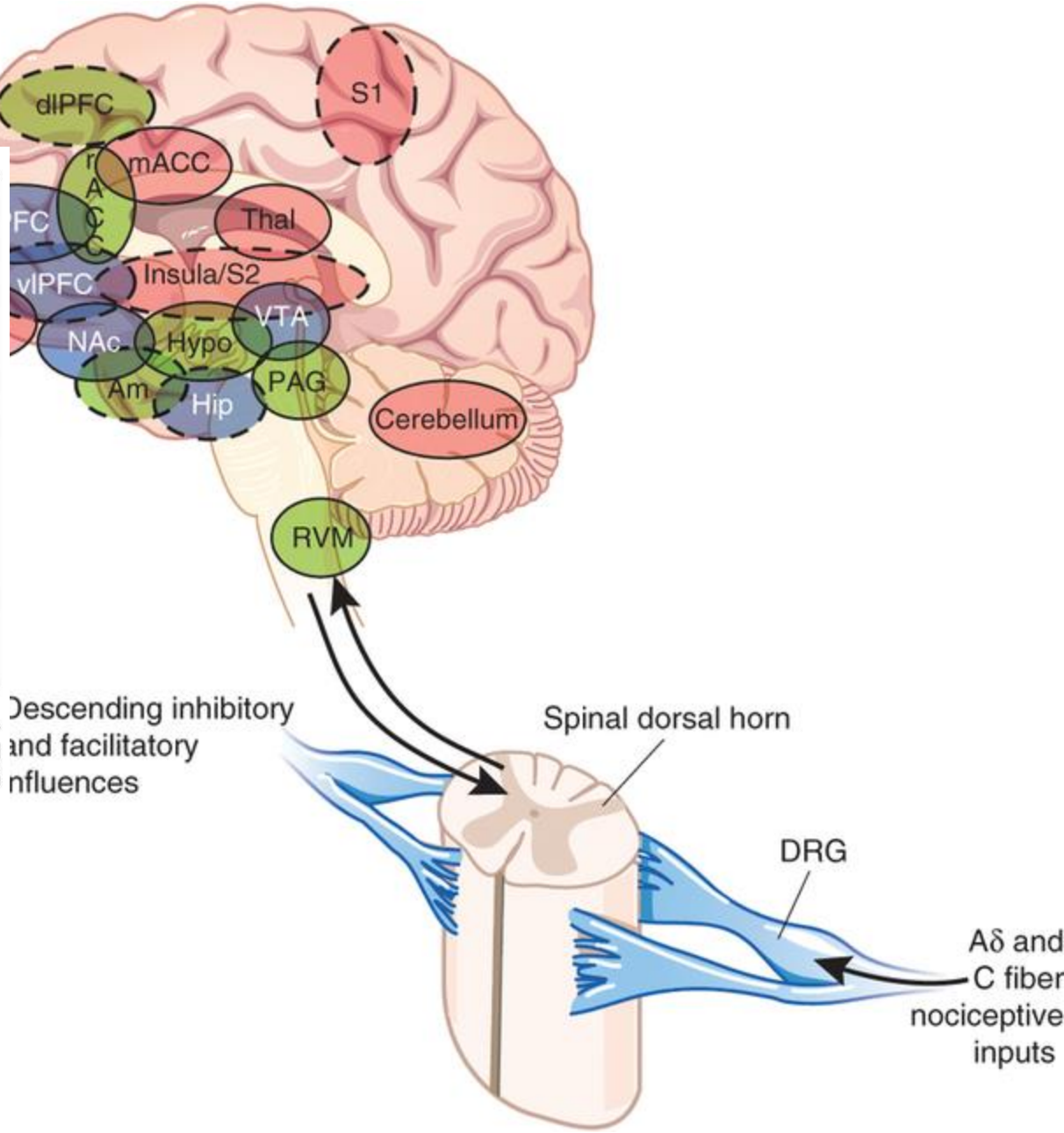
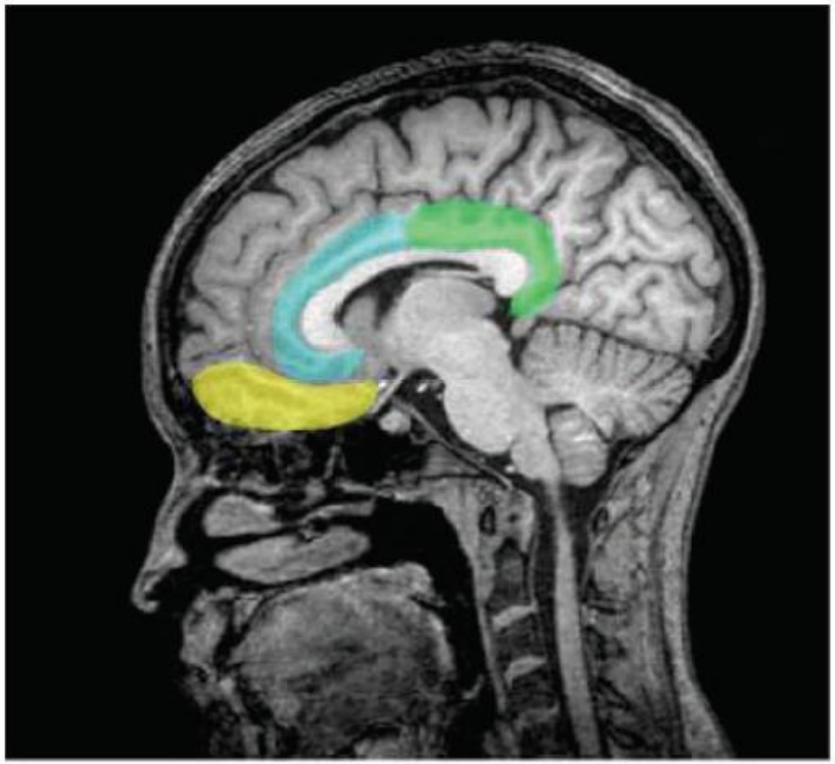


Fig. 2. Brain regions implicated in emotional experience include orbitofrontal cortex (yellow), insular cortex (purple), and anterior (blue) and posterior (green) cingulate cortices. The amygdala (red) is involved in linking perception with automatic emotional responses and memory.




***F. Denk et al.***
***Nature***
***Neuroscience***
***17, 192-200,2014***

# Regioni cerebrali delle emozioni



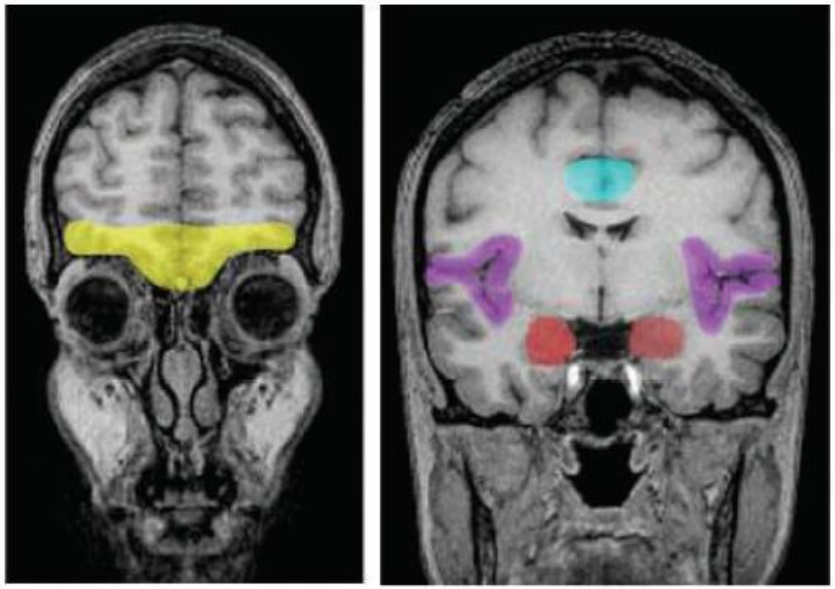
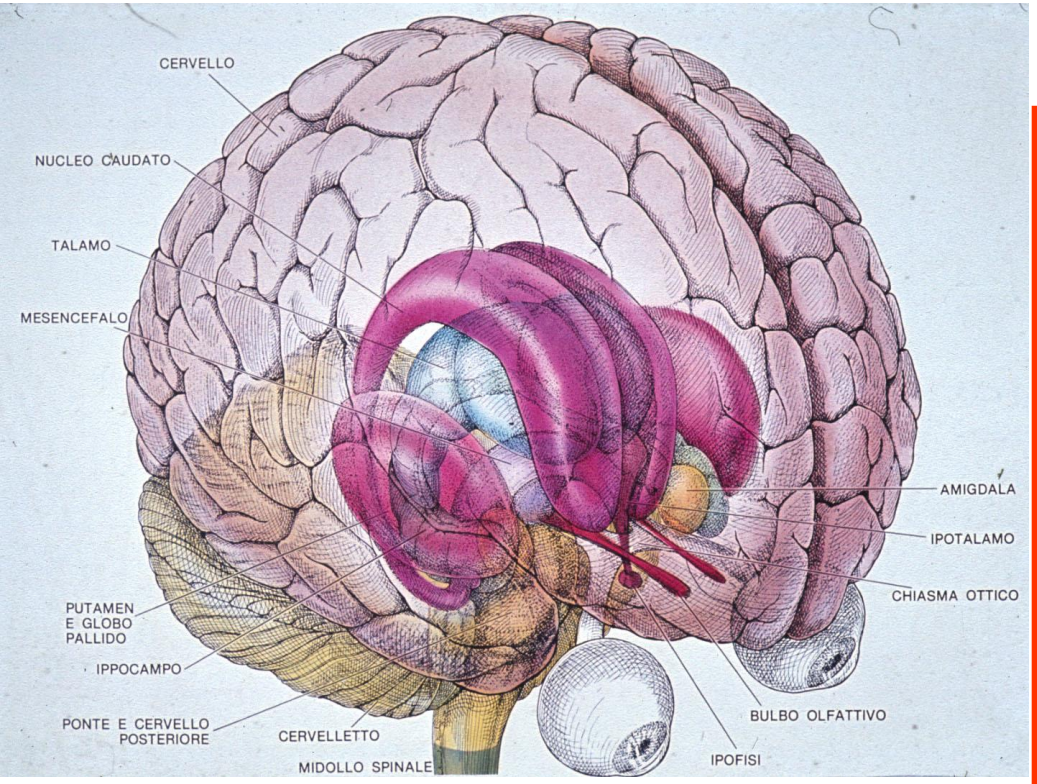


**Fig. 2.** Brain regions implicated in emotional experience include orbitofrontal cortex (yellow), insular cortex (purple), and anterior (blue) and posterior (green) cingulate cortices. The amygdala (red) is involved in linking perception with automatic emotional responses and memory.

# Variazioni morfologiche del cervello nel dolore cronico

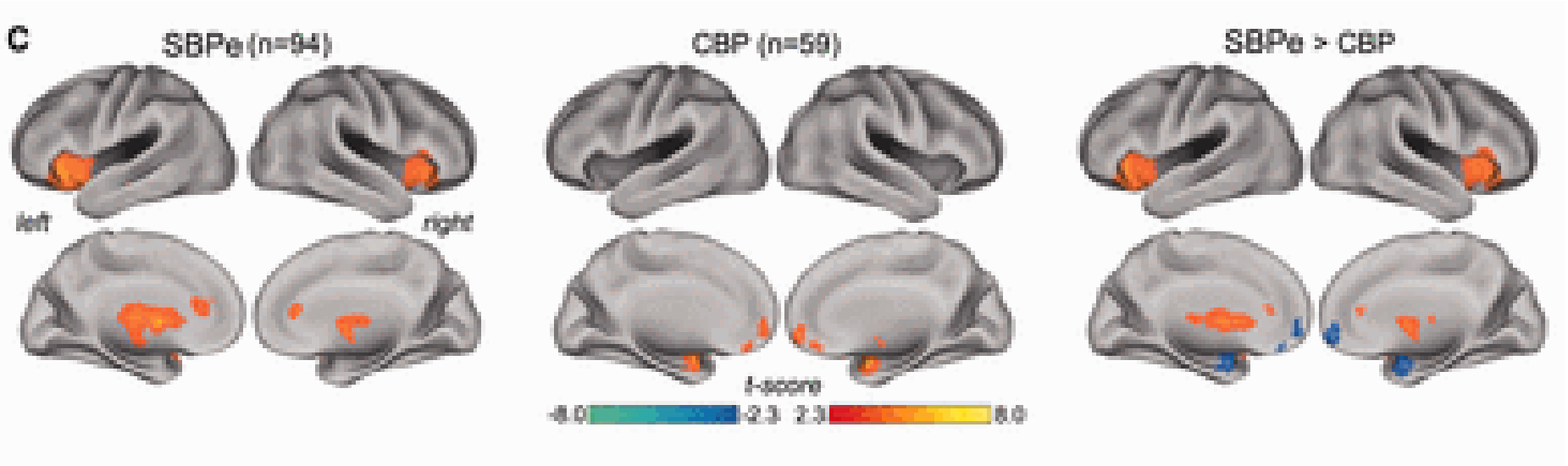



- **Corteccia: diminuzione del volume (5.4%) e della densità (5.9%) della sostanza grigia, specie della parte laterale della corteccia prefrontale (modulaz. discendente)**
- **Ipotrofia del talamo, specie a sn**
- **Neurochimica:**

  **++ glutammato**

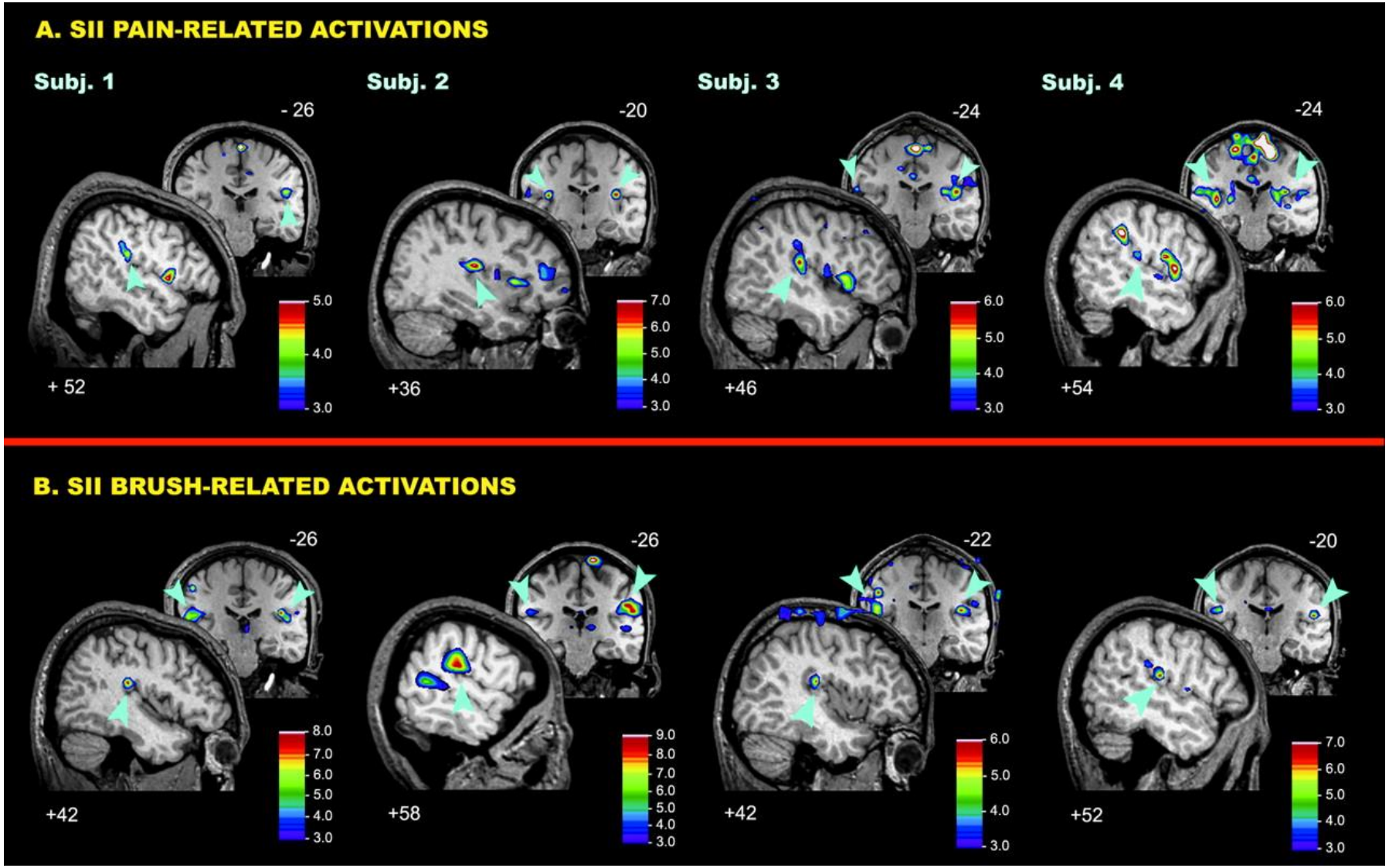
  **--- sensibilità agli oppiodi**

**Brain 136, 2751-2768, 2013; J.of Pain 10, 1113-1120,2009; J.of Neurosci. 17,10410-10515,2004; Nature-Neurosci. 17,1438-1439, 2014; ibidem 17,1607-1615, 2014**



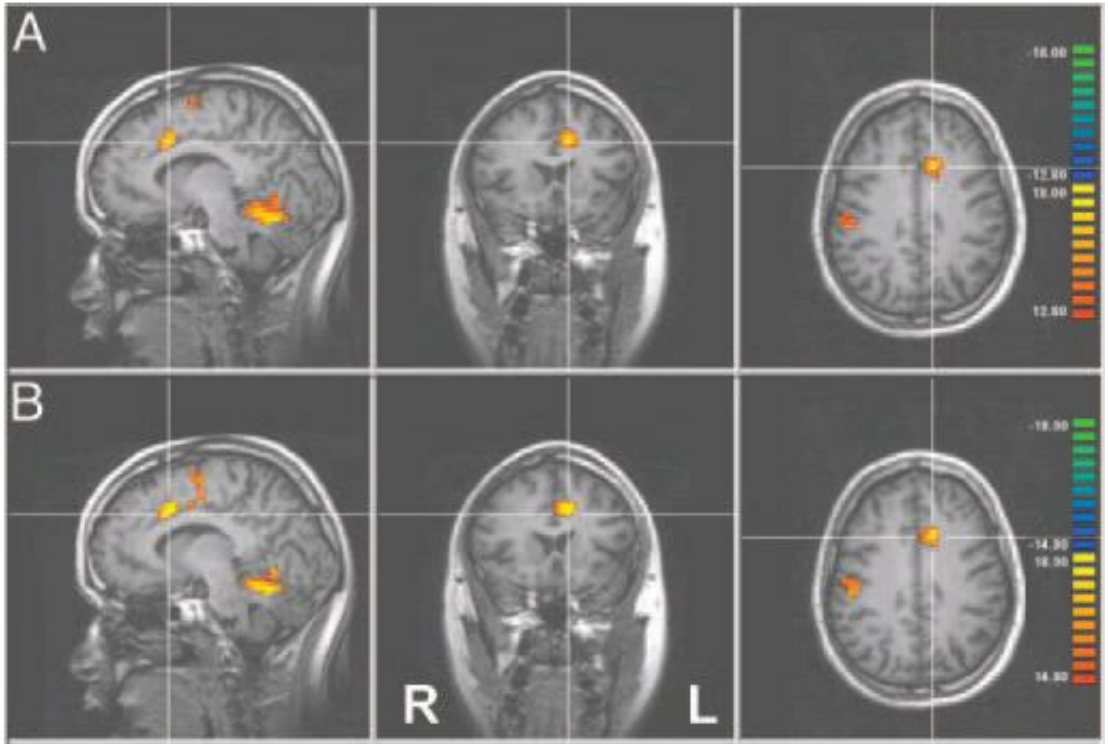

**J.A. Hashmi et al.**

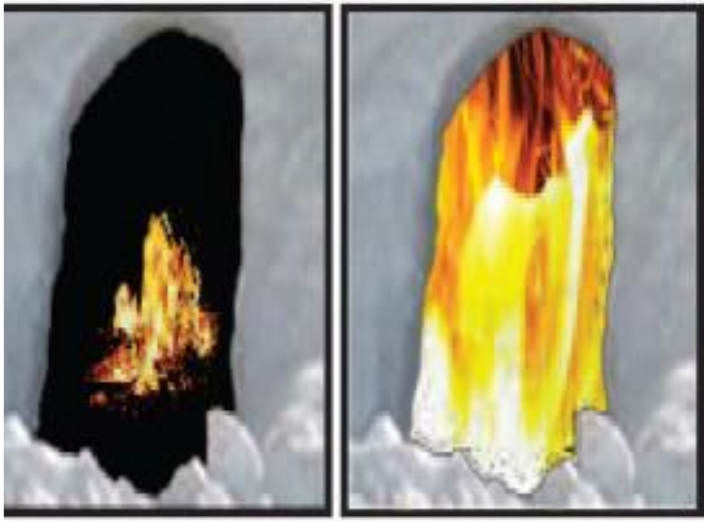
***Brain 136, 2751-2768, 2013***

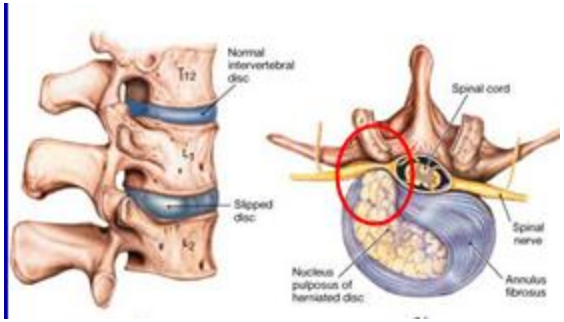



**J. Chen et al. J. Of Neurophysiology 88, 464-474, 2002**

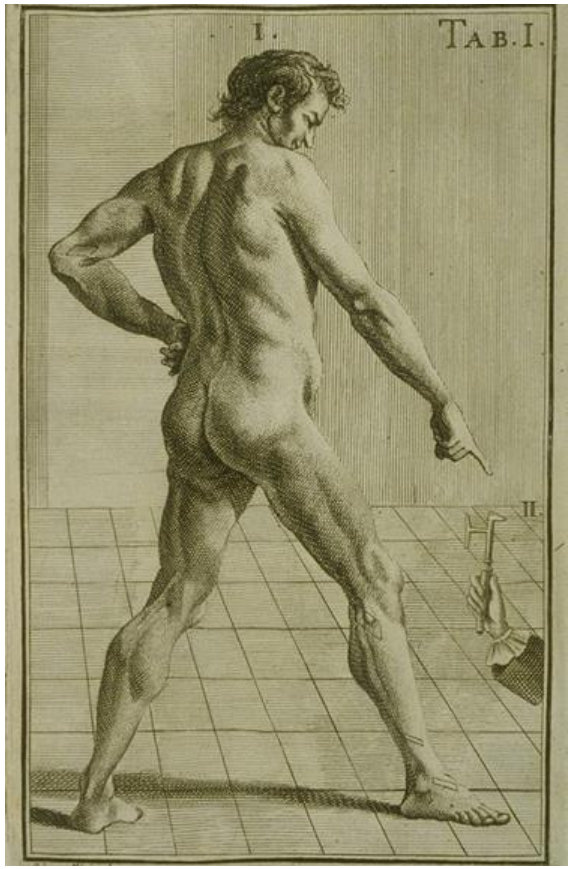
**R.C. de Charms et al.**
**Control over brain activation and pain learned by using real-time functional MRI**
***PNAS 102, 18626-18631,2005***

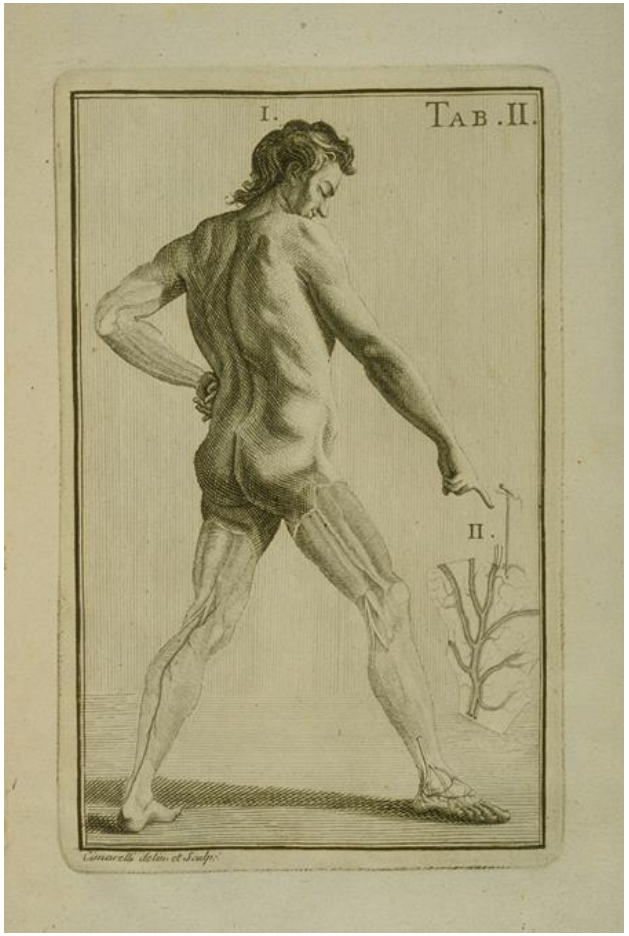


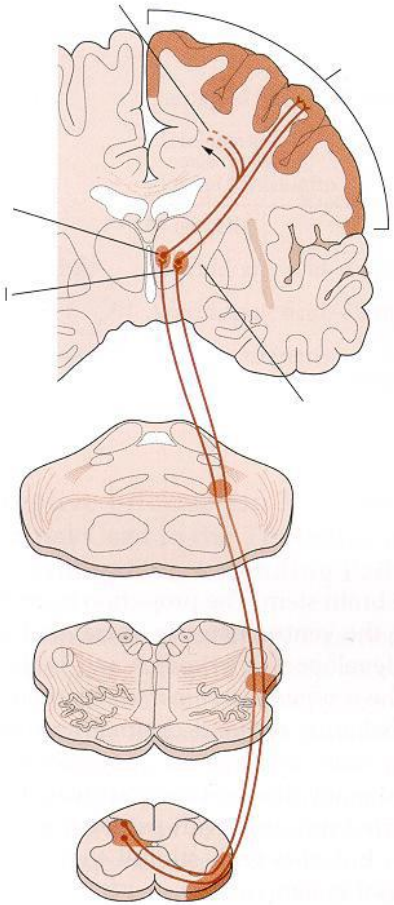




Normal intervertebral disc
T12
L1
Slipped disc
L2
Spinal cord
Spinal nerve
Nucleus pulposus of herniated disc
Annulus fibrosus

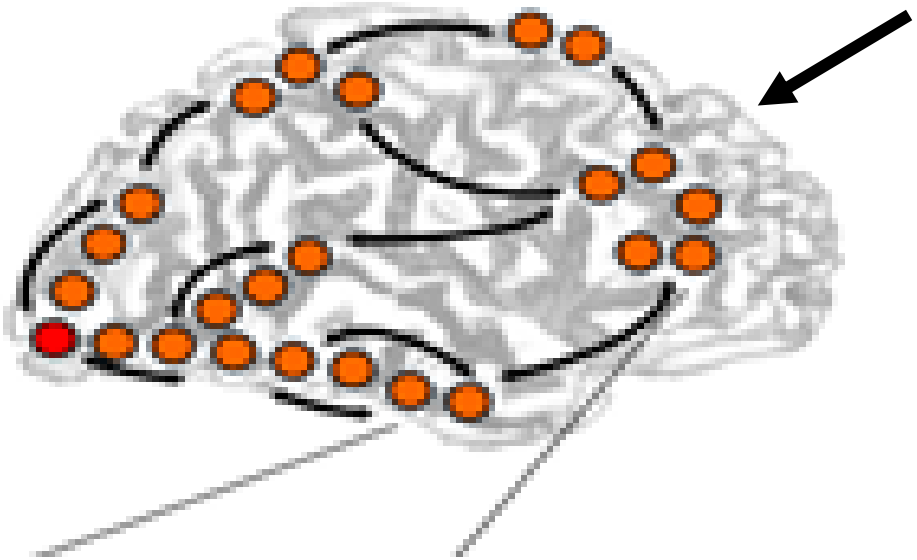
# Disturbi neurogenici alle gambe

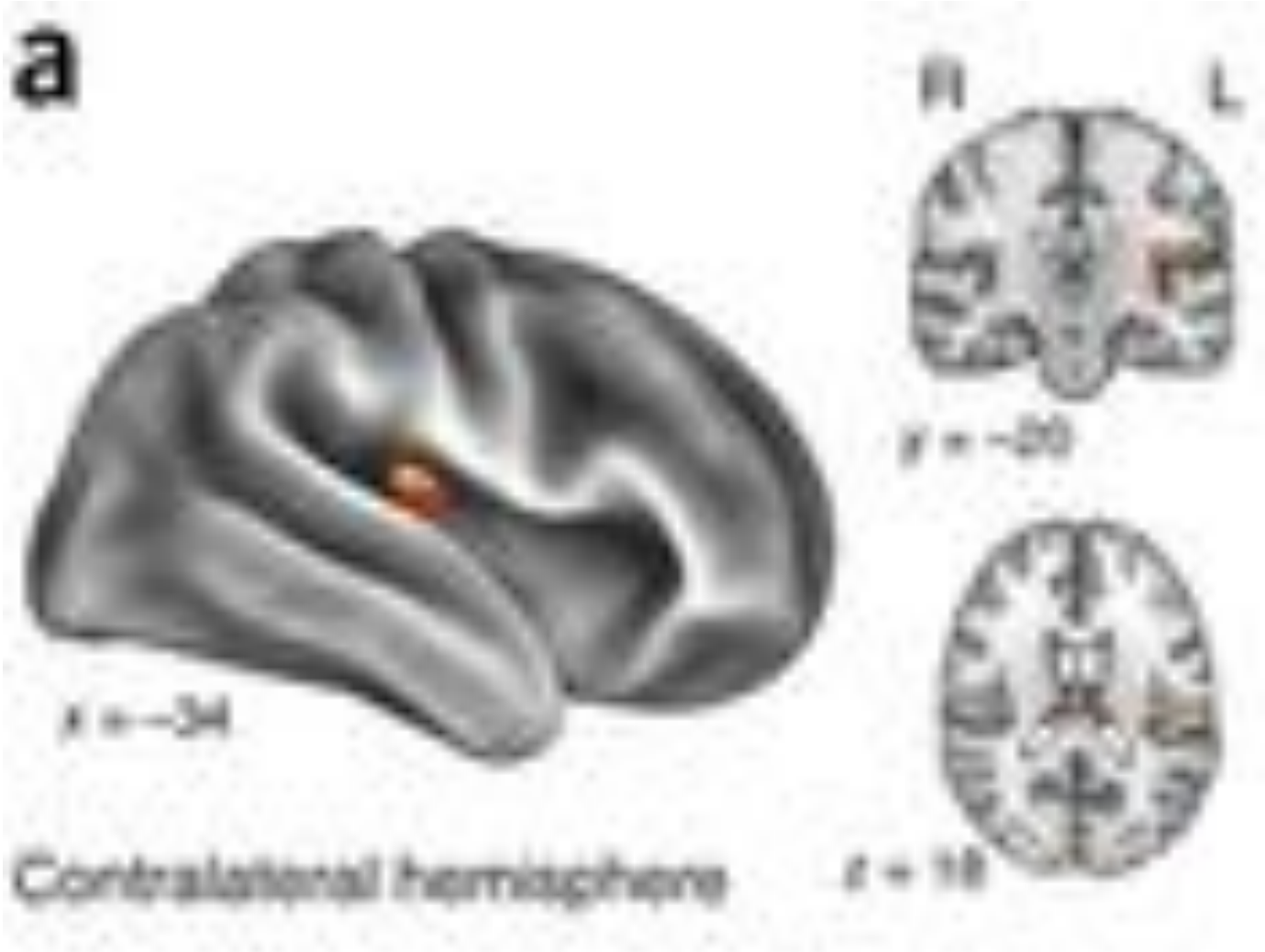




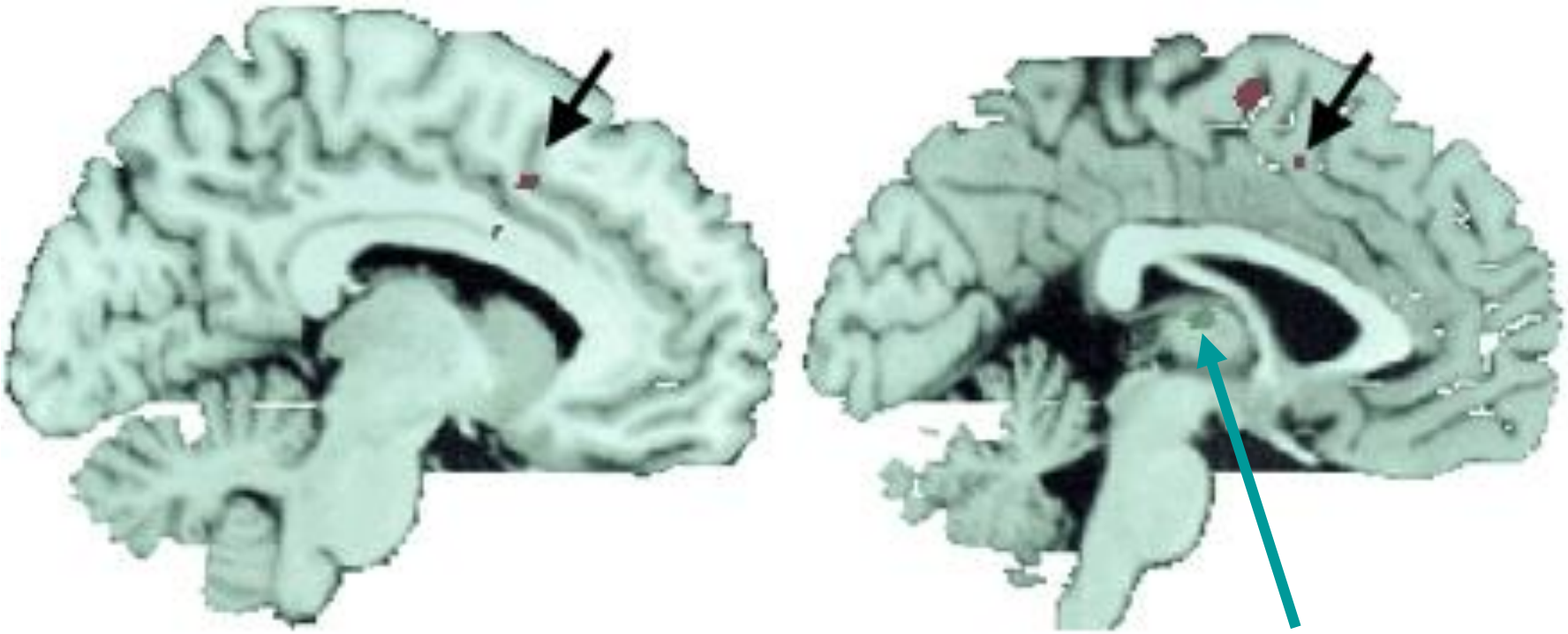
**Corteccia prefrontale**



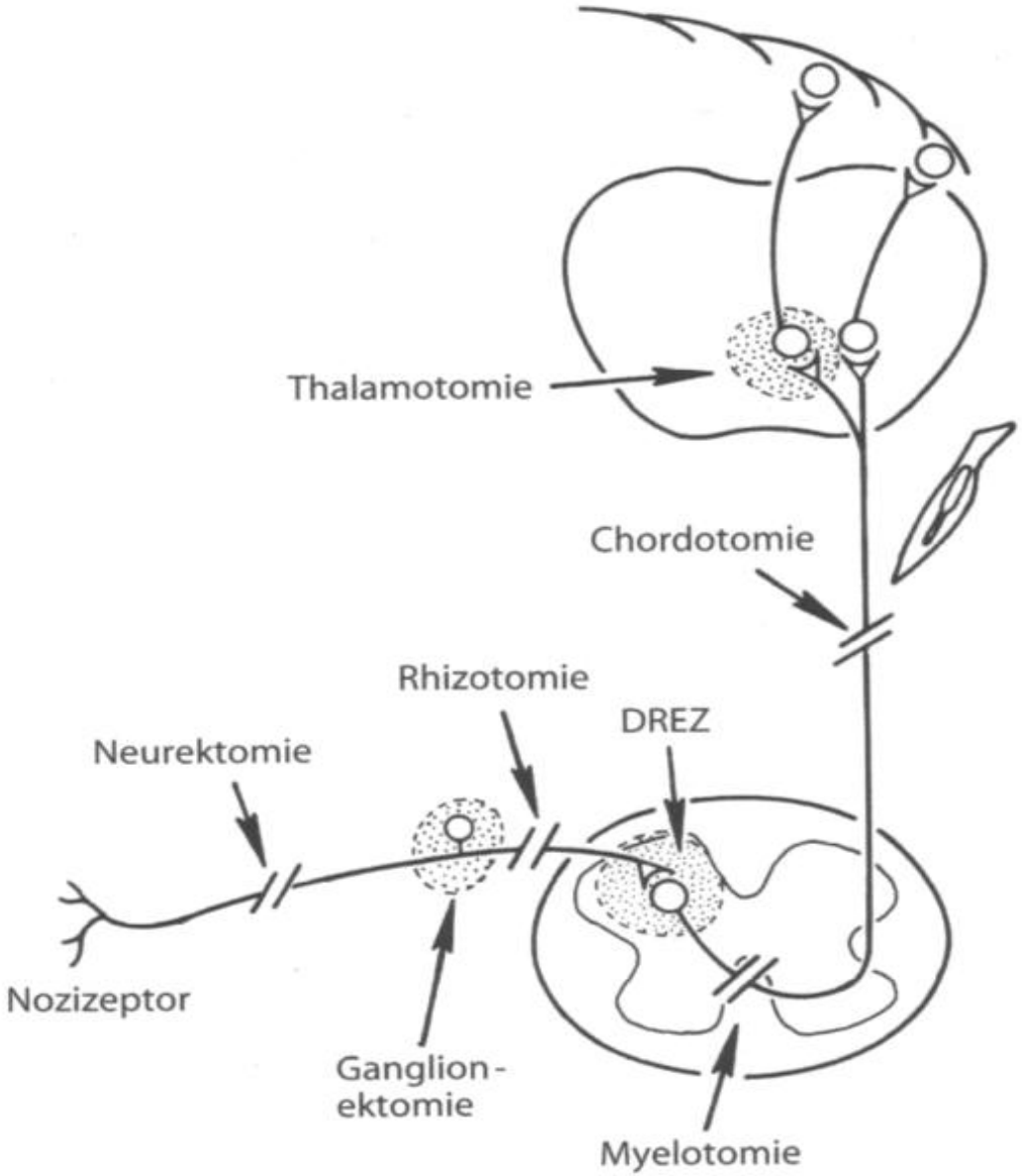


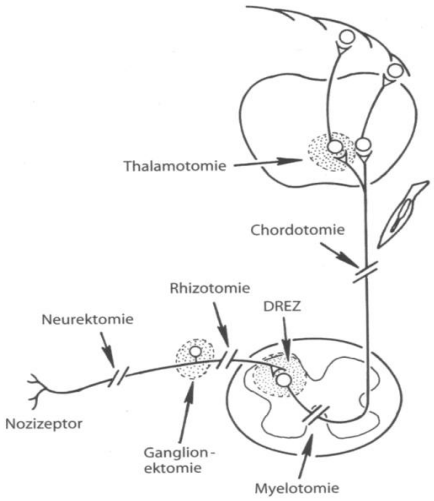

***A.R. Segerdahl et al.***
***Nature Neuroscience 18, 499-500,2015***

# „Pain catastrophizing“ in fibromialgia



**Brain 127, 835-843,2004**


Thalamotomie
Chordotomie
Rhizotomie
DREZ
Neurektomie
Nozizeptor
Ganglion-
ektomie
Myelotomie


Thalamotomie
Chordotomie
Rhizotomie
DREZ
Neurektomie
Nozizeptor
Ganglion-
ektomie
Myelotomie