

# **Il processo di cronicizzazione del dolore**

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Dipartimento di Biotecnologie Mediche e Medicina Traslazionale  
Università degli Studi di Milano

# Dichiarazione di conflitto di interessi

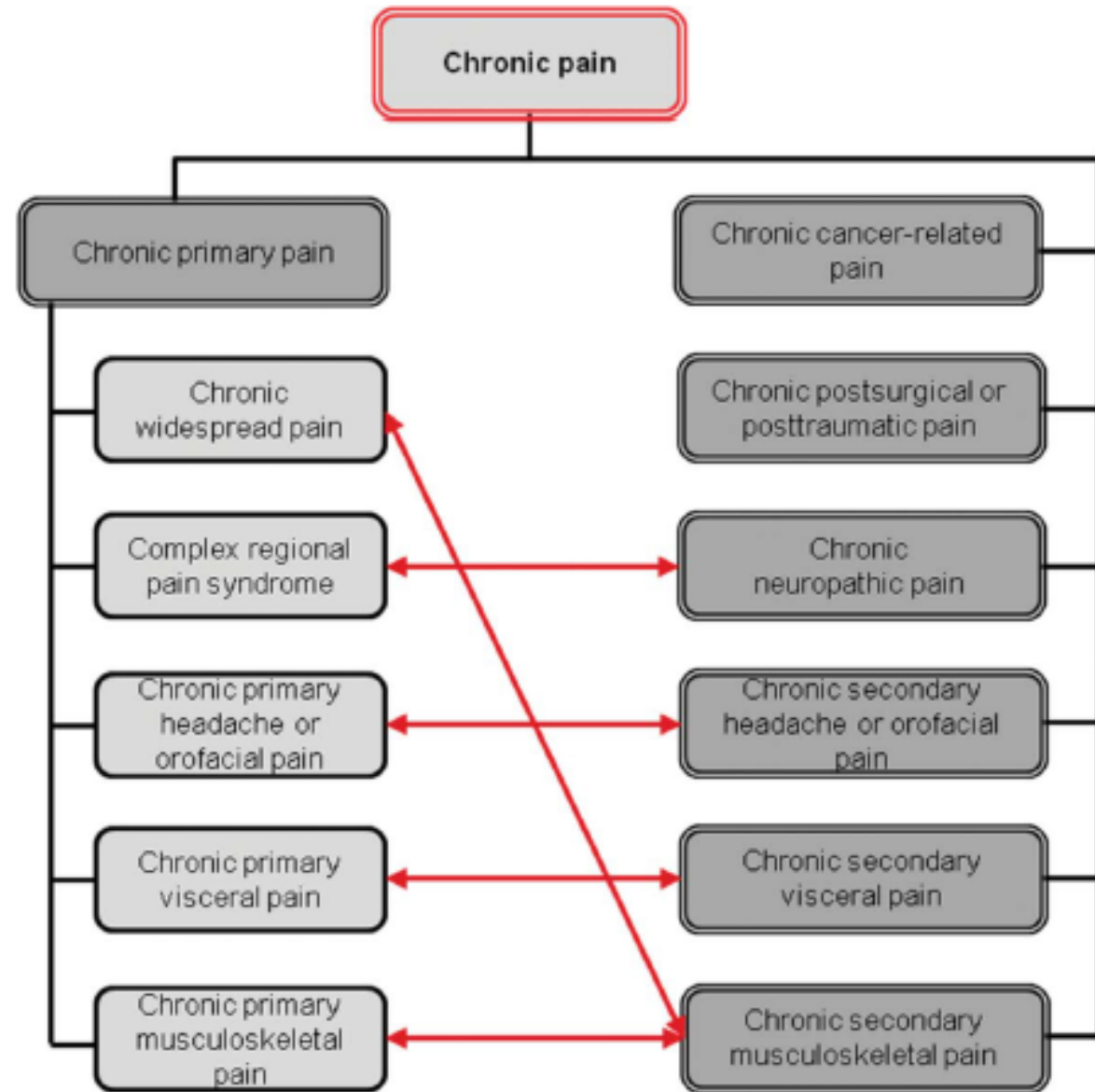
Negli ultimi due anni ho ricevuto compensi per attività di relatore o per la partecipazione ad Advisory Board dalle seguenti Aziende:

Alfasigma, Abiogen, Astellas, Bayer, Daiichi, Grunenthal, Kyowa Kirin, Lundbeck, Neopharmed, Molteni, SPA, Zambon

## **Chronic pain as a symptom or a disease: the IASP Classification of Chronic Pain for the *International Classification of Diseases (ICD-11)***

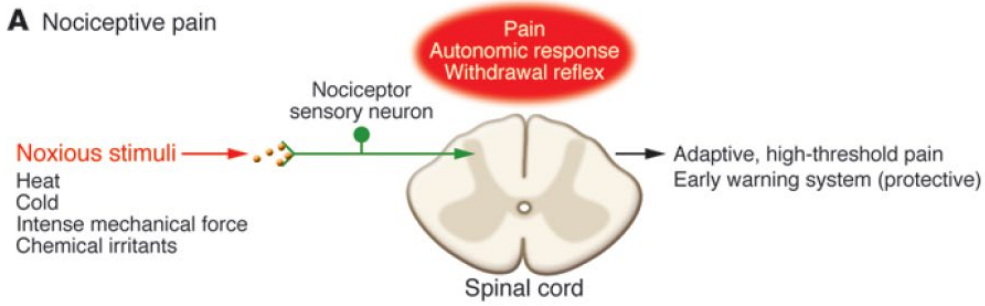
Rolf-Detlef Treede<sup>a,\*</sup>, Winfried Rief<sup>b</sup>, Antonia Barke<sup>b</sup>, Qasim Aziz<sup>c</sup>, Michael I. Bennett<sup>d</sup>, Rafael Benoliel<sup>e</sup>, Milton Cohen<sup>f</sup>, Stefan Evers<sup>g</sup>, Nanna B. Finnerup<sup>h,i</sup>, Michael B. First<sup>j</sup>, Maria Adele Giamberardino<sup>k</sup>, Stein Kaasa<sup>l,m,n</sup>, Beatrice Korwisi<sup>b</sup>, Eva Kosek<sup>o</sup>, Patricia Lavand'homme<sup>p</sup>, Michael Nicholas<sup>q</sup>, Serge Perrot<sup>f</sup>, Joachim Scholz<sup>s</sup>, Stephan Schug<sup>t,u</sup>, Blair H. Smith<sup>v</sup>, Peter Svensson<sup>w,x</sup>, Johan W.S. Vlaeyen<sup>y,z,aa</sup>, Shuu-Jiun Wang<sup>bb,cc</sup>

January 2019 • Volume 160 • Number 1

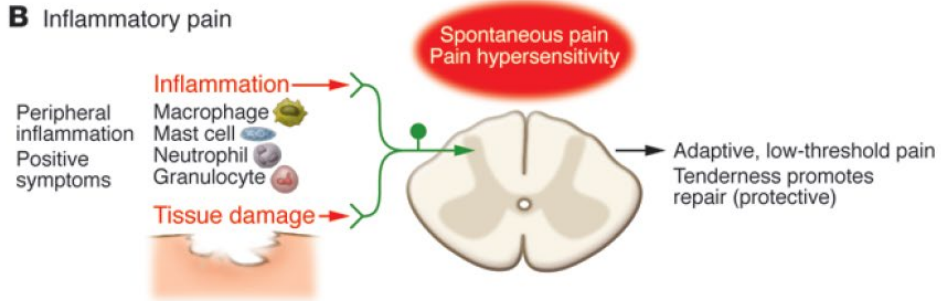


Chronic secondary pain syndromes

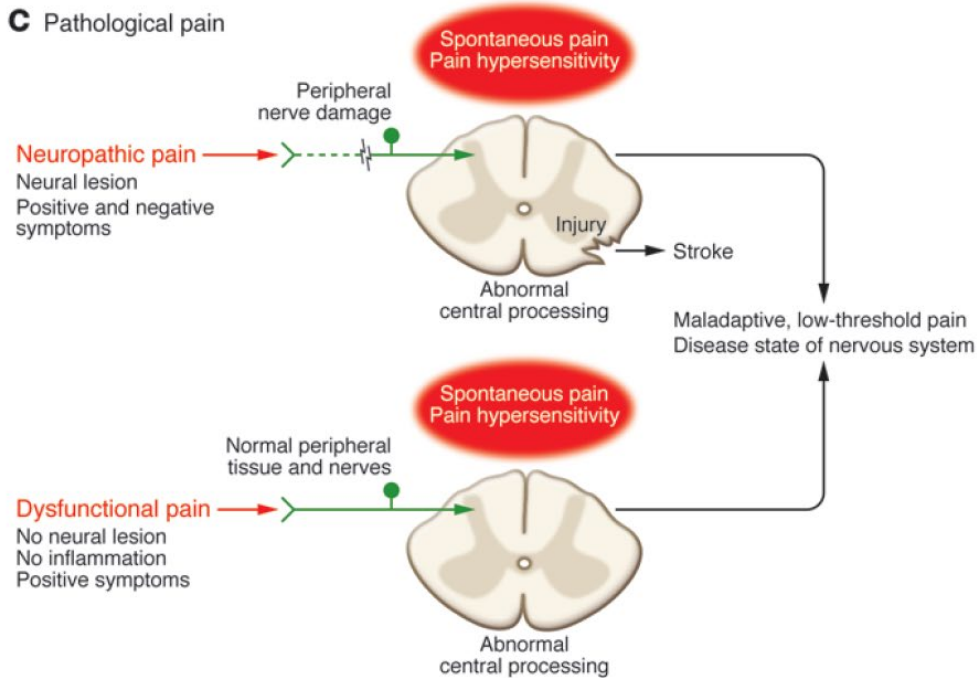
### A Nociceptive pain

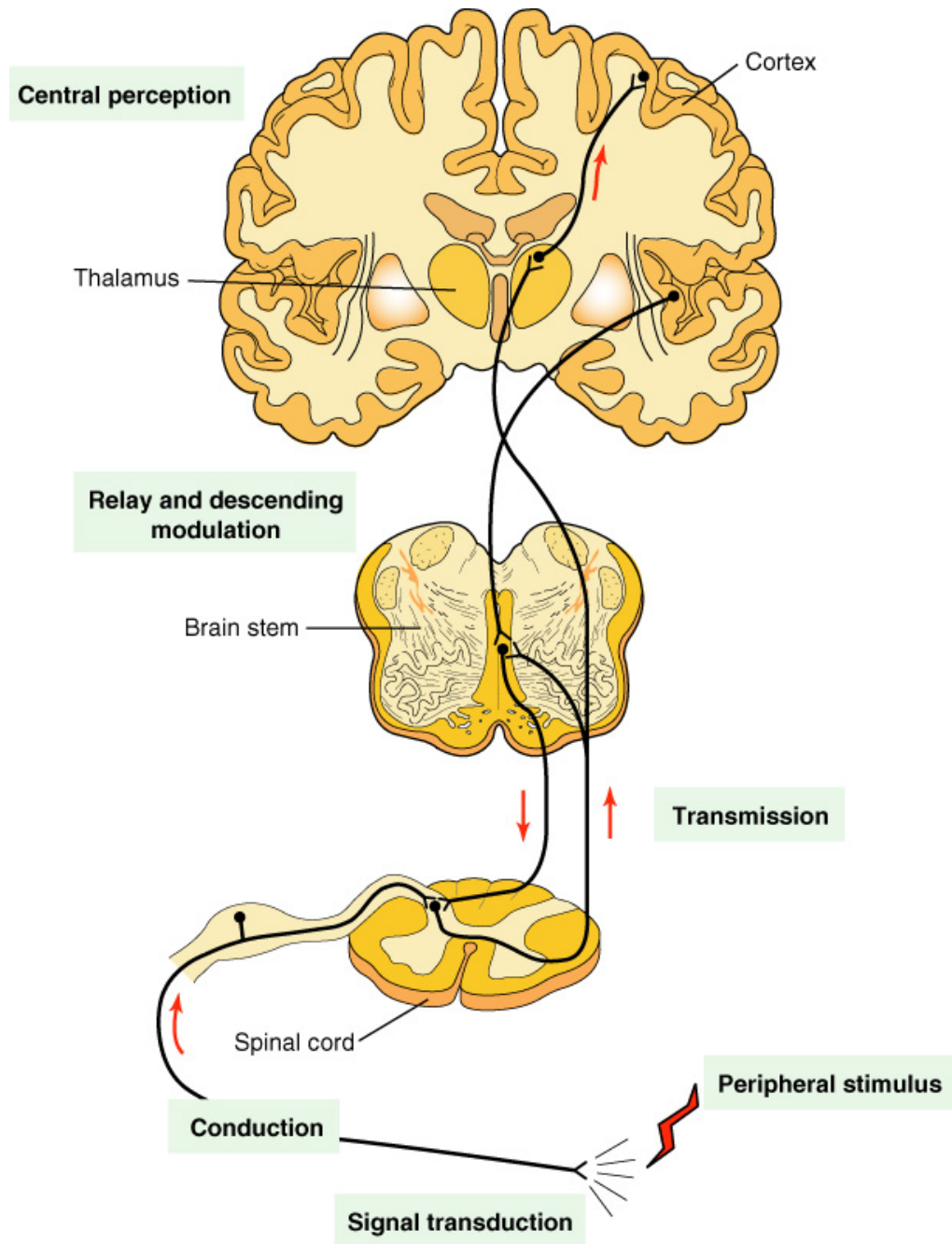


### B Inflammatory pain



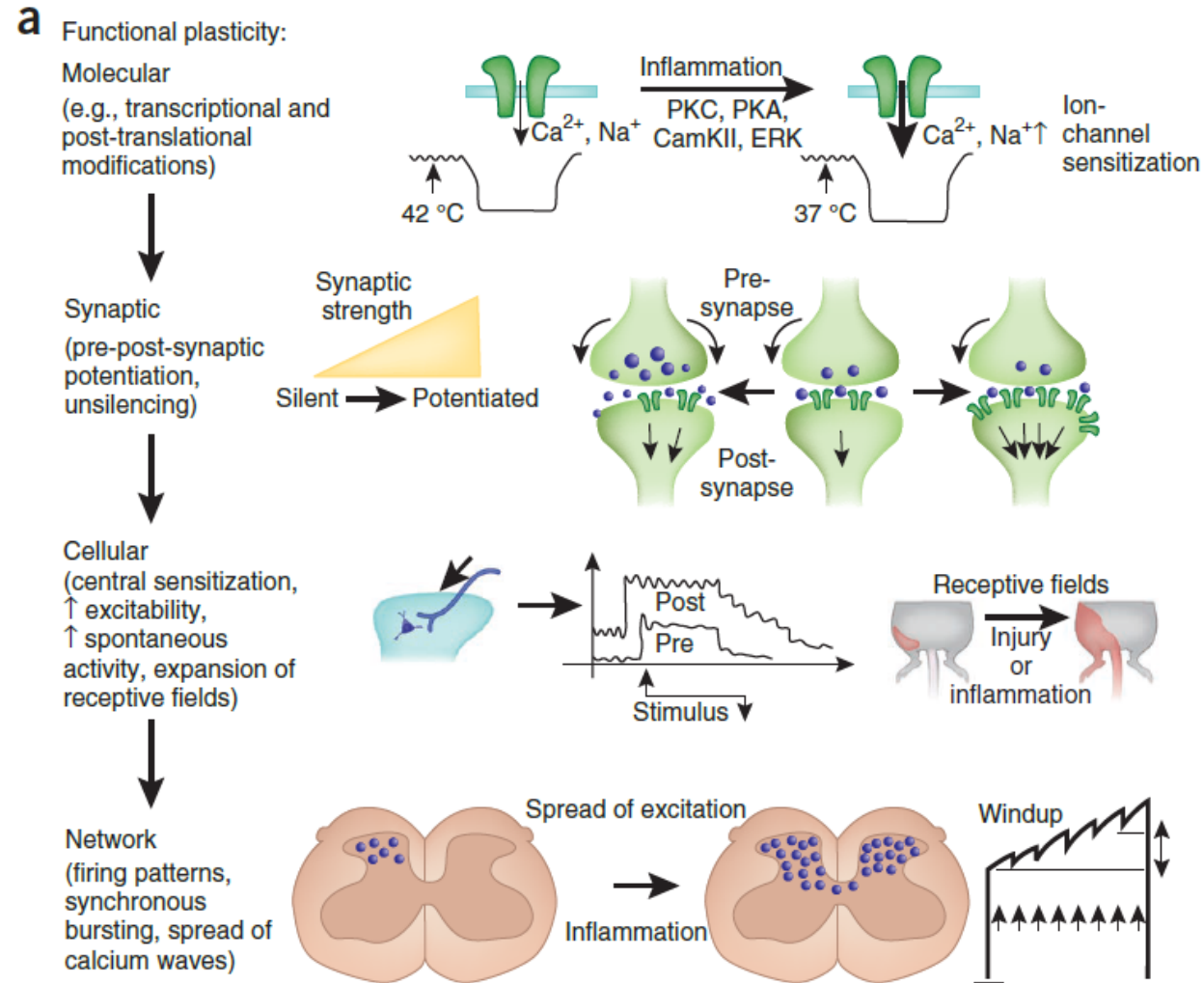
### C Pathological pain





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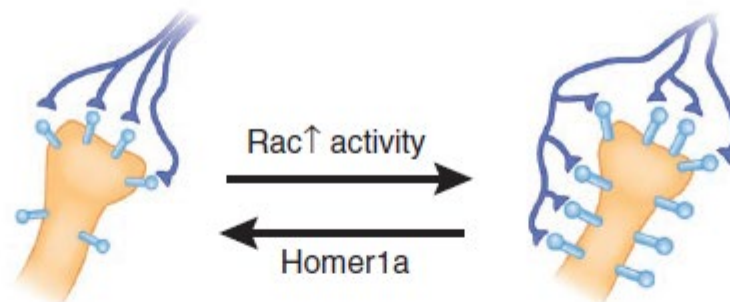
# PLASTICITÀ FUNZIONALE



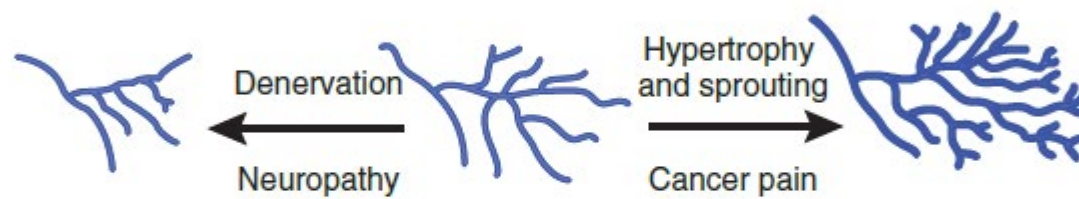
# PLASTICITÀ STRUTTURALE

**b** Structural plasticity:

Synaptic spines:

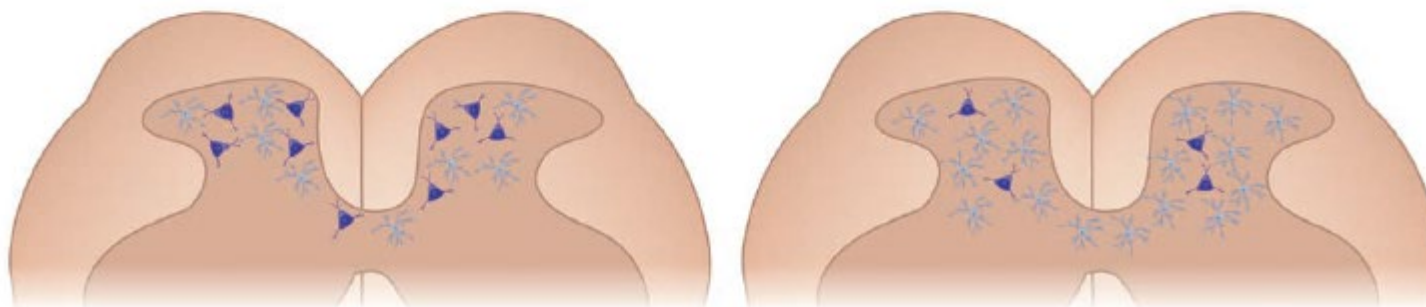


Connectivity:



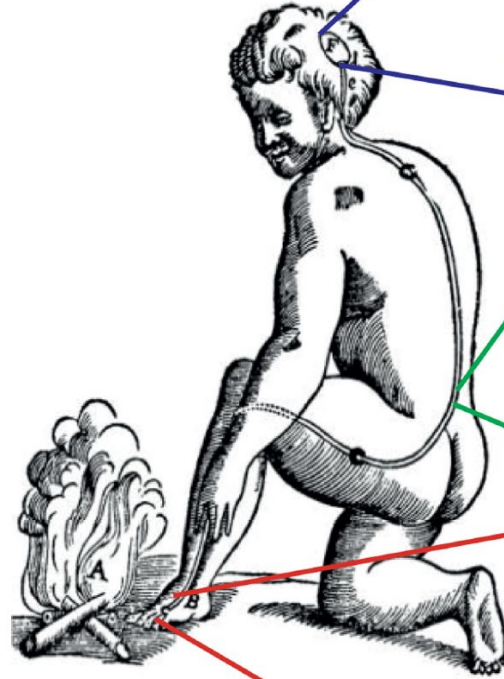
Cell number:

- Microglial and astrocyte proliferation
- Neuronal loss?

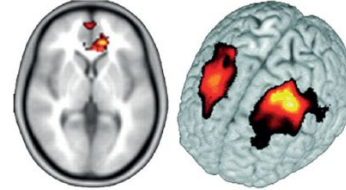




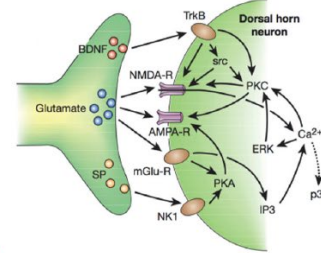
Descartes, 1644



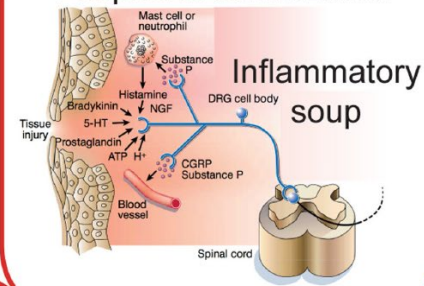
### Cortical reorganization



### Central sensitization

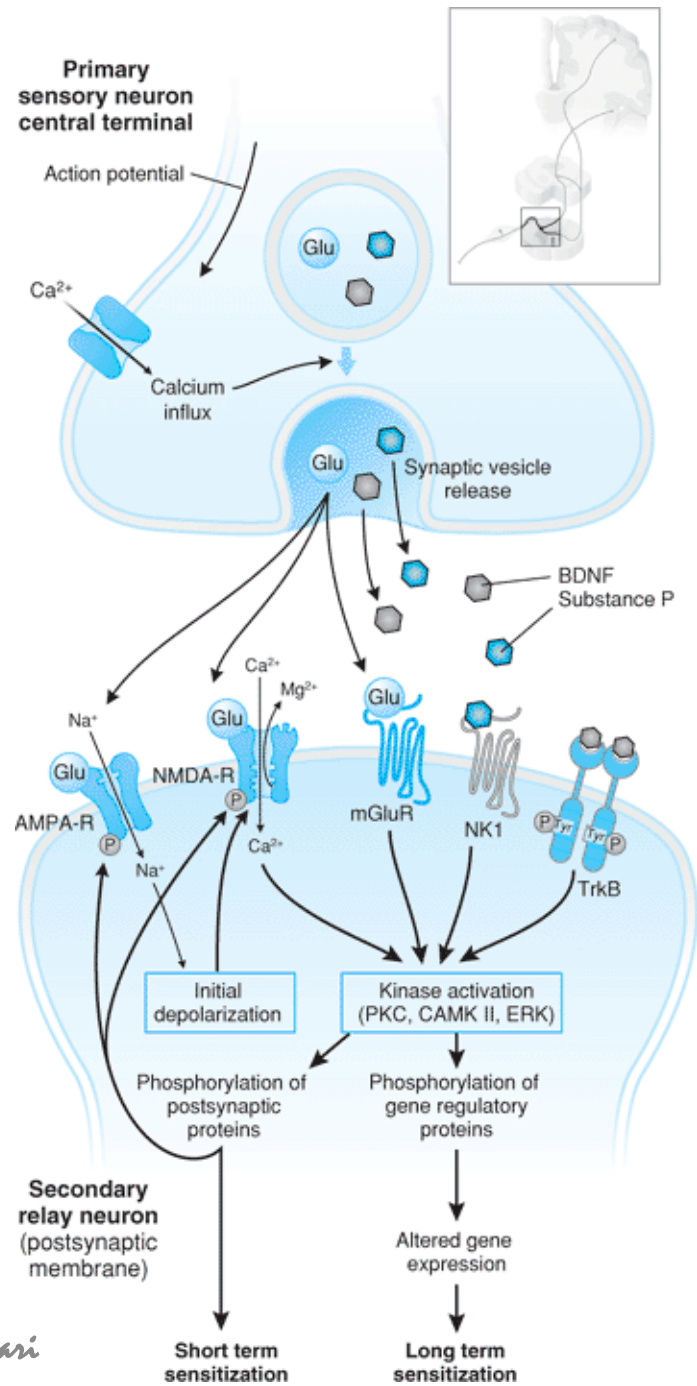


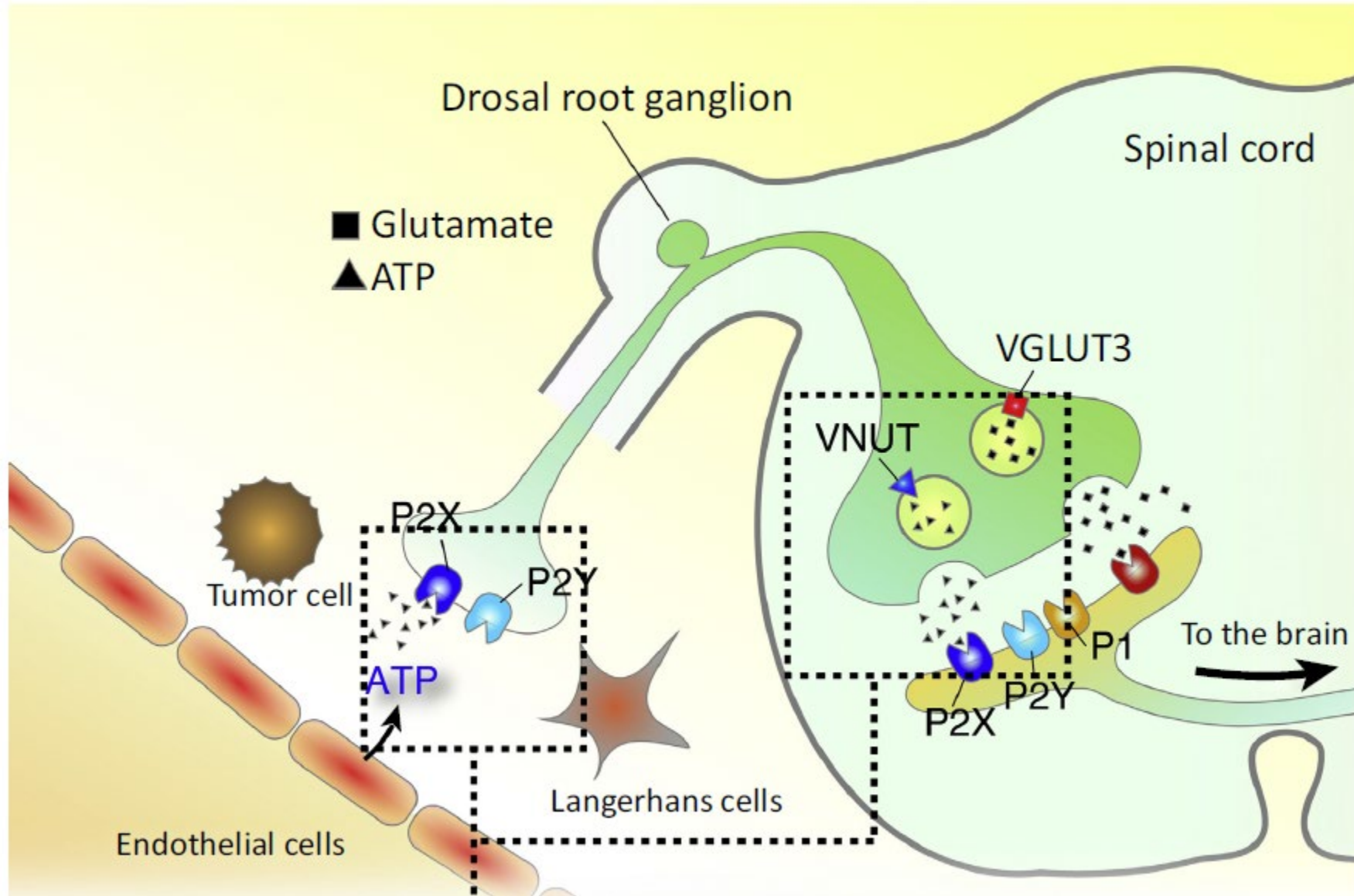
### Peripheral sensitization

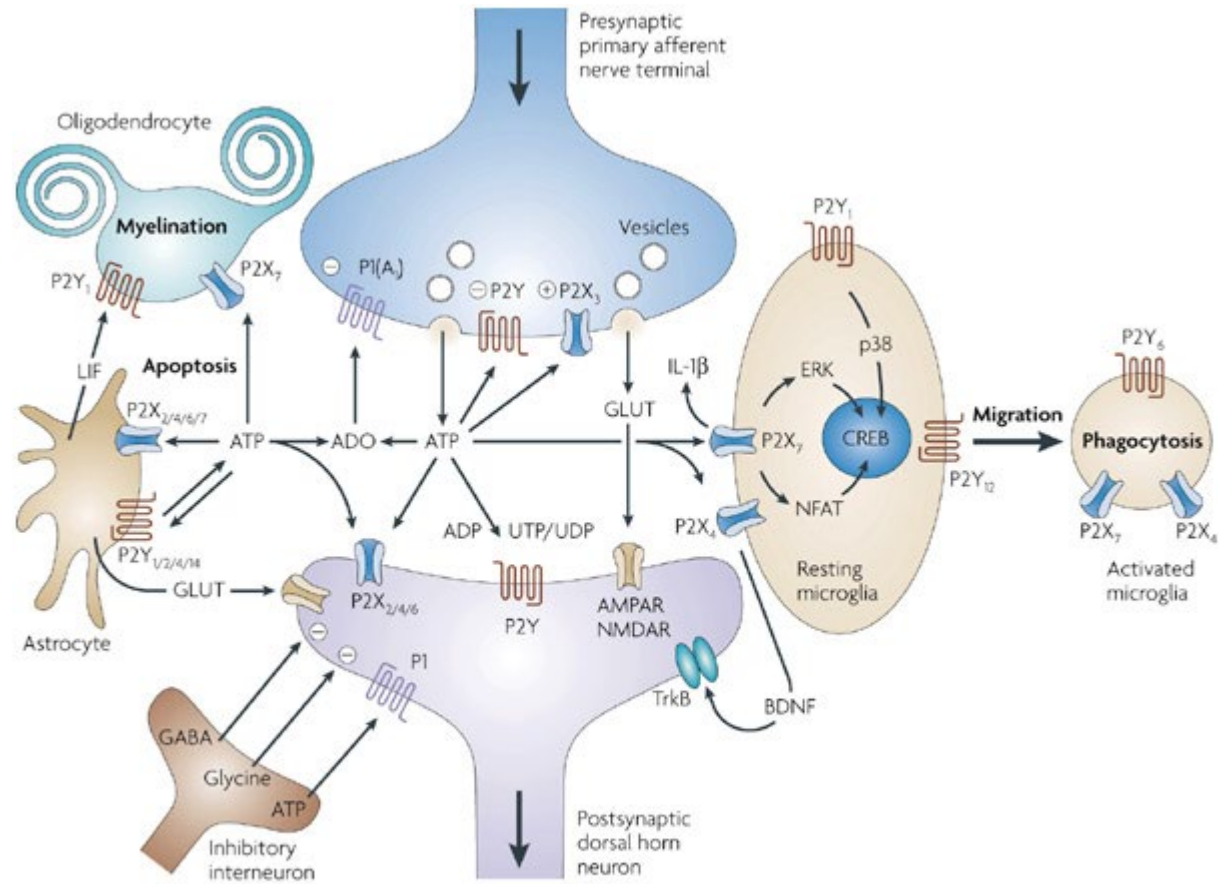


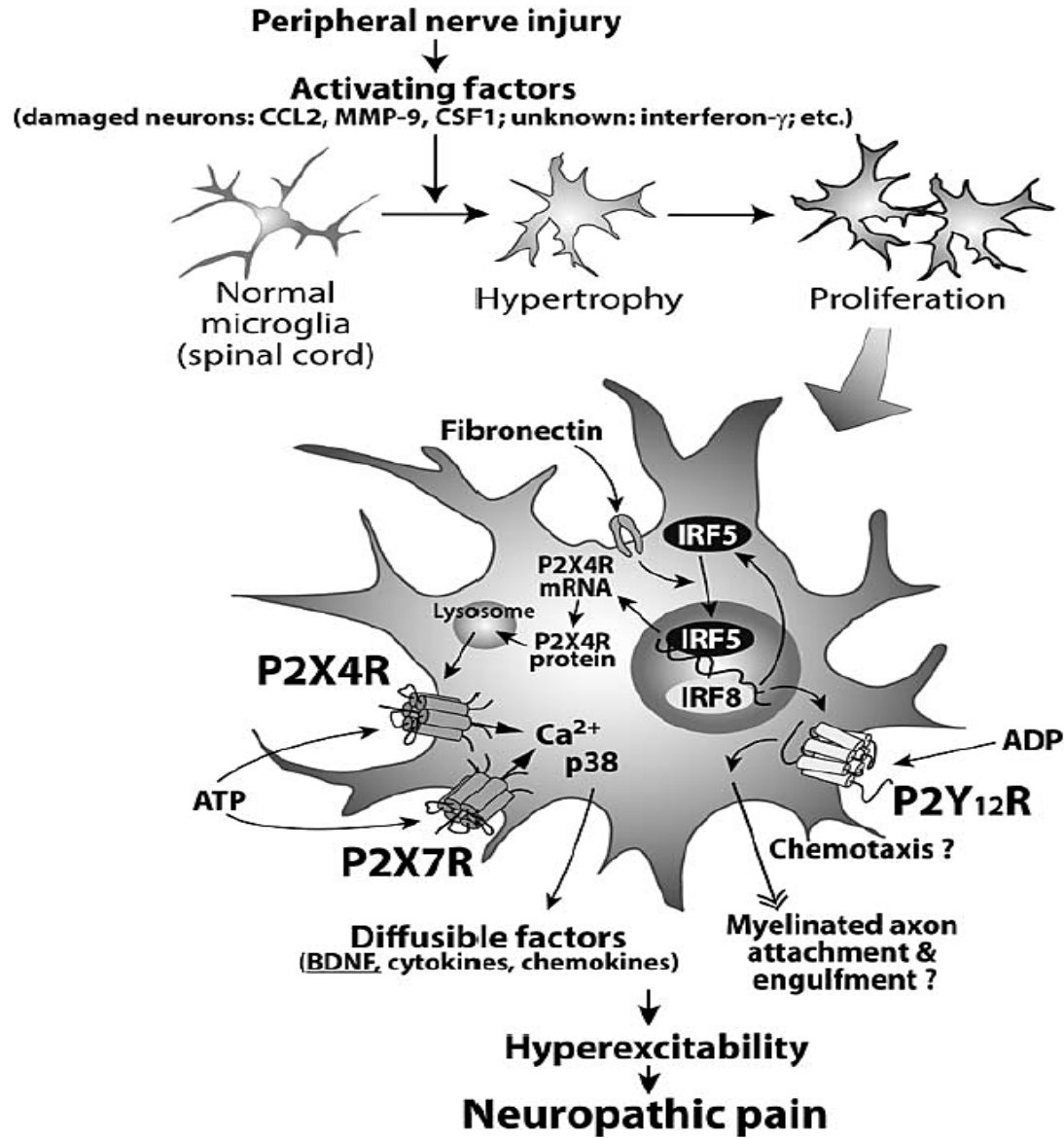
*Neuron*. 2015 August 5; 87(3): 474–491.

# SENSIBILIZZAZIONE SPINALE



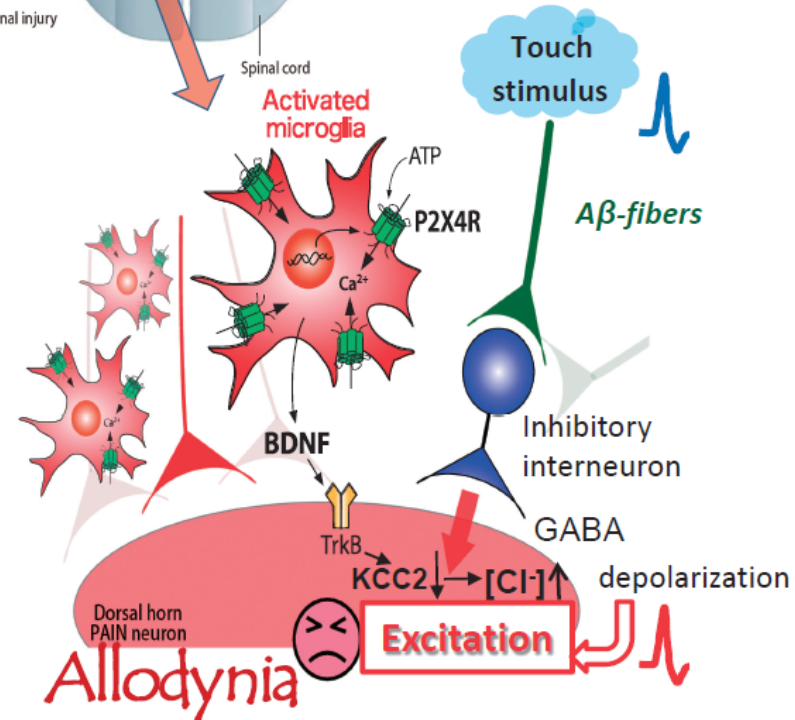
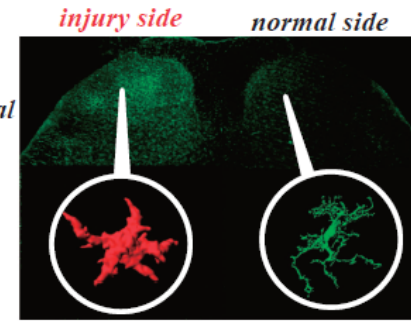
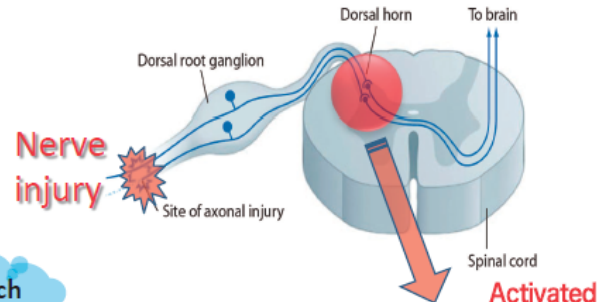
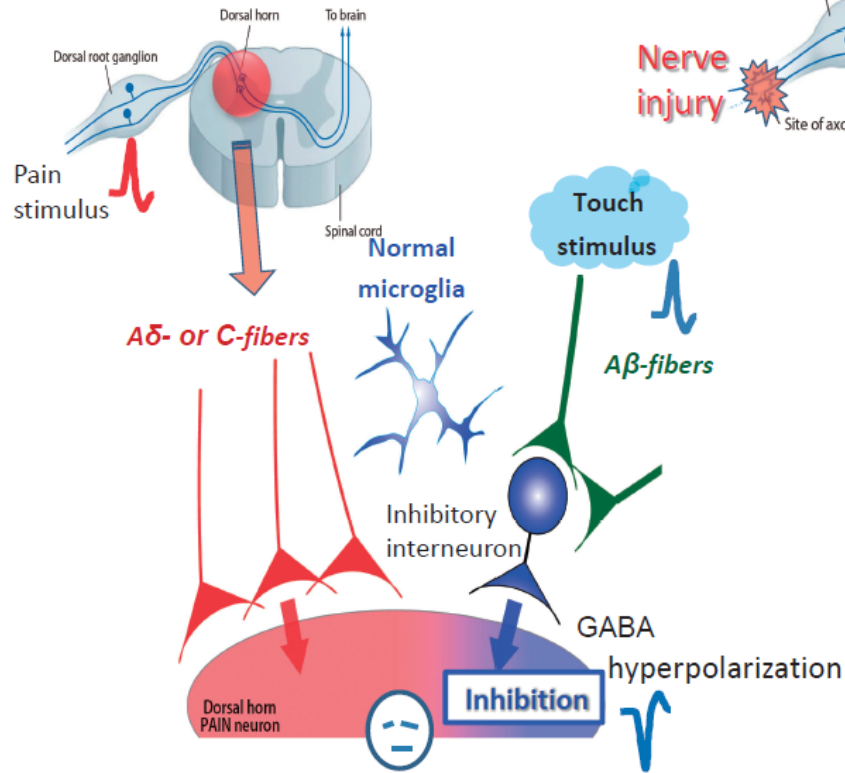


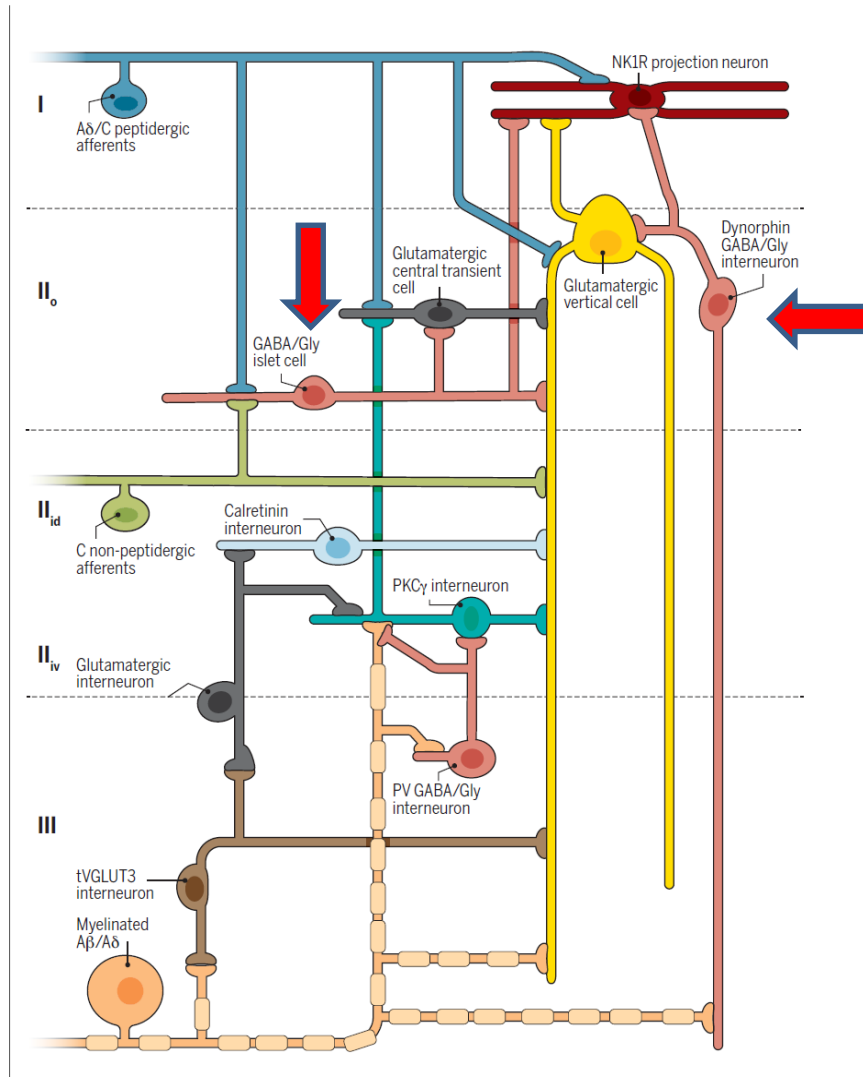




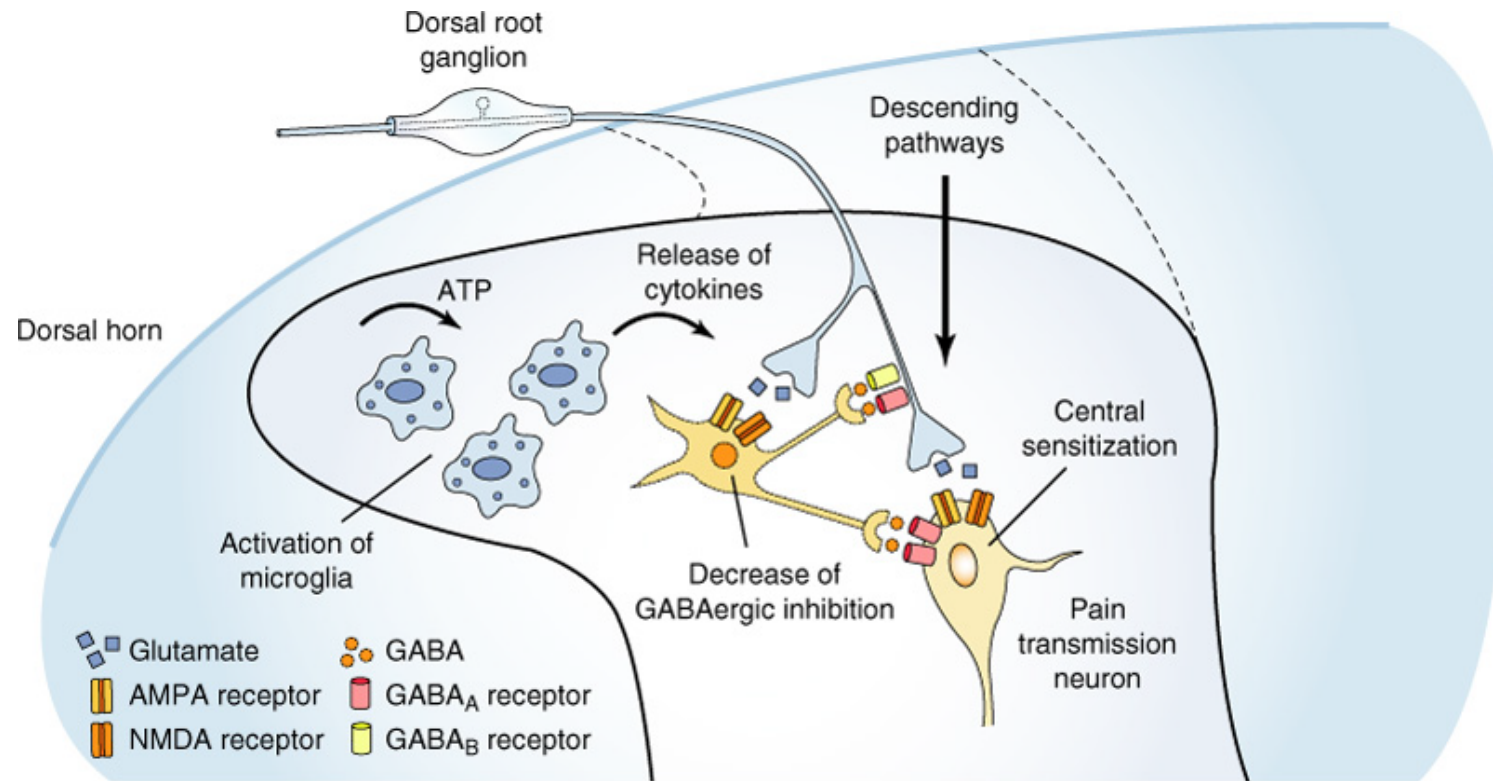
## B. Pathological condition

### A. Normal condition





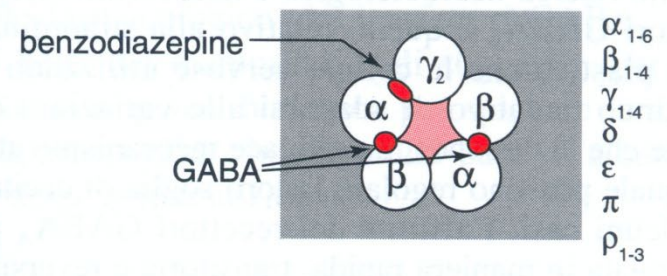
Pharmacol Rev 70:315–347, April 2018



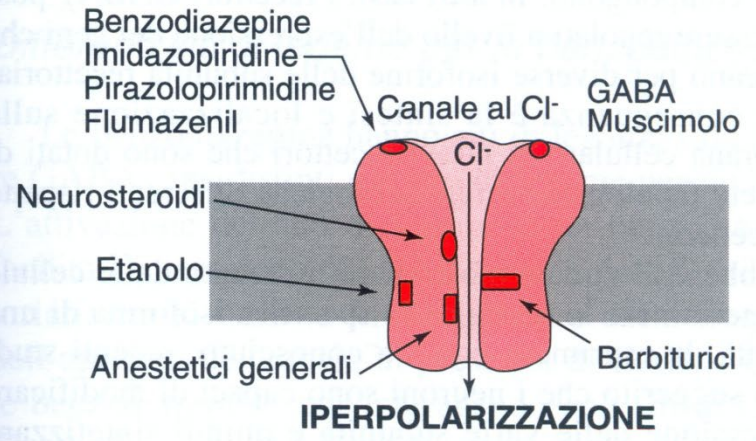
Copyright © 2006, American Society for Neurochemistry. All rights reserved.



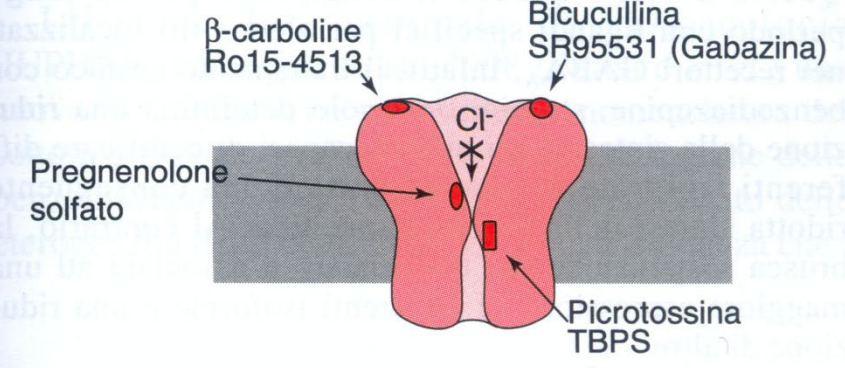
A. Subunità del recettore GABA<sub>A</sub>

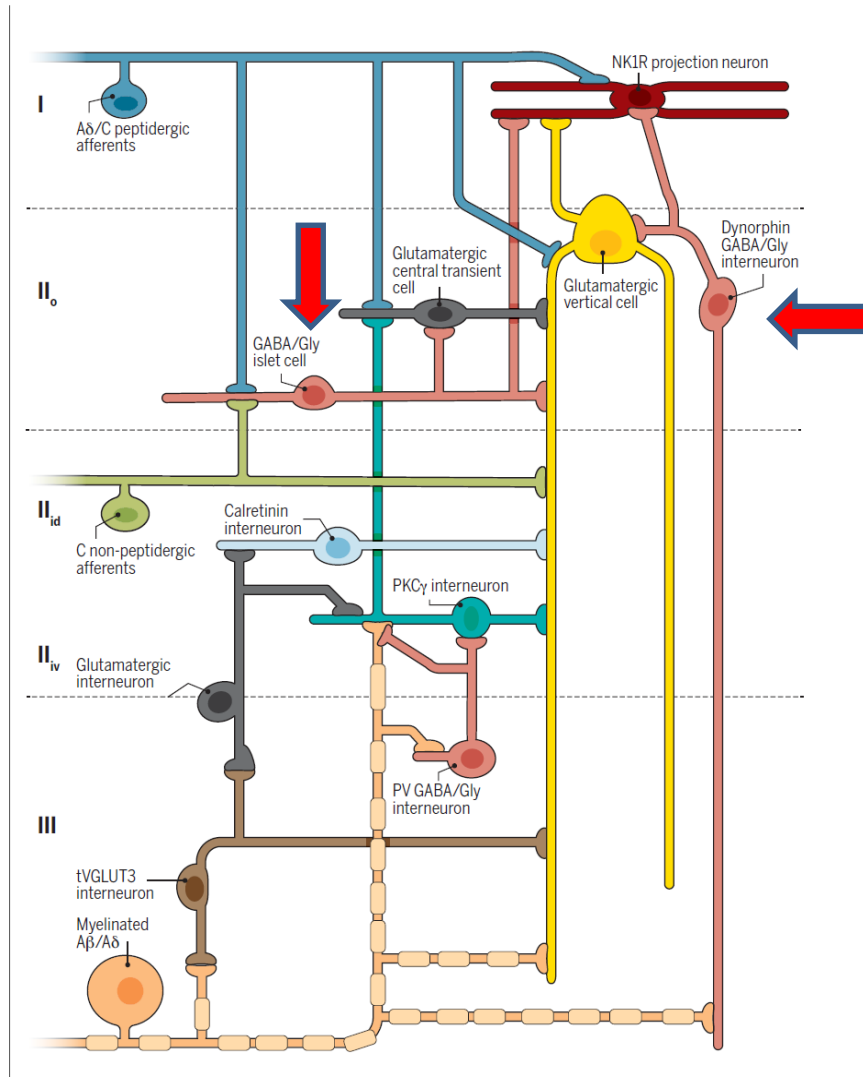


B. Agonisti e modulatori positivi

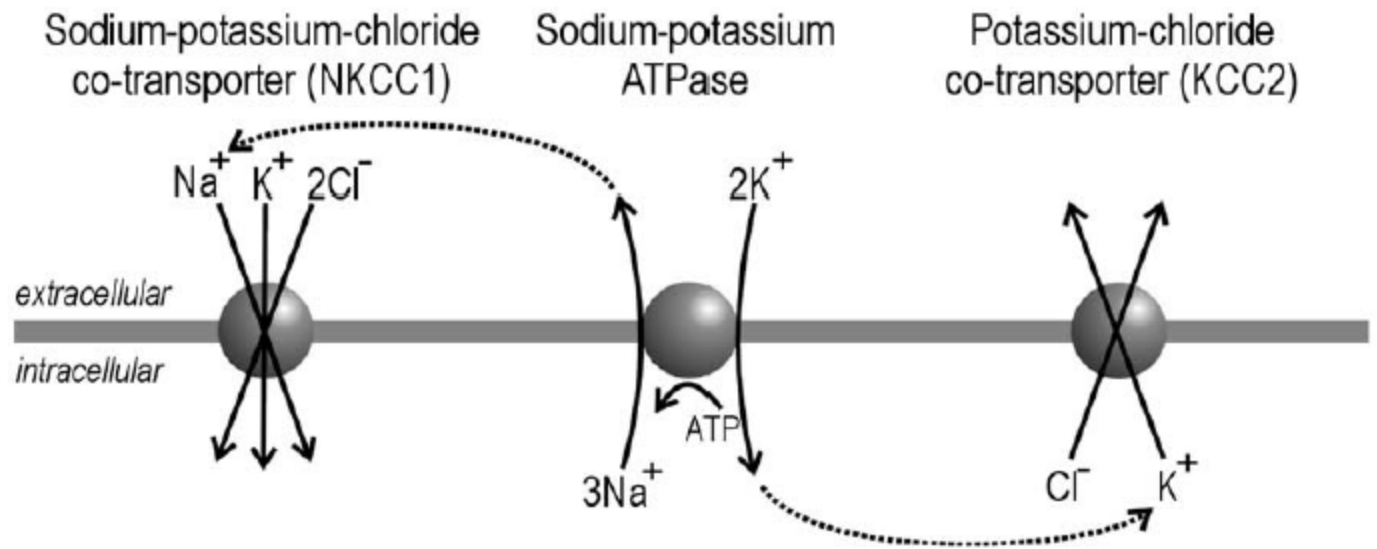


C. Antagonisti e modulatori negativi

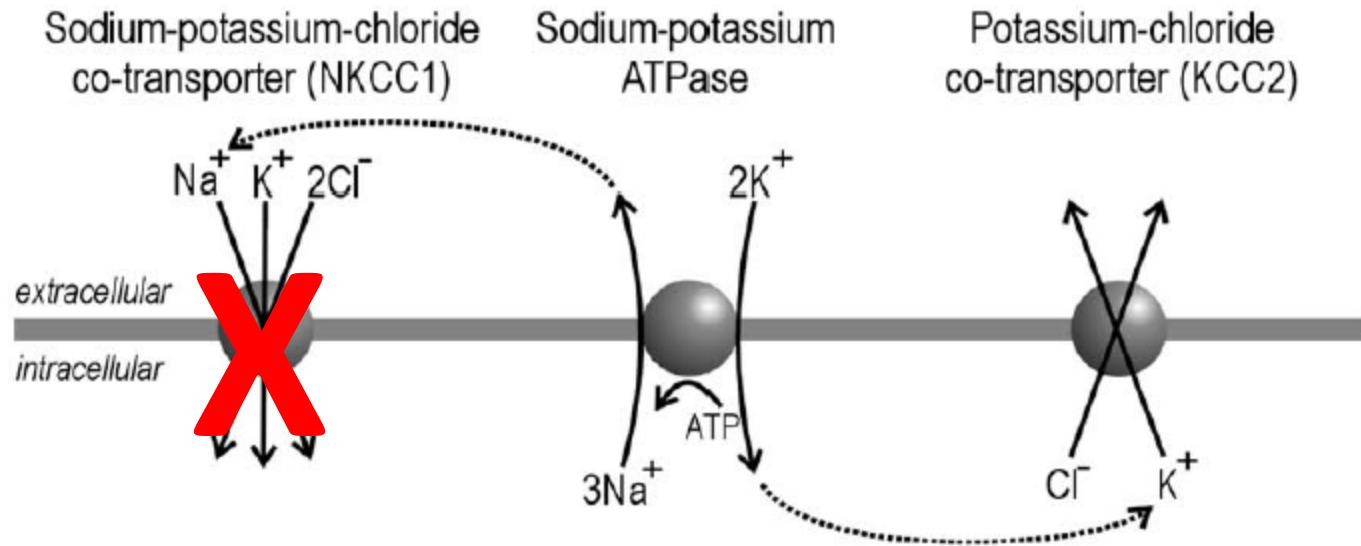




Pharmacol Rev 70:315–347, April 2018

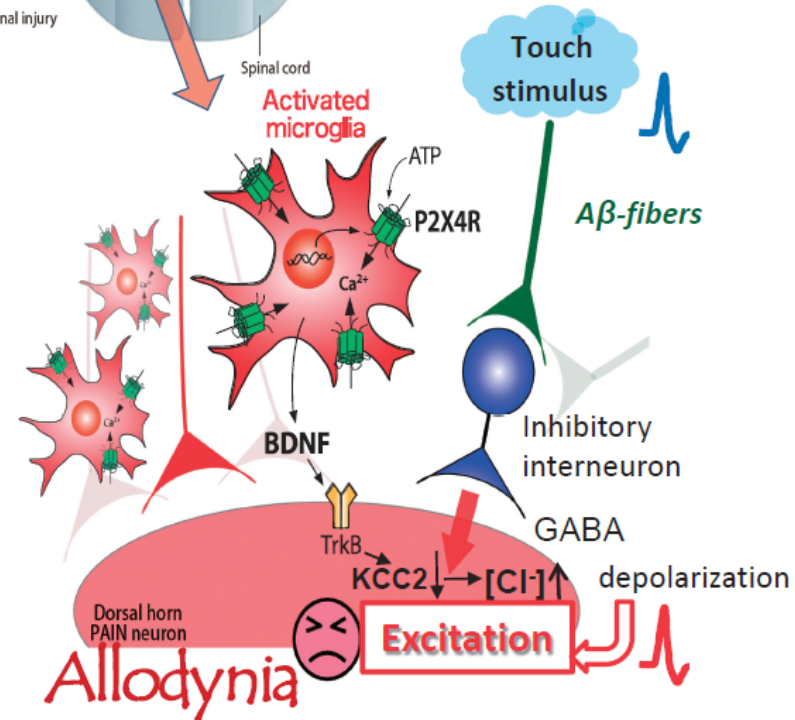
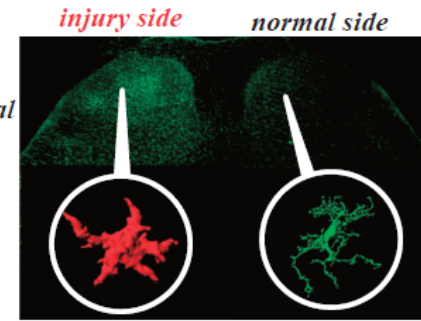
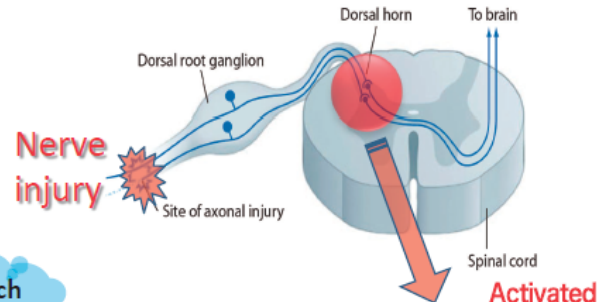
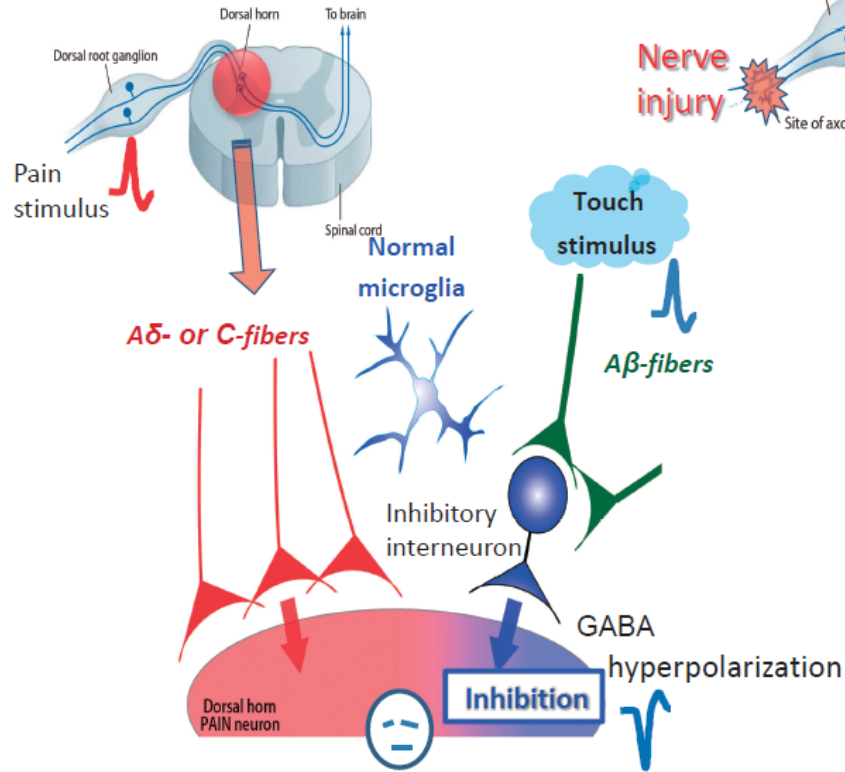


# BUDENAMIDE



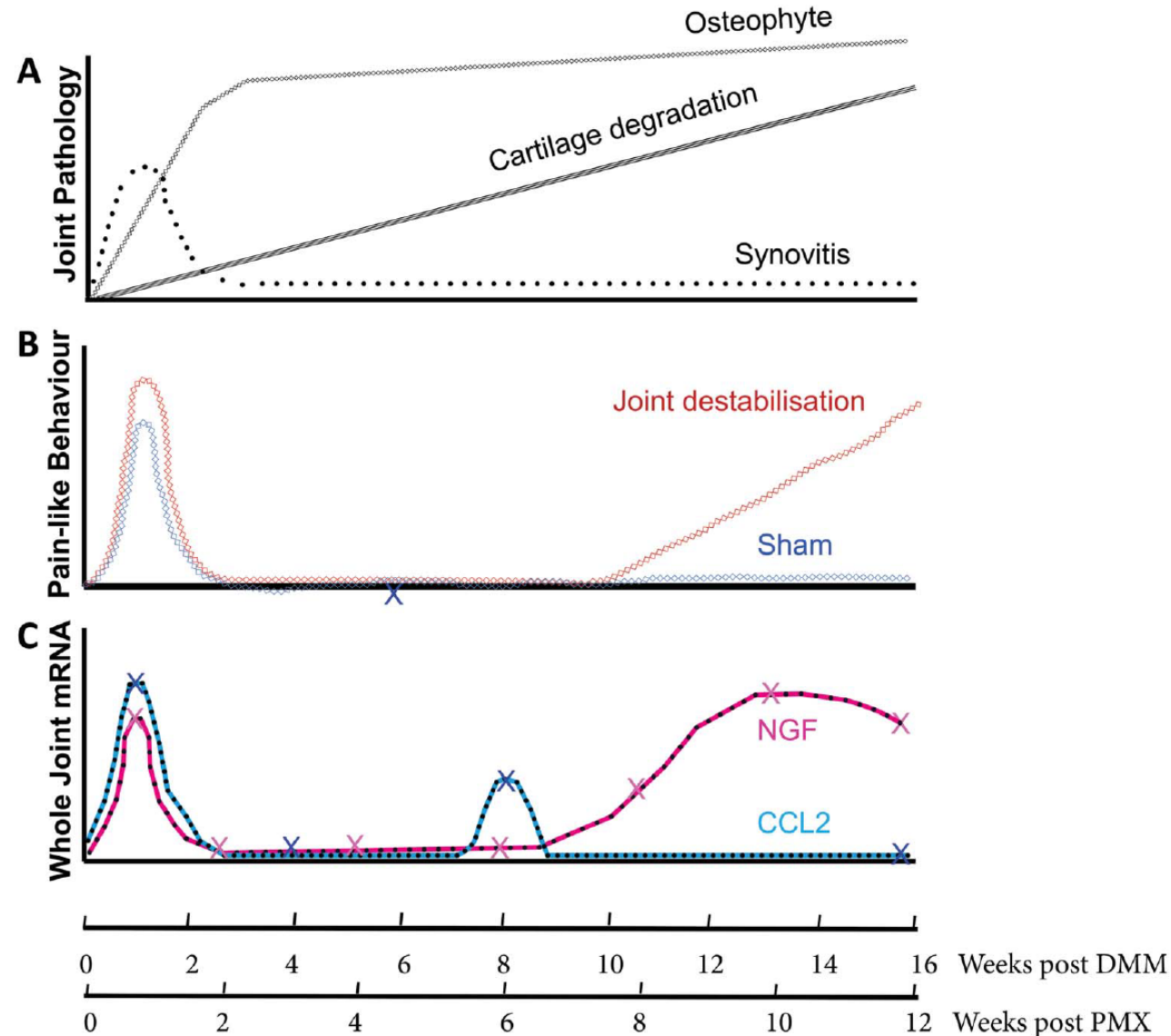
## B. Pathological condition

### A. Normal condition

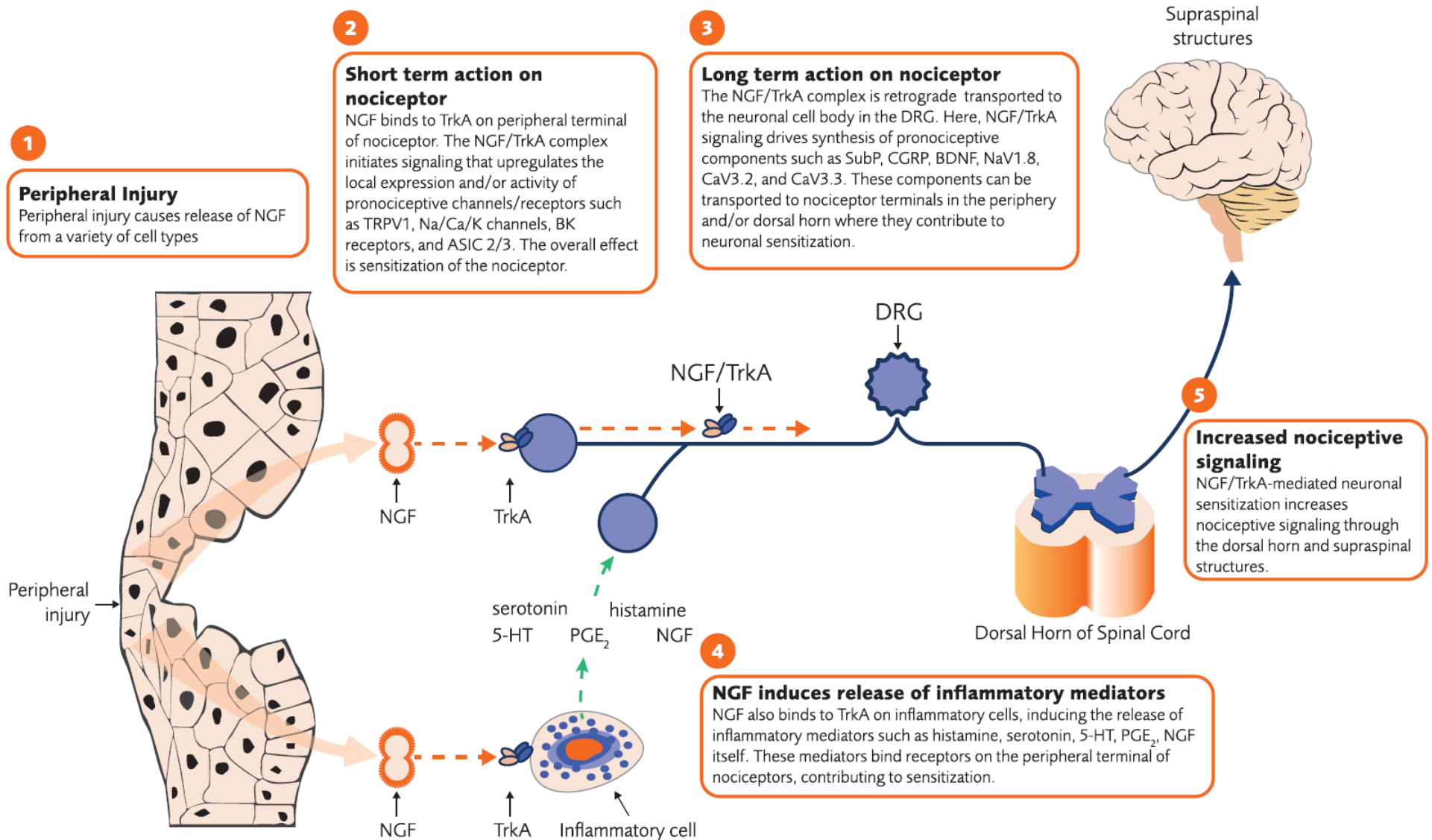


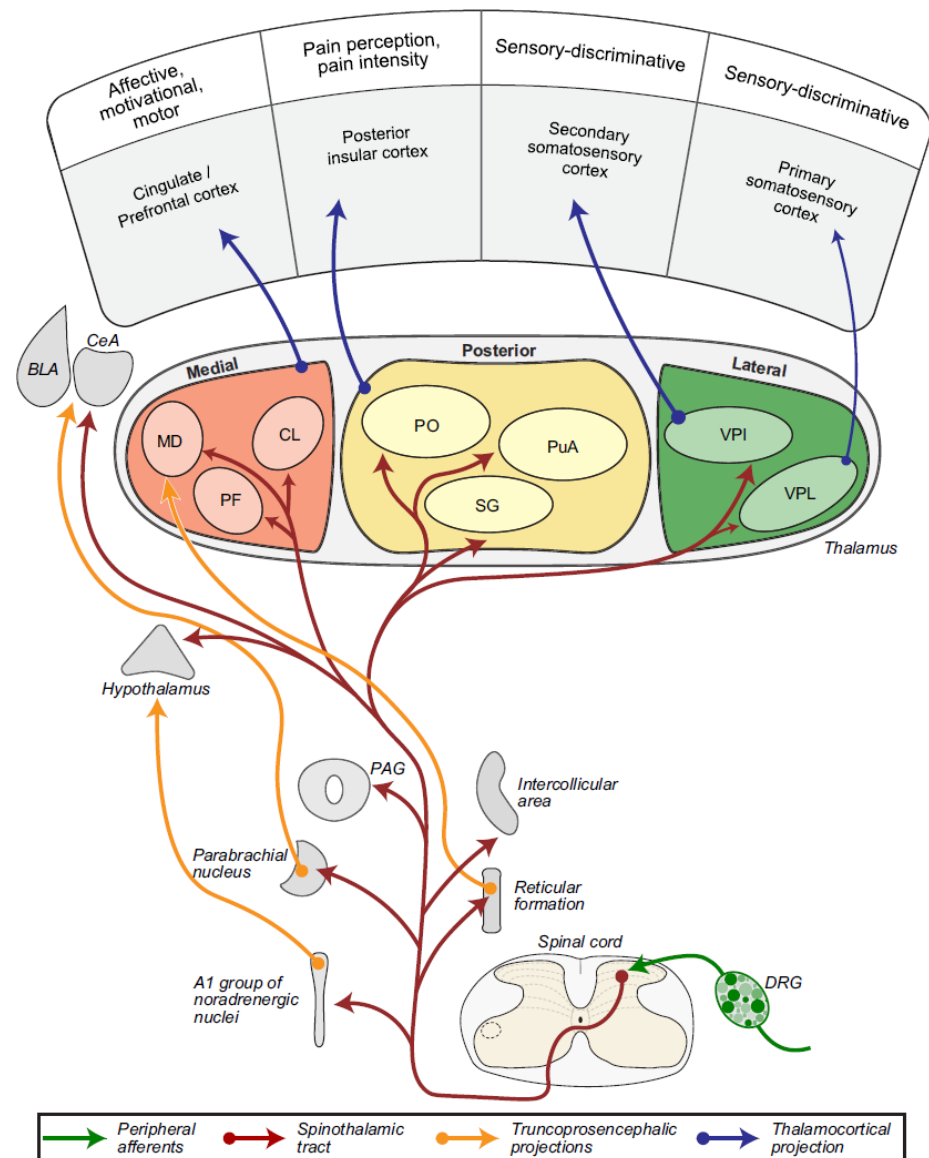
Proc. Jpn. Acad., Ser. B 93 (2017)

# Temporal relationship between pain-like behavior, pathology, and molecular expression in murine osteoarthritis.



# Pronociceptive actions of NGF

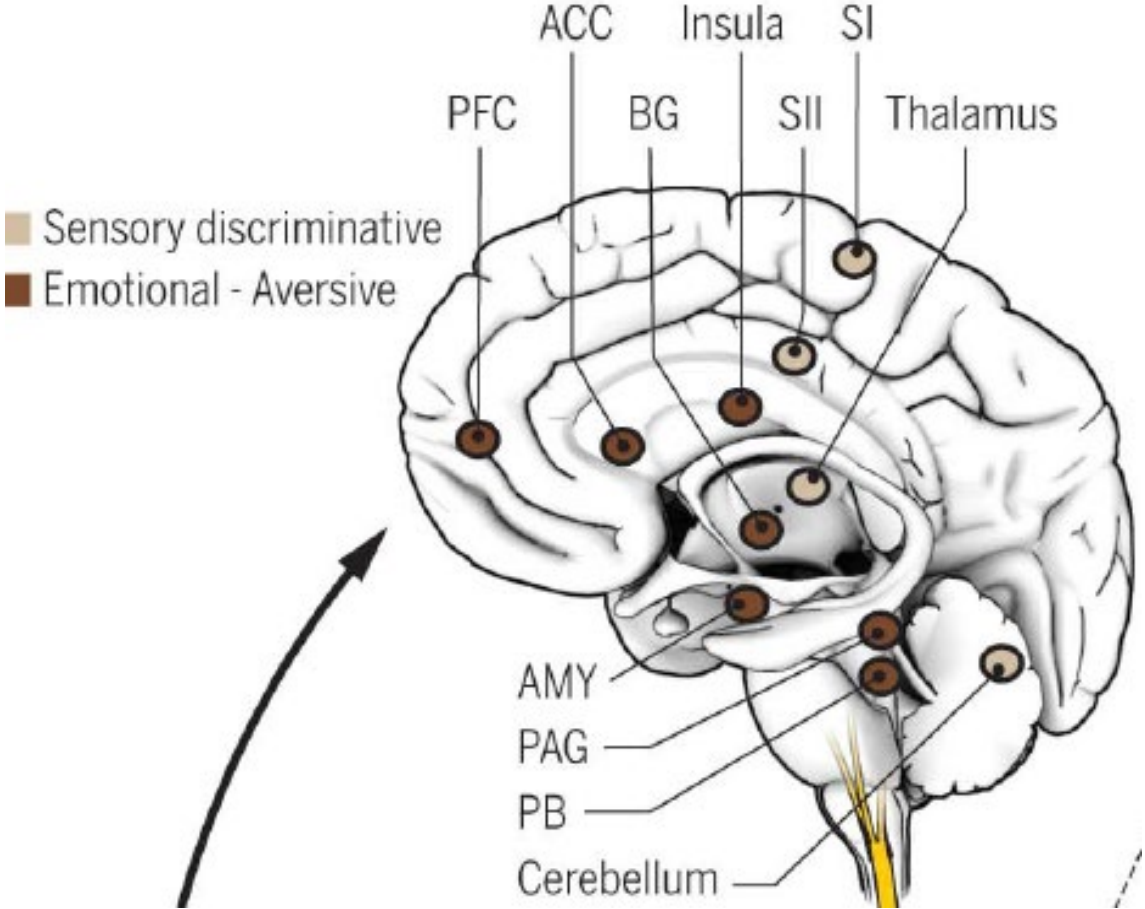




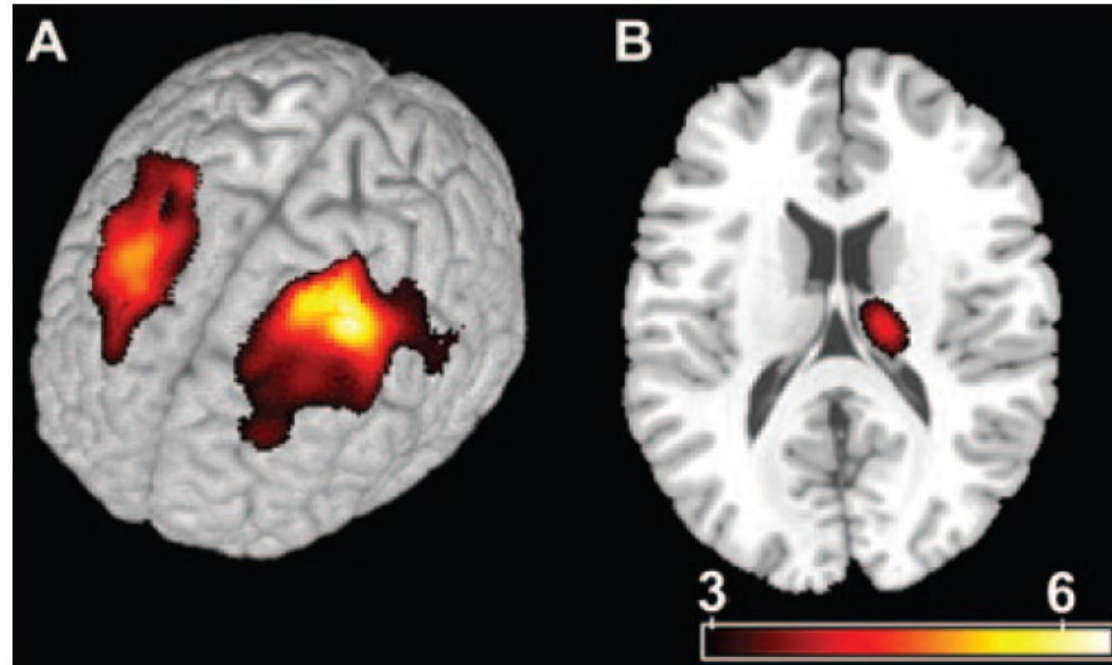
**FIGURE 1.** Scheme depicting spinothalamic tract signaling to thalamus and cortex. *Bottom:* the peripheral sensory inputs, the spinothalamic tract, and its terminations in the brain stem, including pain-relevant projections of brain stem nuclei to prosencephalic areas. *Middle:* the thalamic targets of the spinothalamic tract and connections to the amygdala. Only thalamic nuclei relaying spinothalamic tract inputs are shown. The trigeminothalamic tract and ventral posterior medial thalamic nucleus (VPM) are not shown for clarity. *Top:* the thalamic relay to cortex and functional modalities. CL, centrolateral nucleus; MD, mediodorsal nucleus; PF, parafascicular nucleus; PO, posterior nucleus; PuA, anterior pulvinar nucleus; SG, suprageniculata nucleus; VPI, ventral posterior inferior nucleus; VPL, ventral posterior lateral nucleus.



# PAIN MATRIX



Pharmacol Rev 70:315-347, April 2018



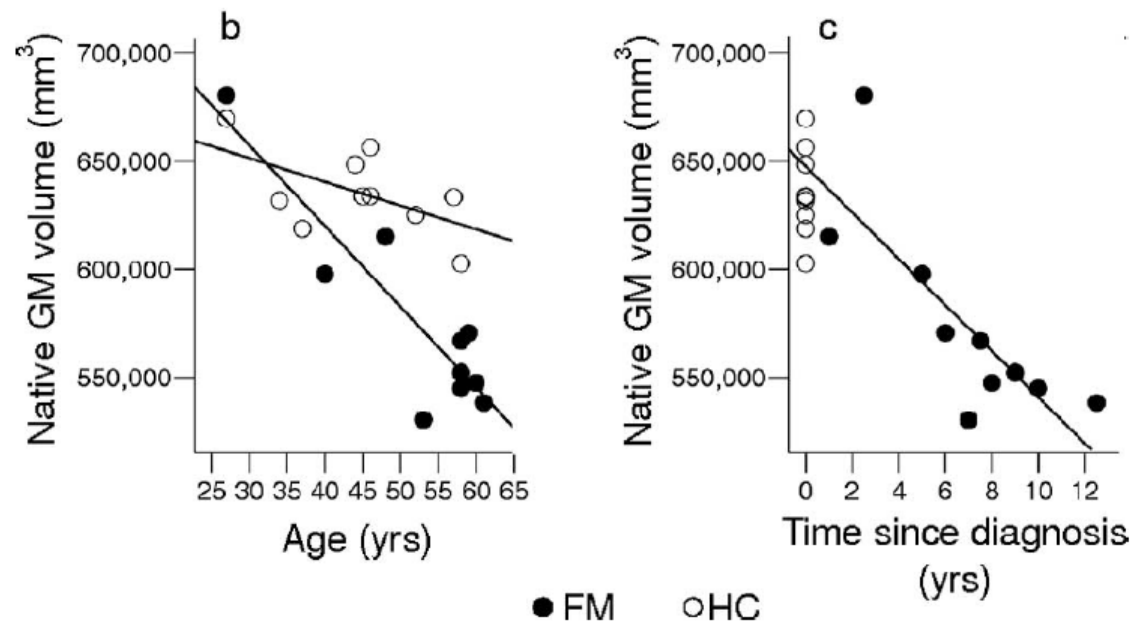
The Journal of Neuroscience, November 17, 2004 • 24(46):10410–10415

Brief Communications

## Accelerated Brain Gray Matter Loss in Fibromyalgia Patients: Premature Aging of the Brain?

**Anil Kuchinad,<sup>1,2</sup> Petra Schweinhardt,<sup>1</sup> David A. Seminowicz,<sup>1</sup> Patrick B. Wood,<sup>1</sup> Boris A. Chizh,<sup>4</sup> and M. Catherine Bushnell<sup>1,2,3</sup>**

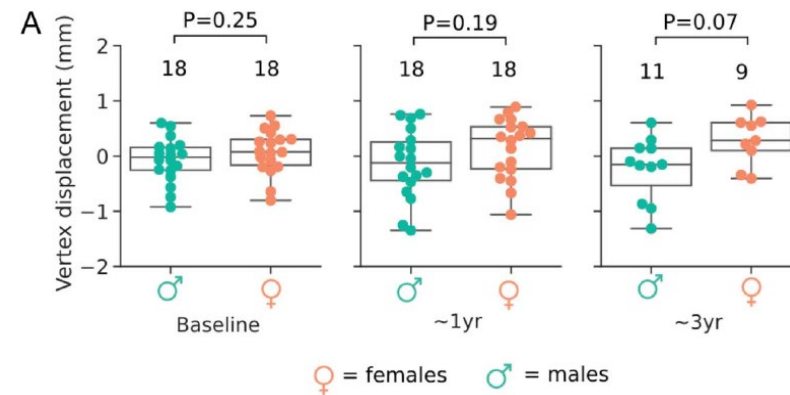
<sup>1</sup>McGill Centre for Research on Pain, <sup>2</sup>Department of Neurology and Neurosurgery, and <sup>3</sup>Department of Anesthesia and Faculty of Dentistry, McGill University, Montreal, Quebec, Canada H3A 2B2, and <sup>4</sup>GlaxoSmithKline, Addenbrooke's Centre for Clinical Investigation, Addenbrooke's Hospital, Cambridge CB2 2GG, United Kingdom



The Journal of Neuroscience, April 11, 2007 • 27(15):4004–4007

# Hippocampus shape deformation: a potential diagnostic biomarker for chronic back pain in women

Diane Reckziegel<sup>a,b</sup>, Taha Abdullah<sup>b,c</sup>, Binbin Wu<sup>d</sup>, Bo Wu<sup>e</sup>, Lejian Huang<sup>a,b</sup>, Thomas J. Schnitzer<sup>a,f,g</sup>, A. Vania Apkarian<sup>a,b,g,h,\*</sup>

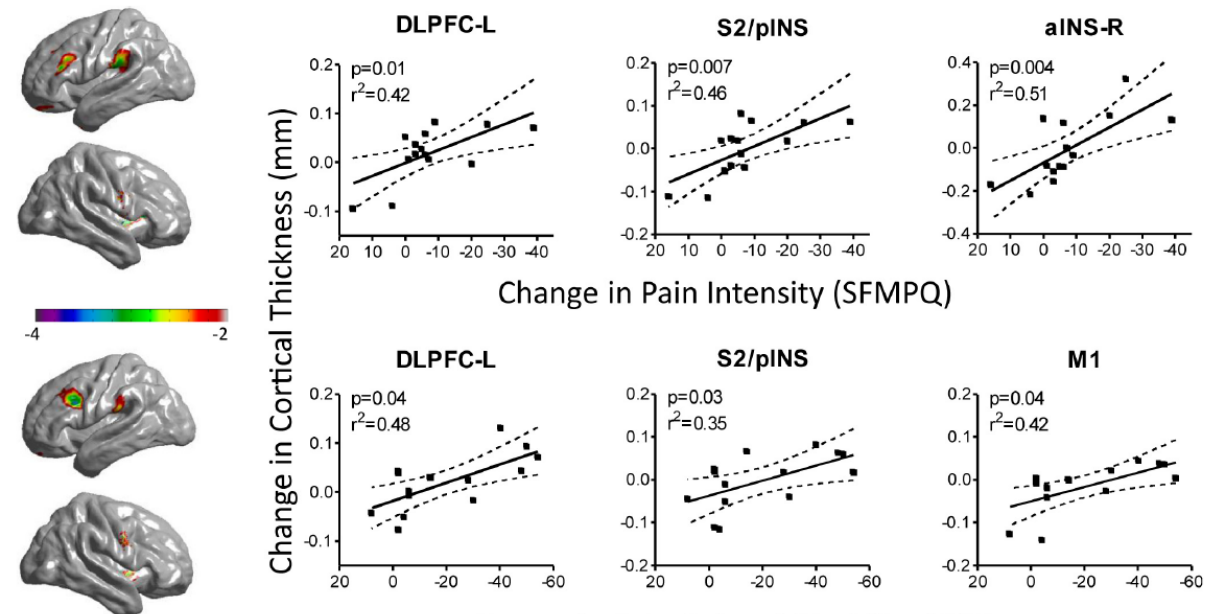
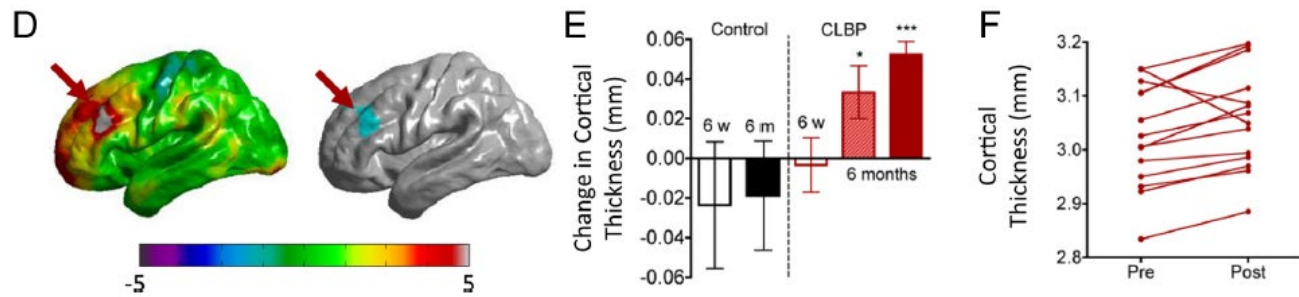


Behavioral/Systems/Cognitive

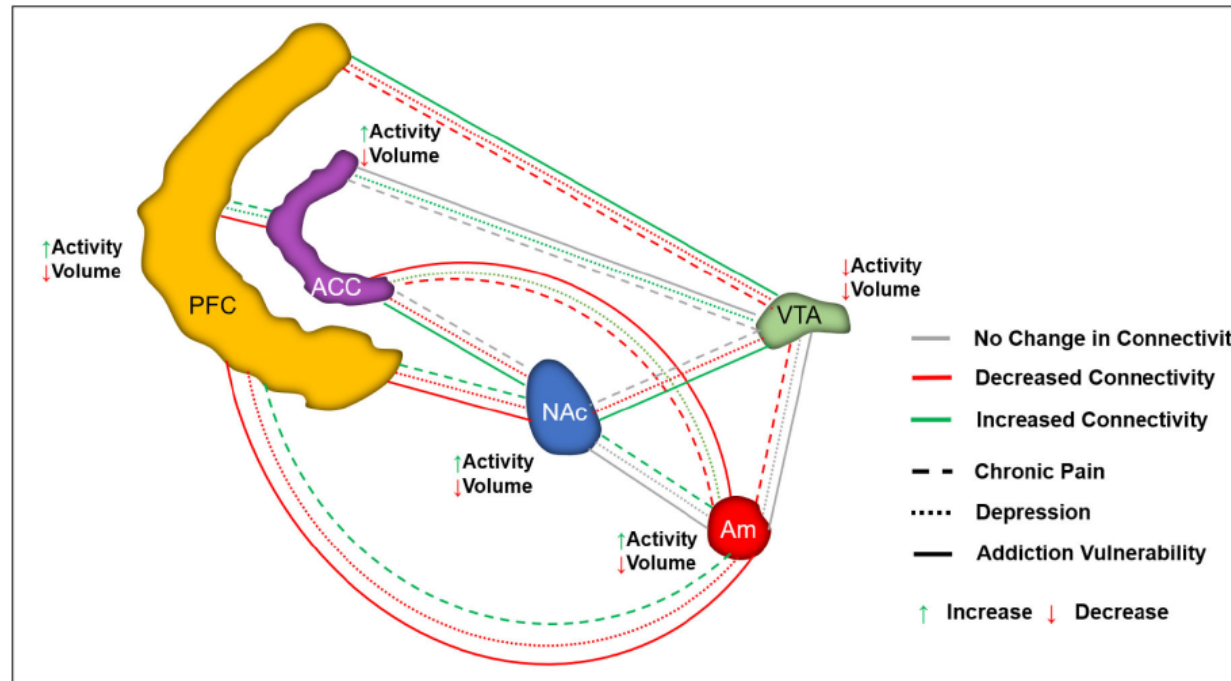
## Effective Treatment of Chronic Low Back Pain in Humans Reverses Abnormal Brain Anatomy and Function

David A. Seminowicz,<sup>1,2,3</sup> Timothy H. Wideman,<sup>1,7,8</sup> Lina Naso,<sup>1,2,3</sup> Zeinab Hatami-Khoroushahi,<sup>1,2,3</sup> Summaya Fallatah,<sup>4,8</sup> Mark A. Ware,<sup>1,8</sup> Peter Jarzem,<sup>2,9</sup> M. Catherine Bushnell,<sup>1,3,4,6</sup> Yoram Shir,<sup>1,8</sup> Jean A. Ouellet,<sup>2,9</sup> and Laura S. Stone<sup>1,2,3,4,5,6</sup>

<sup>1</sup>Alan Edwards Centre for Research on Pain, <sup>2</sup>McGill Scoliosis and Spine Research Group, <sup>3</sup>Faculty of Dentistry, Departments of <sup>4</sup>Anesthesiology, <sup>5</sup>Pharmacology and Therapeutics, and <sup>6</sup>Neurology and Neurosurgery, Faculty of Medicine, and <sup>7</sup>Department of Psychology, Faculty of Science, McGill University, Montreal, Quebec H3A 1A4, Canada, and <sup>8</sup>Alan Edwards Pain Management Unit and <sup>9</sup>Division of Orthopaedics, McGill University Health Centre, Montreal, Quebec H3G 1A4, Canada



The Journal of Neuroscience, May 18, 2011 • 31(20):7540–7550



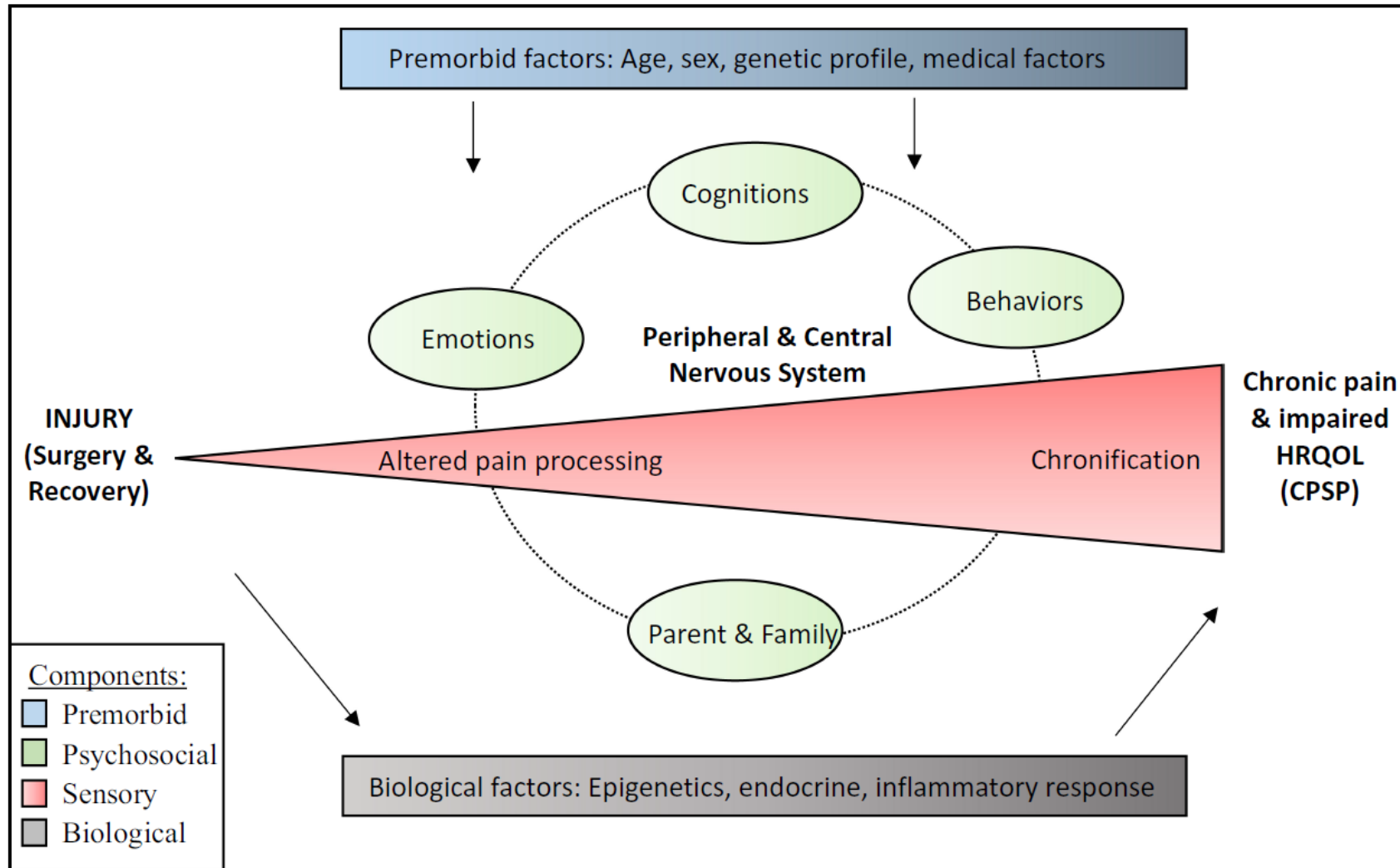
**Figure 1:**

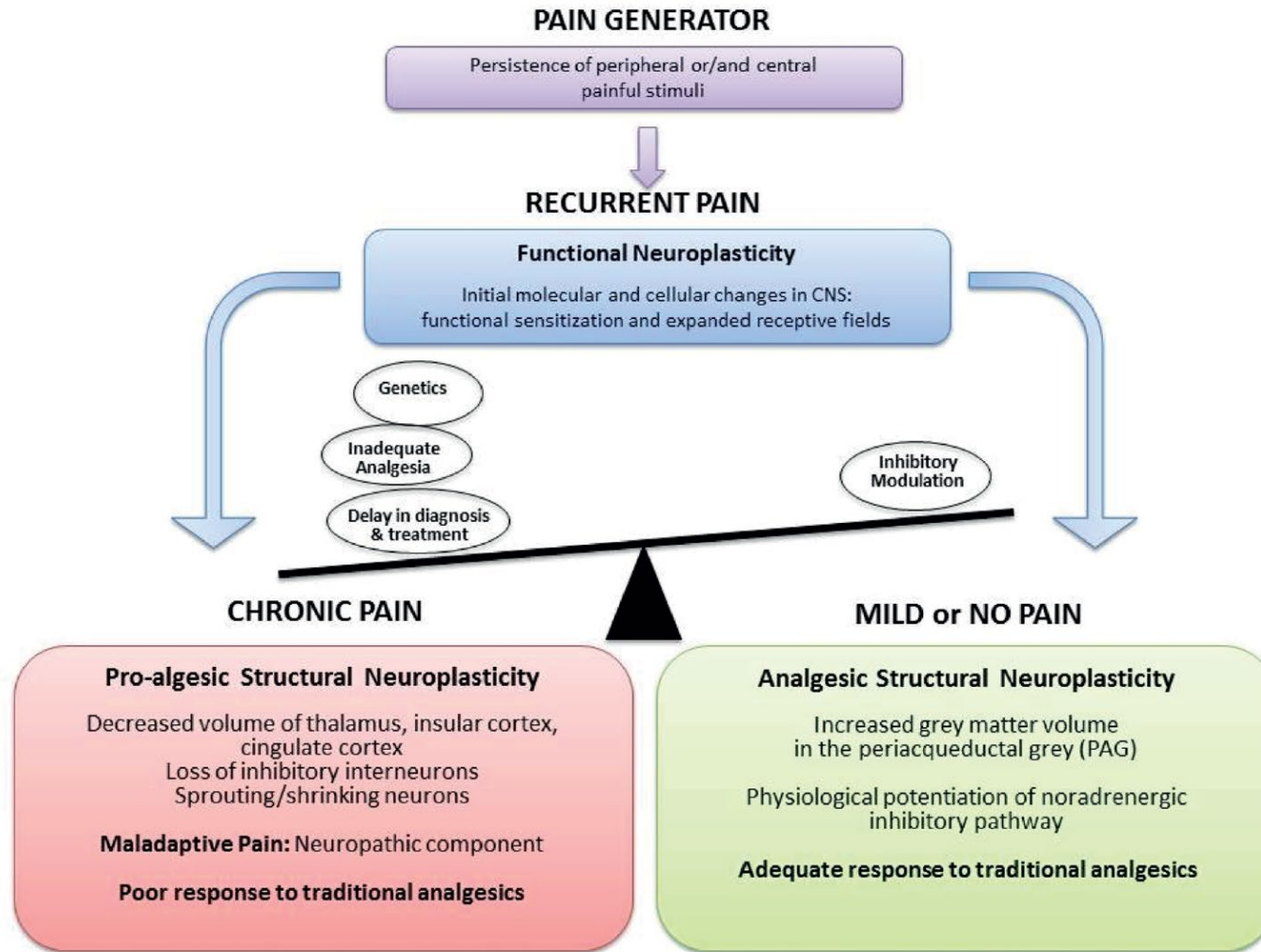
fMRI studies have provided data on structural and functional changes within the mesolimbic circuitry underlying chronic pain and depression, independently and within comorbid states. This schematic highlights intra-regional changes in collective baseline activity and gray matter volume within chronic pain populations, as well as changes in functional connectivity within chronic pain, depression, and addiction populations. PFC=prefrontal cortex; ACC=anterior cingulate cortex; NAc=nucleus accumbens; VTA=ventral tegmental area; Am=amygdala.

*Biol Psychiatry.* 2020 January 01; 87(1): 64–73.



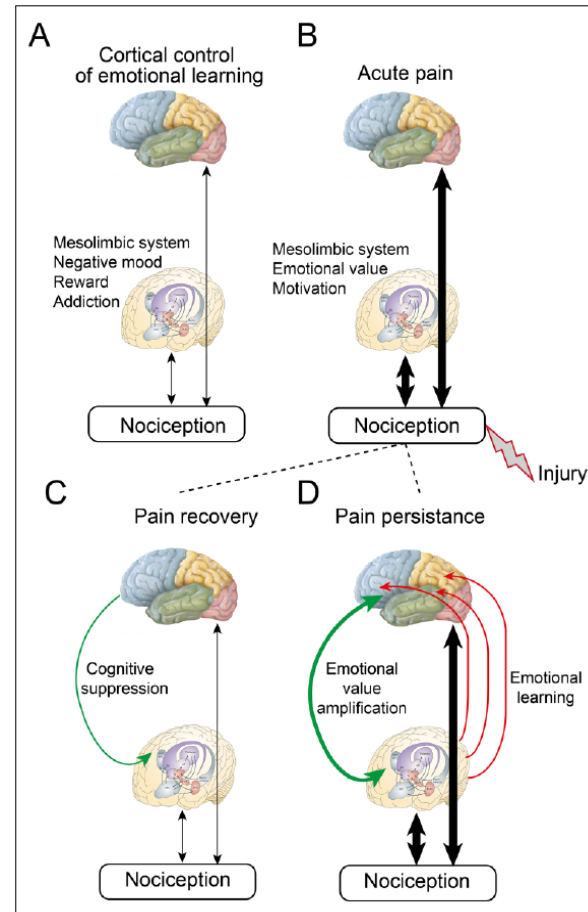
**CONCEPTUAL MODEL OF BIOPSYCHOSOCIAL MECHANISMS OF TRANSITION  
FROM ACUTE TO CHRONIC POSTSURGICAL PAIN.**



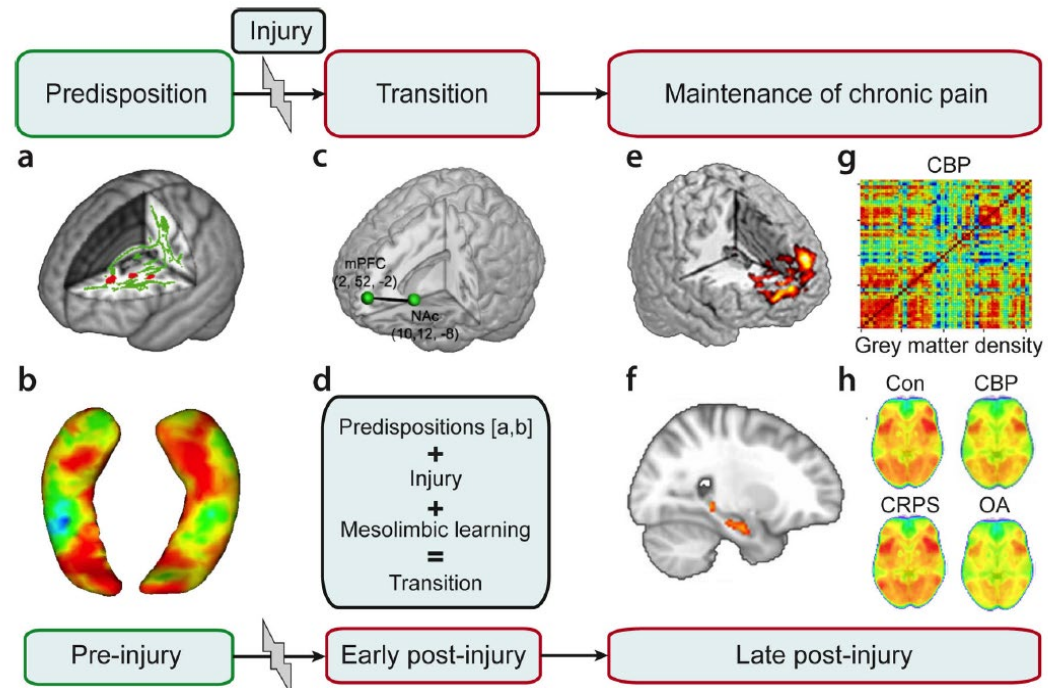


**Figure 2.** Pain chronification is the result of an imbalance between enhanced ascending nociceptive inputs and inadequate inhibitory descending system.

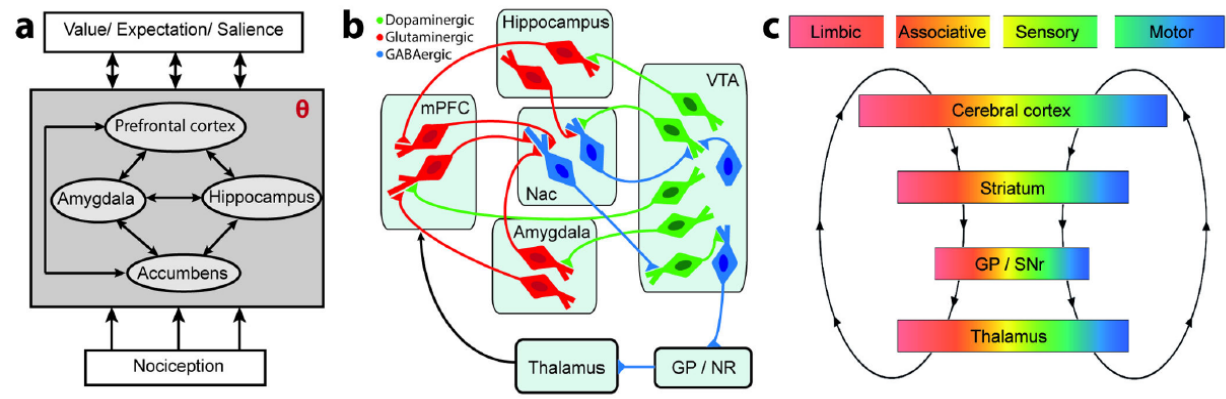
**Chronic pain depends on the corticolimbic properties interacting with nociceptive inputs.**



Journal of Dental Research 2016, Vol. 95(6) 605–612



*Neuron*. 2015 August 5; 87(3): 474–491.

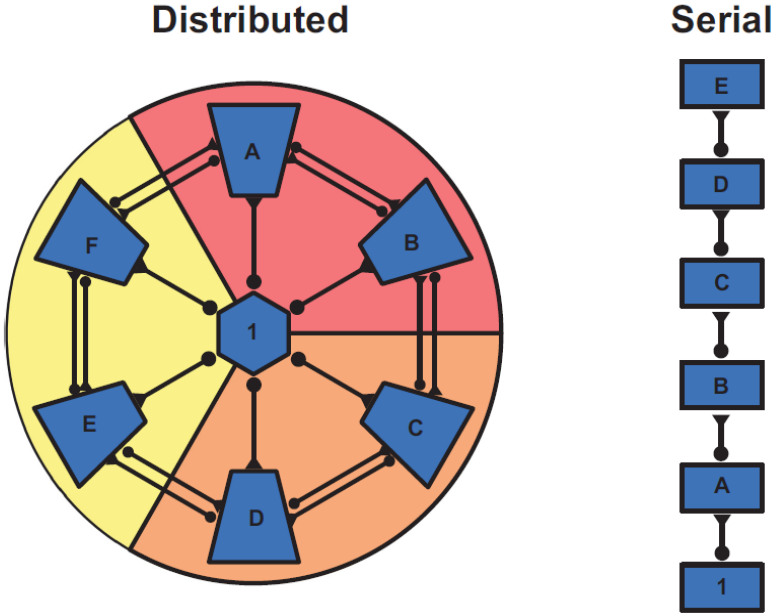


*Neuron*. 2015 August 5; 87(3): 474–491.

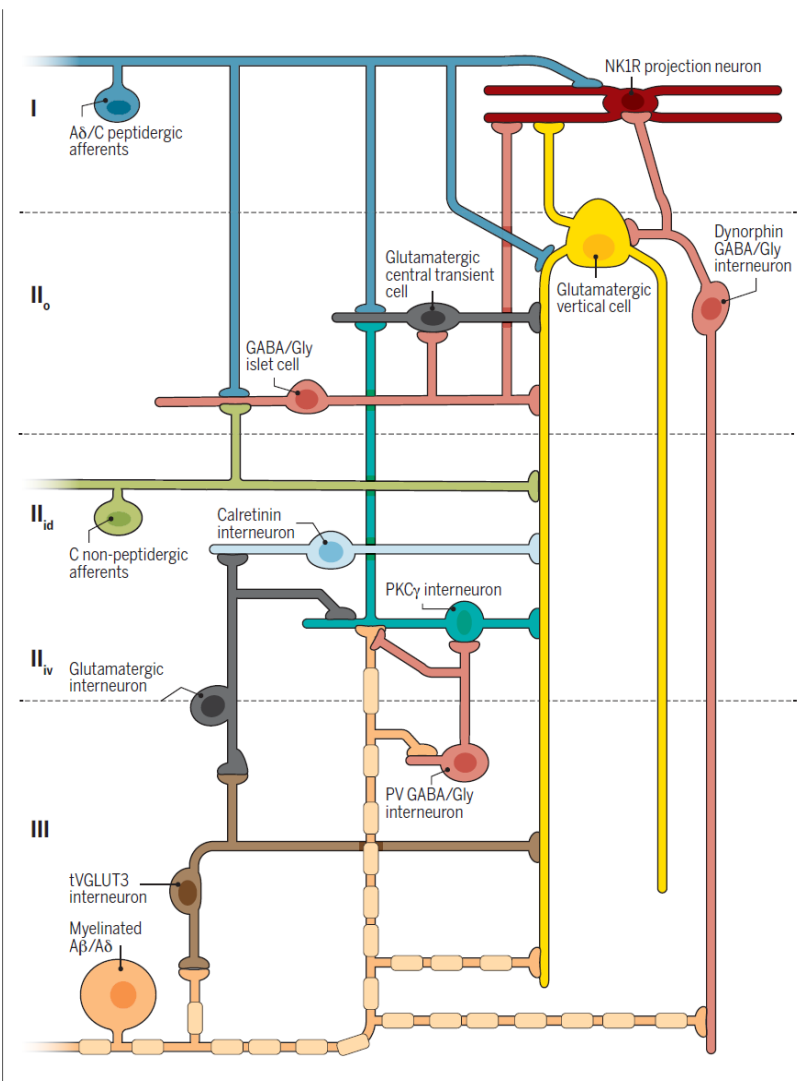


*Diego Fornasari*

# The Distributed Nociceptive System

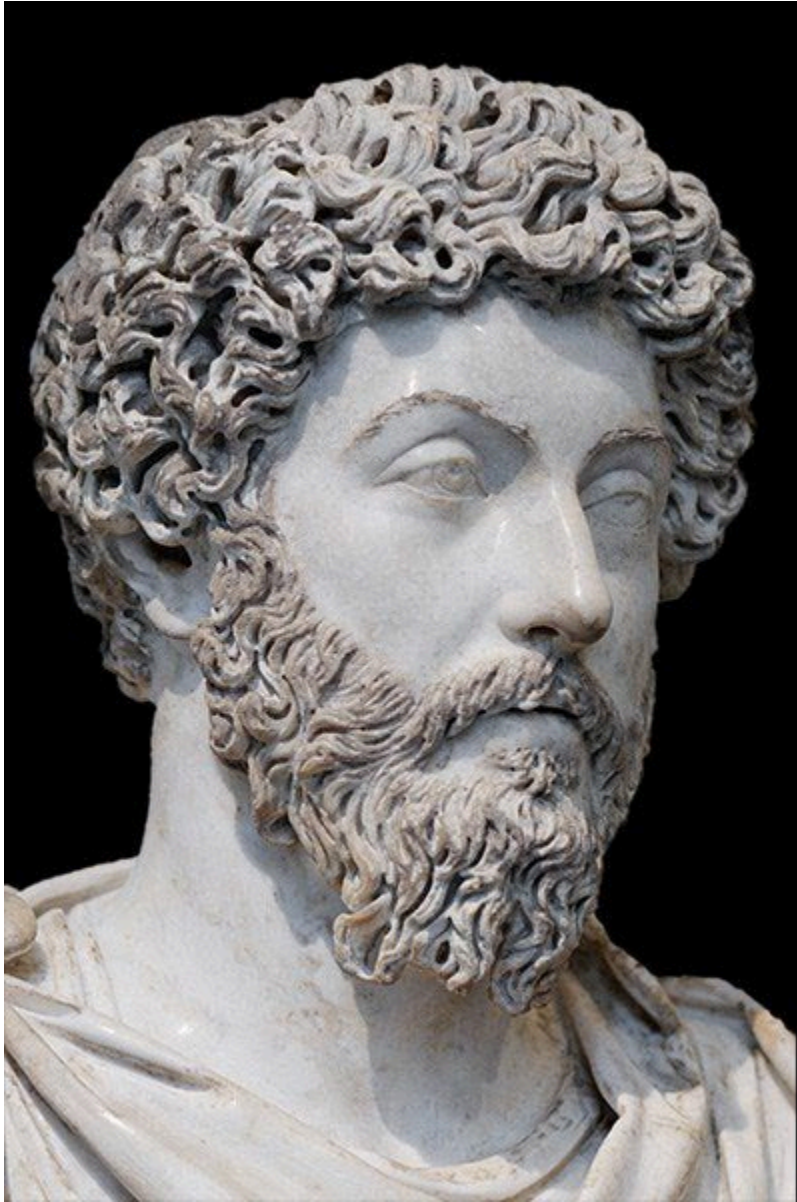


Trends in Neurosciences, October 2020, Vol. 43, No. 10



Pharmacol Rev 70:315–347, April 2018





“If you are distressed by anything external, the pain is not due to the thing itself, but to your estimate of it; and this you have the power to revoke at any moment.”

Marcus Aurelius, *Meditations*



*Diego Fornasari*

