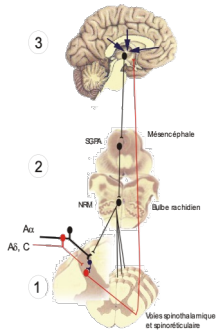
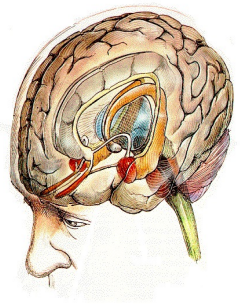




Bases neurophysiologiques de la douleur

Formation des résidents du programme de médecine de la douleur

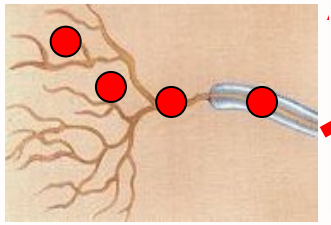
MMD 8800

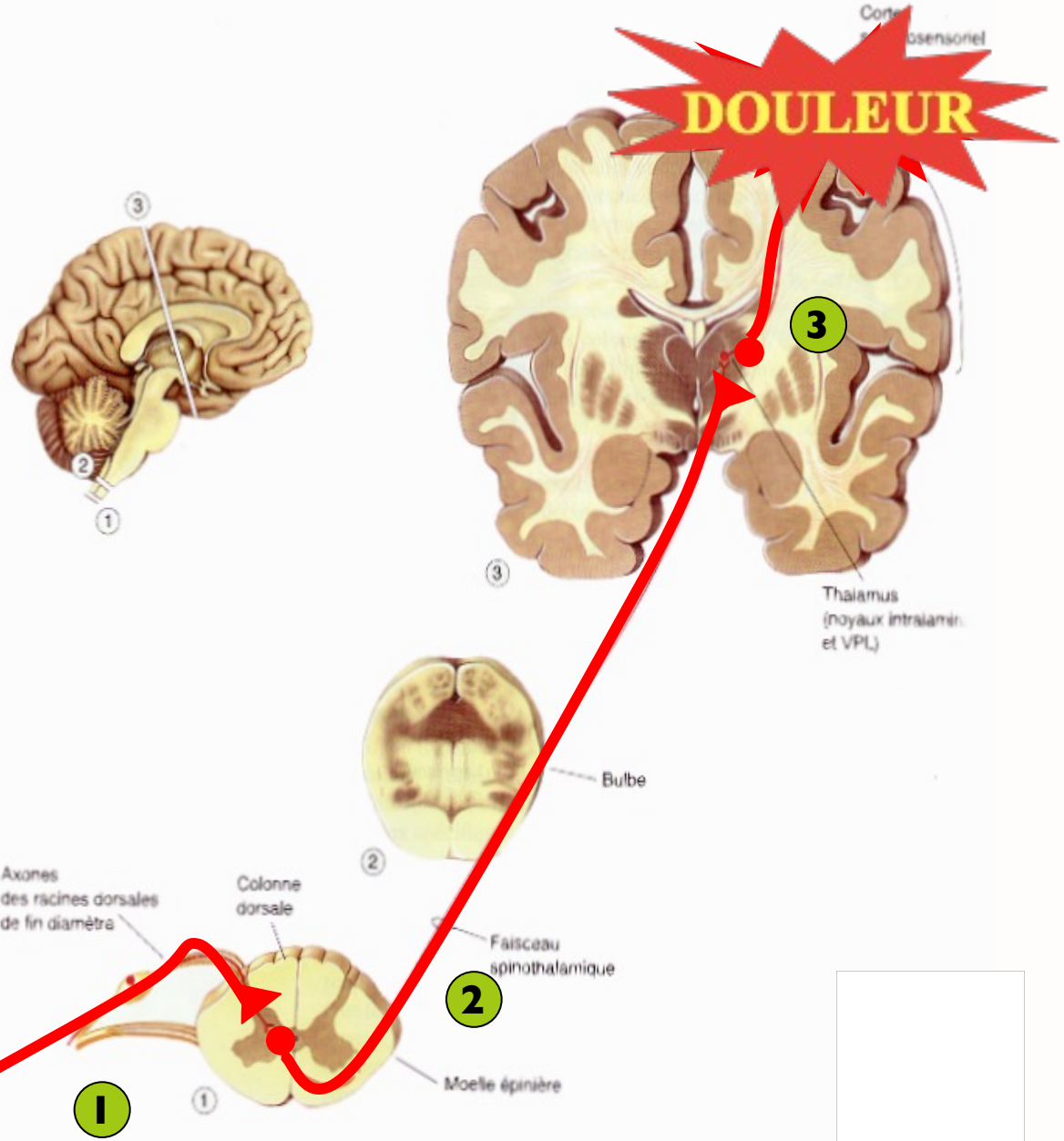
Serge Marchand, Ph.D.

UNIVERSITÉ DE SHERBROOKE
Faculté de médecine et des sciences de la santé

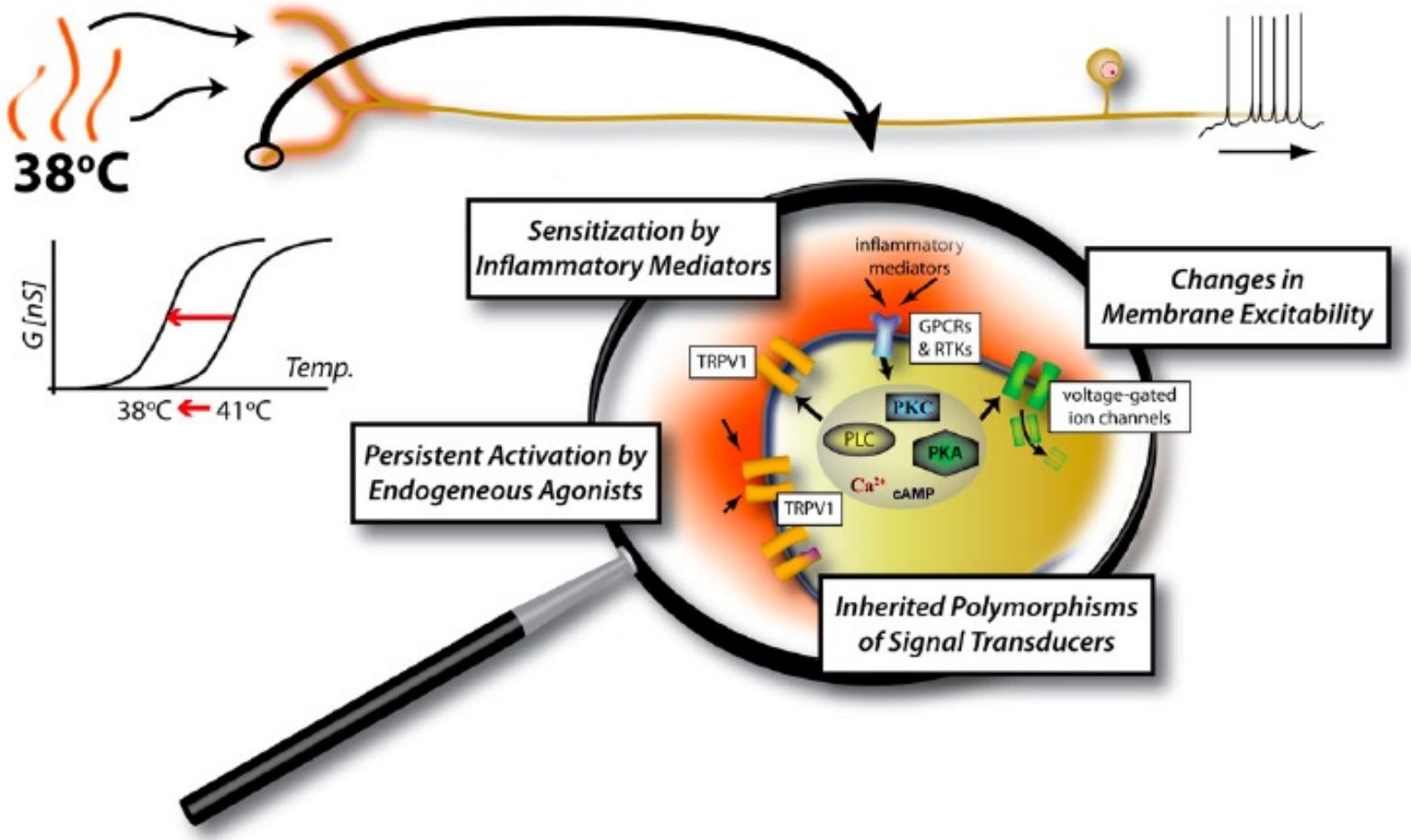
CENTRE DE RECHERCHE | CHUS

DE LA NOCICEPTION À LA DOULEUR





Sensibilisation centrale

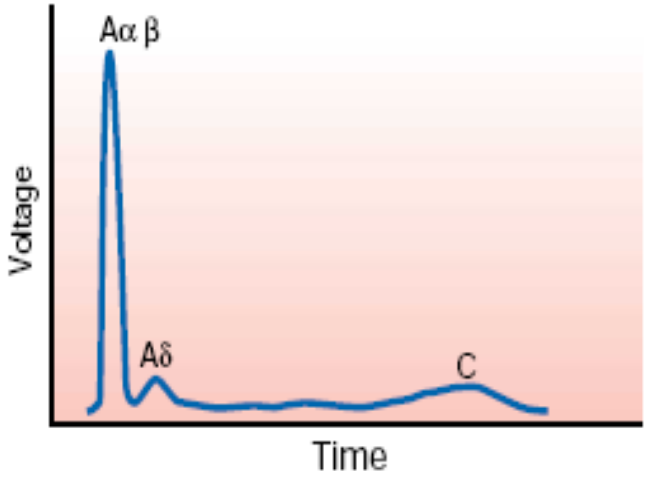


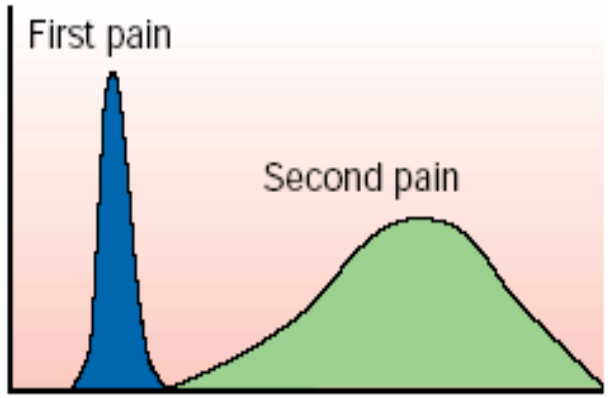
Christian A. von Hehn,[1,2] Ralf Baron,[3] and Clifford J. Woolf[1,2,*] Neuron 73, February 23, 2012

Fibres de la nociception

Primary afferent axons

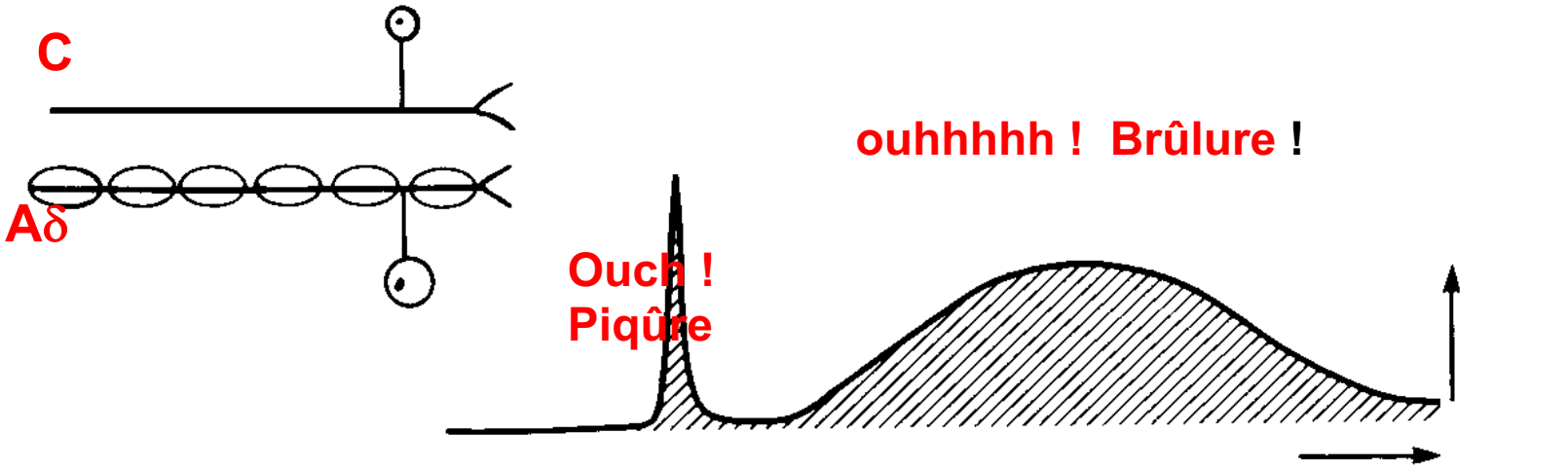
		Thermal threshold
	Aα and Aβ fibres Myelinated Large diameter Proprioception, light touch	None
	Aδ Fibre Lightly myelinated Medium diameter Nociception (mechanical, thermal, chemical)	~ 53 °C Type I ~ 43 °C Type II
	C fibre Unmyelinated Small diameter Innocuous temperature, itch Nociception (mechanical,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

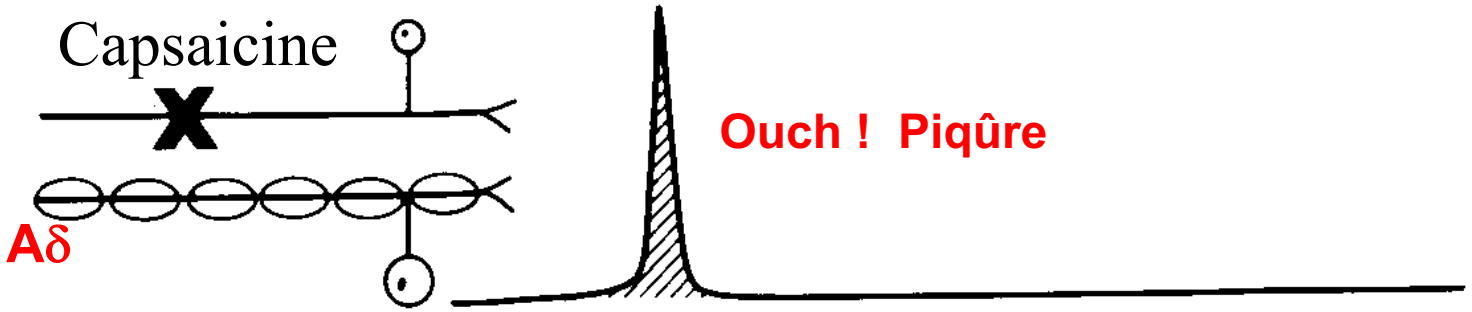




Basbaum, NATURE, 2001

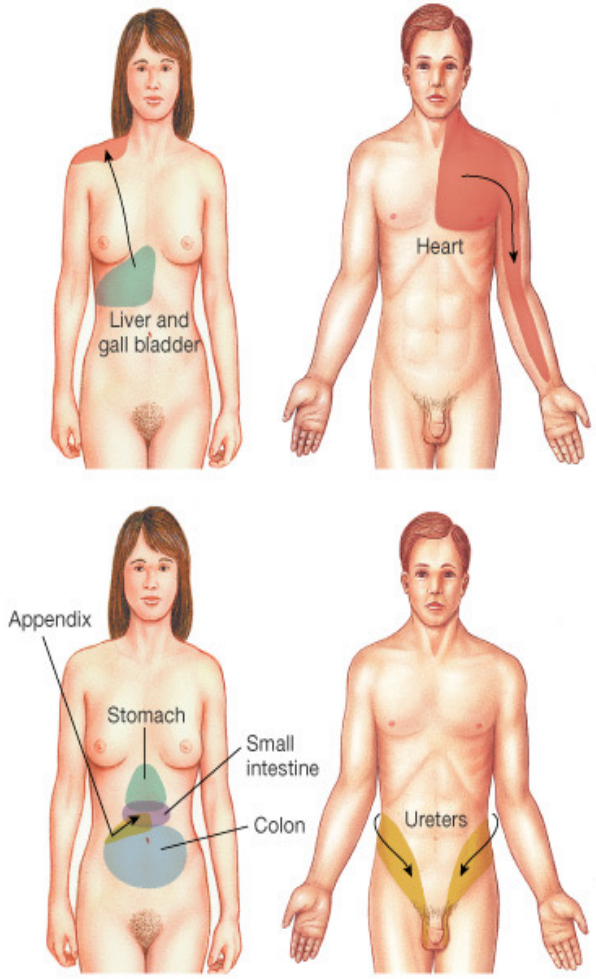
Première et seconde douleur



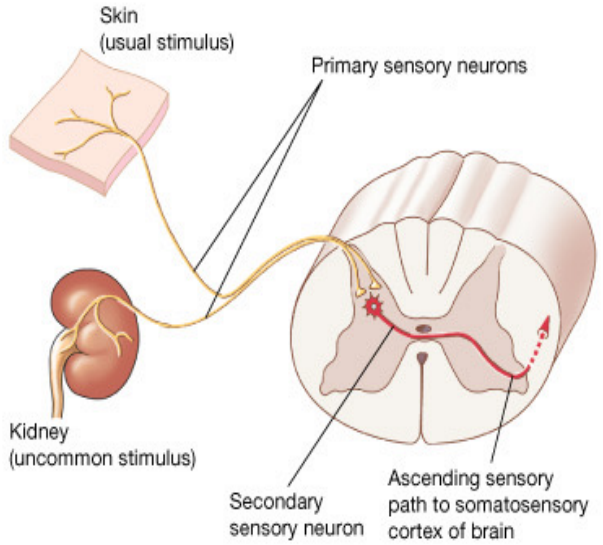


Douleur projetée : Viscéro-somatique

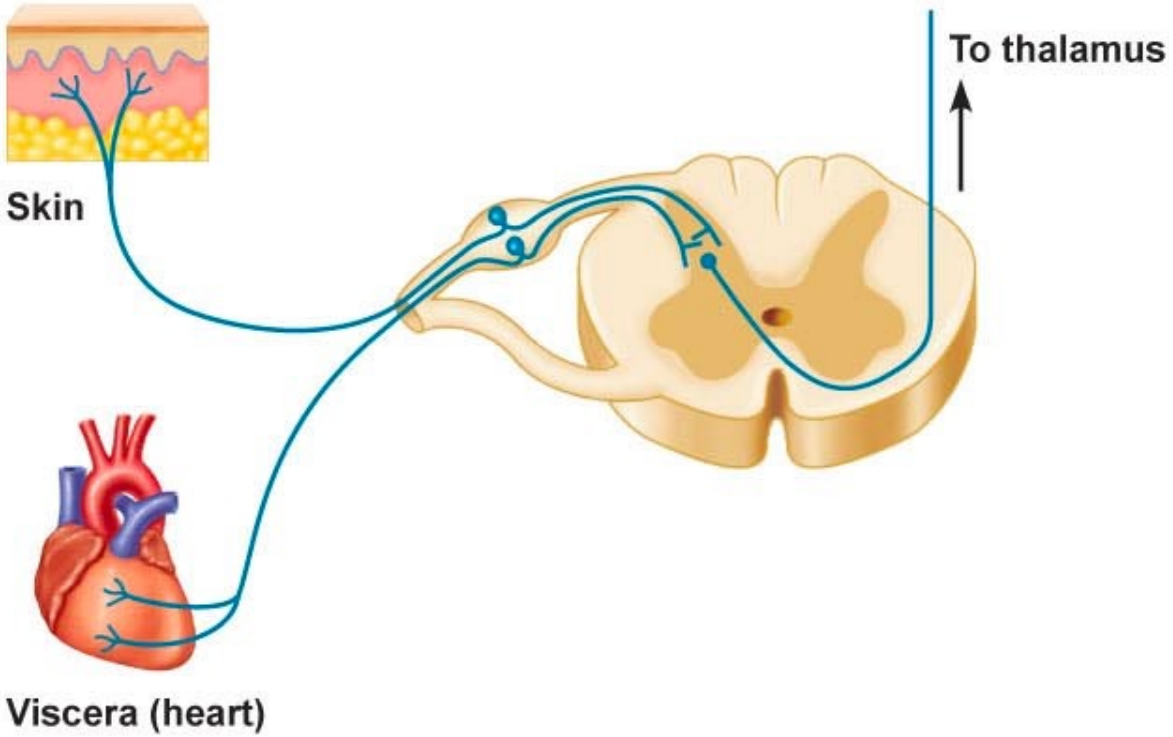
(a) Pain in internal organs is often sensed on the surface of the body, a sensation known as **referred pain**.



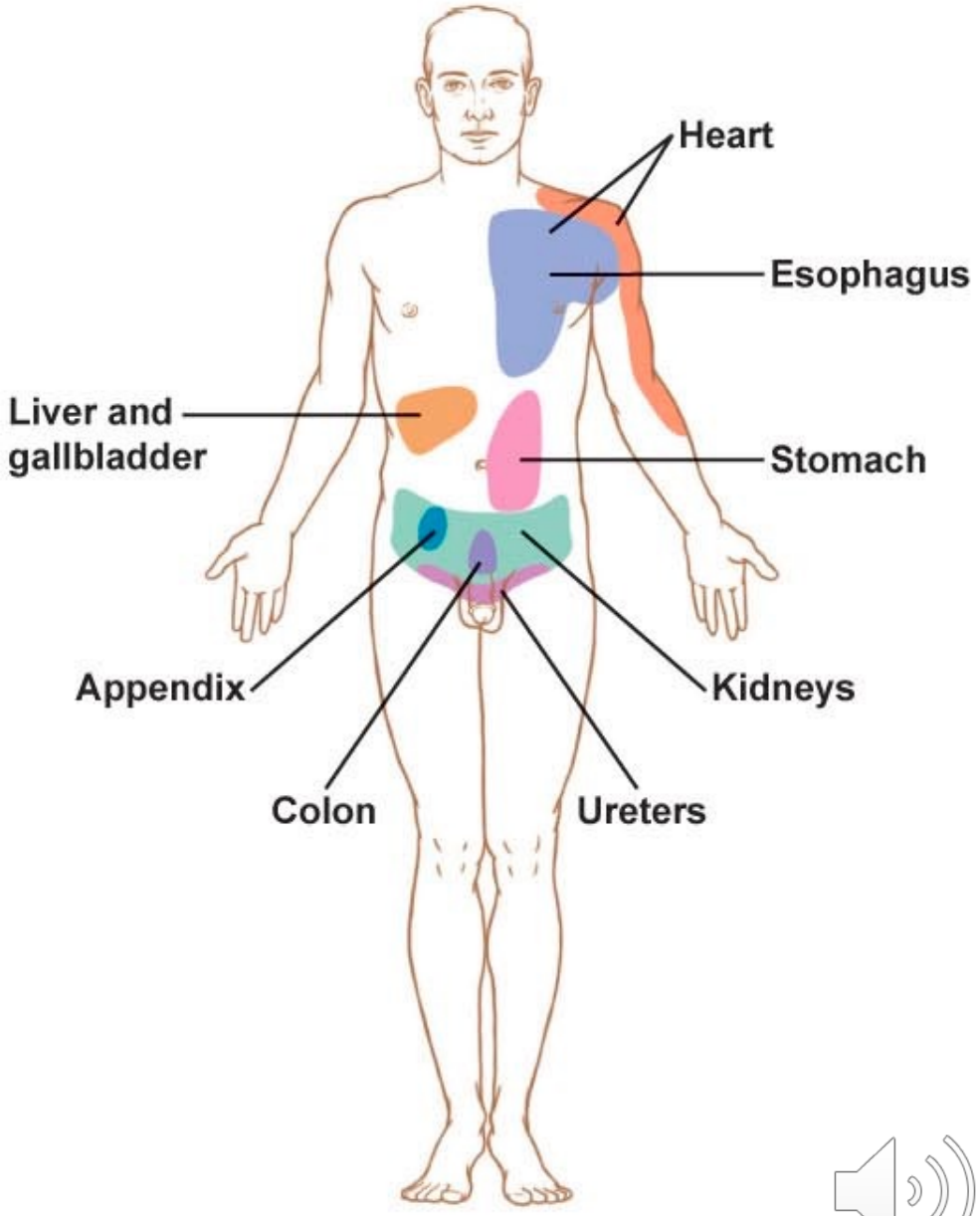
(b) One theory of referred pain says that nociceptors from several locations converge on a single ascending tract in the spinal cord. Pain signals from the skin are more common than pain from internal organs, and the brain associates activation of the pathway with pain in the skin. Adapted from H.L. Fields, *Pain* (McGraw Hill, 1987).



Douleur projetée



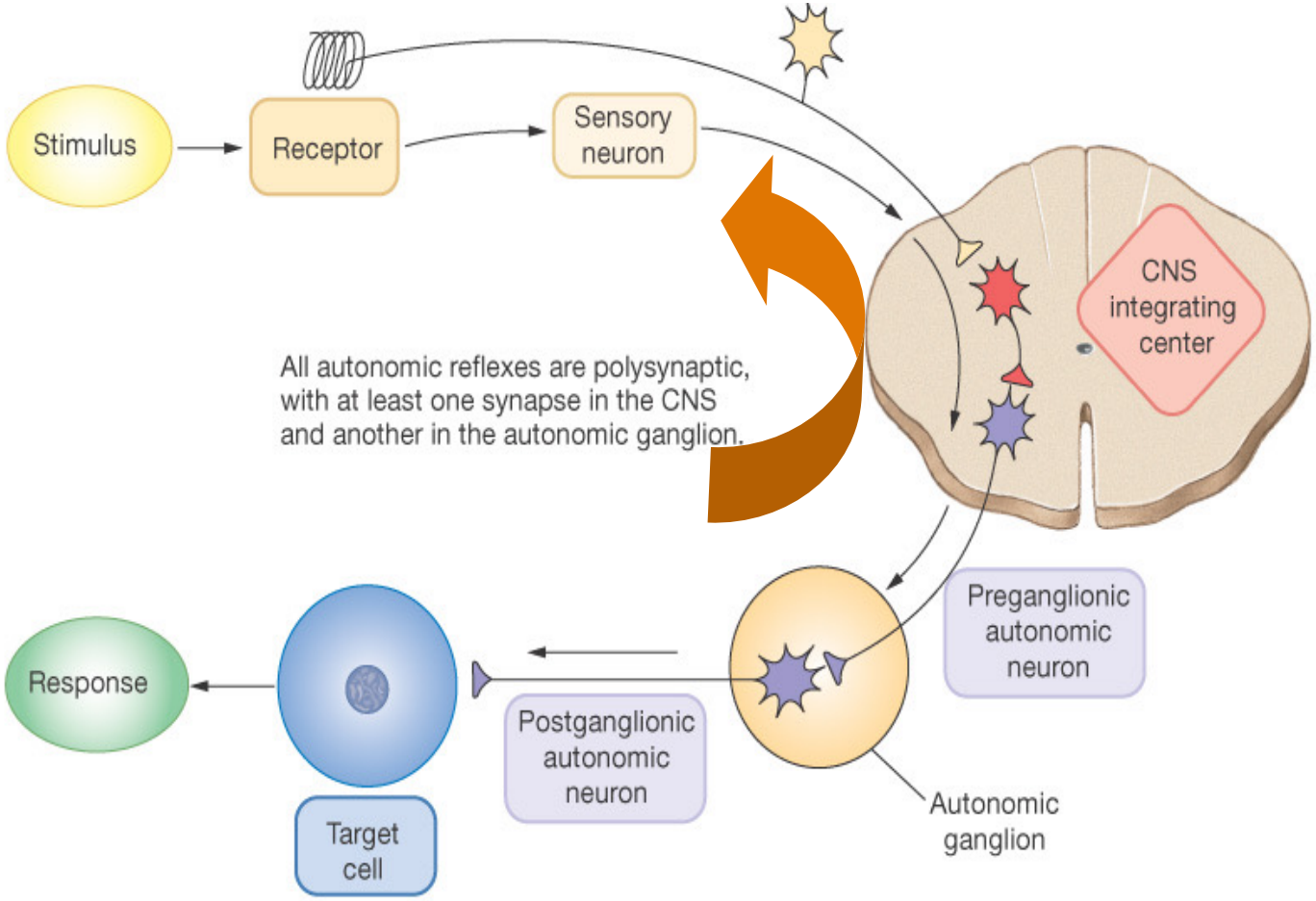
(a) Mechanism of referred pain



(b) Clinical map of referred pain

Réflexe somato-viscéral

Mais aussi viscéro-somatique



Pain Medicine

Pain Medicine 2013; *: **–**
Wiley Periodicals, Inc.

Can Quantitative Sensory Testing Move Us Closer to Mechanism-Based Pain Management?

Cruz-Almeida Y, Fillingim RB. *Pain Med*, (2013).

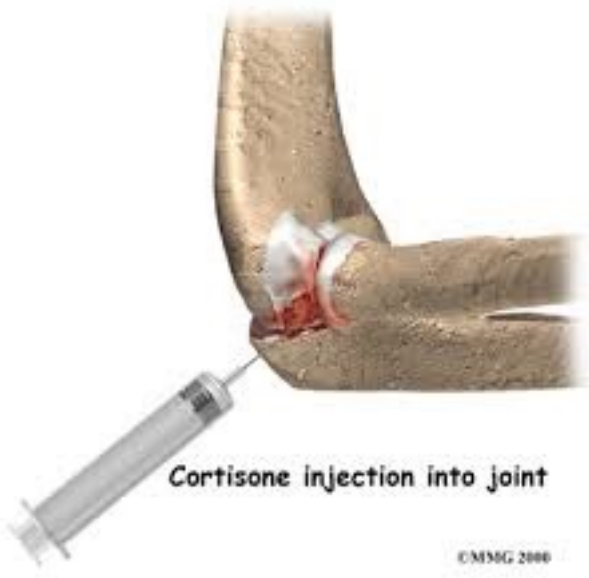
QST (Quantitative Sensory Testing) Périphérie

Aβ : Touch, vibration

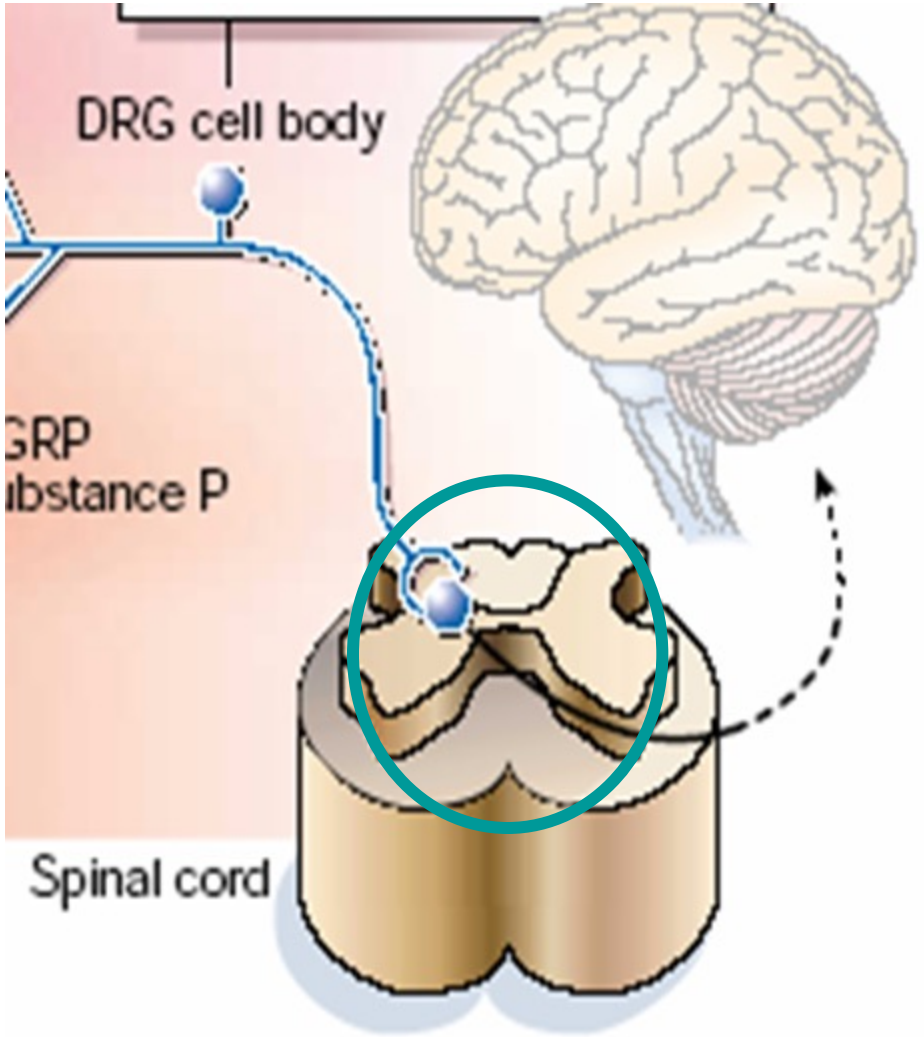
Aδ : Sharp Pain

C: Heat

Mécanismes périphériques: Traitements



Nocicepteurs secondaires – cornes postérieures de la moelle

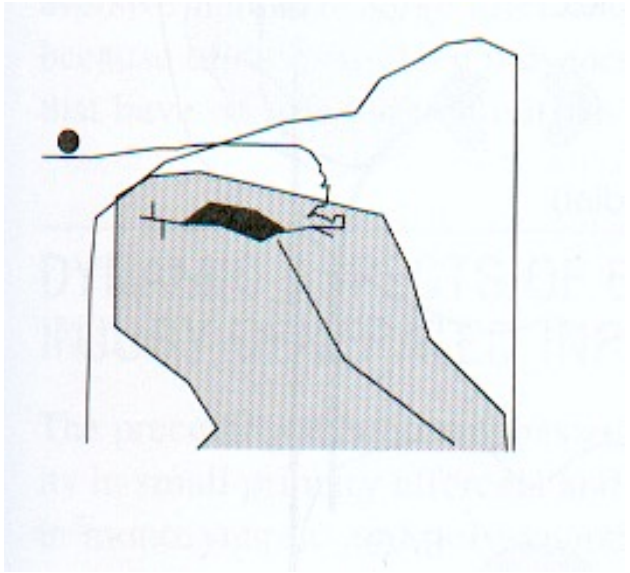


Neurones nociceptifs

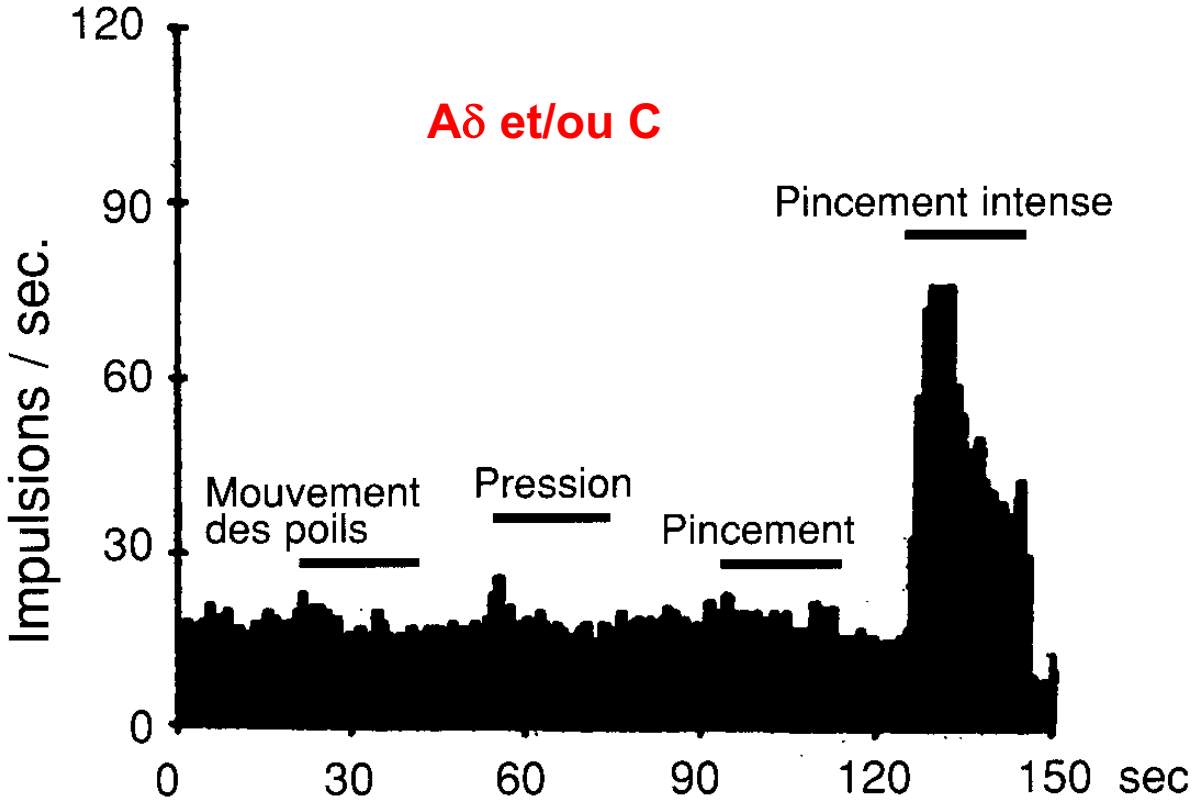
Illustration des caractéristiques des 2 catégories de neurones de la corne dorsale de la moelle impliqués dans la transmission des messages nociceptifs :

B

neurone nociceptif spécifique



Enregistrement d'un neurone Nociceptif spécifique

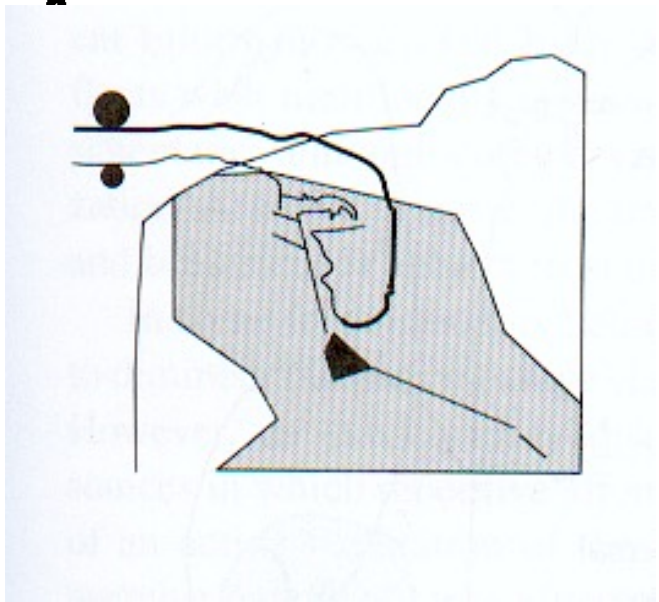


Brasseur (1997) fig.2-4a

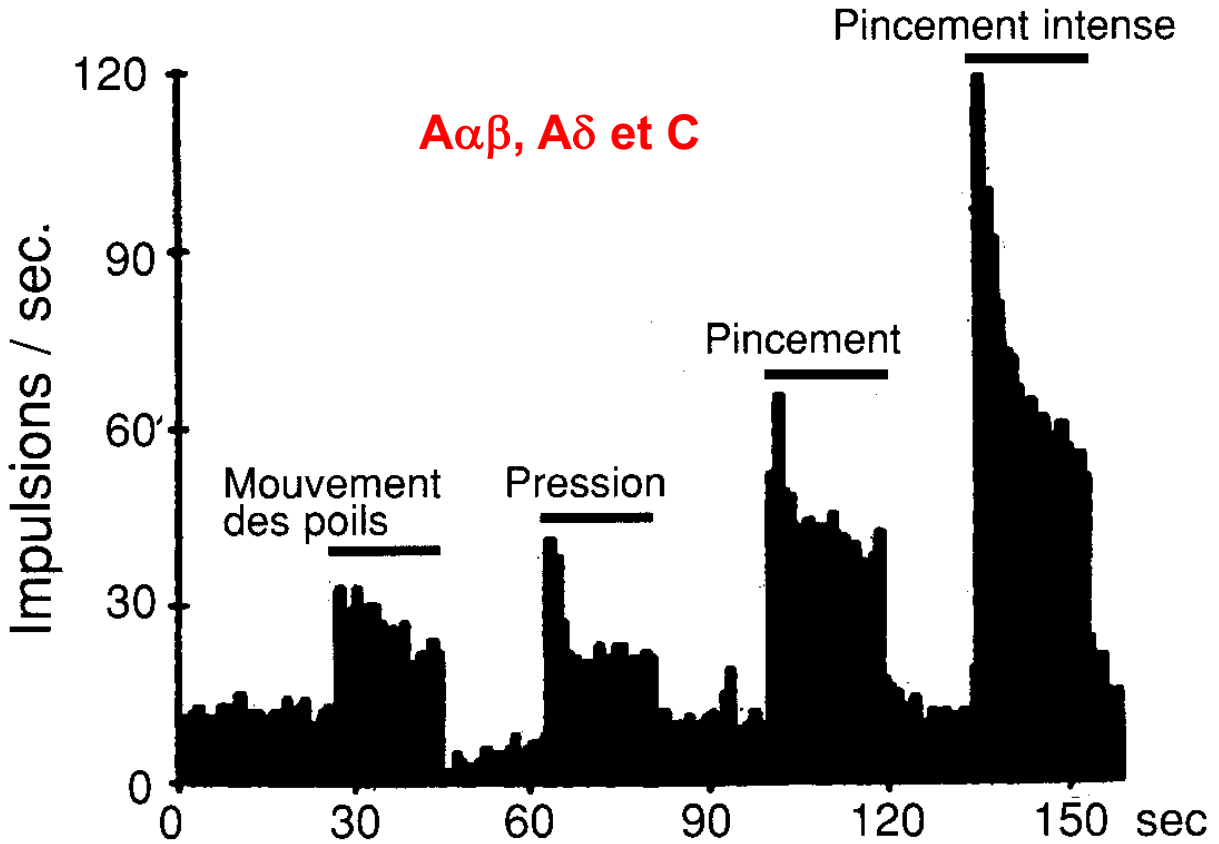
Neurones nociceptifs

Illustration des caractéristiques des 2 catégories de neurones de la corne dorsale de la moelle impliqués dans la transmission des messages nociceptifs :

neurone nociceptif non spécifique

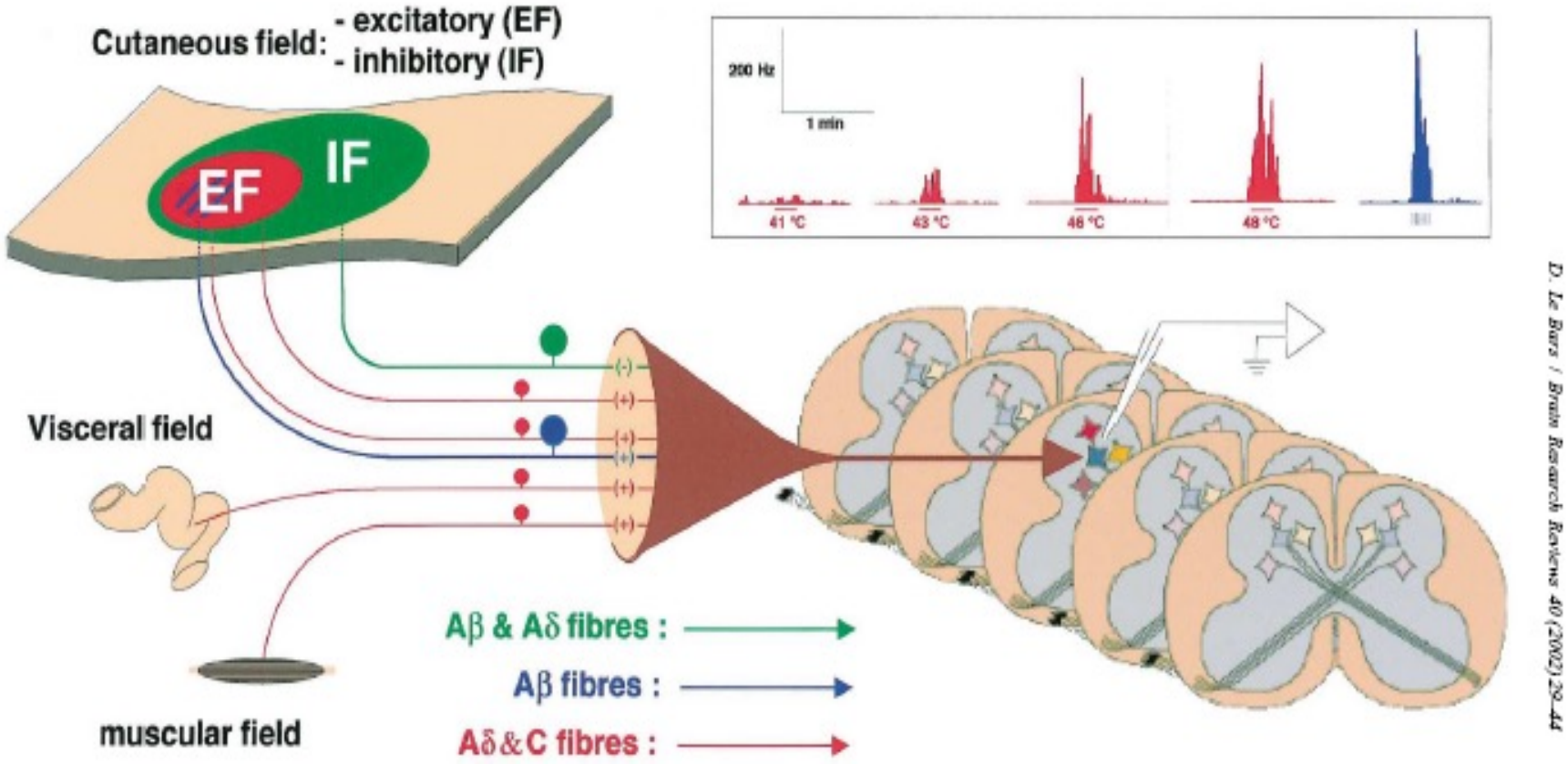


Enregistrement d'un neurone Nociceptif non spécifique

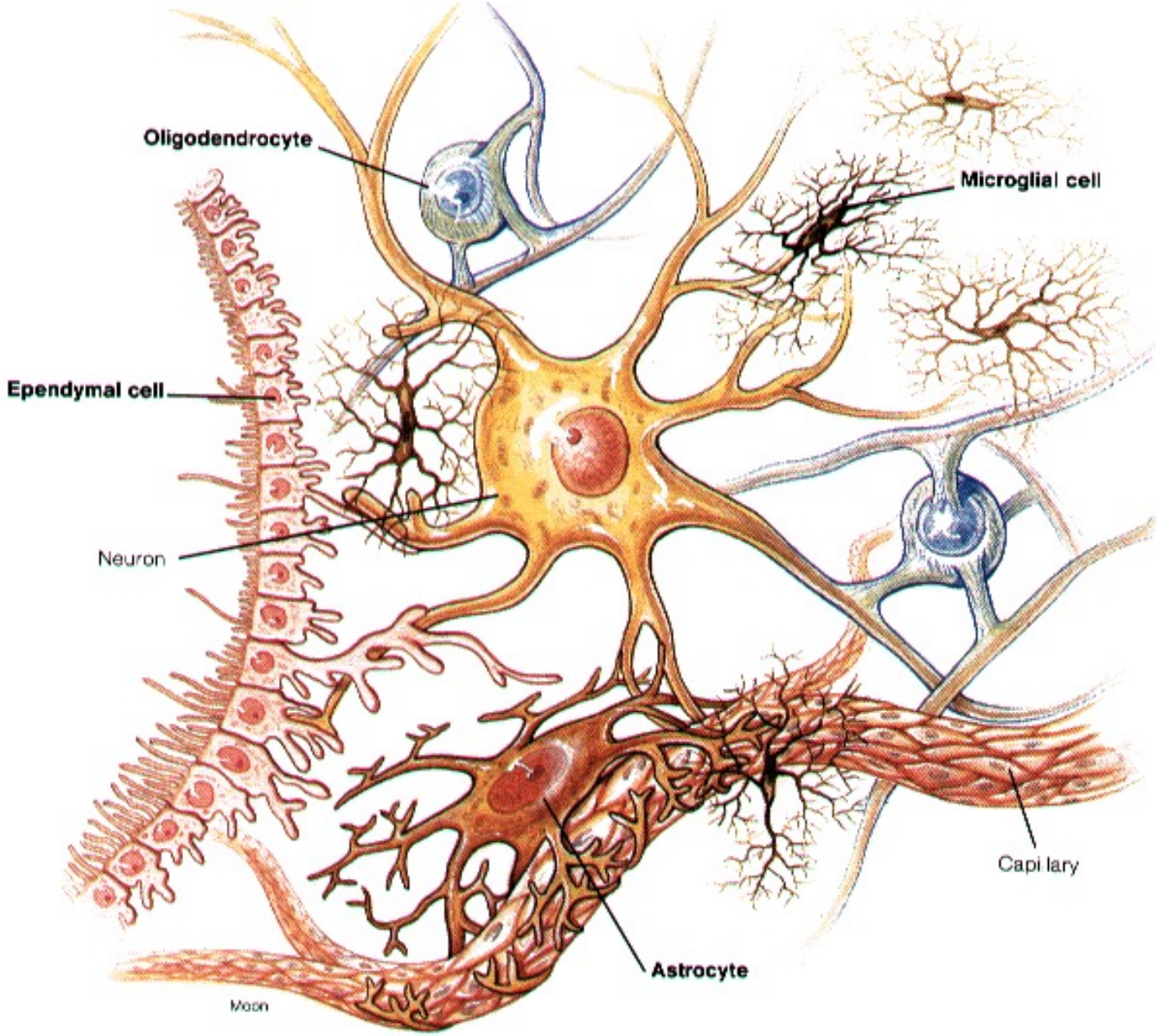


Brasseur (1997) fig.2-4a

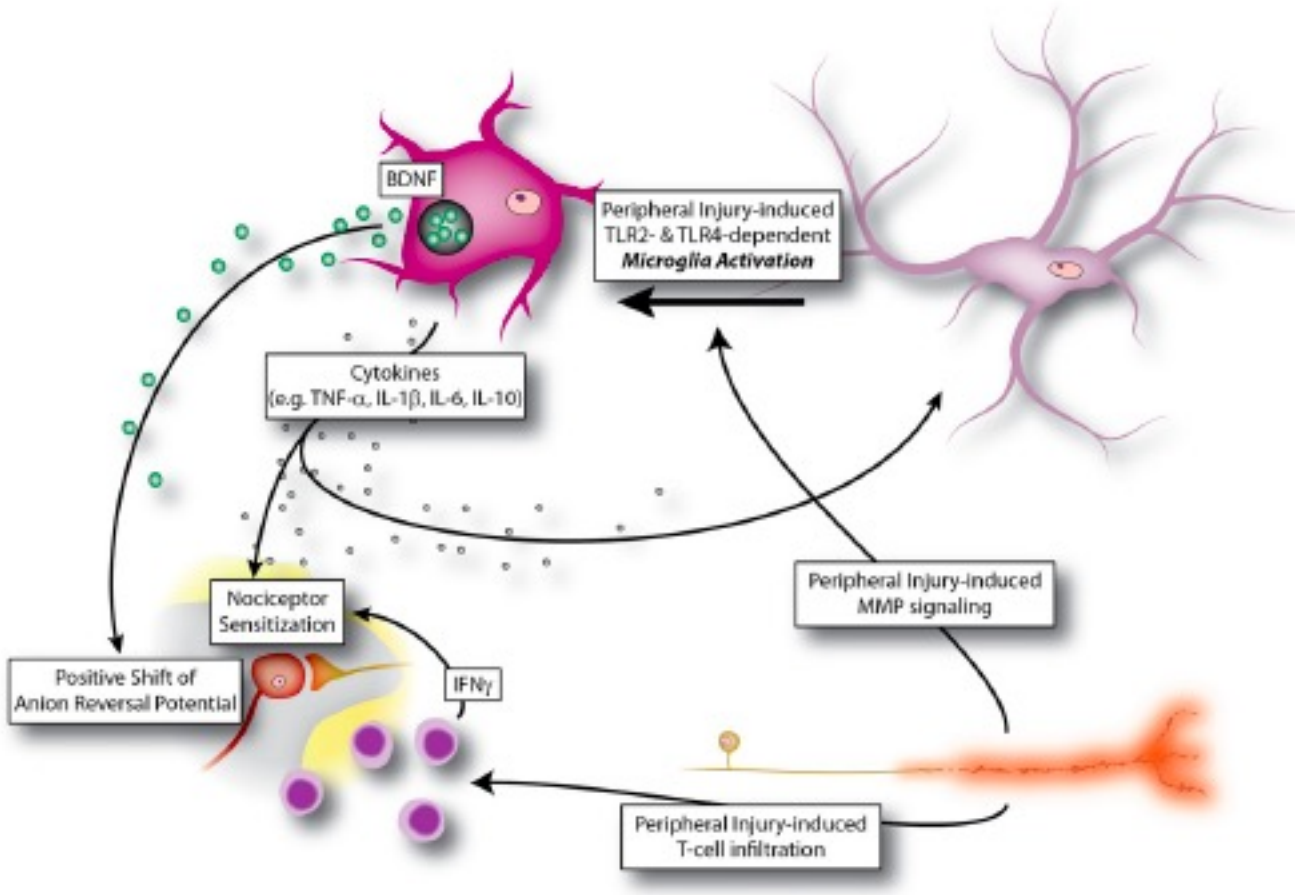
Convergences et réponses nociceptives



Cellules gliales



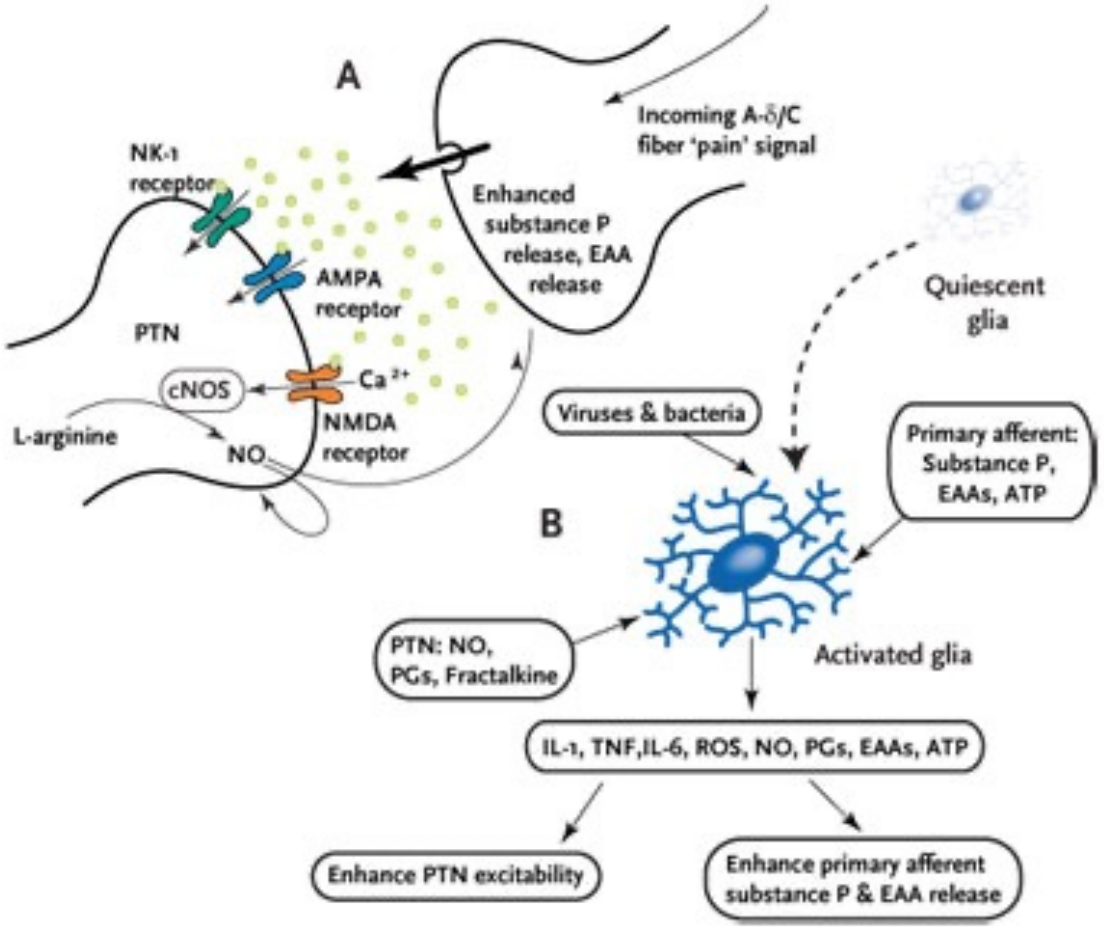
cellules gliales, système immunitaire et douleur



Christian A. von Hehn,[1,2] Ralf Baron,[3] and Clifford J. Woolf[1,2,*] Neuron 73, February 23, 2012

Cellules gliales et douleur

L'activation de la microglie et des astrocytes provoque de l'hyperactivité cellulaire et le relâchement de substance P et d'AAE



Il est important de tenir compte du rôle des cellules gliales qui sont activées par neurones nociceptifs

The Scientist, 28 Mars 2005: Watkins et al., *Trends Neurosci*, 24:450-5, 2001

Review TRENDS in Neurosciences Vol.28 No.2 February 2005

Makoto Tsuda[1,2], Kazuhide Inoue[1,3] and Michael W. Salter[2]

P2X4 receptor is a ligand-gated cation channel activated by ATP required for neuropathic pain.

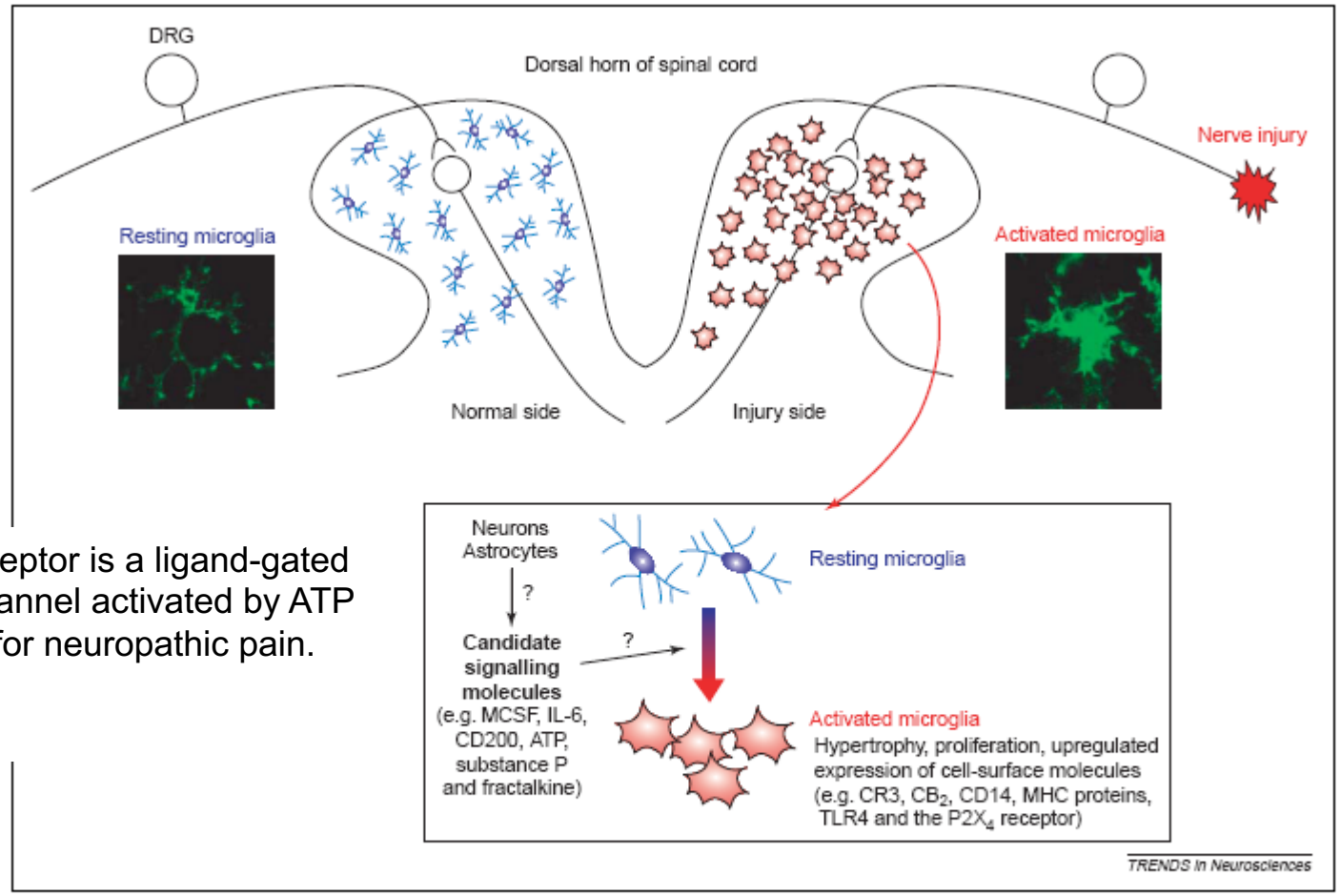
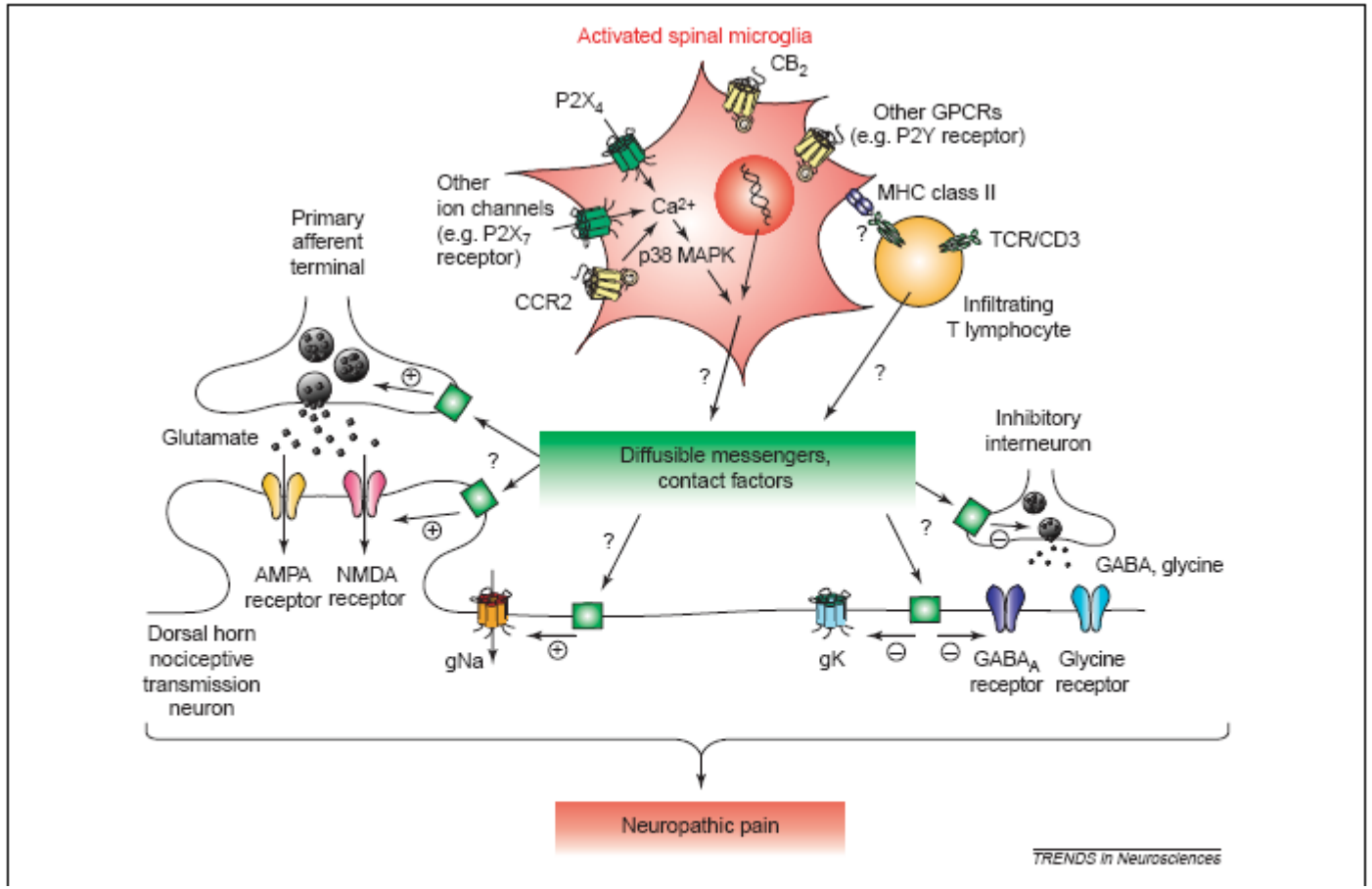


Figure 1. Processes causing activation of microglia in the dorsal horn of the spinal cord following injury to a nerve in the periphery. On the normal side of dorsal horn, microglia have small somas, bearing thin and branched processes, and are homogeneously distributed (i.e. they are 'resting microglia'). After peripheral nerve injury, microglia in the spinal cord ipsilateral to the nerve injury transform from the resting to the 'activated microglia' phenotype, which is characterized by hypertrophy, proliferation and expression of cell-surface molecules (e.g. CR3, CB_2, CD14, MHC proteins, TLR4 and the $P2X_4$ receptor). Photographs show resting (left) and activated (right) microglia staining for CR3. Activation of microglia in the dorsal horn occurs predominantly in the central projection area of the injured peripheral nerve, which implies contribution of signals from injured nerve and/or affected dorsal horn neurons or astrocytes. Candidate signaling molecules include MCSF, IL-6, CD200, ATP, substance P and fractalkine.

Review TRENDS in Neurosciences Vol.28 No.2 February 2005
Full text provided by www.sciencedirect.com

Makoto Tsuda[1,2], Kazuhide Inoue[1,3] and Michael W. Salter[2]



The role of microglia in neuropathic pain:

- Release of glutamate
- Activation of the NMDA receptors
- Blocking of inhibition

Ma, J. Y. and Zhao, Z. Q.
The involvement of glia in long-term plasticity in the spinal dorsal horn of the rat.
Neuroreport 13 (14):1781-1784, 2002.

Stimulation tétanique = **LTP** fibres C spinales

Stimulation tétanique avec fluorocitrate (inh activité gliale) = **LTD** fibres C spinales

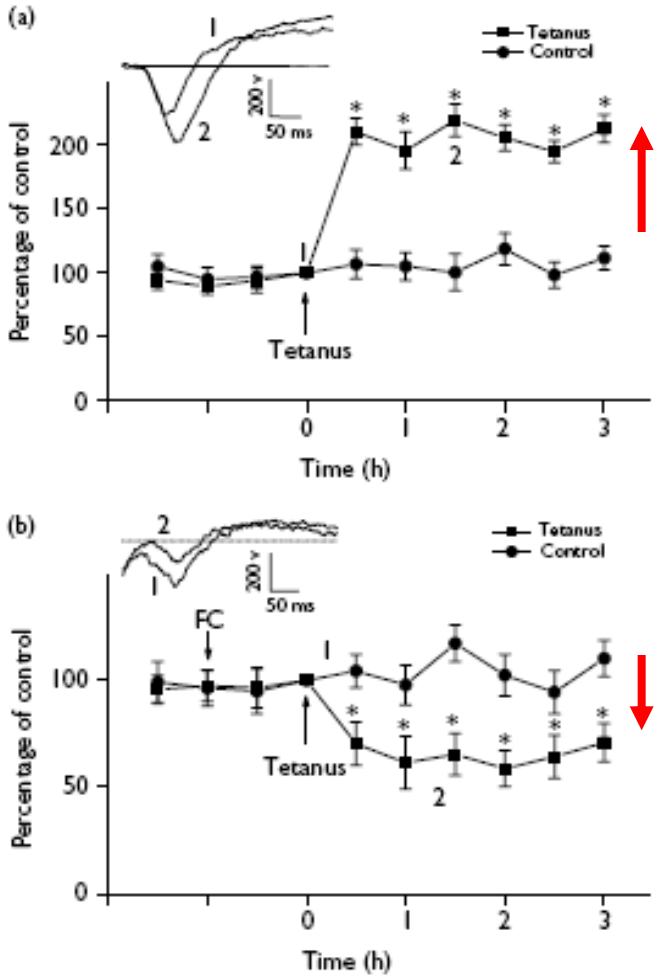


Fig. 1. LTD is induced with prior fluorocitrate administration. Tetanic stimulation induces LTP of C fiber evoked field potentials are shown in (a). (b) Tetanic stimulation produces LTD when fluorocitrate (1 nmol) is given 1 h before. Mean amplitude (± s.e.m.) was expressed as percentage of control and was plotted *vs* time. $*p < 0.05$ *vs* control. Insets illustrate the original C fibers evoked field potentials before and after tetanus. Bars = 200 μV, 50 ms.

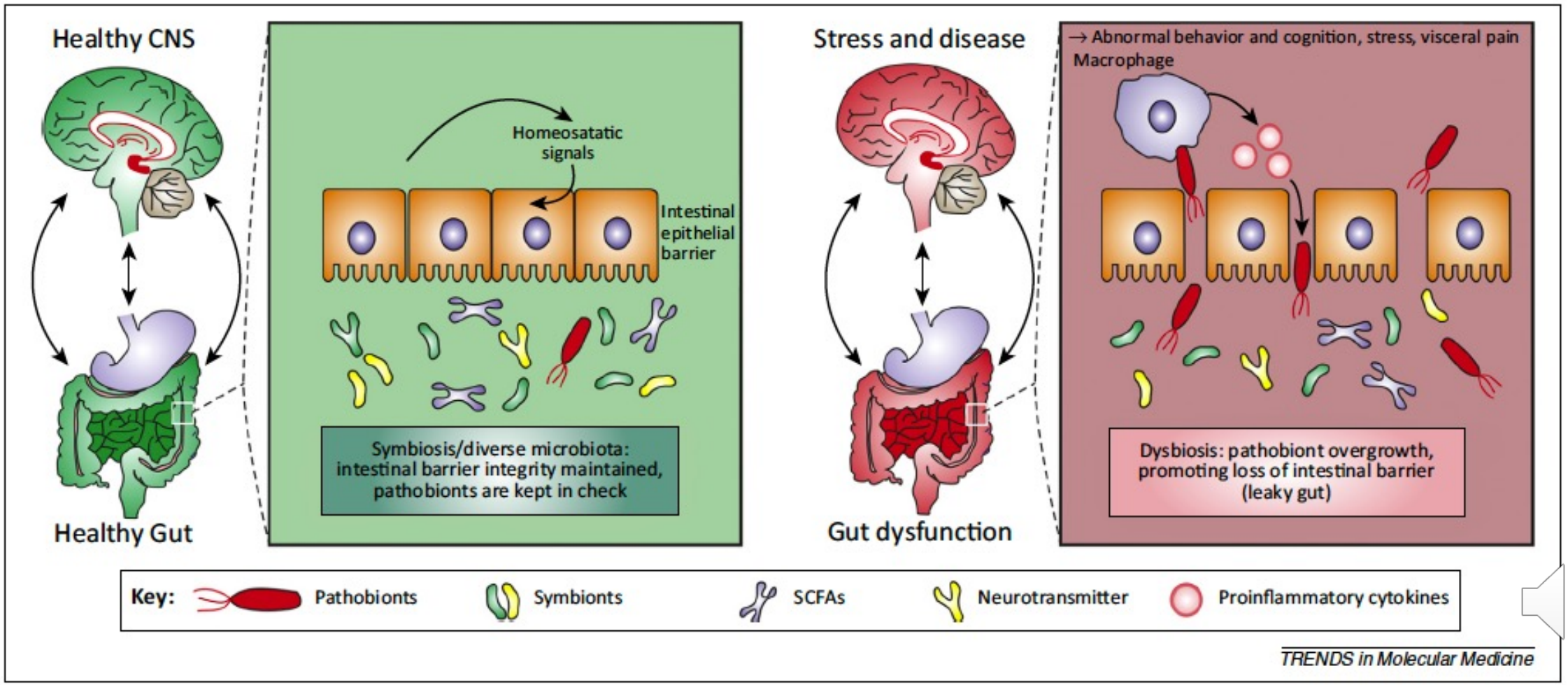
Cellules gliales et LTP

Review

CellPress

Microbiota and neurodevelopmental windows: implications for brain disorders

Yuliya E. Borre[1], Gerard W. O'Keeffe[2,3], Gerard Clarke[1,4], Catherine Stanton[4,5], Timothy G. Dinan[1,4], and John F. Cryan[1,2]



SPECIAL FOCUS REVIEW

Gut Microbes 5:3, 404–410; May/June 2014; © 2014 Landes Bioscience

The effects of gut microbiota on CNS function in humans

Kirsten Tillisch

- Role for the microbiota in broad aspects of human health, including mood, cognition, and chronic pain.

- Altering the microbiota with beneficial bacteria, or probiotics, can lead to changes in brain function, as well as subjective reports of mood.

- Bidirectional communication between the brain and microbiota … provide novel methods to enhance health and treat disease.

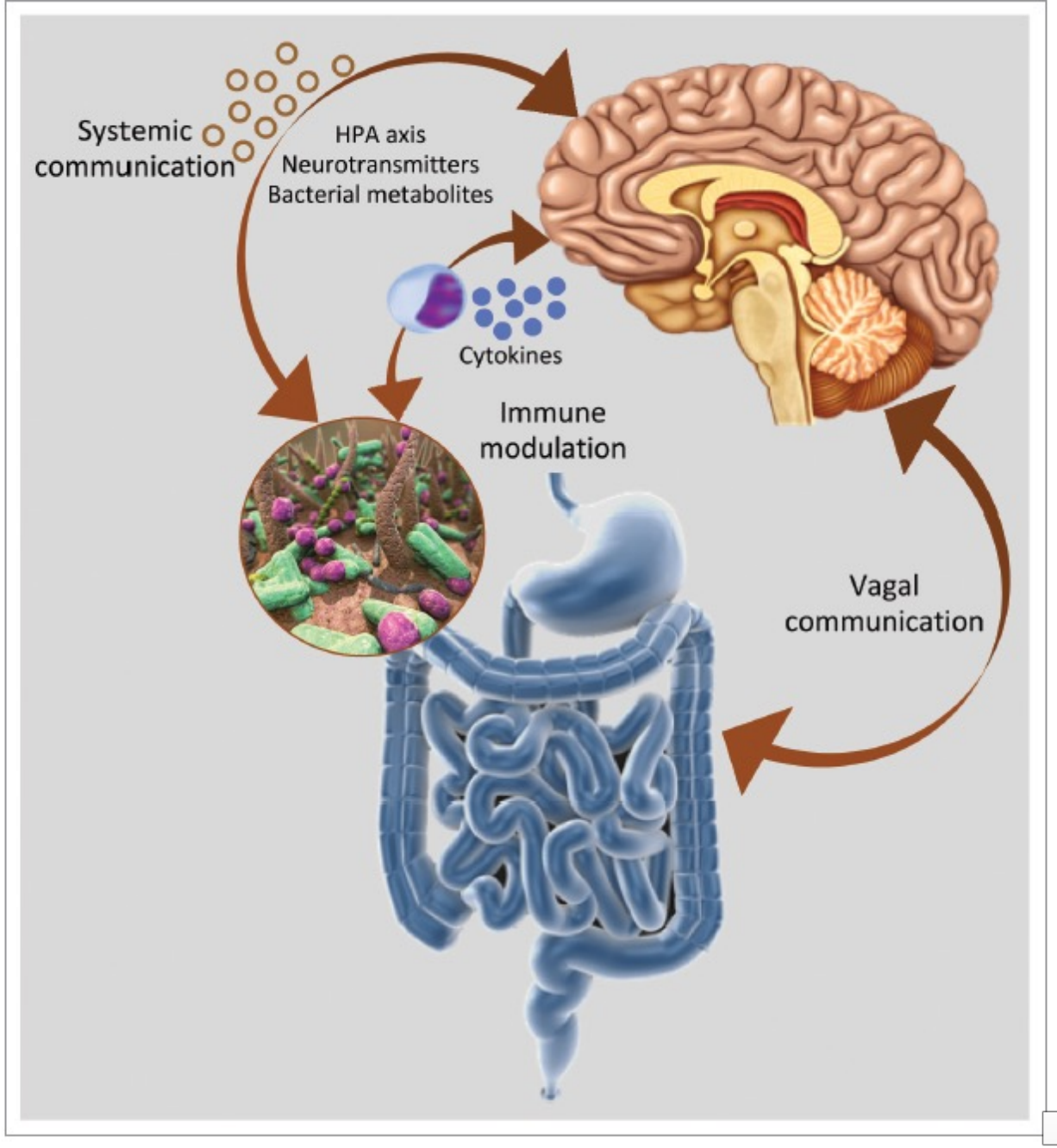
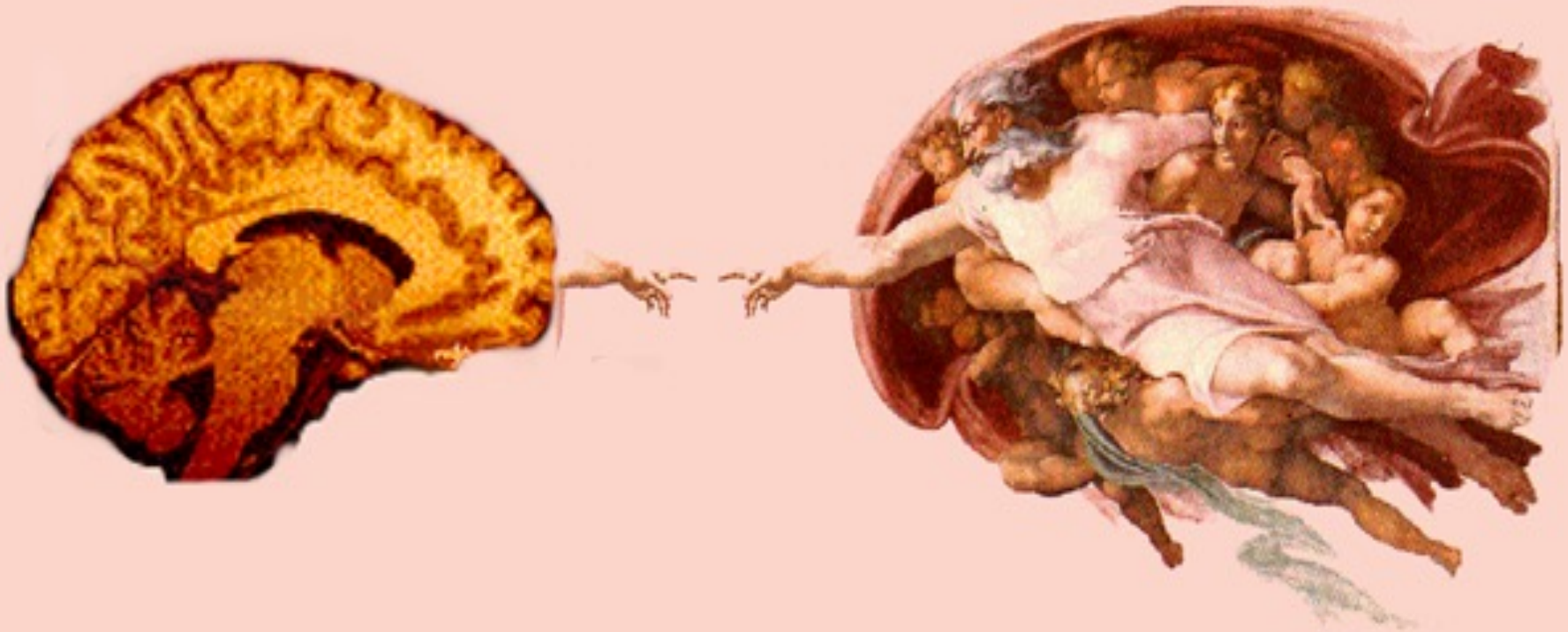
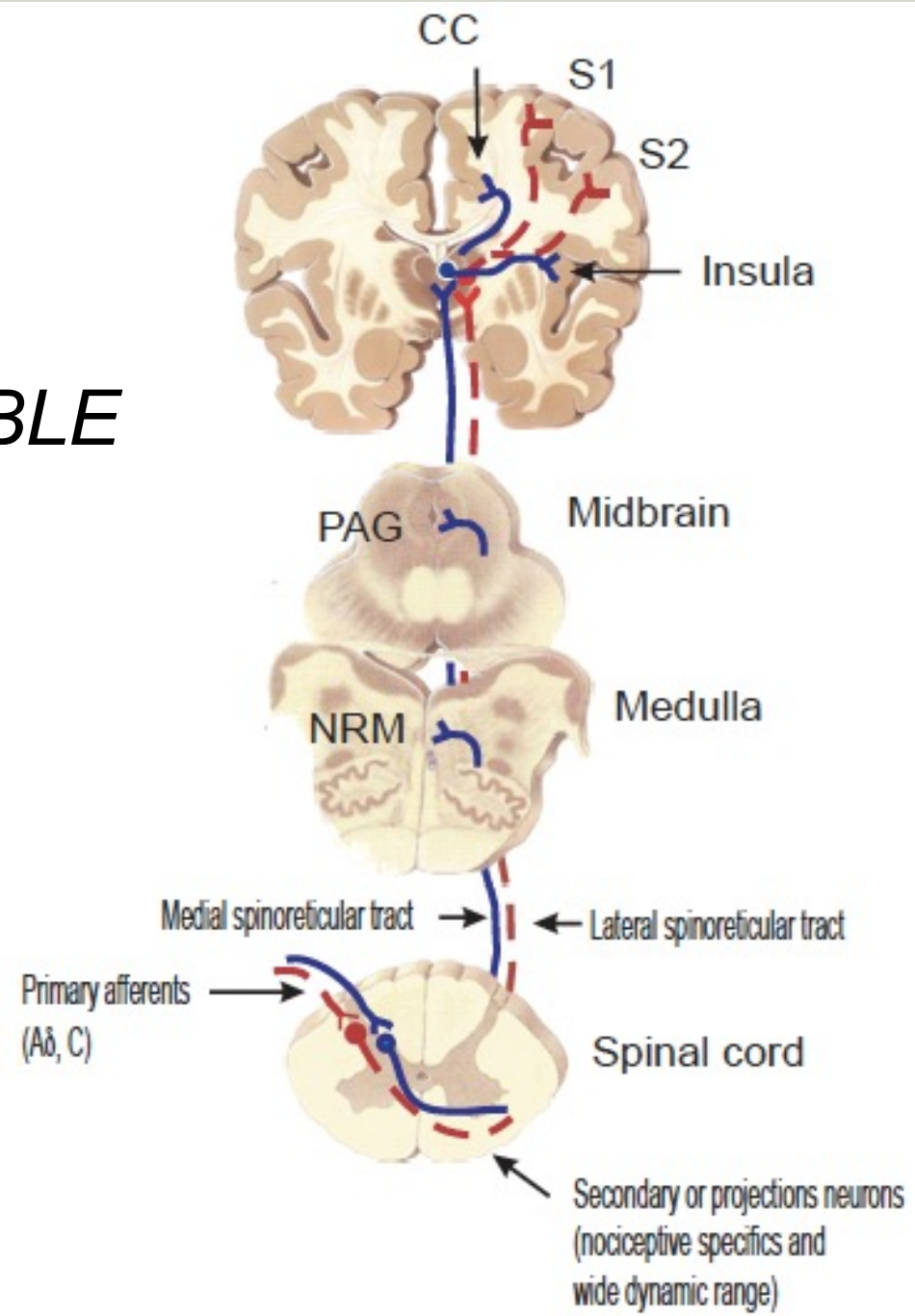


Figure 1. Potential routes of communication between the microbiota and the brain are shown. Multiple inputs from the periphery can act centrally to modulate mood, pain sensitivity, cognition, and behavior.

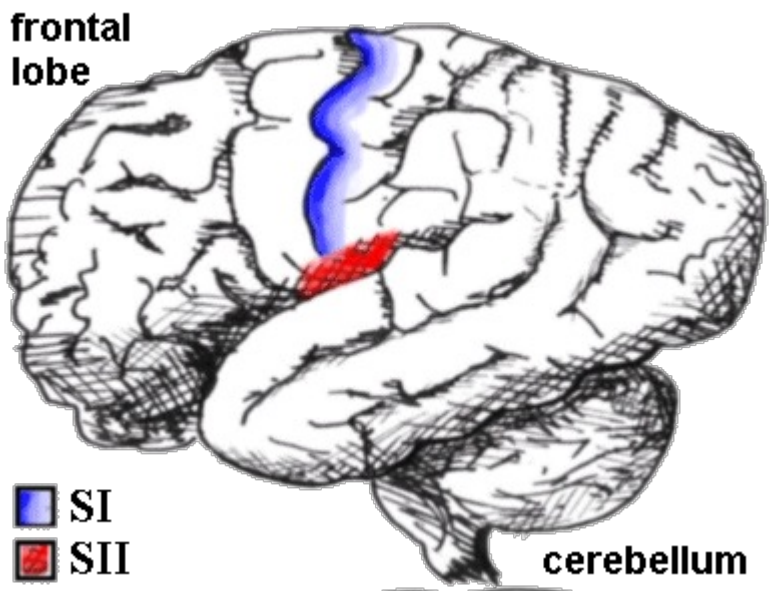
Centres supérieurs et douleur

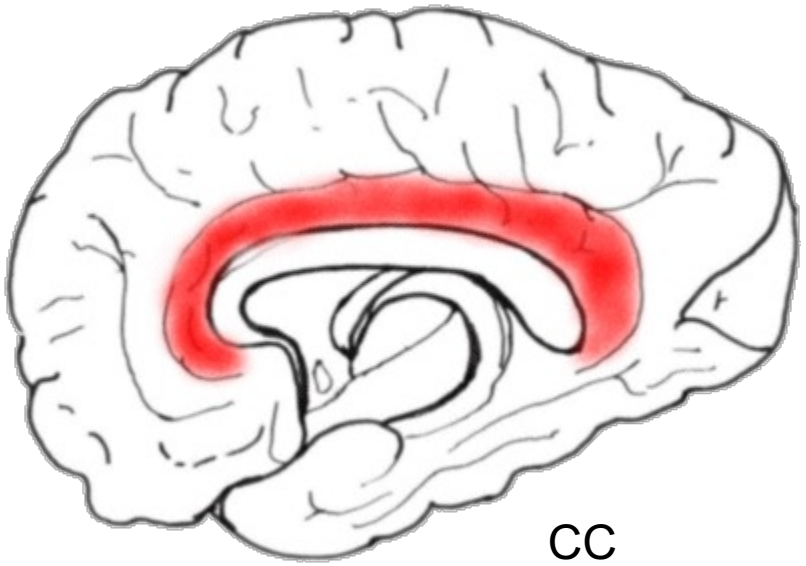


INTENSITÉ
ET
ASPECT DÉSAGRÉABLE

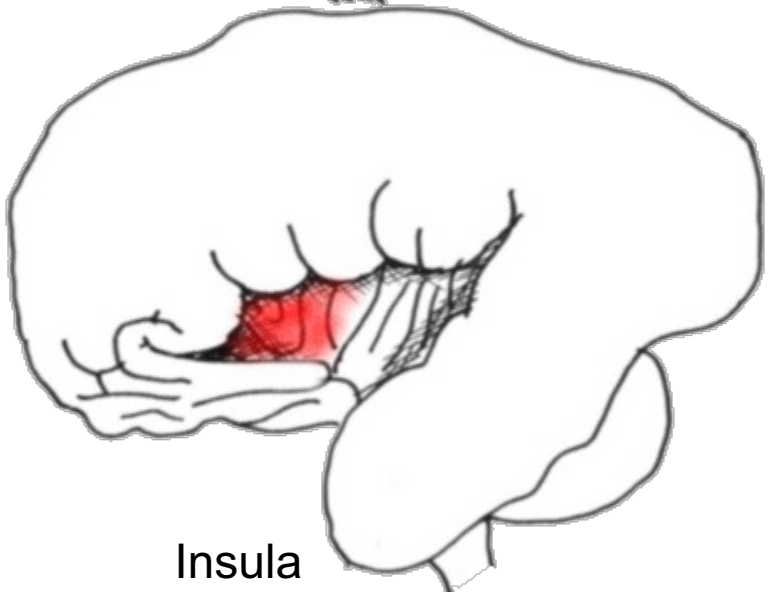


Quatre régions majeures qui sont activées lors de douleurs



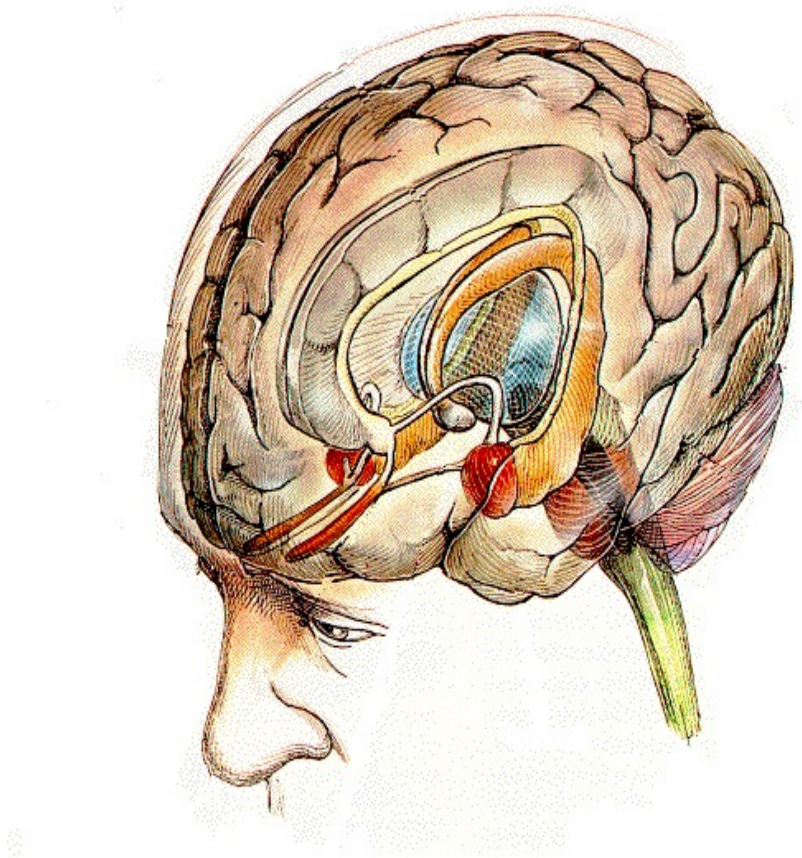


CC



Insula

Système limbique



Influencé par :

Attentes

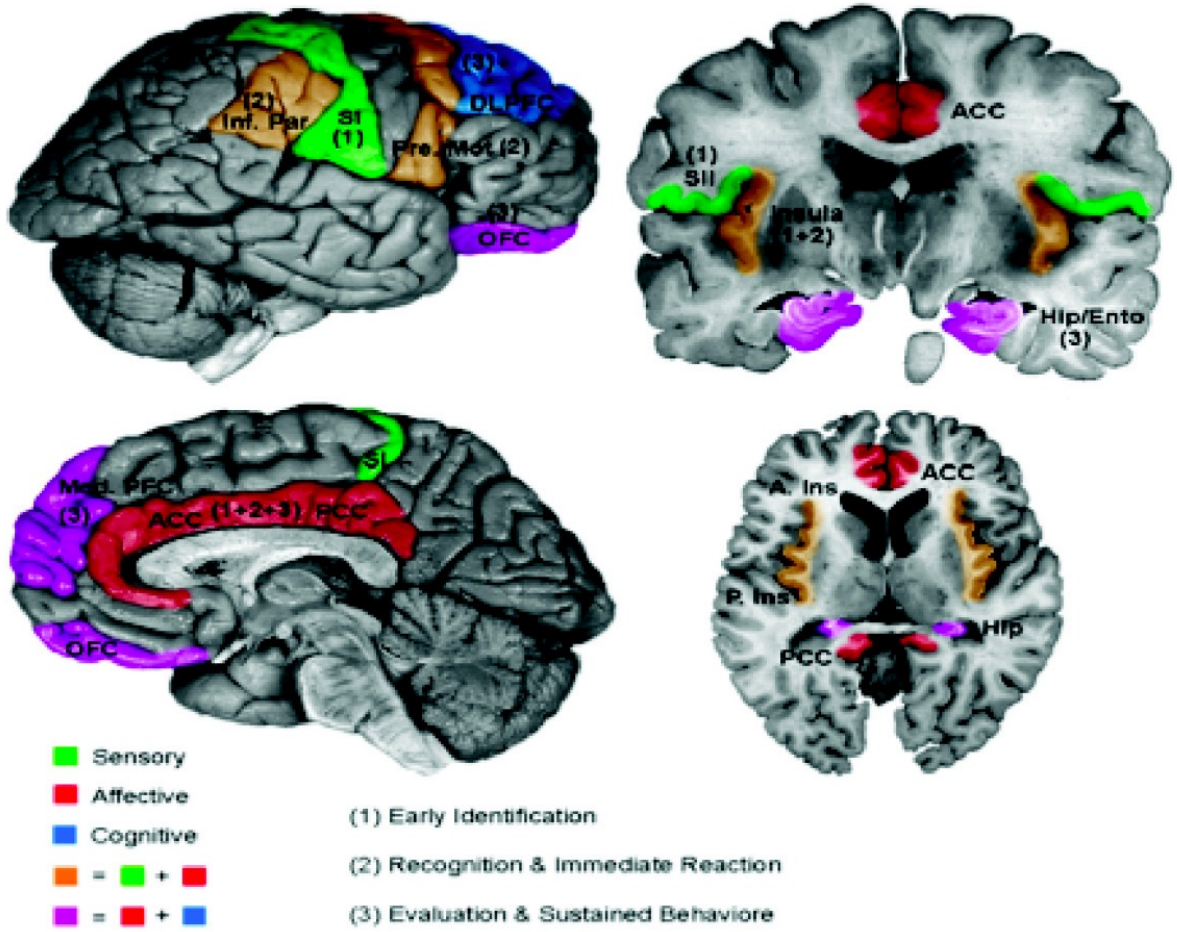
Émotions

Anxiété

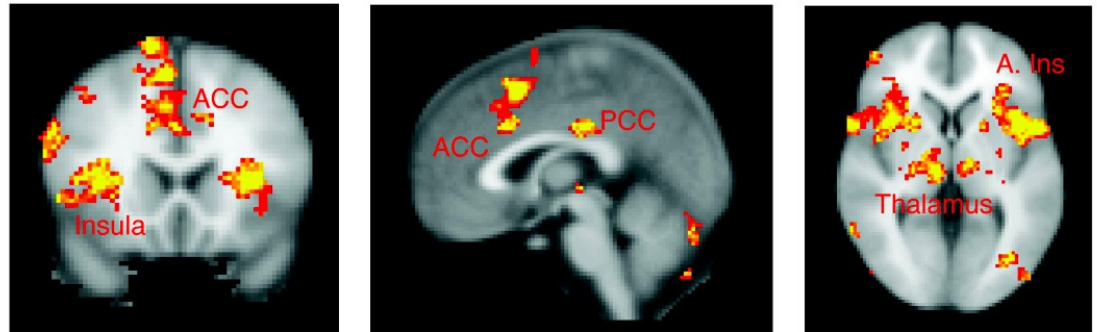
…

Functional measures

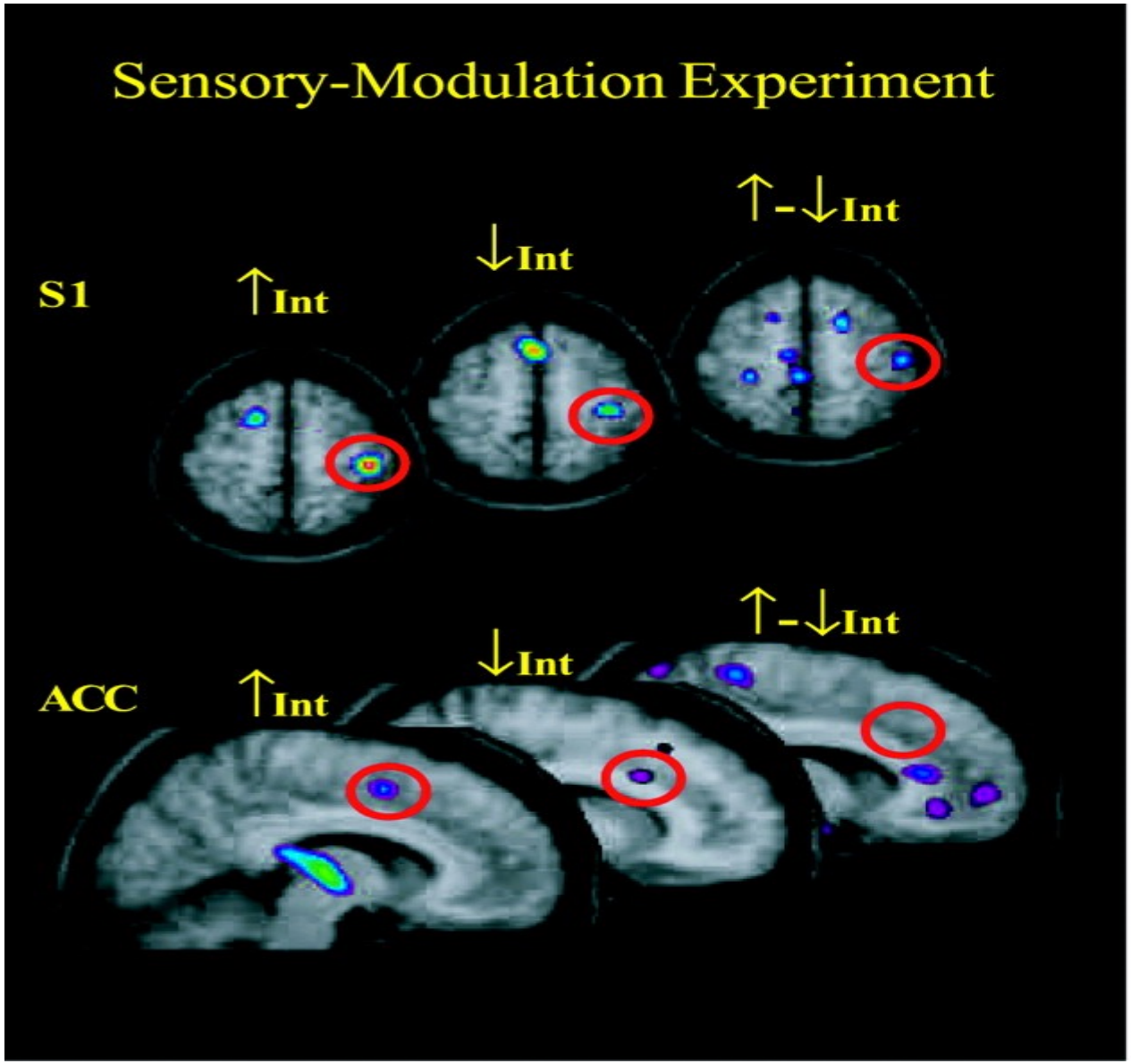
A. Brain areas functionally related to pain processing.

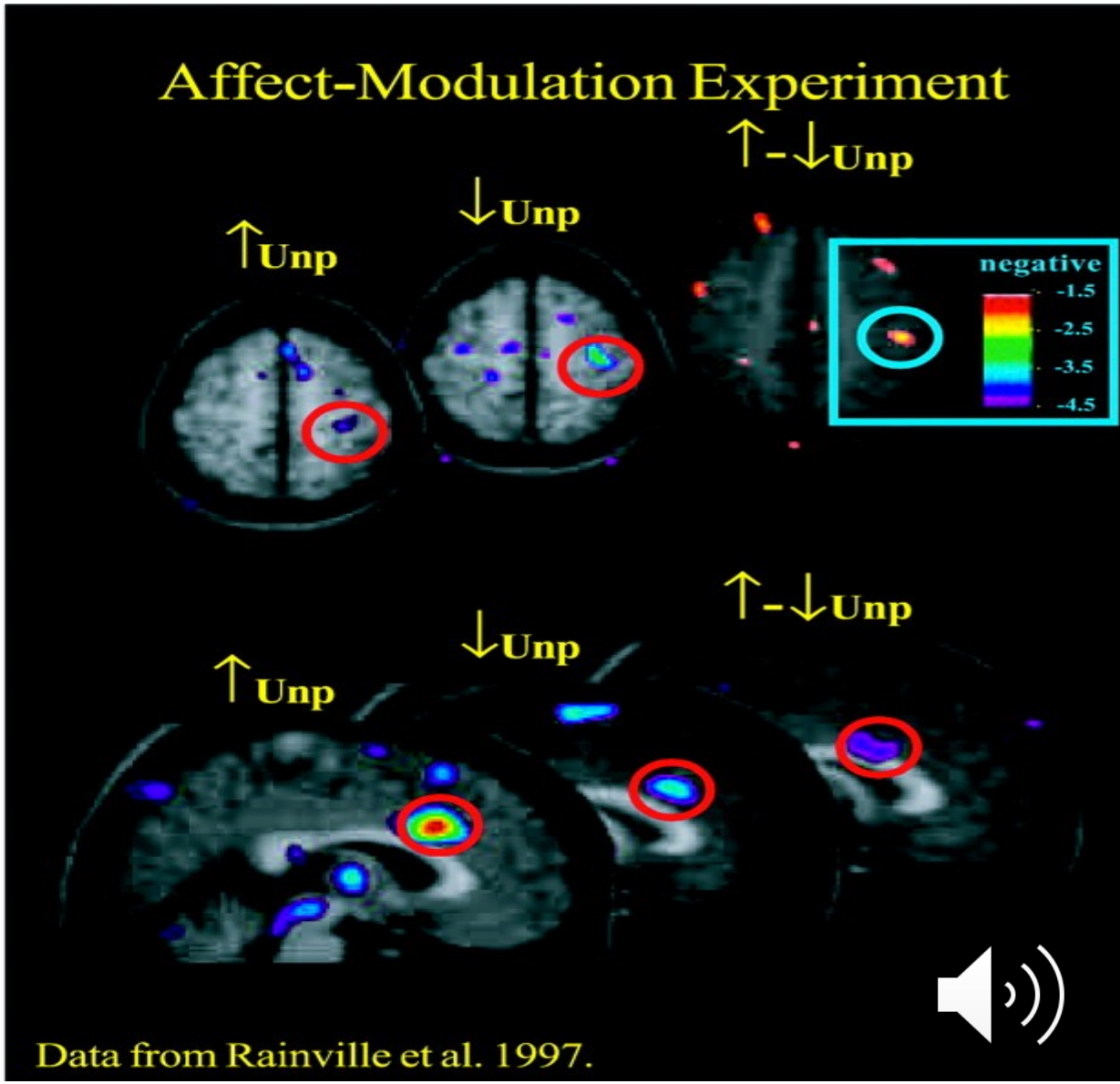


B. Example of functional MRI response to painful stimulation.

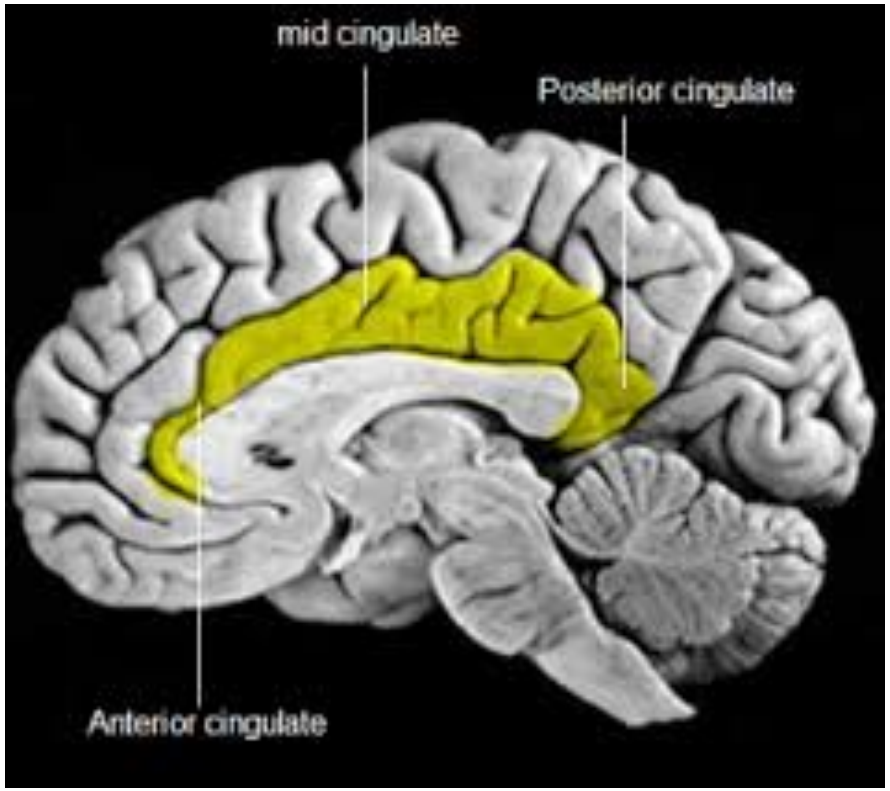


Manipulations indépendantes des composantes sensorielles et affectives de la douleur





Cortex cingulé

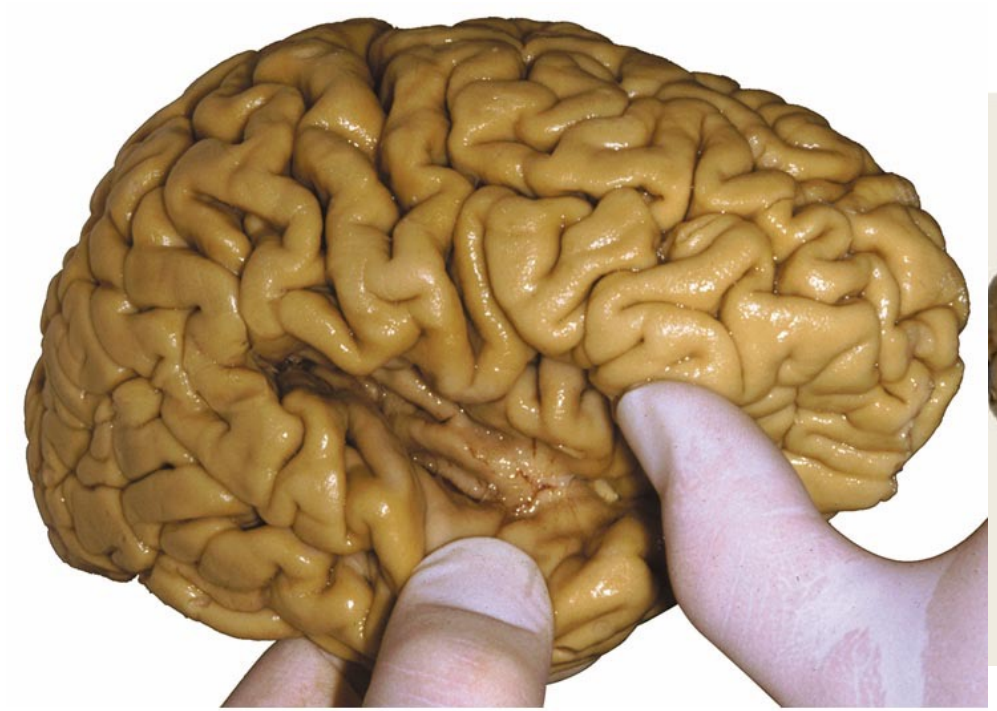


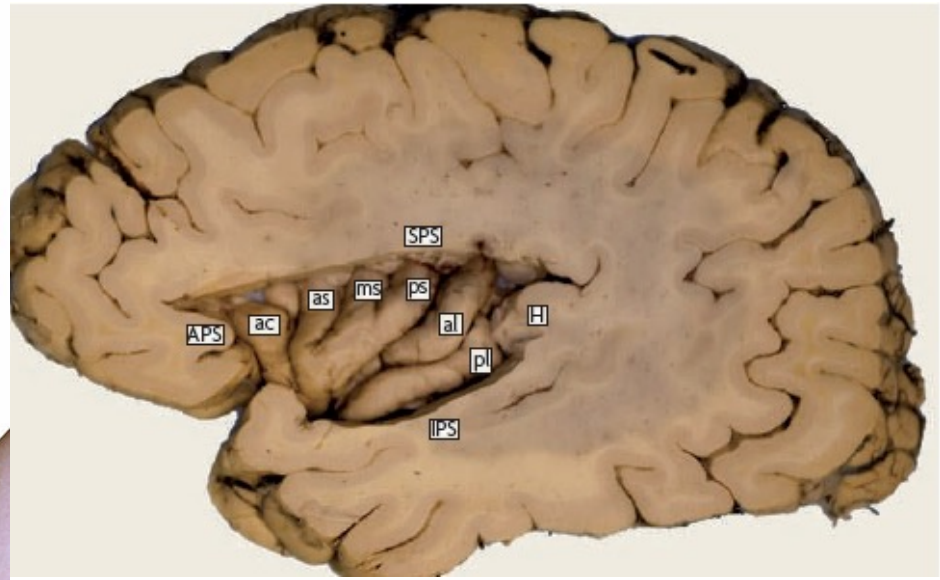
CCA: Émotions et douleur
CCA: Peur et douleur
CCP: Salience

OPINION

How do you feel — now? The anterior insula and human awareness

A. D. (Bud) Craig





OPINION

How do you feel — now? The anterior insula and human awareness

A. D. (Bud) Craig

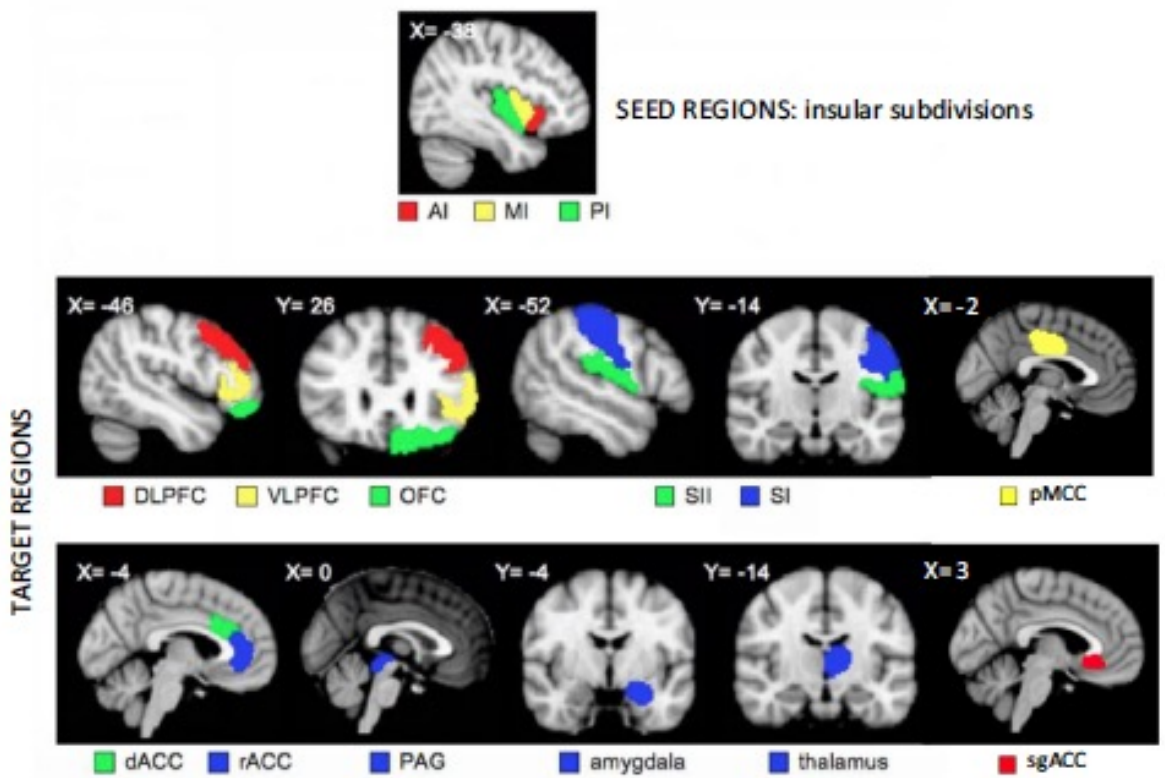
PAIN® 155 (2014) 2047–2055

PAIN®

www.elsevier.com/locate/pain

Differential structural and resting state connectivity between insular subdivisions and other pain-related brain regions

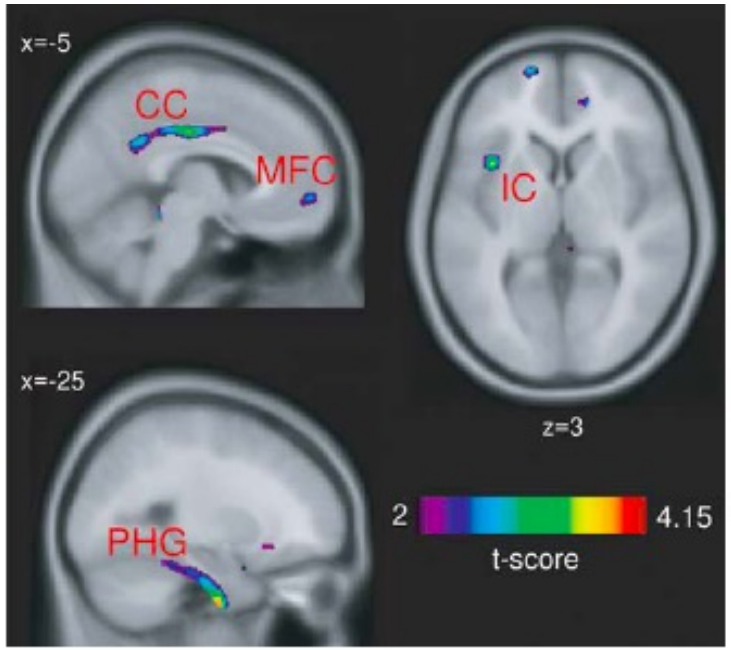
K. Wiech [a,b,*], S. Jbabdi [a], C.S. Lin [a,b], J. Andersson [a], I. Tracey [a,b]

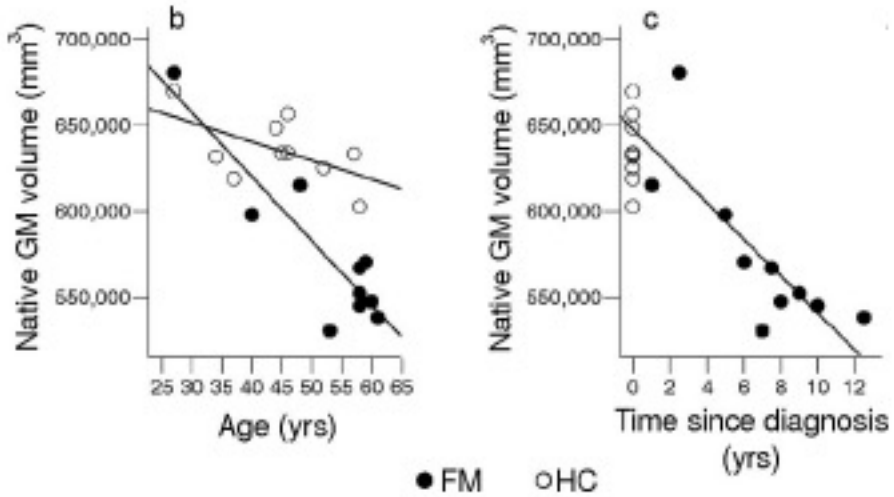


Effet de la douleur sur le cerveau

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

Anil Kuchinad,[1,2] Petra Schweinhardt,[1] David A. Seminowicz,[1] Patrick B. Wood,[1] Boris A. Chizh,[4] and M. Catherine Bushnell[1,2,3]

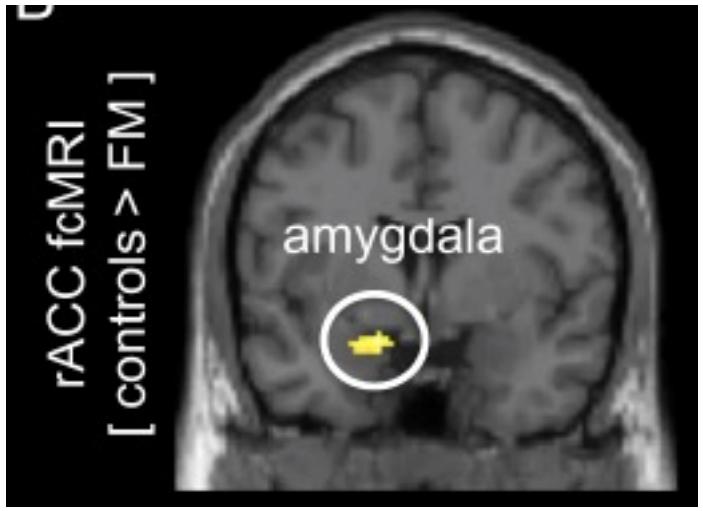




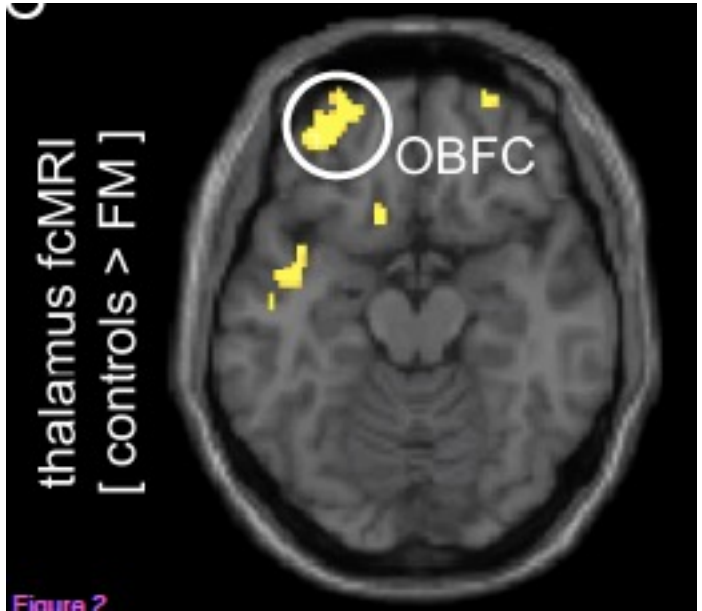
The Journal of Neuroscience, April 11, 2007 • 27(15):4004 – 4007

Patients With Fibromyalgia Display Less Functional Connectivity In The Brain's Pain Inhibitory Network

Molecular Pain 2012, **8**:32 doi:10.1186/1744-8069-8-32



Patients with FM displayed less connectivity within the brain‟s pain inhibitory network during calibrated pressure pain, compared to healthy controls.



Pain 137 (2008) 7–15

PAIN

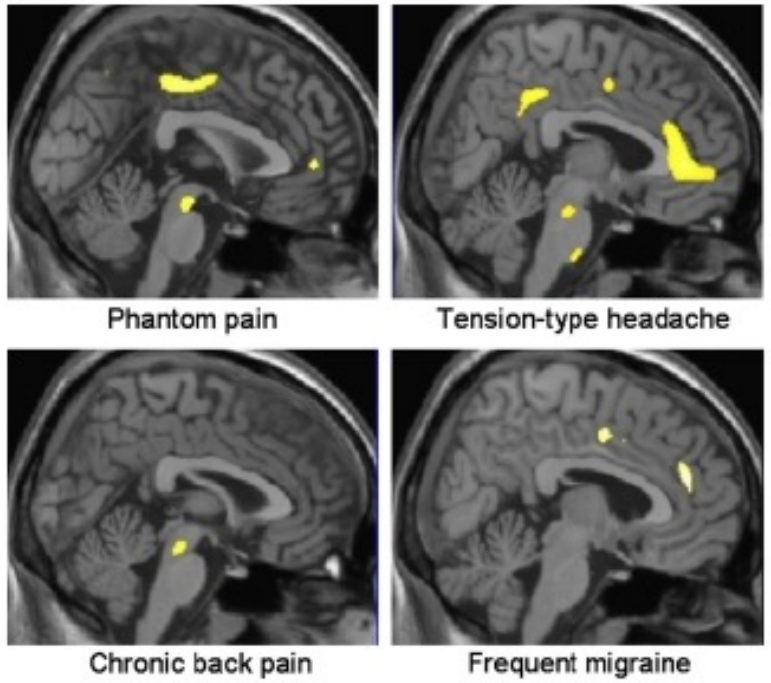
www.elsevier.com/locate/pain

Review

Chronic pain may change the structure of the brain

Arne May*

Statistical parametric maps demonstrating the structural difference in gray matter between chronic pain patients and unaffected control subjects. Significant gray matter decrease is shown for each single group of patients, compared to match healthy controls and is superimposed in yellow color on a normalized image of a healthy control subject.



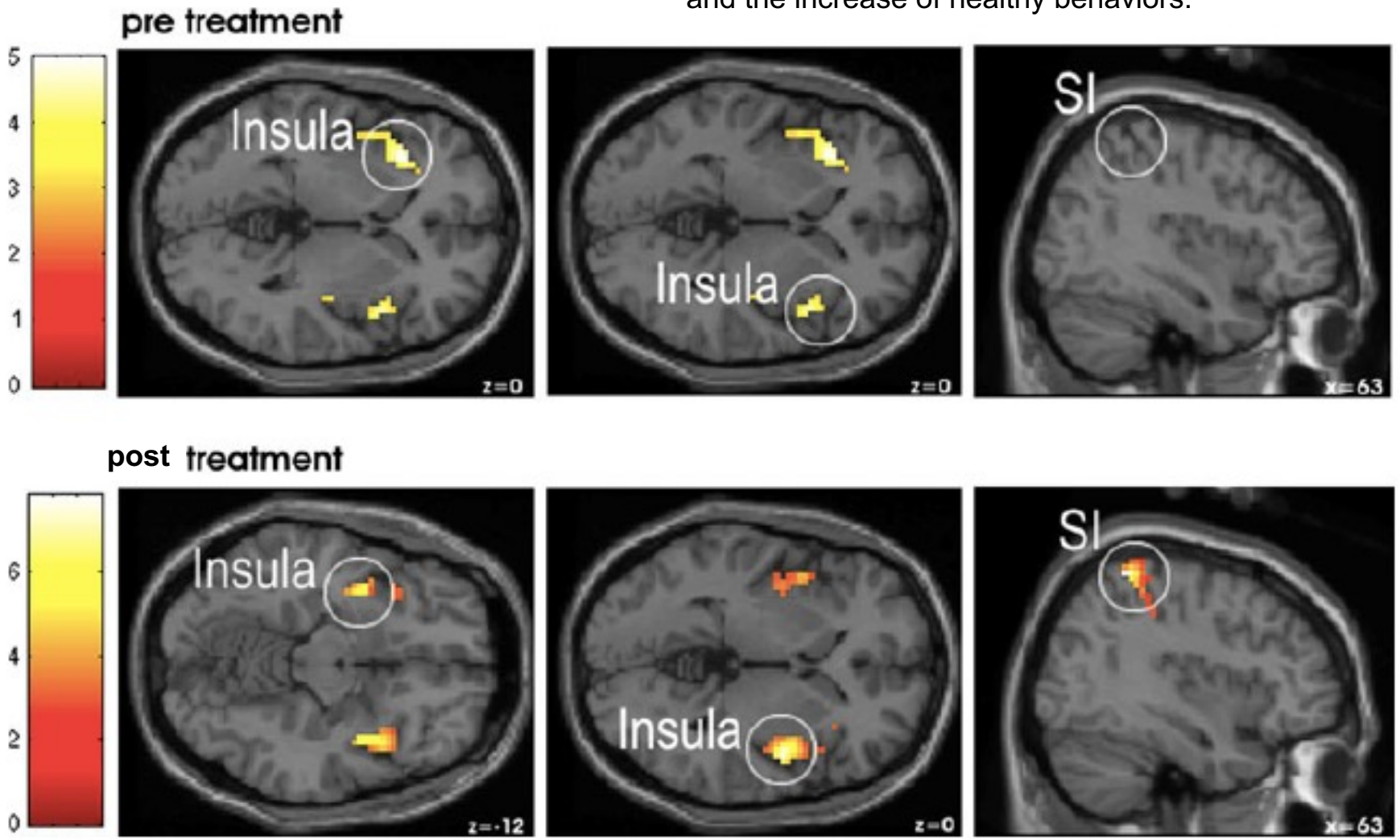
Pas uniquement pour les patients qui souffrent de fibromyalgie !

Treatment-related changes in brain activation in patients with fibromyalgia syndrome

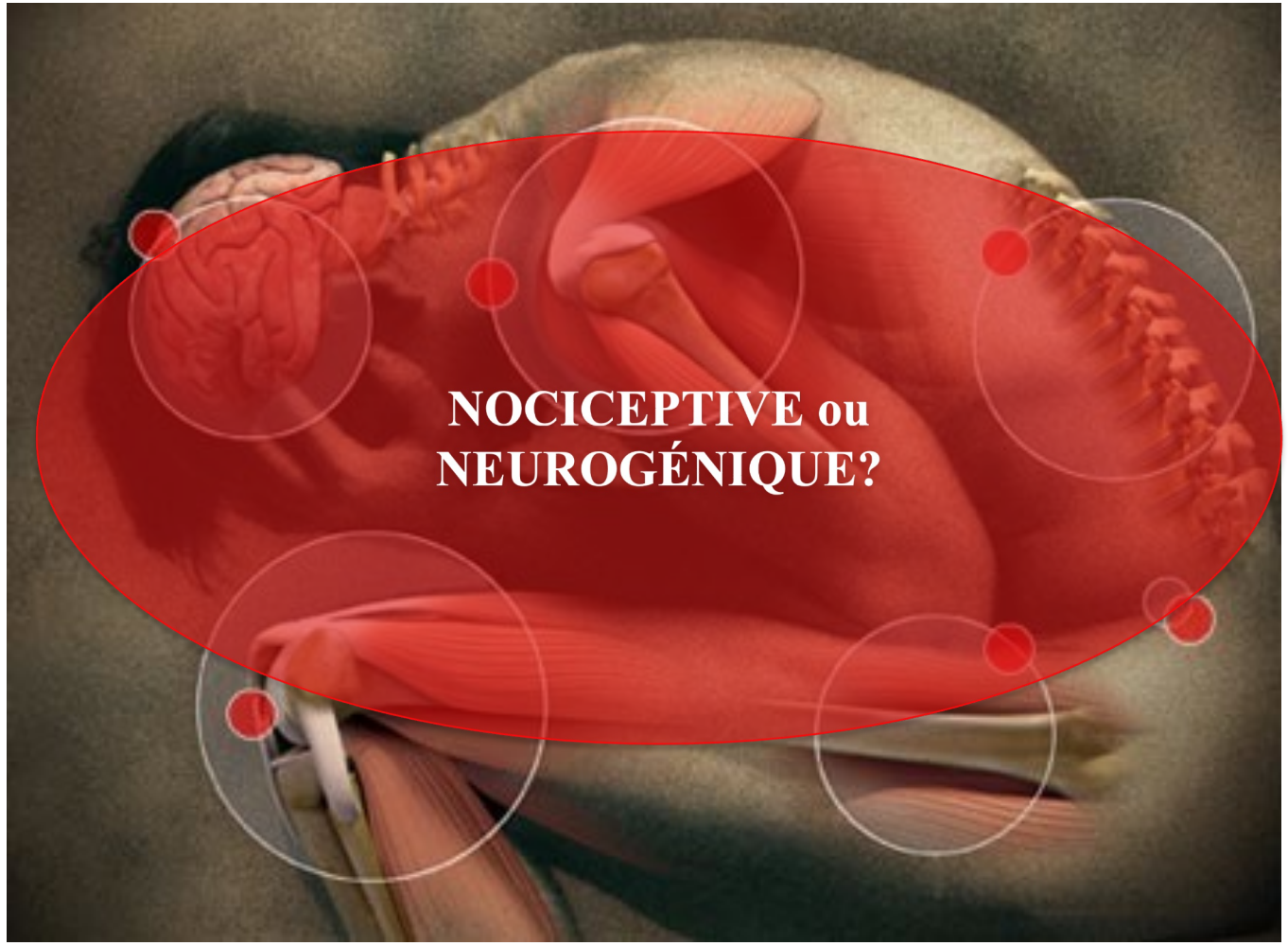
Martin Diers · Pinar Yilmaz · Mariela Rance · Kati Thieme · Richard H. Gracely · Claudia Rolko · Marcus T. Schley · Ulrike Kiessling · Haili Wang · Herta Flor

Exp Brain Res (2012) 218:619–628

The treatment consisted of 12 weekly 2-h sessions led and focused on the extinction of pain-related behaviors and the increase of healthy behaviors.



Douleur



Le patient a mal, mais il souffre de quoi?

Nociceptive

•Réponse à la suite d'une stimulation potentiellement dangereuse pour l'organisme (mécanique, chimique, thermique)

•Lacération, fracture, ischémie…

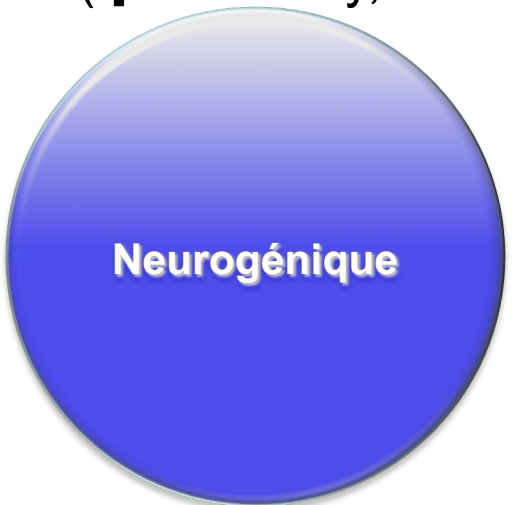
Le patient a mal, mais il souffre de quoi?

Neurogénique

•Douleur à la suite d'une lésion ou une dysfonction du SNC

•Lésion nerf, neuropathies, sensibilisation centrale…

•Sensibilisation centrale : Dysfonction des mécanismes endogènes de modulation (↑excitatory, ↓ inhibitory)



Centre hospitalier universitaire de Sherbrooke
Centre de recherche clinique Étienne-Le Bel

Nociceptive ou neurogénique?

Nociceptive

Neurogénique

Centre hospitalier universitaire de Sherbrooke
Centre de recherche clinique Étienne-Le Bel

Conclusion

- De la périphérie aux centres supérieurs, le signal nociceptif est modulé avant de devenir une douleur.
- Même pour les douleurs chroniques centralisées, il est important de vérifier si une composante nociceptive participe au maintien de la douleur.