

# Que significa “DOLOR” ?

**Jordi Montero Homs**

EX

NEUROLOGO DE “A PIE”

NEUROFISIOLOGO CLINICO DE UN HOSPITAL GRANDE

MIEMBRO ACTIVO DE UNA UNIDAD HOSPITALARIA DE DOLOR

PROFESOR DE NEUROLOGIA EN LA UNIVERSIDAD

DIRECTOR DE MASTERS INERNACIONALES DE ELECTRODIAGNOSTICO NEUROLOGICO

MEDICO DE FAMILIA EN EL BARRIO DE SINGUERLIN

PIONERO DEL SISTEMA MIR

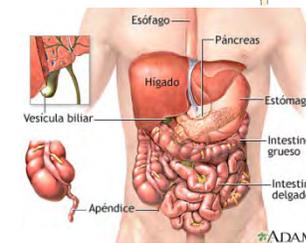
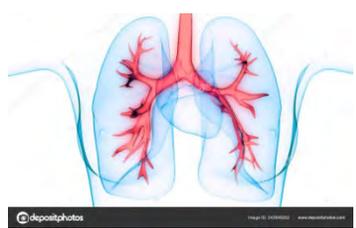
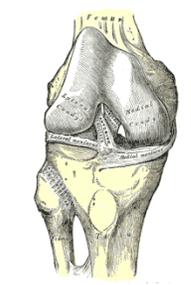
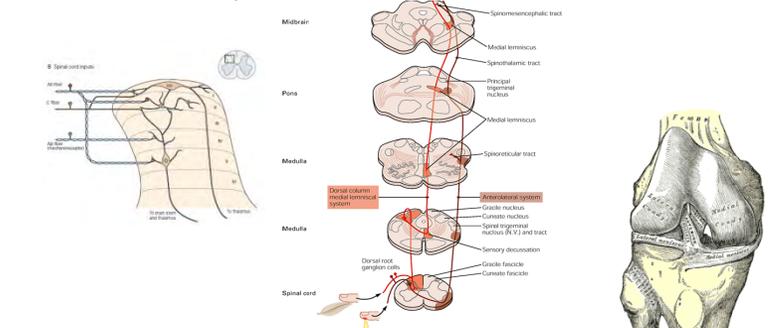
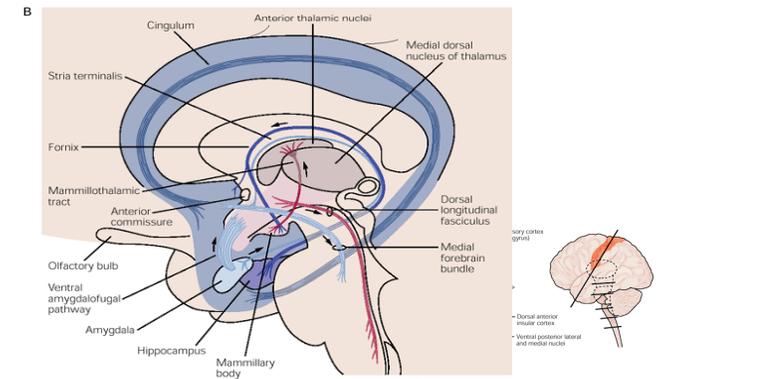
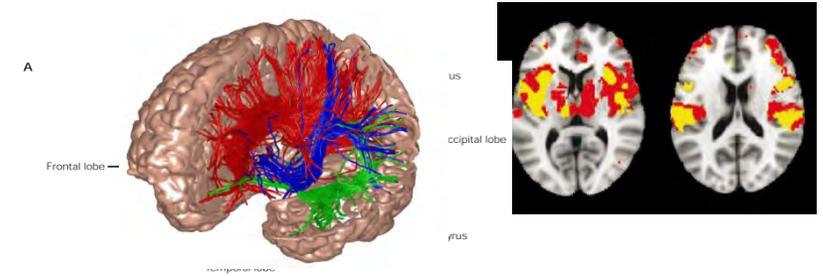
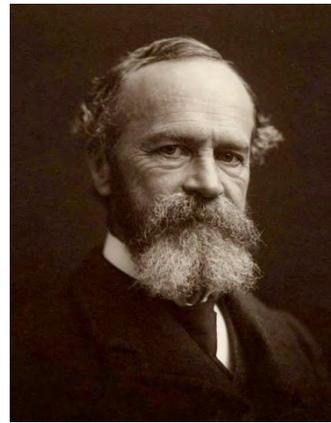
MIEMBRO NUMERARIO DE HONOR DE LA SOCIEDAD ESPAÑOLA DE NEUROLOGIA

AUTOR DE LIBROS SOBRE “DOLOR CRONICO” Y SOBRE EMOCIONES

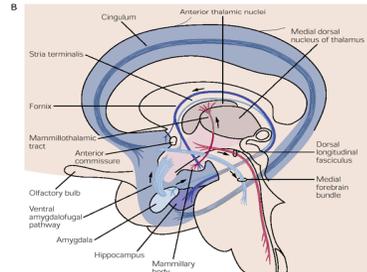
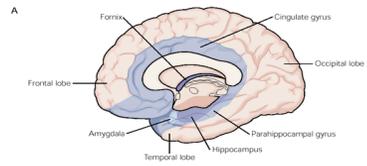
AFICIONADO A LA **NEUROCIENCIA COGNITIVA** DEL SIGLO XXI

# William James

(1842-1910)

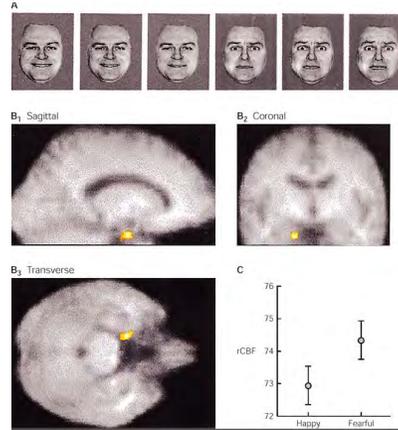


# Daño:

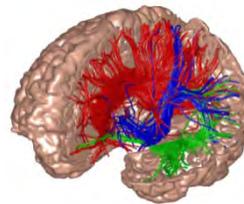


.Damasio

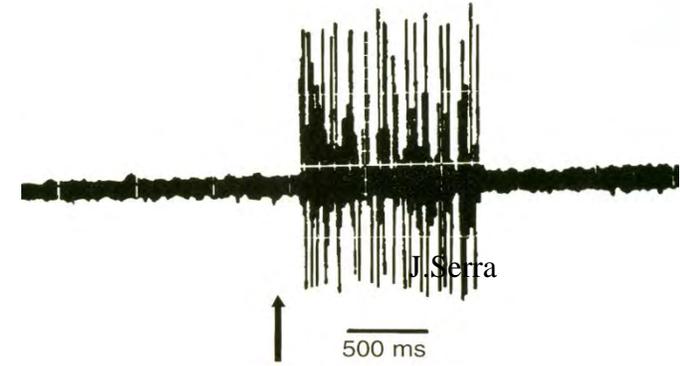
# Emoción



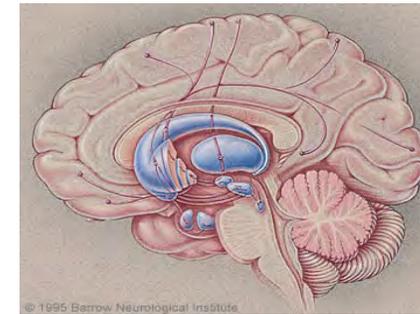
# Miedo



Planificación  
conducta

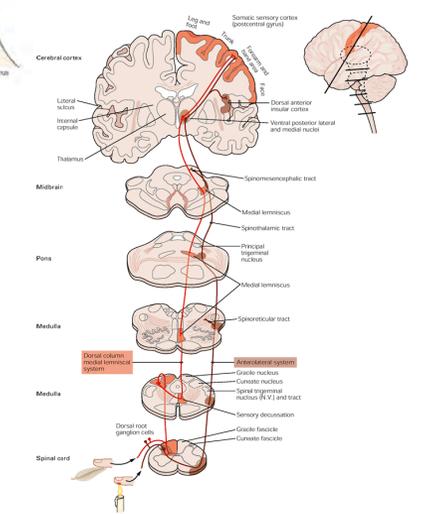
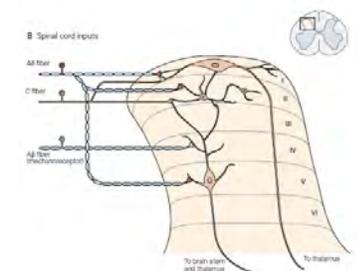
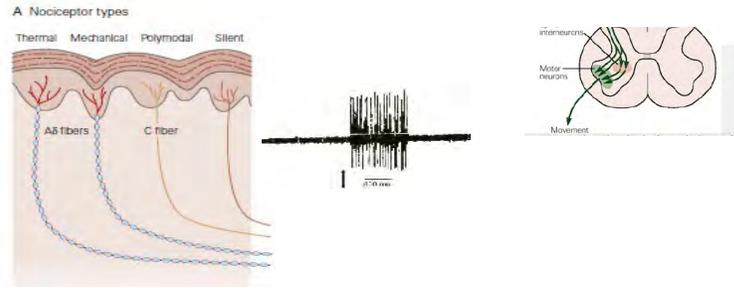


# Sensación

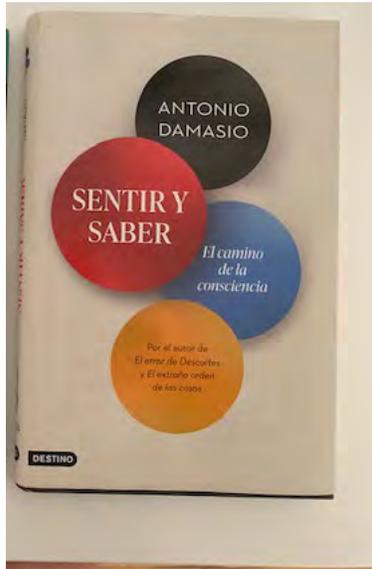
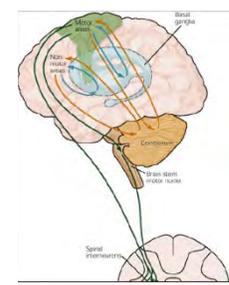
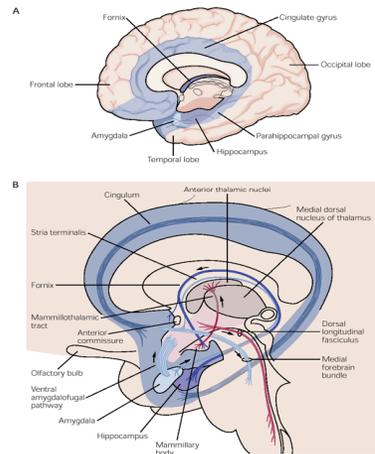


Movimiento  
de huida

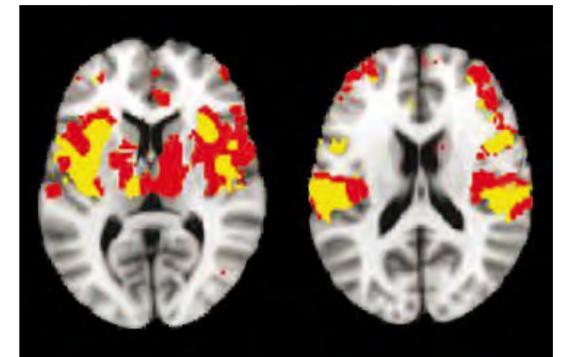
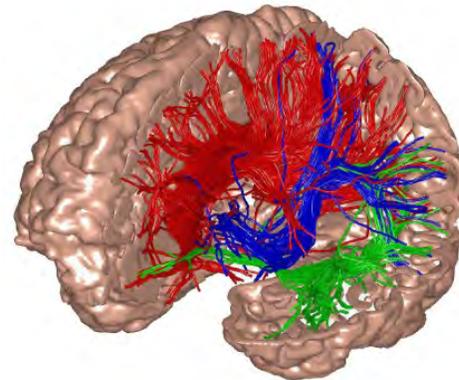
# SENSACION



# EMOCION



# SENTIMIENTO



# DOLOR

Experiencia sensorial desagradable asociada a daño tisular real o potencial, o que es vivida como tal daño.

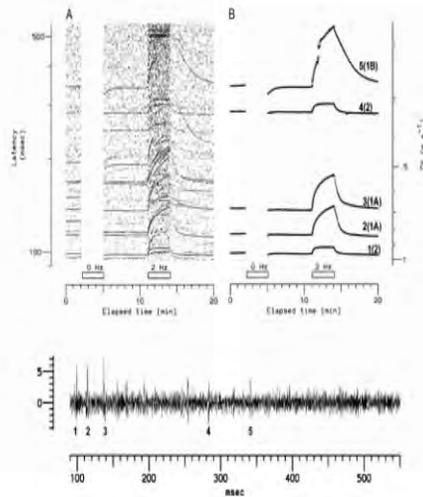
*Merskey 1964, IASP (Pain 1986:3:S1-226)*

# DOLOR

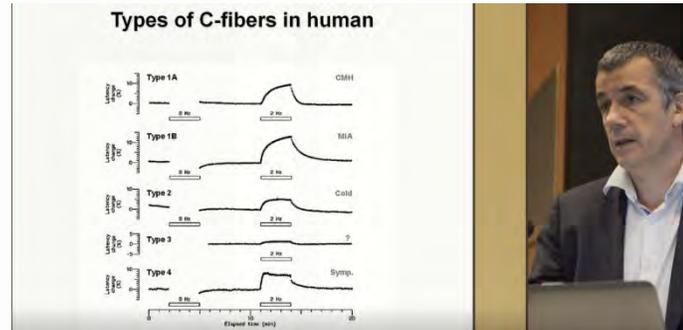
# NOCIOCEPCION

## NOCICEPTORES AMIELINICOS

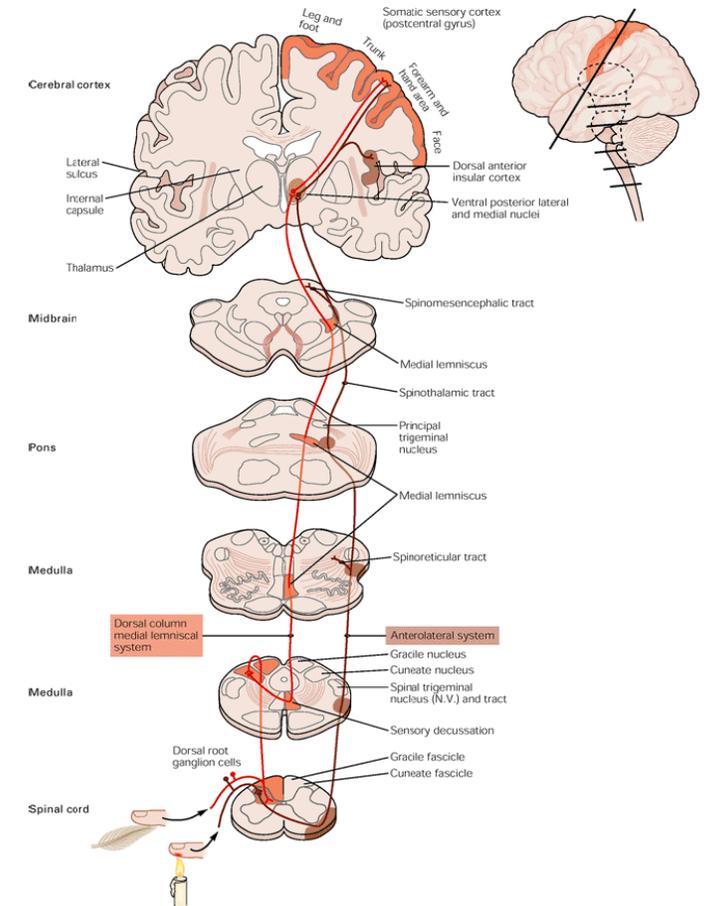
- 1) SENSIBLES.....Polimodales
  - .....Mecánicos
  - .....De calor
- 2) INSENSIBLES (“silentes”) (M=mecánico H=térmico)
  - .....CMi Hi
  - .....CMi H
  - .....CM Hi



- 1A ..... CMH
- 1B ..... Insensibles
- 2 ..... Frío
- 3 ..... ?
- 4 ..... Simpáticos

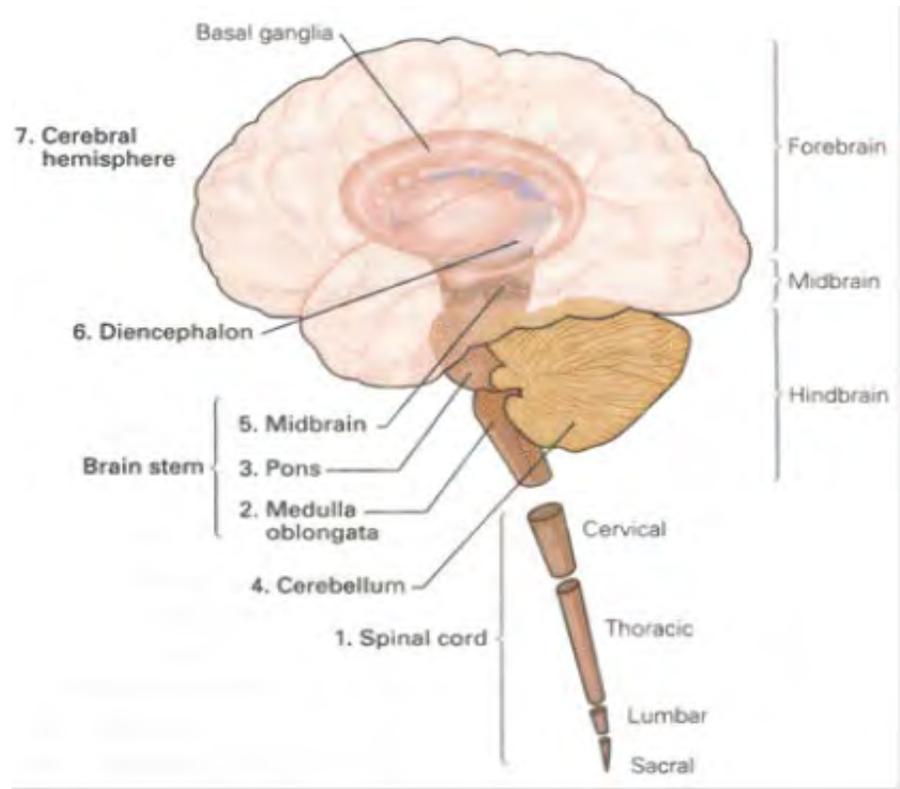


Serra J. SEN 2004



**DOLOR AGUDO**

**DOLOR “SISTEMA DE DEFENSA”**



Ciencia de la Evolución

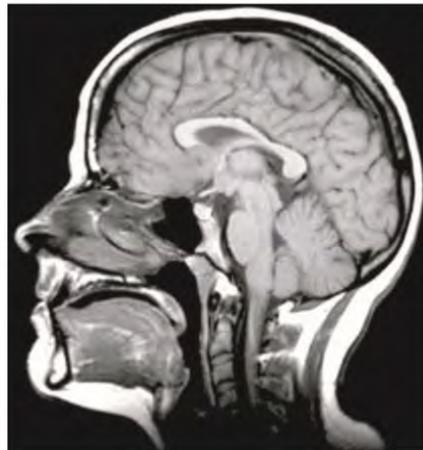
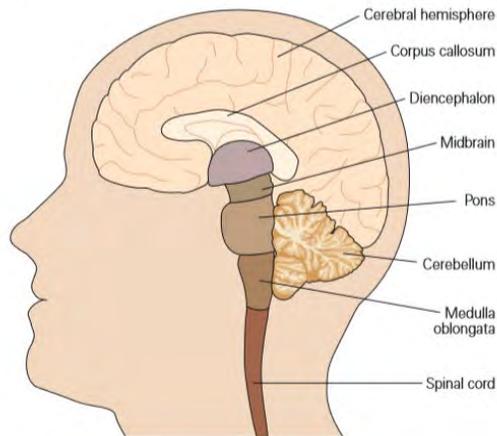
Imagen funcional

Neurofisiología

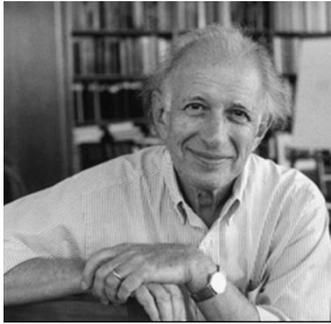
Neurociencia cognitiva

Evidencia del inconsciente

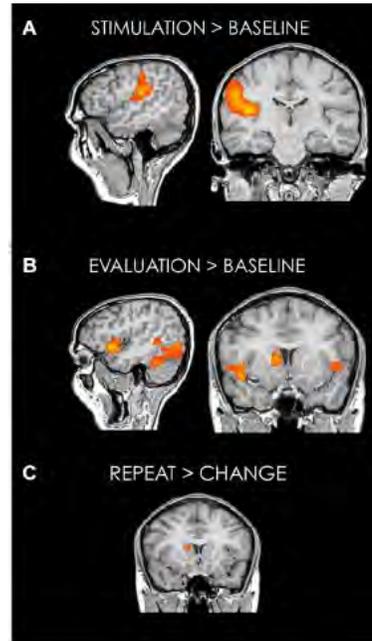
Neurofilosofía: el libre albedrío



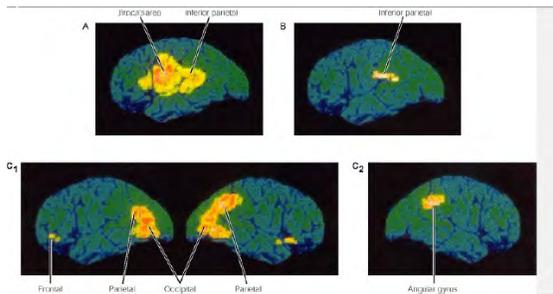
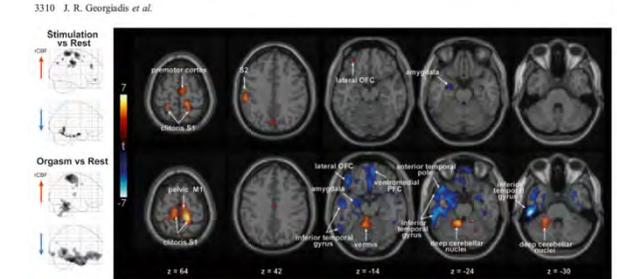
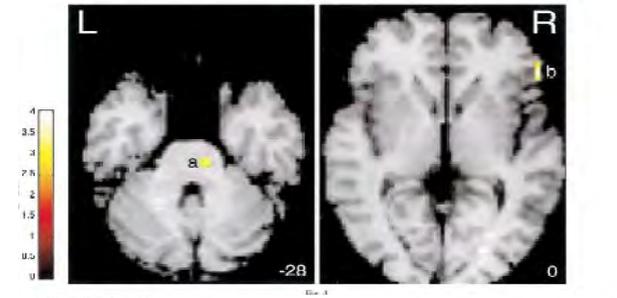
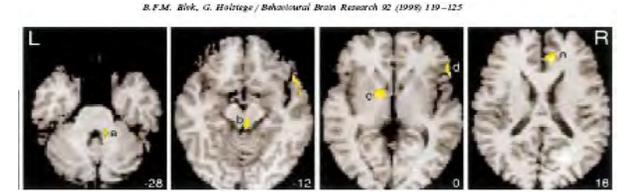
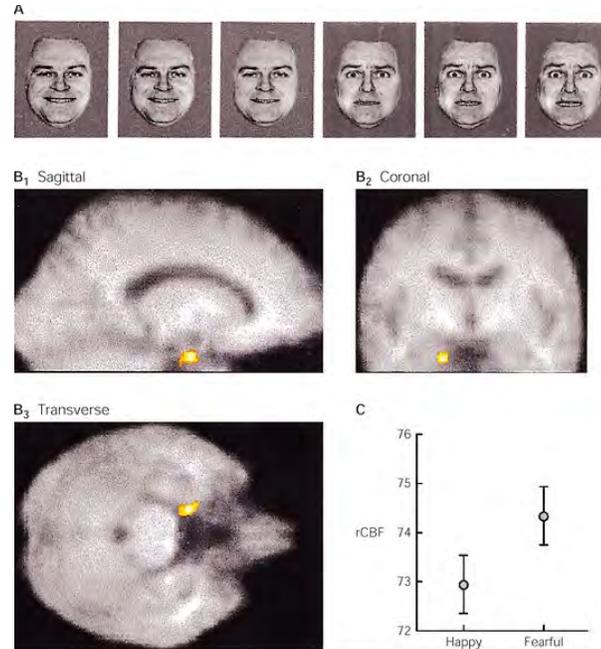
# Conocimiento del cerebro



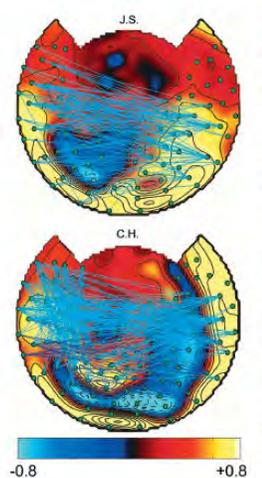
Erik Kandel  
Principles of Neural Science(2013)  
The disordered mind (2019)



## Neuroimagen Funcional



## Inconsciente



## Emociones /Homeostasis



Sentir y Saber  
A.Damasio 2021

## Neurociencia Cognitiva

# Aplicaciones de Tecnología a Redes Cerebrales

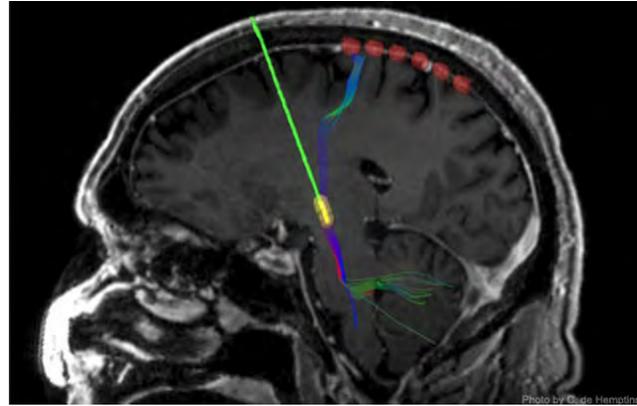
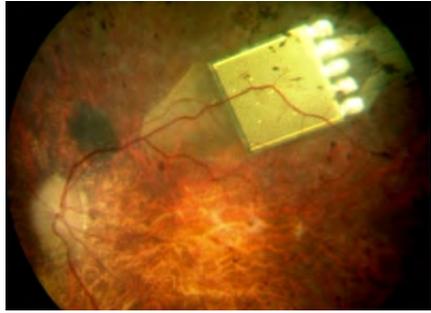
*J Neurophysiol* 95: 3297-3308, 2006.  
doi:10.1152/jn.00166.2006.

Invited Re

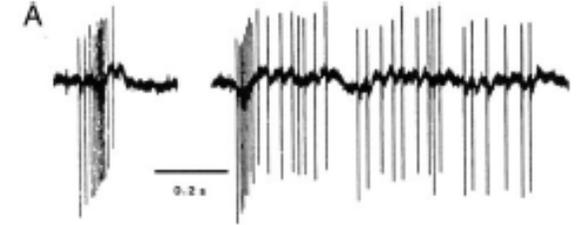
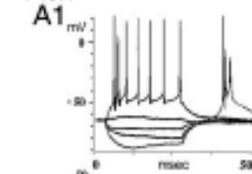
## Bursting of Thalamic Neurons and States of Vigilance

Rodolfo R. Llinás<sup>1</sup> and Mircea Steriade<sup>2</sup>

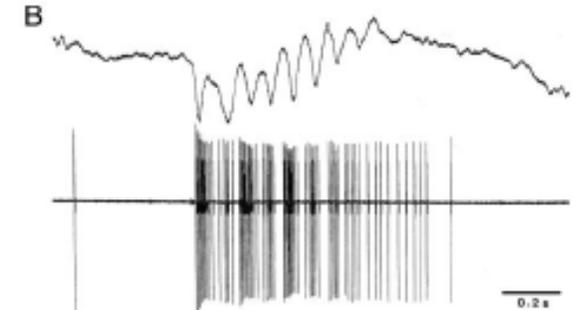
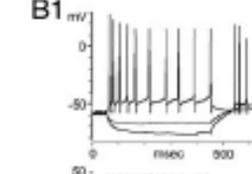
<sup>1</sup>Department of Physiology and Neuroscience, New York University School of Medicine, New York, New York; and <sup>2</sup>Laboratory of Neurophysiology, Faculty of Medicine, Laval University, Quebec, Canada



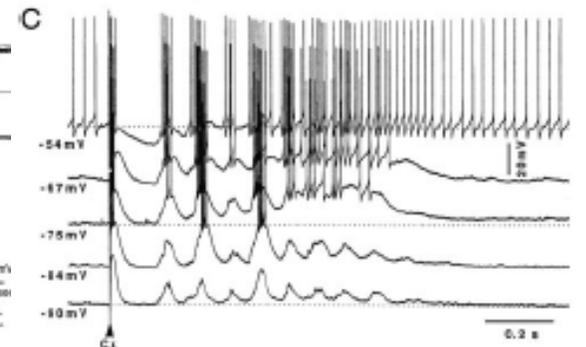
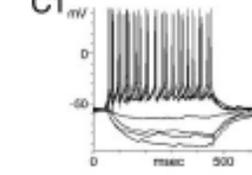
Fish Tonic & Burst Firing



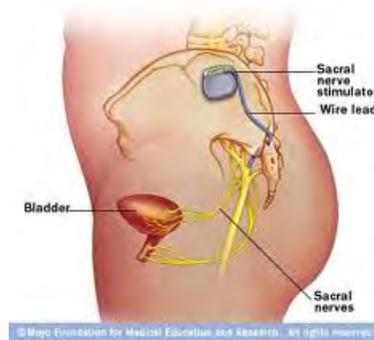
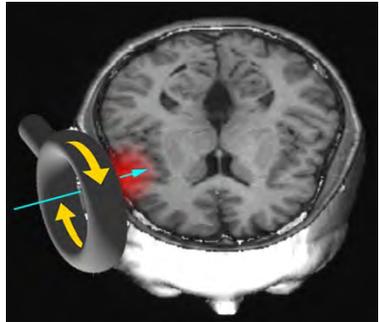
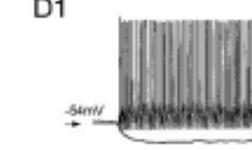
Frog B1



Turtle C1

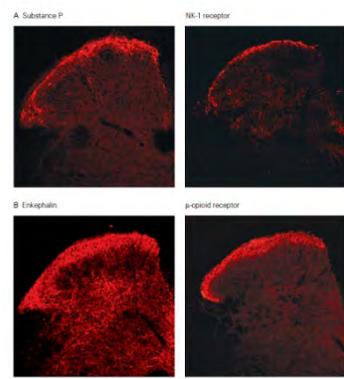
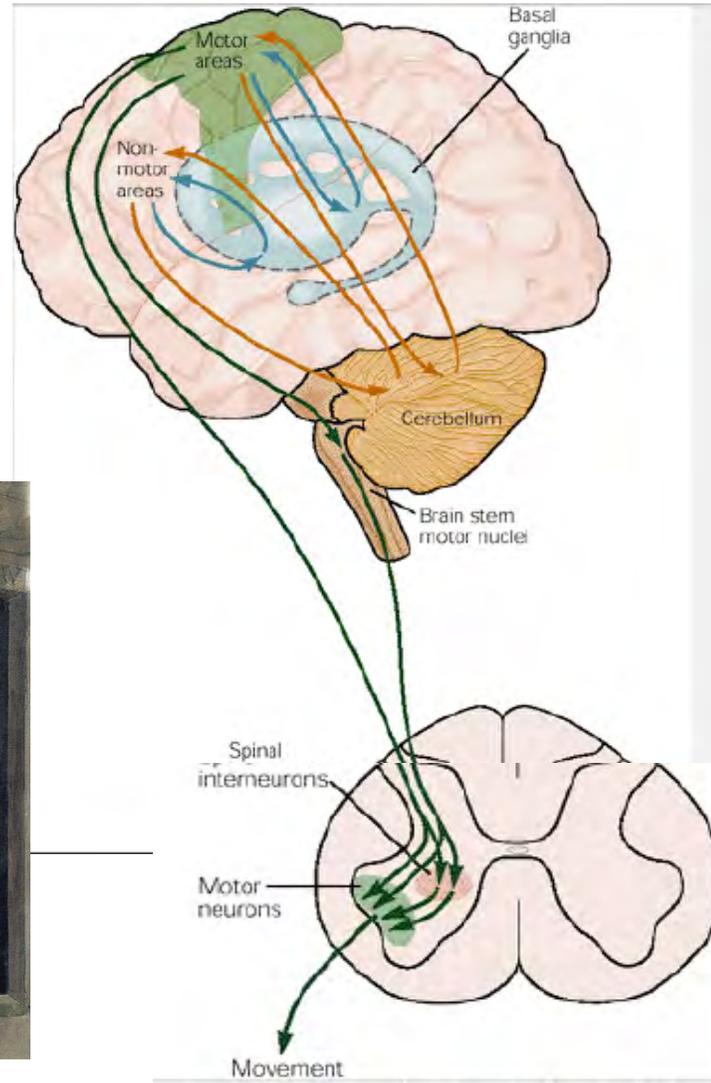


Bird D1



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“Vía final común”



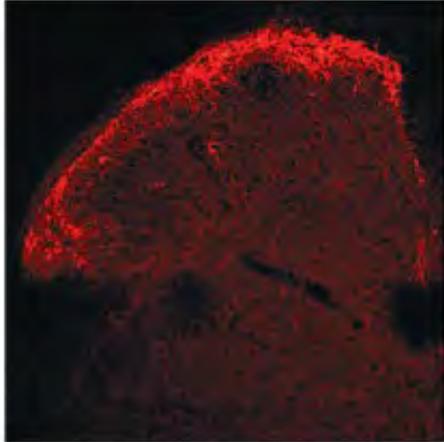
Allan I Basbaum  
Howard Fields

“Con las motoneuronas podemos talar un bosque o escribir una poesia”

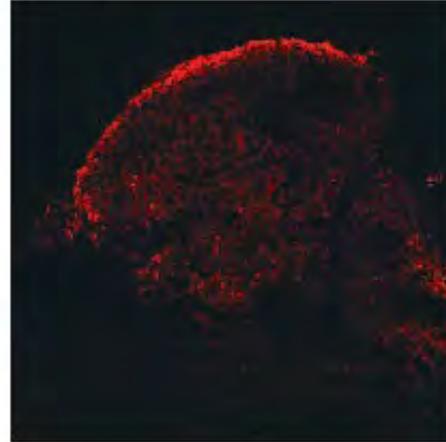
Charles Sherrington

# DOLOR AGUDO = DOLOR “SISTEMA DE DEFENSA”

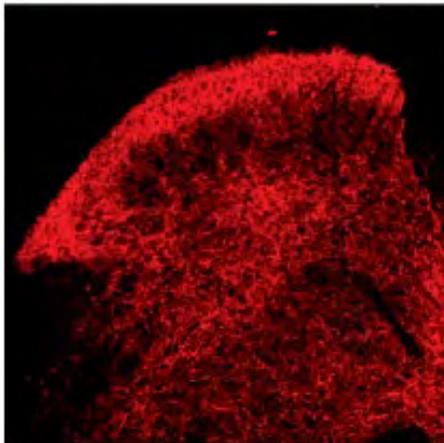
A Substance P



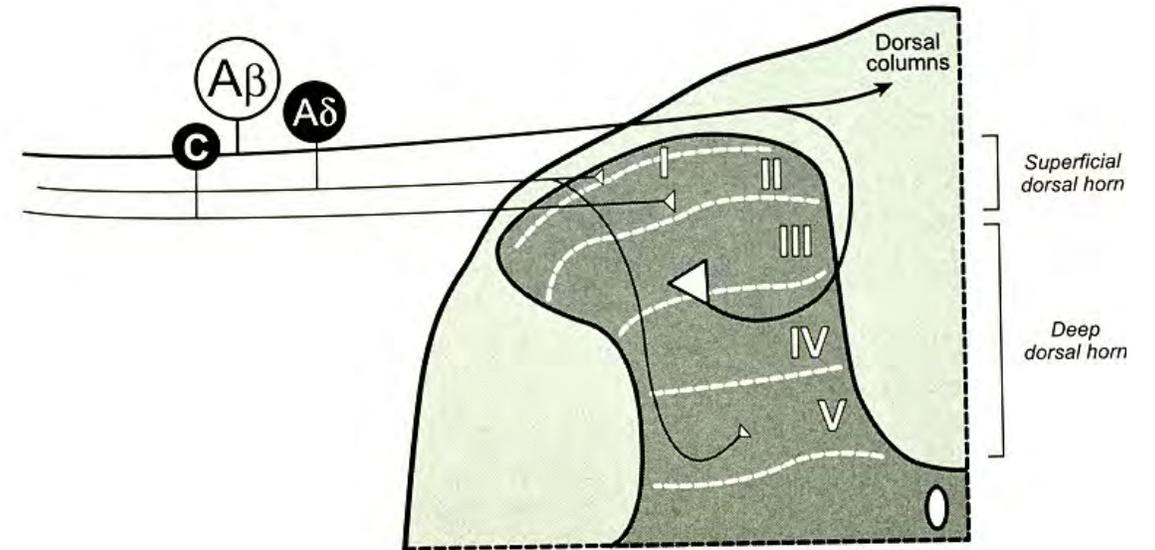
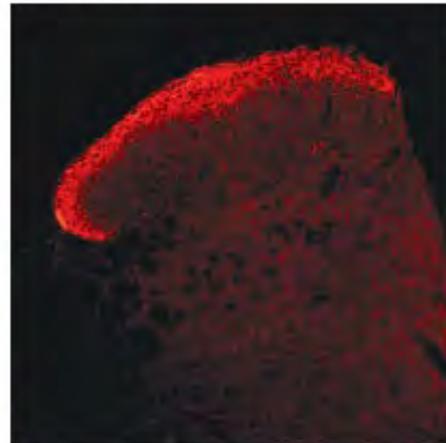
NK-1 receptor



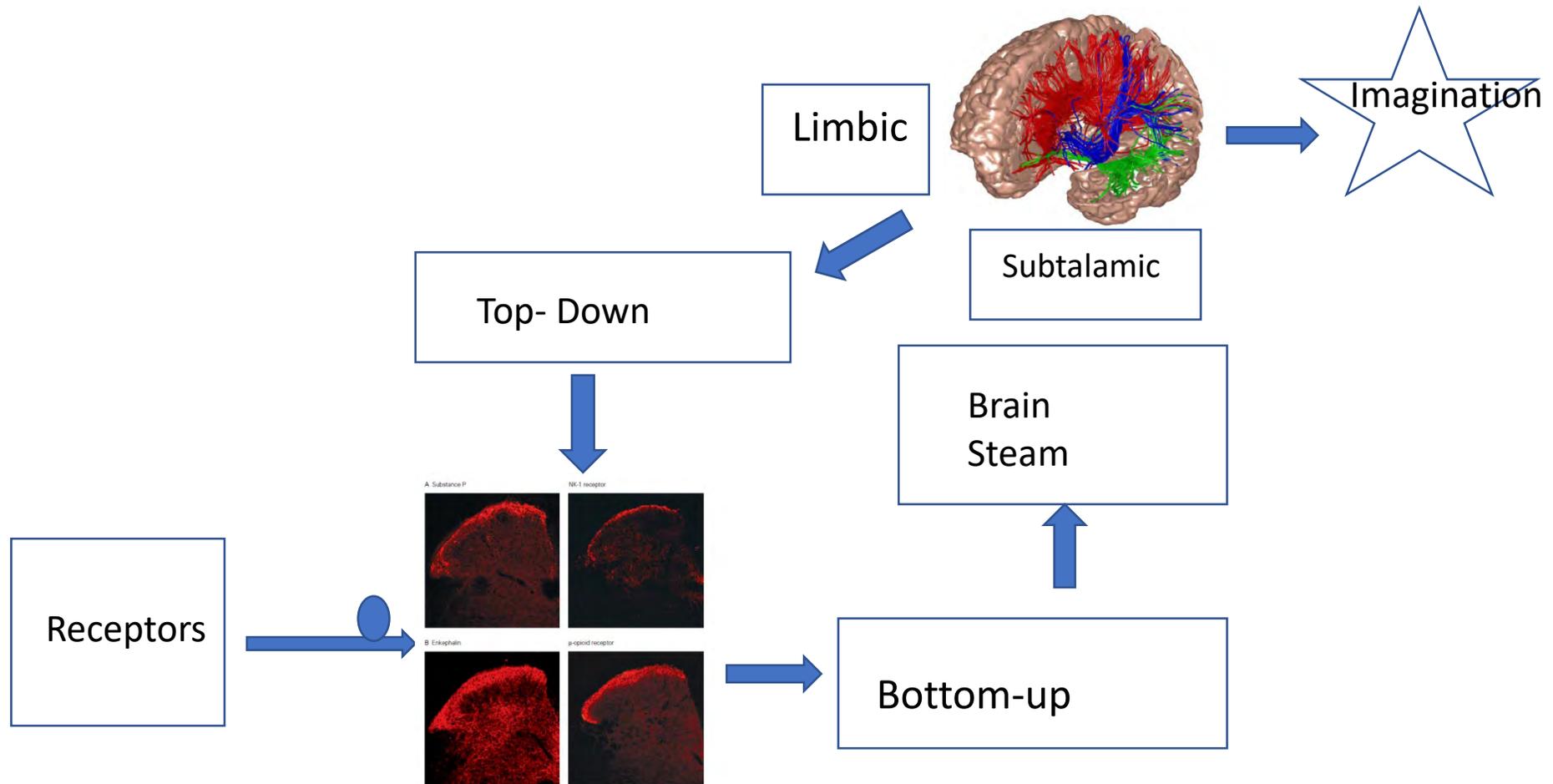
B Enkephalin



$\mu$ -opioid receptor



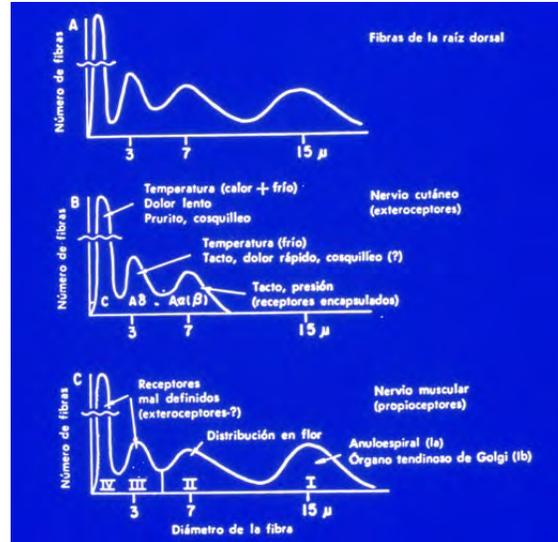




# Fibras nerviosas

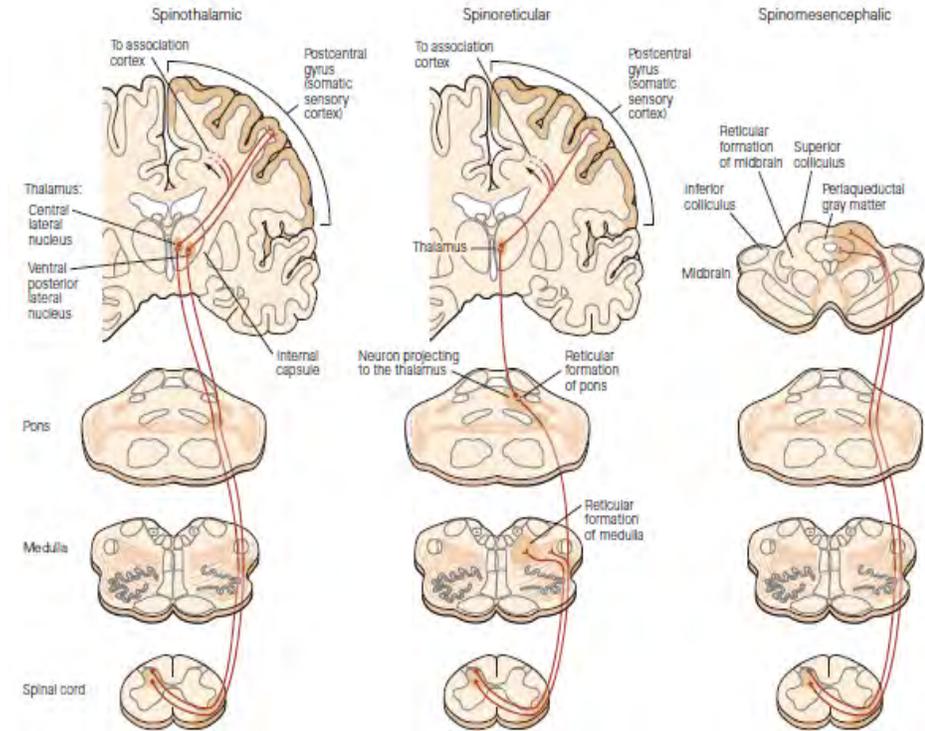
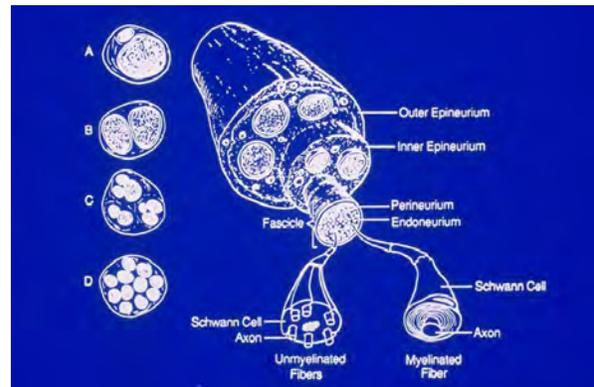
Mielinizadas

- A $\alpha$
- A $\beta$
- A $\lambda$

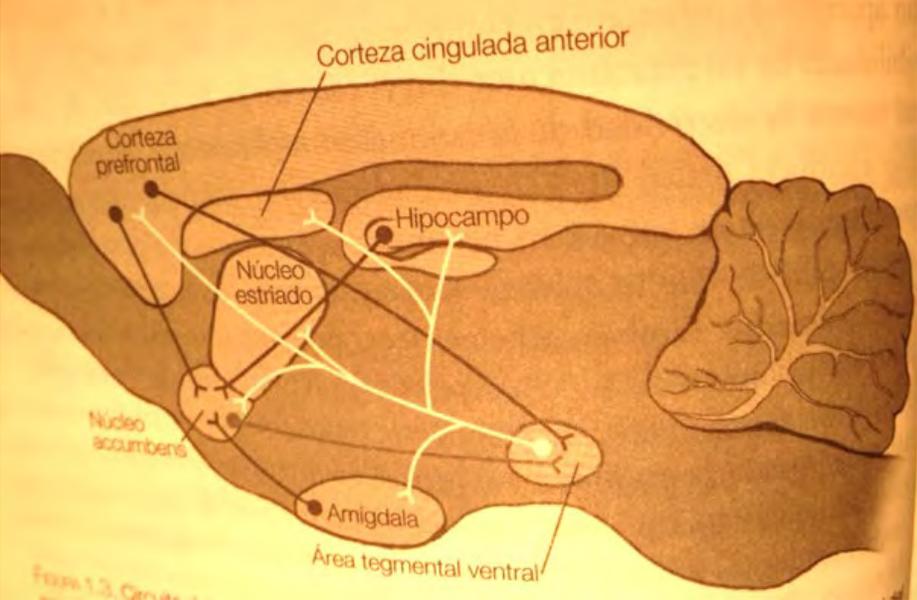
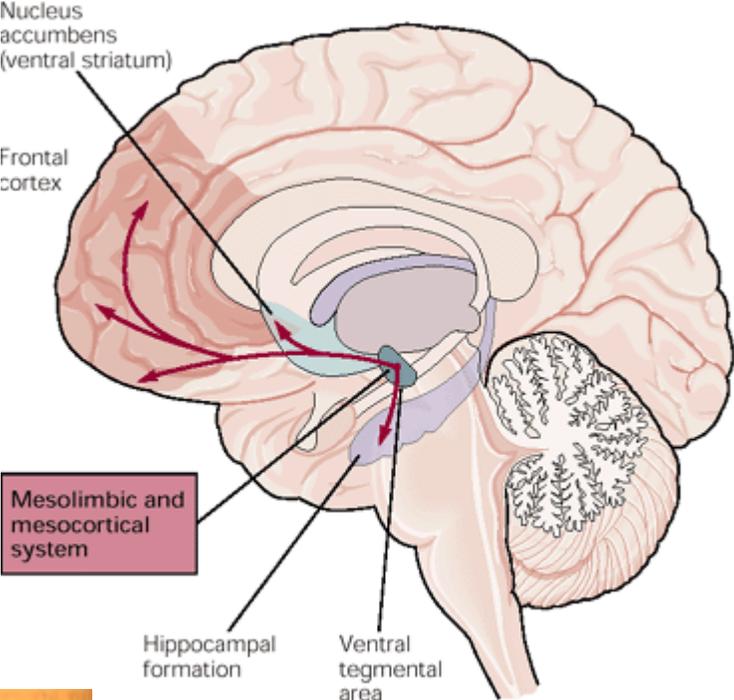


Amielinicas

- C nociceptoras
- C calor
- C “silentes”
- C autonómicas
- C picor
- C táctiles

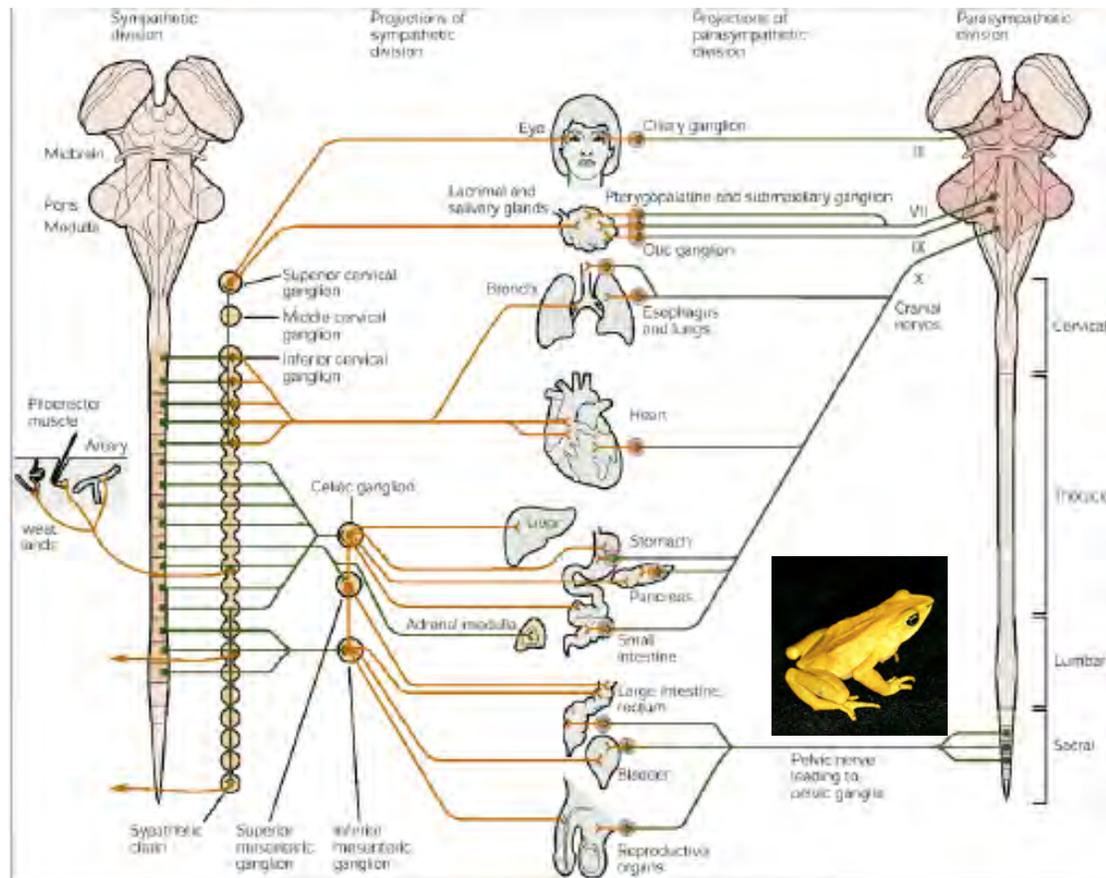


# SISTEMA LIMBICO



Paul Broca (1824-1880)

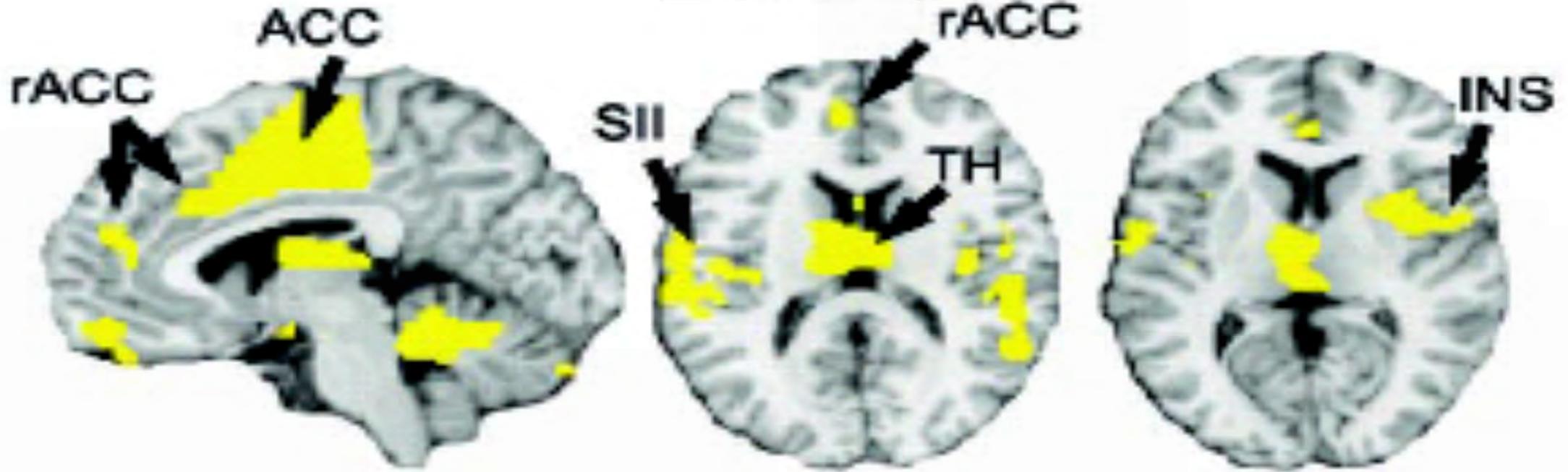
# SISTEMA NERVIOSO ANTIGUO (AUTONOMO)



- Respiración
- Ritmo cardiaco
- Sudoración
- Pupilas
- Eritema y "flair"
- Control digestivo
- Micción/ Defecación



**dolor**

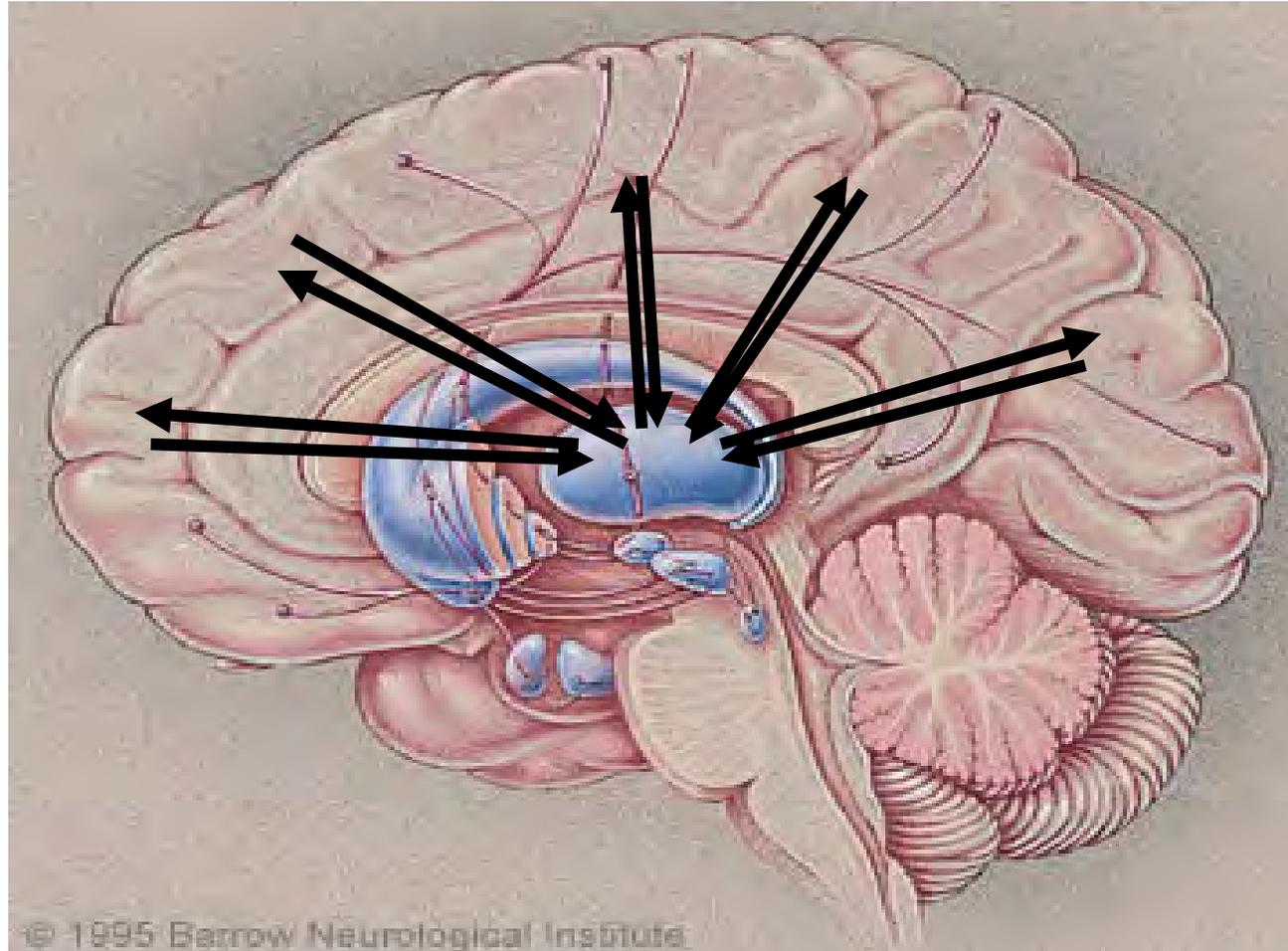


**SI/MI contralateral**  
**SII bilateral**  
**Insula posterior contralateral**  
**Insula anterior y media bilateral**  
**Circunvolución Cingulada Anterior (ACC)**  
**Tálamo (VL y MD) contralateral**  
**Tronco cerebral**  
**Cerebelo contralateral**

Wager TD et al Science 2004; 303:1162

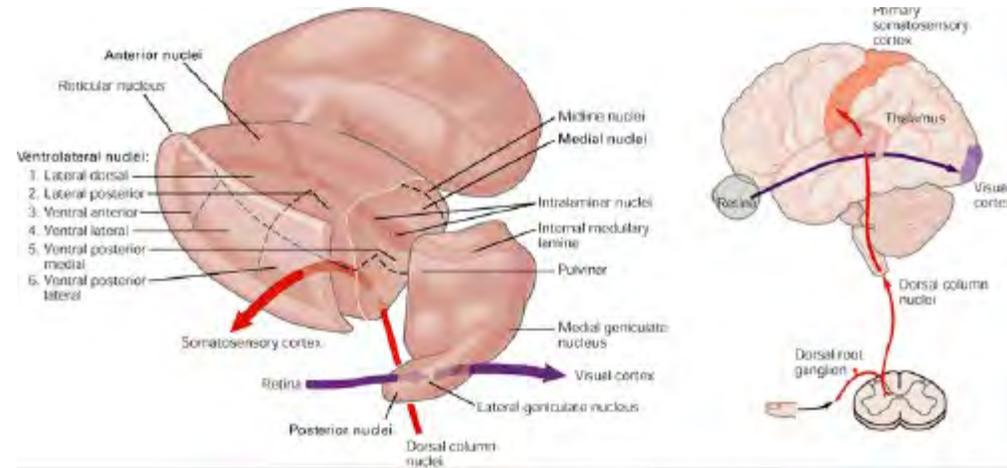
1

## Circuitos de reentrada



GM Edelman y G Tononi  
El Universo de la Conciencia. Ed.Crítica 2002

## Conexión bi direccional TALAMO- CORTEX



10 veces más de conexiones cortico-talámicas que al revés

Solo 6-20% de sinapsis son de “paso” desde la periferia al cortex (moduladores y “drivers”)

Los eventos oscilatorios (ritmos) entre las neuronas corticales y talámicas son los generadores de la cognición.

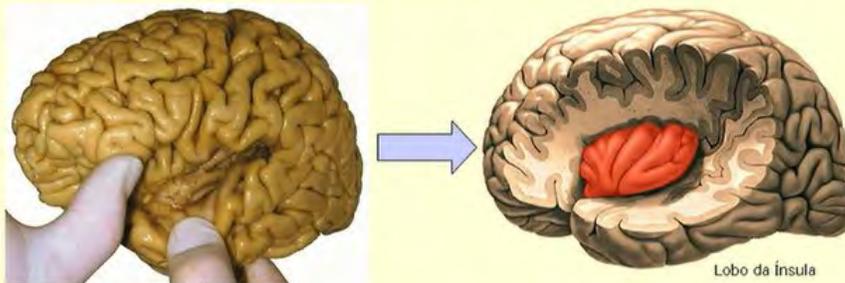
Dos grandes grupos de ritmos talámicos: tónico y en brotes (atención)

Importancia de núcleos intralaminares

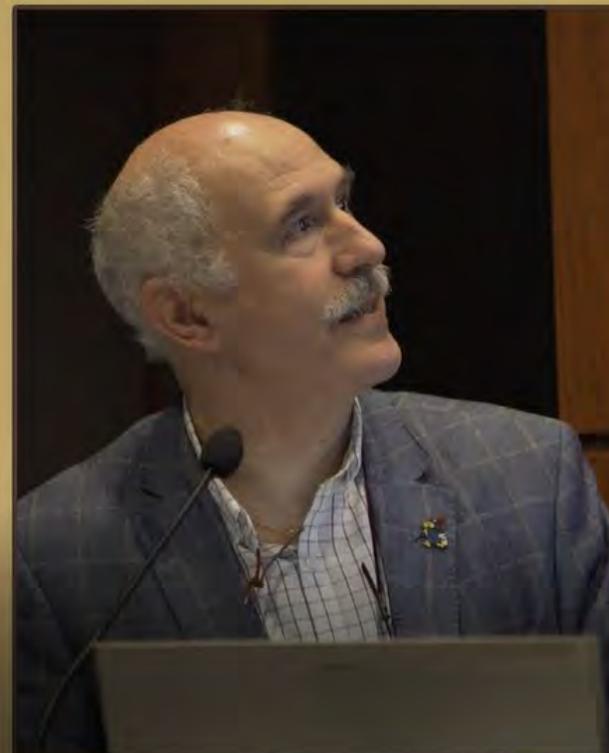
La “RE-ENTRADA” como esencia de este sistema

# MÁSTER EN ELECTRODIAGNÓSTICO NEUROLÓGICO | BARCELONA, 2017

The posterior insula & medial operculum (PIMO):  
a crucial region to *initiate* the pain experience



21\_03\_2017\_Luis\_Garcia\_Larrea



0:10:52

CLÍNIC  
BARCELONA  
Hospital Universitari

Belvitge  
Hospital Universitari

UNIVERSITAT DE  
BARCELONA

0:32:09

## ANTICIPACION

Acumbens  
Cingulado Medial  
Insula anterior

**“Impending pain”**

## PERCEPCION

Cingulado Anterior  
Insula Media y Posterior  
Estriado dorsal

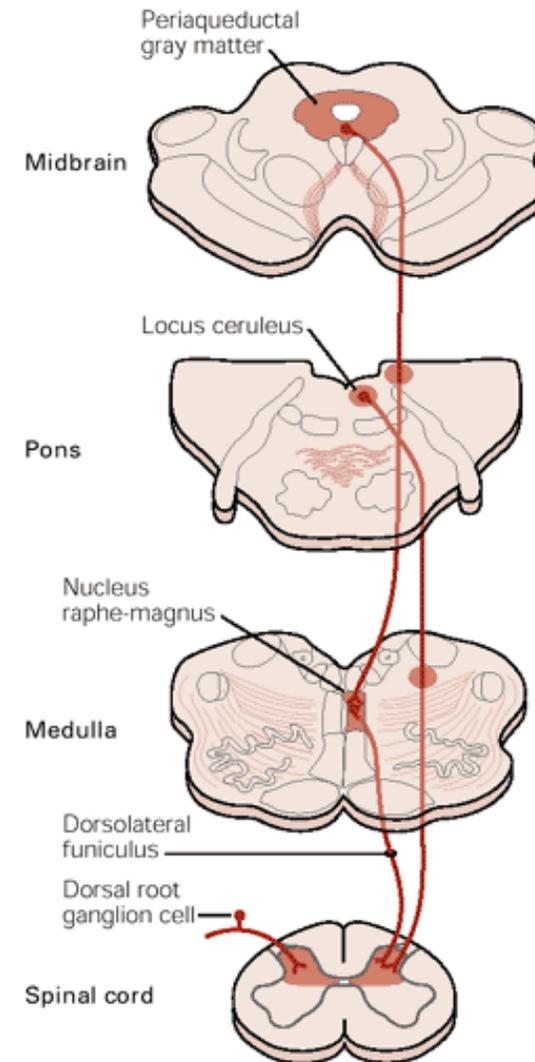
## ALIVIO

Tronco Cerebral (SGP)

## CRITICA A LA TEORIA DE LA PUERTA DE ENTRADA DE MELLZACK Y WALL

- 1- Diversos aferentes primarios responden al estímulo nociceptivo
- 2- El daño excita neuronas del asta posterior (con distintos aferentes)
- 3- La estimulación intensa causa LTP e hiperexcitabilidad en neuronas transmisoras de sensación de daño en el asta posterior
- 4- La mayoría de neuronas del área gelatinosa son excitadoras, no inhibitoras. Su excitación intensa produce LTP.
- 5- Algunas neuronas del área gelatinosa son inhibitoras, pero no se ha demostrado que puedan ser a su vez inhibidas por aferentes amielínicos.
- 6- No hay evidencia del papel de “trigger” de control central por parte de las columnas dorsales.

Howard L.Fields  
Setting the Stage for Pain  
En “Pain and its Transformations”  
Harvard Univ,Press 2007

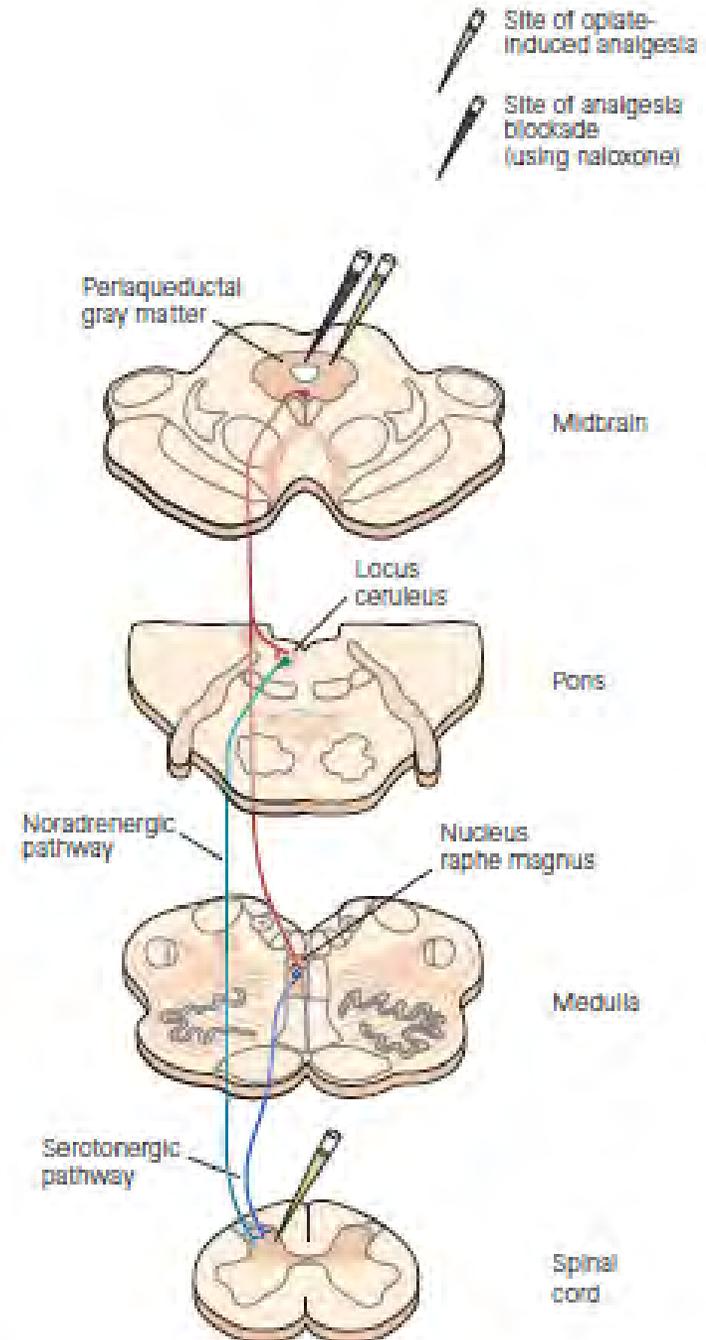


Opiáceos

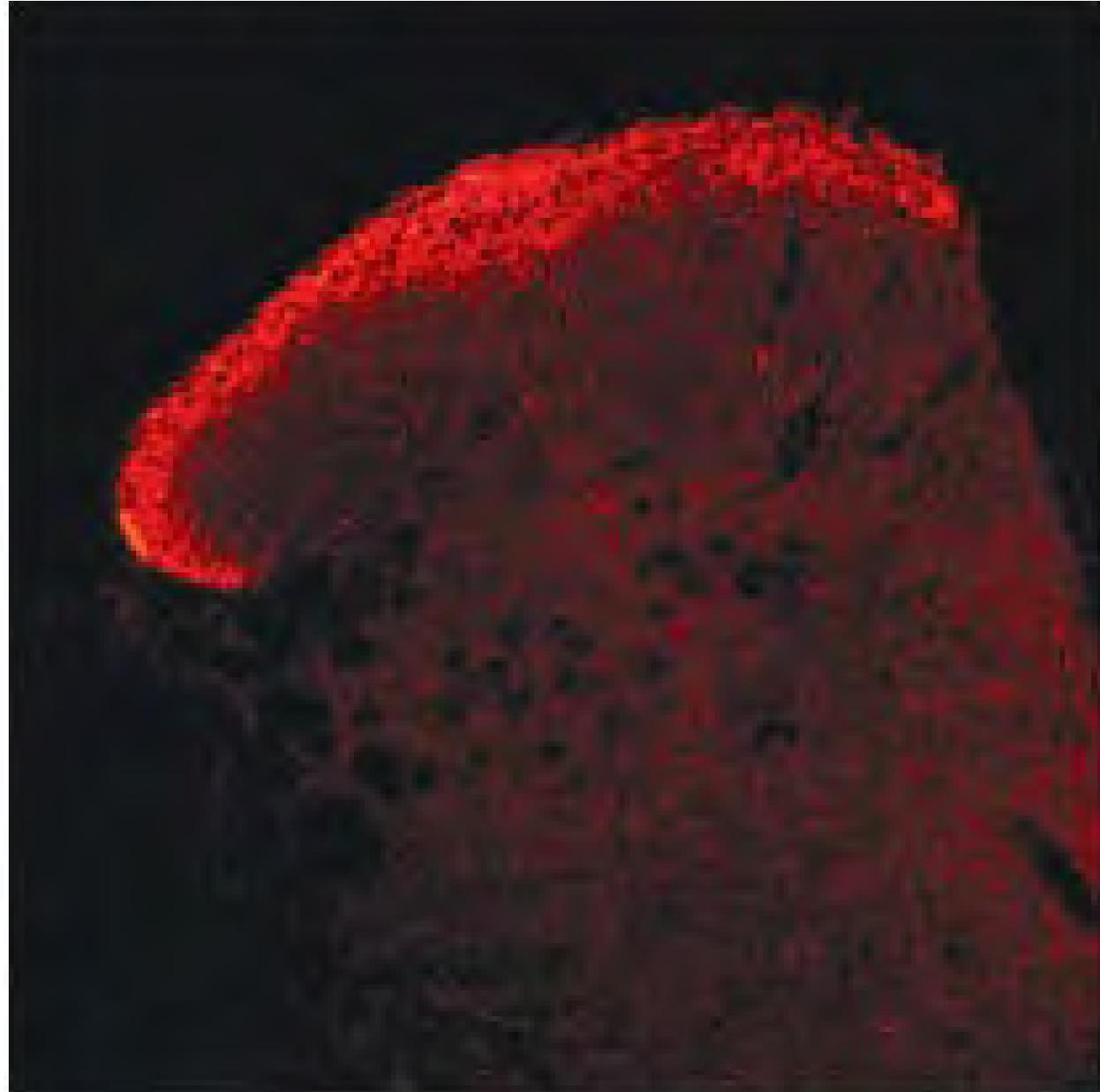
Endorfinas

# Analgesia fisiológica

Propeptide	Peptide(s)	Preferential receptor
POMC	$\beta$ -endorphin	$\mu/\delta$
	Endomorphin-1	$\mu$
	Endomorphin-2	$\mu$
Proenkephalin	Met-enkephalin	$\delta$
	Leu-enkephalin	$\delta$
Prodynorphin	Dynorphin A	$\kappa$
	Dynorphin B	$\kappa$
Pro-orphanin FQ	Orphanin FQ	Orphan receptor



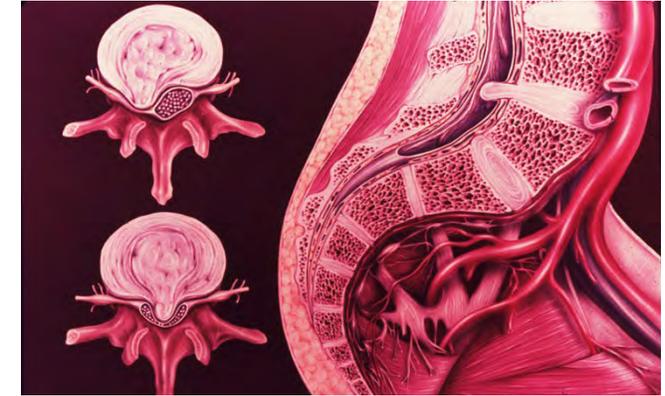
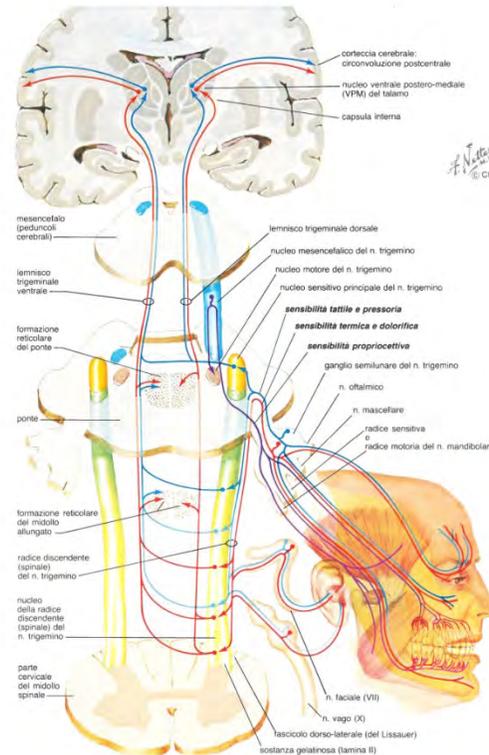
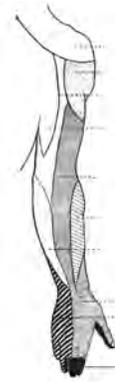
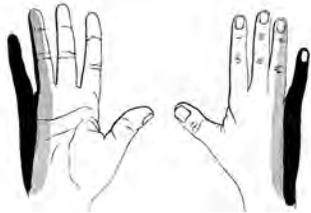
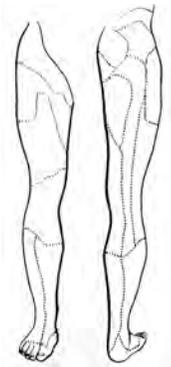
# $\mu$ -opioid receptor



# Dolor Neuropático

“Pain arising as a direct consequence of a lesion or disease affecting the somatosensory system”

(Treede et al, Neurology 2008)



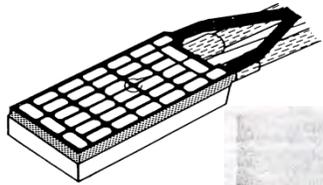
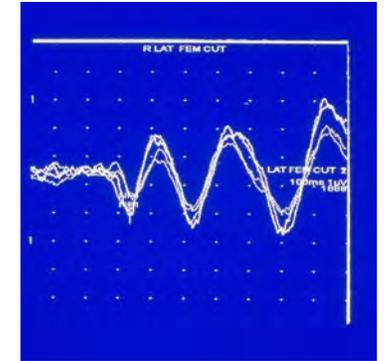
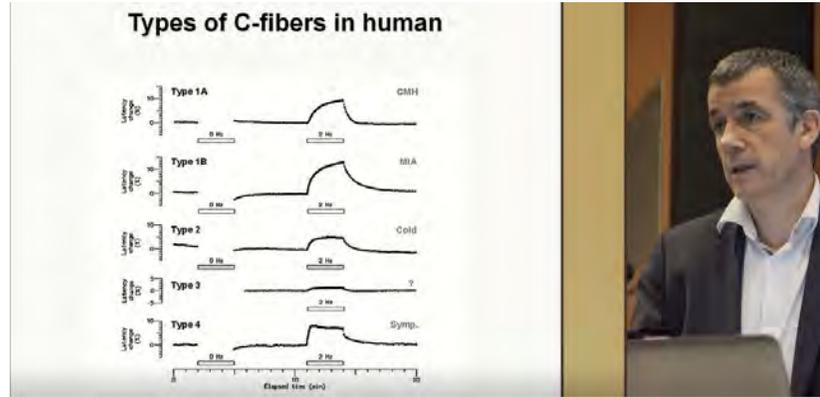
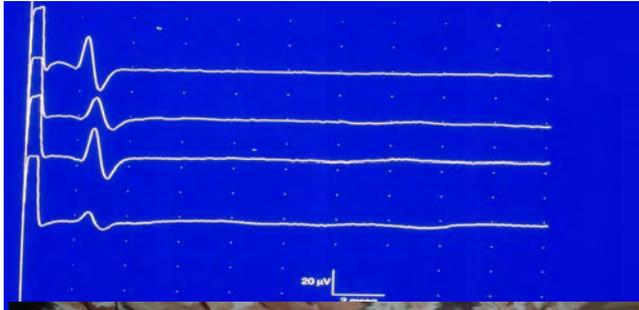
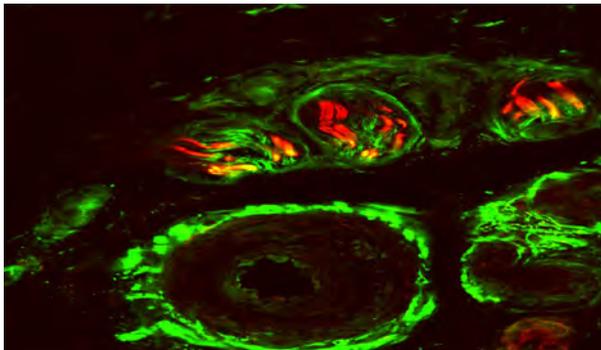


Fig 1 Measurement of temperature thresholds in dig II + III.



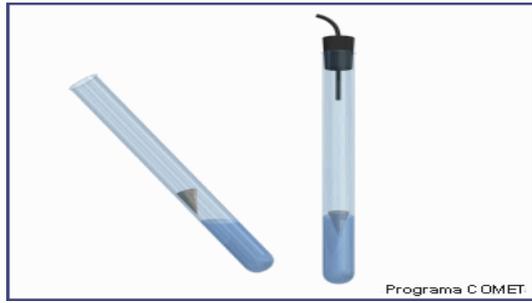


Figure 2: C-shaped curve during testing ensures application of correct pressure



DOLOR AGUDO  
(DOLOR PERSISTENTE)

# DOLOR CRÓNICO

*Mas de 6 meses.*

*No evidencia de daño*

DOLOR “NEUROPÁTICO”

# Clinical Practice Guidelines for management of neuropathic pain

**Table 3. Recommended first- and second-line pharmacologic agents for general peripheral neuropathic pain from selected organisations**

Therapy	National Institute for Health and Care Excellence (NICE) <sup>[18]</sup>	Canadian Pain Society (CPS) <sup>[87]</sup>	Neuropathic Pain Special Interest Group (NeuPSIG) <sup>[50]</sup>
	UK	Canada	International
	Published 2013, updated 2017	Published 2014	Published 2015
First-line pharmacotherapy		Gabapentin	Gabapentin
	Amitriptyline	Pregabalin	Gabapentin XR or enacarbil
	Duloxetine	Tricyclic antidepressants (TCAs)	Pregabalin
	Gabapentin	Serotonin norepinephrine reuptake inhibitors (SNRIs)	SNRIs-duloxetine or venlafaxine*
	Pregabalin		TCA**
Second-line pharmacotherapy	Capsaicin cream	Tramadol	Tramadol
	Short-term tramadol for acute rescue only***	Controlled-release opioids	Capsaicin 8% patch**** Lidocaine patch
Third-line pharmacotherapy		Cannabinoids	
Fourth-line pharmacotherapy		Topical lidocaine	

Deng et al. *BMC Anesthesiology* (2016) 16:12  
DOI 10.1186/s12871-015-0150-5

BMC Anesthesiology

RESEARCH ARTICLE Open Access

CrossMark

## Clinical practice guidelines for the management of neuropathic pain: a systematic review

Yunkun Deng<sup>1,2</sup>, Lei Luo<sup>3</sup>, Yuhuai Hu<sup>3</sup>, Kaiyun Fang<sup>1</sup> and Jin Liu<sup>2\*</sup>

IASP (2007) CPS (2007) Latin American (2009) NICE (2010) MER (2010) SA (2013) Fench (2010) Danish (2010)

*European Journal of Neurology* 2010, **17**: 1113–1123 doi:10.1111/j.1468-1331.2010.02999.x

## EFNS GUIDELINES

### EFNS guidelines on the pharmacological treatment of neuropathic pain: 2010 revision

 **Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis**

Nanna B Finnerup<sup>\*</sup>, Nadine Attal<sup>\*</sup>, Simon Haroutounian, Ewan McNicol, Ralf Baron, Robert H Dworkin, Ian Gilron, Majja Haanpää, Per Hansson, Troels S Jensen, Peter R Kamerman, Karen Lund, Andrew Moore, Srinivasa N Raja, Andrew S C Rice, Michael Rowbotham, Emily Sena, Phillip Siddall, Blair H Smith, Mark Wallace

**Summary**  
Background New drug treatments, clinical trials, and standards of quality for assessment of evidence justify an update

*Lancet Neurol* 2015; 16:2-73







DOLOR AGUDO  
(DOLOR PERSISTENTE)

# DOLOR CRÓNICO

*Mas de 6 meses.*

*No evidencia de daño*

DOLOR “NEUROPÁTICO”

## Astonishing hypothesis

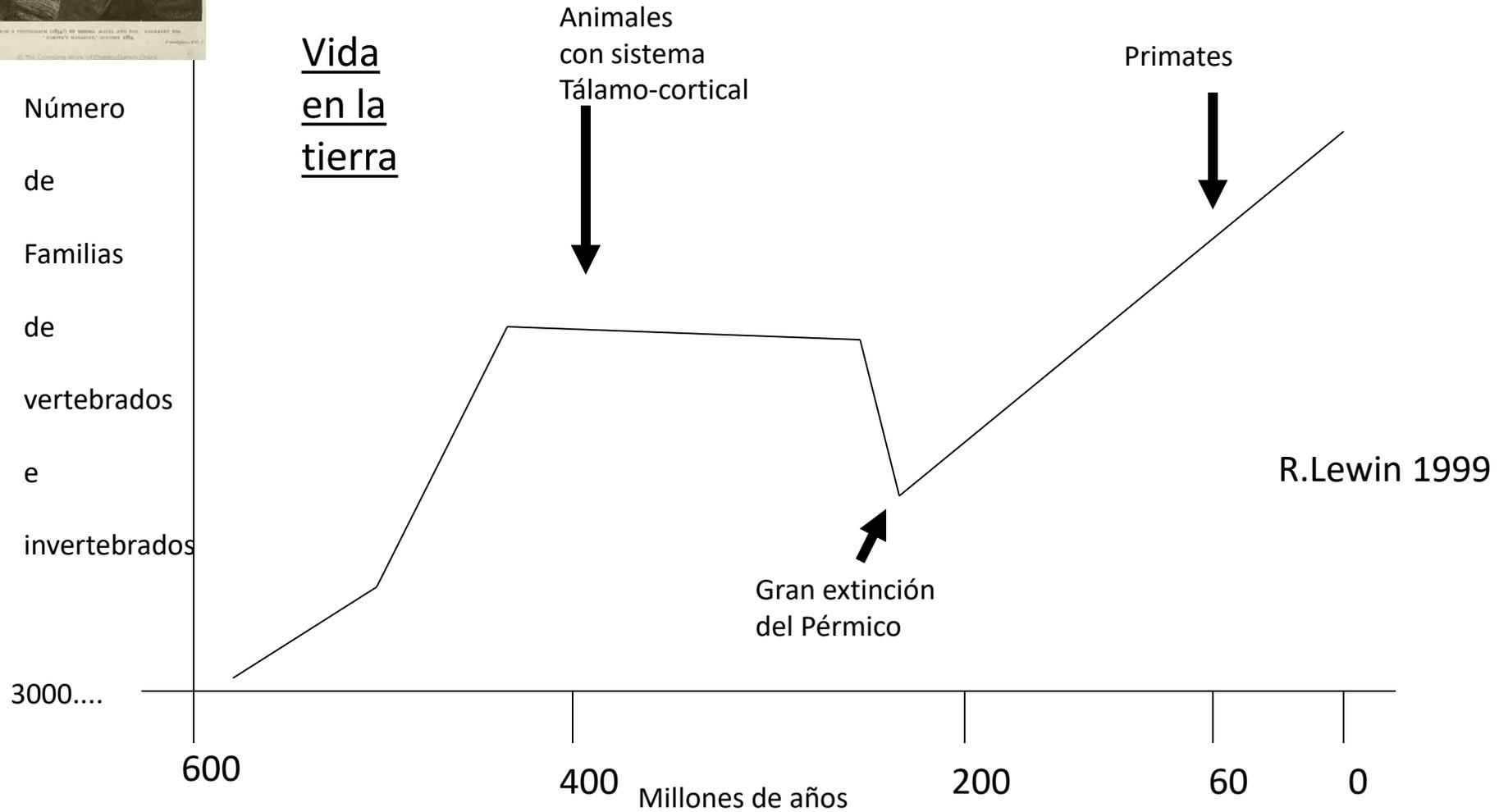
Human feelings, thoughts, and actions-even  
consciousness itself- are just the products of  
neural activity in the brain

Francis Crick 1916-2004



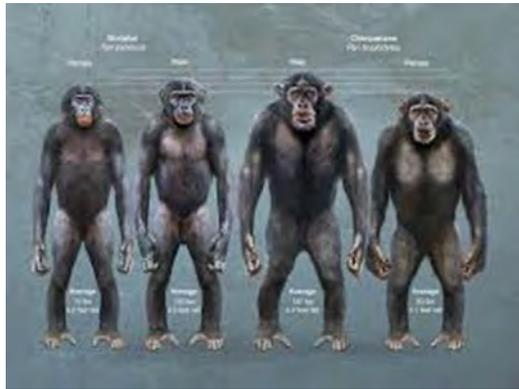


Nada tiene sentido en Biología si no es a la luz de la evolución  
Nada tiene sentido en Medicina si no es a la luz de la Biología





60 millones años



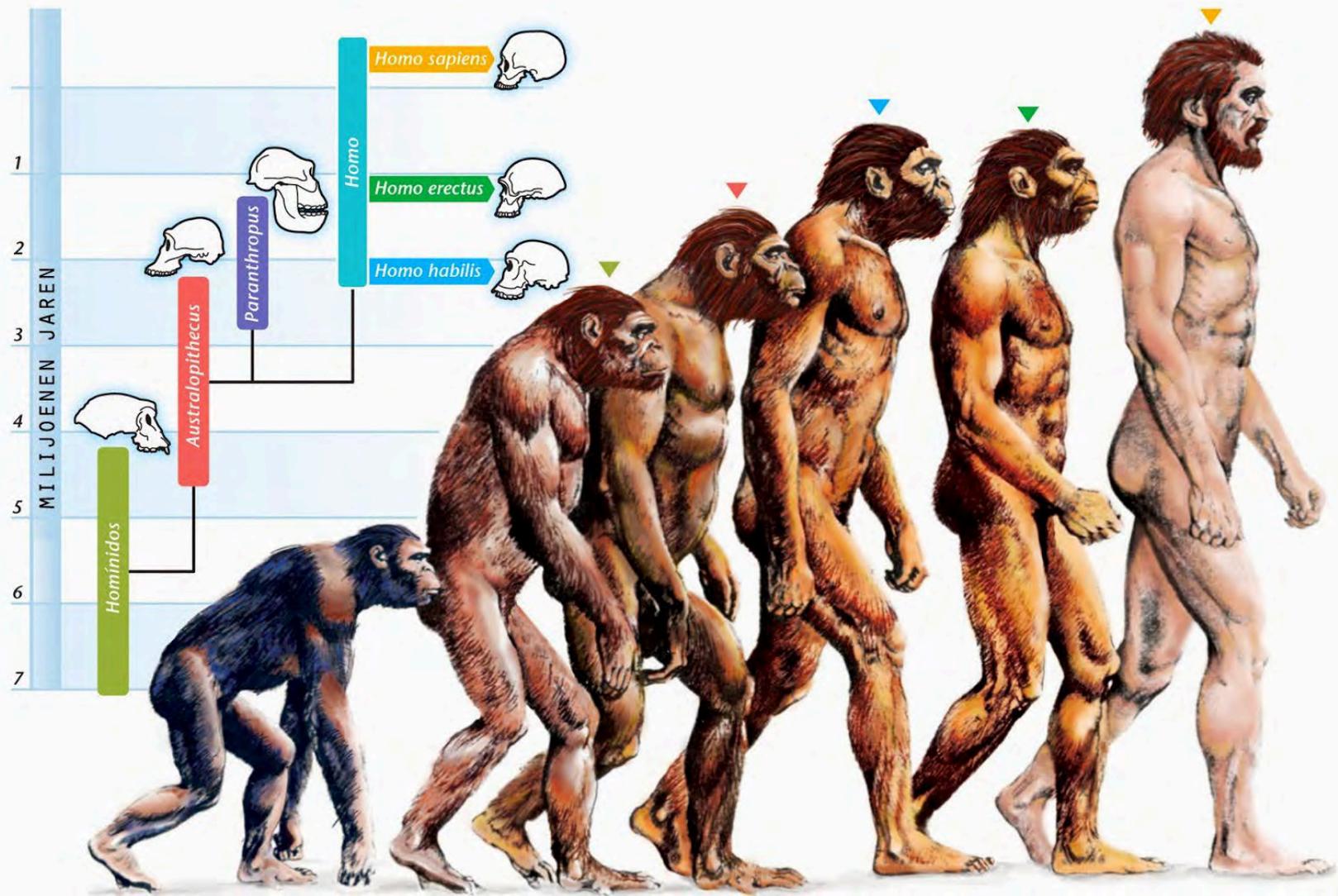
6 millones años



3-4 millones años

1-2 millones años

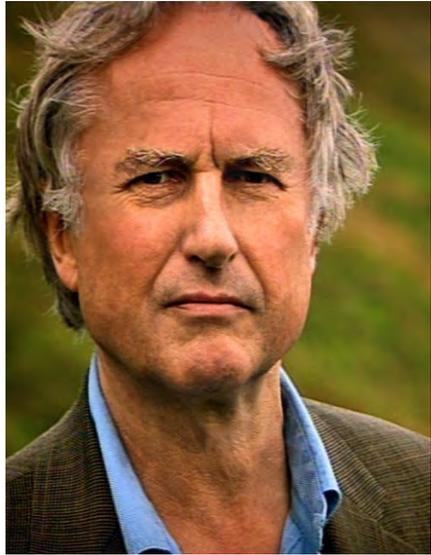
70 mil años



El ser vivo como transportador temporal de GENES

Los GENES construyen animales para protegerse y reproducirse

La Paleontología como una de las grandes Ciencias del siglo XXI



Richard Dawkins

“El Gen Egoista”

Salvat Editores 1994



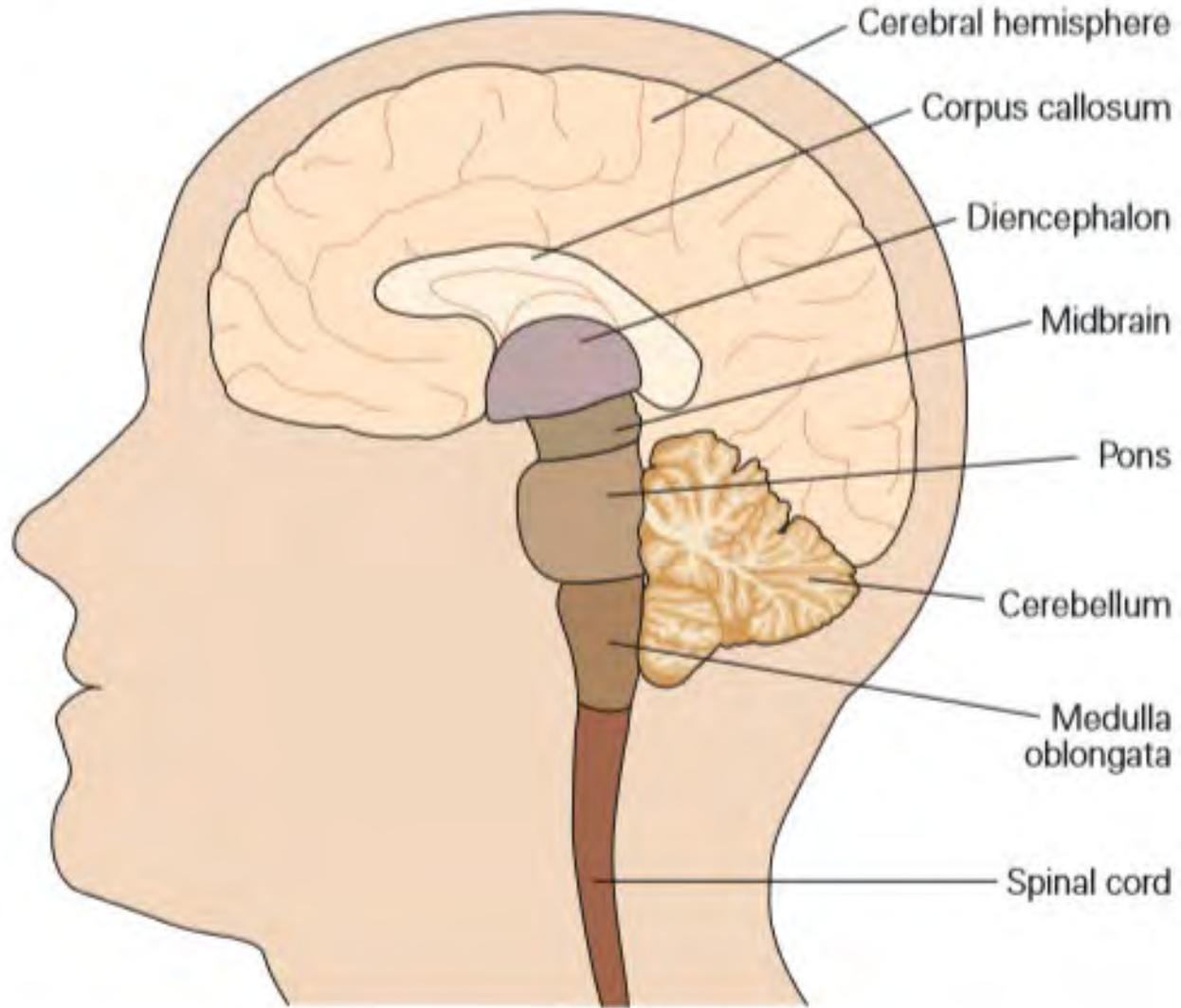
Juan Luis Arsuaga

“El sello Indeleble”

Debolsillo 2014

“Vida.La gran historia”

Destino 2019



Respiración

Hipo

Parpadeo

Tos

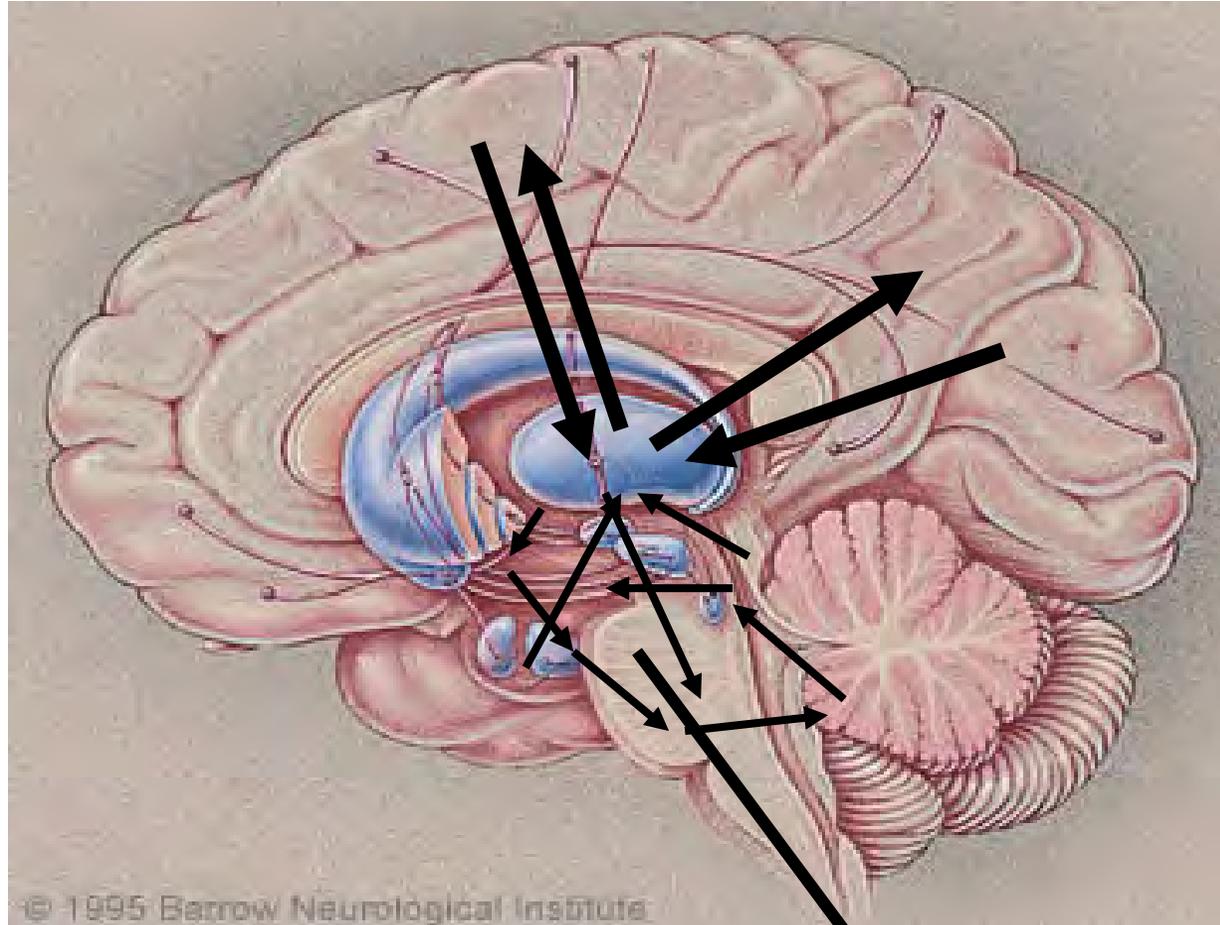
Bostezo

Chupeteo

Prensión

Retirada

Patrones de acción fijos  
Memoria implícita (no declarativa)



Sonrisa

Marcha

Lenguaje

Correr

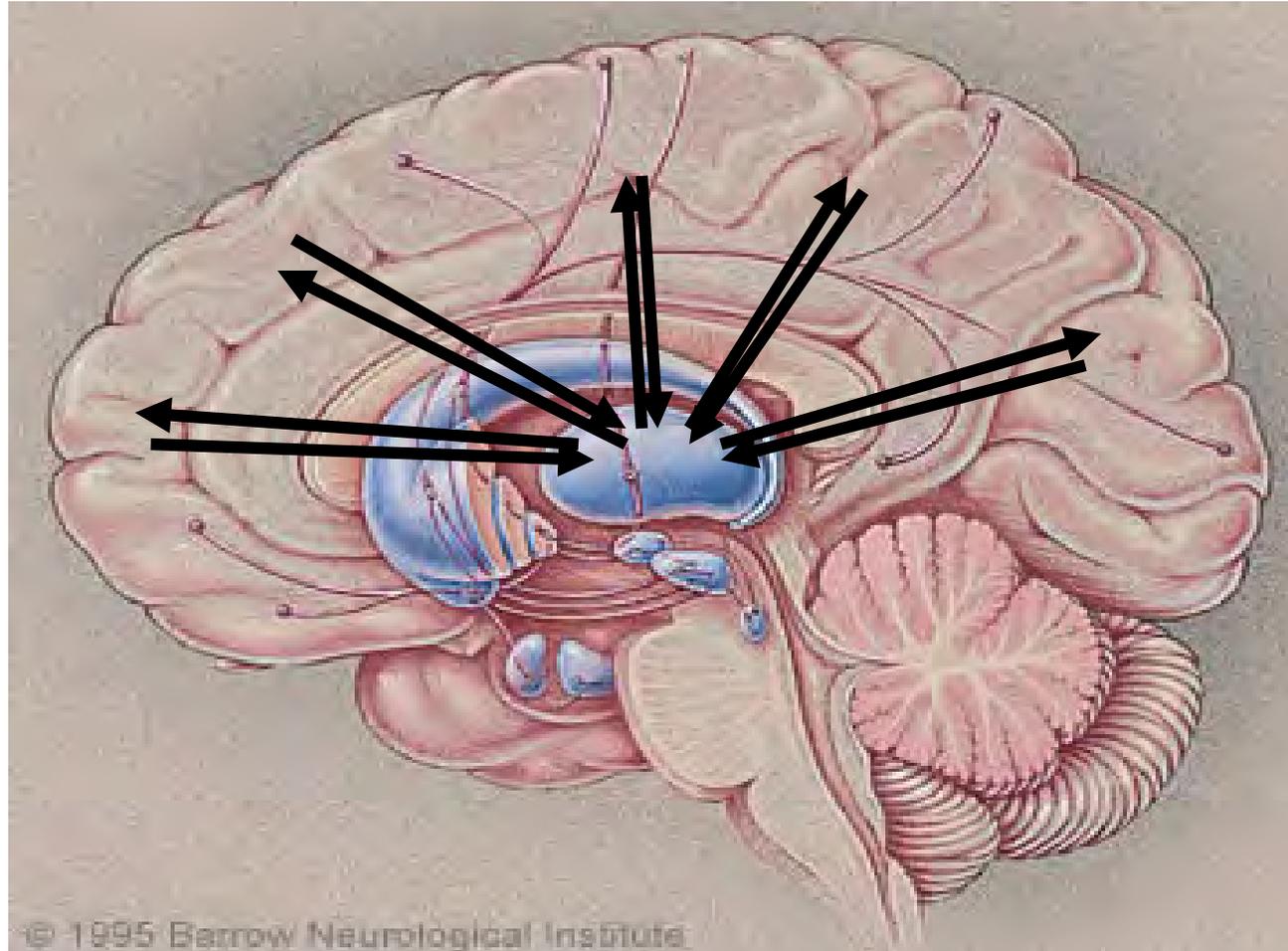
Conducir

“Swing” golf

Drive tennis

1

## Circuitos de reentrada



GM Edelman y G Tononi  
El Universo de la Conciencia. Ed.Crítica 2002



Concepto de “impronta” (Lorenz 1935)

Establecimiento de memorias “fijadas” tras experiencias específicas, intensas, en un momento determinado de la vida del animal, con componente emocional intenso.

No pueden ser eliminadas



Características emocionales fijadas tras una “impronta” en un momento determinado del desarrollo del aprendizaje, fundamentalmente por imitación ??

Base neurobiológica de la teoría freudiana ????



## Cazador – recolector versus especies “eusociales”

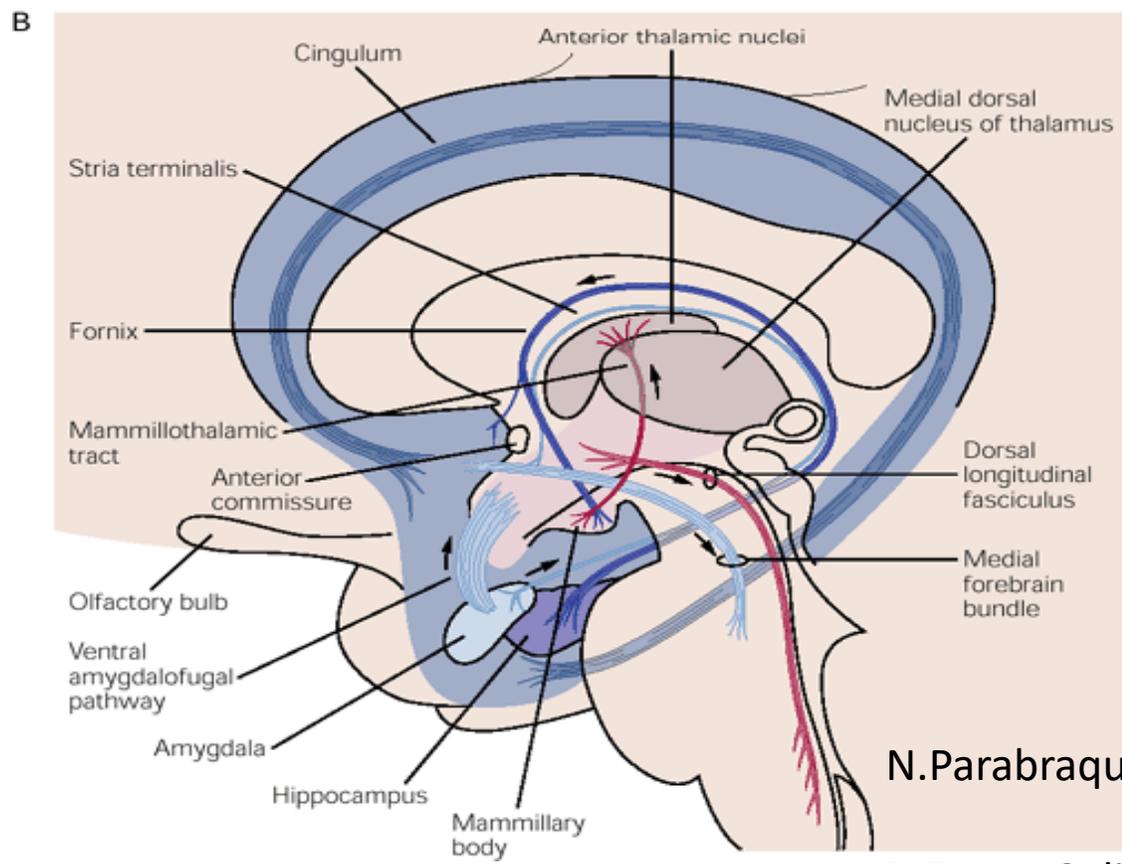
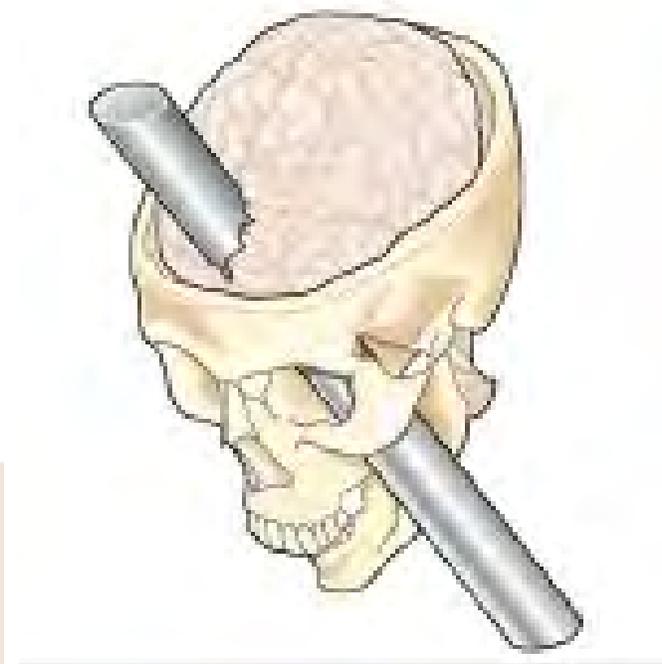
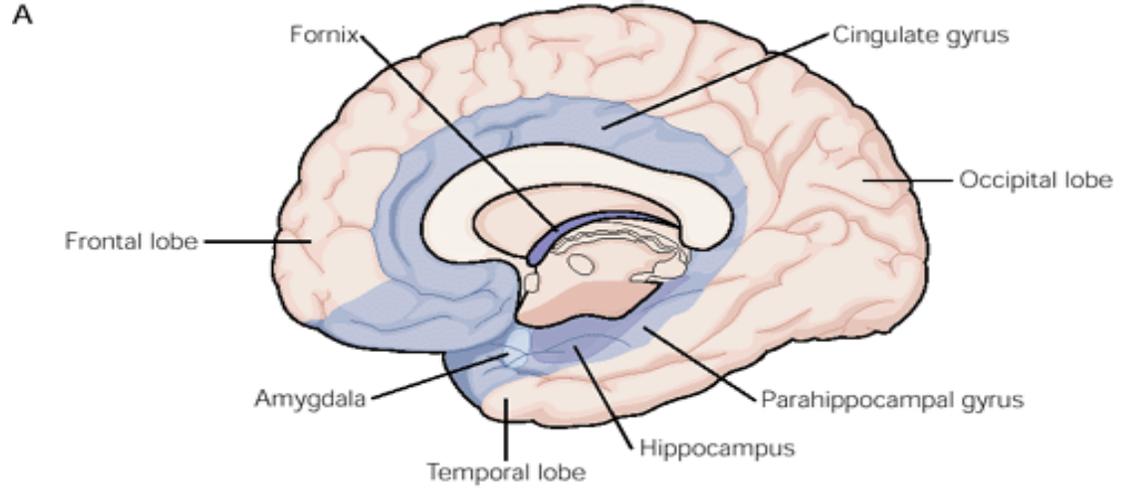


**Eduard O.Wilson**  
**El Sentido de la Existencia Humana**  
**Gedisa Ed 2014**



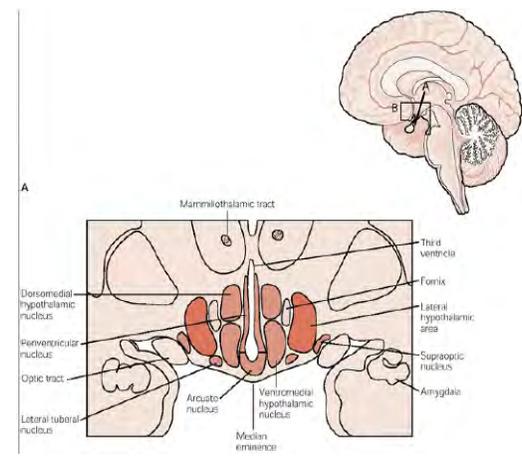
**Frans de Waal**  
**El mono que llevamos dentro 2005**  
**El bonobo y los 10 mandamientos 2014**  
**Tusquets editores**

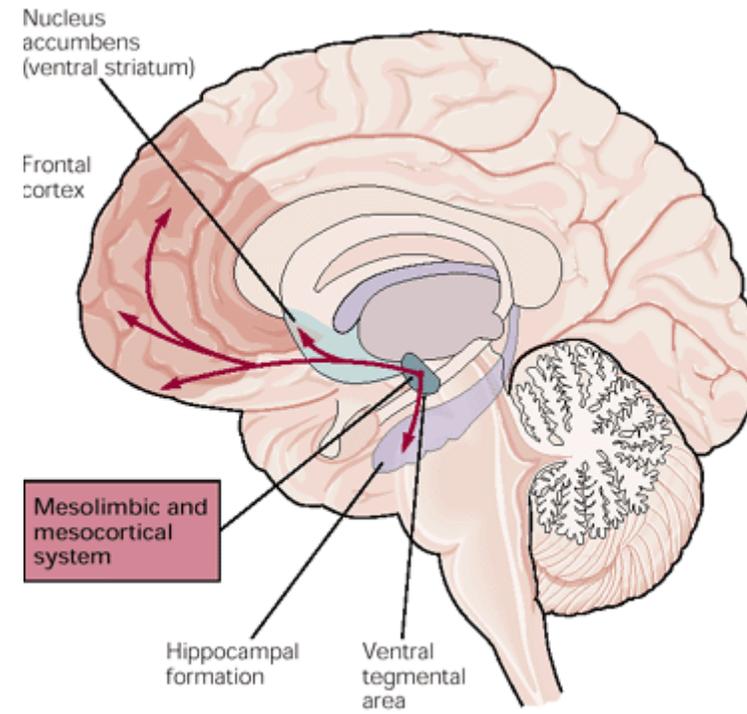
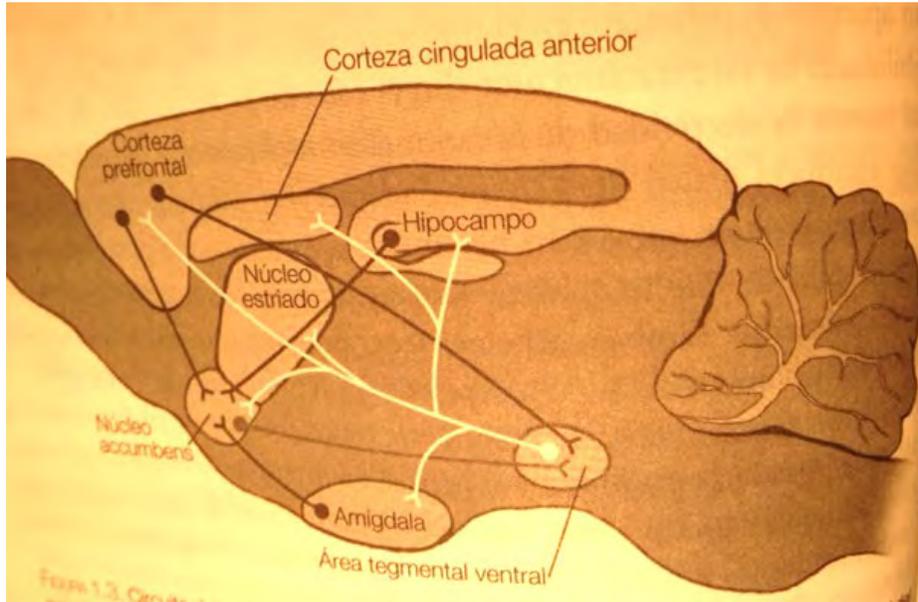


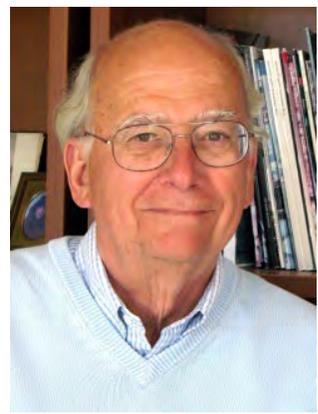
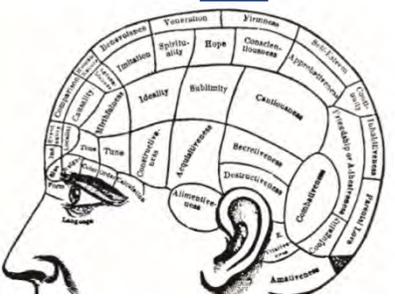
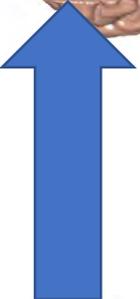
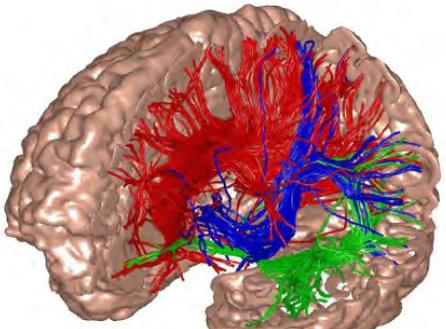


N.Parabraquial

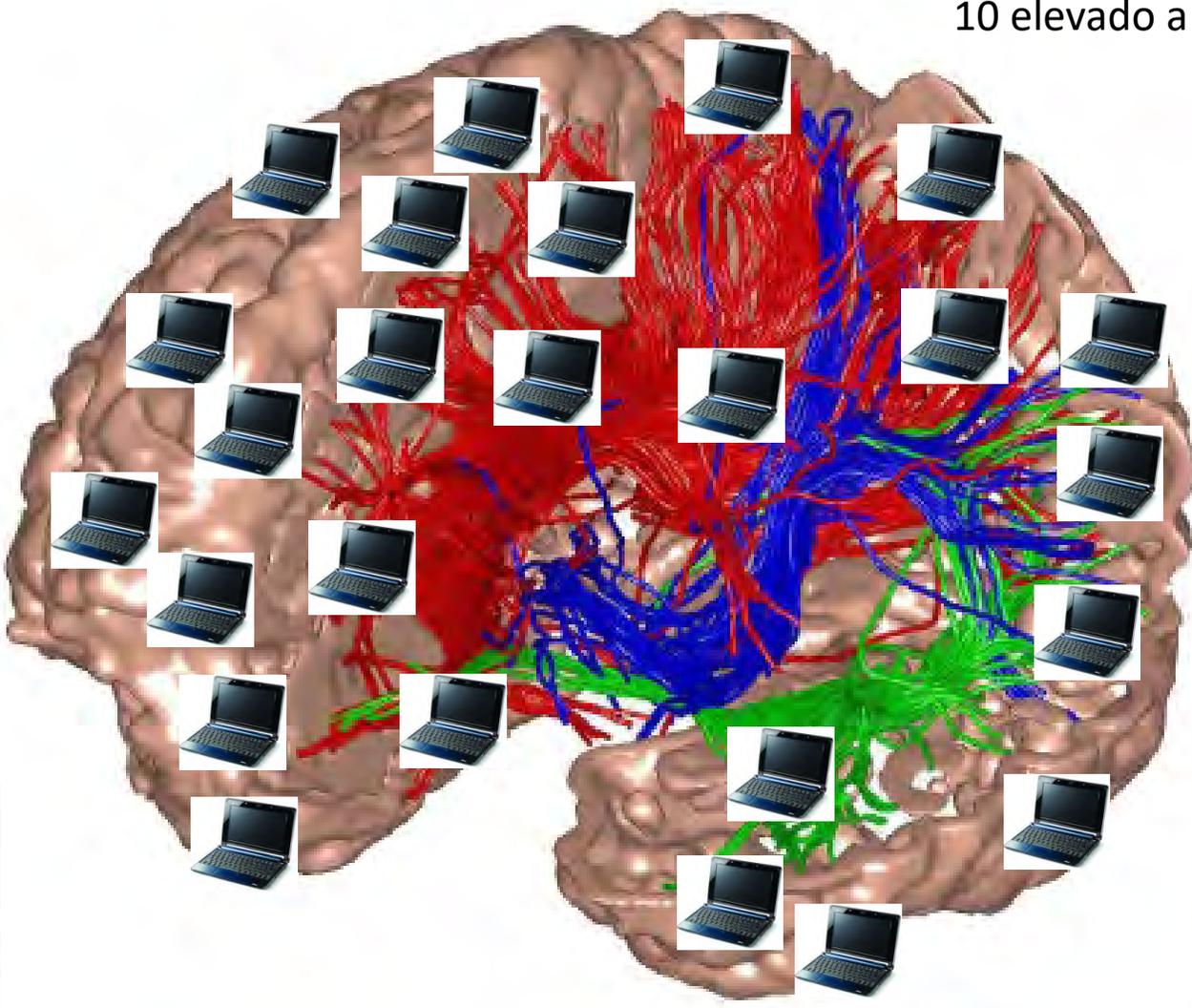
N.Tracto Solitario







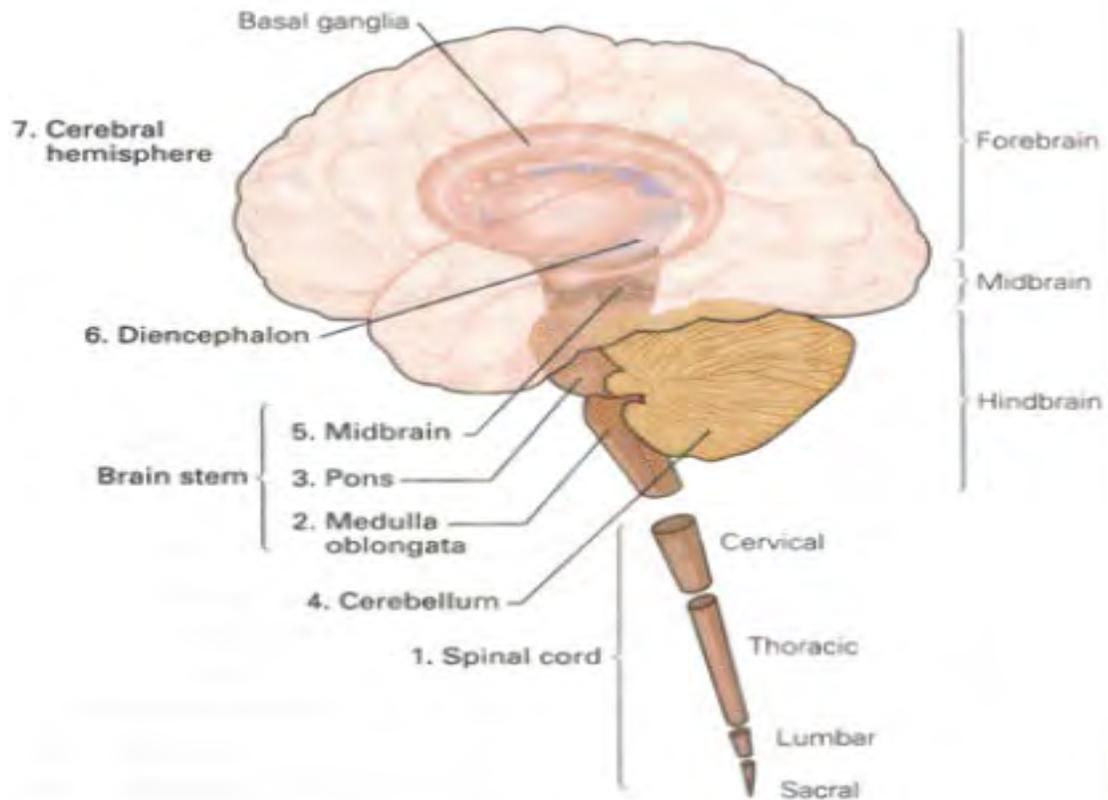
10 elevado a 1 millón de redes neuronales



Una red = Un significado (Howard Fields)

CEREBRO MODULAR  
CEREBRO ESTRATIFICADO (M.Gazzaniga)

Redes que constituyen un "Nucleo Dinámico" = Consciencia (Edelman y Tononi)



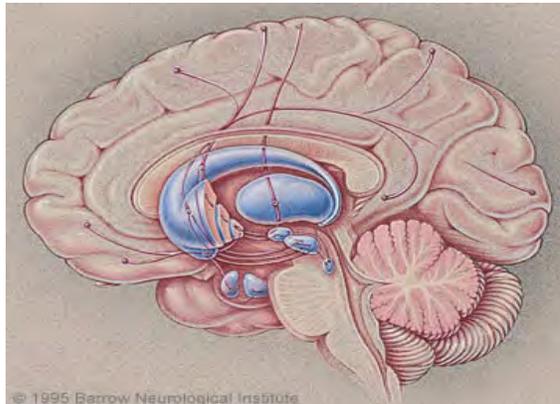
El cerebro **IMAGINA** en su sistema talamo-cortical

Si hay tiempo = REALIDAD

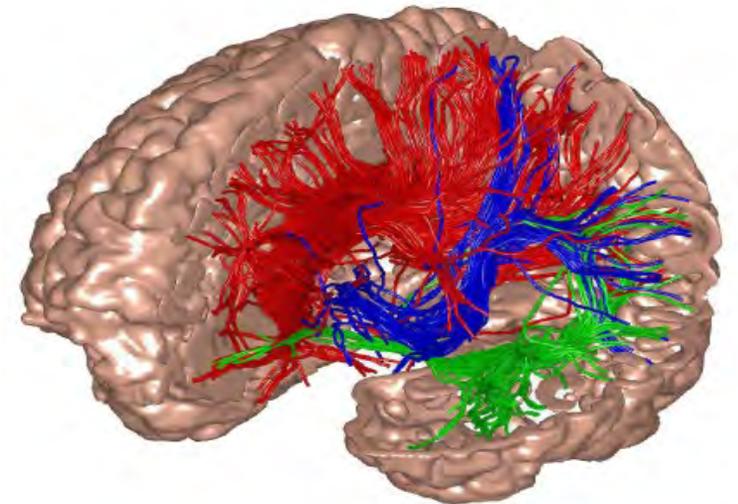
Si está “desconectado” = SUEÑO

Si se “aisla” = FANTASIA

Si no hay control = DELIRIO

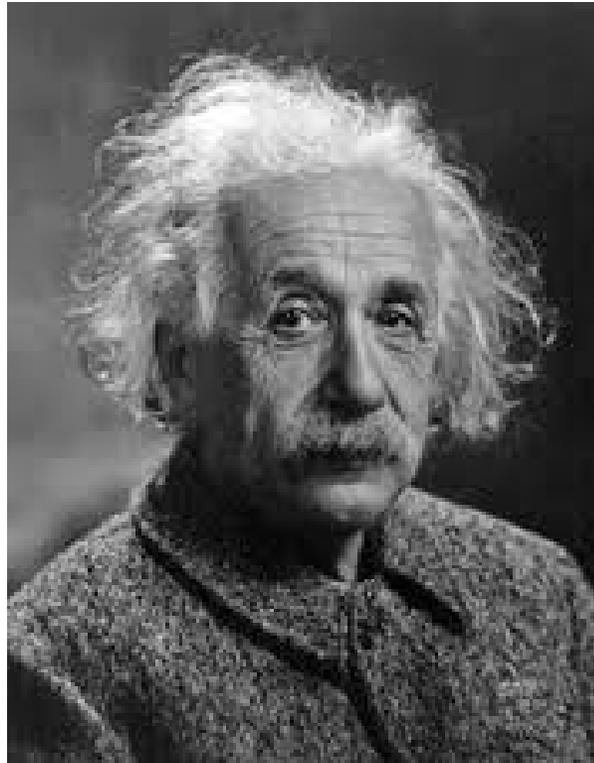


Rodolfo Llinás



**La mente intuitiva es un Don sagrado,  
Y la mente racional es un fiel sirviente.**

**Hemos creado una sociedad que honra al  
sirviente  
Y ha olvidado el Don**



**Albert Einstein**

*“Nada tiene sentido en Biología humana  
si no es a la luz de la evolución cultural”*

## **La Cultura es Biología**

Borsook D, Maleki N, Bercera L, McEwen B. Understanding migraine through the lens of maladaptive stress responses: a model disease of allostatic load. *Neuron* 2012; 73: 219-34



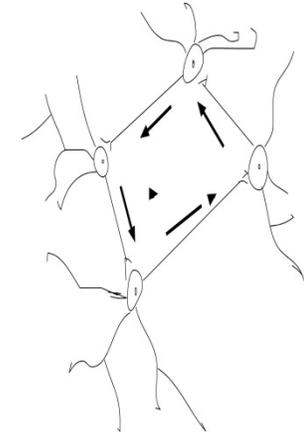


www.shutterstock.com · 285293123

# Long Term Potentiation

**Long- lasting but not necessarily irreversible**

**increase in synaptic strength**



**Early phase: last for up to three hours. Not de-novo protein synthesis**

**Late phase: Protein synthesis. Three hours up to the life span of an animal.**

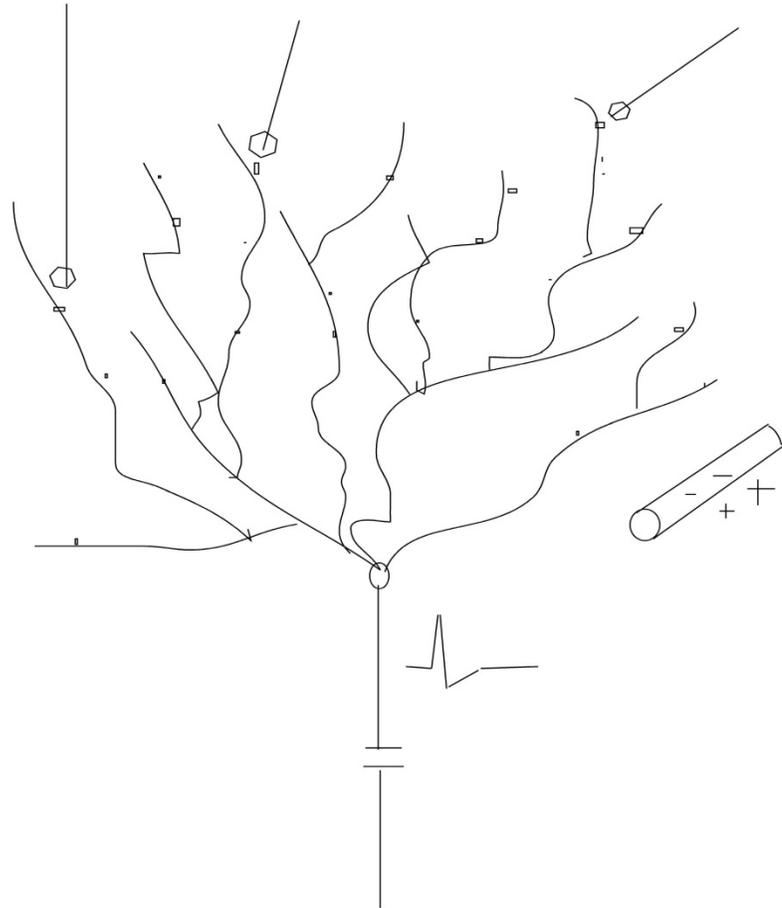
**synaptic strength = magnitude of the postsynaptic response**

Can increase if:

- 1- Release of neurotransmitter is enhanced
- 2- Postsynaptic effects of the neurotransmitters become stronger

Bliss TVP, Collingridge GL, Nature 1993, 361:31  
Malenka RC, Bear MF, Neuron 2004, 44:5





**Neurotransmisor**

**Receptor**

**ELECTROTONO**

**Canales iónicos voltajedependientes**

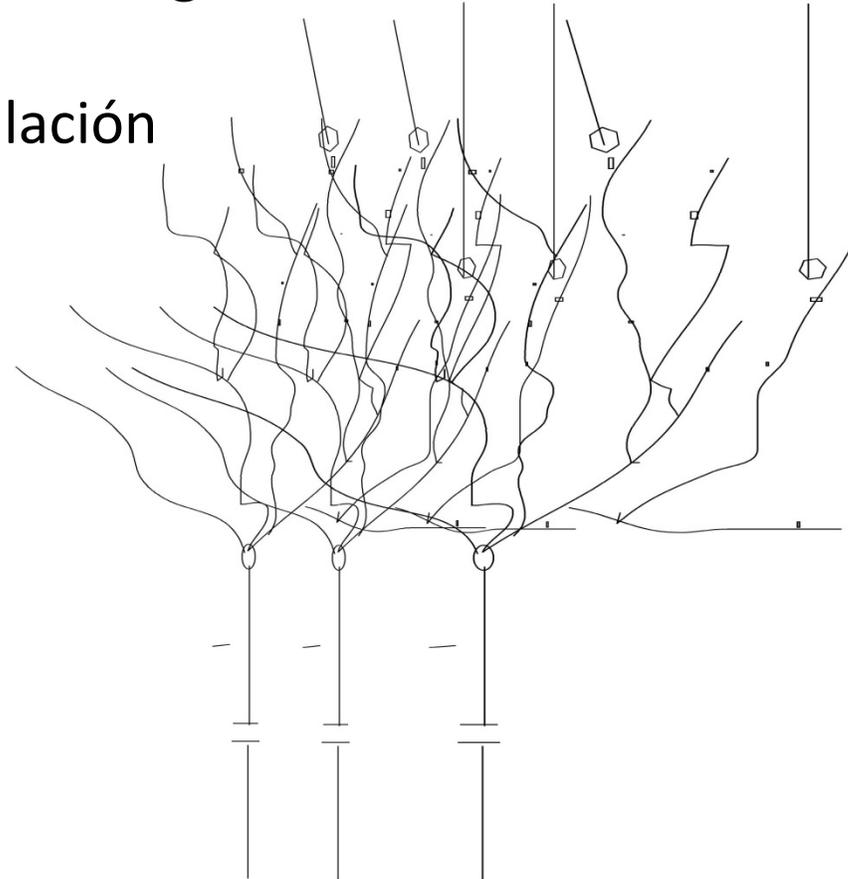
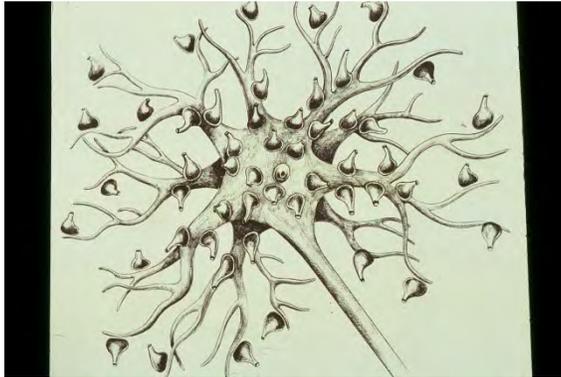
**POTENCIAL DE ACCION  
(todo o nada)**

La neurona es un “promediador”

# Neuromodulación “cognitiva”

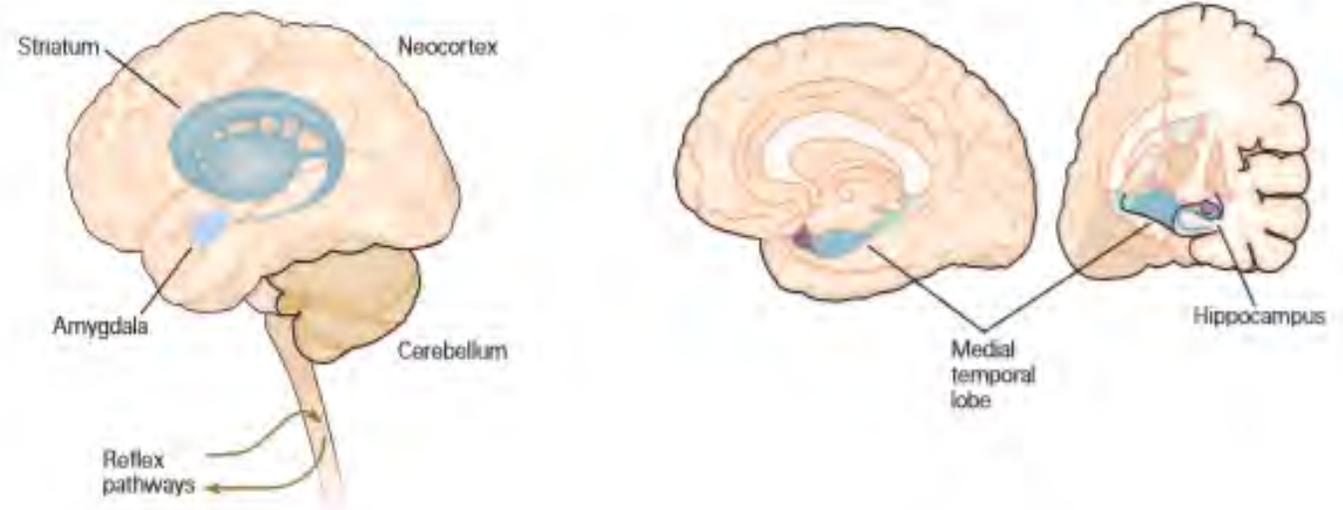
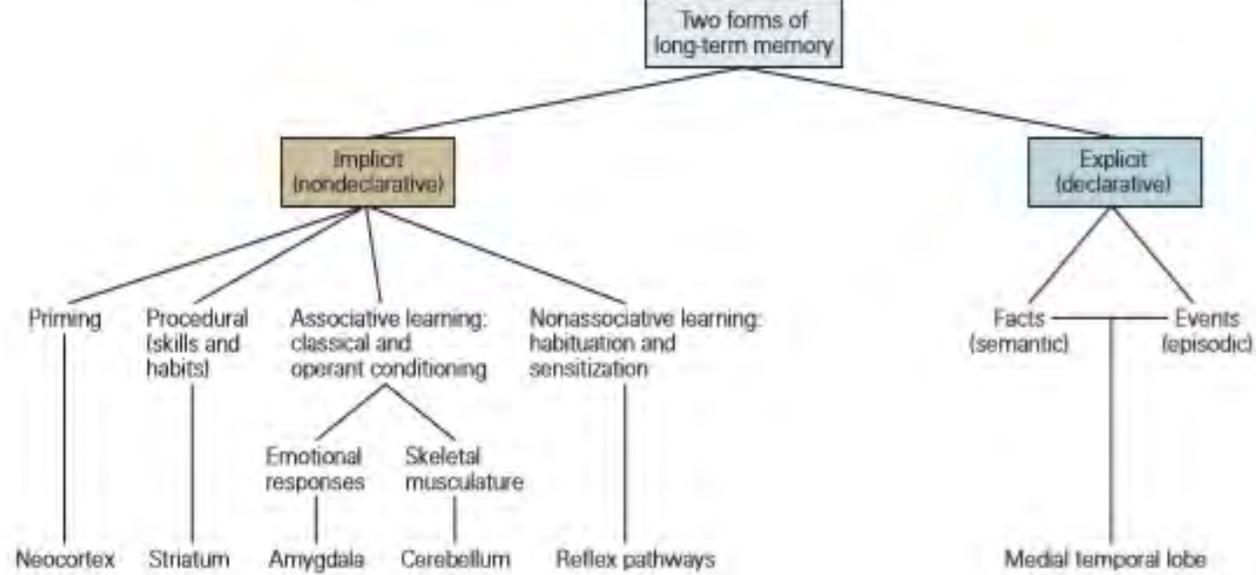
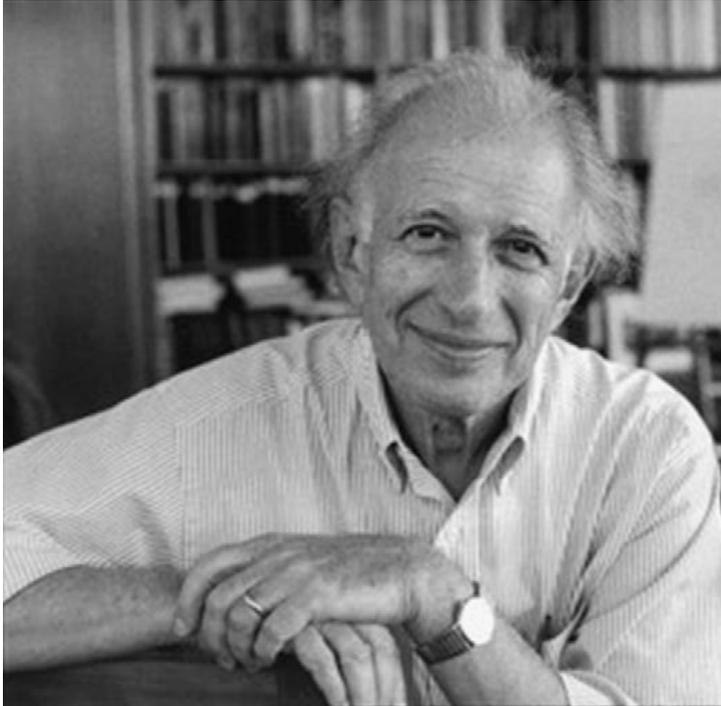
Neuromodulación farmacológica

Neuromodulación por estimulación



El grado de excitabilidad es variable para cada neurona y cada sistema

Eric R. Kandel Ed  
 Principios de Neurociencia 2000  
 Principles of Neural Science 2013



**Figure 66-1** Two forms of long-term memory involve different brain systems. Implicit memory involves the neocortex, striatum, amygdala, cerebellum, and in the simplest cases the

reflex pathways themselves. Explicit memory requires the medial temporal lobe and the hippocampus, as well as certain areas of neocortex (not shown).

**Perceptual Correlates of Nociceptive Long-Term Potentiation and Long-Term Depression in Humans**

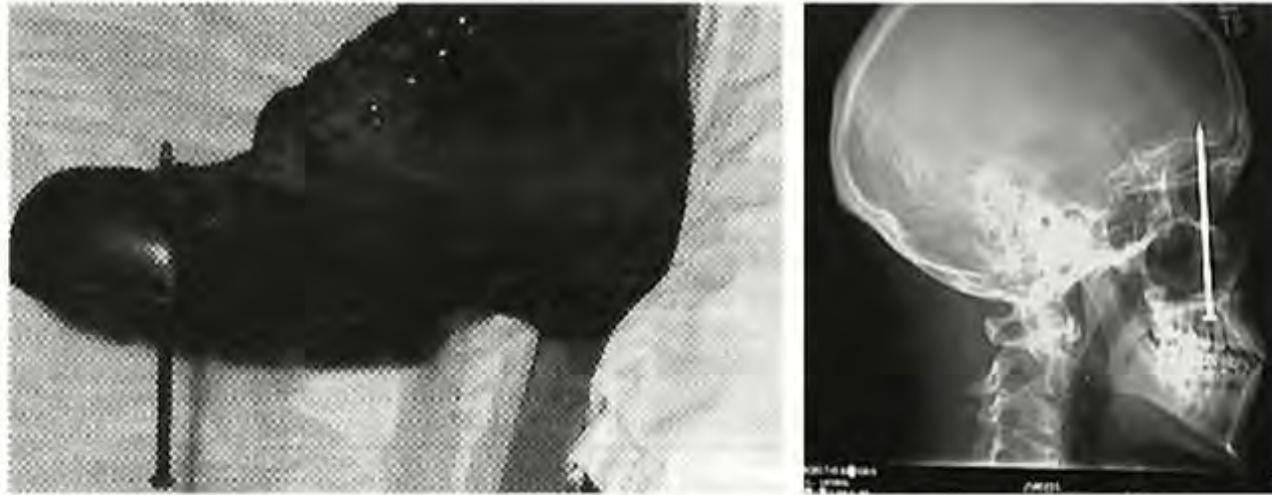
**Thomas Klein,<sup>1,2 \*</sup> Walter Magerl,<sup>1 \*</sup> Hanns-Christian Hopf,<sup>2</sup> Jürgen Sandkühler,<sup>3</sup> and Rolf-Detlef Treede<sup>1</sup>**

<sup>1</sup>Institute of Physiology and Pathophysiology, Johannes Gutenberg University, D-55099 Mainz, Germany,

<sup>2</sup>Department of Neurology, Johannes Gutenberg University, D-55101 Mainz, Germany, and

<sup>3</sup>Brain Research Institute, Vienna University Medical School, A-1090 Vienna, Austria

Journal of Neuroscience, January 28, 2004, 24(4):964-971



Fisher JP, Hassan DT, O' Connor N. Minerva. *Br Med J* 1995;310:70

Lesión imaginada (dolor sin daño)  
versus daño real sin dolor

# “DOLOR SINE MATERIA” (sin “daño”)

Proctalgia

Lumbalgia crónica

Pancreatitis crónica

Dispareumia

Cistitis intersticial

Cefalea crónica

Talalgia

Coxalgia

Precordialgia

Cervicalgia

Vulvodinia

## DOLOR CRÓNICO

**80 % de consultas en una Unidad de Dolor**

**8% de consultas en Medicina de Familia**

**8 millones de personas en España**

- 1- Dolor pélvico
- 2- Cefalea
- 3- Lumbalgia / Cervicalgia

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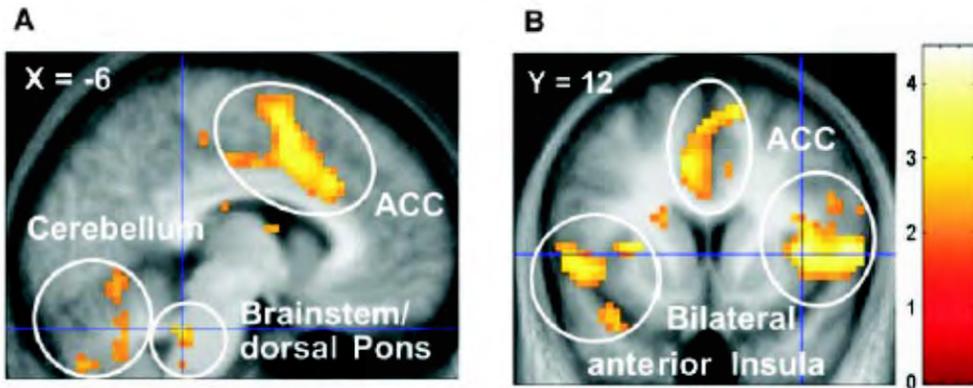
“Fibromialgia”  
“Fascitis plantar”  
Etc

MAS DE 6 MESES

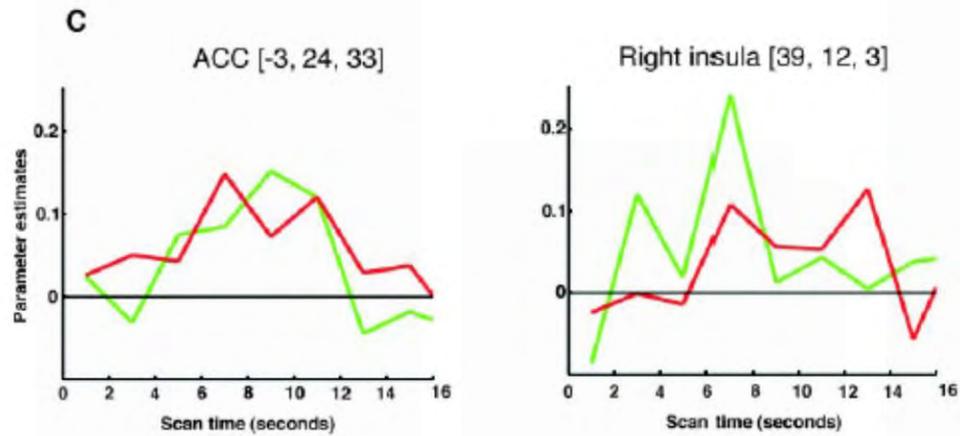
NO EVIDENCIA DE DAÑO

NO DESPIERTA AL DORMIR

NO MEJORA CON ANALGESICOS



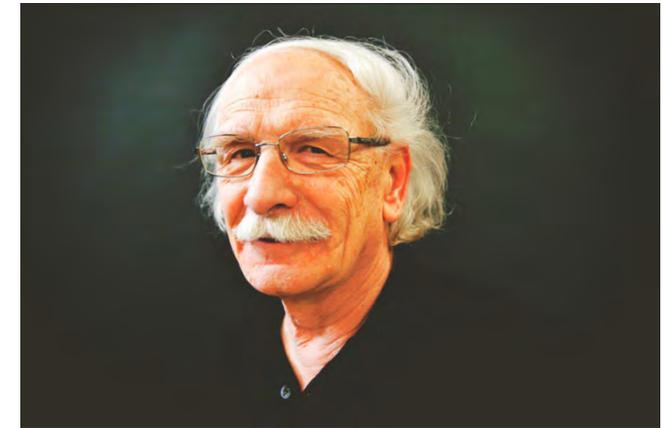
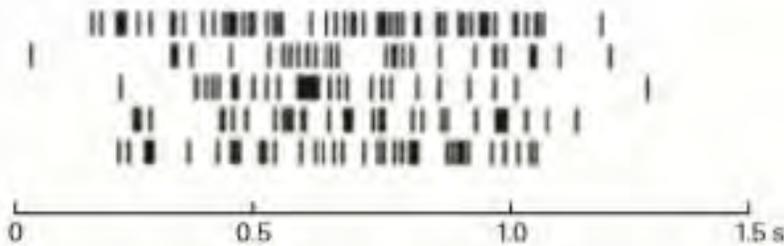
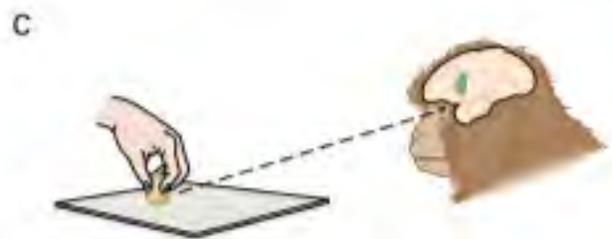
# EMPATIA



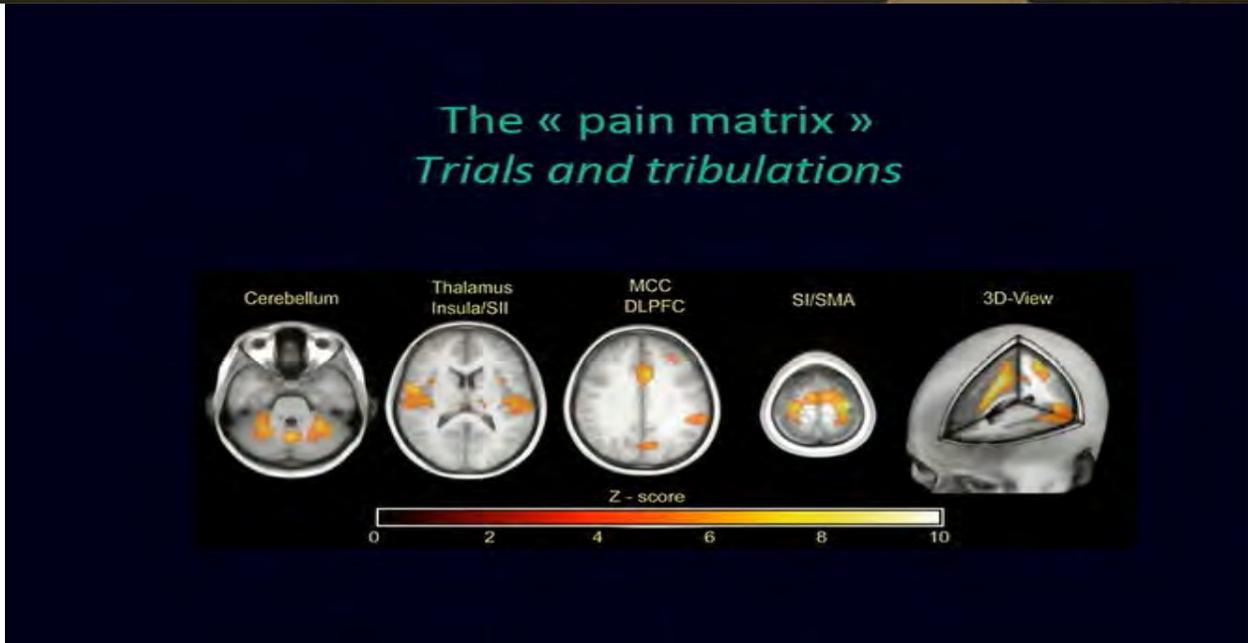
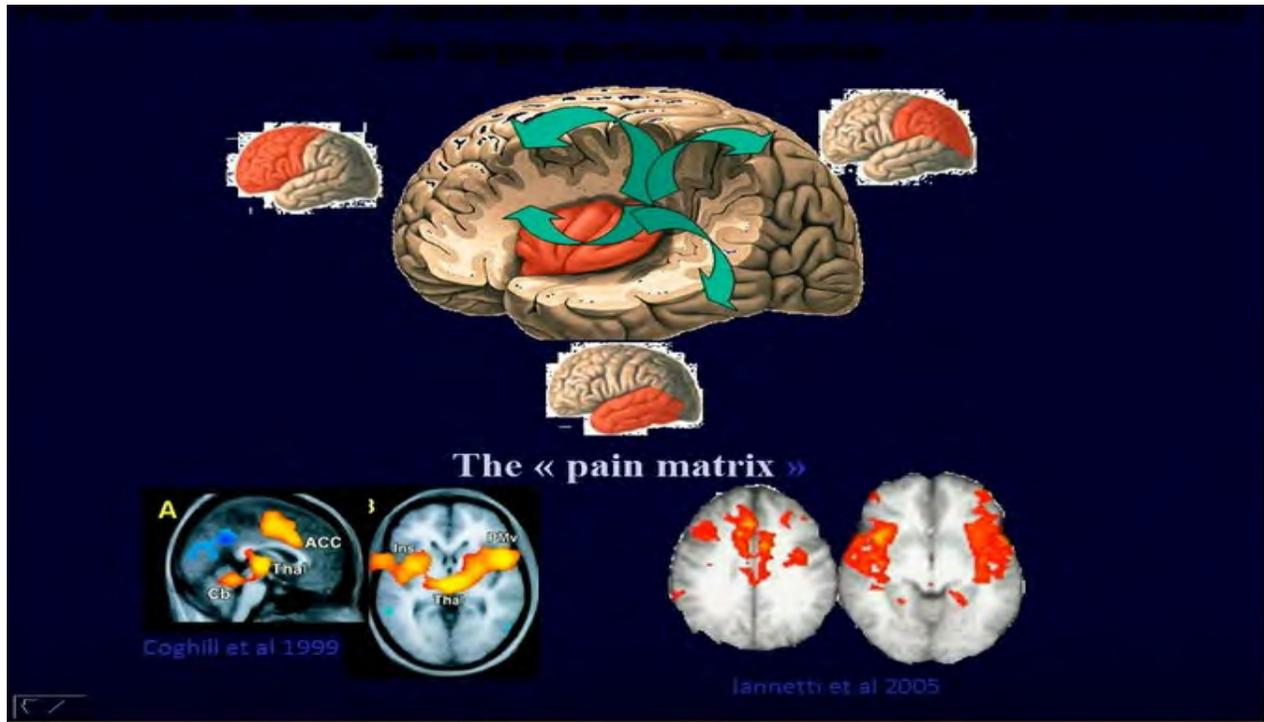
ACC Rostral

Insula anterior

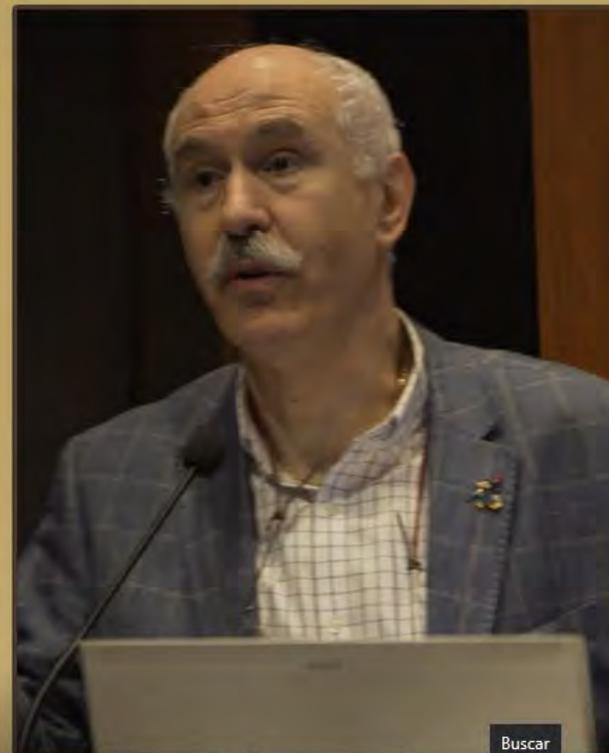
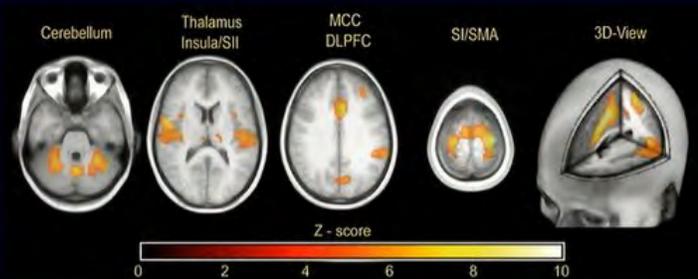
# Mirror neurons



Giacomo Rizzolatti



The « pain matrix »  
*Trials and tribulations*



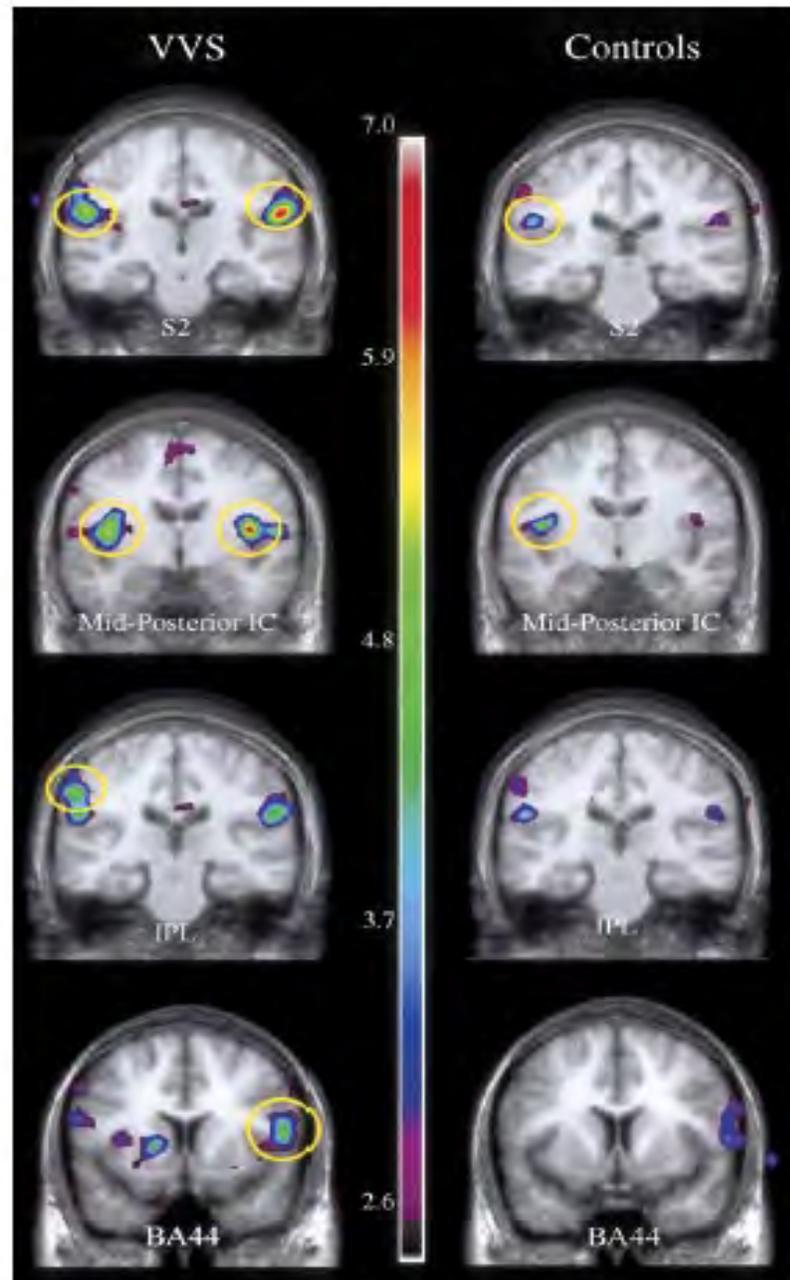
0:01:34



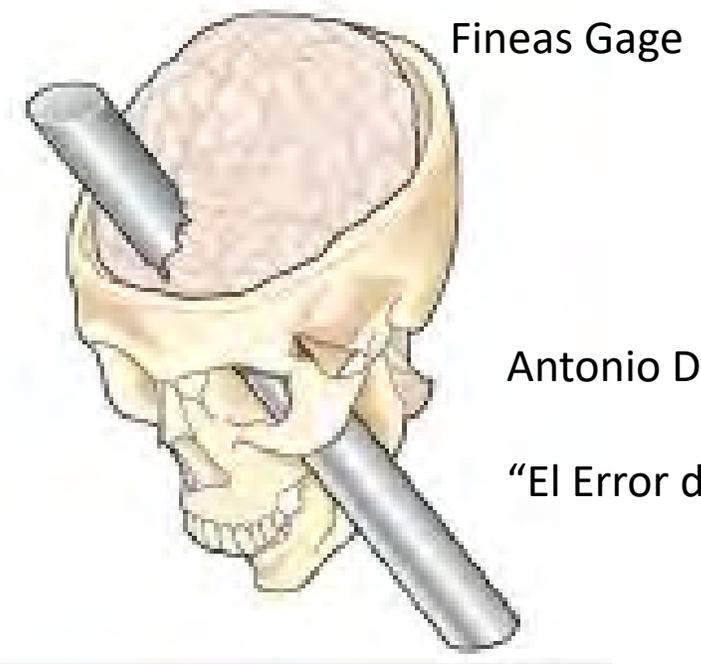
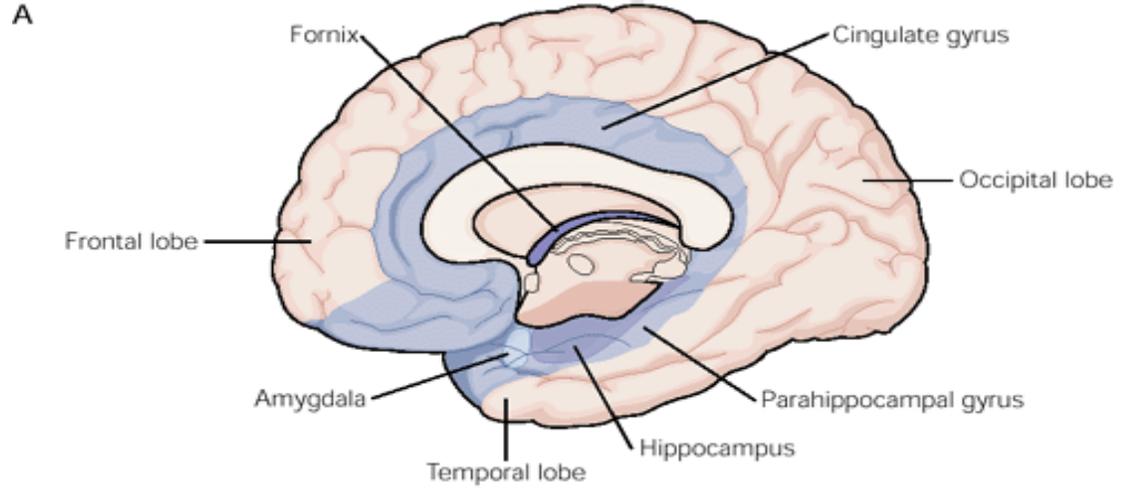
0:41:27



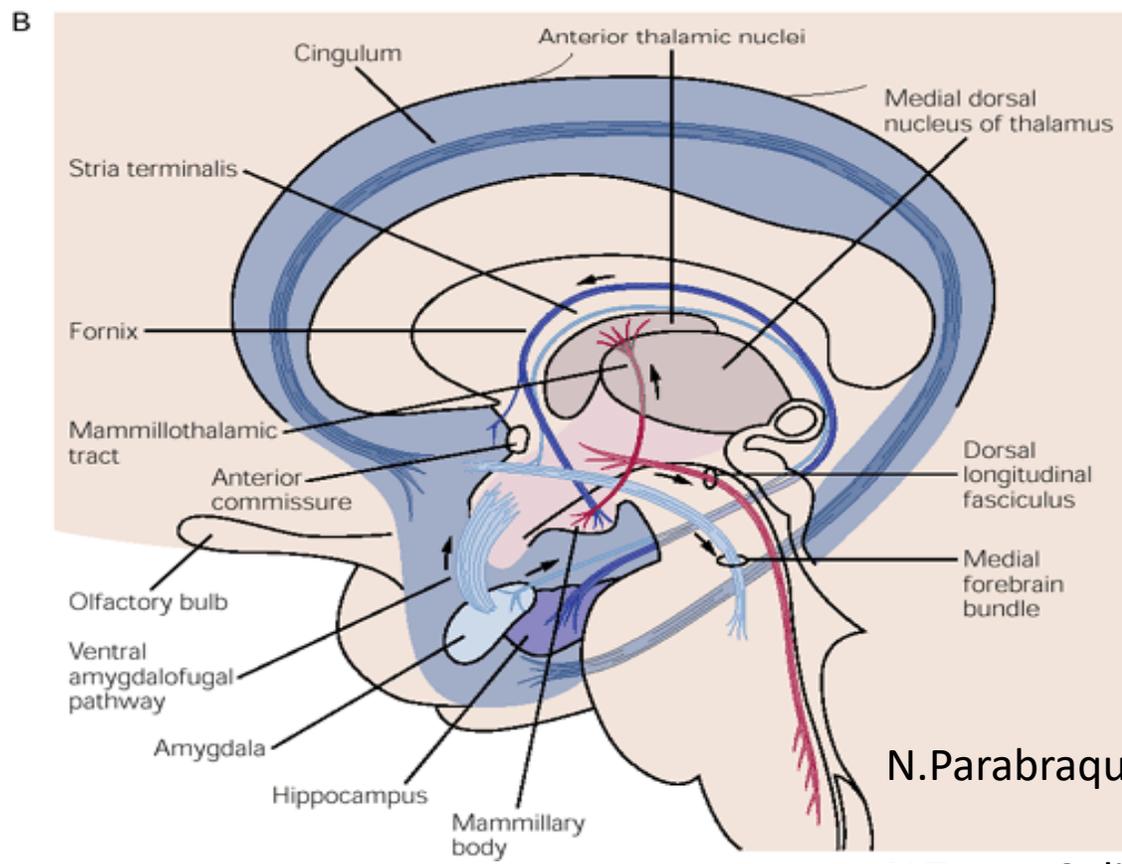
Alodinia  
en vestibulitis vulvar  
que causa  
Dispareunia



Pukall et al. Pain 2005

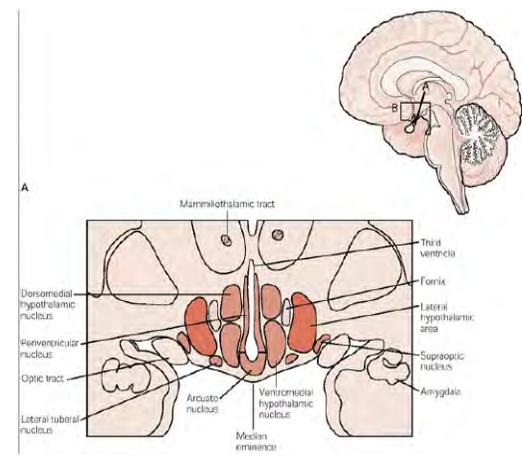


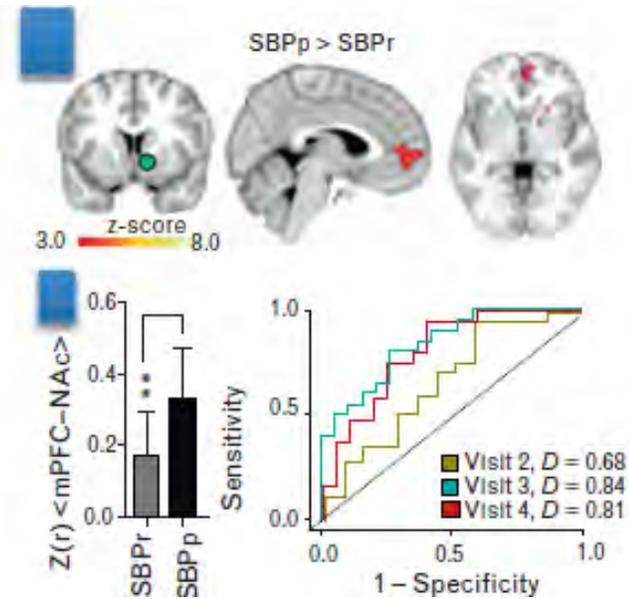
Antonio Damasio  
“El Error de Descartes”



N.Parabraquial

N.Tracto Solitario





## Predicting transition to chronic pain

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*A. Vania Apkarian, Marwan N. Baliki, and Melissa A. Farmer*

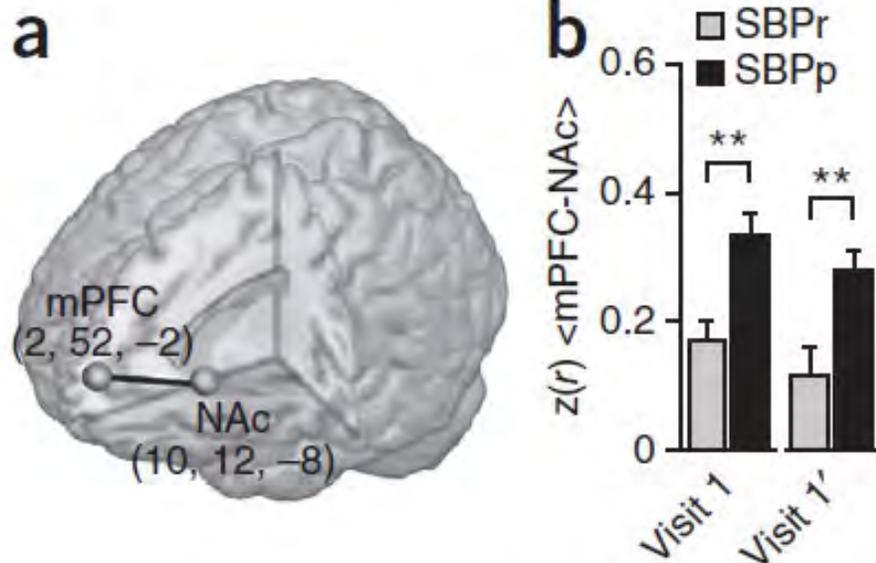
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**Curr Opin Neurol** 2013, 26:360–367

# Corticostriatal functional connectivity predicts transition to chronic back pain

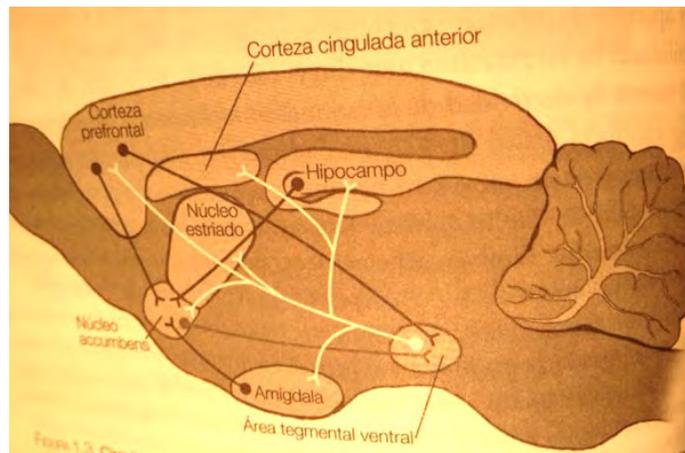
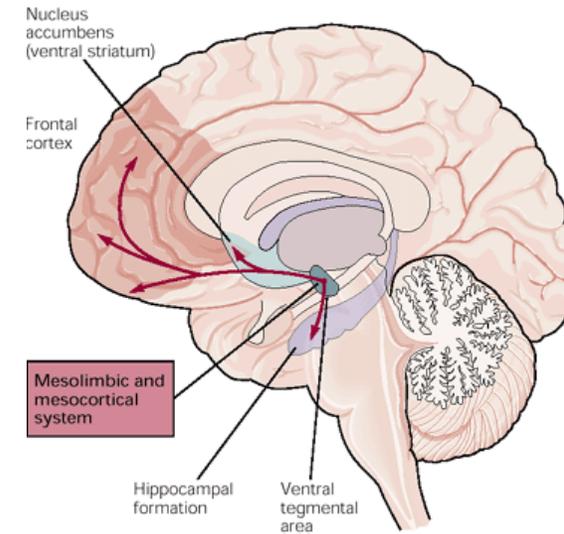
Marwan N Baliki<sup>1</sup>, Bogdan Petre<sup>1</sup>, Souraya Torbey<sup>1</sup>,  
Kristina M Herrmann<sup>1</sup>, Lejian Huang<sup>1</sup>, Thomas J Schnitzer<sup>2</sup>,  
Howard L Fields<sup>3</sup> & A Vania Apkarian<sup>1,4</sup>

NATURE NEUROSCIENCE | VOLUME 15 | NUMBER 8 | AUGUST 2012



# DOLOR y RECOMPENSA

## ESTAN RELACIONADOS



Sadomasoquismo

Descarga dopaminérgica al finalizar dolor agudo

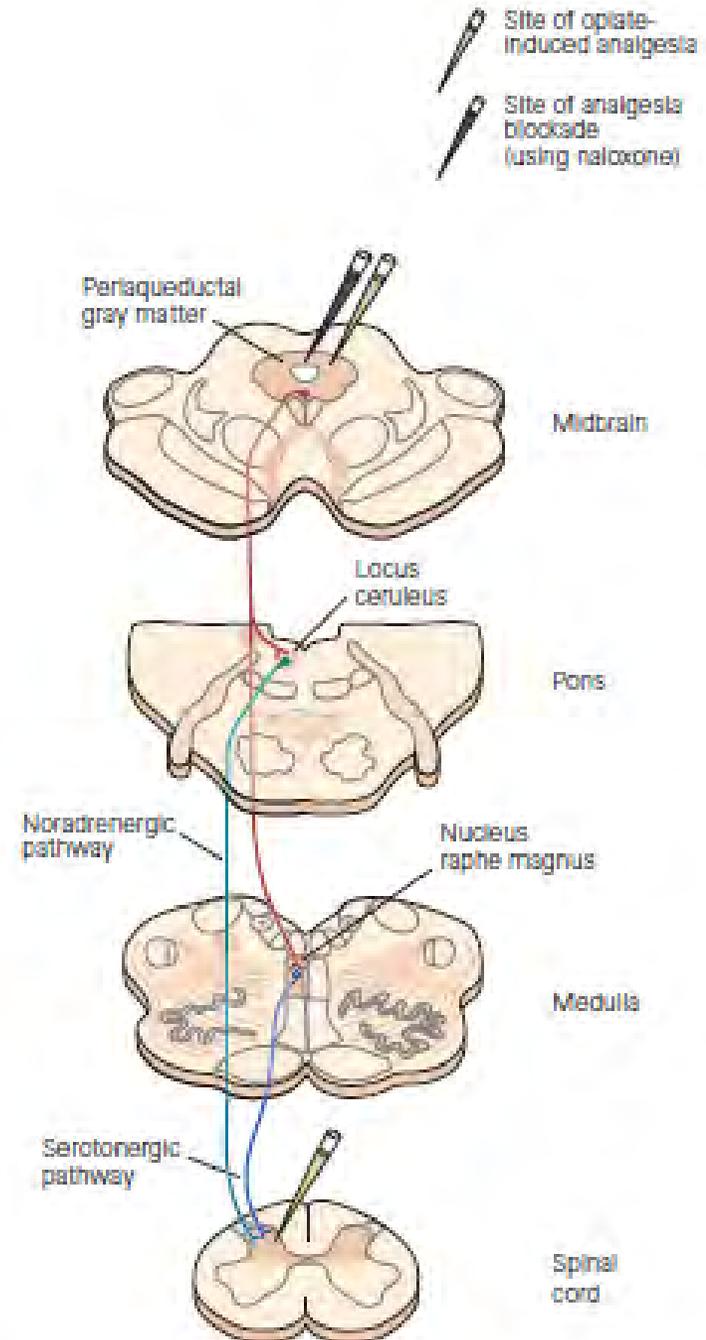
Los opioides activan la recompensa

Opiáceos

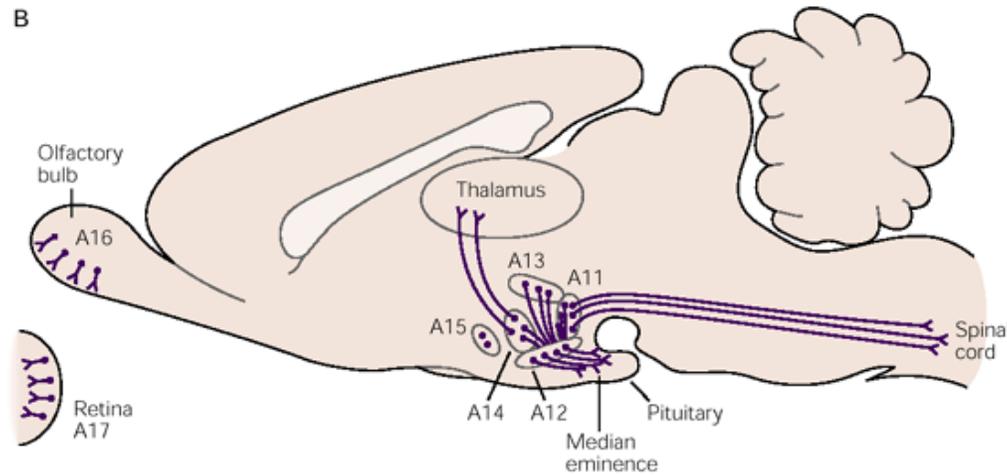
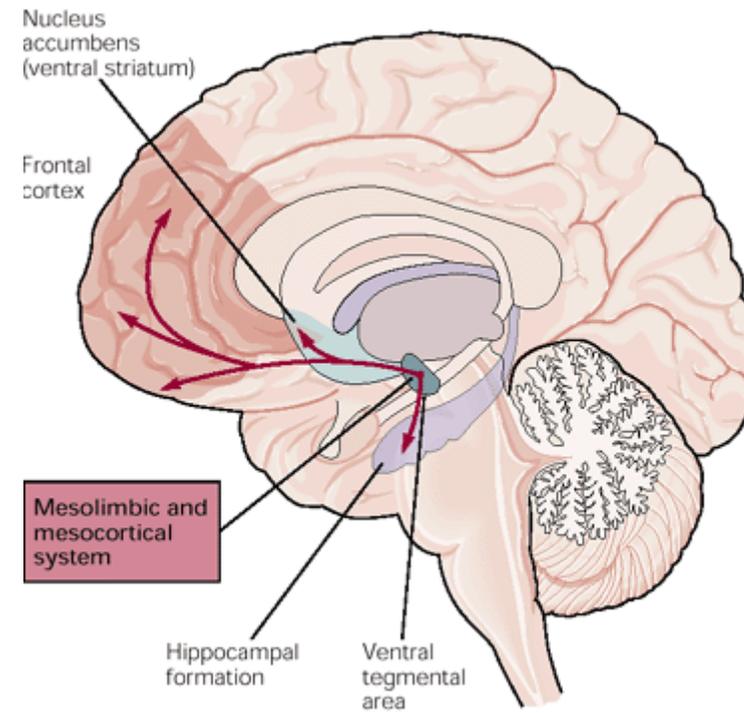
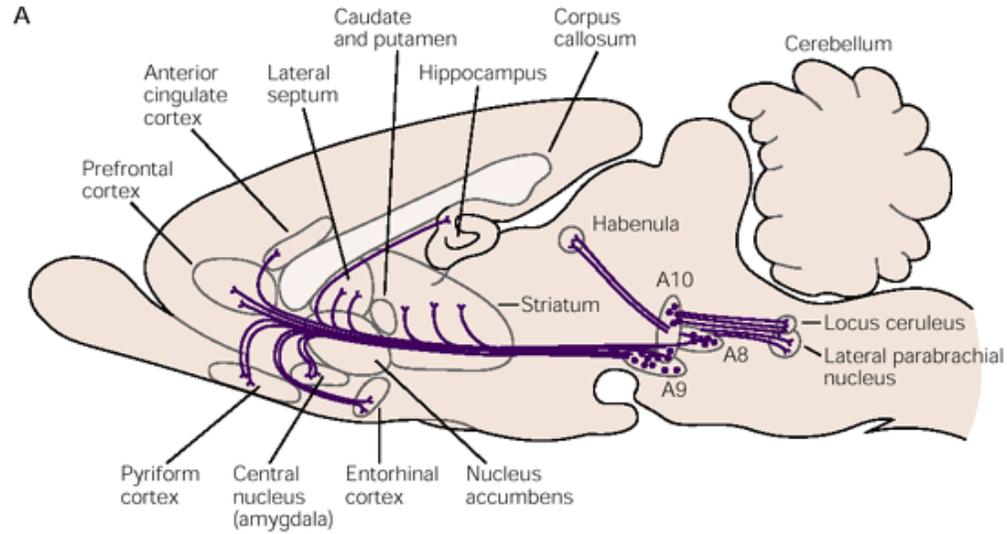
Endorfinas

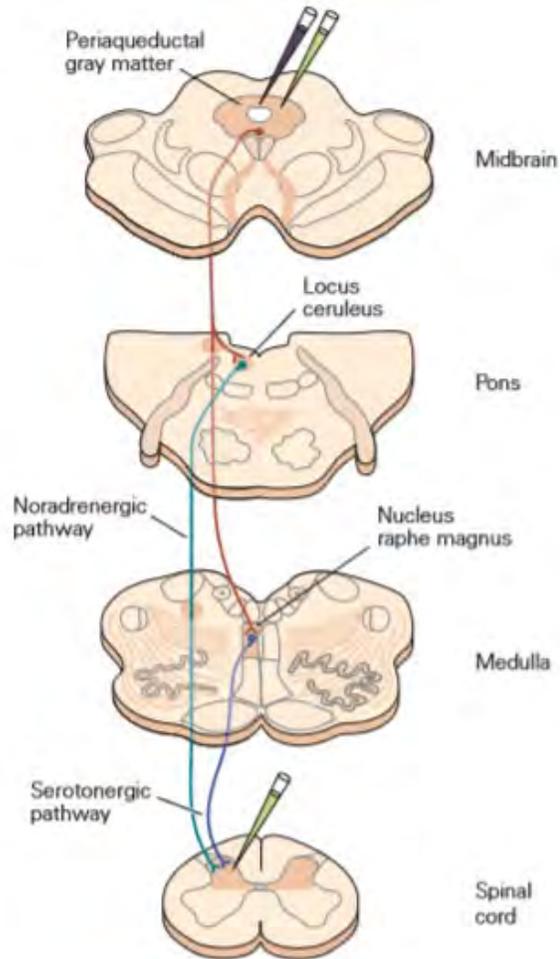
# Analgesia fisiológica

Propeptide	Peptide(s)	Preferential receptor
POMC	$\beta$ -endorphin	$\mu/\delta$
	Endomorphin-1	$\mu$
	Endomorphin-2	$\mu$
Proenkephalin	Met-enkephalin	$\delta$
	Leu-enkephalin	$\delta$
Prodynorphin	Dynorphin A	$\kappa$
	Dynorphin B	$\kappa$
Pro-orphanin FQ	Orphanin FQ	Orphan receptor



# Sistema dopaminérgico





**Los péptidos opioides endógenos**

**son necesarios como analgésicos**

**para anular dolor durante el ataque**

**para no sufrir cuando el animal es comido**

**Table 24–1** Four Major Classes of Endogenous Opioid Peptides

Propeptide	Peptide(s)	Preferential receptor
POMC	$\beta$ -endorphin	$\mu/\delta$
	Endomorphin-1	$\mu$
	Endomorphin-2	$\mu$
Proenkephalin	Met-enkephalin	$\delta$
	Leu-enkephalin	$\delta$
Prodynorphin	Dynorphin A	$\kappa$
	Dynorphin B	$\kappa$
Pro-orphanin FQ	Orphanin FQ	Orphan receptor

Las drogas adictivas “en pico” generan adicción

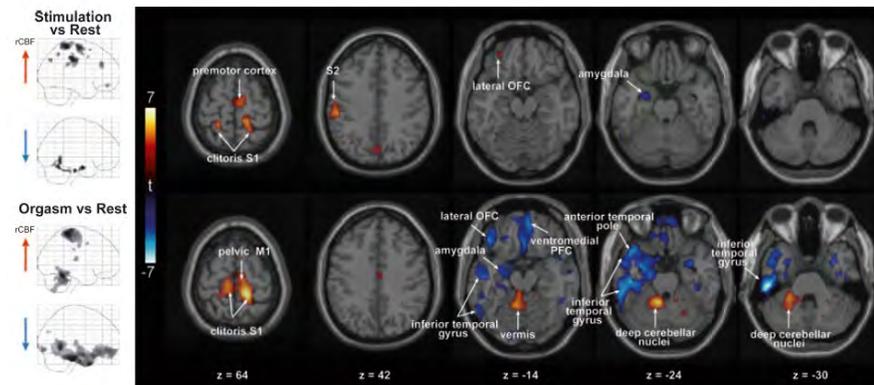
Establecen un “condicionamiento” droga / placer que origina aprendizaje (LTP)

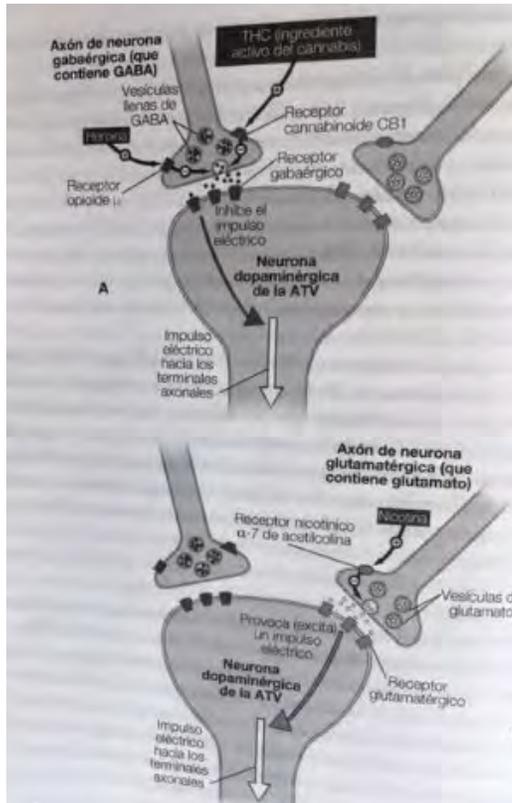
La LTP es mayor

con heroína inyectada que con un opiáceo rectal o en parche

con 200 pequeños “picos” de nicotina al día que con tabaco masticado

3310 J. R. Georgiadis *et al.*





## Los opioides son agentes mediadores e influyen en múltiples funciones

Exaltación de la recompensa

Influencia en el stress

Motivación

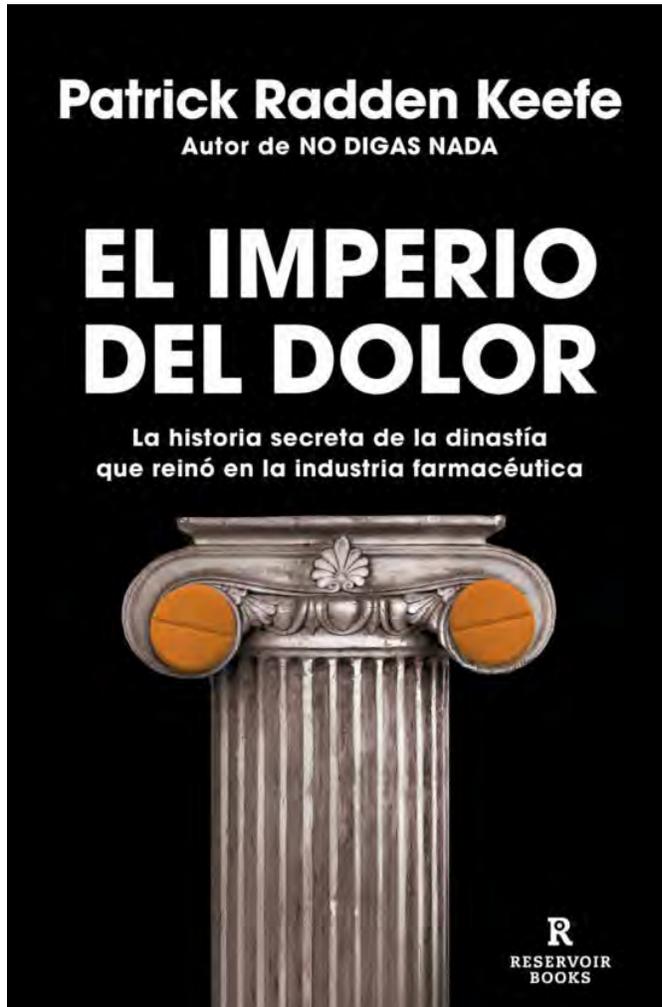
Emociones (miedo, hambre, ira, apego, compasión...)

Capacidad de generar tolerancia

Capacidad de generar adicción

La administración continuada de opioides inhibe la producción de endorfinas

Que sucede con los “picos” fisiológicos de recompensa ??????



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<https://dx.doi.org/10.20986/resed.2016.3482/2016>

## CARTAS AL DIRECTOR

**Prescripción de opioides de acción prolongada y mortalidad en pacientes con dolor crónico no oncológico**

**Prescribing long-acting opioids and mortality in patients with chronic noncancer pain**

**A. Alcántara-Montero<sup>1</sup> , A. González-Curado<sup>1</sup>**

<sup>1</sup>Unidad del Dolor. Hospital Don Benito-Villanueva de la Serena. Don Benito, Badajoz



# Pain and its Transformations

## The Interface of Biology and Culture

Coakley S and Kaufman K Ed.  
Harvard University Press 2007

Clifford J.Wolf: Deconstructing Pain: A Deterministic Dissection of the Molecular Basis of Pain

**Howard L.Fields: Setting the Stage for Pain: Allegorical Tales from Neuroscience (\*)**

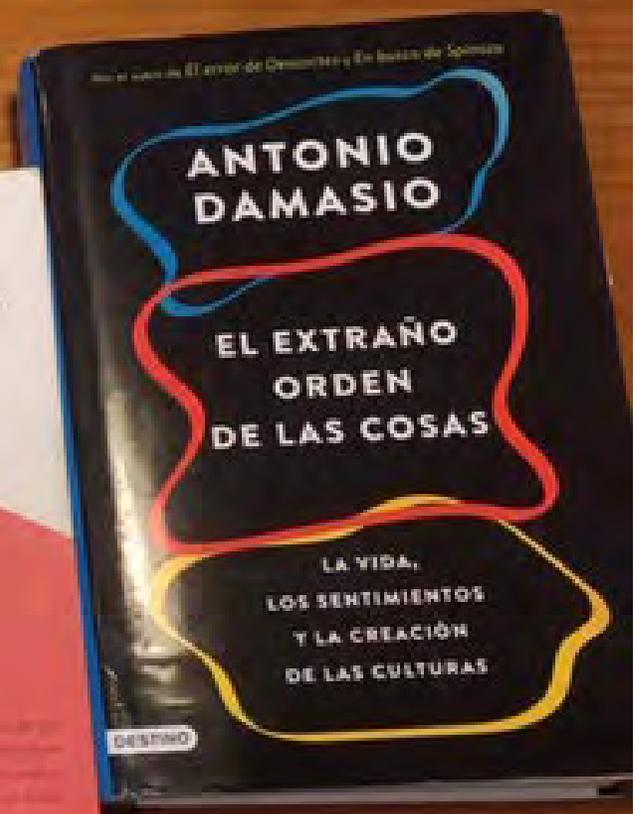
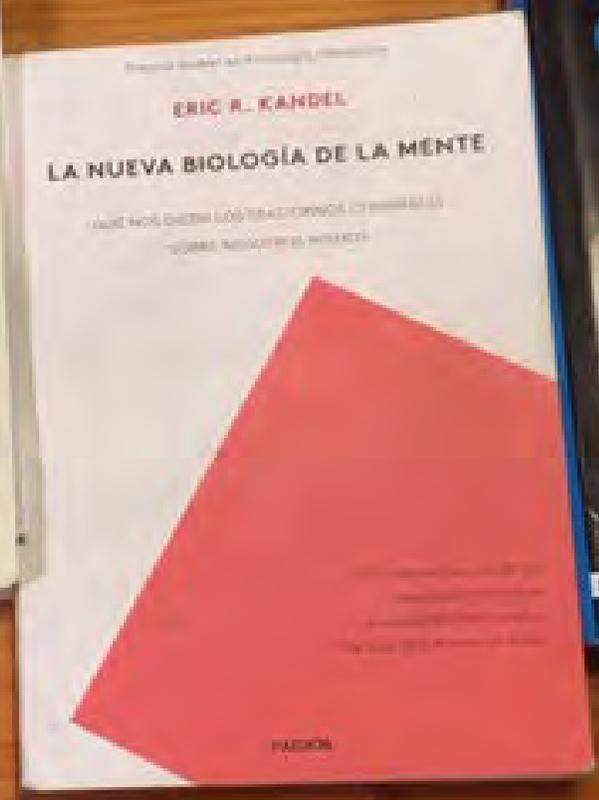
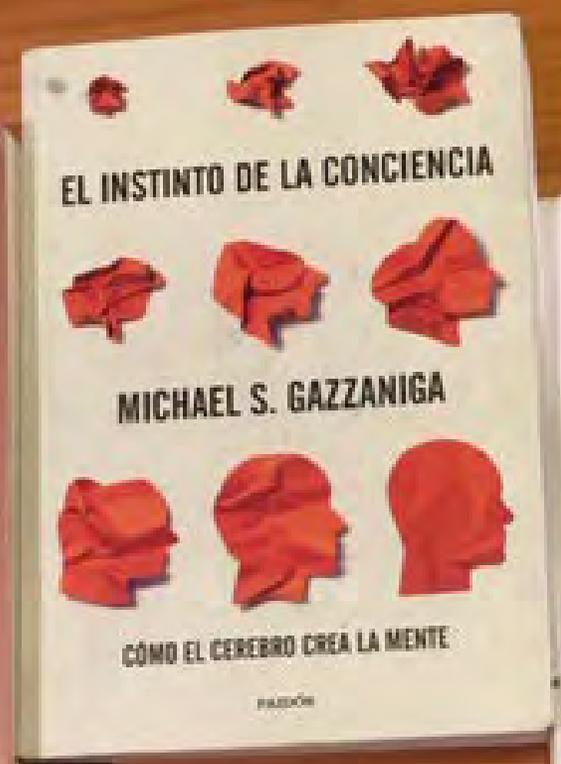
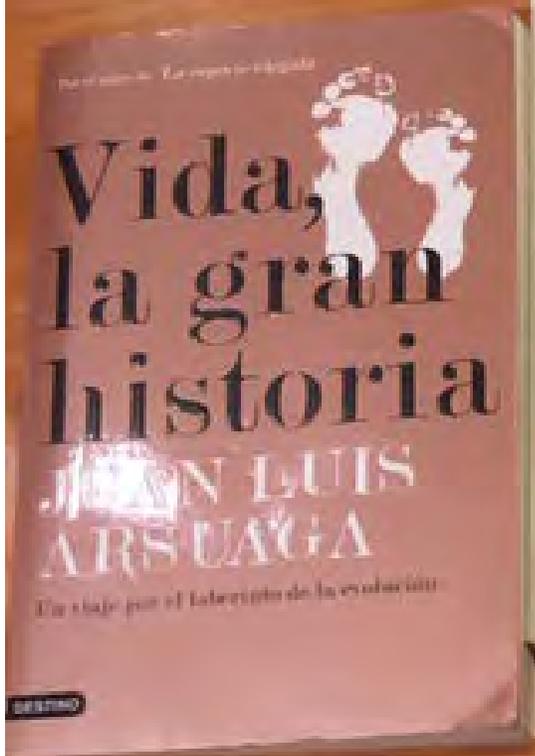
Grief and Pain: The Mediation of Pain in Music

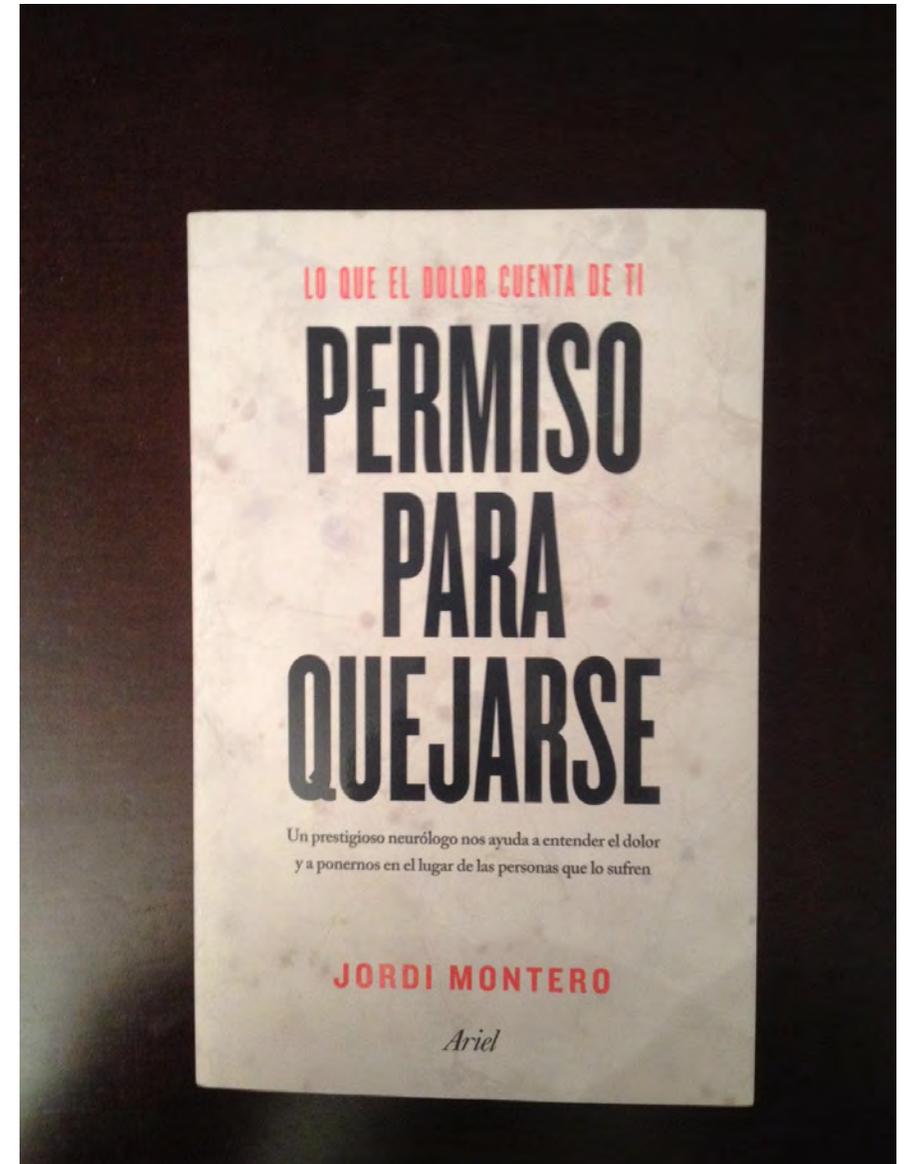
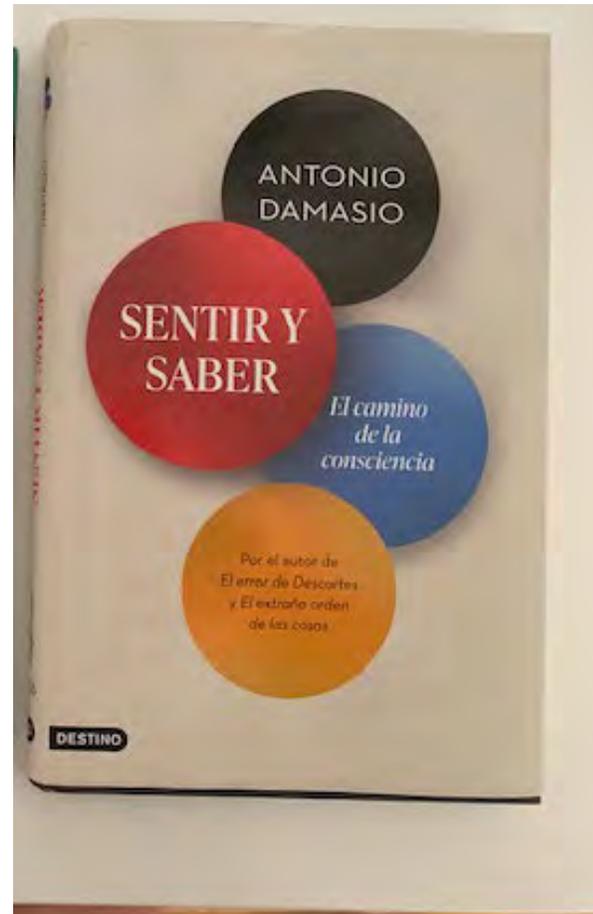
Pain, Ritual and the Somatomoral: Beyond the Individual

When is Pain not Suffering and Suffering not Pain?. Self, Ethics, and Transcendence

.....

(\*) «Pain Transforms Meaning, Meaning Transforms Pain»







**A flor de piel**  
Una interpretación de las caricias y las emociones desde la neurología  
Dr. Jordi Montero

Plataforma Actual

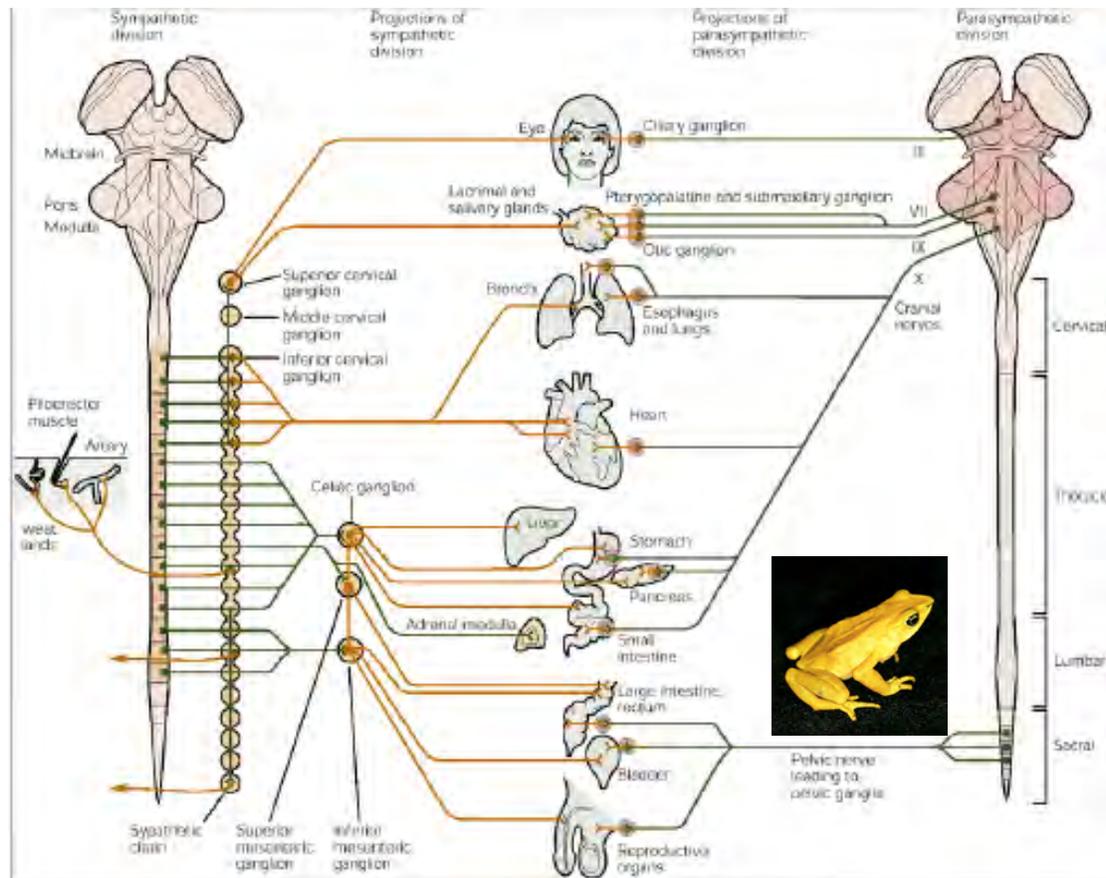


Descubre la importancia del contacto a la luz de la evolución y la neurociencia

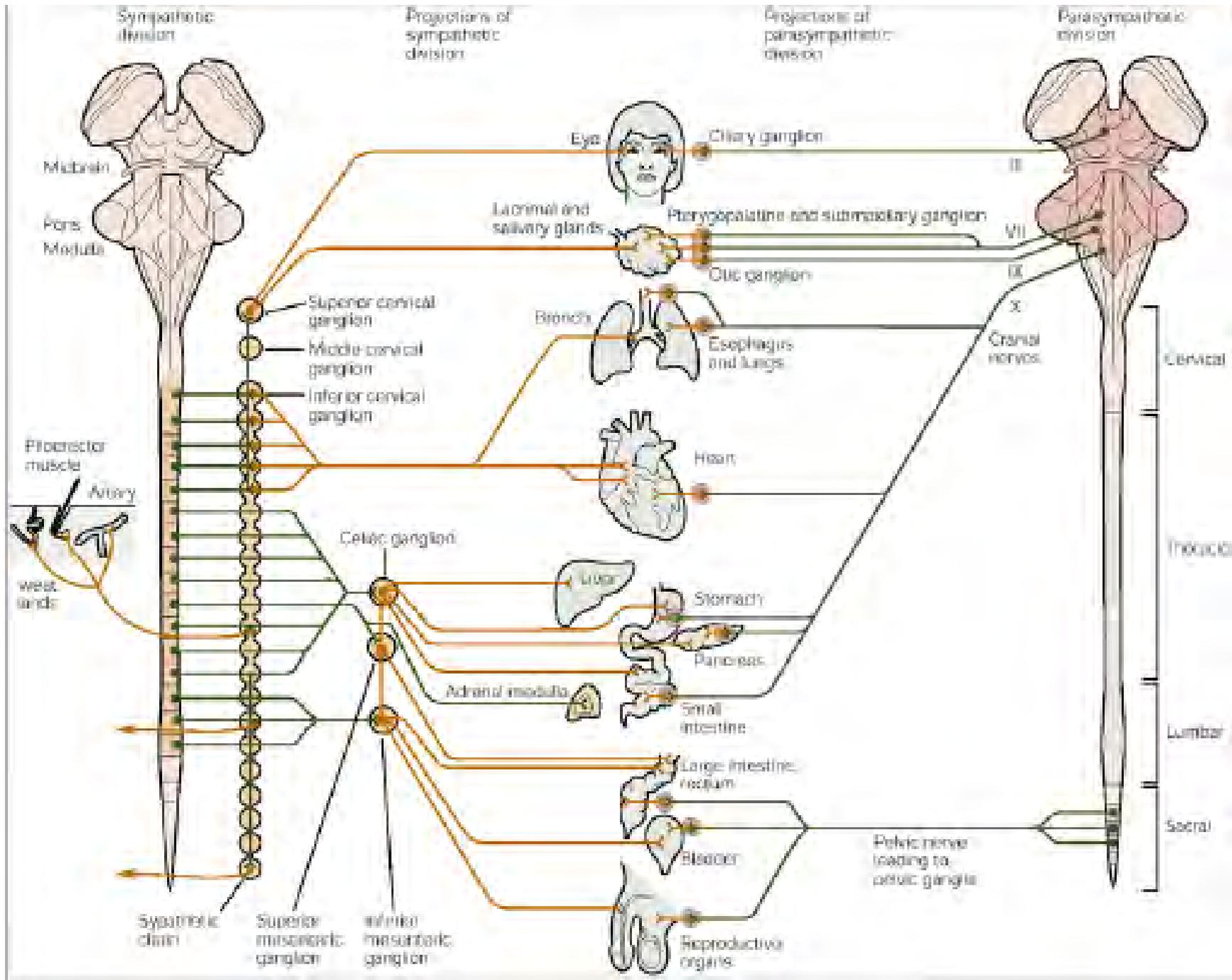


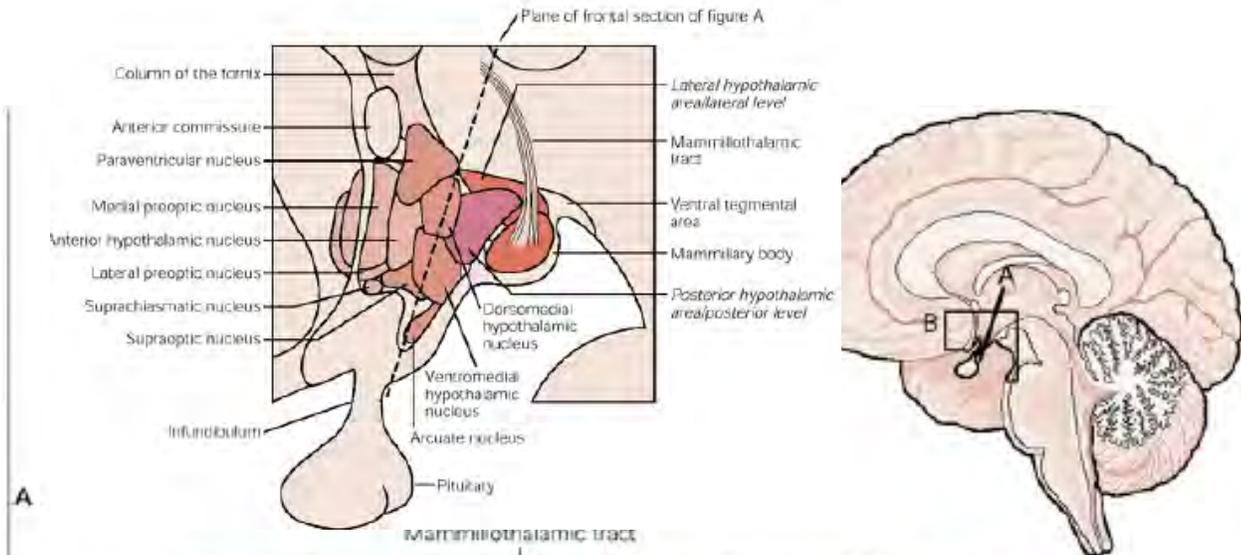


# SISTEMA NERVIOSO ANTIGUO (AUTONOMO)

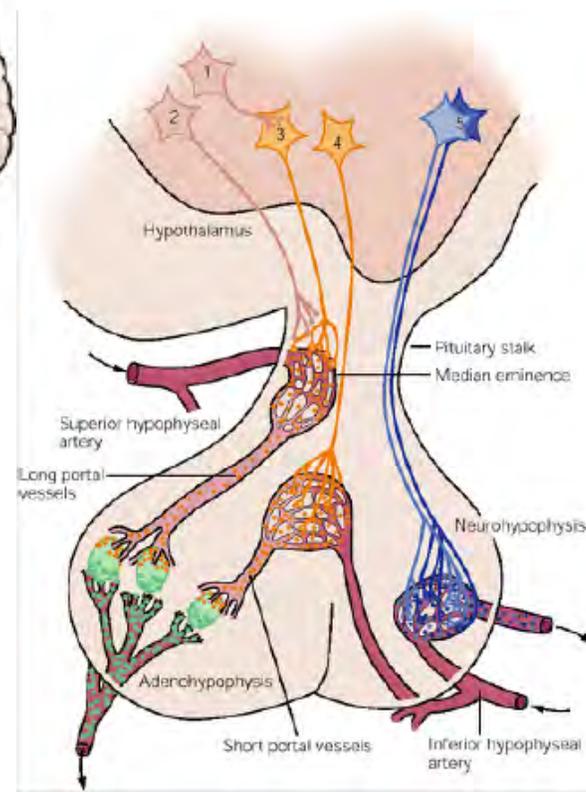
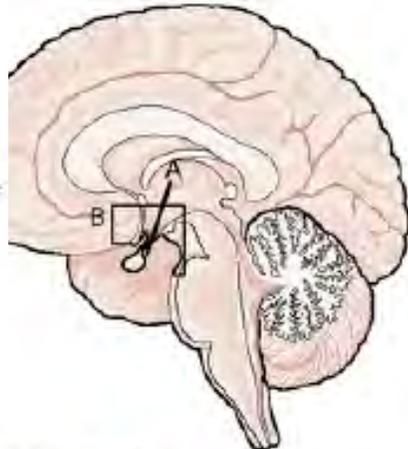
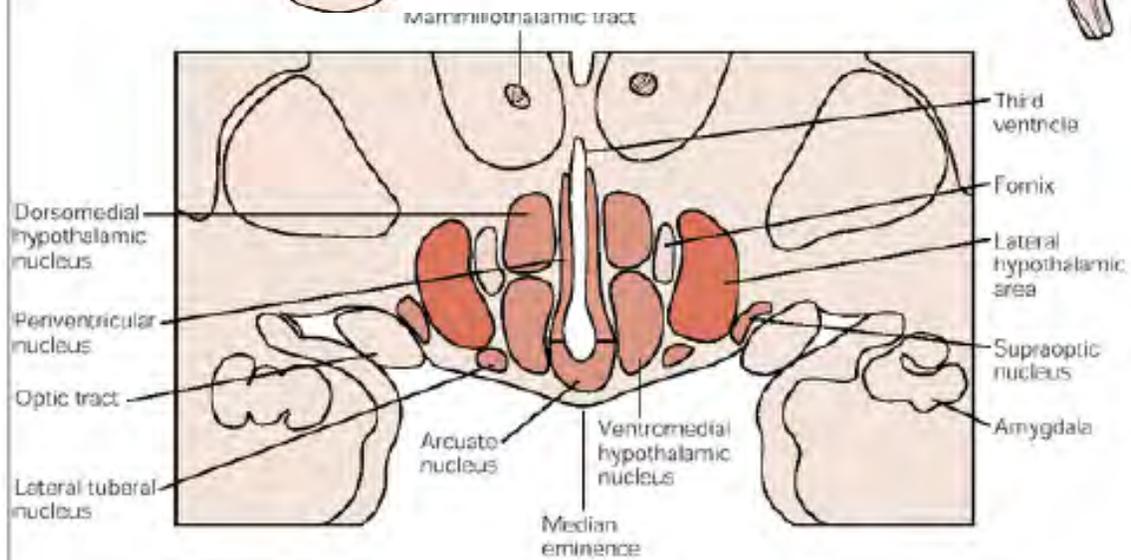


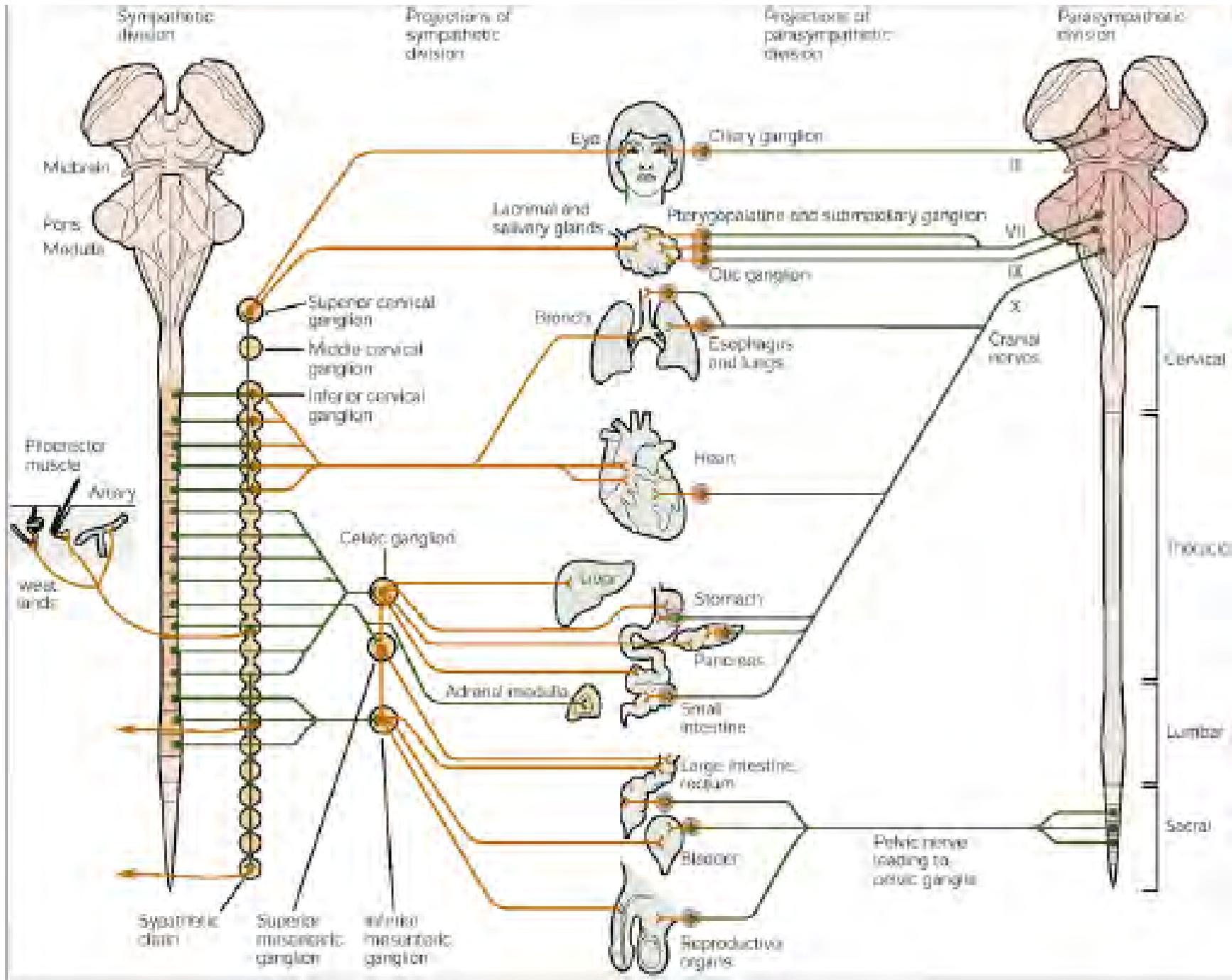
- Respiración
- Ritmo cardiaco
- Sudoración
- Pupilas
- Eritema y "flair"
- Control digestivo
- Micción/ Defecación

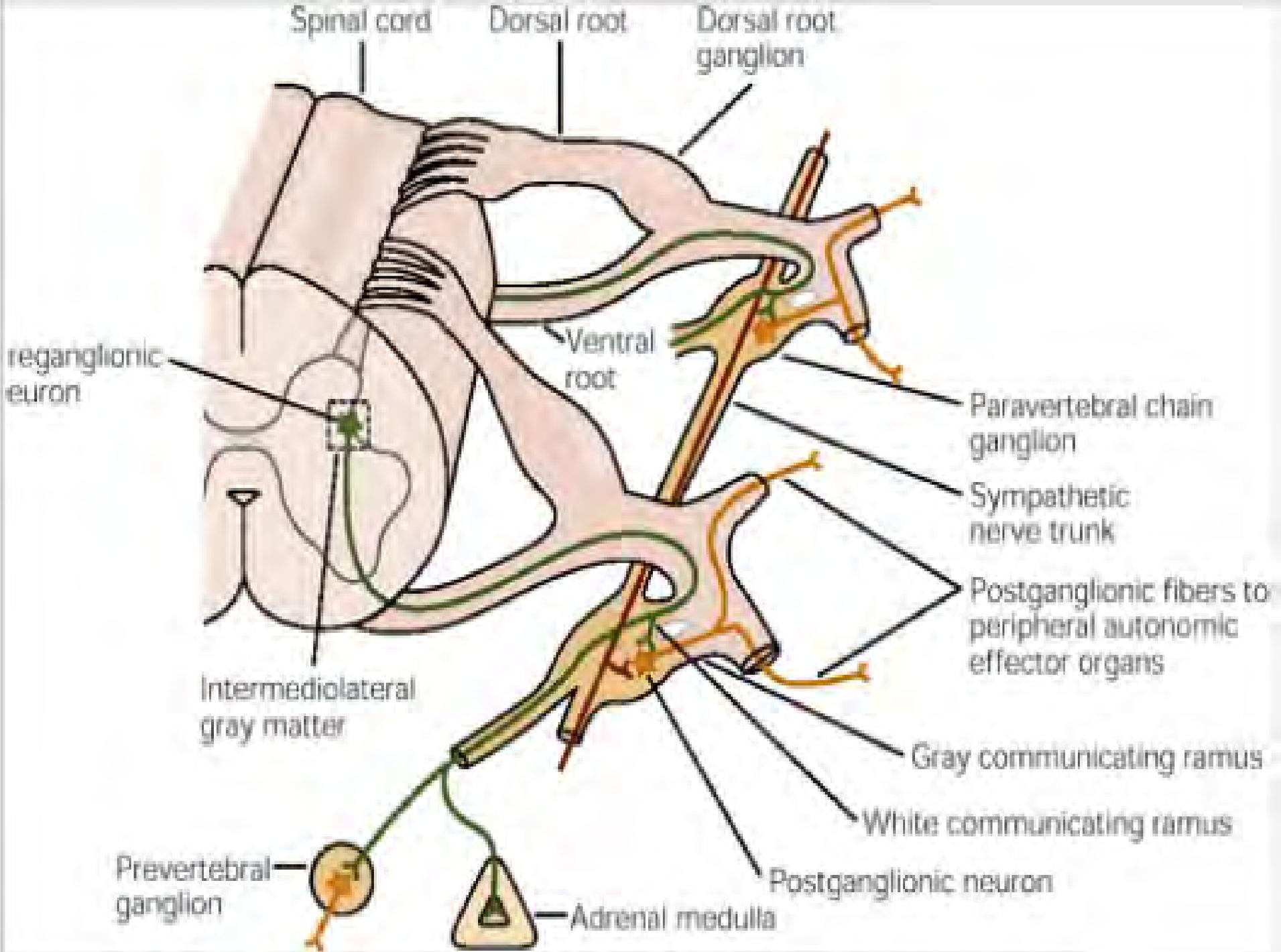




A







Receptor category	Functional roles <sup>1</sup>	Drugs that act selectively at these receptors	Medical use
<b>Norepinephrine</b>			
Adrenergic $\alpha_1$	Contractile effects of NE on smooth muscle, especially blood vessels, urogenital, and sphincter muscles	Prazosin (antagonist)	Hypertension
Adrenergic $\alpha_2$	Presynaptic control (inhibitory) of release of NE, ATP, and ACh from nerve terminals	Yohimbine (antagonist)	Delay ejaculation
Adrenergic $\beta_1$	Stimulatory effects of NE and circulating epinephrine on heart	Atenolol (antagonist)	Hypertension
Adrenergic $\beta_2$	Relaxant effects of NE on smooth muscle in gastrointestinal tract, urinogenital system, and airways	Salbutamol (agonist)	Bronchodilator for asthma
Adrenergic $\beta_3$	Stimulate release of free fatty acids from adipose tissue	None	Potential in obesity
<b>Acetylcholine</b>			
Cholinergic-nicotinic (ganglionic type)	Fast excitation of postganglionic neurons in autonomic ganglia	Hexamethonium (antagonist)	Hypertension (formerly)
Cholinergic-muscarinic $M_1$	Inhibit ACh and NE release from autonomic nerve terminals	Pirenzepine (antagonist)	Anti-ulcerogenic
Cholinergic-muscarinic $M_2$	Effects of ACh on heart and smooth muscle	Atropine (nonselective antagonist)	Mydriatic
Cholinergic-muscarinic $M_3$	ACh-induced secretion from glandular tissues (eg, salivary gland)	Atropine (nonselective antagonist)	Reduced drooling in Parkinson disease
<b>Others</b>			
Purinergic $P_1$ (Four subtypes)	Modulatory effects of adenosine on autonomic effector tissues	Theophylline (antagonist)	Bronchodilator
Purinergic $P_2$ (Two subtypes)	Fast and slow responses to ATP in smooth muscle	Few drugs; suramin is $P_{2Y}$ antagonist	None
Nitric oxide (NO)	Relaxant effects on smooth muscle, especially blood vessels	Glyceryl trinitrate and nitroprusside (generate NO)	Coronary vasodilators for angina
<sup>1</sup> ACh = acetylcholine; ATP = adenosine triphosphate; NE = norepinephrine.			

