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68° CONGRESSO NAZIONALE SIGG
Ritorno al futuro
FIRENZE, 13-16 DICEMBRE 2023
PALAZZO DEI CONGRESSI

LA GESTIONE DEL DOLORE NELL'ANZIANO

Gli approcci metodologici nella rilevazione del dolore

DR.SSA MANUELA BARONIO

SERVIZIO DI ANESTESIA E RIANIMAZIONE IN ORTOPEDIA.
AZIENDA OSPEDALIERA UNIVERSITARIA CAREGGI

Definizioni

Razionale

Strategie

Il dolore è un'esperienza emozionale e sensoriale spiacevole associata ad un danno tissutale in atto, potenziale o percepito come tale

Mannion e Woolf, 2000

International Association for the Study of Pain

Dolore acuto

Difesa

Dolore SINTOMO

Dolore cronico

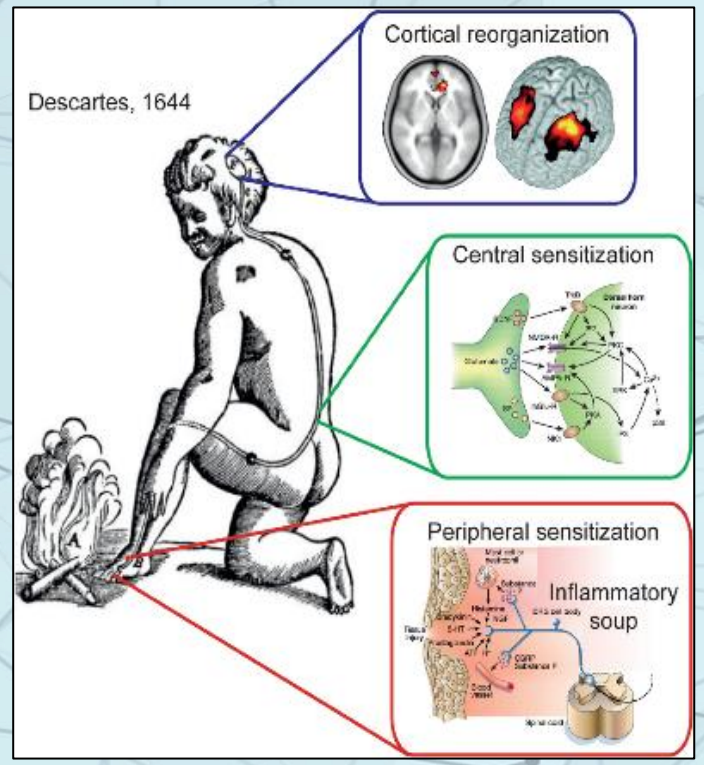
Offesa

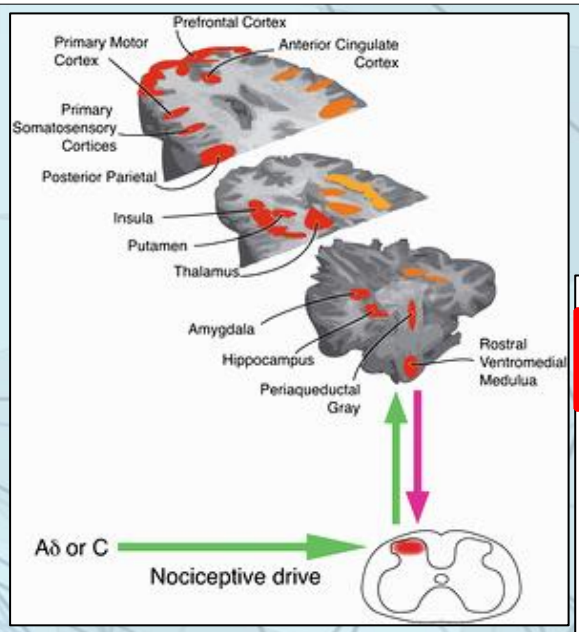
Dolore MALATTIA

2020 PAIN, definition of pain

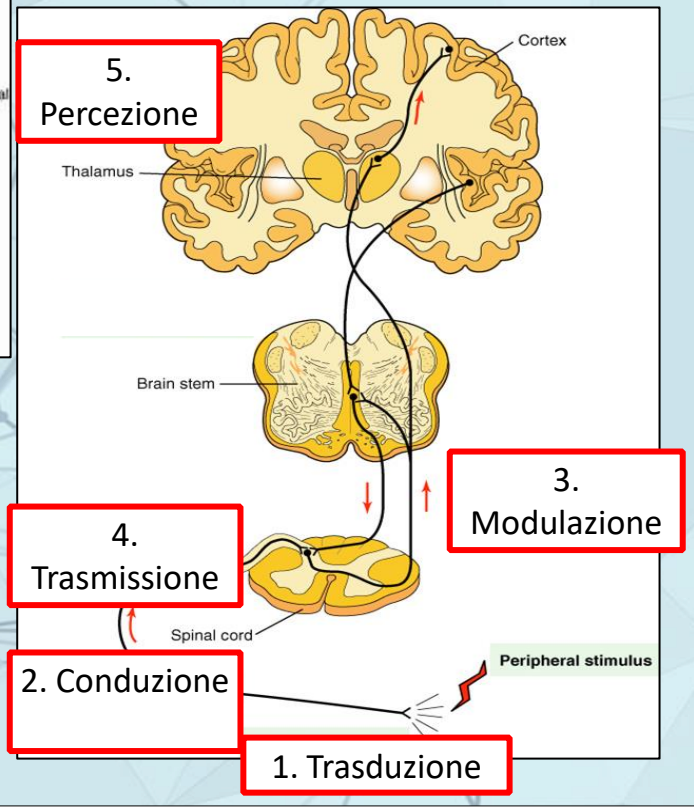
Esperienza sensoriale ed emozionale spiacevole associata, o simile a quella associata, ad un danno tissutale reale o potenziale

LE FASI "NEURONALI" DEL DOLORE

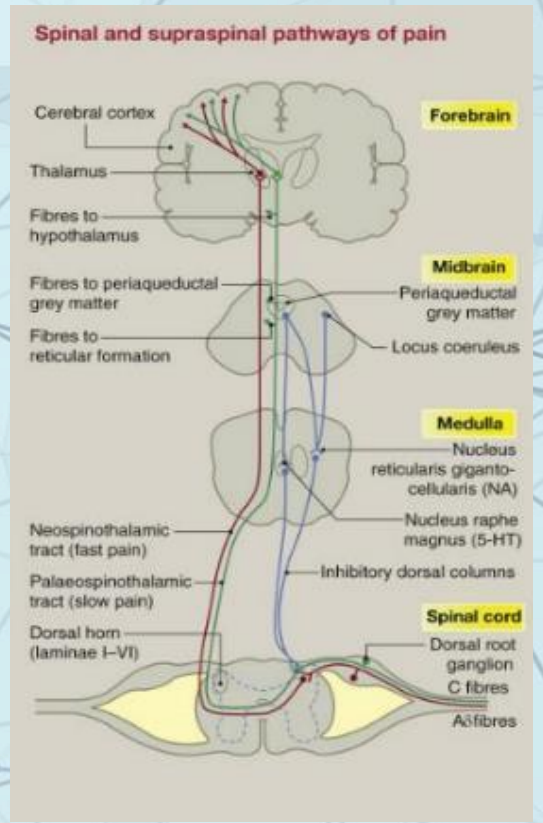




1. **Trasduzione**
2. **Conduzione**
3. **Modulazione**
4. **Trasmissione**
5. **Percezione**



STRUTTURE NERVOSE E DOLORE



ENCEFALO
Corteccia

TALAMO

NEURONE DI TERZO ORDINE

Vie neuromodulatorie discendenti

NEURONE DI SECONDO ORDINE

stimolo

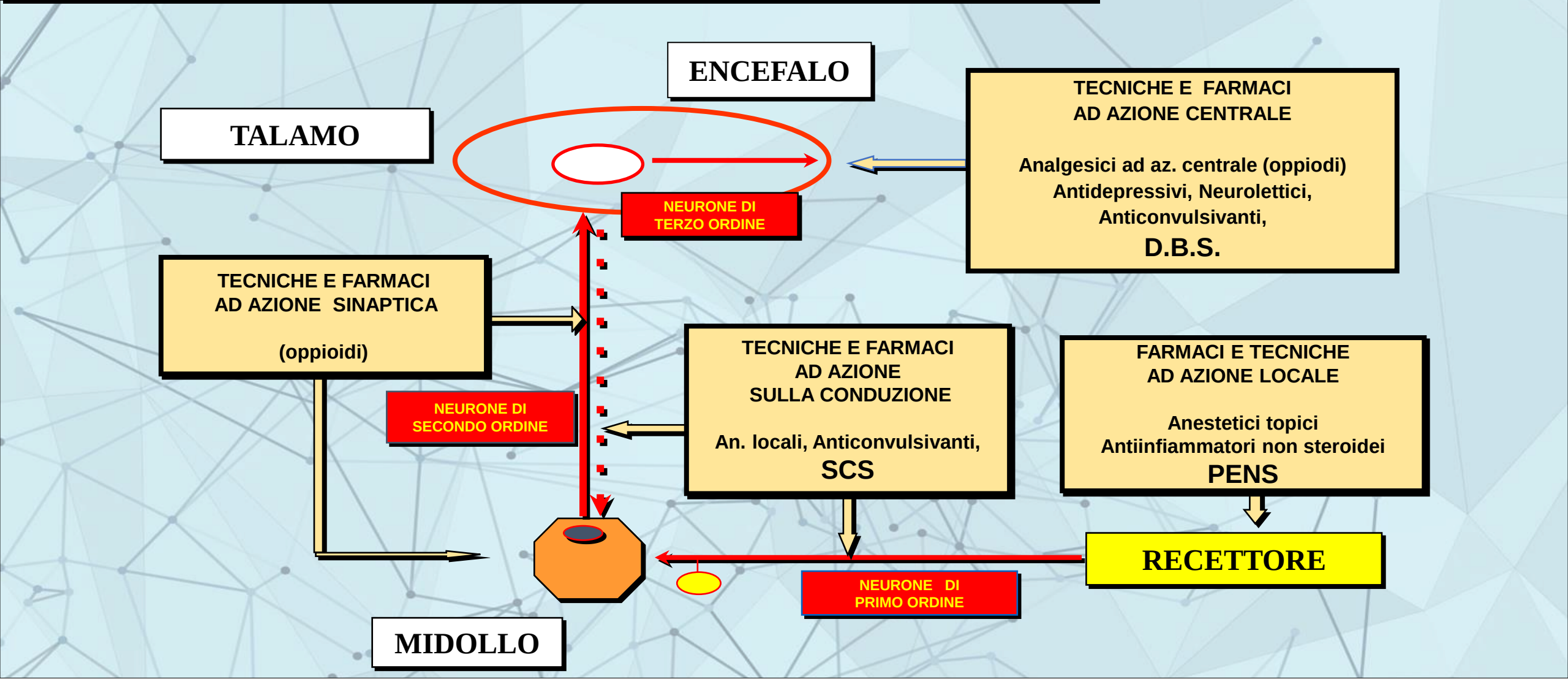
MIDOLLO

NEURONE DI PRIMO ORDINE

CUTE
VISCERI

recettore

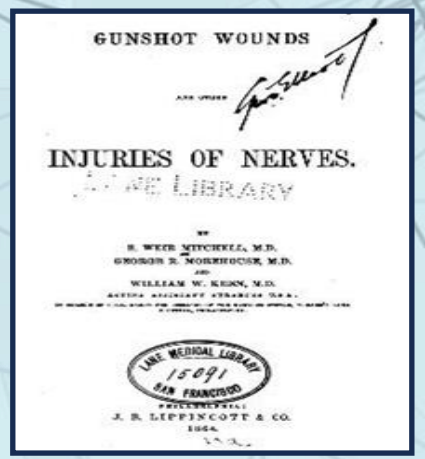
TECNICHE ANTALGICHE E LIVELLI D'AZIONE



NOCICEZIONE processo sensitivo in base al quale uno stimolo lesivo è captato a livello periferico e trasmesso al cervello. Qui riconosciuto, localizzato, potenziato o inibito, e infine memorizzato (**Jacques Jaume, 2006**).

Tale fenomeno si basa sulla presenza all'interno dei tessuti di **NOCICETTORI,** terminazioni libere di nervi periferici afferenti primari, in grado di rispondere in modo differenziato agli stimoli nocicettivi, presenti in ogni organo.

Stato mentale associato all'attivazione dei circuiti della nocicezione cosciente (**Tiengo, 2006**).


GUNSHOT WOUNDS

INJURIES OF NERVES.

IL SISTEMA NOCICETTIVO è un Organo deputato alla Percezione, è suscettibile di ammalarsi e dar luogo a condizioni cliniche di Disfunzione.

Il sistema Nocicettivo è un organo deputato alla percezione, suscettibile di ammalarsi e dar luogo a disfunzioni cliniche

L'assenza del dolore come dannazione

L' incapacità di percepire la fisicità dello stimolo doloroso è una condiziona genetica rara ma presente in alcune persone

In three consanguineous families from northern Pakistan, we mapped the condition as an autosomal-recessive trait to chromosome 2q24.3. mutations (S459X, I767X and W897X).

Nature **444**, 894-898 (14 December 2006)

NUOVI TARGETS SUL DOLORE?

RICONOSCERE I PRINCIPALI TIPI DI DOLORE

- Dolore nocicettivo
- Dolore acuto
- Dolore nociplastico
- Dolore neuropatico
- Dolore cronico
- Dolore misto

PAIN CLASSIFICATIONS

TIME

Acute pain
Chronic pain

PATHOLOGY

Malignant
Non-malignant

TISSUE

Nerve
Viscera
Bone
Skin

PATHOPHYSIOLOGY

Inflammation
Neuropathic
Idiopatic

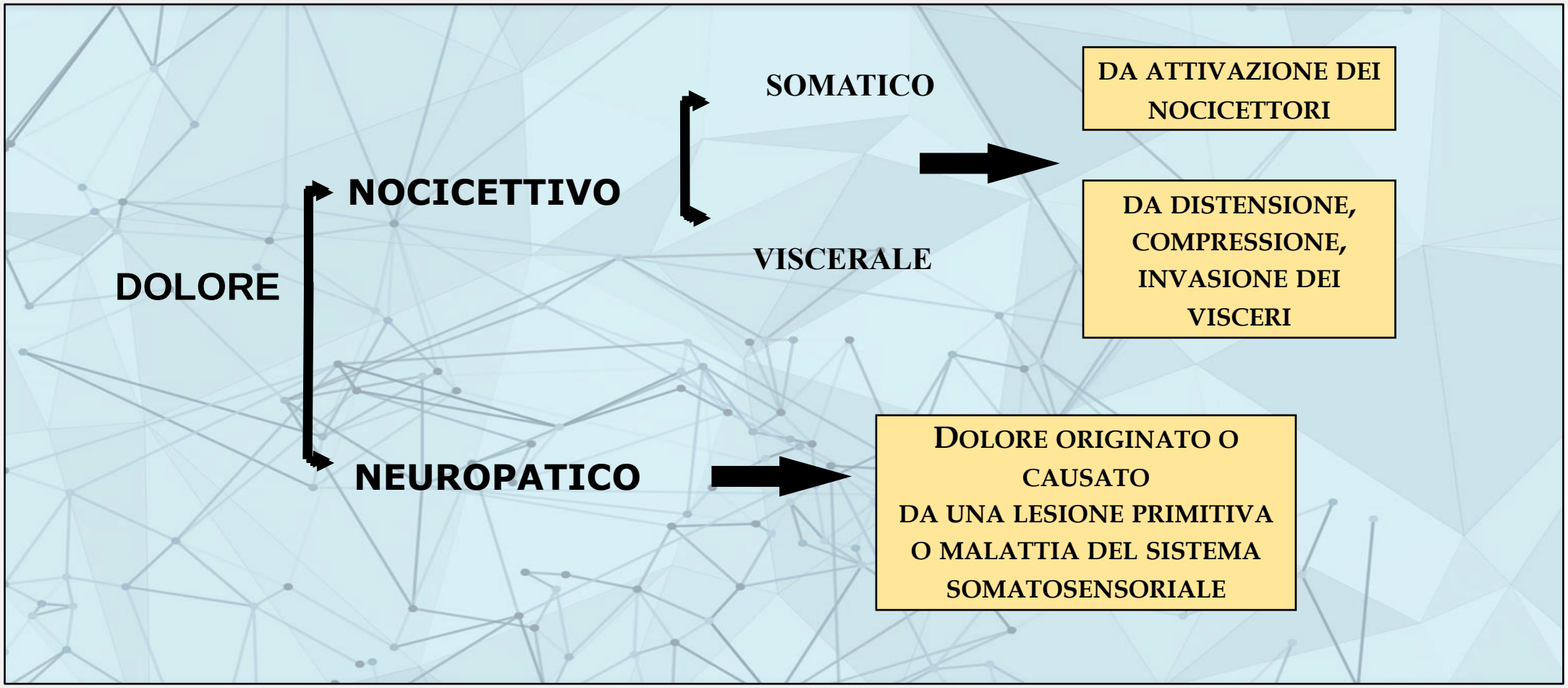
LOCALIZATION

Superficial
Deep

TOPOGRAPHY

Extremity
Thoracic
Spinal
Head
Etc

TIPOLOGIA DEL DOLORE



IL CONTINUUM DEL DOLORE

Trauma

Dolore acuto → **Dolore cronico**

≥ 3-6 mesi

	Origine nei terminali nocicettivi integri ma sensibilizzati o sottoposti a stimoli ad alta soglia	Origine degli impulsi in siti ectopici, ovvero nei punti di lesione, nei terminali nocicettivi alterati, nel ganglio della radice spinale	Origine nel sistema nervoso centrale per fenomeni di plasticità o modificazioni dei sistemi inibitori
	NOCICETTIVO	NEUROPATICO	NOCIPLASTICO
	• Infiammatorio • Meccanico	• Periferico • Centrale	• Plasticità • Inibizione
	PATOLOGIE DEI TESSUTI SOMATO-VISCERALI Vie nocicettive Aδ e C	PATOLOGIE DELLE VIE AFFERENTI AL SNC DEL SISTEMA SOMATO-SENSORIALE Vie nocicettive Aδ e C e vie tattili Aβ	MODIFICAZIONI NEI CENTRI SOVRASPINALI

- Ha una funzione protettiva
- Generalmente caratterizzato da un trauma lesivo manifesto

- Non ha una funzione protettiva
- Causa disfunzione

Koo PJ. Adv Stud Pharm. 2009; Schaible HG Arch Surg 2004.
McMahon SB Wall and Melzack's Textbook of Pain; 2006.

RICONOSCERE IL DOLORE

Dolore ad un arto in seguito a frattura

Dolore dovuto a ustioni o ematomi

Dolore articolare nell'osteoartrosi

DESCRITTORI COMUNI

Dolore pulsante
Dolenzia
Rigidità

Herndon C, et al. Pharmacotherapy 2008;28:788-805.
McMahon SB, Wall and Melzack's Textbook of Pain, 2006, 1099.
Schaible H-G, Arch Surg 2004;389:237-243.

RICONOSCERE IL DOLORE

Dolore post-ictus

Neuropatia diabetica periferica

Nevralgia post-erpetica

DESCRITTORI COMUNI

Dolore lancinante
Tipo scossa
Bruciante
Formicolio
Intorpidimento

Dolore lombare radicolare

Dolore post-chirurgico

IL DOLORE NEUROPATICO

Il dolore che origina come diretta conseguenza di una lesione o di una patologia che interessa le fibre del sistema somato-sensoriale

VIEWS & REVIEWS

Neuropathic pain

Redefinition and a grading system for clinical and research purposes

R.-D. Treede, MD*
T.S. Jensen, MD, PhD*
J.N. Campbell, MD
G. Cruccu, MD
J.O. Dostrovsky, PhD
J.W. Griffin, MD
P. Hansson, MD, DMSc, DDS
R. Hughes, MD
T. Nurmikko, MD, PhD
J. Serra, MD

Address correspondence and reprint requests to Dr. Troels S. Jensen, Department of Neurology, Aarhus University Hospital, Norrebrogade 44, 8000 Aarhus C, Denmark tsjensen@ki.au.dk

ABSTRACT

Pain usually results from activation of nociceptive afferents by actually or potentially tissue-damaging stimuli. Pain may also arise by activity generated within the nervous system without adequate stimulation of its peripheral sensory endings. For this type of pain, the International Association for the Study of Pain introduced the term neuropathic pain, defined as "pain initiated or caused by a primary lesion or dysfunction in the nervous system." While this definition has been useful in distinguishing some characteristics of neuropathic and nociceptive types of pain, it lacks defined boundaries. Since the sensitivity of the nociceptive system is modulated by its adequate activation (e.g., by central sensitization), it has been difficult to distinguish neuropathic dysfunction from physiologic neuroplasticity. We present a more precise definition developed by a group of experts from the neurologic and pain community: pain arising as a direct consequence of a lesion or disease affecting the somatosensory system. This revised definition fits into the nosology of neurologic disorders. The reference to the somatosensory system was derived from a wide range of neuropathic pain conditions ranging from painful neuropathy to central poststroke pain. Because of the lack of a specific diagnostic tool for neuropathic pain, a grading system of definite, probable, and possible neuropathic pain is proposed. The grade possible can only be regarded as a working hypothesis, which does not exclude but does not diagnose neuropathic pain. The grades probable and definite require confirmatory evidence from a neurologic examination. This grading system is proposed for clinical and research purposes. *Neurology*® 2008;70:1630–1635

Task force in collaboration with the IASP Special Interest Group on Neuropathic Pain

IASP
PAIN® 152 (2011) 2204–2205
PAIN®
www.elsevier.com/locate/pain

Commentary

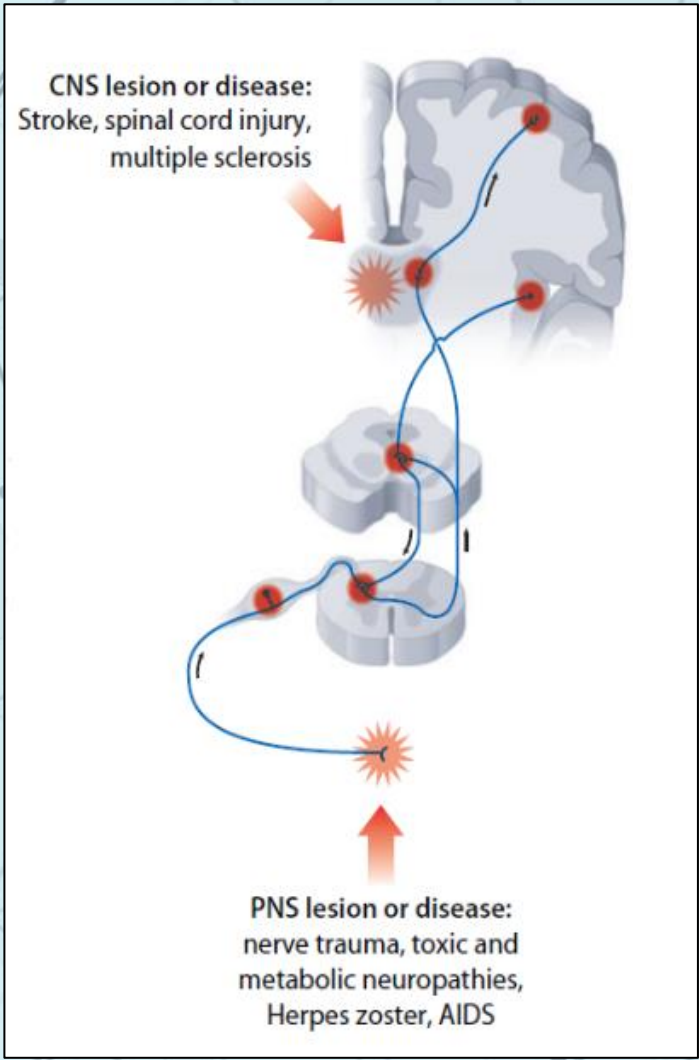
A new definition of neuropathic pain

Tredee, 2008

Neuropathic pain*
Pain caused by a lesion or disease of the somatosensory nervous system.

Note: Neuropathic pain is a clinical description (and not a diagnosis) which requires a demonstrable lesion or a disease that satisfies established neurological diagnostic criteria. The term *lesion* is commonly used when diagnostic investigations (e.g. imaging, neurophysiology, biopsies, lab tests) reveal an abnormality or when there was obvious trauma. The term *disease* is commonly used when the underlying cause of the lesion is known (e.g. stroke, vasculitis, diabetes mellitus, genetic abnormality). *Somatosensory* refers to information about the body per se including visceral organs, rather than information about the external world (e.g., vision, hearing, or olfaction). The

IL DOLORE NEUROPATICO – NEUPSIG 2008



1. **Anamnesi: ci sono lesioni o malattie del sistema nervoso periferico?**
2. **Anatomia: la distribuzione del dolore è neuro anatomicamente plausibile.**
3. **EO: segni sensoriali positivi o negativi nel territorio di innervazione della struttura nervosa lesionata? (esami bed side)**
4. **I test diagnostici neurofisiologici confermano la lesione o la malattia?**

DN
processo clinico ragionato 'step by step'
attraverso livelli progressivi di certezza diagnostica,
secondo un definito grading system

MANIFESTAZIONI DOLOROSE PIÙ FREQUENTI NEL DN

VOLUME 9 | OCTOBER 2013 NATURE REVIEWS | NEUROLOGY

Reappraising neuropathic pain in humans —how symptoms help disclose mechanisms

Andrea Truini, Luis Garcia-Larrea and Giorgio Cruccu

Ongoing burning pain
65,4%

Abnormal spontaneous activity in C fibres

Neuropathic state inducing 'irritable' nociceptors and regenerating sprouts

Denervation 'supersensitivity ' of second-order neurons

Paroxysmal electric shock-like pain
57%

Abnormal Ectopic activity in Aβ fibres

Brush-evoked pain
18-54%

Heterosynaptic spinal sensitization

FISIOPATOLOGIA SEMPLIFICATA DEL DN

Boyce-Rustay JM, et al. Curr Pharm Des 2009;15:1711-6.
Gilron I, et al. Can Med Assoc J 2006;175:265-75.

MECCANISMI PERIFERICI

Ipereccitabilità neuronale periferica

MECCANISMI CENTRALI

Perdita dei controlli inibitori

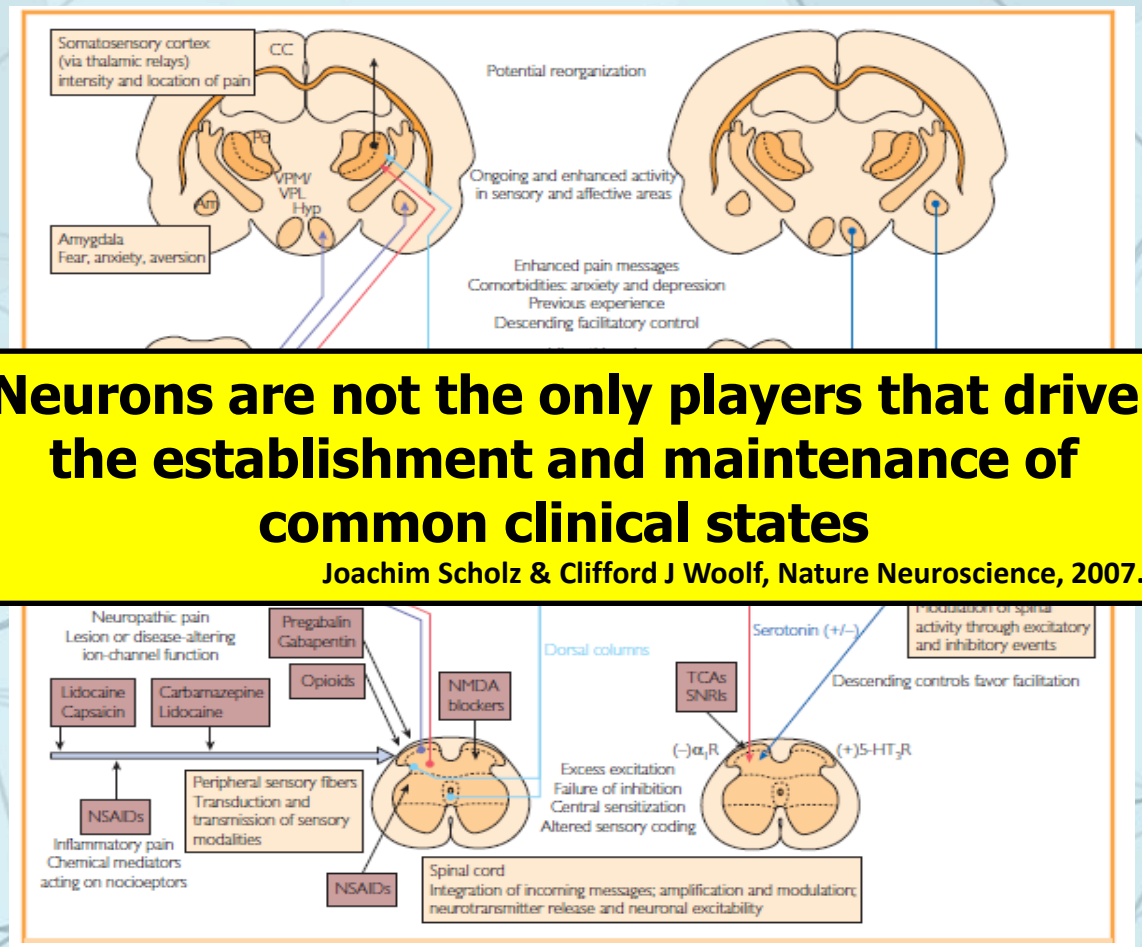
MECCANISMI CENTRALI

Ipereccitabilità neuronale centrale (sensibilizzazione centrale)

Scariche anormali

NeP

IL NEURONE *TARGET* PRIMARIO DELLE CLASSICHE TERAPIE ANTALGICHE PER IL CONTROLLO DEL DOLORE CRONICO NEUROPATICO



Neurons are not the only players that drive the establishment and maintenance of common clinical states

Joachim Scholz & Clifford J Woolf, Nature Neuroscience, 2007.

Mayo Clin Proc. 2015;90(4):532-545

Emerging targets in neuroinflammation-driven chronic pain

Ru-Rong Ji[1], Zhen-Zhong Xu[1], and Yong-Jing Gao[2]

Abstract | Current analgesics predominately modulate pain transduction and transmission in neurons and have limited success in controlling disease progression. Accumulating evidence suggests that neuroinflammation, which is characterized by infiltration of immune cells, activation of glial cells and production of inflammatory mediators in the peripheral and central nervous system, has an important role in the induction and maintenance of chronic pain. This Review focuses on emerging targets — such as chemokines, proteases and the WNT pathway — that promote spinal cord neuroinflammation and chronic pain. It also highlights the anti-inflammatory and pro-resolution lipid mediators that act on immune cells, glial cells and neurons to resolve neuroinflammation, synaptic plasticity and pain. Targeting excessive neuroinflammation could offer new therapeutic opportunities for chronic pain and related neurological and psychiatric disorders.

Nature review drug discovery 2014.

NATURE MEDICINE ADVANCE ONLINE PUBLICATION
Published online 14 October 2010; doi:10.1038/nm.2234

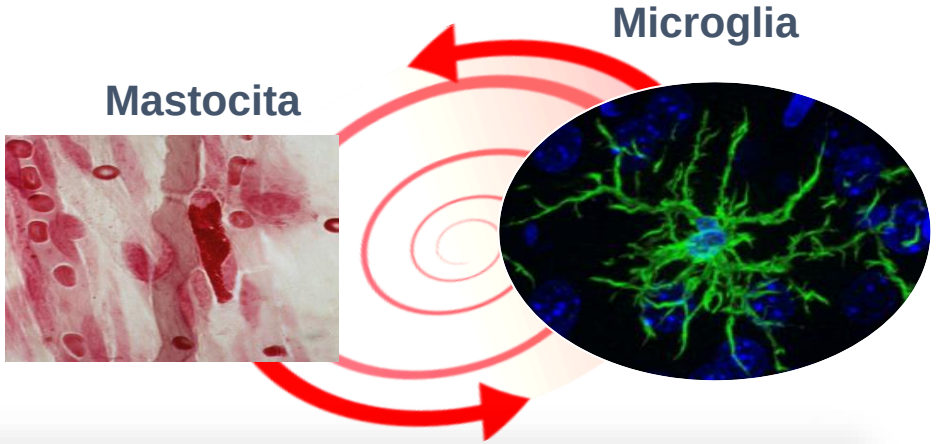
FOCUS ON PAIN REVIEW

nature medicine

Interactions between the immune and nervous systems in pain

Ke Ren & Ronald Dubner

Immune cells and glia interact with neurons to alter pain sensitivity and to mediate the transition from acute to chronic pain. In response to injury, resident immune cells are activated and blood-borne immune cells are recruited to the site of injury. Immune cells not only contribute to immune protection but also initiate the sensitization of peripheral nociceptors. Through the synthesis and release of inflammatory mediators and interactions with neurotransmitters and their receptors, the immune cells, glia and neurons form an integrated network that coordinates immune responses and modulates the excitability of pain pathways. The immune system also reduces sensitization by producing immune-derived analgesic and anti-inflammatory or proresolution agents. A greater understanding of the role of the immune system in pain processing and modulation reveals potential targets for analgesic drug development and new therapeutic opportunities for managing chronic pain.



Topical review

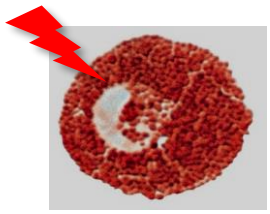
PAIN

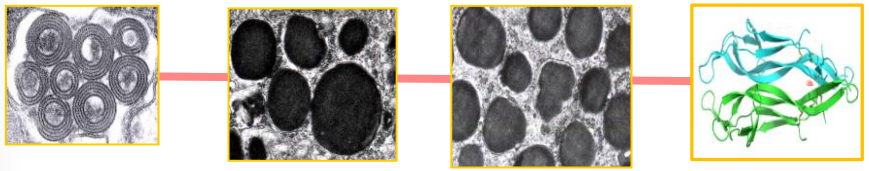
The role of neuroinflammation and neuroimmune activation in persistent pain

Joyce A. DeLeo[a,*], Robert P. Yezierski[b]

Esiste una correlazione diretta tra attivazione di specifiche cellule immunitarie non neuronali, neuroinfiammazione e insorgenza di Dolore.

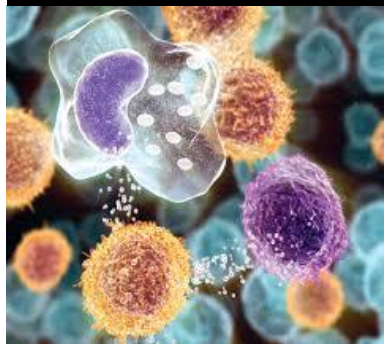
Dong H et all, 2015



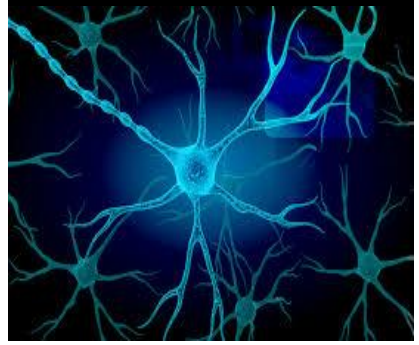


Dolore infiammatorio, Lesioni tissutali, Neoinnervazione, Iperalgesia/Allodinia, iperestesie

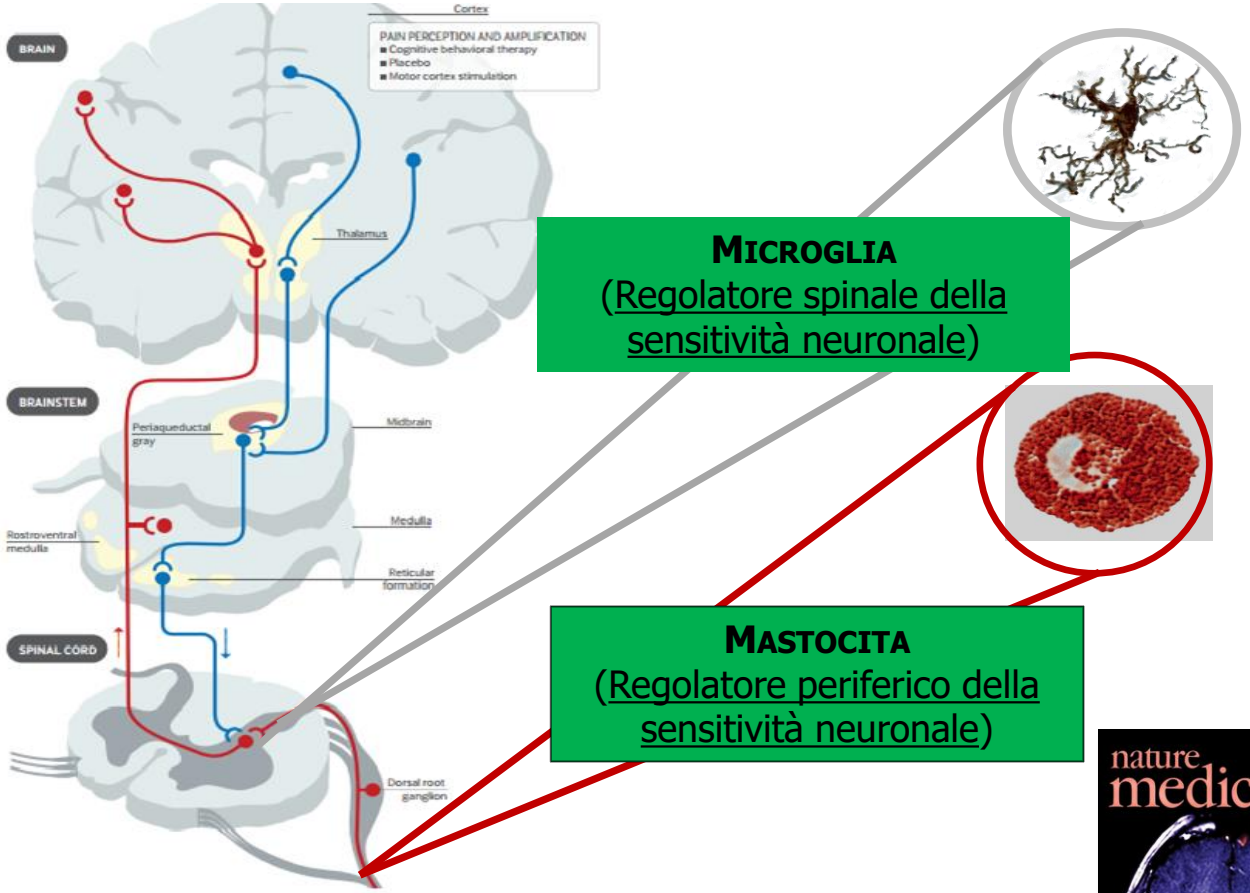
Sistema immune (Mastocita-Microglia)



Sistema nervoso (periferico e centrale)



DeLeo et al., 2001; Pain. 2001;90(1-2):1-6.



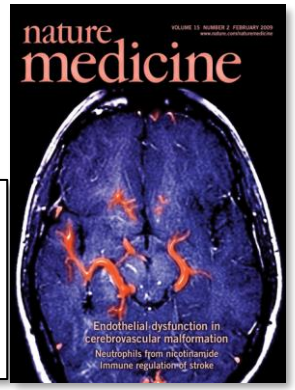
MICROGLIA
(Regolatore spinale della sensitività neuronale)

MASTOCITA
(Regolatore periferico della sensitività neuronale)

Interactions between the immune and nervous systems in pain

Ke Ren & Ronald Dubner

Nat Med. 2010;16(11):1267-76.



The FASEB Journal
The Journal of the Federation of American Societies for Experimental Biology

Microglia and mast cells: two tracks on the road to neuroinflammation

Stephen D. Skaper,[1] Pietro Giusti, and Laura Facci
Dipartimento di Scienze del Farmaco, Largo Egidio Meneghetti 2, University of Padova, Padua, Italy

Le cellule immunitarie e la glia interagiscono con i neuroni per alterare la sensibilità al dolore e mediare la transizione dal dolore acuto a quello cronico.

“Pain in the elderly is a difficult pain:

difficult to understand and difficult to treat”

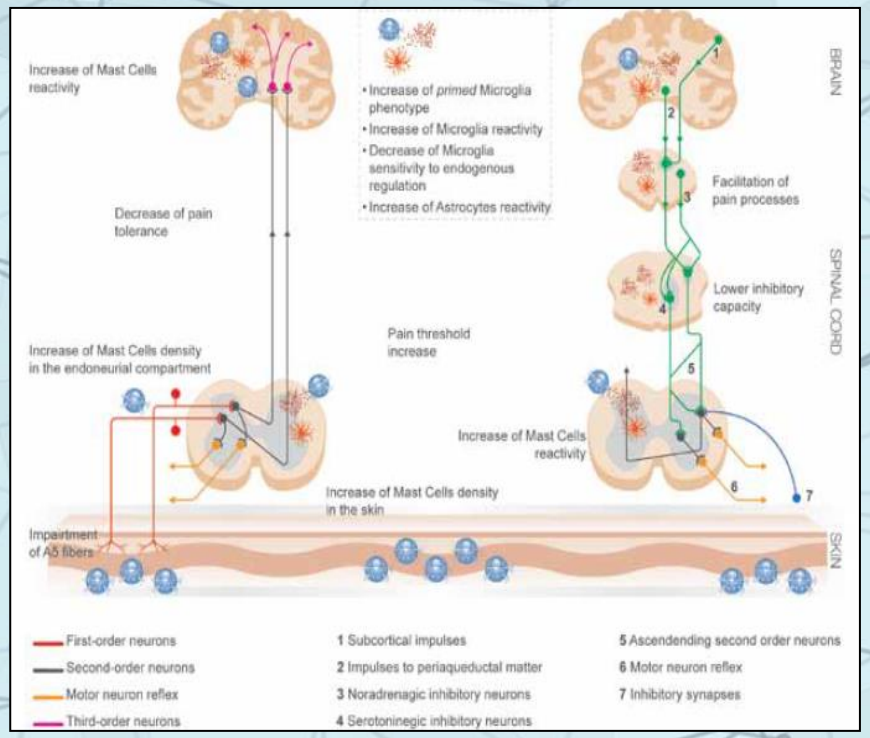
Abdulla et al., 2013
Skaper et al., 2015

Narrative Review

Chronic Pain in the Elderly: The Case for New Therapeutic Strategies

Antonella Paladini, MD, PhD[1], Mariella Fusco, PhD[2], Stefano Coaccioli, MD, PhD[3], Stephen D. Skaper, PhD[4], and Giustino Varrassi MD, PhD[5]

Pain Physician 2015;



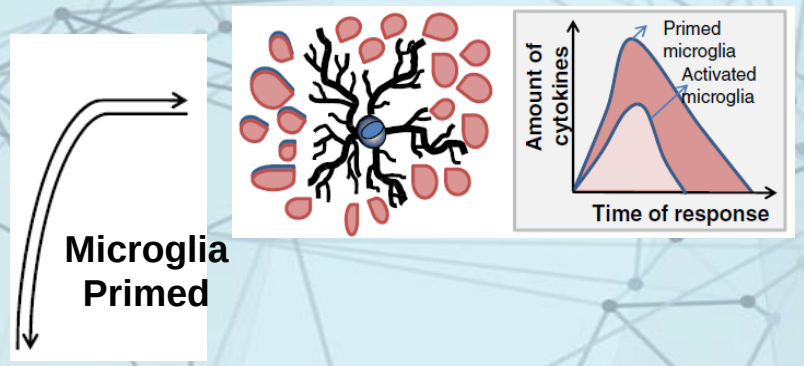
Le alterazioni delle cellule immunitarie, **mastociti** e **microglia**, partecipano fortemente all'alterazione del sistema somatosensoriale in corso di invecchiamento.

La **microglia** nel SNC spinale dell'**Anziano**

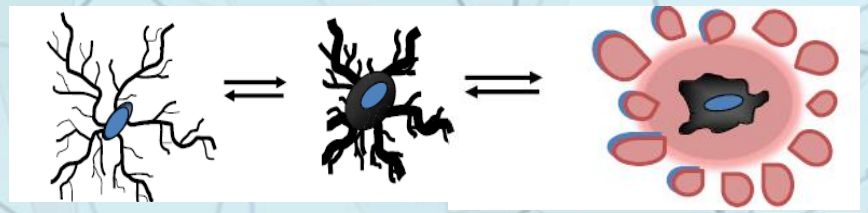
Review: Microglia of the aged brain: primed to be activated and resistant to regulation

D. M. Norden* and J. P. Godbout*†‡

La microglia senescente o primed costituisce un fenotipo parzialmente attivato di questa importante cellula non neuronale caratterizzato da una marcata espressione del complesso di istocompatibilità (MHCII), di specifici recettori e di citochine pro-infiammatorie che inducono una intensa risposta della cellula a **noxae anche di blanda entità**.
Boche et al., 2013; Norden e Godbout, 2013; Torres- Platas et al., 2014



La risposta infiammatoria della **Microglia Primed,** rispetto a quella attivata, è più violenta e duratura nel tempo

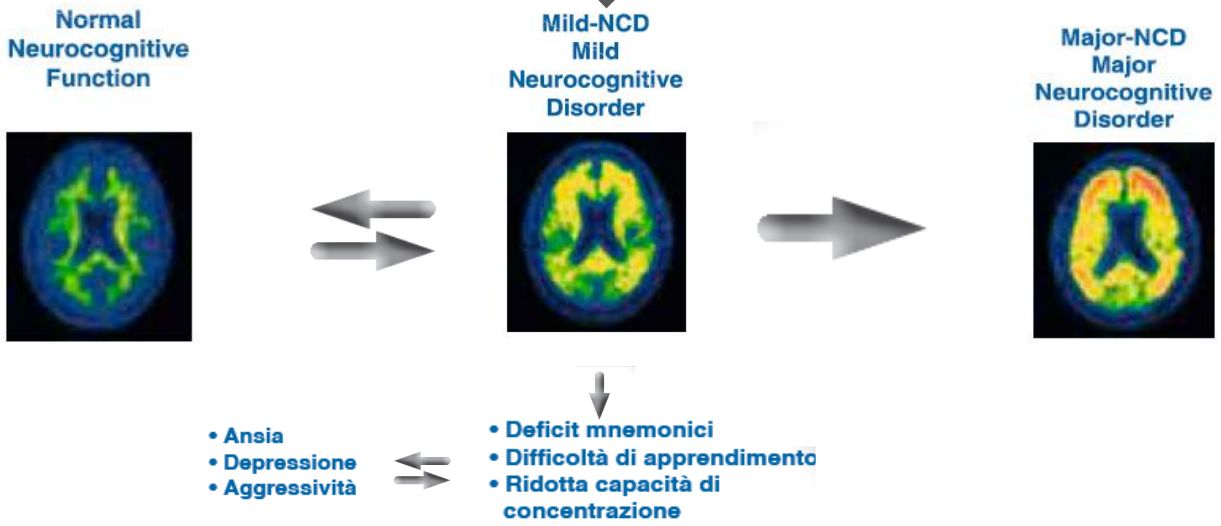


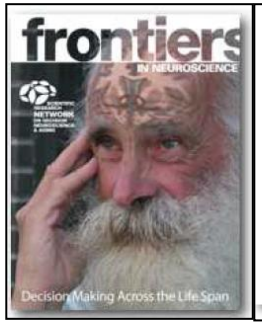
Eggen et al., 2013
Hains et al., 2010
Norden et al., 2013

Malattia:

- vascolare
- degenerativa
- traumatica
- dismetabolica
- virale
- multipla

low-grade chronic neuroinflammation





Glial Modulation by *N*-acylethanolamides in Brain Injury and Neurodegeneration

*María I. Herrera[1,2], Rodolfo Kölliker-Frers[1], George Barreto[3], Eduardo Blanco[4] and Francisco Capani[1,5,6,7]**

"Le disfunzioni neuro-immunitarie dell'età avanzata si associano alla ***low-grade chronic neuroinflammation*** *che contribuisce* all'evoluzione del declino cognitivo e rende l'anziano suscettibile alle patologie neurodegenerative e neuropsiachiatriche"