

Approccio globale al paziente con emofilia

Il percorso per la gestione del dolore

Nicola Luxardo

S.C.Terapia del Dolore e Cure Palliative

Presidio Molinette

Dipartimento di Anestesia

A.O. Città della Salute e della Scienza di Torino

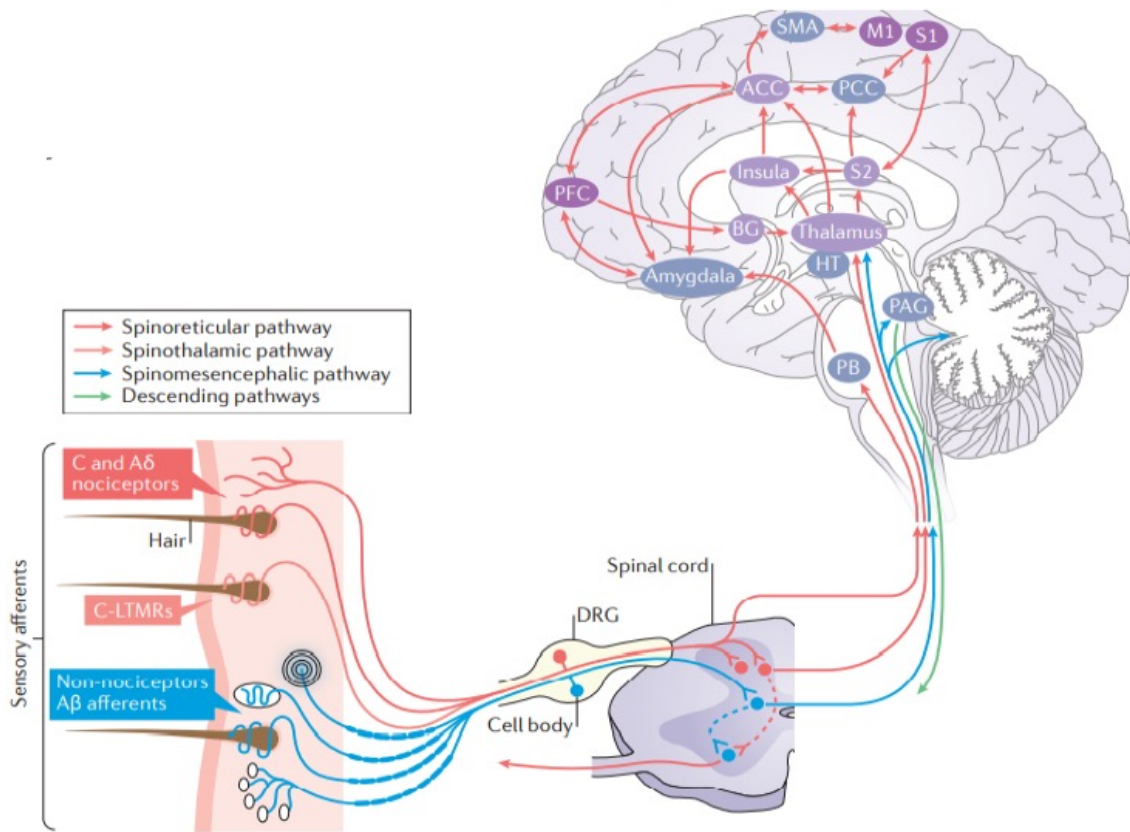
Il sistema nocicettivo

- **Meccanismo di difesa**
- **Sintomo di una attivazione del sistema di allarme da parte di stimoli nocivi interni o esterni**

NOVITÀ IN COAGULAZIONE

attraverso i centri emostasi e trombosi

Torino, 12-13 novembre 2021



Nociplastic

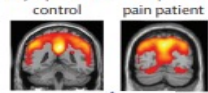
Causes

- Diffuse sensitisation (fibromyalgia)
- Functional visceral pain (irritable bowel syndrome, bladder pain syndrome)
- Regional somatic sensitisation (complex regional pain syndrome type 1, temporomandibular disorder)

Altered nociception

- Peripheral sensitisation (proliferation of sodium channels, sympatho-afferent coupling)
- Central sensitisation (N-methyl-D-aspartate activation, cortical reorganisation)
- Diminished descending inhibition (periaqueductal grey and rostroventromedial medulla)
- Immune system activation (glial cells, chemokines, cytokines, and other inflammatory mediators)

Asymptomatic control vs Nociplastic pain patient



Irritable bowel syndrome

Neuropathic

Causes

- Central**
 - Traumatic (spinal cord injury)
 - Vascular (stroke)
 - Neurodegenerative (Parkinson's disease)
 - Autoimmune (multiple sclerosis)
 - Inflammatory (transverse myelitis)
- Peripheral**
 - Infections (HIV, acute herpes zoster or postherpetic neuralgia)
 - Nerve compression (carpal tunnel syndrome)
 - Trauma (complex regional pain syndrome type 2)
 - Metabolic (amyloidosis, nutritional deficiencies)
 - Ischaemic (peripheral vascular disease, diabetes)
 - Toxic (chemotherapy-induced peripheral neuropathy)
 - Auto-immune (Guillain-Barré syndrome)
 - Genetic (inherited neuropathy)

Spinal cord injury



Stroke



Peripheral vascular disease, diabetes

Nociceptive

Causes

Somatic

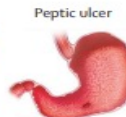
- Bones (bone fracture, metastases)
- Muscles (dystonia, muscle spasm)
- Joints (osteoarthritis)
- Skin (postoperative pain, burns)

Visceral

- Mucosal injury (peptic ulcer)
- Obstruction or capsular distension (gallstones, kidney stones)
- Ischaemia (angina, mesenteric ischaemia)
- Tissue injury (cancer, cirrhosis)



Trochanteritis



Peptic ulcer



Angina



Kidney stones



Osteoarthritis

Treatment considerations

- Anticonvulsants
- Analgesic antidepressants
- Image guided injections
- Behavioural interventions
- Neuromodulation
- Non-steroidal anti-inflammatory drugs
- Opioids
- Exercise

NOVITÀ IN COAGULAZIONE
attraverso i centri emostasi e trombosi

Torino, 12-13 novembre 2021

Il continuum del dolore



Dolore
acuto

Dolore
cronico

≥ 3-6 mesi

Ha una funzione protettiva
Generalmente eziologia evidente e unica

Non ha una funzione protettiva
Fattori multipli
Causa il deterioramento dello stato di
salute e delle funzioni

Cronicizzazione del dolore: Transizione

Un processo complesso

Il Sistema Nervoso reagisce nel tempo ai
due parametri di stimolazione

- Intensità
- Frequenza

Meccanismo della plasticità si modifica

- SNP
- SNC

NOVITÀ IN COAGULAZIONE

attraverso i centri emostasi e trombotici

Torino, 12-13 novembre 2021

Plasticità : abilità di modificare le proprietà funzionali e strutturali in seguito a variazioni di attività del sistema

NATIONAL INSTITUTES OF HEALTH
OR HEALTH

NIH Public Access
Author Manuscript
Pain. Author manuscript; available in PMC 2012 March 1.

Published in final edited form as:
Pain. 2011 March ; 152(3 Suppl): S49-S64. doi:10.1016/j.pain.2010.11.010.

Pain and the brain: Specificity and plasticity of the brain in clinical chronic pain

A.V. Apkarian^{1,2,*}, J.A. Hashmi¹, and M.N. Baliki¹

¹ Department of Physiology, Northwestern University, Feinberg School of Medicine, Chicago, Illinois, 60611

² Departments of Anesthesia, Surgery, Northwestern University, Feinberg School of Medicine, Chicago, Illinois, 60611

Abstract

We review recent advances in brain imaging in humans, concentrating on advances in our understanding of the human brain in clinical chronic pain. Understanding regarding anatomical and functional reorganization of the brain in chronic pain is emphasized. We conclude by proposing a brain model for the transition of the human from acute to chronic pain.

Keywords

fMRI; VBM; brain activity; brain reorganization; acute pain; chronic pain

Descartes proposed that all observable human behavior could be divided into two categories, the simple and the complex. Simple behaviors were those in which a given sensation always, deterministically, produced the same behavioral response Complex behaviors, in contrast were those in which the linkage between sensation and action was unpredictable and subject to the vagaries of volition They were produced when sensory data were transmitted from the nervous system

REVIEWS

Structural plasticity and reorganisation in chronic pain

Rohini Kumer^{1,3} and Herta Flor^{2,3}

Abstract (Chronic pain is not simply a temporal continuum of acute pain. Studies on functional plasticity in neural circuits of pain have provided mechanistic insights and linked various modulatory factors to a change in perception and behaviour. However, plasticity also occurs in the context of structural remodelling and reorganisation of synapses, cells and circuits, potentially contributing to the long-term nature of chronic pain. This Review discusses maladaptive structural plasticity in neural circuits of pain, spanning multiple anatomical and spatial scales in animal models and human patients, and addresses key questions on structure-function relationships.

Introduction

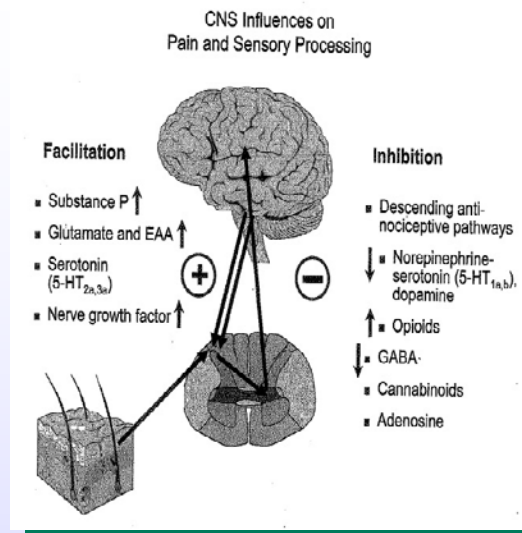
Noception and acute pain serve an important protective function in preventing tissue damage. However, pain can become chronic when maladaptive processes that are triggered by pathophysiological factors (such as neural injury, trauma, amputation, viral infections, inflammation, tumour growth, exposure to neurotoxins, autoimmune disease, vascular diseases, metabolic disorders or stress-related alterations) are exacerbated early on by a range of psychosocial variables. Indeed, chronic pain is a major cause of human suffering worldwide¹, especially because effective, specific and safe therapies have yet to

along multiple scales of plasticity. Mechanisms involving functional plasticity have been studied extensively and have revealed a range of modulatory factors that change the sensory, emotional and cognitive components of pain (reviewed in REFs 2-4). However, recent data show that structural plasticity changes are accompanied by structural remodelling and reorganization of synapses, cells and circuits that can also occur at various anatomical and temporal scales^{5,6}, thereby further adding complexity and a large dynamic range, and potentially accounting for the development of pain that extends over longer periods of

Acute pain
A transient form of pain that is acutely associated with a noxious stimulus.

Chronic pain
A pain that persists for one

- Alterata elaborazione del dolore per squilibrio fattori di amplificazione e inibizione



- Rischio-grado-decorso cronicizzazione dipende da fattori genetici- psicologici-socioambientali

Classificazione Definizione

- Esperienza sensoriale ed emotiva spiacevole, associata a un danno tissutale potenziale o reale o comunque descritta come tale
- Esperienza di sofferenza, associata a danni effettivi o potenziali ai tessuti con connotazioni sensoriali, emotive, cognitive e sociali

Narrative Review

PAIN

ICD-11

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

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

Abstract

Chronic pain is a major source of suffering. It interferes with daily functioning and often is accompanied by distress. Yet, in the *International Classification of Diseases*, chronic pain diagnoses are not represented systematically. The lack of appropriate codes renders accurate epidemiological investigations difficult and impedes health policy decisions regarding chronic pain such as adequate financing of access to multimodal pain management. In cooperation with the WHO, an IASP Working Group has developed a classification system that is applicable in a wide range of contexts, including pain medicine, primary care, and low-resource environments. Chronic pain is defined as pain that persists or recurs for more than 3 months. In chronic pain syndromes, pain can be the sole or a leading complaint and requires special treatment and care. In conditions such as fibromyalgia or nonspecific low-back pain, chronic pain may be conceived as a disease in its own right; in our proposal, we call this subgroup "chronic primary pain." In 6 other subgroups, pain is secondary to an underlying disease: chronic cancer-related pain, chronic neuropathic pain, chronic secondary visceral pain, chronic posttraumatic and postsurgical pain, chronic secondary headache and orofacial pain, and chronic secondary musculoskeletal pain. These conditions are summarized as "chronic secondary pain" where pain may at least initially be conceived as a symptom. Implementation of these codes in the upcoming 11th edition of *International Classification of Diseases* will lead to improved classification and diagnostic coding, thereby advancing the recognition of chronic pain as a health condition in its own right.

Keywords: Classification, ICD-11, Chronic pain, Symptom, Disease, Chronic primary pain, Chronic secondary pain, Functioning, Diagnoses, Coding

NOVITÀ IN COAGULAZIONE
attraverso i centri emostasi e trombosi

Torino, 12-13 novembre 2021

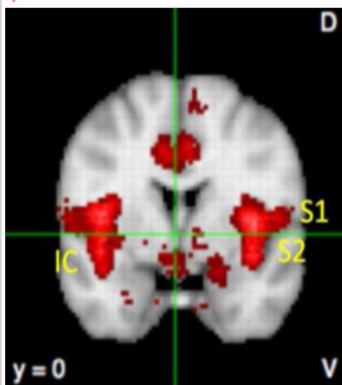
Criteri diagnostici del D.C.P.

- Presenza di dolore persistente o ricorrente per più di 3 mesi
- Associato ad almeno 1 delle seguenti situazioni

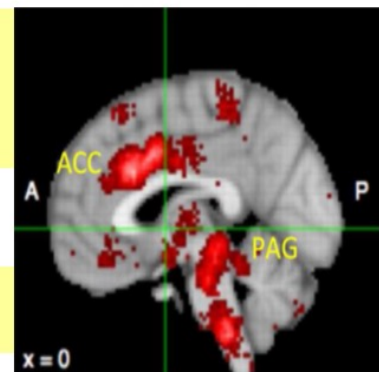
sofferenza emotiva causata dal dolore
interferenza con le attività quotidiane e le relazioni sociali

- Primario o secondario

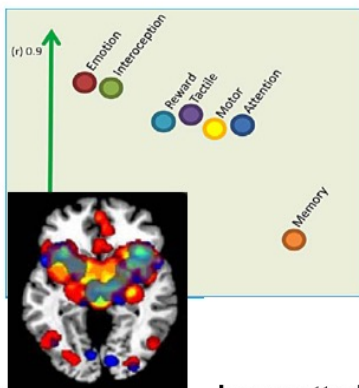
Navratilova et al., 2016



I pazienti con dolore cronico tendono a processare il dolore nelle aree emozionali del cervello più che in quelle sensoriali



così nel dolore cronico la relazione fra emozioni e dolore è più intensa



PLOS ONE

Shared "Core" Areas between the Pain and Other Task-Related Networks

August 2012 | Volume 7 | Issue 8 | e41929

Franco Cauda^{1,2*}, Diana M.E. Torta², Katuscia Sacco^{1,2}, Elisabetta Geda¹, Federico D'Agata^{1,2,3}, Tommaso Costa², Sergio Duca¹, Giuliano Geminiani^{1,2}, Martina Amanzio^{2,4}

Gray matter alterations in chronic pain: A network-oriented meta-analytic approach

NeuroImage: Clinical 4 (2014) 676-686

Franco Cauda^{a,b,c,*}, Sara Palermo^b, Tommaso Costa^{a,b,c}, Riccardo Torta^{d,e}, Sergio Duca^{a,b}, Ugo Vercelli^f, Giuliano Geminiani^{a,c}, Diana M.E. Torta^{a,b,c}

il concetto della «pain matrix» è cambiato,
da un modello anatomico ad uno più funzionale.

Le caratteristiche di un paziente, il differente tipo di dolore e la sua durata possono modificare la rilevanza delle aree coinvolte nel dolore

NOVITÀ IN COAGULAZIONE

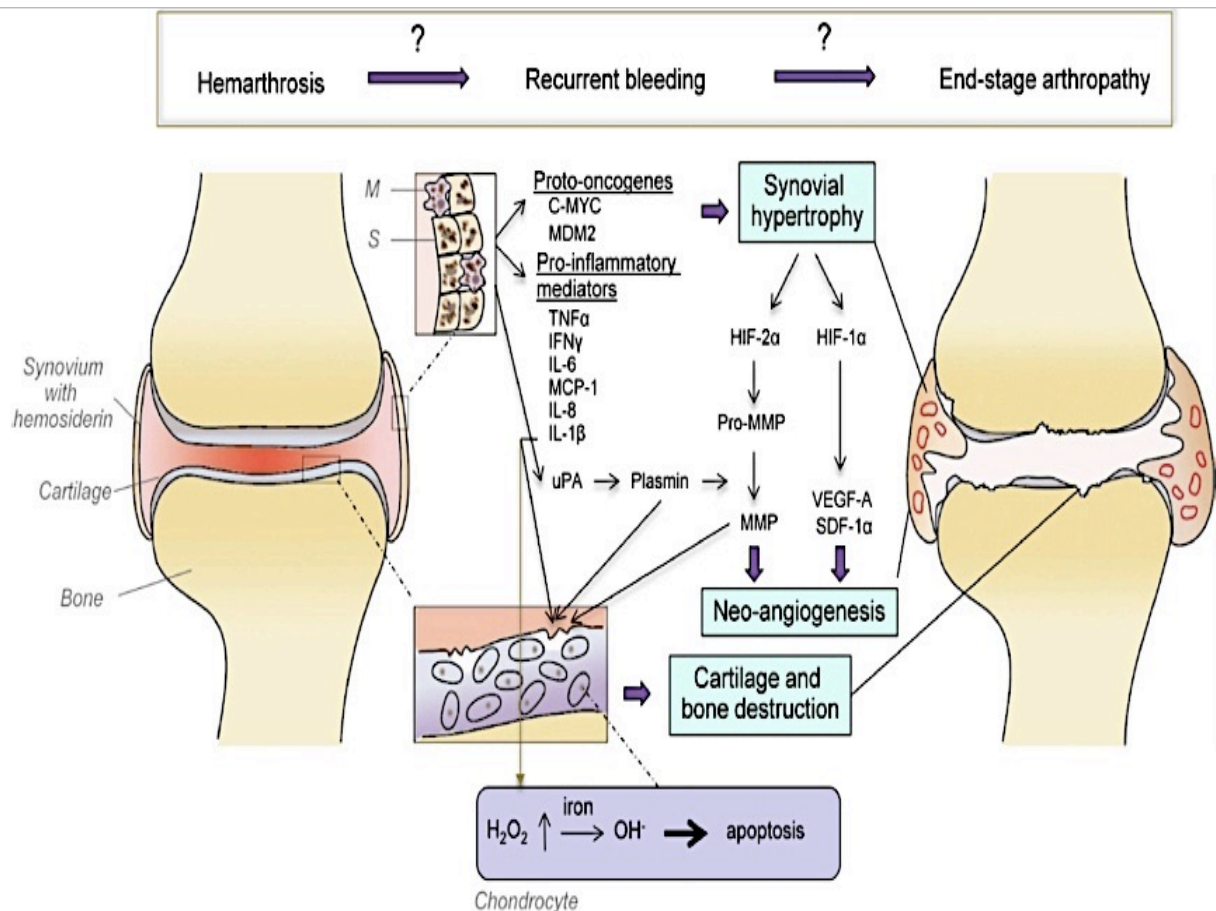
attraverso i centri emostasi e trombosi

Torino, 12-13 novembre 2021

Dolore in emofilia: stato dell'arte

- 50% delle persone adulte con emofilia soffre di dolore articolare (Riley et al., Haemophilia, 2011)
- Nel 29% dei pazienti il dolore in acuto persiste anche dopo l'infusione di FVIII (Riley et al., Haemophilia, 2011)
- Il dolore comporta una limitazione nello svolgimento delle attività quotidiane e impatta negativamente sulla qualità di vita (Riley et al., Haemophilia, 2011)
- Necessità di prevenire il dolore cronico e identificare un approccio di trattamento a gradino (prendendo come esempio il WHO pain ladder per il dolore oncologico) (Holstein, Haemophilia, 2012)

Età	Frequenza Dolore
0-17 aa	10%
18-39 aa	46%
≥40 aa	67%



NOVITÀ IN COAGULAZIONE
attraverso i centri emostasi e trombosi

Torino, 12-13 novembre 2021

Neuropathic pain in patients with haemophilia, that is the question

Hämostaseologie 2015; 35

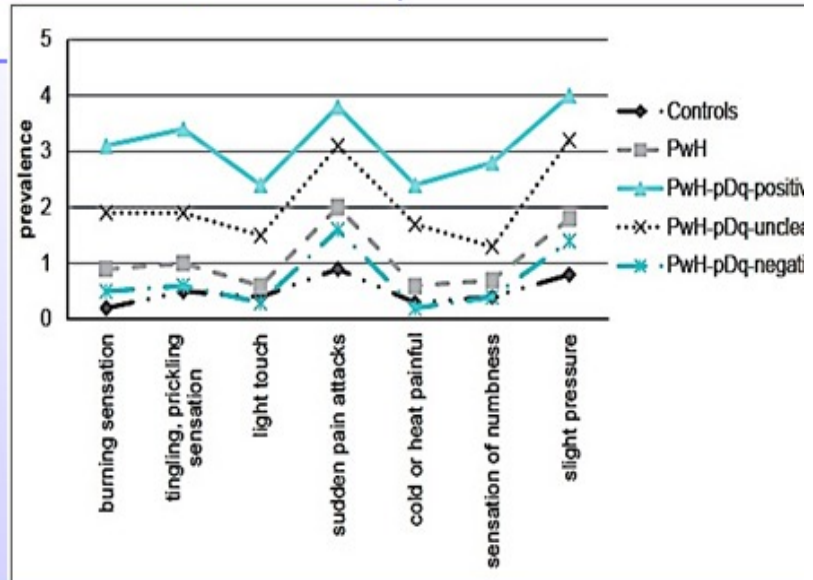
S. Krüger; T. Hilberg

there is a potential risk to misunderstand underlying pain mechanisms in PwH.

In chronic pain conditions based on haemophilic arthropathy, a differential diagnosis seems to be unalterable

for comprehensive and individualised pain management in PwH.

[painDETECT-questionnaire \(pDq\)](#), identifies neuropathic components in a pain profile.



Although inflammatory pain is a central theme in PwH, neuropathic pain is present in approximately **seven percent** of the patients based on our study

TDL

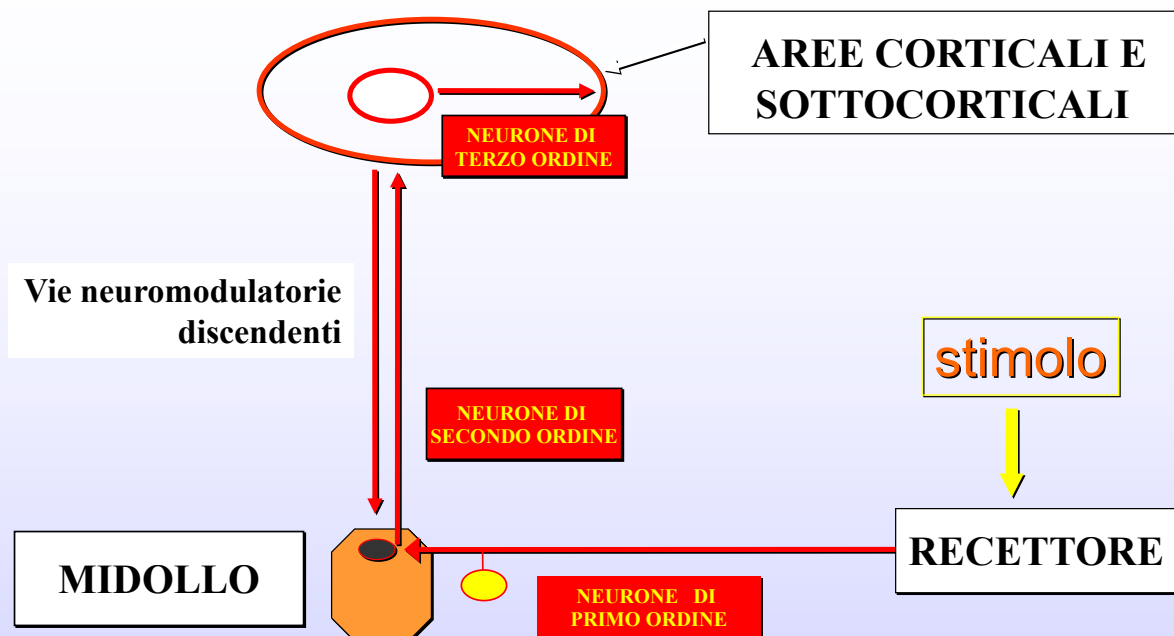
NOVITÀ IN COAGULAZIONE
attraverso i centri emostasi e trombosi

Torino, 12-13 novembre 2021

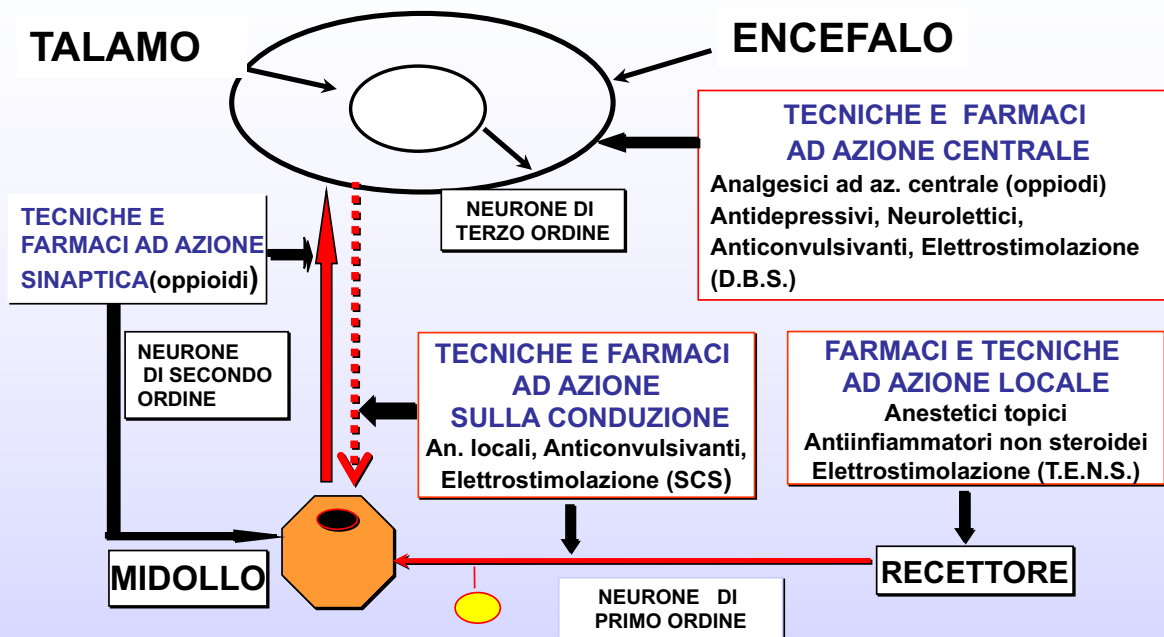
Valutare il paziente

- Componente sensoriale
- Disagio emotivo
- Componente funzionale

Componente sensoriale



TECNICHE ANTALGICHE E LIVELLI DI AZIONE



Disagio emotivo

- Depressione, ansia
- Disturbi psicofisiologici su base neurovegetativa (tachicardia respirazione)
- Disturbi psichici (fobie; autostima)
- Disturbi del comportamento (alimentazione; irritabilità; sonno)
- Ipervigilanza; tensione muscolare; paura

NOVITÀ IN COAGULAZIONE

attraverso i centri emostasi e trombosi

Torino, 12-13 novembre 2021

Conclusioni

Individuale, basata sulle componenti sensoriali, emotive e cognitive del singolo soggetto

Riflessione di efficacia, tollerabilità e sicurezza di un programma terapeutico

Collegialità

NOVITÀ IN COAGULAZIONE

attraverso i centri emostasi e trombotici

Torino, 12-13 novembre 2021

Grazie