

# **IL DOLORE:CLASSIFICAZIONE E FISIOPATOLOGIA**

**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**

# classificare

- Complessità del dolore
- Bussola di orientamento
- Scelte individuali –PDTA
- Multidisciplinarietà
- Organizzazione: peso
- Economia: valore

# 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

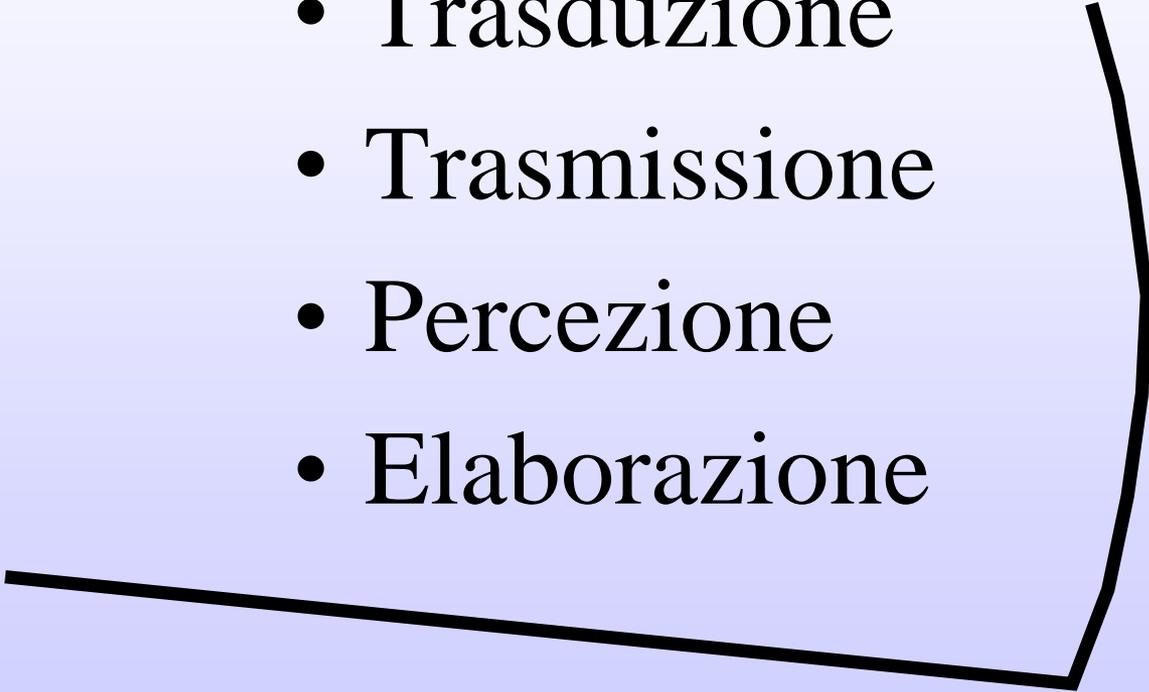
Comune denominatore: la soggettività  
ma

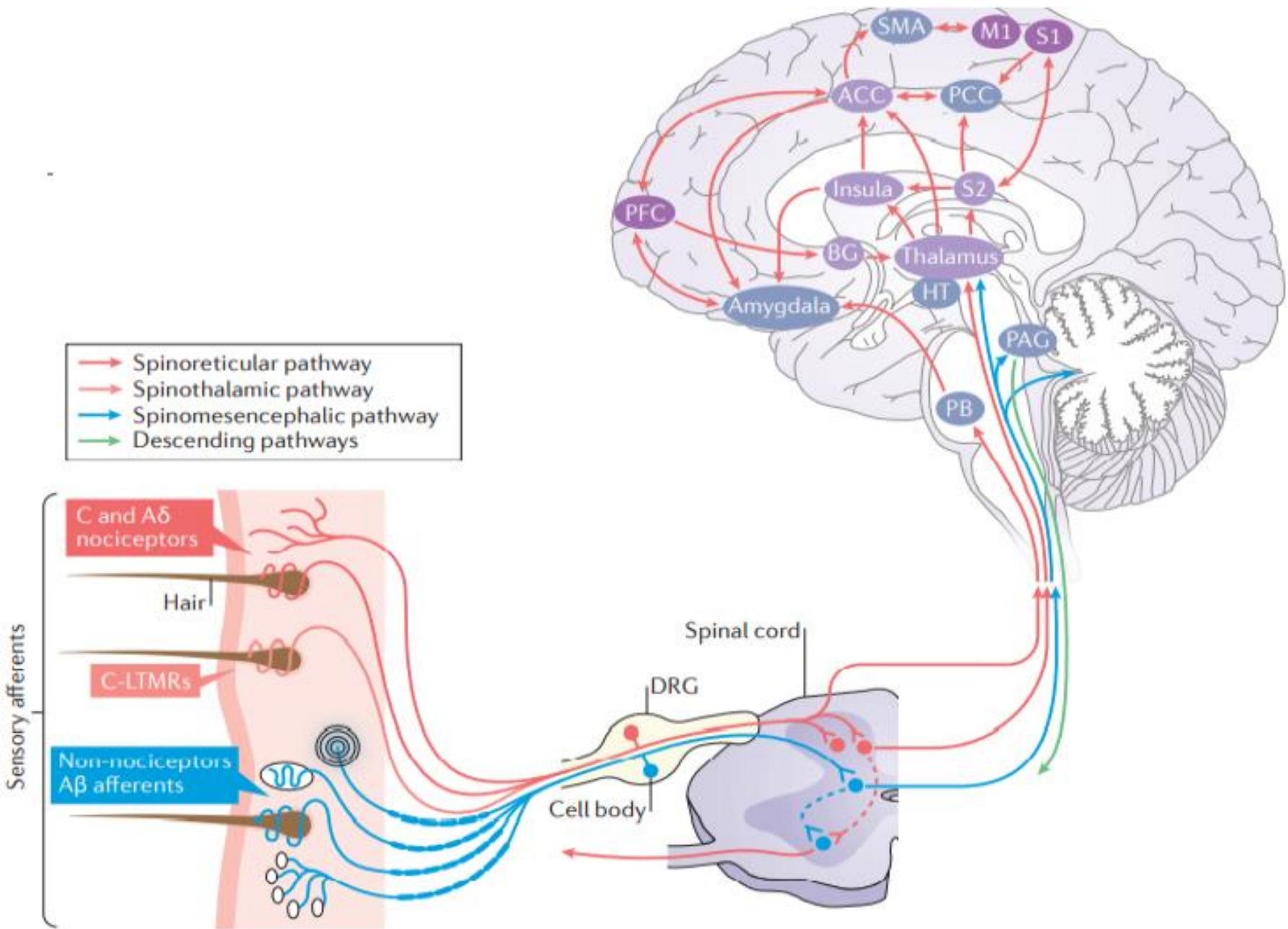
Diventa una funzione cognitiva  
dell'individuo

# Il sistema nocicettivo

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

# FISIOLOGIA DEL DOLORE

- Trasduzione
  - Trasmissione
  - Percezione
  - Elaborazione
- 



# 1<sup>^</sup> CLASSIFICAZIONE

- PAIN GENERATOR

## Nociplastic

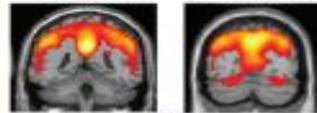
### Causes

- 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      Nociplastic pain patient



Fibromyalgia



Irritable bowel syndrome



Bladder pain syndrome

## 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)

Trochbursitis



Peptic ulcer



Angina



Kidney stones



Osteoarthritis



## 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



Postherpetic neuralgia



Peripheral vascular disease, diabetes



### Treatment considerations

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

# 2^ CLASSIFICAZIONE

- Durata
- Decorso
  
- ACUTO
- CRONICO

# Il continuum del dolore



Dolore  
acuto

Dolore  
cronico

$\geq 3-6$  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

# Dolore Cronico

- ICD d.c. dolore che dura o ricorre per più di 3 mesi
- Sintomo di una condizione cronica alla base
- Frequentemente non è possibile identificare malattie sottostanti
- Fenomeno da biomedico a bio-psico-sociale: terapia multidisciplinare

# **Cronicizzazione del dolore:Transizione**

- Un processo complesso di evoluzione del dolore
- Elementi multifattoriali
  - Flogistici
  - Neuropatici
  - Psicologici e ambientali

da episodico a persistente

Il Sistema Nervoso reagisce a due parametri di stimolazione

- Intensità
- Frequenza

Meccanismo della plasticità si modifica

- SNP
- SNC

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



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<sup>1,2,\*</sup>, J.A. Hashmi<sup>1</sup>, and M.N. Baliki<sup>1</sup>

<sup>1</sup> Department of Physiology, Northwestern University, Feinberg School of Medicine, Chicago, Illinois, 60611

<sup>2</sup> 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 Kuner<sup>1,3</sup> and Herta Flor<sup>2,3</sup>

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.

#### Nociception

The sensing of stimuli that are potentially harmful to the body; the sensory component of pain.

#### Acute pain

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

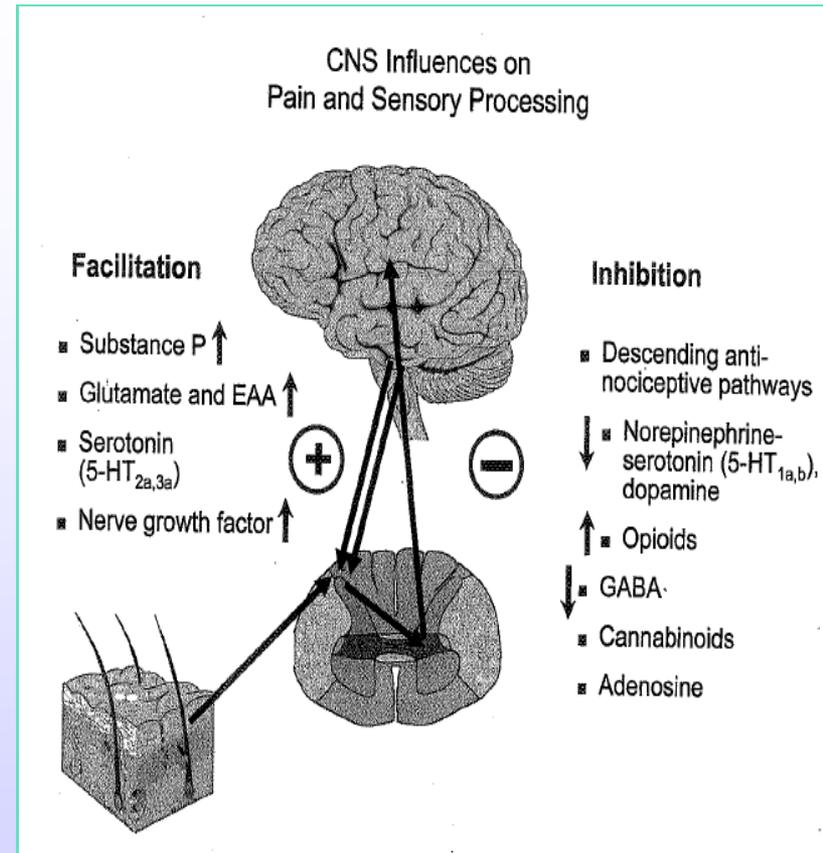
#### Chronic pain

A pain that persists for long

Nociception 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 infection, 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 worldwide<sup>1</sup>, 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 2–7). However, recent data show that functional plasticity changes are accompanied by structural remodelling and reorganization of synapses, cells and circuits that can also occur at various anatomical and temporal scales<sup>2–9</sup>, thereby further adding complexity and a large dynamic range, and potentially accounting for the development of pain that extends over longer periods of

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



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

# Fattori che influenzano il processo di transizione

## Fattori positivi

- supporto sociale
- livello educativo
- strategie di coping
- lavoro soddisf.
- medico di famiglia
- riconosc. di sé

## Fattori negativi

- stato di salute insodd.
- Dolore tipologia /NRS
- Depressione
- Stress
- Contenzioso
- Evitamento per paura
- Ingiustizia percepita
- catastrofismo

# Sintomo-malattia

- Il dolore è l'espressione di un funzionamento patologico del SN: fisico-psicologico-sociale



The Journal of Pain, Vol 10, No 11 (November), 2009; pp 1113-1120  
Available online at [www.sciencedirect.com](http://www.sciencedirect.com)

Critical Review

How Neuroimaging Studies Have Challenged Us to Rethink:  
Is Chronic Pain a Disease?

Irene Tracey\* and M. Catherine Bushnell<sup>†</sup>

\*Oxford Centre for Functional Magnetic Resonance Imaging of the Brain, Nuffield Department of Anaesthetics and Department of Clinical Neurology, University of Oxford, John Radcliffe Hospital, Headington, England, UK.  
<sup>†</sup>Alan Edwards Centre for Research on Pain, Department of Anesthesia and Faculty of Dentistry, McGill University, Montreal, Quebec, Canada.

**Abstract:** In this review, we present data from functional, structural, and molecular imaging studies in patients and animals supporting the notion that it might be time to reconsider chronic pain as a disease. Across a range of chronic pain conditions, similar observations have been made regarding changes in structure and function within the brains of patients. We discuss these observations within the framework of the current definition of a disease.

**Perspective:** Neuroimaging studies have made a significant scientific impact in the study of pain. Knowledge of nociceptive processing in the noninjured and injured central nervous system has grown considerably over the past 2 decades. This review examines the information from these functional, structural, and molecular studies within the framework of a disease state.

© 2009 by the American Pain Society  
**Key words:** Chronic pain, disease, neuroimaging, central nervous system.



**HHS Public Access**  
Author manuscript  
*Neuron*. Author manuscript; available in PMC 2020 March 06.

Published in final edited form as:  
*Neuron*. 2019 March 06; 101(5): 783-800. doi:10.1016/j.neuron.2019.02.019.

**Composite pain biomarker signatures for objective assessment and effective treatment**

Irene Tracey<sup>1,\*</sup>, Clifford J Woolf<sup>2,\*</sup>, Nick Andrews<sup>2</sup>

<sup>1</sup>Nuffield Department of Clinical Neurosciences, University of Oxford, West Wing, John Radcliffe Hospital, Oxford, OX3 9DU, England UK.

<sup>2</sup>Kirby Neurobiology Center, Boston Children's Hospital and Department of Neurobiology, Harvard Medical School, Boston, 02115 MA, USA

**IN BRIEF:**

This perspective highlights the significance of chronic pain, its underpinning biology and the need for composite biomarker signatures alongside self-report. Combining evidence from animal and human research spanning genetics through to neuroimaging, we highlight a few key areas of promise.

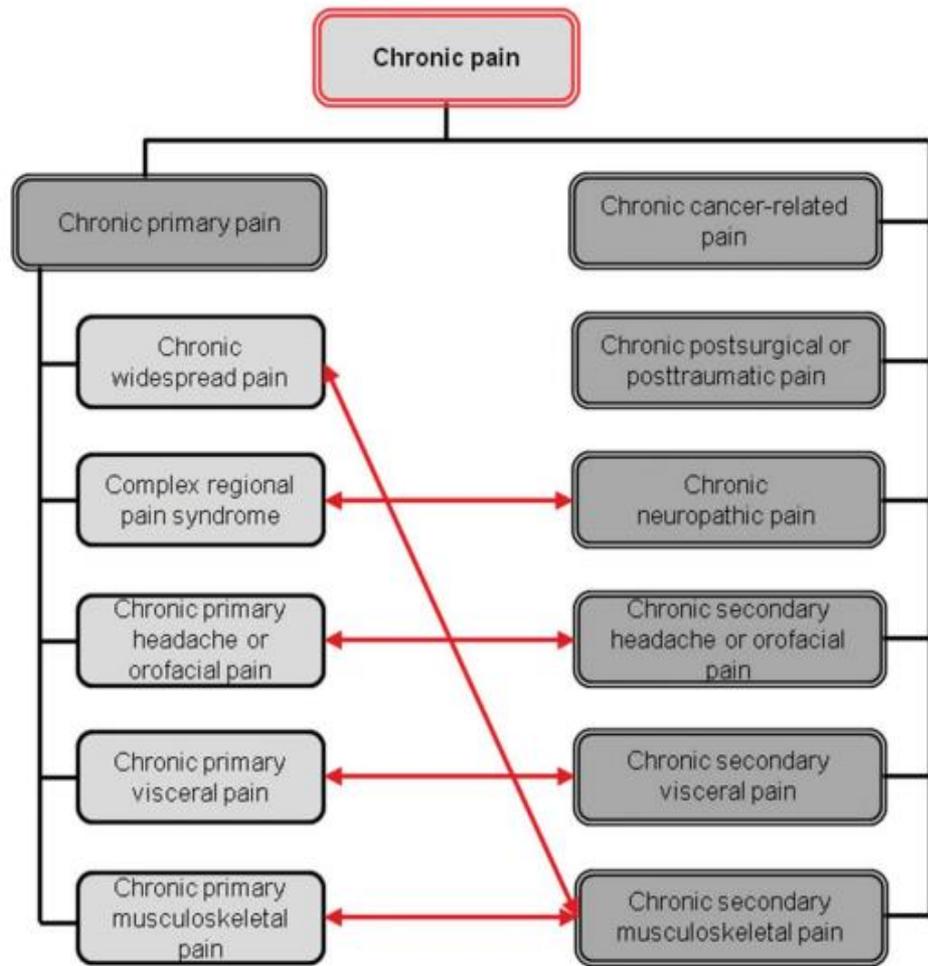
# Chronic pain as a symptom or a disease: the IASP Classification of Chronic Pain for the *International Classification of Diseases (ICD-11)*

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

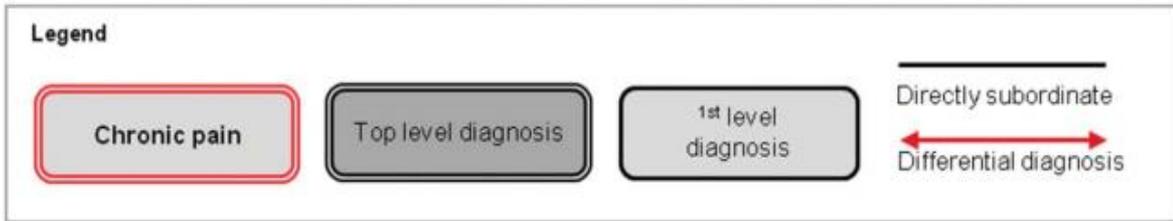
## Abstract

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



Chronic secondary pain syndromes



# The IASP classification of chronic pain for *ICD-11*: chronic primary pain

Michael Nicholas<sup>a</sup>, Johan W.S. Vlaeyen<sup>b,c,d</sup>, Winfried Rief<sup>e</sup>, Antonia Barke<sup>e</sup>, Qasim Aziz<sup>f</sup>, Rafael Benoliel<sup>g</sup>, Milton Cohen<sup>h</sup>, Stefan Evers<sup>i</sup>, Maria Adele Giamberardino<sup>j</sup>, Andreas Goebel<sup>k</sup>, Beatrice Korwisi<sup>e</sup>, Serge Perrot<sup>l</sup>, Peter Svensson<sup>m,n</sup>, Shuu-Jiun Wang<sup>o,p</sup>, Rolf-Detlef Treede<sup>q,\*</sup>, The IASP Taskforce for the Classification of Chronic Pain

## Abstract

This article describes a proposal for the new diagnosis of chronic primary pain (CPP) in *ICD-11*. Chronic primary pain is chosen when pain has persisted for more than 3 months and is associated with significant emotional distress and/or functional disability, and the pain is not better accounted for by another condition. As with all pain, the article assumes a biopsychosocial framework for understanding CPP, which means all subtypes of the diagnosis are considered to be multifactorial in nature, with biological, psychological, and social factors contributing to each. Unlike the perspectives found in *DSM-5* and *ICD-10*, the diagnosis of CPP is considered to be appropriate independently of identified biological or psychological contributors, unless another diagnosis would better account for the presenting symptoms. Such other diagnoses are called "chronic secondary pain" where pain may at least initially be conceived as a symptom secondary to an underlying disease. The goal here is to create a classification that is useful in both primary care and specialized pain management settings for the development of individualized management plans, and to assist both clinicians and researchers by providing a more accurate description of each diagnostic category.

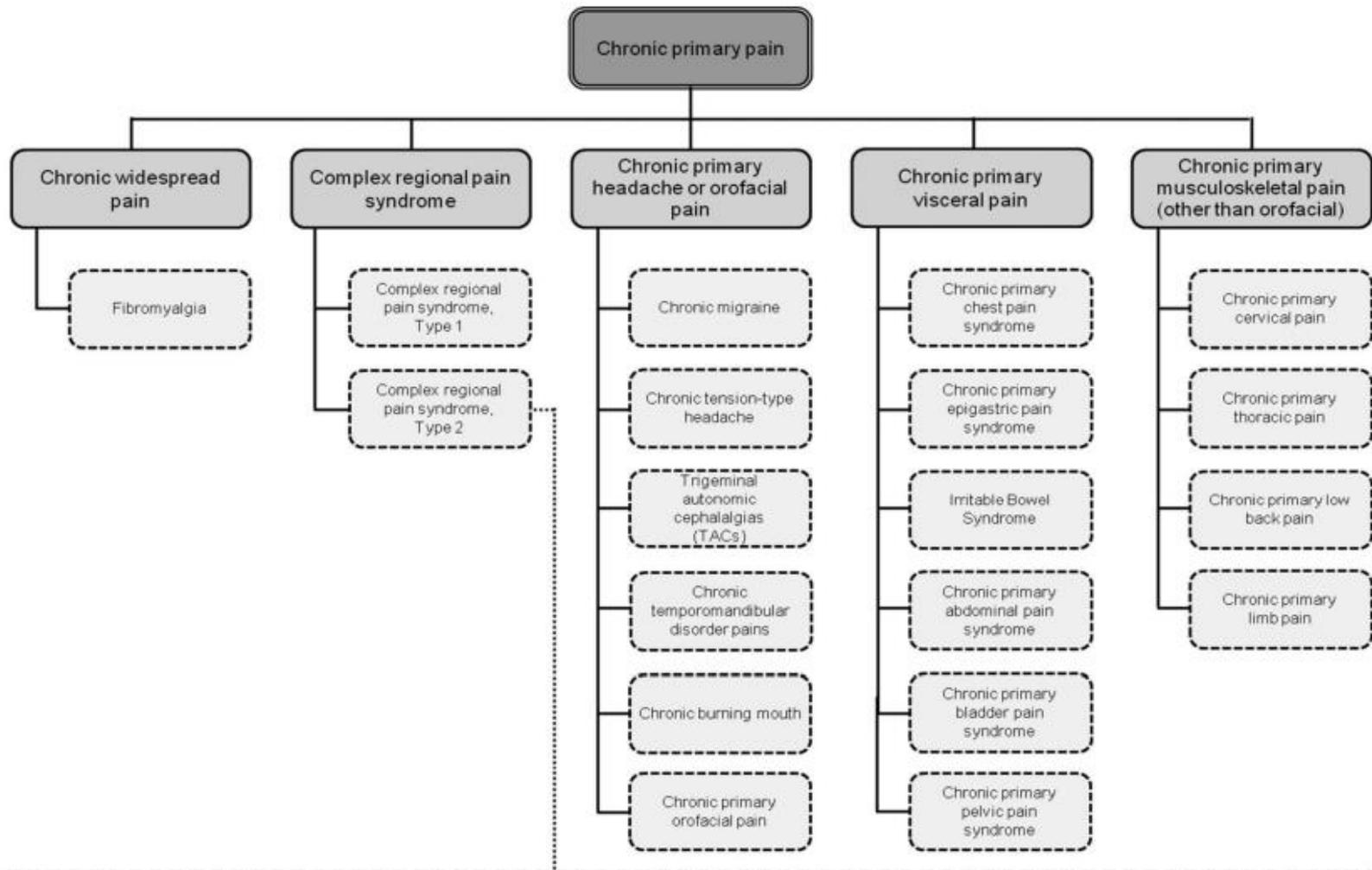
**Keywords:** *ICD-11*, Classification, Chronic pain, Chronic primary pain, CRPS, CWP, Fibromyalgia, Headache, Orofacial pain, Visceral pain, Musculoskeletal pain, Idiopathic pain, Functional pain

## 1. Background on chronic primary pain

There are 2 main diagnostic classification systems used internationally for chronic pain, apart from headaches: the *Diagnostic and Statistical Manual (DSM)* published by the American Psychiatric Association (APA), and the *International Classification of Diseases (ICD)* published by the World Health Organization (WHO). However, both have been found wanting in their accounts of chronic pain conditions. In particular, neither system reflects the developments in pain research over the last 2 decades, and they do not have clear treatment or management implications.<sup>10,15,16,38,61</sup> To illustrate,

*ICD-10* refers to pain attributable exclusively to an underlying pathophysiological mechanism.<sup>19</sup> In the absence of a clear (pathophysiological) etiology, and when biological, psychological, and social factors seem to be contributing to a chronic pain presentation,<sup>15</sup> *ICD-10* offers only the option of "somatoform pain disorder." However, this classification cannot be used when pathophysiological factors are also considered to be contributing to the pain problem.<sup>39</sup>

These distinctions have important treatment implications. As Taylor and colleagues pointed out, if we accept that chronic pain is



Multiple parents

*Chronic pain after peripheral nerve injury*

**Legend**

Top (1 <sup>st</sup> ) level diagnosis	2 <sup>nd</sup> level diagnosis	3 <sup>rd</sup> level diagnosis	Additional parent of the diagnosis	Directly subordinate
				Additional parent

# **Criteria 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
- Il dolore non è correlato a un'altra condizione morbosa

# Disturbi correlati

Livello psicologico-comportamentale

depressione-disturbi del sonno-ansia

capacità di reazione-paura-alimentazione

Livello sociale

interazioni sociali-famiglia-lavoro

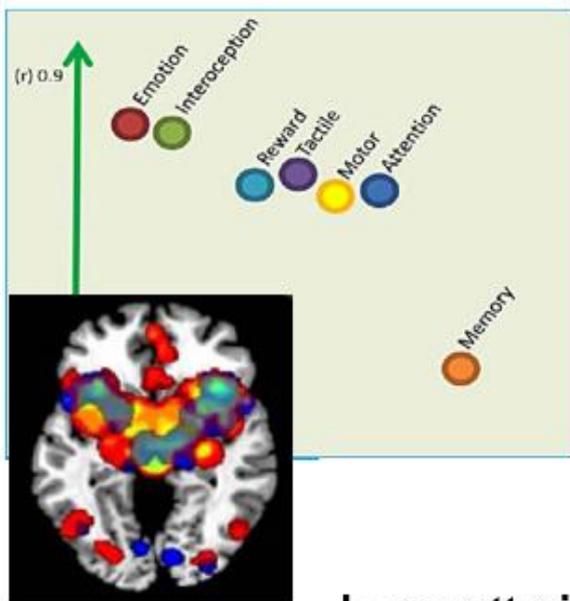
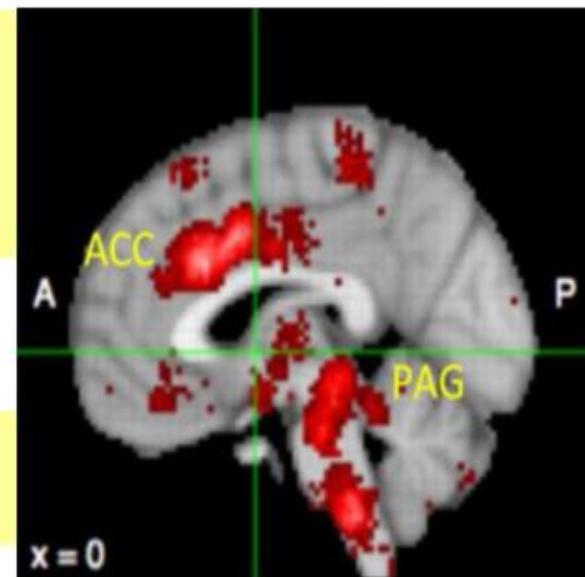
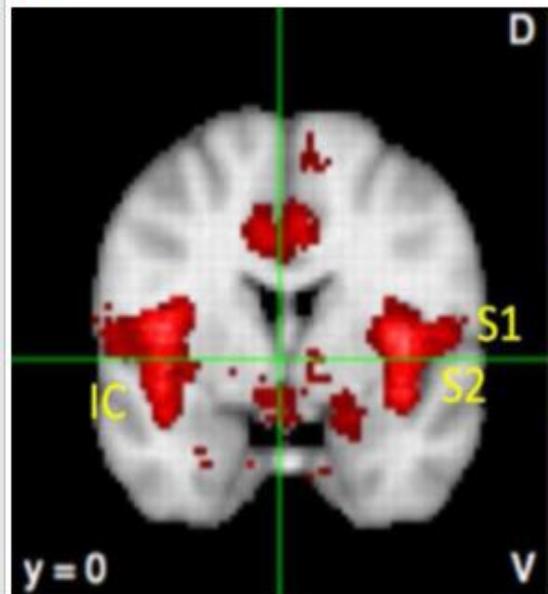
Qualità di vita

salute mentale-attività sociali-attività fisica

attività quotidiane

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<sup>1,2\*</sup>, Diana M-E. Torta<sup>2</sup>, Katuscia Sacco<sup>1,2</sup>, Elisabetta Geda<sup>1</sup>, Federico D'Agata<sup>1,2,3</sup>, Tommaso Costa<sup>2</sup>, Sergio Duca<sup>1</sup>, Giuliano Geminiani<sup>1,2</sup>, Martina Amanzio<sup>2,4</sup>

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

NeuroImage: Clinical 4 (2014) 676-686

Franco Cauda<sup>a,b,c,\*</sup>, Sara Palermo<sup>b</sup>, Tommaso Costa<sup>a,b,c</sup>, Riccardo Torta<sup>d,e</sup>, Sergio Duca<sup>a,b</sup>, Ugo Vercelli<sup>a</sup>, Giuliano Geminiani<sup>a,c</sup>, Diana M.E. Torta<sup>a,b,c</sup>

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

**analgesici**



**dolore**

40 % dei pazienti  
soddisfatti



resistenza al  
trattamento

farmaco  
inadeguato

dosaggi  
inadeguati

**PERCHE' ?**

altre componenti  
sottovalutate?

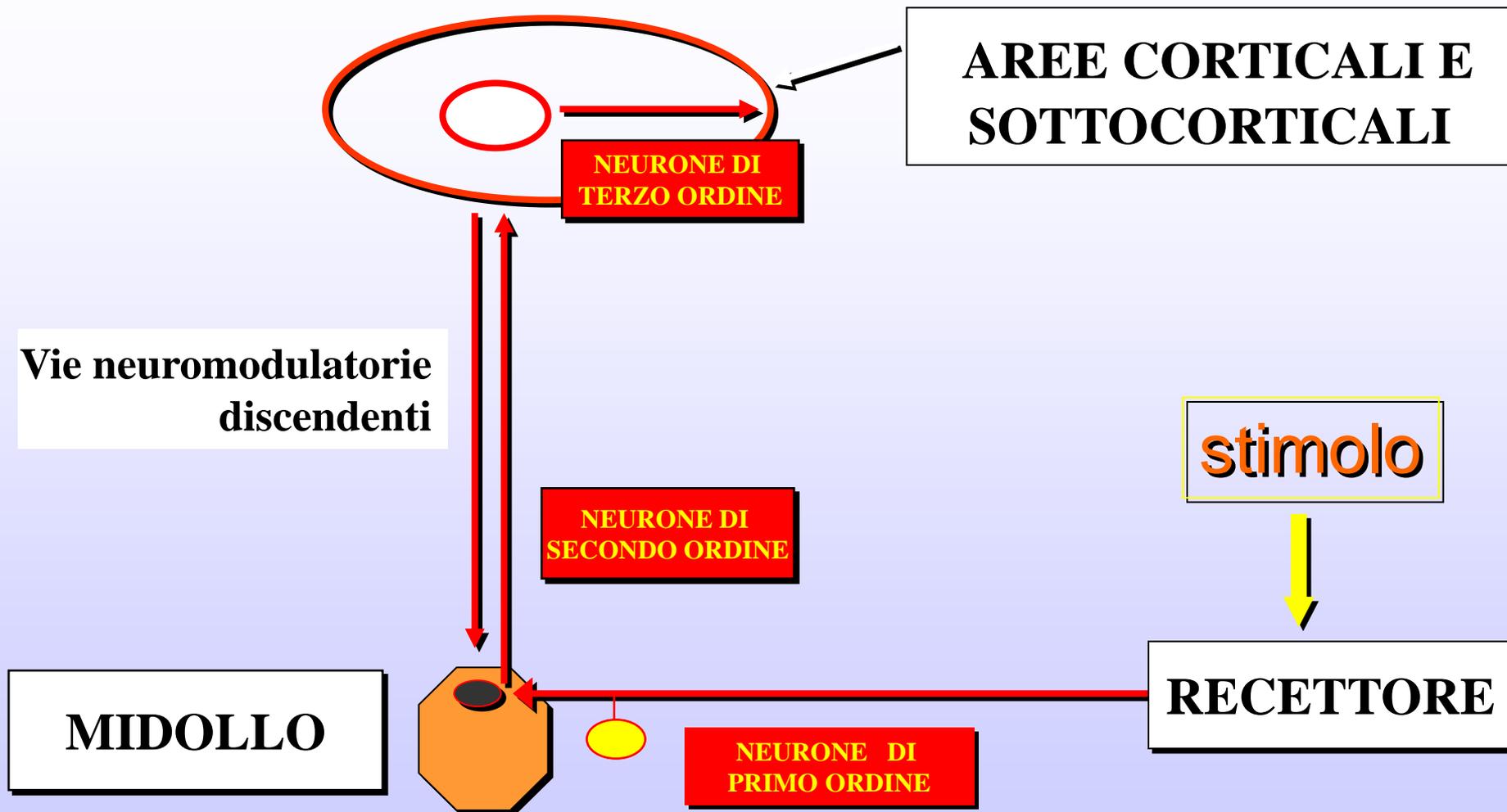
**cognitive**

**emozionali**

**sociali**

Interferenza con senso di benessere, qualità di vita,  
intensità e cronicizzazione del dolore  
e sulla efficacia del trattamento farmacologico

# Strutture nervose e Dolore



# Conclusioni

Terapia basata sulla complessità

# Cosa trattare

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

# Terapia non farmacologica

identificare

atteggiamenti verso il dolore associati con comportamenti disadattivi

Terapista

modificare

correggere le convinzioni inappropriate e migliorare i comportamenti adattivi

aumentare la resilienza verso il dolore

ottenere un maggior controllo cognitivo sullo stimolo algico

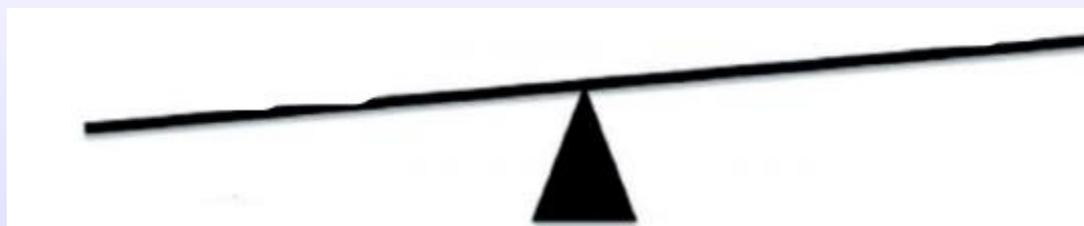
da:

“ il mio dolore è terribile e io non posso farci niente ”

a:

“ per quanto il mio dolore sia forte c'è sempre qualcosa che io possa fare per stare un po' meglio ”

# Programma multimodale integrato



vulnerabilità

resilienza

Per step

Valutazione /primi interventi

Ruolo attivo

Emancipazione

Medico di famiglia

Grazie