



XII EDIZIONE ■■■■
MALATTIA DOLORE
E RETE TERRITORIALE
■ IL DIRITTO DEL PAZIENTE AD ESSERE CREDUTO ■



**DIFFERENZE DI GENERE NEL DOLORE:
aspetti psico-emozionali**

Riccardo Torta

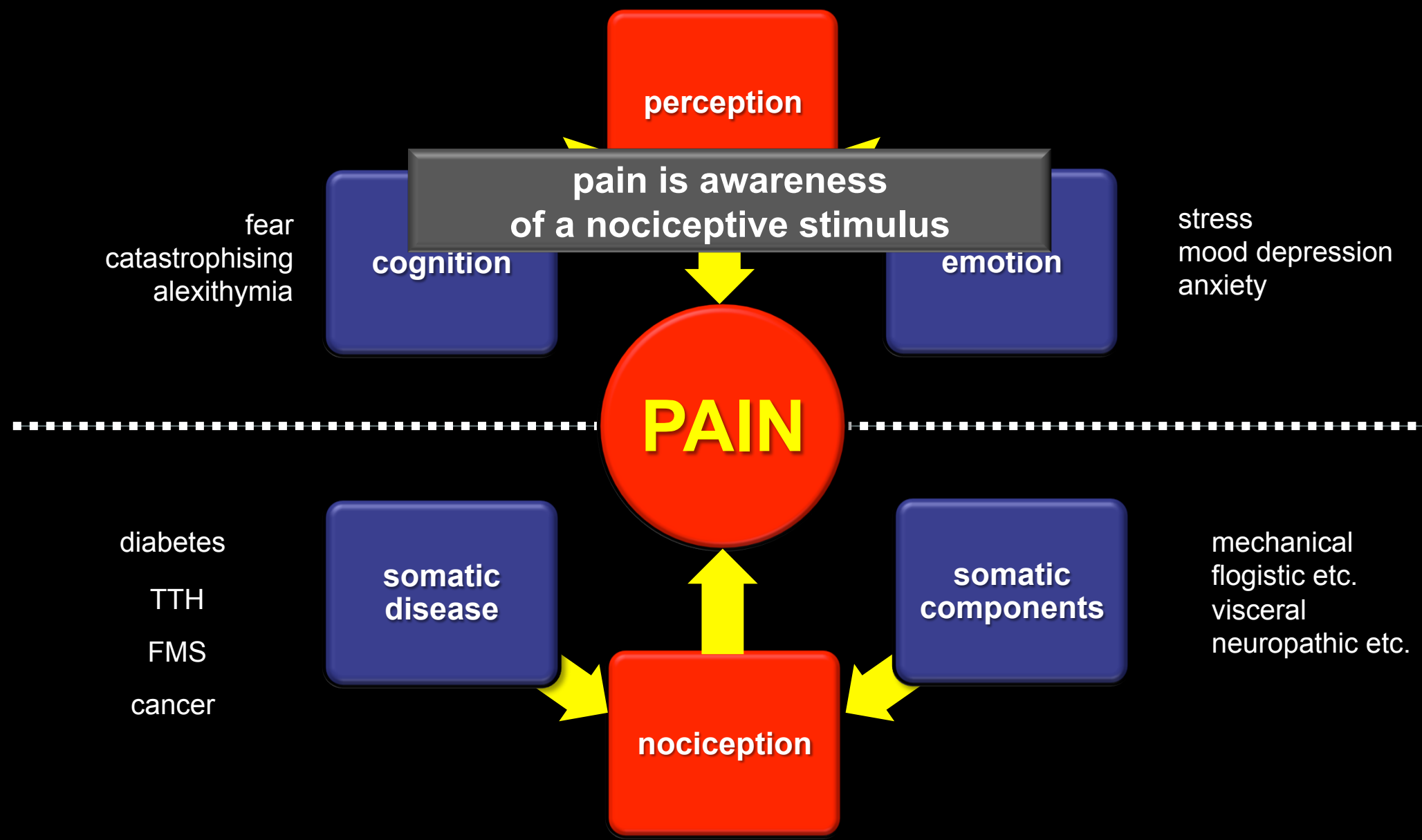
Psicologia Clinica e Oncologica
Città della Salute e della Scienza
Università di Torino

Argomenti

la patogenesi del dolore oggi

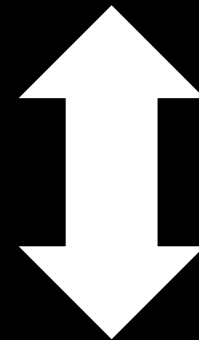
le differenze di genere nel dolore

antidepressivi ed analgesici



depression

central sensitization
reduction of pain threshold

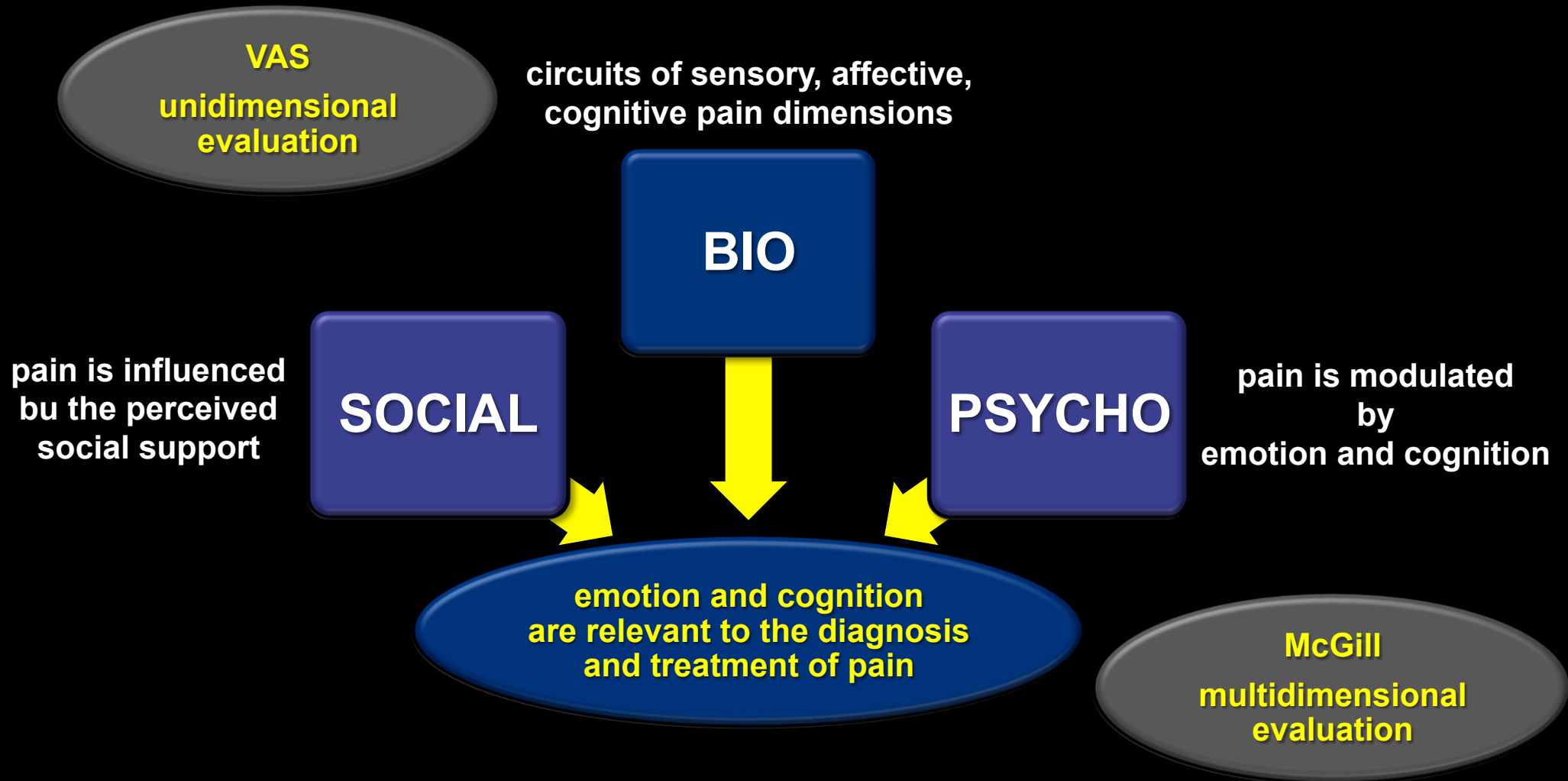


chronicity
disability
strained relationships

pain

*Torta and Lacerenza, 2002;
Leo, 2003*

bio-psycho-social model of pain

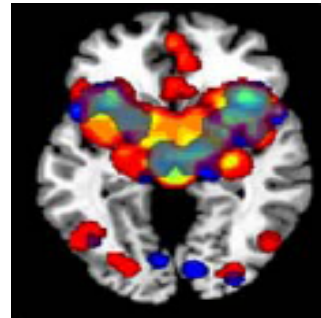
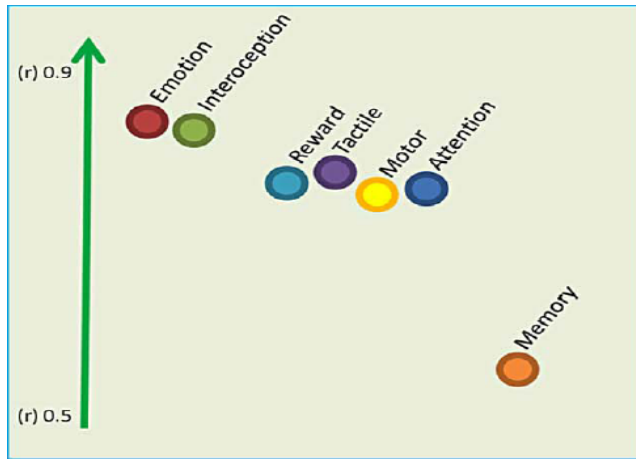


Shared "Core" Areas between the Pain and Other Task-Related Networks

August 2012 | Volume 7 | Issue 8 | e41929

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

the concept of PAIN MATRIX is changed



Contents lists available at ScienceDirect

NeuroImage: Clinical

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

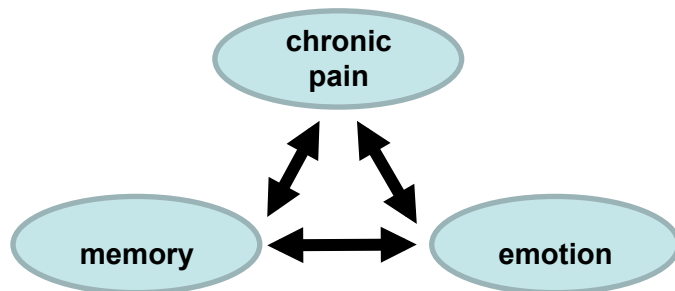


Franco Cauda^{a,b,c,*}, Sara Palermo^b, Tommaso Costa^{a,b,c}, Riccardo Torta^{d,e}, Sergio Duca^{a,b}, Ugo Vercelli^a, Giuliano Geminiani^{a,c}, Diana M.E. Torta^{a,b,c}

• The Journal of Neuroscience, February 6, 2008 • 28(6):1398 –1403

Beyond Feeling: Chronic Pain Hurts the Brain, Disrupting the Default-Mode Network Dynamics

Marwan N. Baliki,¹ Paul Y. Geha,¹ A. Vania Apkarian,^{1,2,3,4} and Dante R. Chialvo¹



Chronic pain selectively alters large-scale brain networks.
Some common areas represent a "core group" of regions altered by almost all the chronic pain pathologies and some other areas that are differentially damaged and that may represent the specific damage of each pathology.

Long-term pain alters the functional connectivity of cortical regions known as *pain matrix*

Chronic pain has to be prevented as early as possible in order to keep "pain memory" from being established

the concept
of MOOD
DEPRESSION
is changed

reduced brain
monoaminergic
transmission

neurotransmitter
receptor dysfunction

oxidative stress
and nitric oxide

Major
depression

dysregulation HPA
HPG HPT axis

reduction of
neurotrophic factors

increase of
proinflammatory
cytokines



Review

Open Access

Depressive Disorders and Pain: A Joint Model of Diagnosis and Treatment

Torta RG[†] and Ieraci V

Clinical and Oncological Psychology, Department of Neuroscience, University of Turin, Italy

CNS & Neurological Disorders - Drug Targets, 2016, 15, 000-000

Disease-Induced Neuroinflammation and Depression

Cristina Benatti^{1,§}, Joan M.C. Blom^{2,§}, Giovanna Rigillo¹, Silvia Alboni¹, Francesca Zizzi³,
Riccardo Torta³, Nicoletta Brunello¹ and Fabio Tascedda^{*.1}

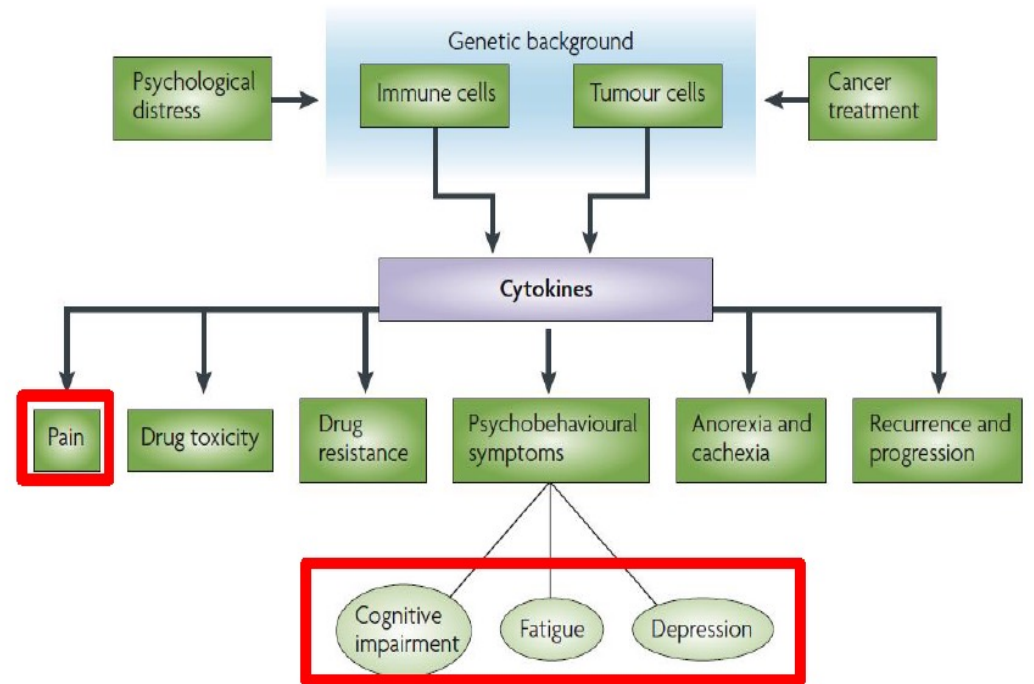
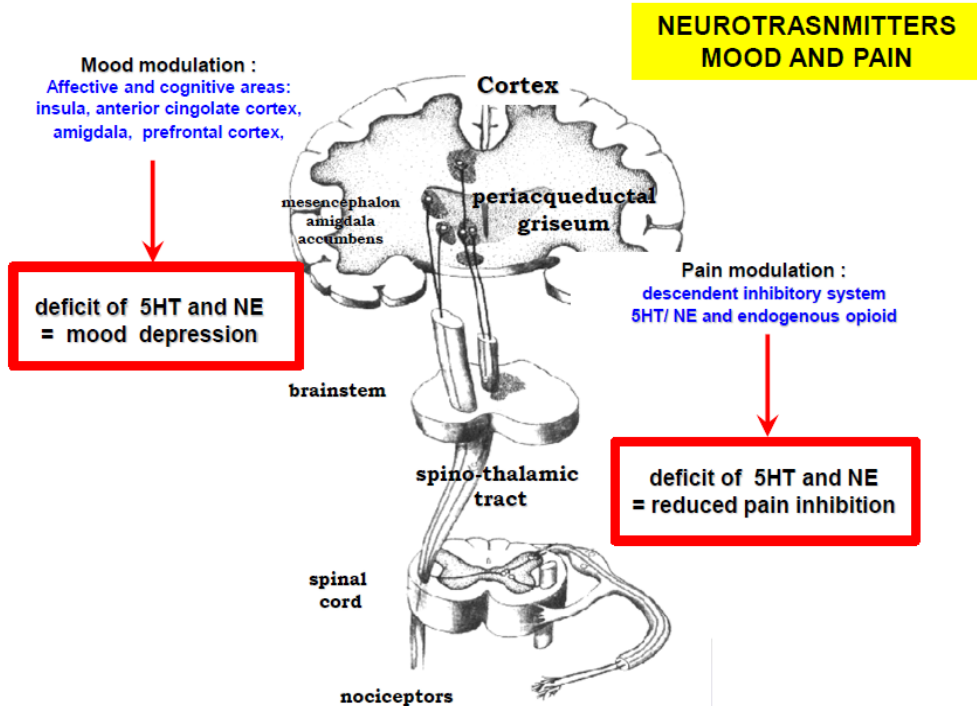
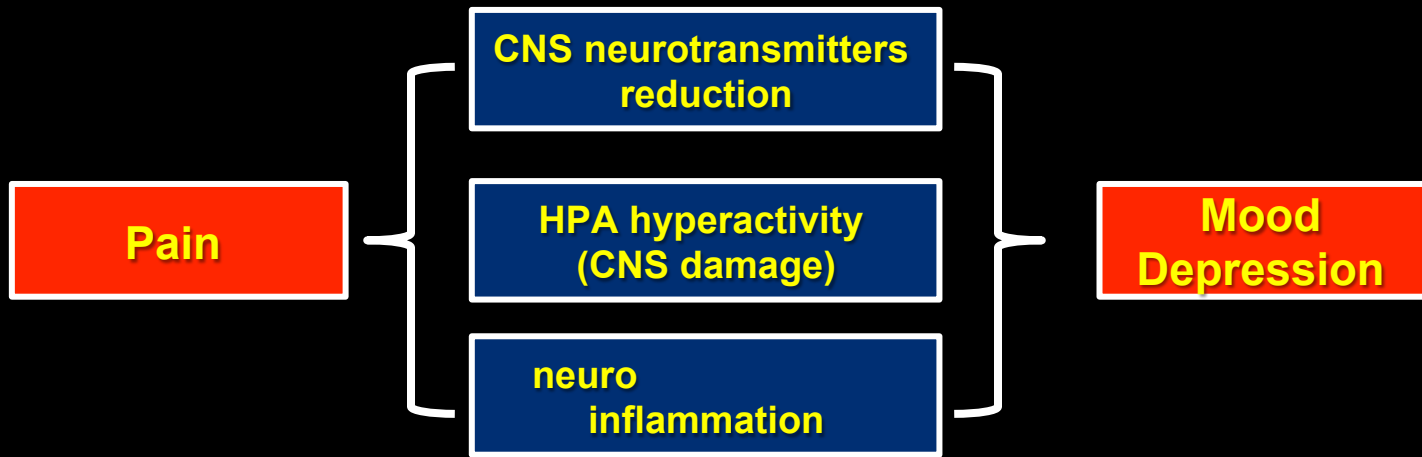
Pharmacol Rev 66:80–101, January 2014

Neuroinflammation and Comorbidity of Pain and Depression

A. K. Walker, A. Kavelaars, C. J. Heijnen, and R. Dantzer

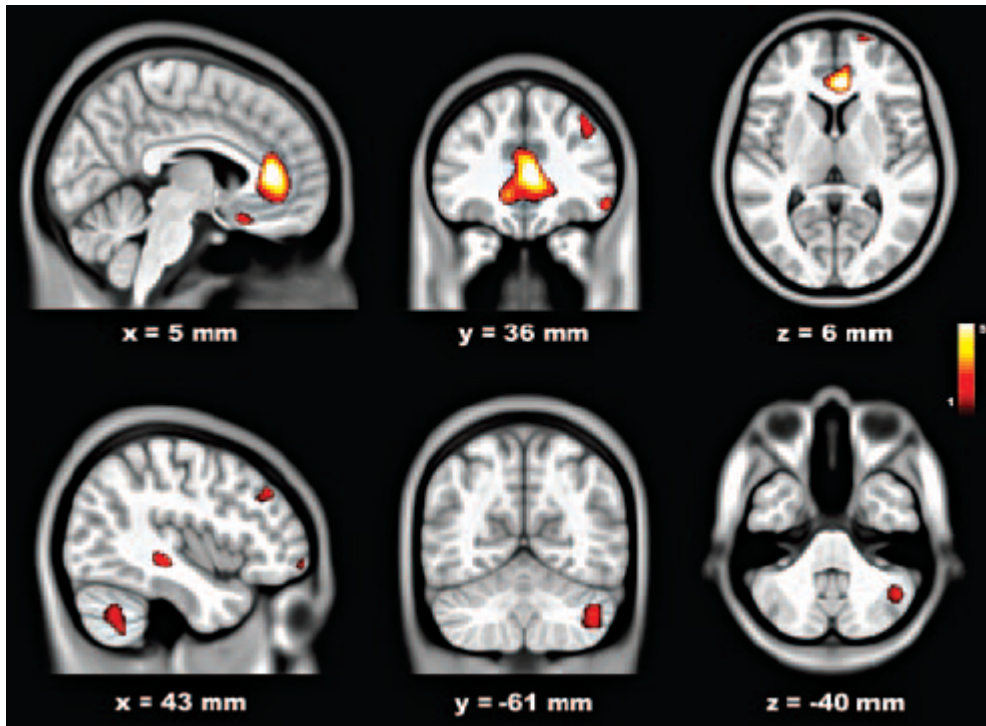


from co-morbidity to co-pathogenesis



The chemotherapy long-term effect on cognitive functions and brain metabolism in lymphoma patients

B. BAUDINO ¹, F. D'AGATA ^{2,3}, P. CAROPPO ², G. CASTELLANO ¹, S. CAUDA ¹
M. MANFREDI ¹, E. GEDA ³, L. CASTELLI ³, P. MORTARA ², L. ORSI ², F. CAUDA ³
K. SACCO ³, R. B. ARDITO ³, L. PINESSI ², G. GEMINIANI ³, R. TORTA ⁴, G. BISI ¹



The involvement of frontal lobes could be a factor guiding the changes and the adaptation mechanisms activated as a response by the system (e.g. cytokines production, stress system activation, immune system responses).



High cytokines levels correlate with mood depression, cognitive dysfunction, pain and stress levels

Argomenti

la patogenesi del dolore oggi

le differenze di genere nel dolore

meccanismi biologici, psichici e sociali

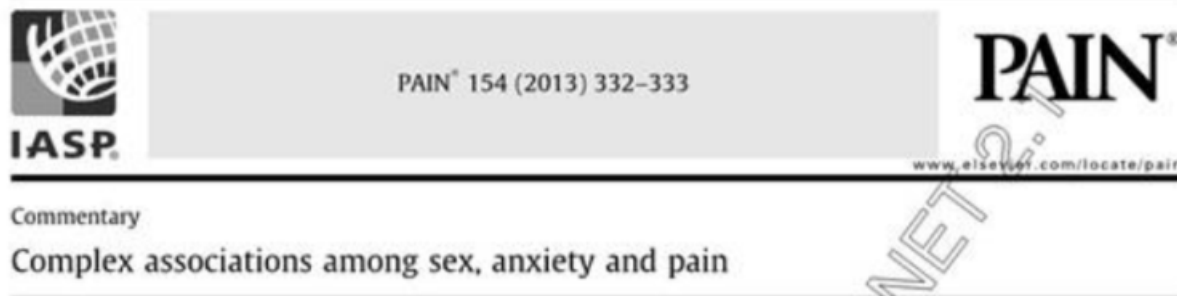
la fibromialgia: il dolore incompreso

Sex differences in pain: a brief review of clinical and experimental findings

E. J. Bartley* and R. B. Fillingim

Sex, Stress, and Mood Disorders: At the Intersection of Adrenal and Gonadal Hormones
Horm Metab Res. 2012

A. Fernández-Guasti¹, J. L. Fiedler², L. Herrera³, and R. J. Handa⁴



The Neuroanatomy of Sexual Dimorphism in Opioid Analgesia

Dayna R. Loyd¹ and Anne Z. Murphy² *Exp Neurol.* 2014

Sex differences in opioid analgesia and addiction:
interactions among opioid receptors and
estrogen receptors

Cynthia Wei-Sheng Lee^{1,2*} and Ing-Kang Ho^{1,3,4}



Pain, 65 (1996) 123–167

Gender variations in clinical pain experience

Anita M. Unruh

Women and men may have different pain experiences from similar diseases

Stress and depression may be more closely associated with pain in women than in men

Severity of pain may be more important as a risk for depression in women than in men

Journal of the National Cancer Institute Monographs No. 32, 2004
Gender Differences in Pain, Fatigue, and Depression in Patients With Cancer

Christine Miaskowski

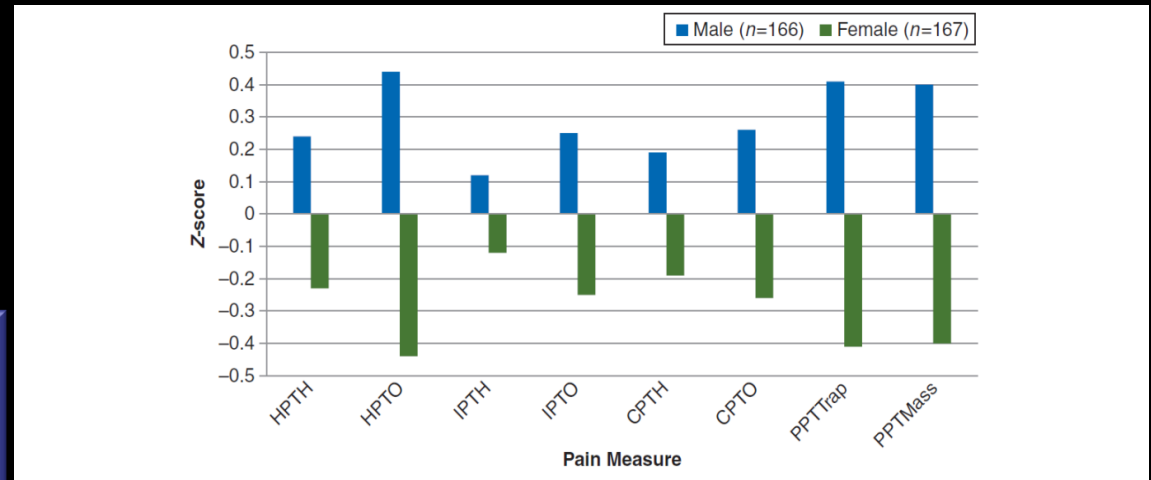
Women were 1.5 times as likely to be undertreated for their cancer pain

Sex differences in opioid analgesia and addiction:
interactions among opioid receptors and
estrogen receptors

Lee and Ho *Molecular Pain* 2013, 9:45

Ovarian steroids have been found to modulate the activity of opioid receptors in healthy women and migraine sufferers

HPTH= heat pain threshold
 HPTO= heat pain tolerance
 IPTH = ischaemic pain threshold
 IPTO = ischaemic pain tolerance
 CPTH= cold pain threshold
 CPTO=cold pain tolerance
 PPTTrap = pressure pain threshold



differenze di genere



le donne dimostrano una maggiore sensibilità al dolore quando paragonate ai maschi (1,2)

**ridotta prescrizione oppioide post-chirurgica (3)
 maggior utilizzo di ansiolitici/sedativi nel dolore(4)
 maggiore prescrizione di oppioidi al proprio sesso (5)**

(1) Hastie et al. 2012; 2) Rahim-Williams et al. 2012; 3) Miaskowski et al., 2000 ; 4) Calderone 1990; 5) Weisse et al., 2001)

differenze di genere

meccanismi biologici

ormoni sessuali

testosterone più antinocicettivo

aumentata sensibilità al dolore in catamenio (fase luteinica)

attivazione del SNC

ridotta attivazione estroprogestinica e bassi livelli di testosterone nelle aree inibenti il dolore (PEG)

sistema oppioide

bassi livelli di estradiolo: < trasmissione oppioide

meccanismi psichici

maggiore frequenza di depressione dell'umore

aspettativa comportamentale

mascolinità vs femminilità

meccanismi sociali

espressione culturale

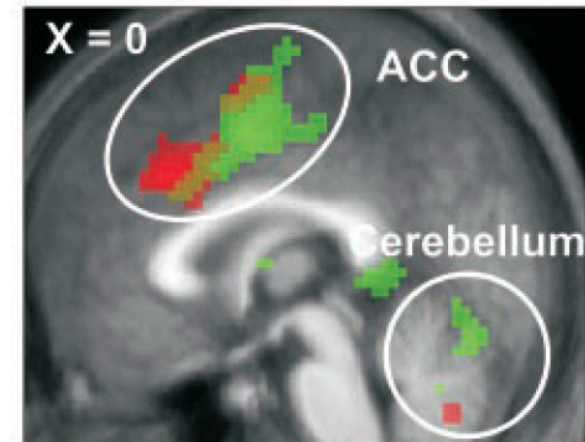
latini vs.anglosassoni

sensibilizzazione algica

esperienze traumatiche (es.abuso) memoria del dolore

Empathy for Pain Involves the Affective but not Sensory Components of Pain

Tania Singer,^{1*} Ben Seymour,¹ John O'Doherty,¹ Holger Kaube,² Raymond J. Dolan,¹ Chris D. Frith¹



Volontarie (donne) attivano le loro aree affettive del dolore (corteccia cingolata anteriore -ACC), in correlazione significativa on il livello di empatia, quando osservano I loro amati che ricevono una (finta) stimolazione dolorosa sulla mano

PSYCHOLOGICAL SCIENCE

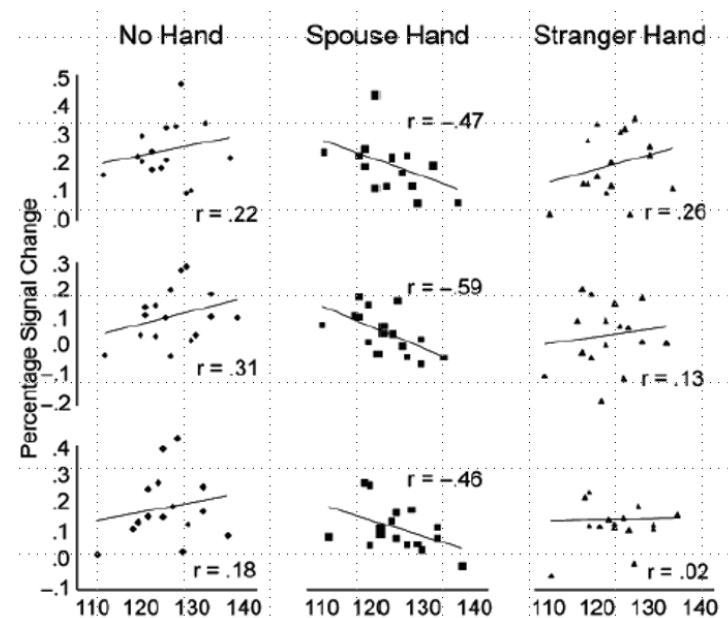
Research Article

Lending a Hand

Social Regulation of the Neural Response to Threat

James A. Coan,¹ Hillary S. Schaefer,² and Richard J. Davidson²

¹University of Virginia and ²W.M. Keck Laboratory for Functional Brain Imaging and Behavior and Department of Psychology, University of Wisconsin-Madison



**distress del caregiver e percezione
dolorosa del paziente**

DISTRESS THERMOMETER

analogo visivo

problem list

livello di
distress

caregiver

numero aree
stressogene

$p \leq 0.2$



$p \leq 0.007$



dolore percepito dal Paziente

**ANTIDEPRESSANTS AND
ANALGESICS
BETWEEN MOOD AND PAIN**

**if antidepressants act also on pain,
pain killers act also on mood ?**

neurotransmitters

increased
neurotransmitters
availability

immune system

reduced
pro-inflammatory
cytokines levels

mood depression

HPA, HGA axis
modulation

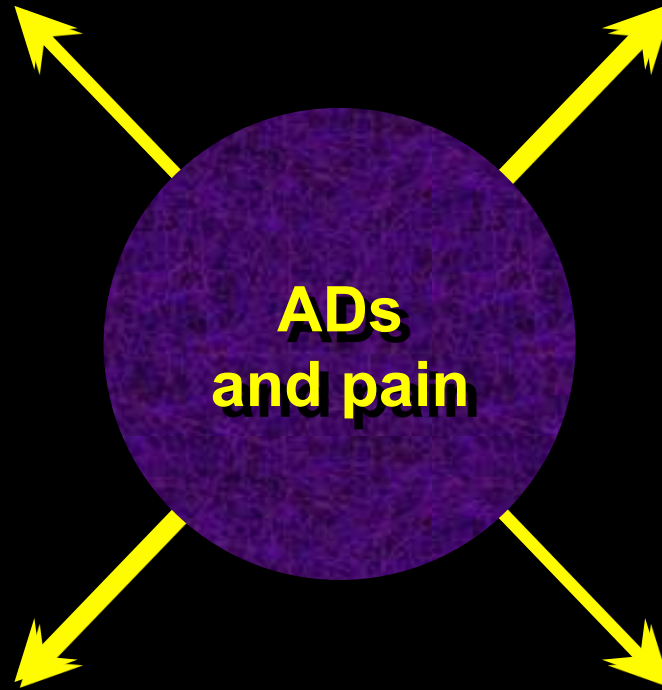
hormones

ADs
and pain

stress and anxiety

increased
BDNF-NGF
expression

CNS trophism



Tramadol (MOR + SRI activities)
Tapentadol (MOR + NRI activities)

NE and 5HT

Pregabalin /Gabapentin
($\alpha 2\delta$ receptors Ca channels)
Neuropathic pain /Anxiety / Mood

GLUTAMATE

**Pain Killer
and mood**

Opioid system

Opioids ($\mu + \delta$ opioid receptors)
Cannabinoids (CB1 + CB2 receptors)
TCAs (δ receptors + endocannab.)

flogosis

ASA / Cox 2 inhibition
(Pain and mood)

Take home messages

**Both mood depression and pain
have a multifactorial pathogenesis**

**Depression and pain share
several pathogenetic mechanisms**

**Sex differences in pain are present
both from biological point of view
and in clinical pain management**