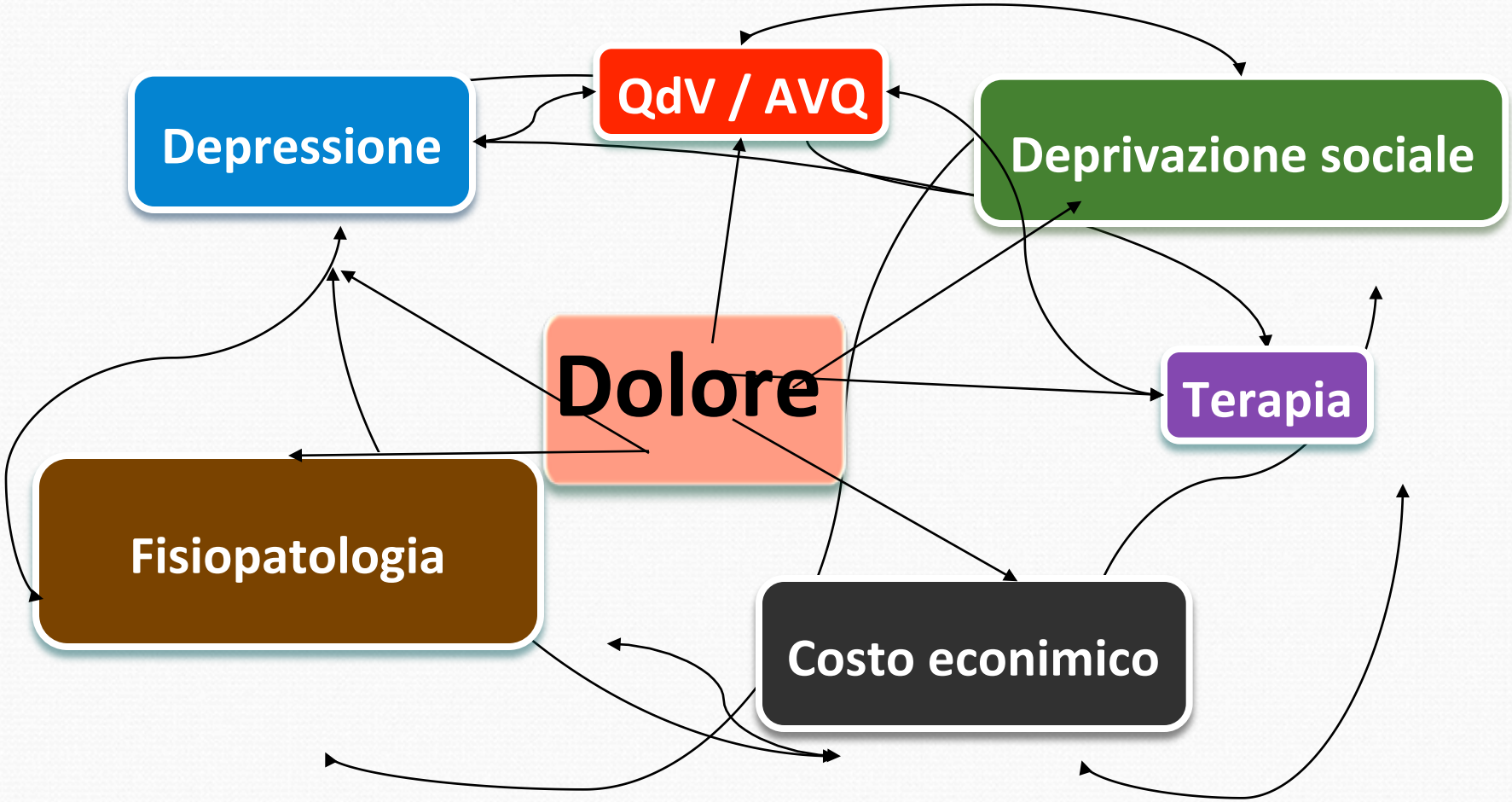
il dolore

Stefano Coaccioli

da: Dolore come condizione …

a: Dolore come Malattia



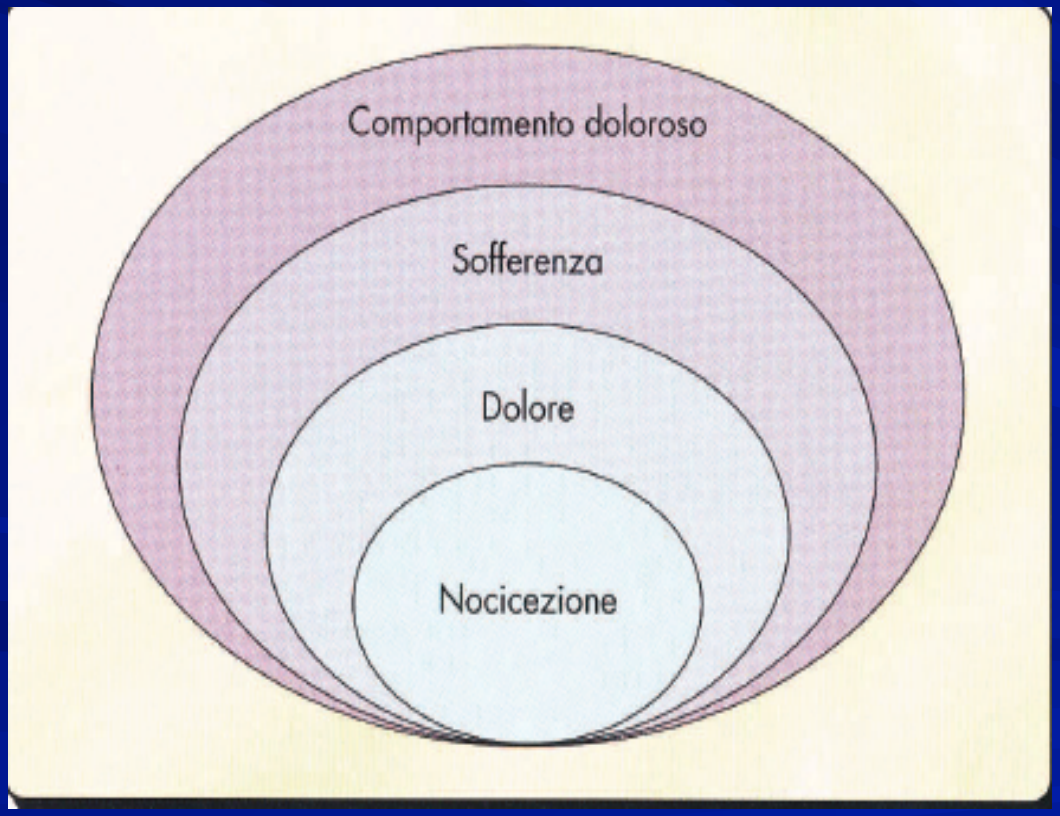
DOLORE

ESPERIENZA PLURIDIMENSIONALE

"Esperienza sensoriale ed emozionale spiacevole, associata a danno tissutale potenziale o effettivo o descritta in termini di tale danno"

iasp

DOLORE



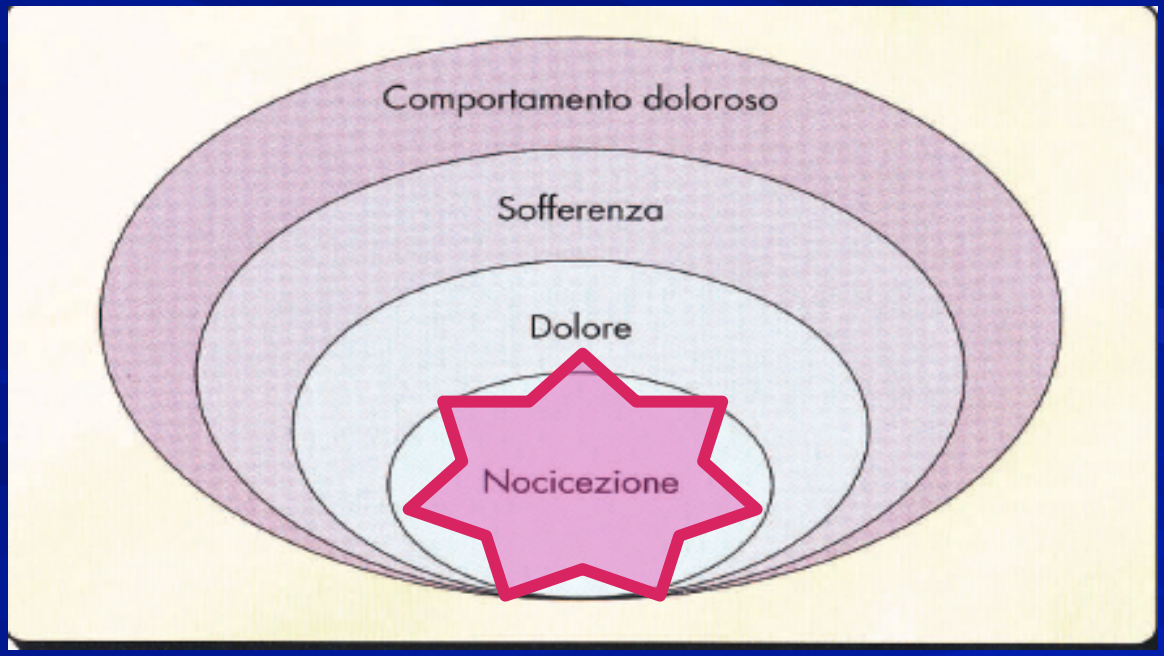
" Il dolore è ciò che il paziente dice che esso sia ed esiste ogni qualvolta egli ne afferma l'esistenza"

Sternbeck 1974

LE DIMENSIONI DEL DOLORE

NOCICEZIONE

I recettori per il dolore vengono attivati da un danno e trasmettono l'impulso alle strutture centrali.



DIMENSIONI DEL DOLORE

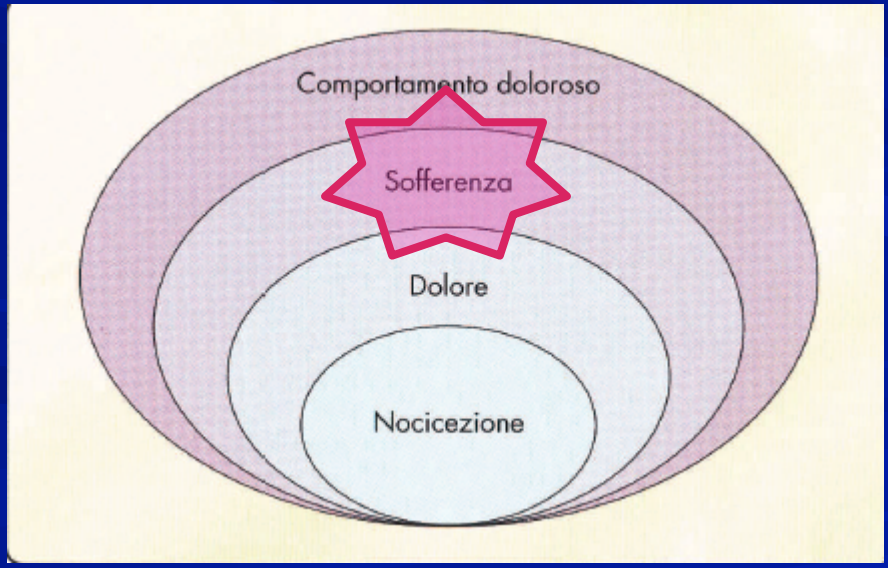
DOLORE

Rappresenta il risultato dell'elaborazione di un segnale trasmesso al Sistema Nervoso Centrale

DIMENSIONI DEL DOLORE

SOFFERENZA

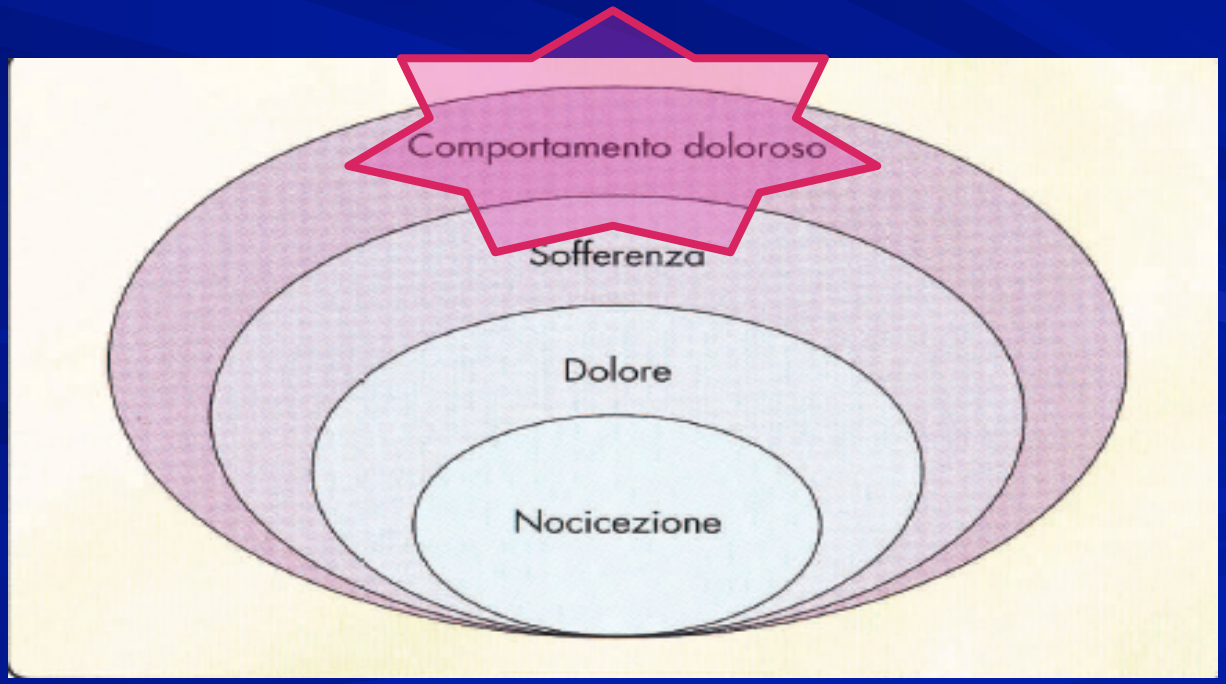
Rappresenta la risposta affettiva al dolore, è generata da processi corticali più elevati e conferisce al dolore stesso la sua tonalità spiacevole, aggressiva, penosa, difficilmente sopportabile



DIMENSIONI DEL DOLORE

COMPORTAMENTO DOLOROSO

Dall'influenza del dolore sulla sfera cognitiva derivano un insieme di manifestazioni verbali e non verbali osservate nella persona che soffre



FISIOLOGICO

Dolore Acuto “*buono*”:

- Causato da lesione, danno esterno o interno
- Transitorio e adattativo
- Allerta prevenzione e protezione dal danno

PATOLOGICO

Dolore Cronico “*cattivo*”:

- Non sempre riferibile ad un evento causale
- Non transitorio e mal adattativo
- No caratteristiche difensive

Dolore acuto

Dolore associato a danno tissutale che ha avuto insorgenza recente ed una probabile durata limitata; possiede una relazione causale e temporale identificabile con un danno od una patologia

Ready and Edwards. Management of acute of acute pain: a pratical guide *1992*. *Taskforce on acute pain. Seattle: IASP Publication*

DOLORE CRONICO

..persistente oltre il periodo di guarigione del danno e frequentemente senza una causa d'origine chiara ed identificabile

Merskey H. Bogduk N. Classification of chronic pain. Descriptions of chronic pain syndromes and definitions of pain terms. *1994 Second edition Seattle: IASP Press*.

Dolore

NOCICETTIVO
(fisiologico) - senza lesione tessutale

INFIAMMATORIO

Somatico

Viscerale

NEUROPATICO

Periferico

Centrale

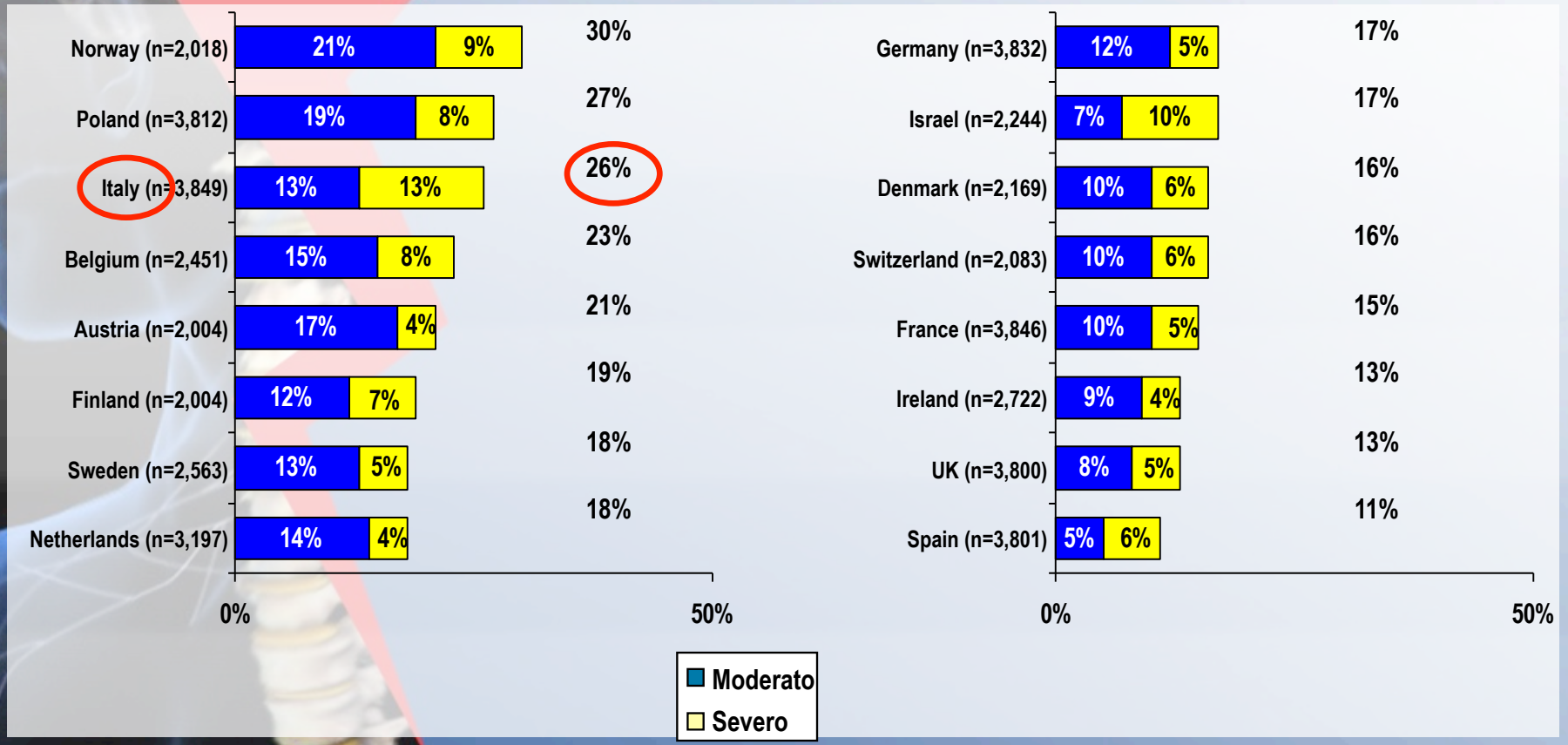
DISFUNZIONALE
(cefalee, fibromialgia etc.)

Prevalenza del Dolore Cronico per Paese
– *Basata sull'esame completo dei dati* –

PAIN IN EUROPE

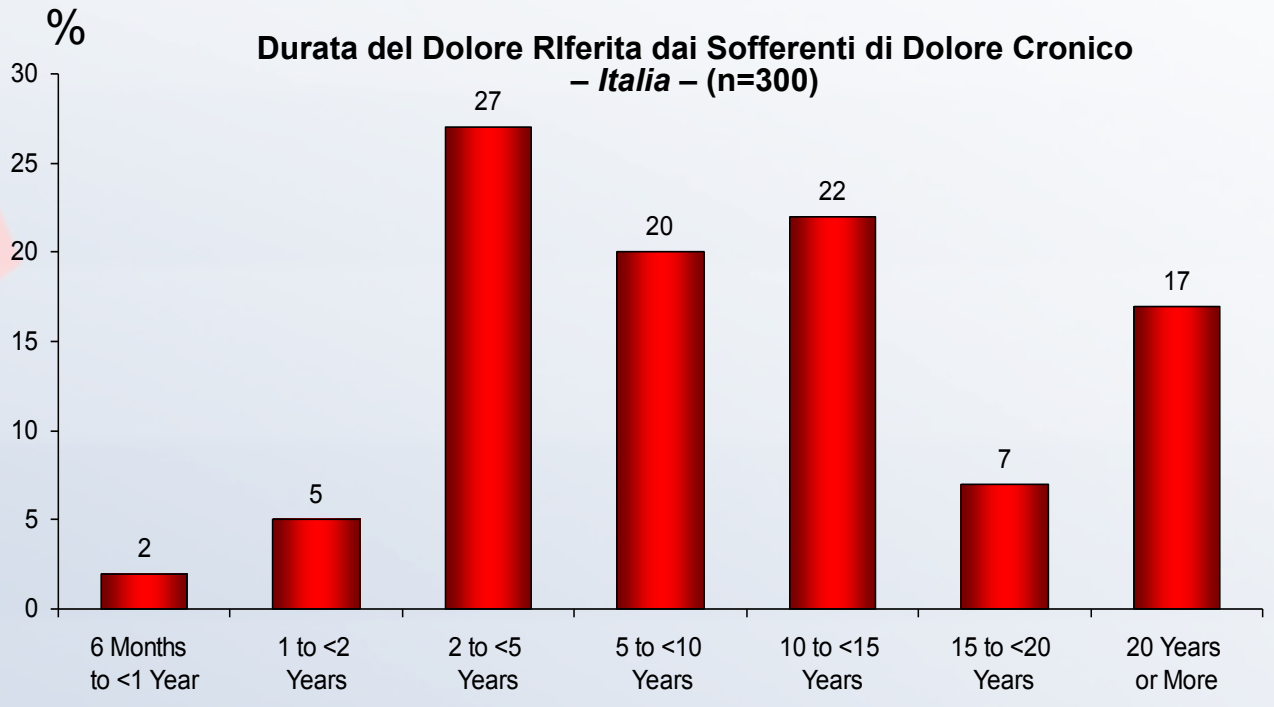
Prevalenza Generale = 19%
(n=46,394)

Moderato 13% Severo 6%



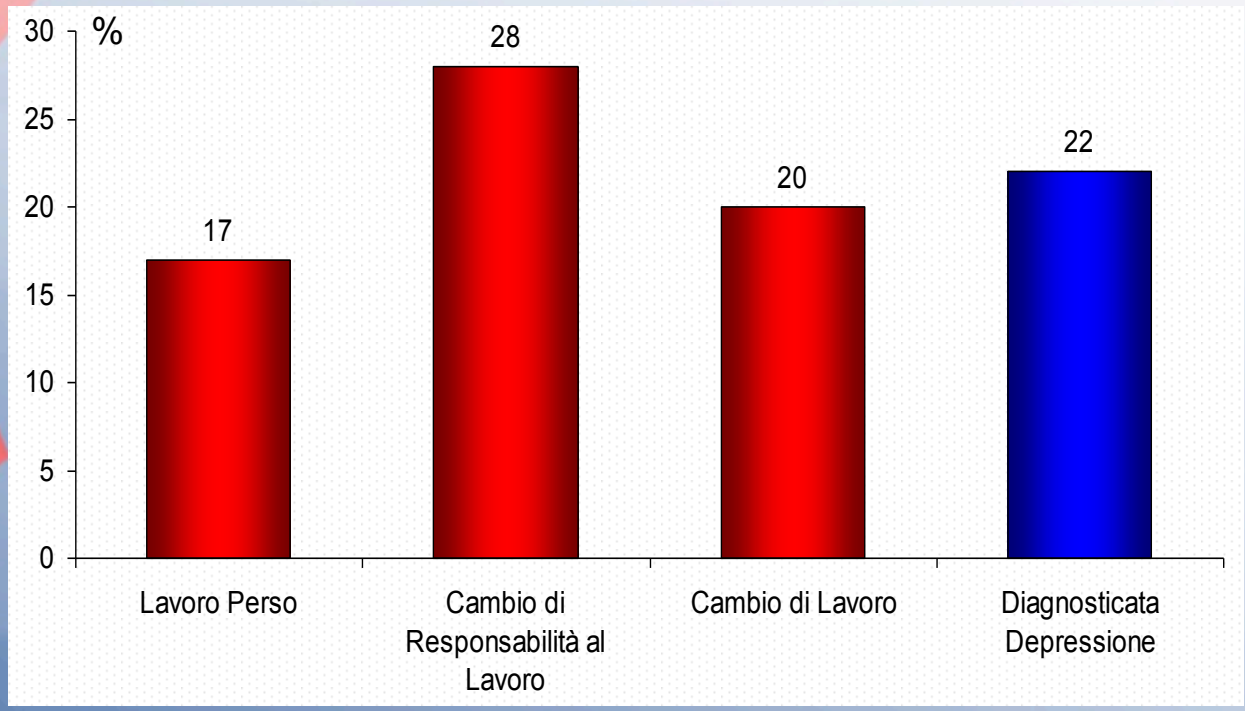
Pazienti Costretti a Vivere con il Dolore

- In media, I sofferenti sono vissuti con il dolore cronico per 7,7 anni
- Quasi un quinto è vissuto con il dolore per oltre 20 anni



Source: SQ6. For how long have you suffered from pain due to your illness or medical condition?

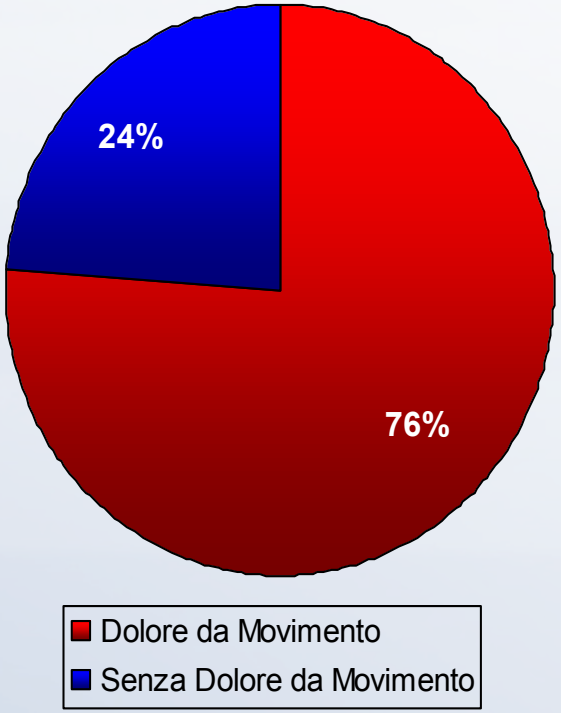
Il Dolore Cronico Può Devastare le Vite



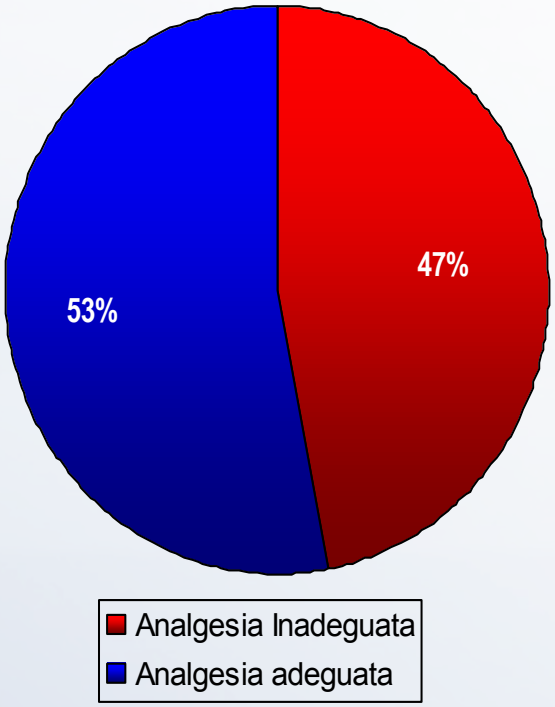
Source: Q6a. Have any of the following ever happened as a result of your pain…? (Read list) Q6b. Have you ever been diagnosed with depression by a medical doctor as a result of your pain?

Come i Pazienti Valutano il Trattamento

Dolore da movimento
– Italia – (n=294)



Adeguatezza del Trattamento
– Italia – (n=96)



Source: Q21. Do you ever experience an increase in pain during the day as a direct result of an activity you did? Q20. Are there ever times when your pain medicines are not adequate to control your pain?

il dolore come un “puzzle”

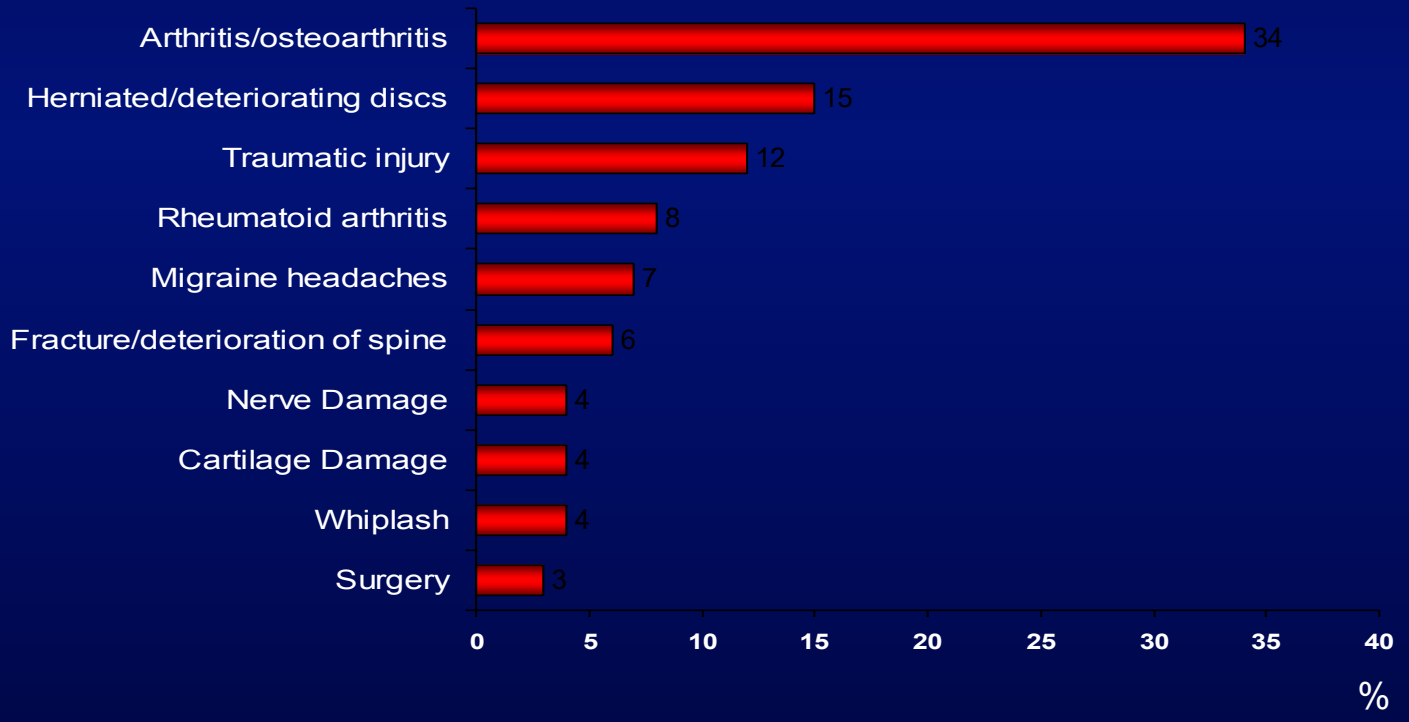
Interessante similitudine che evidenzia come il dolore sia un fenomeno complesso, in cui vari elementi concorrono alla sua determinazione e alle diverse modalità della sua presentazione.

Tipi di dolore

- nocicettivo
- infiammatorio
- neuropatico
- dis-funzionale

Principali cause di dolore cronico *(Pain Europe Survey, 2006)*

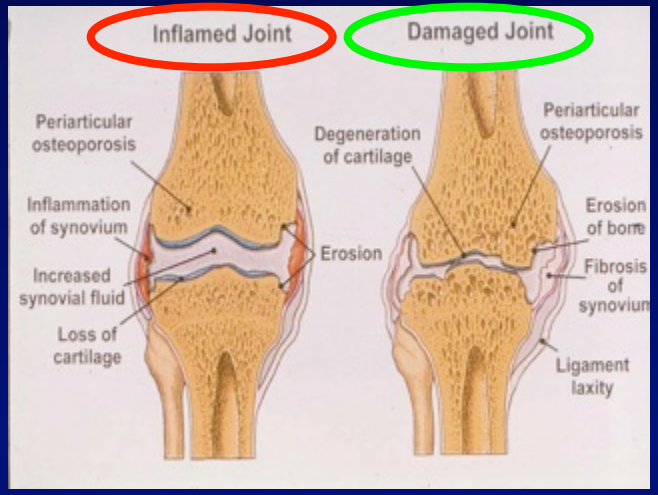
Malattie reumatologiche: 53 %

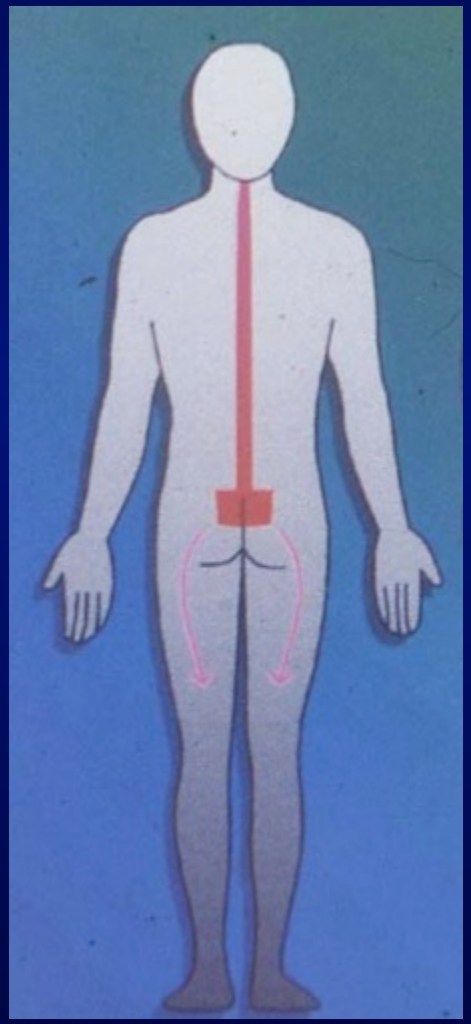


Source: SQ11. Where is your pain located? SQ12. Please tell me the illness or medical condition that is the cause of your pain. Q1. Is your pain caused by…?

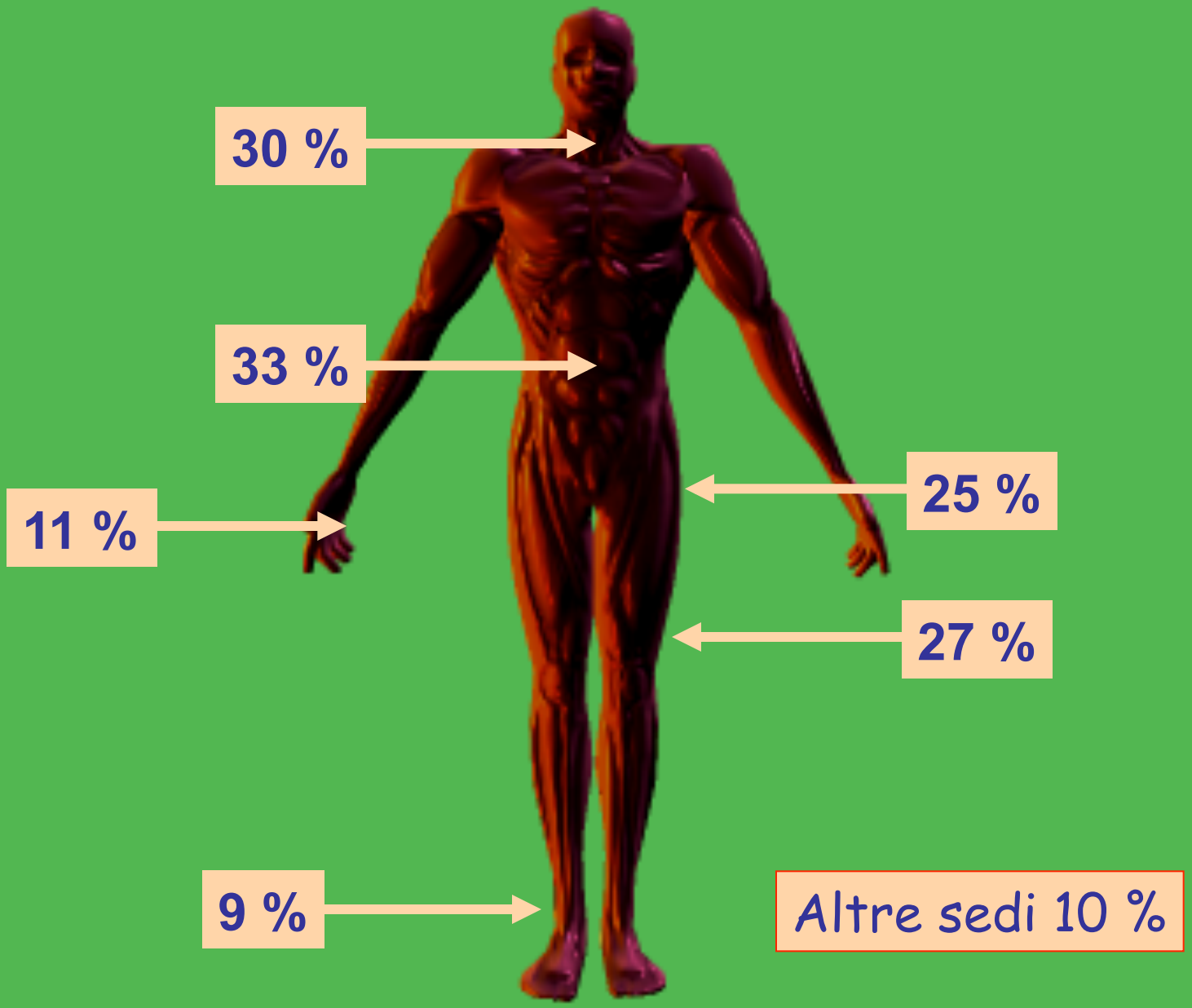
Malattie Reumatiche Croniche:

degenerative e infiammatorie – funzionali e strutturali

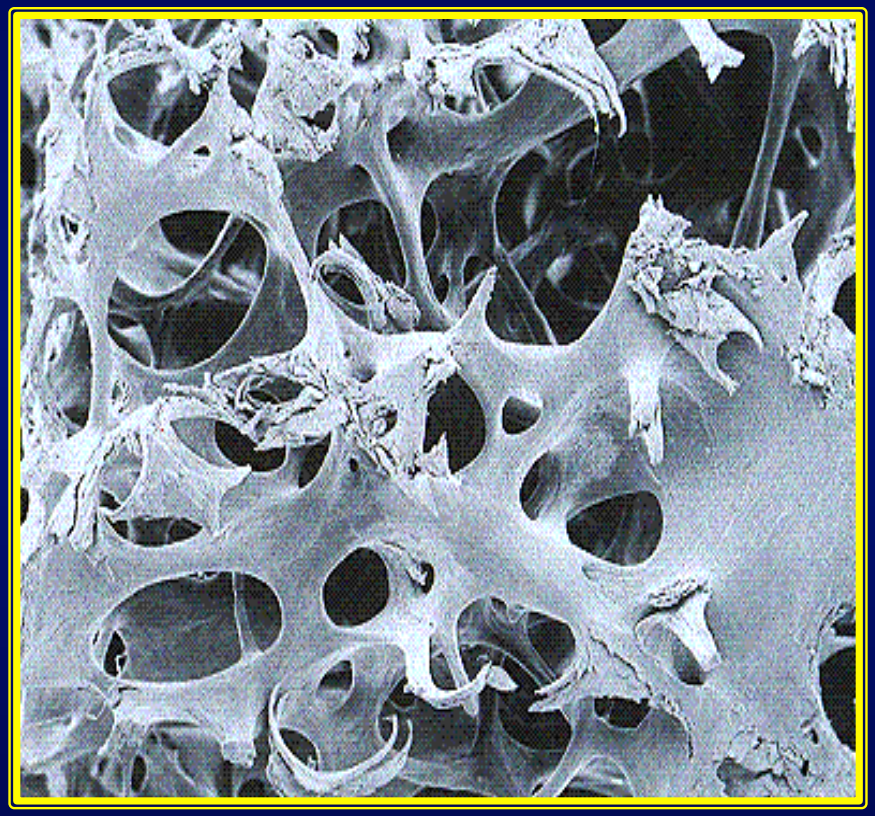




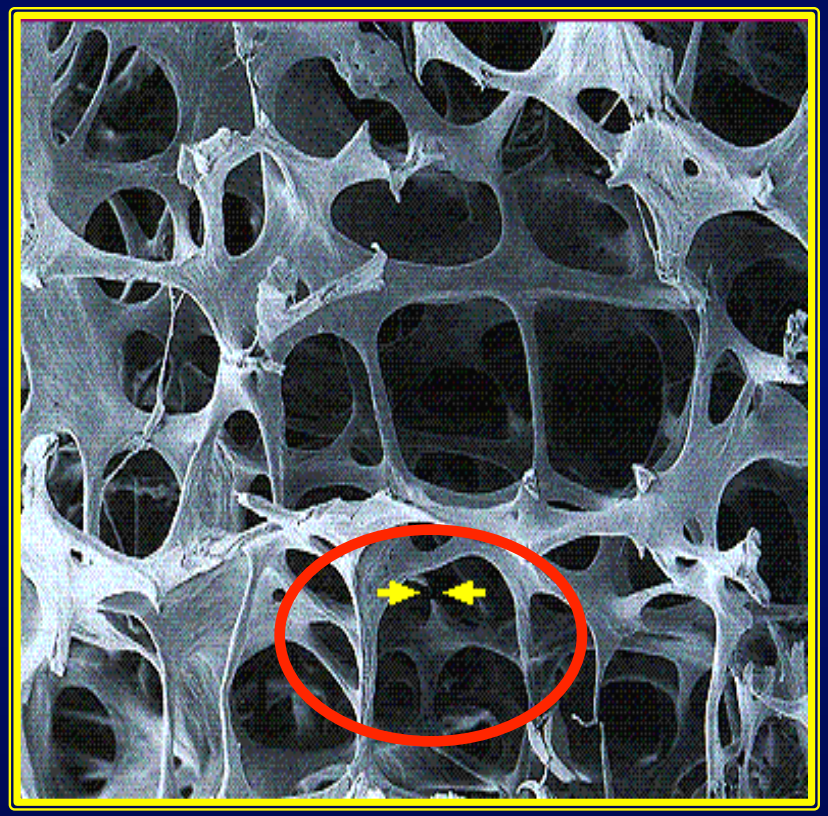
OA: frequenza delle localizzazioni



Osteoporosi: non solo BMD



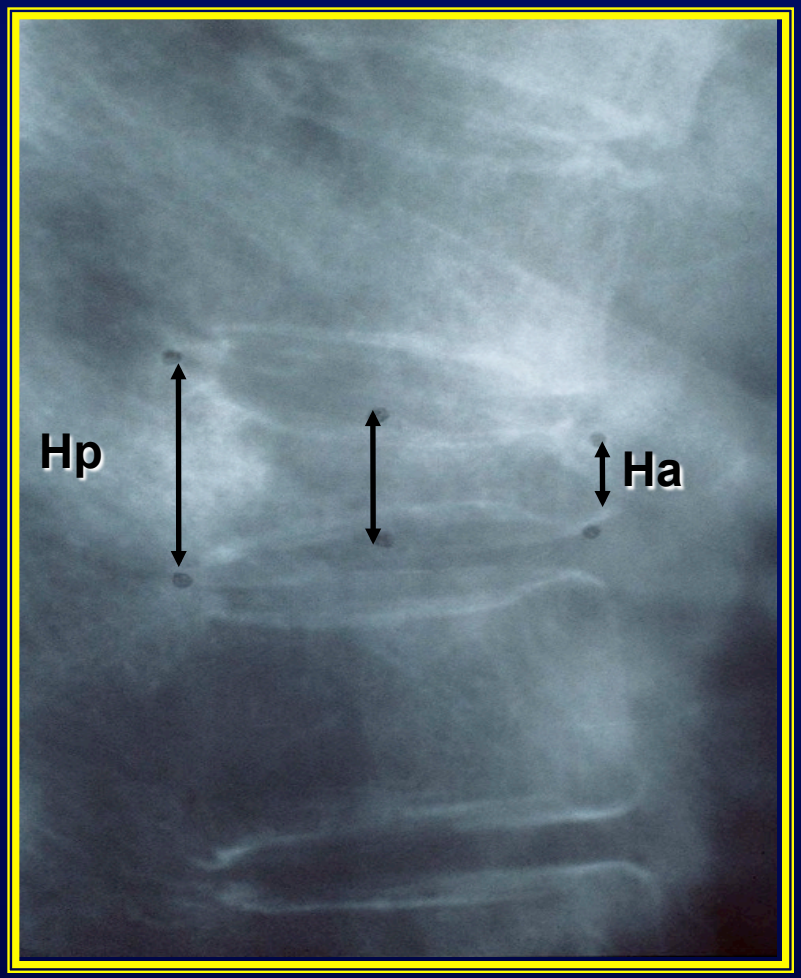
Normale

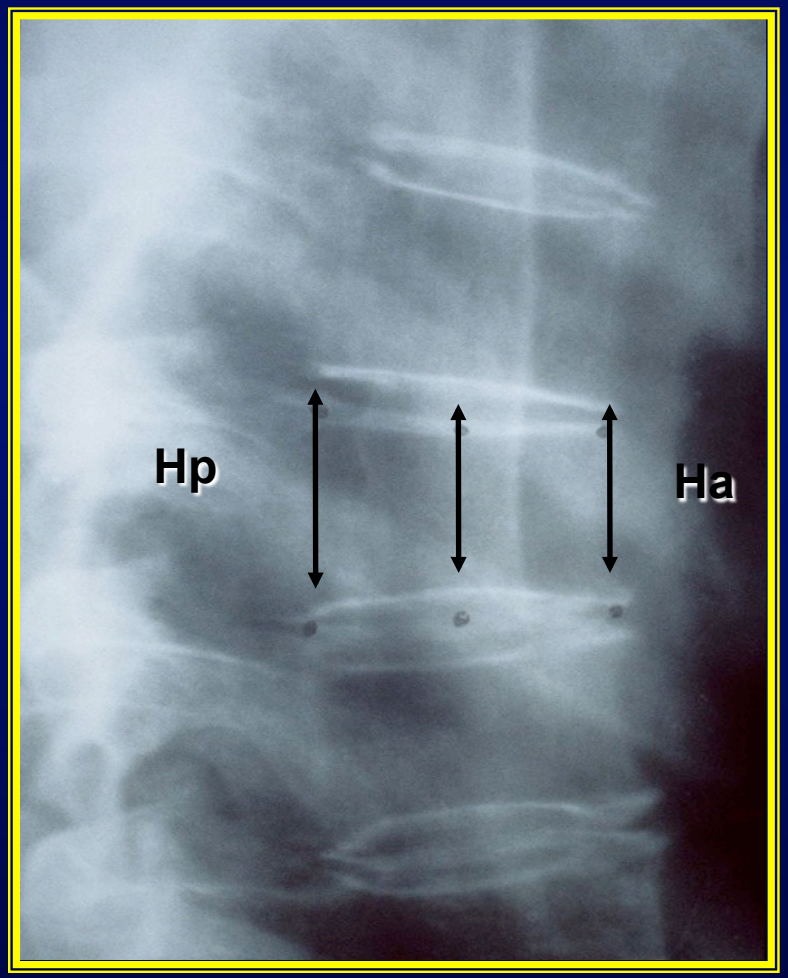


Osteoporosi

1. Consensus Development Conference, JAMA 2001;285:785-95
2. Dempster DW et al., JBMR 1986;1:15-21

All’esame Rx
non sempre le Fx vertebrali sono di facile individuazione





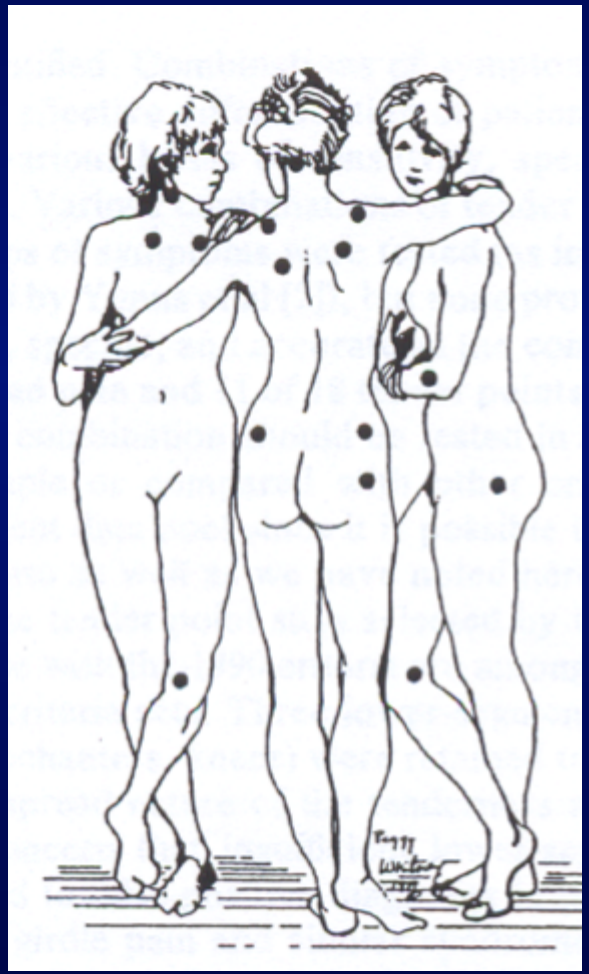
Artrite Reumatoide come Malattia Sistemica

non solo malattia articolare …

… ma precoce impegno d'organo

- **Rene**: *amiloidosi, NTA, IRC*
- **Polmone**: *IP, fibrosi*
- **Cuore**: *peri-mio-endo-carditi*
- **Midollo osseo**: *anemie, γ.patie*
- **Vasi**: *vasculiti, crioglobulinemia*
- **Osso**: *OP, necrosi avascolari*
- **Fegato**: *epatite autoimmune*
- *Occhio, Cute/Derma, ecc.*

Fibromialgia – ACR, 1990



Low Back Pain - Lombalgia

- LBP rappresenta uno dei sintomi più frequenti, secondo solo al comune raffreddore.
- La "sorgente anatomica" del LBP meccanico può non essere facilmente identificata.
- Il dolore di tipo infiammatorio è caratterizzato da rigidità al mattino, riduzione durante le ore diurne, ricomparsa nel tardo pomeriggio (dolore bimodale).

Conseguenze di un dolore non rilevato e non trattato

- Cuore e CV: *↑ rischio infarto*
- Respiratorio: *↑ rischio polmoniti*
- GI: *↓ motilità – anoressia, perdita di peso*
- Muscoloscheletrico: *↓ performance mioarticolari*
- Personali: *inabilità per AVQ/QdV, depressione*

Valutazione clinica del Dolore

CARATTERISTICHE

- Qualitative
- Quantitative
- Temporali

Valutazione del Dolore

QUALITÀ DI VITA

Propria personale esperienza, connessa alla percezione di:

- Stato funzionale
- Livello di autonomia
- Benessere psicosociale
- Stato di salute
- Sintomi della malattia
- Effetti del trattamento

Legge 38 / 15.3.2010 – *il Paziente*

Art. 2
Definizioni

Cure Palliative

L'insieme degli **interventi** […] rivolti sia **alla persona malata sia al suo nucleo familiare**, [in presenza di una] malattia di base, caratterizzata da un'inarrestabile evoluzione e da una **prognosi infausta**, non risponde più a trattamenti specifici.

Terapia del Dolore

L'insieme degli **interventi** [per] applicare […] appropriate terapie […] allo scopo di elaborare idonei **percorsi diagnostico-terapeutici per la soppressione e il controllo del dolore**.

Persona Malata

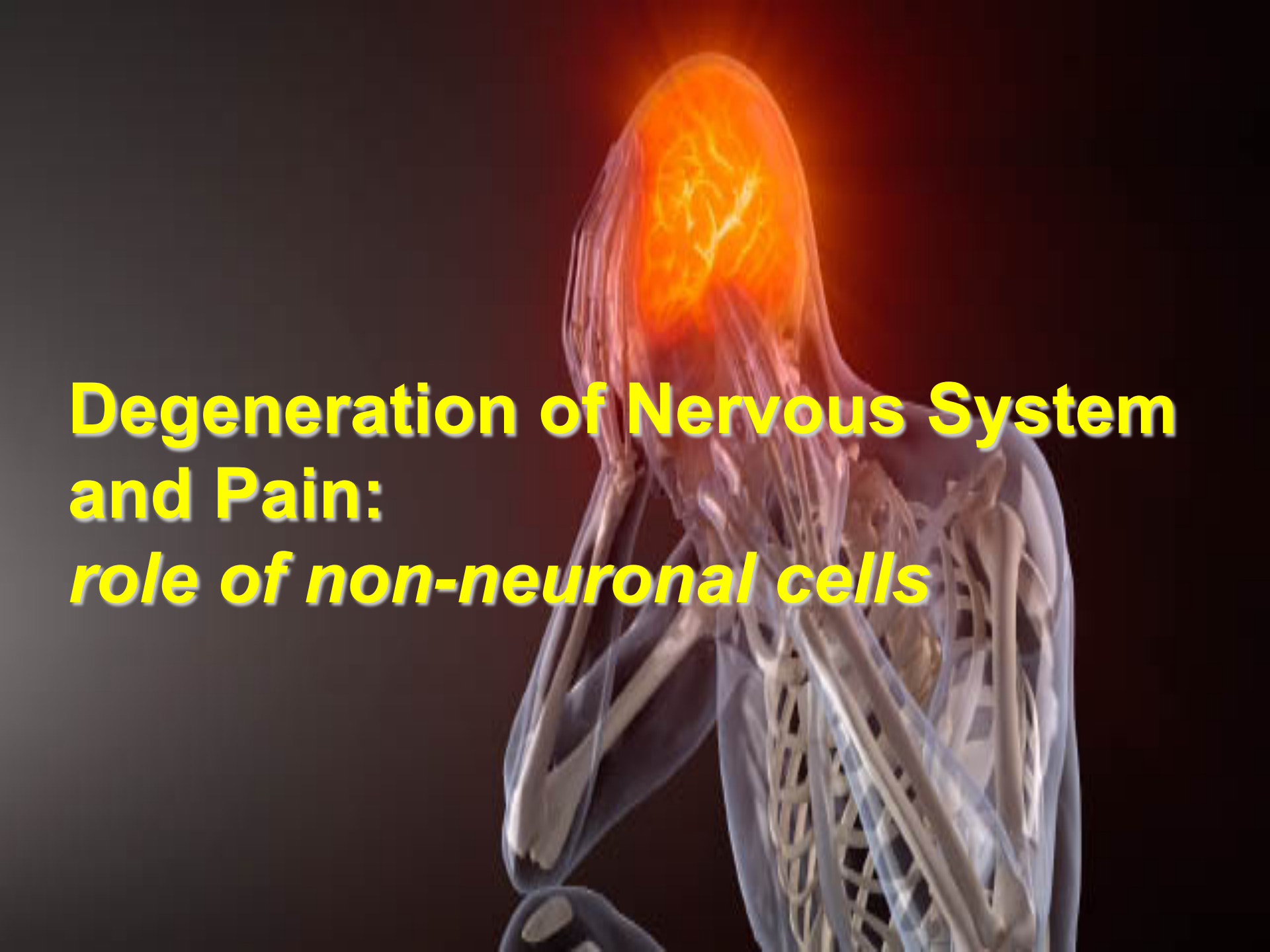
[…] Affetta da una **patologia ad andamento cronico ed evolutivo** […], nonché la persona affetta da una **patologia dolorosa cronica da moderata a severa**;

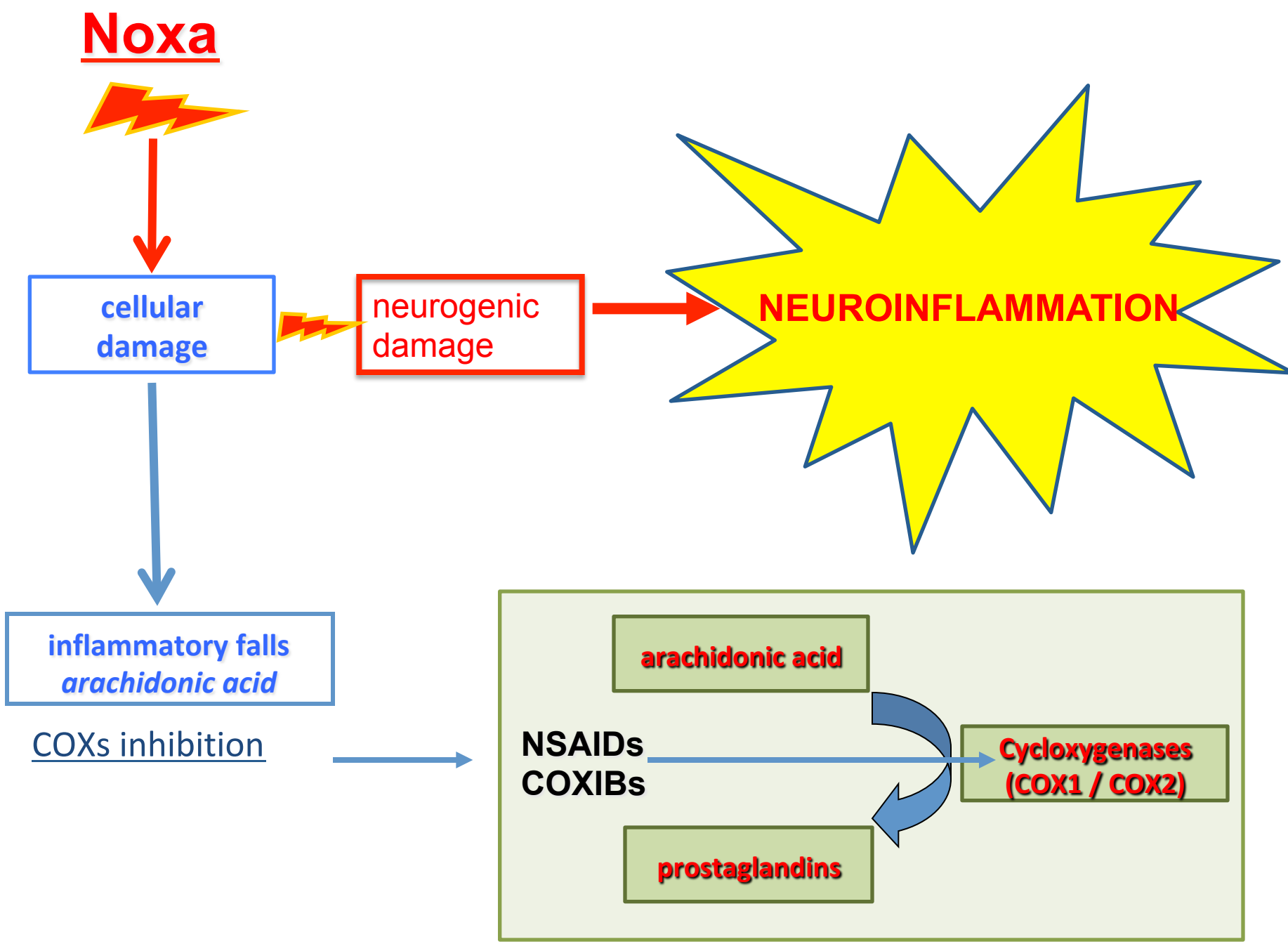
Art. 7

Il dolore come parametro vitale:
Rilevazione costante in cartella clinica e report delle decisioni terapeutiche

Ethics Code for Pain

Coaccioli S., et al. European Journal of Pain, 2012


Degeneration of Nervous System
and Pain:
role of non-neuronal cells

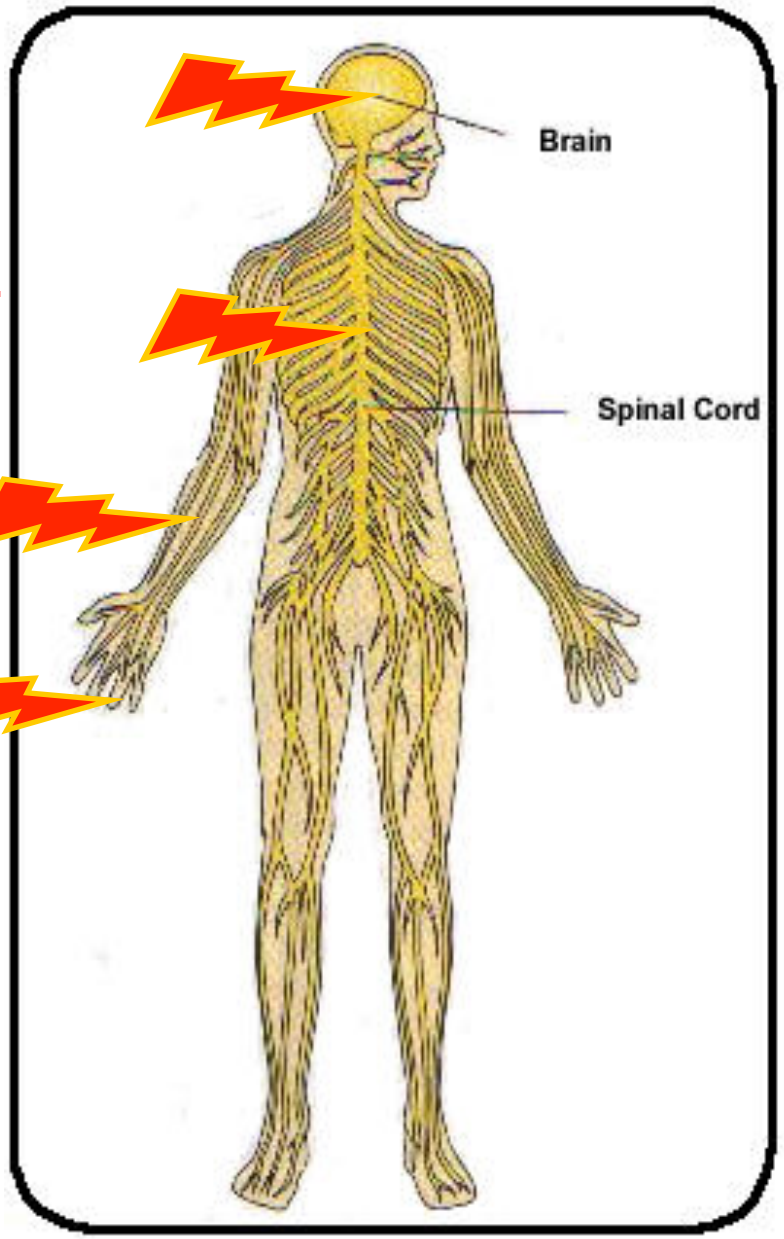

Noxa
cellular damage
neurogenic damage
NEUROINFLAMMATION
inflammatory falls
arachidonic acid
COXs inhibition
arachidonic acid
NSAIDs
COXIBs
Cycloxygenases (COX1 / COX2)
prostaglandins

SUPER-SPINAL NEUROINFLAMMATION

SPINAL NEUROINFLAMMATION

ENDONEURAL NEUROGENIC INFLAMMATION

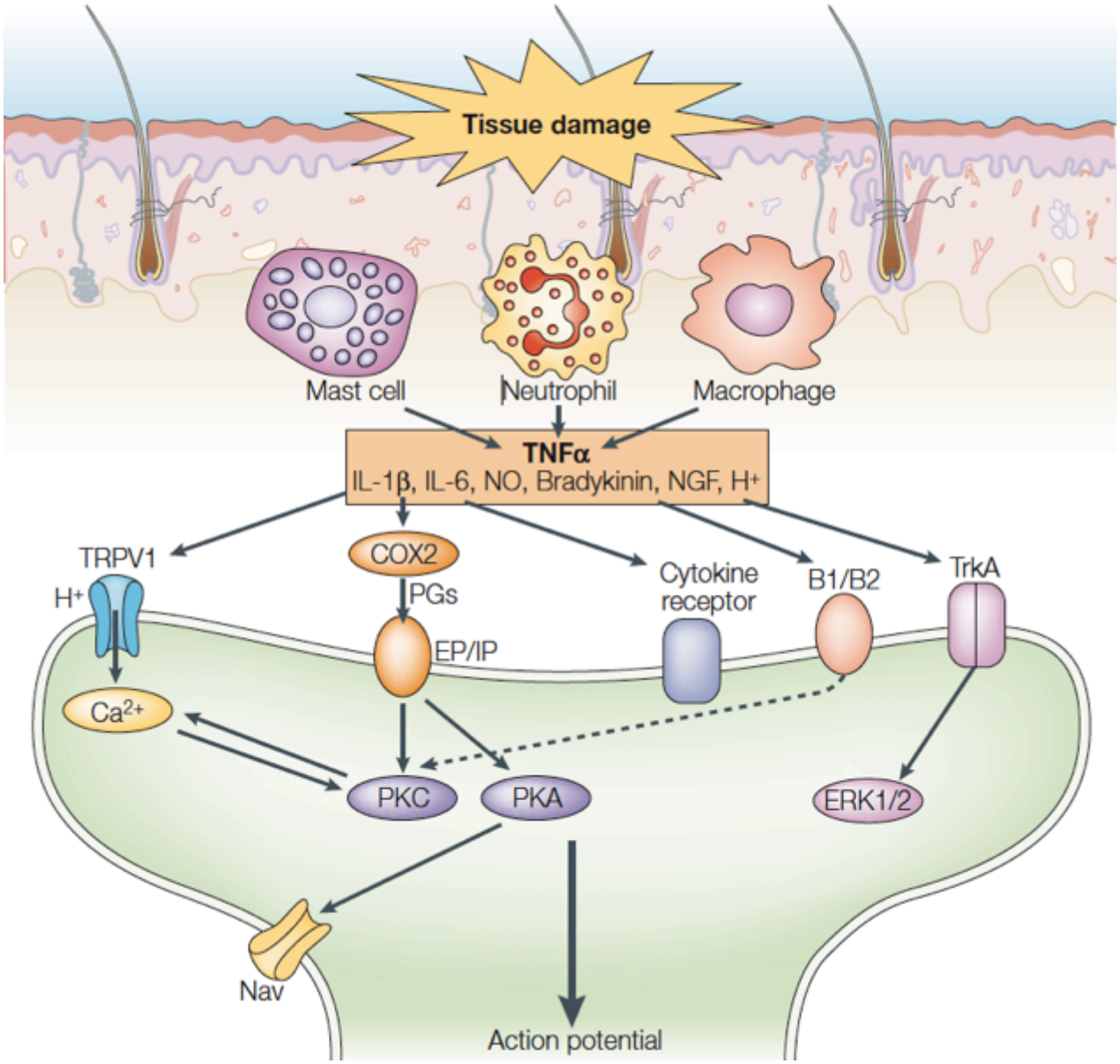
TISSUE NEUROGENIC INFLAMMATION



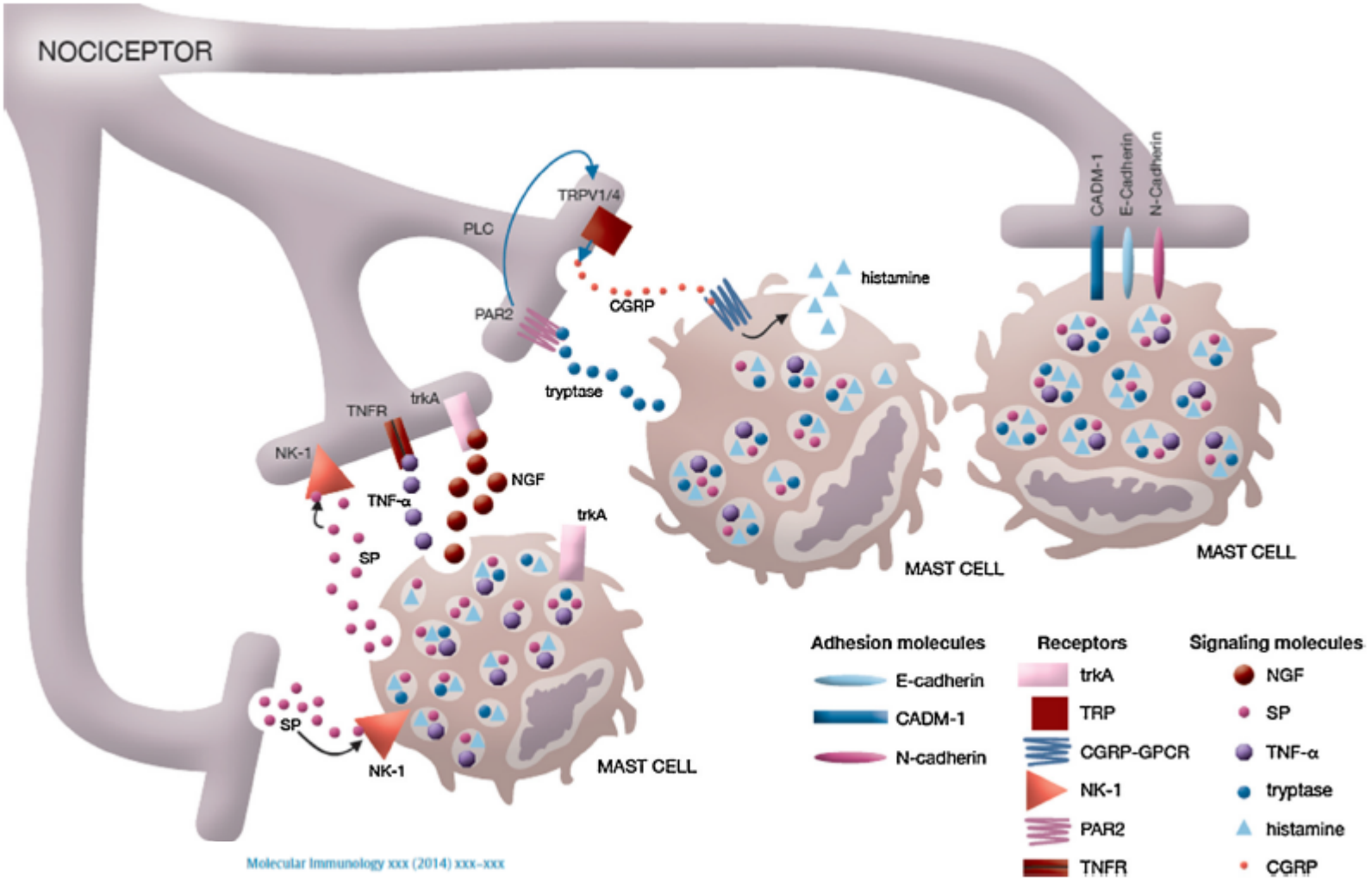
"The term ***neuroinflammation***, in its broadest sense, of course encompasses any inflammatory processes, whether acute or cronic, involving the nervous system."

Boche D.and Nicoll JA
Neuropathology and Applied Neurobiology (2013), **39**, 1-2

TISSUE NEURONAL DAMAGE



Marchand F, Perretti M, McMahon SB.
Nat Rev Neurosci. 2005 Jul;6(7):521-32. Review.



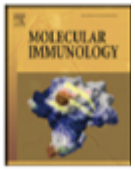
Molecular Immunology xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

Molecular Immunology

journal homepage: www.elsevier.com/locate/molimm

ELSEVIER



Article history:
Received 15 October 2013
Received in revised form 3 March 2014
Accepted 3 March 2014
Available online xxx

Keywords:
Mast cells
Pain
Cytokines
Neurons

Review

Mast cells: Versatile gatekeepers of pain☆

Devavani Chatterjea*, Tijana Martinov

Department of Biology, Macalester College, St. Paul, MN, USA

Mast cells produce a plethora of mediators, which include:

- biogenic amines (histamine, serotonin),
- cytokines [interleukin (IL-1 to IL-6, leukemia inhibitory factor, tumor necrosis factor (TNF) , interferon-, transforming growth factor-, granulocyte-microphage colony-stimulating factor],
- enzymes (acid hydrolyzes, chymase, phospholipases, rat mast-cell protease I and II, trypase),
- lipid metabolites (prostaglandins, leukotrienes, platelet-activating factor),
- ATP,
- neuropeptides(vasoactive intestinal peptide),
- growth factors, *e.g.*,nerve growth factor (NGF), nitric oxide, and heparin.

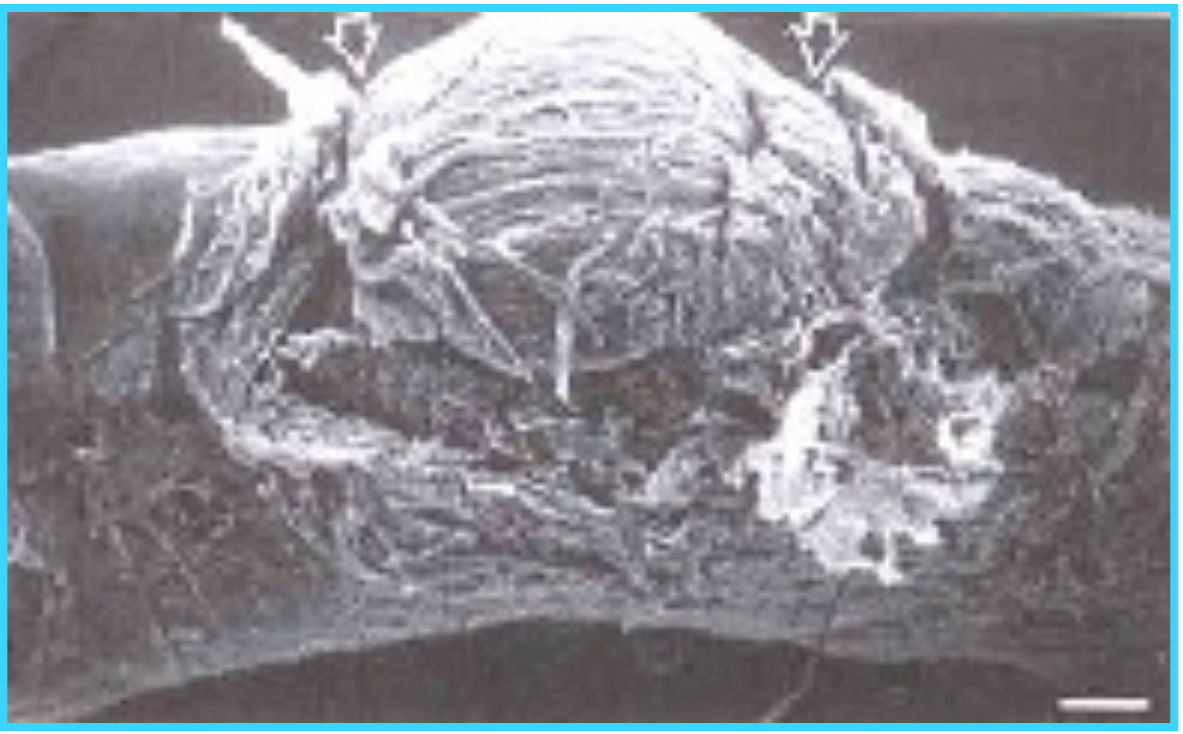
The FASEB Journal • Review

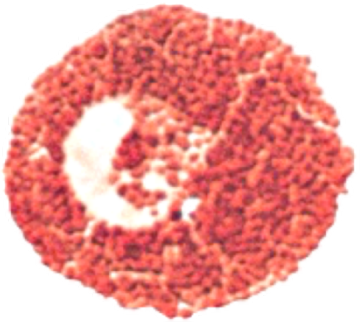
Microglia and mast cells: two tracks on the road to neuroinflammation

Stephen D. Skaper,[1] Pietro Giusti, and Laura Facci

The FASEB Journal article fj.11-197194. Published online April 19, 2012.

Endoneural Oedema





Release
of vasoactive amines

extravascular fluidis

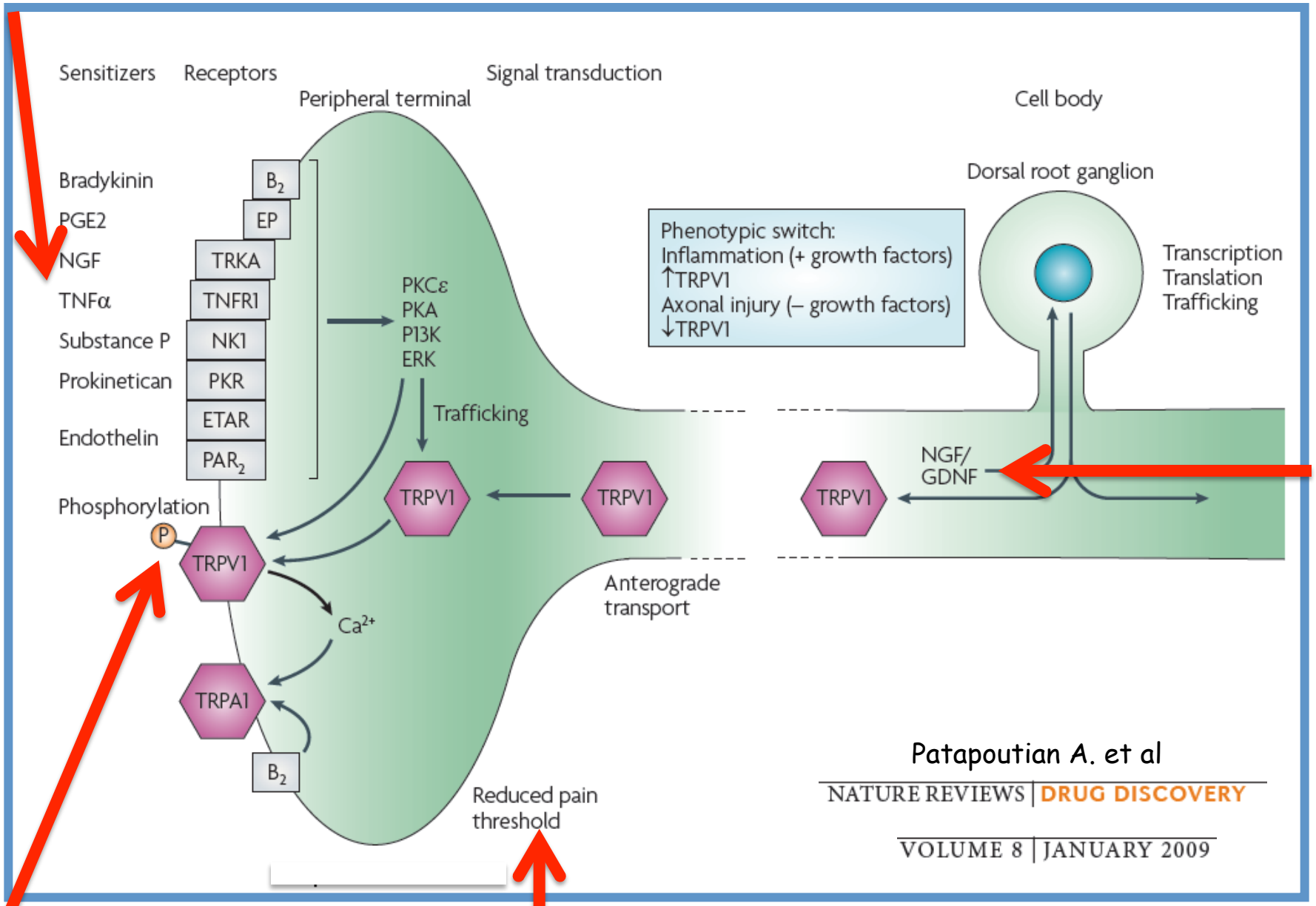
endoneural oedema

hydraulic endoneural pressure
> vascular pressure

collapse of *vasa nervorum*

endoneural ischemia

functional alteration of nervous fibers



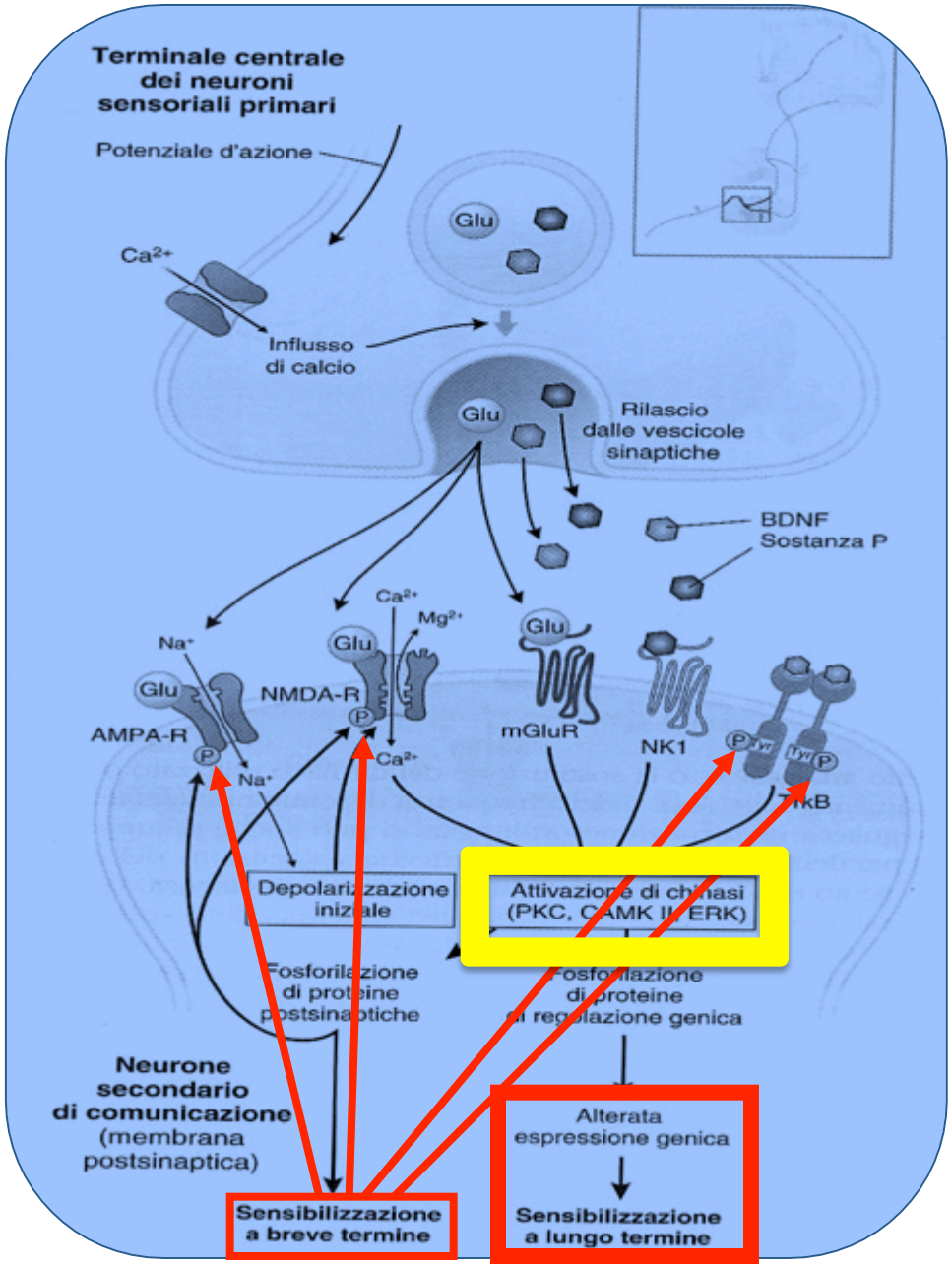
Patapoutian A. et al

NATURE REVIEWS | DRUG DISCOVERY

VOLUME 8 | JANUARY 2009

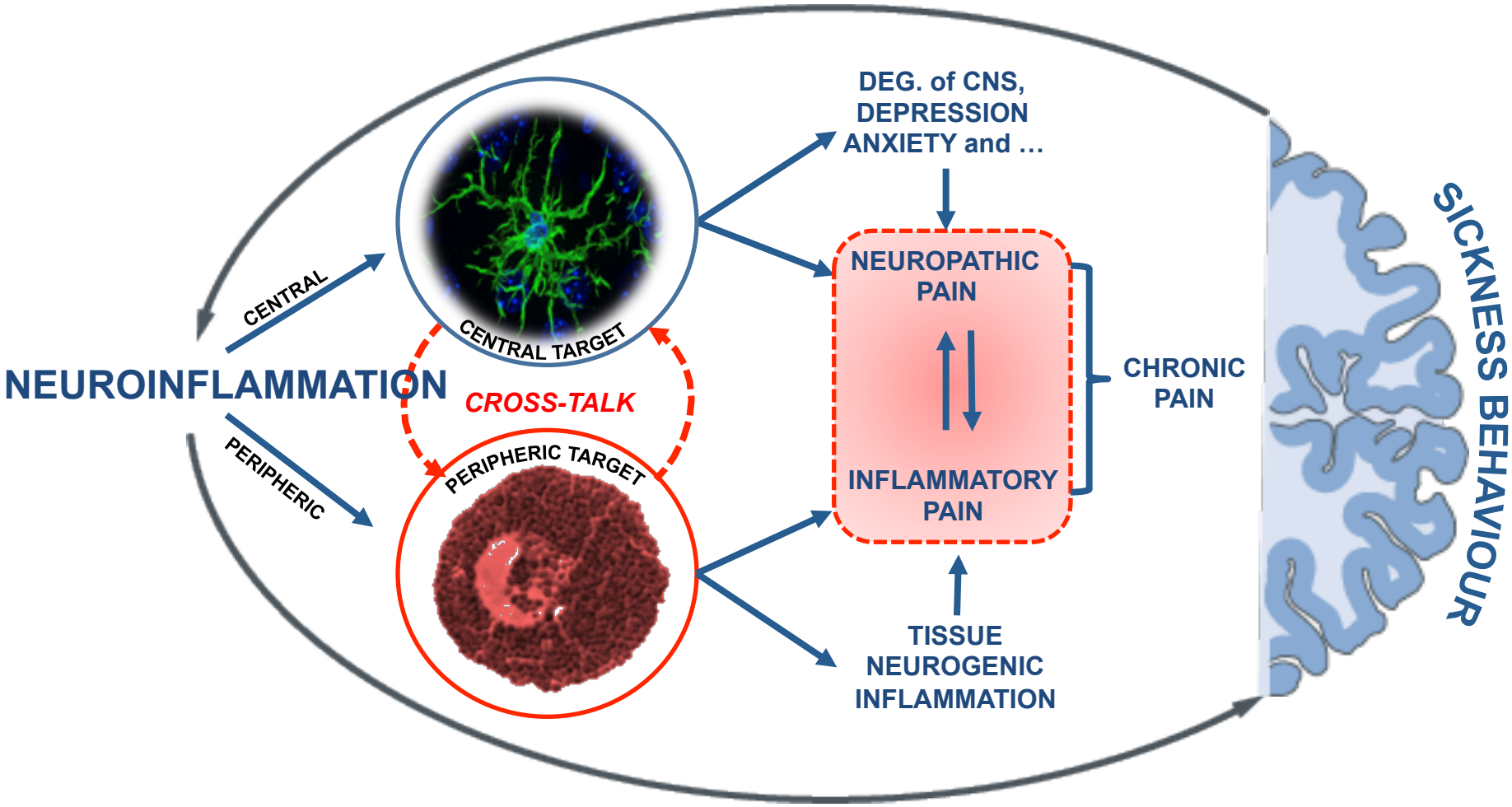
Peripheral sensitization mechanism

Central sensitization mechanisms

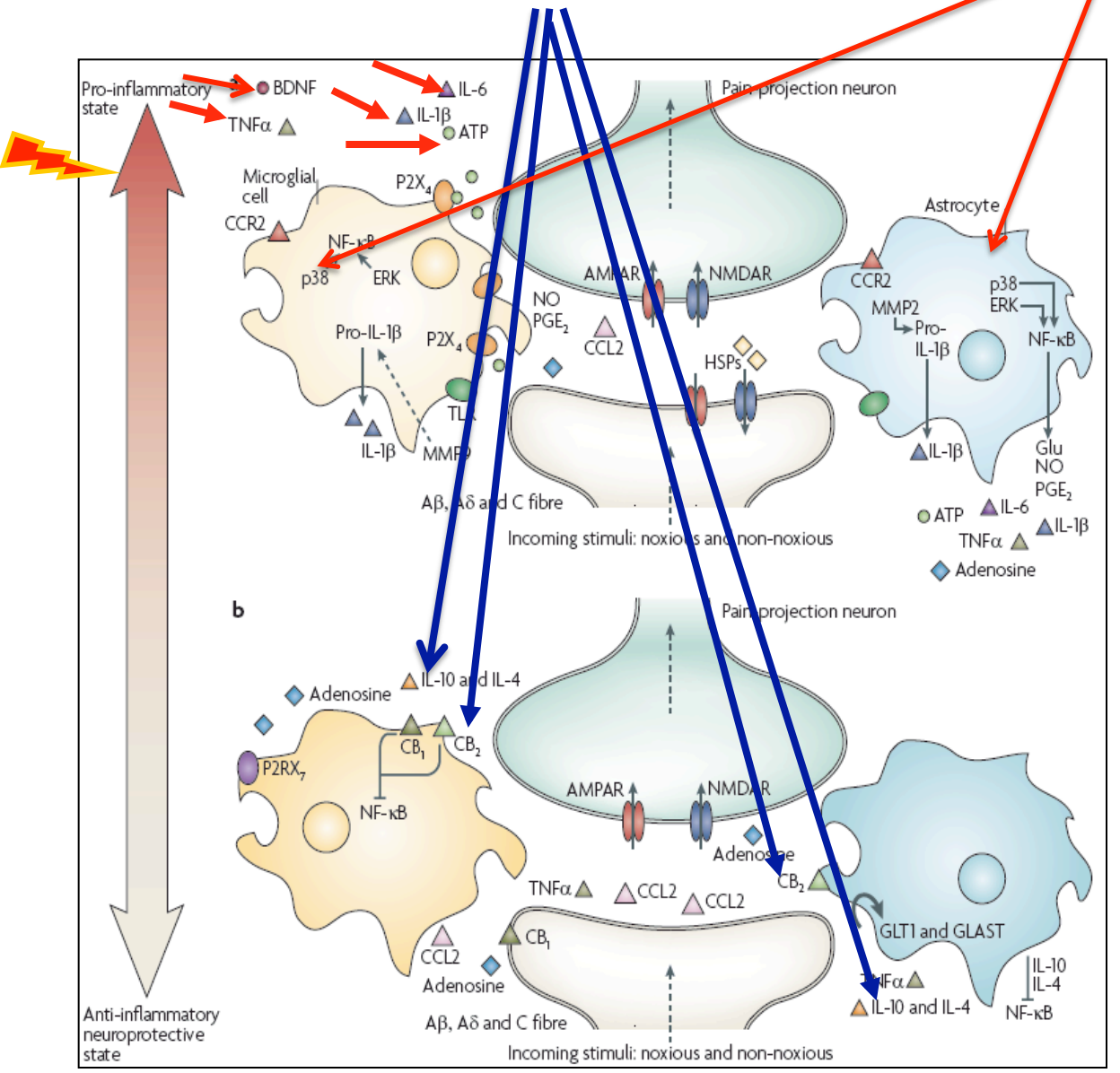


Not only Pain, but:

Disease behaviour



Glia activation: from pro-inflammatory status to anti-inflammatory state (neuroprotective)



- **Marchand F. et al -*Role of the immune system in chronic pain*-**
  Nature Neuroscience (2005)

Inoue K and Tsuda M. *Microglia and neuropathic pain*
Glia (2009)

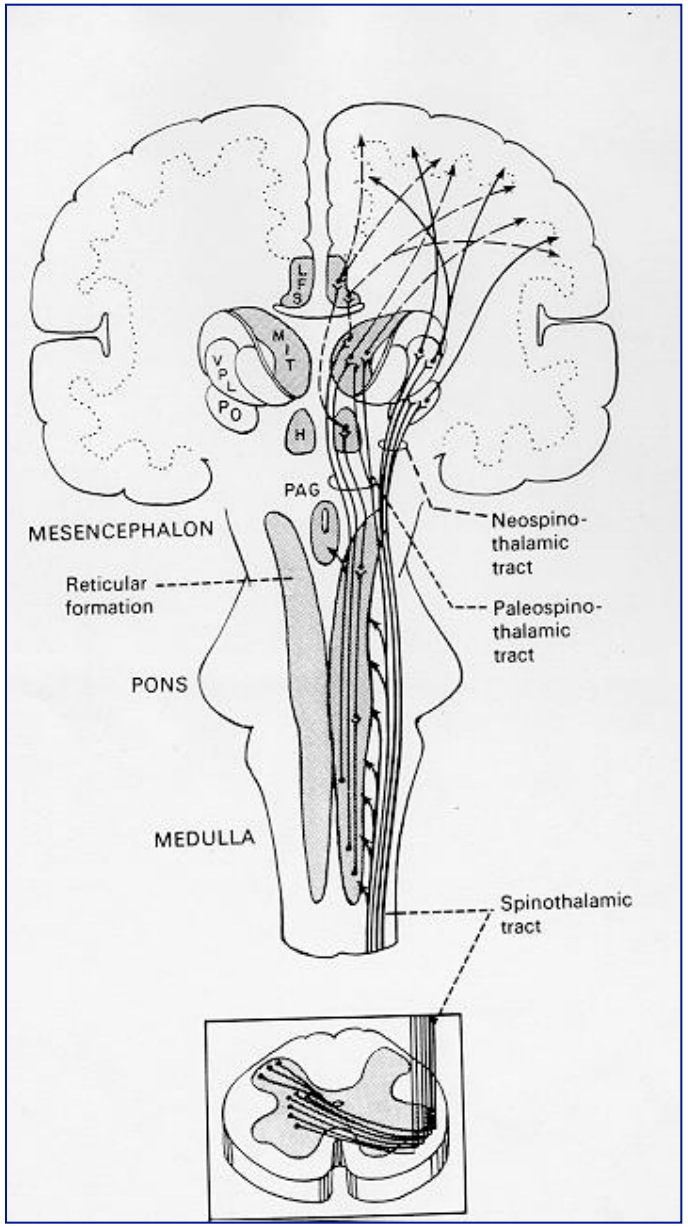
Ren K and Dubner R *Interactions between the immune and nervous systems in pain*
Nature Medicine (2010)

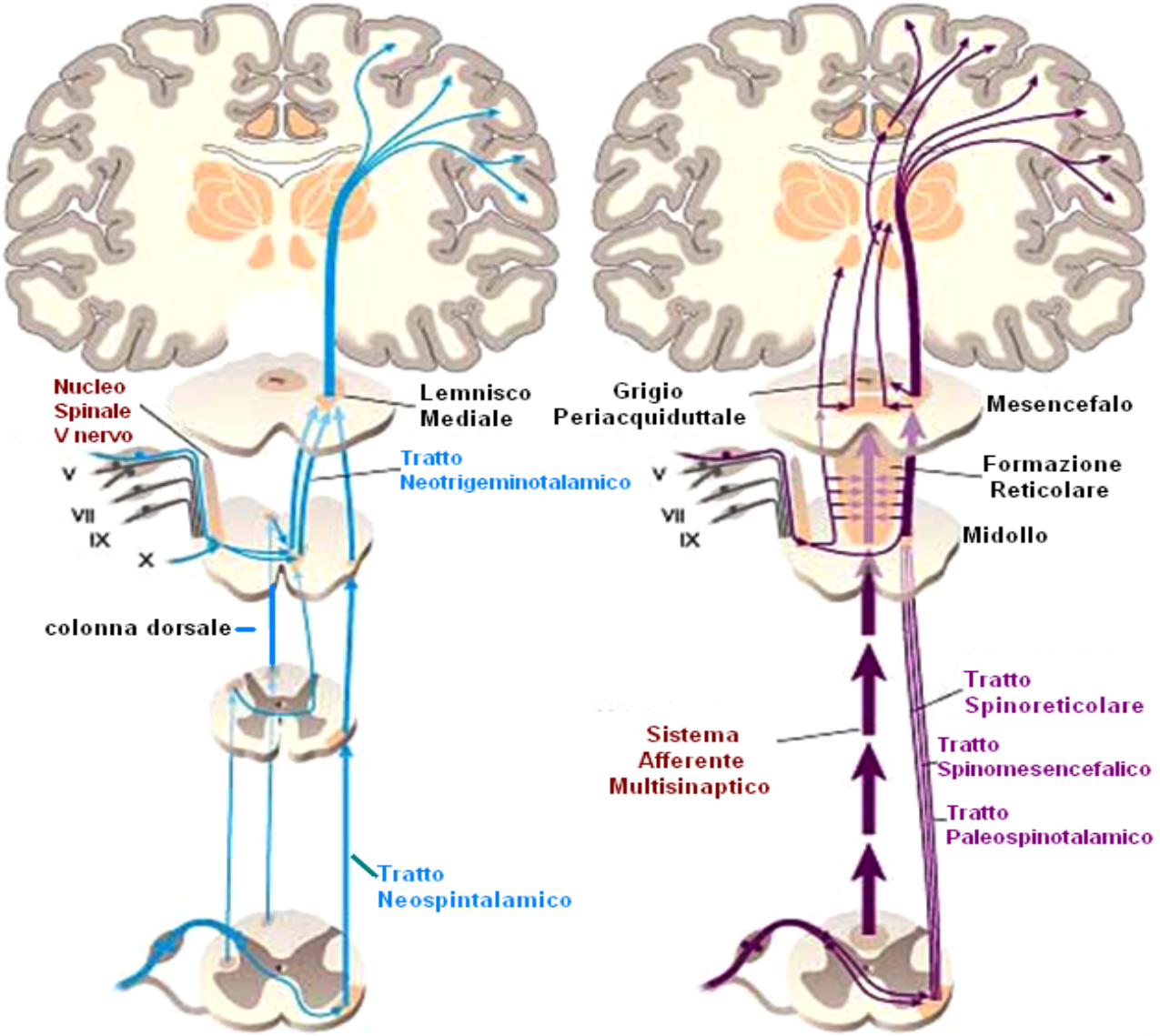
Gao YJ. and Ji RR. *Chemokines, neuronal-glial interactions, and central processing of neuropathic pain*
Pharmacol Ther. (2010)

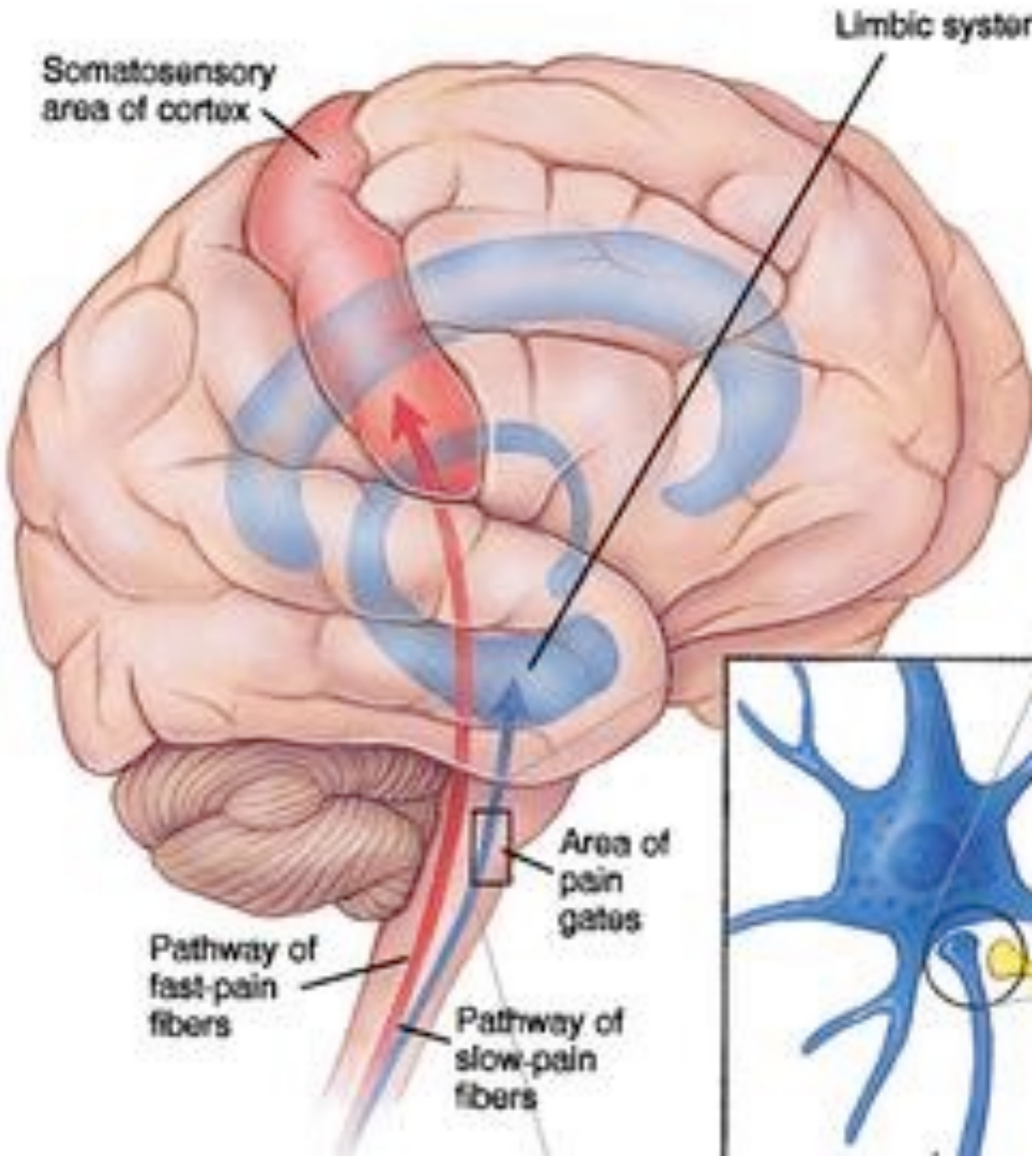
Milligan ED e Watkins LR

NATURE REVIEWS | NEUROSCIENCE
VOLUME 10 | JANUARY 2009 | 23

Fascio spino-talamico

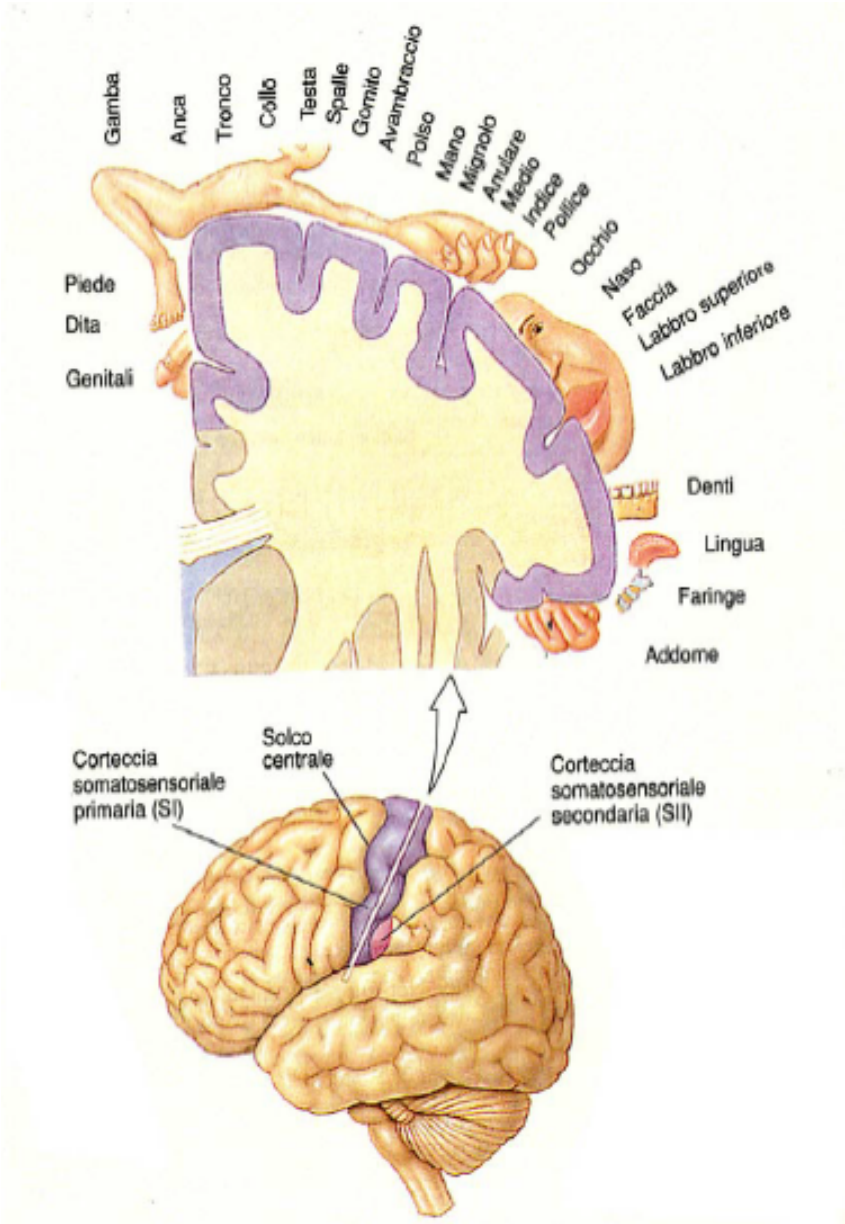


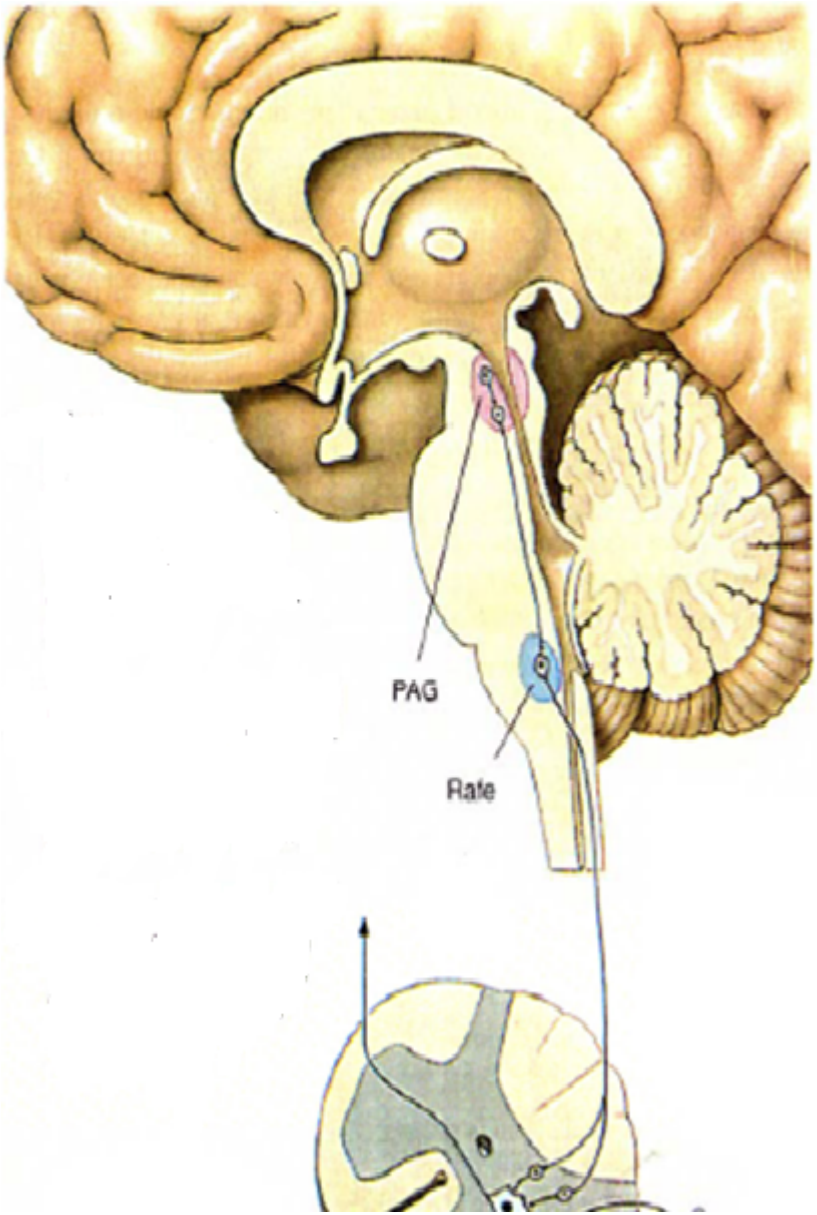

Nucleo
Spinale
V nervo
V
VII
IX
X
Lemnisco
Mediale
Tratto
Neotrigeminotalamico
colonna dorsale
Tratto
Neospintalamico
Grigio
Periacquiduttale
Mesencefalo
V
VII
IX
Formazione
Reticolare
Midollo
Tratto
Spinoreticolare
Sistema
Afferente
Multisinaptico
Tratto
Spinomesencefalico
Tratto
Paleospinotalamico


Limbic syster
Somatosensory area of cortex
Area of pain gates
Pathway of fast-pain fibers
Pathway of slow-pain fibers

Corteccia

- Somatosensoriale primaria SI
- Somatosensoriale secondaria SII
- Corteccia insulare
- Corteccia orbitale ventrolaterale





Reynolds, 1969

DOLORE: “UN EQUILIBRIO INSTABILE”

Processi eccitatori

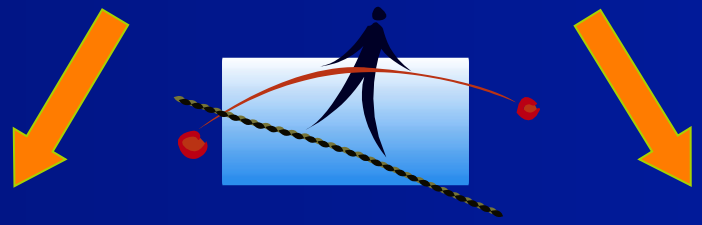
Modulazione inibitoria

Il Dolore “difficile”: *scenario*

1. **Fisiopatologia**
   - *meccanismi «nuovi» per la genesi e la cronicizzazione del dolore*
2. **Clinica**
   - *malattie frequenti e malattie rare*
   - *conseguenze del dolore cronico*
3. **Terapia**
   - *polimodale di associazione*

TERAPIA MULTIMODALE

FARMACI AD AZIONE SINERGICA



↓ Dosaggio

↓ Reazioni avverse

TIPOLOGIA DI DOLORE e TRATTAMENTO

Una terapia antalgica mono-farmacologica non è spesso in grado di trattare efficacemente il dolore ed espone più facilmente il paziente agli effetti avversi ad esso correlati

ANALGESIA MULTIMODALE

Kehlet H and Dahl JB. Anesth Analg 1993
Jin F and Chung F. J Clin Anesth 2001

ANALGESIA MULTIMODALE

AZIONE SUI DIVERSI MECCANISMI DI DOLORE

Trasduzione. FANS, anestetici locali.

Trasmissione. Analgesia tronculare, plessica, caudale, spinale.

Modulazione. Oppioidi, analgesia caudale e spinale.

Percezione. Oppioidi, antidepressivi, paracetamolo.

Neuroinfiammazione periferica e centrale. PEA

Pain Reduction: *Targets and Reasons*

Targets	***Reasons***
• *to reduce pain*	*presence of pain*
• *to decrease inflammation*	*presence of inflammation*
• *to maintain activity*	*to prevent articular degeneration*
• *to permit physiotherapy*	*to improve articular performance*

Pain Relief Ladder (WHO)

pain intensity

strong OPIOIDS

± NSAIDs ± adjuvants

weak OPIOIDS

± NSAIDs ± adjuvants

PCM/NSAIDs

± adjuvants

time (?)

The " *MAGIC BULLETS* " against Pain

FANS

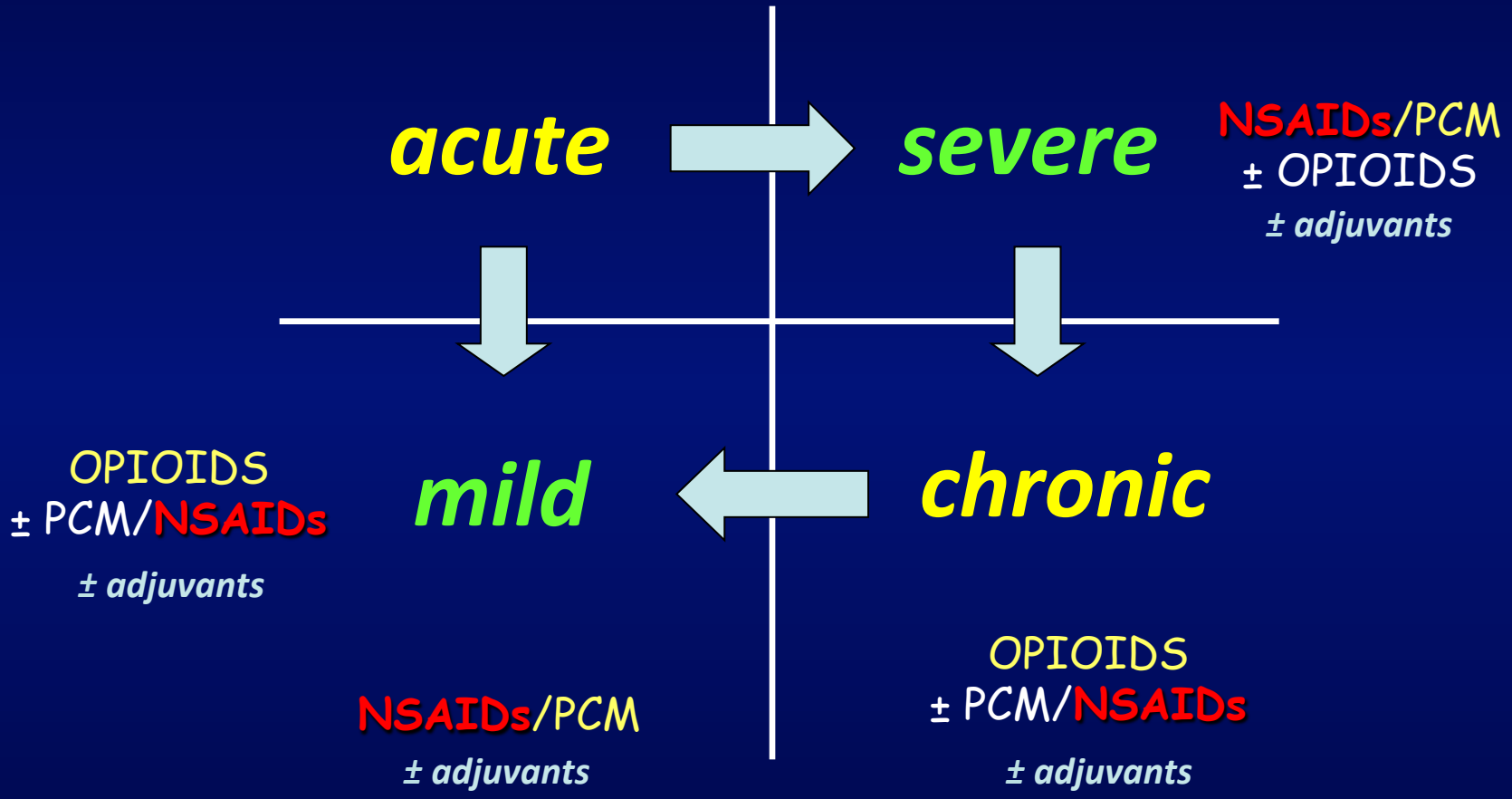
paracetamolo

oppiacei deboli

oppiacei forti

adiuvanti

Towards a *New Pain Relief Flow Sheet* for Chronic Pain



Paracetamolo e FANS nel Trattamento del Dolore

Arthritis Care & Research
Vol. 64, No. 4, April 2012, pp 465–474
DOI 10.1002/acr.21596

SPECIAL ARTICLE

American College of Rheumatology 2012 Recommendations for the Use of Nonpharmacologic and Pharmacologic Therapies in Osteoarthritis of the Hand, Hip, and Knee

MARC C. HOCHBERG,[1] ROY D. ALTMAN,[2] KARINE TOUPIN APRIL,[3] MARIA BENKHALTI,[3] GORDON GUYATT,[4] JESSIE McGOWAN,[3] TANVEER TOWHEED,[5] VIVIAN WELCH,[3] GEORGE WELLS,[3] AND PETER TUGWELL[3]

Results

Results. Both "strong" and "conditional" recommendations were made for OA management. Modalities conditionally recommended for the management of hand OA include instruction in joint protection techniques, provision of assistive devices, use of thermal modalities and trapeziometacarpal joint splints, and use of oral and topical nonsteroidal antiinflammatory drugs (NSAIDs), tramadol, and topical capsaicin. Nonpharmacologic modalities strongly recommended for the management of knee OA were aerobic, aquatic, and/or resistance exercises as well as weight loss for overweight patients. Nonpharmacologic modalities conditionally recommended for knee OA included medial wedge insoles for valgus knee OA, subtalar strapped lateral insoles for varus knee OA, medially directed patellar taping, manual therapy, walking aids, thermal agents, tai chi, self-management programs, and psychosocial interventions. Pharmacologic modalities conditionally recommended for the initial management of patients with knee OA included acetaminophen, oral and topical NSAIDs, tramadol, and intraarticular corticosteroid injections; intraarticular hyaluronate injections, duloxetine, and opioids were conditionally recommended in patients who had an inadequate response to initial therapy. Opioid analgesics were strongly recommended in patients who were either not willing to undergo or had contraindications for total joint arthroplasty after having failed medical therapy. Recommendations for hip OA were similar to those for the management of knee OA.

Current use of prescription medicines

(Pain in Europe Survery, EJP 2005)

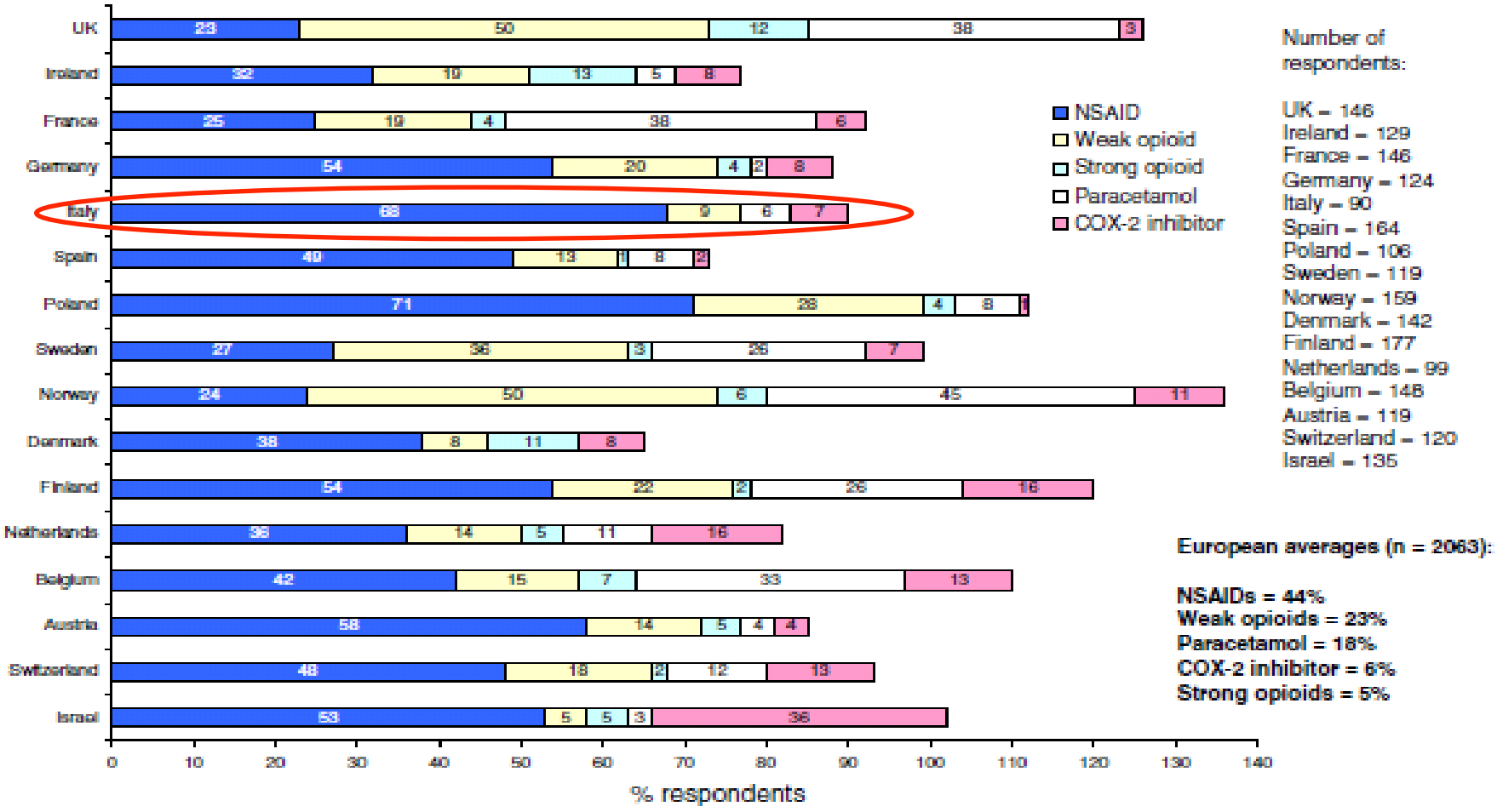
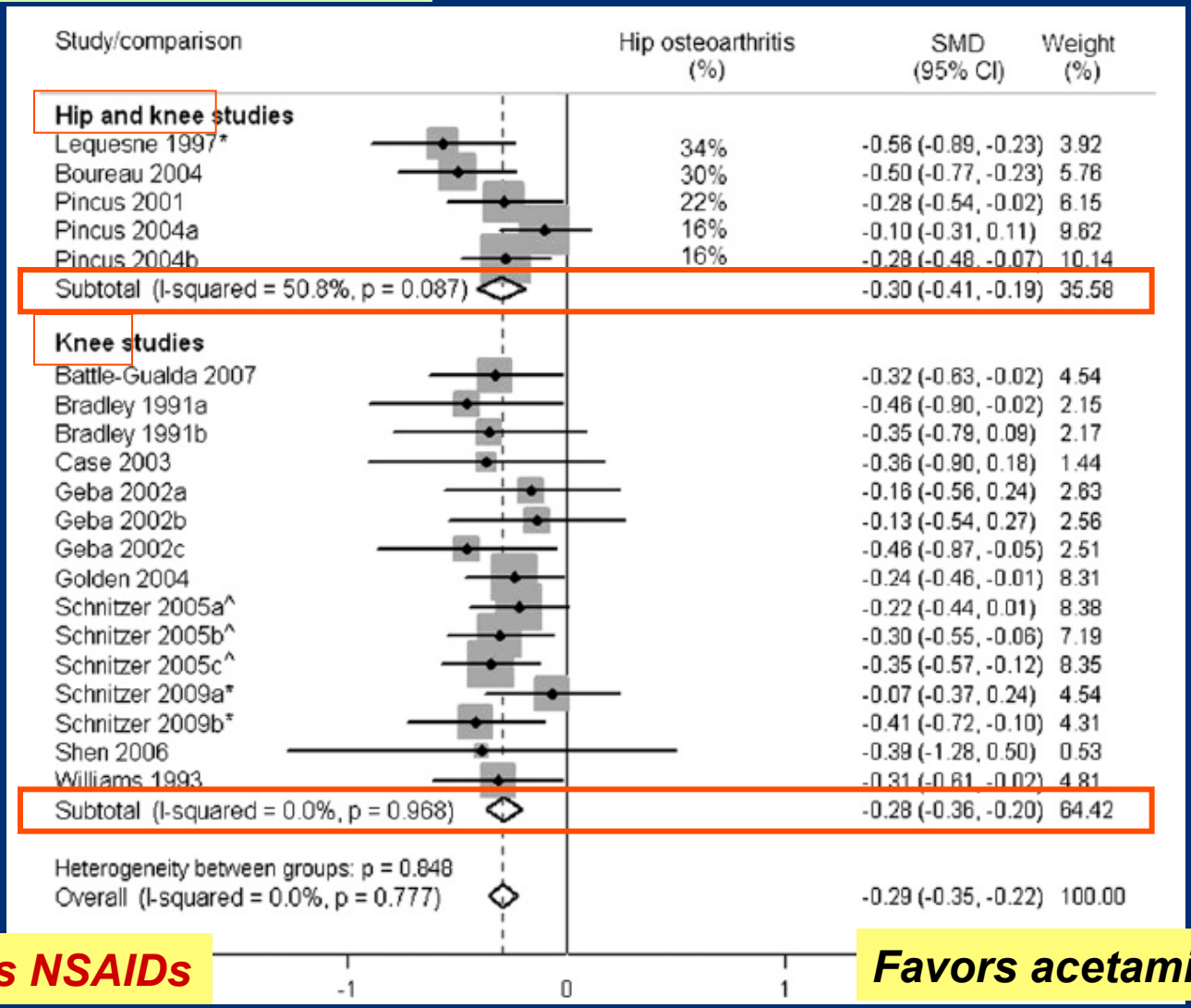


Fig. 22. Current use of prescription medicines in the 16 countries by respondents currently taking such medications. Answers to the structured interview question: "Which prescription pain medicines are you currently taking for the specific pain we have been discussing?".

NSAIDs vs acetaminophen in knee and hip osteoarthritis: a systematic review regarding heterogeneity influencing the outcomes

Efficacy on Pain

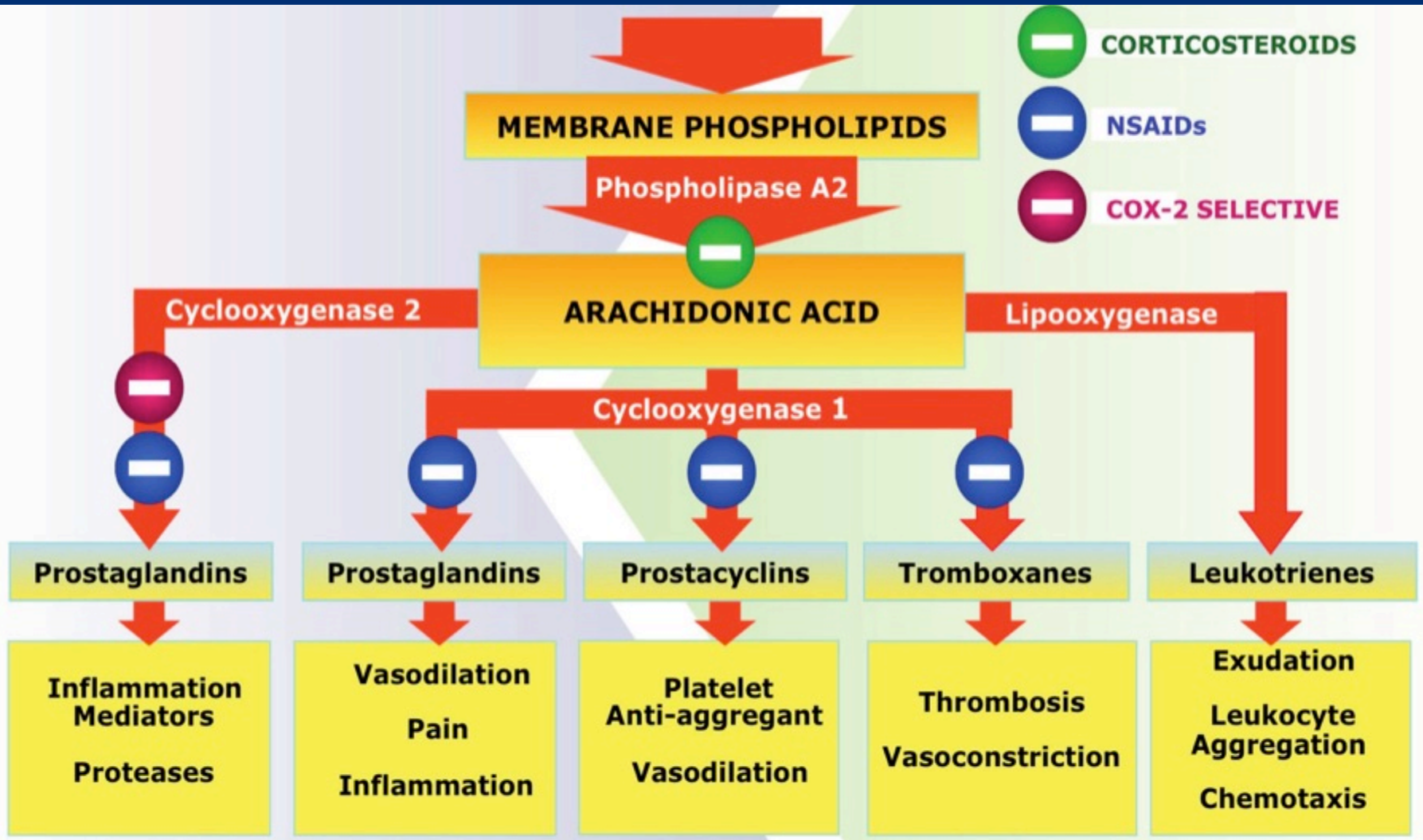
S.P.J. Verkleij et al. / Osteoarthritis and Cartilage 19 (2011) 921–929



Favors NSAIDs

Favors acetaminophen

ARACHIDONIC ACID CASCADE



Analgesic Therapy and NSAIDs

dose analgesica **<** ***dose anti-infiammatoria***

aumento del dosaggio → ***aumento rischio AE***

aumento del dosaggio → ***NON aumenta l'effetto analgesico***

- ***dolore acuto***
- ***stimolo periferico (acuto/cronico)***

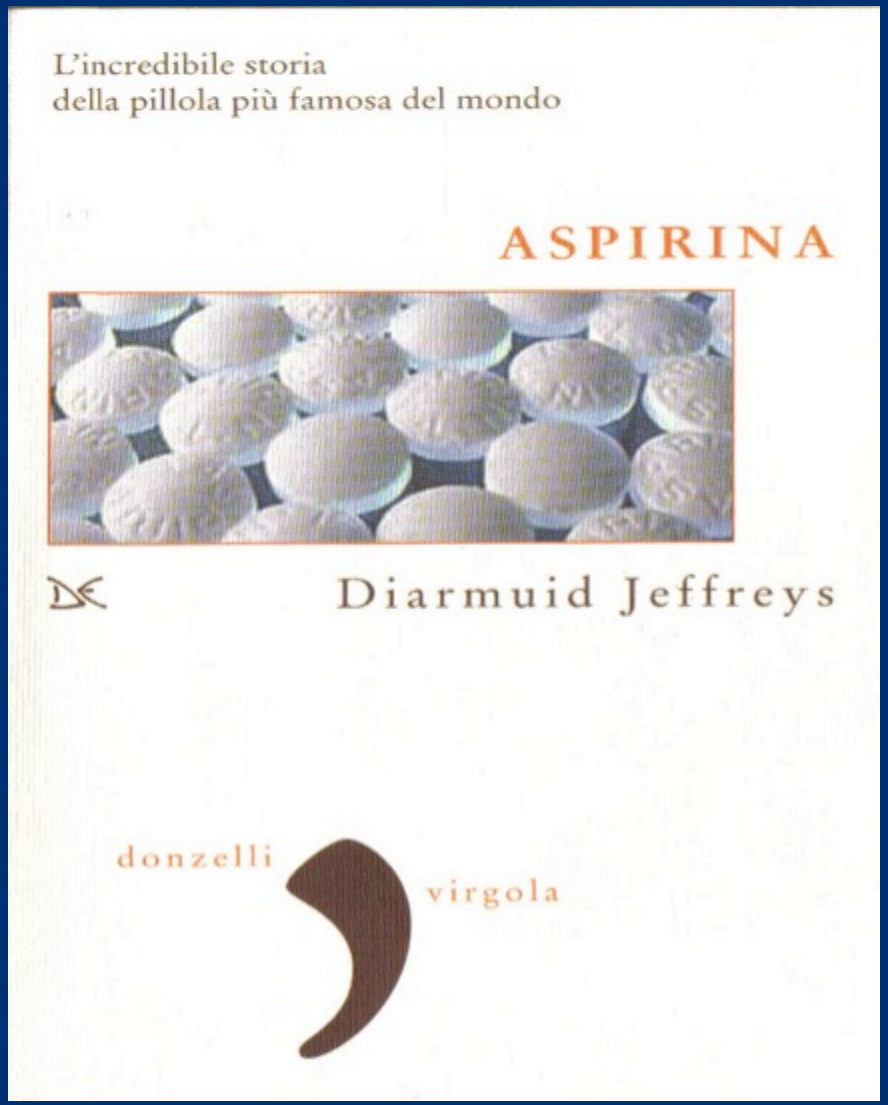
→ ***EFFICACE***

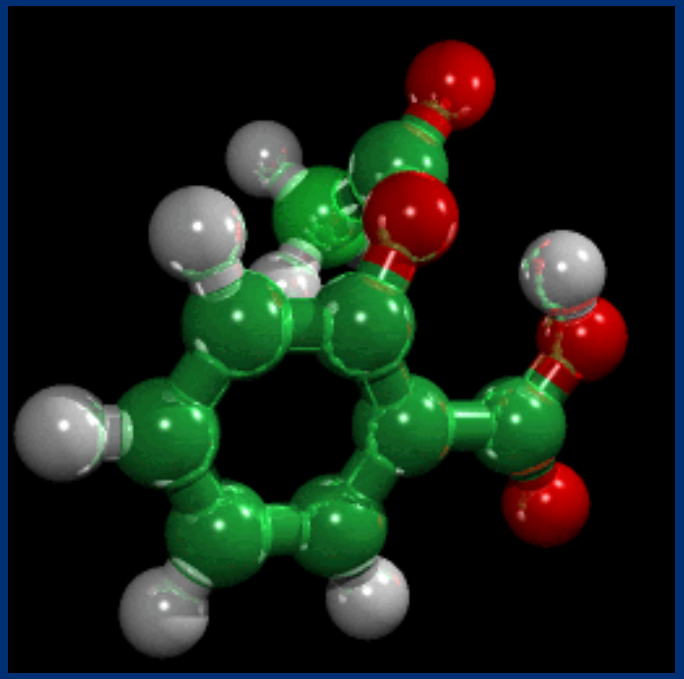
- ***dolore cronico***
- ***da sensibilizzazione centrale***

→ ***NON EFFICACE***

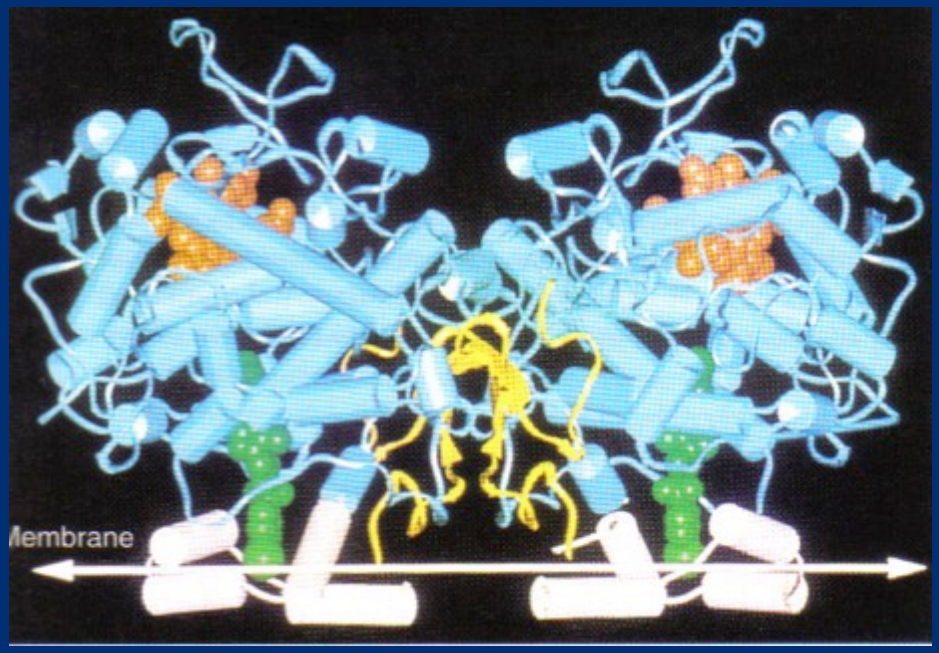
… dal *SALIX ALBA VULGARIS* …

… all'ASPIRINA …





… ai COX-2 inibitori …



Lesioni alla mucosa GI da FANS

Tratto GI superiore

- Esofagite
- Emorragie petecchiali sub-epiteliali
- Erosioni
- Ulcere
  - -Stomaco e duodeno
- Sanguinamenti
  - -Lesioni acute della mucosa
  - -Ulcera
- Perforazione
- Ostruzione

Piccolo intestino

- Aumento della permeabilità intestinale
- Infiammazione
- Anemia
- Ulcera
- Stenosi mucosali a diaframma
- Sanguinamento
- Perforazione
- Enteropatia

Colon

- Colite
- Ulcera
- Stenosi
- Diverticolite
- Sanguinamento
- Perforazione
- Colite collagenosa
- Recidive di IBD

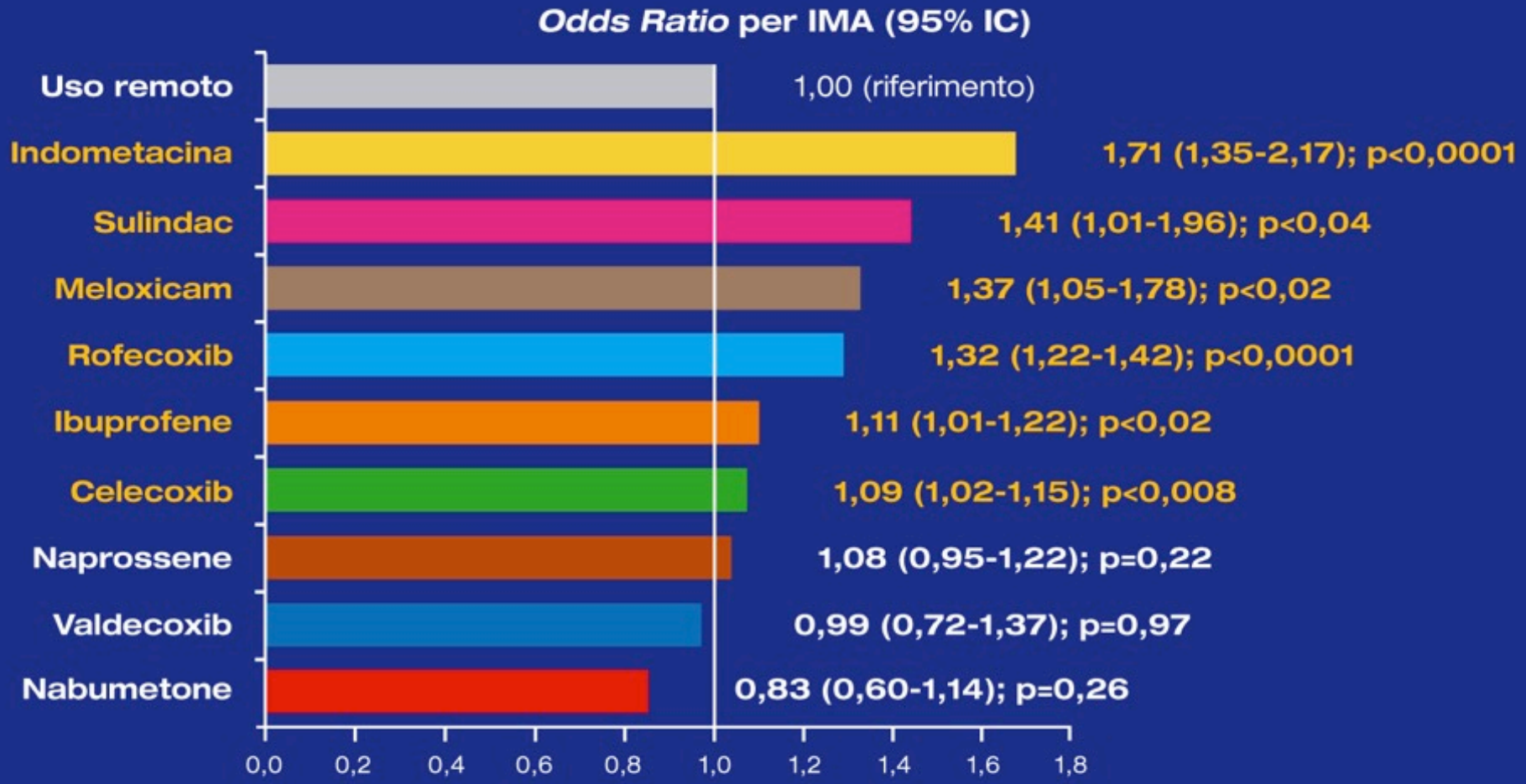
IBD=sindrome del colon irritabile.

Lanas A et al. *Ch J Dig Dis.* 2006;7:127-133.

Studio caso-controllo *nested*

Medi-Cal: FANS tradizionali e rischio di IMA

Popolazione Medi-Cal (>18 anni) con diagnosi di artropatia (1999-2004)*



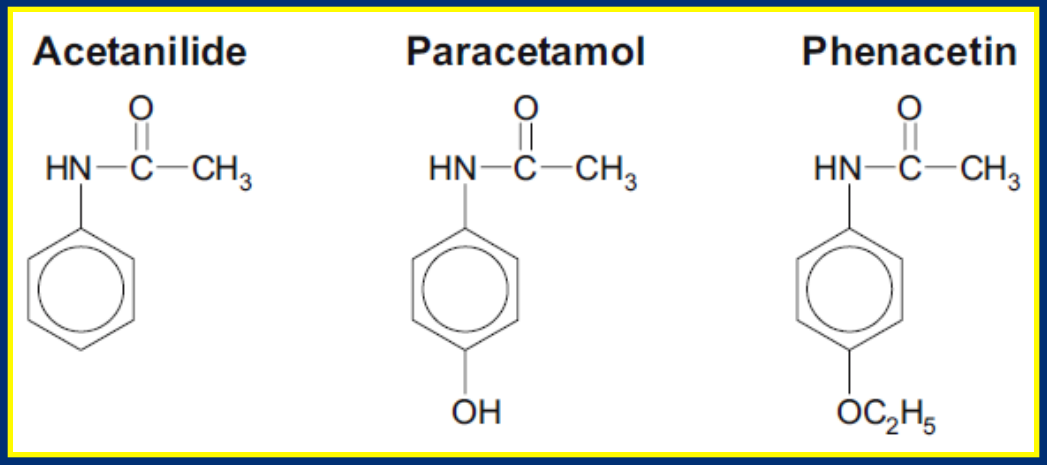
*2.356.885 persone/anno di follow-up; 15.343 casi di IMA.

Singh G et al. *Ann Rheum Dis*. 2005;64(suppl III):85.

Paracetamolo

Sintetizzato nel 1878 da Morse

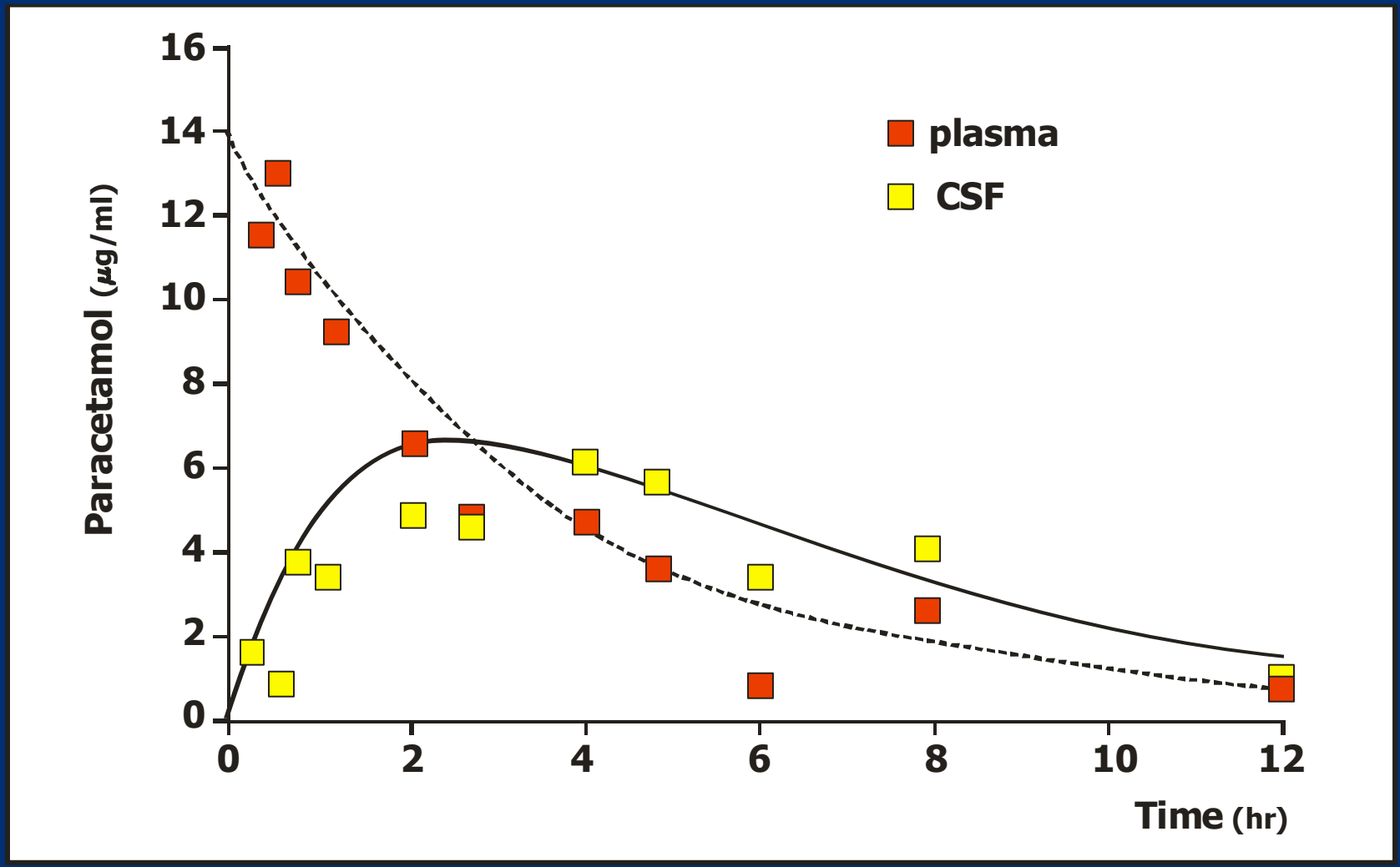
uso clinico nel 1887 da Von Mering fino al 1950 sostituito della Fenacetina



Riscoperta nel 1950 da Brodie e Axelrod, in sostituzione della Fenacetina (nefrotossica)

PLASMA AND CSF [PARACETAMOL] AFTER iv BOLUS

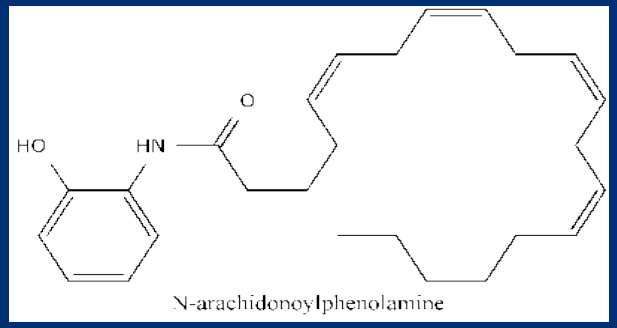
(Bannwarth et al. Br J Clin Pharmacol 1992;34:79-81)

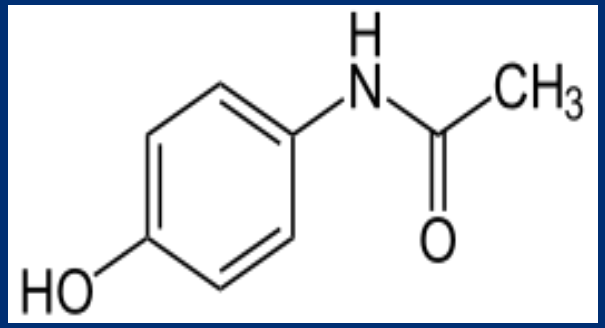


“NUOVI” MECCANISMI D’AZIONE

- **Struttura simile tra paracetamolo e Aminoacido N-arachidonilfenolamina (AM404)**

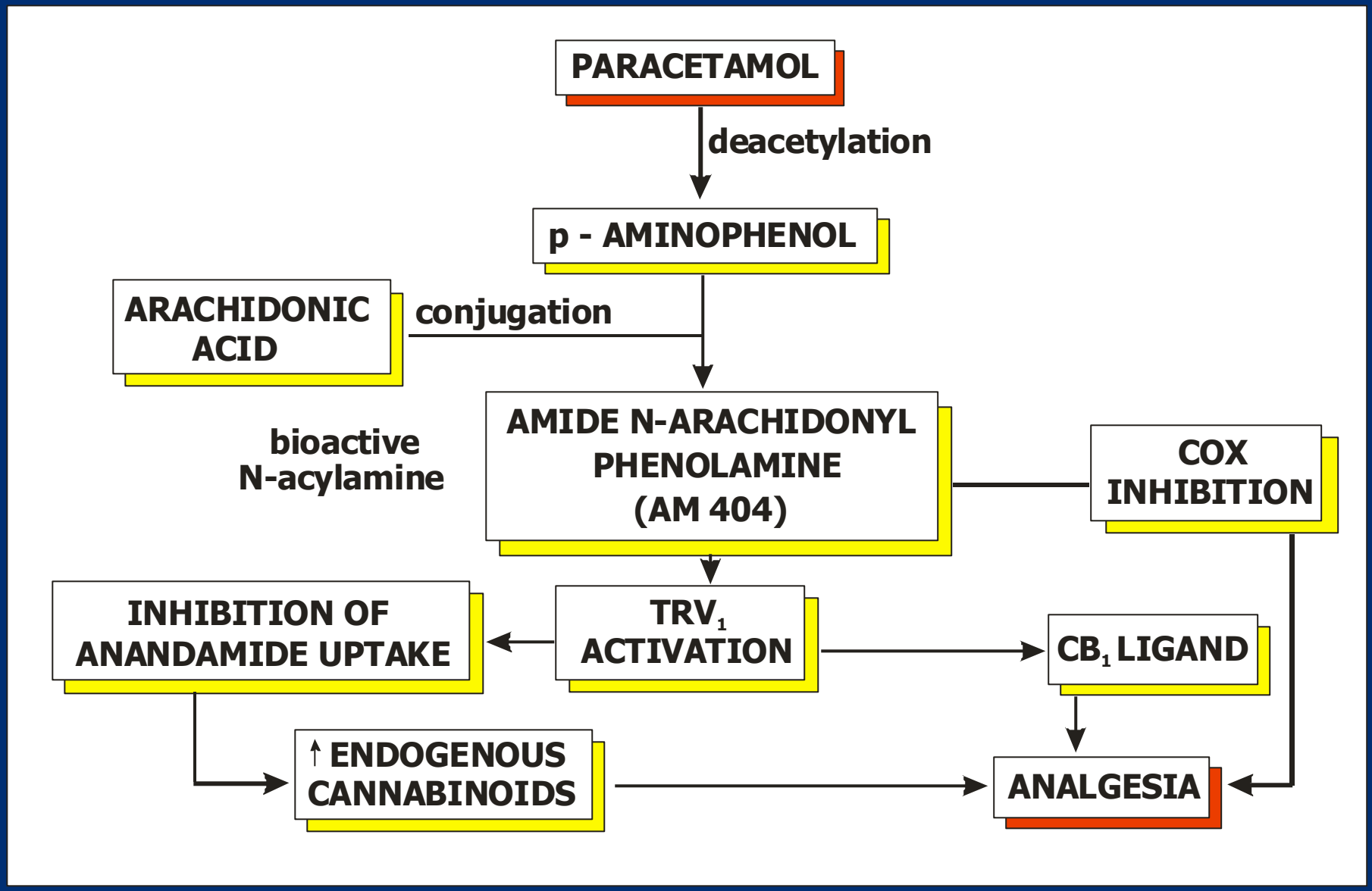
- **AM404 del gruppo delle N-acylamine ed il lipide endogeno anadamide promuovono l’attività analgesica dei cannabinoidi in vari test animali ed a temperature corporee basse.**



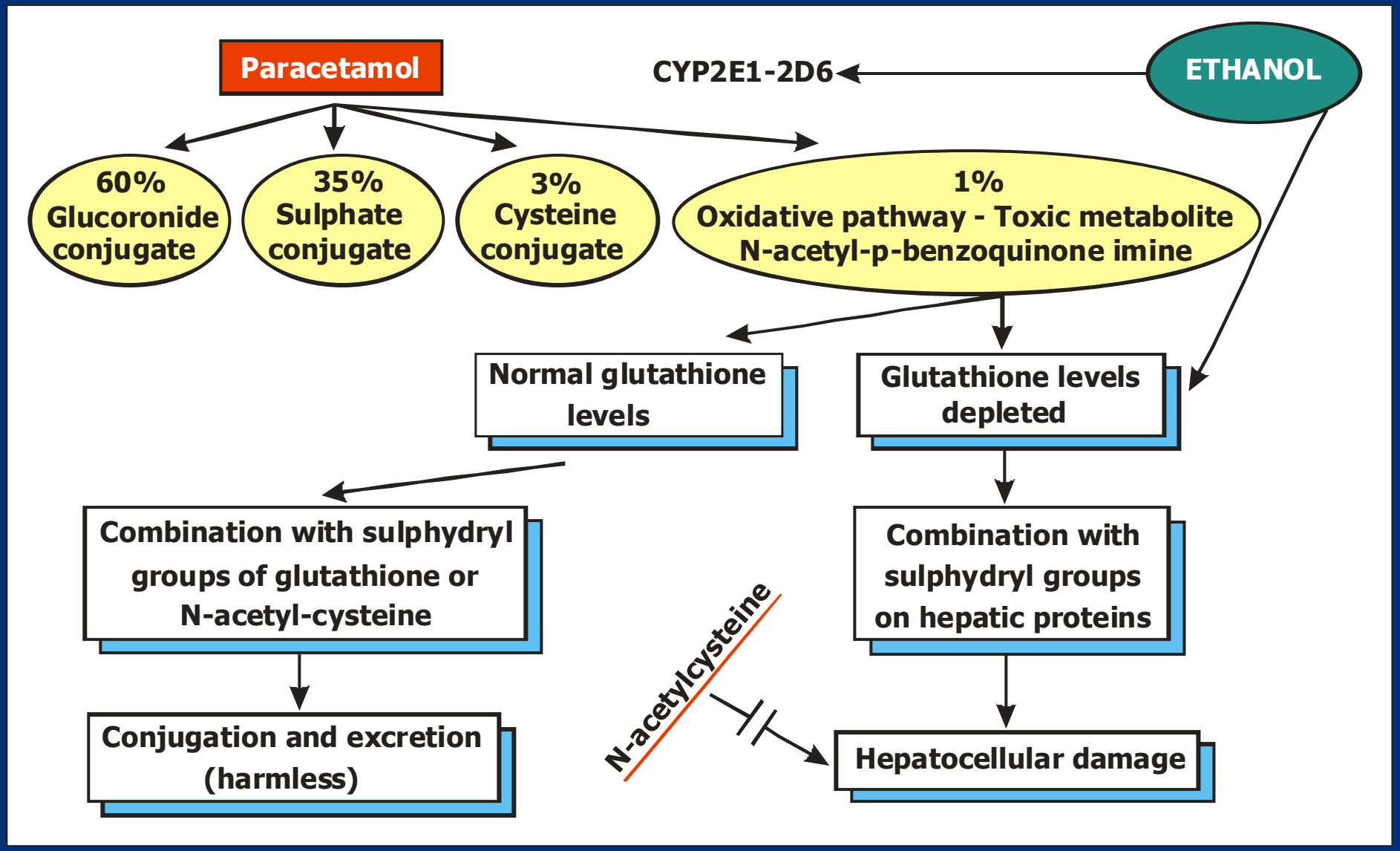


NOVEL MECHANISM OF PARACETAMOL ANTINOCICEPTION

(Hogestatt et al. J Biol Chem 2005;280:31405-12)



PARACETAMOL METABOLISM AND TOXICITY



La Terapia con Oppioidi

Spine

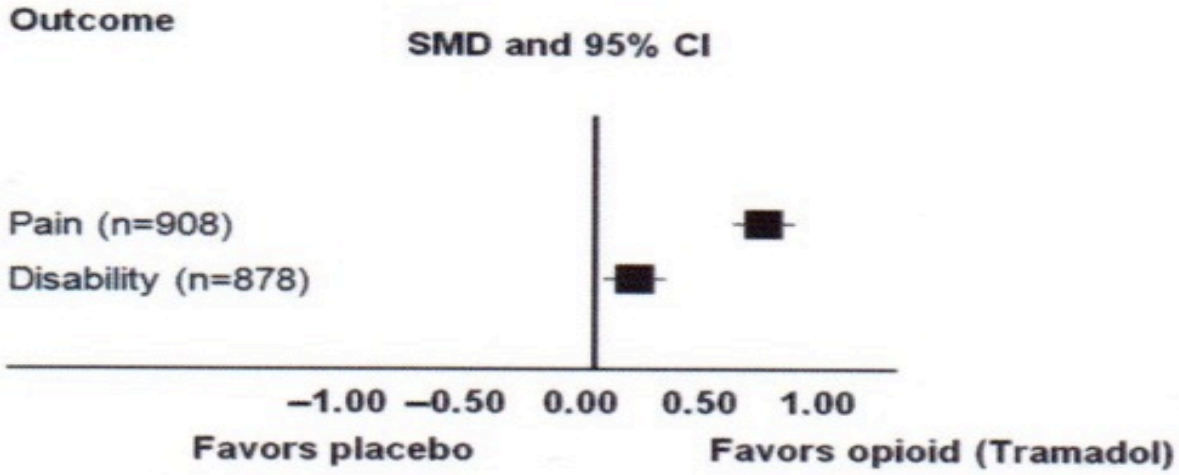
SPINE Volume 36, Number 21S, pp S131–S143

NONSURGICAL CARE OF CHRONIC LOW BACK PAIN

Pharmacologic Management of Chronic Low Back Pain

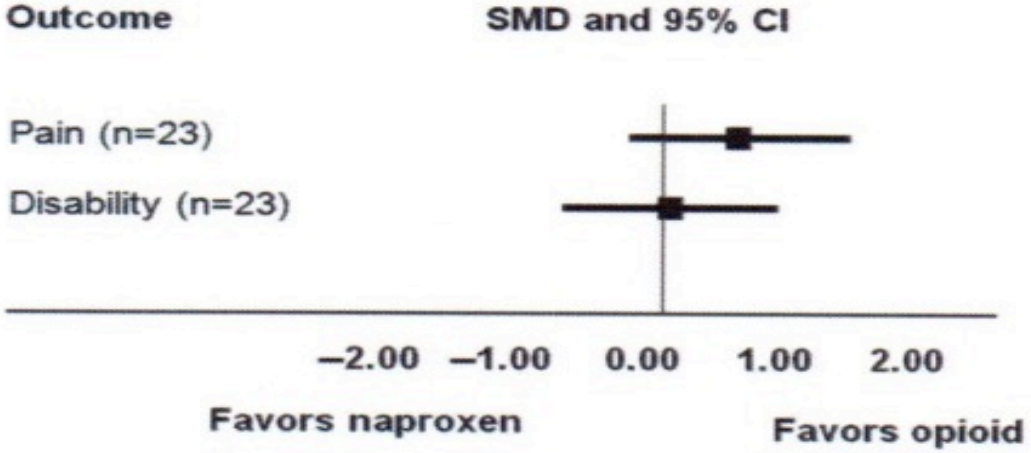
Synthesis of the Evidence

Andrew P. White, MD,* Paul M. Arnold, MD,† Daniel C. Norvell, PhD,‡ Erika Ecker, BS,‡ and Michael G. Fehlings, MD, PhD, FRCSC§



*Treatment effect favors opiods for both pain and disability.

(A)



*Treatment effect favors neither Opioids or NSAIDs for pain or disability. Note very small sample size.

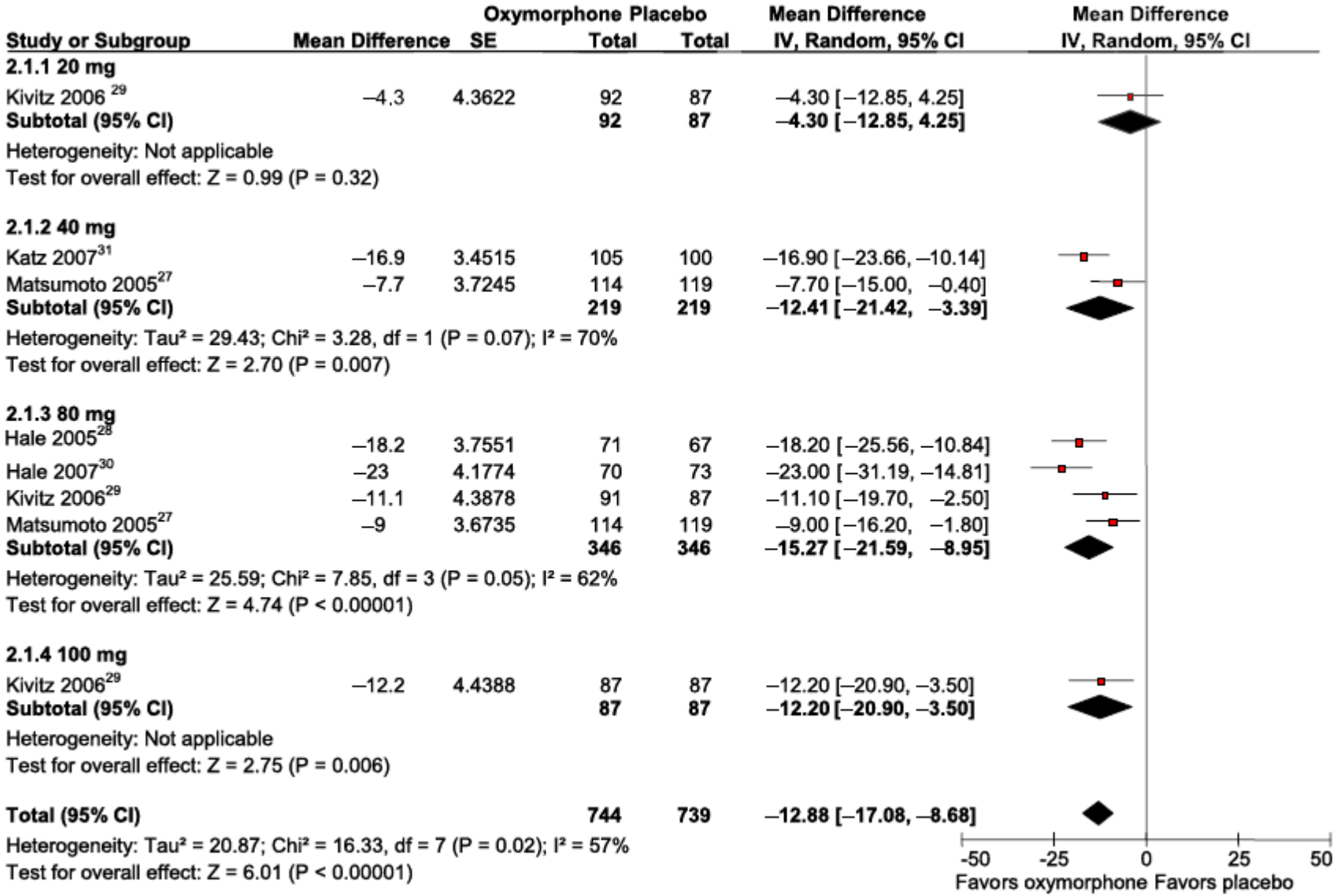
SPINE Volume 36, Number 21S, pp S131–S143

Review Article

A Systematic Review of Oxymorphone in the Management of Chronic Pain

Fadia Mayyas, MS, Peter Fayers, PhD, Stein Kaasa, MD, PhD, and Ola Dale, MD, PhD

Pain and Palliation Research Group (F.M., P.F., S.K., O.D.), Faculty of Medicine, Department of Molecular Biology and Cancer Research (P.F., S.K.), and Department of Circulation and Medical Imaging (F.M., O.D.), Norwegian University of Science and Technology, Trondheim, Norway; Palliative Medicine (S.K.), Department of Oncology, and Department of Anesthesiology and Emergency Medicine (O.D.), St. Olav's University Hospital, Trondheim, Norway; and Department of Public Health (P.F.), University of Aberdeen, Aberdeen, United Kingdom



Standardized Pain Intensity Scores in Chronic Nonmalignant Pain

F. Mayyas et al. J Pain and Symptom Management Vol. 39 No. 2 February 2010

REVIEW ARTICLE

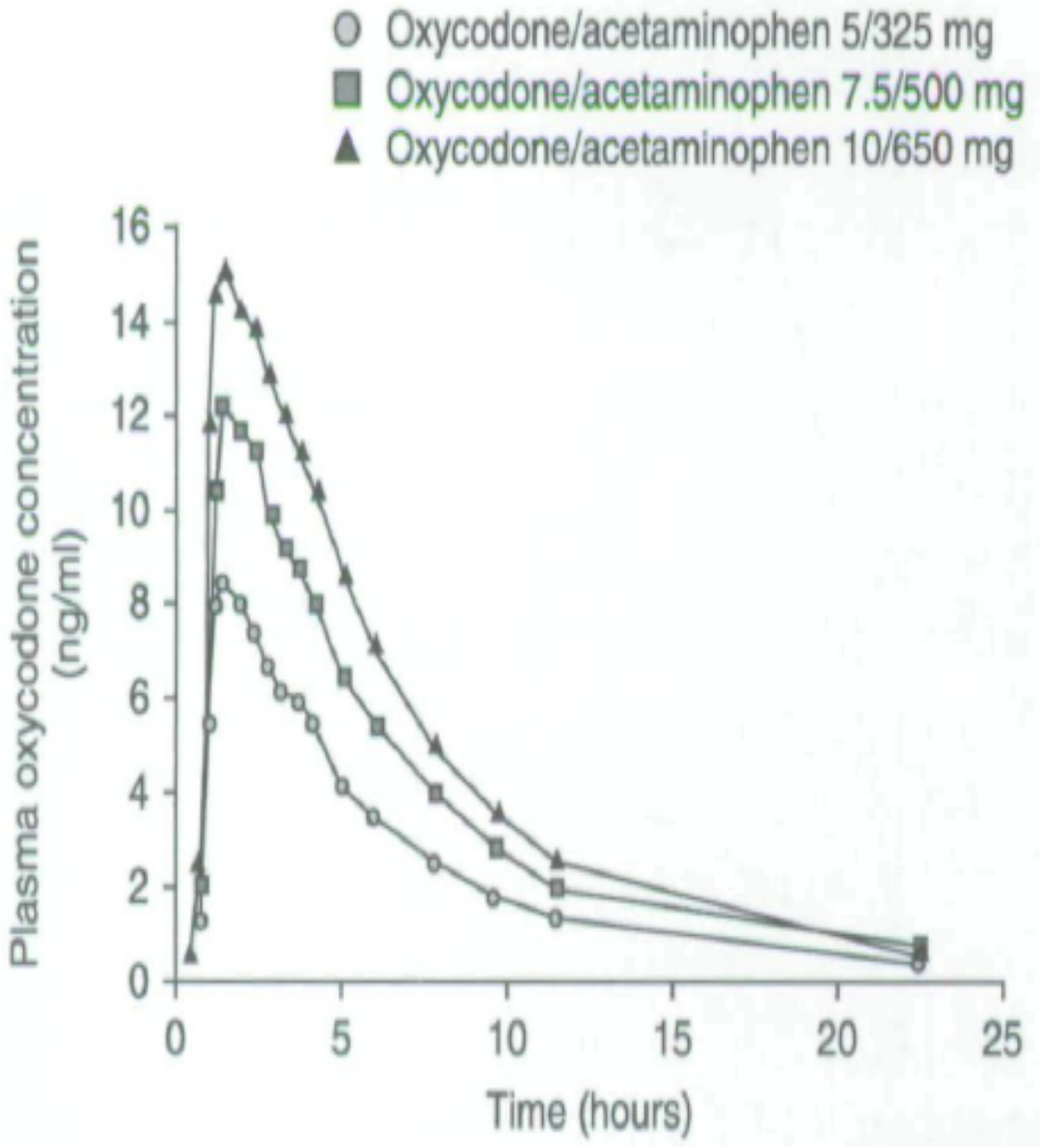
Clin Drug Investig 2010; 30 Suppl. 2: 3-14
1173-2563/10/0002-0003/$49.95/0

Oxycodone/Paracetamol

A Low-Dose Synergic Combination Useful in Different Types of Pain

Antonio Gatti, Elisabetta Sabato, Anna Rita Di Paolo, Massimo Mammucari and *Alessandro Fabrizio Sabato*

Emergency Care, Critical Care Medicine, Pain Medicine and Anaesthesiology Department at Tor Vergata Polyclinic, University of Rome – Tor Vergata, Rome, Italy



Mean oxycodone plasma concentrations in patients who received one of three dosage strengths of the oxycodone/ paracetamol immediate-release fixed-dose combination (5 mg/325 mg, 7.5mg/500mg or 10mg/650mg).

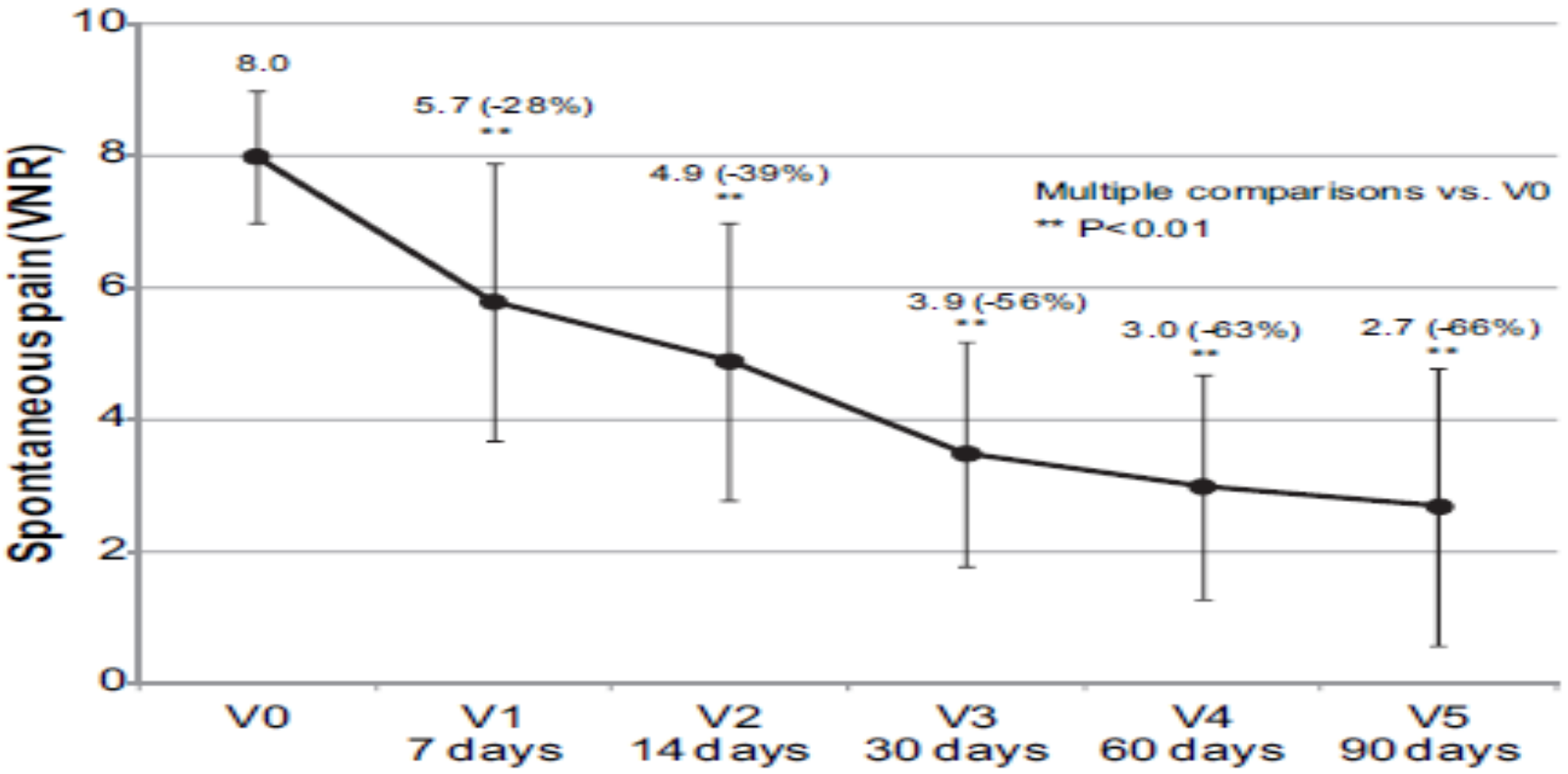
A. Gatti et al.Clin Drug Investig. 2010;30 Suppl.2:3-14

Original Article

Transdermal Buprenorphine for the Treatment of Chronic Noncancer Pain in the Oldest Old

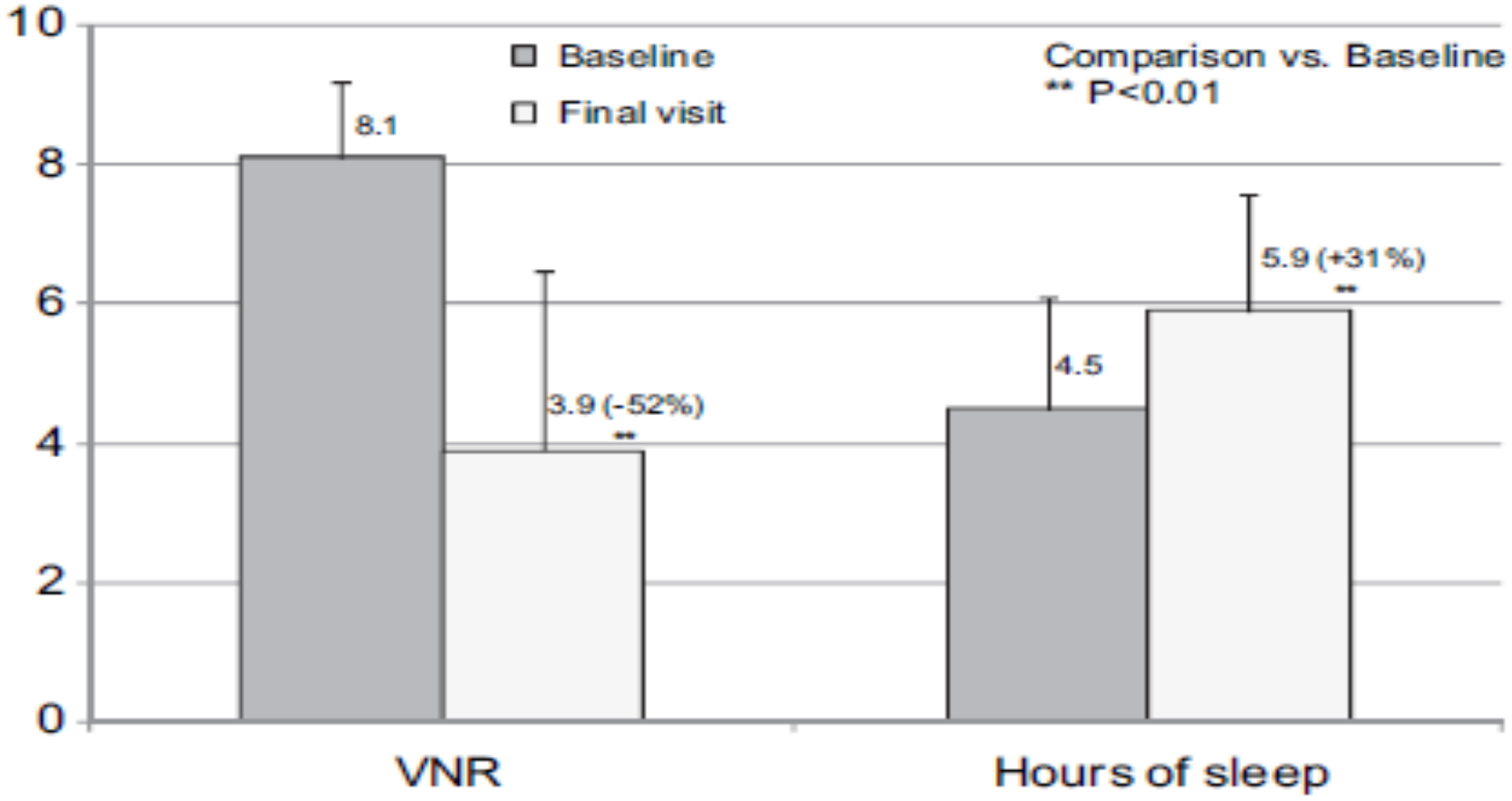
Walter Gianni, MD, Angelo Raffaele Madaio, MD, Moira Ceci, MD, Elena Benincasa, MD, Gianfranco Conati, MD, Fabrizio Franchi, MD, Giuseppe Galetti, MD, Antonio Nieddu, MD, Bernardo Salani, MD, and Stefano Maria Zuccaro, MD

Geriatrics Unit (W.G., M.C.), Istituto Nazionale di Ricovero e Cura per Anziani, Istituto di Ricovero e Cura a Carattere Scientifico, Rome; Department of Medical Oncology (A.R.M., E.B.), and Geriatrics Unit (S.M.Z.), Ospedale Israelitico, Rome; Geriatrics Unit (G.C.), Ospedale Civile, Belluno; Geriatrics Unit (F.F.), Azienda Ospedaliera G. Da Saliceto, Piacenza; Istituto Palazzolo Fondazione Don Gnocchi Nursing Home (G.G.), Milan; Department of Geriatrics (A.N.) and Alzheimer Evaluation Unit (A.N.), Policlinico Sassarese, Sassari; and Geriatrics Division Day Hospital (B.S.), Azienda Ospedaliera Universitaria Careggi, Florence, Italy



Reduction of spontaneous pain in 89 geriatric patients affected from chronic noncancer pain and treated with buprenorphine TDS for three months

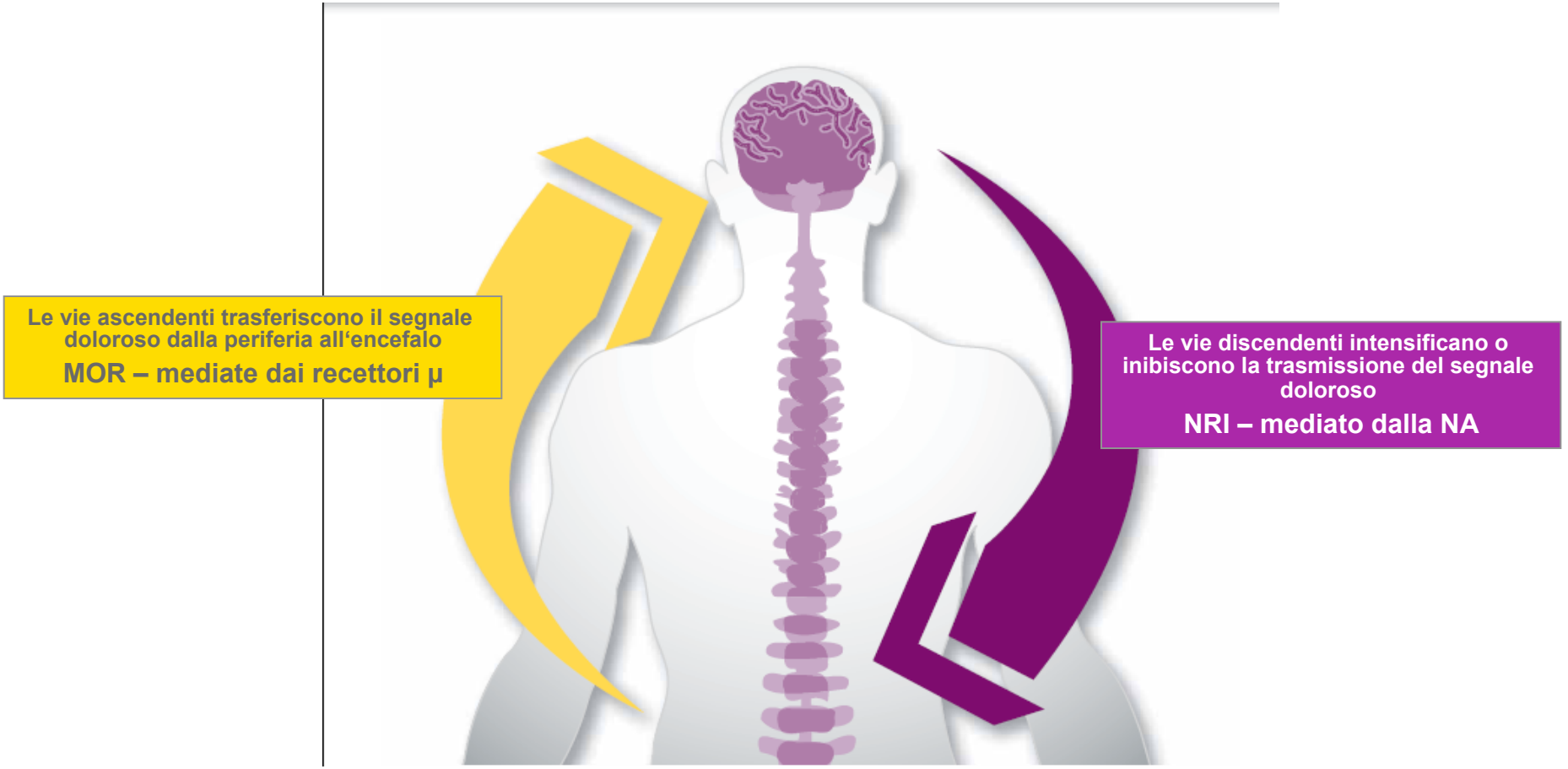
W. Gianni. Journal of Pain and Symptom Management. Vol. 41 No. 4 April 2011



Reduction of spontaneous pain and increase in hours of sleep in 89 geriatric patients affected from chronic noncancer pain and treated with buprenorphine TDS for three months

W. Gianni. Journal of Pain and Symptom Management. Vol. 41 No. 4 April 2011

Comprendere le vie del dolore per scegliere il trattamento ottimale



É evidente una forte rilevanza della componente NRI nel dolore cronico di tipo neuropatico

Tzschentke TM. et al. Drugs of Today 2009, 45 (7): 483-496.

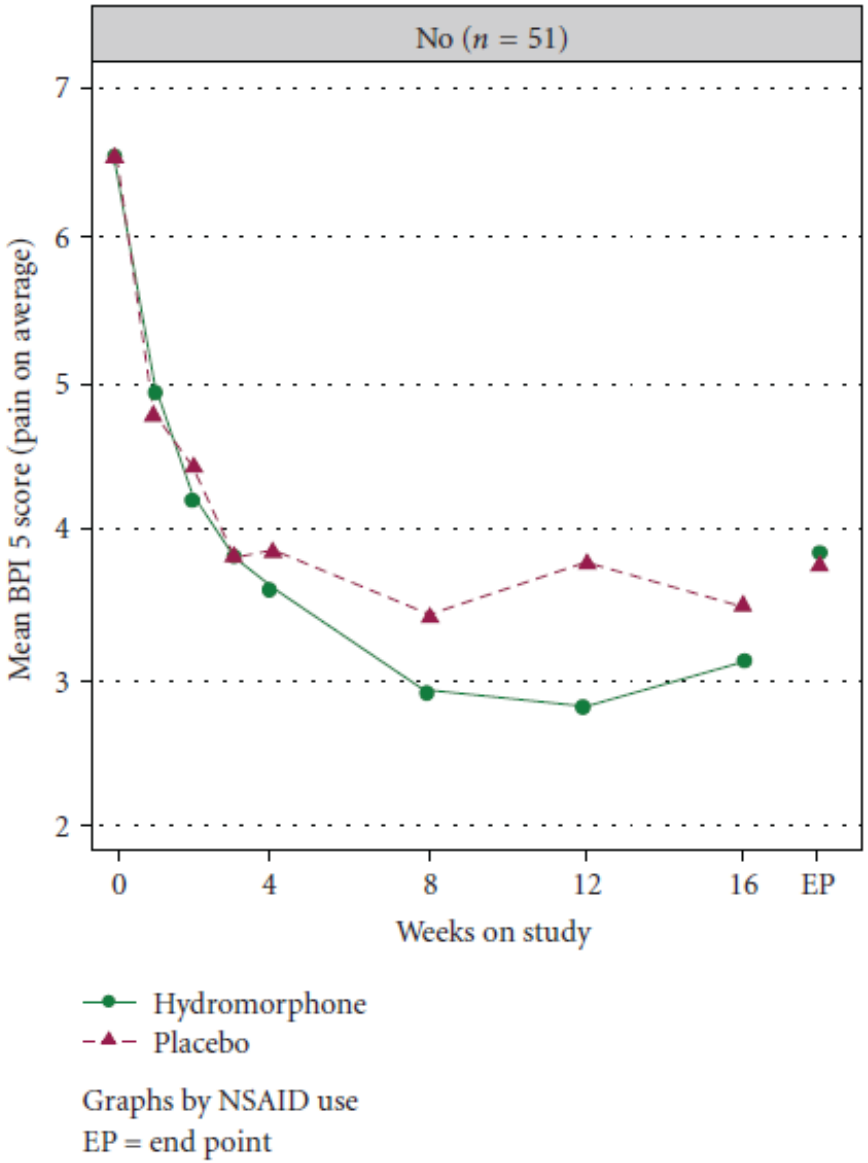
Hindawi Publishing Corporation
Pain Research and Treatment
Volume 2011, Article ID 239501, 9 pages
doi:10.1155/2011/239501

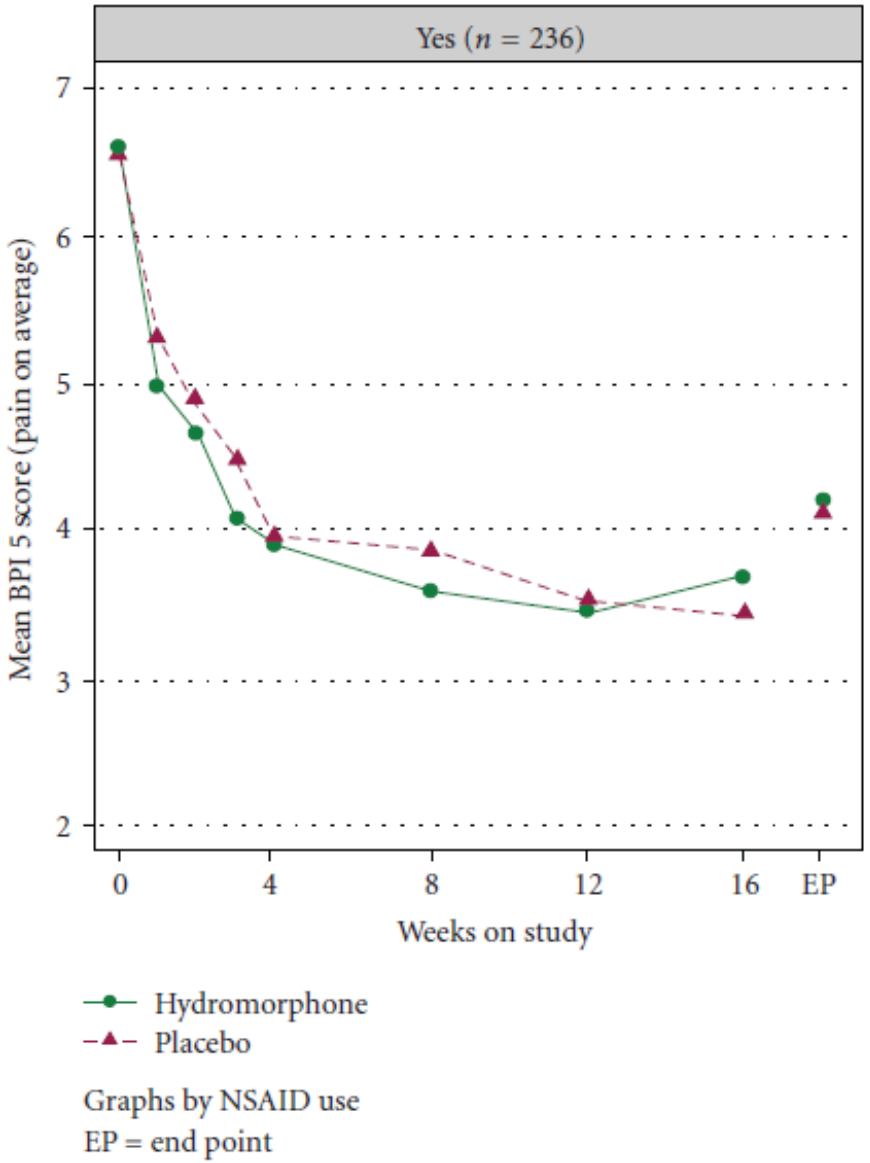
Clinical Study

A Phase IIIb, Multicentre, Randomised, Parallel-Group, Placebo-Controlled, Double-Blind Study to Investigate the Efficacy and Safety of OROS Hydromorphone in Subjects with Moderate-to-Severe Chronic Pain Induced by Osteoarthritis of the Hip or the Knee

Jozef Vojtaššák,[1] Jozef Vojtaššák,[1] Adam Jacobs,[2] Leonie Rynn,[3] Sandra Waechter,[4] and Ute Richarz[5]

[1] *Orthos Paidion, 83263 Bratislava, Slovakia*
[2] *Dianthus Medical Limited, London SW19 2RL, UK*
[3] *EMEA Medical Affairs, Analgesia, Janssen-Cilag, Quarryvale, Co Dublin, Ireland*
[4] *Medical Affairs, Janssen-Cilag Europe, 6341 Baar, Switzerland*
[5] *Global Medical Affairs, GMAL Mature Products, Johnson & Johnson Pharmaceutical Services, LLC, 6341 Baar, Switzerland*





Mean BPI score item 5 (pain on average) by concomitant NSAID use and treatment (ITT population)

J.Vojtassak et al. Pain Research and Treatment Volume 2011, 9

ORIGINAL RESEARCH ARTICLE

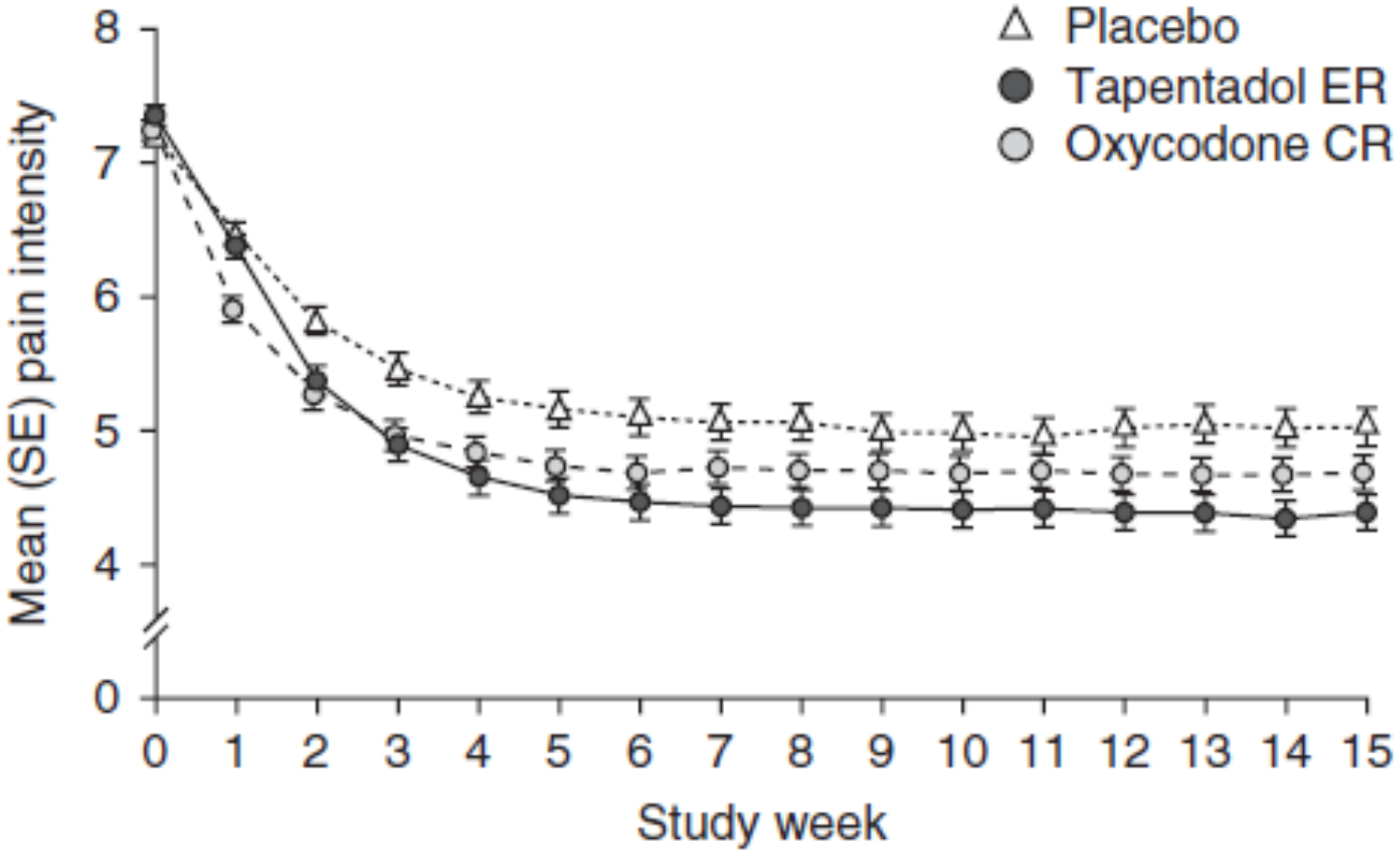
Clin Drug Investig 2010; 30 (8): 489-505
1173-2563/10/0008-0489/$49.95/0

Efficacy and Safety of Tapentadol Extended Release Compared with Oxycodone Controlled Release for the Management of Moderate to Severe Chronic Pain Related to Osteoarthritis of the Knee

A Randomized, Double-Blind, Placebo- and Active-Controlled Phase III Study

Marc Afilalo,[1] *Mila S. Etropolski,*[2] *Brigitte Kuperwasser,*[2] *Kathy Kelly,*[2] *Akiko Okamoto,*[2] *Ilse Van Hove,*[3] *Achim Steup,*[4] *Bernd Lange,*[4] *Christine Rauschkolb*[2] and *Juergen Haeussler*[2]

1 Sir Mortimer B. Davis Jewish General Hospital, Montreal, Quebec, Canada
2 Johnson & Johnson Pharmaceutical Research & Development, L.L.C., Raritan, New Jersey, USA
3 Johnson & Johnson Pharmaceutical Research & Development, Division of Janssen Pharmaceutica, N.V., Beerse, Belgium
4 Global Development, Grünenthal GmbH, Aachen, Germany



Mean (SE) pain intensity scores over time using last observation carried forward (intent-to-treat population). CR= controlled release; ER = extended release; SE = standard error.

M. Afilalo et al. Clin Drug Investig 2010;30(8):489-505

International Guidelines

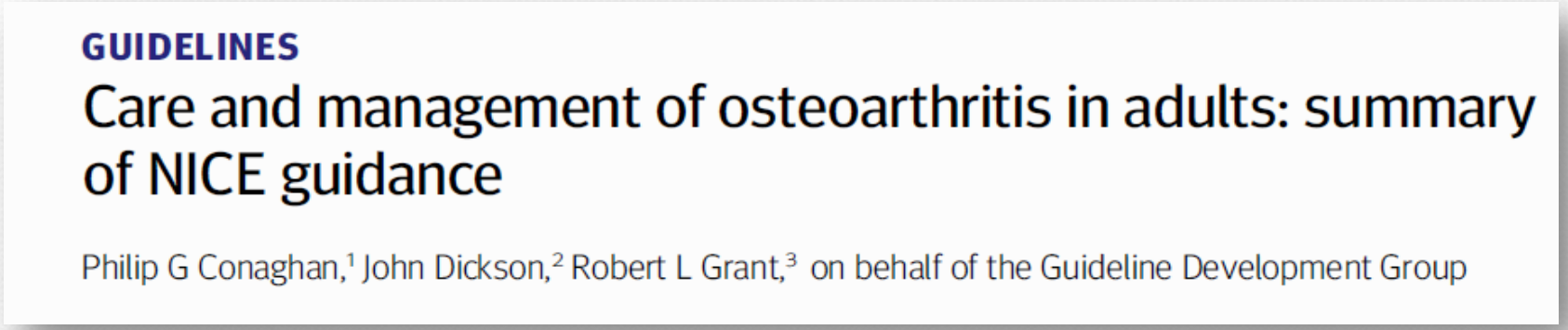
- The **European League Against Rheumatism** recommends opioid analgesics with or without paracetamol as useful alternatives for patients in whom non-steroidal antiinflammatory drugs (NSAIDs), including cyclo-oxygenase-2 (Cox-2) selective inhibitors, are contra-indicated, ineffective and/or poorly tolerated.

Zhang W, *et al.* ***Ann Rheum Dis 2005, 64:*** 669-681.

- The **American Pain Society** and the **American College of Rheumatology** give similar advice for the use of opioids in rheumatoid arthritis (RA) as well as osteoarthritis (OA).

American Pain Society: *APS & ACR guidelines. Guideline for the Management of Pain in Osteoarthritis, Rheumatoid Arthritis, and Juvenile Chronic Arthritis. Glenview, IL: American Pain Society;* 2002.
Arthritis Rheum 2000, 43:1905-1915.

International Guidelines



GUIDELINES

Care and management of osteoarthritis in adults: summary of NICE guidance

Philip G Conaghan,[1] John Dickson,[2] Robert L Grant,[3] on behalf of the Guideline Development Group

- For knee and hand osteoarthritis, consider paracetamol and/or topical non-steroidal anti-inflammatory drugs (NSAIDs) before oral NSAIDs, cyclo-oxygenase-2 (COX 2) inhibitors, and opioids.
- If paracetamol or topical NSAIDs are insufficient for pain relief, then consider adding opioid analgesics or substituting with (or in addition to paracetamol) an oral NSAID or COX 2 inhibitor.

BMJ | 1 MARCH 2008 | VOLUME 336

Choice of Opioids

- No evidence that dosing regimen has any bearing on the development of tolerance
- ***Generally long-acting formulations are preferred***
- Methadone may be a good choice because
  - long-acting and has NMDA-receptor antagonism
- Methadone may be a bad choice because
  - half-life is unpredictable and it may accumulate
- American Society of Anesthesiologists recommends the slow-release forms of morphine and oxycodone

Strategies to Improve Opioid Effectiveness

- Opioids titration
- Equianalgesic dose
- Opioids switch
- Avoid irrational polypharmacy
- Prevent and cure side effects

Opioid rotation

- **Reduce the side effects with another drug**
  - Anti-emetics, laxatives, stimulants
- **Add other analgesics/adjuvants**
  - NSAIDs, TCA, neuropathic agents, steroids, ketamine
- **Interventional techniques**
  - Epidural, intrathecal analgesia

J Pain Symptom Manage 2001; 21:338-54

STEP 1
OPIOID THERAPY: THE BEGINNING

- The opioid should always be started at the lowest available dose and titrated slowly depending on analgesic response and adverse effects

- The efficacy of the opioid should be re-evaluated on a regular basis and it should be discontinued if not effective

STEP 2a

OPIOID THERAPY: STEPS OF INTERVENTION

- Educate patient; provide educational material on opioid therapy to patient and family
- Set realistic goals and reach agreement with patient: opioids are one modality in a multifaceted treatment approach
- Decide whether to start a short-acting opioid analgesic or a low dose of a long-acting opioid analgesic, with or without short-acting rescue doses if break-through pain occurs
- Consider cost, tolerability, ease of administration, and patient compliance

STEP 2b
OPIOID THERAPY: STEPS OF INTERVENTION

- Titrate daily opioid dose to optimal effect
- Manage side effects aggressively
- Continue opioid therapy if the patient reports:
  - *pain relief and / or*
  - *improvement in selected areas of function and /or psychosocial functioning*
- Always consider opioid rotation
- Consider Genetic Variability

Purpose


what
you love
passion
mission
what
you're
good at
what
the world
needs
profession
vocation
what
someone
will pay for
= purpose

… Medical Humanities …