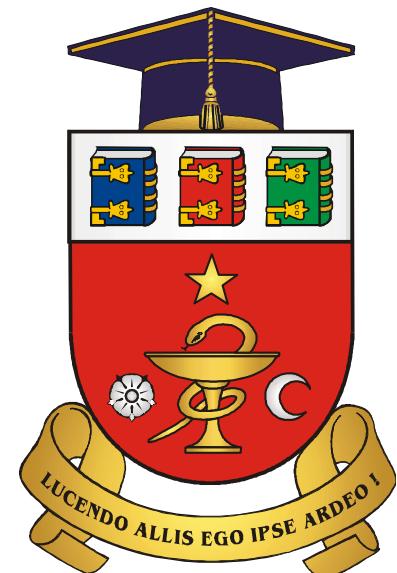


ACTUALITĂȚI ÎN DIAGNOSTICUL ȘI TRATAMENTUL DURERII NEUROPAȚE



Vitalie LISNIC

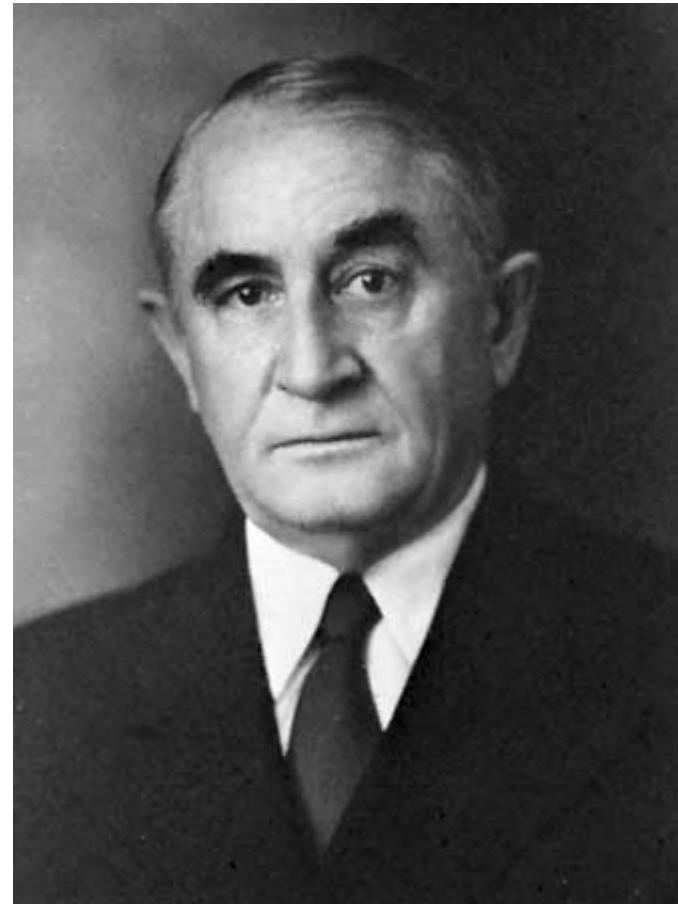
16 aprilie 2019



“Durerea într-o formă sau altă este simptomul care-l determină pe pacient să se adreseze la medic”

**Dr. Charles
H. Mayo**

1931



DURAREA

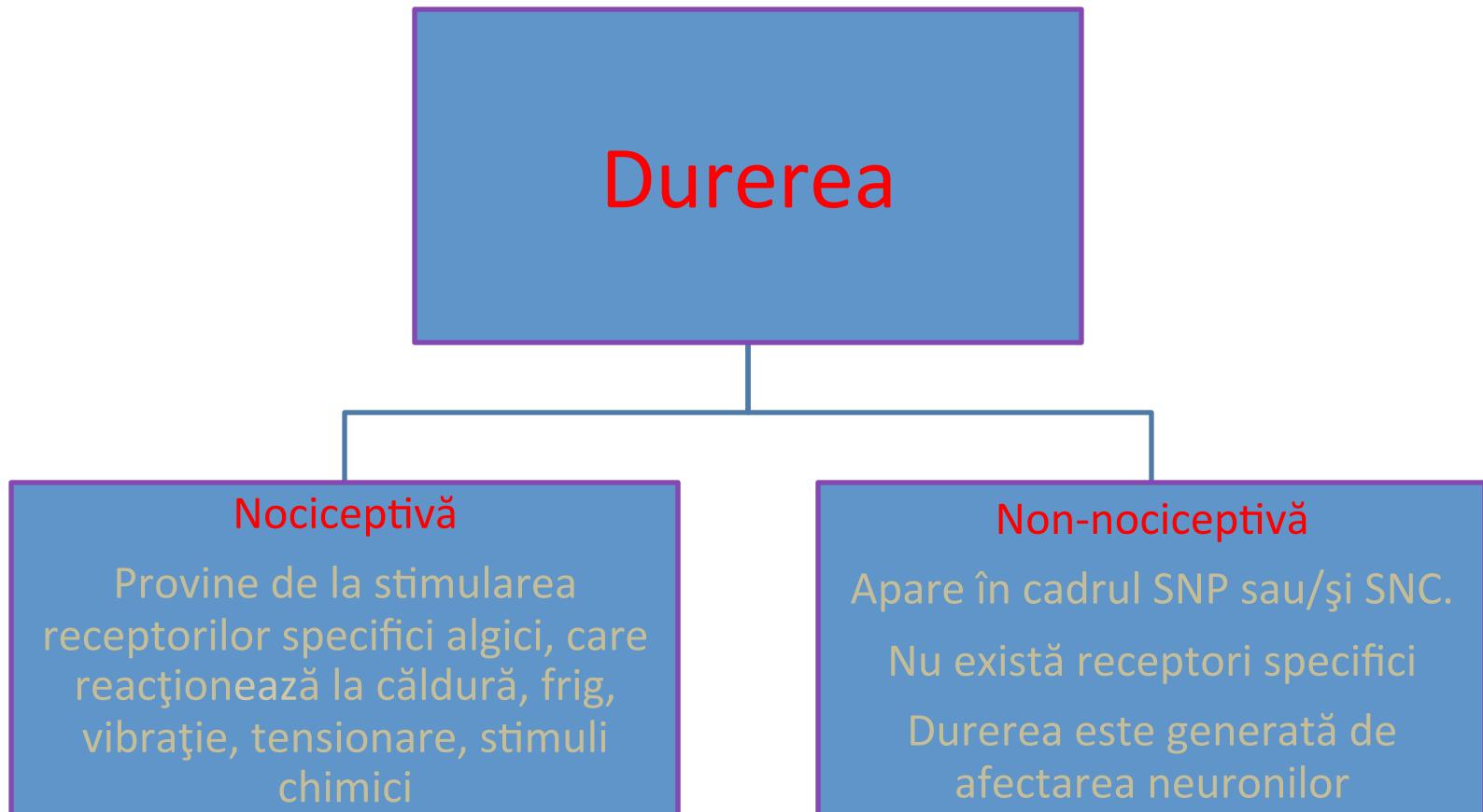
“experiență senzorială și emoțională neplăcută asociată cu leziune tisulară actuală sau potentială sau descrisă în termeni echivalenți unor asemenea stări”

**International Association for
the Study of Pain**

11 septembrie 2011



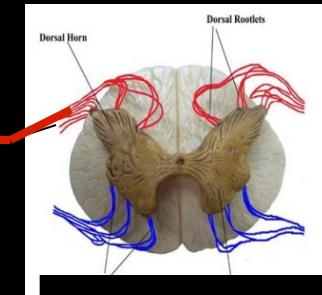
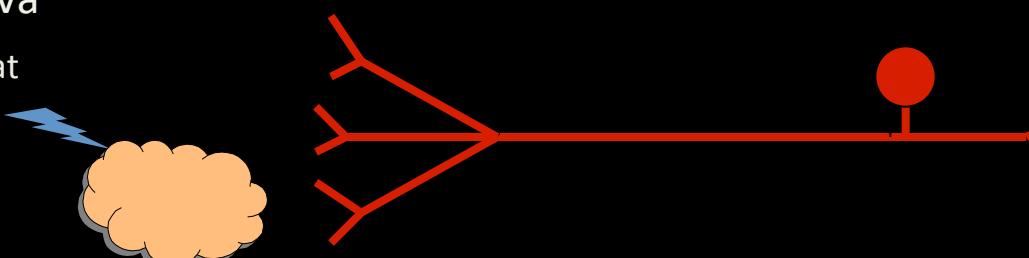
Clasificarea durerii



Clasificarea durerii

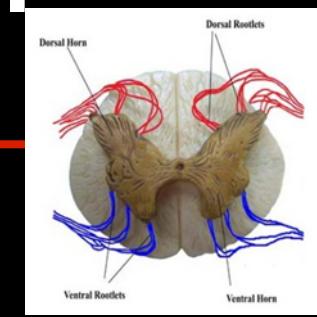
A. Nociceptiva

Tesut afectat



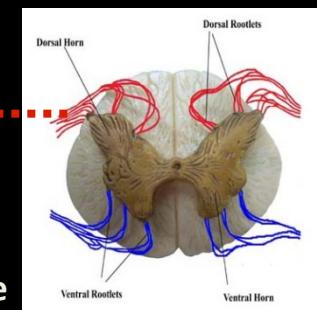
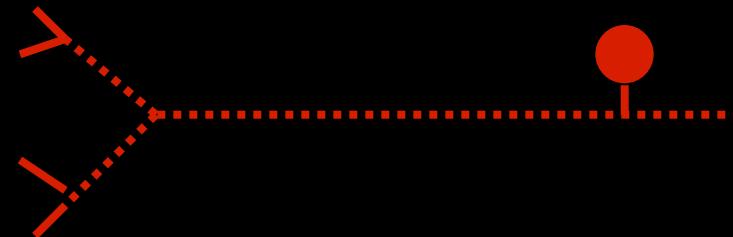
B. Neuropatica

Leziunea nervului



C. Funcțională (Psihogena)

Deregarea proceselor nespecifice centrale



Prevalență durerii neuropatice

7 % populația generală

Bouhassira D, Lanteri-Minet M,
Pain 2008; 136 (3):380-387.

EFNS guidelines on neuropathic pain assessment

G. Cruccu^{a,b}, P. Anand^c, N. Attal^d, L. Garcia-Larrea^{a,e}, M. Haanpää^{a,f}, E. Jørum^{a,g}, J. Serra^{a,h} and T. S. Jensen^{a,i}

^aEFNS Panel on Neuropathic Pain; ^bDepartment of Neurological Sciences, La Sapienza University, Rome, Italy; ^cPeripheral Neuropathy Unit, Imperial College London, Hammersmith Hospital, London, UK; ^dINSERM E-332, Centre d'Evaluation et de Traitement de la Douleur, Hôpital Ambroise Paré and Université Versailles Saint-Quentin, Versailles; ^eCentral Integration of Pain Unit – INSERM E342 and Claude Bernard University, Lyon, France; ^fDepartments of Anaesthesiology and Neurosurgery, Pain Clinic, Helsinki University Hospital, Helsinki, Finland; ^gDepartment of Neurology, The National Hospital, Oslo, Norway; ^hNeuropathic Pain Unit, Hospital General de Catalunya, Barcelona, Spain; and ⁱDepartment of Neurology and Danish Pain Research Center, Aarhus University Hospital, Aarhus, Denmark

Keywords:
laser-evoked potentials

In September 2001, a Task Force was set up under the auspices of the European Federation of Neurological Societies with the aim of evaluating the existing evidence.

European Journal of Neurology 2010, 17: 1113–1123

doi:10.1111/j.1468-1331.2010.02999.x

EFNS GUIDELINES

EFNS guidelines on the pharmacological treatment of neuropathic pain: 2010 revision

N. Attal^{a,b}, G. Cruccu^{a,c}, R. Baron^{a,d}, M. Haanpää^{a,e}, P. Hansson^{a,f}, T. S. Jensen^{a,g} and T. Nurmi^{kko^{a,h}}

^aEFNS Panel Neuropathic Pain; ^bINSERM U987, Centre d'Evaluation et de Traitement de la Douleur, Hôpital Ambroise Paré, APHP, Boulogne-Billancourt, and Université Versailles-Saint-Quentin, Versailles, France; ^cDepartment of Neurological Sciences, La Sapienza University, Rome, Italy; ^dDivision of Neurological Pain Research and Therapy, Department of Neurology, Universitätsklinikum Schleswig-Holstein, Kiel, Germany; ^eRehabilitation ORTON and Department of Neurosurgery, Helsinki University Hospital, Helsinki, Finland;

^fDepartment of Molecular Medicine and Surgery, Clinical Pain Research and Pain Center, Department of Neurosurgery, Karolinska Institutet/University Hospital, Stockholm, Sweden; ^gDepartment of Neurology and Danish Pain Research Center, Aarhus University Hospital, Aarhus, Denmark; and ^hPain Research Institute, Neuroscience Research Unit, School of Clinical Sciences, University of Liverpool, Liverpool, UK

CONTINUUM

LIFELONG LEARNING IN NEUROLOGY®

ContinuumJournal.com

Selected Topics in Outpatient Neurology

Guest Editor: Charles A. Zollinger, MD, FAAN

 Denotes Video Content

 Denotes Supplemental Digital Content

 Denotes Online-Only Article

Editor's Preface 333

REVIEW ARTICLES

Syncope 335

William P. Cheshire Jr, MD, FAAN

Dizziness in the Outpatient Care Setting 359

Terry D. Fife, MD, FAAN

 **Trigeminal Neuralgia** 396

Giorgio Cuccu, MD

Disorders of Taste and Smell 421

Ronald DeVere, MD, FAAN

 **Bell's Palsy** 447

Stephen G. Reich, MD, FAAN

Low Back Pain 467

Jinny O. Tavee, MD; Kerry H. Levin, MD, FAAN

Common Entrapment Neuropathies 487

Lisa D. Hobson-Webb, MD; Vern C. Juel, MD, FAAN

 **Neuropathic Pain** 512

Lindsay A. Zilliox, MD, MS

Urogenital Symptoms in Neurologic Patients 533

Jalesh N. Panicker, MD, DM, FRCP

Neuropathic Pain: Mechanisms, Therapeutic Approach, and Interpretation of Clinical Trials

Nadine Attal, MD, PhD

ABSTRACT

Purpose of Review: Neuropathic pain (NP) is caused by a lesion of the somatosensory system and is characterized by a combination of positive symptoms (ongoing pain, paroxysmal pain, evoked pain) and negative phenomena (sensory deficit in the painful area). Examples of NP include painful diabetic and nondiabetic neuropathies, postherpetic neuralgia, traumatic nerve lesions, radiculopathies, and central pain (eg, spinal cord injury pain, poststroke pain). This review presents the mechanisms and therapeutic options for NP.

Recent Findings: Consensus recommendations for the treatment of NP or of some neuropathic conditions propose using antidepressants, antiepileptics, and topical lidocaine as first-line treatment and using tramadol and other opioids as second- or third-line treatment. Clinical advances in the management of NP include the implementation of comparative studies and combination therapy trials, the study of rarer and often neglected NP conditions, and the identification of responder profiles based on a detailed characterization of symptoms and signs using sensory examination and specific pain questionnaires.

Summary: The management of patients with chronic NP is challenging because of the multiplicity of mechanisms involved in NP conditions. Evidence-based recommendations for the pharmacologic treatment of NP have recently been proposed.

Address correspondence to
Dr Nadine Attal, INSERM U 987
and Centre d'Evaluation et de
Testement De la Douleur,
9 Avenue Charles De Gaulle,
Boulogne-Billancourt 92104,
France; nadine.attal@chaphy.fr.

Relationship Disclosure:
Dr Attal serves on the advisory
boards and speakers' panels of
Astellas Pharma, Eisai Co., Ltd.,
Eli Lilly and Company,
Gruenthal, and Pfizer Inc.

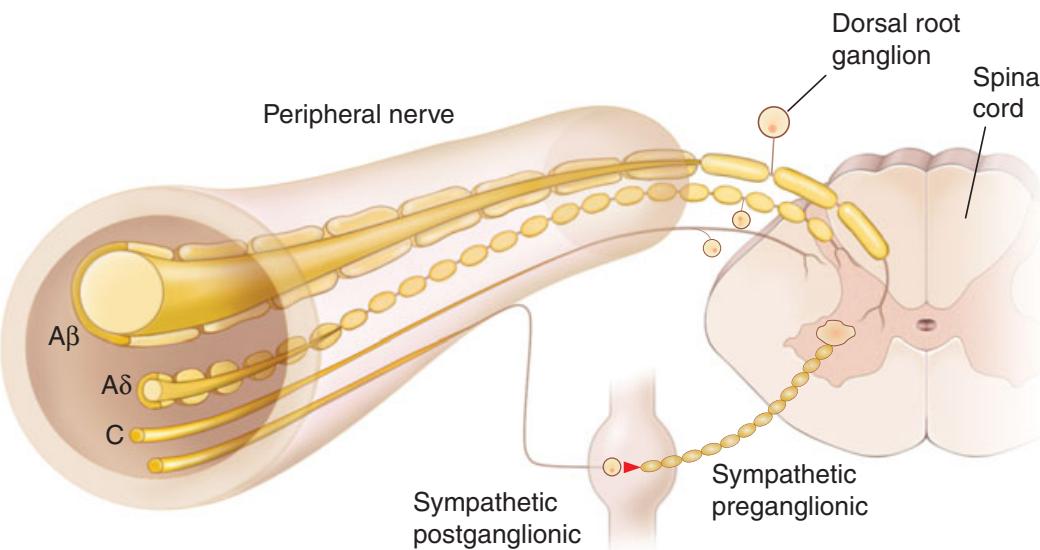
**Unlabeled Use of
Products/Investigational
Use Disclosure:**

Dr Attal discusses the unlabeled
use of botulinum toxin and
cannabidiol cannabinoids to
treat neuropathic pain. Dr Attal
discusses the unlabeled use of
duloxetine to treat central pain.

Copyright © 2012,
American Academy
of Neurology. All rights
reserved.

Mecanisme periferice

- **A-beta (A β)**, fibre groase
stimuli tactili, stimuli determinați de mișcare

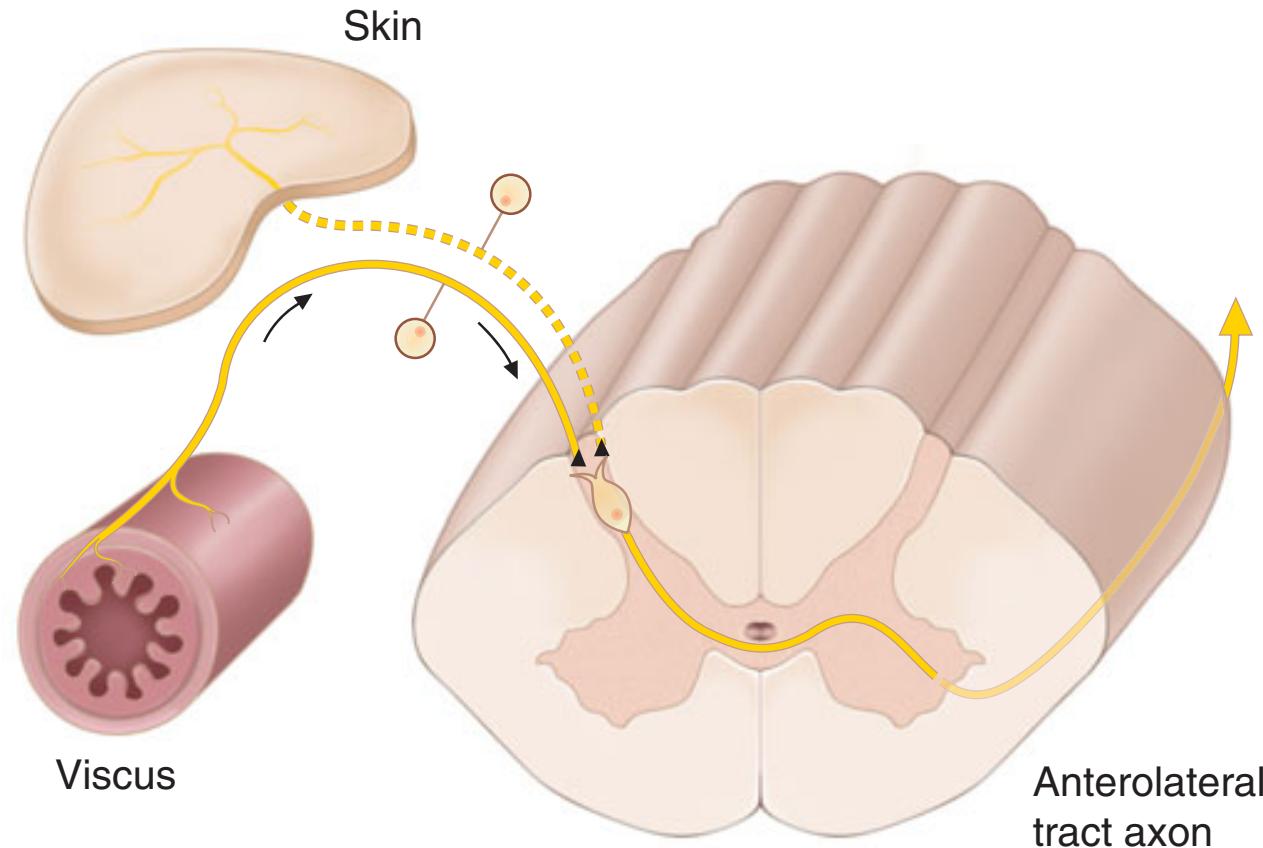


- **A-delta (A δ)**, fibre subțiri mielinizate și **C** nemielinizate
În fibre cutanate și structuri somatice și viscerale

Nociceptorii reacționează la căldură, frig, vibrație, tensionare, stimuli chimici (serotonină, bradichinină, histamină)

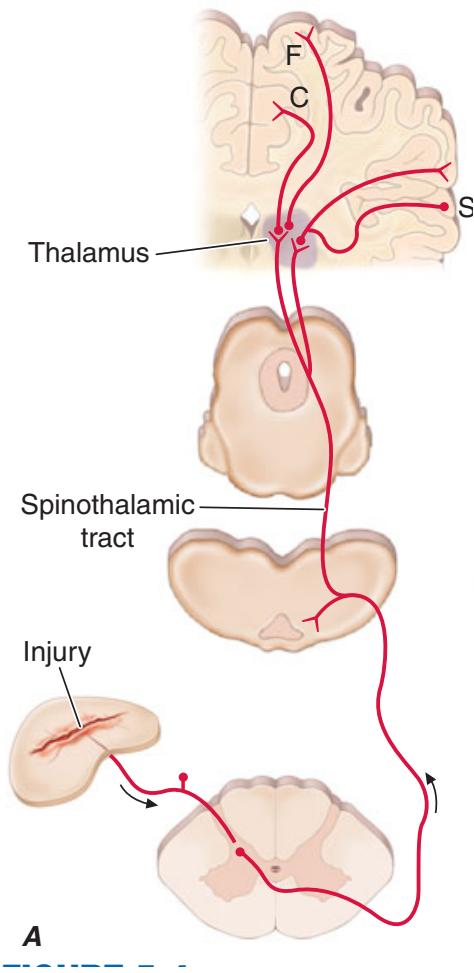
Mécanisme centrale

The Spinal Cord and Referred Pain

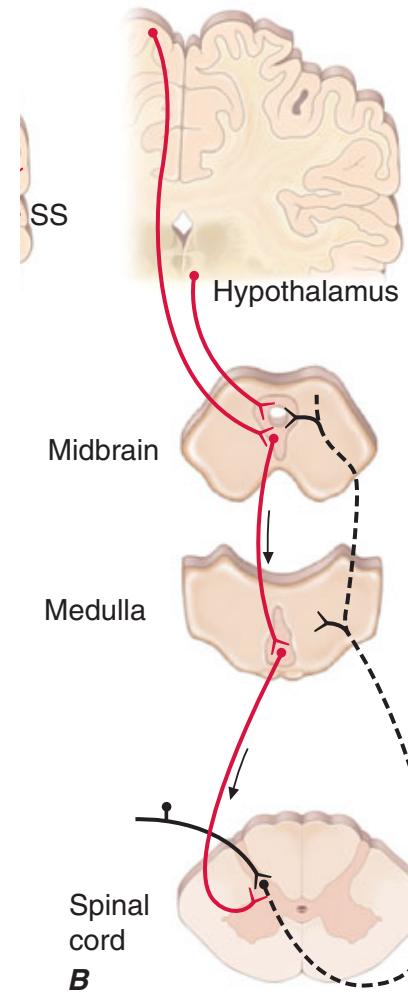


Transmiterea și modularea durerii

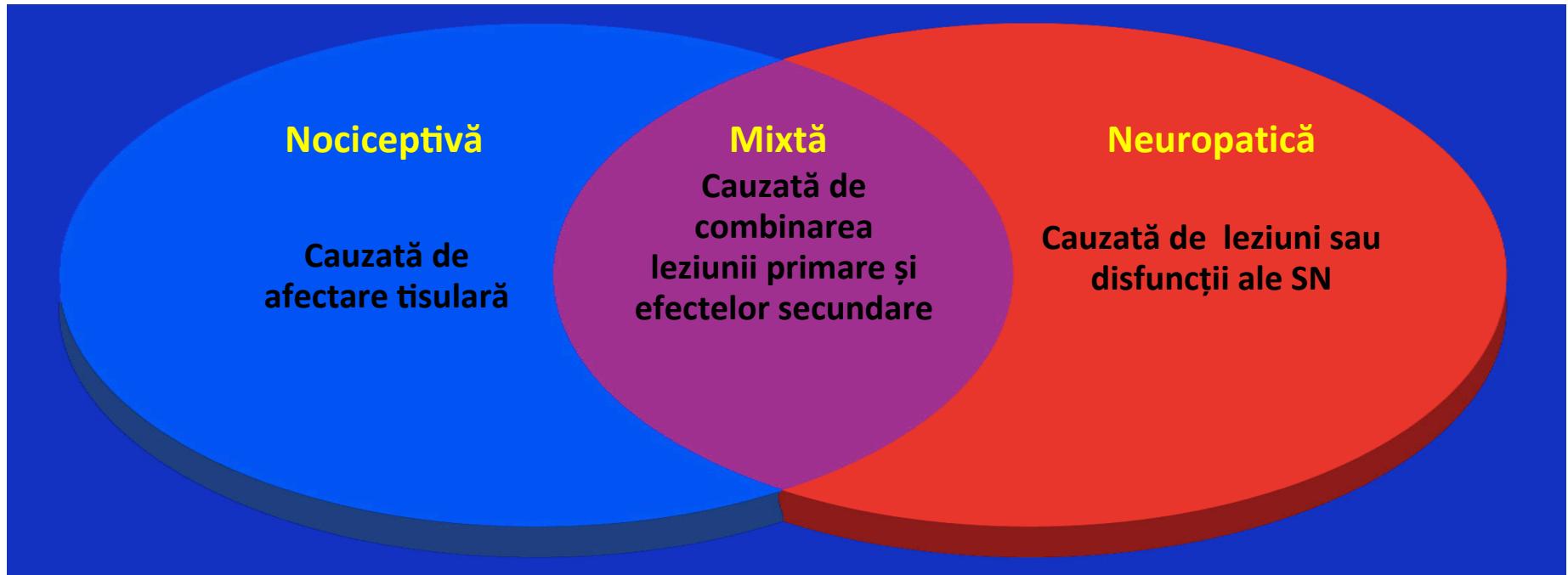
A. Sistemul de transmisiune nociceptiv



B. Rețeaua de modulare a durerii



Exemple de Durere Nociceptivă și Durere Neuropatică



- Artrite
- Dureri lombare
- Leziuni sportive
- Durere postoperatorie
- Dureri lombare
- Fibromialgia
- Dureri cervicale
- Dureri în cadrul cancerului
- Neuropatie diabetică dureroasă
- Nevralgie postherpetică
- Durere lombară neuropatică
- Nevralgie trigemenială
- Durere centrală post-stroke
- Sindrom de durere regională complexă
- Polineuropatie distală în cadrul HIV

Componentele nociceptic și neuropatic în durerea lombară pot fi prezente concomitent

Componentul **nociceptic** al durerii



Componentul **neuropatic** al durerii



Cauzele durerii neuropatice

Cauze centrale

- Stroke
- Leziuni medulare
- Scleroza multiplă
- Tumori

Cauze periferice

- Traume
- Toxice (alcool)
- Infecții (herpes zoster, HIV, Borrelia)
- Maladii autoimune
- Tulburări metabolice și vasculare (Diabet!!!)
- Paraneoplazice
- Ereditare
- Neuropatii de tunel

Simptome spontane



Simptomul

Descrierea

Durerea spontană

Durere arzătoare permanentă, junghiul-

Disestezii

Senzații patologice neplăcute (eg, împușcături, lanciată, frigere)

Parestezii

Senzații patologice, nu neplăcute (eg, gâdilire)

Descrierea posibilă a durerii neuropate

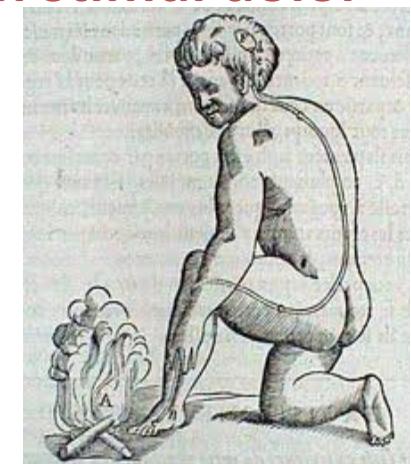
- Senzații

- ✓ Amorțire
- ✓ Gâdilire
- ✓ Ardere
- ✓ Parestezie
- ✓ Paroxismală
- ✓ Lanciată
- ✓ Electricitate
- ✓ Piele brutală
- ✓ Împușcare
- ✓ Profundă, plăcăritoare, durere în os



- Semne/Simptome

- ✓ **alodinia:** durere de la un stimul care de obicei nu evocă durerea
 - ❖ termic
 - ❖ mecanic
- ✓ **hiperalgezia:** răspuns exagerat la un stimul dolor normal



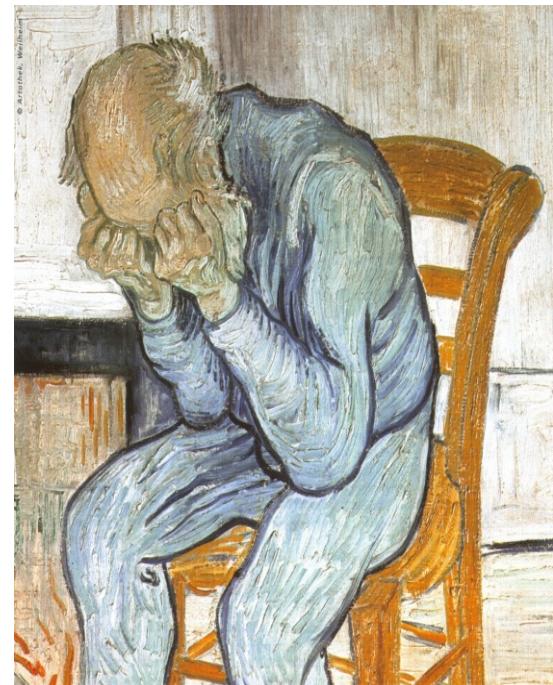
Alodinia

Mecanisme

- Sensitizarea centrală a fibrelor A β
- Reorganizarea centrală a fibrelor A β
- Pierderea controlului inhibitor
- Perturbarea blocajului aferent

Alte simptome ale durerii neuropatice

- Tulburări de somn
- Anxietate
- Depresie
- Modificări ponderale
- Afectarea calității vieții



Screeningul durerii neuropatice

Evaluarea simptomelor

1.NPQ – Neuropathic Pain Questionnaire

2.ID – Pain

3.Pain Detect

Evaluarea semnelor

1.LANSS – Leeds Assessment of Neuropathic Symptoms and Signs

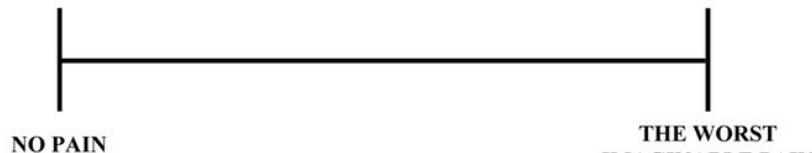
2.DN4 – Douleur Neuropathique en 4 Questions

Scale de apreciere a durerii

- Scala de apreciere numerică (Likert)
- Scala vizuală analogică (Huskisson, 1974)
- Scala de apreciere verbală
- McGill Pain Questionnaire (Melzack, 1975)

PAIN INTENSITY SCALE

WHAT TO ASK THE PATIENT?



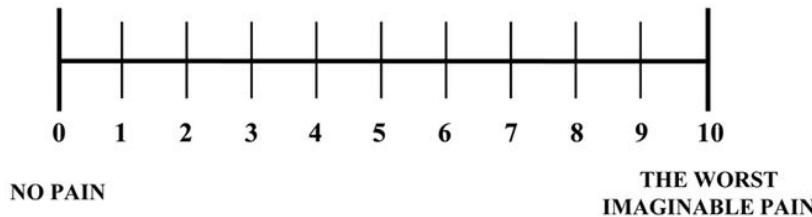
VAS

PLEASE MARK THE INTENSITY OF YOUR PAIN ON THE LINE



NRS

PLEASE CHOOSE THE NUMBER THAT BEST REPRESENTS THE INTENSITY OF YOUR PAIN

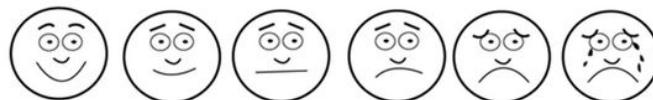


VRS

NO PAIN	MILD PAIN	MODERATE PAIN	INTENSE PAIN	MAXIMUM PAIN
---------	-----------	---------------	--------------	--------------

PLEASE CHOOSE THE TERM THAT BEST REPRESENTS THE INTENSITY OF YOUR PAIN

FPS



PLEASE CHOOSE THE FACE THAT BEST REPRESENTS THE INTENSITY OF YOUR PAIN

Metodele de apreciere a fibrelor senzitive

Fibre	Senzația	Testare clinică	Testare senzorială cantitativă	Examen de laborator
A β	Tactilă	Tifon	Filamente von Frey	Stimulodetectie, PESs
	Vibrație	Diapazon (128 Hz)	Vibrametru	
A δ	Pinprick, durere ascuțită Rece	Baston de lemn Termoroler	Ace dozate Termotest	Reflexe nociceptive, PEL
C	Cald Frigere	Termoroler	Termotest	PEL

Teste diagnostice

Sensorii

- Teste termice
- Filamentele von Frey
- Algometria
- Vibrametria
- Viteza de conducere

Motorii

- Electromiografie (EMG)
- Viteza de conducere

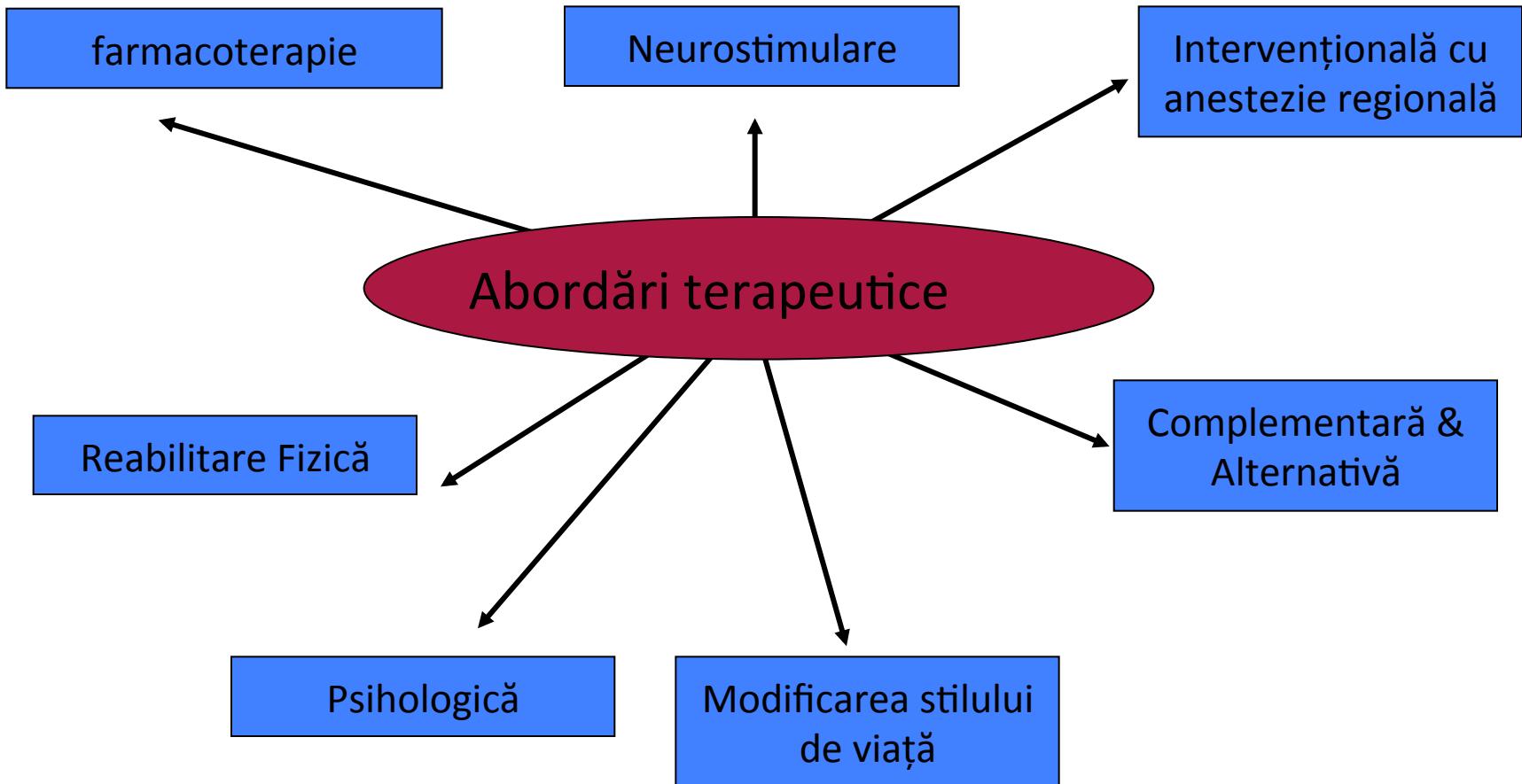
Vegetative

- Variabilitatea ritmului cardiac
- Teste sudomotorii
- Temperatura cutanată
- Fluxul sanguin

Teste diagnostice



Managementul durerii neuropate



Două recomandări esențiale

- ✓ *Primum non nocere („pe prim plan să nu dă unezi”)*

- ✓ *“Compașiunea Dvs pentru pacient – încercarea de a face maximal pentru ei - trebuie să fie forța majoră motivătoare în efortul Dvs de a fi competent”***

** From Dwight C. McGoon: *Ecstasy, a basis for Meaning in the World* Found in: Medicine Quotations: *Views of Health and Disease Through the Ages*: Huth, E.J. and Murray, T.J. eds.; American College of Physicians, Philadelphia 2000

Tratamentul durerii neuropate

- **Antidepresive**
- **Anticonvulsivante**
 - ✓ Prima generație
 - ✓ A doua generație
- **Analgezice opioacee**
- **Agenți topici și dermali**
- **Abordări non-farmacologice**

Antidepresive

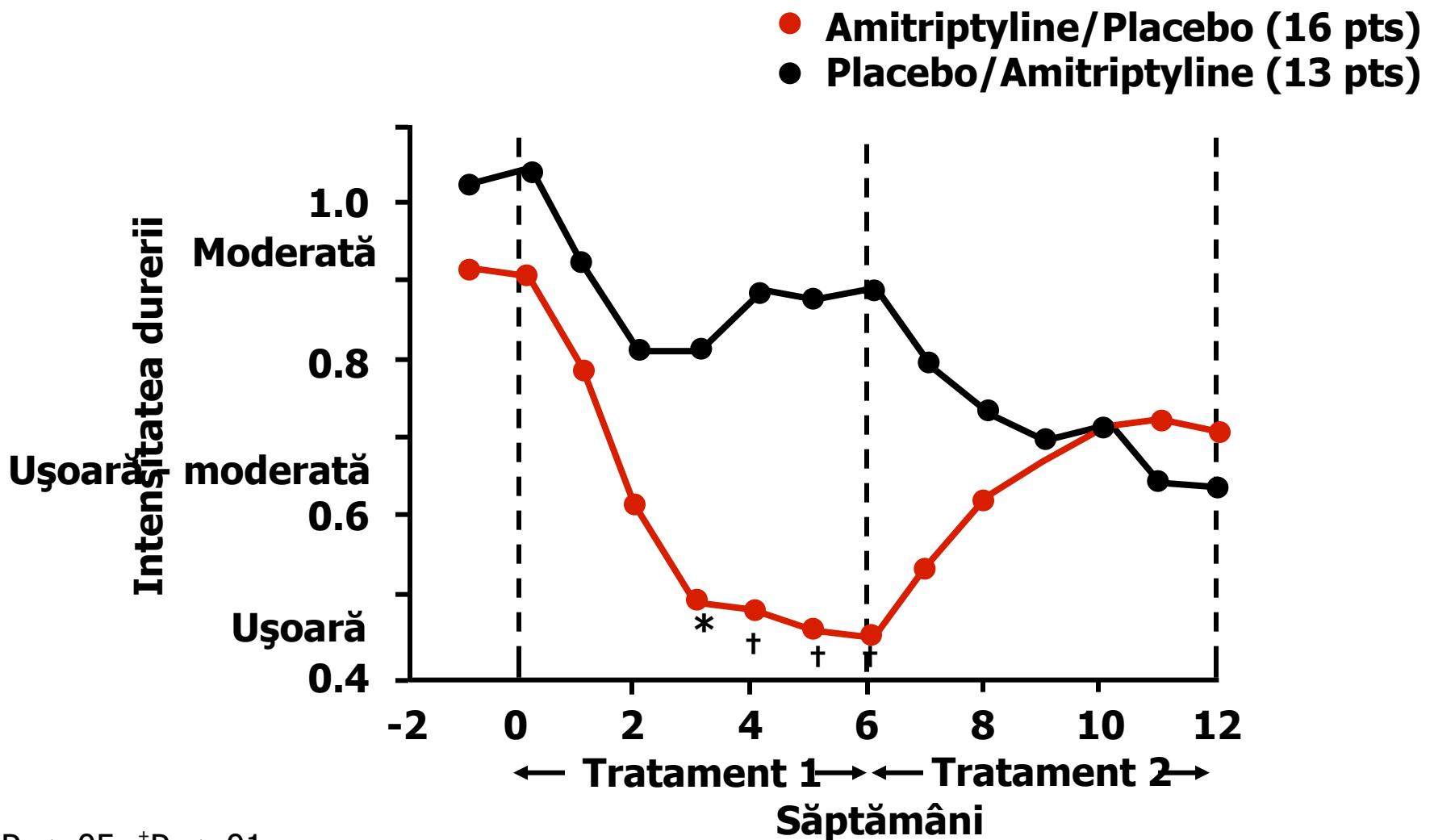
Clasificare

- Antidepresive triciclice (e.g. amitriptyline)
- Antidepresive tetraciclice (e.g. mirtazapine)
- SSRI (e.g. citalopram)
- SNRI (e.g. reboxetine)
- SSNRI – mecanism dual (e.g. duloxetine, venlafaxine)
- Inhibitori ai recaptării noradrenalinei & dopaminei (e.g. bupropion)
- Inhibitori MAO (e.g. moclobemid)
- Remedii melatonergice (e.g. agomelatine)
- Lithium

Antidepresive

- Antidepresivele triciclice au dat dovadă de eficiență semnificativă
- **Duloxetine** și **venlafaxine** de asemenea sunt eficiente
- Majorare treptată a dozei timp de 4 săptămâni
- Doze echivalente la 75 mg **amitriptyline**
- Efecte adverse anticolinergice și sedare

Eficiența Amitriptylinei



* $P < .05$; † $P < .01$.

Max MB et al. Neurology. 1987;37:589-596.

Agenti triciclici

- Amitriptyline
- Imipramine
- Nortriptyline
- Clomipramine
(Anafranil)

- Desipramine
- Doxepin
- Trimipramine
- Amoxapine
- Protriptyline

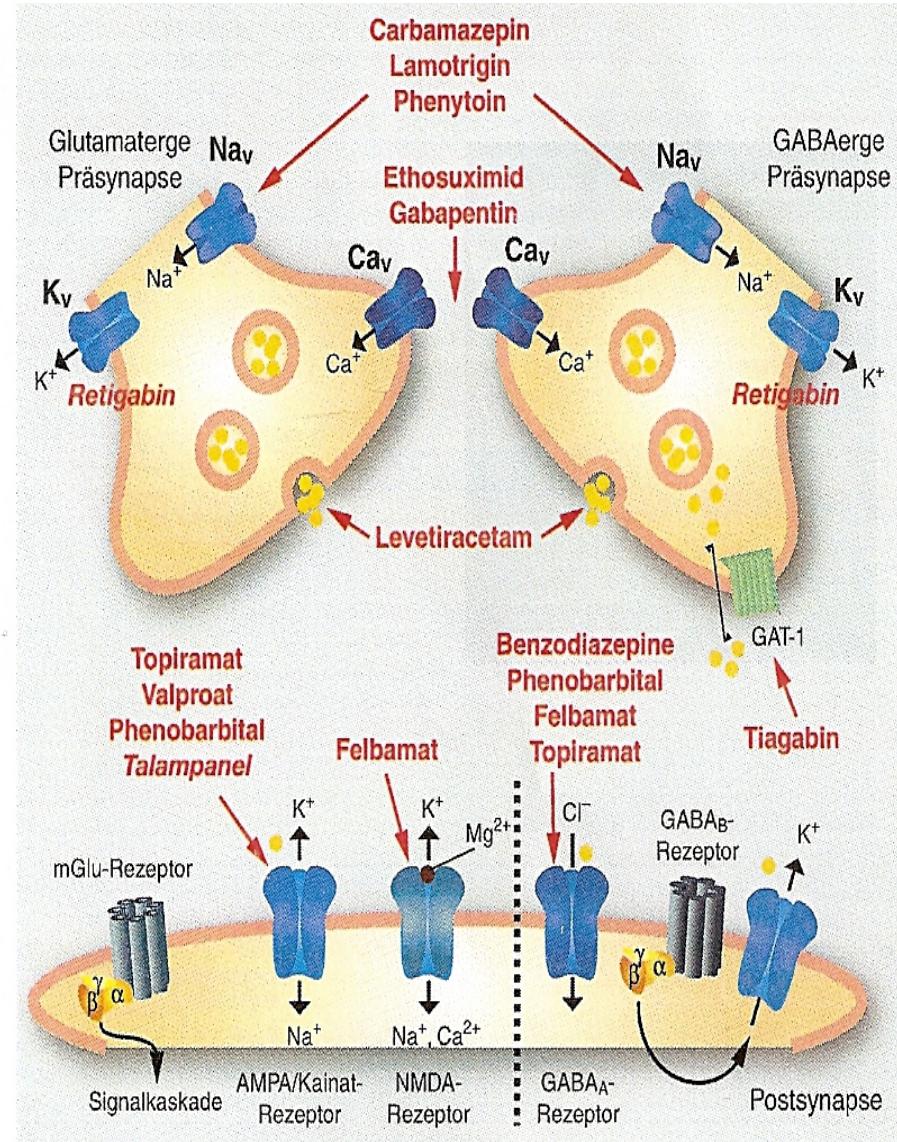
Efecte adverse la administrarea AD

Triciclice

- Somnolentă
 - Anxietate și agitare
 - Tulburări de memorie și cognitive
 - Senzația de uscăciune
 - Constipații
 - Retenția urinei
 - Neclaritatea vederii
 - Tahicardie, aritmii
- Hipotensiune ortostatică
 - Creștere ponderală
 - Creșterea transpirației
 - Amețeală
 - Afecțarea funcției sexuale
 - Contractii musculare
 - Fatigabilitate
 - Slăbiciuni
 - Grețuri

Anticonvulsivante

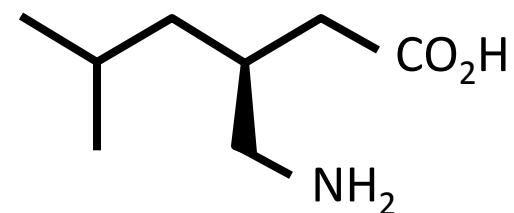
- Dovezi în tratamentul durerii:
 - gabapentin/pregabalin
 - phenytoin
 - acid valproic
 - carbamazepine/oxcarbazepine
 - topiramate
 - lamotrigine
 - lacosamide
- Majorare treptată a dozei timp de 4 săptămâni
- Intravenos phenytoin, acid valproic, lacosamide



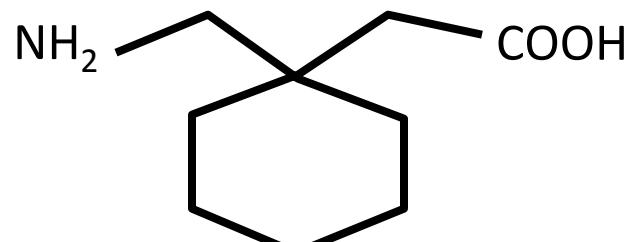
Anticonvulsivante de generația a două

Gabapentin și Pregabalin

- Sunt analogi ai GABA

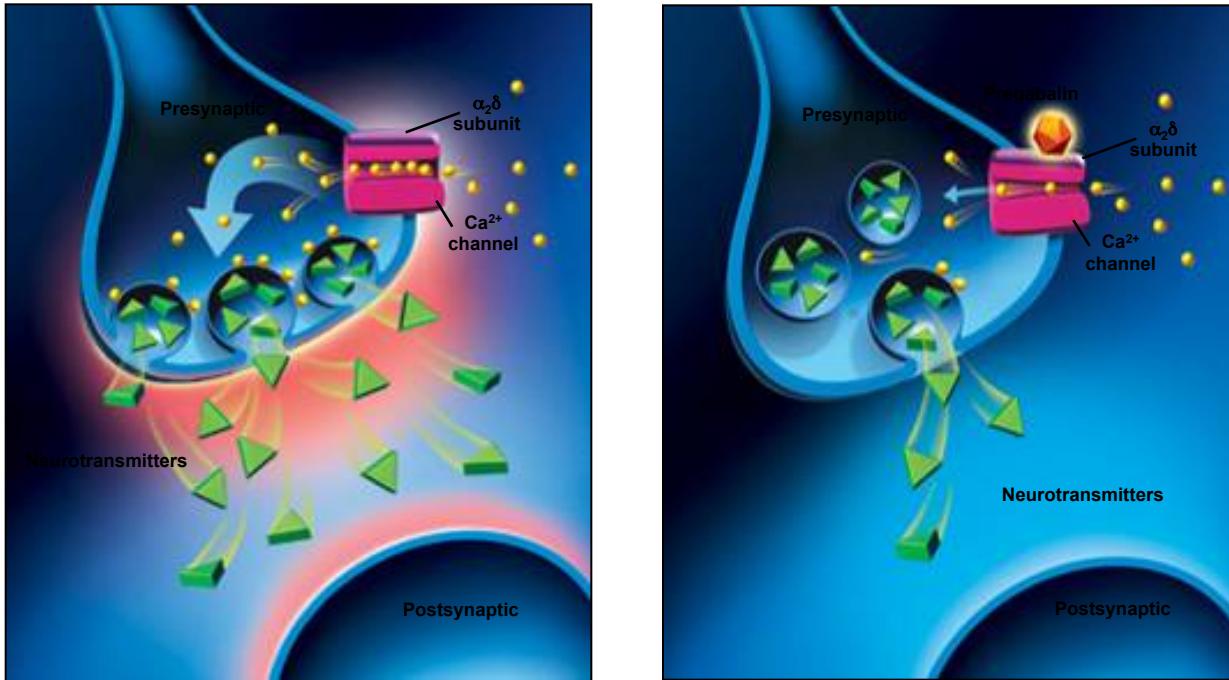


Pregabalin



Gabapentin

Pregabalin: Mecanismul de Acțiune



- Pregabalin selectiv se unește cu subunitățile $\alpha_2\delta$ a canalelor de calciu
 - ✓ Modulează influxul calciului în neuronii hiperexcitați
 - ✓ Reduce eliberarea neurotransmiterelor (eg, substanța P, glutamat, noradrenalina)

Fink K et al. *Neuropharmacology*. 2002;42:229-236; Dooley DJ et al. *Synapse*. 2002;45:171-190; Taylor CP. *CNS Drug Rev*. 2004;10:183-188.

Pregabalin Dozaj

- **Initial 50 mg 3 ori pe zi sau 75 mg x 2 ori – prima săptămână**
- **Majorare la 100 mg x 3 ori sau 150 mg x 2 ori peste o săptămână**
- **În caz de dureri exprimate – 450 - 600 mg/zi.**
- **Efectele adverse devin mai frecvente odată cu mărirea dozei**
- **Poate fi administrat indiferent de mese**
- **Nu sunt date de adicție**

Pregabalin – reacții adverse

- Amețeală
- Somnolență
- **Edeme periferice**
- Cefalalgii

Gabapentin

- Același mecanism de acțiune cu **PGB**, dar afinitate de 6 ori mai mică pt receptori
- Studiu multicentric, dublu orb placebo controlat, 165 pacienți cu doze de până la 3600 mg/zi
- Scorul durerii de la 6,4 la 3,9 **GBP** comparativ cu modificarea 6,5 la 5,1 placebo
- Reacții adverse **GBP**: ameteală și somnolentă
- Inițierea cu doze mici: 100-300 mg
- Dacă nu este ameliorare la 1800 mg/zi ,stop
- Eficiența începe la 3-8 săptămâni

Echivalență dintre Gabapentin și Pregabalin (mg/24 ore)

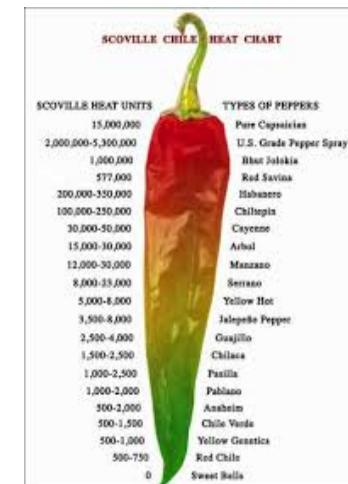
Gabapentin	Pregabalin
300	75
400	100
600	100-150
900	150
1200	150-300
1800	300
2400	400
3200	450
3600	600

[Pain. 2004 May;109(1-2):26-35] and clinical trial experience with Pregabalin
R.J. Tanenberg, MD ECU Diabetes Research Center, Greenville, NC (1999-2005)

Substanțe de uz local în durerea neuropatică



- Anestetici topici
 - Solutii cu lidocaină/procaină
 - Blocaj al nervilor periferici
- Capsaicin
- Toxină botulinică



Capsaicina în tratamentul durerii neuropatice

Degenerare reversibilă a fibrelor C

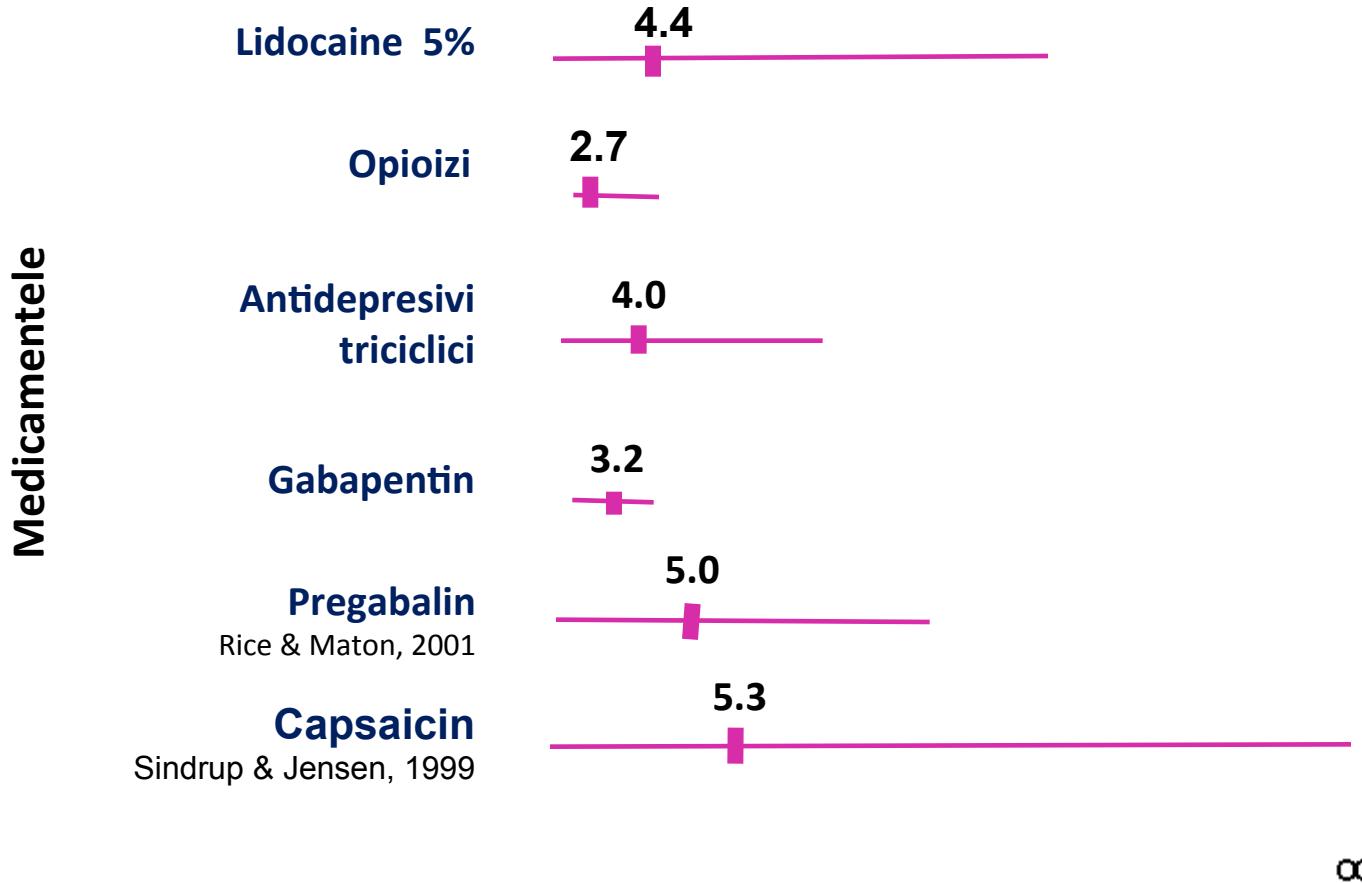


Analgezicele în durerea neuropată

- Antiinflamatoare NS, inclusiv paracetamol
- Opioizi:
 - codein
 - oxycodon



Eficiența tratamentului durerii în neuropatiile focale

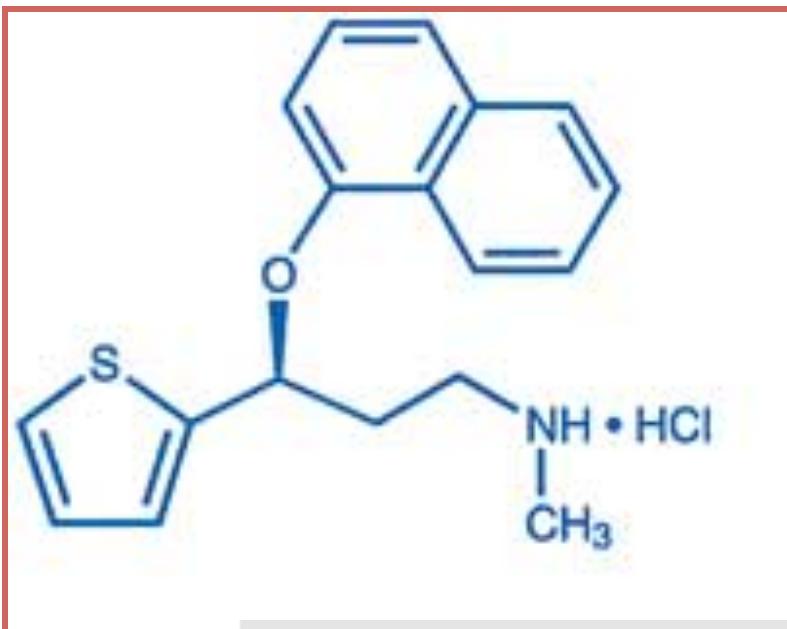


CI = interval de siguranță

**Numărul necesar de a fi tratați
(NNT)**

M ± 95% CI Meier et al. *Pain*. 2003;151-158.

Duloxetine



- Inițial produs de Eli Lilly (Cymbalta)

TABLE 8-4 Neuropathic Pain Medications Approved by the US Food and Drug Administration

Indication	Medication
Trigeminal neuralgia	Carbamazepine
Painful diabetic neuropathy	Duloxetine, pregabalin, capsaicin cream
Postherpetic neuralgia	Gabapentin, pregabalin, topical lidocaine, capsaicin 8% patch, capsaicin cream

Inhibitorii recaptării 5-HT și Norepinephrinei (NE)

Duloxetine și Venlafaxine

- Inhibă recaptarea NE și serotoninei și cresc disponibilitatea lor sinaptică
- Unele efecte adverse sunt datorate intercalării cu mai mulți receptori ai neurotransmisiei

Duloxetine

- Inhibitor al recaptării serotoninei și norepinefrinei (SNRI)
- Aprobat pentru tratamentul tulburărilor depresive majore și neuropatiei diabetice periferice
- Se administrează într-o singură priză 60 mg (marja 30-120 mg)
- Efecte adverse:
 - ✓ grețuri (20%)
 - ✓ insomnia (11%)
 - ✓ xerostomia (15%)
 - ✓ constipații (11%)
 - ✓ ușoară nepăsare
- Raportate cazuri de toxicitate hepatică

Duloxetine

Trial clinic de 12 săptămâni la 457 pacienți cu neuropatie diabetică doloră

- ✓ **O reducere de 50% a scorului de durere a fost atinsă la:**

26% pacienți grupul placebo,

49% - Duloxetine 60 mg/zi,

52% Duloxetine 120 mg/zi.

- ✓ **Ameliorare comparativ cu placebo = 23% (60 mg/zi)**

Goldstein, DJ et.al. *Pain* 116:109, 2005

Duloxetine

Trial clinic de 12 săptămâni la 457 pacienți cu neuropatie diabetică doloră

- ✓ **O reducere de 50% a scorului de durere a fost atinsă la:**

26% pacienți grupul placebo,

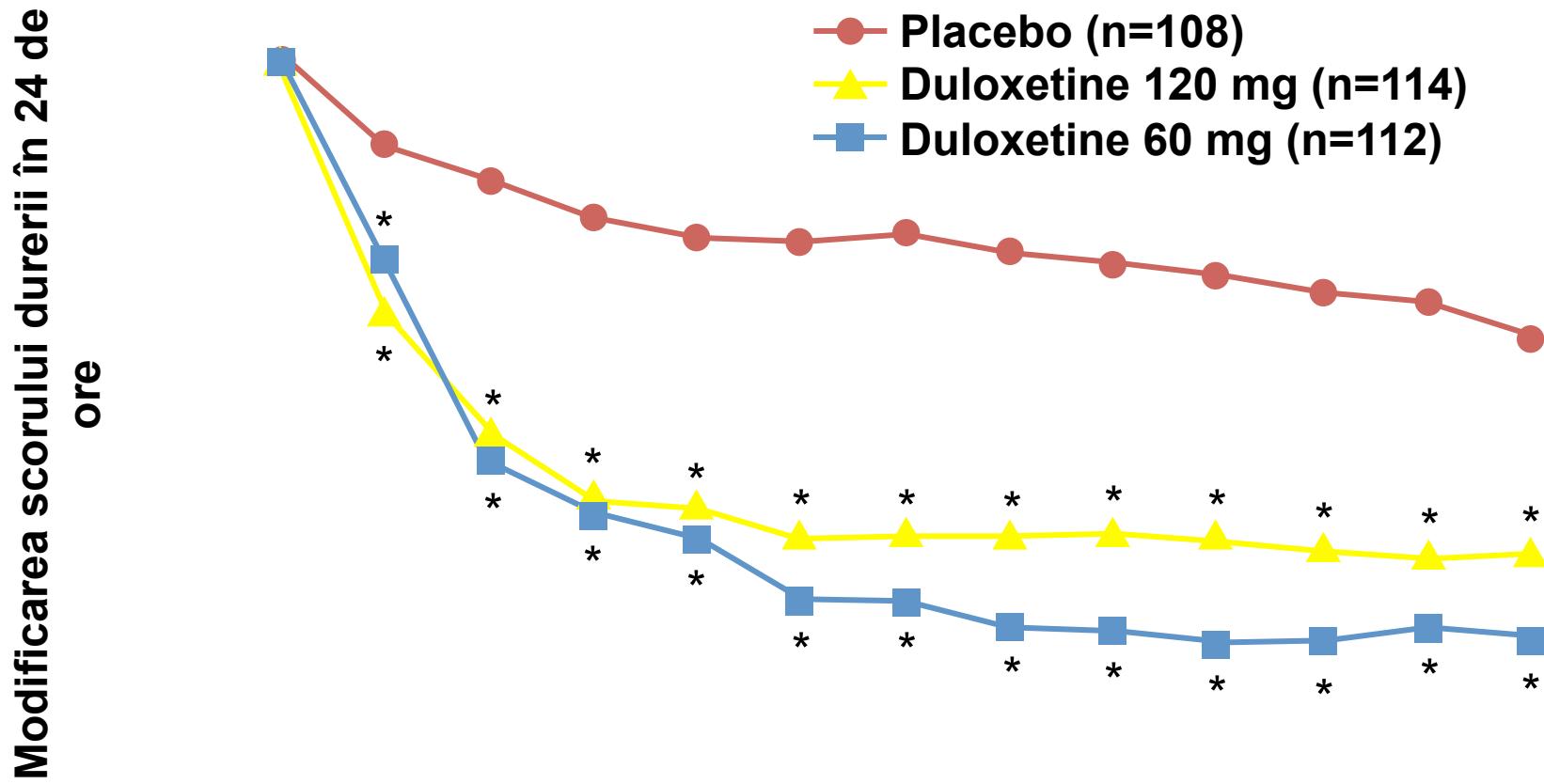
49% - Duloxetine 60 mg/zi,

52% Duloxetine 120 mg/zi.

- ✓ **Ameliorare comparativ cu placebo = 23% (60 mg/zi)**

Goldstein, DJ et.al. *Pain* 116:109, 2005

Duloxetine pentru Neuropatia Diabetică



* $P<0.001$ vs. placebo.

Săptămâna

Wernicke J et al. J Pain. 2004;5(suppl 1)

CONTINUUM Neuropathic Pain

TABLE 8-5 First-Line Pharmacotherapy of Neuropathic Pain

Medication	Dose	Adequate Trial	Side Effects	Comments
Tricyclic antidepressants				
Amitriptyline, nortriptyline	10–25 mg at bedtime, titrate up to a maximum of 150 mg/d	6–8 weeks (2 weeks at maximum dose)	Sedation, anticholinergic effects (eg, dry mouth, blurred vision, urinary retention), cardiac conduction abnormalities	Use with caution in patients with cardiac disease, risk of serotonin syndrome
Serotonin norepinephrine reuptake inhibitors (SNRIs)				
Duloxetine	30 mg once a day, titrate up to 60 mg twice a day	4 weeks	Nausea, increased sweating, increased blood pressure	Risk of serotonin syndrome, risk of hepatic dysfunction; <i>venlafaxine immediate</i>

April, 2017

Duloxetine Dozare

- Administrare într-o singură priză dimineața
- 30 mg – doza de start
- 60 mg – cea mai frecventă doză utilizată
- 120 mg – doza maximală

ORIGINAL ARTICLE

Dosing Pattern Comparison Between Duloxetine and Pregabalin among Patients with Diabetic Peripheral Neuropathic Pain

Peter Sun, MD, PhD*; Yang Zhao, PhD†; Zhenxiang Zhao, PhD†;
Mark Bernauer, BS, RPH†; Peter Watson, MS, MBA†

*Kailo Research Group, Fishers, IN, U.S.A.; †Global Health Outcomes, Eli Lilly and Company, Indianapolis, IN, U.S.A.

■ Abstract

Objective: To compare medication dosing patterns of duloxetine and pregabalin among patients with diabetic peripheral neuropathic pain (DPNP).

Methods: Applying a retrospective cohort study design on a large U.S. healthcare claims database, we examined the dosing patterns of duloxetine and pregabalin among commercially insured patients with DPNP aged 18 to 64 who initiated (a 90-day medication gap) duloxetine or pregabalin therapy in 2006. Selected patients had continuous enrollment during the 12-month pre- and post-index periods. The index mediation was used to classified individuals into the duloxetine or pregabalin cohorts. Initial daily dose, average daily dose over the first post-index year, and average daily dose of the first several prescriptions were estimated and compared across the cohorts.

Results: The study sample included 828 duloxetine and 1934 pregabalin-treated patients with a mean age of 50 years. Cardiovascular diseases, neuropathic pain other than DPNP, osteoarthritis, and diabetic retinopathy were the most common comorbid conditions. The average initial daily doses were 54.3 and 171.8 mg for duloxetine and pregabalin, respectively. The average daily dose over the first post-index year was 55.2 mg for duloxetine and 173.8 mg for pregabalin. The average daily dose for the first 10 duloxetine prescriptions ranged between 54.3 and 61.9 mg, but increased from 171.8 to 264.3 mg for pregabalin.

Conclusions: The commercially insured patients with DPNP who initiated duloxetine or pregabalin therapy had different dosing patterns. The average daily dose for duloxetine was relatively stable over time, while pregabalin-treated patients had significant dose increase over the 12-month post-index period. ■

ORIGINAL PAPER

EUROPEAN
THE INTERNATIONAL JOURNAL OF
CLINICAL PRACTICE

Comparative safety and tolerability of duloxetine vs. pregabalin vs. duloxetine plus gabapentin in patients with diabetic peripheral neuropathic pain

G. Irving,^{1,2} R. J. Tanenberg,³ J. Raskin,⁴ R. C. Risser,⁴ S. Malcolm⁴

Studiu comparativ Duloxetine vs Pregabalin

- ✓ Duloxetine are un profil mai bun pentru efecte adverse comparativ cu Pregabalin
- ✓ Pregabalin este de asemenea indicat în PND și este indicat la pacienții cu durere mai exprimată
- ✓ Ambele medicamente pot fi utilizate cu precauție – recomandare off label



The Journal of Pain, Vol 11, No 2 (February), 2010: pp 109-118
Available online at www.sciencedirect.com

Original Reports

The Clinical Importance of Changes in the 0 to 10 Numeric Rating Scale for Worst, Least, and Average Pain Intensity: Analyses of Data from Clinical Trials of Duloxetine in Pain Disorders

John T. Farrar,* Yili L. Pritchett,† Michael Robinson,‡ Apurva Prakash,§ and Amy Chappell§

**Department of Biostatistics and Epidemiology, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania.*

†*Global Pharmaceutical R&D, Abbott Laboratories, Abbot Park, Illinois.*

‡*Lilly USA, LLC, Indianapolis, Indiana.*

§*Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, Indiana.*

A double-blind, randomized trial of duloxetine versus placebo in the management of chronic low back pain

V. Skljarevski^a, M. Ossanna^a, H. Liu-Seifert^a, Q. Zhang^a, A. Chappell^a, S. Iyengar^a, M. Detke^a and M. Backonja^b

^aLilly Research Laboratories, Indianapolis, IN, USA; and ^bUniversity of Wisconsin Medical School, Madison, WI, USA

Keywords:

chronic low back pain,
duloxetine, randomized
controlled trial

Received 30 May 2008

Accepted 9 April 2009

Background: Duloxetine has demonstrated analgesic effect in chronic pain states. This study assesses the efficacy of duloxetine in chronic low back pain (CLBP).

Methods: Adult patients with non-radicular CLBP entered this 13-week, double-blind, randomized study comparing duloxetine 20, 60 or 120 mg once daily with placebo. The primary measure was comparison of duloxetine 60 mg with placebo on weekly mean 24-h average pain. Secondary measures included Roland-Morris Disability Questionnaire (RMDQ-24), Patient's Global Impressions of Improvement (PGI-I), Brief Pain Inventory (BPI), safety and tolerability.

Results: Four hundred four patients were enrolled, 267 completed. No significant differences existed between any dose of duloxetine and placebo on reduction in weekly mean 24-h average pain at end-point. Duloxetine 60 mg was superior to placebo from

Diagnosis and Management of Anxiety Disorders

By Peter Giacobbe, MD, MSc, FRCPC; Alastair Flint, MD, FRCPC, FRANZCP

REVIEW ARTICLE



CONTINUUM AUDIO
INTERVIEW AVAILABLE
ONLINE

ABSTRACT

PURPOSE OF REVIEW: This article provides a synopsis of the current understanding of the pathophysiology of anxiety disorders, the biological and environmental risk factors that contribute to their development and maintenance, a review of the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)* diagnostic criteria, and a practical approach to the treatment of anxiety disorders in adults.

RECENT FINDINGS: Despite the ubiquity of anxiety, the evidence is that most individuals with an anxiety disorder are not identified and do not receive guideline-level care. In part, this may be because of the manifold clinical

CITE AS:

CONTINUUM (MINNEAP MINN)
2018;24(3, BEHAVIORAL NEUROLOGY
AND PSYCHIATRY):893-919.

Address correspondence to
Dr Peter Giacobbe, Toronto
Western Hospital, 399 Bathurst
St, Room 7M-415, Toronto, ON
M5T 2S8, Canada, peter.
giacobbe@uhn.ca.

TABLE 12-2

Medications With US Food and Drug Administration-Approved Indications for Anxiety Disorders

Medication	Panic Disorder	Generalized Anxiety Disorder	Social Anxiety Disorder
Selective serotonin reuptake inhibitors (SSRIs)			
Escitalopram		X	
Fluvoxamine XR			X
Fluoxetine	X		
Paroxetine	X	X	X
Paroxetine CR			X
Sertraline	X		X
Serotonin norepinephrine reuptake inhibitors (SNRIs)			
Duloxetine		X	
Venlafaxine XR	X	X	X
Azapurones			
Buspirone		X	
Benzodiazepines			
Alprazolam	X		
Clonazepam	X		

CR = controlled release; XR = extended release.

TABLE 7-6

Antidepressants Used in Major Depressive Disorder

Class/Drug	Mechanism of Action	Possible Adverse Effects
Selective serotonin reuptake inhibitors (SSRIs)		
Fluoxetine, paroxetine, sertraline, citalopram, escitalopram, fluvoxamine	Blocks the 5-HT reuptake transporter	Headache, nausea, yawning, sweating, fatigue, insomnia, anxiety, sexual dysfunction, tremors, hyponatremia, serotonin syndrome
Vortioxetine	Blocks the 5-HT reuptake transporter and blocks 5-HT ₇ , 5-HT ₃ , and 5-HT _{1D} receptor; agonizes 5-HT _{1A} receptor; partial agonist at 5-HT _{1B}	Headache, nausea, yawning, sweating, fatigue, insomnia, anxiety, sexual dysfunction, tremors, hyponatremia, serotonin syndrome
Vilazodone	Blocks the 5-HT reuptake transporter and is a 5-HT _{1A} receptor partial agonist	Headache, nausea, yawning, sweating, fatigue, insomnia, anxiety, sexual dysfunction, tremors, hyponatremia, serotonin syndrome
Serotonin norepinephrine reuptake inhibitors (SNRIs)		
Venlafaxine, desvenlafaxine, duloxetine, levomilnacipran	Blocks 5-HT and norepinephrine reuptake transporters	Headache, yawning, fatigue, insomnia, anxiety, decreased libido, tremors, hypertension, nausea, diarrhea, sweating

Duloxetine

- Indicații:
 - Tulburare depresivă majoră (AAN – A)
 - Anxietate generalizată (AAN –A)
 - Fibromialgie (AAN –A)
 - Durere neuropată (AAN – B, EFNS –A)

Algoritmul de tratament al durerii neuropatice

FIRST LINE AGENTS:

- 1) gabapentin or pregabalin
- 2) duloxetine

SECOND LINE AGENTS:

- 1) amitriptyline or nortriptyline,
- 2) topiramate

THIRD LINE AGENTS

- 1) phenytoin
- 2) lamotrigine
- 3) carbamazepine

FOURTH LINE AGENTS

- 1) venlafaxine
- 2) levetiracetam
- 3) oxcarbazepine
- 4) zonisamide
- 5) mexiletine

FIFTH LINE AGENTS

- capsaicin cream
lidocaine cream 5%
sports creams