KLINIČKI PRISTUP DIJAGNOSTICI, PATOFIZIOLOGIJI I LIJEČENJU NEUROPATSKE BOLI

Mira Fingler

11. svibnja 2019.g.

HRVATSKI LIJEČNIČKI ZBOR
HRVATSKO DRUŠTVO ZA LIJEČENJE BOLI

DEFINICIJA BOLI

Bol - neugodni osjetni i emocionalni doživljaj povezan s aktualnim ili potencijalnim oštećenjem tkiva

IASP 1986.g.

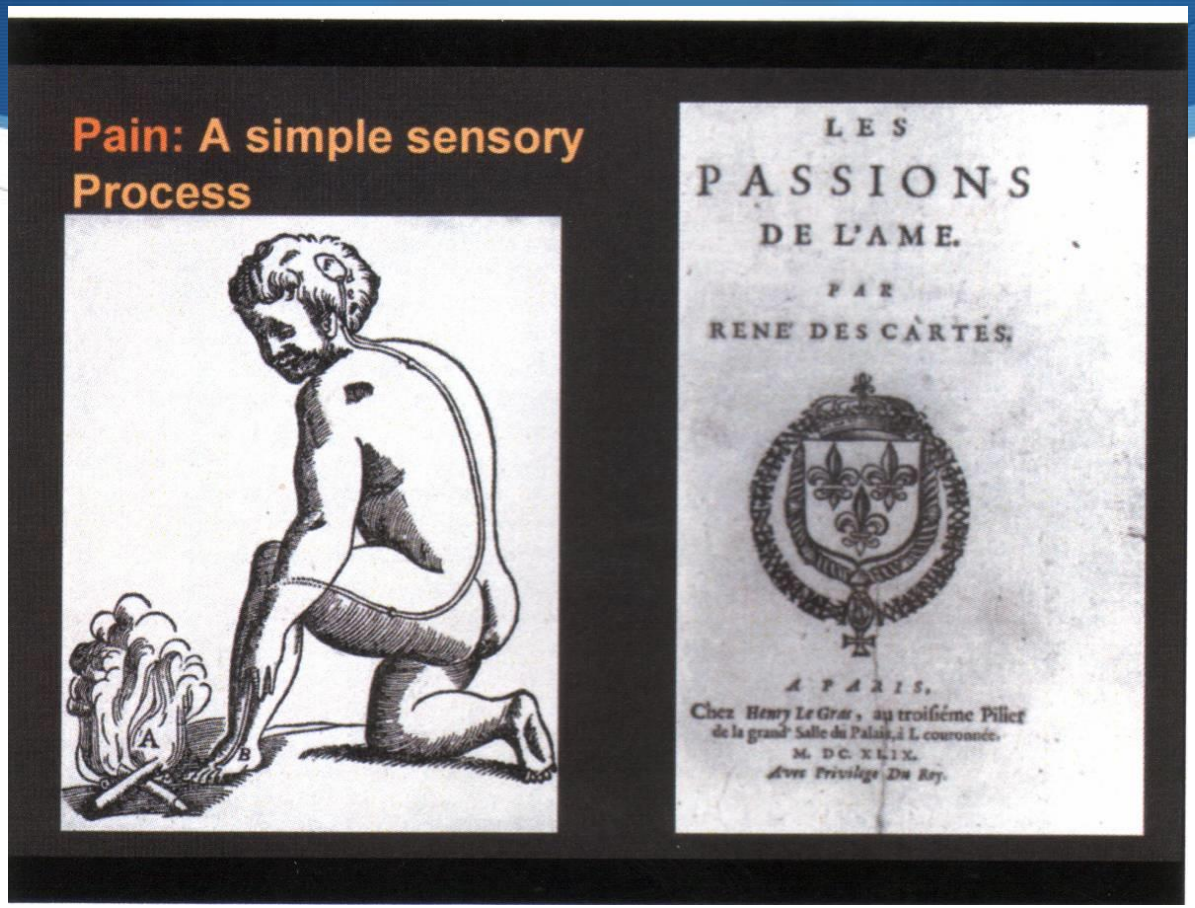
Neuropatska bol – uzrokovana oštećenjem ili bolešću somatosenzornog sustava

NeuPSIG 2007.g.

IASP - International Association for the Study of Pain

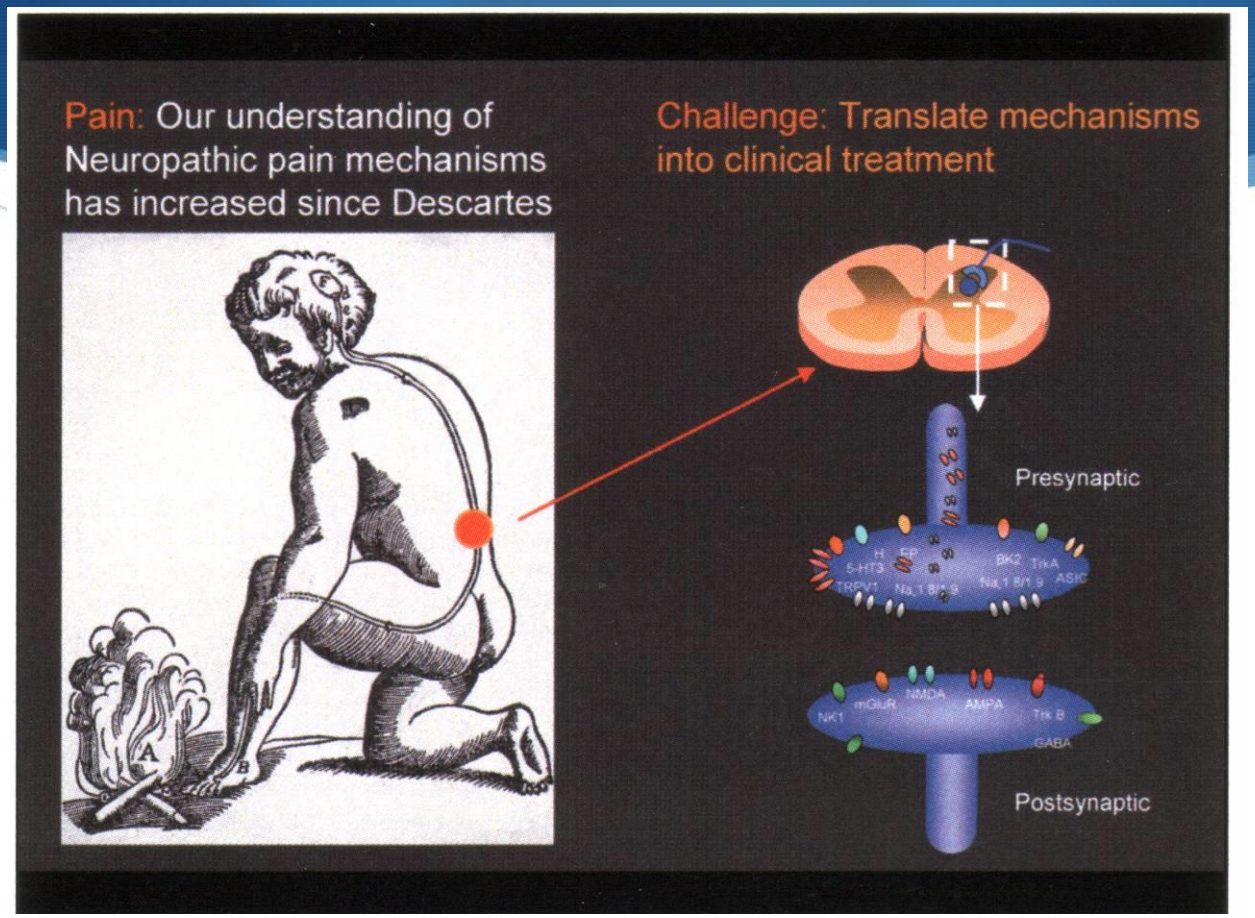
NeuPSIG – Special Interest Group on Neuropathic Pain of the IASP

NEUROPATSKA BOL



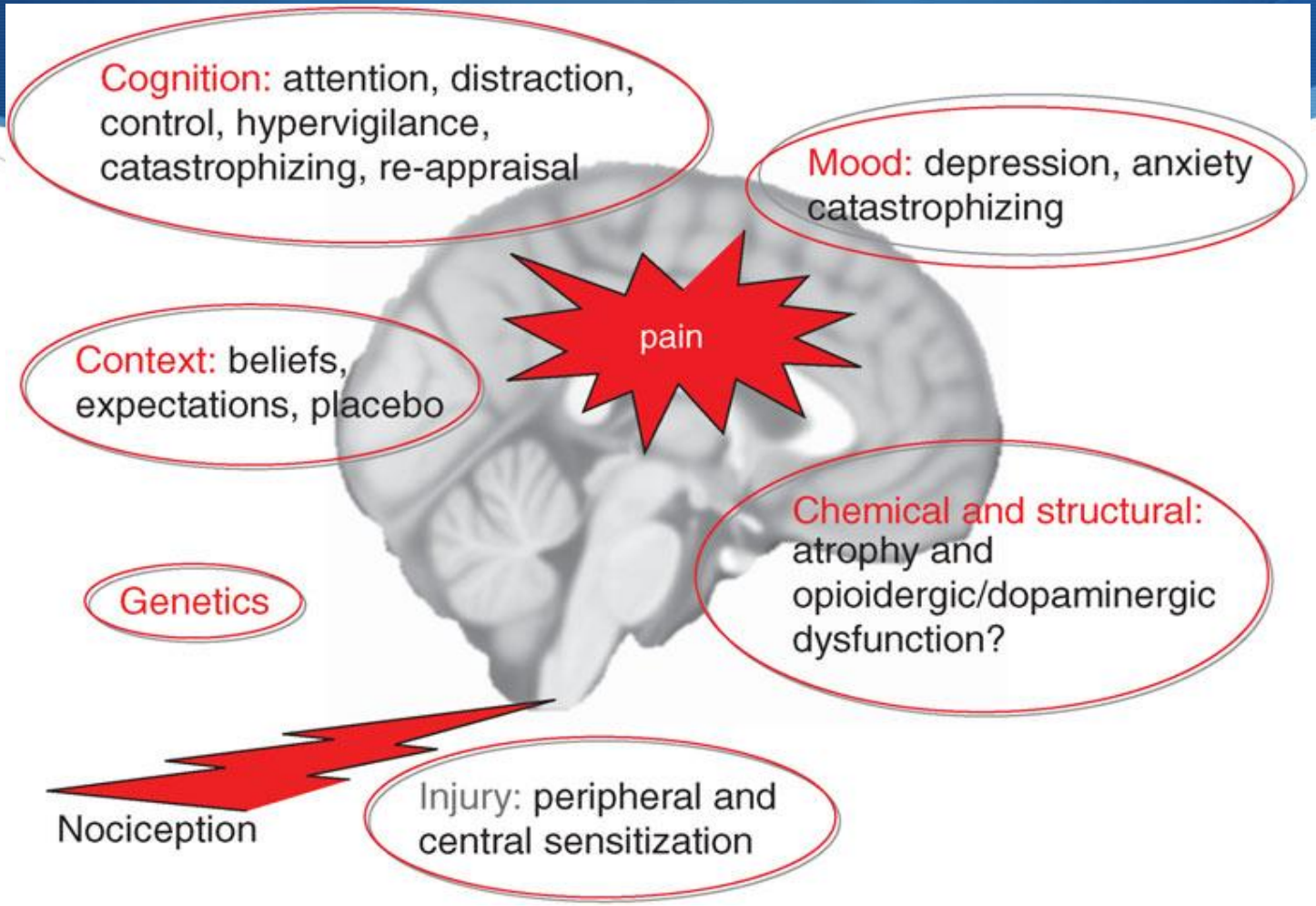
Troels.S.Jensen. The "Burning Issues" of Neuropathic Pain: New Partnerships in Managing Neuropathic Pain, International Congress of NeuPSIG 2004

NEUROPATSKA BOL



Troels.S.Jensen. The "Burning Issues" of Neuropathic Pain: New Partnerships in Managing Neuropathic Pain, International Congress of NeuPSIG 2004

KOMPLEKSNOST BOLNOG FENOMENA



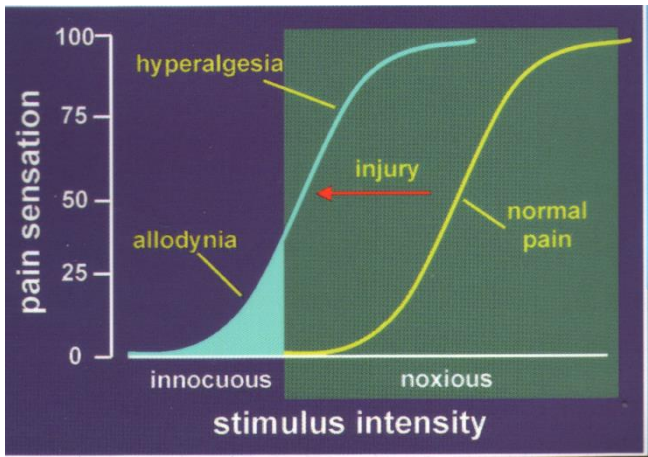
Tracey I. Imaging pain. Br J Anaesth 2008; 101: 32-9.

KLINIČKE KONTROVERZE U LIJEČENJU NEUROPATSKE BOLI

- Etiološki i klinički heterogena bolest
- Prevalencija 7-10%
- Refrakterna na konvencionalne analgetike
- Općenito ishod liječenja nije zadovoljavajući
- Neprepoznati aktualni patofiziološki mehanizmi svakog pojedinog bolesnika
- Nedovoljno specifični lijekovi

KLINIČKI PRISTUP NEUROPATSKOJ BOLI

- NeP bol predstavlja jedan od najvećih izazova u medicini boli
- U posljednjem desetljeću došlo je do značajnog napretka u razumijevanju i liječenju NeP boli, no ipak današnja razina uspješnosti liječenja još uvijek nije zadovoljavajuća.



KLINIČKI PRISTUP NEUROPATSKOJ BOLI

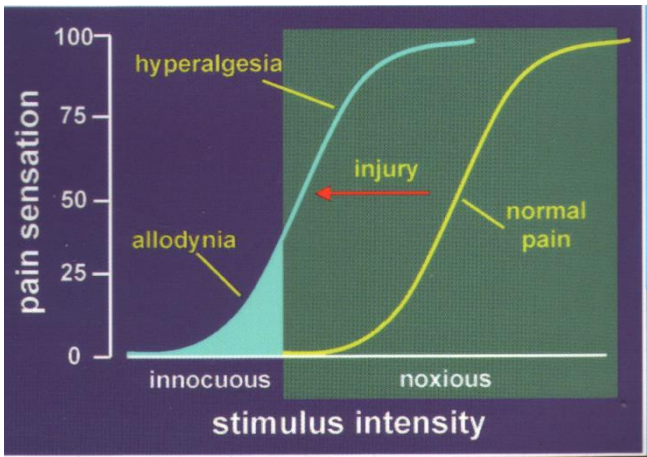
GORUĆI PROBLEMI U NeP BOLI:

1. **Nepredvidiv put od neurobiologije do kliničke slike**

2. **“Link” simptoma i mehanizama**

3. **Klasifikacija NeP boli**

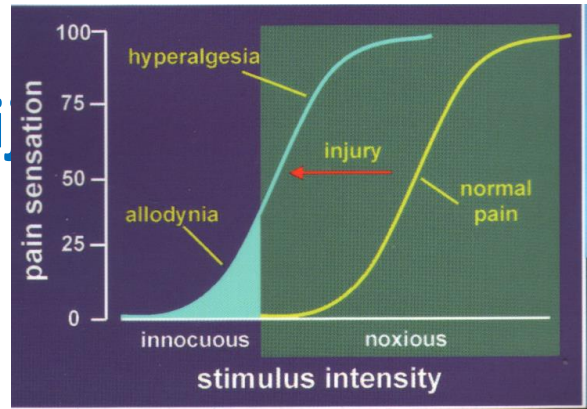
4. **Liječenje neuropatske boli**



KLINIČKI PRISTUP NEUROPATSKOJ BOLI

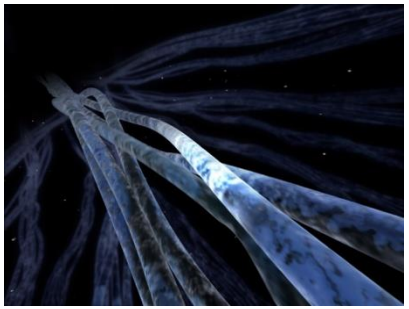
PREDVIDIVOST NeP BOLI:

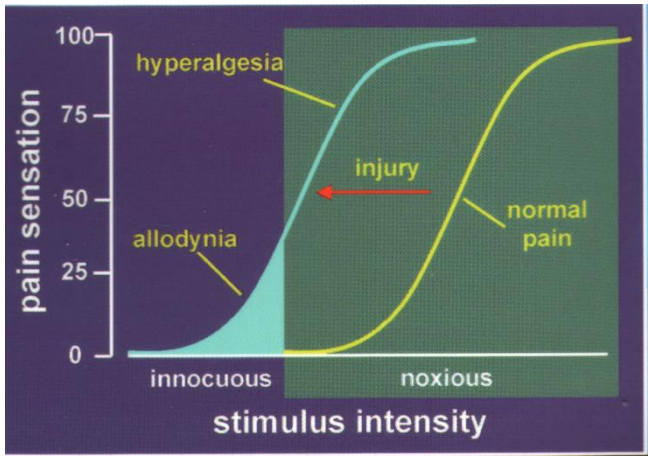
- Kronična bol=NeP bol?
- Čista i miješana NeP bol?
- Moguća NeP bol?
- Prevalencija 7-10 % ukupne populacij
- Neuropatija bez boli



NEUROPATHIC PAIN

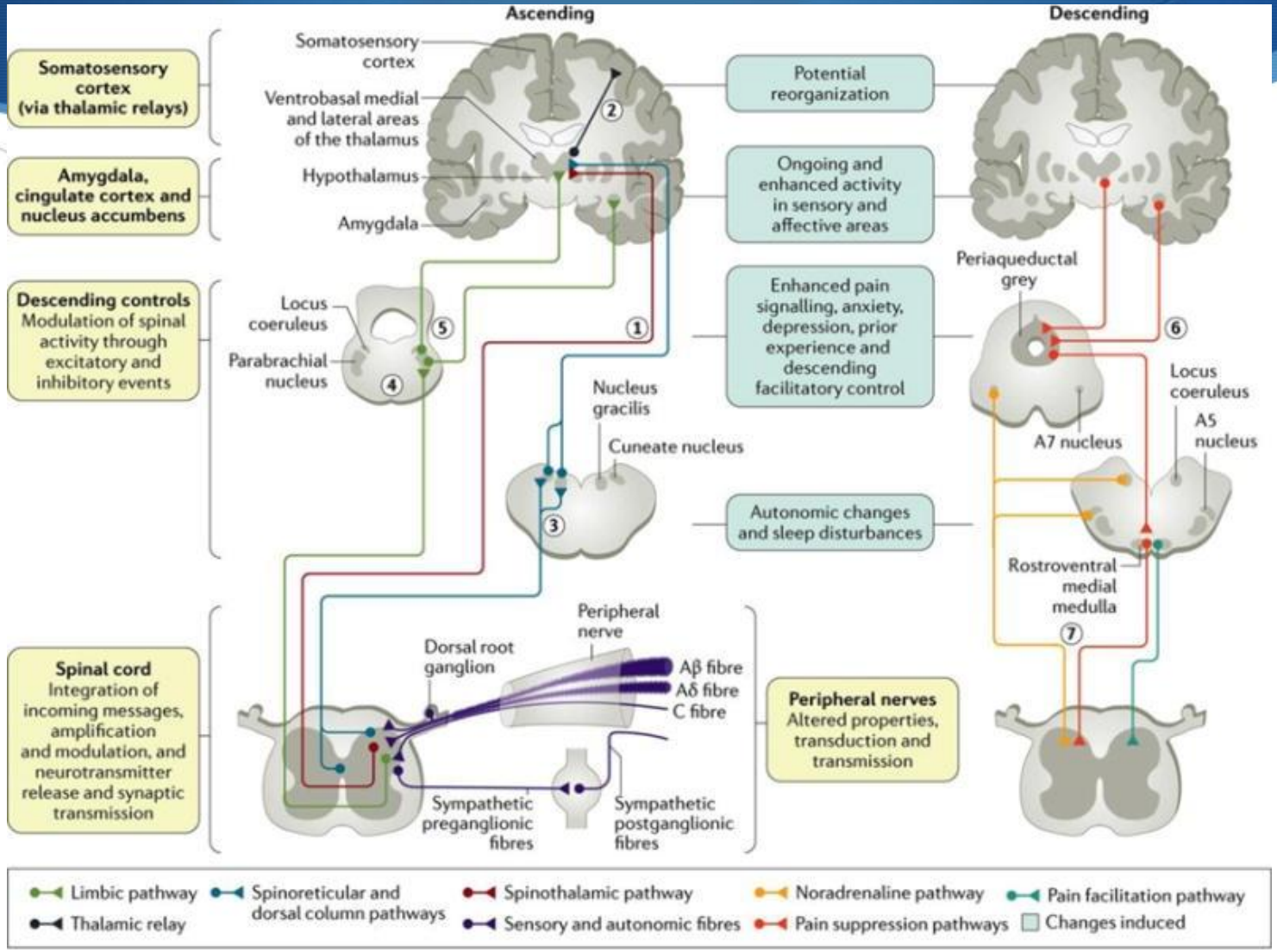
NeuP
SIG
2002





NEWSLETTER of IASP
Special Interest Group on Neuropathic Pain

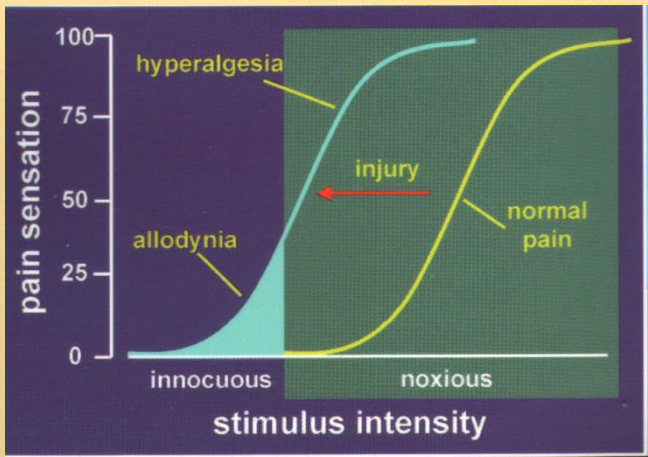
SENZORNI PUTEVI I PROMJENE U NEUROPATSKOJ BOLI



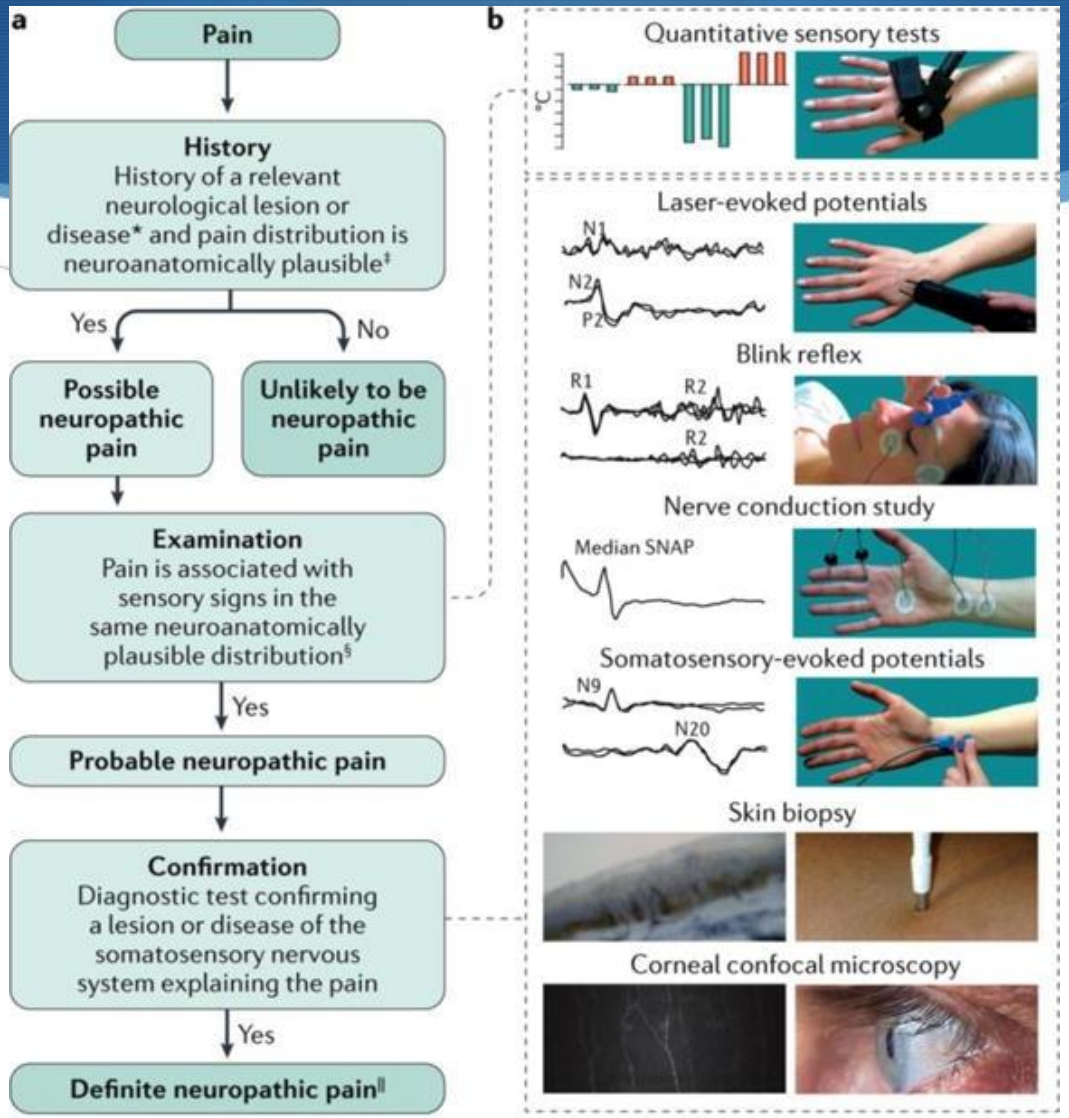
KLINIČKE KARAKTERISTIKE NEUROPATSKE BOLI

Clinical features of neuropathic pain

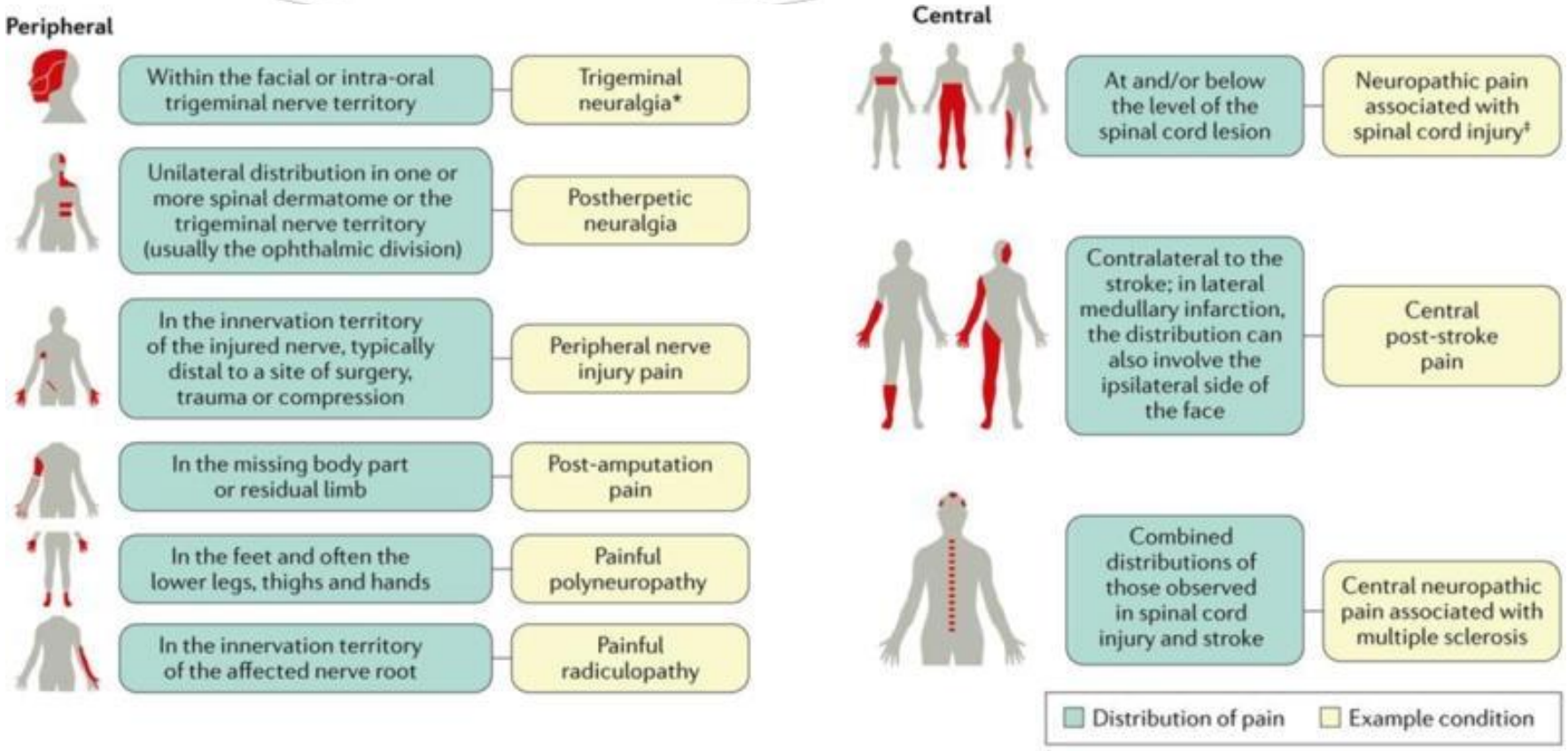
- **Positive phenomena**
  - **Spontaneous pain** *pain without stimulus*
    - **Continuous**
      - cutaneous
      - deep
      - visceral
    - **Paroxysmal**
  - **Evoked pain** *pain with stimulus*
    - **Allodynia** *qualitative abnormalities*
      - mechanical
        - dynamic
        - static
      - thermal
    - **Hyperalgesia** *quantitative abnormalities*
    - **Hyperpathia** *spatial and temporal abnormalities*
- **Autonomic dysfunction**
  - **Vasomotor** *vascular dysfunction*
  - **Sudomotor** *sweat and hair dysfunction*
- **Negative phenomena**
  - **Sensory loss**
    - thermal
    - vibration
    - soft



DIJAGNOSTIKA NEUROPATSKE BOLI



PERIFERNI I CENTRALNI ENTITETI NEUROPATSKE BOLI

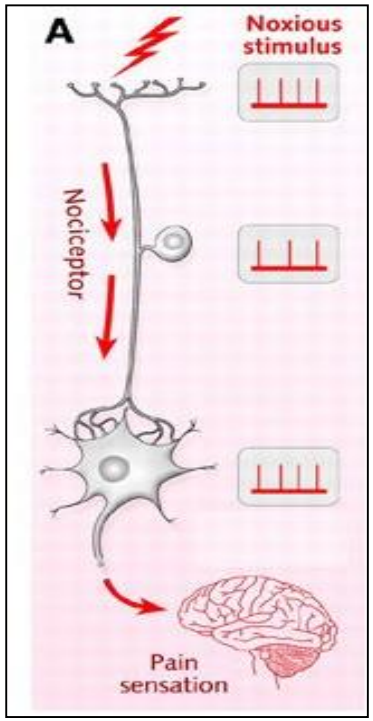


ALATI ZA SVAKODNEVNU RUTINSKU PRAKSU

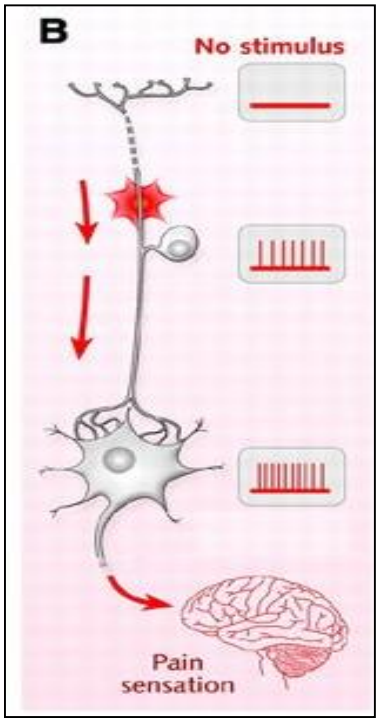
- Questionnaire DN4
- PainDetect
- Lansse

VRSTE BOLI PREMA PATOFIZIOLOGIJI

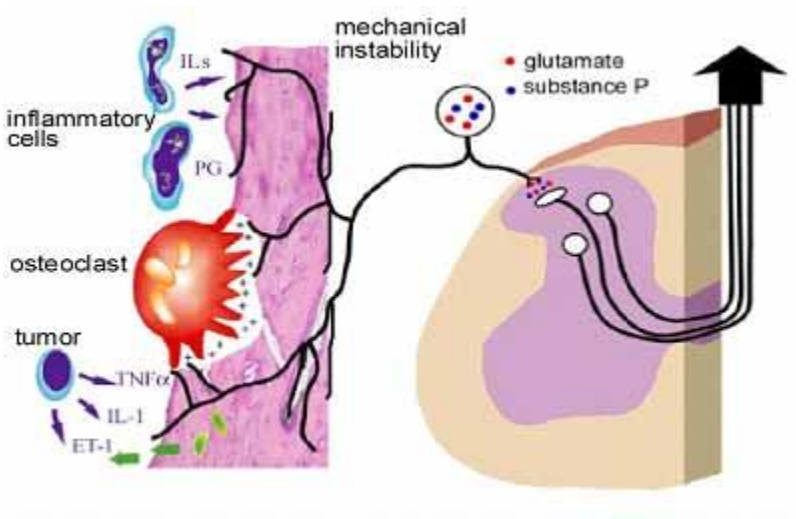
NOCICEPTIVNA BOL



NEUROPATSKA BOL

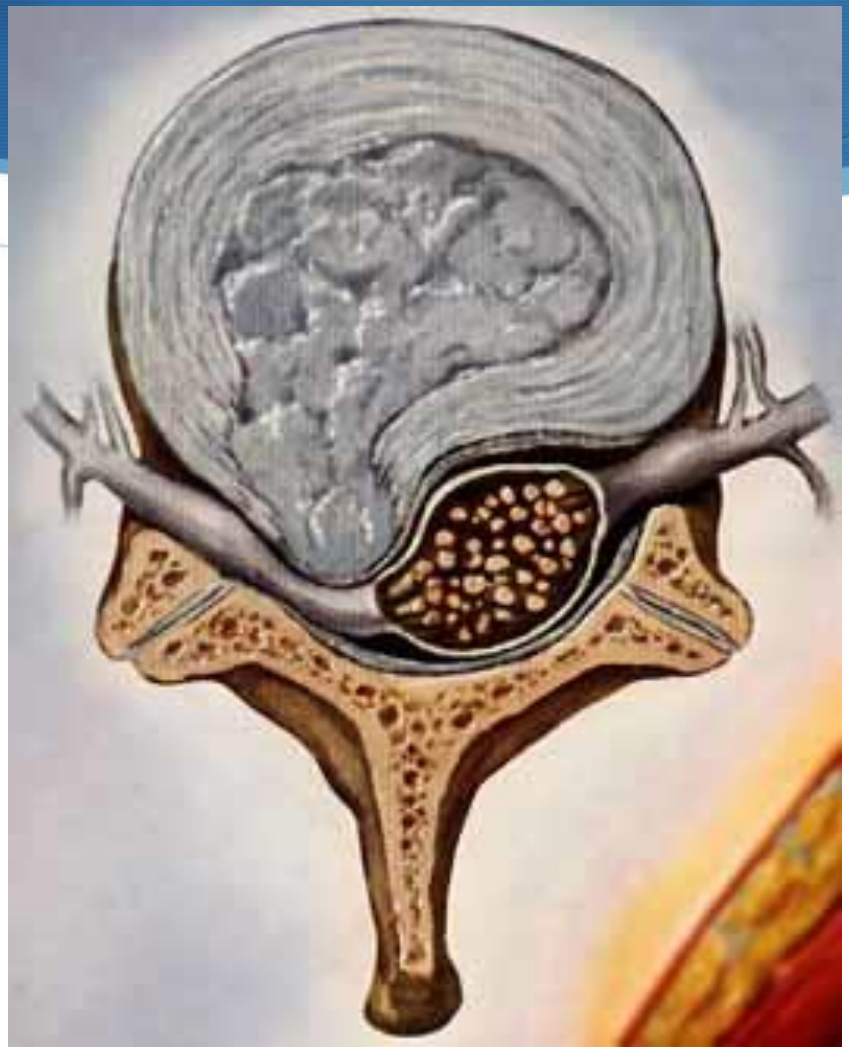


INFLAMATORNA BOL

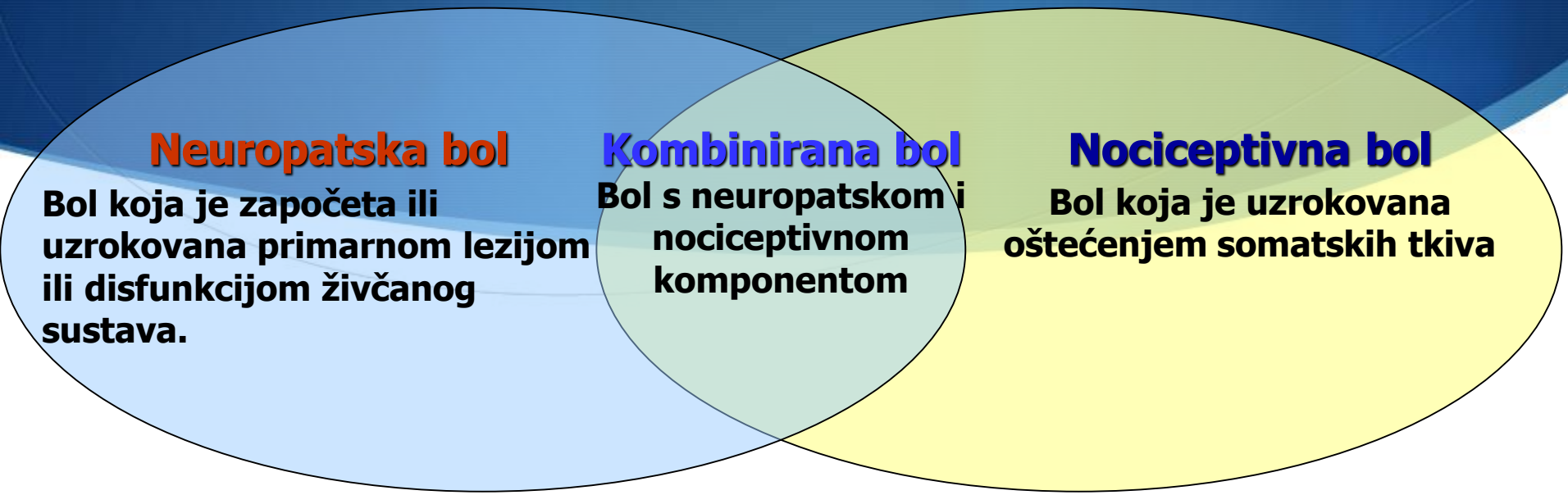


NAJČEŠĆE: MIJEŠANA
NOCICEPTIVNO-INFLAMATORNA-NEUROPATSKA BOL

NEUROPATSKA I/ILI NOCICEPTIVNA BOL?



Baron R, Binder A. 2004 Orthopade. 2004;33(5):568-75



Primjeri:

PŽS

- **Postherpetička neuralgija**
- **Trigeminalna neuralgija**
- **Diajabetička polineuropatija**

SŽS

- **Postinzultna bol**

Primjeri:

- **Lumbosakralni sindrom s radikulopatijom**
- **Karcinomska bol**
- **Sindrom karpalnog tunela**

Primjeri:

- **Upale**
- **Bol kod koštanog prijeloma**
- **Postoperativna bol**

1. International Association for the Study of Pain. IASP Pain Terminology.
2. Raja et al. in Wall PD, Melzack R (Eds). Textbook of pain. 4th Ed. 1999.;11-57

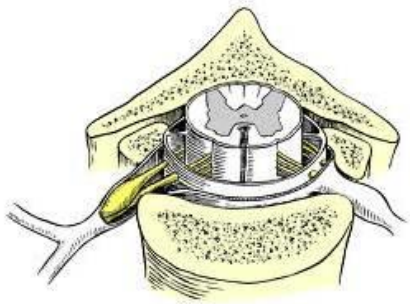
NEUROPATSKA BOL PRIDRUŽENA KARCINOMSKOM BOLNOM SINDROMU

CENTRALNI PATOFIZIOLOŠKI MEHANIZMI

- Centralna senzitizacija
- Neravnoteža ekscitacije i inhibicije
- Neuroglijalna aktivacija
- Anatomska reorganizacija
- Neuroglijalni modulatori (glutamat, GABA, P2X, kemokini)

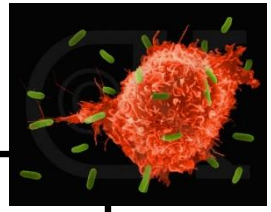
IZMJENJENA GENSKA EKSPRESIJA

- Čimbenici ozljede
- Trofički faktori
- Citokini, neutrofini



CENTRALNI PATOFIZIOLOŠKI MEHANIZMI

- Descendentna inhibicija
- Descendentna fascilitacija
- Monoamini, endorfini



TUMOR

- Rast
- Neurokemija
- Inune stanice
- Upalni medijatori

PERIFERNI PATOFIZIOLOŠKI MEHANIZMI

- Senzitizacija
- Hiperekscitabilnost
- Ektopičnost
- Ionski kanali, GPCRs, kinaze

KOMORBIDITET

- poremećaj spavanja zbog bola
- potencira anksioznost
- uzrokuje depresiju
- narušava kvalitetu života

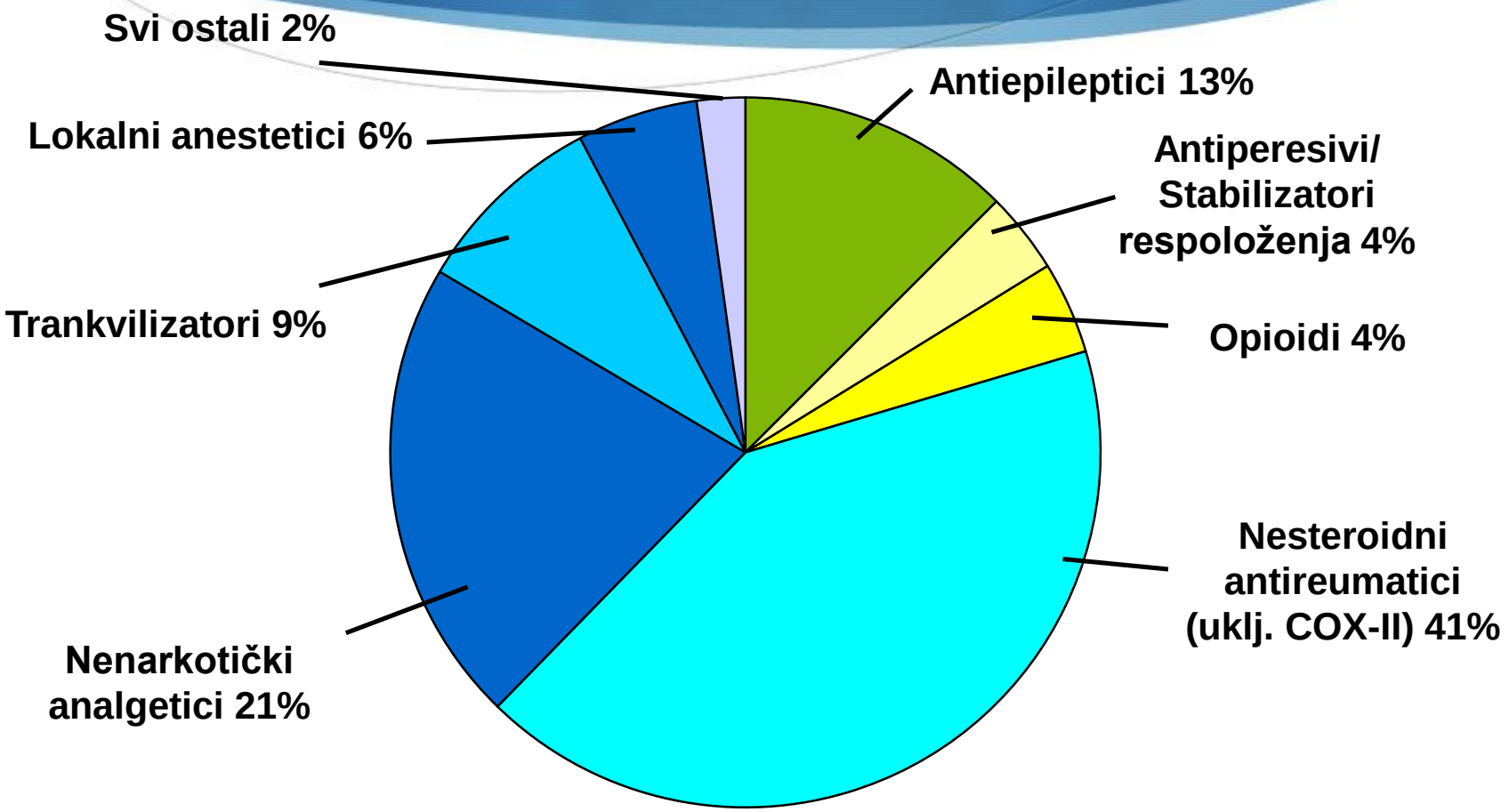
1. Baron. Clin J Pain. 2000;16:S12-S20.
2. Merskey H et al. (Eds) In: Classification of Chronic Pain:
Descriptions of Chronic Pain Syndromes and Definitions of Pain Terms. 1994:209-212.

ODNOSI IZMEĐU BOLI, SPAVANJA I ANKSIOZNOSTI/DEPRESIJE

Nicholson and Verma. Pain Med. 2004;5 (suppl. 1):S9-S27

NAJČEŠĆE KORIŠTENI LIJEKOVI U BOLESNIKA S NEUP

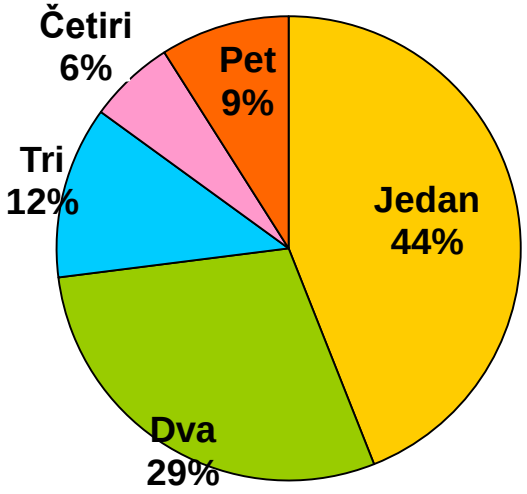
Premalo se koriste lijekovi dokazane učinkovitosti



IMS global Rx data 4Q 2003 (n=143 million Rx)

VIŠE OD POLOVICE BOLESNIKA S NEUROPATSKOM BOLI UZIMA VIŠE OD JEDNOG LIJEKA ZA SVOJU BOL

Polifarmakoterapija = 56%



Data on file, Pfizer Inc. Elderly PHN survey

SMJERNICE ZA FARMAKOLOŠKO LIJEČENJE NEUROPATSKE BOLI

- Attal N, Cruccu G, Haanpaa M, Hansson P, Jensen TS, Nurmikko T, et al. **EFNS Task Force. EFNS guidelines on pharmacological treatment of neuropathic pain.** *Eur J Neurol*. 2006;13:1153–1169

- Dworkin RH, O'Connor AB, Backonja M, Farrar JT, Finnerup NB, Jensen TS, et al. **Pharmacologic management of neuropathic pain: evidence-based recommendations.** *PAIN®*. 2007;132:237–251

- Moulin DE, Clark AJ, Gilron I, Ware MA, Watson CPN, Sessle BJ, et al. **Velly A; Canadian Pain Society. Pharmacological management of chronic neuropathic pain: consensus statement and guidelines from the Canadian Pain Society.** *Pain Res Manage*. 2007;12:13–21

- Hrvatsko društvo za liječenje boli Hrvatskog liječničkog zbora. Smjernice za farmakološko liječenje neuropatske boli. 2009.

MEHANISTIČKA KLASIFIKACIJA ANALGETIKA – FARMAKOLOŠKA MODULACIJA BOLI

Lussier D, Beaulieu P 2010

Antinociceptivni analgetici

- Neopioidi
- Acetaminofen
- NSAIL
- Opioidi
- Kanabinoidi

Modulatori periferne transmisije ili senzitizacije

- Lokalni anestetici
- Karbamazepin
- Okskarbazepin
- Topiramat
- Kapsaicin

Antihiperalgezici

- NMDA antagonisti
- Gabapentinoidi (gabapentin,pregabalin9
- Levetiracetam
- Koksibi

Modulatori descedentne inhibicije ili ekscitacije

- Triciklički antidepresivi
- SNRI
- SSRI
- Alfa-2-adenergički agonisti

Mješani antinociceptivni analgetici i modulatori

- descedentne inhibicije ili ekscitacije
- Tramadol
- Tapentadol

Ostali

- Kalcitonin
- Bifosfanati

SMJERNICE ZA FARMAKOLOŠKO LIJEČENJE NEUROPATSKE BOLI

Summary of recommendations for pharmacological management of neuropathic pain

	EFNS [7]			NICE [10]		CPS [2]		NeuPSIG [4
	Diabetic neuropathy	**Post-herpetic neuralgia**	**Trigeminal neuralgia**	**Central neuropathic pain**	**All neuropathic pain**	**Trigeminal neuralgia**	**All neuropathic pain**	**Trigeminal neuralgia**	**All neuropa pain**
First-line therapy	Duloxetine Gabapentin Pregabalin TCA Venlafaxine[d]	Gabapentin Pregabalin TCA Lidocaine plasters[a]	Carbamazepine Oxcarbazepine	Gabapentin Pregabalin TCA	Amitriptyline Duloxetine Gabapentin Pregabalin Capsaicin cream[b] (localized pain in patients who wish to avoid or who cannot tolerate oral treatments)	Carbamazepine	Gabapentin Pregabalin Duloxetine Venlafaxine[d] TCA	Carbamazepine	Gapabentin Gabapentin ER/enacarbil Pregabalin Duloxetine Venlafaxine[d] TCAs
Second-line therapy	Tramadol	Strong opioids Capsaicin cream		Tramadol Strong opioids	One of the remaining 3 oral drugs of the First-line therapy		Tramadol Strong opioids Lidocaine cream[c] Lidocaine patches[c]		Capsaicin patches[b] Lidocaine patches[b] Tramadol
Third-line therapy	Strong opioids			Strong opioids	One of the remaining 3 oral drugs of the First-line therapy		Cannabinoids		Botulinum tox type A Strong opioids
Fourth-line therapy				Lamotrigine (in central post-stroke pain) Cannabinoids (in multiple sclerosis)			Other opioids Lacosamide Lamotrigine Botulinum toxin Lidocaine cream Lidocaine patches		

CPS Canadian Pain Society, *EFNS* European Federation of Neurological Societies, *ER* extended release, *NeuPSIG* Neuropathic Pain Special Interest Group, *NICE* National Institute for Health and Care Excellence

[a]For use in the elderly; [b]for use in localized pain; [c]for use in post-herpetic neuralgia; [d]in most European countries, including Italy, venlafaxine is not approved for the indication of "neuropathic pain", and therefore any s use should be considered off-label

- Giorgio Cruccu and Andrea Truini**A review of Neuropathic Pain: From Guidelines to Clinical Practice.** Pain Ther. 2017 Dec; 6(Suppl 1): 35–42.

POGLED U BUDUĆNOST

NeuPSIG Reviews

PAIN

NeuP SIG

Individualized neuropathic pain therapy based on phenotyping: are we there yet?

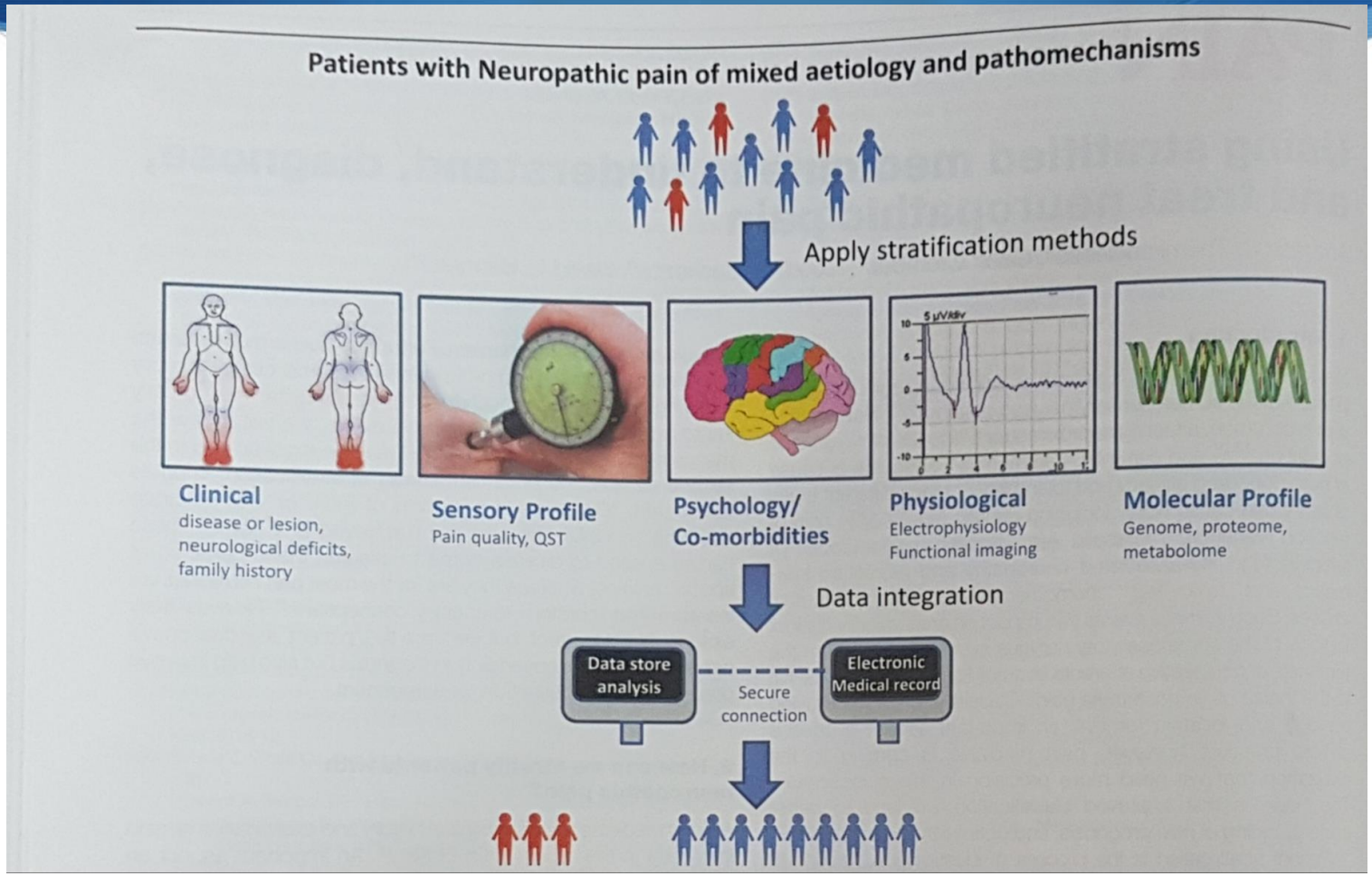
Julia Forstenpointner, Jan Otto, Ralf Baron*

Abstract

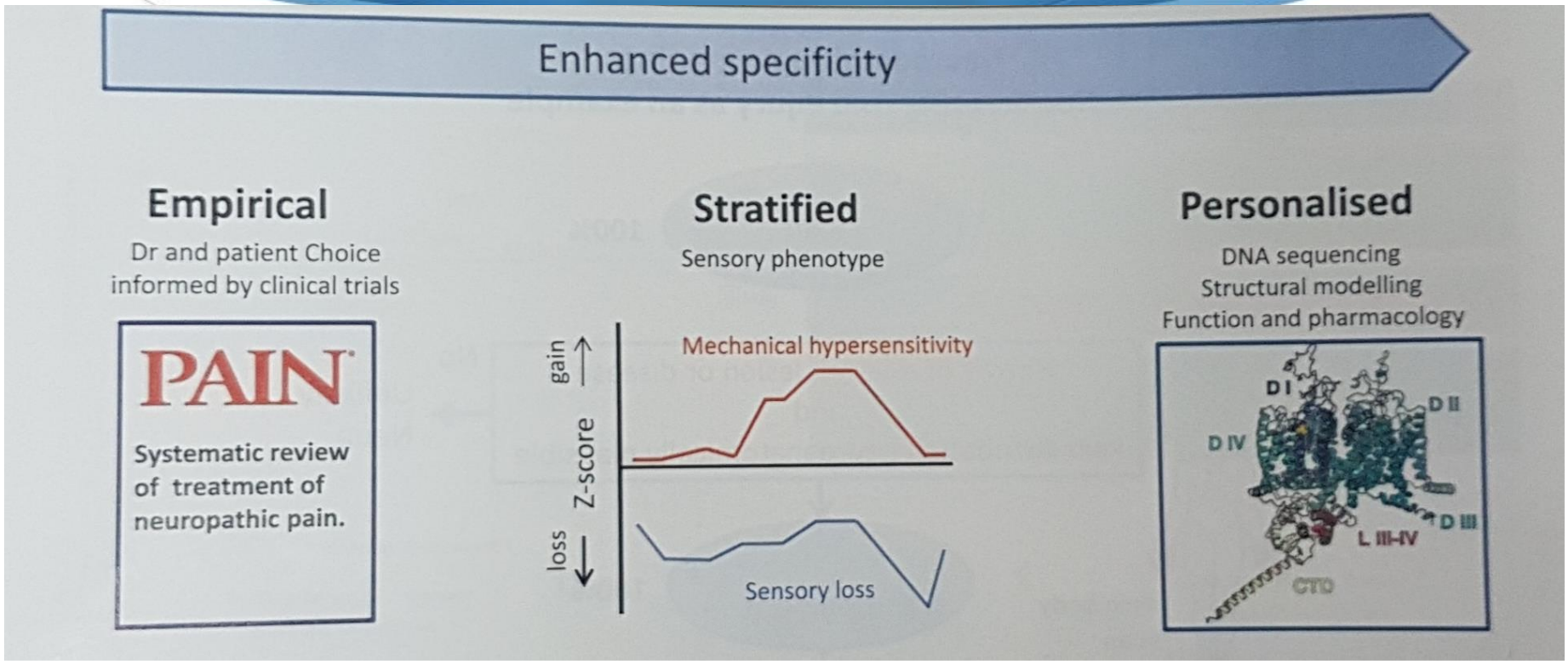
Patients with the same neuropathic pain disorder may have completely different sensory signs and symptoms yet receive the same medicinal treatment. New concepts suggest that patient stratification according to their pain mechanisms, reflected in their sensory phenotype, could be promising to implement an individualized therapy in neuropathic pain. Retrospective classification of patients according to their sensory phenotype showed predictive validity and reliability for treatment response in certain subgroups of patients. Recent prospective studies using stratification based on sensory phenotypes confirm this concept. In this article, we review the recent accomplishments towards an individualized pharmacological treatment of neuropathic pain.

Keywords: Chronic pain, Sensory phenotype, Mechanism-based treatment, Human pain model, Quantitative sensory testing, Patient-reported outcome

SVJETLO NA KRAJU TUNELA



INDIVIDUALNI PRISTUP PREMA PATOFIZIOLOŠKIM MEHANIZMIMA JE UČINKOVITIJI



ZAKLJUČAK

- Interdisciplinarno
- Multimodalno
- Individualno
- Utemeljeno na dokazima

"The Future of Pain Therapy: Something Old, Something New, Something Borrowed, and Someting Blue and a Silver Sixpence in her Shoe."

Allan I. Basbaum, The Patch of Pain 1975-2005.