BOL

Prof dr D.Golić

Project number: 585927-EPP-1-2017-1-RS-EPPKA2-CBHE-JP (2017 – 3109 / 001 – 001)

Definicija

- Prema definiciji Međunarodne asocijacije za istraživanjje bola (*IASP - International Association for the Study of Pain),* **bol je neprijatno emocionalno i osećajno iskustvo povezano sa stvarnom ili potencijalnom povredom tkiva, ili uzrokovano tim oštećenjem ili povredom.**

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Why treat pain?

- 50-75% of patients who die in the hospital die with pain[1]
- 25% of all cancer patients die with pain[2]
- It is estimated that 85-90% of pain is easily treated with medication, usually opioids and adjuvants
- It is considered the "Fifth vital sign"

1-www.painmed.org/PatientCenter/Facts_on_Pain.aspx

2-Medtronics Cancer Pain Fact Sheet

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Podjela bola

- akutni i hronični
- Prema mehanizmu nastanka bola, postoji nociceptivni i neuropatski bol (rezultat neposrednog oštećenja nervnog sistema)

USA

- 1. Acute
- 2. Cancer
- 3. Chronic non-malignant

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Nociceptivni sistem

- Nocere-povrijediti, oštetiti
- Elementi nociceptivnog sistema su periferni receptori za bol - nociceptori, senzitivna nervna vlakna, dorzalni rog kičmene moždine, ushodni putevi, te centralna područja koja uključuju talamus i senzorni korteks

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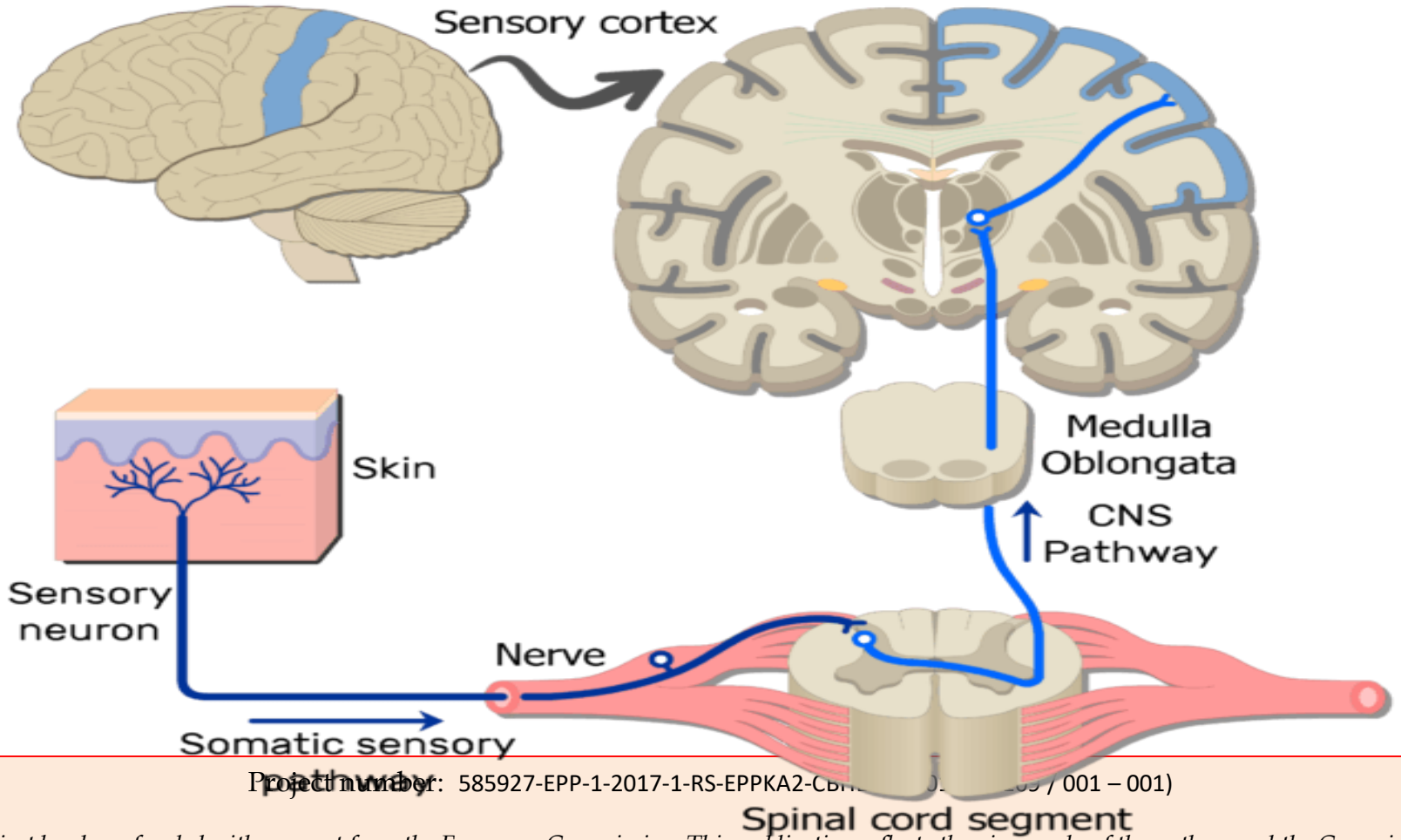
Nociceptivni sistem



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Pojava bola

- Mehanizam bola započinje pojavom nervnih impulsa u receptorima za bol, koji su većinom **slobodni nervni završeci**. Oni su ogranci senzitivnih nervnih vlakana koji se nalaze u površinskim slojevima kože, pokosnici, zidovima arterija, zglobnim površinama, te strukturama unutrašnjih organa. Manji dio receptora za bol čine mehanoreceptorna tjelašca, koja pri uobičajenoj stimulaciji dovode do odgovarajućih mehaničkih osjećaja, dok intenzivniji podražaji izazivaju osjećaj bola. Kada je riječ o slobodnim nervnim završecima kao nociceptorima, oni su **uglavnom polimodalni**, što znači da reaguju na termičke, hemijske i mehaničke stimuluse.

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Transdukcija

- Pretvaranje energije stimulusa u električni potencijal na membrani nervnog završetka
- Ovaj proces se odvija zahvaljujući brojnim receptorima na membrani nociceptora od kojih su do sada najbolje, ali ne dovoljno, proučene porodice ASIC (*acid-sensing ion channels),* TRP (*transient receptor potential)* katjonskih kanala i voltažno-zavisnih Na^+ kanala

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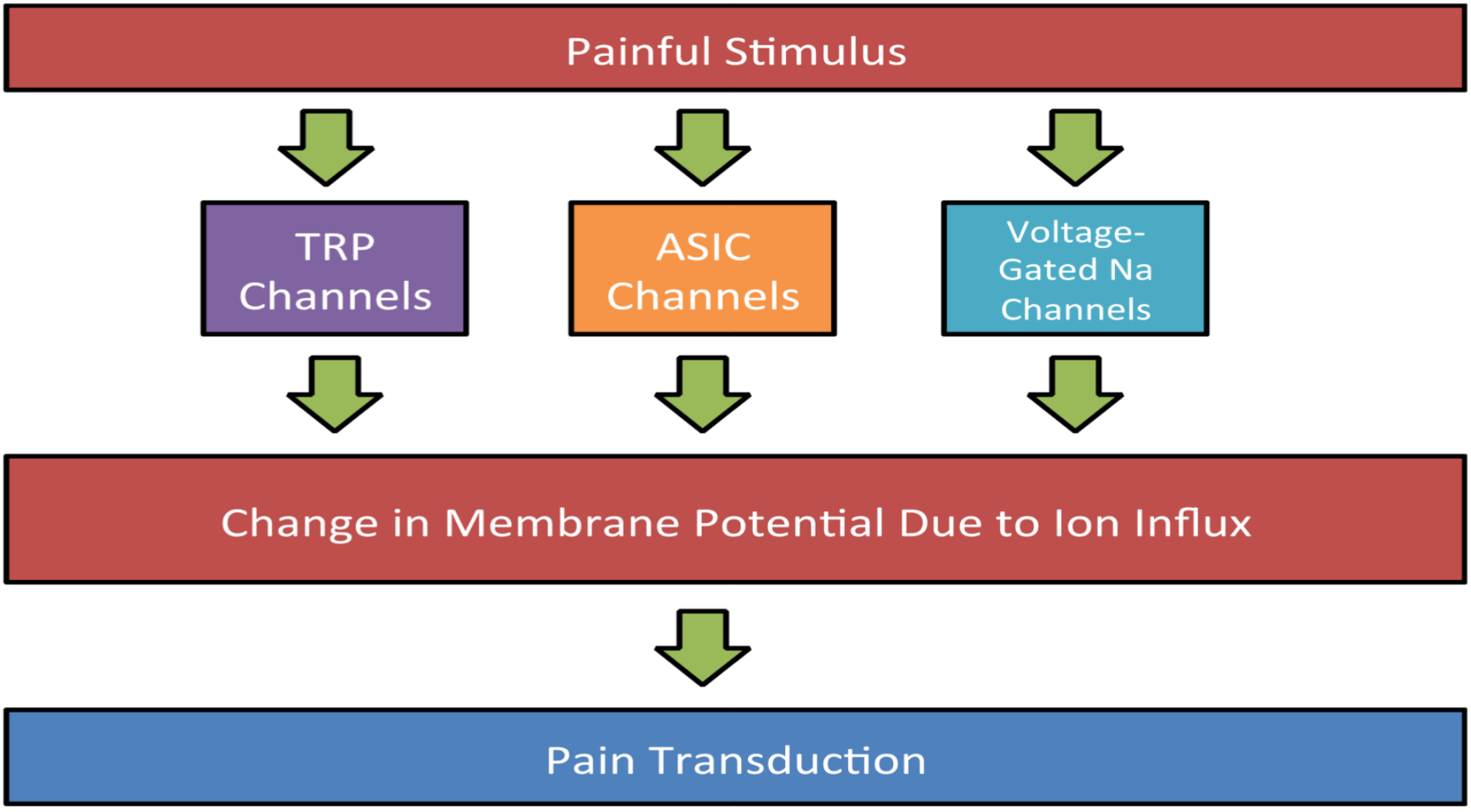
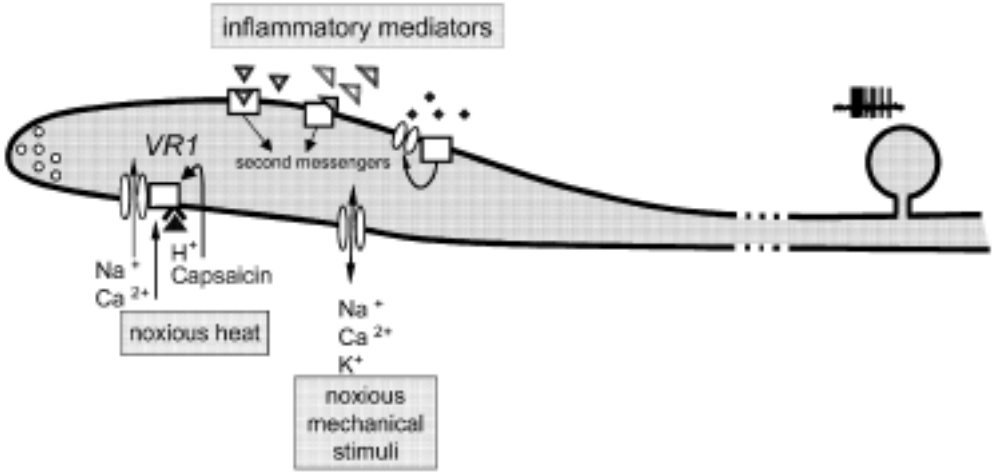
Pain transduction



Završetak nociceptora



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Prenos impulsa

- Nakon generisanja akcionog potencijala na nivou nociceptora dolazi do njegove transmisije prema centralnom nervnom sistemu.
- Impulsi se uglavnom prenose putem A-delta i C perifernih nervnih vlakana primarnih aferentnih neurona
- C vlakna su nemijelinizirana, brzina prenosa ne prelazi 2 m/s-tup i slabo lokalizovan bol
- A-delta vlakna prenose impulse brzinom do 30 m/s-oštar i lokalizovan bol

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Prenos impulsa

- Ova vlakna preko dorzalnih rogova ulaze u kičmenu moždinu gdje prave sinapse sa neuronima drugog reda.
- Na tom nivou transmisija se odvija uglavnom zahvaljujući ekscitatornim aminokiselinama (npr. glutamat) i neuropeptidima (supstanca P).
- Vlakna neurona drugog reda većinom ulaze u sastav kontralateralnog spinotalamičkog puta kojim se impulsi prenose ka talamusu, a zatim i višim centrima.
- Manji dio vlakana ushodnim putevima odlazi prema retikularnoj formaciji, mezencefalonu i hipotalamusu
- sinapse sa neuronima sive mase kičmene moždine daju i osnov puta koji preko ventralnih rogova napušta kičmenu moždinu, te u obliku motornih i simpatičkih vlakana odlazi prema efektornim organima, čime se uspostavlja refleksni sistem reakcije i odbrane od bolnih stimulusa.
- Treba spomenuti i prisustvo interneurona čija je uloga da, oslobađajući inhibitorne aminokiseline (npr. GABA) i neuropeptide (endogene opioide), suprimiraju nociceptivnu transmisiju

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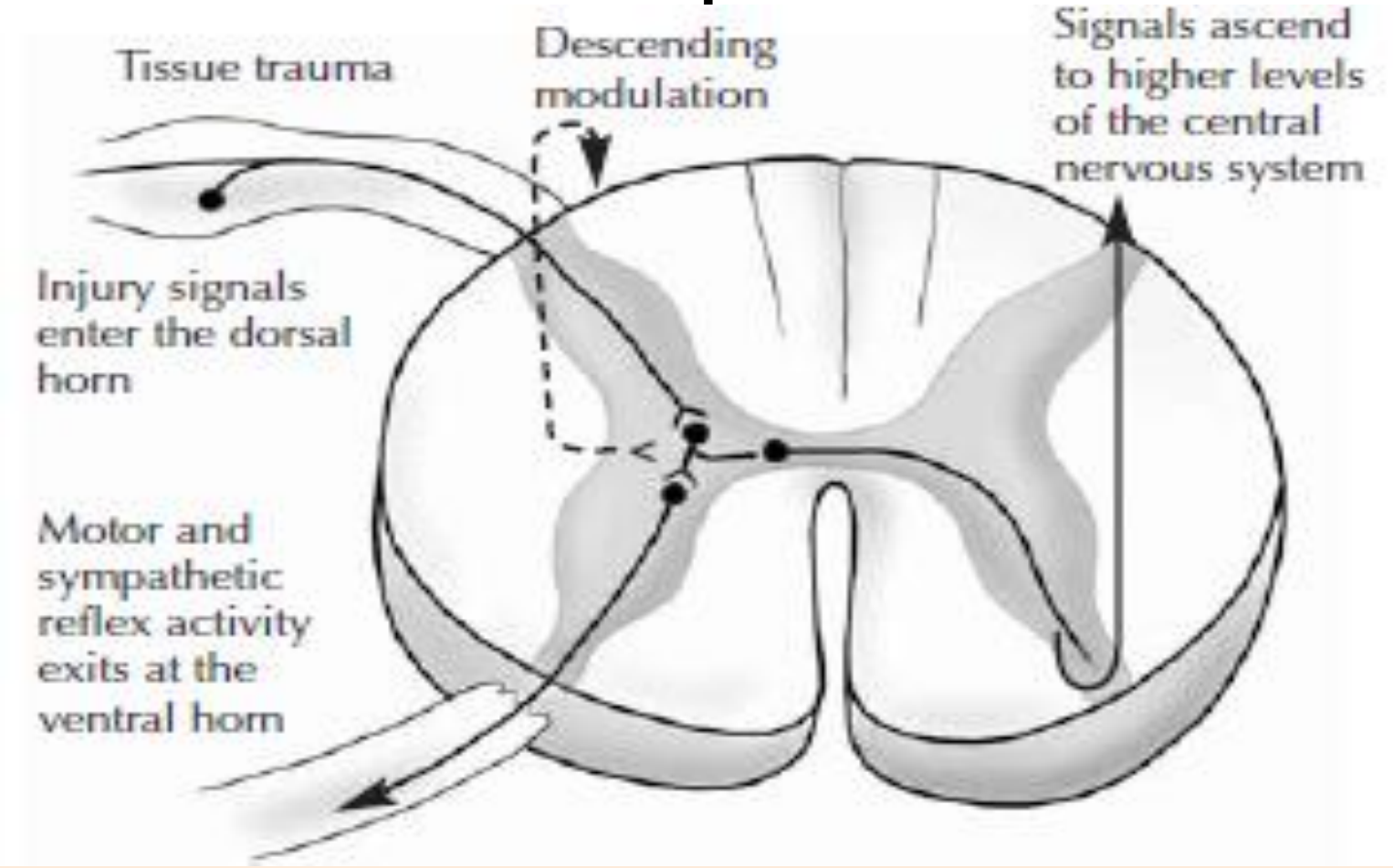
Prenos impulsa bola



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Percepcija bola

- Percepcija bola je neprijatna svjesnost određenog dijela tijela, okarakterisana prisustvom negativnih emocija.
- Na nivou somatosenzorne kore se tumači lokalizacija, intenzitet i kvalitet bola, dok limbički sistem daje emotivnu komponentu percepciji bola.
- Iz tog razloga se može reći da svaka osoba ima svoj jedinstven obrazac percepcije bola i reakcije na isti.

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Modulacija

- sposobnost centralnog nervnog sistema da posredstvom jasnih organskih mehanizama suprimira bolni impuls sa periferije.
- descedentni sistem koji u tome učestvuje je unutrašnji analgezijski sistem.
- On se sastoji iz tri komponente, a to su periakveduktna siva masa i periventrikularne zone mezencefalona, *nucleus raphe magnus*, te inhibitorni kompleks u dorzalnim rogovima sive mase kičmeme moždine gdje konačno dolazi do inhibicije prenosa bolnih impulsa.
- Neurotransmiteri modulacije: serotonin i enkefalini (receptori:μ,κ i δ receptori)
- Enkefalini pripadaju grupi endogenih opioida, pored β-endorfina i dinorfina.
- aktivnost ispoljavaju preko opioidnih receptora (μ,κ i δ receptori), a upravo ovi receptori cu meta za vrstu lijekova bez kojih je moderna hirurgija nezamisliva, opioidne analgetike

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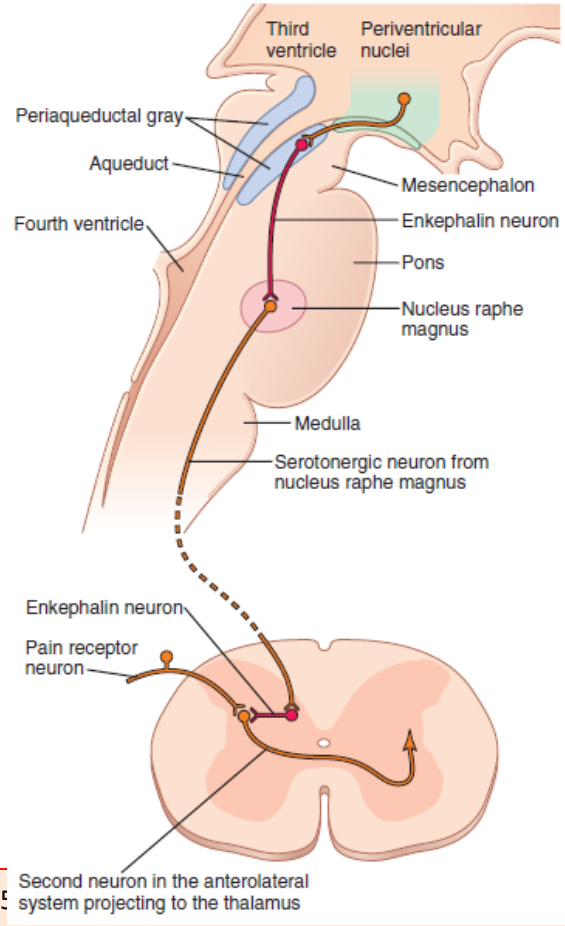
Modulacija-unutrašnji analgezijski sistem



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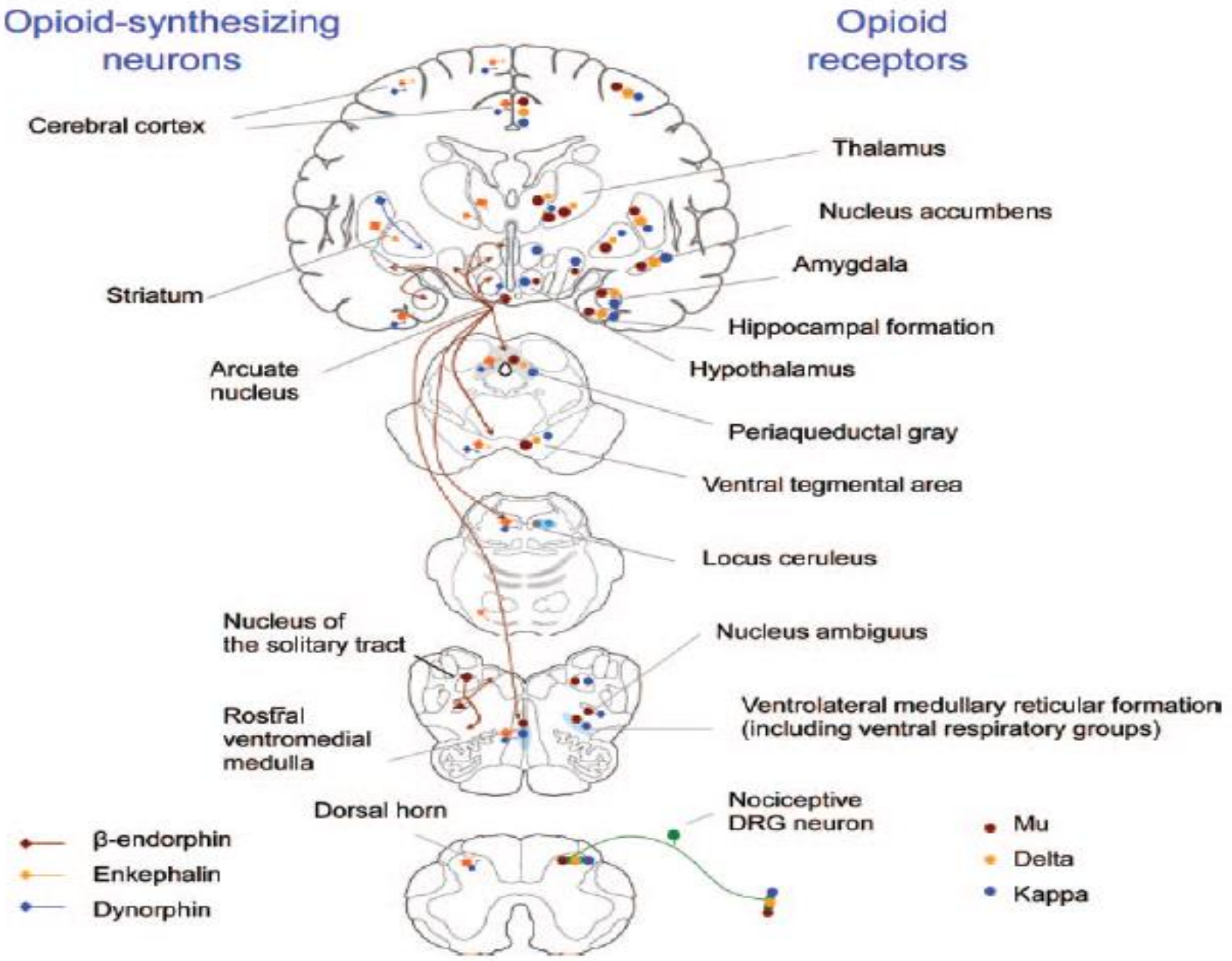

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Postoperativni bol

- posljedica inflamacije na mjestu traume tkiva (incizija tkiva, opekotine), te istovremeno posljedica direktnog oštećenja neurona usljed presijecanja, istezanja ili kompresije istih.
- Dakle, može se reći da postoperativni bol istovremeno ima nociceptivnu i neuropatsku komponentu.
- Veliki značaj u nastanku akutnog postoperativnog bola i perzistentnog bola nakon operacije imaju mehanizmi periferne i centralne senzitizacije.

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Periferna senzitizacija

- Periferna senzitizacija posledica: inflamacije i direktne hemijske stimulacije stimulacije nociceptora-šnižen prag
- Tako termički i taktilni stimulusi koji obično ne izazivaju bol sada dovode do osjećaja bola (alodinija), a uobičajeni bolni stimulusi sada daju izraženiji intenzitet bola (hiperalgezija).
- Dakle, neposredna postoperatvna hiperalgezija (primarna hiperalgezija) se javlja zbog periferne senzitizacije

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Centralna senzitizacija

- Centralna senzitizacija podrazumijeva senzitizaciju neurona na nivou kičmene moždine, te dovodi do sekundarne hiperalgezije
- Ova pojava predstavlja osnov za razvoj perzistentnog, tj. hroničnog postoperativnog bola.

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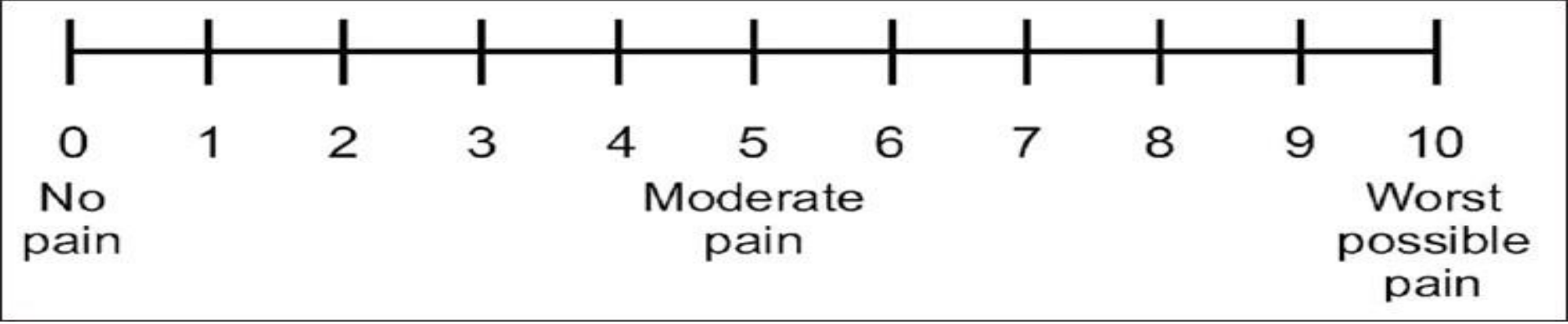
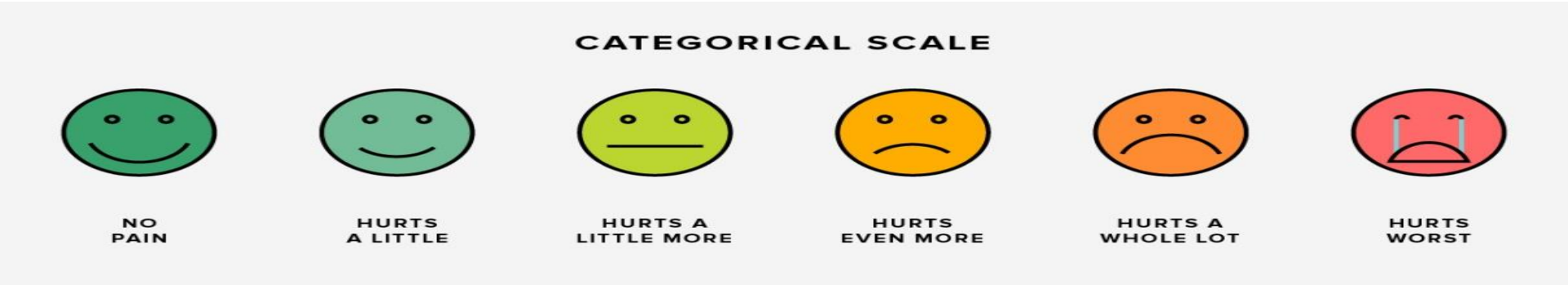


Visual Analog Scale (VAS) for pain severity measurement (not to scale)

No pain — Most pain



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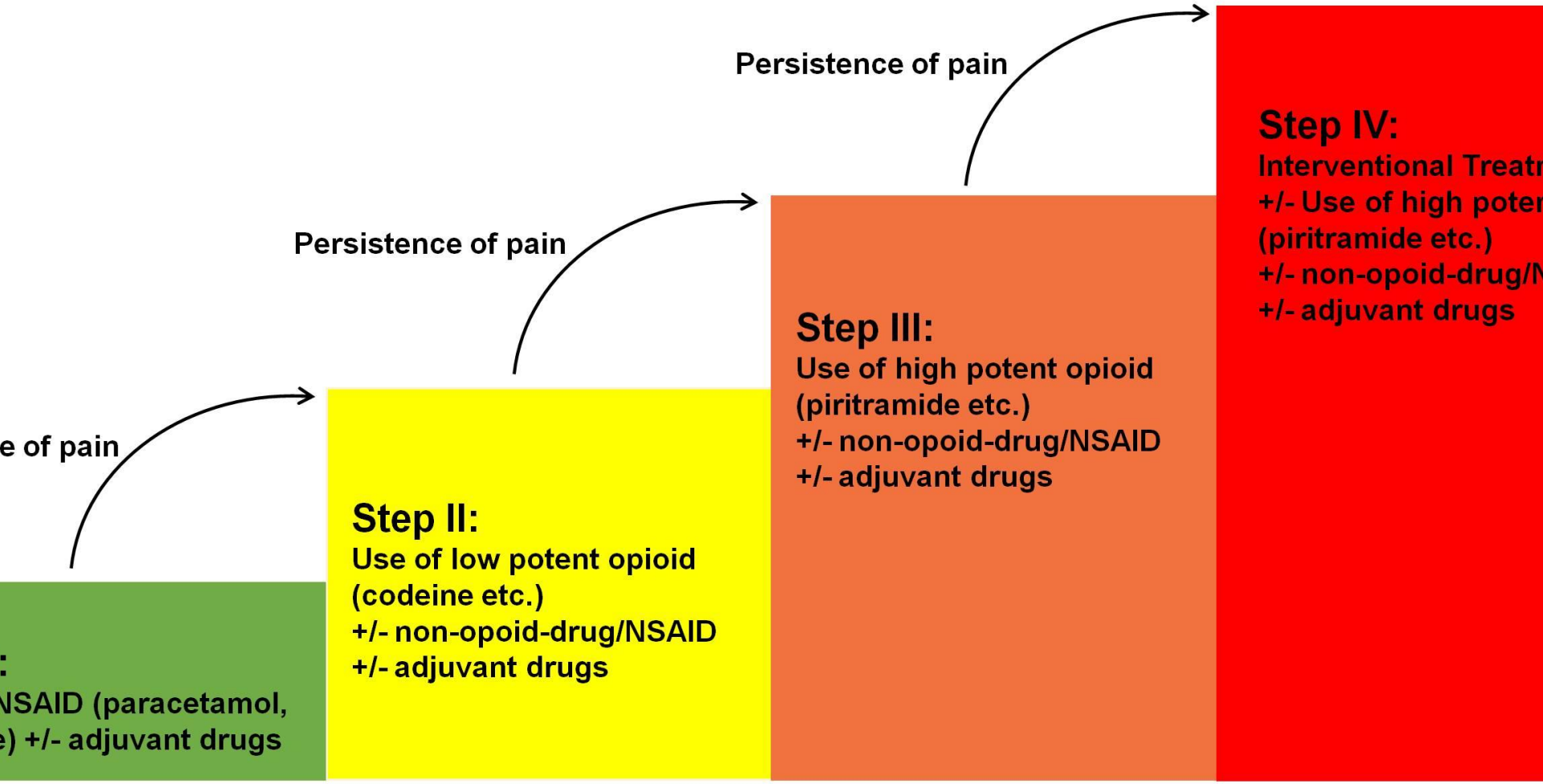

= Non-Steroidal Anti-Inflammatory Drugs

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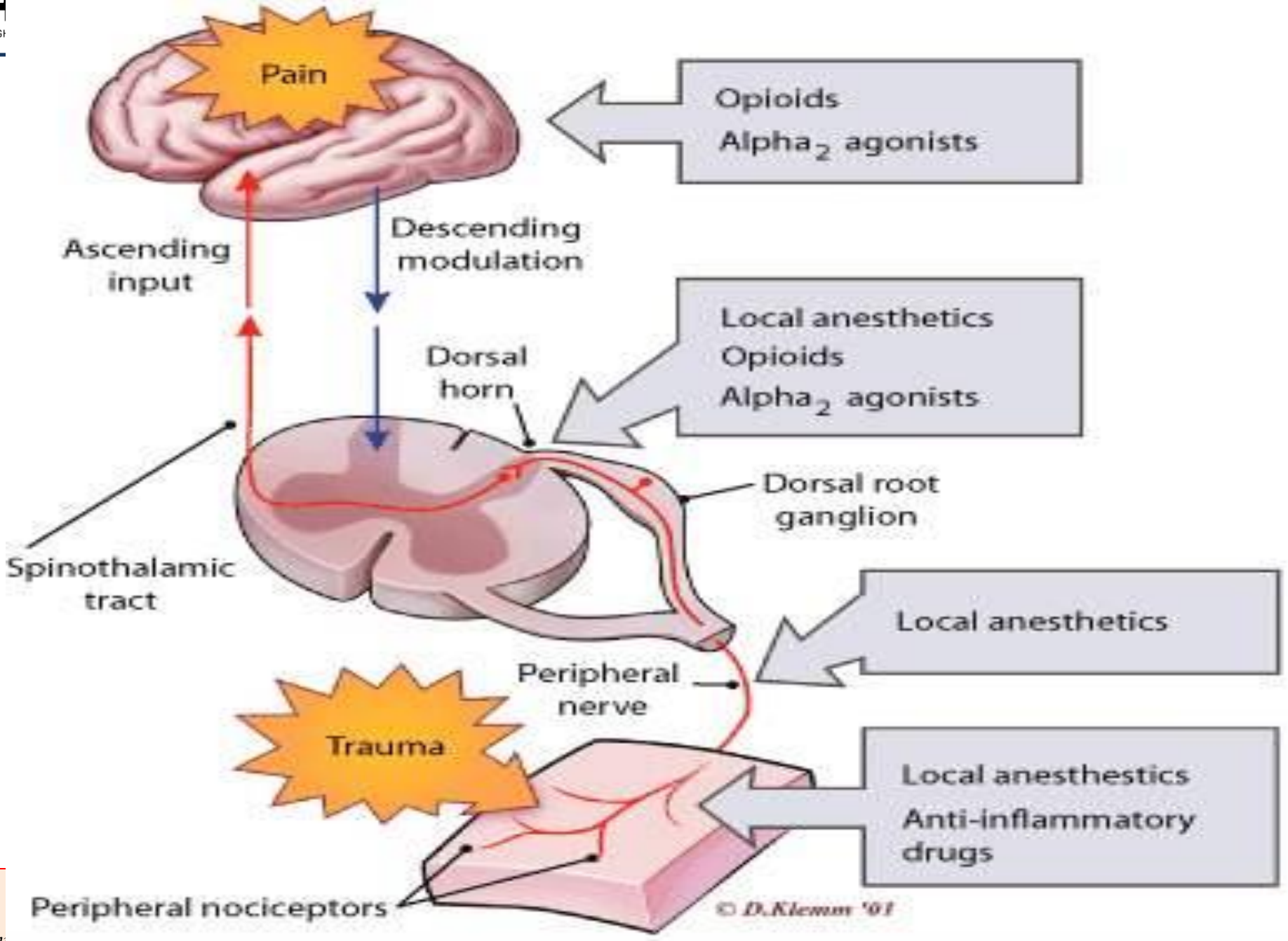

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Opioid v. non-opioid analgesics

- Opioids
  - Morphine
  - Fentanyl
  - Oxycodone
  - Hydromorphone
  - Hydrocodone
  - Methadone
  - Codeine
  - Tramadol
  - Oxymorphone
  - Tapentadol
  - Buprenorphine
- Non-opioids
  - NSAIDs
  - Acetominophen
  - Cox-2 inhibitors
  - Tri-cyclic antidepressants
  - Steroids
  - Anti-convulsants
  - SSNRIs
  - other

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Kontrola bola

- *PCA - patient controlled analgesia)*
- *on-demand analgesia*
- *PROSPECT - Procedure specific postoperative pain management)*

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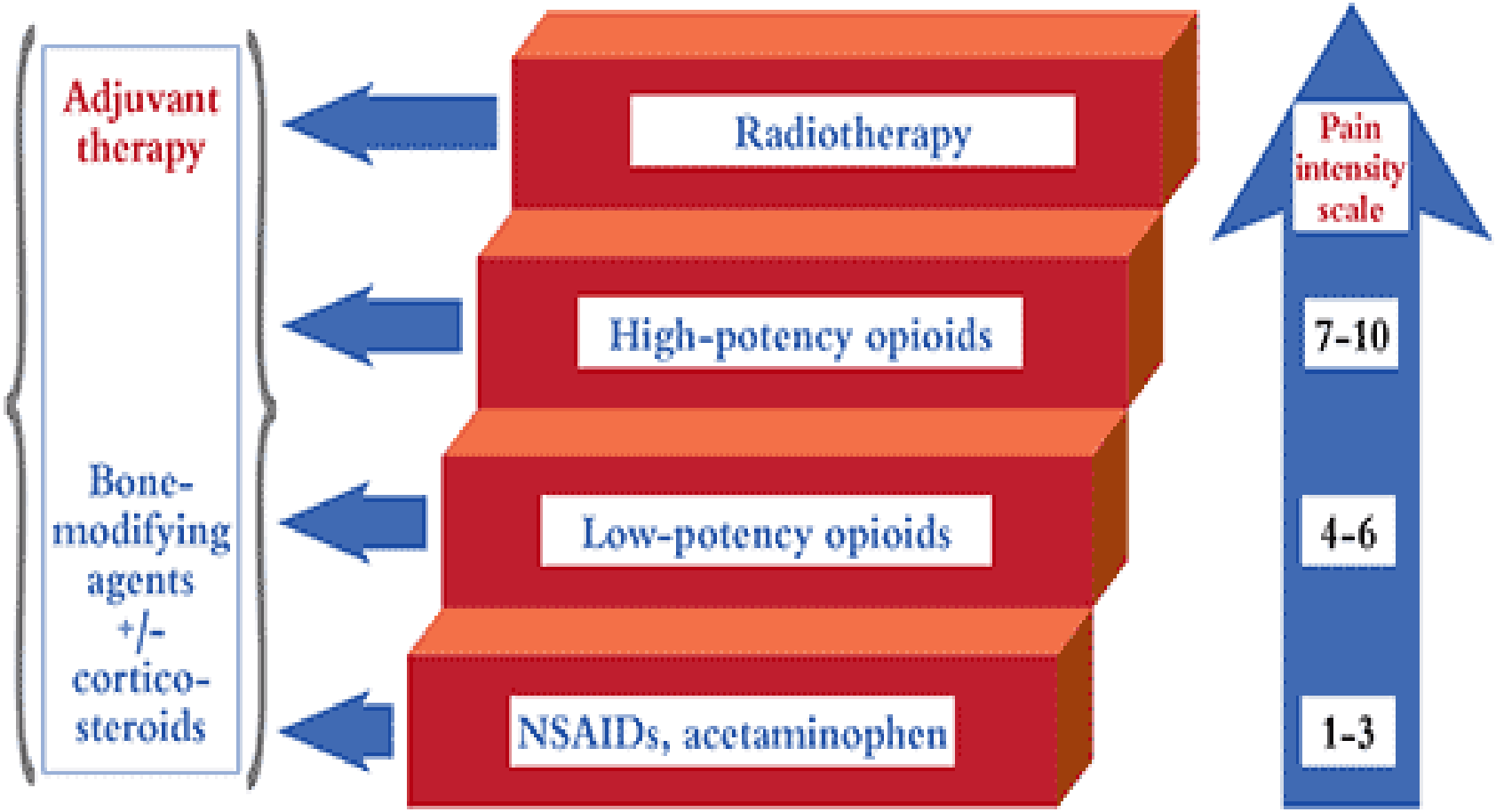
Figure 1. Stepwise Approach to Cancer Pain Management of Bone Metastases



NSAID: nonsteroidal anti-inflammatory drug. Pain intensity scale: 1-3 (mild); 4-6 (moderate); 7-10 (severe).
Source: References 6, 7.

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Pregabalin: The Good, The Bad and the Ugly

- The Good
  - Chronic pain in region of surgery, when pronociceptive mechanisms play a role such as joint arthroplasty, bowel surgery in IBD patients, chronic limb ischemic pain, opioid tolerant patients
- The Bad
  - Mild pain when simple analgesics like acetaminophen, NSAIDs or low dose opioid or Tramacet suffice.
- The Ugly
  - Too large a dose in sleep deprived patient already in state of “morphine-failure”

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