Managing Pain & Irritability in Non-verbal Children

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Vignette's – Encephalopathy

Static – 15yr old male with cerebral palsy (GMFCS IV)

- spastic quadriplegia – largely bed-bound
- non-verbal
- seizures
- bulbar palsy requiring gastrostomy feeding
- excessive secretions with recurrent aspirations
- frequent admissions for pneumonia resulting in longer hospital stays
- main issue is **irritability & agitation**

Progressive – 15yr old male with juvenile NCL

- mostly in bed; less tolerant of wheelchair
- essentially non-verbal
- seizures
- oral feeding; prolonged with associated choking episodes
- excessive secretions
- increasing admissions to hospital for **irritability & agitation**

Definitions

- **Agitation** – unpleasant state of arousal manifesting as irritability, restlessness, & increased motor activity

- **Irritability** – abnormal response to stimuli or physiological arousal

US Dept Health & Human Services; National Institutes of Health; National Cancer Institute.

Common Terminology Criteria for Adverse Events.

View agitation & irritability as a communication of need

Causes – pain, anxiety, acute illness, medications

Pain Assessment

- tools available for non-verbal children
- observational scales
  - Revised FLACC (R-FLACC)
  - Individualized Numeric Rating Scale (I-NRS)
  - Non-Communicating Children's Pain Checklist-Revised (NCCPC-R)
  - Paediatric Pain Profile (PPP)

AAP Clinical Report, Table 4

Clinical Utility Comparison

Tool	Utility
r-FLACC	**Demonstrated feasibility for use in the acute care setting related to ease of use.** Crosta et al. 2014
NCCPC-R	Clinicians indicated too complex and long compared with other tools for use with this group of children. Voepel-Lewis et al. 2008
Paediatric Pain Profile (PPP)	Use in acute clinical setting limited by time required to complete and teaching needed to use. Hunt & Franck 2011; Chen-Lim et al. 2012 **Parents perceived it as more accurate even though difficult to use in clinical setting.** Chen-Lim et al. 2012

Revised FLACC Scale

FACE		
0	1	2
No particular expression or smile **Individual behaviour:**	Occasional Grimace or frown, withdrawn, disinterested *Appears sad or worried* **Individual behaviour:**	Frequent to constant frown, clenched jaw, quivering chin *Distressed- looking face; expression of fright or panic* **Individual behaviour:**
LEGS		
0	1	2
Normal position or relaxed *Usual tone & motion to limbs* **Individual behaviour:**	Uneasy, restless, tense *Occasional tremors* **Individual behaviour:**	Kicking or legs drawn up *Marked increase in spasticity, constant tremors or jerking* **Individual behaviour:**
ACTIVITY		
0	1	2
Lying quietly, normal position, moves easily *Regular, rhythmic respirations* **Individual behaviour:**	Squirming, shifting back & forth, tense *Tense or guarded movements; mildly agitated (e.g. head back and forth, aggression); shallow, splinting respirations, intermittent sighs* **Individual behaviour:**	Arched, rigid or jerking *Severe agitation; head banging; shivering (not rigors); breath holding, gasping or sharp intake of breaths, severe splinting* **Individual behaviour:**
CRY		
0	1	2
No cry, awake or asleep **Individual behaviour:**	Moans or whimpers, occasional complaint *Occasional verbal outburst or grunt* **Individual behaviour:**	Crying steadily, screams or sobs, frequent complaints *Repeated outbursts, constant grunting* **Individual behaviour:**
CONSOLABILITY		
0	1	2
Content relaxed **Individual behaviour:**	Reassured by occasional touching, hugging or "talking to", distractable **Individual behaviour:**	Difficult to console or comfort *Pushing away care giver, resisting care or comfort measures* **Individual behaviour:**

Interpreting the Score Total ?/10			
0	1-3	4-6	7-10
Relaxed and comfortable	**Mild discomfort**	**Moderate discomfort**	**Severe pain or discomfort or both**

The *revised* FLACC observational pain tool: improved reliability and validity for pain assessment in children with cognitive impairment. Pediatric Anaesthesia 2006 16: 258-265

Princess Margaret Hospital for Children, Pain Services. September 2007.

Revised FLACC

- improved reliability & validity in children with cognitive impairment
- additional descriptors validated in children with cognitive impairment

Malviya et al. Pediatr Anesth 2006

- clinical utility more highly rated than other tools for neurologically impaired children

Voepel-Lewis et al 2008

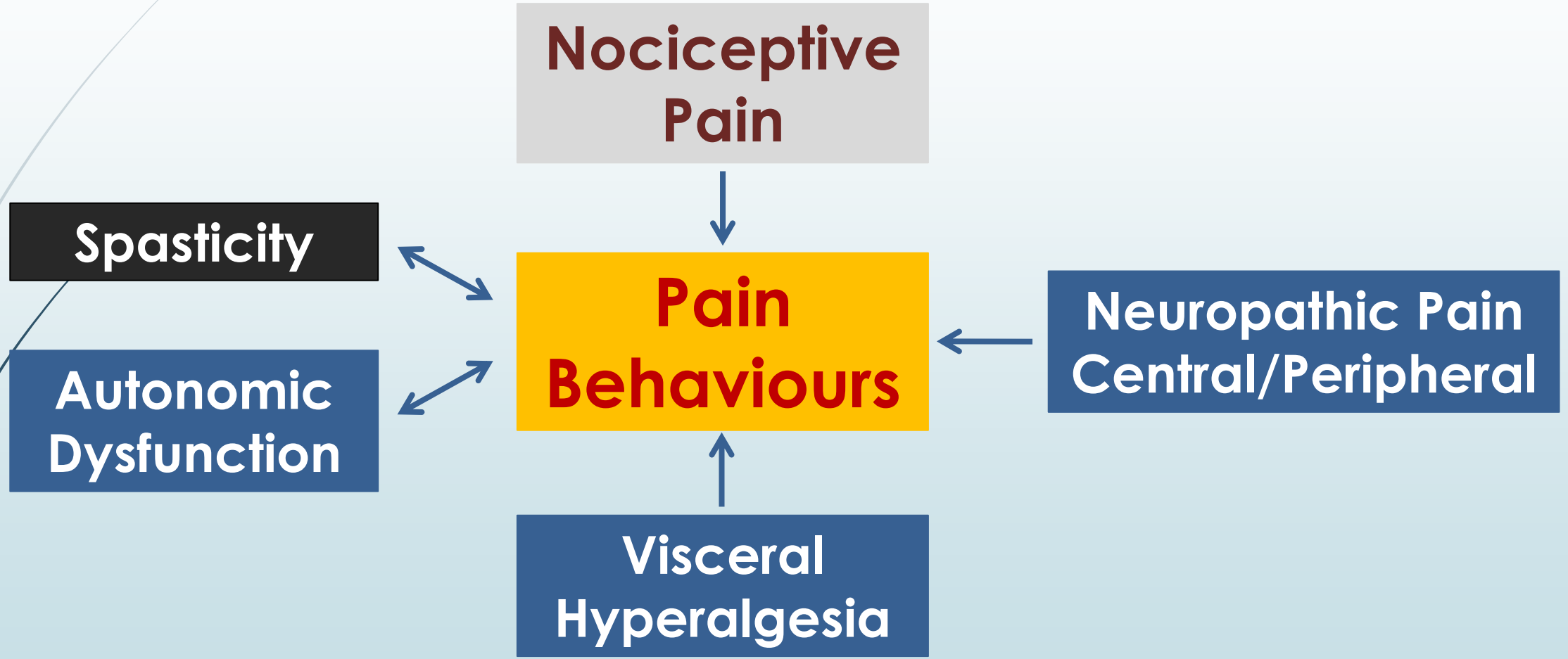
- nurse can review descriptors with parents
  - ask about additional behaviors that are better indicators in their child
  - add these to the tool in the appropriate category

Pain Behaviours

- vocalisations – crying, moaning
- facial expression – grimacing
- consolability – less consolable
- interactivity – withdrawn, less active
- physiological responses – pale, sweating
- movement – pulls legs up, restless
- tone & posture – arching, stiffening
- idiosyncratic behaviors – laughing

Breau 2002, Hunt 2004, Malviya 2006

Sources of Pain Behaviours



Blue boxes = impaired nervous system

Spasticity **Muscle spasm**	Velocity dependent; not painful Intermittent; **can result in pain and be triggered by pain**
Dystonia	Twisting and repetitive movements and/or abnormal postures; **worsened by pain**
Dysautonomia, PAID, Storms	Facial flushing, sweating, hyperthermia, vomiting, GI pain
Central Pain	**Abrupt onset of pain "out of the blue"; pain localized to GI tract**
Visceral Hyperalgesia	**Sensitization of visceral afferents**; GI pain with distension

Vignette – Episodes of Distress

15 year old with CP

- frequent, daily episodes of crying, grimacing, sweating, tachycardia, increased muscle spasms, seizures

15 year old with NCL

- in constant / perpetual motion
- associated rocking, groaning, grimacing, sweating, increased muscle tone, seizures
- prolonged periods of insomnia

Consider pain as cause

- **Nociceptive**
- **Neuropathic**
- **Nociplastic**

Nociceptive Pain

Pain due to activation of nociceptors arising from actual or threatened damage to non-neural tissue

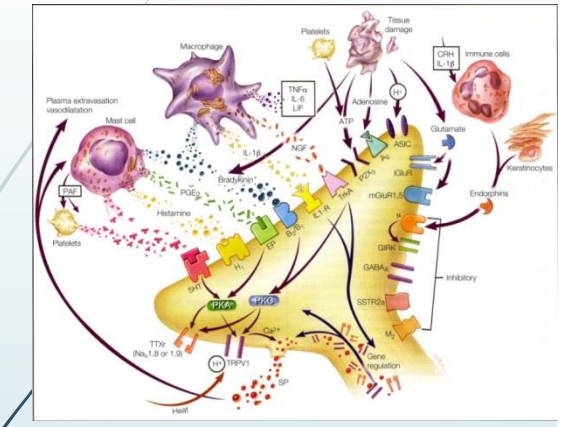
Somatic

- dental
- otitis media
- corneal abrasion
- urinary tract infection
- osteoporosis
- fracture
- hip subluxation

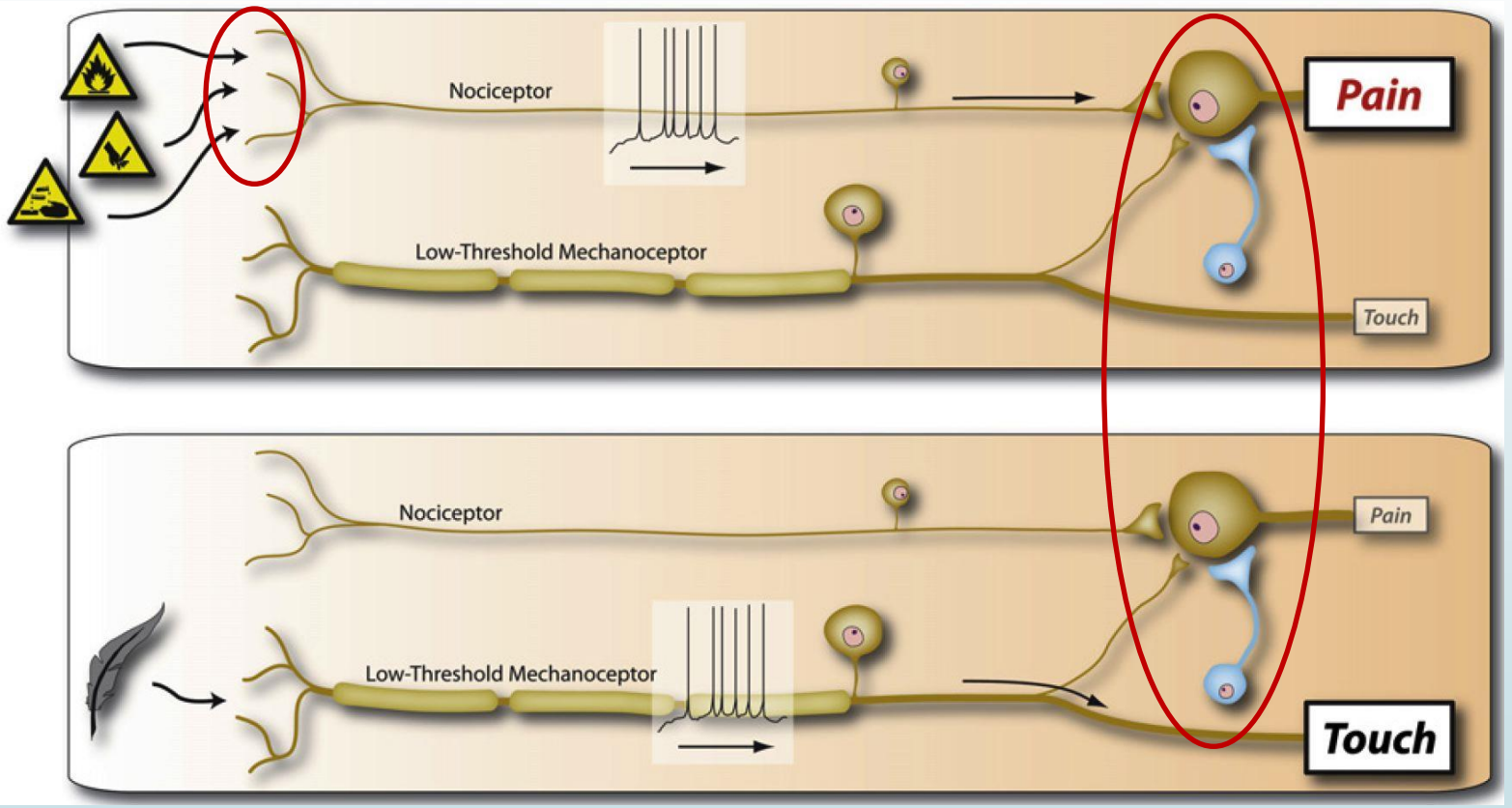
Visceral

- GOR disease
- G-tube site
- GI distension
- cholecystitis
- pancreatitis
- renal stones

Normal Sensation



- inflammatory response
- peripheral sensitisation



Woolf C. Pain 2011;152:S2

Vignette – Nociceptive Stimuli

Medical assessment CP

- aspiration pneumonia – antibiotics
- review personal cares
  - positioning, bowel habit, gastrostomy venting…
- review medication use
- gastrostomy feeding; not tolerating full feeds – reduce to 2/3rd's

Pain behaviours improve but not resolved after 1 month

Medical assessment NCL

- pneumonia – antibiotics
- review personal cares
- review medication use
  - not tolerating volume; rationalize
- not tolerating oral feeds; parents to consider NG feeding – 50% oral/50% NG
- parent welfare discussed

Pain behaviours continue

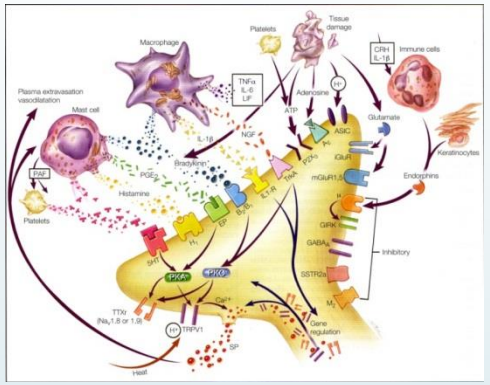
Neuropathic Pain

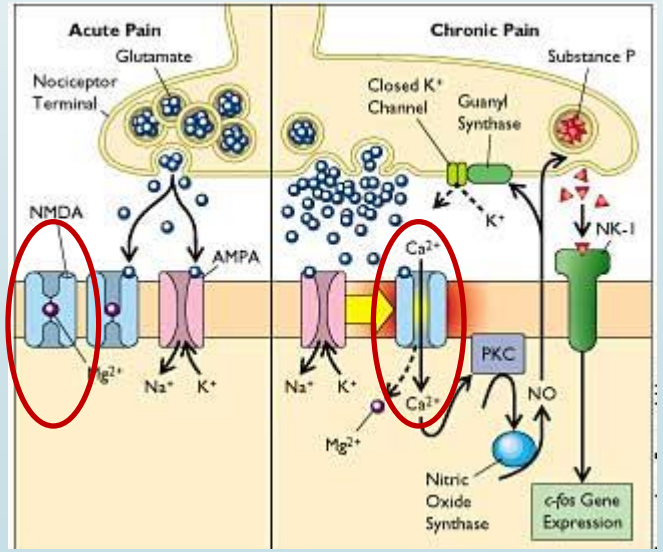
Pain caused by a lesion or disease of the somatosensory nervous system

- Peripheral
- Central

Mechanism – Neuropathic Pain

- peripheral
  - inflammatory response
  - peripheral sensitisation
- central
  - glutamate – excitatory neurotransmitter
  - **NMDA channel opens**
  - **inflammatory response**
  - **loss of inhibition**
  - **hyperexcitability of spinal cord dorsal horn neurons**



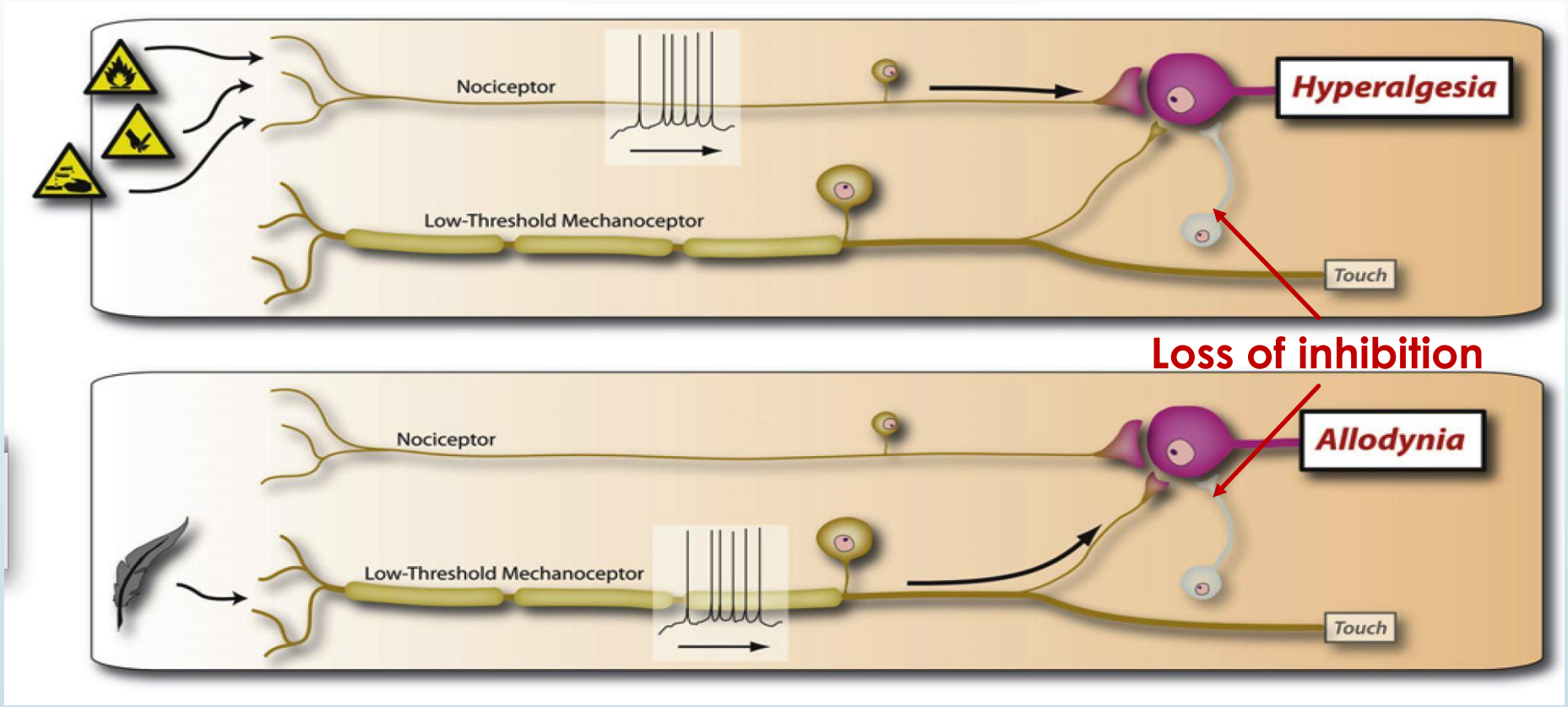


Nociplastic Pain

Pain arising from altered nociception despite no clear evidence of actual or threatened tissue damage causing activation of peripheral nociceptors or evidence for disease or lesion of somatosensory system causing pain

Nociplastic Pain = Central Sensitisation

Top – mismatch between stimulus & response



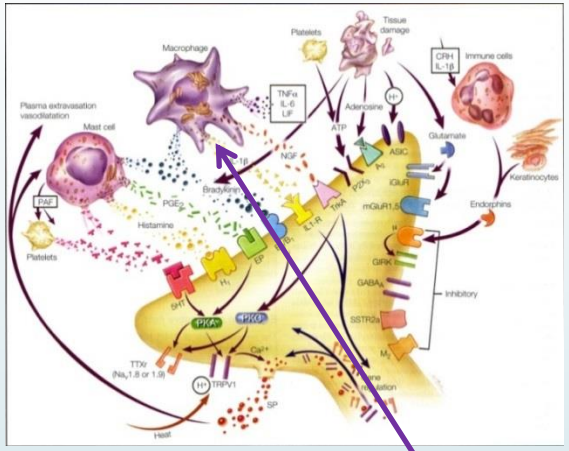
Bottom – disruption of normal specialisation results in aberrant convergence

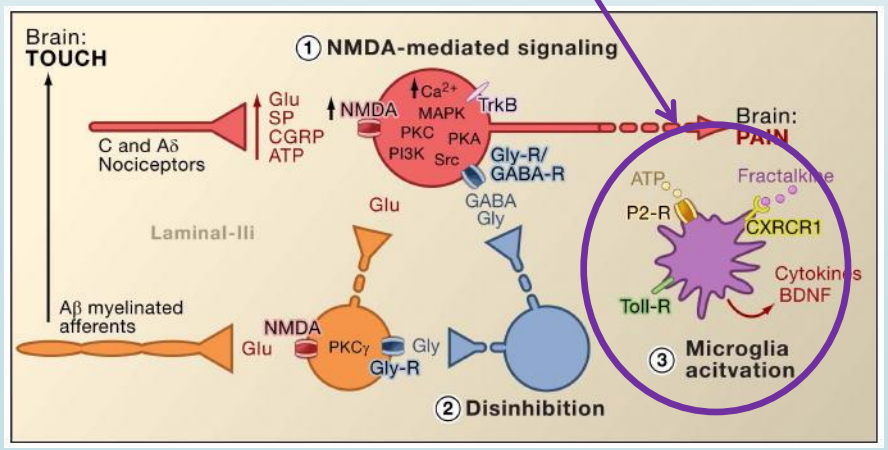
Woolf C. Pain 2011;152:S2

Mechanism – Nociplastic Pain

- peripheral
  - inflammatory response
  - peripheral sensitisation
- central (at spinal cord DHN)
  - **microglia activation**
    - **inflammatory response**
    - **loss of inhibition**

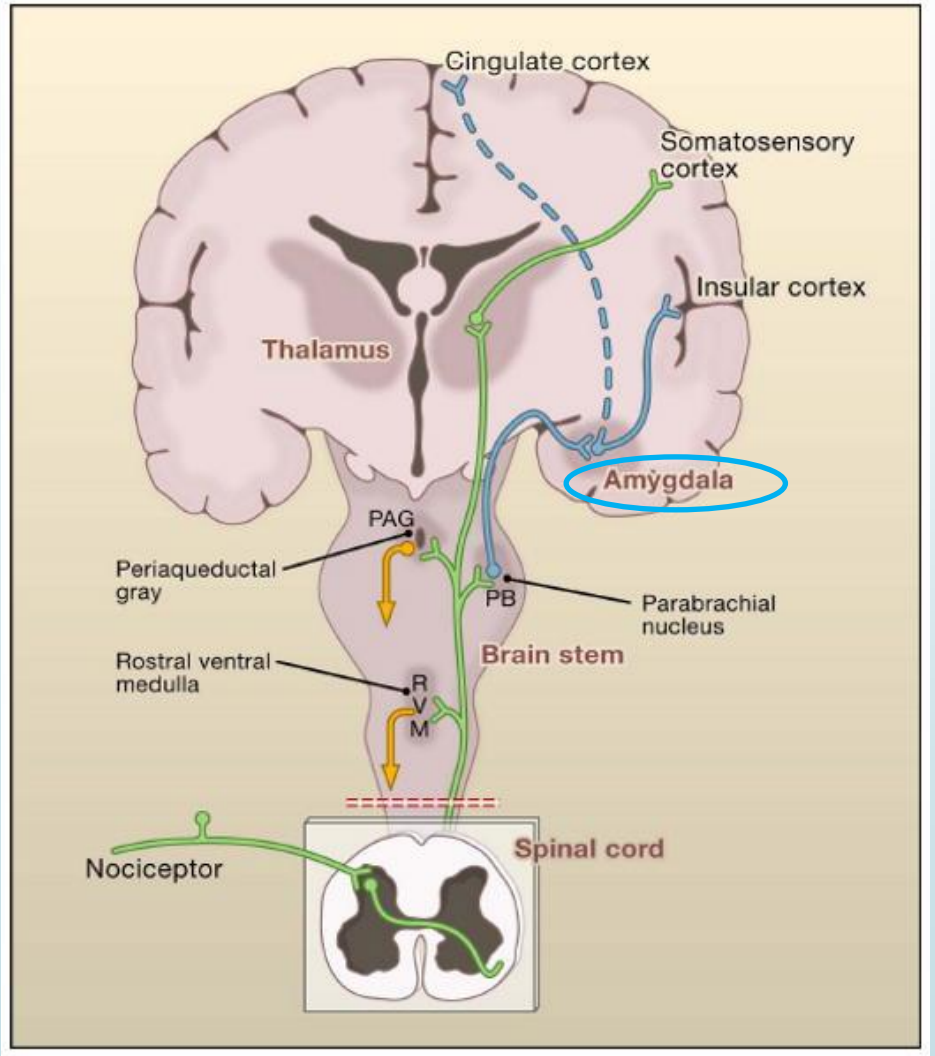
= Central Sensitisation



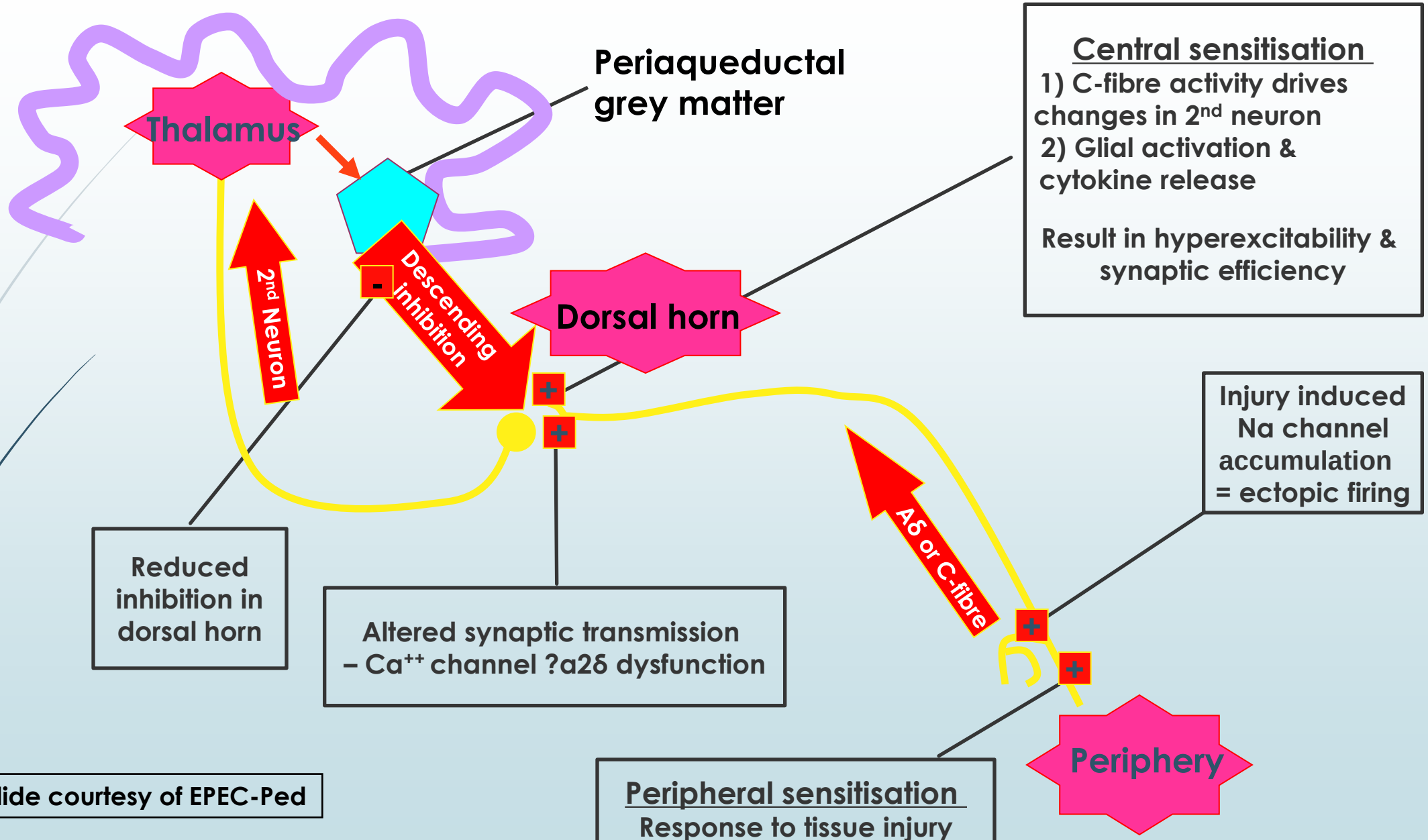


Somatosensory Pathways

- projection neurons send information to **SS cortex** via thalamus (VP)
  - **location & intensity of the painful stimulus**
- other neurons engage cingulate & insular cortices via brainstem (parabrachial nucleus & **amygdala**)
  - **affective component of pain experience**
- ascending information accesses neurons of **RVM & midbrain PAG**
  - **engage descending feedback to regulate output from spinal cord**



CNS Pain



Slide courtesy of EPEC-Ped

Vignette's – Unresolved Symptoms

- introduce integrated pain management strategies
- mix of pharmacological & non-pharmacological

Fix vs. Modify

"Fix" = nociceptive pain

- urinary tract infection
- fracture
- renal stones
- medication toxicity

"Modify" = intractable (not easily "fixed") symptoms

- seizures
- CNS pain
- dysautonomia
- GI motility

Non-Pharmacological

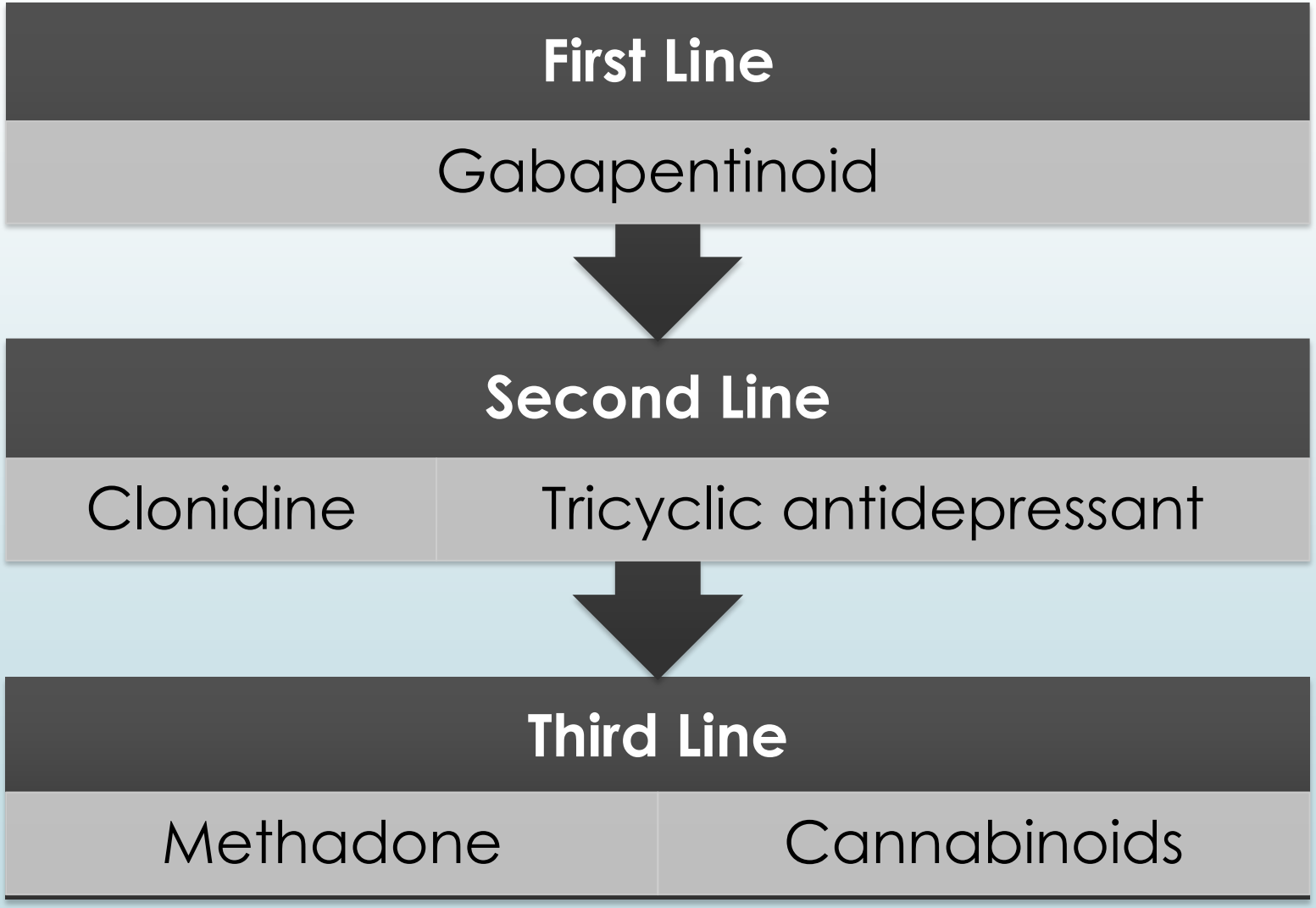
- rocking, massage, repositioning
- fan, cool air, music, water, aromatherapy
- vibratory stimulation – mats, pillows
- supportive equipment – seating, pillows
- calm environment
- day/night routine – sleep
- GI tract distention – overfeeding, constipation

Vignette CP – Introduce Gabapentin

Weight 30kg

- start at 10 mg/kg/day; x3 per day = 100 mg tds
  - can start at lower dose of 5 mg/kg/day
- increase at 4 day intervals
- reasonable dose is 30 mg/kg/day or 300 mg tds
- can maximize to 60 mg/kg/day or 600 mg tds
- effect noticed by 3rd day of starting
- titrated to 300 mg tds
- significant improvement
  - smiling/giggling
  - improved sleep
  - no day-time sedation
- continued benefit over time

Medication Options

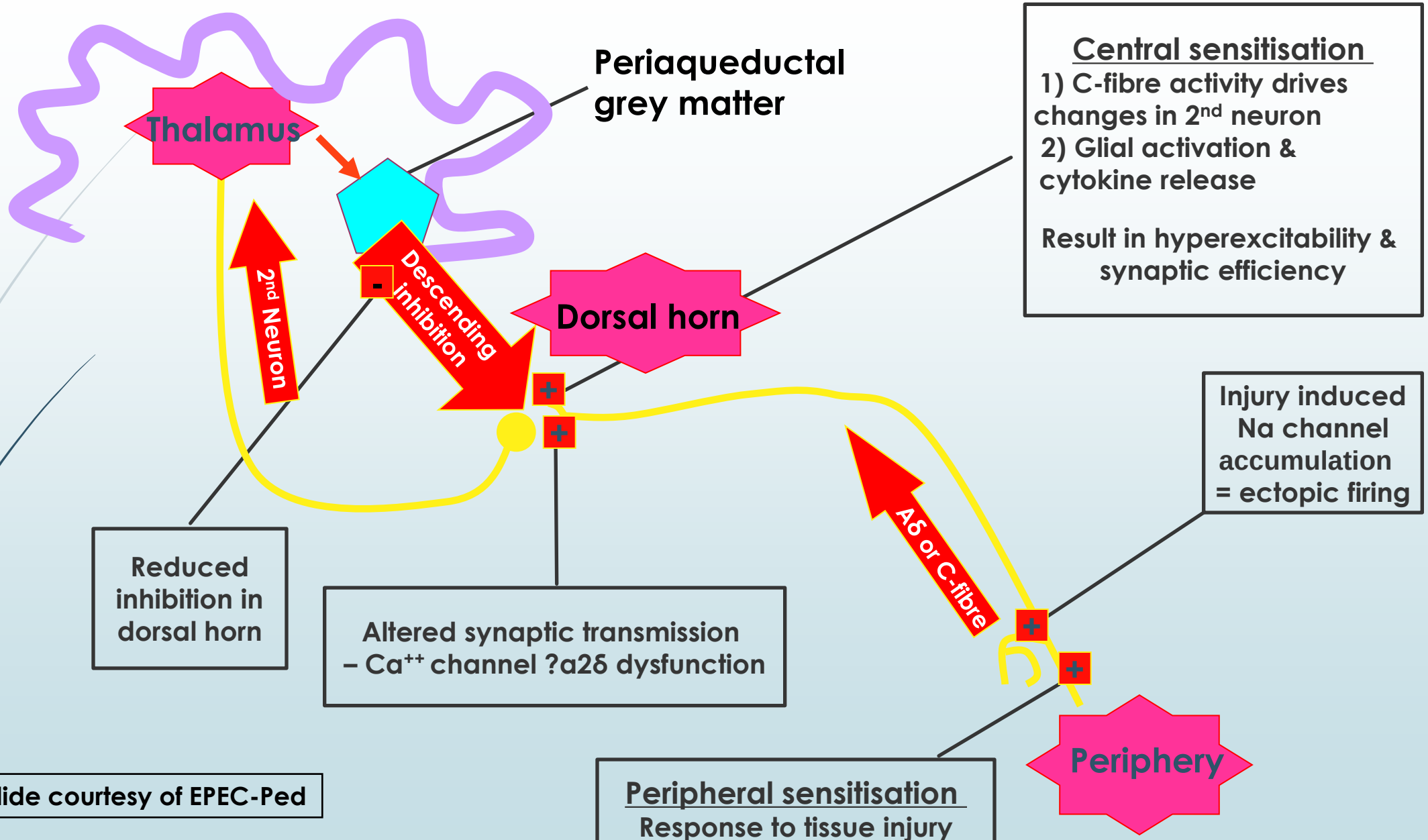


Rationale for Medication

Clonidine	Dysautonomia, Spasticity, Sleep
Tricyclic (TCA)	Central neuropathic pain, Sleep
Methadone	Central neuropathic pain
Cannabinoids	Spasticity, Muscle Spasms
PRN (opioids, benzodiazepines, clonidine)	Breakthrough pain, Spasticity, Autonomic storm

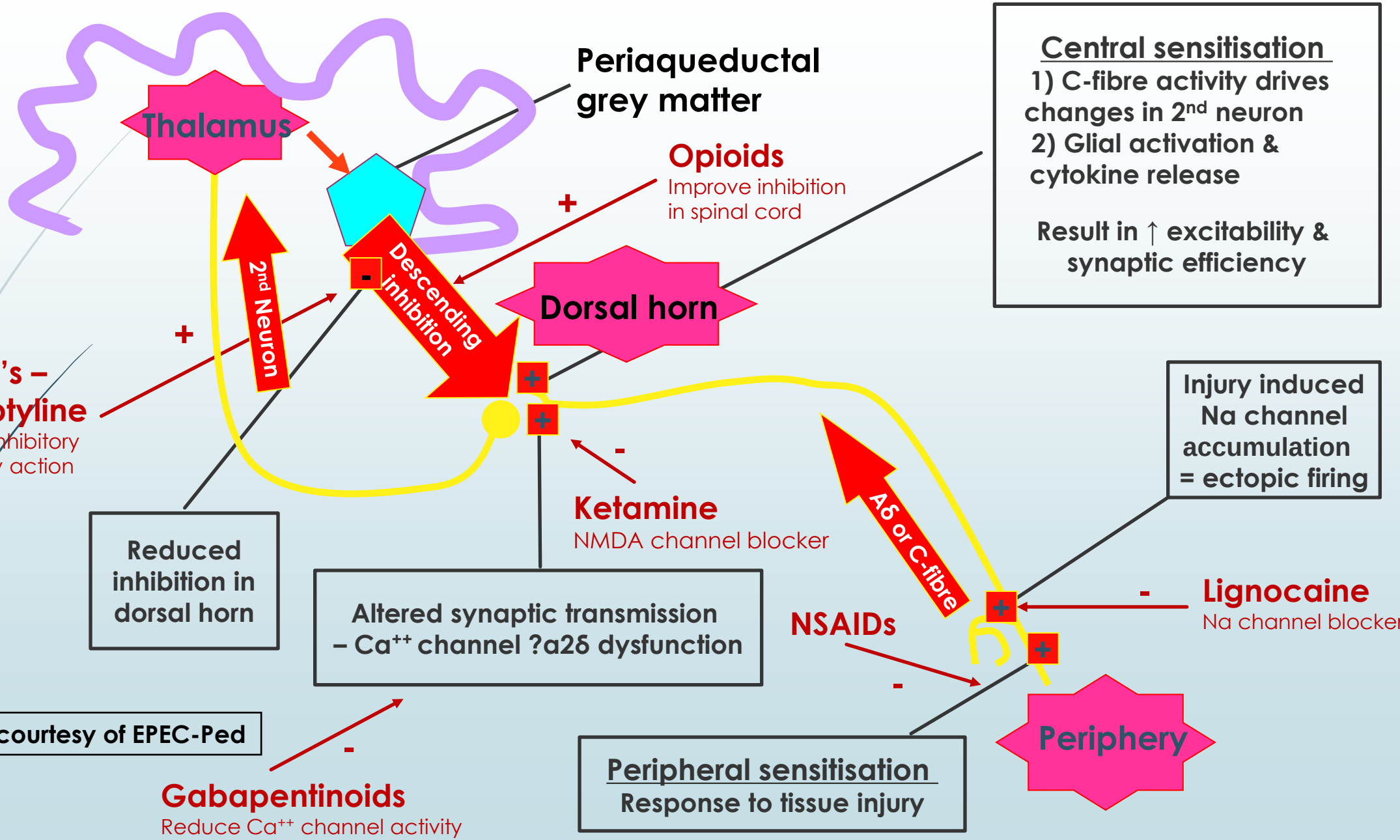
Dosing guidelines in AAP Clinical Report Table 8

CNS Pain



Slide courtesy of EPEC-Ped

CNS Pain & Medication



Vignette NCL – Medication Review

- Paracetamol 1Gm bd; 1Gm PRN
- Gabapentin 1200mg mane, 900mg midday, 1500mg nocte
- Amitriptyline 75mg nocte
- Morphine 2.5 to 5mg q1h PRN
- THC & CBD oil
  - dose of THC has been escalating
- Quetiapine 200mg nocte; 200mg after 2 hrs PRN
- Temazepam 30mg nocte
- Midazolam 10mg SL PRN for seizures

Suggested Alterations

Stop – not helping

- Paracetamol
- Morphine
- Gabapentin (large volume)
- CBD oil

Alter – rationalize

- Amitriptyline
- THC oil (wean)
- Quetiapine (wean)
- Temazepam (wean)

New Regimen (Recommended)

- Pregabalin 300mg bd
- Amitriptyline 25mg mane, 50mg nocte
- THC oil 6 mL QID – weaning

For Breakthrough Agitation/Pain

- Oxycodone 5-7.5mg after 1 hr; then
- Diazepam 5-10mg after 1 hr; then
- THC oil 6 mL after 30 min

- Quetiapine 200mg nocte; 100mg after 2 hrs PRN – weaning
- Temazepam 15mg at night – weaning
- Midazolam 5-10mg SL PRN for seizures

Vignette NCL – Introduce Methadone

Weight 65kg

- Methadone 2.5mg mane, 2.5mg midday, 5mg nocte
- can increase for unresolved pain/agitation

- effect noticed within 48hr
- significant improvement in pain behaviours
  - minimal agitation
  - improved sleep
  - no sedation
- increases with time to 5 mg then 10 mg tds

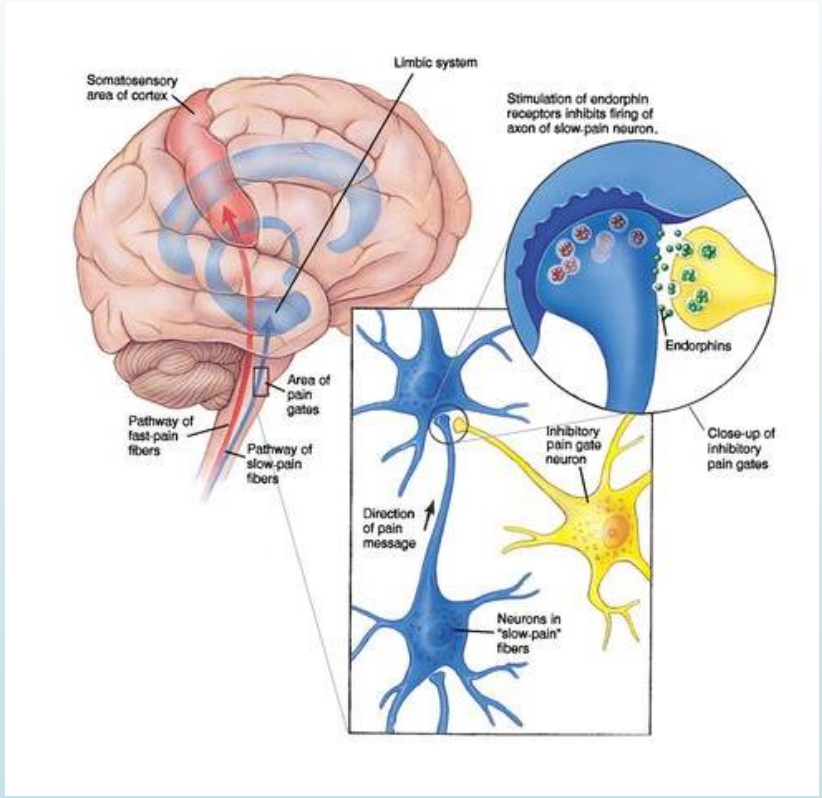
Opioids & Pain

Endogenous opioids released by inhibitory neuron in dorsal horn

- bind to opioid receptors
- inhibits pre-synaptic release of glutamate
- prevent transmission to higher centres

Exogenous opioids

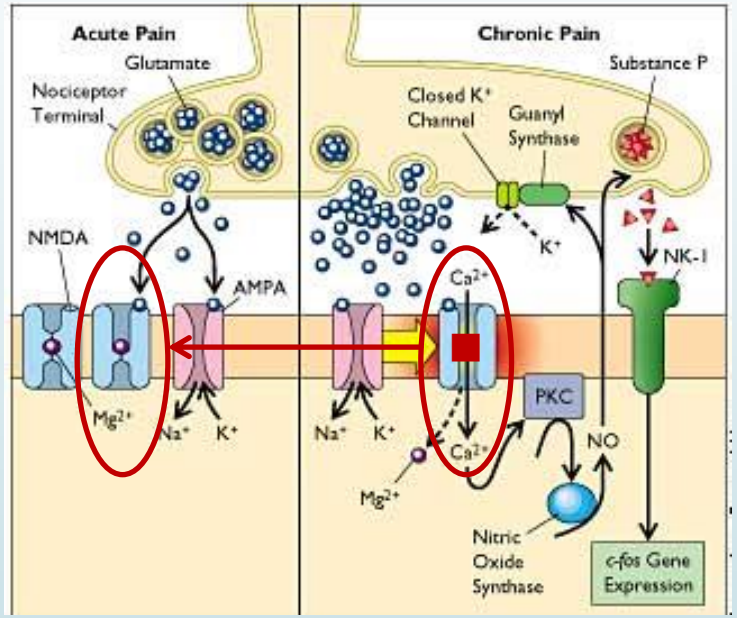
- **bind to opioid receptor**
- **prevent transmission to higher centres**



Ketamine & Pain

Excitatory (glutamate) neurotransmitters activate NMDA channel

Ketamine resets by blocking NMDA channel



General Principles

- testable & treatable vs. non-testable CNS symptoms
- unable to “fix” CNS problems
- clear communication; lessen mixed messages
- preparing & hoping
- intractable problems require goals of care

Hauer 2014

Management Principles

- review symptom(s)
  - episodes – frequency, duration, severity, triggers…
- check for correctable causes of nociceptive pain
- adjust symptom care plan
  - review non-pharmacological strategies
  - maximize/rationalize medication doses & timing
  - effectiveness of breakthrough symptom care plan

Hauer J, Houtrow A. AAP clinical report, June 2017

AAP Clinical Report

Optimal treatment of pain in children with impaired nervous system **often requires considerable time and effort** to achieve & is most likely accomplished if the overall treatment of pain for the child is guided by broader management strategies and considerations.

CLINICAL REPORT Guidance for the Clinician in Rendering Pediatric Care

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Pain Assessment and Treatment in Children With Significant Impairment of the Central Nervous System

Julie Hauer, MD, FAAP,[a,b] Amy J. Houtrow, MD, PhD, MPH, FAAP,[c] SECTION ON HOSPICE AND PALLIATIVE MEDICINE, COUNCIL ON CHILDREN WITH DISABILITIES

abstract

gnificant problem for children with impairment
ystem, with the highest frequency and severity
th the greatest impairment. Despite the significance
ulation remains vulnerable to underrecognition
ain. Barriers to treatment may include uncertainty

FREE