OPIOIDS: LIGHTS AND SHADOWS

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SISTEMA SANITARIO REGIONALE
AZIENDA OSPEDALIERO-UNIVERSITARIA
SANT'ANDREA

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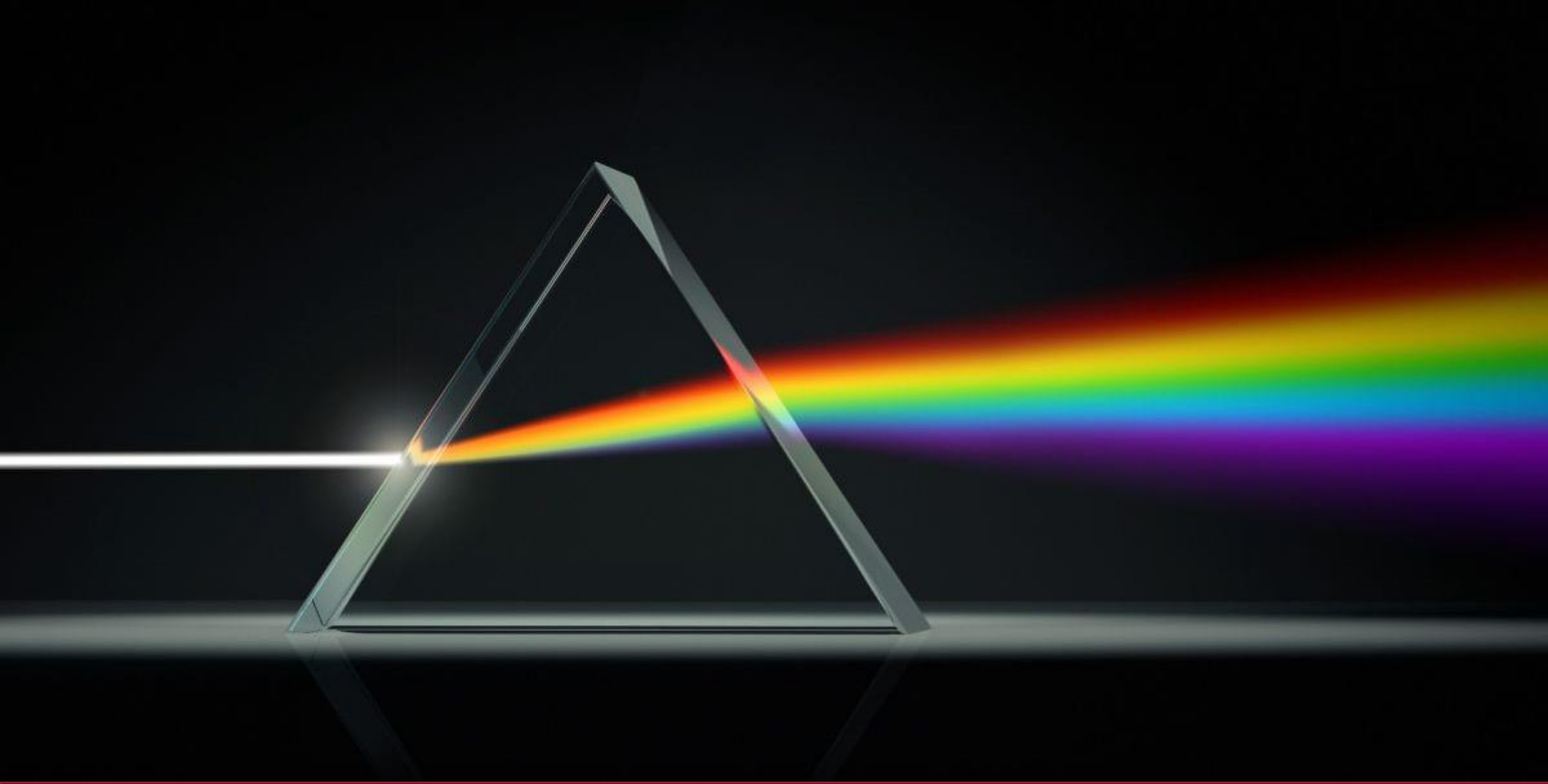
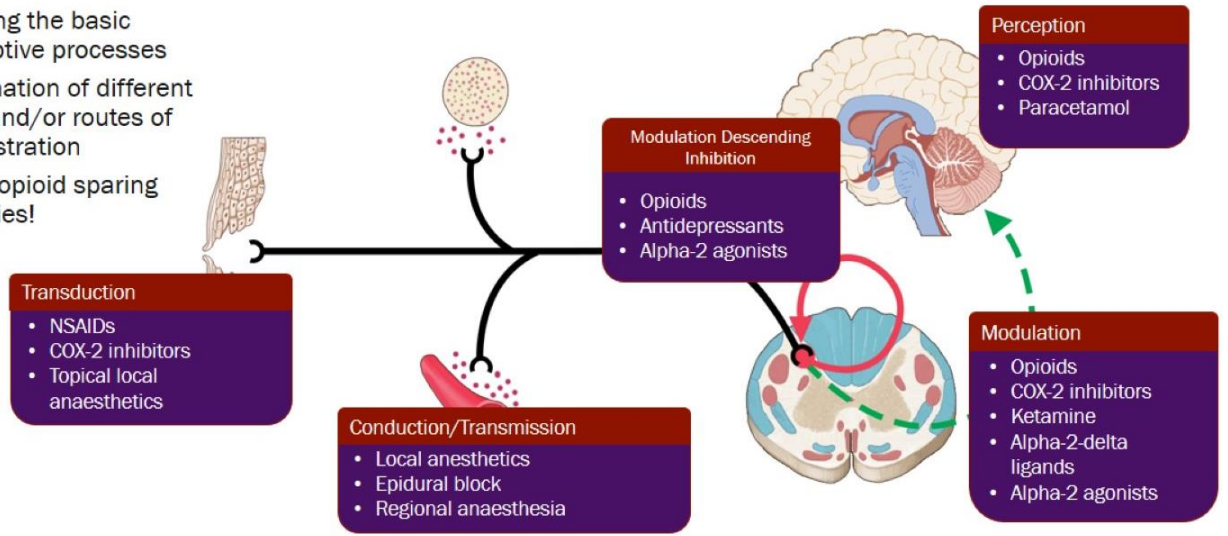


OPIOIDS: RATIONAL FOR USE

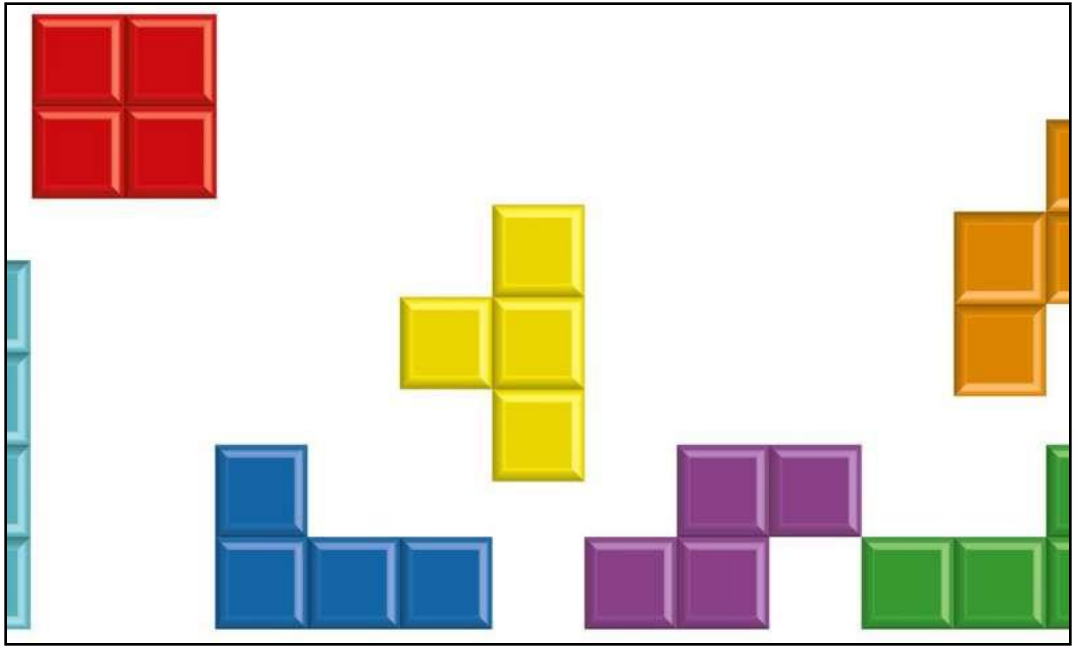
Pharmacotherapy of Pain: multimodal analgesia

- Targeting the basic nociceptive processes
- Combination of different drugs and/or routes of administration
- Mostly opioid sparing strategies!



Kumar S, et al. *OA Anaesthetics*. 2014;2:2; Julius D, et al. *Nature*. 2001;413:203-210; Lee B, et al. *Best Pract Res Clin Anaesthesiol*. 2018;32:101-111; Dunkman WJ, et al. *Surg Clin North Am*. 2018;98:1171-1184.

Any drug has its role



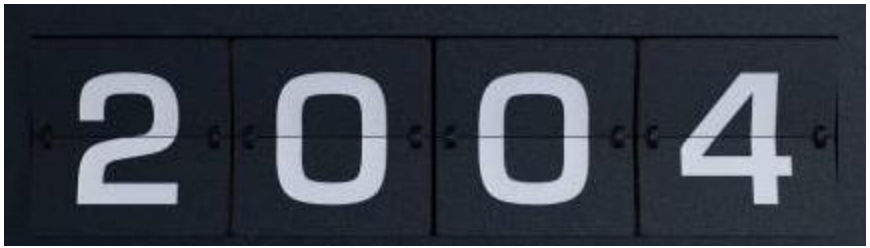
PHYSIOLOGY IN MEDICINE: A SERIES OF ARTICLES LINKING MEDICINE WITH SCIENCE
Physiology in Medicine
Dennis A. Ausiello, MD, *Editor*; Dale J. Benos, PhD, *Deputy Editor*; Francois Abboud, MD, *Associate Editor*; William Koopman, MD, *Associate Editor*

Annals of Internal Medicine
Paul Epstein, MD, *Series Editor*

REVIEW

Pain: Moving from Symptom Control toward Mechanism-Specific Pharmacologic Management

Clifford J. Woolf, MD



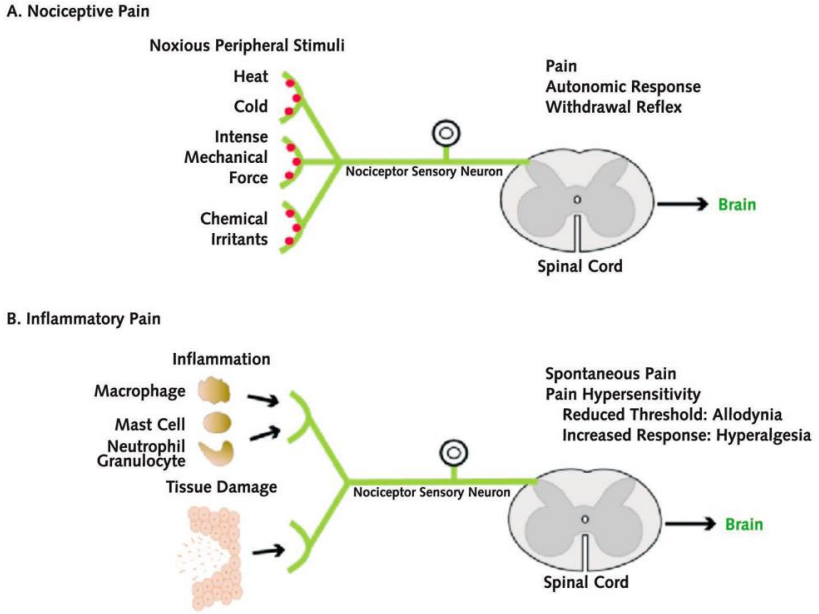
ADAPTIVE PAIN

The somato-sensorial peripheral and central system is intact

Adaptive Pain

Nociceptive

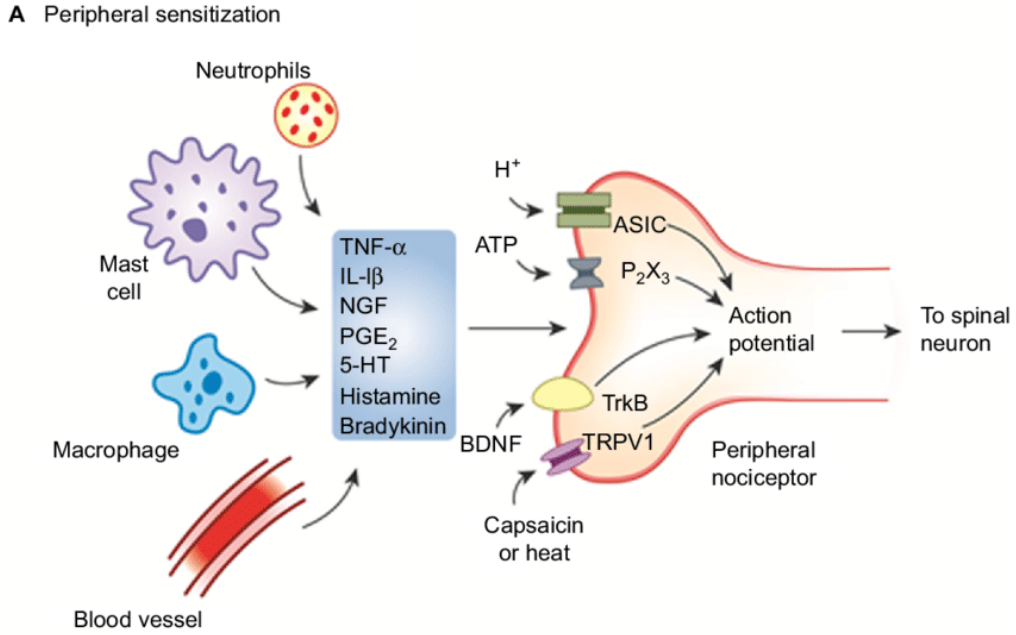
Inflammatory



ADAPTIVE PAIN

PERIPHERAL SENSITIZATION

Sensitization of the nociceptive terminals in skin and muscle



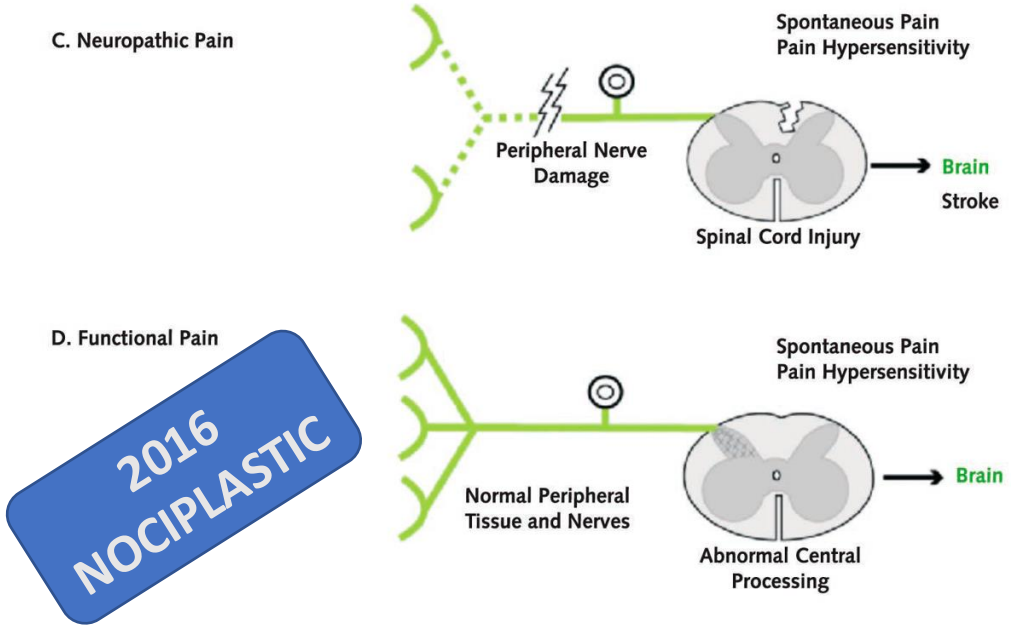
MALADAPTIVE PAIN

Absence of external potentially noxious inputs

Maladaptive Pain

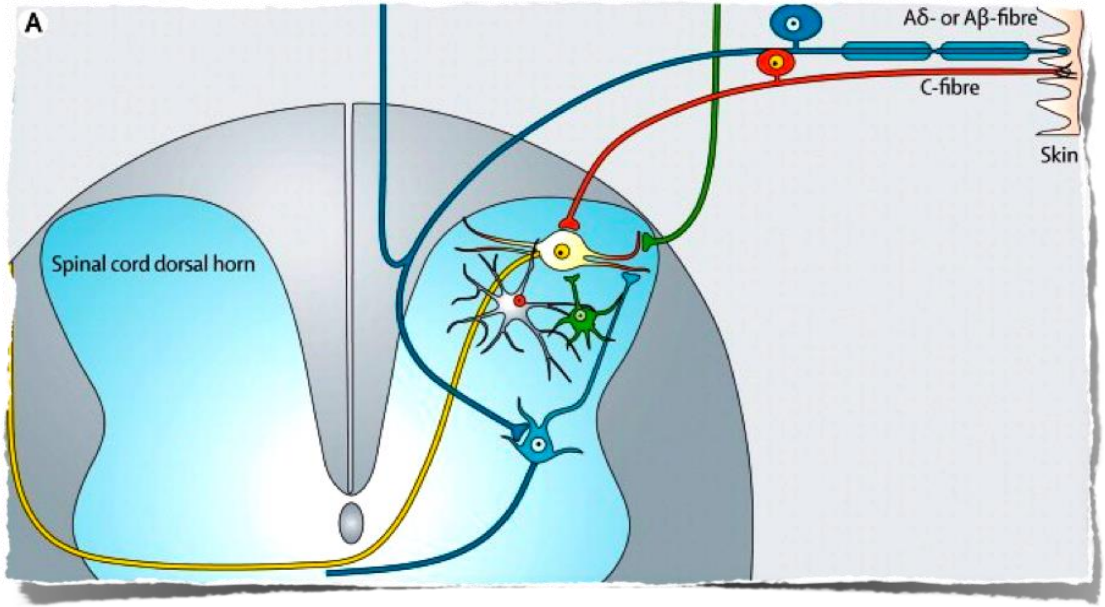
Neuropathic

Nociplastic

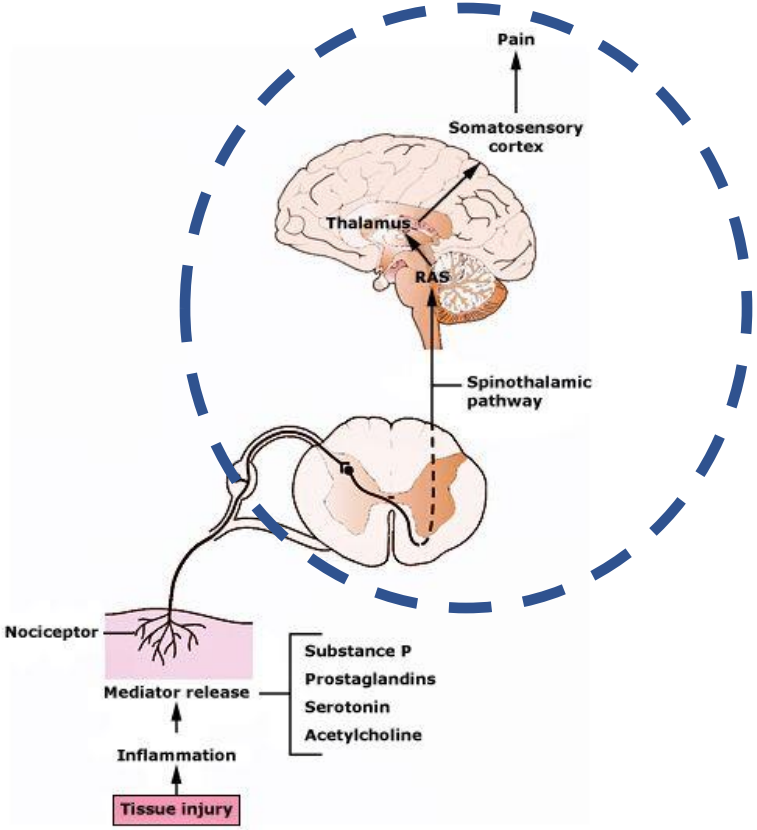


MALADAPTIVE PAIN

CENTRAL SENSITIZATION



CENTRAL ANALGESICS



EXPERT OPINION ON PHARMACOTHERAPY
https://doi.org/10.1080/14656566.2021.1970135

Taylor & Francis
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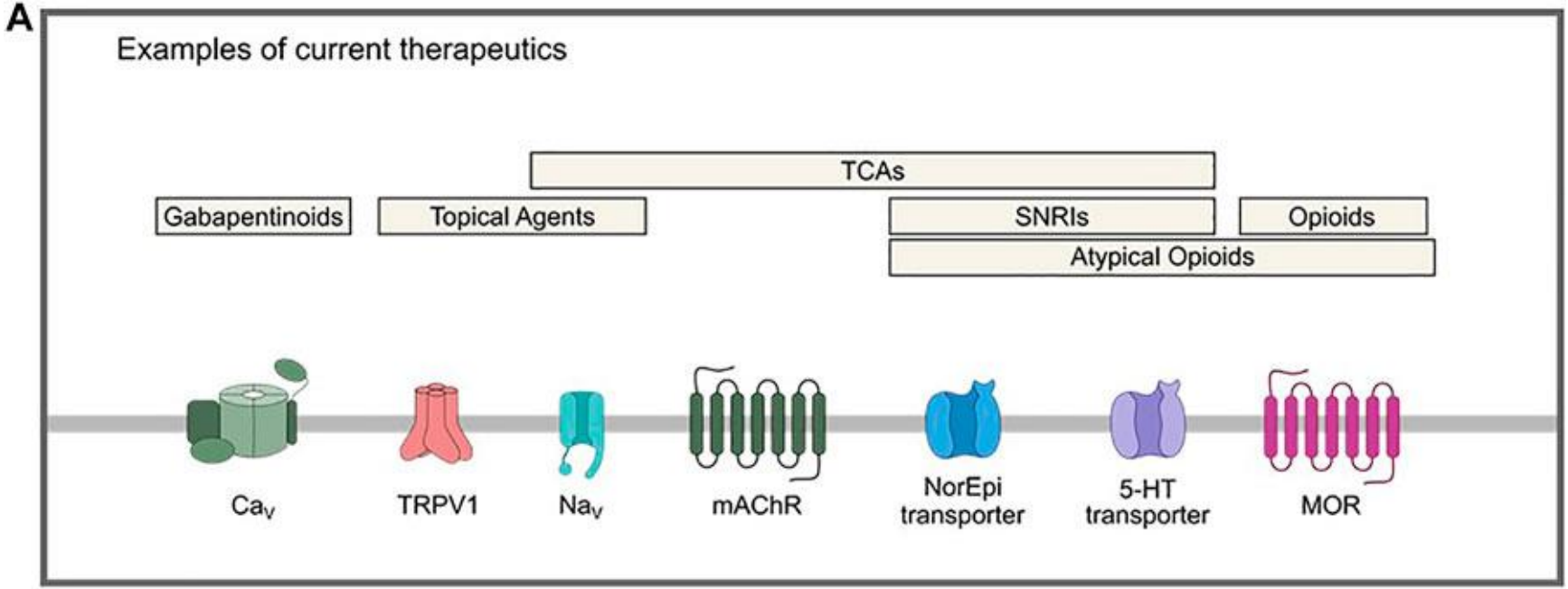
REVIEW

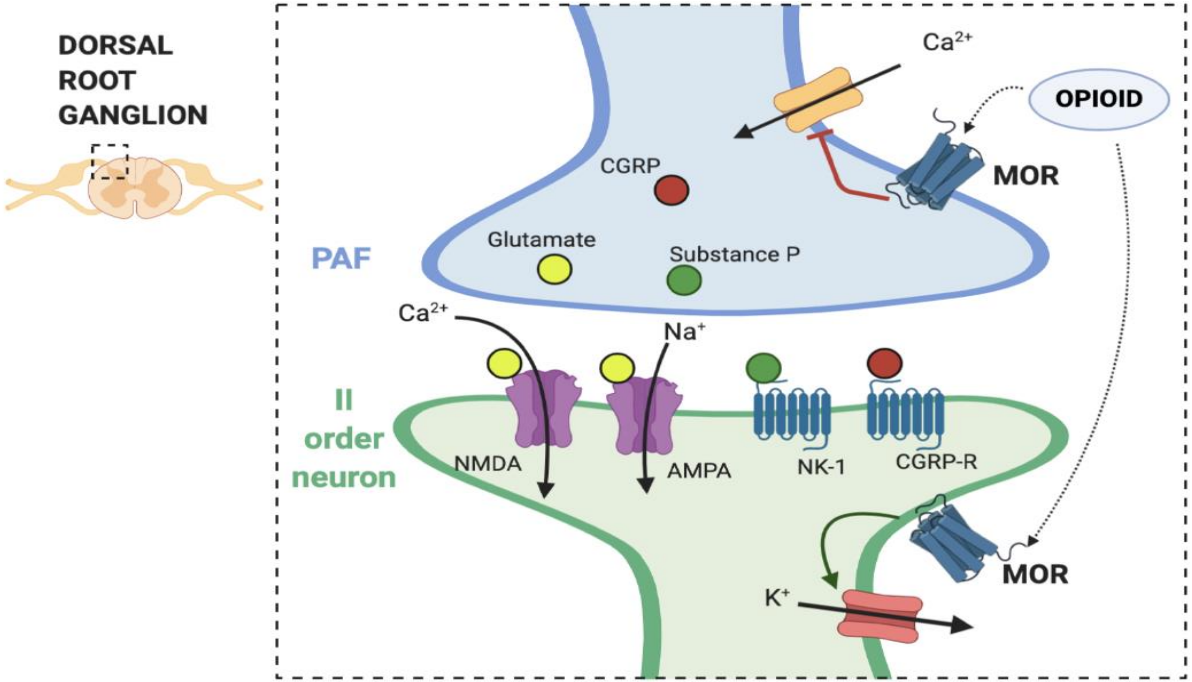
Pharmacologic agents directed at the treatment of pain associated with maladaptive neuronal plasticity

Joseph V. Pergolizzi Jr.[a], Giustino Varrassi [b], Peter Magnusson [c,d], Frank Breve[e], Robert B. Raffa [f,g], Paul J. Christo[h], Maninder Chopra[i], Antonella Paladini [j], Jo Ann LeQuang [a], Kailyn Mitchell[a] and Flaminia Coluzzi[k]

[a]NEMA Research, Inc, Naples, USA; [b]Paolo Procacci Foundation, Rome, Italy; [c]Centre for Research and Development, Region Gävleborg/Uppsala University, Gävle, Sweden; [d]Department of Medicine, Cardiology Research Unit, Karolinska Institutet, Stockholm, Sweden; [e]Department of Pharmacy Practice, Temple University School of Pharmacy, Philadelphia, USA; [f]College of Pharmacy (Adjunct), University of Arizona, Tucson, USA; [g]Temple University School of Pharmacy (Professor Emeritus), Philadelphia, USA; [h]Associate Professor, the Johns Hopkins School of Medicine, Baltimore, USA; [i]Decision Alternatives, LLC, Frederick, USA; [j]Department MESVA, University of L'Aquila, L'Aquila, Italy; [k]Department Medical and Surgical Sciences and Biotechnologies, Sapienza University of Rome, Latina, Italy


A
Examples of current therapeutics
TCAs
Gabapentinoids
Topical Agents
SNRIs
Opioids
Atypical Opioids
Ca_V
TRPV1
Na_V
mAChR
NorEpi transporter
5-HT transporter
MOR

OPIOIDS: MOR-mediated modulation

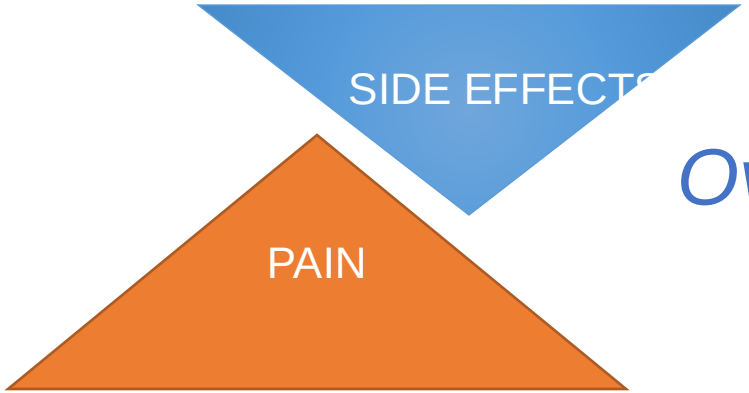


Coluzzi F,
Therapeutics and Clinical Risk Management 2020:16 1–17

OPIOIDS: RATIONAL USE

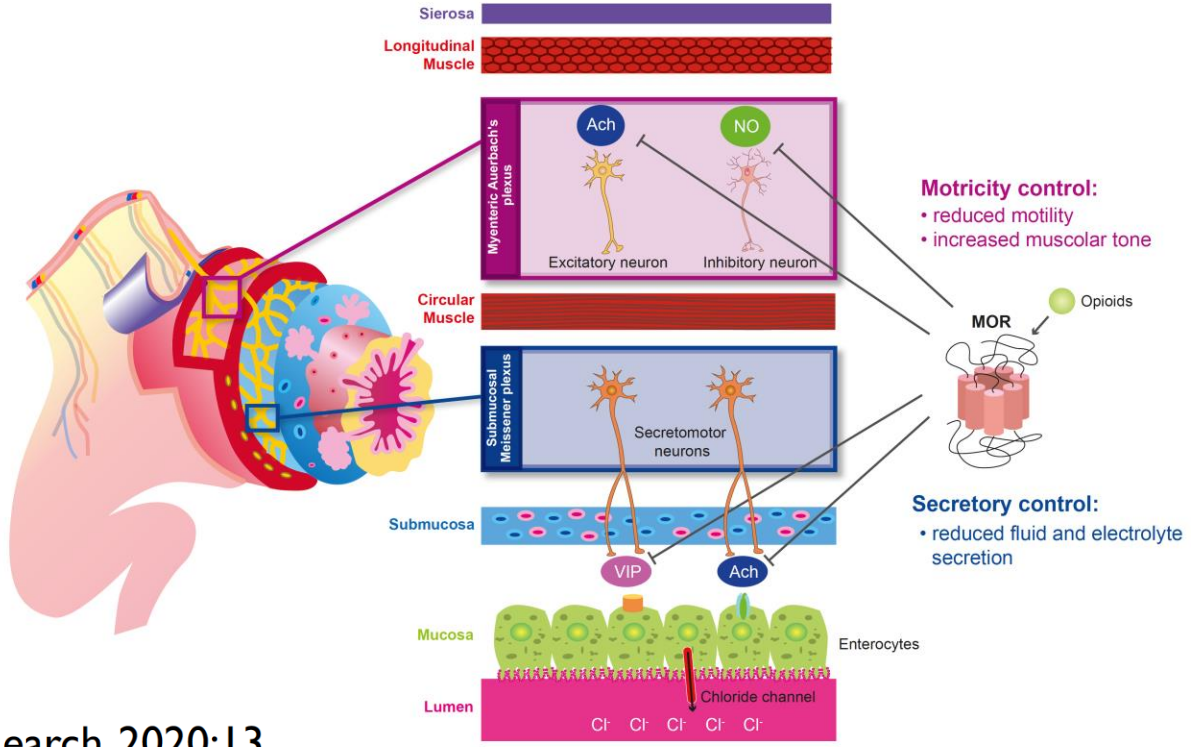
TITRATION is the first step

- Reach to lowest effective dose
- Minimize side effects
- Tailored therapy



Overlapping

Opioid-Induced Constipation



Coluzzi F et al.

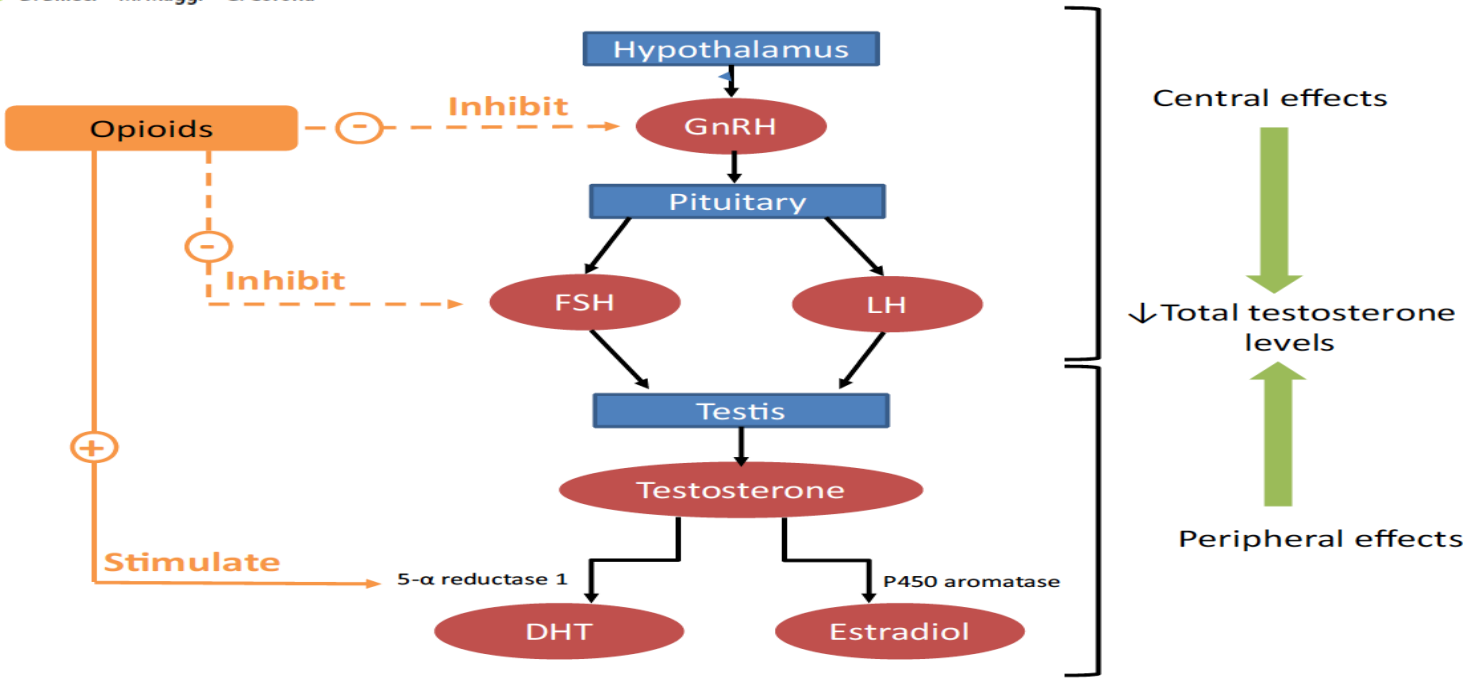
Journal of Pain Research 2020:13

Journal of Endocrinological Investigation
https://doi.org/10.1007/s40618-018-0964-3

REVIEW ARTICLE

Testosterone deficiency in non-cancer opioid-treated patients

F. Coluzzi[1] · D. Billeci[2] · M. Maggi[3] · G. Corona[4]

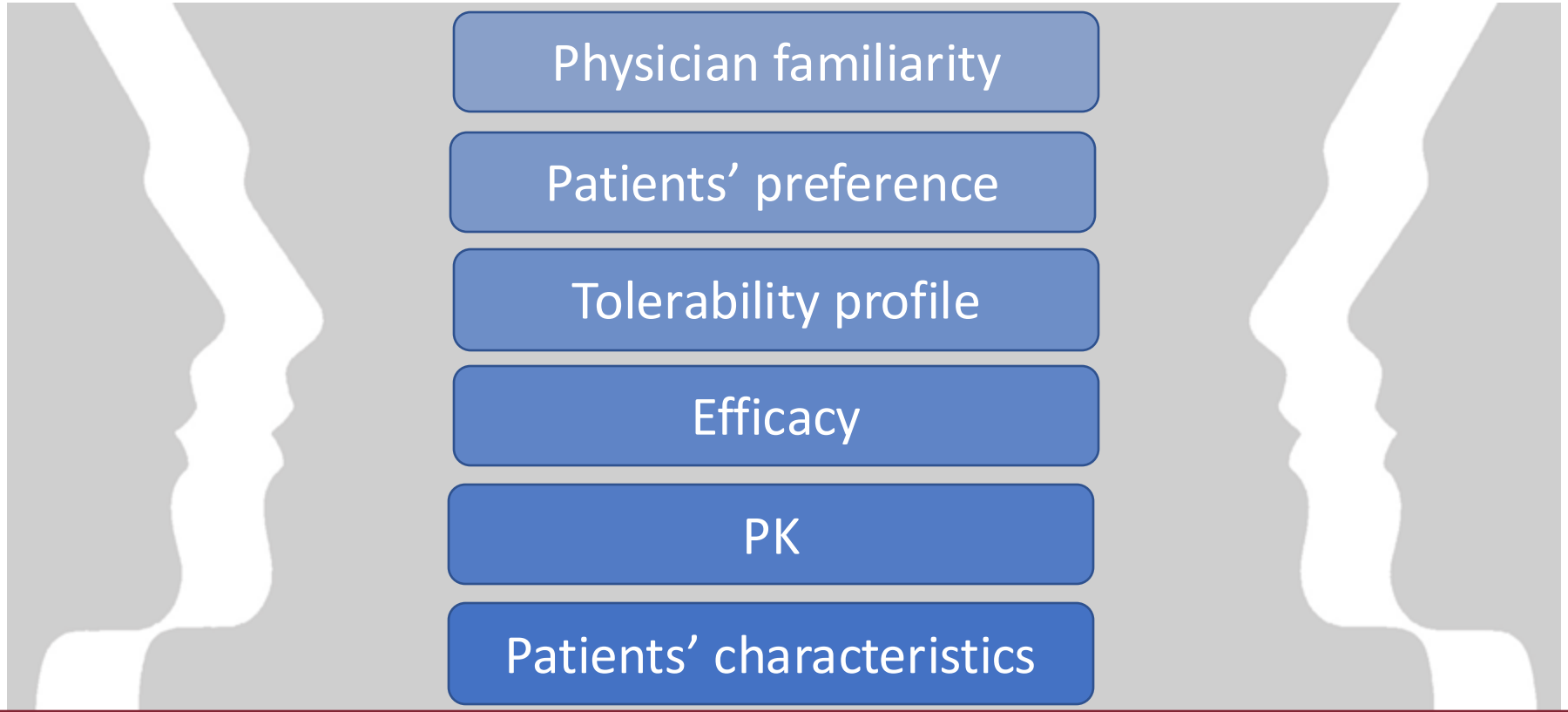


Opioid Classification

	LAO	SAO	ROO
ANALGESIA	**Long Acting**	**Short Acting**	**Rapid Onset**
Onset	1-2 hrs	30-40 min	15 min
Duration	8-12 + hrs	4 hrs	1-2 hrs

How to choose…

Choosing the right LAO



Drugs
https://doi.org/10.1007/s40265-018-0980-9

REVIEW ARTICLE

CrossMark

Assessing and Treating Chronic Pain in Patients with End-Stage Renal Disease

Flaminia Coluzzi[1]

Table 3 Pharmacological treatment for chronic pain management in ESRD

Drugs	Route of administration	Starting dosage	Indications	Clinical considerations
Opioids				
Buprenorphine patch	Transdermal	5 µg/h	Severe chronic pain	Safer profile
Fentanyl patch	Transdermal	12 µg/h	Severe chronic pain	Safer profile. No clinically significant accumulation in CKD
Hydromorphone	Oral	4 mg bid	Severe chronic pain (second-line treatment)	Safe, but use with caution. Dose adjustment required
Oxycodone	Oral	5 mg bid	Severe chronic pain (second-line treatment)	Safe, but use with caution. Dose adjustment required
Tramadol	Oral	50 mg bid	Severe chronic pain (second-line treatment)	Safe, but use with caution. Dose adjustment required
Tapentadol	Oral	25 mg bid	Severe chronic pain (second-line treatment)	No dose adjustment needed for CrCl ≥ 30 ml/min. Data are not available in ESRD
Morphine				Not recommended due to accumulation. To be avoided
Codeine				Not recommended due to accumulation. To be avoided

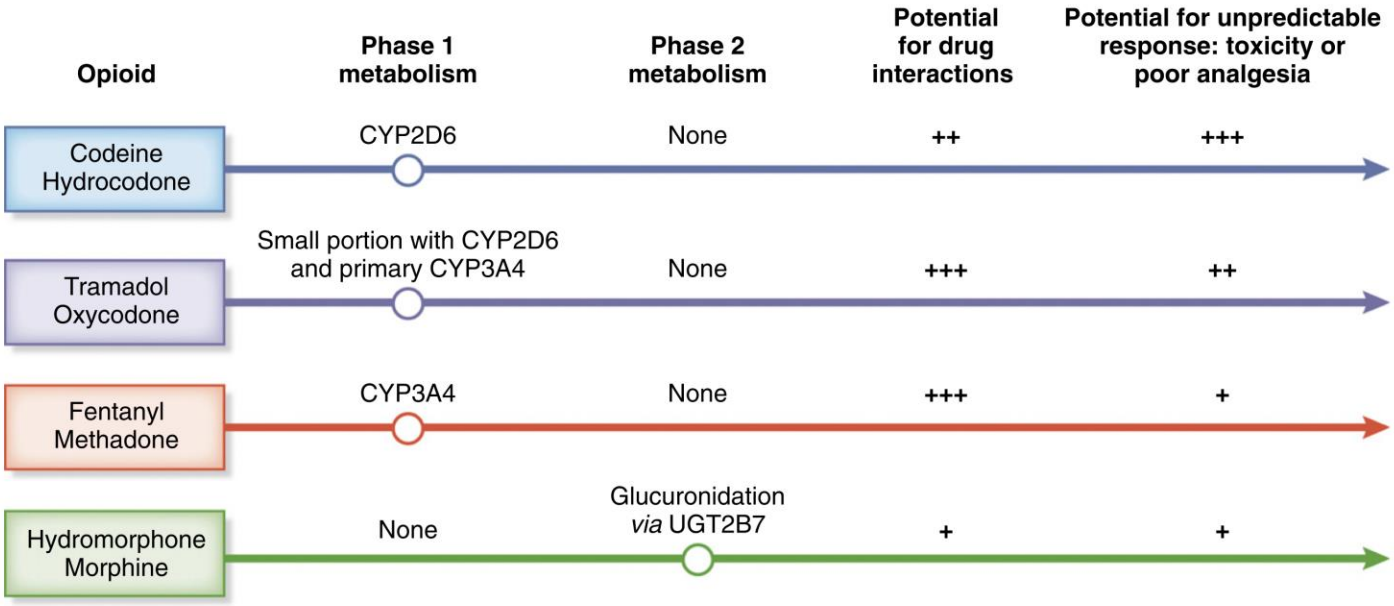
Opioids in liver failure

Table 3. Recommendations for Opioids in Hepatic Impairment

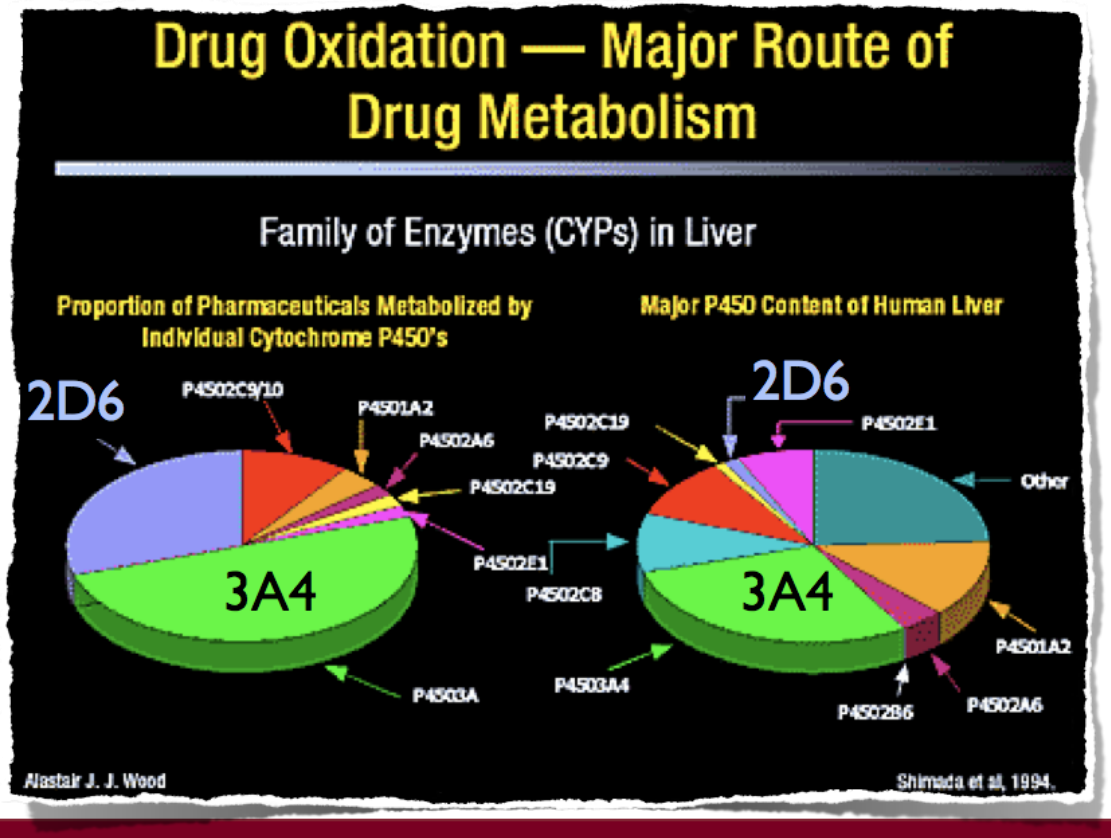
Opioid	Recommendations
Codeine	Not recommended; in severe hepatic dysfunction codeine is not converted to morphine, leading to poor analgesia
Fentanyl	99% metabolized in liver; studies have not demonstrated PK alterations; careful monitoring is warranted
Hydrocodone	Use with caution; monitor for overdose due to parent compound not being converted to metabolites
Hydromorphone	Undergoes phase II reaction; however, use with caution due to its intermediate extraction ratio
Methadone	Use with caution; risk of accumulation because of increased free drug
Meperidine	Not recommended; toxic metabolite, normeperidine, may accumulate
Morphine	Use with caution; monitor for overdose due to high extraction ratio
Oxycodone	Use with caution; dose adjustment recommended (1/2 to 1/3 of original dose)
Oxymorphone	Contraindicated in moderate-to-severe hepatic impairment
Tramadol	Not recommended; significant PK changes in moderate-to-severe hepatic impairment

PK: pharmacokinetics. Source: References 8, 16.

PK: Opioids'Metabolism



Drug-Drug Interactions: Role of CYP450



PK: potential drug-drug interactions

CYP2D6

- Codeine
- Tramadol
- Hydrocodone
- Oxycodone
- Methadone

CYP3A4

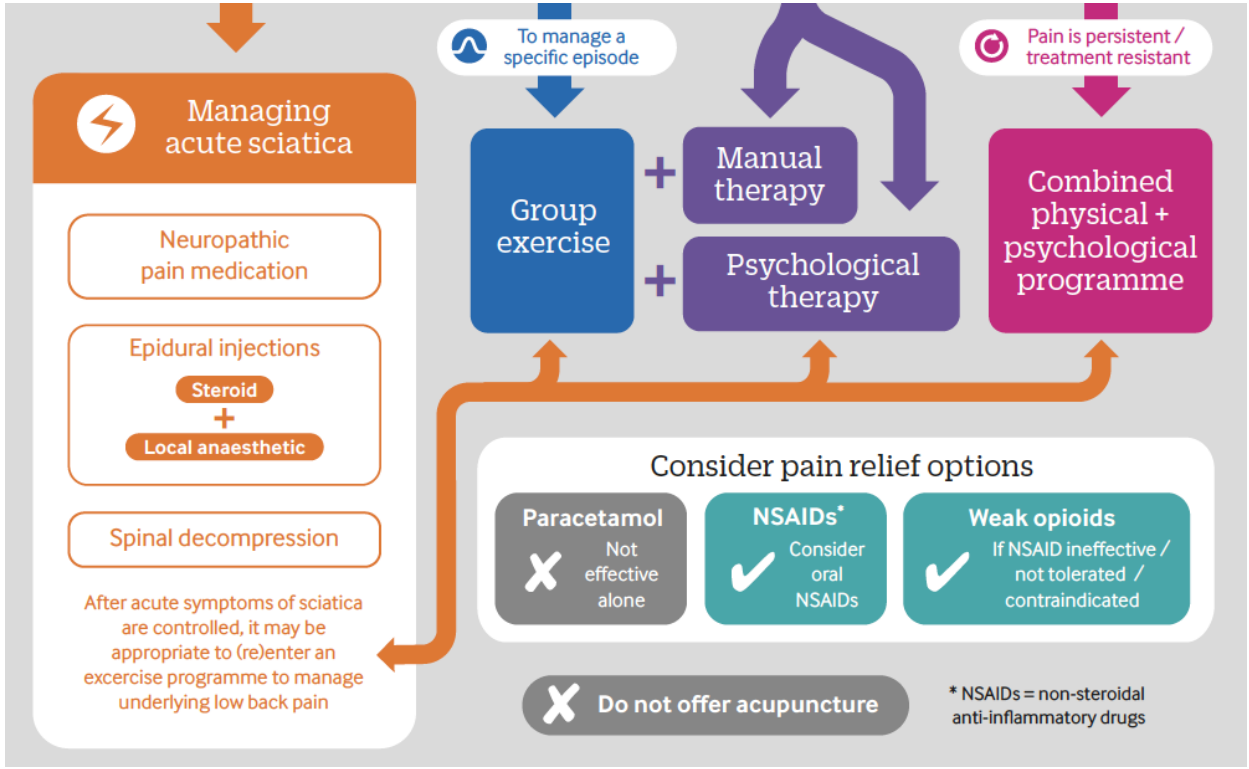
- Codeine
- Tramadol
- Fentanyl
- Methadone

- Morphine
- Hydromorphone
- Oxymorphone
- Tapentadol

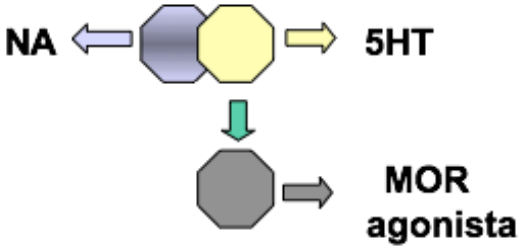
Ideal Analgesic Drug

- Potent analgesic effect
- Low abuse potential
- No tolerance
- Reduced risk of respiratory depression and other AEs
- Safe for long term use

NICE guidelines LBP

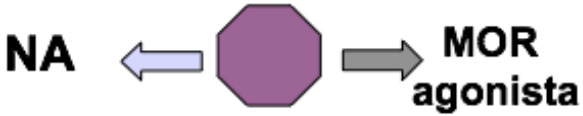


TRAMADOL



Racemic mixture
Prodrug
MOR/SNRI
Metabolic activation (CYP2D6)

TAPENTADOL



Single molecule
No metabolic activation
No active metabolites
Synergic MOR/NRI activity

Tapentadol: more than “MOR” …

STRONG ANALGESIC ≠ **STRONG OPIOID**

EXPECTED ADVANTAGES:

Similar Analgesia

Lower incidence of side effects

Adv Ther
https://doi.org/10.1007/s12325-018-0778-x

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COMMENTARY

Does ‘Strong Analgesic’ Equal ‘Strong Opioid’? Tapentadol and the Concept of ‘μ-Load’

Robert B. Raffa · Christian Elling · Thomas M. Tzschentke

Reduced μ load

Tapentadol: the concept of Mu-Load

Adv Ther
https://doi.org/10.1007/s12325-018-0778-x

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COMMENTARY

Does 'Strong Analgesic' Equal 'Strong Opioid'? Tapentadol and the Concept of 'μ-Load'

Robert B. Raffa · Christian Elling · Thomas M. Tzschentke

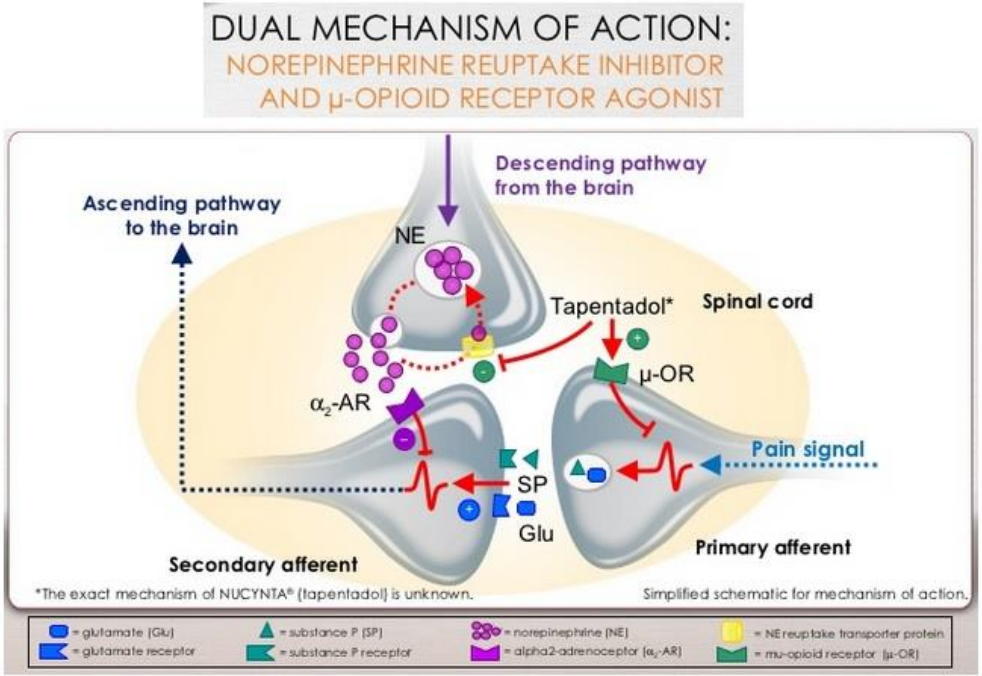
Table 1 Summary of the calculated estimates of the contribution of tapentadol's opioid component to its analgesic (antinociceptive) action

Pain type	Source of data	Estimate (%)
Nociceptive	Animal model: LITF-r (low-intensity tail-flick test, rat)	54
Neuropathic	Animal model: SNL-r (spinal nerve ligation test, rat)	36

54% **36%**

NEUROPATHIC

Tapentadol is ATYPICAL



Sources: Tzschentke et al, 2007; Vanderah, 2007; Pertovaara, 2006; Janssen Pharmaceuticals, Inc.

Tapentadol: LBP with or without NP component

CMRO

Current Medical Research & Opinion Vol. 28, No. 6, 2012, 1–26

0300-7995
doi:10.1185/03007995.2012.679254

Article FT-0043.R1/679254

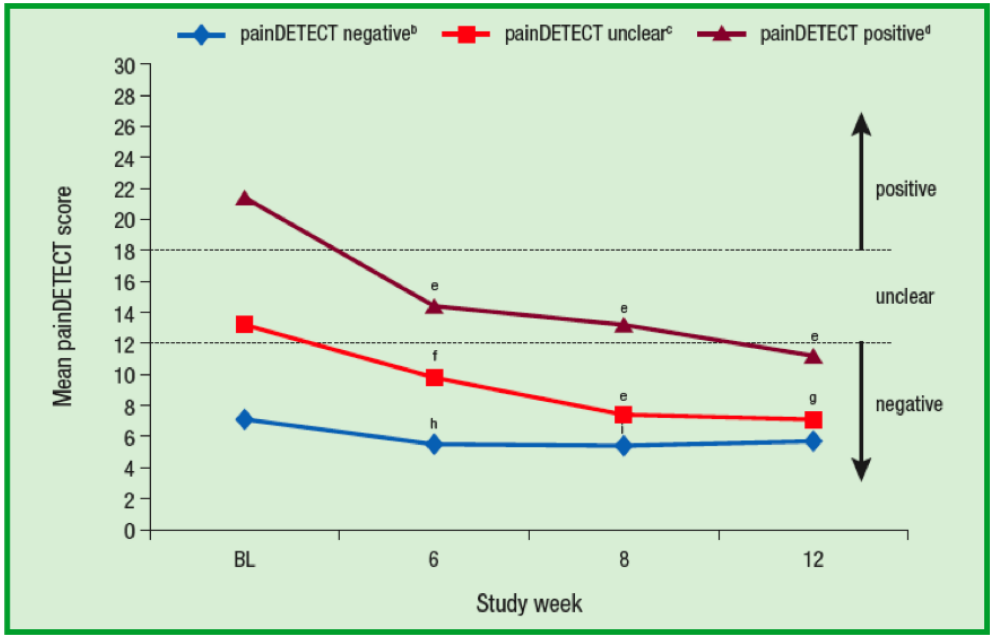
Original article

Effectiveness and safety of tapentadol prolonged release for severe, chronic low back pain with or without a neuropathic pain component: results of an open-label, phase 3b study

Ilona Steigerwald
Matthias Müller
Medical Affairs Europe & Australia, Grünenthal GmbH, Aachen, Germany

Abstract

Objective:
This open-label, phase 3b study evaluated the effectiveness and tolerability of tapentadol prolonged release and tapentadol immediate release (for acute pain episodes) for severe, chronic low back pain with or without



Tapentadol: NECK PAIN

with or without NP component

CURRENT MEDICAL RESEARCH AND OPINION
2020, VOL. 36, NO. 4, 651–659
https://doi.org/10.1080/03007995.2020.1722083
Article ST-0636/1722083

Taylor & Francis
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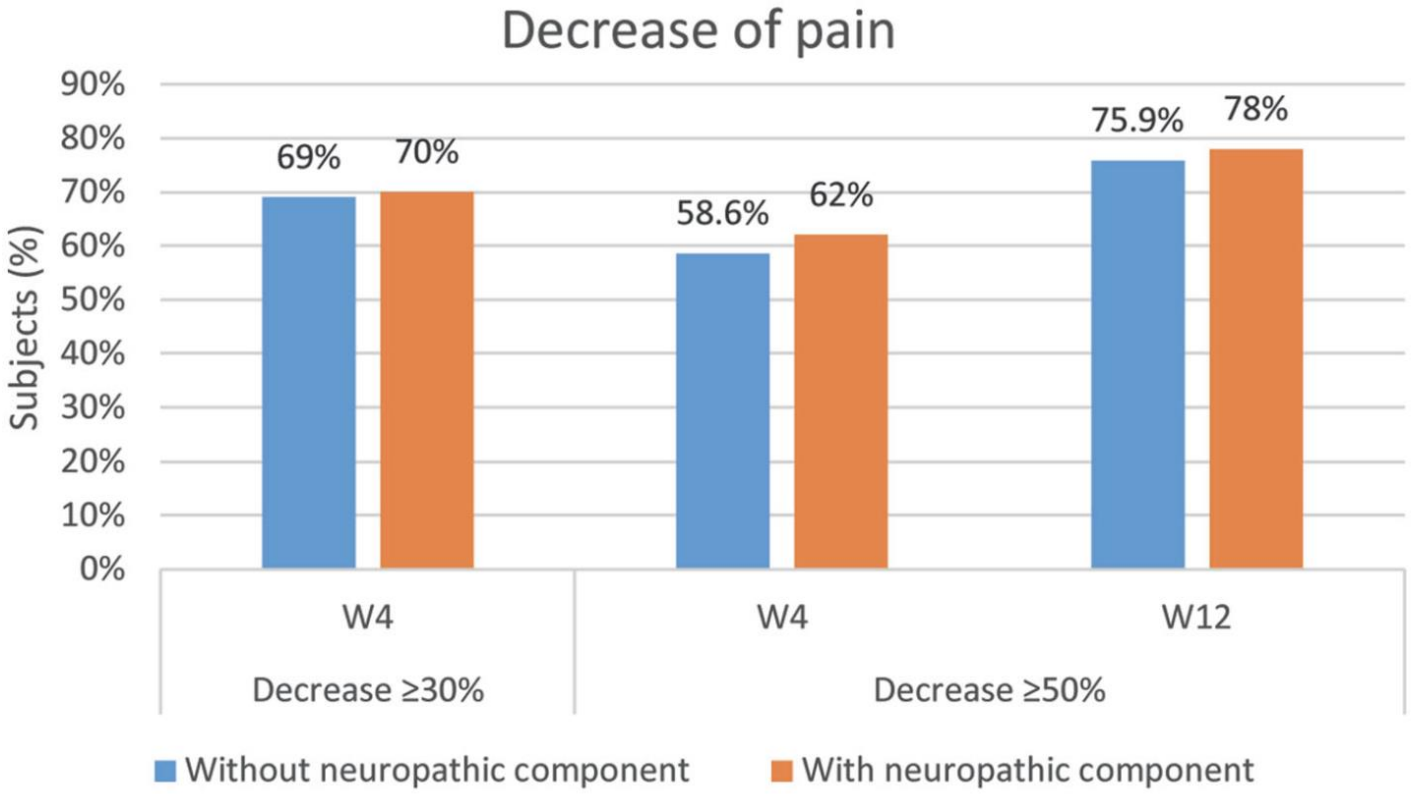
ORIGINAL ARTICLE

Tapentadol prolonged release for managing moderate to severe chronic neck pain with or without a neuropathic component

Flaminia Coluzzi[a], Joseph V. Pergolizzi Jr[b], Enrico Giordan[c], Pamela Locarini[a], Alessandro Boaro[c] and Domenico Billeci[c]



CURRENT MEDICAL RESEARCH AND OPINION
2020, VOL. 36, NO. 4, 651–659
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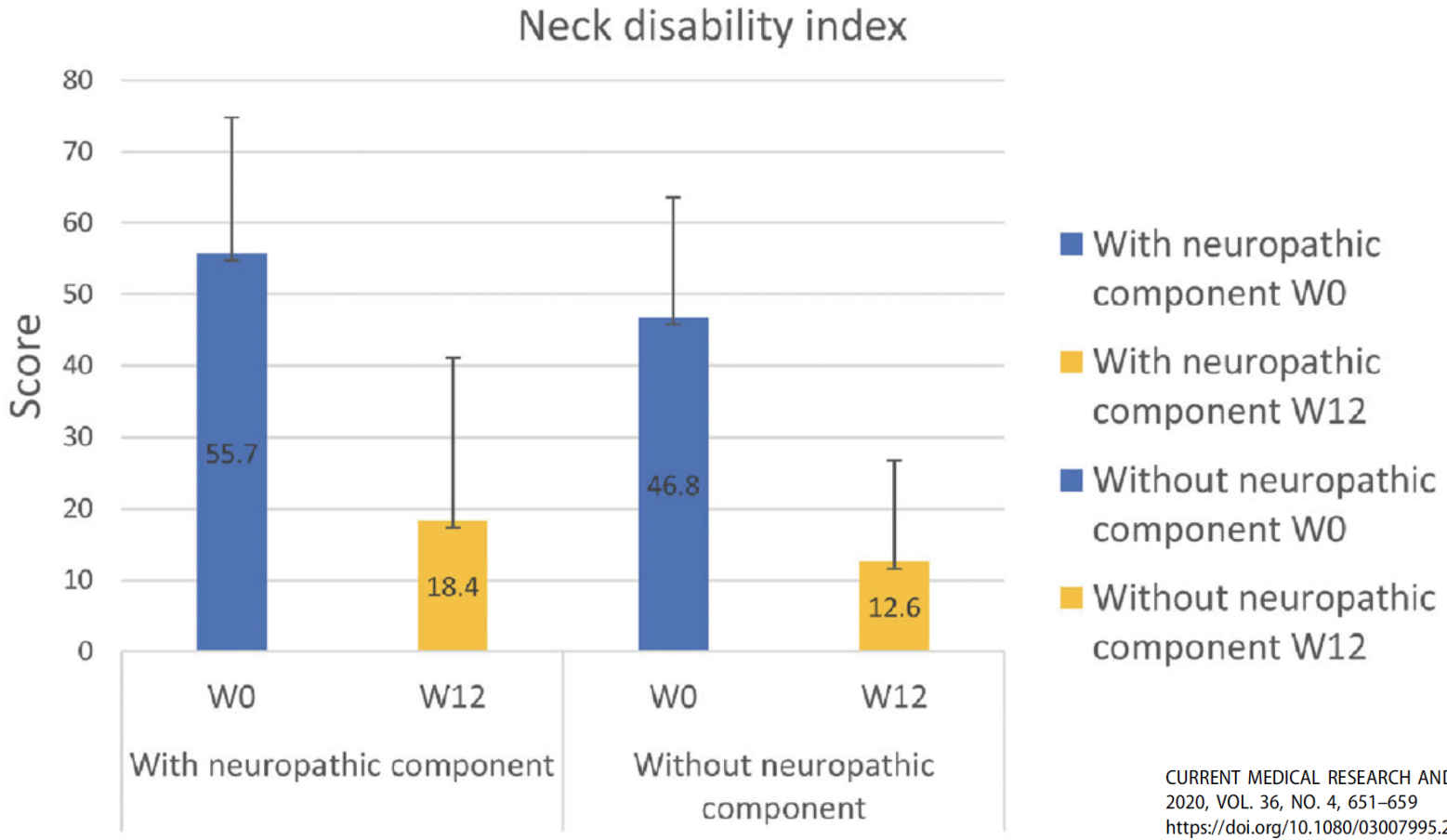


CURRENT MEDICAL RESEARCH AND OPINION
2020, VOL. 36, NO. 4, 651–659
https://doi.org/10.1080/03007995.2020.1722083

Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis

Nanna B Finnerup*, Nadine Attal*, Simon Haroutounian, Ewan McNicol, Ralf Baron, Robert H Dworkin, Ian Gilron, Maija Haanpää, Per Hansson, Troels S Jensen, Peter R Kamerman, Karen Lund, Andrew Moore, Srinivasa N Raja, Andrew S C Rice, Michael Rowbotham, Emily Sena, Philip Siddall, Blair H Smith, Mark Wallace

NeuP SIG

IASP
International Association for the Study of Pain

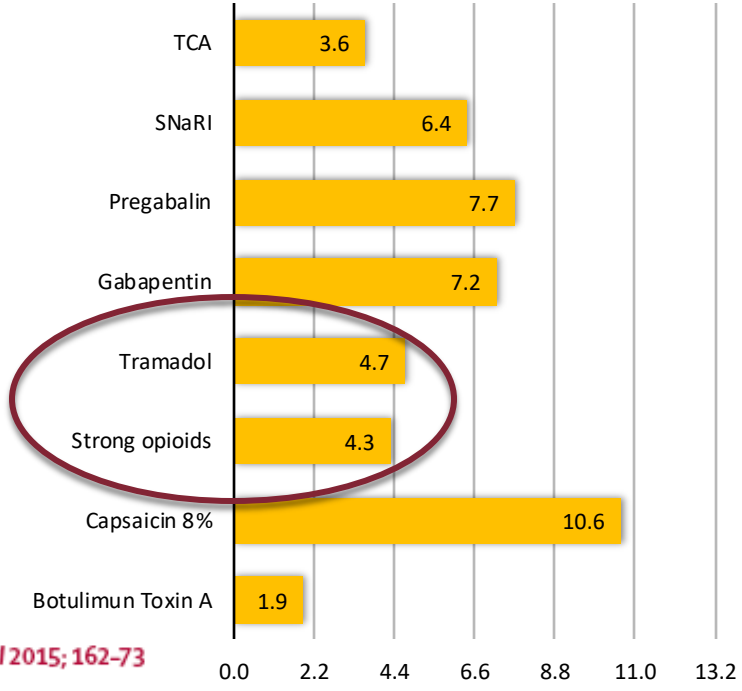
	Total daily dose and dose regimen	Recommendations
Strong recommendations for use		
Gapabentin	1200–3600 mg, in three divided doses	First line
Gabapentin extended release or enacarbil	1200–3600 mg, in two divided doses	First line
Pregabalin	300–600 mg, in two divided doses	First line
Serotonin-noradrenaline reuptake inhibitors duloxetine or venlafaxine*	60–120 mg, once a day (duloxetine); 150–225 mg, once a day (venlafaxine extended release)	First line
Tricyclic antidepressants	25–150 mg, once a day or in two divided doses	First line†
Weak recommendations for use		
Capsaicin 8% patches	One to four patches to the painful area for 30-60 min every 3 months	Second line (peripheral neuropathic pain)‡
Lidocaine patches	One to three patches to the region of pain once a day for up to 12 h	Second line (peripheral neuropathic pain)
Tramadol	200–400 mg, in two (tramadol extended release) or three divided doses	Second line
Botulinum toxin A (subcutaneously)	50–200 units to the painful area every 3 months	Third line; specialist use (peripheral neuropathic pain)
Strong opioids	Individual titration	Third line§

Lancet Neurol 2015; 162–73

NeuP SIG 2015

IASP
International Association for the Study of Pain

NNT



Lancet Neurol 2015; 162–73

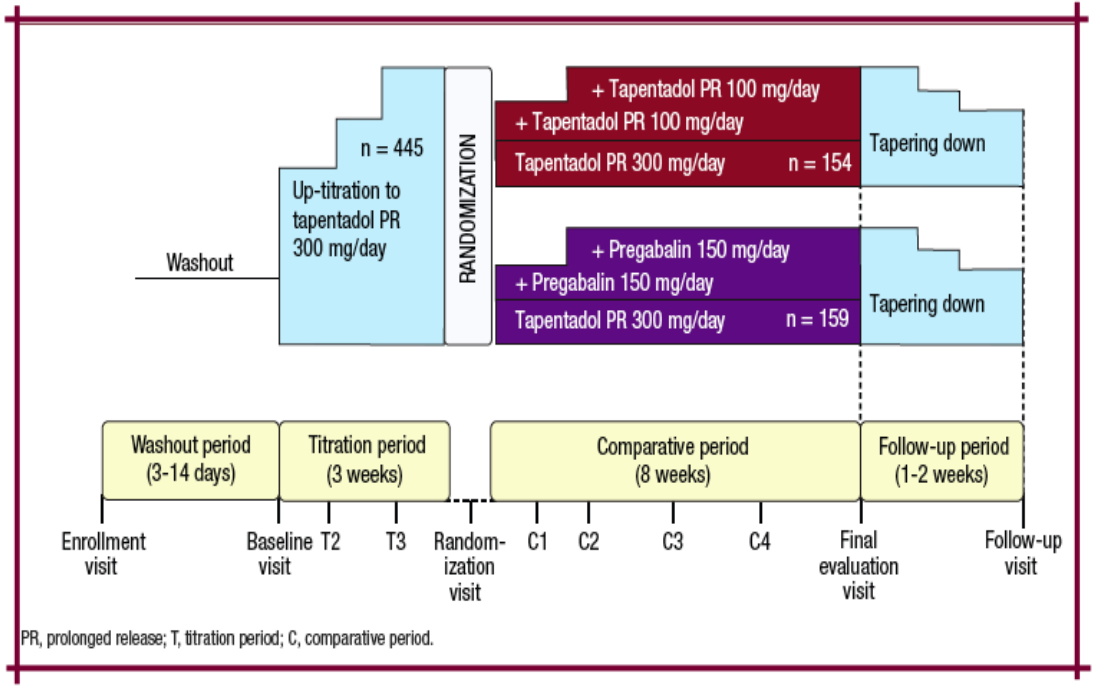
	Comparisons*	Participants†	Active pain relief	Placebo	Number needed to treat (95% CI)	Susceptibility to bias‡
Tricyclic antidepressants	15	948	217/473	85/475	3·6 (3·0–4·4)	1973
Serotonin-noradrenaline reuptake inhibitors	10	2541	676/1559	278/982	6·4 (5·2–8·4)	1826
Pregabalin	25	5940	1359/3530	578/2410	7·7 (6·5–9·4)	2534
Gabapentin§	14	3503	719/2073	291/1430	7·2 (5·9–9·1)	1879
Tramadol	6	741	176/380	96/361	4·7 (3·6–6·7)	982
Strong opioids	7	838	211/426	108/412	4·3 (3·4–5·8)	1326
Capsaicin 8%	6	2073	466/1299	212/774	10·6 (7·4–18·8)	70¶
Botulinum toxin A	4	137	42/70	4/67	1·9 (1·5–2·4)	678

LBP with NP: Tapentadol + Pregabalin

ORIGINAL ARTICLE

Effectiveness and Safety of Tapentadol Prolonged Release (PR) Versus a Combination of Tapentadol PR and Pregabalin for the Management of Severe, Chronic Low Back Pain With a Neuropathic Component: A Randomized, Double-blind, Phase 3b Study

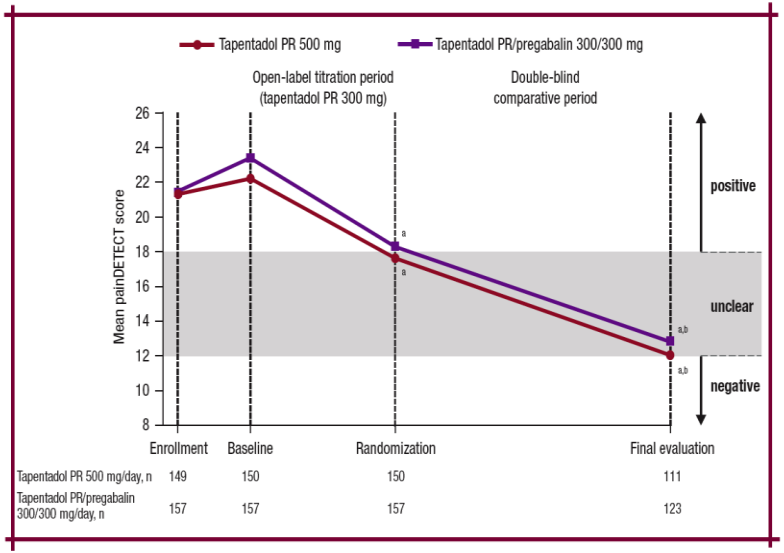
Ralf Baron, MD, PhD*; Emilio Martin-Mola, MD, PhD†; Matthias Müller, MD, MSc‡; Cecile Dubois, MS§; Dietmar Falke, PhD‡; Ilona Steigerwald, MD‡



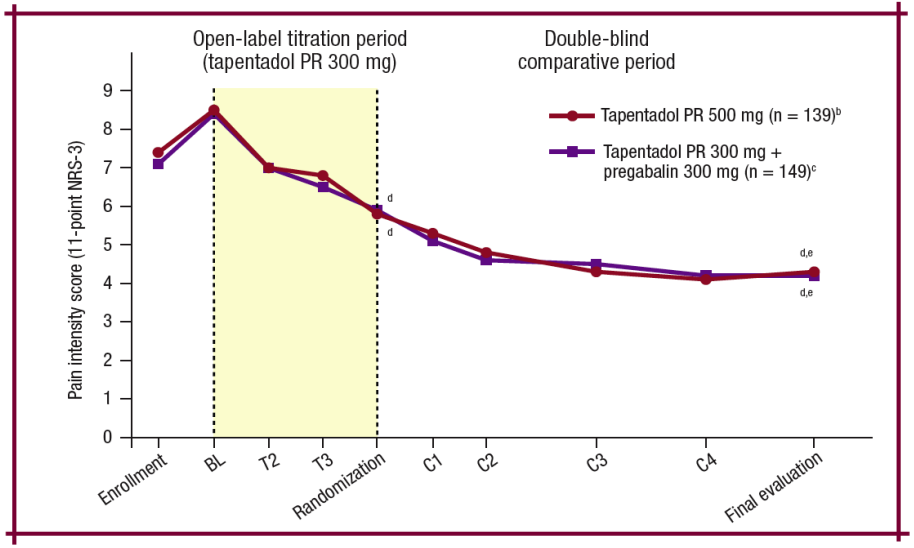
Baron R et al. Pain Pract 2016; 16(5):580-99

LBP with NP: Tapentadol + Pregabalin

NEUROPATHIC PAIN SYMPTOMS



MEAN PAIN INTENSITY

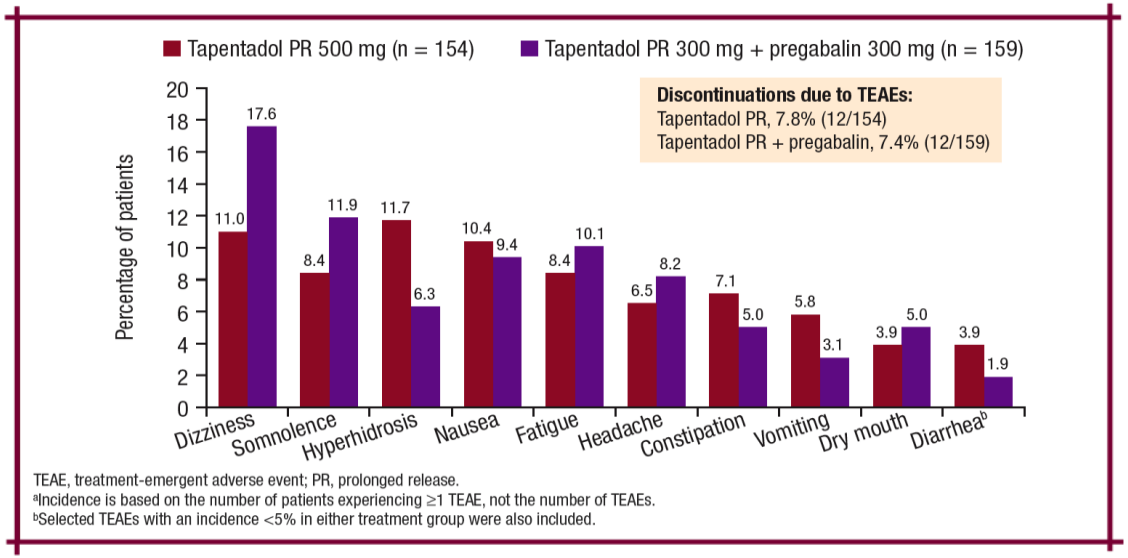


Baron R et al. Pain Pract 2016; 16(5):580-99

LBP with NP: Tapentadol + Pregabalin

Baron R et al. Pain Pract 2016; 16(5):580-99

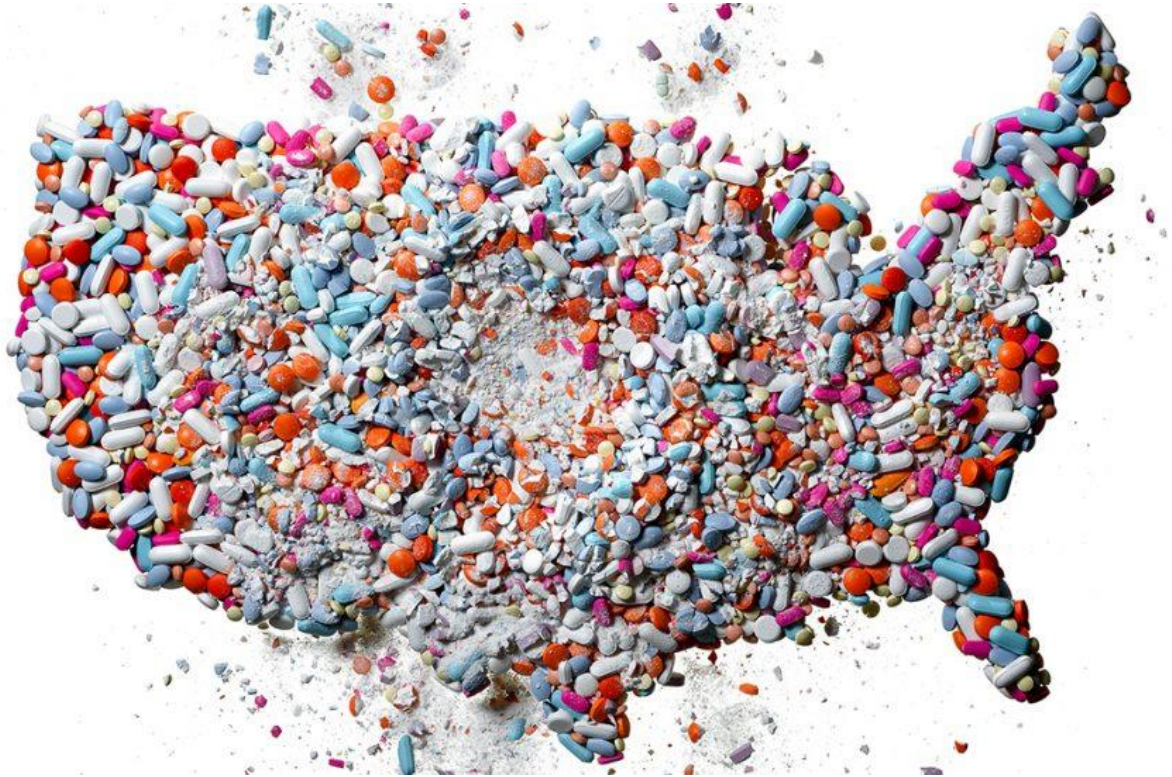
TEAEs > 5%



TEAE, treatment-emergent adverse event; PR, prolonged release.
[a]Incidence is based on the number of patients experiencing ≥1 TEAE, not the number of TEAEs.
[b]Selected TEAEs with an incidence <5% in either treatment group were also included.

OPIOIDS for chronic non-cancer pain

Unmet NEED from "OPIOID EPIDEMIC"

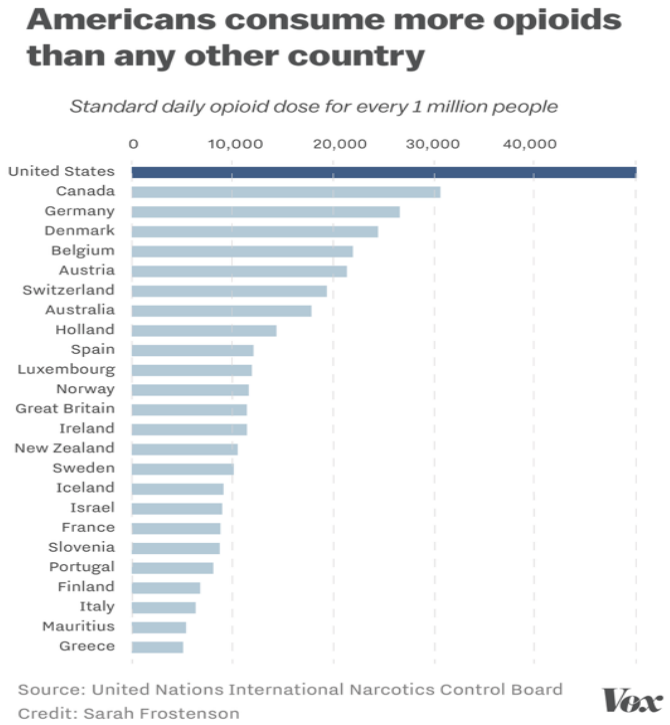


The US “OPIOID EPIDEMIC”

2015’s US opioid deaths…

more than one 747 plane crashing every week

US 70% of global opioid consumption

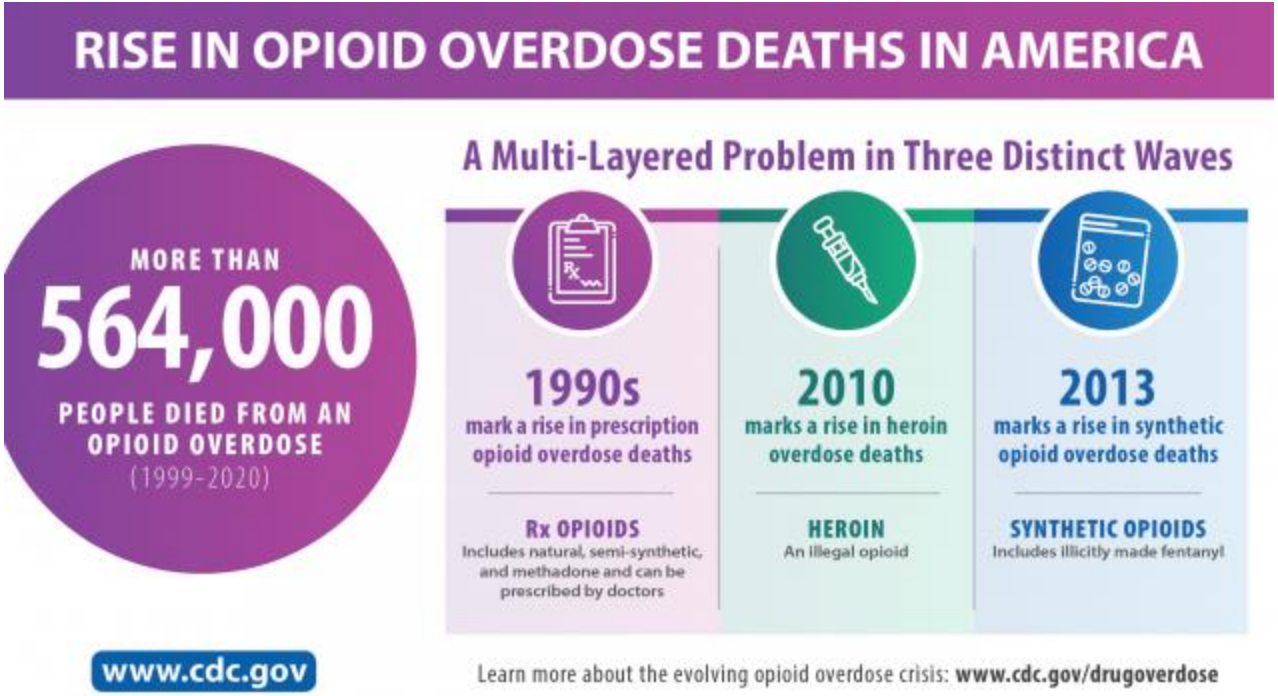


US vs EU

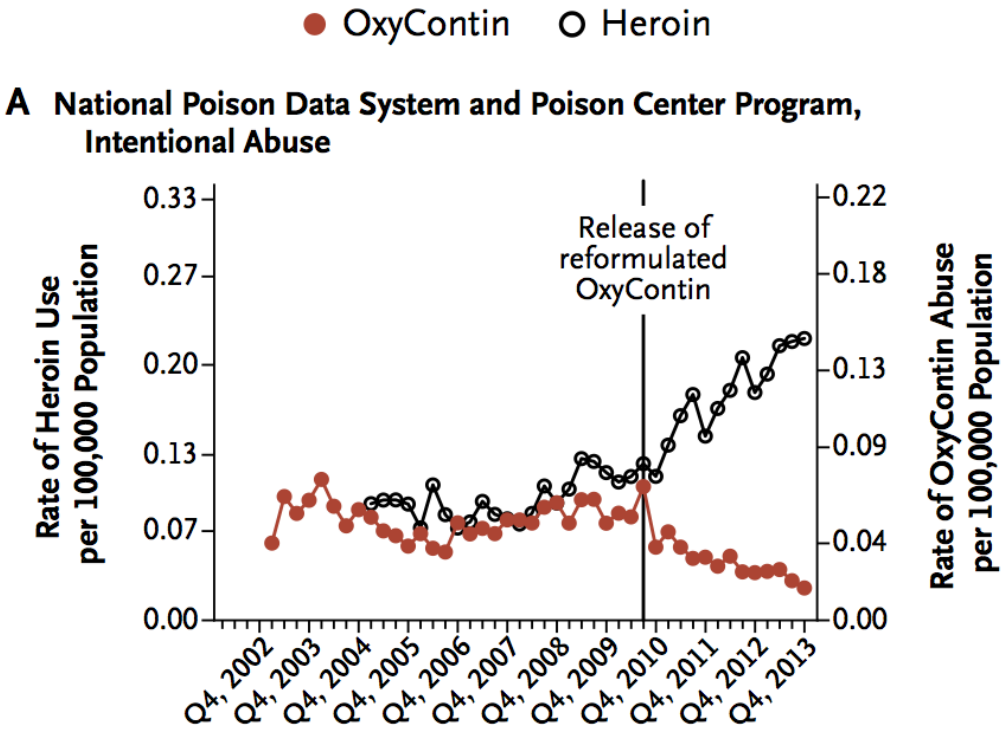
- 323 million: **4%** of the world's population
- 8.5 million misuse opioids: **3%**
- 22000 (2016): 27% of the world's drug overdose death

- 741 million: **10%** of the world's population
- 1.3 million misuse opioids: **0.4%**
- 6800 (2016): 8.3% of the world's drug overdose death

The triple wave epidemic



The US political of OPIOID restriction



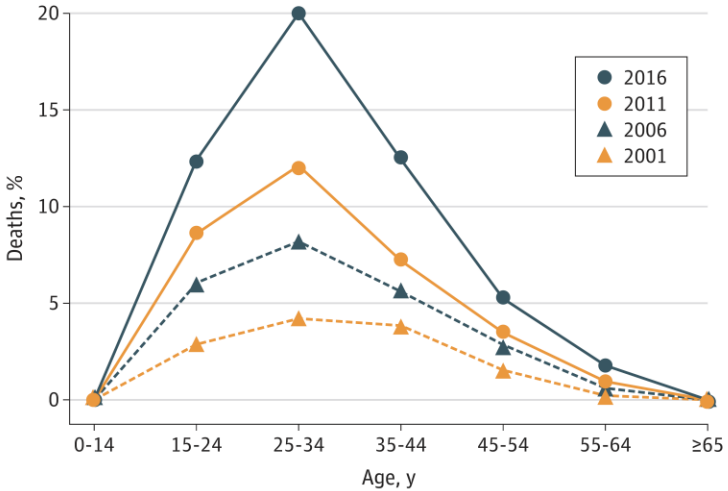
JAMA Network Open

Original Investigation | Substance Use and Addiction

The Burden of Opioid-Related Mortality in the United States

Tara Gomes, PhD; Mina Tadrous, PharmD, PhD; Muhammad M. Mamdani, PharmD, MA, MPH; J. Michael Paterson, MSc; David N. Juurlink, MD, PhD

Figure. Proportion of Deaths Related to Opioid Use by Age Group in 2001, 2006, 2011, and 2016



JAMA Network Open. 2018;1(2):e180217. doi:10.1001/jamanetworkopen.2018.0217

WHAT'S THE DIFFERENCE BETWEEN

the killer's knife and the surgeon's knife?

WHAT'S THE DIFFERENCE BETWEEN

the killer's knife and the surgeon's knife?

…the intention

How Addiction Affects the Brain

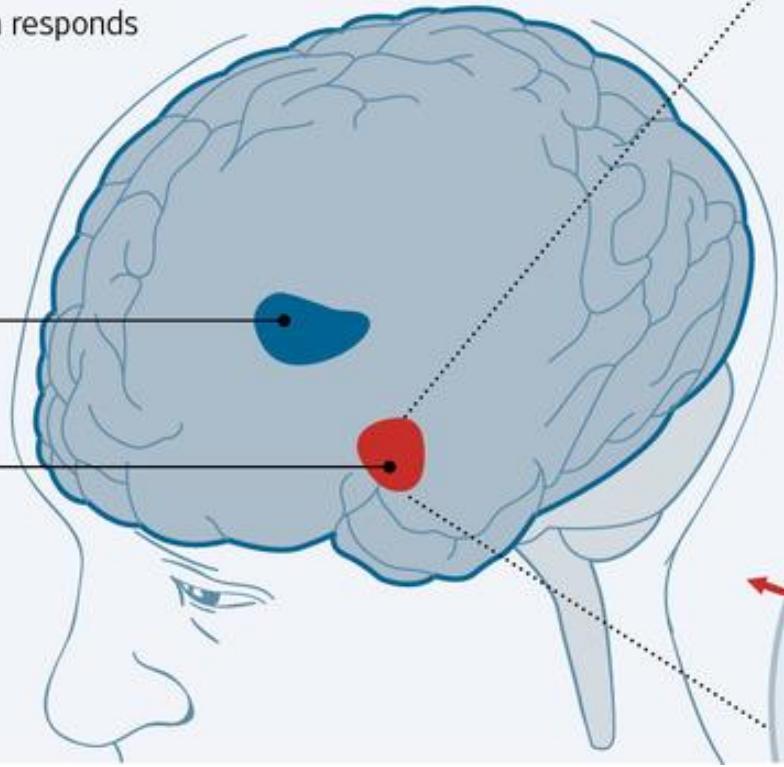
Two ways scientists say the brain responds to alcohol and drug abuse

In the nucleus accumbens, the brain's reward center, drug and alcohol use boosts dopamine, a neurotransmitter that helps produce pleasurable feelings, thus promoting more cravings.

In the amygdala, which processes memory and emotions, long-term substance abuse can send the stress-response system into overdrive.

Source: George Koob, Scripps Research Institute

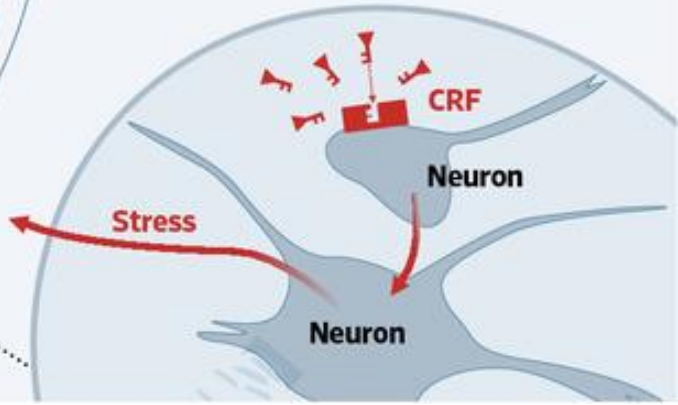
The Wall Street Journal



Blocking Bad Feelings

Scientists hope that by blocking a 'misery neurotransmitter' known as **CRF**, they can hinder the brain's stress response to addiction on a molecular level. A drug called gabapentin recently showed promising results.

Inside the amygdala



Not all opioids are created equal in the eyes of dopamine

EJN EUROPEAN JOURNAL OF NEUROSCIENCE FENS

European Journal of Neuroscience, Vol. 40, pp. 3041–3054, 2014 doi:10.1111/ejn.12709

NEUROSYSTEMS

Rapid dopamine transmission within the nucleus accumbens: Dramatic difference between morphine and oxycodone delivery

Caitlin M. Vander Weele,[1,†] Kirsten A. Porter-Stransky,[1,†] Omar S. Mabrouk,[2] Vedran Lovic,[1] Bryan F. Singer,[1] Robert T. Kennedy[2] and Brandon J. Aragona[1,3]

[1]Department of Psychology, University of Michigan, Ann Arbor, MI 48109, USA

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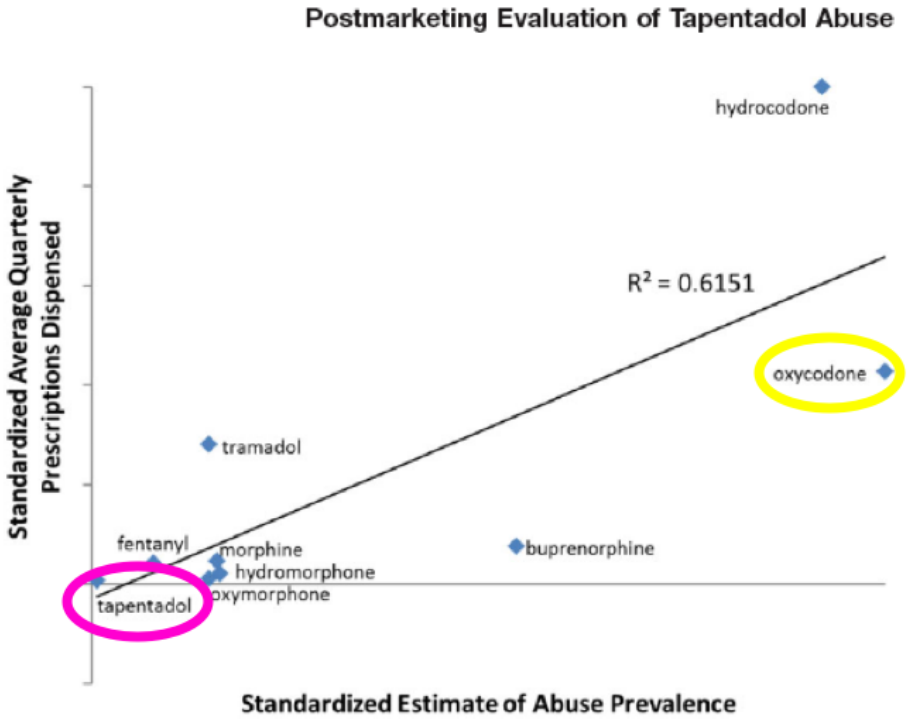
[3]Program in Neuroscience, University of Michigan, Ann Arbor, MI, USA

Keywords: addiction, motivation, opioid, reward

Opioids' Abuse Potential



Pain Medicine

Pain Medicine 2014; *: **–**
Wiley Periodicals, Inc.

Tapentadol Abuse Potential: A Postmarketing Evaluation Using a Sample of Individuals Evaluated for Substance Abuse Treatment

Minerva Anestesiologica
EDIZIONI MINERVA MEDICA

"I am in pain": is it really the magic formula to open the door of opioid abuse?

Flaminia COLUZZI

Minerva Anestesiologica 2017 Jul 20
DOI: 10.23736/S0375-9393.17.12269-8

Minerva Anestesiologica
EDIZIONI MINERVA MEDICA

ARTICLE ONLINE FIRST
This provisional PDF corresponds to the article as it appeared upon acceptance.
A copyedited and fully formatted version will be made available soon.
The final version may contain major or minor changes.

"I am in pain": is it really the magic formula to open the door of opioid abuse?

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DOI: 10.23736/S0375-9393.17.12269-8

YES, there is a problem in the US

The US cannot export national issues globally

Cannabis products account for the largest share of the illicit drug market

Opioids : Cannabis = 1:17

1.3 million : 22.1 million

EJP
European Journal of Pain

POSITION PAPER

European Pain Federation position paper on appropriate opioid use in chronic pain management

T. O'Brien[1,2], L.L. Christrup[3], A.M. Drewes[4], M.T. Fallon[5], H.G. Kress[6], H.J. McQuay[7], G. Mikus[8], B.J. Morlion[9], J. Perez-Cajaraville[10], E. Pogatzki-Zahn[11], G. Varrassi[12], J.C.D. Wells[13]

Inappropriate and exaggerated fear concerning the **legitimate scientific use of opioid medications** as part of a comprehensive pain management strategy…

O'Brien T, ChristrupLL, Drewes AM et al.
European Pain Federation Position Paper.
EurJ Pain **21** (2017) 3-19

EJP
European Journal of Pain

POSITION PAPER

European Pain Federation position paper on appropriate opioid use in chronic pain management

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EFIC

O'Brien T, ChristrupLL, Drewes AM et al. European Pain Federation Position Paper. EurJ Pain **21** (2017) 3-19

Silent epidemic of pain

Uncomplaining patients & unquestioning doctors
- a lethal conspiracy of silence -

EFIC position 2021: RATIONAL USE of OPIOIDS

DOI: 10.1002/ejp.1736

POSITION PAPER

EJP European Journal of Pain

European* clinical practice recommendations on opioids for chronic noncancer pain – Part 1: Role of opioids in the management of chronic noncancer pain

Winfried Häuser[1,2] | Bart Morlion[3] | Kevin E. Vowles[4] | Kirsty Bannister[5] | Eric Buchser[6] | Roberto Casale[7] | Jean-François Chenot[8] | Gillian Chumbley[9] | Asbjørn Mohr Drewes[10] | Geert Dom[11] | Liisa Jutila[12] | Tony O'Brien[13] | Esther Pogatzki-Zahn[14] | Martin Rakusa[15] | Carmen Suarez–Serrano[16] | Thomas Tölle[17] | Nevenka Krčevski Škvarč[18]

Eur J Pain. 2021;25:949–968.

1. Comprehensive clinical evaluation
   a. Medical and psychosocial history
   b. Medical and if necessary psychological and physiotherapeutic examination
   c. Technical examinations
   d. Interdisciplinary assessment if needed
2. Start treatment
   a. Education
   b. Non-pharmacological therapies
   c. Non-opioids if needed
3. Consider a trial with opioids if
   a. There is a relative indication for opioids for the type of the pain syndrome of the patient and
   b. non-pharmacological treatment and non-opioid analgesics are
   (i) Not effective and/or
   (ii) Not tolerated and/or
   (iii) Contraindicated

Eur J Pain. 2021;25:949–968.

4. Shared decision making with patients
   a. Assess individual benefit risk-ratio
   b. Consider patient's treatment preferences
   c. Obtain informed consent and agreement
   d. Establish individual and realistic treatment goals (sustained improvement of daily functioning, pain reduction)
5. Initial dose adjustment phase (8–12 weeks)
   a. Start slow, go slow
   b. Monitor and treat side effects if needed
   c. Find the optimal dosage (predefined treatment goals met; no or tolerable/manageable side effects)
   d. Discontinue if
   (i) Predefined treatment goals not reached
   (ii) Intolerable/manageable side effects
   (iii) Non-medical use of prescribed opioids

Eur J Pain. 2021;25:949–968.

6. Long-term opioid therapy (>12 weeks)
   a. Regular assessments (at least every 3 months)
   b. Assess four A's: Activity, analgesia, aberrant behaviour, adverse effects
   c. Promote non-pharmacological therapies
   d. Continue if
   (i) Stable dosage
   (ii) Sustained improvement of daily functioning and pain reduction
   (iii) tolerable/manageable side effects
   (iv) No signals of non-medical use of prescribed opioids
   e. Discuss tapering/drug holiday after 6 months with the patient
   f. Discontinue if
   (i) Dose escalation
   (ii) Loss of improvement of daily functioning and of pain reduction
   (iii) tolerable/manageable side effects
   (iv) Signals of non-medical use of prescribed opioids

Activity

Analgesia

Aberrant behaviour

Adverse effects

Eur J Pain. 2021;25:949–968.

OPIOIDS: when and how to STOP

LEARN WHEN TO STOP

TAPERING PLANNING

- Intolerable adverse effects
- Treatment goals not reached
- Patient request
- Non-adherence by the patient
- Misuse by the patient

Good clinical practice guide for opioids in pain management: the three Ts – titration (trial), tweaking (tailoring), transition (tapering)

Flaminia Coluzzi[a], Robert Taylor Jr.[b], Joseph V. Pergolizzi Jr.[c,d,e], Consalvo Mattia[a], Robert B. Raffa[f,*]

TITRATION

TAILORING

TAPERING


Opioid Misconceptions

Opioid Misconceptions

O'Brien T, ChristrupLL, Drewes AM et al. European Pain Federation Position Paper. EurJ Pain **21** (2017) 3-19

- Dangerous
- Shorten life / Hasten death
- Respiratory depression
- End of life only
- Opioids kill pain by killing the patient

Opioid Misconceptions

O'Brien T, ChristrupLL, Drewes AM et al. European Pain Federation Position Paper. EurJ Pain **21** (2017) 3-19

- Tolerance
- Addiction
- Compromise function
- Confusion / disorientation
- If a patient dies whilst on opioid medication, the opioid caused the death

Opioid Facts

Opioid Facts (1)

for medical use in properly selected and supervised patients

O'Brien T, ChristrupLL, Drewes AM et al. European Pain Federation Position Paper. EurJ Pain **21** (2017) 3-19

- Indispensable in pain management
- Safe & effective
- Do not compromise function
- Introduce when less potent medicines are ineffective
- Physical dependence is not addiction

Opioid Facts (2)

for medical use in properly selected and supervised patients

O'Brien T, ChristrupLL, Drewes AM et al. European Pain Federation Position Paper. EurJ Pain **21** (2017) 3-19

- No significant respiratory depression
- Bowel dysfunction is main concern
- Inter-individual variation in response
- No single 'ideal' opioid; therefore need a range of opioids
- Opioid misuse causes harm; not opioid use

Medical Use of Opioids (1)

O'Brien T, ChristrupLL, Drewes AM et al. European Pain Federation Position Paper. EurJ Pain **21** (2017) 3-19

- Adequate patient assessment
- Clinicians familiar with best practice
- Non-specialsts need access to export advice
- Opioids prescribed by competent doctors
- Correct dose is the the lowest possible dose

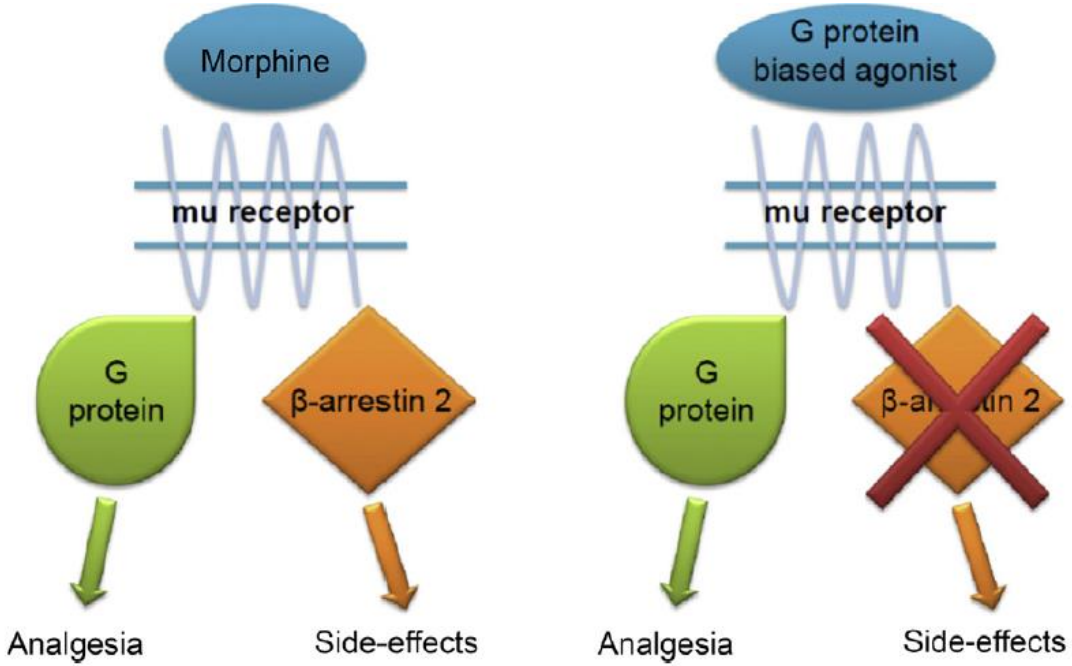
Medical Use of Opioids (2)

O'Brien T, ChristrupLL, Drewes AM et al. European Pain Federation Position Paper. EurJ Pain **21** (2017) 3-19

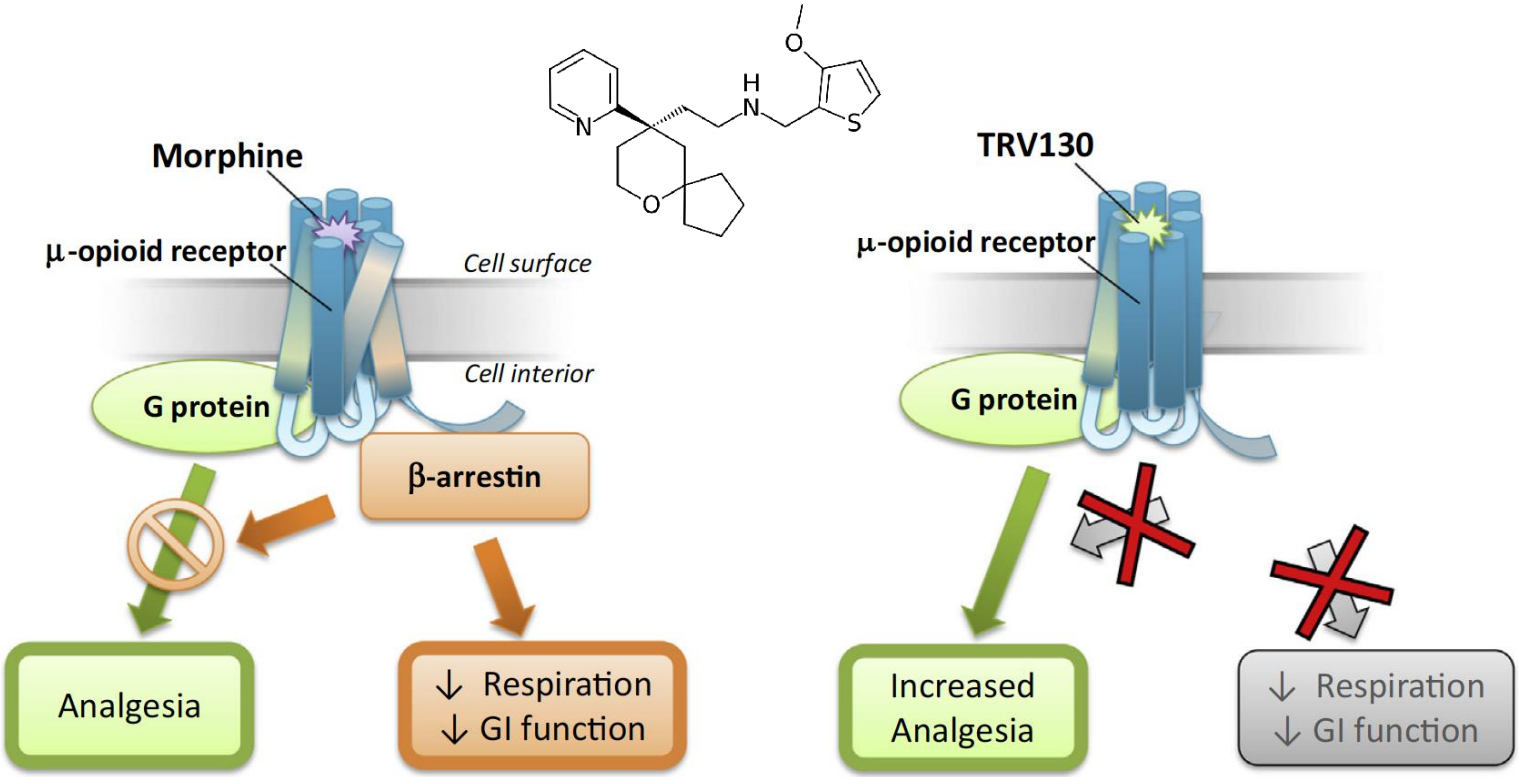
- Close on-going supervision
- Treatment initiated on trial basis
- Patient & Family education on safe use and storage
- Opioids dispensed by competent pharmacists
- Honest doctor/patient relationship

Opioids of the future

Functional selectivity or biased agonism



TRV130 Oliceridine



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