

Evaluation and management of pain in Rare Neuroimmune Disorders

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Disclosures

None

Synopsis

- Pain in the context of Rare Neuroimmune disorders
- What is neuropathic pain? How common is it?
- Causes/mechanisms of neuropathic pain?
- Diagnosis of neuropathic pain?
- Management
 - Medication
 - Non-pharmacological measures
 - Emerging therapies
 - Psychotherapy

What are some RND?

- Transverse Myelitis (TM)/Myelopathy – inflammatory, infectious, vascular (Stroke)
- Optic Neuritis (ON)
- Neuromyelitis Optica Spectrum Disorder (NMOSD) – esp AQP4 disease
- Acute Disseminated Encephalomyelitis (ADEM)
- Acute Flaccid Myelitis (AFM)
- MOG Antibody Disease (MOGAD)

** These are classified as rare because their incidence is much lesser (1-10 per 100,000) than “common” Neuroimmune conditions like MS (100 per 100,000)

Pain in the context of NMOSD..



[J Clin Neurol.](#) 2020 Jan; 16(1): 124–130.

PMCID: PMC6974826

Published online 2019 Dec 30. doi: [10.3988/jcn.2020.16.1.124](https://doi.org/10.3988/jcn.2020.16.1.124)

PMID: [31942768](https://pubmed.ncbi.nlm.nih.gov/31942768/)

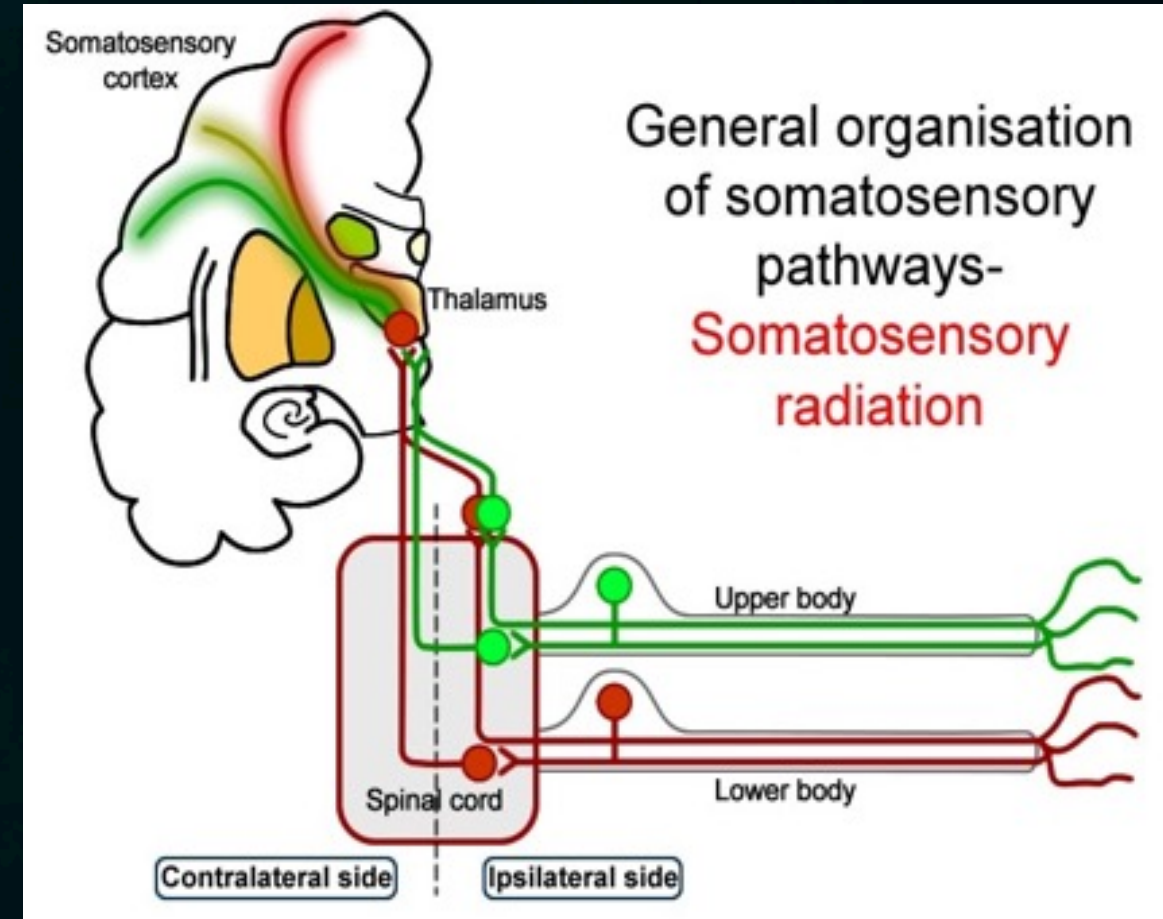
Comparison of Neuropathic Pain in Neuromyelitis Optica Spectrum Disorder and Multiple Sclerosis

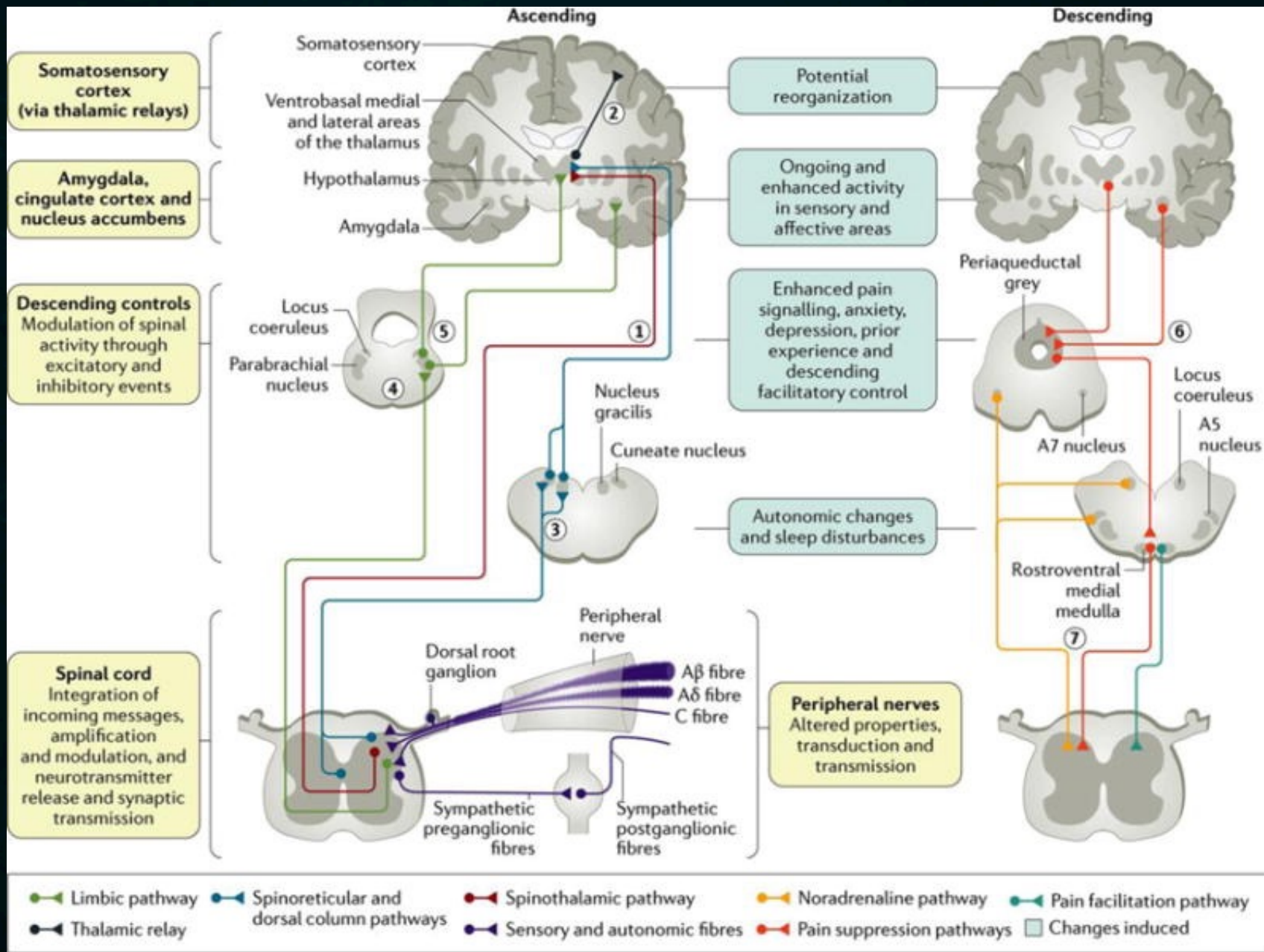
[Jae-Won Hyun](#),^a [Hyunmin Jang](#),^a [JaeBin Yu](#),^a [Na Young Park](#),^a [Su-Hyun Kim](#),^a [So-Young Huh](#),^b [Woojun Kim](#),^c
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****Severity of neuropathic pain and the pain-related interference in daily life were greater in NMOSD patients than in MS patients.**

What is neuropathic pain?

- Pain caused by disease of the somatosensory pathways – 3 wire system
 - Peripheral pathways – DM neuropathy
 - Central pathways – MS, NMO, stroke
- Different from pain from inflammation
 - RA, visceral pain (appendicitis)
- 10% of all patients with chronic pain have neuropathic characteristics.
 - ~50m adults in the U.S have chronic pain!!



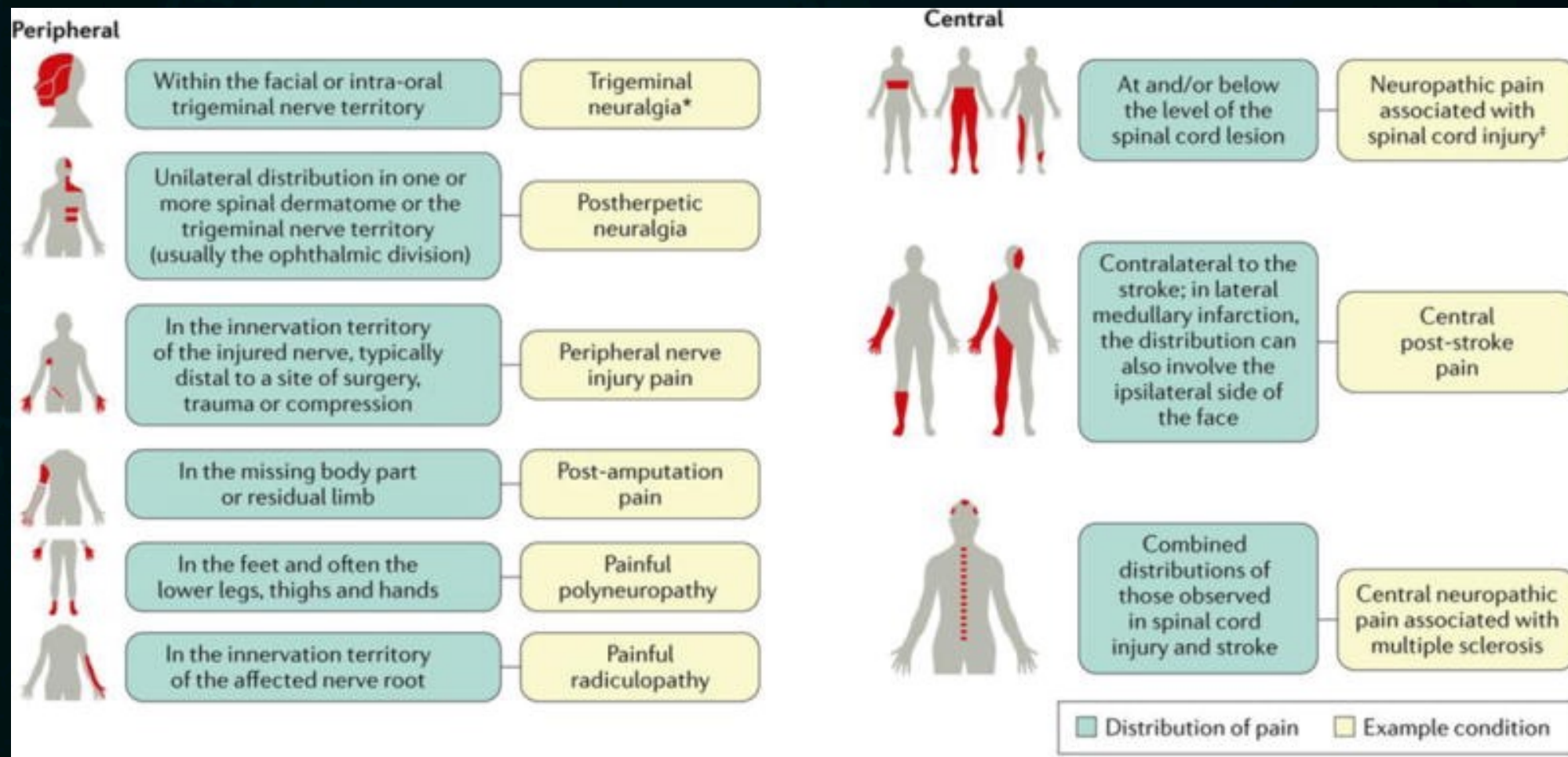


Somatosensory pathways. Nat Rev Dis Primers. 2017 Feb 16; 3: 17002.

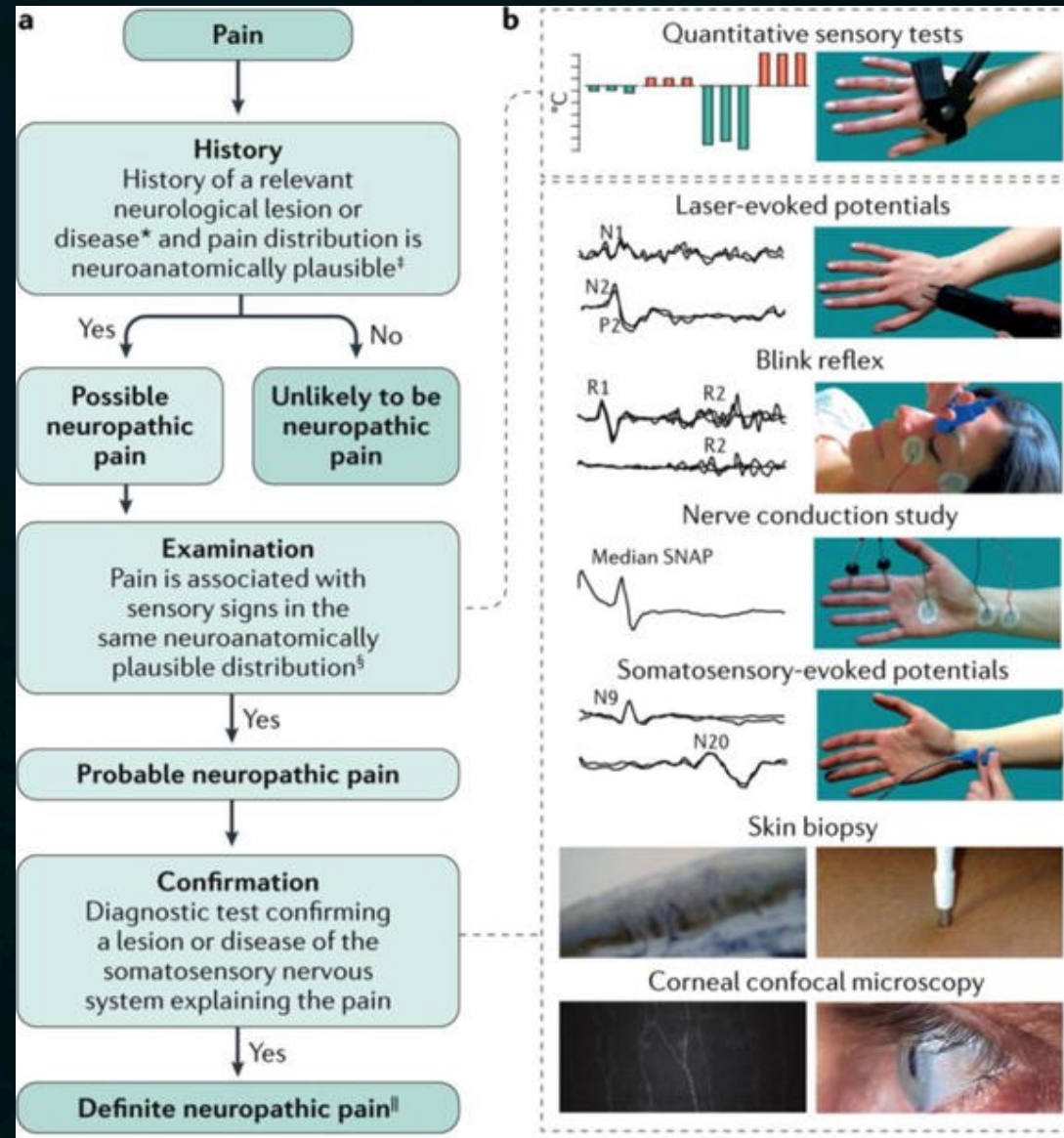
What causes neuropathic pain ?

- Pain signaling changes
- Ion channel alterations
- Second-order nociceptive neuron alternations
- Inhibitory modulation changes
- Reduced central pain modulation

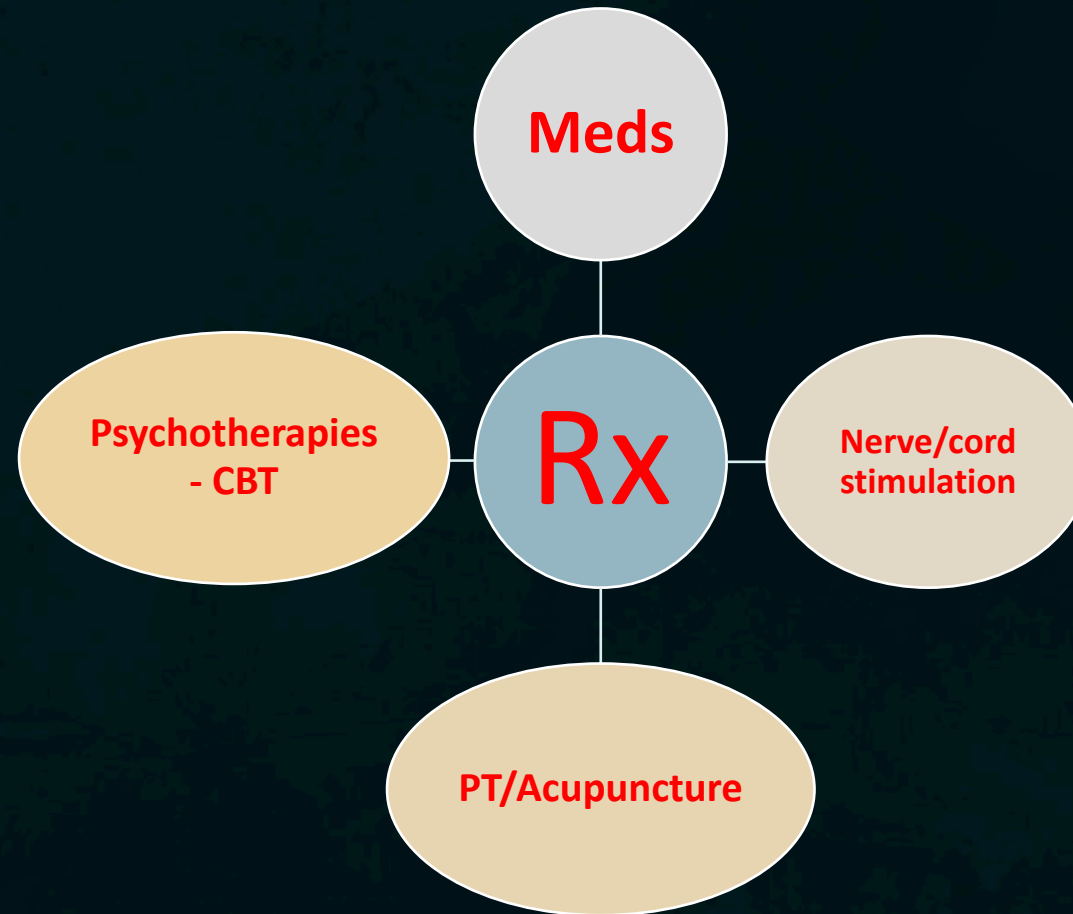
Clinical features of neuropathic pain



Diagnosis of neuropathic pain



Management



Meds

First-line therapies

- Antidepressants
- Anti-epileptics

Second-line therapies

- Topical
Lidocaine/Capsaicin
- Tramadol

Third-line therapies

- Botulinum toxin
- Mexelitene/Clonidine
- Cannabinoids
- Low dose naltrexone
- ? Opioids

Full med list – amitriptyline, nortriptyline (Pamelor), duloxetine (Cymbalta), milnacipran (Savella), gabapentin, lyrica (pregabalin), valproic acid, carbamazepine (tegretal), oxcarbazepine (trileptal), topiramate.

- Beware of polypharmacy
- Typically do not work immediately, require chemical changes to occur over a few weeks for optimal effect
- Slow titration is key to prevent adverse effects
- Trial and error basis mostly. One size does not fit all!
- NSAIDs and OTC meds have limited utility and risk of adverse effects with long term use.

Opioids for neuropathic pain

- Short term studies – equivocal results
- Intermediate term studies – higher efficacy of opioids compared to placebo.
 - Unclear results on QOL measures.
- Caution regarding narcotic overuse/dependence issues!
- Worsening adverse effects in this patient population
 - Cognitive, bladder, etc.

Cannabinoids

- THC – psychoactive and CBD – ?anxiolytic, ?anti-inflammatory, ?neuroprotective
- Mixed outcomes from studies.
 - Cochrane analysis of 16 studies, 1750 people → The benefits of cannabis-based medicine (herbal cannabis, plant-derived or synthetic THC, THC/CBD oromucosal spray) in chronic neuropathic pain might be outweighed by their **potential harms**.
- Caution on interpreting studies
 - Non-neuropathic pain types exist in neurological conditions like NMO, MS, TM
 - Safety and duration
- Personal experience – CBD may indeed have a role for anxiety/depression and spasticity when coexisting with neuropathic pain in select patients.



**<https://www.frontiersin.org/articles/10.3389/fphar.2019.01239/full>

A few clinical trials

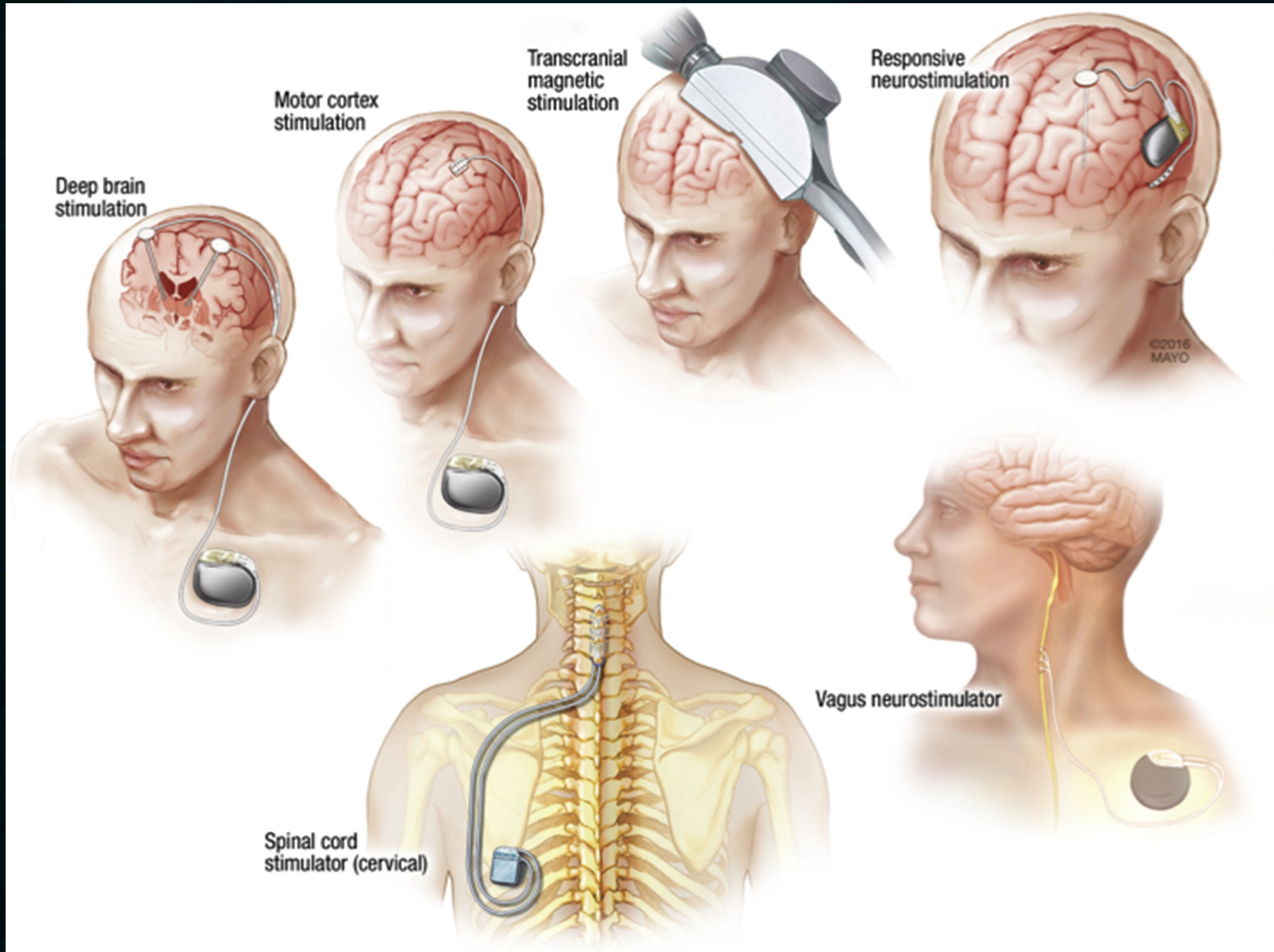
Phase III Clinical Trials.

NCT number	Study title	Drug	Results
NCT01536314	Prophylaxis of neuropathic pain by memantine	Memantine EBIXA [®] Placebo: lactose	Memantine prevented post-mastectomy pain and diminished chemotherapy-induced pain symptoms
NCT00313378	Effects of perioperative systemic ketamine on development of long-term neuropathic pain after thoracotomy	Ketamine	Ketamine did not prevent chronic pain after thoracotomy
NCT00224588	KETOR: Effects of peri-operative administration of ketamine on long-term post thoracotomy pain	Ketamine	Data not available
NCT00872144	Sativex for the treatment of chemotherapy-induced neuropathic pain	Sativex [®]	Sativex reduced chemotherapy-induced neuropathic pain in five participants that trended toward statistical significance
NCT01604265	A study of Sativex in the treatment of central neuropathic pain due to multiple sclerosis	Sativex [®]	Sativex reduced pain and sleep disturbance in patients with multiple sclerosis
NCT01606202	A study of cannabis-based medicine extracts and placebo in patients with pain due to spinal cord injury	GW-1000-02 Placebo	GW-1000-02 improved pain score
NCT00713817	A study to determine the maintenance of effect after long-term treatment of	Sativex [®] Placebo	Sativex showed no effect

Phase III Clinical Trials.

NCT00713817	A study to determine the maintenance of effect after long-term treatment of Sativex [®] in subjects with neuropathic pain	Sativex [™] Placebo	Sativex showed no effect
NCT00713323	A study to compare the safety and tolerability of Sativex [®] in patients with neuropathic pain	Sativex [®] Placebo	Sativex improved pain score
NCT00711880	A study of Sativex [®] for relief of peripheral neuropathic pain associated with allodynia	Sativex [®] Placebo	Sativex reduced global neuropathic pain score, sleep disturbance, dynamic and punctate allodynia
NCT00710554	A study of Sativex [®] for pain relief of peripheral neuropathic pain, associated with allodynia	Sativex [®] Placebo	Sativex reduced the peripheral neuropathic pain NRS scores and the sleep quality score
NCT00391079	Sativex versus placebo when added to existing treatment for central neuropathic pain in MS	Sativex [®] Placebo	Sativex reduced neuropathic pain and improved sleep and quality of life
NCT00710424	A study of Sativex [®] for pain relief due to diabetic neuropathy	Sativex [®] Placebo	Sativex improved diabetic neuropathy pain
NCT00959218	Efficacy and safety of the pain relieving effect of dronabinol in central neuropathic pain related to multiple sclerosis	Dronabinol [®] Placebo	Dronabinol reduced pain intensity and adverse events over time
NCT01555983	Vaporized cannabis and spinal cord injury pain	Vaporization of cannabis	Vaporized cannabis decreased pain associated with injury or disease of

Devices



Scrambler therapy for neuropathic pain



Mealy MA, Kozachik SL, Cook LJ, Totonis L, Salazar RA, Allen JK, Nolan MT, Smith TJ, Levy M. Scrambler therapy improves pain in neuromyelitis optica: A randomized controlled trial. *Neurology*. May 2020

THOUGHTS

What we **think** affects
how we feel and act

CBT

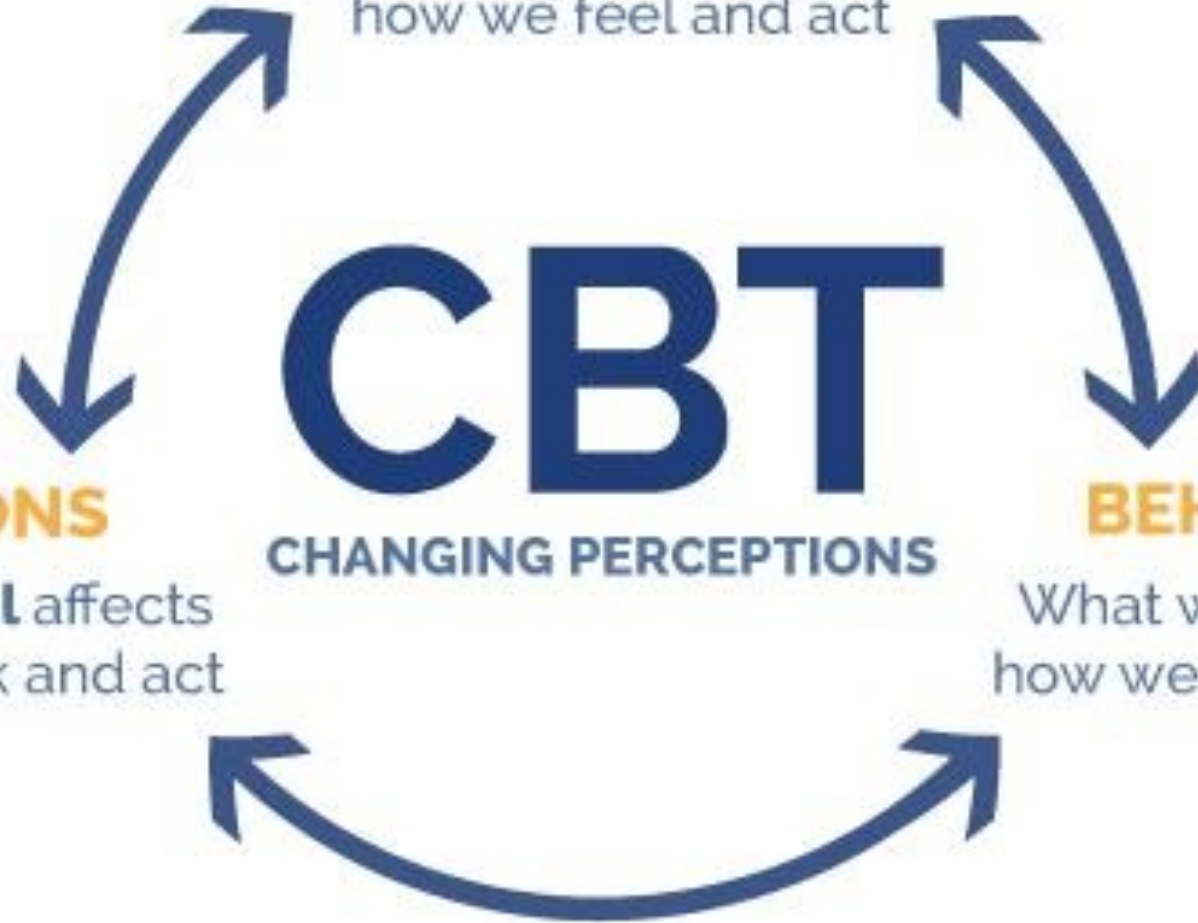
CHANGING PERCEPTIONS

BEHAVIORS

What we **do** affects
how we think and feel

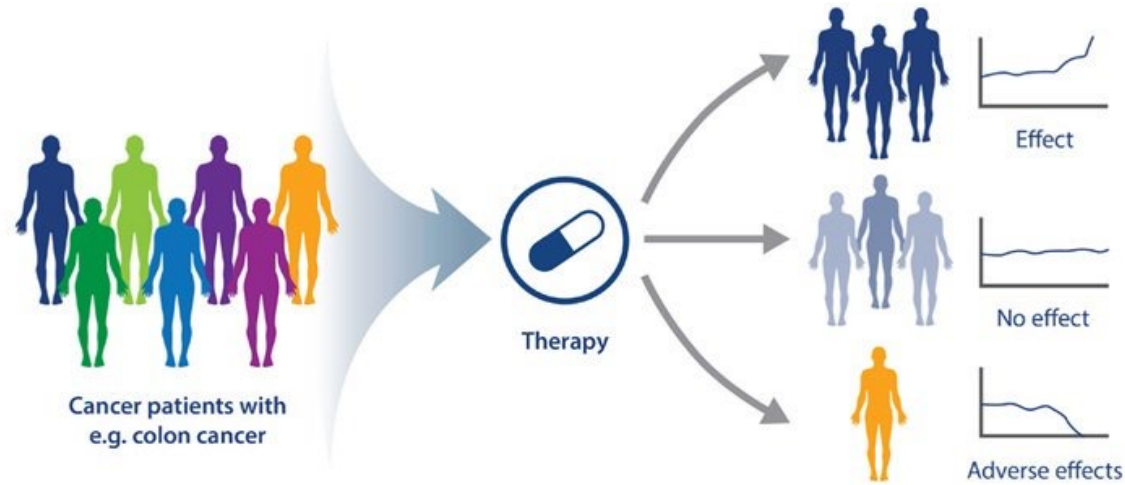
EMOTIONS

What we **feel** affects
how we think and act



Current Medicine

One Treatment Fits All



Future Medicine

More Personalized Diagnostics

