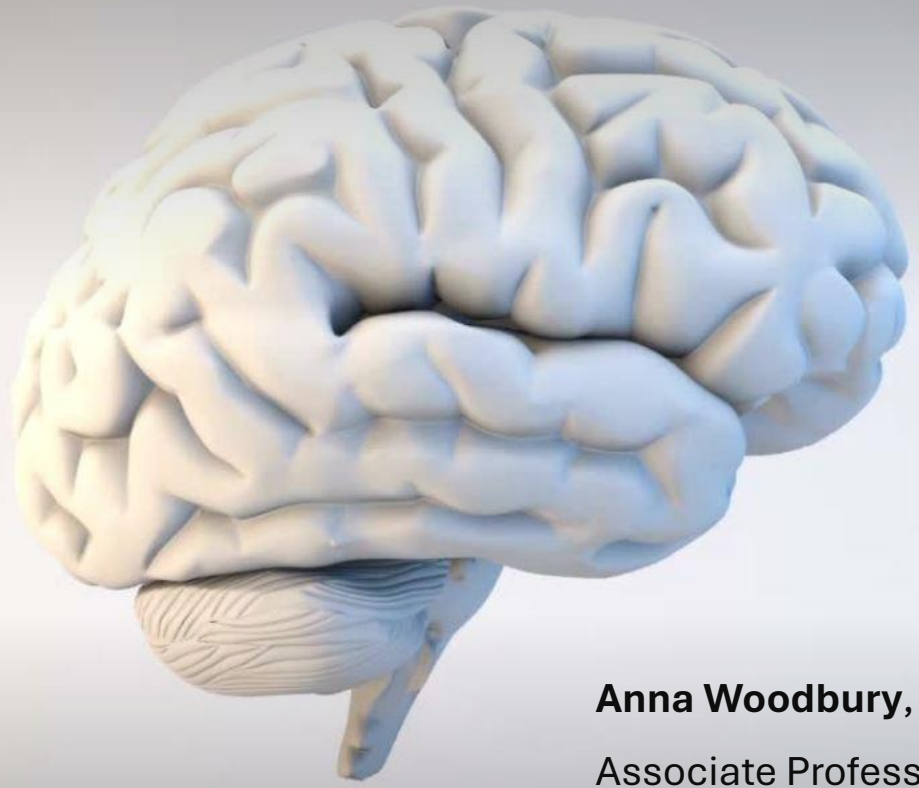
Fibromyalgia and Centralized Pain



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January 30, 2026 | Southern Pain Society

Learning Objectives

1

Understand nociplastic pain, its diagnosis, and its relevance

2

Evaluate alternative strategies for pain management, especially in central sensitivity syndromes

3

Compare existing neuromodulatory techniques and explore their neural bases

What is Pain?

- **IASP Definition:**
  - An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage.

Type of Pain	Definition	Examples
Nociceptive	Due to tissue damage or inflammation (via nociceptors)	Osteoarthritis, cuts, surgery
Neuropathic	Due to nerve injury or disease	Diabetic neuropathy, shingles
Nociplastic	Due to altered pain processing without clear tissue/nerve injury	Fibromyalgia, IBS, primary headaches (tension-type and migraine), some low back and knee pain

What is Nociplastic Pain?

- Chronic pain that is neither fully nociceptive or neuropathic
- Altered nervous system pain processing despite no clear evidence of actual tissue damage or nerve injury (amplified pain signals/ central sensitization)

- **Diagnosis and Recognition:**
  - Chronic pain > 3 months
  - Hypersensitivity
  - Absence of clear nociceptive/neuropathic cause
  - Other symptoms (fatigue or cognitive issues)
- **Importance:**
  - Validates pain is real, even without visible injury
  - Improves treatment (understanding mechanism helps target therapies)


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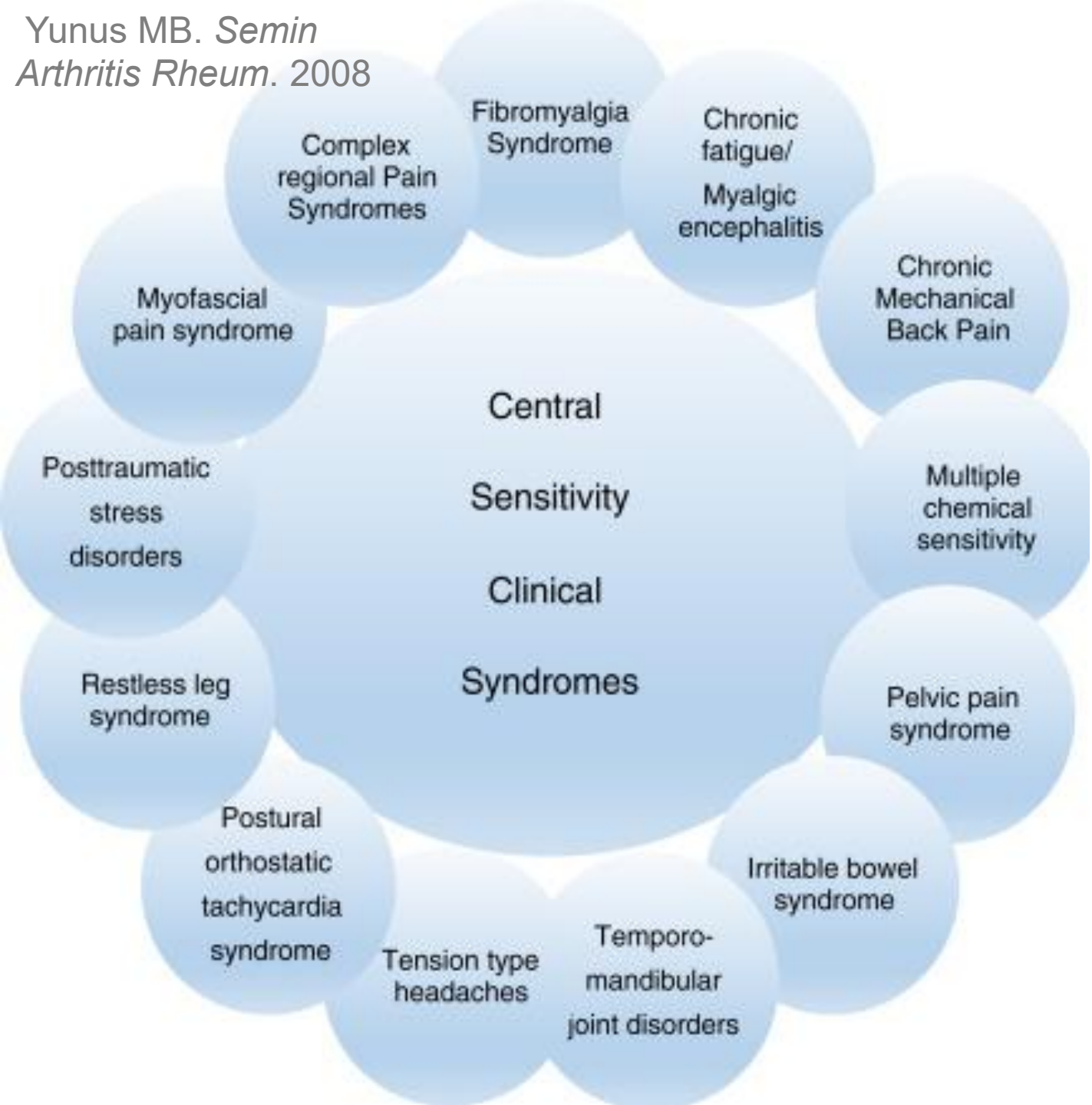
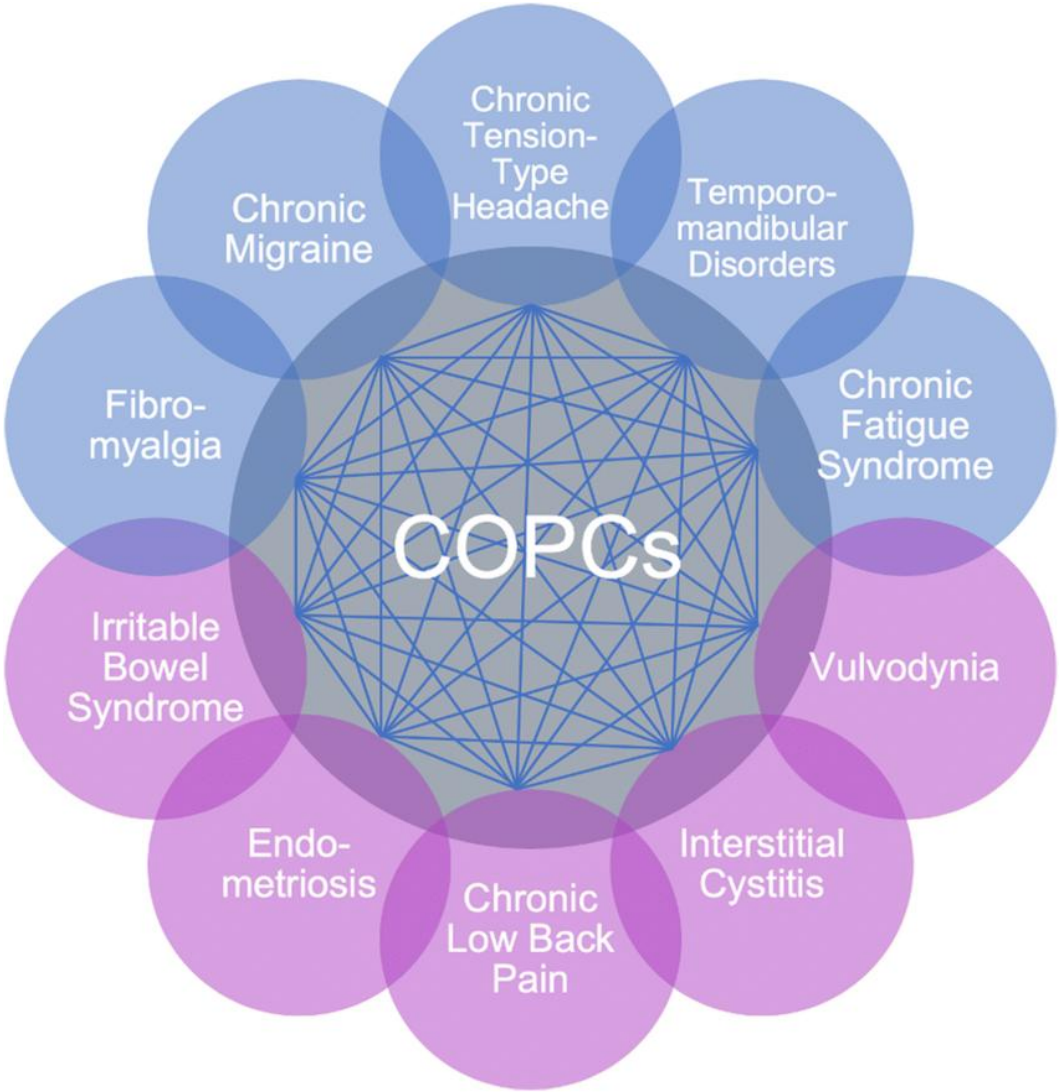
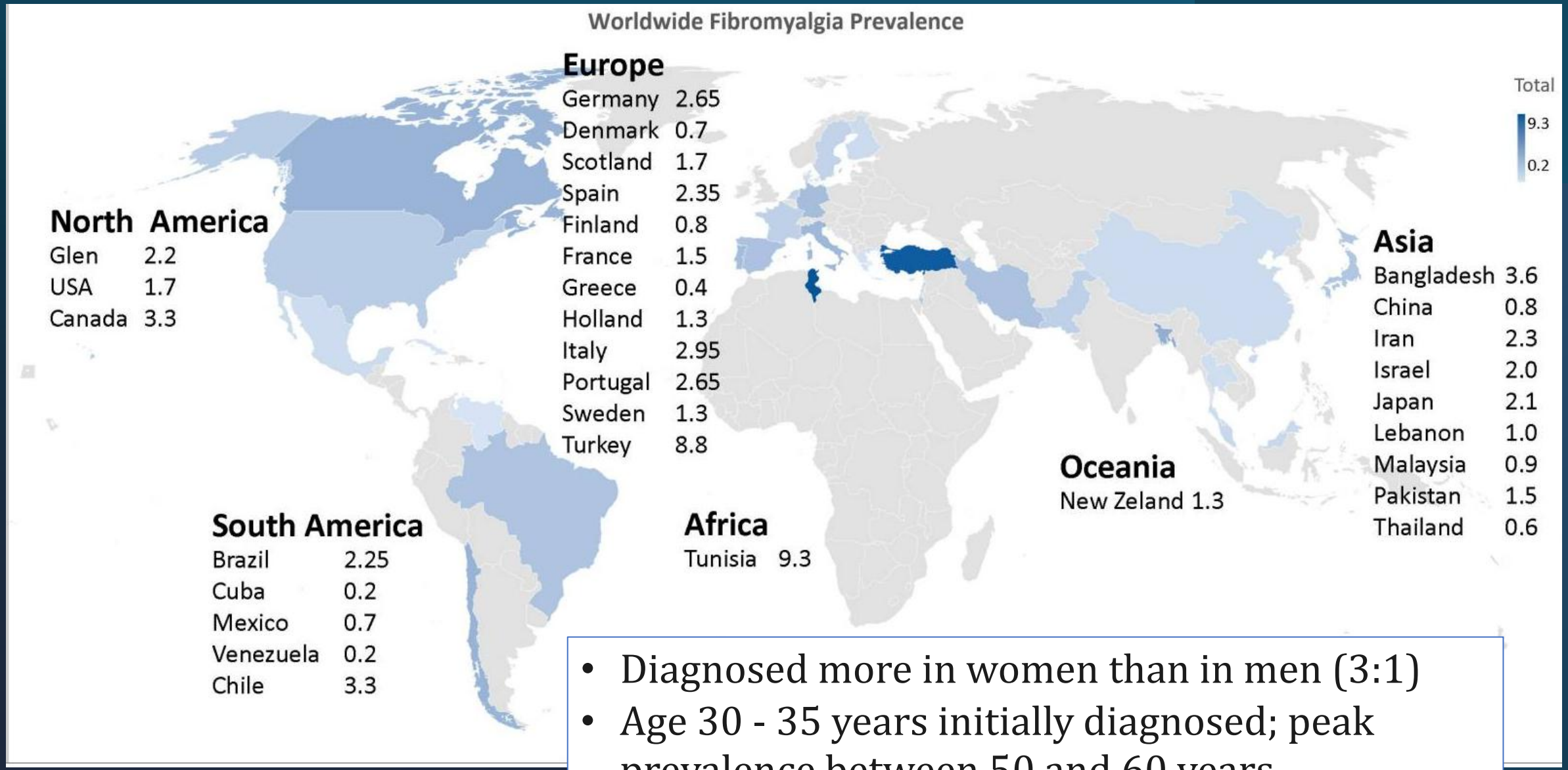
THE PAIN STARTS IN MY HUSBAND'S LOWER BACK, THEN IT TRAVELS UP HIS SPINE TO HIS NECK, THEN IT COMES OUT HIS MOUTH AND INTO MY EARS. AND THAT'S WHY I GET THESE HEADACHES.
CHIROPRACTOR
GLASBERGEN

Yunus MB. *Semin Arthritis Rheum*. 2008







- Diagnosed more in women than in men (3:1)
- Age 30 - 35 years initially diagnosed; peak prevalence between 50 and 60 years

Jurado-Priego et al. 2024. PMC11275111

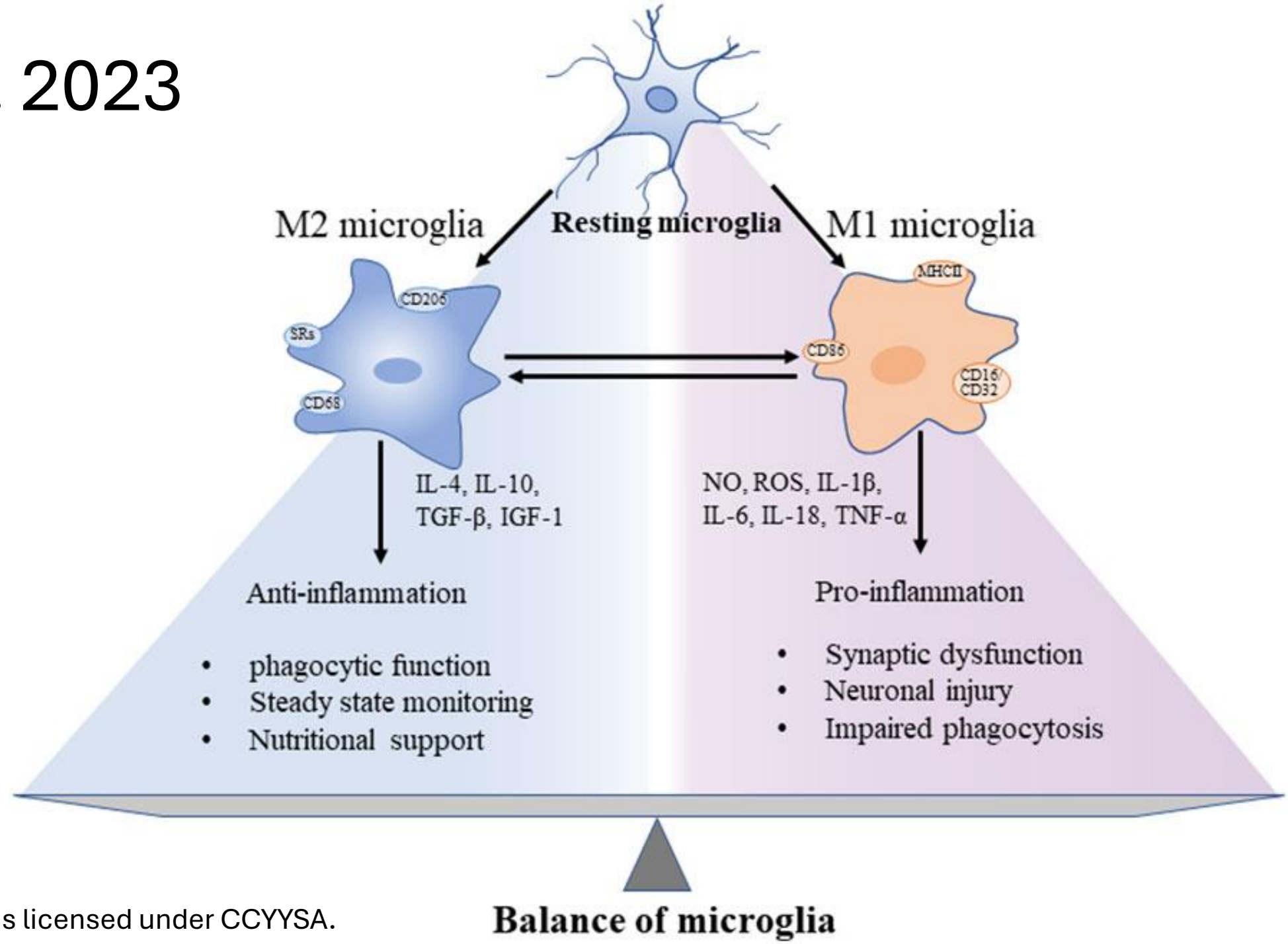
Mechanisms

Neuroimaging & Neuroinflammation (Pathophysiology)

- Changes in brain regions involved in pain processing.
  - Disrupted intrinsic connectivity within multiple brain networks in FM patients.
  - Increased connectivity to the insula is directly associated with increasing spontaneous pain.
- TSPO PET imaging suggest microglia are predominant glial population driving PET abnormalities in fibromyalgia
- Normalization of rs-fcMRI with exercises, pregabalin, acupuncture, and other therapies that benefit pain.

Nishigami T, et al . 2023. PMC10380903.
Harris & Napadow. 2011. PMC2921024
Albrecht et al. 2019. PMC6541932

Wang et al. 2023



Autonomic Nervous System Imbalance

HRV studies with higher resting heart rate, reduced overall HRV, lower vagal tone in FMS

Persistent sympathetic overactivity

Fatigue, sleep disturbance, anxiety/depression, and sometimes orthostatic intolerance or POTS-like features

Measurement and Diagnosis

- CSI
- PSD (ACR 2016)
- FIQ-R
- QST

*standard labs just to r/o other diagnoses

Central Sensitization Inventory

CSI Inventory (Part A)

Name _____ Date _____

Please circle the best response to the right of each statement.
Key for Scoring: **Never = 0, Rarely = 1, Sometimes = 2, Often = 3, Always = 4**

1. I feel tired and unrefreshed when I wake from sleeping.	Never	Rarely	Sometimes	Often	Always
2. My muscles feel stiff and achy.	Never	Rarely	Sometimes	Often	Always
3. I have anxiety attacks.	Never	Rarely	Sometimes	Often	Always
4. I grind or clench my teeth.	Never	Rarely	Sometimes	Often	Always
5. I have problems with diarrhea and/or constipation.	Never	Rarely	Sometimes	Often	Always
6. I need help in performing my daily activities.	Never	Rarely	Sometimes	Often	Always
7. I am sensitive to bright lights.	Never	Rarely	Sometimes	Often	Always
8. I get tired very easily when I am physically active.	Never	Rarely	Sometimes	Often	Always
9. I feel pain all over my body.	Never	Rarely	Sometimes	Often	Always
10. I have headaches.	Never	Rarely	Sometimes	Often	Always
11. I feel discomfort in my bladder and/or burning when I urinate.	Never	Rarely	Sometimes	Often	Always
12. I do not sleep well.	Never	Rarely	Sometimes	Often	Always
13. I have difficulty concentrating.	Never	Rarely	Sometimes	Often	Always
14. I have skin problems such as dryness, itchiness, or rashes.	Never	Rarely	Sometimes	Often	Always
15. Stress makes my physical symptoms get worse.	Never	Rarely	Sometimes	Often	Always
16. I feel sad or depressed.	Never	Rarely	Sometimes	Often	Always
17. I have low energy.	Never	Rarely	Sometimes	Often	Always
18. I have muscle tension in my neck and shoulders.	Never	Rarely	Sometimes	Often	Always
19. I have pain in my jaw.	Never	Rarely	Sometimes	Often	Always
20. Certain smells, such as perfumes, make me feel dizzy and nauseated.	Never	Rarely	Sometimes	Often	Always
21. I have to urinate frequently.	Never	Rarely	Sometimes	Often	Always
22. My legs feel uncomfortable and restless when I am trying to go to sleep at night.	Never	Rarely	Sometimes	Often	Always
23. I have difficulty remembering things.	Never	Rarely	Sometimes	Often	Always
24. I suffered trauma as a child.	Never	Rarely	Sometimes	Often	Always
25. I have pain in my pelvic area.	Never	Rarely	Sometimes	Often	Always
Total Each Column					
				Overall Total	

Worksheet

CSI Inventory (Part B)

Name _____ Date _____

Have you been diagnosed by a doctor with any of the following disorders?

Please check the box to the right for each diagnosis and write the year of the diagnosis.

		No	Yes	Year Diagnosed
1	Restless Leg Syndrome			
2	Chronic Fatigue Syndrome			
3	Fibromyalgia			
4	Temporomandibular Joint Disorder			
5	Migraine or tension headaches			
6	Irritable Bowel Syndrome			
7	Multiple Chemical Sensitivities			
8	Neck injury (including whiplash)			
9	Anxiety or panic attacks			
10	Depression			

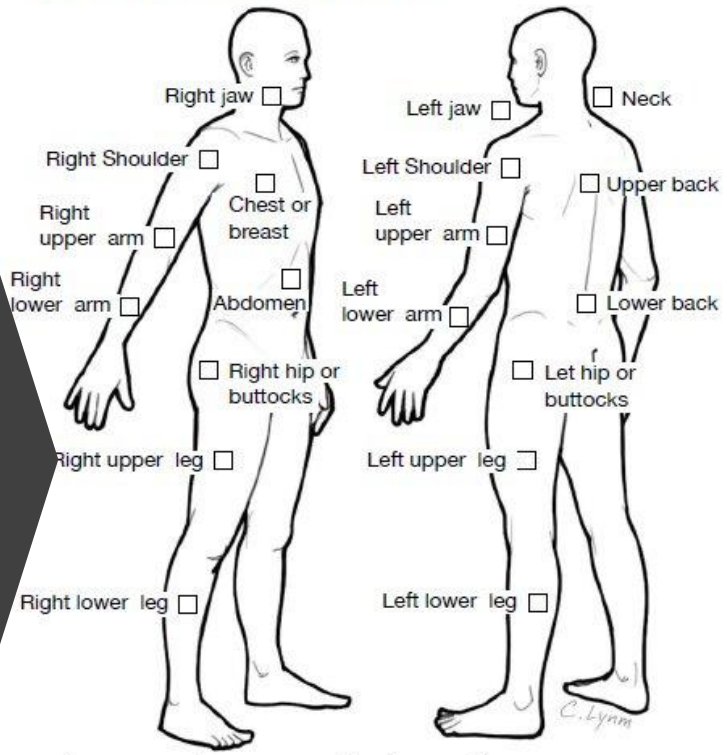
Mayer TG, et al. Pain Pract. 2012.
PMID: 21951710; PMCID: PMC3248986.

ACR 2016 Fibromyalgia Diagnostic Criteria PSD = WPI + SSS

2016 Revised Fibromyalgia Diagnostic Criteria Seminars in Arthritis and Rheumatism 46 (2016) 319 - 329

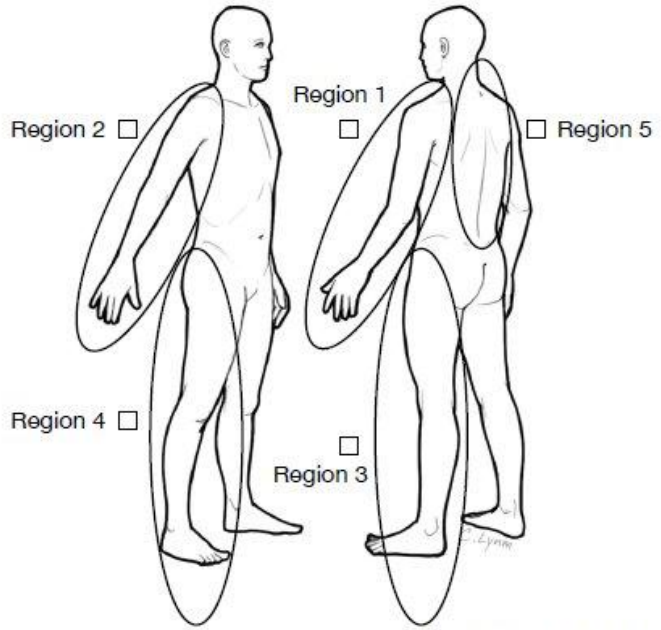
(1) Widespread Pain Index (WPI score range 0 - 19)

Pain and tenderness *during the past week*



Widespread Pain Index Total (maximum 19) ____

(2) Generalized pain - do not count jaws, chest, or abdomen



Generalized Pain Total (maximum 5) ____

All of the following criteria must be met to make a diagnosis of Fibromyalgia

1. WPI ≥ 7 and SSS ≥ 5 OR WPI 4 to 6 and SSS ≥ 9	☐ No	☐ Yes
2. Generalized pain: at least 4/5 regions	☐ No	☐ Yes
3. Have the symptoms in section 3 and pain been present at a similar clinical level for **at least 3 months**?	☐ No	☐ Yes
Fulfills all diagnostic criteria for FM	☐ No	☐ Yes

(3) Symptom Severity Score (SSS score range 0 - 12)

Over the past week:
No problem
Slight or mild problem: genrally mild or intermittent
Moderate problem: considerable problems; often present and/or at a moderate level
Severe problem: continuous, life-disturbing

	No problem	Slight/mild	Moderate	Severe
• Fatigue	☐ = 0	☐ = 1	☐ = 2	☐ = 3
• Trouble thinking or remembering	☐ = 0	☐ = 1	☐ = 2	☐ = 3
• Waking up tired (unrefreshed)	☐ = 0	☐ = 1	☐ = 2	☐ = 3

During the past 6 months:

• Pain or cramps in the abdomen	☐ No = 0	☐ Yes = 1
• Depression	☐ No = 0	☐ Yes = 1
• Headache	☐ No = 0	☐ Yes = 1

Symptom Severity Score Total (maximum 12) ____

Fibromyalgia Impact Questionnaire - Revised

The Revised Fibromyalgia Impact Questionnaire

Domain 1 directions: For each of the following nine questions, check the one box that best indicates how much your fibromyalgia made it difficult to do each of the following activities over the past 7 days:

Brush or comb your hair	No difficulty ☐☐☐☐☐☐☐☐☐☐☐ Very difficult
Walk continuously for 20 minutes	No difficulty ☐☐☐☐☐☐☐☐☐☐☐ Very difficult
Prepare a homemade meal	No difficulty ☐☐☐☐☐☐☐☐☐☐☐ Very difficult
Vacuum, scrub, or sweep floors	No difficulty ☐☐☐☐☐☐☐☐☐☐☐ Very difficult
Lift and carry a bag full of groceries	No difficulty ☐☐☐☐☐☐☐☐☐☐☐ Very difficult
Climb one flight of stairs	No difficulty ☐☐☐☐☐☐☐☐☐☐☐ Very difficult
Change bed sheets	No difficulty ☐☐☐☐☐☐☐☐☐☐☐ Very difficult
Sit in a chair for 45 minutes	No difficulty ☐☐☐☐☐☐☐☐☐☐☐ Very difficult
Go shopping for groceries	No difficulty ☐☐☐☐☐☐☐☐☐☐☐ Very difficult

Domain 2 directions: For each of the following two questions, check the one box that best describes the overall impact of your fibromyalgia over the past 7 days:

Fibromyalgia prevented me from accomplishing goals for the week	Never ☐☐☐☐☐☐☐☐☐☐☐ Always
I was completely overwhelmed by my fibromyalgia symptoms	Never ☐☐☐☐☐☐☐☐☐☐☐ Always

Domain 3 directions: For each of the following 10 questions, check the one box that best indicates the intensity of your fibromyalgia symptoms over the past 7 days:

Please rate your level of pain	No pain ☐☐☐☐☐☐☐☐☐☐☐ Unbearable pain
Please rate your level of energy	Lots of energy ☐☐☐☐☐☐☐☐☐☐☐ No energy
Please rate your level of stiffness	No stiffness ☐☐☐☐☐☐☐☐☐☐☐ Severe stiffness
Please rate the quality of your sleep	Awoke rested ☐☐☐☐☐☐☐☐☐☐☐ Awoke very tired
Please rate your level of depression	No depression ☐☐☐☐☐☐☐☐☐☐☐ Very depressed
Please rate your level of memory problems	Good memory ☐☐☐☐☐☐☐☐☐☐☐ Very poor memory
Please rate your level of anxiety	Not anxious ☐☐☐☐☐☐☐☐☐☐☐ Very anxious
Please rate your level of tenderness to touch	No tenderness ☐☐☐☐☐☐☐☐☐☐☐ Very tender
Please rate your level of balance problems	No imbalance ☐☐☐☐☐☐☐☐☐☐☐ Severe imbalance
Please rate your level of sensitivity to loud noises, bright lights, odors, and cold	No sensitivity ☐☐☐☐☐☐☐☐☐☐☐ Extreme sensitivity

Scoring: Step 1. Sum the scores for each of the three domains (function, overall, and symptoms). Step 2. Divide domain 1 score by three, divide domain 2 score by one (that is, it is unchanged), and divide domain score 3 by two. Step 3. Add the three resulting domain scores to obtain the total Revised Fibromyalgia Impact Questionnaire score.

Bennett RM, Friend R, Jones KD, Ward R, Han BK, Ross RL. The Revised Fibromyalgia Impact Questionnaire (FIQR): validation and psychometric properties. Arthritis Res Ther. 2009;11(4):R120.

Quantitative Sensory Testing

Heightened pain sensitivity(hyperalgesia) and allodynia due to central and peripheral sensitization(QST).

Test battery b	Cold pain (CPT)	Heat pain (HPT)	Mechanical pain (MPT)
QST Criteria: Z > 1.96			
CST Criteria: Increased perception			 

Treatments

- Pharmacotherapy
- Non-pharmacological Therapies
- Neuromodulatory Therapies

FDA-approved Medications

- **Pregabalin** – a calcium channel alpha-2-delta subunit ligand (anticonvulsant)
- **Duloxetine** – SNRI
- **Milnacipran** – an SNRI with a somewhat more noradrenergic profile, approved for fibromyalgia (but not depression in the U.S.).
- **TNX-102 SL** (Tonmya, sublingual **cyclobenzaprine** HCl) – a once-daily, bedtime, sublingual formulation recently approved as a non-opioid treatment for fibromyalgia, with evidence for improvements in pain, sleep, and function.

Low-Dose Naltrexone (Experimental)

Crossover trial (4.5 mg nightly, n=31), LDN produced about a 29% reduction in baseline pain vs ~18% with placebo (P≈0.016), with improvements in life satisfaction and mood but not sleep or fatigue. (Younger 2013)

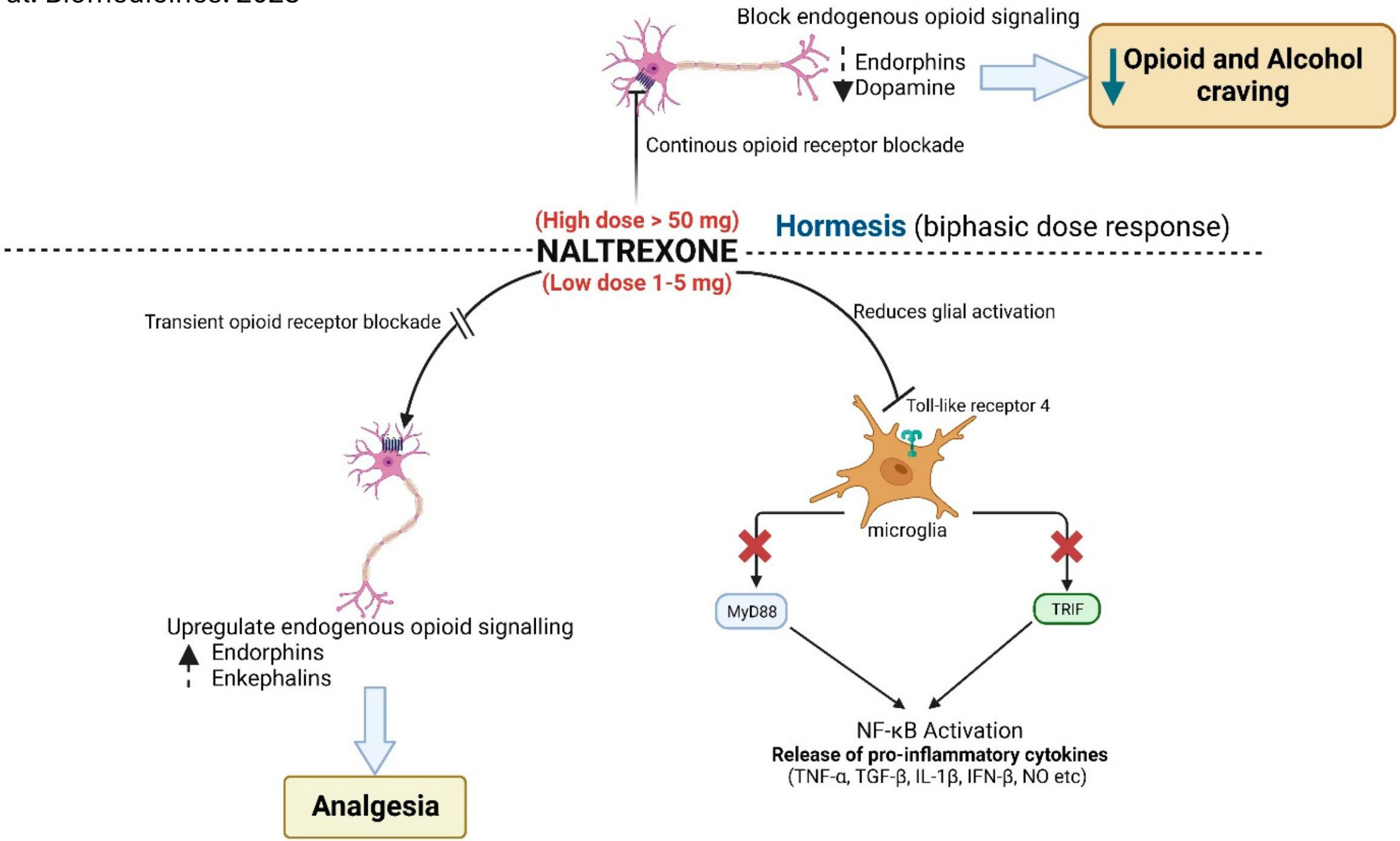
Subsequent small studies and case series suggest that ~50–70% of patients report clinically meaningful pain improvement, with generally good tolerability; dizziness and vivid dreams are among the more common side effects.

Fibromyalgia and Naltrexone: The FINAL Study (FINAL), Danish, 99 participants did not show LDN to be superior to placebo at 12 weeks. (Due Brunn 2023)

~ $45/month - worth a try for refractory pain?

Scoping Review for Centralized Pain: Rupp, Young, Chadwick 2023

Dara et al. Biomedicines. 2023



Non-Pharmacological Treatments

Exercise therapy and physical therapy

- Stretching, aerobic, strengthening, pilates
- Manual and manipulative therapies, hydrotherapy

Nutrition

- (Vit D, Magnesium, Protein, Water, B-vitamins)

Cognitive behavioral therapy and other psychological therapies

Virtual reality and others…

Balanced Diet

- **Fresh fruits and vegetables**
  - increase antioxidant intake with color
- **Whole grains**
- **Lean proteins**
  - Fish, poultry, beans, nuts
- **Healthy fats**
  - Avocado, fish, nuts
- **Low-fat dairy**
- **H2O**
- Limit processed foods, added sugars, fats
- **Special Diets**: Mediterranean, low FODMAP, anti-inflam, gluten-free

Metyas C, Aung TT, Cheung J, Joseph M, Ballester AM, Metyas S. Diet and Lifestyle Modifications for Fibromyalgia. Curr Rheumatol Rev. 2024;20(4):405-413. doi: 10.2174/0115733971274700231226075717. PMID: 38279728; PMCID: PMC11107431.

Supplements

Vitamin D

Lower in FM than in control groups

Low levels correlate with musculoskeltal pain

Supplementation improved FIQ and VAS in 180 female FM patients

Shouild target normal levels (can result in toxicity)

Magnesium

Helps with healthy nerve, bone, muscle function

200-400 mg/day

Iron

Only if anemic

Probiotics

Help with gut health/function and IBS symptoms

Psychological Therapies

Cognitive Behavioral Therapy	• Greatest evidence for pain reduction in FM • Recognize negative thought patterns, improve coping and self-management
Mindfulness-Based Interventions	• Mindfulness-based stress reduction for pain, sleep, depression
Relaxation Techniques	• Progressive muscle relaxation • Guided imagery
Acceptance and Commitment Therapy	• Effectiveness in managing pain, sleep, depression • Stanza (Swing Therapeutics) smartphone-based app received FDA approval for FM
Biofeedback	• Help with sleep in FM when combined with relaxation techniques
Hypnosis	• More effective than usual care for pain, sleep, depression in FM

Hassett AL, Gevirtz RN. Nonpharmacologic treatment for fibromyalgia: patient education, cognitive-behavioral therapy, relaxation techniques, and complementary and alternative medicine. Rheum Dis Clin North Am. 2009 May;35(2):393-407. doi: 10.1016/j.rdc.2009.05.003. PMID: 19647150; PMCID: PMC2743408.

Virtual Reality

- 11 RCTs with 535 women showed reduction in FMS pain, fatigue, anxiety, depression, and increases in dynamic balance, aerobic capacity, and quality of life
- One study found a 40% reduction in pain scores and 24% reduction in pain intensity after VR use
- Patients generally find VR acceptable, with limited side effects, and are open to using it at home for pain management

Cortés-Pérez I, 2021. PMC8621064.

Novel Treatments

(Neuromodulatory Off-Label)

- Transcutaneous electrical nerve stimulation (**TENS**)
- Integrative Approaches
  - Battlefield Acupuncture (BFA)
- Vagus nerve stimulation (**VNS**)
- Percutaneous electrical nerve field stimulation (**PENFS**)
- Cranial electrotherapy stimulation (**CES**)
- Repetitive transcranial magnetic stimulation (**rTMS**)

NOT DISCUSSED

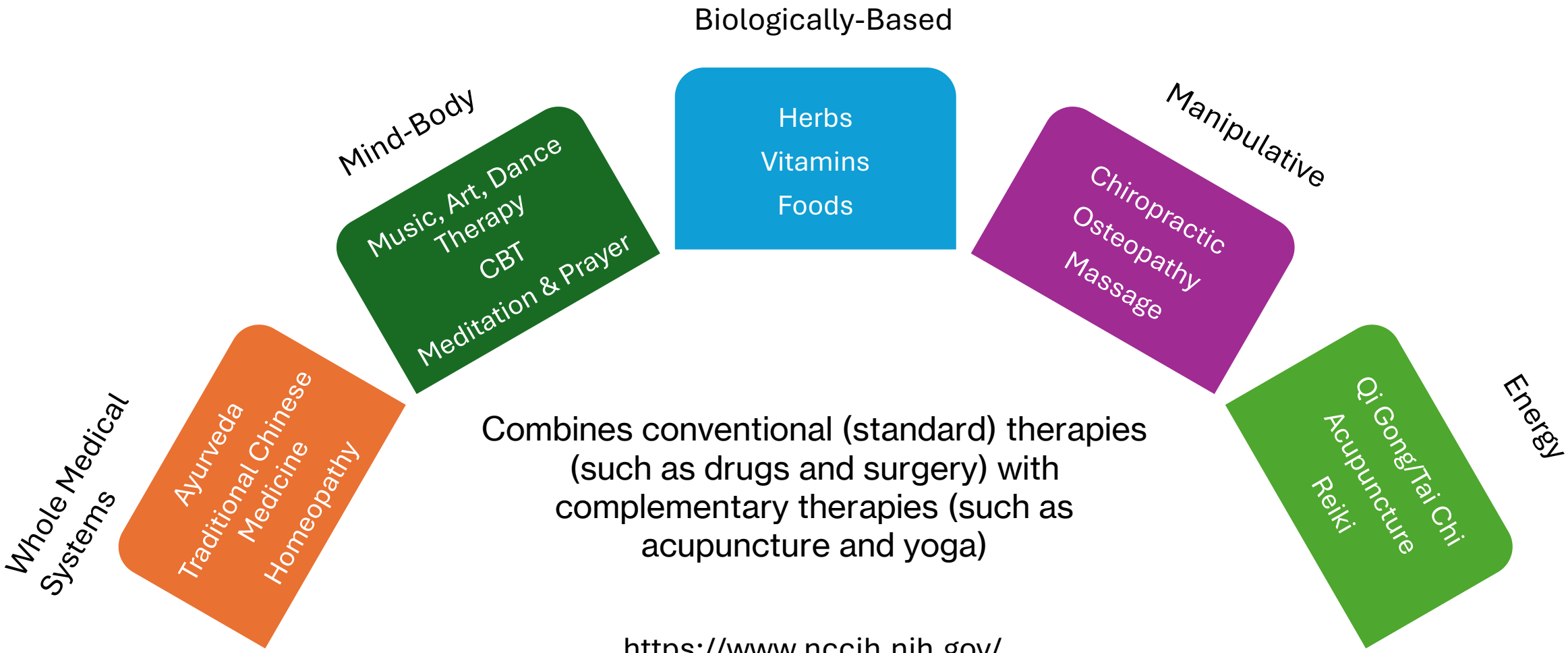
- Transcranial direct current stimulation (**tDCS**)
- Electroconvulsive therapy (**ECT**) or non-convulsive(**nECT**)
- Transcranial focused ultrasound (**tFUS**)
- Transcranial random noise stimulation (**tRNS**)
- Spinal cord stimulation (**SCS**)

Wearable TENS-based neuromodulation devices for fibromyalgia and neuropathic pain

- Quell - first FDA-cleared, non-pharmacological wearable device for fibromyalgia (De Novo authorization in 2022 for this indication)
- Approved based on a double-blind RCT showing statistically significant improvement in most FIQR domains; better results when pain sensitivity was higher

Jamison RN. J Pain Res. 2021.
PMID: 34335055; PMCID: PMC8318714.

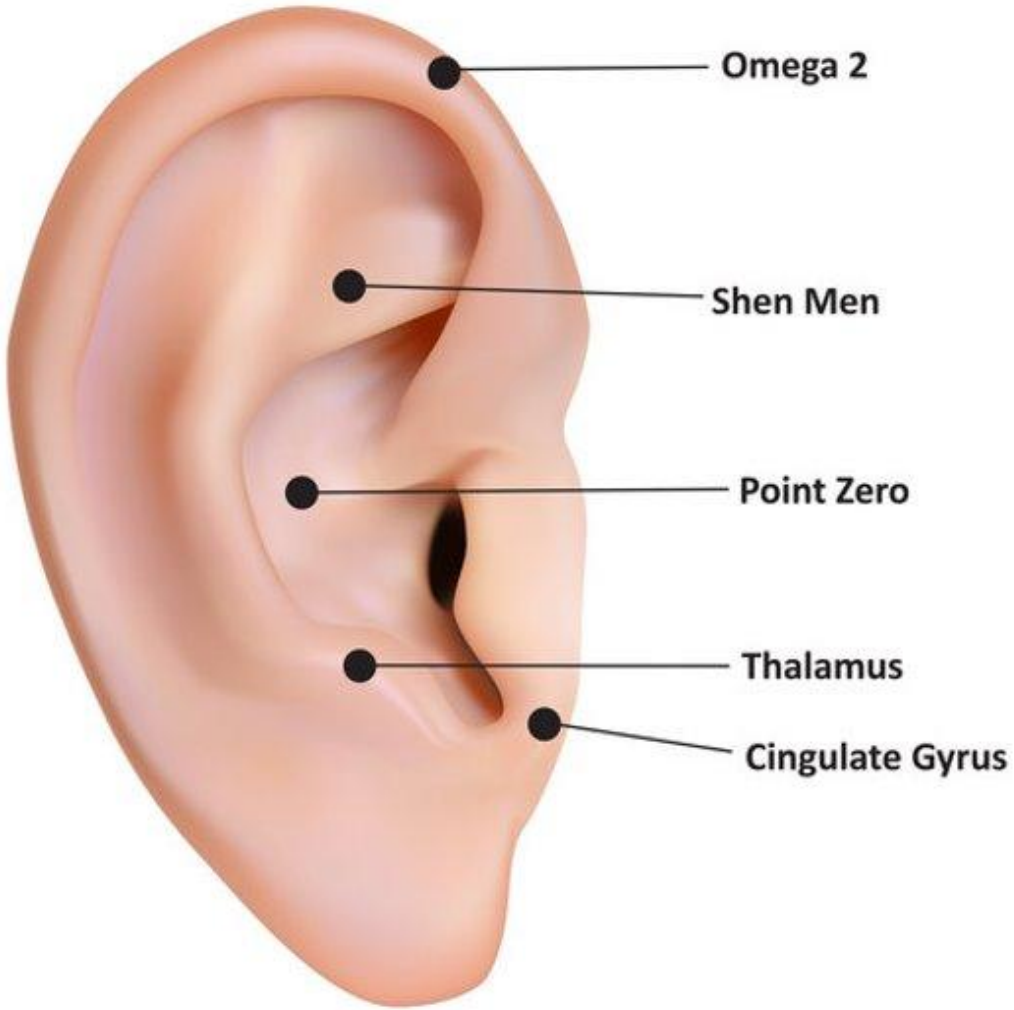
Integrative Medicine

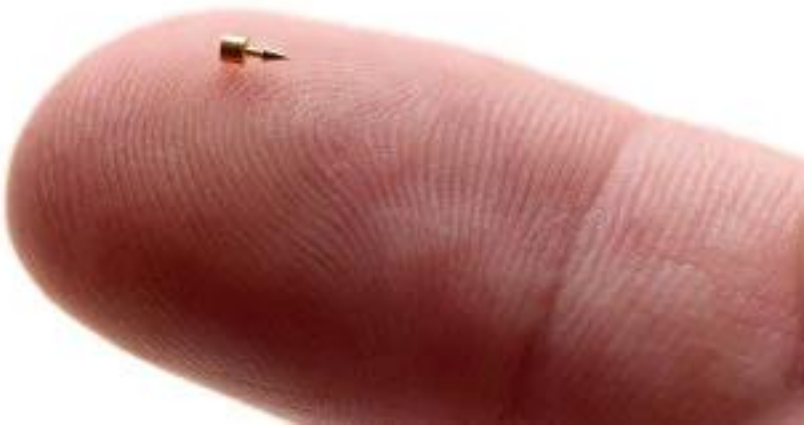


Combines conventional (standard) therapies (such as drugs and surgery) with complementary therapies (such as acupuncture and yoga)

https://www.nccih.nih.gov/

Battlefield Acupuncture Protocol

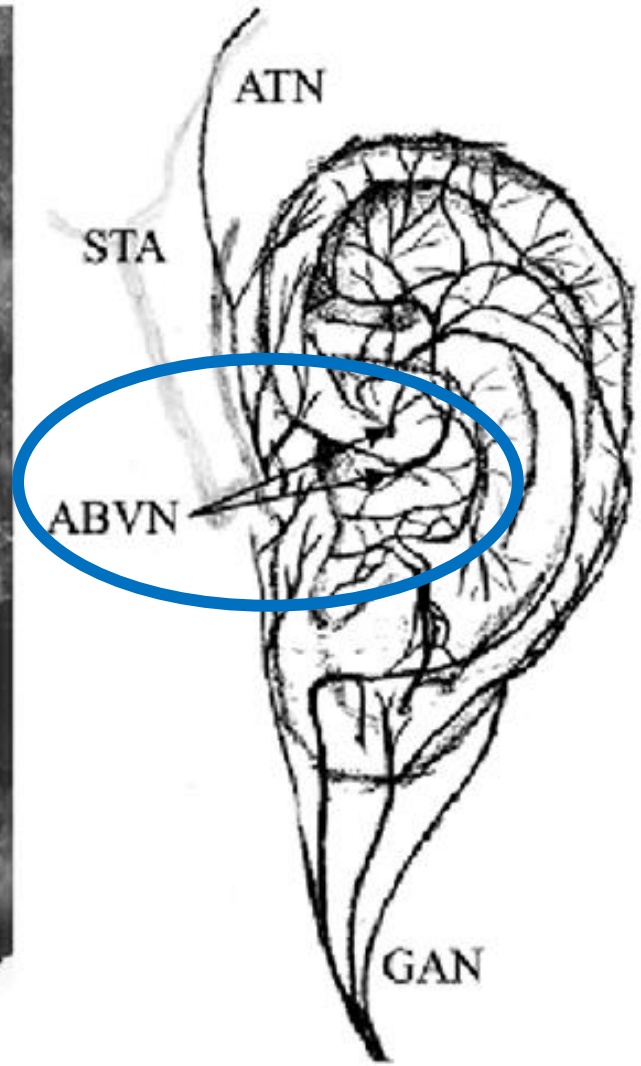




Patient Feedback on the Effectiveness of Auricular Acupuncture on Pain in Routine Clinical Care: The Experience of 11,406 Veterans

Steven B Zeliadt [1] [2], Eva R Thomas [1], Juli Olson [3], Scott Coggeshall [1], Karleen Giannitrapani [4], Princess E Ackland [5] [6], Kavitha P Reddy [7] [8], Daniel G Federman [9] [10], David F Drake [11] [12] [13], Benjamin Kligler [12] [14], Stephanie L Taylor [15] [16]

- Retrospective analysis
- Over ¾ experienced immediate pain decrease
- 60% reported MCID; average decrease was 2.5 points
- Opioid use in the past year = less improvement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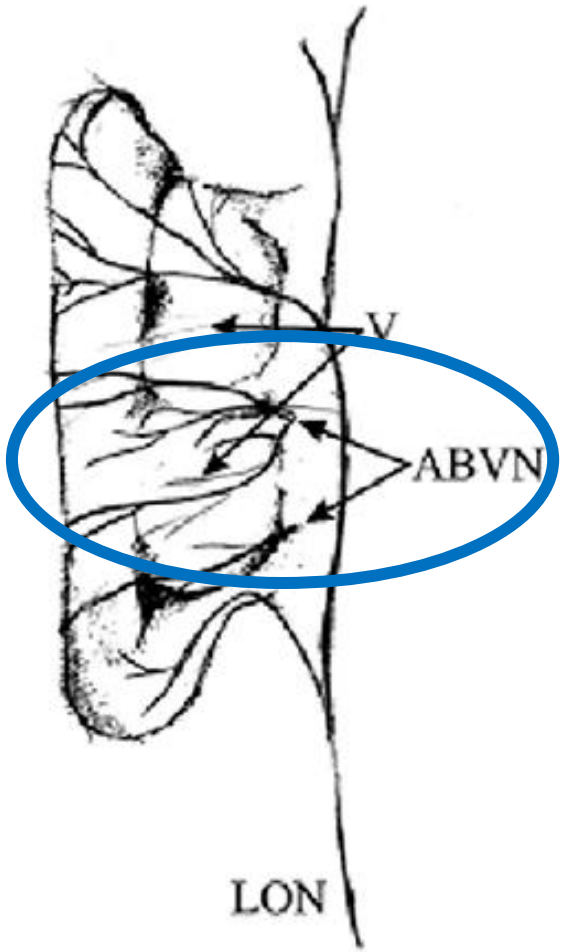
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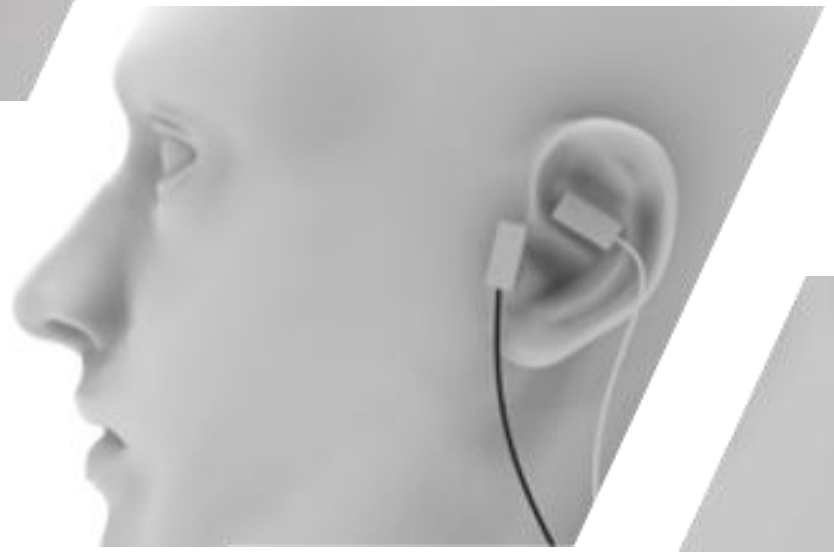
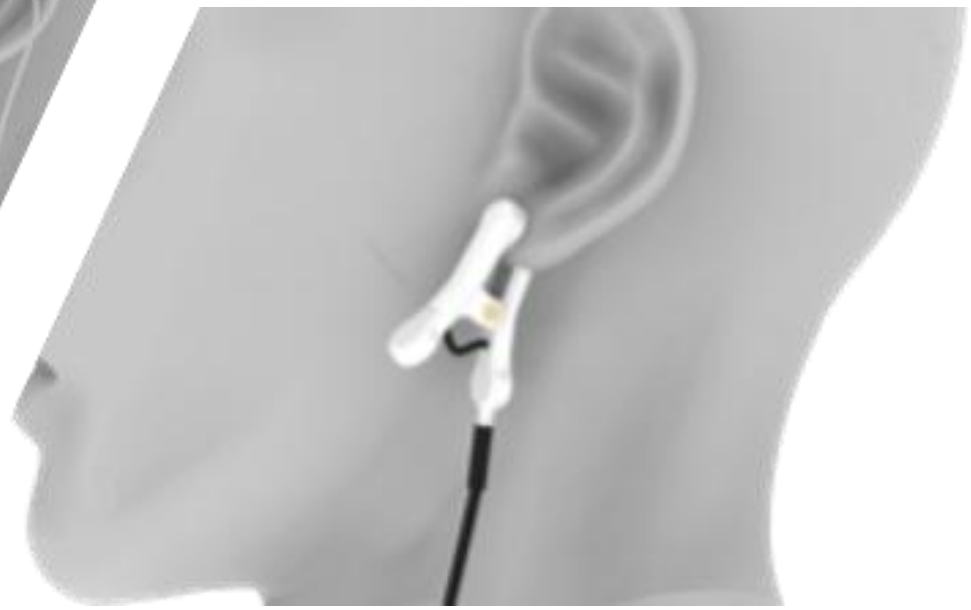
Trans-auricular Vagus Nerve Stimulation (taVNS)

- Non-invasive technology applied to the auricular branch of the vagus nerve to modulate autonomic nervous system





Mixed Nerve

- 80% afferent fibers
- (input to CNS)
- 20% efferent fibers
- (output to body)

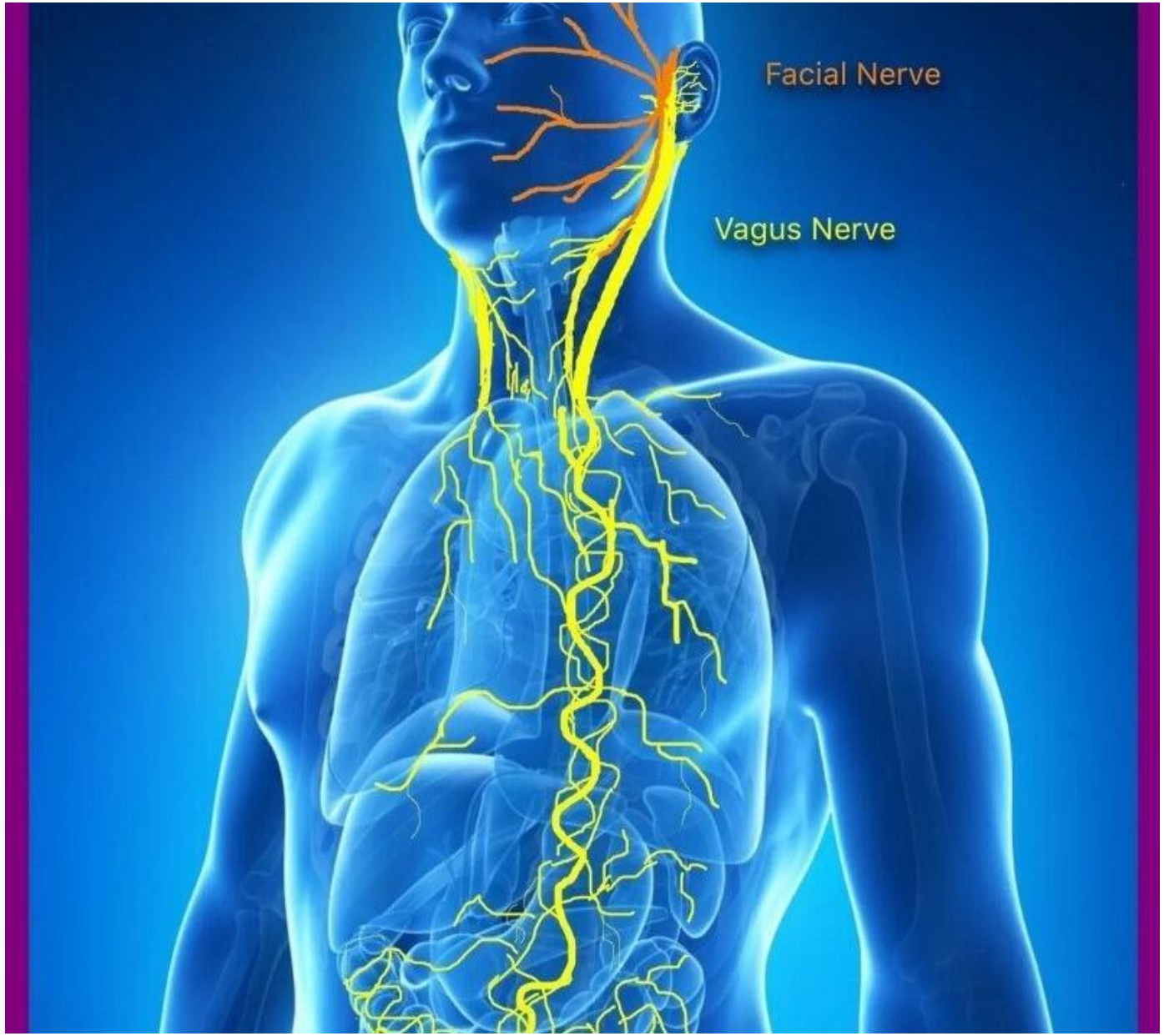


Photo Credit: Bruno Bordoni, PhD in StatPearls

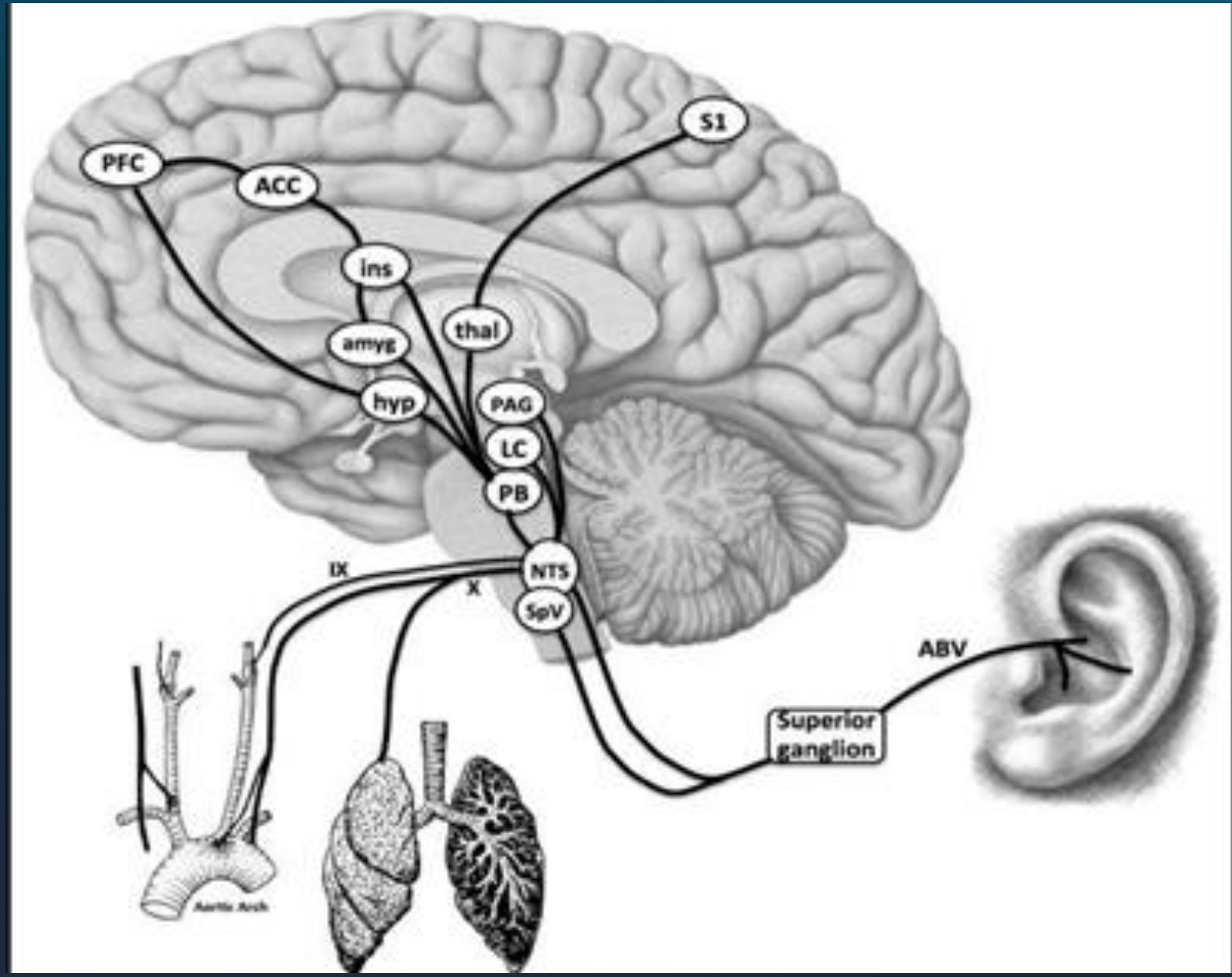
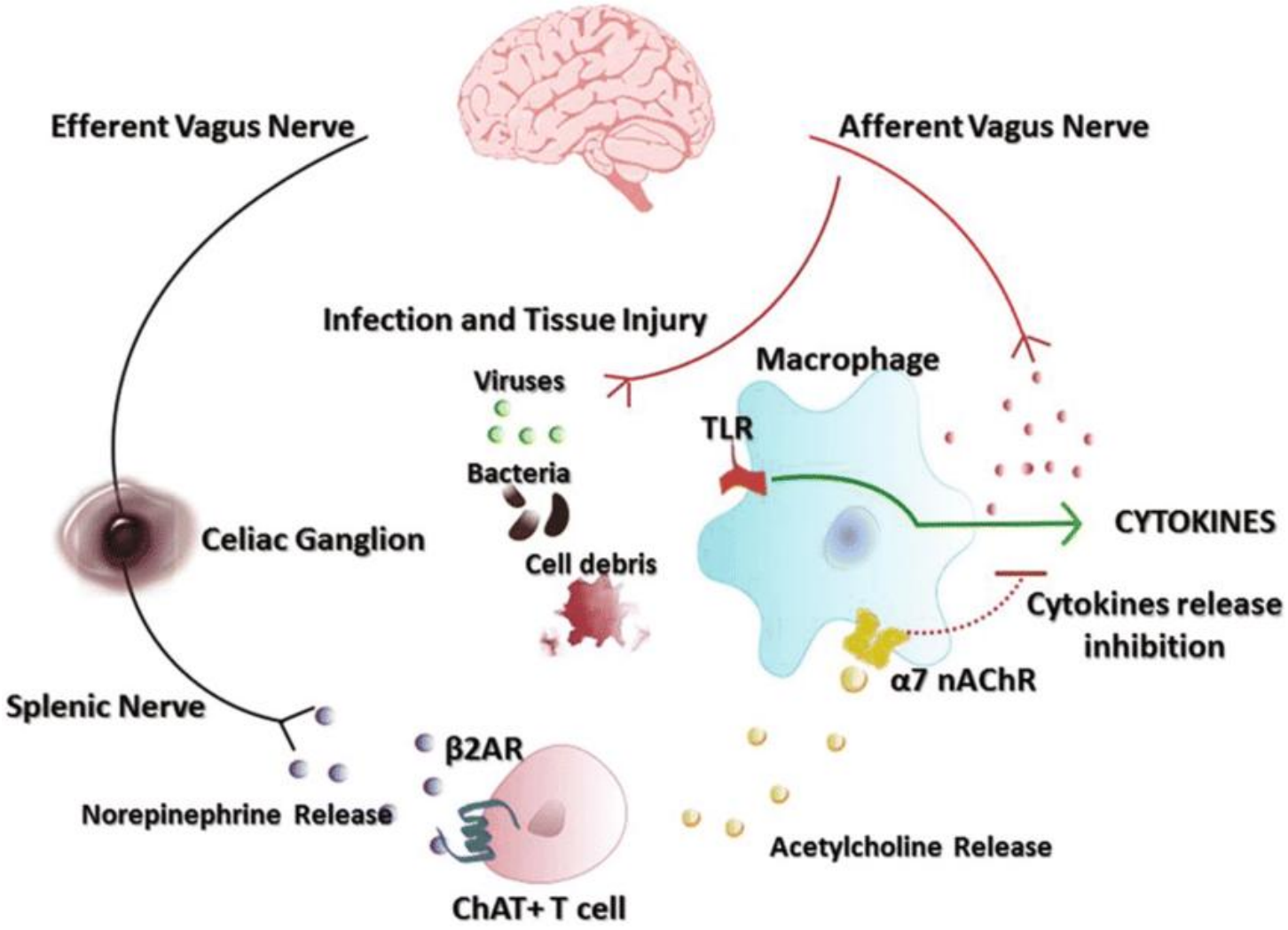


Figure A. Schematic of Integrative Innervation of the Nucleus Tractus Solitarius. From[1] The nucleus tractus solitarius (NTS) in the medulla integrates afferent inputs from the cervical vagus (X, e.g. aortic arch baroreceptors, lungs), glossopharyngeal nerve (IX, e.g. carotid baroreceptors), and auricular branch ofthe vagus (ABV). NTS input to higher brain regions processing different aspects of pain is thought to underlie the anti-nociceptive effects of vagus nerve stimulation (VNS). N.b. SpV = trigeminal nucleus, PB = parabrachial nucleus, LC = locus ceruleus, PAG = periaqueductal gray, hyp = hypothalamus, amyg = amygdala, thal = thalamus, ins = insula, ACC = anterior cingulate cortex, PFC = prefrontal cortex, S1 = primary somatosensory cortex.

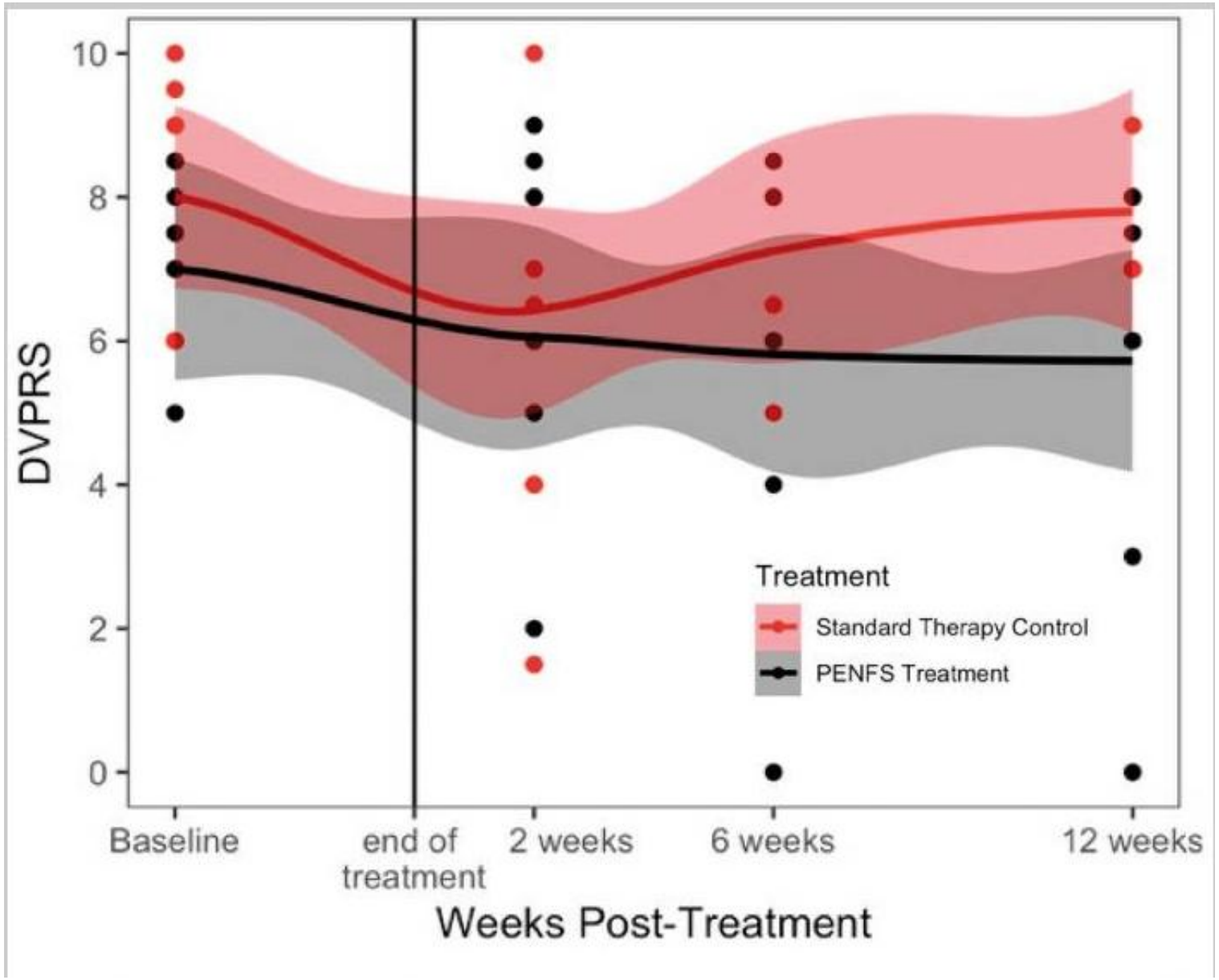
Vagus and The Cholinergic Anti-Inflammatory Pathway

- The afferent arm of the vagus nerve activated by peripheral inflammatory stimuli (i.e., infection and tissue injury) signals the nucleus tractus solitarius that, by stimulating the efferent vagus nerve, causes norepinephrine release from the vagal splenic terminations.
- This in turn stimulates ACh secretion by the ChAT^{+} T cells in the spleen that by binding α7nAChR expressed by macrophages induces anti-inflammatory response

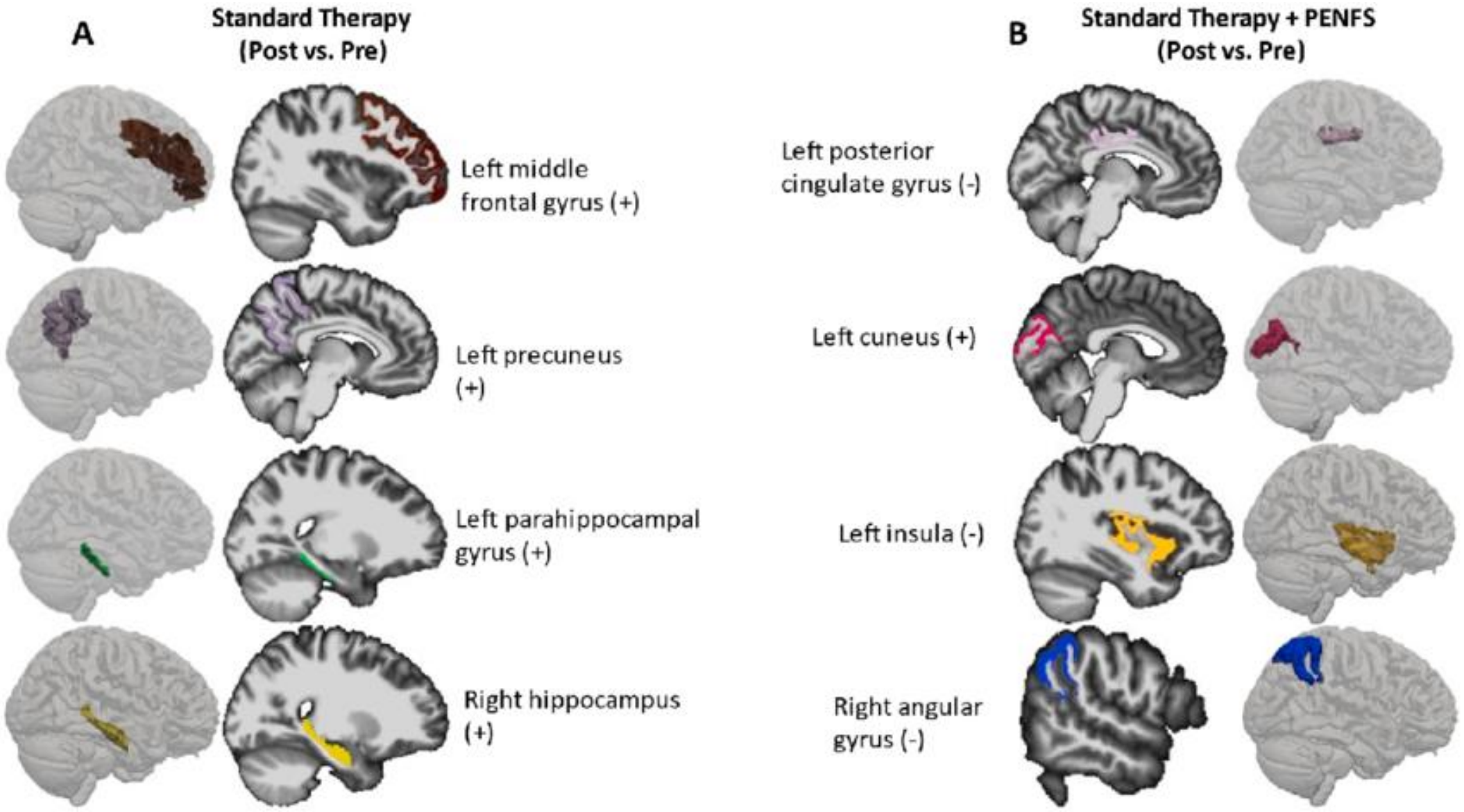


Benfante R, Di Lascio S, Cardani S, Fornasari D. Acetylcholinesterase inhibitors targeting the cholinergic anti-inflammatory pathway: a new therapeutic perspective in aging-related disorders. Aging Clin Exp Res. 2021 Apr;33(4):823-834. doi: 10.1007/s40520-019-01359-4. Epub 2019 Oct 3. PMID: 31583530.

Percutaneous Electric Nerve Field Stimulation



Woodbury et al. Pain Medicine. 2021.



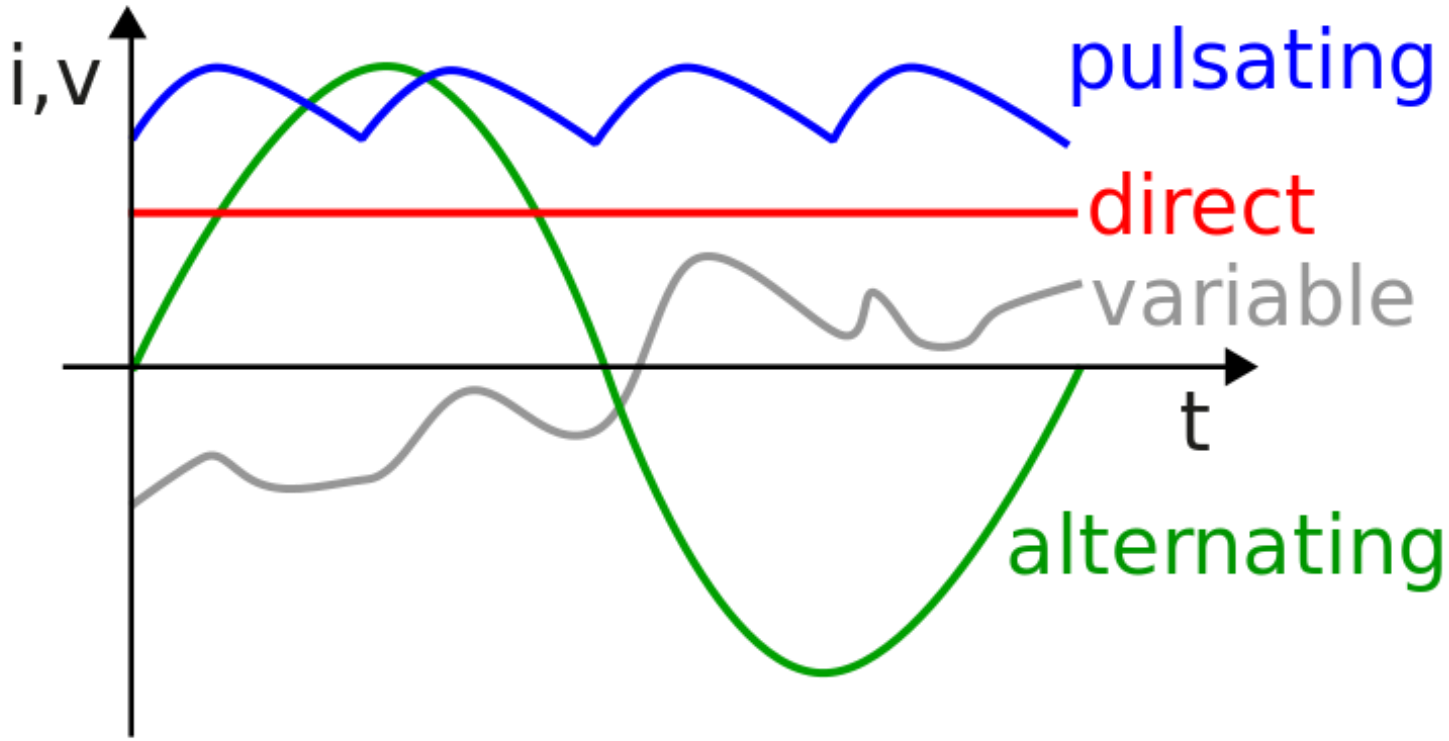
Woodbury et al. Neurobiology of Pain. 2022.

Cranial Electrotherapy Stimulation (CES)

Mechanism of Action

- CES is a type of treatment in which the brain is stimulated by a tiny current of electricity, no more than 600 millionths of an ampere
- The FDA recognizes CES as a Class II device for the treatment of depression, anxiety, and insomnia, and research backs its efficacy at treating pain and stress disorders.
- It is thought to modulate brain cells to return them to a healthy, normal state.

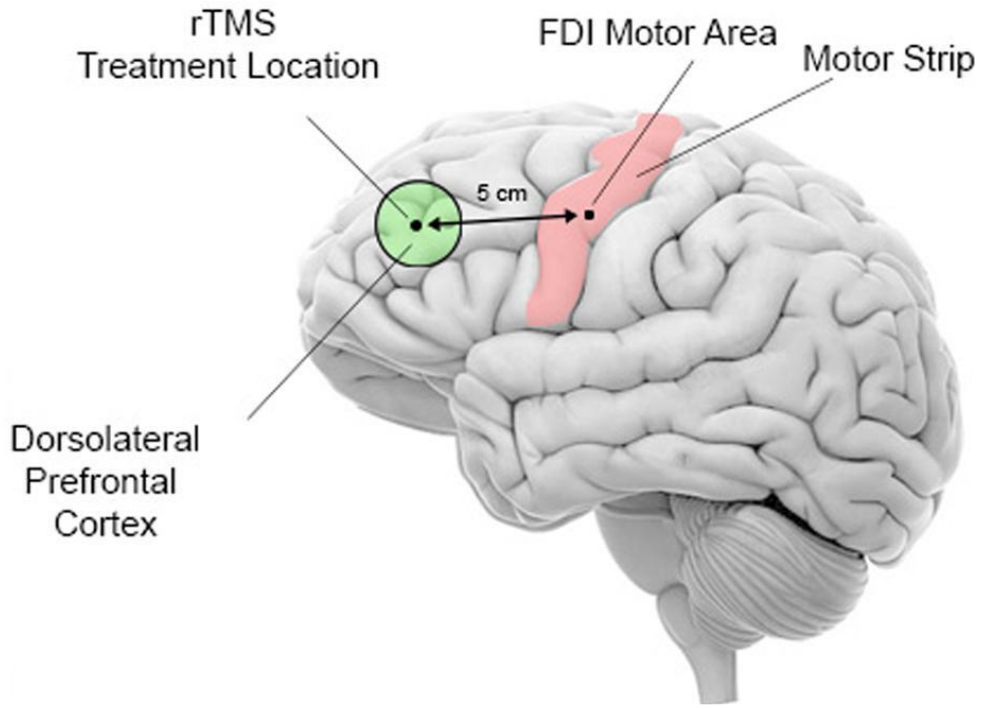
Alternating Current



Activate/Deactivate (get neurons to fire more or less)

Entrainment (synchronize neurons to the same firing pattern as the stimulation)

rTMS (2021 Review)



- Large body of research supporting use in fibromyalgia
- Multiple meta-analyses showing efficacy
- 19 studies of 643 participants found reduction in disease on FIQ, with larger reduction in older patients (p=0.008)
- Effects persist 2 weeks after final treatment
- Targeted areas were M1 and dlPFC

Su YC, 2021. PMC8538417.

Take Away Points

Fibromyalgia and Central Sensitivity Syndromes (CSS) have a pathophysiological basis – validate your patients!
Work towards novel lab-based and imaging biomarkers is under way; clinical diagnoses that can be gauged using validated instruments (CSI, PSD, etc.)
Only 4 FDA-approved medications for fibromyalgia; many off-label options.
Non-pharmacological therapies are a mainstay of treatment, with strongest evidence for CBT.
Neuromodulatory therapies hold promise, with some wearable and digital devices receiving FDA indications for fibromyalgia.

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