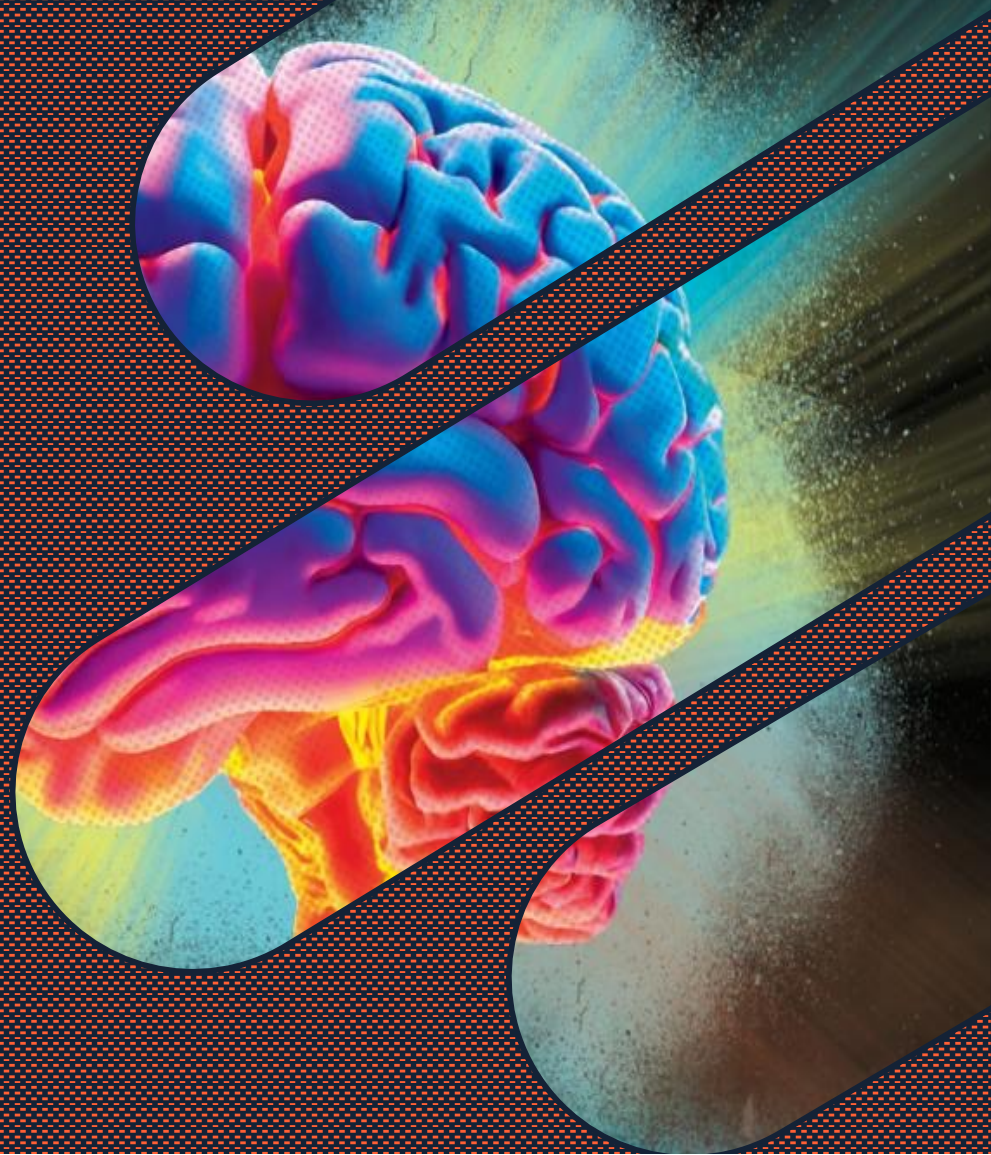


# Fibromyalgia Unmasked: Unveiling the Complexities of Chronic Pain and Management

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# Objectives

Review the possibilities of how fibromyalgia may present

Demonstrate how to use the fibromyalgia rapid screening tool (FiRST) to evaluate patients for fibromyalgia

Evaluate the AAPT 2019 Diagnostic Criteria for Fibromyalgia and 2016 American College of Rheumatology Fibromyalgia Diagnostic Criteria

Analyze the need and possibilities of diagnostic testing in the evaluation of a patient with fibromyalgia

Identify non-pharmacologic and pharmacologic therapies indicated for the management of fibromyalgia

# Fibromyalgia

Fibromyalgia is characterized by diffuse musculoskeletal pain, fatigue, poor sleep, and other somatic symptoms

Chronic diffuse pain affects 10% to 15% of adults in the general population worldwide, many of whom have fibromyalgia

Approximately 2% of people in the United States have fibromyalgia, although the prevalence varies across populations and with the diagnostic criteria used

# Fibromyalgia

Fibromyalgia can occur in children and adults and is found worldwide and across cultures

Women are diagnosed more frequently than men;

- A Scottish survey found that women are diagnosed between 2 and 14 times as often as men depending on the criteria used

Changes in the diagnostic criteria over the past decade, including the elimination of specific tender points, have resulted in more patients with chronic pain meeting the criteria for fibromyalgia

# Pathophysiology

- Likely caused by disordered central nociceptive signal processing leading to sensitization expressed as hyperalgesia and allodynia
  - Similar to chronic pain conditions such as irritable bowel syndrome, painful bladder syndrome, chronic pelvic pain, and chronic low back pain

Functional brain imaging suggests that this aberrant processing may be attributed to an imbalance between excitatory and inhibitory neurotransmitters, particularly within the insula

Suggested etiologies include:

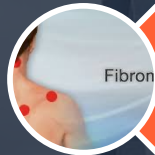
- Dysfunction of the hypothalamic-pituitary-adrenal axis and the autonomic nervous system
  - Diffuse inflammation
  - Glial cell activation
  - Small fiber neuropathy
- Infections such as the Epstein-Barr virus, Lyme disease, and viral hepatitis



# Clinical Presentation



Chronic diffuse pain is the predominant symptom in most patients with fibromyalgia



Patients may also experience muscle stiffness and tenderness



The physical examination in patients with fibromyalgia generally finds diffuse tenderness without other unusual findings

- If joint swelling, inflammation, or deformities are present, an alternative or additional diagnosis should be investigated



Fatigue and sleep disturbances are also common

- Sleep disturbances include difficulty falling and staying asleep, frequent awakenings, or feeling unrefreshed after sleeping

# Clinical Presentation

Comorbid mental health diagnoses are common, as are cognitive symptoms such as poor concentration, forgetfulness, or altered thinking

This cognitive dysfunction has been termed "fibrofog" and is described by patients as a mental slowing that adversely affects daily activities

The presence of another painful disorder does not exclude the diagnosis of fibromyalgia

The Fibromyalgia Rapid Screening Tool can screen patients with diffuse chronic pain to help distinguish between fibromyalgia and other conditions

The tool may also be used to detect coexisting fibromyalgia in patients with confirmed rheumatologic conditions

**TABLE 1**

**Fibromyalgia Rapid Screening Tool (FiRST)**

Yes

I have pain all over my body.

My pain is accompanied by a continuous and very unpleasant general fatigue.

My pain feels like burns, electric shocks, or cramps.

My pain is accompanied by other unusual sensations throughout my body, such as pins and needles, tingling, or numbness.

My pain is accompanied by other health problems such as digestive problems, urinary problems, headaches, or restless legs.

My pain has a significant impact on my life, particularly on my sleep and my ability to concentrate, making me feel slower in general.

Total\*

\*—One point for each yes answer. A score of 5 or greater suggests fibromyalgia.

*Adapted with permission from Perrot S, Bouhassira D, Fermanian J; CEDR (Cercle d'Etude de la Douleur en Rhumatologie). Development and validation of the Fibromyalgia Rapid Screening Tool (FiRST). Pain. 2010;150(2):255.*



# Diagnosis

Fibromyalgia should be considered in patients with chronic pain without a history of tissue injury that has been present for **more than three months** and who also have fatigue, mood issues, and sleep disturbances

The initial American College of Rheumatology (ACR) classification criteria included widespread pain and multiple specific muscular tender points

When these criteria were updated in 2010, 2011, and 2016, the physical examination of tender points was eliminated, and a symptom severity scale and self-reported widespread pain index were added

# AAPT 2019 Diagnostic Criteria

The AAPT (Analgesic, Anesthetic, and Addiction Clinical Trial Translations Innovations Opportunities and Networks-American Pain Society Pain Taxonomy) diagnostic criteria are an alternate framework created in 2019

The criteria require at least three months of pain in at least six of nine anatomic regions and moderate to severe sleep problems or fatigue

**TABLE 2**

**AAPT 2019 Diagnostic Criteria  
for Fibromyalgia**

1. Multisite pain, defined as six or more pain sites from a total of nine possible sites:

Head

Left arm

Right arm

Chest

Abdomen

Upper back and spine

Lower spine, including buttocks

Left leg

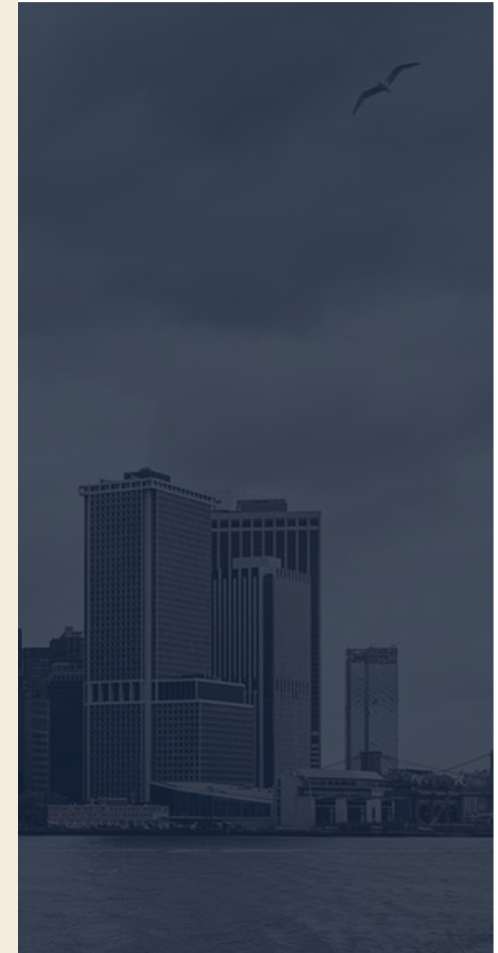
Right leg

2. Moderate to severe sleep problems or fatigue

3. Symptoms present for at least three months

AAPT = Analgesic, Anesthetic, and Addiction Clinical Trial Translations Innovations Opportunities and Networks–American Pain Society Pain Taxonomy.

*Adapted with permission from Arnold LM, Bennett RM, Crofford LJ, et al. AAPT diagnostic criteria for fibromyalgia. J Pain. 2019;20(6):*



# ACR 2016 Diagnostic Criteria

1. Symptoms present > 3 months

2. Generalized Pain in 4/5 Regions

3. WPI  $\geq 7$  and SSS  $\geq 5$  or  
WPI 4-6 and SSS  $\geq 9$

The diagnosis of fibromyalgia can now be made **irrespective of other diagnoses** (you do not need to rule out all other conditions that could explain the symptoms, **if criteria 1-3 are all met**).

**TABLE 3**

**2016 American College of Rheumatology Fibromyalgia Diagnostic Criteria**

Criterion	Areas	Met
1. Generalized pain affecting at least four of five body regions	Left shoulder/arm	Y/N
	Right shoulder/arm	Y/N
	Neck/back	Y/N
	Left hip/leg	Y/N
	Right hip/leg	Y/N
	Total:	_____
2. Symptom duration	At least 3 months	Y/N
3. Compare widespread pain index and symptom severity score	Widespread pain index is $\geq 7$ and the symptom severity score is $\geq 5$ <i>or</i>	Y/N
	Widespread pain index is $\geq 4$ and symptom severity score is $\geq 9$	Y/N
Widespread pain index: locations where the patient had pain in the past week; one point per location	Left jaw	Upper back
	Right jaw	Lower back
	Left shoulder	Chest
	Right shoulder	Abdomen
	Left upper arm	Left hip/buttock
	Right upper arm	Right hip/buttock
	Left lower arm	Left upper leg
	Right lower arm	Right upper leg
	Neck	Left lower leg
		Right lower leg
	Total widespread pain index score:	_____

**Symptom severity score\*;** add parts 1 and 2

Part 1 – sum for each area:	Fatigue	_____
0 – no problem	Waking unrefreshed	_____
1 – slight or intermittent	Cognitive symptoms	_____
2 – moderate		
3 – severe, pervasive, life-altering		
Part 2 – add 1 point for each symptom present	Headache	_____
	Lower abdominal pain or cramps	_____
	Depression	_____
	Total symptom severity score:	_____

\*—The symptom severity score is the sum (0 to 9) of the severity scores of the three symptoms (fatigue, waking unrefreshed, cognitive symptoms) plus the sum (0 to 3) of the number of symptoms (headache, lower abdominal pain or cramps, depression) the patient has been bothered by that occurred during the previous six months.

*Adapted with permission from Wolfe F, Clauw DJ, Fitzcharles MA, et al. 2016 revisions to the 2010/2011 fibromyalgia diagnostic criteria. Semin Arthritis Rheum. 2016;46(3):326.*



# Diagnosis

In patients with existing fibromyalgia the diagnosis was made in 56.8% using the AAPT criteria



However, fibromyalgia was confirmed in 94.7% of those patients using the 2016 ACR criteria



Although the AAPT criteria have simplified the diagnostic criteria, their poor diagnostic accuracy will limit the adoption and spread of these criteria

# Comorbidities

Fibromyalgia and other chronic pain conditions may represent a single patient presentation

- The coexistence of these conditions is termed chronic overlapping pain

Other painful conditions that may coexist with fibromyalgia include:

- Temporomandibular pain, irritable bowel syndrome, vulvodynia, myalgic encephalomyelitis (i.e., chronic fatigue syndrome), painful bladder syndrome/interstitial cystitis, endometriosis, chronic tension headaches, migraine headaches, and chronic low back pain


Restless legs syndrome may occur with fibromyalgia, exacerbating sleep disturbances

Psychiatric comorbidities are common in patients with fibromyalgia

# Comorbidities

More than one-half of patients with fibromyalgia also experience depression

- Other mental health conditions including bipolar disorder, generalized anxiety, and substance use disorder



Patients with fibromyalgia and inflammatory conditions tend to have higher self-rated disease activity scores than the degree of inflammation, which can lead to overtreatment of the inflammatory condition

# Diagnostic Testing

Fibromyalgia is a clinical diagnosis, and laboratory testing is not routinely needed

Because fatigue, myalgia, arthralgias, etc. can be from many causes, clinicians can consider

Tests for rheumatoid factor or antinuclear antibody levels **are not recommended** in patients without features concerning for a rheumatologic condition because of their high false-positive rates

CBC to exclude anemia

CMP

TSH

# Diagnostic Testing

A cytokine array-based blood test, known as the FM/a Test, has the potential to help confirm the diagnosis of fibromyalgia

Patients with fibromyalgia demonstrate higher cytokine production in stimulated immune cells than in the general population

The FM/a Test demonstrated 93% sensitivity and 89% specificity in 160 patients with fibromyalgia compared with patients in the control group

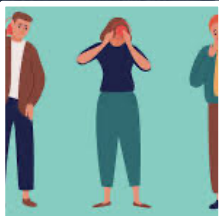
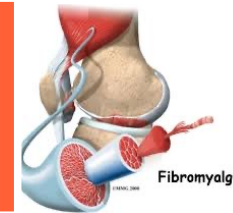


# Management



The initial benefit of establishing the diagnosis of fibromyalgia is to reassure patients and prevent further unnecessary testing and anxiety

The goal of fibromyalgia treatment is to manage symptoms such as pain, fatigue, poor sleep, and cognitive issues



A multidisciplinary individualized treatment regimen that includes pharmacologic and nonpharmacologic elements is recommended

# Management

An industry-funded initiative called the FibroCollaborative convened a panel of fibromyalgia experts to make clinical recommendations

It emphasizes a multimodal approach that includes patient education, treatment of comorbid conditions, lifestyle modification, pharmacologic therapy, cognitive behavior therapy (CBT), and self-management support

# Non-Pharmacologic Treatment

There is moderate-quality evidence that exercise (i.e. aerobic, resistance, stretching, or a combination) produces small improvements in quality of life, pain, and physical function in patients with fibromyalgia

The strongest evidence exists for aerobic exercise of moderate intensity. In addition to improvements in pain and function, exercise can decrease fatigue and improve sleep quality

# Non-Pharmacologic Treatment



CBT teaches patients how to change negative thoughts and behaviors, and helps promote skills to improve chronic pain, fatigue, and poor sleep



Options include traditional CBT, acceptance-based cognitive therapies, and operant therapy



Three systematic reviews demonstrated moderate-quality evidence that patients with fibromyalgia treated with CBT experience modest improvements in pain and disability in the short and medium term

# Non-Pharmacologic Treatment

Most complementary and alternative medicine options have not been extensively studied, and there is no consistently high-quality evidence to support them

A systematic review found that yoga, Pilates, and tai chi improved function and reduced pain

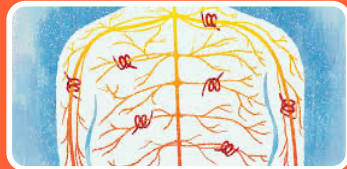
- One randomized trial found that performing tai chi for one hour twice per week for 12 to 24 weeks led to moderate symptomatic improvement in pain and function



# Non-Pharmacologic Treatment



A Cochrane review concluded that acupuncture could improve short-term pain and stiffness compared with usual care, but it is not consistently better than sham acupuncture



Manual therapy, specifically myofascial release, may decrease symptoms and improve the quality of life in patients with fibromyalgia



A small trial suggested that patient self-myofascial release improves pain and quality of life

# Non-Pharmacologic Treatment

There are limited studies showing uncertain benefits of cannabinoids for the treatment of fibromyalgia, although use is becoming more common

Other possible treatments that have not been well studied in patients with fibromyalgia include:

- Transcutaneous electrical nerve stimulation units
- Thermal therapies
- Hyperbaric oxygen
- Laser and phototherapy
- Transdermal magnesium
- Vibroacoustic and rhythmic sensory stimulation

**TABLE 4**

**Nonpharmacologic Treatments for Fibromyalgia**

<b>Intervention</b>	<b>Comments</b>
Patient education and self-management <sup>27,30</sup>	Provide information about diagnosis, pathophysiology, and prognosis Discuss treatment expectations Offer resources such as the National Fibromyalgia Association ( <a href="https://www.fmaware.org">https://www.fmaware.org</a> ) and the University of Michigan's Pain Guide ( <a href="https://painguide.com">https://painguide.com</a> )
Exercise <sup>27,31,32</sup>	Provide a prescription for low-intensity and low-frequency exercise and increase to moderate intensity, if able
Cognitive behavior therapy <sup>33-35</sup>	Can decrease pain and disability
Complementary and alternative medicine <sup>36-38</sup>	Yoga, Pilates, and tai chi can reduce pain and improve function Massage, specifically myofascial release, decreases symptoms

*Information from references 27-38.*

# Pharmacologic Treatment

Because nonpharmacologic measures often do not provide adequate symptom relief, medications are also used to treat the most problematic symptoms

Potentially useful medication classes include tricyclic antidepressants, SNRIs, and gabapentinoids

A single medication should be started at a low dosage, slowly increased to the recommended dosage, and then continued for at least three months to ensure an adequate trial, unless adverse effects are intolerable

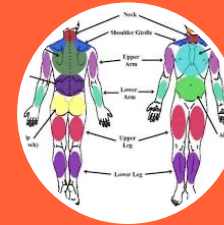
# Pharmacologic Treatment



If a satisfactory clinical response is achieved, treatment should be continued for at least 12 months



Few studies compare monotherapy with combination pharmacotherapy for fibromyalgia; however, combinations are sometimes needed

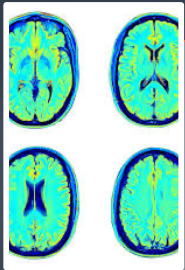


Duloxetine, milnacipran, and pregabalin are approved by the U.S. Food and Drug Administration for the treatment of fibromyalgia in the United States; however, several other medications are beneficial





# Pharmacologic Treatment



Tricyclic antidepressant medications improve several symptoms of fibromyalgia



A systematic review of amitriptyline demonstrated reduced pain, improved sleep, and improved patient satisfaction after six to eight weeks

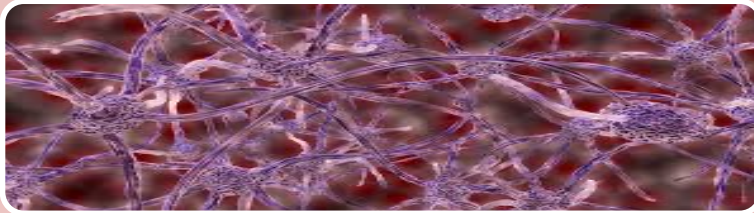


Other tricyclic agents such as nortriptyline have fewer adverse effects and may be better tolerated; however, there are few studies evaluating their use in fibromyalgia



For patients unable to tolerate amitriptyline, cyclobenzaprine, a muscle relaxant that is a tricyclic derivative, can be a reasonable option

# Pharmacologic Treatment



A meta-analysis of five randomized trials found that cyclobenzaprine produced modest pain reduction without affecting fatigue or sleep



There is insufficient evidence for other muscle relaxants in the treatment of fibromyalgia

# Pharmacologic Treatment

A systematic review showed that duloxetine (SNRI) produced greater pain relief compared with placebo and other antidepressants such as sertraline, paroxetine, fluoxetine, and bupropion

Milnacipran (SNRI) improves pain, fatigue, and cognition compared with placebo over three months

Other serotonin-norepinephrine reuptake inhibitors, such as venlafaxine, have not been examined as extensively

# Pharmacologic Treatment



Gabapentinoids (Pregabalin) may be helpful in fibromyalgia with severe sleep disturbances



Pregabalin reduces pain by up to 50% with a number needed to treat of 10, and improves sleep, fatigue, and quality of life



The evidence is insufficient to determine if gabapentin is effective for fibromyalgia



**TABLE 5****Medications for Fibromyalgia**

<b>Medication (class)</b>	<b>Starting dosage</b>	<b>Recommended dosage</b>	<b>Common adverse effects</b>	<b>Potential benefits</b>
Amitriptyline (tricyclic antidepressant) <sup>47</sup>	5 to 10 mg at night	20 to 30 mg at night	Dry mouth, constipation, dizziness, urinary retention, somnolence	Pain reduction
Cyclobenzaprine (muscle relaxant; tricyclic derivative) <sup>28,48</sup>	5 to 10 mg at night	10 to 40 mg daily in 1 to 3 divided doses	Sedation, seizures, arrhythmias, confusion	Pain reduction
Duloxetine (Cymbalta; serotonin-norepinephrine reuptake inhibitor) <sup>28,49</sup>	20 to 30 mg every morning	60 mg every morning	Nausea, dry mouth, somnolence, fatigue, constipation, decreased appetite; FDA boxed warning for increased suicidality risk in children, adolescents, and young adults with major depressive disorder or other psychiatric disorders	Pain reduction
Milnacipran (Savella; serotonin-norepinephrine reuptake inhibitor) <sup>28,50,51</sup>	12.5 mg every morning	50 mg twice daily	Nausea, constipation, hyperhidrosis, vomiting, palpitations, increased heart rate, dry mouth, hypertension; FDA boxed warning for increased suicidality risk in children, adolescents, and young adults with major depressive disorder or other psychiatric disorders	Pain reduction, fatigue reduction, improvement in cognition
Pregabalin (Lyrica; gabapentinoid) <sup>27,52</sup>	25 to 50 mg at bedtime	150 to 450 mg at bedtime	Dizziness, somnolence, dry mouth, blurred vision	Pain reduction, fatigue reduction, improved sleep, improved quality of life

FDA = U.S. Food and Drug Administration.

Information from references 27, 28, and 47-52



# Pharmacologic Treatment



Opioids are not recommended for fibromyalgia as they do not target the processes involved in centralized sensitization, and their use may cause additional harm because of the risk of dependence, misuse, worsening of hyperalgesia, and other significant adverse effects



A Cochrane review concluded that nonsteroidal anti-inflammatory medications are not superior to placebo for pain in fibromyalgia and can have significant adverse effects



The data is insufficient to determine the benefit of acetaminophen for pain in fibromyalgia

# Treatment Resistance - Neuromodulation

## Transcranial magnetic stimulation (TMS)

- Most studied has been transcranial direct current stimulation (tRGS)
- The change in pain was significantly greater in those who received treatment to the motor cortex than in the groups receiving sham or dorsolateral prefrontal cortex stimulation

## Occipital and C2 nerve stimulation

- After occipital nerve stimulation, positron emission tomography demonstrated activation of the descending pain inhibitory pathway and the lateral pain pathway in fibromyalgia patients

# The Jury Is Still Out...

## Esreboxetine and Reboxetine

- Have been tested in fibromyalgia but are not commonly used and offer **no advantages over the FDA-approved SNRIs (duloxetine and milnacipran)**

## Naltrexone

- A pilot study found that low-dose naltrexone reduced pain more than placebo (29 versus 18 percent)
- Low-dose naltrexone was also associated with **improved general satisfaction with life and with improved mood** but was not associated with improved fatigue or sleep

# The Jury Is Still Out...



Memantine, pramipexole, and sodium oxybate, had looked promising in early fibromyalgia clinical trials but, either from lack of efficacy or adverse side effects, are not considered current pharmacologic options



## Vitamin D supplementation

- A 2018 systematic review did not find conclusive evidence that symptoms correlated with low vitamin D or that supplementation was effective



# Resources

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