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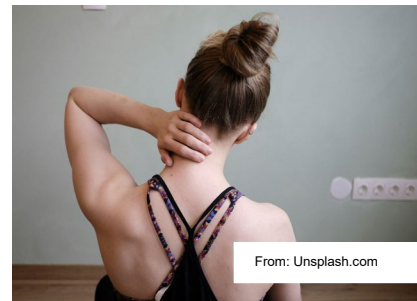


Key Inforbits

- What is fibromyalgia?
- National Fibromyalgia Awareness Day
- Common Comorbidities of Fibromyalgia
- Managing Fibromyalgia

What is fibromyalgia?

Epidemiology: Fibromyalgia is characterized by a form of chronic, maladaptive pain that has continued to perplex the medical field. This specific form of maladaptive pain consists of disturbances in the central nervous system's pain processing resulting in widespread pain that may include spontaneous pain and/or increased hypersensitization to painful stimuli.¹ The first preliminary reference to fibromyalgia symptoms was in 1824, which were described as “tender points”.² In 1904, the term “fibrositis” was used to diagnose patient symptoms.² It wasn't until 1987 that the American Medical Association (AMA) recognized the term and condition of fibromyalgia as a disease and cause of illness or disability.² Fibromyalgia affects up to 5% of the global population and 6.4% of Americans.^{3,4} Within the U.S., 7.7% of presentations are in women while only 4.9% are in men.⁴ The prevalence of fibromyalgia also seems to increase with age.⁴



Pathology: Normally, the descending pathway of the nervous system utilizes endogenous opioids, γ -aminobutyric acid (GABA), norepinephrine, and serotonin to regulate pain perception, while glutamate and substance P increase the intensity of the pain signaling.⁴ In fibromyalgia, there are abnormalities within these levels of neurotransmitters, specifically lower levels of serotonin and norepinephrine while levels of glutamate and substance P have been noted to be higher.⁵ The regulation of these neurotransmitters has played a key role in the management of fibromyalgia and continues to be the focus in the creation of new fibromyalgia therapies. In addition to neurotransmitter dysfunctions, the use of magnetic resonance imaging (MRI) has been used to observe common structural abnormalities within these patients, including decreased cortical thickness and diminished brain volumes.⁶

Symptoms: Fibromyalgia is associated with many symptoms that dramatically impact a patient's quality of life. The main symptoms that characterize fibromyalgia include:⁷

- Chronic pain throughout multiple areas of the body
- Chronic fatigue
- Pain described as aching, burning, or throbbing
- Unrefreshing sleep

Other symptoms may manifest as:⁷

- Muscle and joint stiffness
- Tenderness to touch
- Digestive issues (bloating/constipation)
- Numbness/tingling in the extremities
- Decreased abilities in concentration and memory
- Sensitivity to temperature

Diagnosis: There is currently no gold standard for the diagnosis of fibromyalgia. However, some organizations have created criteria for the treatment of fibromyalgia based on several validated studies that evaluated the symptoms and comorbidities associated with fibromyalgia. The 2016 Revision to the 2010/2011 American College of Rheumatology (ACR) fibromyalgia diagnostic criteria states that patients must meet 3 of the following criteria to be diagnosed with fibromyalgia:



From: Unsplash.com

widespread pain index (WPI) ≥ 7 and symptom severity scale (SSS) score ≥ 5 or WPI of 4-6 and SSS score ≥ 9 ; generalized pain (defined as pain in 4 or 5 regions), must be present.⁸ Jaw, chest, and abdominal pain are not included in the generalized pain definition; symptoms have been present generally for at

least 3 months; a diagnosis of fibromyalgia is valid irrespective of other diagnoses and does not exclude the presence of other clinically important illnesses.⁸

Many medical professionals stated that the ACR criteria was not useful in a clinical setting and did not address any of the co-occurring symptoms of fibromyalgia.⁹ As a result, the ACTION-APS Pain Taxonomy (AAPT) published its own criteria for fibromyalgia in an effort to create criteria that was more representative of the disease state.⁹ The AAPT diagnostic criteria consists of the following:⁹

- Multiple site pain (MSP), defined as 6 or more pain sites from a total of 9 possible sites:
 - Head
 - Left arm
 - Right arm
 - Chest
 - Abdomen
 - Upper back and spine
 - Left leg
 - Right leg
 - Lower back spine, including the buttocks
- Moderate to severe sleep problems/fatigue
- MSP plus fatigue/sleep problems must be present for at least 3 months

National Fibromyalgia Awareness Day

The National Fibromyalgia Association (NFA) has been bringing global awareness to the condition and effects of fibromyalgia since 1998.¹⁰ After many years of working with local and national lawmakers, May 12th was assigned as National Fibromyalgia Awareness Day.¹⁰ The NFA hosts annual events on this day to bring people together who are living with fibromyalgia and highlight their experiences to educate others in the community about the impacts fibromyalgia has on their lives. NFA has held an Annual Walk of FAME (Fibromyalgia Awareness Means Everything) to raise money and show support for these individuals.¹⁰ Educational seminars have also been a part of the Awareness Day activities including presentations from physicians and other healthcare workers to speak on the condition and provide information on fibromyalgia management.¹⁰ To stay up to date on events and webinars hosted by the NFA, please visit <https://www.fmaware.org/>.

Common Comorbidities with Fibromyalgia

Fibromyalgia is associated with many disease states, and although the mechanisms behind these associations are unclear, it is thought to be related to the central sensitization. The coexistence of these diseases can lead to further impacts on patient care and their quality of life. Below is a list of comorbidities that should be taken into consideration when caring for fibromyalgia patients and be managed appropriately to optimize patient outcomes.

Table 1: Common Comorbidities Associated with Fibromyalgia⁹

Somatic Pain Disorders	Irritable Bowel Syndrome Chronic Pelvic Pain Interstitial Cystitis Otologic Symptoms Chronic Headaches and Migraine Disorders
Psychiatric Conditions	Major Depressive Disorder Bipolar Disorder General Anxiety Disorder Panic Disorder Post Traumatic Stress Disorder Social Phobia Obsessive Compulsive Disorder Substance Use Disorder
Sleep Disorders	Central and Obstructive Sleep apnea Restless Leg Syndrome Insomnia
Rheumatic Diseases	Rheumatoid and osteoarthritis Systemic lupus erythematosus Sjögren's Syndrome

Managing Fibromyalgia

As more studies have been conducted and their data interpretation included the overall understanding of fibromyalgia, recommendations have emerged based on available evidence.



The level of recommendation for each pharmacological and non-pharmacological activity varies based on agreement from several multidisciplinary professional organizations such as the European League Against Rheumatism (EULAR), the Canadian Pain Society, and the Canadian Rheumatology Association (CRA).^{11,12} Several pharmacologic therapies have received increased recommendations for off-label use, however, currently, there are only 3 medications with FDA approval for management of fibromyalgia symptoms: pregabalin (Lyrica), duloxetine (Cymbalta), and milnacipran (Savella).¹³ Though

there may be suggested therapy, all guidelines are in consensus that each patient should have care tailored to their needs noting that any one treatment will not be appropriate for all patients, with monotherapy and combination therapies seeing widespread use. Pharmacological treatments are generally adjunctive use with non-pharmacologic interventions and not recommended for use alone, while non-pharmacological options are tried first in the management of symptoms.^{11,12} As there is the possibility for patients with fibromyalgia to experience any or all of the common symptoms, therapy can be made most efficient by utilizing overlapping suggested interventions. However, since each patient should still be considered on a case-by-case basis, this type of strategy may not always prove feasible. To provide more options for treatment of mood disturbance, in cases of patients with comorbid depression, the selective serotonin reuptake inhibitors (SSRIs) fluvoxamine and paroxetine have been recommended as possible treatments despite their showing no efficacy for the treatment of fibromyalgia, as do duloxetine and milnacipran (SNRIs).¹⁴



Several interventions have less overall consensus for inclusion into guidelines. Organizations suggested more research be conducted prior to guideline inclusion on these medications: cyclobenzaprine (centrally acting muscle relaxant), cannabinoids, and non-steroidal anti-inflammatory drugs (NSAIDs).¹⁴ Several medications were rejected by all current guidelines for the treatment of fibromyalgia including, monoamine oxidase inhibitors (MAOIs), hormone therapies, sodium oxybate, and all opioid therapies (with the exception of the weak opioid, tramadol).



Table 2: Current Medications and Non-Pharmacologic Interventions for Fibromyalgia ^{11, 12, 14}			
Symptom	Medications	Drug Class	Non-pharmacologic treatment
Pain	Amitriptyline (Elavil)	TCA	Physical Activity: Biking, walking, swimming, and other aerobic exercise, with daily stretching Cognition: Improving sleep habits and cognitive behavioral therapy Stress-relief: Meditative movement (yoga, tai chi), mindfulness-based stress reduction
	Tramadol (Ultram)	Weak opioid	
	Pregabalin (Lyrica)	Anticonvulsant	
	Duloxetine (Cymbalta) and milnacipran (Savella)	SNRIs	
Fatigue	Duloxetine (Cymbalta) and milnacipran (Savella)	SNRIs	
Sleep disturbance	Amitriptyline (Elavil)	TCA	
	Pregabalin (Lyrica)	Anticonvulsant	
Mood disturbance	Duloxetine (Cymbalta) and Milnacipran (Savella)	SNRIs	

Tricyclic antidepressant = TCA, Serotonin-Norepinephrine Reuptake Inhibitors = SNRI

Emerging Therapies

On August 1, 2024, it was announced that the United States Food and Drug Administration (FDA) had granted Fast Track designation to Tonix Pharmaceuticals for the development of TNX-102 SL (cyclobenzaprine HCl sublingual tablets, brand name: Tonmya™) as a treatment for fibromyalgia.¹⁵ The press release states that phase 3 control trials which show statistically significant evidence of pain reduction have been conducted but have not been published at the time of this statement. A phase 2 controlled trial, with 503 patients total, was published in 2023 showing the treatment to be effective and well-tolerated.¹⁶ A phase 3 randomized controlled trial of TNX-102 SL 5.6 mg, with a total of 358 patients, was published in the context of the treatment of posttraumatic stress disorder (PTSD) in US service members.¹⁷ Common adverse reactions reported were somnolence (15.4%), dry mouth (3.4%), and headache (2.3%), though dry mouth and headache were seen less frequently in the TNX-102 SL group than in the placebo group.¹⁷

Summary

With fibromyalgia affecting many patients, the need for awareness is imperative. Fibromyalgia is commonly referred to as a “catch-all” diagnosis when pain is present, but no other diagnosis can be determined. Being able to identify the specific symptoms and physiologic changes associated with fibromyalgia can lead to more accurate diagnosis and treatment. Utilizing therapies that target the unique symptoms of each patient and implementing appropriate non-pharmacologic therapies are key to improving these patients’ quality of life.

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The last “dose” ...

“Time is not a cure for chronic pain, but it can be crucial for improvement. It takes time to change, to recover and to make progress.”

—Dr. Mel Pohl, *A Day Without Pain* [Physician specializing in treatment of chronic pain and addiction, 1951 -]



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