CLINICAL PRACTICE

Fibromyalgia

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This Journal *feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the authors' clinical recommendations.*

SUMMARY

Fibromyalgia is characterized by widespread pain involving any body tissue and typically accompanied by fatigue and problems with sleep, mood, and memory. Fibromyalgia can occur alone or in combination with other chronic overlapping primary pain conditions, or it can be superimposed on other conditions, such as autoimmune disorders (secondary pain). In fibromyalgia, the central nervous system (CNS) is hyperresponsive to sensory stimuli generally. Successful pharmacologic and nonpharmacologic interventions focus on the CNS to support CNS quiescence and a return to homeostasis. Although fibromyalgia is rarely curable, most cases can be well managed in the context of primary care.

A 43-year-old man presents with a 3-year history of chronic low back pain that has been unresponsive to muscle relaxants, nonsteroidal antiinflammatory drugs (NSAIDs), epidural glucocorticoid injections, and physical therapy. A recent diagnostic workup revealed a normal erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) level, thyroid-stimulating hormone (TSH) level, and complete blood count and normal results of liver-function tests. Magnetic resonance imaging of the lumbar spine showed mild degenerative changes and a protruding disk (at L5 or S1). At intake, he used a body map (i.e., a paper and pencil mannequin) to indicate sites of pain in his back, head, shoulders, and legs. He reports a long history of tension headache and noncardiac chest pain and a previous diagnosis of chronic prostatitis. He reports long-term insomnia, fatigue, and sensitivity to bright lights and multiple drug allergies. The physical examination is generally unremarkable except for tenderness in many regions but otherwise normal strength and sensation throughout and negative findings on provocative maneuvers of the lower back and sacroiliac joint. He is frustrated and wondering whether he should have lumbar surgery to relieve his pain or whether opioids would be helpful. How would you treat this patient?

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N Engl J Med 2026;395:267-77.
DOI: 10.1056/NEJMcp2411656

CME

THE CLINICAL PROBLEM

Fibromyalgia affects approximately 4 to 6% of the U.S. population, with a similar prevalence worldwide.[1] As with most chronic pain conditions, it affects 1.5 to 2 times as many women and girls as men and boys. The cardinal symptom of fibromyalgia is persistent widespread pain,[2] but problems with sleep, mood, fatigue, and memory and sensitivity to nonpainful sensory stimuli such as lights, noises, and odors are commonly reported.[3] Persons with

fibromyalgia tend to be frequent users of health care services, with one study estimating health care costs to be 3 times higher than for matched controls.[4]

Fibromyalgia has a long and controversial history.[5] Originally called fibrositis and later fibrositis syndrome, the condition was thought to involve tender and inflamed muscle tissue accompanied by sleep problems. The name was later changed to fibromyalgia syndrome and then simply to fibromyalgia when no evidence of peripheral inflammation could be detected. Failure to identify a source of inflammation or observable damage to peripheral tissues led many to cast doubt on the legitimacy of this condition.

Over the past 20 years, however, considerable research has repeatedly shown fibromyalgia to have many objective neurobiologic underpinnings. The strength of these findings helped support the formal acknowledgment by the International Association for the Study of Pain that pain could arise from the central nervous system (CNS) with little to no input from peripheral tissues. This form of pain, termed nociplastic pain,[6,7] connotes central neural plasticity resulting in sensitization of the CNS to both nociceptive input and non-nociceptive input. Hypersensitization to both painful and nonpainful sensory stimuli is now thought to underlie many of the symptoms of fibromyalgia. Thus, the goal of therapy is not to "fix" peripheral pathologic features but instead to calm the sensory hyperresponsiveness that promotes CNS-augmented pain.

Fibromyalgia is not the only painful condition influenced by nociplastic pain processes. In 2016, the National Institutes of Health identified 10 chronic pain conditions that appeared to co-occur more commonly than other chronic pain conditions in patients with fibromyalgia, affected women and girls more than men and boys, were refractory to traditional biomedical interventions, and probably were neurobiologically underpinned by nociplastic pain.[8] These conditions were termed chronic overlapping pain conditions (Fig. 1). More recently, the 11th revision of the *International Classification of Diseases* refers to many of the chronic overlapping pain conditions as primary pain, meaning that the pain is the primary problem as opposed to a problem that is secondary to some other disease (e.g., osteoarthritis).[12] Understanding how and why the CNS becomes sensitized can help clinicians form rational approaches to fibromyalgia treatment.

RISK FACTORS FOR FIBROMYALGIA AND NOCIPLASTIC PAIN

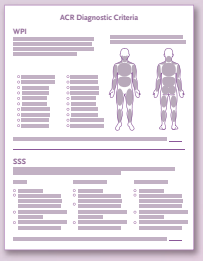
Nociplastic pain appears to evolve by means of two processes. The top-down process is a CNS-driven process by which characteristics of nociplasticity are present even before the onset of a painful event.[13] In the large Adolescent Brain and Cognitive Development (ABCD) study, symptoms of sleep difficulties, memory problems, and heightened sensitivity to sensory stimuli, alone or in combination, antedated the development of pain.[14] Thus, these symptoms are core components rather than effects of nociplastic pain. In a different ABCD study, pain-free healthy children who were 9 to 11 years of age received brain imaging at baseline and then again 1 year later.[15] Although most of the children had remained free of pain by the 1-year follow-up, widespread pain had developed in approximately 2%. As compared with healthy controls, the children with widespread pain by year 1 had neuroimaging findings characteristic of nociplastic pain at baseline, before any pain had been reported.

In the bottom-up process, nociplastic pain evolves over time, secondary to repeated exposure to injury or illness.[13] Examples include the high prevalence of fibromyalgia and nociplastic pain associated with most chronic pain conditions. Bottom-up processes begin primarily as nociceptive or inflammatory conditions, including autoimmune disease, hypermobility syndrome, sickle cell disease, and cancer. With repeated exposure to painful events, the CNS becomes hypersensitive to both noxious and non-noxious stimuli, thus sensitizing the CNS to preferentially process pain experiences.

STRATEGIES AND EVIDENCE

DIAGNOSIS

The first research-based diagnostic criteria for fibromyalgia were published in 1990 and included the presence of widespread pain and tender points (specific areas of the body that evoke pain even when lightly touched) in at least 11 of 18 prespecified sites.[16] The first diagnostic criteria that did not require a tender-point ex-



ACR Diagnostic Criteria

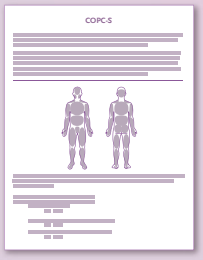
The 2016 ACR diagnostic criteria for fibromyalgia combine data from the Widespread Pain Index with those from the Symptom Severity Scale to obtain the Fibromyalgia Severity score. A diagnosis of fibromyalgia is presumed if pain is indicated in at least four of five regions on the Widespread Pain Index body map and the Fibromyalgia Severity score is greater than 13.

PROMIS-29+2

The PROMIS-29+2 tool is used to assess the following fibromyalgia symptoms:

- physical function
- anxiety
- depression
- fatigue
- sleep disturbance
- pain
- pain interference
- ability to participate in social roles and activities
- cognitive function

Scores on the PROMIS-29+2 are converted to T scores with a mean of 50 and standard deviation of 10 for comparison with population means.



COPC-S

The COPC-S is used by the patient to assess the following conditions on the basis of standardized diagnostic criteria: fibromyalgia, temporomandibular disorder, irritable bowel syndrome, chronic tension headache, chronic migraine headache, chronic urologic pelvic pain, chronic low back pain, painful endometriosis, vulvodynia, and myalgic encephalomyelitis (also known as chronic fatigue syndrome). This assessment tool can be administered in less than 10 to 15 minutes.

Figure 1. Diagnosis and Assessment of Fibromyalgia.

Shown are clinician resources for diagnosing fibromyalgia, monitoring symptoms, and identifying chronic overlapping pain conditions. The 2016 revisions to the 2010/2011 fibromyalgia diagnostic criteria[9] include several tools to diagnose the condition: the Widespread Pain Index (WPI) is used to assess chronic pain at 19 sites on a body map, the Symptom Severity Scale (SSS) is used to record nonpain symptoms, and the Fibromyalgia Severity score is a continuous measure of the burden of fibromyalgia symptoms and can serve as a proxy measure of the degree of nociplasticity. The Patient-Reported Outcomes Measurement Information System (PROMIS)–29+2 tool,[10] developed by the National Institutes of Health, is used to assess the effects of fibromyalgia symptoms on physical and mental health during a 7-day recall period. The Chronic Overlapping Pain Conditions–Screener (COPC-S)[11] is used to help identify chronic overlapping pain conditions that may be present in patients with fibromyalgia. ACR denotes American College of Rheumatology.

amination were published in 2010,[17] and revised criteria published in 2011 relied entirely on symptoms as reported by the patient.[18] The 2011 criteria have two components — the Widespread Pain Index (WPI) and the Symptom Severity Score (SSS). The WPI is used to assess chronic pain at 19 sites and thus documents the widespread nature of pain in fibromyalgia. The SSS is used to record the presence and severity of other centrally mediated symptoms (e.g., fatigue, sleep problems, and depressed mood). In 2016, the authors of the 2011 report refined the criteria again, defining widespread pain as the presence of pain in multiple sites located within four of five regions included in the WPI and emphasizing that fibromyalgia is not a diagnosis of exclusion and should be diagnosed irrespective of other diagnoses.[9] Although there are no specific laboratory tests for fibromyalgia, laboratory testing can be used to identify other potential coexisting medical conditions.[2] Tests that should generally be performed are those that are used to screen for conditions mimicking fibromyalgia and include measurement of the ESR and CRP

level to screen for inflammatory conditions, measurement of the TSH level to screen for thyroid abnormalities, and performance of a complete blood count and liver-function tests to screen for general medical conditions.

MANAGEMENT

Fibromyalgia is common in the general population. The first provider to encounter patients with fibromyalgia is likely to be in the primary care setting, where this condition can generally be managed successfully. However, it can be useful to refer patients with refractory or complex cases to a specialist in rheumatology or neurology in order to confirm the diagnosis or rule out mimicking conditions or to refer such patients to a pain-management provider.

Management of fibromyalgia can be frustrating for both providers and patients because none of the available therapies have more than modest effects. Several attempts are often needed to identify the combination of therapies that best align with the needs of a given patient. New treatments should be introduced one at a time to assess benefits or side effects before the treatment is retained or additional treatments are added. Finally, involving patients in treatment decision making is key because patient engagement is critical to the success of many nonpharmacologic treatments.

EDUCATION AND SELF-CARE

Given that patients may believe that pain always involves observable tissue damage or inflammation, reassurance that pain can also be related to problems with CNS processing is often needed. Patient education includes messaging that fibromyalgia is chronic and noncurable but manageable and not life threatening, that treatment focuses on calming and resetting a hypersensitive CNS, and that nonpharmacologic self-care strategies play an important role in promoting health.[19]

Pain self-care occurs outside the medical office, in the context of family, friends, and community. Self-management strategies are health-promoting lifestyle changes that can increase positive affect and calm CNS hypersensitivity[19] (Fig. 2). Because each strategy involves the formation of a new habit, consistent use of the strategy is needed to produce the desired benefits. Encouragement from the provider team at follow-up visits can help with habit formation and self-care maintenance. A meta-analysis of randomized, controlled trials that examined many different self-care interventions for managing fibromyalgia supports the use of self-care in reducing pain, increasing functioning, and modulating mood over the short and long terms.[20] PainGuide (available at https://painguide.com/) is an online source for education and resources regarding self-care skills.

BEHAVIORAL TREATMENTS

Cognitive behavioral therapy (CBT) is the best-studied behavioral therapy for fibromyalgia. CBT helps patients manage fibromyalgia by challenging negative and irrational thought patterns, minimizing maladaptive responses to pain and illness, and teaching adaptive skills for living and functioning with pain. A systematic review of CBT for fibromyalgia suggested that it can offer modest benefits in terms of reduced pain, improved mood, and decreased disability immediately after treatment and over the long term.[21] Several newer forms of behavioral therapy that are based on CBT include acceptance and commitment therapy (which focuses on mindfulness and mental flexibility for living with pain),[22] pain reprocessing therapy (which focuses on retraining the brain to interpret harmless physical sensations as safe), and emotional awareness and expression therapy (which focuses on adaptively confronting unresolved trauma and difficult emotions in order to calm the CNS and reduce pain).[23] Given the importance of sleep in nociplastic pain,[7] CBT for insomnia can also be beneficial[2] (Table 1).

PHYSICAL ACTIVITY INTERVENTIONS

Physical therapists and occupational therapists can assist with training that promotes physical and aerobic capacity and improves physical functioning.[27] Strong evidence indicates that varied forms of exercise can reduce pain and fibromyalgia symptoms and improve health-related quality of life.[28] Protocols to improve aerobic capacity, strength, and flexibility have been shown to reduce many of the symptoms of fibromyalgia, but these interventions require a "start low and go slow" approach because physical therapy can otherwise exacerbate symptoms[29] (Table 1).

Figure 2. Self-Care Approaches for Fibromyalgia.

Shown are selected evidence-based self-care activities for pain that provide a foundation for the long-term management of fibromyalgia.[19]

COMPLEMENTARY AND INTEGRATIVE THERAPIES

Complementary and integrative therapies are commonly used in fibromyalgia. The most commonly used treatments include spiritual healing (in 54% of cases), massage (in 50%), chiropractic treatment (in 38%), and aromatherapy (in 39%).[30] A systematic review of complementary and integrative therapies for fibromyalgia led to strong recommendations for qigong, tai chi, and yoga, with considered recommendations for acupuncture and for diet when fibromyalgia is present in patients with obesity[26] (Table 1).

PHARMACOLOGIC TREATMENTS

Many classes of drugs can be helpful in managing fibromyalgia, but all have small effect sizes and the potential for clinically significant side effects. Tricyclic drugs can be of benefit, especially if a single dose is given a few hours before bedtime to maximize the hypnotic effects. Amitriptyline and nortriptyline are classic tricyclics that are known to be effective in many chronic pain conditions, but sublingual cyclobenzaprine recently received Food and Drug Administration (FDA) approval for use in fibromyalgia. It is

Table 1. Nonpharmacologic Treatments with the Strongest Support.*

Treatment and Outcome Measure	Standardized Mean Difference (95% CI)†	Effect Size‡
Physical activity[24]		
Exercise		
Pain	−1.11 (−1.52 to −0.71)	Large
Fibromyalgia symptoms	−0.67 (−0.89 to −0.45)	Medium
HRQOL–physical health	0.77 (0.47 to 1.08)§	Medium
HRQOL–mental health	0.39 (0.27 to 0.52)§	Small
Depression	−0.40 (−0.55 to −0.24)	Small
Aerobic exercise		
Pain	−1.05 (−1.78 to −0.33)	Large
Fibromyalgia symptoms	−0.65 (−1.14 to −0.16)	Medium
Depression	−0.39 (−0.77 to −0.01)	Small
Muscle strengthening		
Pain	−1.39 (−2.16 to −0.62)	Large
Fibromyalgia symptoms	−0.84 (−1.23 to −0.45)	Large
HRQOL–physical health	0.72 (0.23 to 1.21)§	Medium
HRQOL–mental health	0.44 (0.17 to 0.71)§	Small
Depression	−0.37 (−0.61 to −0.13)	Small
Stretching		
HRQOL–physical health	1.15 (0.61 to 1.69)§	Large
HRQOL–mental health	0.57 (0.06 to 1.08)§	Medium
Depression	−0.36 (−0.72 to 0.00)	Small
Psychological and behavioral therapies		
Cognitive behavioral therapy[25]		
Pain	−0.45 (−0.80 to −0.10)	Medium
Acceptance and commitment therapy[22]		
Fibromyalgia symptoms	−1.43 (−2.17 to −0.69)	Large
Depression	−0.81 (−1.31 to −0.31)	Large
Anxiety	−0.94 (−1.29 to −0.59)	Large
Mindfulness[25]		
Fatigue	−0.49 (−0.91 to −0.07)	Medium
Depression	−0.46 (−0.75 to −0.17)	Medium
Multidisciplinary treatment[25]		
Pain	−1.33 (−2.16 to −0.49)	Large
Sleep	−1.15 (−2.11 to −0.18)	Large
Depression	−1.26 (−2.06 to −0.45)	Large
Complementary and integrative therapies[26]		
Electroacupuncture		
Pain	−0.63 (−1.02 to −0.23)	Medium
Sleep	−0.40 (−0.01 to −0.79)	Small
HRQOL	−0.65 (−1.05 to −0.26)	Medium

Table 1. (Continued.)

Treatment and Outcome Measure	Standardized Mean Difference (95% CI)†	Effect Size‡
Qigong		
Pain	−0.69 (−1.25 to −0.12)	Medium
Sleep	−0.67 (−1.01 to −0.34)	Medium
Fatigue	−0.56 (−1.07 to −0.34)	Medium
Tai chi		
Sleep	−0.71 (−1.28 to −0.13)	Medium
Yoga		
Pain	−0.54 (−0.96 to −0.11)	Medium
HRQOL	−0.72 (−1.32 to −0.12)	Medium

* CI denotes confidence interval, and HRQOL health-related quality of life.
† The standardized mean difference is a summary measure that quantifies the difference between two groups in standard deviation units and is calculated as the difference in group means divided by the pooled standard deviation. Unless otherwise indicated, a better outcome in the intervention group than in the comparison group is indicated by a negative standardized mean difference. P<0.05 for all comparisons.
‡ A standardized mean difference with an absolute value of less than 0.20 indicates a negligible effect size, 0.20 to 0.49 a small effect size, 0.50 to 0.79 a medium effect size, and 0.80 or higher a large effect size.
§ A better outcome in the intervention group than in the comparison group is indicated by a positive standardized mean difference.

often helpful to increase the dose of these drugs slowly until the patient reports improved sleep. A similar dose-escalation strategy may be helpful with gabapentinoid agents, such as gabapentin and pregabalin (the latter has also been approved by the FDA for fibromyalgia), because many of the palliative effects of tricyclics and gabapentinoids seem to be due to improved deep sleep[31] (Table 2).

Serotonin–norepinephrine reuptake inhibitors (SNRIs) have shown efficacy in the treatment of fibromyalgia.[34,35] Although these drugs were originally used as antidepressants in patients with fibromyalgia, they do not appear to reduce pain and other symptoms simply by reducing coexisting depression. The selective serotonin-reuptake inhibitors and SNRIs with greater noradrenergic activity (e.g., duloxetine and milnacipran), which have been approved by the FDA for use in fibromyalgia, are more efficacious than highly selective serotonin-reuptake inhibitors (e.g., citalopram). Pure norepinephrine-reuptake inhibitors such as esreboxetine have also been shown to be efficacious.[36-38] Combination therapy has been shown to be more efficacious than the individual drugs alone. For example, a clinical trial showed that moderate or greater global pain relief at 6 weeks was achieved in 68% of the participants who received a gabapentinoid at bedtime and an SNRI during the day, as compared with 42% who received duloxetine alone, 39% who received pregabalin alone, and 18% who received placebo.[39]

Classic analgesic drugs such as acetaminophen, NSAIDs, and opioid analgesics are generally not helpful in treating fibromyalgia. However, it is not uncommon for persons with fibromyalgia to have coexisting nociceptive pain conditions, such as osteoarthritis, for which nonopioid analgesics may be beneficial. Opioids should be avoided in fibromyalgia and other nociplastic pain conditions for many reasons. Overrelease of endogenous opioids may promote nociplastic pain by means of endogenous opioid-induced hyperalgesia,[40] overdose and addiction may occur, and all-cause mortality nearly doubles with opioid use[41] owing to increases in the risk of death from myocardial infarction, falls, suicides, and motor vehicle collisions. If opioids are used, it may be preferable to use a mixed opioid agonist, such as tramadol, buprenorphine, or tapentadol. Some evidence even indicates that low-dose naltrexone, an opioid antagonist, may be helpful in fibromyalgia.[42]

Table 2. Medications for Fibromyalgia with the Strongest Support.*

Drug and Outcome Measure	Standardized Mean Difference (95% CI or 95% Credible Interval)†	Effect Size‡
Tricyclic agents		
Amitriptyline[32]		
Sleep	−0.97 (−1.10 to −0.83)	Large
Fatigue	−0.64 (−0.75 to −0.53)	Medium
HRQOL	−0.80 (−0.94 to −0.65)	Large
Cyclobenzaprine[33]		
Pain	−0.25 (−0.34 to −0.16)	Small
Sleep	−0.21 (−0.32 to −0.11)	Small
Function	−0.18 (−0.35 to −0.02)	Negligible
Fibromyalgia symptoms	−0.23 (−0.33 to −0.13)	Small
SNRIs		
Duloxetine[32]		
Pain	−0.33 (−0.36 to −0.30)	Small
Sleep	−0.21 (−0.30 to −0.13)	Small
Depression	−0.25 (−0.32 to −0.17)	Small
Fatigue	−0.12 (−0.16 to −0.08)	Small
HRQOL	−0.39 (−0.55 to −0.23)	Small
Milnacipran[32]		
Pain	−0.17 (−0.20 to −0.15)	Negligible
Depression	−0.10 (−0.12 to −0.07)	Negligible
Fatigue	−0.10 (−0.14 to −0.05)	Negligible
Gabapentinoid agent		
Pregabalin[32]		
Pain	−0.30 (−0.32 to −0.27)	Small
Sleep	−0.60 (−0.67 to −0.54)	Medium
Depression	−0.22 (−0.26 to −0.19)	Small
Fatigue	−0.27 (−0.29 to −0.24)	Small
HRQOL	−0.18 (−0.29 to −0.06)	Negligible

* Cyclobenzaprine, duloxetine, milnacipran, and pregabalin are approved by the Food and Drug Administration for the treatment of fibromyalgia. SNRI denotes serotonin–norepinephrine reuptake inhibitor.

† A better outcome in the intervention group than in the comparison group is indicated by a negative standardized mean difference. The differences for all drugs include 95% credible intervals, except for differences for cyclobenzaprine, which include 95% confidence intervals. $P<0.05$ for all comparisons.

‡ A standardized mean difference with an absolute value of less than 0.20 indicates a negligible effect size, 0.20 to 0.49 a small effect size, 0.50 to 0.79 a medium effect size, and 0.80 or higher a large effect size.

GUIDELINES

Three commonly cited evidence-based treatment guidelines for fibromyalgia are the Canadian Guidelines,[43] the American Family Physician guidelines,[44] and the European League against Rheumatism guidelines.[27] Combined, these guidelines show consensus in supporting a multidisciplinary approach to treatment rather than single treatment methods, prioritizing patient education, and emphasizing active participation by patients in their care.

KEY POINTS

FIBROMYALGIA

- Fibromyalgia is associated with widespread pain plus other centrally mediated symptoms, such as poor sleep, fatigue, impaired cognition, depressed mood, and general sensory sensitivity.
- Fibromyalgia is common and can manifest as the primary problem (i.e., primary pain) or be superimposed on other conditions (e.g., autoimmune disorders or osteoarthritis).
- The workup of fibromyalgia depends on the context. Persons who have widespread pain that developed during childhood and evolved slowly over time need very little workup, and those who have acute or subacute onset of symptoms need a more extensive workup.
- The treatment of fibromyalgia begins with education and self-care activities such as physical activity, resilience training, and improvement of sleep. Nonpharmacologic integrative approaches, including cognitive behavioral therapy, movement-promoting therapies (e.g., yoga and tai chi), and stress-reduction therapies (e.g., meditation and mindfulness), are the most effective treatments.
- Classes of drugs that can be helpful include tricyclic drugs, gabapentinoid agents, and serotonin–norepinephrine reuptake inhibitors. Nonsteroidal antiinflammatory drugs and opioid agents are not useful, and opioids may be harmful.

AREAS OF UNCERTAINTY OR CONTROVERSY

Attempts to develop blood tests and other biologic or objective tests for the diagnosis of fibromyalgia have been unsuccessful. This lack of tests is due in part to misinterpretation of the underlying root cause and pathophysiology of fibromyalgia. Claims that fibromyalgia is an autoimmune disorder, a small-fiber neuropathy, or primarily a psychological problem remain unsubstantiated.[5,45] For example, although there is no debate that persons with fibromyalgia have evidence of decreased intraepidermal nerve fiber density (e.g., small-fiber neuropathy), it is not clear whether this finding is of pathologic importance.[46] Small-fiber neuropathy is an extremely nonspecific finding in hundreds of medical conditions[47] and can occur with or without pain, and it remains unclear whether this phenomenon plays a pathogenic role in fibromyalgia. Similarly, although psychiatric issues can result from inadequate pain treatment,[48] there is little evidence that such factors are the primary cause of fibromyalgia.

A number of emerging treatments for fibromyalgia deserve mention. A variety of neurostimulation treatments are being explored for fibromyalgia owing to the strong CNS component to this condition. Studies of direct-current stimulation and transcranial magnetic stimulation for fibromyalgia are promising, but further clinical trials are needed.[49] Peripheral stimulation with transcutaneous electrical nerve stimulation devices is also promising.[50]

Cannabinoid agents may also be useful in the management of fibromyalgia, but more work is needed to understand whether cannabidiol alone might be helpful (thus avoiding the psychoactive effects of cannabis) or whether a small amount of tetrahydrocannabinol may be needed for benefit.[51] Other emerging treatments include brief forms of behavioral interventions, light-based therapy, low-intensity focused ultrasound to stimulate deeper brain regions, psychedelic agents, and resilience training.

CONCLUSIONS AND RECOMMENDATIONS

The case vignette intentionally described a male patient, since providers often consider fibromyalgia only in female patients. He reports pain in many body regions (i.e., chronic overlapping pain conditions) and is sensitive to touch and other nonpainful sensory stimuli. This man has a classic presentation for fibromyalgia and, like most patients with fibromyalgia, does not need a referral to subspecialty care or further workup. For patients with fibromyalgia who may have an underlying autoimmune disorder, neuropathy, or radiculopathy, referral to the appropriate subspecialist for a one-time consultation might be helpful. Often, however, fibromyalgia can be treated in primary care. We would reassure this patient that he does not need surgery and would prescribe a low nighttime dose of a tricyclic agent (e.g., cyclobenzaprine or nortriptyline), in combination with a graduated physical activity and

exercise plan (e.g., a yoga or walking program). If he does not have a response to these treatments, we would consider trying other classes of centrally acting nonopioid analgesics (e.g., SNRIs or gabapentinoids), as well as a wide range of integrative nonpharmacologic therapies (e.g., various forms of CBT, movement therapy, and neurostimulation therapy) that can be helpful in persons with fibromyalgia.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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