MAYO CLINIC

Fibromyalgia and Related Conditions

Daniel J. Clauw, MD

From the University of Michigan, Ann Arbor, MI.

CME Activity

Target Audience: The target audience for *Mayo Clinic Proceedings* is primarily internal medicine physicians and other clinicians who wish to advance their current knowledge of clinical medicine and who wish to stay abreast of advances in medical research.

Statement of Need: General internists and primary care physicians must maintain an extensive knowledge base on a wide variety of topics covering all body systems as well as common and uncommon disorders. *Mayo Clinic Proceedings* aims to leverage the expertise of its authors to help physicians understand best practices in diagnosis and management of conditions encountered in the clinical setting.

Accreditation: Mayo Clinic College of Medicine is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Credit Statement: Mayo Clinic College of Medicine designates this journal-based CME activity for a maximum of 1.0 *AMA PRA Category 1 Credit(s).*™ Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Learning Objectives: On completion of this article, you should be able to (1) understand the three underlying mechanisms of chronic pain; (2) recognize centralized pain, either as a distinct entity or as a co-morbidity with other underlying pain mechanisms; (3) treat chronic pain based on the underlying mechanisms operative in each patient rather than based on the disease that is purported to be causing the pain.

Disclosures: As a provider accredited by ACCME, Mayo Clinic College of Medicine (Mayo School of Continuous Professional Development) must ensure balance, independence, objectivity, and scientific rigor in its educational activities. Course Director(s), Planning Committee members, Faculty, and all others who are in a position to control the content of this educational activity are required to disclose all relevant financial relationships with any commercial interest related to the subject matter of the educational activity. Safeguards against commercial bias have been put in place. Faculty also will disclose any off-label and/or investigational use of pharmaceuticals or instruments discussed in their presentation. Disclosure of this information will be published in course materials so that those participants in the activity may formulate their own judgments regarding the presentation.

In their editorial and administrative roles, William L. Lanier, Jr, MD, Terry L. Jopke, Kimberly D. Sankey, and Nicki M. Smith, MPA, have control of the content of this program but have no relevant financial relationship(s) with industry.

Dr Clauw has performed consulting services for and/or served on scientific advisory boards of Pfizer, Lilly, Forest Laboratories, Johnson & Johnson, Purdue Pharma, Nuvo, Cerephex, Tonix, Iroko, Takaeda, Cerephex, IMC, Zynerba, and Samumed. He has received grant support from Pfizer, Forest, Merck, Nuvo, and Cerephex.

Method of Participation: In order to claim credit, participants must complete the following:

1. Read the activity.
2. Complete the online CME Test and Evaluation. Participants must achieve a score of 80% on the CME Test. One retake is allowed.

Visit www.mayoclinicproceedings.com, select CME, and then select CME articles to locate this article online to access the online process. On successful completion of the online test and evaluation, you can instantly download and print your certificate of credit.

Estimated Time: The estimated time to complete each article is approximately 1 hour.

Hardware/Software: PC or MAC with Internet access.

Date of Release: 5/1/2015

Expiration Date: 4/30/2017 (Credit can no longer be offered after it has passed the expiration date.)

Privacy Policy: http://www.mayoclinic.org/global/privacy.html

Questions? Contact dletcsupport@mayo.edu.

Abstract

Fibromyalgia is the currently preferred term for widespread musculoskeletal pain, typically accompanied by other symptoms such as fatigue, memory problems, and sleep and mood disturbances, for which no alternative cause can be identified. Earlier there was some doubt about whether there was an "organic basis" for these related conditions, but today there is irrefutable evidence from brain imaging and other techniques that this condition has strong biological underpinnings, even though psychological, social, and behavioral factors clearly play prominent roles in some patients. The pathophysiological hallmark is a sensitized or hyperactive central nervous system that leads to an increased volume control or gain on pain and sensory processing. This condition can occur in isolation, but more often it co-occurs with other conditions now being shown to have a similar underlying pathophysiology (eg, irritable bowel syndrome, interstitial cystitis, and tension headache) or as a comorbidity in individuals with diseases characterized by ongoing peripheral damage or inflammation (eg, autoimmune disorders and osteoarthritis). In the latter instance, the term *centralized pain* connotes the fact that in addition to the pain that might be caused by peripheral factors, there is superimposed pain augmentation occurring in the central nervous system. It is important to recognize this phenomenon (regardless of what term is used to describe it) because individuals with centralized pain do not respond nearly as well to treatments that work well for peripheral pain (surgery and opioids) and preferentially respond to centrally acting analgesics and nonpharmacological therapies.

 ■ Mayo Clin Proc. 2015;90(5):680-692

Clinicians often encounter individuals who present with pain that they cannot adequately explain on the basis of the degree of damage or inflammation noted in peripheral tissues. This typically prompts an evaluation for the cause of pain. If no cause is found, these individuals are often given a diagnostic label that merely connotes that they have chronic pain in a region of the body without an underlying mechanistic cause (eg, chronic low back pain, headache, and temporomandibular joint disorder [TMJD]). In other cases, the label given alludes to an underlying pathologic abnormality that may or may not be responsible for the individual's pain (eg, endometriosis and facet syndrome). In other instances, the patients may be told that there is nothing wrong with them, advised that the disorder is "all in their head," and given a label such as "somatizer" without being offered any treatment.

Fibromyalgia (FM) is the currently preferred term for widespread musculoskeletal pain for which no alternative cause can be identified. Every subspecialist sees the same individuals, typically because these individuals present with pain in the region of the body the subspecialist specializes in. Gastroenterologists see the very same patients and focus on their gastroenterological symptoms and often use the terms such as *functional gastrointestinal disorder*, *irritable bowel syndrome* (IBS), *nonulcer dyspepsia*, or *esophageal dysmotility* to explain the patients' symptoms. Urologists focus on their genitourinary symptoms and use terms such as *interstitial cystitis* or *chronic prostatitis*, and gynecologists use terms such as *vulvodynia*, *vulvar vestibulitis*, and *endometriosis*. Until recently these unexplained pain syndromes perplexed researchers, clinicians, and patients.

We have come to understand that although individuals sometimes have only one of these idiopathic pain syndromes over the course of their lifetime, more commonly individuals with one of these entities will have many, and their family members also have high rates of pain in many regions of the body. Many terms have been used to describe these co-occurring syndromes and symptoms, such as *functional somatic syndromes*, *somatization disorders*, *allied spectrum conditions*, *chronic multisymptom illnesses*, and *medically unexplained symptoms*. Although some of these individuals will have comorbid psychiatric conditions, and these are often blamed by physicians as the cause of these otherwise unexplained pains, most individuals who have these conditions do not have a definable psychiatric disorder. There is now much evidence that these syndromes are clearly different and separable from depression and anxiety and have different (yet strong) genetic underpinnings. A hallmark of these conditions (eg, FM, IBS, TMJD, and headache) is that individuals display diffuse hyperalgesia (increased pain to normally painful stimuli) and/or allodynia (pain to normally nonpainful stimuli). This and many other pieces of evidence suggest that these individuals have a fundamental problem with augmented pain or sensory processing (ie, an increased gain setting) in the central nervous system (CNS) rather than a pathologic abnormality confined to the region of the body in which the person is currently experiencing pain.

Even if a practitioner has a problem with considering FM as a discrete disorder, it is critical to understand the diagnostic and therapeutic importance of centralization of pain as exemplified by a typical patient with FM. Once this phenomenon is recognized, it helps determine what types of treatments will work (centrally acting analgesics and nondrug therapies) and, just as importantly, what will not (opioids and surgery).

OVERVIEW

Fibromyalgia is generally considered to be the second most common "rheumatic" disorder, behind osteoarthritis. Depending on the diagnostic criteria used, the prevalence in the population ranges from 2% to 8%.[1-3] The diagnostic criteria for FM published in 1990 require chronic widespread pain plus a certain number of tender points to make the diagnosis. According to this definition, FM was an almost exclusively female disease because women have many more tender points than do men (population-based studies suggest that women are 10 times as likely to have 11 tender points as do men[4]). The new diagnostic criteria for FM published in 2010 and 2011 no longer require performing a tender point count to make the diagnosis and instead ask about the constellation of nonpain somatic symptoms that are typically present in addition to widespread pain (eg, fatigue, sleep