

EDITORIAL

Fibromyalgia: Where Are We a Decade After the American College of Rheumatology Classification Criteria Were Developed?

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The American College of Rheumatology (ACR) published classification criteria for fibromyalgia (FM) in 1990 (1). These criteria allow investigators around the world to investigate mechanisms of symptom expression in FM with assurance that research subjects share the presence of chronic widespread pain and evidence of altered pain processing, as demonstrated by the presence of tender points. With publication of the classification criteria, the ACR assumed a leadership position in research into basic mechanisms underlying FM symptoms and management of patients with FM. What progress has been made in the decade since the ACR classification criteria were developed?

A strength of the criteria from a research standpoint is that FM patients meeting the ACR classification criteria are at the extreme end of the spectrum of pain and tenderness. As a result, a number of studies have demonstrated important alterations in pain processing in FM. These studies use subjective ratings of experimental pain paradigms as well as objective demonstration of an altered central representation of painful stimuli.

Petzke et al demonstrated that patients with FM had low mechanical and thermal pain thresholds regardless of whether the stimulus was presented in a predictable, ascending manner (as with tender point determinations or dolorimetry) or randomly (2). These data suggest that, compared with healthy individuals, FM patients do not rate pain stimuli higher because of psychological hypervigilance or “expectancy.” Staud et al showed that patients with FM exhibit altered temporal summation of pain stimuli administered as a thermal stimulus to skin or as a mechanical stimulus to muscle

(3,4). The results of these studies suggest a parallel between the human condition of FM and the “wind-up” phenomenon that leads to hyperalgesia and has been extensively studied in animal models (5).

Other data corroborating the veracity of FM patients’ descriptions of pain have been collected using paradigms that are not dependent on subjective reports by patients. For example, Lorenz et al demonstrated altered laser-evoked potentials as objective representation of the central nervous system (CNS) response to cutaneous stimulation (6). Patients with FM were shown by Mountz et al and by Cianfrini et al to have reduced thalamic blood flow under resting conditions (a finding observed in other chronic pain states) and altered responses to mechanical pain stimuli (7,8). Finally, Grant et al demonstrated that increased blood flow to brain regions known to receive pain input correlates with the intensity of perceived pain rather than the absolute level of the stimulus (9).

All these data arguably complement the most consistent biologic finding supporting aberrant central pain transmission in FM—the ~3-fold higher concentrations of substance P in cerebrospinal fluid (CSF) of FM patients compared with those in the CSF of normal controls (10–13). Taken together, the data on pain processing in FM demonstrate that the central representation of pain correlates with patient reports of pain, and that purely behavioral or psychological factors are not primarily responsible for the pain and tenderness seen in FM.

The ACR classification criteria focus only on pain, however, and disregard other important FM symptoms, including fatigue, cognitive disturbance, sleep disturbance, and psychological distress. If one takes a more general view of FM that includes these symptoms and commonly associated syndromes (e.g., chronic fatigue syndrome, irritable bowel syndrome, and depression), then the ACR criteria fail to capture the essence of the FM syndrome. When research subjects are identified using the ACR criteria, there is greater variability

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in studies of physiologic mechanisms other than pain processing. For example, studies of the hypothalamic–pituitary–adrenal (HPA) axis must consider the impact of comorbid conditions (e.g., mood disorders and chronic fatigue syndrome, neither of which is an exclusion to the diagnosis of FM) that might independently alter HPA axis activity. Nevertheless, studies of the HPA axis (14–17) and the sympathetic nervous system (18–22) have demonstrated alterations in most instances. It is plausible that alterations of these stress-response systems identify a population vulnerable to the development of FM. Alternatively, altered neuroendocrine axis activity could cause or occur as a consequence of some FM symptoms. It is likely that these neurobiologic alterations are shared with other poorly understood somatic syndromes and psychiatric disorders that frequently occur concurrently with FM.

In this issue of *Arthritis & Rheumatism*, Paiva et al describe an important neuroendocrine disturbance seen in FM patients. This study represents an extension of previous work by this group demonstrating that serum levels of insulin-like growth factor 1 are diminished in a substantial percentage of FM patients, and that treating these individuals with human recombinant growth hormone (GH) leads to improvement of symptoms (23,24). The present study demonstrates that failure of the GH axis to respond to an exercise stress is attributable to increased levels of somatostatin. Somatostatin tone is critically important to physiologic alteration in GH secretion, both acutely (e.g., exercise) and chronically (e.g., aging, obesity). Although the study by Paiva et al does not determine the reason for increased somatostatin tone, all of the possibilities suggested by the authors include regulatory mechanisms localized to the CNS and revolving around an altered physiologic response to stress. Thus, the results of this study provide additional evidence that central mechanisms are involved in the pathophysiology of the FM syndrome.

In addition to neurobiologic mechanisms, behavioral factors play a role in symptom expression in many FM patients. A typical pattern is that as a result of pain and other symptoms of FM, individuals begin to function less well in their various roles. They may have difficulties with spouses, children, and work inside or outside the home, which exacerbate symptoms and lead to maladaptive illness behaviors. Such behaviors include isolation, cessation of pleasurable activities, and reductions in activity and exercise. In the worst cases, patients become involved with disability and compensation systems, which almost ensures that they will not improve (25).

The complex interaction of biologic and behav-

ioral mechanisms is not, however, unique to FM. Nonbiologic factors play a prominent role in symptom expression in all rheumatic diseases. In fact, in conditions such as rheumatoid arthritis and osteoarthritis (OA), nonbiologic factors such as level of formal education, coping strategies, and socioeconomic variables account for more of the variance in pain reporting and disability than do biologic factors, such as joint space width or erythrocyte sedimentation rate (25,26). Why, then, should we be surprised that nonbiologic factors play a significant role in FM?

Nevertheless, many rheumatologists express enormous frustration aimed specifically at FM patients or the FM “construct.” The most simplistic reason for this frustration may be psychological distress on the part of patients, physicians, or both. Patients with FM display higher average levels of distress than do individuals with other rheumatic disorders (27). Previous unsatisfactory interactions with the health care system may increase the likelihood of an adversarial relationship between patient and physician. Distress on the part of physicians is likely, because mechanisms underlying FM symptoms are poorly understood and are outside the realm of mechanisms traditionally studied by rheumatologists (e.g., immunology, inflammation, connective tissue biology). In addition, current pharmacologic therapies are often ineffective, nonpharmacologic therapies require time to implement, and dealing with contentious issues surrounding FM such as disability compensation or litigation is frustrating and counterproductive.

Population-based studies have demonstrated that chronic pain and fatigue syndromes affect huge numbers of individuals; the results are similar regardless of where the studies are performed or what labels are used to identify these individuals (28). It has been suggested that our specialty should exclude treatment of FM patients for the stated reason that there are not enough rheumatologists to treat the diseases we are uniquely qualified to manage. However, musculoskeletal pain is properly evaluated by rheumatologists, using our specialized knowledge to facilitate the correct diagnosis and institute a treatment plan. What is, perhaps, even more germane is the fact that many of our patients with inflammatory arthritides, connective tissue diseases, OA, and regional soft tissue disorders also manifest symptoms of FM. Studies have demonstrated that ~20% of individuals with nearly any type of rheumatic disease will meet ACR criteria for FM (29). An even higher percentage will have some elements of pain or other somatic symptoms not explained by immune activation

or tissue damage or will manifest behaviors that play a prominent role in symptom expression.

Rheumatologists have established a leadership position in research on the mechanisms underlying FM symptoms and the most appropriate treatments for FM patients. That position can be used to educate patients and primary care physicians and dictate how this disorder is best managed. Even if a rheumatologist is required to make the initial diagnosis of FM, treatment can be implemented effectively by primary care physicians. Abandoning our leadership position is not likely to further basic research on the mechanisms underlying FM symptoms, decrease the number of individuals with chronic widespread musculoskeletal pain, or improve management of these patients.

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