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Editorial

Fibromyalgia: Hamlet's Soliloquy and the State of the Art

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1. Perspectives

Fibromyalgia might be considered as the body's response to the slings and arrows of outrageous fortune. Analogous is the relationship to sleep and how the afflicted deal with it. This editorial heads a special issue of Rheumato, dedicated to that manifestation: fibromyalgia.

The question of how to diagnose fibromyalgia pales alongside the very question as to its actual existence and significance [1–8]—to be or not to be? There has been a dichotomy of opinions on this subject, and this editorial is intended as the "point" in a point-counterpoint discussion in Rheumato.

Fibromyalgia is the current term for what Baillou [9] called muscular rheumatism, and Traut [10] called muscular fibrositis, incorporating it into the spectrum of non-articular rheumatism [11] and Hench [12] suggested the term, based on the Latin fibro for fibrous tissue and the Greek words mio for muscle and alga for pain.

Fibromyalgia has a complicated history as a medical diagnosis, analogous to the anecdote of the blind people and the elephant. Symptoms observed by practitioners of various specialties resulted in a Venn diagram, with each specialty noting findings specific to that specialty and amalgamating them with other disorders sharing such findings. Thus, physiatrists recognized myofascial pain syndrome; rheumatologists, fibrositis and subsequently fibromyalgia; neurologists, nerve entrapment syndromes; orthopedic surgeons, regional pain syndromes; and psychiatrists, perhaps psychogenic rheumatism, with others using the term fibromyalgia when they are unable to recognize a physical source for a given patient's complaints [13–15]. This has resulted in controversy even as to its very existence e.g., [16]. Wolfe perceived a spectrum of pain complaints, of which fibromyalgia was simply a part, and that the appellation was a "social concept."

Depending on the definitions and populations surveyed, the prevalence of fibromyalgia ranges from 0.5 to 12% [17], increasing with age but paradoxically lower after age 80 [18]. Much of the suggested prevalence seems to derive from patient self-assessments, and it should be noted that less than a third of those claiming they had fibromyalgia actually fulfilled current criteria [19].

The term fibromyalgia, originally referred to as fibrositis by rheumatologists, was itself originally defined on the basis of gestalt, a pattern of symptoms and physical findings. Patients presented with what seemed to be generalized body pain. Their pain differed from that of other individuals, for whom disorders were responsible, in that fibromyalgia-related pain actually occurred in highly "predictable" patterns and was reproducible through physical examination.

Those physical examination findings are referred to as trigger or tender points at which pressure (four pounds or enough to "whiten" the nailbeds of the examining physician) does not just produce pain at the site of pressure, but pain is perceived in highly reproducible patterns that are not necessarily in juxtaposition to the site of pressure application. Misdiagnoses have been emphasized by Srinivasan et al. [20] and by Walitt et al. [19]. Given the apparent discrepancy between their observations and my own, one might hypothesize as to their derivation. Visiting numerous medical schools, it has been my perspective that training as to the recognition of signs of fibromyalgia has been limited and, more importantly, that the ability of those involved to apply the techniques is often not witnessed, let alone

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verified. I believe that explains the perspective offered by Jacobs et al. [21] that trigger point recognition is not a reproducible skill. I respectfully disagree, noting that this is at variance with the performance of those whom I have trained [22]. This issue unfortunately seems quite widespread and not limited to fibromyalgia, but that is a subject for another editorial addressing "quality control".

More importantly, confirmation of the diagnosis of fibromyalgia is obtained with the patient's admission that the induced pattern of pain reproduces the symptomatology that brought them to the physician's attention. Attention to these details clearly rebuts prior suggestions e.g., Vanderschueren et al. [23], Wolfe et al. [24] to use the term fibromyalgia as a diagnostic term to encompass any regional or general body pain.

Sleep disturbance and stress are major phenomena associated with fibromyalgia and may actually have an etiologic role [25–27], as apparently do traumatic life events [28,29]. Herein lies another controversy: Wolfe et al. [30] have disputed causation by trauma. Arnold et al. [17] suggested a genetic contribution. Pain specialists [31] have suggested the term "dyscognition" for the associated concentration challenges, including forgetfulness, memory loss, and disrupted thinking, and suggested environmental sensitivity (e.g., cold and heat). The latter has been attributed to the centralization of pain, and functional MRI demonstrates brain processing area activation to stimuli that those without fibromyalgia perceive as touch [11,32–36]. Curiously, allodynia is also associated with brain abnormalities [37–39]. Arnold et al. [31] also emphasize muscle stiffness, a finding that causes diagnostic confusion with polymyalgia rheumatica. Other phenomena observed in association with fibromyalgia include anxiety, headaches, depression, oral and ocular dryness, irritable bowel syndrome, urinary urgency, and dysmenorrhea. These are associations, not diagnostic criteria.

Smythe and Moldofsky [40] suggested the first criteria for disease recognition, emphasizing the importance of trigger points in such assessments. Yunus et al. [41] suggested the formalization of those criteria. Given controversy as to the nature of fibromyalgia, committees have been charged with suggesting criteria for disease recognition. Mindful of the anecdote that a camel is a horse designed by a committee, let us examine the results of some of those efforts.

The 1990 criteria made acceptance of trigger points as criteria dependent on the number present, suggesting that involvement in 11 of 14 designated locations was required but not requiring the presence of widespread pain [42]. However, Straud et al. [43] reported that the new criteria were no better than the old ones. A specificity of 67% and a sensitivity of 83%, with "accuracy" of 74%, was reported by Bennett et al. [44]. I found this intriguing because the classification committee, in its wisdom, deleted the one physical finding that many of us perceive as essential for diagnosis: Evaluation for the presence of trigger points [45]. This deletion actually resulted in a loss of accuracy, and the 2010 criteria were actually documented as inferior to those suggested by the committee responsible for the 1990 criteria, especially for differential diagnostic application [46,47].

I am unclear as to what entity is represented by the 25% additional individuals [48] identified by the 2010 classification. They certainly do not appear to be derived from the same cohort as those with trigger points. This is mindful of some drug studies in the 1970's, when the participation of massive numbers of patients was desired. That resulted in tremendous numbers for statistical purposes, but interpretation was compromised by the many diseases with very different pathophysiologies that were actually represented. So too, it seems that use of the 2010 criteria diluted the data set, such that the efficacy of intervention among individuals who had trigger points that reproduced a given patient's symptomatology (the seemingly pathognomonic sign of fibromyalgia) was potentially overlooked [44,48,49].

More importantly, the 2010 and 2011 criteria failed to separate regional pain syndromes [3,11,25,33,50–54]. Another major complicating phenomenon that compromises the applicability of the 2010/2011 criteria was the patient-derived questionnaire. The authors

and others e.g., Arnold et al., [31] emphasized that these were not clinically applicable, but only designed for research studies.

The 2016 criteria altered the inclusion of widespread pain to require pain in "4 of 5 regions" and eliminated the exclusions of the 2010/2011 version [7,50,55]. The deletion of trigger point identification in both the 2010/2011 and 2016 versions related to the perspective that practitioners are unable to reliably assess their presence [56].

Pain specialists [31] listed the following as mimicking fibromyalgia: hypothyroidism, inflammatory rheumatic diseases, statins, aromatase inhibitors, bisphosphonates, and opioids. However, fibromyalgia is often found in association with rheumatic diseases [53,54,57–59]. Thus, the presence of a rheumatic disease does not obviate the diagnosis (co-occurrence) of fibromyalgia. That being said, the list should be extended to include back pain. Back pain is an extraordinarily common problem that prompts the afflicted to seek medical care and, unfortunately, is one for which many physicians find themselves ill-prepared for diagnosis, let alone intervention [60]. Fibromyalgia is an extremely common cause of back pain; the diagnosis is often overlooked because of the misdirection brought about by X-rays that are ordered as a response to a physician's feeling of helplessness. When other modalities have failed, utilizing those specifically addressing fibromyalgia resolves their back pain, often completely [27,61,62]. X-rays often reveal vertebral osteophytes, which may seem alarming but are actually asymptomatic, so much so that the old term "osteoarthritis of the spine" has been replaced by "lumbar spondylosis" to emphasize their benignity [63].

Perhaps the most important and most common differential consideration is the phenomenon variously reported as allodynia, dysbiosis, or general body tenderness. This describes individuals who apparently perceive touch (non-noxious stimuli applied anywhere, not just at trigger points) as pain [64–68]. Visual, auditory, and olfactory stimuli can be similarly perceived as pain [26,68,69]. This diagnostic group is critical to identify, as it does not seem to respond to interventions that are effective in the management of fibromyalgia, only placing them at risk of treatment side effects. Complicating diagnosis is the entity referred to as small-fiber neuropathy [70]. It shares symptoms with both fibromyalgia and allodynia, including paresthesia, ocular dryness, and altered adrenergic function, as manifest by sweating and skin color variation.

Complications/associations of/with fibromyalgia include sleep disturbance, fatigue, morning stiffness length, paresthesia, anxiety, headache, depression, irritable bowel, sicca, urinary urgency, and dysmenorrhea. Thus, it is critical to facilitate the primary care physician's ability to distinguish between these entities and other musculoskeletal diseases that share symptoms/signs.

Fibromyalgia is actually amenable to treatment. In my experience, restoring Stage IV and non-REM sleep and stress management are extremely effective, as are trigger point-specific interventions. The latter involves injection with lidocaine, electroprobe stimulation or acupuncture. Kang et al. [71] specifically noted the benefit of aquatic, aerobic, resistance, and strengthening exercises. Somatosensory rehabilitation [53], counter stimulation [66], and spa therapy [72,73] are other interventions under consideration.

Pharmaceutical intervention is controversial. Kang et al. [71] compared committee assessments of medication efficacy in Canadian, Italian, German, and EULAR studies, noting universal disagreement among the studies, especially the latter, which perceived the evidence as weak. Canadian and Italian investigators felt that pregabalin, duloxetine/milnacipran, and amitriptyline were effective. The Italians supported the use of cyclobenzaprine, and the Canadians noted that tramadol lacked efficacy. However, I perceive the issue as even more complicated. Fibromyalgia can be extremely frustrating, depressing, and demoralizing. It is of concern to utilize medications that can elicit suicidal tendencies. Thus, amitriptyline is best avoided. If sleep restoration is so effective, the use of hypnotics (which restore stage IV, non-REM sleep) rather than soporifics (which make individuals groggy) seems appropriate.

2. Conclusions

Fibromyalgia is a common clinical problem for which diagnostic criteria have been suggested. Application of those criteria misses the diagnosis of one-fifth of patients on the basis of clinical gestalt. It must be asked: Does it matter with respect to therapeutic response? The current criteria create a cohort, the purity of which some may question. In this era of evidence-based research, the definition of study groups is even more important. If we are to be more effective in treating fibromyalgia, we must promulgate the concept, examine what interventions are effective, and not place the patient at risk.

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