

The Significance of Dysfunctions of the Sleeping/Waking Brain to the Pathogenesis and Treatment of Fibromyalgia Syndrome

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KEYWORDS

- Nonrestorative sleep • Fibromyalgia syndrome • Pain
- Fatigue • Treatment

Since the publication of the American College of Rheumatology (ACR) criteria for fibromyalgia (FM) in 1990,¹ the essential clinical features of widespread musculoskeletal pain and multiple tender points in specific anatomic sites have taken root in the scientific literature and the clinic to characterize a population of patients having a specific pain diagnosis or disease. This FM descriptive diagnostic label substituted for an earlier nonspecific ailment termed “fibrositis.” The fibrositis term fell into disrepute because of a lack of confirmed evidence for inflammatory disease involving fibrous tissue. Nevertheless, the FM diagnosis continues to suggest a rheumatologic pathogenesis where the source of the pain resides in the muscles and connective tissue. Both the ACR clinical criteria and the presumed rheumatic pathogenesis, however, have generated considerable controversy within the rheumatology community. Some rheumatologists argue that the current ACR diagnostic criteria for FM are useful in identifying patients of rheumatologic interest;² others use epidemiologic methodology to argue that FM is not a specific rheumatologic entity.^{3,4} Once more, some authors continue to hypothesize that the source of the illness lay in muscles⁵ even though the specific sites of tenderness, which are designated as a clinical feature of FM, are not specific for characterizing such patients with diffuse pain.⁶ Other authors

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argue against the significance of histopathological claims for muscle and fibrous tissue abnormalities.^{7,8}

Because of the lack of definitive evidence for peripheral indications of muscular or fibrous tissue structural pathology, attention has shifted away from the idea of a peripheral painful disease. Current interest resides in the role of the nervous system in the clinical features and pathogenesis of FM. This article reviews the evidence in favor of the diffuse muscular pain and body tenderness being aspects of a clinical syndrome that includes dysfunctions of the sleeping/waking brain and its contribution to unrefreshing sleep, fatigue, psychological disturbances, and impaired quality of life of patients who have FM. In particular, the author proposes that the pathogenesis of the widespread pain of patients who have FM involves disturbances of the functions of the sleeping/waking brain and coincident adverse effects on somatic and behavioral functions. As such, the author intends to summarize some recent evidence of therapeutic agents that improve sleep physiology, thus facilitating restorative sleep and ameliorating the pain and fatigue symptoms.

CLINICAL STUDIES ON THE CONTRIBUTION OF UNREFRESHING SLEEP TO WIDESPREAD PAIN AND FATIGUE IN FIBROMYALGIA SYNDROME

Common experience, confirmed by numerous clinical research studies, reveal that poor nighttime sleep interferes with our energy, alertness, mood, and ability to think. If FM is a syndrome involving malfunctions of the sleeping/waking brain, then there should be clinical evidence for such disturbances in patients with widespread pain and fatigue. From a purely descriptive perspective, patients diagnosed with FM commonly complain of poor sleep.^{9,10} Indeed, among the many features of patients who have FM, unrefreshing or nonrestorative sleep ranks with pain and fatigue as the most common of all symptoms. Furthermore, problems with sleep, low energy, emotional distress, and poor health are independent predictors of chronic widespread pain.¹¹

A series of prospective clinical studies support the notion of the interplay of poor sleep and widespread pain. A prospective study of a group of subjects who have FM who completed sleep/wake behavioral diaries showed that a night of poorer sleep results in complaints of more pain the following day. A more painful day is followed by a night of poorer sleep.¹¹ A 15-month population-based study of subjects who initially had no symptoms of chronic widespread pain showed that poor sleep increases the risk of such pain symptoms.¹² In another large-scale prospective study of FM subjects, increased disturbances in sleep result in increased pain, then disability, followed by depression.¹³

These clinical research studies highlight a broader conception of FM than originally proposed by the ACR criteria.¹ This broader conception of FM is embraced by the Outcome Measures in Rheumatology Clinical Trials (OMERACT) FM working group, which proposes an extension of the ACR criteria to include unrefreshing sleep as one of the key outcome domains for assessing the treatment of patients who have FM.¹⁴ Recently, the author and colleagues have incorporated the proposal into a simple six-item screening instrument known as the Fibromyalgia Moldofsky Questionnaire. In an United Kingdom epidemiologic study, this instrument proved to be a valid tool for identifying subjects with widespread pain, hyperesthesia, unrefreshing sleep, fatigue, psychological distress, and impaired quality of life.¹⁵ The identification of people with this constellation of symptoms in the general population allows for more detailed clinical study of the prevalence of such patients in clinical practice and with it

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