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Juvenile Fibromyalgia: A Primary Pain, or Pain Processing, Disorder

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Juvenile fibromyalgia (JFM), a chronic disorder of widespread musculoskeletal pain in combination with autonomic, sensory, and cognitive dysfunction, is responsible for considerable morbidity and impaired quality of life in affected patients and their families. Historically, fibromyalgia has been incorrectly characterized as a psychosomatic or psychogenic disorder, but new understanding of the science of pain has demonstrated unambiguously that it is an organic disorder of the pain processing system itself. This new science provides a framework for understanding the pathophysiology of fibromyalgia and for developing rational therapeutic interventions. Advances in JFM include the verification of adult criteria for diagnosis in pediatric patients and the publication of effective therapies based on cognitive and physical neuromuscular intervention. Although primarily nonpharmacologic therapy can include adjunctive medications as well. Finally, the recognition that JFM is a disorder of the central and peripheral nervous systems suggests that neurologists can be important in the care of these patients.

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Introduction

Juvenile fibromyalgia (JFM; also known as juvenile primary fibromyalgia [FM] syndrome) is a chronic disorder characterized by widespread musculoskeletal pain in combination with a number of other associated symptoms, including persistent fatigue, nonrestorative sleep, and sensory, autonomic, and cognitive dysfunction.[1-3] The disorder is responsible for considerable morbidity and impaired quality of life in affected children and their families.[4-6]

JFM is one of the so-called "functional pain syndromes,"[7-11] diseases in which persistent pain in an organ system or body site is not adequately explained by inflammation or other readily apparent disease at the site where the pain is experienced. For decades these disorders have eluded insight into both their pathophysiology and effective treatment. However, recent developments have led to a transformation in understanding pain perception and processing,[5,12-14] and have laid the groundwork for a consistent scientific framework to explain chronic pain disorders such as FM.[10,11,15,16] In addition, a growing, robust evidence base of effective interventions for JFM fits this new framework, and holds promise for continued improvement in the treatment of this common and disabling condition.

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Epidemiology and Impact

Chronic musculoskeletal pain, defined as pain experienced 3 or more times per week over at least 3 months, is surprisingly frequent in children and adolescents, with a prevalence of 5%-20% in various studies.[17-20] As many as 25%-40% of these children meet criteria for FM, and although disease is significant enough to bring them to medical attention is less common, there is a consensus that 1%-2% of the pediatric population has functionally significant JFM.[2,17,20,21] As with all the "functional" pain syndromes, girls are more commonly affected than boys. Onset is generally in early adolescence but has been identified in children as young as 4 years old.[17,20] There are genetic factors at play as well, and it is more common in certain genetic backgrounds[2] and in the family members of patients with FM or other chronic pain syndromes.[14,19] It would not be uncommon for FM to be present in 2 or 3 generations in a family.

There is a significant overlap among the functional pain syndromes, with many patients who report symptoms primarily of 1 disorder, such as FM, also suffering comorbid

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Table 1 Central Pain Syndromes With Symptoms Overlapping Those of Fibromyalgia

Primary Diagnosis	Degree of Overlap With Secondary Condition (%)				
	FMS	CFS	IBS	TMD	MCS
FMS		70	32-80	75	55
CFS	35-70		58-92	20	41-67
IBS	32-65	58-92		32-65	ND
TMD	13-18	20	64		ND
MCS	33-55	30	ND	ND	

The numbers represent the fraction of patients with a primary diagnosis who also have symptoms meeting the definition of other disorders. CFS, chronic fatigue syndrome; FMS, fibromyalgia syndrome; IBS, irritable bowel syndrome; MCS, multiple chemical sensitivity; ND, not determined; TMD, temporomandibular disorder. (Adapted with permission from Dadabhoy and Clauw.[8])

irritable bowel syndrome, chronic fatigue, daily tension-type or mixed headaches, and vice versa[8,10,11,15] (Table 1).

The effect of JFM on patients and families is considerable. There is poor quality of life, worse than in other chronic conditions such as migraine headaches, missed school, adverse effects on other family members, and family function and, in adult FM, there is a lower rate of full-time work and marriage.[3,6,20,22-25] The economic cost of chronic pain syndromes in adolescents has been estimated to be $19.5 billion/year,[24] a figure in line with estimates in adults. As at least 20% of young patients with chronic pain become adults with chronic pain,[23] earlier effective intervention may help mitigate a growing adult public health issue.[26]

Historical Context and Reconceptualization

The use of the term "functional" to describe certain pain disorders was initially intended to emphasize the disruption in proper operation (so to speak) of the involved organ system, but became used to imply no "organic" cause to the pain.

That few objective abnormalities can be found on physical examination or in diagnostic studies, in the context of considerable subjective distress and disability, is frustrating to both patients and their medical providers.[10,19] This has led in the past to the widespread misconception of "functional" as synonymous with "psychosomatic," "psychogenic," or even "factitious,"[11,15] especially as there is often an accompanying mood disorder.

In addition to FM, these so-called functional disorders include irritable bowel syndrome and related gastrointestinal (GI) disorders, chronic daily headaches, nonspecific low back pain, chronic pelvic pain including endometriosis, temporomandibular joint disorder, interstitial cystitis, and others.[11,27] A number of other syndromes in which not pain, but other sensory or autonomic dysfunctions are the primary symptoms such as chronic fatigue syndrome, postural orthostatic tachycardia syndrome (POTS), and multiple chemical sensitivity, share with functional pain syndromes a related underlying mechanism of central sensitization causing disordered processing of pain and other sensory input.[9,11,15]

This fundamental shift in understanding of disease mechanism means that these syndromes are no longer medically unexplained, but have an organic etiology that lies in the nervous system itself. As a result, it may well be time to change the name of functional pain syndromes.[11,28] Schechter has suggested "primary pain disorders," placing focus on the dysfunctional system at the heart of the diseases,[28] and Yunus[11] has proposed "central sensitization syndromes," reflecting the unifying concept that connects these seemingly disparate but in fact related conditions. We might suggest "pain processing disorders," which encompasses the important points of both of these proposals without seeming to exclude central pain comorbid with pain-causing diseases such as juvenile idiopathic arthritis, or to exclude other pathophysiologic mechanisms such as aberrant gate control.

Science of FM

The premise that nociception is not the same as pain is fundamental to understanding the pathophysiology of FM.

Historically, pain signaling was viewed as a passive transfer of information from the peripheral receptors of a noxious stimulus to the parts of the brain responsible for the awareness of pain (discussed in Ref. 32). However, this simple unidirectional model is unable to explain many characteristics of pain in experimental systems or in clinical practice, such as secondary hyperalgesia, allodynia, and temporal summation (windup). Two concepts, gate control theory and central sensitization, alter this model of information flow in pain and allow a fuller understanding of the critical role of the central nervous system (CNS) in the experience of pain.

Normal Pain Processing

The afferent limb of pain processing, nociception, begins with activation of primary nociceptive myelinated A delta and nonmyelinated C fibers at the site of a stimulus such as heat, pressure, tissue damage, etc. These travel to the dorsal horn of the spine and from there through secondary nerves of the spinothalamic tract to the thalamus, projecting to the somatosensory cortex, which mediates the sensory discriminatory dimension of the pain report, and to many other regions including the anterior cingulate cortex, the insula, the amygdala, and the prefrontal cortex, which together are responsible for the autonomic, affective, and cognitive dimensions.[11,29]

Gate Control

Pain processing also involves descending inhibitory and facilitating pathways, which modulate pain at the level of the spinal cord, integrating signals descending from a complex network including the same areas of the brain involved in the afferent pathway, as well as the periaqueductal gray and medulla[30,31] (Fig. 1). These modulatory inputs change the level and character of the ascending pain signal, as proposed in the "gate control" theory of Melzack and Wall.[32] The experience of pain is the final result of the interaction of these ascending and descending pathways, interpreted through cognitive and affective as well as sensory cortical regions of the brain.