Understanding Fibromyalgia and its Resultant Disability
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The introduction of the American College of Rheumatology fibromyalgia classification criteria 20 years ago heralded two decades of professional acceptance and enhanced multidisciplinary research in the pathogenesis and therapy of fibromyalgia [1]. Whereas the initial criteria included tenderness on pressure (tender points) in at least 11 of 18 defined anatomic sites with the presence of widespread pain in the 2010 set of proposed criteria it is clear that apart from the pain other seminal features of the disorder – namely cognitive dysfunction, unrefreshing sleep, fatigue and mood disorders – play an important role in the diagnosis [2]. Many journals today dedicate scientific papers to the pathogenesis and treatment of fibromyalgia, and grants are provided worldwide to investigate the disorder.

Fibromyalgia is a chronic manifestation of diffuse musculoskeletal pain that is more commonly encountered in women (9:1 female: male ratio) and is present in all ethnic groups, climates and cultures [3-7]. In the following review we will explore the emergence of the fibromyalgia syndrome and its implications with regard to disability of disability.

PATHOGENETIC ASPECTS OF FIBROMYALGIA
Although a clear sequence of events to explain the clinical manifestations of fibromyalgia is lacking, many advances have been made in unraveling its pathogenesis. Firstly, a deficiency of serotonin and a surplus of substance P have been recorded in the cerebrospinal fluid of patients with fibromyalgia [8]. Serotonin deficiency may be related to the altered sleep patterns, especially during stage 4 sleep (deep sleep) in whose initiation serotonin plays a major role [9]. On the other hand, a surfeit of substance P, a brain and spinal cord neuropeptide released from the terminals of specific sensory nerves, plays a role in pain signaling, integration and modulation, suggesting that fibromyalgia patients have an enhanced sensitivity to pain.

In addition, central sensitization is another mechanism to explain this increased perception of pain in fibromyalgia patients. Central sensitization includes spontaneous nerve activity, expanded receptive fields (resulting in a larger geographic distribution of pain), and augmented stimulus responses within the spinal cord [10]. This pathway involves triggering an N-Methyl-D-aspartate (NMDA) receptor, which is thought to be involved in this abnormal temporal summation of pain stimuli [11].

Muscular pathology has also been implicated in the pathophysiology of tender points in the fibromyalgia syndrome. Decreased growth hormone concentration, which is essential for muscle function, may explain the extended muscle pain seen after exercise in fibromyalgia patients [12]. More convincing arguments have been published regarding abnormal pain amplification at the level of the spine as the likely mechanism for increased pain in fibromyalgia patients [13].

It is currently recognized that familial aggregation is often encountered in fibromyalgia. Hudson et al. [14] reported that the odds ratio for fibromyalgia in a relative of a fibromyalgia proband versus a relative of a rheumatoid arthritis proband was 8.5. Learned patterns of behavior probably portray certain families. Several candidate genes have been suggested to mediate this association. Early research into the genetic basis of fibromyalgia was directed towards the possibility of linkage to human leukocyte antigens. Burda and collaborators [15] reported that the HLA1 DR4 antigen was detected in 64% of patients with fibromyalgia versus 30% of healthy controls. Several teams observed a higher frequency of the S/S genotype of the serotonin transporter gene (5-HTT) promoter region in fibromyalgia patients compared to healthy controls. An increased frequency of the 5-HTT gene was demonstrated among patients versus controls [16]. Other studies focusing on the serotonin receptor subunit genes HTR3A and HTR3B failed to exhibit any polymorphism among fibromyalgia patients [17].

Several inciting factors have been shown to trigger the emergence of fibromyalgia. Some studies show that infections...
such as hepatitis B virus, hepatitis C virus, human immunodeficiency virus and Lyme disease triggered fibromyalgia [18]. Past history of negative life events has often been described among patients with fibromyalgia, and increased rates of post-traumatic stress disorder associated with childhood abuse, trauma or anxiety have been reported [16,19,20]. Many fibromyalgia patients have psychological disorders that have further challenged its validity: Is fibromyalgia a reflection of a psychiatric illness or an illness on its own? Although approximately 30%–50% have anxiety, depression, somatization or hypochondriasis, many fibromyalgia patients do not have psychiatric comorbidities [21].

**DISABILITY IN FIBROMYALGIA**

Chronic pain conditions are the most common reason for disability leave from work. In addition, these conditions account for the highest indirect costs for society and also account for an individual economic, social, educational and vocational burden [22]. Musculoskeletal disorders and gender interact in a way that increases sick-leave rates.

In Sweden in 2001, women accounted for 58% of costs resulting from sickness absence from work [22]. Excluding pregnant women, the sick-leave rate was 25% higher than in men [23]. In an 11 year prospective cohort study of people with spinal and shoulder pain, 27% of the women and 14% of the men had been granted a disability pension. Interestingly, the leading causes that were related to approval of disability pensions were foreign citizenship, gender, and number of sick-leave days per spell [24].

The most frequently mentioned symptoms that affected vocational activities were found to be pain, sleep disturbances, and difficulties in performing motor tasks. The leading symptoms limiting vocational tasks in patients with fibromyalgia were found to be pain (87%), tiredness (80%), muscle weakness (73%), and memory and concentration problems (51%) [25].

This economic burden often affects fibromyalgia individuals, particularly those of lower socioeconomic status. These individuals are more often dependent on the government health care system, which has not accounted for the complexity and implications of this syndrome sufficiently. In fact, fibromyalgia is more prevalent in the lower socioeconomic status population perhaps due to other confounding variables. First, this population tends to work in more manual labor jobs, which may facilitate more pain and injuries. Second, this population tends to be overweight – another risk factor for pain; and third, this population tends to do more household work, in general and because they are less likely to afford housekeeping services, an additional risk factor for pain [26]. Other reports have also showed an inverse relationship between chronic pain and educational level [27].

**Vocational rehabilitation ameliorates depressive symptoms and improves functional ability, although pain symptoms do not disappear**

Children with fibromyalgia are usually diagnosed months to years following the initial manifestations; the precious time lost until proper diagnosis is made is characterized by social isolation and malfunction and loss of days at school, which directly contribute to a lower educational level in adulthood [28]. Sleep disturbances also greatly affect how well children pay attention in school and even their overall attendance in school. In addition, lack of sleep may lead to muscle deconditioning, which leads to loss of muscle strength particularly in women. Kilbom [29] suggested that the differences in body size, muscle strength, oxygen uptake and hormones contribute to musculoskeletal disorders. This muscle deterioration may even perpetuate musculoskeletal pain but, as discussed earlier, is less convincing than the central sensitization theory of pain in these individuals. Physicians and caregivers should recognize these problems and try to promote full attendance at school or, if the implications are severe enough, consider homeschooling. The impaired learning may have lasting effects on their ability to succeed in future workplaces in addition to their inability to attain jobs in a higher echelon.

Therefore, fibromyalgia patients may experience a vocational and socioeconomic vicious cycle. Fibromyalgia symptoms such as sleepiness and inability to concentrate may affect individuals as early as childhood, which may result in poor academic performance, limiting these individuals to lower echelon jobs, mainly manual labor. Manual labor jobs may then further disable these patients at the workplace.

**CURRENT IMPLICATIONS FOR DISABILITY**

Now that fibromyalgia is gaining general acceptance in the medical community, many patients are applying for modifications at their workplace to relieve these burdens. Several recent reports show that 34%–77% of women with fibromyalgia have succeeded in preserving their jobs [22,30-32]. Those who continued working tended to be older, had fewer difficulties in daily activities and lower severity of symptoms, especially pain [27]. The needs of fibromyalgia patients should be understood, and the importance of identifying necessary individual adjustments should be considered to keep these women working and to lessen the economic, social and vocational burdens on themselves, their family and society. Possible explanations may be that although these individuals are applying for modifications, employers, physicians and other health care administrators are not familiar with this syndrome or with the required modifications that are necessary to keep women at work. This fact, in addition to other social and economic burdens, may contribute to them leaving work. Therefore, it is recommended that younger patients be provided with the appropriate aid and setting for their disability at work, to enable them to continue working [22,30-32].
Although previous studies have shown that patients who were diagnosed with fibromyalgia have not sought medical care since they are apprehensive and reluctant to believe that their syndrome is real, recent studies show otherwise [33]. In a study conducted in the Negev district in southern Israel, fibromyalgia patients were compared with hypertensive and diabetic patients regarding the costs for hospitalization, day care, specialists and diagnostic services. The study concluded that although the hospitalization costs were similar for the three chronic diseases, the need for specialists and diagnostic services was statistically significantly greater among patients with fibromyalgia in comparison to the other two diseases [34]. Perhaps this statistic may be elucidated by the fact that only 55% of primary care providers in that region were familiar with the fibromyalgia syndrome [3]. These studies underlined the significant burden that the fibromyalgia syndrome casts on the health care budget. It was indicated that patients spend much time with specialists and undergoing unnecessary diagnostic procedures, which impose a significant economic burden in addition to the time taken off from work, costs of transportation to the medical services, and diagnostic studies that are not always completely covered by their medical insurance [3,34]. Furthermore, specialists who evaluate the necessity of worker’s compensation for these patients are essential since physicians are usually not able to assess these needs.

In a study analyzing the way 23 assessment centers in the United States evaluated chronic pain patients at the workplace, it was found that these assessors focused mainly on the physical factors of work performance rather than the individuals as a whole, the specific work demands, the environmental conditions, and how their disorder was influenced by their ability to work [35]. A study in Finland demonstrated that a specific multidisciplinary fibromyalgia rehabilitation program was not superior to a non-specific musculoskeletal multidisciplinary rehabilitation program, further supporting the uncertainty of the type of multidisciplinary programs needed while at the same time supporting the need for them [36]. However, another study, where non-intensive (six sessions, one weekly) multidisciplinary treatment was given to 94 patients who were on the verge of not returning to work or filing for disability pension and were followed at discharge and 6 and 12 months later, showed that although pain symptoms did not disappear, depressive symptoms subsided and functional ability improved [37]. Additionally, another study showed that individuals who had more negative expectations about pain progression and a high perceived functional disability were least likely to return to work after a multidisciplinary treatment program [38].

Many fibromyalgia patients value their work role and it is therefore crucial to assess ways to rehabilitate them and generate solutions so that these individuals will be able to preserve their positions at work [22]. Although rehabilitation programs in the future may help resolve the disabilities these patients experience at the workplace, adjustments should be made now. Firstly, it has been found that various types of work situations involving heavy physical tasks, working above shoulder height, using power grip, and dynamic repetitive tasks should be avoided [22]. Secondly, flexibility at work, including replacing certain tasks and allowing those who work full time to take a break at mid-day as well as short breaks can significantly reduce the number of fibromyalgia patients who leave their jobs. Moreover, flexibility in adjusting working hours day-by-day may help women with fibromyalgia to remain at work. Lastly, a positive social environment where the supervisors and colleagues appreciate the patient was found to be integral in keeping these women working [22].

Fibromyalgia patients have been struggling for years to have their disability acknowledged by the medical community, as have scholars of disability studies. These individuals have been hindered socially and economically by misconceptions held by the medical, social and general communities regarding their clinical condition. These misunderstandings have led to negative attitudes towards rehabilitation programs and compensations for these individuals in the workplace [22]. However, these programs are essential to battle the long-term pain, fatigue and associated symptoms that will lead to increased disability pension for fibromyalgia patients.

In order to keep patients with fibromyalgia at work it is crucial to change current views and to seek and establish constructive strategies for employers as well as medical personnel in order to keep these patients fit for work.

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**Capsule**

**Interleukin-6 enhances insulin secretion by increasing glucagon-like peptide-1 secretion from L cells and alpha cells**

Exercise, obesity and type 2 diabetes are associated with elevated plasma concentrations of interleukin-6 (IL-6). Glucagon-like peptide-1 (GLP-1) is a hormone that induces insulin secretion. Ellingsgaard and co-workers show that administration of IL-6 or elevated IL-6 concentrations in response to exercise stimulates GLP-1 secretion from intestinal L cells and pancreatic alpha cells, improving insulin secretion and glycemia. IL-6 increased GLP-1 production from alpha cells through increased proglucagon (which is encoded by GCG) and prohormone convertase 1/3 expression. In models of type 2 diabetes, the beneficial effects of IL-6 were maintained, and IL-6 neutralization resulted in further elevation of glycemia and reduced pancreatic GLP-1. Hence, IL-6 mediates crosstalk between insulin-sensitive tissues, intestinal L cells and pancreatic islets to adapt to changes in insulin demand. This previously unidentified endocrine loop implicates IL-6 in the regulation of insulin secretion and suggests that drugs modulating this loop may be useful in type 2 diabetes.

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Eitan Israeli

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“Be the master of your will and the slave of your conscience”

Hasidic saying