

**Research Abstracts**  
**FMS**  
**2000**

*Emphasis added*

*Author*

Bendtsen L

*Title*

**Central sensitization in tension-type headache--possible pathophysiological mechanisms**

*Source*

Cephalalgia 2000 Jun;20(5):486-508 PubMed 11037746

*Author's Affiliation*

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*Abstract*

The aim of the present thesis was to investigate the pathophysiology of chronic tension-type headache with special reference to central mechanisms. Increased tenderness to palpation of pericranial myofascial tissues is the most apparent abnormality in patients with tension-type headache. A new piece of equipment, a so-called palpometer, that makes it possible to control the pressure intensity exerted during palpation, was developed. Thereafter, it was demonstrated that the measurement of tenderness could be compared between two observers if the palpation pressure was controlled, and that the Total Tenderness Scoring system was well suited for the scoring of tenderness during manual palpation. Subsequently, it was found that pressure pain detection and tolerance thresholds were significantly decreased in the finger and tended to be decreased in the temporal region in chronic tension-type headache patients compared with controls. In addition, the electrical pain threshold in the cephalic region was significantly decreased in patients. It was concluded that the central pain sensitivity was increased in the patients probably due to sensitization of supraspinal neurones. The stimulus-response function for palpation pressure vs. pain was found to be qualitatively altered in chronic tension-type headache patients compared with controls. The abnormality was related to the degree of tenderness and not to the diagnosis of tension-type headache. In support of this, the stimulus-response function was found to be qualitatively altered also in patients with fibromyalgia. It was concluded that the qualitatively altered nociception was probably due to central sensitization at the level of the spinal dorsal horn/trigeminal nucleus. Thereafter, the prophylactic effect of amitriptyline, a non-selective serotonin (5-HT) reuptake inhibitor, and of citalopram, a highly selective 5-HT reuptake inhibitor, was examined in patients with chronic tension-type headache. Amitriptyline reduced headache significantly more than placebo, while citalopram had only a slight and insignificant effect. It was concluded that the blockade of 5-HT reuptake could only partly explain the efficacy of amitriptyline in tension-type headache, and that also other actions of amitriptyline, e.g. reduction of central sensitization, were involved. Finally, the plasma 5-HT level, the platelet 5-HT level and

the number of platelet 5-HT transporters were found to be normal in chronic tension-type headache. On the basis of the present and previous studies, a pathophysiological model for tension-type headache is presented. **According to the model, the main problem in chronic tension-type headache is central sensitization at the level of the spinal dorsal horn/trigeminal nucleus due to prolonged nociceptive inputs from pericranial myofascial tissues. The increased nociceptive input to supraspinal structures may in turn result in supraspinal sensitization. The central neuroplastic changes may affect the regulation of peripheral mechanisms and thereby lead to, for example, increased pericranial muscle activity or release of neurotransmitters in the myofascial tissues. By such mechanisms the central sensitization may be maintained even after the initial eliciting factors have been normalized, resulting in the conversion of episodic into chronic tension-type headache. Future basic and clinical research should aim at identifying the source of peripheral nociception in order to prevent the development of central sensitization and at ways of reducing established sensitization. This may lead to a much needed improvement in the treatment of chronic tension-type headache and other chronic myofascial pain conditions.**

*Authors*

Bernard AL, Prince A, Edsall P

*Title*

**Quality of life issues for fibromyalgia patients**

*Source*

Arthritis Care Res 2000 Feb;13(1):42-50

*Author's Affiliation*

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*Abstract*

**OBJECTIVE:** To collect information from patients with fibromyalgia syndrome (FMS) in regard to quality of life, impact of FMS, coping strategies, and what they want from their health care providers.

**METHODS:** Two hundred seventy support group members in Washington, Illinois, and Pennsylvania completed an 85-item questionnaire.

**RESULTS:** On a scale from 1 to 10 (10 being highest positive rating), patients ranked past quality of life as 8.6, present quality of life as 4.8, and future quality of life without FMS as 9.2. **Respondents indicated that FMS has had a negative impact on personal relationships, career, and mental health. Many also reported a lack of social support. Most respondents reported a variety of coping responses including talking to friends, praying, exercise, hobbies, relaxation techniques, talking to a professional, and meditation. Patients reported needing more support, better educated health professionals, for people to believe that this disease exists, more funding for research, and better diagnostic tools. CONCLUSIONS:** Health care workers need to be cognizant of the effect FMS has on quality of life.

Treatment options should not be limited to prescription medication therapy. Patients are using a variety of methods to cope with their FMS symptoms, some positive, but others that are negative, and health care providers need to be alert to negative coping strategies such as alcohol and nonprescription medication abuse.

*Authors*

Bradley LA, McKendree-Smith NL, Alberts KR, Alarcon GS, Mountz JM, Deutsch G

*Title*

**Use of Neuroimaging to Understand Abnormal Pain Sensitivity in Fibromyalgia.**

*Source*

Curr Rheumatol Rep 2000 Apr;2(2):141-148 PubMed 11123051

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*Abstract*

This paper examines the use of neuroimaging to measure change in regional cerebral blood flow (rCBF) produced by pain in patients with fibromyalgia and in healthy individuals. **Fibromyalgia patients differ from healthy persons in rCBF distribution in several brain structures involved in pain processing and pain modulation both at rest and during experimental pain induction. These abnormalities may contribute to abnormal pain sensitivity as well as the maladaptive pain behaviors that characterize many patients with fibromyalgia. We anticipate that future neuroimaging studies will enhance our understanding of abnormal pain sensitivity and of pain management interventions aimed at altering central nervous system function in patients with fibromyalgia.**

*Authors*

Elenkov IJ, Wilder RL, Chrousos GP, Vizi ES

*Title*

**The sympathetic nerve-An integrative interface between two super systems: the brain and the immune system**

*Source*

Pharmacol Rev 2000 Dec;52(4):595-638

*Author's Affiliation*

Inflammatory Joint Diseases Section, Arthritis and Rheumatism Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, Maryland.

### *Abstract*

The brain and the immune system are the two major adaptive systems of the body. During an immune response the brain and the immune system "talk to each other" and this process is essential for maintaining homeostasis. Two major pathway systems are involved in this cross-talk: the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system (SNS). This overview focuses on the role of SNS in neuroimmune interactions, an area that has received much less attention than the role of HPA axis. Evidence accumulated over the last 20 years suggests that norepinephrine (NE) fulfills the criteria for neurotransmitter/neuromodulator in lymphoid organs. Thus, primary and secondary lymphoid organs receive extensive sympathetic/noradrenergic innervation. Under stimulation, NE is released from the sympathetic nerve terminals in these organs, and the target immune cells express adrenoreceptors. Through stimulation of these receptors, locally released NE, or circulating catecholamines such as epinephrine, affect lymphocyte traffic, circulation, and proliferation, and modulate cytokine production and the functional activity of different lymphoid cells. Although there exists substantial sympathetic innervation in the bone marrow, and particularly in the thymus and mucosal tissues, our knowledge about the effect of the sympathetic neural input on hematopoiesis, thymocyte development, and mucosal immunity is extremely modest. In addition, recent evidence is discussed that NE and epinephrine, through stimulation of the beta(2)-adrenoreceptor-cAMP-protein kinase A pathway, inhibit the production of type 1/proinflammatory cytokines, such as interleukin (IL-12), tumor necrosis factor-alpha, and interferon-gamma by antigen-presenting cells and T helper (Th) 1 cells, whereas they stimulate the production of type 2/anti-inflammatory cytokines such as IL-10 and transforming growth factor-beta. Through this mechanism, systemically, endogenous catecholamines may cause a selective suppression of Th1 responses and cellular immunity, and a Th2 shift toward dominance of humoral immunity. On the other hand, in certain local responses, and under certain conditions, catecholamines may actually boost regional immune responses, through induction of IL-1, tumor necrosis factor-alpha, and primarily IL-8 production. Thus, the activation of SNS during an immune response might be aimed to localize the inflammatory response, through induction of neutrophil accumulation and stimulation of more specific humoral immune responses, although systemically it may suppress Th1 responses, and, thus protect the organism from the detrimental effects of proinflammatory cytokines and other products of activated macrophages. The above-mentioned immunomodulatory effects of catecholamines and the role of SNS are also discussed in the context of their clinical implication in certain infections, major injury and sepsis, autoimmunity, chronic pain and fatigue syndromes, and tumor growth. Finally, the pharmacological manipulation of the sympathetic-immune interface is reviewed with focus on new therapeutic strategies using selective alpha(2)- and beta(2) adrenoreceptor agonists and antagonists and inhibitors of phosphodiesterase type IV in the treatment of experimental models of autoimmune diseases, fibromyalgia, and chronic fatigue syndrome.

### *Authors*

Jason LA, Taylor RR, Kennedy CL

### *Title*

## **Chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivities in a community-based sample of persons with chronic fatigue syndrome-like symptoms**

### *Source*

Psychosom Med 2000 Sep;62(5):655-63

### *Author's Affiliation*

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ljason@wppost.depaul.edu

### *Abstract*

**OBJECTIVE:** The aim of this study was to determine illness comorbidity rates for individuals with chronic fatigue syndrome (CFS), fibromyalgia (FM), and multiple chemical sensitivities (MCS). An additional objective was to identify characteristics related to the severity of fatigue, disability, and psychiatric comorbidity in each of these illness groups.

**METHODS:** A random sample of 18,675 residents in Chicago, Illinois, was first interviewed by telephone. A control group and a group of individuals with chronic fatigue accompanied by at least four minor symptoms associated with CFS received medical and psychiatric examinations.

**RESULTS:** Of the 32 individuals with CFS, 40.6% met criteria for MCS and 15.6% met criteria for FM. Individuals with MCS or more than one diagnosis reported more physical fatigue than those with no diagnosis. Individuals with more than one diagnosis also reported greater mental fatigue and were less likely to be working than those with no diagnosis. Individuals with CFS, MCS, FM, or more than one diagnosis reported greater disability than those with no diagnosis.

**CONCLUSIONS:** **Rates of coexisting disorders were lower than those reported in prior studies. Discrepancies may be in part attributable to differences in sampling procedures. People with CFS, MCS, or FM endure significant disability in terms of physical, occupational, and social functioning, and those with more than one of these diagnoses also report greater severity of physical and mental fatigue. The findings illustrate differences among the illness groups in the range of functional impairment experienced.**

### *Authors*

Jeschonneck M, Grohmann G, Hein G, Sprott H

### *Title*

**Abnormal microcirculation and temperature in skin above tender points in patients with fibromyalgia.**

### *Source*

Rheumatology (Oxford) 2000 Aug;39(8):917-21 PubMed 10952750

### *Author's Affiliation*

Department of Internal Medicine IV and. Department of Internal Medicine III, Friedrich Schiller University, Jena, Germany.

*Abstract*

**OBJECTIVE:** Skin temperature and skin blood flow were studied above different tender points in 20 patients with fibromyalgia (FM) and 20 healthy controls.

**METHODS:** Blood flow was measured by laser Doppler flowmetry and skin temperature was measured with an infrared thermometer.

**RESULTS:** In the skin above the five tender points examined in each subject, we found an increased concentration of erythrocytes, decreased erythrocyte velocity and a consequent decrease in the flux of erythrocytes. A decrease in temperature was recorded above four of the five tender points.

**CONCLUSION: Vasoconstriction occurs in the skin above tender points in FM patients, supporting the hypothesis that FM is related to local hypoxia in the skin above tender points.**

*Authors*

Liu Z, Welin M, Bragee B, Nyberg F

*Title*

**A high-recovery extraction procedure for quantitative analysis of substance P and opioid peptides in human cerebrospinal fluid.**

*Source*

Peptides 2000 Jun;21(6):853-60

*Author's Affiliation*

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*Abstract*

This study reports an improved approach for the determination of neuropeptide levels in human cerebrospinal fluid (CSF). The method is based on sample acidification followed by liquid-liquid extraction (LLE) combined with radioimmunoassay. It was applied to study the recovery and level of some opioid peptides (Met-enkephalin-Arg(6)-Phe(7) and Leu-enkephalin-Arg(6)), substance P and the substance P(1-7) fragment, which are all compounds known to be present in human CSF. The results indicated that the use of LLE highly improved the recovery of these peptides compared to current liquid-solid-phase extraction methods by using silica gel cartridges or mini-columns for ion-exchange chromatography. Peptides added to CSF in concentrations down to 10 fmol/ml were recovered in yields exceeding 80%. The mean recovery of synthetic peptides as recorded by radioimmunoassay in the LLE procedure was significantly improved when HCl was added to the sample. In contrast, when the (125)I-labeled analogues of the peptides were added to CSF samples, the mean recovery of the four labeled peptides using the LLE procedure was markedly reduced in acidified samples. We also found that

the inclusion of HCl effectively improved the removal of proteins present in the samples. **As an application the levels of substance P and Met-enkephalin-Arg(6)-Phe(7) in CSF samples from patients with chronic pain (fibromyalgia syndrome) were measured using the new procedure. It was possible to confirm a significant difference in the CSF levels of both peptides when comparing patients and controls.**

*Authors*

Maes M, Verkerk R, Delmeire L, Van Gastel A, van Hunsel F, Scharpe S

*Title*

**Serotonergic markers and lowered plasma branched-chain-amino acid concentrations in fibromyalgia**

*Source*

Psychiatry Res 2000 Dec 4;97(1):11-20

*Author's Affiliation*

Department of Psychiatry & Neuropsychology, University Hospital of Maastricht, Postbus 5800, 6202 AZ, Maastricht, The Netherlands.

*Abstract*

The aims of the present study were to examine serotonergic markers, i.e. [3H]paroxetine binding characteristics and the availability of plasma tryptophan, the precursor of serotonin (5-HT), and the plasma concentrations of the branched chain amino acids (BCAAs), valine, leucine and isoleucine, in fibromyalgia. The [3H]paroxetine binding characteristics, B(max) and K(d) values, and tryptophan and the competing amino acids (CAA), known to compete for the same cerebral uptake mechanism (i.e. valine, leucine, isoleucine, phenylalanine and tyrosine), were determined in fibromyalgia patients and normal controls. There were no significant differences in the [3H]paroxetine binding characteristics (B(max) and K(d)) between fibromyalgia and control subjects. There were no significant differences in plasma tryptophan or the tryptophan/CAA ratio between fibromyalgia patients and normal controls. In the fibromyalgia patients, there were no significant correlations between [3H]paroxetine binding characteristics or the availability of tryptophan and myalgic or depressive symptoms. **Patients with fibromyalgia had significantly lower plasma concentrations of the three BCAAs (valine, leucine and isoleucine) and phenylalanine than normal controls. It is hypothesized that the relative deficiency in the BCAAs may play a role in the pathophysiology of fibromyalgia, since the BCAAs supply energy to the muscle and regulate protein synthesis in the muscles. A supplemental trial with BCAAs in fibromyalgia appears to be justified.**

*Author*

Mense S

*Title*

## Neurobiological concepts of fibromyalgia--the possible role of descending spinal tracts

### Source

Scand J Rheumatol Suppl 2000;113:24-9

### Author's Affiliation

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### Abstract

In the spinal cord, long descending pathways are known to exist which modulate pain sensations by either inhibiting or facilitating the discharges of spinal nociceptive neurones. In this article, the hypothesis is discussed that the pain of fibromyalgia may be due to a dysfunction of these pain-modulating pathways. Theoretically, two kinds of disturbance could lead to pain, namely reduced activity in the pain-inhibiting (antinociceptive) system or increased activity in the pain-facilitating (pronociceptive) pathways. Data from animal experiments show that interruption of the dorsal descending systems leads to hyperactivity of spinal nociceptive neurones, namely increase in background activity, lowering in stimulation threshold, and increase in response magnitude to noxious stimuli. The responses of the neurones to input from nociceptors in deep tissues were more strongly inhibited by the descending pathways than were responses to input from cutaneous nociceptors. **Collectively, the findings indicate that the dorsal descending systems are tonically active and have a particularly strong inhibitory action on neurones that mediate pain from deep tissues. If these systems operate in a similar way also in patients, an impairment of their function is likely to lead to 1. spontaneous deep pain (because of an increased background activity in nociceptive neurones supplying deep tissues), 2. tenderness of deep tissues (because of a lowered mechanical threshold of the same neurones), and 3. hyperalgesia of deep tissues (because of increased neuronal responses to noxious stimuli). These changes will affect large areas of the body because the descending inhibitory systems have widespread terminations in the spinal cord. Thus, a dysfunction of the descending inhibitory pathways could mimic to a large extent the pain of fibromyalgia.**

### Author

Neeck G

### Title

**Neuroendocrine and hormonal perturbations and relations to the serotonergic system in fibromyalgia patients**

### Source

Scand J Rheumatol Suppl 2000;113:8-12

### Author's Affiliation

Department of Rheumatology, Kerckhoff Clinic and Foundation, Bad Nauheim, Germany.

### *Abstract*

The symptomatology of the fibromyalgia syndrome (FMS) often resembles an alteration in central nervous set points at least in three systems. The patients suffer under chronic pain in the region of the locomotor system, presumably reflecting a disturbed central processing of pain. Anxiety and depression often characterizes the clinical picture. Almost all of the hormonal feedback mechanisms controlled by the hypothalamus are altered. Characteristic for FMS patients are the elevated basal values of ACTH, follicle-stimulating hormone (FSH), and cortisol as well as lowered basal values of insulin-like growth factor 1 (IGF-1, somatomedin C), free triiodothyronine (FT3), and oestrogen. In FMS patients, the systemic administration of the relevant releasing hormones of corticotropin-releasing hormone (CRH), growth hormone-releasing hormone (GHRH), thyrotropin-releasing hormone (TRH), and luteinizing hormone-releasing hormone (LHRH) leads to increased secretion of ACTH and prolactin, whereas the degree to which TSH can be stimulated is reduced. The stimulation of the hypophysis with LHRH in female FMS patients during their follicular phase results in a significantly reduced LH response. **All in all, the typical alterations in set points of hormonal regulation that are typical for FMS patients can be explained as a primary stress activation of hypothalamic CRH neurons caused by the chronic pain. In addition to the stimulation of pituitary ACTH secretion, CRH activates somatostatin on the hypothalamic level, which in turn inhibits the release of GH and TSH on the hypophyseal level. The lowered oestrogen levels could be accounted for both via an inhibitory effect of the CRH on the hypothalamic release of LHRH or via a direct CRH-mediated inhibition of the FSH-stimulated oestrogen production in the ovary. Serotonin (5HT), precursors like tryptophan (5HTP), drugs which release 5HT or act directly on 5HT receptors stimulate HPA axis, indicating a stimulatory serotonergic influence on HPA axis function. Therefore activation of the HPA axis may reflect an elevated serotonergic tonus in the central nervous system of FMS patients.**

### *Authors*

Neeck G, Crofford LJ

### *Title*

**Neuroendocrine perturbations in fibromyalgia and chronic fatigue syndrome**

### *Source*

Rheum Dis Clin North Am 2000 Nov;26(4):989-1002 *PubMed* 11084955

### *Author's Affiliation*

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### *Abstract*

A large body of data from a number of different laboratories worldwide has demonstrated a general tendency for reduced adrenocortical responsiveness in CFS. It is still not clear if this is secondary to CNS abnormalities leading to decreased activity of CRH- or AVP-producing hypothalamic neurons. Primary hypofunction of the CRH neurons has been described on the basis of genetic and environmental influences. Other pathways could

secondarily influence HPA axis activity, however. For example, serotonergic and noradrenergic input acts to stimulate HPA axis activity. Deficient serotonergic activity in CFS has been suggested by some of the studies as reviewed here. In addition, hypofunction of sympathetic nervous system function has been described and could contribute to abnormalities of central components of the HPA axis. One could interpret the clinical trial of glucocorticoid replacement in patients with CFS as confirmation of adrenal insufficiency if one were convinced of a positive therapeutic effect. If patient symptoms were related to impaired activation of central components of the axis, replacing glucocorticoids would merely exacerbate symptoms caused by enhanced negative feedback. Further study of specific components of the HPA axis should ultimately clarify the reproducible abnormalities associated with a clinical picture of CFS. **In contrast to CFS, the results of the different hormonal axes in FMS support the assumption that the distortion of the hormonal pattern observed can be attributed to hyperactivity of CRH neurons. This hyperactivity may be driven and sustained by stress exerted by chronic pain originating in the musculoskeletal system or by an alteration of the CNS mechanism of nociception. The elevated activity of CRH neurons also seems to cause alteration of the set point of other hormonal axes. In addition to its control of the adrenal hormones, CRH stimulates somatostatin secretion at the hypothalamic level, which, in turn, causes inhibition of growth hormone and thyroid-stimulating hormone at the pituitary level. The suppression of gonadal function may also be attributed to elevated CRH because of its ability to inhibit hypothalamic luteinizing hormone-releasing hormone release; however, a remote effect on the ovary by the inhibition of follicle-stimulating hormone-stimulated estrogen production must also be considered. Serotonin (5-HT) precursors such as tryptophan (5-HTP), drugs that release 5-HT, or drugs that act directly on 5-HT receptors stimulate the HPA axis, indicating a stimulatory effect of serotonergic input on HPA axis function. Hyperfunction of the HPA axis could also reflect an elevated serotonergic tone in the CNS of FMS patients. The authors conclude that the observed pattern of hormonal deviations in patients with FMS is a CNS adjustment to chronic pain and stress, constitutes a specific entity of FMS, and is primarily evoked by activated CRH neurons.**

*Authors*

Park JH, Niermann KJ, Olsen N

*Title*

**Evidence for Metabolic Abnormalities in the Muscles of Patients with Fibromyalgia.**

*Source*

Curr Rheumatol Rep 2000 Apr;2(2):131-140 *PubMed* 11123050

*Author's Affiliation*

Vanderbilt University School of Medicine, Department of Radiology, Division of Rheumatology and Immunology, Department of Medicine, 3219 Medical Center North, Vanderbilt University, Nashville, TN 37232-2681, USA.

*Abstract*

Widespread muscle pain, fatigue, and weakness are defining characteristics of patients with fibromyalgia (FM). The aim of this review is to summarize recent investigations of muscle abnormalities in FM, which can be classified as structural, metabolic, or functional in nature. **Histologic muscle abnormalities of membranes, mitochondria, and fiber type have been well described at both the light microscopic and ultrastructural levels. These structural abnormalities often correlate with biochemical abnormalities, defective energy production, and the resultant dysfunction of FM muscles. The observed abnormalities in FMS muscles are consistent with neurologic findings and disturbances in the hypothalamic-pituitary-adrenal axis. Functional changes in FM muscles are assessed most directly by strength and endurance measurements, but pain and psychologic factors may interfere with accurate assessments. To compensate for diminished effort, the decreased efficiency of the work performance by patients with FM can be verified from P-31 magnetic resonance spectroscopy (MRS) data by calculation of the work/energy-cost ratio for various tasks. In the disease course, muscle abnormalities may be elicited by intrinsic changes within the muscle tissue itself and/or extrinsic neurologic and endocrine factors.** The accurate assignment of intrinsic or extrinsic factors has been substantially clarified by a recent surge of experimental findings. Irrespective of the multifaceted causes of muscle dysfunction and pain, an in-depth understanding of the muscle defects may provide ideas for characterization of the underlying pathogenesis and development of new therapeutic approaches for fibromyalgia syndrome.

*Authors*

Pongratz DE, Sievers M

*Title*

**Fibromyalgia-symptom or diagnosis: a definition of the position**

*Source*

Scand J Rheumatol Suppl 2000;113:3-7

*Author's Affiliation*

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*Abstract*

According to the American College of Rheumatology the diagnosis of fibromyalgia is based on criteria for the classification of fibromyalgia consisting entirely of clinical signs and symptoms. For diagnostic reasons autonomic disturbances and mental features have to be considered. The distinction between fibromyalgia (tender points) and myofascial pain syndrome (trigger points) is essential. Internal and neurological disorders as a primary cause of fibromyalgia have to be excluded. The etiology and pathogenesis of fibromyalgia still remain uncertain. **The myopathological patterns in fibromyalgia are non-specific: type II fiber atrophy, an increase of lipid droplets, a slight proliferation of mitochondria, and a slightly elevated incidence of ragged red fibers. Initial reports on some allelic abnormalities in the serotonin system seem to highlight the important role of serotonin already presumed earlier. Significantly high levels of substance P in the cerebrospinal fluid of FM patients**

**additionally support the impact of these neurotransmitters on both nociceptive and antinociceptive mechanisms.**

*Authors*

Raj SR, Brouillard D, Simpson CS, Hopman WM, Abdollah H

*Title*

**Dysautonomia among patients with fibromyalgia: a noninvasive assessment**

*Source*

J Rheumatol 2000 Nov;27(11):2660-5

*Author's Affiliation*

Department of Medicine and Mackenzie Health Services Research, Queen's University, Kingston, Ontario, Canada.

*Abstract*

**OBJECTIVE:** Fibromyalgia (FM) is a prevalent and poorly understood disorder associated with a significant amount of disability. Some clinical characteristics are common to both FM and vasovagal syncope (which is caused by dysautonomia). We assessed the response of patients with FM to a head up tilt table test (HUT). We also examined sympathovagal balance by assessing heart rate variability (HRV).

**METHODS:** We studied 17 women with FM and 14 female control subjects. After baseline functional assessments, they underwent a 3 stage HUT (with isoproterenol). HRV was assessed over a 24 h period and also before and during HUT. Quality of life was assessed using the Medical Outcomes Study SF-36 Short Form Health Survey.

**RESULTS:** HUT was positive in 64.7% of the patients with FM compared with 21.3% of controls ( $p = 0.016$ ). **FM patients had less HRV, as measured by either time domain or frequency domain analysis. The FM group had a different response to HUT than controls. Quality of life was significantly lower in patients with FM compared to controls ( $p < \text{or} = 0.001$  in all domains).**

**CONCLUSION:** Patients with FM have abnormal responses to 2 tests of autonomic nervous system function. Further research is needed to determine if dysautonomia plays a role in the pathogenesis of FM or is a result of FM.

*Authors*

Shanklin DR, Stevens MV, Hall MF, Smalley DL

*Title*

**Environmental immunogens and T-cell-mediated responses in fibromyalgia: evidence for immune dysregulation and determinants of granuloma formation**

*Source*

Exp Mol Pathol 2000 Oct;69(2):102-18

*Author's Affiliation*

Department of Pathology.

*Abstract*

Thirty-nine patients with fibromyalgia syndrome (FMS) according to American College of Rheumatology criteria were studied for cell-mediated sensitivity to environmental chemicals. Lymphocytes were tested by standard [(3)H]thymidine incorporation in vitro for T cell memory to 11 chemical substances. Concanavalin A (Con A) was used to demonstrate T cell proliferation. Controls were 25 contemporaneous healthy adults and 252 other concurrent standard controls without any aspect of FMS. **Significantly higher (P < 0.01) stimulation indexes (SI) were found in FMS for aluminum, lead, and platinum; borderline higher (0.05 > P > 0.02) SI were found for cadmium and silicon. FMS patients showed sporadic responses to the specific substances tested, with no high-frequency result (>50%) and no obvious pattern. Mitogenic responses to Con A indicated some suppression of T cell functionality in FMS. Possible links between mitogenicity and immunogenic T cell proliferation, certain electrochemical specifics of granuloma formation, maintenance of connective tissue, and the fundamental nature of FMS are considered.** Copyright 2000. Reprinted from Experimental Molecular Pathology, Vol. 69, No. 2, 2000, pp 102-118, Shankilin DR, Stevens MV, Hall MF, Smalley DL, **Environmental immunogens and T-cell-mediated responses in fibromyalgia: evidence for immune dysregulation and determinants of granuloma formation**, with permission from Elsevier Science Inc.

*Authors*

Wolfe F, Hawley DJ, Goldenberg DL, Russell IJ, Buskila D, Neumann L

*Title*

**The assessment of functional impairment in fibromyalgia (FM): Rasch analyses of 5 functional scales and the development of the FM Health Assessment Questionnaire**

*Source*

J Rheumatol 2000 Aug;27(8):1989-99

*Author's Affiliation*

University of Kansas School of Medicine, Wichita, USA.

*Abstract*

**OBJECTIVE:** Functional assessment by self-report questionnaire plays an important role in most rheumatic conditions, but psychometric properties of questionnaires have not been studied in fibromyalgia (FM), particularly by Rasch analysis, which allows for examining adequacy of the questionnaire scale. To assess currently used instruments, we examined the Fibromyalgia Impact Scale (FIQ), 4 versions of the Health Assessment Questionnaire (HAQ), and the Medical Outcome Survey Short Form (SF-36).

**METHODS:** More than 2,500 patients from 4 sites (3 US, 1 Israel) completed the FIQ. The HAQ questionnaires were completed by 1438 patients participating in the US National Data Bank for Rheumatic Diseases. Seven hundred sixty patients from Wichita, Kansas, completed the SF-36. Rasch analysis was applied separately to each of these data sets.

**RESULTS:** The FIQ systematically underestimated functional impairment by its handling of activities not usually performed. All questionnaires had problems with non-unidimensionality and ambiguous items when applied to patients with FM. In addition, scales were found to be non-linear. Because of these findings we used the 20 item HAQ questionnaire as an item bank to develop a new questionnaire more suitable for use in FM, the fibromyalgia HAQ (FHAQ). This questionnaire fits the Rasch model well, is relevant, is linear, and has a long, well spaced scale.

**CONCLUSION:** **No available functional assessment questionnaire works well in FM. A new questionnaire, the FHAQ, was developed. It has appropriate metric properties and should function well in this condition. Since the FHAQ is a subset of the larger HAQ questionnaire, a new questionnaire is not required; only a different method of scoring is needed. Additional studies regarding sensitivity to change are required to fully validate the FHAQ.**