ME/CFS Research Abstracts

2000

Authors
Aaron LA, Burke MM, Buchwald D.

Title
Overlapping conditions among patients with chronic fatigue syndrome, fibromyalgia, and temporomandibular disorder.

Source
Arch Intern Med. 2000 Jan 24;160(2):221-7. *PubMed* 10647761

Author's Affiliation
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Abstract
BACKGROUND: Patients with chronic fatigue syndrome (CFS), fibromyalgia (FM), and temporomandibular disorder (TMD) share many clinical illness features such as myalgia, fatigue, sleep disturbances, and impairment in ability to perform activities of daily living as a consequence of these symptoms. A growing literature suggests that a variety of comorbid illnesses also may commonly coexist in these patients, including irritable bowel syndrome, chronic tension-type headache, and interstitial cystitis.

OBJECTIVE: To describe the frequency of 10 clinical conditions among patients with CFS, FM, and TMD compared with healthy controls with respect to past diagnoses, degree to which they manifested symptoms for each condition as determined by expert-based criteria, and published diagnostic criteria.

METHODS: Patients diagnosed as having CFS, FM, and TMD by their physicians were recruited from hospital-based clinics. Healthy control subjects from a dermatology clinic were enrolled as a comparison group. All subjects completed a 138-item symptom checklist and underwent a brief physical examination performed by the project physicians.

RESULTS: With little exception, patients reported few past diagnoses of the 10 clinical conditions beyond their referring diagnosis of CFS, FM, or TMD. In contrast, patients were more likely than controls to meet lifetime symptom and diagnostic criteria for many of the conditions, including CFS, FM, irritable bowel syndrome, multiple chemical sensitivities, and headache. Lifetime rates of irritable bowel syndrome were particularly striking in the patient groups (CFS, 92%; FM, 77%; TMD, 64%) compared with controls (18%) ($P<.001$). Individual symptom analysis revealed that patients with CFS, FM, and TMD share common symptoms, including generalized pain sensitivity, sleep and concentration difficulties, bowel complaints, and headache. However, several symptoms also distinguished the patient groups.

CONCLUSIONS: **This study provides preliminary evidence that patients with CFS, FM, and TMD share key symptoms. It also is apparent that other localized and systemic conditions may frequently co-occur with CFS, FM, and TMD.** Future research that seeks to identify the temporal relationships and other pathophysiologic mechanism(s) linking CFS, FM, and TMD will likely advance our understanding and treatment of these chronic, recurrent conditions.

Authors
Ablashi DV, Eastman HB, Owen CB, Roman MM, Friedman J, Zabriskie JB, Peterson DL, Pearson GR, Whitman JE.

Title
Frequent HHV-6 reactivation in multiple sclerosis (MS) and chronic fatigue syndrome (CFS) patients.

Source
J Clin Virol. 2000 May;16(3):179-91. *PubMed* 10738137

Author's Affiliation
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Abstract
BACKGROUND: HHV-6 is a ubiquitous virus and its infection usually occurs in childhood and then becomes a latent infection. HHV-6 reactivation has been shown to play a role in the pathogenesis of AIDS and several other diseases.

OBJECTIVES: To determine what role HHV-6 infection or reactivation plays in the pathogenesis of multiple sclerosis (MS) and chronic fatigue syndrome (CFS).

RESULTS: Twenty-one MS and 35 CFS patients were studied and followed clinically. In these patients, we measured HHV-6 IgG and IgM antibody levels and also analyzed their peripheral blood mononuclear cells (PBMCs) for the presence of HHV-6, using a short term culture assay. In both MS and CFS patients, we found higher levels of HHV-6 IgM antibody and elevated levels of IgG antibody when compared to healthy controls. Seventy percent of the MS patients studied contained IgM antibodies for HHV-6 late antigens (capsid), while only 15% of the healthy donors (HD) and 20% of the patients with other neurological disorders (OND) had HHV-6 IgM antibodies. Higher frequency of IgM antibody was also detected in CFS patients (57.1%) compared to HD (16%). Moreover, 54% of CFS patients exhibited antibody to HHV-6 early protein (p41/38) compared to only 8.0% of the HD. Elevated IgG antibody titers were detected in both the MS and the CFS patients. PBMCs from MS, CFS and HD were analyzed in a short term culture assay in order to detect HHV-6 antigen expressing cells and to characterize the viral isolates obtained as either Variant A or B. Fifty-four percent of MS patients contained HHV-6 early and late antigen producing cells and 87% of HHV-6 isolates were Variant B. Isolates from CFS, patients were predominately Variant A (70%) and isolates from HD were predominately Variant B (67%). Moreover, one isolate from OND was also Variant B. Persistent HHV-6 infection was found in two CFS patients over a period of 2.5 years and HHV-6 specific cellular immune responses were detected in PBMCs from ten CFS patients.

CONCLUSION: **In both MS and CFS patients, we found increased levels of HHV-6 antibody and HHV-6 DNA. A decrease in cellular immune responses was also detected in CFS patients. These data suggest that HHV-6 reactivation plays a role in the pathogenesis of these disorders.**

Authors
Bradley LA, McKendree-Smith NL, Alarcon GS.

Title

Pain complaints in patients with fibromyalgia versus chronic fatigue syndrome.

Source
Curr Rev Pain. 2000;4(2):148-57. *PubMed* 10998728

Author's Affiliation
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Abstract
Individuals with fibromyalgia (FM) and/or chronic fatigue syndrome (CFS) report arthralgias and myalgias. However, only persons with FM alone exhibit abnormal pain responses to mild levels of stimulation, or allodynia. We identify the abnormalities in the neuroendocrine axes that are common to FM and CFS as well as the abnormalities in central neuropeptide levels and functional brain activity that differentiate these disorders. **These two sets of factors, respectively, may account for the similarities and differences in the pain experiences of persons with FM and CFS.**

Authors
Brooks JC, Roberts N, Whitehouse G, Majeed T.

Title

Proton magnetic resonance spectroscopy and morphometry of the hippocampus in chronic fatigue syndrome.

Source
Br J Radiol. 2000 Nov;73(875):1206-8. *PubMed* 11144799

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Abstract
Seven patients with chronic fatigue syndrome (CFS) were matched with ten healthy control subjects of similar age. Hippocampal volume, obtained from magnetic resonance images using an unbiased method, showed no difference between the two groups, whereas **proton magnetic resonance spectroscopy showed a significantly reduced concentration of N-acetylaspartate in the right hippocampus of CFS patients (p = 0.005).**

Authors
Chaudhuri A, Watson WS, Pearn J, Behan PO.

Title

The symptoms of chronic fatigue syndrome are related to abnormal ion channel function.

Source
Med Hypotheses. 2000 Jan;54(1):59-63. *PubMed* 10790725

Author's Affiliation
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Abstract
The pathogenesis of chronic fatigue syndrome (CFS) is unknown but one of the most characteristic features of the illness is fluctuation in symptoms which can be induced by physical and/or mental stress. Other conditions in which fluctuating fatigue occurs are caused by abnormal ion channels in the cell membrane. These include genetically determined channelopathies, e.g. hypokalemic periodic paralysis, episodic ataxia type 2 and acquired conditions such as neuromyotonia, myasthenic syndromes, multiple sclerosis and inflammatory demyelinating polyneuropathies. Our hypothesis is that abnormal ion channel function underlies the symptoms of CFS and this is supported also by the finding of abnormal cardiac-thallium201 SPECT scans in CFS, similar to that found in syndrome X, another disorder of ion channels. **CFS and syndrome X can have identical clinical symptoms. CFS may begin after exposure to specific toxins which are known to produce abnormal sodium ion channels. Finally, in CFS, increased resting energy expenditure (REE) occurs, a state influenced by transmembrane ion transport. The hypothesis that ion channels are abnormal in CFS may help to explain the fluctuating fatigue and other symptoms.**

Authors
De Becker P, Roeykens J, Reynders M, McGregor N, De Meirleir K.

Title
Exercise capacity in chronic fatigue syndrome.

Source
Arch Intern Med. 2000 Nov 27;160(21):3270-7. *PubMed* 11088089

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Abstract
BACKGROUND: Patients with chronic fatigue syndrome (CFS) suffer from various symptoms, including debilitating fatigue, muscle pain, and muscle weakness. Patients with CFS can experience marked functional impairment. In this study, we evaluated the exercise capacity in a large cohort of female patients with CFS. METHODS: Patients with CFS and matched sedentary control subjects performed a maximal test with graded increase on a bicycle ergometer. Gas exchange ratio was continuously measured. In a second stage, we examined only those persons who achieved a maximal effort as defined by 2 end points: a respiratory quotient of at least 1.0 and an age-predicted target heart rate of at least 85%. Data were assessed using univariate and multivariate statistical methods.

RESULTS: The resting heart rate of the patient group was higher, but the maximal heart rate at exhaustion was lower, relative to the control subjects. The maximal workload and maximal oxygen uptake attained by the patients with CFS were almost half those achieved by the control subjects. Analyzing only those persons who performed a maximal exercise test, similar findings were observed.

CONCLUSIONS: **When compared with healthy sedentary women, female patients with CFS show a significantly decreased exercise capacity. This could affect their physical abilities to a moderate or severe extent. Reaching the age-predicted target heart rate seemed to be a limiting factor of the patients with CFS in achieving maximal effort, which could be due to autonomic disturbances.**

Authors
De Meirleir K, Bisbal C, Campine I, De Becker P, Salehzada T, Demettre E, Lebleu B.

Title
A 37 kDa 2-5A binding protein as a potential biochemical marker for chronic fatigue syndrome.

Source
Am J Med. 2000 Feb;108(2):99-105. *PubMed* 11126321
Author's Affiliation Department of Human Physiology and Medicine, Vrije Universiteit Brussels, Belgium.

Abstract
PURPOSE: Recent studies have revealed abnormalities in the ribonuclease L pathway in peripheral blood mononuclear cells of patients with the chronic fatigue syndrome. We conducted a blinded study to detect possible differences in the distribution of 2-5A binding proteins in the cells of patients with chronic fatigue syndrome and controls.

PATIENTS AND METHODS: We studied 57 patients with fatigue syndrome and 53 control subjects (28 healthy subjects and 25 patients with depression or fibromyalgia). A radioactive probe was used to label 2-5A binding proteins in unfractionated peripheral blood mononuclear cell extracts and to compare their distribution in the three groups.

RESULTS: **A 37 kDa 2-5A binding polypeptide was found in 50 (88%)** of the 57 patients with chronic fatigue syndrome compared with 15 (28%) of the 53 controls ($P < 0.01$). When present, the amount of 37 kDa protein was very low in the control groups. When expressed as the ratio of the 37 kDa protein to the 80 kDa protein, 41 (72%) of the 57 patients with chronic fatigue syndrome had a ratio > 0.05, compared with 3 (11%) of the 28 healthy subjects and none of the patients with fibromyalgia or depression.

CONCLUSION: **The presence of a 37 kDa 2-5A binding protein in extracts of peripheral blood mononuclear cells may distinguish patients with chronic fatigue syndrome from healthy subjects and those suffering from other diseases.**

Authors
Friedberg F, Dechene L, McKenzie MJ 2nd, Fontanetta R.

Title
Symptom patterns in long-duration chronic fatigue syndrome.

Source
J Psychosom Res. 2000 Jan;48(1):59-68. *PubMed* 10750631

Author's Affiliation

Department of Mathematics, Fitchburg State College, MA, USA.

Abstract
OBJECTIVE: Our objective was to evaluate symptom patterns in patients with chronic fatigue syndrome (CFS) who were ill for 10 or more years.

METHODS: This cross-sectional self-report study compared patient groups with long-duration (median = 18 years; n = 258) and short-duration (median = 3 years; n = 28) CFS to a group of healthy significant others (n = 79) on symptomatic, neurocognitive, and psychological variables. Data were gathered from a 574-item postal questionnaire.

RESULTS: A principal-components analysis of CFS symptom data yielded a three-factor solution: cognitive problems; flu-like symptoms; and neurologic symptoms. **Compared with the short-duration CFS group, the long-duration group had significantly higher CFS symptom severity scores ($p < 0.04$), largely attributable to increased cognitive difficulties.** A subgroup comparison of subjects ill for < 3 years versus those ill 4-7 years suggested that denial coping strategies were more likely in those participants with the shorter illness duration. Significant differences between both CFS groups and healthy controls were found in a number of comorbid disorders. Participants with CFS most often endorsed immune/viral abnormalities and persistent stress as important perceived causes of their illness.

CONCLUSION: **Participants with long-duration CFS reported a large number of specific cognitive difficulties that were greater in severity than those reported by participants with short-duration CFS. The pattern of comorbid disorders in the CFS groups was consistent with hypersensitivity and viral reactivation hypotheses.**

Authors
Fulle S, Mecocci P, Fano G, Vecchiet I, Vecchini A, Racciotti D, Cherubini A, Pizzigallo E, Vecchiet L, Senin U, Beal MF.

Title
Specific oxidative alterations in vastus lateralis muscle of patients with the diagnosis of chronic fatigue syndrome.

Source
Free Radic Biol Med. 2000 Dec 15;29(12):1252-9. *PubMed* 11118815

Author's Affiliation
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Abstract
Chronic fatigue syndrome (CFS) is a poorly understood disease characterized by mental and physical fatigue, most often observed in young white females. Muscle pain at rest, exacerbated by exercise, is a common symptom. Although a specific defect in muscle metabolism has not been clearly defined, yet several studies report altered oxidative metabolism. In this study, we detected oxidative damage to DNA and lipids in muscle specimens of CFS patients as compared to age-matched controls, as well as increased activity of the antioxidant enzymes catalase, glutathione peroxidase, and transferase, and increases in total glutathione plasma levels. **From these results we hypothesize that in CFS there is oxidative stress in muscle, which results in an increase in antioxidant defenses. Furthermore, in muscle membranes, fluidity and fatty acid composition are significantly different in specimens from CFS patients as compared to**

controls and to patients suffering from fibromyalgia. These data support an organic origin of CFS, in which muscle suffers oxidative damage.

Authors
Kavelaars A, Kuis W, Knook L, Sinnema G, Heijnen CJ.

Title
Disturbed neuroendocrine-immune interactions in chronic fatigue syndrome.

Source
J Clin Endocrinol Metab. 2000 Feb;85(2):692-6. *PubMed* 10690878

Author's Affiliation
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Abstract
The present study was designed to investigate the interaction between neuroendocrine mediators and the immune system in chronic fatigue syndrome (CFS). We examined the sensitivity of the immune system to the glucocorticoid agonist dexamethasone and the beta2-adrenergic agonist terbutaline in 15 adolescent girls with CFS and 14 age- and sex-matched controls. Dexamethasone inhibits T-cell proliferation in healthy controls and in CFS patients. However, the maximal effect of dexamethasone on T-cell proliferation is significantly reduced in CFS patients as compared with controls. The beta2-adrenergic receptor agonist terbutaline inhibits tumor necrosis factor-alpha production and enhances interleukin-10 production by monocytes. Our data demonstrate that the capacity of a beta2-adrenergic agonist to regulate the production of these two cytokines is also reduced in CFS patients. We did not observe differences in baseline or CRH-induced cortisol and ACTH between CFS patients and controls. Baseline noradrenaline was similar in CFS and controls, whereas baseline adrenaline levels were significantly higher in CFS patients. **We conclude that CFS is accompanied by a relative resistance of the immune system to regulation by the neuroendocrine system. Based on these data, we suggest CFS should be viewed as a disease of deficient neuroendocrine-immune communication.**

Authors
Moorkens G, Berwaerts J, Wynants H, Abs R.

Title
Characterization of pituitary function with emphasis on GH secretion in the chronic fatigue syndrome.

Source
Clin Endocrinol (Oxf). 2000 Jul;53(1):99-106. *PubMed* 10931086

Author's Affiliation
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Abstract
OBJECTIVE: Previous studies have revealed that hormonal disturbances may accompany the chronic fatigue syndrome (CFS). Changes in the secretion of the pituitary-adrenal axis have been demonstrated, as well as abnormalities in the GH-IGF-I axis. However, data have not always been

well characterized and were sometimes conflicting. The small number of CFS patients investigated in earlier studies may have played a role in the interpretation of the results.

SUBJECTS AND DESIGN: Hormonal testing was performed in 73 nonobese CFS patients and nonobese 21 age-and gender-matched healthy controls. We investigated GH, ACTH and cortisol responses to insulin-induced hypoglycaemia. In a subgroup of patients arginine and clonidine stimulation for GH was also performed. Nocturnal secretion of GH, ACTH and cortisol were determined. Serum levels of IGF-I, prolactin, TSH, and free thyroxine were also measured. Visceral fat mass was assessed by CT scanning.

RESULTS: GH response to insulin induced hypoglycaemia assessed by peak value (17.0 +/- 13.1 microg/l vs. 22. 1 +/- 9.8 microg/l; P =0.01) and by AUC (450.0 +/- 361.3 microg/l vs. 672.3 +/- 393.0 microg/l; P = 0.002) was significantly decreased in CFS patients vs. controls. Nocturnal GH secretion assessed by GH peak value (5.4 +/- 3.7 vs. 9.0 +/- 5.1 microg/l; P = 0.44) and by AUC (34.4 +/- 20.2 vs. 67.4 +/- 43.1; P = 0.045) was also significantly impaired in CFS patients. Arginine and clonidine administration showed no differences in GH secretion between CFS patients and controls. In the CFS group, GH peak values were significantly higher after ITT than after arginine (P = 0.017) or clonidine (P = 0.001). No differences in serum IGF-I levels were found between CFS patients and controls. Except for a significantly lower nocturnal cortisol peak value, no differences were found in ACTH and cortisol secretion between CFS patients and controls. Significantly higher serum prolactin levels (7.4 +/- 4.7 microg/l vs. 4.4 +/- 1.3 microg/l; P = 0.004) and significantly higher serum TSH levels (1.6 +/- 1.0 mU/l vs. 1.0 +/- 0.4 mU/l; P = 0.011) were found in CFS patients. Serum free thyroxine was comparable in both groups. Visceral fat mass was significantly higher in CFS patients (86.6 +/- 34.9 cm2 vs. 51.5 +/- 15.7 cm2; P < 0.001).

CONCLUSIONS: We observed a significant impairment of GH response during insulin-induced hypoglycaemia and a low nocturnal GH secretion in CFS patients. These changes did, however, not lead to different concentrations in serum IGF-I. The clinical expression of this inadequate GH secretion can thus be questioned, although the alteration in body composition may be related to this relative GH deficiency. Significantly increased prolactin and TSH levels were found when compared to controls. These findings give support to the hypothesis of a decreased dopaminergic tone in CFS. Further investigations are required in order to identify specific adaptations within the neurotransmitter system in CFS and to determine the clinical importance of the impaired GH homeostasis.

Authors
Naschitz JE, Rosner I, Rozenbaum M, Gaitini L, Bistritzki I, Zuckerman E, Sabo E, Yeshurun D.

Title
The capnography head-up tilt test for evaluation of chronic fatigue syndrome.

Source
Semin Arthritis Rheum. 2000 Oct;30(2):79-86. *PubMed* 11071579

Author's Affiliation
Department of Internal Medicine A, Bnai Zion Medical Center and Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel.

Abstract
OBJECTIVES: To compare the hemodynamic and ventilatory responses to autonomic challenge evoked by upright tilt table testing in patients with chronic fatigue syndrome (CFS) to healthy individuals.

METHODS: Thirty-two consecutive patients with CFS and 32 healthy volunteers were evaluated with the aid of the recently introduced capnography head-up tilt test (CHUTT). The main outcome measures were values of blood pressure (BP), heart rate (HR), respiratory rate (RR), and end-tidal pressure of co2 (ETPco2) recorded during recumbence and tilt. In addition, the end points of vasodepressor and cardioinhibitory reactions, hyperventilation (defined by ETPco2 <25 mm Hg) and the postural tachycardia syndrome, were recorded.

RESULTS: The BP, HR, RR, and ETPco2 recorded during recumbence were similar in both groups. During tilt, patients with CFS developed significantly lower systolic BP, diastolic BP, and ETPco2, and a significant rise in HR and RR (P<.01). In CFS patients, the postural tachycardia syndrome occurred in 44%, vasodepressor reaction in 41%, cardioinhibitory reaction in 13%, and hyperventilation in 31% of cases. One or more end points of the CHUTT were reached in 78% of patients with CFS but in none of the controls (P<.0001).

CONCLUSIONS: **In most patients with CFS, a spectrum of abnormal homeostatic reactions is diagnosed with the aid of the CHUTT. Data provided by the CHUTT may reinforce the clinical diagnosis by adding objective and unbiased criteria to the subjective assessment of CFS.**

Authors
Richards RS, Roberts TK, Dunstan RH, McGregor NR, Butt HL.

Title
Free radicals in chronic fatigue syndrome: cause or effect?

Source
Redox Rep. 2000;5(2-3):146-7. *PubMed* 10939298

Author's Affiliation
Department of Biological Sciences, University of Newcastle, New South Wales, Australia

Abstract
We have demonstrated that certain morphological and biochemical changes occur in chronic fatigue syndrome (CFS) and in rheumatoid arthritis (RA). These changes in RA can be explained by the well-established inappropriate increase in free radical generation. The similar changes in CFS suggest a similar explanation and a possible role for free radicals in the aetiology of this condition.

Authors
Richards RS, Roberts TK, McGregor NR, Dunstan RH, Butt HL.

Title
Blood parameters indicative of oxidative stress are associated with symptom expression in chronic fatigue syndrome.

Source
Redox Rep. 2000;5(1):35-41. *PubMed* 10905542

Author's Affiliation

Department of Biological Sciences, University of Newcastle, Australia.

Abstract
Full blood counts, ESR, CRP, haematinics and markers for oxidative stress were measured for 33 patients diagnosed with chronic fatigue syndrome (CFS) and 27 age and sex matched controls. All participants also completed symptom questionnaires. CFS patients had increases in malondialdehyde (P <0.006), methaemoglobin (P <0.02), mean erythrocyte volume (P <0.02) and 2,3-diphosphoglycerate (P <0.04) compared with controls. Multiple regression analysis found methaemoglobin to be the principal component that differentiated between CFS patients and control subjects. Methaemoglobin was found to be the major component associated with variation in symptom expression in CFS patients (R(2) = 0.99, P <0.00001), which included fatigue, musculoskeletal symptoms, pain and sleep disturbance. Variation in levels of malondialdehyde and 2,3-diphosphoglycerate were associated with variations in cognitive symptoms and sleep disturbance (R(2) = 0.99, P <0.00001). These data suggest that oxidative stress due to excess free radical formation is a contributor to the pathology of CFS and was associated with symptom presentation.

Authors
Starr A, Scalise A, Gordon R, Michalewski HJ, Caramia MD.

Title
Motor cortex excitability in chronic fatigue syndrome.

Source
Clin Neurophysiol. 2000 Nov;111(11):2025-31. *PubMed* 11068238

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Abstract
OBJECTIVE: To use transcranial magnetic stimulation (TMS) to define motor cortical excitability in chronic fatigue syndrome (CFS) subjects during a repetitive, bilateral finger movement task.

METHODS: A total of 14 CFS patients were tested and compared with 14 age-matched healthy control subjects. TMS of the motor cortex (5% above threshold) was used to elicit motor evoked potentials (MEPs). Subjects performed regular (3-4/s) repetitive bilateral opening-closing movements of the index finger onto the thumb. MEPs of the first dorsal interosseus (FDI) were measured before, immediately following exercise periods of 30, 60 and 90 s, and after 15 min of rest.

RESULTS: Performance, defined by rate of movement, was significantly slower in CFS subjects (3.5/s) than in controls (4. 0/s) independent of the hand measured. The rate, however, was not significantly affected by the exercise duration for either group. The threshold of TMS to evoke MEPs from the FDI muscle was significantly higher in CFS than in control subjects, independent of the hemisphere tested. A transient post-exercise facilitation of MEP amplitudes immediately after the exercise periods was present in controls independent of the hemisphere tested, but was absent in CFS subjects. A delayed facilitation of MEPs after 15-30 min of rest was restricted to the non-dominant hemisphere in controls; delayed facilitation was absent in CFS subjects.

CONCLUSIONS: **Individuals with CFS do not show the normal fluctuations of motor cortical excitability that accompany and follow non-fatiguing repetitive bimanual finger movements.**

Authors
Streeten DH, Thomas D, Bell DS.

Title
The roles of orthostatic hypotension, orthostatic tachycardia, and subnormal erythrocyte volume in the pathogenesis of the chronic fatigue syndrome.

Source
Am J Med Sci. 2000 Jul;320(1):1-8. *PubMed* 10910366

Authors Affiliation
Department of Medicine, State University of New York Health Science Center, Syracuse 13210, USA.

Abstract
BACKGROUND: Orthostatic hypotension during upright tilt is an important physical disorder in patients with chronic fatigue syndrome. We have tested its occurrence during prolonged standing, whether it is correctable, and whether reduced circulating erythrocyte volume is present.

METHODS: Fifteen patients were randomly selected from a large population of patients with chronic fatigue syndrome, studied, and observed for several years (by DSB). Blood pressure (BP) and heart rate (HR) measured with Dinamap every minute for 30 minutes supine and 60 minutes standing were compared with these findings in 15 healthy age- and gender-matched control subjects and later during lower body compression with military antishock trousers (MAST). Plasma catecholamines and circulating erythrocyte and plasma volumes were also measured by isotopic dilution methods.

RESULTS: Abnormal findings in the patients included excessive orthostatic reductions in systolic ($P < 0.001$) and diastolic BP ($P < 0.001$) and excessive orthostatic tachycardia ($P < 0.01$), together with presyncopal symptoms in 11 of the 15 patients and in none of the control subjects after standing for 60 min. Lower body compression with the MAST restored all orthostatic measurements to normal and overcame presyncopal symptoms within 10 min. Circulating erythrocyte but not plasma volumes were subnormal in the 12 women ($P < 0.01$) and plasma norepinephrine concentration rose excessively after standing for 10 min.

CONCLUSION: **Delayed orthostatic hypotension and/or tachycardia caused by excessive gravitational venous pooling, which is correctable with external lower-body compression, together with subnormal circulating erythrocyte volume, are very frequent, although not invariably demonstrable, findings in moderate to severe chronic fatigue syndrome. When present, they may be involved in its pathogenesis.**

Authors
Visser JT, De Kloet ER, Nagelkerken L.

Title
Altered glucocorticoid regulation of the immune response in the chronic fatigue syndrome.

Source
Ann N Y Acad Sci. 2000;917:868-75. *PubMed* 11268418

Author's Affiliation
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Abstract
It is increasingly recognized that glucocortiocoids (GCs) can have subtle modulatory effects in immunoregulation rather than having generalized immunosuppressive effects. GCs suppress Th1 cells and cellular immunity, but may favor Th2 responses and humoral immunity. **The chronic fatigue syndrome (CFS) appears to be associated with a disturbed HPA-axis. Moreover, CFS patients show several immunological changes suggestive of decreased cellular immunity. It is postulated herein that in CFS patients a decreased Th1/Th2 balance may be the result of selective effects of GC on the IL-10/IL-12 regulatory circuit.**

Authors
Woo SB, Schacterle RS, Komaroff AL, Gallagher GT.

Title
Salivary gland changes in chronic fatigue syndrome: a case-controlled preliminary histologic study.

Source
Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2000 Jul;90(1):82-7. *Pub Med* 10884641

Author's Affiliation
Dept of Oral Medicine and Diagnostic Sciences, Harvard School of Dental Medicine, Brigham and Women's Hospital, USA.

Abstract
OBJECTIVE: The purpose of this preliminary study is to compare labial salivary gland changes of 11 patients with chronic fatigue syndrome with control subjects.

STUDY DESIGN: Changes in labial salivary glands were graded from 0 to 3+ for acinar dilatation, ductal dilatation, periductal fibrosis, plasmacytic infiltrate, lymphocytic infiltrate, mast cell infiltrate, and lymphocytic aggregates or foci.

RESULTS: Four of the 11 subjects had 2+ to 3+ changes in at least 4 of the 7 parameters examined. Only the presence of mast cells was statistically significant between the 2 groups. Two of these 4 patients had 1 lymphocytic focus per 4 mm(2) of tissue.

CONCLUSIONS: **The salivary gland changes in patients with chronic fatigue syndrome show varying degrees of ductal and acinar dilatation, periductal fibrosis, lymphoplasmacytic infiltrates, and occasional lymphocytic foci, all suggestive of primary gland damage. The one parameter that showed statistical significance was the presence of mast cells.**