

Authors	Author Address	Title	Publication	Abstract
Aboudiab T, Leke L, Skonieczny M, Chouraki JP.	Departement de pediatrie, unite de neonatologie, CHU, 80000 Amiens, France.	[Are IgE-independent food hypersensitivity and chronic fatigue syndrome related?][Article in French]	Arch Pediatr. 2004 Aug;11(8):975-977.	
Aceves-Avila FJ, Ferrari R, Ramos-Remus C.	Hospital General Regional No. 46, Instituto Mexicano del Seguro Social, Unidad de Investigacion en Enfermedades Cronico-Degenerativas SC, Guadalajara, Jalisco, Mexico.	New insights into culture driven disorders.	Best Pract Res Clin Rheumatol. 2004 Apr;18(2):155-71.	Rheumatologists frequently encounter patients whose illnesses lack face-value; that is, they lack the typical objective features of pathology that rheumatologists traditionally rely on for diagnosis and developing effective treatment approaches: namely fibromyalgia, chronic fatigue syndrome, Gulf War syndrome, chronic whiplash, chronic low back pain, etc. In this article, we examine this group of illnesses as culture-driven disorders to emphasize the central importance of various societal constraints in the ultimate presentation of patients with these illnesses. We will examine them by first understanding the purpose they serve, the underlying factors that compel societal institutions to sanctify these disorders as diseases, and how research is beginning to examine the behaviour that captures and packages these symptoms to produce their clinical presentation. With this research understanding, rheumatologists may be able to offer patients more useful action plans, but likely changes in societal approaches to the expressions of distress and changes in disability and compensation systems will also be required.
Adler RH.	University of Berne Medical School, Kehrsatz, Switzerland. rolf.adler@tele2.ch	Chronic fatigue syndrome (cfs).	Swiss Med Wkly. 2004 May 15;134(19-20):268-76.	The Chronic Fatigue Syndrome (CFS) is described based on the revision of Fukuda et al. The question "whether CFS can be discussed as a homogenous disorder?" has been reviewed and the answer is "no". Other overlapping syndromes are mentioned. Disorders with fatigue as a symptom are depression, somatisation, irritable bowel syndrome, effort-syndrome, hyperventilation, conservation-withdrawal. Among the pathogenetic factors of CFS immune systems disorders, neuroendocrine abnormalities, autonomic activity, neuroimaging, neuropsychological abnormalities, exercise capacity and muscle function and psychological processes (attribution, perception, symptom avoidance and neutralisation of conflicts) are discussed. Since CFS cannot be comprehended without knowledge of the ontogenetic development of the affect "fatigue", it is extensively described. Based on this knowledge, fatigue as an affect and the CFS are embedded in a context, which has as its basis the fight-flight reaction and the conservation-withdrawal reaction. Weighing the evidence, it is concluded that CFS in its varieties can best be understood as a manifestation of the activation of the two biological emergency reactions: fight-flight and conservation-withdrawal. The physician should interview and examine each individual patient according to the Harvey Cushing dictum: The physician should not only study the diseased organ, but the man with his diseased organ, and not only these. He should comprehend the man with his diseased organ in his environment. This leads to study of the biological, psychological and social factors contributing to each patient's illness. Work-up and therapy have to be based on this integrated approach. The latter encompasses conflict centred psychotherapy, stepwise increasing physical activation and antidepressive drugs.
Andersen MM, Permin H, Albrecht F.	Department of Infectious Diseases M5132, Rigshospitalet, Blegdamsvej 9, DK-2100 Copenhagen, Denmark.	Illness and disability in Danish Chronic Fatigue Syndrome patients at diagnosis and 5-year follow-up.	J Psychosom Res. 2004 Feb;56(2):217-29.	OBJECTIVE: Evaluation of the life impact of Chronic Fatigue Syndrome (CFS) over 5 years. METHODS: Thirty-three adult patients meeting 1988 and 1994 CDC case criteria answered identical questionnaires at diagnosis and 5 years later, when a retrospective questionnaire was also completed. RESULTS: Work disability was very high and increased further, social isolation remained high, emotional adjustment improved. There were increased problems with reading and with allergies. Two measures of improvement were used: The relation between these measures was weak. Length of illness, extent of disability and emotional adjustment were poorly related to measures of improvement. Average illness scores were unchanged, but most individuals improved in some ways while worsening or remaining the same in others. Only one participant (3%) neared recovery, one other was substantially better but still severely disabled. CONCLUSION: CFS patients exhibit severe, long-term functional impairment. Substantial improvement is uncommon, less than 6%. Allergies and aspects of cognition may worsen, emotional adjustment often improves.
Arashima Y, Kato K, Komiya T, Kumasaka K, Matsukawa Y, Murakami M, Takahashi K, Ikeda T, Arakawa Y.	Department of Laboratory Medicine, Nihon University School of Medicine, Tokyo,	Improvement of chronic nonspecific symptoms by long-term minocycline treatment in Japanese patients with Coxiella burnetii infection considered to have post-Q fever fatigue syndrome.	Intern Med. 2004 Jan;43(1):49-54. Comment in: Intern Med. 2004 Jan;43(1):1-2.	OBJECTIVE: To address the presence of post-Q fever fatigue syndrome (post-QFS) in Japan, and to evaluate the efficacy of minocycline for this condition. PATIENTS AND METHODS: In 20 Coxiella burnetii (C. burnetii) seropositive patients with persistent nonspecific symptoms including general fatigue, low-grade fever, myalgia and arthralgia, changes in subjective symptoms, C. burnetii antibody titers and C. burnetii DNA were evaluated after antibiotic treatment. RESULTS: After treatment mainly with minocycline (100 mg/day for 3 months), the clinical picture improved in all 20 patients as evidenced by decreases in body temperature (13/17), general fatigue (20/20) and headache (9/12). The mean performance status (PS) score improved from 5.0 to 1.8 (p<0.01). All 7 who had been positive for C. burnetii DNA, became negative together with an improvement in subjective symptoms. Indirect immunofluorescence tests demonstrated 6 of the 20 patients to be positive for C. burnetii IgM antibody to phase II antigen (1:32), and 18 to be positive for IgG antibody (1:128, 1:256). Antibody titers of both IgM (6/6, 1:16) and IgG (18/18, 1:16) decreased markedly after treatment. CONCLUSION: These results of an open label study in Japan suggest that minocycline administration is useful for improving chronic nonspecific symptoms considered to be post-Q fever fatigue

				syndrome caused by <i>C. burnetii</i> infection.
Asbring P, Narvanen AL.	Stockholm Center of Public Health, Department of Public Health Sciences, Karolinska Institutet, Stockholm, Sweden.	Patient power and control: a study of women with uncertain illness trajectories.	Qual Health Res. 2004 Feb;14(2):226-40.	The authors interviewed 12 women diagnosed with chronic fatigue syndrome and 13 with fibromyalgia with the aim of determining the strategies they perceive themselves as using to gain control over their situation during the health care process. The results highlight various strategies that the women report applying to find a way of managing the illness and to influence caregivers. They describe, for example, how they try to gain control over their situation by acquiring knowledge about the illness. The women also describe various power strategies they use in their interaction with the caregivers to take command of their situation, namely exiting, noncompliance, confrontation, persuasion/insistence, making demands, and demonstrative distancing.
Ball N, Buchwald DS, Schmidt D, Goldberg J, Ashton S, Armitage R.	Virginia Mason Sleep Disorders Center, University of Washington, Seattle, WA, USA.	Monozygotic twins discordant for chronic fatigue syndrome: objective measures of sleep.	J Psychosom Res. 2004 Feb;56(2):207-12.	PURPOSE: Chronic fatigue syndrome (CFS) is characterized by profound fatigue accompanied by disturbances of sleep, cognition, mood, and other symptoms. Our objective was to describe sleep architecture in CFS-discordant twin pairs. METHODS: We conducted a co-twin control study of 22 pairs of monozygotic twins where one twin met criteria for CFS and the co-twin was healthy. Twins underwent two nights of polysomnography. RESULTS: The percentage of Stage 3 and REM sleep was greater among the CFS twins than their healthy co-twins ($P < .05$ for both), but no other differences in sleep architecture including sleep latency, REM latency, and total sleep time were observed. Compared to their co-twins, CFS twins had higher values for the apnea-hypopnea index and apnea-hypopnea arousal index ($P < .05$ for both). CONCLUSION: These results do not provide strong evidence for a major role for abnormalities in sleep architecture in CFS. Respiration appears impaired in CFS, but these clinical abnormalities cannot alone account for the prominence of sleep complaints in this illness. The co-twin control methodology highlights the importance of selecting well-matched control subjects.
Barlow JH, Ellard DR.	Interdisciplinary Research Centre in Health, School of Health and Social Sciences, Coventry University, Coventry, UK. j.barlow@coventry.ac.uk	Psycho-educational interventions for children with chronic disease, parents and siblings: an overview of the research evidence base.	Child Care Health Dev. 2004 Nov;30(6):637-45.	BACKGROUND: The role of psycho-educational interventions in facilitating adaptation to chronic disease has received growing recognition and is in keeping with policy developments advocating greater involvement of patients in their own care. The purpose of this paper is to provide an overview of the current literature regarding the effectiveness of psycho-educational interventions for children and adolescents with chronic disease, their parents and siblings. METHODS: Electronic searches were conducted using AMED, CINAHL, Cochrane Database, DARE, HTA, MEDLINE, NHS EED, PsycLIT, PsycINFO, and PubMed. Inclusion criteria were systematic reviews, meta-analyses and overviews based on traditional reviews of published literature. The titles of papers were reviewed, abstracts were obtained and reviewed, and full copies of selected papers were obtained. RESULTS: No reviews of psycho-educational interventions were found for either parents or siblings. Twelve reviews of interventions for children and adolescents were identified: chronic disease in general (three); chronic pain (one); asthma (three); chronic fatigue syndrome (CFS)/myalgic encephalomyelitis (ME) (one); diabetes (two); juvenile idiopathic arthritis (JIA) (one) and one informational intervention for paediatric cancer patients. The main focus was on disease management (particularly in asthma and diabetes) with less attention being paid to psychosocial aspects of life with a chronic condition. Overall, there is evidence of effectiveness for interventions incorporating cognitive-behavioural techniques on variables such as self-efficacy, self-management of disease, family functioning, psychosocial well-being, reduced isolation, social competence, knowledge, hope, pain (for chronic headache), lung function (asthma), days absent from school (asthma), visits to A & E (asthma), fatigue (CFS), and metabolic control (diabetes). A number of gaps and limitations were identified across all disease categories, such as inadequate description of interventions, small sample sizes, and lack of evidence regarding cost-effectiveness. CONCLUSION: This overview has highlighted the need to extend the evidence base for psycho-educational interventions, particularly in a UK context. It is essential that effective interventions are implemented and embedded in service provision in order to maximize empowerment through self-care for children, adolescents and their parents.
Baschetti R.		Cost-effectiveness of cognitive behaviour therapy for patients with chronic fatigue syndrome. [Letter]	QJM. 2004 Jun;97(6):378-9.	
Baschetti R.		Chronic fatigue syndrome, pregnancy, and Addison disease.	Arch Intern Med. 2004 Oct 11;164(18):2065. Comment on: Arch Intern Med. 2004 Feb 23;164(4):401-4.	
Bates MN, Fawcett J, Garrett N, Cutress T, Kjellstrom T.	Institute of Environmental Science and Research Ltd. (ESR), PO Box 50-348,	Health effects of dental amalgam exposure: a retrospective cohort study.	Int J Epidemiol. 2004 Aug;33(4):894-902. Epub 2004 May 20.	BACKGROUND: Whether dental amalgam fillings (containing mercury) are hazardous is a long-standing issue, with few epidemiological investigations. Allegations have particularly involved nervous system disorders, such as multiple sclerosis, Alzheimer's disease, and chronic fatigue syndrome. This retrospective cohort study, the largest of its kind, contained people in the New Zealand Defence Force (NZDF) between 1977 and 1997. The NZDF has its own dental service, providing all personnel with

	Porirua, New Zealand.			regular and consistent treatment. Comprehensive treatment records are maintained and archived. METHODS: Yearly dental treatment histories, including amalgam filling placements, were compiled from individual records. To minimize amalgam exposure misclassification the cohort was restricted to people who, at NZDF entry, were aged <26 years and had all their posterior teeth. The cohort was linked with morbidity records. Data were analysed with a proportional hazards model, using a time-varying exposure unit of 100 amalgam surface-years. RESULTS: The final cohort contained 20 000 people, 84% males. Associations with medical diagnostic categories, particularly disorders of the nervous system and kidney, were examined. Of conditions allegedly associated with amalgam, multiple sclerosis had an adjusted hazard ratio (HR) of 1.24 (95% CI: 0.99, 1.53, P = 0.06), but there was no association with chronic fatigue syndrome (HR = 0.98, 95% CI: 0.94, 1.03), or kidney diseases. There were insufficient cases for investigation of Alzheimer's or Parkinson's diseases. CONCLUSIONS: Results were generally reassuring, and provide only limited evidence of an association between amalgam and disease. Further follow-up of the cohort will permit investigation of diseases more common in the elderly.
Benca RM, Ancoli-Israel S, Moldofsky H.	University of Wisconsin, Madison, USA.	Special considerations in insomnia diagnosis and management: depressed, elderly, and chronic pain populations.	J Clin Psychiatry. 2004;65 Suppl 8:26-35.	Patients with insomnia who also have chronic pain or depression or who are elderly represent segments of the population that are particularly difficult to treat. These populations tend to be at higher risk for experiencing difficulty sleeping and are more likely to experience chronic insomnia, sleep maintenance problems, and/or nonrestorative sleep. Worsening insomnia may exacerbate other somatic and psychological symptoms and vice versa. Conversely, there is evidence that appropriate recognition and management of the sleep complaint may alleviate other symptoms related to the associated condition and help interrupt this vicious cycle.
Berger J.		On chronic fatigue syndrome. Comment on: Am J Psychiatry. 2003 Feb;160(2):221-36.	Am J Psychiatry. 2004 Jun;161(6):1133; author reply 1133-4.	
Bierl C, Nisenbaum R, Hoaglin DC, Randall B, Jones AB, Unger ER, Reeves WC.	Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA. wcr1@cdc.gov	Regional distribution of fatiguing illnesses in the United States: a pilot study.	Popul Health Metr. 2004 Feb 4;2(1):1.	BACKGROUND: Chronic fatigue syndrome (CFS) is a debilitating illness with no known cause or effective therapy. Population-based epidemiologic data on CFS prevalence are critical to put CFS in a realistic context for public health officials and others responsible for allocating resources. METHODS: We conducted a pilot random-digit-dialing survey to estimate the prevalence of fatiguing illnesses in different geographic regions and in urban and rural populations of the United States. This report focuses on 884 of 7,317 respondents 18 to 69 years old. Fatigued (440) and randomly selected non-fatigued (444) respondents completed telephone questionnaires concerning fatigue, other symptoms, and medical history. RESULTS: We estimated 12,186 per 100,000 persons 18 to 69 years of age suffered from fatigue lasting for at least 6 months (chronic fatigue), and 1,197 per 100,000 described an illness that, though lacking clinical evaluation, met criteria for CFS (CFS-like). Chronic fatigue and CFS-like illness were more common in rural than in urban populations, although the differences were not significant. The prevalence of these fatiguing illnesses did not differ meaningfully among the four regions surveyed, and no significant geographic trends were observed. CONCLUSIONS: This investigation estimated that nearly 2.2 million American adults suffer from CFS-like illness. The study also suggested the need to focus future investigations of fatigue on populations with lower incomes and less education. There was no evidence for regional differences in the occurrence of fatiguing illnesses.
Blacker CV, Greenwood DT, Wesnes KA, Wilson R, Woodward C, Howe I, Ali T.	Department of Health and Social Sciences, University of Exeter, Exeter, England. c.v.r.blacker@btinternet.com	Effect of galantamine hydrobromide in chronic fatigue syndrome: a randomized controlled trial.	JAMA. 2004 Sep 8;292(10):1195-204.	CONTEXT: There is no established pharmacological treatment for the core symptoms of chronic fatigue syndrome (CFS). Galantamine hydrobromide, an acetyl cholinesterase inhibitor, has pharmacological properties that might benefit patients with CFS. OBJECTIVE: To compare the efficacy and tolerability of galantamine hydrobromide in patients with CFS. DESIGN, SETTING, AND PATIENTS: Randomized, double-blind trial conducted June 1997 through July 1999 at 35 outpatient centers in the United Kingdom (n = 17), United States (n = 14), the Netherlands (n = 2), Sweden (n = 1), and Belgium (n = 1) involving 434 patients with a clinical diagnosis of CFS (modified US Centers for Disease Control and Prevention criteria). INTERVENTIONS: A total of 89 patients were randomly assigned to receive 2.5 mg of galantamine hydrobromide; 86 patients, 5.0 mg; 91 patients, 7.5 mg; and 86 patients, 10 mg (these patients received medicine in the tablet form 3 times per day); a total of 82 patients received matching placebo tablets 3 times per day. MAIN OUTCOME MEASURES: The primary efficacy variable was the global change on the Clinician Global Impression Scale after 4, 8, 12, and 16 weeks of treatment. Secondary outcomes were changes in core symptoms of CFS on the Chalder Fatigue Rating Scale, the Fibromyalgia Impact Questionnaire, and the Pittsburgh Sleep Quality Index; changes in quality of life on the Nottingham Health Profile; and assessment of plasma-free cortisol levels and cognitive performance on a computer-based battery of tests. RESULTS: After 16 weeks, there were no statistically significant differences between any of the galantamine or placebo groups in clinical condition on the Clinician Global Impression Scale, or for any of the secondary end points. Exploratory regression analysis failed to detect any consistent prognostic factor that might have influenced the primary or any secondary outcome measures. CONCLUSION: This trial did not demonstrate any benefit of galantamine over placebo in the treatment of patients with CFS.
Bobo WV, Hall WC.		On chronic fatigue	Am J Psychiatry. 2004	

		syndrome. Comment on: Am J Psychiatry. 2003 Feb;160(2):221-36.	Jun;161(6):1132-3; author reply 1133-4.	
Bruera E, Moyano JR, Sala R, Rico MA, Bosnjak S, Bertolino M, Willey J, Strasser F, Palmer JL.	Department of Palliative Care & Rehabilitation Medicine, The University of Texas MD Anderson Cancer Center, Houston 77030, USA.	Dexamethasone in addition to metoclopramide for chronic nausea in patients with advanced cancer: a randomized controlled trial.	J Pain Symptom Manage. 2004 Oct;28(4):381-8.	Chronic nausea occurs in most patients with advanced cancer. This study was done to assess the antiemetic effects of dexamethasone in patients with chronic nausea refractory to metoclopramide. Secondary outcomes included appetite, fatigue, and pain. Fifty-one patients who had nausea (> or = 3/10 on a 0-10 scale) for > or = 2 weeks despite 48 hours of oral metoclopramide therapy (40-60 mg/day) were enrolled. Patients received 20 mg/day dexamethasone (DM) orally (n = 25) or placebo (n = 26) for severe nausea in addition to metoclopramide (60 mg/day orally). At baseline the mean nausea intensity ratings in the DM and placebo groups were 8.0 and 7.4. At Day 8 they were 2.1 and 2.0, respectively. At Day 3 and Day 8, the mean difference in nausea intensity for the DM and placebo groups was 4.5 and 2.9 (P = 0.16) and 5.9 and 5.7 (P = 0.85), respectively. Improvement in appetite and fatigue were observed on Day 3 and Day 8 in both groups as compared with the baseline. Pain, vomiting, well-being, and quality of life remained unchanged in both groups at both times. We conclude that DM was not superior to placebo in the management of chronic nausea in our patients with advanced cancer.
Brustia D, Uglietti A, Garavelli PL.	SCDO Malattie Infettive, Azienda Sanitaria Ospedaliera Maggiore della Carita, Novara.	[Polyneuritis cranialis HHV-6 infection associated][Article in Italian]	Recenti Prog Med. 2004 May;95(5):257-8.	Human herpesvirus 6 (HHV-6) has been shown to be a common cause of acute febrile disease in young children, including exanthema subitum. HHV-6 has also been associated with a number of neurologic disorders including encephalitis and the virus has been postulated to play a role in acquired immunodeficiency syndrome, multiple sclerosis and chronic fatigue syndrome. The disorder of multiple cranial nerve palsies without spinal cord involvement is referred to as polyneuritis cranialis and is rare. The Authors describe a case of polyneuritis cranialis in a 52-year old woman treated with ganciclovir and only complete eradication of the virus.
Burnet RB, Chatterton BE.		Gastric Emptying is Slow in Chronic Fatigue Syndrome.	BMC Gastroenterol. 2004 Dec 26;4(1):32 [Epub ahead of print]	BACKGROUND: Gastrointestinal symptoms are common in patients with Chronic Fatigue Syndrome (CFS). The objective of this study was to determine the frequency of these symptoms and explore their relationship with objective (radionuclide) studies of upper GI function. METHODS: Thirty-two (32) patients with CFS and 45 control subjects completed a questionnaire on upper GI symptoms, and the 32 patients underwent oesophageal clearance, and simultaneous liquid and solid gastric emptying studies using radionuclide techniques compared with historical controls. RESULTS: The questionnaires showed a significant difference in gastric (p>0.01) symptoms and swallowing difficulty. Nocturnal diarrhoea was a significant symptom not previously reported. 5/32 CFS subjects showed slightly delayed oesophageal clearance, but overall there was no significant difference from the control subjects, nor correlation of oesophageal clearance with symptoms. 23/32 patients showed a delay in liquid gastric emptying, and 12/32 a delay in solid gastric emptying with the delay significantly correlated with the mean symptom score (for each p<<0.001). CONCLUSION: GI symptoms in patients with chronic fatigue syndrome are associated with objective changes of upper GI motility.
Busichio K, Tiersky LA, Deluca J, Natelson BH.	Chronic Fatigue Syndrome Center, Newark, New Jersey 07666, USA.	Neuropsychological deficits in patients with chronic fatigue syndrome.	J Int Neuropsychol Soc. 2004 Mar;10(2):278-85.	The degree of neuropsychological dysfunction across multiple domains was examined in individuals suffering from chronic fatigue syndrome (CFS). In this descriptive study, a similar series of neuropsychological tests was administered to a group of CFS patients and healthy participants. More specifically, CFS patients (n = 141) who met the 1994 Case Definition criteria were compared to 76 healthy control participants on tests of memory, attention (concentration), speed of information processing, motor speed, and executive functioning. On the 18 measures administered, CFS patients scored 1 standard deviation below the healthy mean on nine measures and scored 2 standard deviations below the healthy mean on four of the measures. Moreover, results indicated that CFS patients were more likely than healthy controls to fail (1.6 SD below the healthy mean) at least one test in each of the following domains: attention, speed of information processing, and motor speed, but not on measures of memory and executive functioning. Finally, CFS patients demonstrated a greater total number of tests failed across domains.
Busichio K, Tiersky LA, Deluca J, Natelson BH.	Chronic Fatigue Syndrome Center, Newark, New Jersey.	Neuropsychological deficits in patients with chronic fatigue syndrome.	J Int Neuropsychol Soc. 2004 Feb;:278-285. [Epub ahead of print]	The degree of neuropsychological dysfunction across multiple domains was examined in individuals suffering from chronic fatigue syndrome (CFS). In this descriptive study, a similar series of neuropsychological tests was administered to a group of CFS patients and healthy participants. More specifically, CFS patients (n = 141) who met the 1994 Case Definition criteria were compared to 76 healthy control participants on tests of memory, attention (concentration), speed of information processing, motor speed, and executive functioning. On the 18 measures administered, CFS patients scored 1 standard deviation below the healthy mean on nine measures and scored 2 standard deviations below the healthy mean on four of the measures. Moreover, results indicated that CFS patients were more likely than healthy controls to fail (1.6 SD below the healthy mean) at least one test in each of the following domains: attention, speed of information processing, and motor speed, but not on measures of memory and executive functioning. Finally, CFS patients demonstrated a greater total number of tests failed across domains. (JINS, 2004, 10, 278285.)
Candy B, Chalder T, Cleare AJ, Wessely S,	Department of Psychological	A randomised controlled trial of a	J Psychosom Res. 2004 Jul;57(1):89-94.	OBJECTIVES: Glandular fever is associated with an approximate fivefold increase in fatigue at 6 months. Reduced levels of fitness and illness beliefs may be important predictors of fatigue following glandular fever. We therefore developed a brief

Hotopf M.	Medicine, Guy's, King's and St. Thomas' School of Medicine, 103 Denmark Hill, London SE5 8AZ, UK.	psycho-educational intervention to aid recovery in infectious mononucleosis.		psycho-educational intervention aimed at improving recovery from infectious mononucleosis, and piloted a randomised controlled trial to evaluate the intervention. METHODS: We performed a randomised-controlled trial in primary health care in Southeast London and Kent. Sixty-nine patients aged between 16 and 45 years who were diagnosed, serologically and clinically, with acute infectious mononucleosis between December 1999 and December 2000 were randomised. The control group received a standardised fact-sheet about infectious mononucleosis, which gave no advice on rehabilitation. Patients who were randomised to the intervention received an individual treatment session, two follow-up telephone calls, and an information booklet. Fatigue score 6 months after the onset of infectious mononucleosis was the main outcome measure. RESULTS: Sixty-nine out of 139 patients referred were recruited and randomised. Eighty-seven percent of those recruited completed the Fatigue Questionnaire at 6 months. The intervention was acceptable to all who received it. There were fewer fatigue cases in the intervention group than the control group at 6 months follow-up (odds ratio 0.31, 95% confidence interval 0.09-0.91). CONCLUSIONS: A brief intervention at the diagnosis of infectious mononucleosis is acceptable, and may help prevent the development of chronic fatigue. Definitive randomised controlled trials are required to test the intervention.
Carlo-Stella N, Lorusso L, Candura SM, Cuccia M.	Laboratorio di Immunogenetica, Dipartimento di Genetica e Microbiologia, Universita, Pavia.	[Chronic fatigue syndrome: a review] [Article in Italian]	Recenti Prog Med. 2004 Nov;95(11):546-52;	Chronic fatigue syndrome is a relatively unknown and underdiagnosed entity in Italy where its epidemiology remains uncertain, as well as its etiology, although it causes important disability in those affected. Classification criteria by Fukuda are available to diagnose the syndrome. Its epidemiology indicates that it is probably more frequent in Northern countries and it is described in Gulf War veterans. Etiological hypotheses include infectious diseases, immunology and neurology. Among these hypotheses sickness behavior mimics certain aspects of this syndrome and is characterized by a cytokine imbalance in the central nervous system and in the periphery. There are no valid therapies available at the moment. In the laboratory of Immunogenetics, we are constituting a biological bank of the syndrome to study the immunogenetic aspects of the disease in the hope of delucidating some of the obscure areas of its etiopathogenesis.
Cevik R, Gur A, Acar S, Nas K, Sarac AJ.	Physical Medicine and Rehabilitation, School of Medicine, Dicle University, Diyarbakir, Turkey. fremzi@dicle.edu.tr	Hypothalamic-pituitary-gonadal axis hormones and cortisol in both menstrual phases of women with chronic fatigue syndrome and effect of depressive mood on these hormones.	BMC Musculoskelet Disord. 2004 Dec 08;5(1):47.	BACKGROUND: Chronic fatigue syndrome (CFS) is a disease which defined as medically unexplained, disabling fatigue of 6 months or more duration and often accompanied by several of a long list of physical complaints. We aimed to investigate abnormalities of hypothalamic-pituitary-gonadal (HPG) axis hormones and cortisol concentrations in premenopausal women with CFS and find out effects of depression rate on these hormones. METHODS: We examined follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol, progesterone and cortisol concentrations in 43 premenopausal women (mean age: 32.86 +/- 7.11) with CFS and compared matched 35 healthy controls (mean age: 31.14 +/- 6.19). Patients were divided according to menstrual cycle phases (follicular and luteal) and compared with matched phase controls. Depression rate was assessed by Beck Depression Inventory (BDI), and patients with high BDI scores were compared to patients with low BDI scores. RESULTS: There were no significant differences in FSH, LH, estradiol and progesterone levels in both of menstrual phases of patients versus controls. Cortisol levels were significantly lower in patients compared to controls. There were no significant differences in all hormone levels in patients with high depression scores versus patients with low depression scores. CONCLUSION: In spite of high depression rate, low cortisol concentration and normal HPG axis hormones of both menstrual phases are detected in premenopausal women with CFS. There is no differentiation between patients with high and low depression rate in all hormone levels. Depression condition of CFS may be different from classical depression and evaluation of HPG and HPA axis should be performed for understanding of pathophysiology of CFS and planning of treatment.
Chaudhuri A, Behan PO.	Division of Clinical Neurosciences, Institute of Neurological Sciences, Southern General Hospital, University of Glasgow, 1345 Govan Road, Glasgow G51 4TF, UK. ac54p@udcf.gla.ac.uk	In vivo magnetic resonance spectroscopy in chronic fatigue syndrome.	Prostaglandins Leukot Essent Fatty Acids. 2004 Sep;71(3):181-3.	The pathogenic mechanisms of chronic fatigue syndrome (CFS) are not clearly known. Fatigue, poor short-term memory and muscle pain are the most disabling symptoms in CFS. Research data on magnetic resonance spectroscopy (MRS) of muscles and brain in CFS patients suggest a cellular metabolic abnormality in some cases. 31P MRS of skeletal muscles in a subset of patients indicate early intracellular acidosis in the exercising muscles. 1H MRS of the regional brain areas in CFS have shown increased peaks of choline derived from the cell membrane phospholipids. Cell membrane oxidative stress may offer a common explanation for the observed MRS changes in the muscles and brain of CFS patients and this may have important therapeutic implications. As a research tool, MRS may be used as an objective outcome measure in the intervention studies. In addition, regional brain 1H MRS has the potential for wider use to substantiate a clinical diagnosis of CFS from other disorders of unexplained chronic fatigue.
Chaudhuri A, Behan PO.	Division of Clinical Neurosciences, University of Glasgow, Glasgow G51 4TF, UK. ac54p@udcf.gla.ac.uk	Fatigue in neurological disorders.	Lancet. 2004 Mar 20;363(9413):978-88.	Chronic fatigue is a typical symptom of neurological diseases, and is most disabling in multiple sclerosis, postpoliomyelitis, poststroke, and in chronic fatigue syndrome. Disorders of neuromuscular junction transmission and metabolic diseases cause muscle fatigability, which is characterised by failure to sustain the force of muscle contraction (peripheral fatigue). Fatigue is also seen in diseases that affect the central, peripheral, and autonomic nervous systems (central fatigue). Enhanced perception of effort and limited endurance of sustained physical and mental activities are the main characteristics of central fatigue. Metabolic and structural lesions that disrupt the usual process of activation in pathways interconnecting the basal ganglia, thalamus, limbic system, and higher cortical centre are implicated in the pathophysiological process of central fatigue. A state of pre-existing relative hypocortisolaemia might sensitise the hypothalamic-pituitary-adrenal axis to development of persistent central fatigue

				after stress. The contributions of physiological, cognitive, and affective changes underlying fatigue are variable, and treatment is largely symptomatic and rehabilitative.
Clark C.		Patient organisations in ME and CFS seek only understanding. Comment on: BMJ. 2004 Jun 5;328(7452):1354-7.	BMJ. 2004 Jul 10;329(7457):112-3.	
Cleare AJ, O'Keane V, Miell JP.	Division of Psychological Medicine, The Institute of Psychiatry and Guy's, King's and St Thomas' School of Medicine, London SE5 8AF, UK. a.cleare@iop.kcl.ac.uk	Levels of DHEA and DHEAS and responses to CRH stimulation and hydrocortisone treatment in chronic fatigue syndrome.	Psychoneuroendocrinology. 2004 Jul;29(6):724-32.	Background: An association between chronic fatigue syndrome (CFS) and abnormalities of the hypothalamo-pituitary-adrenal axis has been described, and other adrenal steroid abnormalities have been suggested. Dehydroepiandrosterone (DHEA) and its sulphate (DHEA-S), apart from being a precursor of sex steroids, have other functions associated with memory, depression and sleep. It has been suggested that CFS may be associated with a state of relative DHEA(-S) deficiency. Therefore we investigated basal levels of DHEA(-S), the cortisol/DHEA molar ratio and the responsiveness of DHEA to stimulation by corticotrophin-releasing hormone (CRH). Recent studies have also suggested that low dose hydrocortisone may be effective at reducing fatigue in CFS. We therefore also assessed these parameters prior to and following treatment with low dose oral hydrocortisone. Methods: Basal levels of serum DHEA, DHEAS and cortisol were measured in 16 patients with CFS without depression and in 16 controls matched for age, gender, weight, body mass index and menstrual history. CRH tests (1 g/kg i.v.) were carried out on all subjects and DHEA measured at 0, +30 and +90 min. In the patient group, CRH tests were repeated on two further occasions following treatment with hydrocortisone (5 or 10 mg, p.o.) or placebo for 1 month each in a double-blind cross over study protocol. Results: Basal levels of DHEA were higher in the patient, compared to the control, group (14.1+/-2.2 vs. 9.0+/-0.90 ng/ml, P=0.04), while levels of DHEAS in patients (288.7+/-35.4 microg/dl) were not different from controls (293.7+/-53.8, P=NS). Higher DHEA levels were correlated with higher disability scores. Basal cortisol levels were higher in patients, and consequently the cortisol/DHEA molar ratio did not differ between patients and controls. Levels of DHEA (8.9+/-0.97 ng/ml, P=0.015) and DHEAS (233.4+/-41.6 microg/dl, P=0.03) were lower in patients following treatment with hydrocortisone. There was a rise in DHEA responsiveness to CRH in the patients after treatment but this did not attain significance (AUCc: 2.5+/-1.7 ng/ml h pre-treatment vs. 6.4+/-1.2 ng/ml h post-hydrocortisone, P=0.053). However, those patients who responded fully to hydrocortisone in terms of reduced fatigue scores did show a significantly increased DHEA responsiveness to CRH (AUCc: -1.4+/-2.5 ng/ml h at baseline, 5.0+/-1.2 ng/ml h after active treatment, P=0.029). Conclusions: DHEA levels are raised in CFS and correlate with the degree of self-reported disability. Hydrocortisone therapy leads to a reduction in these levels towards normal, and an increased DHEA response to CRH, most marked in those who show a clinical response to this therapy.
Cleare AJ.	Section of Neurobiology of Mood Disorders, Division of Psychological Medicine, The Institute of Psychiatry, London, SE5 8AF, UK. a.cleare@iop.kcl.ac.uk	The HPA axis and the genesis of chronic fatigue syndrome.	Trends Endocrinol Metab. 2004 Mar;15(2):55-9.	Many studies of patients with long-standing chronic fatigue syndrome (CFS) have found alterations to the hypothalamo-pituitary-adrenal (HPA) axis, including mild hypocortisolism, heightened negative feedback and blunted responses to challenge. However, recent prospective studies of high-risk cohorts suggest that there are no HPA axis changes present during the early stages of the genesis of fatiguing illnesses. Moreover, HPA axis changes can be reversed by modifying behavioural features of the illness, such as inactivity, deconditioning and sleep disturbance. Nevertheless, raising levels of cortisol pharmacologically can temporarily alleviate symptoms of fatigue. This article presents the case that there is no specific change to the HPA axis in CFS and that the observed changes are of multifactorial aetiology, with some factors occurring as a consequence of the illness. Nevertheless, the HPA axis might play a role in exacerbating or perpetuating symptoms late on in the course of the illness.
Cook DB, Lange G, Ciccone DS, Liu WC, Steffener J, Natelson BH.	Chronic Fatigue Syndrome Cooperative Research Center, New Jersey Medical School, Newark, New Jersey 07018, USA. cookdb@njneuromed.org	Functional imaging of pain in patients with primary fibromyalgia.	J Rheumatol. 2004 Feb;31(2):364-78.	OBJECTIVE: To examine the function of the nociceptive system in patients with fibromyalgia (FM) using functional magnetic resonance imaging (fMRI). METHODS: Two groups of women, 9 with FM and 9 pain-free, volunteered to participate. In Experiment 1, we assessed psychophysical responses to painful stimuli and prepared participants for fMRI testing. For Experiment 2, subjects underwent fMRI scanning while receiving painful and nonpainful heat stimuli. Conventional and functional MR images were acquired using a 1.5 T MR scanner. Scanning occurred over 5 conditions. Condition 1 served as a practice session (no stimuli). Conditions 2 and 5 consisted of nonpainful warm stimuli. Conditions 3 and 4 consisted of an absolute thermal pain stimulus (47 degrees C) and a perceptually equivalent pain stimulus delivered in counterbalanced order. RESULTS: Experiment 1 indicated that subjects with FM were significantly more sensitive to experimental heat pain than controls (p < 0.001). In Experiment 2, fMRI data indicated that the FM group exhibited greater activity than controls over multiple brain regions in response to both nonpainful and painful stimuli (p < 0.01). Specifically, in response to nonpainful warm stimuli, FM subjects had significantly greater activity than controls in prefrontal, supplemental motor, insular, and anterior cingulate cortices (p < 0.01). In response to painful stimuli, FM subjects had greater activity in the contralateral insular cortex (p < 0.01). Data from the practice session indicated brain activity in pain-relevant areas for the FM group but not for controls.

				CONCLUSION: Our results provide further evidence for a physiological explanation for FM pain.
Cox IJ, Puri BK.	Faculty of Medicine, Imaging Sciences Department, Imperial College London, Division of Clinical Sciences, Robert Steiner Magnetic Resonance Unit, Hammersmith Campus, Du Cane Road, London W12 0HS, UK. j.cox@imperial.ac.uk	In vivo MR spectroscopy in diagnosis and research of neuropsychiatric disorders.	Prostaglandins Leukot Essent Fatty Acids. 2004 Apr;70(4):357-60.	Magnetic resonance spectroscopy is one of the most important tools for quantitative analysis of chemical composition and structure, and this non-invasive technique is now being applied in vivo to study biochemical processes in those neuropsychiatric disorders that are part of the phospholipid spectrum. Interpretation of a clinical magnetic resonance spectrum can provide information about membrane phospholipid turnover, cellular energetics, neuronal function, selected neurotransmitter activity and intracellular pH. Cerebral proton and phosphorus magnetic resonance spectroscopy findings are summarized in relation to schizophrenia, dyslexia and chronic fatigue syndrome.
Crofford LJ, Young EA, Engleberg NC, Korszun A, Brucksch CB, McClure LA, Brown MB, Demitrack MA.	Department of Internal Medicine, University of Michigan School of Medicine, Ann Arbor, MI, USA. crofford@umich.edu	Basal circadian and pulsatile ACTH and cortisol secretion in patients with fibromyalgia and/or chronic fatigue syndrome.	Brain Behav Immun. 2004 Jul;18(4):314-25.	The objective of this study was to evaluate and compare the basal circadian and pulsatile architecture of the HPA axis in groups of patients with FMS, CFS, or both syndromes with individually matched control groups. Forty patients with either FMS (n = 13), FMS and CFS (n = 12), or CFS (n = 15) were matched by age (18-65), sex, and menstrual status to healthy controls. Subjects were excluded if they met criteria for major Axis I psychiatric disorders by structured clinical interview (SCID). Subjects were admitted to the General Clinical Research Center where meals and activities were standardized. Blood was collected from an intravenous line every 10 min over 24 h for analysis of ACTH and cortisol. Samples were evaluable for ACTH in 36 subject pairs and for cortisol in 37 subject pairs. There was a significant delay in the rate of decline from acrophase to nadir for cortisol levels in patients with FMS (P <.01). Elevation of cortisol in the late evening quiescent period was evident in half of the FMS patients compared with their control group, while cortisol levels were numerically, but not significantly, lower in the overnight period in patients with CFS compared with their control group. Pulsatility analyses did not reveal statistically significant differences between patient and control groups. We conclude that the pattern of differences for basal circadian architecture of HPA axis hormones differs between patients with FMS and CFS compared to their matched control groups. The abnormalities in FMS patients are consistent with loss of HPA axis resiliency.
de Lange FP, Kalkman JS, Bleijenberg G, Hagoort P, van der Werf SP, van der Meer JW, Toni I.	F.C. Donders Centre for Cognitive Neuroimaging, University of Nijmegen, NL-6500 HB Nijmegen, The Netherlands E-mail: floris.delange@fcdonders.kun.nl	Neural correlates of the chronic fatigue syndrome--an fMRI study.	Brain. 2004 Sep;127(Pt 9):1948-57. Epub 2004 Jul 07.	Chronic fatigue syndrome (CFS) is characterized by a debilitating fatigue of unknown aetiology. Patients who suffer from CFS report a variety of physical complaints as well as neuropsychological complaints. Therefore, it is conceivable that the CNS plays a role in the pathophysiology of CFS. The purpose of this study was to investigate neural correlates of CFS, and specifically whether there exists a linkage between disturbances in the motor system and CFS. We measured behavioural performance and cerebral activity using rapid event-related functional MRI in 16 CFS patients and 16 matched healthy controls while they were engaged in a motor imagery task and a control visual imagery task. CFS patients were considerably slower on performance of both tasks, but the increase in reaction time with increasing task load was similar between the groups. Both groups used largely overlapping neural resources. However, during the motor imagery task, CFS patients evoked stronger responses in visually related structures. Furthermore, there was a marked between-groups difference during erroneous performance. In both groups, dorsal anterior cingulate cortex was specifically activated during error trials. Conversely, ventral anterior cingulate cortex was active when healthy controls made an error, but remained inactive when CFS patients made an error. Our results support the notion that CFS may be associated with dysfunctional motor planning. Furthermore, the between-groups differences observed during erroneous performance point to motivational disturbances as a crucial component of CFS.
d'Elia G.	Center for kognitiv psykoterapi i Linkoping. gidelia@telia.com	[Chronic fatigue syndrome in a cognitive perspective. A therapeutic model] [Article in Swedish]	Lakartidningen. 2004 Jan 29;101(5):358-64.	The cognitive approach to the treatment of chronic fatigue syndrome (CSF) is based on a multifactor etiological hypothesis, i.e. inaccurate beliefs and attitudes to the illness interact with pathophysiological processes, ineffective coping behaviours, negative states of mood, social problem, to perpetuate the illness. Patients suffering from CFS are supposed to be hypervigilant to somatic sensations and to interpret them as signs of impending physical catastrophe. The aim of the this paper is to describe the clinical implementation of principles of cognitive therapy in the treatment of CFS. Basic to the treatment approach is a collaborative, listening and empathic attitude, sensitive to the patient's personal beliefs and potential threats to self-esteem. The aim is to develop more useful, functional, formulations of the illness. The patient and the therapist work together to look at how the patient thinks about herself/himself and the illness, detect unhelpful attitudes, thoughts and mental images about the illness, and to make them accessible to Socratic reasoning. Graded behavioural interventions are planned in order to disconfirm unhelpful beliefs and reverse the spiral of tiredness, demoralization and reduced activity. The treatment is structured according to the general principles of cognitive therapy.
Deluca J, Christodoulou C,	Department of Physical Medicine and	Working memory deficits in chronic	J Int Neuropsychol Soc. 2004 Jan;10(1):101-9.	To examine the relative influence of speed of information processing versus working memory ability, CFS participants with psychiatric comorbidity (CFS-Psych) and CFS without a psychiatric history (CFS-noPsych) were examined on tests of visual and

Diamond BJ, Rosenstien ED, Kramer N, Natelson BH.	Rehabilitation, University of Medicine and Dentistry of New Jersey, New Jersey Medical School, Newark, New Jersey, USA. Jdeluca@kmrrec.org	fatigue syndrome: differentiating between speed and accuracy of information processing.		auditory processing speed and visual and auditory working memory. Compared to healthy controls (HC) and a group of participants with rheumatoid arthritis (RA), the CFS-noPsych group displayed significantly reduced performance on tests of information processing speed, but not on tests of working memory. No significant differences were observed between the CFS-Psych group and any other group in the study. The implications of group heterogeneity on the understanding of cognitive impairment in CFS are discussed.
DiVasta AD, Alexander ME.	Division of Adolescent and Young Adult Medicine, Department of Cardiology, Children's Hospital Boston, Harvard Medical School, Boston, Massachusetts 02115, USA. amy.divasta@childrens.harvard.edu	Fainting freshmen and sinking sophomores: cardiovascular issues of the adolescent.	Curr Opin Pediatr. 2004 Aug;16(4):350-6.	PURPOSE OF REVIEW: Syncope is a common symptom in adolescents. The vast majority of cases are the result of benign neurocardiogenic syncope, without associated risk of sudden death. This paper reviews the mainstays of diagnosis and treatment for syncopal episodes, differentiation of syncope from life-threatening arrhythmia and aborted sudden cardiac death, and the patient populations at highest risk for cardiac symptoms and cardiac disease. RECENT FINDINGS: A detailed history (including past medical history and family history that focus on cardiac disease) combined with dynamic physical examination and electrocardiogram identifies the vast majority of adolescents with significant heart disease. Further diagnostic modalities have limited utility. Reassurance and supportive measures remain the treatment of choice, although drug therapy can sometimes be helpful, even if data are limited. Divergent approaches to the screening of the young competitive athlete exist. Particular attention is required in adolescents and young adults with exercise-associated syncope, eating disorders, chronic fatigue syndrome, or history of congenital heart disease. Their symptoms may be either more serious or challenging to manage. SUMMARY: Syncope in the adolescent patient is very common; true cardiac disease is not. The traditional diagnostic screen of history and physical combined with an electrocardiogram will identify the overwhelming majority of patients with significant disease. Patients with abnormalities on this initial office evaluation, history of cardiac disease, or complicating medical illness may benefit from referral to a cardiologist. Even within this patient subset, many will prove to have benign disease.
Dyer C.		Paediatrician cleared of serious professional misconduct.	BMJ. 2004 May 1;328(7447):1035.	
Dyer C.		Teenager seeks to overturn GMC judgment.(Letter)	BMJ. 2004 Feb 7;328(7435):310.	
Edmonds M, McGuire H, Price J.		Exercise therapy for chronic fatigue syndrome.	Cochrane Database Syst Rev. 2004;(3):CD003200.	BACKGROUND: Chronic fatigue syndrome (CFS) is an illness characterised by persistent medically unexplained fatigue. CFS is a serious health-care problem with a prevalence of up to 3%. Treatment strategies for CFS include psychological, physical and pharmacological interventions. OBJECTIVES: To investigate the relative effectiveness of exercise therapy and control treatments for CFS. SEARCH STRATEGY: CCDANCTR-Studies and CENTRAL were searched using "Chronic Fatigue" and Exercise. The Journal of Chronic Fatigue Syndrome and CFS conferences were handsearched. Experts in the field were contacted. Clinicaltrials.gov and controlled-trials.com were searched. SELECTION CRITERIA: Only Randomised Controlled Trials (RCT) including participants with a clinical diagnosis of CFS and of any age were included. DATA COLLECTION AND ANALYSIS: The full articles of studies identified were inspected by two reviewers (ME and HMG). Continuous measures of outcome were combined using standardised mean differences. An overall effect size was calculated for each outcome with 95% confidence intervals. One sensitivity analysis was undertaken to test the robustness of the results. MAIN RESULTS: Nine studies were identified for possible inclusion in this review, and five of those studies were included. At 12 weeks, those receiving exercise therapy were less fatigued than the control participants (SMD -0.77, 95% CIs -1.26 to -0.28). Physical functioning was significantly improved with exercise therapy group (SMD -0.64, CIs -0.96 to -0.33) but there were more dropouts with exercise therapy (RR 1.73, CIs 0.92 to 3.24). Depression was non-significantly improved in the exercise therapy group compared to the control group at 12 weeks (WMD -0.58, 95% CIs -2.08 to 0.92). Participants receiving exercise therapy were less fatigued than those receiving the antidepressant fluoxetine at 12 weeks (WMD -1.24, 95% CIs -5.31 to 2.83). Participants receiving the combination of the two interventions, exercise + fluoxetine, were less fatigued than those receiving exercise therapy alone at 12 weeks, although again the difference did not reach significance (WMD 3.74, 95% CIs -2.16 to 9.64). When exercise therapy was combined with patient education, those receiving the combination were less fatigued than those receiving exercise therapy alone at 12 weeks (WMD 0.70, 95% CIs -1.48 to 2.88). REVIEWERS' CONCLUSIONS: There is encouraging evidence that some patients may benefit from exercise therapy and no evidence that exercise therapy may worsen outcomes on average. However the treatment may be less acceptable to patients than other management approaches, such as rest or pacing. Patients with CFS who are similar to those in these trials should be offered exercise therapy, and their progress monitored. Further high quality randomised studies are needed.

Endresen GK.	Rvematologisk avdeling, Rikshospitalet, 0027 Oslo. gerhard.endresen@rikshospitalet.no	[Systemic Mycoplasma blood infection in fibromyalgia and chronic fatigue syndrome][Article in Norwegian]	Tidsskr Nor Laegeforen. 2004 Jan 22;124(2):203-5.	
Engstrom JW.	Professor of Neurology, Department of Neurology, University of California, San Francisco, California 94143-0114, USA.	Myasthenia gravis: diagnostic mimics.	Semin Neurol. 2004 Jun;24(2):141-7.	The clinical hallmark of myasthenia gravis (MG) is fluctuating, painless weakness of muscles that most often affect extraocular, lower bulbar, or limb musculature. Predicting the probability of successful treatment for the patient assumes that the physician has made an accurate diagnosis. In this review, the practical differential diagnosis of MG is reviewed from the perspective of conditions (at presentation of symptoms and signs) that may mimic the disorder. The differential diagnosis includes disorders that limit eye movements (with or without associated diplopia), cause false-positive laboratory studies, and mimic MG but have normal eye movements. The differential diagnosis includes disorders that affect the upper brainstem, cranial nerves, neuromuscular junction, muscles, or local orbit anatomy. Nonneurological systemic diseases (i.e., encephalopathy, sepsis) can produce fluctuating ptosis or eye movements that can occasionally be confused with MG. Although MG is considered often in the differential diagnosis of weakness or fatigue symptoms that lack a correlate on neurological examination (subjective fatigue, breakaway weakness, chronic fatigue syndrome), MG is almost never found. Copyright 2004 Thieme Medical Publishers, Inc.
Eriksen HR, Ursin H.	Department of Biological and Medical Psychology, University of Bergen, Jonas Lies vei 91, N-5009 Bergen, Norway.	Subjective health complaints, sensitization, and sustained cognitive activation (stress).	J Psychosom Res. 2004 Apr;56(4):445-8.	INTRODUCTION: This review argues that "subjective health complaints" is a better and neutral term for "unexplained medical symptoms." The most common complaints are musculoskeletal pain, gastrointestinal complaints and "pseudoneurology" (tiredness, sleep problems, fatigue, and mood changes). These complaints are common in the general population, but for some these complaints reach a level that requires care and assistance. THEORETICAL ASSUMPTIONS: We suggest that these complaints are based on sensations from what in most people are normal physiological processes. In some individuals these sensations become intolerable. In some cases it may signal somatic disease, in most cases not. Cases without somatic disease, or with minimal somatic findings, occur under diagnoses like burnout, epidemic fatigue, multiple chemical sensitivity, chronic musculoskeletal pain, chronic low back pain, chronic fatigue syndrome, and fibromyalgia. These complaints are particularly common in individuals with low coping and high levels of helplessness and hopelessness. CONCLUSION: The psychobiological mechanisms for this is suggested to be sensitization in neural loops maintained by sustained attention and arousal.
Famularo G, DE Simone C, Trinchieri V, Mosca	Department of Internal Medicine, San Camillo Hospital, Circonvallazione Gianicolense, 00152 Rome, Italy. gfamularo@scamilloforlanini.rm.it.	Carnitines and its congeners: a metabolic pathway to the regulation of immune response and inflammation. .	Ann N Y Acad Sci. 2004 Nov;1033:132-8.	Carnitine and its congeners may regulate the immune networks, and their influence on functions of immune cells predominantly or exclusively relies on carnitine-dependent energy production from fatty acids. A reduced pool of carnitines has been demonstrated in either serum or tissues, or both, from patients with a wide spectrum of disorders characterized by unregulated or impaired immune responses ranging from sepsis syndrome to systemic sclerosis, infection with human immunodeficiency virus, and chronic fatigue syndrome. Furthermore, experimental studies have consistently reported that the deranged immune responses and the less efficient inflammation towards infectious organisms associated with aging may be enhanced or modulated by treatment with carnitines. There is also evidence that carnitine deprivation could adversely affect the course of the sepsis syndrome, at least in experimental models, and preliminary studies suggest that carnitine deficiency is ultimately implicated in the pathophysiology of endotoxin-mediated multiple organ failure. Several data indicate that carnitine deficiency is a contributing factor to the progression of infection with human immunodeficiency virus, and carnitine therapy in those patients could counteract the unregulated process of lymphocyte apoptosis and improve CD4 counts. Some case reports have suggested the use of carnitine for the treatment of the severe lactic acidosis that complicates in some patients the use of reverse transcriptase inhibitors.
Farmer A, Fowler T, Scourfield J, Thapar A.	MRC Social, Genetic, Developmental Psychiatric Research Centre, Institute of Psychiatry, London, UK. spjuaef@iop.kcl.ac.uk.	Prevalence of chronic disabling fatigue in children and adolescents.	Br J Psychiatry. 2004 Jun;184:477-81.	BACKGROUND: The epidemiology of chronic fatiguing illnesses in young people is poorly understood. AIMS: To estimate the lifetime prevalence of different definitions of chronic fatigue in 8- to 17-year-olds. METHOD: Participants came from two population-based twin series. Parents completed self-report questionnaires that inquired whether either child had ever experienced more than a few days of disabling fatigue. Telephone interviews were undertaken for individuals who had experienced such an episode. RESULTS: Questionnaires were returned by 1468 families (65% response rate) and telephone interviews were undertaken regarding 99 of the 129 subjects (77%) who had experienced fatigue. The lifetime prevalence estimates ranged from 2.34% (95% CI 1.75-2.94) for disabling fatigue lasting 3 months to 1.29% (95% CI 0.87-1.71) for a disorder resembling adult operationally defined chronic fatigue syndrome. CONCLUSIONS: From the age of 11 years, young people have similar rates and types of chronic fatiguing illnesses to adults.
Farney RJ, Lugo A, Jensen RL, Walker JM, Cloward TV.	Intermountain Sleep Disorders Center, LDS Hospital, Salt Lake City, UT 84143, USA.	Simultaneous use of antidepressant and antihypertensive medications increases	Chest. 2004 Apr;125(4):1279-85.	BACKGROUND: Essential hypertension and symptoms of depression such as unexplained fatigue and tiredness are frequently encountered in primary medical care clinics. Although, exhaustive evaluation rarely detects unsuspected underlying disorders, obstructive sleep apnea (OSA) is commonly associated with each of these conditions. We tested the hypothesis that therapy with antihypertensive and antidepressant medications predicts the increased likelihood of OSA. METHODS: We analyzed the

	rjfund@msn.com	likelihood of diagnosis of obstructive sleep apnea syndrome.		computer archive of 212,972 patients for prescriptions for antihypertensive medications, antidepressant medications, and International Classification of Diseases, Ninth Revision codes for OSA. Prevalence, prevalence odds ratio (POR), and confidence intervals (CIs) were calculated correcting for gender and age group. RESULTS: The prevalence rates of OSA were 0.8%, 2.8%, and 3.2% for men and 0.4%, 1.4%, and 1.8% for women aged 20 to 39 years, 40 to 59 years, and \geq 60 years, respectively. Compared to groups of corresponding age and gender who had not received prescriptions for either hypertension or depression, the highest PORs were found in patients receiving medications from both categories: 18.30 (95% CI, 10.69 to 25.66), 5.72 (95% CI, 4.10 to 6.70), and 4.47 (95% CI, 2.45 to 7.01) for men, and 17.43 (95% CI, 9.54 to 28.67), 7.29 (95% CI, 5.20 to 9.29), and 2.72 (95% CI, 1.48 to 4.73) for women. CONCLUSIONS: We found that the likelihood of having a diagnosis of OSA increases when either antihypertensive or antidepressant medications have been prescribed. The probability is highest in the young and middle-age groups receiving prescriptions for both medications. The possibility of OSA should be considered in any patient with hypertension and depression or unexplained fatigue who is receiving antihypertensive and antidepressant medications.
Gaab J, Engert V, Heitz V, Schad T, Schurmeyer TH, Ehlert U.	Center for Psychobiological and Psychosomatic Research, University of Trier, Germany.	Associations between neuroendocrine responses to the Insulin Tolerance Test and patient characteristics in chronic fatigue syndrome.	J Psychosom Res. 2004 Apr;56(4):419-24.	OBJECTIVE: Subtle dysregulations of the hypothalamic-pituitary-adrenal (HPA) axis have been proposed as an underlying pathophysiological mechanism in chronic fatigue syndrome (CFS). This study attempted to assess the relationship between patient characteristics and HPA axis functioning using a neuroendocrine challenge test. METHOD: A test battery designed to assess different dimensions of CFS was given to 18 CFS patients and 17 controls. To evaluate the integrity of the HPA axis, the Insulin Tolerance Test (ITT), a centrally acting neuroendocrine challenge test, was performed on patients and controls. ACTH, salivary free cortisol and total plasma cortisol levels were assessed as a measure of the HPA axis stress response. Correlations of patient characteristics were calculated with integrated responses for all endocrine parameters. RESULTS: CFS patients had a significantly reduced area under the ACTH response curve (AUC) in the ITT. The AUC was significantly associated with the duration of CFS symptoms ($r=-.592$, $P=.005$) and the severity of fatigue symptomatology ($r=-.41$, $P=.045$). In addition, duration of CFS was correlated with the severity of fatigue symptoms ($r=.38$, $P=.045$). Similar associations were not observed for cortisol parameters. CONCLUSION: It has been postulated that neuroendocrine dysregulations observed in CFS are of an acquired nature. The results of a strong association between the integrated ACTH response and the duration of CFS emphasizes the need to consider factors known to be risk factors for the chronicity of CFS symptoms, such as profound inactivity, deconditioning and sleep abnormalities, as possible candidates for secondary causes of neuroendocrine dysregulations in CFS.
Gallagher AM, Thomas JM, Hamilton WT, White PD.	Centre for Psychiatry and Department of Information Services, Queen Mary School of Medicine and Dentistry, St Bartholomew's Hospital, London EC1A 7BE.	Incidence of fatigue symptoms and diagnoses presenting in UK primary care from 1990 to 2001.	J R Soc Med. 2004 Dec;97(12):571-5.	Little is known about whether the incidence of symptoms of fatigue presented in primary care, and the consequent diagnoses made, change over time. The UK General Practice Research Database was used to investigate the annual incidence of both fatigue symptoms and diagnoses recorded in UK primary care from 1990 to 2001. The overall incidence of all fatigue diagnoses decreased from 87 per 100 000 patients in 1990 to 49 in 2001, a reduction of 44%, while postviral fatigue syndromes decreased from 81% of all fatigue diagnoses in 1990 to 60% in 2001. Chronic fatigue syndrome (CFS) and myalgic encephalomyelitis (ME) together increased from 9% to 26% of all fatigue diagnoses. The incidence of fibromyalgia increased from less than 1 per 100 000 to 35 per 100 000. In contrast, there was no consistent change in the incidence of all recorded symptoms of fatigue, with an average of 1503 per 100 000, equivalent to 1.5% per year. CFS/ME and fibromyalgia were rarely diagnosed in children and were uncommon in the elderly. All symptoms and diagnoses were more common in females than in males. The overall incidence of fatigue diagnoses in general has fallen, but the incidence rates of the specific diagnoses of CFS/ME and fibromyalgia have risen, against a background of little change in symptom reporting. This is likely to reflect fashions in diagnostic labelling rather than true changes in incidence.
Garralda ME, Rangel L.	Academic Unit of Child and Adolescent Psychiatry, Imperial College, Faculty of Medicine, London, UK. e.garralda@imperial.ac.uk	Impairment and coping in children and adolescents with chronic fatigue syndrome: a comparative study with other paediatric disorders.	J Child Psychol Psychiatry. 2004 Mar;45(3):543-52.	BACKGROUND: Functional impairment is a key feature of chronic fatigue syndrome (CFS) of childhood. AIM: To compare impairment, illness attitudes and coping mechanisms in childhood CFS and in other paediatric disorders. METHOD: Participants were 28 children and adolescents with CFS, 30 with juvenile idiopathic arthritis (JIA) and 27 with emotional disorders (ED). The measures used were interviews with children and parents, with detailed enquiry on impairment, including the Functional Disability Inventory (FDI), Illness Attitudes Scales (IAS), and Kidcope to measure coping styles in relation to common problems, illness and disability. RESULTS: Children with CFS reported significantly more illness impairment, especially in school attendance, than those with JIA and ED. They had higher 'worry about illness' scores on the IAS. On the Kidcope they named school issues (work, expectations, attendance) as illness- or disability-related problems more than the other two groups. Fewer CFS participants reported using problem solving as a strategy to cope with illness and disability than with other problems in their lives. More in the CFS than in the JIA group used emotional regulation to cope with illness and disability. Fewer in the CFS than in the ED groups used social withdrawal to cope with illness and self-criticism for disability, but more used resignation to cope with disability. CONCLUSION: Severe illness-related impairment, particularly through school non-attendance, and high levels of illness-related school concerns appear specific to CFS. CFS may also have characteristically high levels of generalised illness worry and particular styles of coping with illness and disability.
Gill AC, Dosen A,	Department of General	Chronic fatigue	Arch Pediatr Adolesc	OBJECTIVES: To compare the frequency of persistent symptoms up to 8 years after illness onset in adolescents diagnosed as

Ziegler JB.	Pediatrics, Sydney Children's Hospital, Sydney, Australia.	syndrome in adolescents: a follow-up study. Comment in: Arch Pediatr Adolesc Med. 2004 Mar;158(3):207-8.	Med. 2004 Mar;158(3):225-9.	having chronic fatigue syndrome, idiopathic chronic fatigue, and unexplained fatigue for less than 6 months, and to determine if hospital admission is associated with outcome. DESIGN: A cohort study using questionnaire follow-up. SETTING: A tertiary referral hospital. PATIENTS: Consecutive adolescents referred for assessment of persistent fatigue were identified and retrospectively divided into 3 groups according to the diagnostic criteria for chronic fatigue syndrome and idiopathic chronic fatigue. INTERVENTION: A questionnaire was designed and administered by telephone at a mean of 4.57 years after the initial examination. MAIN OUTCOME MEASURE: The persistence of self-reported symptoms was compared with respect to patient group and admission. RESULTS: Outcome data were obtained for 34 (69%) of the 49 eligible subjects. Twenty-five percent of the chronic fatigue syndrome group showed near to complete improvement, 31% showed partial improvement, and 44% showed no improvement. The idiopathic chronic fatigue group had near to complete recovery in 50%, partial in 10%, and no improvement in 40%. Those with unexplained fatigue for less than 6 months had all recovered. There was no difference between the outcome of the subjects admitted to the hospital and those managed as outpatients. CONCLUSIONS: Adolescents with less than 6 months of fatigue have a good outcome. Unexplained fatigue lasting more than 6 months has a similar outcome regardless of the presence of minor criteria for chronic fatigue syndrome.
Glass JM, Lyden AK, Petzke F, Stein P, Whalen G, Ambrose K, Chrousos G, Clauw DJ.	Department of Psychiatry and Institute for Social Research, University of Michigan, Ann Arbor, MI, USA. jglass@umich.edu	The effect of brief exercise cessation on pain, fatigue, and mood symptom development in healthy, fit individuals.	J Psychosom Res. 2004 Oct;57(4):391-8.	OBJECTIVE: Abnormalities of the biological stress response (hypothalamic-pituitary-adrenal axis and the autonomic nervous system) have been identified in both fibromyalgia (FM) and chronic fatigue syndrome (CFS). Although these changes have been considered to be partly responsible for symptom expression, we examine an alternative hypothesis that these HPA and autonomic changes can be found in subsets of healthy individuals in the general population who may be at risk of developing these conditions. Exposure to "stressors" (e.g., infections, trauma, etc.) may lead to symptom expression (pain, fatigue, and other somatic symptoms) in part by precipitating lifestyle changes. In particular, we focus on the effect of deprivation of routine aerobic exercise on the development of somatic symptoms. METHODS: Eighteen regularly exercising (≥ 4 h/week) asymptomatic, healthy adults refrained from physical activity for 1 week. We predicted that a subset of these individuals would develop symptoms of FM/CFS with exercise deprivation, and this manuscript focuses on the baseline HPA axis, immune, and autonomic function measures that may predict the development of symptoms. RESULTS: Eight of the subjects reported a 10% increase in one or more symptoms (pain, fatigue, mood) after 1 week of exercise deprivation. These symptomatic subjects had lower HPA axis (baseline cortisol prior to VO ₂ max testing), immune (NK cell responsiveness to venipuncture), and autonomic function (measured by heart rate variability) at baseline (prior to cessation of exercise) when compared to the subjects who did not develop symptoms. CONCLUSIONS: A subset of subjects developed symptoms of pain, fatigue, or mood changes after exercise deprivation. This cohort was different from the individuals who did not develop symptoms in baseline measures of HPA axis, immune, and autonomic function. We speculate that a subset of healthy individuals who have hypoactive function of the biological stress response systems unknowingly exercise regularly to augment the function of these systems and thus suppress symptoms. These individuals may be at risk for developing chronic multisymptom illnesses (CMIs) (e.g., FM or CFS among others) when a "stressor" leads to lifestyle changes that disrupt regular exercise.
Glise K, Bjorkman A.	Institutet for stressmedicin, Goteborg. kristina.glise@stressmedicin.com	[The burnout syndrome-clinical picture and therapy][Article in Swedish]	Lakartidningen. 2004 Mar 25;101(13):1202-6.	
Gur A, Cevik R, Nas K, Colpan L, Sarac S.	Department of Physical Medicine and Rehabilitation, School of Medicine, Dicle University, Diyarbakir, Turkey. alig@dicle.edu.tr	Cortisol and hypothalamic-pituitary-gonadal axis hormones in follicular-phase women with fibromyalgia and chronic fatigue syndrome and effect of depressive symptoms on these hormones.	Arthritis Res Ther. 2004;6(3):R232-8. Epub 2004 Mar 15.	We investigated abnormalities of the hypothalamic-pituitary-gonadal axis and cortisol concentrations in women with fibromyalgia and chronic fatigue syndrome (CFS) who were in the follicular phase of their menstrual cycle, and whether their scores for depressive symptoms were related to levels of these hormones. A total of 176 subjects participated - 46 healthy volunteers, 68 patients with fibromyalgia, and 62 patients with CFS. We examined concentrations of follicle-stimulating hormone, luteinizing hormone (LH), estradiol, progesterone, prolactin, and cortisol. Depressive symptoms were assessed using the Beck Depression Inventory (BDI). Cortisol levels were significantly lower in patients with fibromyalgia or CFS than in healthy controls ($P < 0.05$); there were no significant differences in other hormone levels between the three groups. Fibromyalgia patients with high BDI scores had significantly lower cortisol levels than controls ($P < 0.05$), and so did CFS patients, regardless of their BDI scores ($P < 0.05$). Among patients without depressive symptoms, cortisol levels were lower in CFS than in fibromyalgia ($P < 0.05$). Our study suggests that in spite of low morning cortisol concentrations, the only abnormalities in hypothalamic-pituitary-gonadal axis hormones among follicular-phase women with fibromyalgia or CFS are those of LH levels in fibromyalgia patients with a low BDI score. Depression may lower cortisol and LH levels, or, alternatively, low morning cortisol may be a biological factor that contributes to depressive symptoms in fibromyalgia. These parameters therefore must be taken into account in future investigations.
Hamlen R.	rhamlen@iximd.com	Lyme borreliosis:	Lancet Infect Dis. 2004	

		perspective of a scientist-patient.	Oct;4(10):603-4. Comment on: Lancet Infect Dis. 2003 Aug;3(8):489-500.	
Hartz AJ, Bentler S, Noyes R, Hoehns J, Logemann C, Sinift S, Butani Y, Wang W, Brake K, Ernst M, Kautzman H. .	University of Iowa, College of Medicine, Department of Family Medicine, Iowa City 52242-1097, USA	Randomized controlled trial of Siberian ginseng for chronic fatigue.	Psychol Med. 2004 Jan;34(1):51-61.	BACKGROUND: Chronic fatigue greatly affects quality of life and is a common reason for consulting a physician. Since conventional therapy is often of limited help, fatigued patients may use herbal treatments. This randomized controlled trial evaluated the effectiveness of Siberian ginseng. METHOD: Subjects were recruited from advertisements in Iowa (82%) and members of chronic fatigue syndrome support groups (18%). Potential subjects were required to have substantial fatigue > or = 6 months with no identifiable cause. The mean change in a fatigue measure was compared for placebo and Siberian ginseng at 1 and 2 months. Comparisons were for all subjects and for subjects with characteristics previously identified in the literature as important for categorizing chronic fatigue. RESULTS: Ninety-six subjects were randomized to treatment groups, and 76 provided information at 2 months of follow-up. Fatigue among subjects assigned to either placebo or Siberian ginseng was substantially reduced during the study, but differences between treatment groups were not statistically significant in the full sample. Fatigue severity and duration had a statistically significant interaction with response to Siberian ginseng at the P < 0.05 level. Treatment was effective at 2 months for 45 subjects with less severe fatigue (P = 0.04 unadjusted for multiple comparisons) and for 41 subjects with fatigue for > or = 5 years (P = 0.09 unadjusted for multiple comparisons). CONCLUSION: Overall efficacy was not demonstrated. However, the findings of possible efficacy for patients with moderate fatigue suggests that further research may be of value.
Hausotter W.		[Appraisal of Lyme borreliosis][Article in German]	Versicherungsmedizin. 2004 Mar 1;56(1):25-9.	Lyme borreliosis is due to infection with a tick-borne spirochete. The variety of signs and symptoms and also the laboratory tests of this multisystem illness often cause great problems in the appraisal of this disease. Frequently indispositions are associated with positive antibody tests for Borrelia burgdorferi. Terms as fibromyalgia or chronic fatigue syndrome are often connected with the diagnosis of Lyme disease. Outdoor workers such as farmers, foresters, hunters, woodcutters and gamekeepers in areas of endemic disease take a great occupational risk of infection with borreliosis. In the German health and social insurance the appraisal of this disease is of great importance. Affected working people can receive financial compensation. Not only serological investigations with the presence of specific antibodies, but also clinical findings must be considered.
Heim C, Bierl C, Nisenbaum R, Wagner D, Reeves WC.	Division of Viral and Rickettsial Diseases, Viral Exanthems and Herpesvirus Branch, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, USA. cmheim@emory.edu	Regional prevalence of fatiguing illnesses in the United States before and after the terrorist attacks of September 11, 2001.	Psychosom Med. 2004 Sep-Oct;66(5):672-8.	OBJECTIVE: Stress or emotional traumas are considered risk factors for unexplained fatiguing illnesses. From July to December 2001, the Centers for Disease Control and Prevention conducted a multigeographical pilot study to test the feasibility of a survey to estimate the prevalence of fatiguing illnesses in the United States. We used data obtained during this survey to estimate the effect of the coincidentally occurring terrorist attacks of September 11, 2001, on the regional prevalence of fatiguing illnesses. METHODS: Identified by random-digit dialing, 2,728 households in eight regional strata were interviewed, and 7,317 respondents were screened for severe fatigue of at least 1 month duration. Identified fatigued people of age 18 to 69 years (N = 440) and a sample of nonfatigued people of the same age range (N = 444) were interviewed in detail concerning fatigue, other symptoms, and medical and psychiatric histories. RESULTS: Weighted prevalence estimates based on interviews performed after the attacks were significantly lower compared with estimates based on interviews performed before the attacks (prolonged fatigue: 5,450 vs. 1,530/100,000, p = .010; chronic fatigue: 18,510 vs. 10,070/100,000, p = .002; chronic fatigue syndrome-like illness: 2,510 vs. 960/100,000, p = .014). CONCLUSION: Our findings suggest decreased regional prevalence of fatiguing illnesses in the aftermath of the terrorist attacks. The causes of this effect are unknown but might involve acute psychological and physiological adaptations that modify the perception or manifestation of fatigue. Future studies should be specifically designed to scrutinize the relationship between stress and fatiguing illnesses and the mediating mechanisms of such a relationship.
Henderson M, Tannock C.	Academic Department of Psychological Medicine, GKT School of Medicine and Institute of Psychiatry, Guys Kings and St. Thomas' Hospital, Weston Education Centre, Cutcombe Road, London SE5 9RJ, UK. m.henderson@iop.kcl.ac.uk	Objective assessment of personality disorder in chronic fatigue syndrome.	J Psychosom Res. 2004 Feb;56(2):251-4.	OBJECTIVES: This study aims to objectively assess the prevalence and nature of personality disorders in depressed and nondepressed chronic fatigue syndrome (CFS) patients and compare this to depressed and healthy control groups. METHODS: Sixty-one patients attending a tertiary referral clinic with chronic fatigue syndrome, 40 psychiatric inpatients with depressive disorder and 45 healthy medical students completed the Structured Clinical Interview for DSM-III-R Diagnoses (SCID-II) in addition to providing routine clinical and demographic information. RESULTS: Thirty-nine percent of the CFS group, 73% of the depressed group and 4% of the healthy group were diagnosed with personality disorders. Cluster C disorders were the most common in both the CFS and depressed group. The depressed CFS patients had more Cluster B personality disorders than nondepressed CFS patients. Overall for CFS patients there was no association between mood state and personality disorder. CONCLUSIONS: High levels of personality disorder are found on objective assessment of CFS patients attending a teaching hospital clinic. This cannot be accounted for by comorbid depression.
Horton-Salway M.	Department of Social	The local production of	Health (London). 2004	This article uses discursive psychology to analyse how knowledge claims and entitlements are locally produced in an ME support

	Sciences, Open University, UK. mkhs2@tutor.open.ac.uk	knowledge: disease labels, identities and category entitlements in ME support group talk.	Jul;8(3):351-71.	group meeting and a research interview. The article demonstrates how 'expertise' and 'experience' associated with lay and professional membership are locally constituted in the activity of reasoning, arguing and claims making. The analysis shows how expertise and experiential claims are constructed, disclaimed, warranted and undermined in relationship to membership categorization and entitlements to knowledge that are co-constructed in the process of a discussion about disease labels and the nature of the illness as physical or psychological. In a discussion about the definition of contested disease categories, what is 'at stake' for the group members is the entitlement to speak from experience as members who can 'know' their own minds.
Huibers MJ, Bleijenberg G, van Amelsvoort LG, Beurskens AJ, van Schayck CP, Bazelmans E, Knottnerus JA.	Department of Epidemiology, Maastricht University, P.O. Box 616, Maastricht 6200 MD, The Netherlands; Department of Medical Psychology, UMC Nijmegen, The Netherlands; Department of General Practice, Maastricht University, P.O. Box 616, Maastricht 6200 MD, The Netherlands.	Predictors of outcome in fatigued employees on sick leave Results from a randomised trial.	J Psychosom Res. 2004 Nov;57(5):443-449.	OBJECTIVE: The main objective of this study was to identify predictors of fatigue caseness, work resumption and chronic fatigue syndrome (CFS)-like caseness in a sample of fatigued employees on sick leave. METHODS: For 12 months, 151 fatigued employees on sick leave, 44% of whom met research criteria for CFS at baseline, were followed. Measures included fatigue, health aspects, psychological problems, burnout, causal attributions and self-efficacy. Logistic regression analysis was used to determine associations between predictor variables at baseline and outcome at follow-up. RESULTS: After 12 months, 43% of the patients were no longer fatigue cases, and 62% had resumed work. Recovery from fatigue caseness was predicted by stronger psychological attributions and other perception-related factors, whereas work resumption was predicted by lower age, male sex, CFS-like caseness and less cognitive difficulties. Lower physical functioning scores were predictive of (the development of) CFS-like caseness. CONCLUSION: Recovering from persistent fatigue and work resumption seem to result from different underlying processes and do not necessarily fall together. As many factors associated with outcome in fatigue reflect illness perception, the prevention of persistent fatigue and CFS may partly be achieved by the modification of perception.
Huibers MJ, Beurskens AJ, Van Schayck CP, Bazelmans E, Metsemakers JF, Knottnerus JA, Bleijenberg G.	Department of Epidemiology, Maastricht University, The Netherlands. m.huibers@dmkep.unimaa.nl	Efficacy of cognitive-behavioural therapy by general practitioners for unexplained fatigue among employees: Randomised controlled trial.	Br J Psychiatry. 2004 Mar;184:240-6.	BACKGROUND: Fatigue is a common complaint that may lead to long-term sick leave and work disability. AIMS: To assess the efficacy of cognitive-behavioural therapy by general practitioners for unexplained, persistent fatigue among employees. METHOD: A randomised controlled trial, using a pre-randomisation design in primary care, investigated 151 employees on sick leave with fatigue. Participants in the experimental group were offered five to seven 30 min sessions of cognitive-behavioural therapy by a general practitioner; those in the control group were offered no treatment. Main outcome measures (fatigue severity, self-reported absenteeism, registered absenteeism and clinical recovery) were assessed at 4 months, 8 months and 12 months. RESULTS: At baseline, 44% of the patients already met research criteria for chronic fatigue syndrome. There was no significant difference between the experimental group and the control group on primary or secondary outcomes at any point. CONCLUSIONS: Cognitive-behavioural therapy by general practitioners for unexplained, persistent fatigue did not prove to be an effective intervention. Since these doctors were unable to deliver this therapy effectively under ideal circumstances, it is unlikely that doctors in routine practice would be more successful in doing so.
Huibers MJ, Kant IJ, Knottnerus JA, Bleijenberg G, Swaen GM, Kasl SV.	Department of Epidemiology, Maastricht University, PO Box 616, 6200 MD Maastricht, Netherlands. m.huibers@dmkep.unimaa.nl	Development of the chronic fatigue syndrome in severely fatigued employees: predictors of outcome in the Maastricht cohort study.	J Epidemiol Community Health. 2004 Oct;58(10):877-82.	STUDY OBJECTIVE: To identify risk factors of the development of the chronic fatigue syndrome (CFS), the persistence or recurrence of fatigue, or recovery from fatigue in a large sample of fatigued employees. DESIGN: Analyses were based on the Maastricht cohort study (MCS), a prospective population based cohort study among more than 12 000 employees. Multiple regression models were used to identify predictors of CFS-like caseness (meeting research criteria for CFS), non-CFS fatigue caseness, or no fatigue caseness. SETTING: The working population in the Netherlands. PARTICIPANTS: 1143 employees with medically unexplained fatigue were followed up prospectively for 44 months. MAIN RESULTS: At 44 month follow up, 8% of the employees were CFS-like cases (none of who reported to have received a CFS diagnosis), 40% were non-CFS fatigue cases, and 52% were no longer fatigue cases. Factors that predicted CFS-like caseness compared with non-CFS fatigue caseness were high age, exhaustion, female sex, low education, and visits to the general practitioner. Factors that predicted CFS-like caseness compared with no fatigue caseness were fatigue, exhaustion, low education, visits to the GP and occupational physician, and bad self rated health. Factors that predicted non-CFS fatigue caseness compared with no fatigue caseness were fatigue, low self perceived activity, exhaustion, anxious mood, and bad self rated health. CONCLUSIONS: Unexplained fatigue among employees in some instances is a precursor of the development of CFS. The prognostic role of self rated health suggests that prevention and treatment of chronic fatigue should be aimed at changing the perception of health or illness. Less clear is the role of health care seeking or receiving a CFS diagnosis.
Huibers MJ, Kant IJ, Swaen GM, Kasl SV.	Department of Medical, Clinical & Experimental Psychology, Maastricht University, Netherlands. marcus.huibers@hag.un	Prevalence of chronic fatigue syndrome-like caseness in the working population: results from the Maastricht cohort	Occup Environ Med. 2004 May;61(5):464-6.	AIM: To determine the prevalence of chronic fatigue syndrome (CFS)-like caseness in the working population. METHODS: Using data from the prospective Maastricht Cohort Study on Fatigue at Work, the prevalence and incidence of CFS-like cases (employees meeting research criteria for CFS) were determined among 5499 employees who responded to the follow up assessment 3 years and 8 months after baseline. RESULTS: Of the 5499 employees, 199 (3.6%) were identified as CFS-like cases. By deleting possible CFS-like cases at baseline, the annual incidence of CFS-like caseness was estimated to be 85 per 10

	imaas.nl	study.		000. Twenty employees (0.36%) reported having been diagnosed with CFS by a physician. CONCLUSIONS: The prevalence of CFS-like cases (3.6%) was considerably higher than the prevalence of CFS reported in previous studies (0.006-3%). These findings suggest that the CFS-like caseness may be underdetected in the working population and perhaps in other populations as well.
Jason LA, Torres-Harding SR, Jurgens A, Helgerson J.		Comparing the Fukuda et al. Criteria and the Canadian Case Definition for Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2004; 12(1):37-52.	Fibromyalgia syndrome (FMS) is characterized by widespread pain, fatigue, sleep abnormalities, and distress. Because FMS lacks consistent evidence for tissue abnormalities, recent investigations have focused on central nervous system mechanisms of pain. Abnormal temporal summation of second pain (AWindup@) and central sensitization (CS) have recently been described in FMS patients. Windup (WU) and central sensitization, which rely on central pain mechanisms, occur after prolonged C-nociceptor input and depend on activation of nociceptor specific neurons as well as wide dynamic range neurons in the dorsal horn of the spinal cord. The important role of WU is also supported by its ability to predict the clinical pain intensity of FMS patients. Furthermore, brain-imaging techniques that can detect neuronal activation following nociceptive stimuli have provided additional evidence for abnormal central pain mechanisms in FMS. Most importantly, brain images have corroborated the augmented reported pain experience of FMS patients during experimental pain stimuli. These findings may have important implications for future research as well as the treatment of FMS pain.
Jason LA PhD, Susan R. Torres-Harding PHD, Amber Jurgens BA, Jean Helgerson BA		Article: Comparing the Fukuda et al. Criteria and the Canadian Case Definition for Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2004 12 (1): 37- 52	Because the pathogenesis of Chronic Fatigue Syndrome (CFS) has yet to be determined, case definitions have relied on clinical observation in classifying signs and symptoms for diagnosis. The selection of diagnostic signs and symptoms has major implications for which individuals are diagnosed with CFS and how seriously the illness is viewed by health care providers, disability insurers and rehabilitation planners, and patients and their families and friends. Diagnostic criteria also have implications for whether research based on varying definitions can be synthesized. The current investigation examined differences between CFS as defined by Fukuda et al. (1994) and a set of criteria that has been proposed for a clinical Canadian Case definition. There were twentythree participants who met the Canadian criteria, 12 in the CFS (Fukuda et al. (7) criteria) group and the 33 from the chronic fatigue (CF)-psychiatric group. Dependent measures included: work status, psychiatric comorbidity, symptoms, and functional impairment (measured by the Medical Outcomes Study). People meeting the Fukuda et al. and Canadian criteria were compared with people who had a chronically fatiguing illness explained by a psychiatric condition. Statistical tests used included binomial logistic regression and analysis of variance. The Canadian criteria group, in contrast to the Fukuda et al. criteria group, had more variables that statistically significantly differentiated them from the psychiatric comparison group. Overall, there were 17 symptom differences between the Canadian and CF-psychiatric group, but only 7 symptom differences between the CFS and CF-psychiatric group. The findings suggest that both the Canadian and Fukuda et al. case definitions select individuals who are statistically significantly different from psychiatric controls with chronic fatigue, with the Canadian criteria selecting cases with less psychiatric co-morbidity, more physical functional impairment, and more fatigue/weakness, neuropsychiatric, and neurological symptoms.
Jiang SY, Yan JT, Fang M.	Department of Tuina, Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine, Shanghai 200437, China. jsysy@tom.com	[Progress in research on chronic fatigue syndrome] [Article in Chinese]	Zhong Xi Yi Jie He Xue Bao. 2004 Nov;2(6):459-63.	
Jones JF, Nisenbaum R, Solomon L, Reyes M, Reeves WC.	National Jewish Medical and Research Center, Denver, Colorado, USA.	Chronic fatigue syndrome and other fatiguing illnesses in adolescents: a population-based study.	J Adolesc Health. 2004 Jul;35(1):34-40.	PURPOSE: To estimate the prevalence of chronic fatigue syndrome (CFS) and describe characteristics of other fatiguing illnesses in adolescents (aged 12 through 17 years). METHODS: We conducted a random digit dialing survey of the residents of Wichita, Kansas. Adults identified fatigued adolescents in the household and answered questions relating to the child's health. Selected adolescents were invited to attend a clinic with a parent/guardian. After clinical evaluation they were classified as CFS or another fatigue state as defined in the 1994 CFS definition. Annual telephone interviews and clinical evaluations monitored subjects' fatigue status. Data were analyzed using the Kruskal-Wallis test, the Mantel-Haenszel test, and the exact McNemar test. RESULTS: The survey contacted 34,018 households with 90,316 residents. Of 8586 adolescents, 138 had fatigue for > or =1 month and most (107 or 78%) had chronic fatigue (> or =6 months) at some point during the 3-year follow-up. Twenty-eight had exclusionary diagnoses. Thirty-one were considered to have a CFS-like illness and were invited for clinical evaluation. Eleven agreed to participate and none met the CFS case definition. The baseline weighted prevalence of CFS-like illness was 338 per 100,000. Significant differences existed between parental and adolescents' descriptions of illness. CONCLUSIONS: The

				prevalence of CFS among adolescents was considerably lower than among adults. Evaluation of CFS in adolescents must consider both parent and patient perception of fatigue and other illnesses that might explain the symptom complex.
Kapfhammer HP, Rothenhausler HB.	Universitätsklinik für Psychiatrie Auenbruggerplatz 31, A-8036 Graz/Osterreich. Hans-Peter.Kapfhammer@klinikum-graz.at	[Chronic fatigue syndrome] [Article in German]	MMW Fortschr Med. 2004 Jul 22;146(29-30):29, 31-3.	The symptoms of fatigue and exhaustion, which are central to chronic fatigue syndrome and neurasthenia, can lay claim to being "psychopathological entities" in their own right. Although ubiquitous, they by no means reflect a homogeneous clinical picture. Chronic fatigue may occur after physical illness, such as viral infections, or be associated with a range of different psychiatric disorders. There is wide overlap with affective, anxiety, somatoform, and personality disorders, and this should be borne in mind when it comes to classifying these symptoms. To investigate the etiopathogenesis, multifactorial models are required. For treatment, adapted cognitive-behavioral therapy, possibly accompanied by an antidepressant, is effective.
Kennedy G, Spence V, Underwood C, Belch JJ.	Vascular Diseases Research Unit, University Department of Medicine, Ninewells Hospital and Medical School, Dundee DD1 9SY, UK. g.kirk@dundee.ac.uk	Increased neutrophil apoptosis in chronic fatigue syndrome.	J Clin Pathol. 2004 Aug;57(8):891-3.	BACKGROUND/AIMS: Many patients with chronic fatigue syndrome (CFS) have symptoms that are consistent with an underlying viral or toxic illness. Because increased neutrophil apoptosis occurs in patients with infection, this study examined whether this phenomenon also occurs in patients with CFS. METHODS: Apoptosis was assessed in patients with CFS in conjunction with concentrations of the anti-inflammatory cytokine, transforming growth factor beta1 (TGFbeta1). RESULTS: The 47 patients with CFS had higher numbers of apoptotic neutrophils, lower numbers of viable neutrophils, increased annexin V binding, and increased expression of the death receptor, tumour necrosis factor receptor-I, on their neutrophils than did the 34 healthy controls. Patients with CFS also had raised concentrations of active TGFbeta1 (p < 0.005). CONCLUSIONS: These findings provide new evidence that patients with CFS have an underlying detectable abnormality in their immune cells.
Kennedy G, Abbot NC, Spence V, Underwood C, Belch JJ.	Vascular Diseases Research Unit, University Department of Medicine, Ninewells Hospital & Medical School, Dundee, UK. g.kirk@dundee.ac.uk	The specificity of the CDC-1994 criteria for chronic fatigue syndrome: comparison of health status in three groups of patients who fulfill the criteria.	Ann Epidemiol. 2004 Feb;14(2):95-100.	PURPOSE: The Centers for Disease Control (CDC)-1994 definition of chronic fatigue syndrome (CFS) is very broad, and there have been suggestions that it lacks specificity. To test this, we have compared three groups of patients, all of whom fulfill the criteria but self-report different etiologies. METHODS: Patients with self-reported symptoms which developed sporadically (sCFS, n=48); after Gulf War service (GW, n=24); and following exposure to organophosphate insecticides (OP, n=25) underwent a clinical examination, completed the MOS SF-36 quality of life and Hospital Anxiety and Depression scales, and were assessed for major and minor criteria for CDC-1994 CFS. RESULTS: Significant differences in simple clinical measures and outcome measures were observed between groups. The GW group had significantly more severe physical symptoms-fatigue, muscle and multi-joint pain-than OP or sCFS, and the sCFS group was significantly less impaired than the other two groups in terms of role emotional and mental health. In all three groups, a majority of patients exhibited muscle weakness in the lower limbs, and significant numbers of patients had absent or abnormal reflexes. CONCLUSIONS: Differences in simple, easily performed clinical outcome measurements can be observed between groups of patients, all of whom fulfill the CDC-1994 criteria for CFS. It is likely that their response to treatment may also vary. The specificity of the CFS case definition should be improved to define more homogeneous groups of patients for the purposes of treatment and research.
Kennedy G, Spence V, Khan F, Belch JJ.	Vascular Diseases Research Unit, University Department of Medicine, Ninewells Hospital & Medical School, Dundee, UK. g.kirk@dundee.ac.uk	Plasma endothelin-1 levels in chronic fatigue syndrome.	Rheumatology (Oxford). 2004 Feb;43(2):252-3; author reply 253-4.	
Khan F, Kennedy G, Spence VA, Newton DJ, Belch JJ.	Vascular Diseases Research Unit, University Department of Medicine, Ninewells Hospital and Medical School, Dundee DD1 9SY, Scotland, U.K. f.khan@dundee.ac.uk	Peripheral cholinergic function in humans with chronic fatigue syndrome, Gulf War syndrome and with illness following organophosphate exposure.	Clin Sci (Lond). 2004 Feb;106(2):183-9.	In the present study, we have investigated whether the peripheral cholinergic abnormalities that we have reported previously [Spence, Khan and Belch (2000) Am. J. Med. 108, 736-739] in patients with chronic fatigue syndrome (CFS) are also present in those with Gulf War syndrome (GWS) and agricultural workers exposed to organophosphate pesticides, where cholinesterase inhibition is specifically implicated. We also looked at whether these abnormalities might be due to a reduction in the activity of cholinesterase expressed on the vascular endothelium. We used laser Doppler imaging to measure the forearm skin blood flow responses to iontophoresis of acetylcholine and of methacholine (which is resistant to breakdown by cholinesterase) in patients with CFS, GWS and those with a history of ill health after definite organophosphate exposure, as well as in matched healthy controls. The response to acetylcholine was significantly higher in patients with CFS than in controls (P = 0.029, repeated-measures ANOVA), but was normal in those with GWS and those exposed to organophosphates. The methacholine response was higher than the acetylcholine response in all patient groups except for those with CFS, where there was no difference between the responses. Although there are many clinical similarities between these three illnesses, our results indicate peripheral cholinergic abnormalities in the vascular endothelium of only patients with CFS, suggesting that this syndrome has a different aetiology, which might involve inhibition of vascular cholinesterase.
Kreyberg S.		[Chronic/post-viral	Tidsskr Nor	Seksjon for forebyggende medisin og epidemiologi, Institutt for allmenn- og samfunnsmedisin, Universitetet i Oslo, Postboks

		fatigue syndrome][Article in Norwegian]	Laegeforen. 2004 Sep 23;124(18):2382-3.	1130 Blindern 0318 Oslo. s.e.kreyberg@medisin.uio.no
Lerner AM, Dworkin HJ, Sayyed T, Chang CH, Fitzgerald JT, Beqaj S, Deeter RG, Goldstein J, Gottipolu P, O'Neill W.	Department of Medicine, William Beaumont Hospital, Royal Oak, Michigan, USA. lerner@cdimed.com	Prevalence of abnormal cardiac wall motion in the cardiomyopathy associated with incomplete multiplication of Epstein-barr Virus and/or cytomegalovirus in patients with chronic fatigue syndrome.	In Vivo. 2004 Jul-Aug;18(4):417-24.	We reported unique incomplete herpesvirus (Epstein-Barr Virus (EBV) and/or nonstructural (HCMV) cytomegalovirus) multiplication in 2 distinct subsets of CFS patients. The CFS subsets were identified by: a) presence of IgM serum antibodies to HCMV nonstructural gene products p52 and CM2 (UL44 and UL57), and/or b) IgM serum antibodies to Epstein-Barr virus viral capsid antigen (EBV, VCA IgM). Diagnostic IgM serum antibodies were found in two independent blinded studies involving 49 CFS patients, but the same antibodies were absent in 170 control patients (p<0.05). Abnormal 24 Hr-electrocardiographic monitoring, tachycardias at rest and, in severe chronic cases, abnormal cardiac wall motion (ACWM) were seen in these same CFS patients. We now report a prospective consecutive case control study from 1987--1999 of cardiac dynamics as measured by radionuclide ventriculography in 98 CFS patients from 1987--1999. Controls were patients with various malignancies who were evaluated in protocols requiring radionuclide ventriculography before initiation of cardiotoxic chemotherapeutic agents. The prevalence of abnormal cardiac wall motion (ACWM) at rest in CFS patients was 10 out of 87 patients (11.5%). With stress exercise, 21 patients (24.1%) demonstrated ACWM. Cardiac biopsies in 3 of these CFS patients with ACWM showed a cardiomyopathy. Among the controls, ACWM at rest was present in 4 out of 191 patients (2%) (p=0.0018). A progressive cardiomyopathy caused by incomplete virus multiplication of EBV and/or HCMV in CFS patients is present.
Lerner AM, Beqaj SH, Deeter RG, Fitzgerald JT.	Department of Medicine, William Beaumont Hospital and Wayne State University School of Medicine, Royal Oak, Michigan, USA. lerner@cdimed.com	IgM serum antibodies to Epstein-Barr virus are uniquely present in a subset of patients with the chronic fatigue syndrome.	In Vivo. 2004 Mar-Apr;18(2):101-6.	BACKGROUND: A unique subset of patients with chronic fatigue syndrome (CFS) and IgM serum antibodies to cytomegalovirus (HCMV) non-structural gene products p52 and CM2 (UL 44 and UL 57) has been described. PATIENTS AND METHODS: Fifty-eight CFS patients and 68 non-CFS matched controls were studied. Serum antibodies to EBV viral capsid antigen (VCA) IgM and EBV Early Antigen, diffuse (EA, D) as well HVCMV(V), IgM and IgG; VP (sucrose, density purified V); p52 and CM2 IgM serum antibodies were assayed. RESULTS: Mean age of CFS patients was 44 years (75% women). Control patients were 9 years older (73% women). Serum EBV VCA IgM positive antibody titers were identified in 33 CFS patients (Group A subset EBV VCA IgM 62.3+/-8.3, neg. <20), but were not present in other CFS patients, (Group B subset EBV VCA IgM 6.8+/-0.7) controls (p<0.0001). EBV VCA IgM titers remained positive in CFS patients from Group A for 24-42 months. CONCLUSION: Serum antibody to EBV VCA IgM may be a specific diagnostic test for a second subset of CFS patients.
Liu Z, Wang D, Xue Q, Chen J, Li Y, Bai X, Chang L.	Department of Neurology, Beijing Friendship Hospital, Affiliated Hospital of Capital University of Medical Science, 95 Yong-an Rd, Beijing 100050, China. liuzhandong99@sina.com.cn	Determination of fatty acid levels in erythrocyte membranes of patients with chronic fatigue syndrome.	Nutr Neurosci. 2003 Dec;6(6):389-92.	Chronic fatigue syndrome (CFS) is an illness characterized by persistent and relapsing fatigue, often accompanied by numerous symptoms involving various systems of whole body. The etiology of CFS remains unclear. Literature reported whether the concentrations of the essential fatty acids in red cell membranes of CFS patients were decreased is controversial. In our study, Forty-two patients who fulfilled the diagnostic criteria defined by Centers for Disease Control and Prevention (CDC). Thirty-seven age- and sex-matched controls were selected from healthy medical staffs and volunteers. After lipid analysis, we found that the levels of the arachidonic acid (ARA) and docosahexanoic acid (DHA) were decreased in patients suffered from CFS. However, the levels of the palmitic acid and oleic acid were increased. We speculated that there are two possible mechanisms--one of which is that oxidative stress has led to an excessive oxidation and resulting in the above fatty acids. Alternatively, insufficiency of ingestion of fatty acids might not be the major cause.
Lloyd AR.	Inflammation Research Unit, School of Medical Sciences, University of New South Wales, Kensington, NSW 2052, Australia. a.lloyd@unsw.edu.au	To exercise or not to exercise in chronic fatigue syndrome? No longer a question.	Med J Aust. 2004 May 3;180(9):437-8.	
Looper KJ, Kirmayer LJ.	Department of Psychiatry, Sir Mortimer B. Davis-Jewish General Hospital, 3755 Chemin de la Cote-Ste-Catherine, Montreal,	Perceived stigma in functional somatic syndromes and comparable medical conditions.	J Psychosom Res. 2004 Oct;57(4):373-8.	OBJECTIVE: To determine if patients with functional somatic syndromes (FSS) perceive greater levels of stigma than patients with comparable medical conditions that have a clear medical pathology. METHODS: Patients with chronic fatigue syndrome (CFS), fibromyalgia (FM), or irritable bowel syndrome (IBS) were compared to multiple sclerosis (MS), rheumatoid arthritis (RA), and inflammatory bowel disease (IBS), respectively. RESULTS: There were greater levels of perceived stigma in the combined group of FSS compared to the medical control group. When each FSS was compared to its matched control group, only CFS had a higher level of perceived stigma. These results remained when controlling for other variables relevant to stigma. CONCLUSIONS: The higher level of perceived stigma in CFS may be due to the ambiguity of its status as a medical condition.

	PQ, Canada. karl.looper@mail.mcgill.ca			The absence of this effect in FM and IBS is consistent with a greater level of acceptance of these disorders as medical illnesses.
Lorenzo Gomez MF, Gomez Castro S.	Area de Urologia Femenina de la Clinica San Marcos, Investigadora en el Centro Biosanitario de Investigacion Experimental de la Universidad de Salamanca, Salamanca. mflorenzogo@yahoo.es	[Physiopathologic relationship between interstitial cystitis and rheumatic, autoimmune, and chronic inflammatory diseases][Article in Spanish]	Arch Esp Urol. 2004 Jan-Feb;57(1):25-34.	OBJECTIVES: To evaluate the current knowledge about interstitial cystitis pathophysiology and its relationship with rheumatic, autoimmune and chronic inflammatory diseases. METHODS: Literature search under "interstitial cystitis pathophysiology" either clinical or experimental trials and reports, in Medline, PubMed, Digital Urology Journal and Doctor's Guide, in addition to our own clinical research experience results. RESULTS: Both human and experimental trials show resemblances between interstitial cystitis and rheumatic, autoimmune, and chronic inflammatory diseases on clinical presentations, pathophysiology. Some interstitial cystitis patients show the bladder infiltrated with specific mononuclear cells, high incidence of circulating antinuclear antibodies, good response to anti-inflammatory and/or immunosuppressive therapies. Interstitial cystitis in association with rheumatic, autoimmune and chronic inflammatory diseases is very common. Many patients with systemic lupus erythematosus, Sjogren syndrome and fibromyalgia syndrome show antibodies against urothelium and/or muscle cells and/or other connective tissue components of urinary bladder. Systemic lupus erythematosus and Sjogren syndrome are the autoimmune diseases which bear strongest similarity with interstitial cystitis. Moreover, rheumatoid arthritis, chronic pelvic pain syndrome, irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, Evan's syndrome and atopic dermatitis share some pathogenic characteristics. CONCLUSIONS: Nowadays, interstitial cystitis pathophysiology is unknown. Based on clinical presentations, epidemiology, pathology and laboratory findings and treatment response, there is an important correlation among interstitial cystitis and rheumatic, autoimmune and chronic inflammatory diseases. These disorders may share some pathophysiologic mechanisms. Rigorous studies of pathophysiology of these group of diseases are needed to confirm consistently this approach for such conditions.
Luthra A, Wessely S.	King's College School of Medicine, Institute of Psychiatry, 103 Denmark Hill, London SE5 8AZ, UK.	Unloading the trunk: neurasthenia, CFS and race.	Soc Sci Med. 2004 Jun;58(11):2363-9.	The aetiologies of both chronic fatigue syndrome (CFS) and its predecessor neurasthenia, have been linked to technological advances in 'developed' countries. This paper discusses how this has led to a form of race thinking within discussions about fatigue which has persisted for more than a century. We review the historical development of this race thinking from neurasthenia to CFS and describe how it is manifested in both the lay- and medical literature. We also review the epidemiological literature on CFS and ethnicity to better understand the relatively low percentage of non-white patients seen in tertiary referral clinics for CFS. The aim of this paper is to act as a starting point for a debate on race and CFS.
Mahurin RK, Claypoole KH, Goldberg JH, Arguelles L, Ashton S, Buchwald D.	Department of Radiology, University of Washington, Seattle, WA 98195-6465, USA. mahurin@u.washington.edu	Cognitive processing in monozygotic twins discordant for chronic fatigue syndrome.	Neuropsychology. 2004 Apr;18(2):232-9.	Twenty-one pairs of monozygotic twins discordant for chronic fatigue syndrome (CFS) and 21 matched healthy control (HC) subjects were assessed with 5 untimed tests and 5 timed tests from the computer-based NeuroCognitive Assessment Battery (R. K. Mahurin, 1993). Random effects regression showed no difference between CFS and healthy twins on any of the cognitive tests. Further, the twin groups did not differ from the HC group on any content-dependent measure. In contrast, both sets of twins performed worse than the HC group on all speed-dependent tests except Finger Tapping. Self-rated fatigue and dysphoric mood were only weakly correlated with cognitive performance. These data point toward a shared genetic trait related to information processing that is manifest in the CFS context. The findings have implications for differentiating genetic and acquired vulnerability in the symptomatic expression of the disorder. ((c) 2004 APA, all rights reserved)
Madill PV.		Chronic fatigue syndrome and the cholinergic hypothesis.	JAMA. 2004 Dec 8;292(22):2723; author reply 2723. Comment on: JAMA. 2004 Sep 8;292(10):1195-204.	
Martinez S, Guilleminault C.	Stanford University Sleep Disorders Clinic, Stanford, California 94305, USA.	Periodic leg movements in prepubertal children with sleep disturbance.	Dev Med Child Neurol. 2004 Nov;46(11):765-70.	This study's aims were to determine: (1) prevalence of periodic leg movements (PLMs) in walking prepubertal children consulting a sleep clinic for any sleep disorder; (2) associations between PLMs and other sleep and medical disorders; and (3) the response of other sleep disorders to treatment with the dopamine agonist pramipexol. Clinical evaluation and polysomnography were carried out for a period of 12 months on 252 consecutively seen, prepubertal children with sleep disorders (156 males, 96 females; aged 15mo to 11y, mean 7y 1mo, SD3y 10mo). Sleep disorders unrelated to PLMs were treated, and six children received pramipexol for PLMs. Follow-up included clinical evaluation and polysomnography. Twenty-three per cent of children were diagnosed with PLMs on the basis of polysomnography. The presence of PLMs had usually been unrecognized clinically. The only clinical symptom that could be related to periodic limb movement disorder was a report of leg pains at morning awakening. Only two of 58 children had PLMs without other clinical or polysomnographic findings. Comorbidity seen with PLMs included neuropsychiatric syndromes (n=20), isolated sleep disordered breathing (SDB; n=29), and several other comorbid conditions (n=7). Seven of 11 children seen with attention-deficit-hyperactivity disorder also had PLMs. Surgery for SDB was associated with subsequent cessation of PLMs in 15 of 29 children. Five out of six children with PLMs who received pramipexol were able to tolerate the drug and experienced a complete disappearance of their PLMs. Presence of chronic fatigue, sleepiness,

				disrupted nocturnal sleep, and difficulties in falling asleep should lead to a systematic search for PLMs that is independent of associated syndromes. Isolated treatment of SDB might help eliminate some, but not all, PLMs.
McCrone P, Ridsdale L, Darbishire L, Seed P.	Centre for the Economics of Mental Health, Health Services Research Department, Institute of Psychiatry, King's College, London, UK. p.mccrone@iop.kcl.ac.uk	Cost-effectiveness of cognitive behavioural therapy, graded exercise and usual care for patients with chronic fatigue in primary care.	Psychol Med. 2004 Aug;34(6):991-9.	BACKGROUND: Chronic fatigue is a common condition, frequently presenting in primary care. The aim of this study was to compare the cost-effectiveness of cognitive behavioural therapy (CBT) and graded exercise therapy (GET), and to compare therapy with usual care plus a self-help booklet (BUC). METHOD: Patients drawn from general practices in South East England were randomized to CBT or GET. The therapy groups were then compared to a group receiving BUC recruited after the randomized phase. The main outcome measure was clinically significant improvements in fatigue. Cost-effectiveness was assessed using the net-benefit approach and cost-effectiveness acceptability curves. RESULTS: Costs were available for 132 patients, and cost-effectiveness results for 130. Costs were dominated by informal care. There were no significant outcome or cost differences between the therapy groups. The combined therapy group had significantly better outcomes than the standard care group, and costs that were on average 149 pounds higher (a non-significant difference). Therapy would have an 81.9% chance of being cost-effective if society were willing to attach a value of around 500 pounds to each four-point improvement in fatigue. CONCLUSION: The cost-effectiveness of cognitive behavioural therapy and graded exercise were similar unless higher values were placed on outcomes, in which case CBT showed improved cost-effectiveness. The cost of providing therapy is higher than usual GP care plus a self-help booklet, but the outcome is better. The strength of this evidence is limited by the use of a non-randomized comparison. The cost-effectiveness of therapy depends on how much society values reductions in fatigue.
McCully KK, Smith S, Rajaei S, Leigh JS Jr, Natelson BH.	Department of Exercise Science, University of Georgia, Athens, GA 30602, USA. kmccully@coe.uga.edu	Muscle metabolism with blood flow restriction in chronic fatigue syndrome.	J Appl Physiol. 2004 Mar;96(3):871-8. Epub 2003 Oct 24.	The purpose of this study was to determine whether chronic fatigue syndrome (CFS) is associated with reduced blood flow and muscle oxidative metabolism. Patients with CFS according to Centers for Disease Control criteria (n = 19) were compared with normal sedentary subjects (n = 11). Muscle blood flow was measured in the femoral artery with Doppler ultrasound after exercise. Muscle metabolism was measured in the medial gastrocnemius muscle with ³¹ P-magnetic resonance spectroscopy. Muscle oxygen saturation and blood volume were measured using near-infrared spectroscopy. CFS and controls were not different in hyperemic blood flow or phosphocreatine recovery rate. Cuff pressures of 50, 60, 70, 80, and 90 mmHg were used to partially restrict blood flow during recovery. All pressures reduced blood flow and oxidative metabolism, with 90 mmHg reducing blood flow by 46% and oxidative metabolism by 30.7% in CFS patients. Hyperemic blood flow during partial cuff occlusion was significantly reduced in CFS patients (P < 0.01), and recovery of oxygen saturation was slower (P < 0.05). No differences were seen in the amount of reduction in metabolism with partially reduced blood flow. In conclusion, CFS patients showed evidence of reduced hyperemic flow and reduced oxygen delivery but no evidence that this impaired muscle metabolism. Thus CFS patients might have altered control of blood flow, but this is unlikely to influence muscle metabolism. Furthermore, abnormalities in muscle metabolism do not appear to be responsible for the CFS symptoms.
Mears CJ, Taylor RR, Jordan KM, Binns HJ; Pediatric Practice Research Group.	Department of Pediatrics, Feinberg School of Medicine, Northwestern University, Chicago, Illinois, USA.	Sociodemographic and symptom correlates of fatigue in an adolescent primary care sample.	J Adolesc Health. 2004 Dec;35(6):528e.21-6.	PURPOSE: To describe the prevalence of prolonged fatigue, chronic fatigue syndrome (CFS)-like illness, and associated symptom patterns in adolescents attending primary care. METHODS: The design was cross-sectional. A questionnaire designed by the authors assessing fatigue and associated symptoms was administered to 901 adolescents (aged 11-18 years) attending 12 primary care clinics in the Chicago area. Prevalence rates for prolonged fatigue and CFS-like illness were calculated. Univariate comparisons involving sociodemographic data and fatigue severity were made between adolescents with and without prolonged fatigue, and sociodemographic and symptom predictors of prolonged fatigue were identified using logistic regression analysis. RESULTS: Prolonged fatigue (> or = 1 month) occurred at a rate of 8.0% and CFS-like illness occurred at a rate of 4.4%. Adolescents with prolonged fatigue were significantly older and also reported greater fatigue severity than those without fatigue. Findings from logistic regression indicated that, in addition to increasing age, headaches, muscle pains, fever, and fatigue made worse by exercise were significantly associated with prolonged fatigue. CONCLUSIONS: Abnormal fatigue is a disabling and prevalent condition in adolescents in primary care. It is associated with a number of additional symptoms, many of which may have viral origins.
Miike T, Tomoda A, Jhodoi T, Iwatani N, Mabe H.	Department of Child Development, Faculty of Medical and Pharmaceutical Sciences, Kumamoto University Graduate School, 1-1-1 Honjo, Kumamoto 860-8556, Kumamoto, Japan. miketeru@kaiju.medic.kumamoto-u.ac.jp	Learning and memorization impairment in childhood chronic fatigue syndrome manifesting as school phobia in Japan.	Brain Dev. 2004 Oct;26(7):442-7.	For the last 15 years, we have tried to understand the pathophysiology of childhood chronic fatigue syndrome (CCFS) in Japan. In this condition, two major symptoms are important: easy fatigability and disturbed learning and memorization. In CCFS patients we clinically evaluated autonomic nervous system function, circadian rhythm of hormonal secretion (melatonin, cortisol and 3-endorphin), core body temperature, and sleep-wake pattern. Most patients showed autonomic nervous system dysfunction and circadian rhythm disturbances, similar to those observed in jet lag. Radiological imaging studies (SPECT, Xe-CT, and MRS) revealed decreased blood flow in the frontal and thalamic areas, and accumulation of choline in the frontal lobe. We analyzed the relationship between the laboratory data and clinical symptoms in CCFS.

Mourot L, Bouhaddi M, Perrey S, Cappelle S, Henriet MT, Wolf JP, Rouillon JD, Regnard J.	Laboratoire de Physiologie Medecine, Faculte de Medecine, Besancon Cedex, France. mourotlaurent@hotmail.com	Decrease in heart rate variability with overtraining: assessment by the Poincare plot analysis.	Clin Physiol Funct Imaging. 2004 Jan;24(1):10-8.	Numerous symptoms have been associated with the overtraining syndrome (OT), including changes in autonomic function. Heart rate variability (HRV) provides non-invasive data about the autonomic regulation of heart rate in real-life conditions. The aims of the study were to: (i) characterize the HRV profile of seven athletes (OA) diagnosed as suffering of OT, compared with eight healthy sedentary (C) and eight trained (T) subjects during supine rest and 60 degrees upright, and (ii) compare the traditional time- and frequency-domain analysis assessment of HRV with the non-linear Poincare plot analysis. In the latter each R-R interval is plotted as a function of the previous one, and the standard deviations of the instantaneous (SD1) and long-term R-R interval variability are calculated. Total power was higher in T than in C and OA both in supine (1158 +/- 1137, 6092 +/- 3554 and 2970 +/- 2947 ms ² for C, T and OA, respectively) and in upright (640 +/- 499, 1814 +/- 806 and 1092 +/- 712 ms ² for C, T and OA, respectively; P<0.05) positions. In supine position, indicators of parasympathetic activity to the sinus node were higher in T compared with C and OA (high-frequency power: 419.1 +/- 381.2, 1105.3 +/- 781.4 and 463.7 +/- 715.8 ms ² for C, T and OA, respectively; P<0.05; SD1: 29.5 +/- 18.5, 75.2 +/- 17.2 and 37.6 +/- 27.5 for C, T and OA, respectively; P<0.05). OA had a marked predominance of sympathetic activity regardless of the position (LF/HF were 0.47 +/- 0.35, 0.47 +/- 0.50 and 3.96 +/- 5.71 in supine position for C, T and OA, respectively, and 2.09 +/- 2.17, 7.22 +/- 6.82 and 12.04 +/- 10.36 in upright position for C, T and OA, respectively). The changes in HRV indexes induced by the upright posture were greater in T than in OA. The shape of the Poincare plots allowed the distinction between the three groups, with wide and narrow shapes in T and OA, respectively, compared with C. As Poincare plot parameters are easy to compute and associated with the 'width' of the scatter gram, they corroborate the traditional time- and frequency-domain analysis. We suggest that they could be used to indicate fatigue and/or prevent OT.
Murphy BE, Abbott FV, Allison CM, Watts C, Ghadirian AM.	Department of Psychiatry, McGill University, 1033 Pine Avenue West, Montreal, Canada H3A 1A1. bev.murphy@mcgill.ca	Elevated levels of some neuroactive progesterone metabolites, particularly isopregnanolone, in women with chronic fatigue syndrome.	Psychoneuroendocrinology. 2004 Feb;29(2):245-68.	Chronic fatigue syndrome (CFS) is a controversial entity whose cause is unknown. In this study we have explored the possibility that progesterone metabolites may be involved. Plasma levels of the progesterone precursor pregnenolone, progesterone itself, and five ring A-reduced metabolites of progesterone were measured in 20 women with CFS and in 13 age-matched controls. To minimize the contribution of the ovary, women were either post-menopausal or in the follicular phase of the menstrual cycle (day 4-8), and progesterone levels were all well within the expected range (< or = 3.5 nmol/l). Mean values for progesterone and all of its metabolites were higher in CFS patients, the most marked being a 2.3-fold elevation in isopregnanolone (3beta,5alpha-tetrahydroprogesterone; p < or = 0.001). Progesterone levels were correlated with those of its metabolites, but even after controlling for progesterone by ANCOVA, isopregnanolone levels were still elevated (p < or = 0.001). These elevated levels of isopregnanolone could not be attributed to medications (antidepressants and anxiolytics). When the CFS patients were divided into two groups according to their Hamilton depression scale ratings, mean (+/-SD) isopregnanolone levels were higher (274 +/- 160 vs 197 +/- 119 pmol/l) in the less depressed group (ratings 2-14) than in the more depressed group (ratings 17-28), although this difference did not reach significance. Progesterone levels were negatively correlated with Hamilton depression rating scores (r=-0.56; p<0.01). These results suggest that increases in ring A-reduced progesterone metabolites, particularly isopregnanolone, are associated with CFS, and that the pathophysiology of CFS is unlikely to be due to depression.
Naschitz J, Dreyfuss D, Yeshurun D, Rosner I.	Department of Internal Medicine A, Bnai Zion Medical Center and Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel. Naschitz@tx.technion.ac.il	Midodrine treatment for chronic fatigue syndrome.	Postgrad Med J. 2004 Apr;80(942):230-2.	The long term results of midodrine treatment in a patient having debilitating chronic fatigue syndrome (CFS) are reported. Midodrine treatment, directed at the autonomic nervous system, resulted in correction of the dysautonomia followed by improvement of fatigue. This finding is consistent with the hypothesis that dysautonomia plays a major part in the pathophysiology of CFS and that therapies directed at the autonomic nervous system may be effective in the treatment of CFS.
Naschitz JE, Rozenbaum M, Fields M, Isseroff H, Enis S, Babich JP, Peck S, Rubin Peck E, Gaitini L, Naschitz S, Sabo E, Rosner I.		Search for disease-specific cardiovascular reactivity patterns - Developing the methodology.	Clin Sci (Lond). 2004 Aug 26 [Epub ahead of print]	Objectives. Aberrations of cardiovascular reactivity (CVR), an expression of autonomic function, lack specificity for a particular disorder. Recently, a CVR pattern particular to chronic fatigue syndrome has been observed. We aimed to develop methodologies for assessment of disease-specific CVR patterns. Subjects. As a prototype, a population of 50 consecutive patients with Familial Mediterranean Fever (FMF) was studied compared with control populations. Methods. A 10-minute supine-30 minute head-up tilt test with recording the heart rate and blood pressure or the pulse transit time was performed. Five studies were conducted, applying different methods. In each study, statistical analysis identified independent predictors of the CVR in FMF. Based on regression coefficients of these predictors, a linear discriminant score (DS) was computed for every subject. Each study established an equation to assess the CVR, calculate the DS for FMF and determine the sensitivity and specificity of the DS cut-off. Results. In each of the five studies, abnormal CVR was observed in FMF patients. The best accuracy (88% sensitivity and 90.1% specificity for FMF) was obtained by a method based on beat-to-beat heart rate and pulse transit time recordings. Data was

				processed by fractal and recurrence quantitative analysis with recordings in FMF patients compared with a mixed control population. Conclusions. Identification of disease-specific CVR patterns became possible with methodologies like those described in the present work. In FMF, disease-specific CVR may be explained by the interplay between neuro-endocrine loops specific to FMF with cardiovascular homeostatic mechanisms. Recognition of disease-specific CVR patterns may advance the understanding of homeostatic mechanisms and have implications in clinical practice.
Naschitz JE, Rosner I, Rozenbaum M, Fields M, Isseroff H, Babich JP, Zuckerman E, Elias N, Yeshurun D, Naschitz S, Sabo E.	Departments of Internal Medicine A and Rheumatology, Bnai Zion Medical Center and Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel. naschitz@tx.technion.ac.il	Patterns of cardiovascular reactivity in disease diagnosis.	QJM. 2004 Mar;97(3):141-51.	BACKGROUND: Aberrations of cardiovascular reactivity (CVR), an expression of autonomic function, occur in a number of clinical conditions, but lack specificity for a particular disorder. Recently, a CVR pattern particular to chronic fatigue syndrome was observed. Aim: To assess whether specific CVR patterns can be described for other clinical conditions. METHODS: Six groups of patients, matched for age and gender, were evaluated with a shortened head-up tilt test: patients with chronic fatigue syndrome (CFS) (n = 20), non-CFS fatigue (F) (n = 15), neurally-mediated syncope (SY) (n = 21), familial Mediterranean fever (FMF) (n = 17), psoriatic arthritis (PSOR) (n = 19) and healthy subjects (H) (n = 20). A 10-min supine phase was followed by recording 600 cardiac cycles on tilt (5-10 min). Beat-to-beat heart rate (HR) and pulse transit time (PTT) were measured. Results were analysed using conventional statistics, recurrence plot analysis and fractal analysis. RESULTS: Multivariate analysis evaluated independent predictors of the CVR in each patient group vs. all other groups. Based on these predictors, equations were determined for a linear discriminant score (DS) for each group. The best sensitivities and specificities of the DS, consistent with disease-related phenotypes of CVR, were noted in the following groups: CFS, 90.0% and 60%; SY, 93.3% and 62.5%; FMF, 90.1% and 75.4%, respectively. DISCUSSION: Pathological disturbances may alter cardiovascular reactivity. Our data support the existence of disease-related CVR phenotypes, with implications for pathogenesis and differential diagnosis.
Naschitz JE, Yeshurun D, Rosner I.	Department of Internal Medicine A, Bnai Zion Medical Center and Bruce Rappaport Faculty of Medicine, Technion - Israel Institute of Technology, PO Box 4940, Haifa 31048, Israel. naschitz@tx.technion.ac.il	Dysautonomia in chronic fatigue syndrome: facts, hypotheses, implications.	Med Hypotheses. 2004;62(2):203-6.	The diagnosis of chronic fatigue syndrome (CFS) is based on patient history and treatment on cognitive behavior therapy and graded exercise. There is increasing evidence that dysautonomia occurs in CFS manifest primarily as disordered regulation of cardiovascular responses to stress. We impart our experience relating to diagnosis, monitoring, and treatment of CFS based on identification and management of dysautonomia. Recently proposed methods for assessment of the cardiovascular reactivity, the 'hemodynamic instability score' (HIS) and the 'Fractal and Recurrence Analysis-based Score' (FRAS), served for this purpose. On HUTT, a particular dysautonomia is revealed in CFS patients that differ from dysautonomia in several other disorders. This distinct abnormality in CFS can be identified by HIS >-0.98 (sensitivity 84.5% and specificity 85.1%) and FRAS > +0.22 (sensitivity 70% and specificity 88%). Therefore, the HIS and FRAS may be used, in the appropriate clinical context, to support the diagnosis of CFS, which until now, could only be subjectively inferred. A pilot study suggested that midodrine treatment, directed at the autonomic nervous system in CFS, results first in correction of dysautonomia followed by improvement of fatigue. This finding implies that dysautonomia is pivotal in the pathophysiology CFS, at least in a large part of the patients, and that manipulating the autonomic nervous system may be effective in the treatment of CFS.
Ng BY, Lim CC, Yeoh A, Lee WL.	Department of Behavioral Medicine, Singapore General Hospital, Republic of Singapore. gdmnby@sgh.com.sg	Neuropsychiatric sequelae of Nipah virus encephalitis.	J Neuropsychiatry Clin Neurosci. 2004 Fall;16(4):500-4.	The authors followed nine patients with Nipah virus encephalitis over the course of 24 months. Eight of the nine developed psychiatric features assigned to the encephalitis. Three patients developed major depressive disorder immediately after recovering from the encephalitis, and two developed depression approximately 1 year after the outbreak. Two patients developed personality changes, and two suffered chronic fatigue syndrome. Neuropsychological testing was accomplished in eight of the nine patients. Deficits in attention, verbal, and/or visual memory were substantial in seven of the eight patients tested. Verbal memory was more impaired than visual memory in these patients. Comparison between psychiatric and cognitive impairment and total number of brain lesions showed no discernible trends.
Nijs J PhD, MSc, Garth L. Nicolson PhD		Article: Gulf War Veterans: Evidence for Chromosome Alternations and Their Significance	Journal of Chronic Fatigue Syndrome 2004 12 (1): 79 - 83	
Nijs J, De Meirleir K, Duquet W.	Department of Human Physiology, Vrije Universiteit Brussel, Brussel, Belgium. Jo.Nijs@vub.ac.be	Kinesiophobia in chronic fatigue syndrome: assessment and associations with disability.	Arch Phys Med Rehabil. 2004 Oct;85(10):1586-92.	OBJECTIVES: To investigate aspects of the validity of the total scores of the Tampa Scale for Kinesiophobia (TSK), Dutch Version, which was modified to make it an appropriate questionnaire for the assessment of kinesiophobia (fear of movement) in chronic fatigue syndrome (CFS) patients (the Dutch TSK-CFS), and, using this assessment tool, to examine the associations between kinesiophobia, exercise capacity, and activity limitations and participation restrictions in patients with CFS. DESIGN: Prospective observational studies. SETTING: An outpatient fatigue clinic. PARTICIPANTS: In the first study, 40 patients fulfilling the 1994 US Centers for Disease Control and Prevention (CDC) criteria for CFS were enrolled. The sample of the second study consisted of 51 CDC-defined patients with CSF. INTERVENTIONS: Not applicable. Main outcome measures Study 1: Subjects completed a set of questionnaires; the Utrechtse Coping List (UCL), the Dutch TSK-CFS, and the Dutch Baecke Questionnaire of Habitual Physical Activity. Study 2: All patients completed 2 questionnaires (Chronic Fatigue Syndrome Activities and Participation Questionnaire [CFS-APQ], Dutch TSK-CFS) and performed a maximal exercise stress test on a

				bicycle ergometer. The heart rate was monitored continuously by use of an electrocardiograph. Metabolic and ventilatory parameters were measured through spirometry. RESULTS: Study 1: The Cronbach alpha coefficient for the individual item scores on the TSK-CFS was .80. The total scores on the Dutch TSK-CFS showed a statistically significant correlation with both the avoidance/abide subscale of the UCL (Spearman rho=.35, P=.029) and the total score of the Baecke Questionnaire (rho=-.45, P=.004). Study 2: The total scores on the Dutch TSK-CFS showed a statistically significant correlation with the total scores on the CFS-APQ (rho=.39, P=.004). No statistically significant associations were observed between the exercise capacity parameters and the total scores on the Dutch TSK-CFS. CONCLUSIONS: These results provide evidence for the internal consistency and the convergent and congruent validity of the scores obtained by use of the Dutch TSK-CFS. Kinesiophobia appears to be associated with activity limitations/participation restrictions but not with exercise capacity in patients with CFS.
Nijs J, De Meirleir K.	Department of Human Physiology, Faculty of Physical Education and Physical Therapy and Chronic Fatigue Clinic, Vrije Universiteit Brussel, Belgium. Jo.Nijs@vub.ac.be	Prediction of peak oxygen uptake in patients fulfilling the 1994 CDC criteria for chronic fatigue syndrome.	Clin Rehabil. 2004 Nov;18(7):785-92.	PURPOSE: To establish an inexpensive, simple method of predicting peak oxygen uptake (VO ₂ peak) in patients fulfilling the 1994 Centers for Disease Control and Prevention (CDC) criteria for chronic fatigue syndrome (CFS). DESIGN: A retrospective observational study. SETTING: An outpatient tertiary care chronic fatigue clinic. SUBJECTS: Two hundred and forty consecutive patients fulfilling the 1994 CDC criteria for CFS. INTERVENTIONS: Heart rate, metabolic and ventilatory parameters were measured continuously during a maximal exercise stress test on a bicycle ergometer. Using the equation peak oxygen uptake = 13.1 x peak workload +284 (used by Mullis et al., Br J Sports Med 1999; 33: 352-56), VO ₂ peak was predicted from the peak workload of a maximal exercise capacity test. Pearson correlation coefficient and linear regression analysis were used to establish the most accurate way to predict VO ₂ peak. RESULTS: Percentage error encountered when comparing actual measured VO ₂ peak with predicted value was 17.3% (+/-10.0). A strong correlation between VO ₂ peak and peak workload was observed (r= 0.89, p < 0.001). A regression analysis established the relation as VO ₂ peak = 10.47 x peak workload +284.1, where VO ₂ peak is given in ml/min and peak workload in W (error in prediction = 11.0+/-9.5%). CONCLUSIONS: Monitoring of the peak workload during a maximal, graded bicycle ergometric test suffices to predict the VO ₂ peak. When predicting VO ₂ peak the used operational definition for the diagnosis of CFS could be taken into account. Compared with the equation used by Mullis et al., peak workload is multiplied by 10.47 in order to predict peak oxygen uptake in CDC-defined CFS patients.
Nijs J, Vanherberghen K, Duquet W, De Meirleir K.	Department of Human Physiology, Faculty of Physical Education and Physical Therapy Science, Vrije Universiteit Brussel, Brussels, Belgium. Jo.Nijs@vub.ac.be	Chronic fatigue syndrome: lack of association between pain-related fear of movement and exercise capacity and disability.	Phys Ther. 2004 Aug;84(8):696-705.	BACKGROUND AND PURPOSE: Patients who experience pain, a symptom of chronic fatigue syndrome (CFS), often exhibit kinesiophobia (irrational fear of movement). The purpose of this study was to examine whether pain-related fear of movement is associated with exercise capacity, activity limitations, or participation restrictions in patients with CFS who experience widespread pain. SUBJECTS AND METHODS: Sixty-four subjects met the inclusion criteria. All subjects fulfilled the 1994 Centers for Disease Control and Prevention case definition for CFS and experienced widespread myalgias or arthralgias. The subjects completed the Tampa Scale for Kinesiophobia-Dutch Version (TSK-DV) and the Dutch Chronic Fatigue Syndrome-Activities and Participation Questionnaire (CFS-APQ). They then performed a maximal exercise test on a bicycle ergometer. Heart rate was monitored continuously by use of an electrocardiograph. Ventilatory factors were measured through spirometry. Correlations between the TSK-DV scores and both the exercise capacity data and the CFS-APQ scores were assessed using the Spearman rank correlation coefficient. Using the Mann-Whitney U test, the TSK-DV scores were compared between subjects who performed a maximal exercise stress test and those who did not perform the test. RESULTS: Forty-seven subjects (73.4%) attained a total score of greater than 37 on the TSK-DV, indicating high fear of movement. Neither the exercise capacity data nor the CFS-APQ scores indicated a correlation with the TSK-DV scores (n=64). Subjects who did not perform a maximal exercise capacity test had more fear of movement (median TSK-DV score=43.0, interquartile range=10.3) compared with those who did perform a maximal exercise capacity test (median TSK-DV score=38.0, interquartile range=13.2; Mann-Whitney U-test score=322.5, z=-1.974, P=.048), but the correlation analysis was unable to reveal an association between exercise capacity and kinesiophobia in either subgroup. DISCUSSION AND CONCLUSION: These results indicate a lack of correlation between kinesiophobia and exercise capacity, activity limitations, or participation restrictions, at least in patients with CFS who are experiencing widespread muscle or joint pain.
Nijs J, De Meirleir K, Meeus M, McGregor NR, Englebienne P.	Department of Human Physiology, Faculty of Physical Education and Physical Therapy Science, Vrije Universiteit Brussel (VUB), Brussel 1090, Belgium.	Chronic fatigue syndrome: intracellular immune deregulations as a possible etiology for abnormal exercise response.	Med Hypotheses. 2004;62(5):759-65.	The exacerbation of symptoms after exercise differentiates Chronic fatigue syndrome (CFS) from several other fatigue-associated disorders. Research data point to an abnormal response to exercise in patients with CFS compared to healthy sedentary controls, and to an increasing amount of evidence pointing to severe intracellular immune deregulations in CFS patients. This manuscript explores the hypothetical interactions between these two separately reported observations. First, it is explained that the deregulation of the 2-5A synthetase/RNase L pathway may be related to a channelopathy, capable of initiating both intracellular hypomagnesaemia in skeletal muscles and transient hypoglycemia. This might explain muscle weakness and the reduction of maximal oxygen uptake, as typically seen in CFS patients. Second, the activation of the protein kinase R enzyme, a characteristic feature in atleast subsets of CFS patients, might account for the observed excessive nitric oxide (NO) production in patients with CFS. Elevated NO is known to induce vasodilation, which may limit CFS patients to increase blood flow during exercise, and may even cause and enhanced postexercise hypotension. Finally, it is explored how several types of infections, frequently

				identified in CFS patients, fit into these hypothetical pathophysiological interactions.
Nijs J, De Meirleir K, Wolfs S, Duquet W.	Department of Human Physiology, Faculty of Physical Education and Physical Therapy and Chronic Fatigue Clinic, Vrije Universiteit Brussel (VUB), Belgium. Jo.Nijs@vub.ac.be	Disability evaluation in chronic fatigue syndrome: associations between exercise capacity and activity limitations/participation restrictions.	Clin Rehabil. 2004 Mar;18(2):139-48.	OBJECTIVE: In an attempt to examine whether impairments in cardiorespiratory fitness are associated with daily functioning in patients with chronic fatigue syndrome (CFS), this study addresses the correlations between exercise capacity and activity limitations/participation restrictions. DESIGN: Prospective observational study. SETTING: An outpatient tertiary care, chronic fatigue clinic at the Vrije Universiteit Brussel (VUB), Belgium. SUBJECTS: Seventy-seven patients fulfilling the 1994 Centers for Disease Control and Prevention (CDC) case definition for CFS. INTERVENTIONS: All patients filled in the Chronic Fatigue Syndrome Activities and Participation Questionnaire (CFS-APQ) and performed a maximal exercise stress test on a bicycle ergometer. Heart rate was monitored continuously by use of an electrocardiograph. Metabolic and ventilatory parameters were measured through spirometry. RESULTS: A statistically significant correlation between the score obtained with the CFS-APQ and the body weight-adjusted peak oxygen uptake (Spearman rho = -0.32; p = 0.005), functional aerobic impairment (rho = 0.33; p = 0.004), workload/body weight (rho = -0.30; p = 0.009), exercise duration (rho = -0.30; p = 0.008), and the percentage of target heart rate achieved (rho = -0.33; p = 0.004) was observed. The correlations between the remaining exercise capacity parameters and the scores obtained with the CFS-APQ all indicated a trend towards association (0.01 <p<0.05). CONCLUSIONS: These results suggest a moderate association between exercise capacity and activity limitations/participation restrictions in patients with CFS. The observed correlations lack strength to predict activity limitations/ participation restriction based on exercise capacity parameters. Disability evaluation in CFS should therefore encompass both exercise capacity testing and measurements at the activity/participation dimension.
Nijs J, Nicolson GL.		Gulf War Veterans: Evidence for Chromosome Alternations and Their Significance	Journal of Chronic Fatigue Syndrome 2004; 12(1):79-83.	
Nijs J, Vaes P, McGregor N, Lambrecht L, Van Hoof E, De Meirleir K	Department of Human Physiology, Faculty of Physical Education and Physical Therapy, Vrije Universiteit Brussel (VUB), Belgium, Jo.Nijs@vub.ac.be	Comparison of Activity Limitations/Participation Restrictions Among Fibromyalgia and Chronic Fatigue Syndrome Patients	Journal of Chronic Fatigue Syndrome 2004; Mar;11(4):3-18.	Fibromyalgia (FM) and Chronic Fatigue Syndrome (CFS) are related yet overlapping disorders; the current case definitions prohibit a clear-cut differential diagnosis. These diagnostic criteria mainly address the impairment level of the World Health Organization's International Classification of Functioning, Disability and Health. This study aimed at comparing activity limitations and participation restrictions in patients with FM (n = 90) and CFS (n = 47). The Chronic Fatigue Syndrome Activities and Participation Questionnaire (CFS-APQ) was used for assessing functionality in both groups. The convergent validity of the scores obtained with the questionnaire with visual analogue scales for pain, fatigue and concentration was investigated in FM patients, as well as the content validity. No differences in total scores and 25 out of 26 individual items on the CFS-APQ were observed between the 2 groups (independent samples Mann-Whitney U test). This sample of FM patients reported to be more disabled in 'sitting for two hours' as compared to the CFS group (mean scores 3.0 ± 1.0 and 2.3 ± 1.0; P = .004). Four hundred and thirty-seven of the 497 (87.9 %) responses to the request to list difficult activities matched the content of the CFS-APQ. The overall scores of the CFS-APQ correlated statistically significant in respect to visual analogue scales for pain and concentration (Spearman rho for the total scores ranged between .44 and .49). These data question the disease specificity of the CFS-APQ for CFS, but suggests its applicability in 'the Chronic Pain-Fatigue Syndromes'. The present report provides evidence for both the content and convergent validity of the CFS-APQ in FM patients.
Nisenbaum R, Reyes M, Unger ER, Reeves WC.	Viral Exanthems and Herpesvirus Branch, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases/CDC, 1600 Clifton Road, Mail Stop A-15, Building 6, Room 116, Atlanta, GA 30333, USA. ran7@cdc.gov	Factor analysis of symptoms among subjects with unexplained chronic fatigue: what can we learn about chronic fatigue syndrome?	J Psychosom Res. 2004 Feb;56(2):171-8.	OBJECTIVE: Chronic fatigue syndrome (CFS) case definitions agree that fatigue must be unexplained, debilitating and present for at least 6 months, but they differ over accompanying symptoms. Our objective was to compare the 1994 CFS case-defining symptoms with those identified by factor analysis. METHODS: We surveyed the Wichita population and measured the occurrence of 21 symptoms in 1391 chronically fatigued subjects who did not report fatigue-associated medical or psychiatric conditions. We used factor analyses to identify symptom dimensions of fatigue and cluster analysis to assign subjects to subgroups. RESULTS: Forty-three subjects had CFS. We confirmed three factors: musculoskeletal, infection and cognition-mood-sleep, essentially defined by CFS symptoms. Although factor scores were higher among CFS subjects, CFS and non-CFS distributions overlapped substantially. Three clusters also showed overlap between CFS and non-CFS subjects. CONCLUSION: CFS symptomatology is a multidimensional phenomenon overlapping with other unexplained fatiguing syndromes and this must be considered in CFS research.
Noakes TD.		Physiological factors limiting exercise performance in CFS. Comment on: Med Sci	Med Sci Sports Exerc. 2004 Jun;36(6):1087.	

		Sports Exerc. 2003 Jun;35(6):908-13.		
Ohashi K, Bleijenberg G, van der Werf S, Prins J, Amaral LA, Natelson BH, Yamamoto Y.	Educational Physiology Laboratory, Graduate School of Education, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan. yamamoto@edcom.p.u-tokyo.ac.jp	Decreased fractal correlation in diurnal physical activity in chronic fatigue syndrome.	Methods Inf Med. 2004;43(1):26-9.	OBJECTIVES: Our objectives were to study the temporal correlation of physical activity time series in patients with chronic fatigue syndrome (CFS) during normal daily life and to examine if it could identify the altered physical activity in these patients. METHODS: Fractal scaling exponents of diurnal and nocturnal physical activity time series in 10 CFS patients and 6 healthy control subjects (CON) were calculated by the detrended fluctuation analysis (DFA) and the wavelet transform modulus maxima (WTMM) method. We hypothesized that, due to their illness- and/or fatigue-induced resting episodes, altered physical activity patterns in CFS patients might be observed at the interruption of activity bursts. Thus, we further developed a new method, the wavelet transform negative modulus maxima (WTNMM) method, which could evaluate the temporal correlation at the interruption of activities. We compared the fractal scaling exponents for CFS and CON by each method. RESULTS: Both for CFS and CON, we found the fractal time structures in their diurnal physical activity records for at least up to 35 minutes. No group difference was found in nocturnal activities. The WTNMM method revealed that, in diurnal activities, CFS patients had significantly ($p < 0.01$) smaller fractal scaling exponent (0.87 ± 0.03) compared to controls (1.01 ± 0.03). Such a difference was identified neither by the DFA nor WTMM method. CONCLUSIONS: CFS patients had more abrupt interruptions of voluntary physical activity during diurnal periods in normal daily life, probed by the decreased correlation in the negative modulus maxima of the wavelet-transformed activity data, possibly due to their exaggerated fatigue.
Okada T, Tanaka M, Kuratsune H, Watanabe Y, Sadato N.	National Institute for Physiological Sciences, 38 Nishigonaka, Myodaiji, Okazaki, Aichi 444-8585, Japan. tomokada@ibri-kobe.org <tomokada@ibri-kobe.org>	Mechanisms underlying fatigue: a voxel-based morphometric study of chronic fatigue syndrome.	BMC Neurol. 2004 Oct 04;4(1):14.	BACKGROUND: Fatigue is a crucial sensation that triggers rest, yet its underlying neuronal mechanisms remain unclear. Intense long-term fatigue is a symptom of chronic fatigue syndrome, which is used as a model to study the mechanisms underlying fatigue. METHODS: Using magnetic resonance imaging, we conducted voxel-based morphometry of 16 patients and 49 age-matched healthy control subjects. RESULTS: We found that patients with chronic fatigue syndrome had reduced gray-matter volume in the bilateral prefrontal cortex. Within these areas, the volume reduction in the right prefrontal cortex paralleled the severity of the fatigue of the subjects. CONCLUSION: These results are consistent with previous reports of an abnormal distribution of acetyl-L-carnitine uptake, which is one of the biochemical markers of chronic fatigue syndrome, in the prefrontal cortex. Thus, the prefrontal cortex might be an important element of the neural system that regulates sensations of fatigue.
Papanicolaou DA, Amsterdam JD, Levine S, McCann SM, Moore RC, Newbrand CH, Allen G, Nisenbaum R, Pfaff DW, Tsokos GC, Vgontzas AN, Kales A.	Department of Medicine/Endocrinology, Emory University, Atlanta, GA, USA.	Neuroendocrine aspects of chronic fatigue syndrome.	Neuroimmunomodulation. 2004;11(2):65-74.	Chronic fatigue syndrome (CFS) is a serious health concern affecting over 800000 Americans of all ages, races, socioeconomic groups and genders. The etiology and pathophysiology of CFS are unknown, yet studies have suggested an involvement of the neuroendocrine system. A symposium was organized in March 2001 to explore the possibility of an association between neuroendocrine dysfunction and CFS, with special emphasis on the interactions between neuroendocrine dysfunction and other abnormalities noted in the immune and autonomic nervous systems of individuals with CFS. This paper represents the consensus of the panel of experts who participated in this meeting. Copyright 2004 S. Karger AG, Basel
Pazderka-Robinson H, Morrison JW, Flor-Henry P.	Clinical Diagnostics and Research Centre, Alberta Hospital Edmonton, Box 307, 17480 Fort Road, Edmonton, Alberta, Canada T5J 2J7. hannah@ualberta.ca	Electrodermal dissociation of chronic fatigue and depression: evidence for distinct physiological mechanisms.	Int J Psychophysiol. 2004 Aug;53(3):171-82.	Chronic fatigue syndrome (CFS) has an estimated prevalence between 0.5% and 3%, yet its diagnosis remains contentious. CFS is characterized by subjective symptoms that can be difficult to verify; moreover, depression is a commonly reported CFS complaint, whereas fatigue is a common symptom of depression. Our primary goal was dissociation of these disorders using psychophysiological methods. As previous research has implicated the autonomic nervous system in CFS, we conducted what we believe to be the first analysis of bilateral electrodermal and skin temperature responses of dextral females in a cross-modal orienting task, to investigate differences between these two patient groups and controls. A multivariate analysis of variance (MANOVA) examining three measures of electrodermal activity revealed prestimulus tonic skin conductance levels (SCLs) were markedly lower for the CFS group, with no difference between controls and depressives. Concurrent skin temperature levels were higher for the CFS group than the other two groups. These findings indicate that, despite overtly similar cognitive and symptom profiles, depression and CFS patients can be differentiated with psychophysiological measures. This study adds to the growing body of evidence demonstrating that CFS and depression have distinct neurobiological profiles, consistent with unique aetiologies. Copyright 2004 Elsevier B.V.
Pearce JM.	Emeritus Consultant Neurologist, Department of Neurology, Hull Royal Infirmary, Hull, UK.	Myofascial Pain, Fibromyalgia or Fibrositis?	Eur Neurol. 2004 Jul 13;52(2):67-72.	The terms myofascial pain, fibromyalgia and fibrositis are critically examined. They constitute diagnostic labels for non-specific musculoskeletal aches and pains. Analysis of the evidence shows that none of these labels is substantiated by hard physical signs or by laboratory evidence of consistent pathological or biochemical abnormality. What is the objective evidence for disorder(s) of muscle, fascia or fibrous tissues, so clearly indicated by these diagnostic names? Alternative terms such as 'regional pain syndrome' or 'chronic pain syndrome' merely redefine the clinical problem without providing a mechanism or basis for diagnosis. Despite different diagnostic criteria, these conditions, along with chronic fatigue syndrome, have many demographic and clinical similarities, most notably tender trigger points. Indeed, the terms are often used interchangeably. There are few differences in the symptoms, physical findings, laboratory tests, functional status, psychosocial features and psychiatric disorders. This paper seeks

				not to deny the existence of aches and pains, but to critically examine the utility of these terms. The only claimed physical sign is the presence of tender trigger points over muscles or muscle attachments. Research suggests that tender points are a measure of general distress related to pain complaints but separately associated with fatigue and depression. They are present in some normal subjects and are variable in occurrence in time in the same individual. They reflect no demonstrable pathology. It is therefore argued that none of these commonly used diagnoses represent distinct disease entities. A possible but unproven alternative hypothesis is that such symptoms relate to neural pain with both peripheral and central components, and in some instances psychological or wilful embellishment. Copyright 2004 S. Karger AG, Basel
Pendergast DR, Fisher NM, Meksawan K, Doubrava M, Vladutiu GD.	Department of Physiology, University at Buffalo, Buffalo, New York 14214, USA. dpenderg@buffalo.edu	The distribution of white blood cell fat oxidation in health and disease.	J Inherit Metab Dis. 2004;27(1):89-99.	Fat oxidation is important for maintaining health and for supplying energy for exercise. We have proposed that the predisposition for individual rates of fat oxidation is determined genetically but may be modulated by acute exercise or exercise training. The purpose of this study was to examine cellular fat oxidation in white blood cells (WBC) using [9,10-3H]palmitic acid. Sedentary controls free of symptoms (SED-C, n=32), were compared with known carnitine palmitoyltransferase (CPT) II-deficient patients (n=2), patients with fatiguing diseases (chronic fatigue syndrome, CFS, n=6; multiple sclerosis, MS, n=31), obesity (OB, n=5), eating disorders (ED, n=16), sedentary individuals prior to and after exercise (SED-Ex, n=12), exercise-trained sedentary individuals (SED-Tr, n=12), and elite runners (ER, n=5). Fat oxidation in WBC for all subjects was normally distributed (mean=0.270 +/- 0.090 nmol/h per 10(9) WBC) and ranged from 0.09 nmol/h per 10(9) WBC in CPT II-deficient patients to 0.59 nmol/h per 10(9) WBC in ER. There were no significant sex or acute exercise effects on WBC fat oxidation. Patients with MS, OB or ED were not different from SED-C; however, in CPT II-deficient patients, fat oxidation was low, while that of CFS patients was high. Exercise training in SED-C resulted in a 16% increase in fat oxidation but in ER it was still 97% higher than in SED-C. We propose that while WBC fat oxidation is not significantly affected by sex or acute exercise, and only by 15-20% with training, genetic factors play a role in determining both high and low fat oxidation in certain groups of individuals. The genetic predisposition for individual rates of fat oxidation may be easily measured using WBC fat oxidation, as has been shown for CPT II-deficient patients and for elite runners. Ranges of WBC fat oxidation that are abnormally low (<20 nmol/h per 10(9) WBC, normal 20-35) or high (>35 nmol/h per 10(9) WBC) are proposed based on genetic factors evaluated in this study.
Perski A.	Stressmottagningen vid Institutet for psykosocial medicin och Karolinska institutet, Stockholm. aleksander.perski@ipm.ki.se	[Rehabilitation of stress-related diseases goes on different phases and is often long-lasting][Article in Swedish]	Lakartidningen. 2004 Apr 1;101(14):1292-4.	
Poteliakhoff A.		Etanercept and methotrexate in rheumatoid arthritis. Comment on: Lancet. 2004 Feb 28;363(9410):675-81.	Lancet. 2004 May 22;363(9422):1734.	
Powell P, Bentall RP, Nye FJ, Edwards RH.	Department of Psychology, University of Manchester, UK.	Patient education to encourage graded exercise in chronic fatigue syndrome. 2-year follow-up of randomised controlled trial.	Br J Psychiatry. 2004 Feb;184:142-6.	BACKGROUND: An earlier trial demonstrated good outcomes after 1 year for patients with chronic fatigue syndrome (CFS) who received an educational intervention designed to encourage graded activity. AIMS: To determine 2-year outcomes for the same treated patients and the response to treatment of patients formerly in the control condition. METHOD: Patients in the treatment groups (n=114) were followed up at 2 years; 32 patients from the control group were offered the intervention after 1 year and were assessed 1 year later. Assessments were the self-rated measures used in the original trial. RESULTS: At 2 years 63 of the treated patients (55%) no longer fulfilled trial criteria for CFS compared with 64 patients (56%) at 1 year. Fourteen of 30 crossover patients (47%) achieved a good outcome at 1 year and seven (23%) no longer fulfilled criteria for CFS. CONCLUSIONS: Benefits of the intervention were maintained at 2 years. Delaying treatment is associated with reduced efficacy and required more intensive therapy.
Price JS, Gardner R Jr, Erickson M.	Odintune Place, Plumpton, East Sussex BN7 3AN, UK. john.price@lycosmail.com	Can depression, anxiety and somatization be understood as appeasement displays?	J Affect Disord. 2004 Apr;79(1-3):1-11.	BACKGROUND: No satisfactory basis in normal function characterizes major depression and its co-morbid disorders. Yet these may represent maladaptive expression of adaptive communicational states exhibited normally in many species. METHODS: We examined the signal value of depressive and anxious mood states, fatigue syndrome and somatoform disorders and found them to resemble appeasement or submission to conspecifics (members of a same species) as studied in other animals. Moreover, applying game theory formulations of conflict resolution and the triune brain theory of MacLean supported the hypothesis. LIMITATIONS: Direct experimental evidence must still test hypotheses that emanate from the presented framework. Conclusions: Implications for this approach include improved understanding and treatment of depression, improved research

				strategies, and a potential future pathogenesis-focused nosology.
Prins JB, Bos E, Huibers MJ, Servaes P, van der Werf SP, van der Meer JW, Bleijenberg G.	Department of Medical Psychology, University Medical Centre Nijmegen, Nijmegen, The Netherlands. j.prins@cukz.umcn.nl	Social support and the persistence of complaints in chronic fatigue syndrome.	Psychother Psychosom. 2004 May-Jun;73(3):174-82.	BACKGROUND: Several studies suggested that the surroundings of chronic fatigue syndrome (CFS) patients are of importance in the persistence of complaints. Contrary to what was expected, participation in support groups has not led to clinical improvement. The purpose of the present study was to describe social support in CFS patients as compared with other fatigued and non-fatigued groups. Further, changes in social support and the influence of social support on the course of CFS over a period of more than 1 year were studied in patients with and without treatment. METHODS: Baseline data were assessed in 270 CFS patients, 150 disease-free breast cancer patients, 151 fatigued employees on sick-leave and 108 healthy subjects using the Social Support List and Significant Others Scale. CFS patients were followed in cognitive behaviour therapy (CBT), guided support groups and natural course at 8 and 14 months. RESULTS: CFS patients and fatigued employees reported more negative interactions and insufficiency of supporting interactions than cancer patients and healthy controls. No differences in frequency of supporting interactions were found. Negative interactions decreased significantly after treatment with CBT, but did not change in support groups or natural course. In the natural course, higher fatigue severity at 8 months was predicted by more negative interactions at baseline. CONCLUSIONS: In CFS patients and fatigued employees, social support is worse than in disease-free cancer patients and healthy controls. Lack of social support was identified as a new factor in the model of perpetuating factors of fatigue severity and functional impairment in CFS. Copyright 2004 S. Karger AG, Basel
Puri BK, Holmes J, Hamilton G.	MRI Unit, Imaging Sciences Department, MRC Clinical Sciences Centre, Imperial College School of Medicine, Hammersmith Hospital, London, UK.	Eicosapentaenoic acid-rich essential fatty acid supplementation in chronic fatigue syndrome associated with symptom remission and structural brain changes.	Int J Clin Pract. 2004 Mar;58(3):297-9.	Lateral ventricular enlargement has been reported in chronic fatigue syndrome, while cerebral neurospectroscopy has recently indicated that essential fatty acid treatment may be of value in this condition. An essential fatty acid supplement rich in eicosapentaenoic acid (EPA) was therefore given daily to a female patient with a 6-year history of unremitting symptoms of chronic fatigue syndrome. Cerebral magnetic resonance scanning was carried out at baseline and 16 weeks later. The EPA-rich essential fatty acid supplementation led to a marked clinical improvement in her symptoms of chronic fatigue syndrome, starting within 6-8 weeks. Accurate quantification of the lateral ventricular volumes in the baseline and 16-week follow-up registered images of high-resolution magnetic resonance imaging structural scans showed that the treatment was accompanied by a marked reduction in the lateral ventricular volume during this period, from 28,940-23,660 mm ³ .
Puri BK.	MRI Unit, Imaging Sciences Department, MRC Clinical Sciences Centre, Imperial College School of Medicine, Hammersmith Hospital, Du Cane Road, London W12 0HS, England, UK. basant.puri@csc.mrc.ac.uk	The use of eicosapentaenoic acid in the treatment of chronic fatigue syndrome.	Prostaglandins Leukot Essent Fatty Acids. 2004 Apr;70(4):399-401.	There is evidence that there is an association between chronic fatigue syndrome, a condition of unknown aetiology, and essential fatty acids. This evidence is based on the actions of essential fatty acids, the results of proton neurospectroscopy studies, and essential fatty acid trial data. A series of patients with chronic fatigue syndrome were treated solely with a high-eicosapentaenoic acid-containing essential fatty acid supplement. All showed improvement in their symptomatology within eight to 12 weeks. These results, which are consistent with a recent detailed report of cerebral and clinical changes associated with a high intake of eicosapentaenoic acid, suggest that this n-3 highly unsaturated fatty acid may offer the hope of effective treatment for at least some patients with chronic fatigue syndrome.
Raine R, Sanderson C, Hutchings A, Carter S, Larkin K, Black N.	Health Services Research Unit, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK. rosalind.raine@lshtm.ac.uk	An experimental study of determinants of group judgments in clinical guideline development. Comment in: Lancet. 2004 Jul 31;364(9432):392-3.	Lancet. 2004 Jul 31;364(9432):429-37.	BACKGROUND: Clinical guidelines for improving the quality of care are a familiar part of clinical practice. Formal consensus methods such as the nominal group technique are often used as part of guideline development, but little is known about factors that affect the statements produced by nominal groups, and on their consistency with the research evidence. METHODS: Cognitive behavioural therapy, behavioural therapy, brief psychodynamic interpersonal therapy, and antidepressants for irritable bowel syndrome, chronic fatigue syndrome, and chronic back pain were selected for study. 16 nominal groups in a factorial design allowed comparison of GP-only with mixed groups of GPs and specialists, provision of a literature review with no provision, and ratings made in the context of realistic or ideal levels of health-care resources. Participants rated appropriateness independently, and again after a facilitated meeting. Audiotapes of four group discussions were analysed. FINDINGS: There was agreement with the research evidence for 51% of 192 scenarios. Agreement was more likely if the group was GP-only, if a literature review was provided, or if the evidence was in accordance with clinicians' beliefs. Assumptions about the level of resources available had no impact. Clinical and social cues had mixed effects, irrespective of the research evidence. Qualitative analysis showed the modifying effect of clinical experience and beliefs about research evidence. INTERPRETATION: Guidelines cannot be based on data alone; judgment is unavoidable. The nominal group technique is a method of eliciting and aggregating judgments in a transparent and structured way. It can provide important information on levels of agreement between experts. However, conclusions can be at odds with the published literature. If they are, reasons need to be explicit.
Raine R, Carter S, Sensky T, Black N.	Department of Public Health and Policy,	General practitioners' perceptions of chronic	BMJ. 2004 Jun 5;328(7452):1354-7.	OBJECTIVES: To compare general practitioners' perceptions of chronic fatigue syndrome and irritable bowel syndrome and to consider the implications of their perceptions for treatment. DESIGN: Qualitative analysis of transcripts of group discussions.

	London School of Hygiene and Tropical Medicine, London WC1E 7HT. rosalind.raine@lshtm.ac.uk	fatigue syndrome and beliefs about its management, compared with irritable bowel syndrome: qualitative study. Comment in: BMJ. 2004 Jul 10;329(7457):112-3.	Epub 2004 May 28.	PARTICIPANTS AND SETTING: A randomly selected sample of 46 general practitioners in England. RESULTS: The participants tended to stereotype patients with chronic fatigue syndrome as having certain undesirable traits. This stereotyping was due to the lack of a precise bodily location; the reclassification of the syndrome over time; transgression of social roles, with patients seen as failing to conform to the work ethic and "sick role" and conflict between doctor and patient over causes and management. These factors led to difficulties for many general practitioners in managing patients with chronic fatigue syndrome. For both conditions many participants would not consider referral for mental health interventions, even though the doctors recognised social and psychological factors, because they were not familiar with the interventions or thought them unavailable or unnecessary. CONCLUSIONS: Barriers to the effective clinical management of patients with irritable bowel syndrome and chronic fatigue syndrome are partly due to doctors' beliefs, which result in negative stereotyping of patients with chronic fatigue syndrome and the use of management strategies for both syndromes that may not take into account the best available evidence.
Reeves WC, Lloyd A, Vernon SD, Klimas N, Jason LA, Bleijenberg G, Evengard B, White PD, Nisenbaum R, Unger ER, .	Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America. wcr1@cdc.gov	Identification of ambiguities in the 1994 chronic fatigue syndrome research case definition and recommendations for resolution.	BMC Health Serv Res. 2003 Dec 31;3(1):25.	BACKGROUND: Chronic fatigue syndrome (CFS) is defined by symptoms and disability, has no confirmatory physical signs or characteristic laboratory abnormalities, and the etiology and pathophysiology remain unknown. Difficulties with accurate case ascertainment contribute to this ignorance. METHODS: Experienced investigators from around the world who are involved in CFS research met for a series of three day workshops in 2000, 2001 and 2002 intended to identify the problems in application of the current CFS case definition. The investigators were divided into focus groups and each group was charged with a topic. The investigators in each focus group relied on their own clinical and scientific knowledge, brainstorming within each group and with all investigators when focus group summaries were presented. Relevant literature was selected and reviewed independent of the workshops. The relevant literature was circulated via list-serves and resolved as being relevant by group consensus. Focus group reports were analyzed and compiled into the recommendations presented here. RESULTS: Ambiguities in the current CFS research definition that contribute to inconsistent case identification were identified. Recommendations for use of the definition, standardization of classification instruments and study design issues are presented that are intended to improve the precision of case ascertainment. The International CFS Study Group also identified ambiguities associated with exclusionary and comorbid conditions and reviewed the standardized, internationally applicable instruments used to measure symptoms, fatigue intensity and associated disability. CONCLUSION: This paper provides an approach to guide systematic, and hopefully reproducible, application of the current case definition, so that case ascertainment would be more uniform across sites. Ultimately, an operational CFS case definition will need to be based on empirical studies designed to delineate the possibly distinct biological pathways that result in chronic fatigue.
Reuter K, Harter M.	Freiburg University Medical Center, Department of Psychiatry and Psychotherapy, Freiburg, Germany.	The concepts of fatigue and depression in cancer.	Eur J Cancer Care (Engl). 2004 May;13(2):127-34.	REUTER K. & HARTER M. (2004) European Journal of Cancer Care13, 127-134 The concepts of fatigue and depression in cancer A strong association between fatigue and depression in cancer patients has been reported repeatedly in clinical studies. The distinction remains difficult, mainly because of the similar phenomenology of fatigue and depression. It is the aim of this paper to work out similarities and differences in the conception of fatigue and depressive disorders. For that, a differentiation between depression as emotional distress and depression as clinical syndrome, according to the current classification systems, has to be made. Therefore, the classification of depressive disorders and their criteria is presented in the second section of this paper, especially in view of the diagnosis of depressive disorders in cancer patients. The comparison of the multidimensional fatigue construct and depression shows a strong overlap of symptoms. None of the fatigue symptoms are specific for fatigue, all being elements of depressive syndromes. It is in particular the psychological symptoms of depressive disorders that differentiate between the two concepts. To that end, the question is discussed whether fatigue in its current conceptualization can be defined as a diagnostic entity independent of depressive disorders. Additionally, research approaches are presented from the area of the chronic fatigue syndrome and neurasthenia, which could be adapted to cancer-related fatigue and help to clarify the clinical differences between fatigue and depression. In order to ensure better differential diagnostics in the future, criteria-orientated research in particular is needed.
Reynolds KJ, Vernon SD, Bouchery E, Reeves WC.	Division of Viral and Rickettsial Diseases, Centers for Disease Control and Prevention, Atlanta, U,S,A. wcr1@cdc.gov	The economic impact of chronic fatigue syndrome.	Cost Eff Resour Alloc. 2004 Jun 21;2(1):4.	BACKGROUND: Chronic fatigue syndrome (CFS) is a chronic incapacitating illness that affects between 400,000 and 800,000 Americans. Despite the disabling nature of this illness, scant research has addressed the economic impact of CFS either on those affected or on the national economy. METHODS: We used microsimulation methods to analyze data from a surveillance study of CFS in Wichita, Kansas, and derive estimates of productivity losses due to CFS. RESULTS: We estimated a 37% decline in household productivity and a 54% reduction in labor force productivity among people with CFS. The annual total value of lost productivity in the United States was \$9.1 billion, which represents about \$20,000 per person with CFS or approximately one-half of the household and labor force productivity of the average person with this syndrome. CONCLUSION: Lost productivity due to CFS was substantial both on an individual basis and relative to national estimates for other major illnesses. CFS resulted in a national productivity loss comparable to such losses from diseases of the digestive, immune and nervous systems, and from skin disorders. The extent of the burden indicates that continued research to determine the cause and potential therapies for CFS could provide substantial benefit both for individual patients and for the nation.

Richardson RD, Engel CC Jr.	VA Puget Sound Healthcare System, Seattle, WA, USA.	Evaluation and management of medically unexplained physical symptoms.	Neurologist. 2004 Jan;10(1):18-30.	BACKGROUND: Medically unexplained physical symptoms (MUPS) and related syndromes are common in medical care and the general population, are associated with extensive morbidity, and have a large impact on functioning. Much of medical practice emphasizes specific pharmacological and surgical intervention for discrete disease states. Medical science, with its emphasis on identifying etiologically meaningful diseases comprised of homogeneous groups of patients, has split MUPS into a number of diagnostic entities or syndromes, each with its own hypothesized pathogenesis. However, research suggests these syndromes may be more similar than different, sharing extensive phenomenological overlap and similar risk factors, treatments, associated morbidities, and prognoses. Examples of syndromes consisting of MUPS include chronic fatigue syndrome, fibromyalgia, multiple chemical sensitivities, somatoform disorders, and 'Gulf War Syndrome.' REVIEW SUMMARY: This paper is a narrative review of the increasing body of evidence suggesting that MUPS and related syndromes are common, disabling, and costly. It emphasizes that MUPS occur along a continuum of symptom count, severity, and duration and may be divided into acute, subacute (or recurrent), and chronic types. Predisposing, precipitating, and perpetuating factors influence the natural history of MUPS. CONCLUSIONS: Effective symptom management involves collaborative doctor-patient approaches for identification of problems based on a combination of medical importance and patient readiness to initiate behavioral change, negotiated treatment goals and outcomes, gradual physical activation and exercise prescription. Additionally, efforts should be made to teach and support active rather than passive coping with the symptoms.
Ridsdale L, Darbshire L, Seed PT.	Department of Neurology, Guy's, King's and St Thomas's School of Medicine, London.	Is graded exercise better than cognitive behaviour therapy for fatigue? A UK randomized trial in primary care.	Psychol Med. 2004 Jan;34(1):37-49.	BACKGROUND: Patients frequently present with unexplained fatigue in primary care, but there have been few treatment trials in this context. We aimed to test cognitive behaviour therapy (CBT) and graded exercise therapy (GET) for patients presenting to their family doctor with fatigue. Secondly, we described the outcome for a cohort of patients who presented to the same doctors with fatigue, who received standard care, plus a booklet. METHOD: This was a randomized trial, followed by a prospective cohort study. Twenty-two practices in SE England referred 144 patients aged 16 to 75 years with over 3 months of unexplained fatigue. Self-rated fatigue score, the hospital anxiety and depression rating scale, functional impairment, physical step-test performance and causal attributions were measured. In the trial six sessions of CBT or GET were randomly allocated. RESULTS: In the therapy groups the mean fatigue score decreased by 10 points (95% confidence interval (CI) = -25 to -15), with no significant difference between groups (mean difference = -1.3; CI = -3.9 to 1.3). Fewer patients attended for GET. At outcome one-half of patients had clinically important fatigue in both randomized groups, but patients in the group offered CBT were less anxious. Twenty-seven per cent of the patients met criteria for CFS at baseline. Only 25% of this subgroup recovered, compared to 60% of the subgroup that did not meet criteria for CFS. CONCLUSIONS: Short courses of GET were not superior to CBT for patients consulting with fatigue of over 3 months in primary care. CBT was easier 'to sell'. Low recovery in the CFS subgroup suggests that brief treatment is too short.
Roberts AD, Wessely S, Chalder T, Papadopoulous A, Cleare AJ.	Section of General Hospital Psychiatry, Division of Psychological Medicine, Guy's, King's and St Thomas' School of Medicine and Dentistry, London, UK.	Salivary cortisol response to awakening in chronic fatigue syndrome.	Br J Psychiatry. 2004 Feb;184:136-41.	BACKGROUND: There is accumulating evidence of hypothalamic-pituitary-adrenal (HPA) axis disturbances in chronic fatigue syndrome (CFS). The salivary cortisol response to awakening has been described recently as a non-invasive test of the capacity of the HPA axis to respond to stress. The results of this test correlate closely with those of more invasive dynamic tests reported in the literature; furthermore, it can be undertaken in a naturalistic setting. AIMS: To assess the HPA axis using the salivary cortisol response to awakening in CFS. METHOD: We measured salivary cortisol upon awakening and 10, 20, 30 and 60 min afterwards in 56 patients with CFS and 35 healthy volunteers. RESULTS: Patients had a lower cortisol response to awakening, measured by the area under the curve. CONCLUSIONS: This naturalistic test of the HPA axis response to stress showed impaired HPA axis function in CFS.
Ross SD, Estok RP, Frame D, Stone LR, Ludensky V, Levine CB.	MetaWorks Inc, 10 President's Landing, Medford, MA 02155, USA.	Disability and chronic fatigue syndrome: a focus on function.	Arch Intern Med. 2004 May 24;164(10):1098-107.	BACKGROUND: Evidence was sought in the published literature on how best to measure, monitor, and treat disability in patients with chronic fatigue syndrome (CFS). METHODS: A systematic review was performed of English-language literature published between January 1, 1988, and November 15, 2001. Interventional and observational studies of adults with CFS were eligible if they reported measures of disability and employment. A qualitative synthesis of results relating impairment measures to employment was performed. RESULTS: Of 3840 studies identified, 37 reported employment status and some measure of mental or physical impairment associated with disability. Most patients with CFS in these studies were unemployed. In 22 studies, the employment status of control subjects was also available. Only depression seemed to be associated with unemployment in patients with CFS. No other measurable impairment seemed to be consistently associated with disability or work outcomes. Only cognitive behavior therapy, rehabilitation, and exercise therapy interventions were associated with restoring the ability to work. No specific patient characteristics were identified as best predictors of positive employment outcomes. No quantitative syntheses of results were performed. CONCLUSIONS: For questions of disability and employment in CFS, the limitations inherent in the current literature are extensive. Methodologically rigorous, longitudinal, and interventional studies are needed to determine baseline characteristics that are associated with the inability to work and interventions that are effective in restoring the ability to work in the CFS population. Simple and consistent evaluations of functional capacity in patients with CFS are needed.
Roy-Byrne P, Smith	Department of	Post-traumatic stress	Psychol Med. 2004	BACKGROUND: Fibromyalgia (FM), a chronic pain condition of unknown aetiology often develops following a traumatic

WR, Goldberg J, Afari N, Buchwald D.	Psychiatry and Behavioral Science, University of Washington, Seattle, WA, USA.	disorder among patients with chronic pain and chronic fatigue.	Feb;34(2):363-8.	event. FM has been associated with post-traumatic stress disorder (PTSD) and major depression disorder (MDD). METHOD: Patients seen in a referral clinic (N=571) were evaluated for FM and chronic fatigue syndrome (CFS) criteria. Patients completed questionnaires, and underwent a physical examination and a structured psychiatric evaluation. Critical components of the diagnostic criteria of FM (tender points and diffuse pain) and CFS (persistent debilitating fatigue and four of eight associated symptoms) were examined for their relationship with PTSD. RESULTS: The prevalence of lifetime PTSD was 20% and lifetime MDD was 42%. Patients who had both tender points and diffuse pain had a higher prevalence of PTSD (OR=3.4, 95% CI 2.0-5.8) compared with those who had neither of these FM criteria. Stratification by MDD and adjustment for sociodemographic factors and chronic fatigue revealed that the association of PTSD with FM criteria was confined to those with MDD. Patients with MDD who met both components of the FM criteria had a three-fold increase in the prevalence of PTSD (95% CI 1.5-7.1); conversely, FM patients without MDD showed no increase in PTSD (OR=1.3, 95% CI 0.5-3.2). The components of the CFS criteria were not significantly associated with PTSD. CONCLUSION: Optimal clinical care for patients with FM should include an assessment of trauma in general, and PTSD in particular. This study highlights the importance of considering co-morbid MDD as an effect modifier in analyses that explore PTSD in patients with FM. PMID: 14982142 [PubMed - in process]
Sackner MA, Gummels EM, Adams JA.	Mt. Sinai Medical Center of Greater Miami, Division of Pulmonary Disease and Critical Care Medicine, Miami Beach, FL 33140, USA. artchive@msn.com	Say NO to fibromyalgia and chronic fatigue syndrome: an alternative and complementary therapy to aerobic exercise.	Med Hypotheses. 2004;63(1):118-23.	Increased shear stress to the endothelium increases activity of endothelial nitric oxide synthase (eNOS) with subsequent release of small quantities (nMol) of nitric oxide (NO) into the circulation. It occurs during moderate aerobic exercise mostly as a result of laminar shear stress and with whole body, periodic acceleration as a result of pulsatile shear stress. The latter is administered by means of a new, non-invasive, passive exercise device. Moderate exercise has long been known to alleviate the symptoms of fibromyalgia and chronic fatigue syndrome and in the current study, whole body, periodic acceleration did as well. Since NO through action of eNOS has potent anti-inflammatory properties mainly by suppressing nuclear factor kappa-beta activity, it is hypothesized that both diseases have chronic inflammation as their basis. Whole body periodic acceleration can be applied separately or supplementary to aerobic exercise in the treatment of fibromyalgia and chronic fatigue syndrome.
Schacterle RS, Komaroff AL.	Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts 02115, USA.	A comparison of pregnancies that occur before and after the onset of chronic fatigue syndrome.	Arch Intern Med. 2004 Feb 23;164(4):401-4.	BACKGROUND: Many women with chronic fatigue syndrome (CFS) fear that pregnancy will worsen their condition, increase the risks of maternal complications of pregnancy, or threaten the health of their offspring. Little empirical evidence, however, has been published on this matter. METHODS: A detailed questionnaire was administered to 86 women regarding 252 pregnancies that occurred before or after the onset of CFS and the outcomes of these pregnancies were observed. RESULTS: During pregnancy, there was no change in CFS symptoms in 29 (41%), an improvement of symptoms in 21 (30%), and a worsening of symptoms in 20 (29%) of 70 subjects. After pregnancy, there was no change in CFS symptoms in 21 (30%), an improvement of symptoms in 14 (20%), and a worsening of symptoms in 35 (20%) of the subjects. The rates of many complications were similar in pregnancies occurring before the onset and in those occurring after the onset of CFS. There was a higher frequency of spontaneous abortions in the pregnancies occurring after, vs before, the onset of CFS (22 [30%] of 73 pregnancies after vs 13 [8%] of 171 before; P<.001), but no differences in the rates of other complications. Developmental delays or learning disabilities were reported more often in the offspring of women who became pregnant after, vs before, the onset of CFS (9 [21%] of 43 children vs 11 [8%] of 139 children; P=.01). CONCLUSIONS: Pregnancy did not consistently worsen the symptoms of CFS. Most maternal and infant outcomes were not systematically worse in pregnancies occurring after the onset of CFS. The higher rates of spontaneous abortions and of developmental delays in offspring that we observed could be explained by maternal age or parity differences, and should be investigated by larger, prospective studies with control populations.
Schacterle RS, Milford EL, Komaroff AL	Division of General Medicine and Primary Care, Brigham and Women's Hospital, and Harvard Medical School, Boston, MA, 02115, USA	The Frequency of HLA Class II Antigens in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2004; Mar;11(4):33-42.	Chronic fatigue syndrome is a condition characterized by unexplained, persistent fatigue in conjunction with other generalized symptoms. However, the patients as a group are more likely to have objective abnormalities of the immune system than control subjects. We measured the frequency of certain HLA antigens in a representative group of 35 patients. We restricted our analysis to class II molecules as these appear to be more specific predictors of susceptibility to immunologically based disorders. The frequency of the HLA-DQ1 antigen was increased in patients compared to general population Caucasian controls. This association between chronic fatigue syndrome and the HLA-DQ1 antigen translates into a relative risk of 3.2. This association has not been reported previously in chronic fatigue syndrome. Differences in the ethnic sub-grouping of patients in this study and in previous studies also could have contributed to the difference between our findings and those of previous investigators. Conversely, this study did not find HLA associations that have been reported by previous studies. The sample size of this study could have led to type II statistical errors and a failure to recognize certain HLA associations as significant.
Schillings ML, Kalkman JS, van der Werf SP, van Engelen BG, Bleijenberg G, Zwartz MJ.	Department of Clinical Neurophysiology, University Medical Centre Nijmegen, Internal postal code 314, P.O. Box 9101,	Diminished central activation during maximal voluntary contraction in chronic fatigue syndrome.	Clin Neurophysiol. 2004 Nov;115(11):2518-24.	OBJECTIVE: We have investigated whether central activation failure (CAF) is increased during local muscle fatigue in chronic fatigue syndrome (CFS). METHODS: Fourteen female CFS patients and 14 age-matched healthy female controls made a 2 min sustained maximal voluntary contraction (MVC) of the biceps brachii muscle. Before, during, and after sustained MVC, electrical endplate stimulation was applied. Force and 5 channel surface EMG (sEMG) were registered. RESULTS: Although force responses upon stimulation during rest did not differ between patients and controls, MVC was significantly lower in patients. Already at the beginning of sustained MVC, CFS patients showed significantly larger CAF than controls (36.5+/-17.0% and

	6500 HB Nijmegen, Netherlands.			12.9+/-13.3%, respectively). For all individual patients mean CAF over the first 45 s was higher than 30%, while it was below 30% for all controls. Less peripheral fatigue in patients was demonstrated by the changes in muscle fibre conduction velocity and the differences between force responses before and after contraction. CONCLUSIONS: Central activation is diminished in CFS patients. Possible causes include changed perception, impaired concentration, reduced effort and physiologically defined changes, e.g. in the corticospinal excitability or the concentration of neurotransmitters. As a consequence, demands on the muscle are lower, resulting in less peripheral fatigue. SIGNIFICANCE: CFS patients show reduced central activation during MVC. The underlying pathophysiological processes remain still to be determined.
Scroop GC, Burnet RB.	Lung Function, Royal Adelaide Hospital, North Terrace, Adelaide, SA 5000 gscroop@mail.rah.sa.gov.au.	To exercise or not to exercise in chronic fatigue syndrome?	Med J Aust. 2004 Nov 15;181(10):578-580.	
Severens JL, Prins JB, van der Wilt GJ, van der Meer JW, Bleijenberg G.	Department of Medical Technology Assessment, University Medical Centre Nijmegen, The Netherlands. h.severens@boez.unima.nl	Cost-effectiveness of cognitive behaviour therapy for patients with chronic fatigue syndrome.	QJM. 2004 Mar;97(3):153-61.	BACKGROUND: There is some evidence that cognitive behaviour therapy (CBT) is efficacious in chronic fatigue syndrome (CFS), but little data on its cost-effectiveness. DESIGN: Prospective economic analysis alongside a randomized clinical trial. METHODS: CFS patients were randomly assigned to CBT, guided support groups (SG), or the 'natural course' (NC, no protocol-based interventions). Patients were treated for 8 months and followed-up for another 6 months. Costs per patient showing clinically significant improvement, based on the CIS fatigue scale, and costs per quality-adjusted life year, were determined for a time period of 14 months. RESULTS: Data were available for 171 patients at 8 months and for 128 at 14 months. At 8 and 14 months, the percentages of improved patients were 31% and 27% for CBT, 9% and 11% for SG, and 12% and 20% for NC. Mean QALYs gained at 14 months were, for CBT, SG and NC, respectively, 0.0737, -0.0018 and 0.0458. CBT and SG mean treatment costs were euro1490 and euro424. Other medical costs for CBT, SG, and NC, respectively, were euro324, euro623 and euro412 for the first period, and euro232, euro561 and euro378 for the second period. Non-medical costs for these periods for CBT, SG and NC were euro262, euro550, euro427 and euro226, euro439, euro287, respectively. Productivity costs were considerable, but not significantly different between groups. DISCUSSION: CBT was less costly and more effective than SG. Compared to NC, the baseline incremental cost-effectiveness of CBT was euro20 516 per CFS patient showing clinically significant improvement, and euro21 375 per QALY. The bootstrap ratios showed considerable uncertainty regarding the results. Future research should focus on productivity costs, and follow patients prospectively over a longer period.
Shapiro CM.		Chronic fatigue--chronically confusing but growing information.	J Psychosom Res. 2004 Feb;56(2):153-5.	
Shaver JL.	University of Illinois at Chicago, College of Nursing, M/C 802, 845 South Damen Avenue, Chicago, IL 60612-7350, USA. jshaver@uic.edu	Fibromyalgia syndrome in women.	Nurs Clin North Am. 2004 Mar;39(1):195-204, viii.	Many more women than men experience the chronically fatiguing condition of fibromyalgia syndrome (FMS), a growing diagnosis in the United States. Estimates are that upwards of 2% to 6% of adults have been diagnosed with FMS, and at high societal costs. In this article, common manifestations are described to guide assessment and various lines of research are explored as a basis for understanding contributing factors and potential treatments for FMS and other chronic disorders, such as chronic fatigue syndrome (CFS), irritable bowel syndrome (IBS), and temporomandibular disorders (TMD), and the effectiveness of current treatment options.
Shepherd C.		Patients with chronic fatigue syndrome are being ignored.	BMJ. 2004 Dec 11;329(7479):1405. Comment on: BMJ. 2004 Oct 23;329(7472):928-9.	
Shin HY, An NH, Cha YJ, Shin EJ, Shin TY, Baek SH, Kim CH, Lyu YS, Lee EJ, Kim HM.	Department of Pharmacology, College of Oriental Medicine, Kyung Hee University, Seoul, South Korea.	Effect of Kuibitang on lipopolysaccharide-induced cytokine production in peripheral blood mononuclear cells of chronic fatigue syndrome patients.	J Ethnopharmacol. 2004 Feb;90(2-3):253-9.	Kuibitang (KBT) is clinically used to treat patients suffering from chronic fatigue syndrome (CFS) in South Korea. However, its effect has not been investigated experimentally. Recent reports have shown that CFS patients display an altered cytokine production. We examined the effect of KBT on lipopolysaccharide (LPS)-induced various cytokines production in peripheral blood mononuclear cells (PBMC) of CFS patients and healthy controls. KBT (1 mg/ml) significantly inhibited LPS-induced tumor necrosis factor-alpha, interleukin-10, and transforming growth factor-beta1 production in PBMC of CFS patients. However, LPS-induced interferon-gamma production was significantly increased by KBT (0.01 mg/ml). These results provide evidence of a novel activity of the KBT that regulate cytokines production related with CFS.

Siemionow V, Fang Y, Calabrese L, Sahgal V, Yue GH.	Department of Biomedical Engineering, The Lerner Research Institute, The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195, USA.	Altered central nervous system signal during motor performance in chronic fatigue syndrome.	Clin Neurophysiol. 2004 Oct;115(10):2372-81.	OBJECTIVE: The purpose of this study was to determine whether brain activity of chronic fatigue syndrome (CFS) patients during voluntary motor actions differs from that of healthy individuals. METHODS: Eight CFS patients and 8 age- and gender-matched healthy volunteers performed isometric handgrip contractions at 50% maximal voluntary contraction level. They first performed 50 contractions with a 10 s rest between adjacent trials--'Non-Fatigue' (NFT) task. Subsequently, the same number of contractions was performed with only a 5 s rest between trials--'Fatigue' (FT) task. Fifty-eight channels of surface EEG were recorded simultaneously from the scalp. Spectrum analysis was performed to estimate power of EEG frequency in different tasks. Motor activity-related cortical potential (MRCP) was derived by triggered averaging of EEG signals associated with the muscle contractions. RESULTS: Major findings include: (i) Motor performance of the CFS patients was poorer than the controls. (ii) Relative power of EEG theta frequency band (4-8 Hz) during performing the NFT and FT tasks was significantly greater in the CFS than control group ($P < 0.05$). (iii) The amplitude of MRCP negative potential (NP) for the combined NFT and FT tasks was higher in the CFS than control group ($P < 0.05$) (iv) Within the CFS group, the NP was greater for the FT than NFT task ($P < 0.01$), whereas no such difference between the two tasks was found in the control group. CONCLUSIONS: These results clearly show that CFS involves altered central nervous system signals in controlling voluntary muscle activities, especially when the activities induce fatigue. SIGNIFICANCE: Physical activity-induced EEG signal changes may serve as physiological markers for more objective diagnosis of CFS.
Skapinakis P, Lewis G, Mavreas V.	Department of Psychiatry, University of Ioannina, School of Medicine, Greece. pskapin@cc.uoi.gr	Temporal relations between unexplained fatigue and depression: longitudinal data from an international study in primary care.	Psychosom Med. 2004 May-Jun;66(3):330-5.	OBJECTIVE: Unexplained fatigue syndromes, such as chronic fatigue syndrome and neurasthenia, are strongly associated with depression, but the temporal nature of this association is not clear. METHODS: The authors examined this issue by using data from the World Health Organization collaborative study of psychological problems in general health care. Three thousand two hundred one subjects from 15 primary care centers in 14 countries were followed up for 12 months. The Composite International Diagnostic Interview was the main instrument used. Odds ratios and their 95% confidence intervals (CI) were calculated using logistic regression models adjusted for sociodemographic variables, physical morbidity and intercenter variability. RESULTS: Cases of depression were found to have an increased risk of developing a new episode of unexplained fatigue at follow-up with an adjusted odds ratio of 4.15 (95% CI = 2.64-6.54). Similarly, cases of unexplained fatigue were found to have an increased risk of developing a new episode of depression at follow-up with an adjusted odds ratio of 2.76 (95% CI = 1.32-5.78). Further adjustment for subthreshold symptoms at baseline weakened the reported associations, especially between fatigue and development of a new episode of depression, but these remained significant. CONCLUSIONS: The findings support the view that unexplained fatigue and depression might act as independent risk factors for each other.
Skowera A, Cleare A, Blair D, Bevis L, Wessely SC, Peakman M.	Department of Immunology, Guy's, King's & St Thomas's School of Medicine, King's College London, London, UK.	High levels of type 2 cytokine-producing cells in chronic fatigue syndrome.	Clin Exp Immunol. 2004 Feb;135(2):294-302.	The aetiology of chronic fatigue syndrome (CFS) is not known. However, it has been suggested that CFS may be associated with underlying immune activation resulting in a Th2-type response. We measured intracellular production of interferon (IFN)-gamma and interleukin (IL)-2; type 1 cytokines, IL-4 (type 2) and IL-10 (regulatory) by both polyclonally stimulated and non-stimulated CD4 and CD8 lymphocytes from patients with CFS and control subjects by flow cytometry. After polyclonal activation we found evidence of a significant bias towards Th2- and Tc2-type immune responses in CFS compared to controls. In contrast, levels of IFN-gamma, IL-2 and IL-10-producing cells were similar in both study groups. Non-stimulated cultures revealed significantly higher levels of T cells producing IFN-gamma or IL-4 in CFS patients. Concluding, we show evidence for an effector memory cell bias towards type 2 responsiveness in patients with CFS, as well as ongoing type 0 immune activation in unstimulated cultures of peripheral blood cells.
Smith MS.		Adolescent chronic fatigue syndrome. Comment on: Arch Pediatr Adolesc Med. 2004 Mar;158(3):225-9.	Arch Pediatr Adolesc Med. 2004 Mar;158(3):207-8.	
Solomon L, Reeves WC.	Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA.	Factors influencing the diagnosis of chronic fatigue syndrome.	Arch Intern Med. 2004 Nov 8;164(20):2241-5.	BACKGROUND: Most of what is believed about chronic fatigue syndrome (CFS) is based on clinic-based studies. These studies may not reflect CFS cases in the population. METHODS: We used data from a population-based study of CFS to identify factors associated with receiving a CFS diagnosis. Wichita, Kan, residents were screened by random-digit dialing. Eligible individuals completed a telephone interview. Respondents meeting CFS criteria were invited for a clinical evaluation to confirm CFS. We analyzed all persons with confirmed CFS. The main outcomes of this study, prevalence and incidence of CFS, are published elsewhere. Herein, we present an exploratory analysis with previous CFS diagnosis as the outcome, predicted by demographic and symptom characteristics. RESULTS: We confirmed CFS in 90 subjects; 14 (16%) had been previously diagnosed as having CFS. Persons in the middle- vs the higher-income group were more likely to have been diagnosed as having CFS (9 [29%] of 31 subjects vs 3 [8%] of 39 subjects; $P = .03$), as were those with sudden vs gradual fatigue onset (7 [41%] of 17 subjects vs 4 [6%] of 64 subjects; $P < .01$), those reporting tender lymph nodes (7 [33%] of 21 subjects vs 7 [10%] of 69 subjects; $P = .02$), and those reporting a sore throat (6 [35%] of 17 subjects vs 8 [11%] of 73 subjects; $P = .02$). Only 17 (21%) of 81 subjects had

				sudden fatigue onset, and tender lymph nodes (reported in 21 [23%] of 90 subjects) and a sore throat (reported in 17 [19%] of 90 subjects) were the least common symptoms. CONCLUSION: Most cases of CFS in the population are unrecognized by the medical community; persons diagnosed as having CFS may be different from persons with CFS in the general population.
Spence VA, Khan F, Kennedy G, Abbot NC, Belch JJ.	Vascular Diseases Research Unit, University Department of Medicine, Ninewells Hospital & Medical School, Dundee DD1 9SY, UK.	Acetylcholine mediated vasodilatation in the microcirculation of patients with chronic fatigue syndrome.	Prostaglandins Leukot Essent Fatty Acids. 2004 Apr;70(4):403-7.	The aetiology of chronic fatigue syndrome (CFS) remains controversial and a number of hypotheses have been put forward to explain it. Research into the condition is hindered by the considerable heterogeneity seen across patients but several reports have highlighted disturbances to cholinergic mechanisms in terms of central nervous system activity, neuromuscular function and autoantibodies to muscarinic cholinergic receptors. This paper examines an altogether separate function for acetylcholine and that is its role as an important and generalized vasodilator. Most diseases are accompanied by a blunted response to acetylcholine but the opposite is true for CFS. Such sensitivity is normally associated with physical training so the finding in CFS is anomalous and may well be relevant to vascular symptoms that characterise many patients. There are several mechanisms that might lead to ACh endothelial sensitivity in CFS patients and various experiments have been designed to unravel the enigma. These are reported here.
Staines DR.	Gold Coast Public Health Unit, 10-12 Young Street, Southport, Qld. 4215, Australia.	Is gulf war syndrome an autoimmune disorder of endogenous neuropeptides, exogenous sandfly maxadilan and molecular mimicry?	Med Hypotheses. 2004;62(5):658-64.	Gulf war syndrome (GWS) remains a contentious diagnosis with conflicting laboratory investigation and lack of a biologically plausible aetiology. This paper discusses the potential role of maxadilan, a potent sandfly vasoactive peptide, in causing autoimmune responses in susceptible individuals through possible molecular mimicry with pituitary adenylate cyclase activating polypeptide (PACAP) and the PAC1R receptor. Gulf war syndrome may share some causative pathology with Chronic Fatigue Syndrome (CFS), a disorder characterised by prolonged fatigue and debility mostly associated with post-infection sequelae although ongoing infection is unproven. Immunological aberration associated with an expanding group of vasoactive neuropeptides in the context of molecular mimicry and inappropriate immunological memory has been recently raised as possible cause of CFS. Vasoactive neuropeptides act as hormones, neurotransmitters, immune modulators and neurotrophes. They are readily catalysed to small peptide fragments. They and their binding sites are immunogenic and are known to be associated with a range of autoimmune conditions. Maxadilan, while not sharing substantial sequence homology with PACAP is a known agonist of the PACAP specific receptor (PAC1R) and therefore emulates these functions. Moreover a specific amino acid sequence peptide deletion within maxadilan converts it to a PACAP receptor antagonist raising the possibility of this substance provoking a CFS like response in humans exposed to it. This paper describes a biologically plausible mechanism for the development of a GWS-like chronic fatigue state based on loss of immunological tolerance to the vasoactive neuropeptide PACAP or its receptor following bites of the sandfly <i>Phlebotomus papatasi</i> and injection of the vasodilator peptide maxadilan. Exacerbation of this autoimmune response as a consequence of recent or simultaneous multiple vaccination exposures deserves further investigation. While the possible association between the relatively recently discovered vasoactive neuropeptides and chronic fatigue conditions has only recently been reported in the literature, this paper explores links for further research into GWS and CFS.
Staines DR.	Gold Coast Public Health Unit, 10-12 Young Street, Southport 4215, Qld, Australia.	Is chronic fatigue syndrome an autoimmune disorder of endogenous neuropeptides, exogenous infection and molecular mimicry?	Med Hypotheses. 2004;62(5):646-52.	Chronic fatigue syndrome is a disorder characterised by prolonged fatigue and debility and is mostly associated with post-infection sequelae although ongoing infection is unproven. Immunological aberration is likely and this may prove to be associated with an expanding group of vasoactive neuropeptides in the context of molecular mimicry and inappropriate immunological memory. Vasoactive neuropeptides including vasoactive intestinal peptide (VIP) and pituitary adenylate activating polypeptide (PACAP) belong to the secretin/glucagon superfamily and act as hormones, neurotransmitters, immune modulators and neurotrophes. They are readily catalysed to smaller peptide fragments by antibody hydrolysis. They and their binding sites are immunogenic and are known to be associated with a range of autoimmune conditions. Vasoactive neuropeptides are widely distributed in the body particularly in the central, autonomic and peripheral nervous systems and have been identified in the gut, adrenal gland, reproductive organs, vasculature, blood cells and other tissues. They have a vital role in maintaining vascular flow in organs, and in thermoregulation, memory and concentration. They are co-transmitters for acetylcholine, nitric oxide, endogenous opioids and insulin, are potent immune regulators with primarily anti-inflammatory activity, and have a significant role in protection of the nervous system to toxic assault, promotion of neural development and the maintenance of homeostasis. This paper describes a biologically plausible mechanism for the development of CFS based on loss of immunological tolerance to the vasoactive neuropeptides following infection, significant physical exercise or de novo. It is proposed that release of these substances is accompanied by a loss of tolerance either to them or their receptor binding sites in CFS. Such an occurrence would have predictably serious consequences resulting from compromised function of the key roles these substances perform. All documented symptoms of CFS are explained by vasoactive neuropeptide compromise, namely fatigue and nervous system dysfunction through impaired acetylcholine activity, myalgia through nitric oxide and endogenous opioid dysfunction, chemical sensitivity through peroxynitrite and adenosine dysfunction, and immunological disturbance through changes in immune modulation. Perverse immunological memory established against these substances or their receptors may be the reason for the protracted nature of this condition. The novel status of these substances together with their extremely small concentrations in blood and tissues means that clinical research into them is still in its infancy. A biologically plausible

				theory of CFS causation associated with vasoactive neuropeptide dysfunction would promote a coherent and systematic approach to research into this and other possibly associated disabling conditions.
Staud R.		Abnormal Pain Processing in Patients with Fibromyalgia Syndrome	Journal of Chronic Fatigue Syndrome 2004; 12(1):71-77.	Fibromyalgia syndrome (FMS) is characterized by widespread pain, fatigue, sleep abnormalities, and distress. Because FMS lacks consistent evidence for tissue abnormalities, recent investigations have focused on central nervous system mechanisms of pain. Abnormal temporal summation of second pain (AWindup@) and central sensitization (CS) have recently been described in FMS patients. Windup (WU) and central sensitization, which rely on central pain mechanisms, occur after prolonged C-nociceptor input and depend on activation of nociceptor specific neurons as well as wide dynamic range neurons in the dorsal horn of the spinal cord. The important role of WU is also supported by its ability to predict the clinical pain intensity of FMS patients. Furthermore, brain-imaging techniques that can detect neuronal activation following nociceptive stimuli have provided additional evidence for abnormal central pain mechanisms in FMS. Most importantly, brain images have corroborated the augmented reported pain experience of FMS patients during experimental pain stimuli. These findings may have important implications for future research as well as the treatment of FMS pain.
Steinau M, Unger ER, Vernon SD, Jones JF, Rajeevan MS.	Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, 1600 Clifton Rd., MSG-41, Atlanta, GA 30333, USA.	Differential-display PCR of peripheral blood for biomarker discovery in chronic fatigue syndrome.	J Mol Med. 2004 Nov;82(11):750-5. Epub 2004 Nov.	We used differential-display PCR of peripheral blood mononuclear cells (PBMCs) to search for candidate biomarkers for chronic fatigue syndrome (CFS). PBMCs were collected from a subject with CFS and an age- and sex-matched control before and 24 h after exercise. RNA expression profiles were generated using 46 primer combinations, and the similarity between the individuals was striking. Differentially expressed bands were excised, reamplified, and sequenced, yielding 95 nonredundant sequences, of which 50 matched to known gene transcripts, 38 matched to genes with unknown functions, and 7 had no similarity to any database entry. Most (86%) of the differences between the two subjects were present at baseline. Differential expression of ten genes was verified by real-time reverse-transcription PCR: five (cystatin F, MHC class II, platelet factor 4, fetal brain expressed sequence tag, and perforin) were downregulated, and the remaining five genes (cathepsin B, DNA polymerase epsilon4, novel EST PBMC191MSt, heparanase precursor, and ORF2/L1 element) were upregulated in the subject with CFS. Many of these genes have known functions in defense and immunity, thus supporting prior suggestions of immune dysregulation in the pathogenesis of CFS. Differential-display PCR is a powerful tool for identification of candidate biomarkers. Investigation of these markers in samples from well-designed epidemiological studies of CFS will be required to determine the validity of these candidate biomarkers. The real-time reverse-transcription PCR assays that we developed for assay of these biomarkers will facilitate high-throughput testing of these additional samples.
Stormorken E.		[Harmful psychiatrization] [Article in Norwegian]	Tidsskr Nor Laegeforen. 2004 Jul 1;124(13-14):1826-7; author reply 1827.	
Stormorken E.		[Errors in a textbook on psychiatry] [Article in Norwegian]	Tidsskr Nor Laegeforen. 2004 May 6;124(9):1277; author reply 1277.	
Stouten B.		Cost-effectiveness of cognitive behaviour therapy for patients with chronic fatigue syndrome.	QJM. 2004 Jun;97(6):379-80.	
Stouten B.		Chronic fatigue syndrome: a clinical and laboratory study with a well-matched control group.	J Intern Med. 2004 Sep;256(3):265-7; author reply 268-9. Comment on: J Intern Med. 1995 May;237(5):499-506.	
Straus SE		Pharmacotherapy of chronic fatigue syndrome: another gallant attempt.	JAMA. 2004 Sep 8;292(10):1234-5. Comment on: JAMA. 2004 Sep 8;292(10):1195-204.	
Suhadolnik RG,		Clinical and	Journal of Chronic	Patterns of immune dysfunction have emerged in chronic fatigue syndrome (CFS) that include an immune activation state

<p>Peterson DL, Reichenbach NL, Roen G, Metzger M, McCahan J, O'Brien K, Welsch S, Gabriel J, Gaughan JP, McGregor NR.</p>		<p>Biochemical Characteristics Differentiating Chronic Fatigue Syndrome from Major Depression and Healthy Control Populations: Relation to Dysfunction and RNase L Pathway</p>	<p>Fatigue Syndrome 2004; 12(1):5–35.</p>	<p>(evidenced by increased activated T lymphocytes and circulating cytokines) and poor cellular function (low natural killer (NK) cell cytotoxicity and impaired T lymphocyte response to mitogens). Therefore, the aim of the current study was to examine the relationship between clinical and functional characteristics, immune abnormalities and status of the RNase L pathway in CFS compared with healthy control and depression control populations. All study participants were assessed with respect to their general health, functional status, blood count and chemistry, biochemical and immune parameters. The CFS group (N = 66) demonstrated clinical, functional and biochemical abnormalities distinct from the healthy (N = 62) and depression (N = 51) control groups. The CFS group showed marked functional impairment compared with both control groups (P < .001) as measured by the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36) (P < .001). The CFS group also showed decreased cognitive performance on a computerized test battery compared to healthy (P < .001) and depression controls (P < .009) and significantly higher 37/80 kDa RNase L ratio (P < .001) compared with both control groups. The odds ratios of a 37/80 kDa RNase L ratio > 2 compared with the CFS patients were 3.9 for the healthy controls (95% confidence limit (CL) 1.0-15.2, P < .05) and 65.8 for the depression controls (95% CL 10.7-406.6, P < .001). The CFS group demonstrated low NK cell cytotoxicity compared to healthy controls (P = .045). The correlation between abnormalities in the RNase L pathway and impaired NK cell function (r = .21, P < .006) suggests that both may be part of the same underlying disease mechanism, at least in this homogeneous population of very disabled CFS patients. Healthy contact-control subjects who had exposure to CFS patients showed a number of characteristics similar to the CFS patients, including an increased mean 37/80 kDa RNase L ratio (P < .04) and prevalence of the 37/80 kDa RNase L ratio > 2 (P < .03). In these contact-control subjects, the 37/80 kDa RNase L ratio was correlated with the interferon-α levels (r = .58, P < .02), suggestive of activation of the interferon pathway. The results of the present study support the cytokine/immune activation model in this well-characterized CFS patient group.</p>
<p>Taylor RR, Braveman B, Hammel J.</p>	<p>Department of Occupational Therapy (MC 811), College of Applied Health Sciences, University of Illinois at Chicago, 1919 West Taylor Street, 3rd Floor, Chicago, Illinois 60612-7250, USA. rtaylor@uic.edu</p>	<p>Developing and evaluating community-based services through participatory action research: two case examples.</p>	<p>Am J Occup Ther. 2004 Jan-Feb;58(1):73-82.</p>	<p>Occupational therapy has a strong history of embracing concepts of client empowerment. However there is limited literature in the field on how to achieve empowerment, or on how to extend empowerment to the level of the community and social groups and services within it. This article discusses how concepts and strategies of participatory action research, an extension of empowerment theory, can be used to inform service development and evaluation in occupational therapy. The participatory action research approach is illustrated using two case examples of participatory action research programs for persons with chronic fatigue syndrome and individuals with autoimmune deficiency syndrome (AIDS). A critical analysis of the application of this approach to research and practice is provided. Finally, the paper identifies key principles of participatory action research that can be used to guide occupational therapy services and empower both individuals and communities.</p>
<p>Taylor RR.</p>	<p>University of Illinois at Chicago, Department of Occupational Therapy (MC 811), College of Applied Health Sciences, 1919 West Taylor Street, 3rd Floor, Chicago, Illinois 60612-7250, USA. rtaylor@uic.edu</p>	<p>Quality of life and symptom severity for individuals with chronic fatigue syndrome: findings from a randomized clinical trial.</p>	<p>Am J Occup Ther. 2004 Jan-Feb;58(1):35-43.</p>	<p>OBJECTIVE: Chronic fatigue syndrome is a profoundly disabling condition characterized by severe, unrelenting fatigue and a number of other physical and cognitive symptoms. Currently, there is no cure or widely accepted treatment for chronic fatigue syndrome, and few rehabilitation programs exist to address quality of life issues in chronic fatigue syndrome. In the present randomized clinical trial, the effects of an integrative, consumer-driven rehabilitation program on quality of life and symptom severity for individuals with chronic fatigue syndrome were examined. METHOD: Forty-seven participants were randomly assigned to either an immediate program group (n = 23) or a delayed program control group (n = 24) and assessed with the Chronic Fatigue Syndrome Symptom Rating Scale and the Quality of Life Index before the program, after program participants completed the group phase, and after program participants completed the one-on-one phase. It was hypothesized that the program would lead to improvements in quality of life and an overall reduction in symptom severity. RESULTS: Linear growth models were estimated comparing program and control conditions over time using random-effects regression analyses. Significant condition by time interactions were observed for the main outcomes of symptom severity and overall quality of life. Effect sizes for these interactions involving symptom severity (Cohen's d = 0.71) and overall quality of life (Cohen's d = .66) were moderate. CONCLUSIONS: Findings indicate that consumer driven programs such as this one can have a positive impact on symptom severity and quality of life over time for individuals with chronic fatigue syndrome.</p>
<p>Tomassini V, Pozzilli C, Onesti E, Pasqualetti P, Marinelli F, Pisani A, Fieschi C.</p>	<p>Department of Neurological Sciences, University of Rome "La Sapienza", viale dell'Universita 30, Rome 00185, Italy.</p>	<p>Comparison of the effects of acetyl L-carnitine and amantadine for the treatment of fatigue in multiple sclerosis: results of a pilot, randomised, double-</p>	<p>J Neurol Sci. 2004 Mar 15;218(1-2):103-8.</p>	<p>Treatment with acetyl L-carnitine (ALCAR) has been shown to improve fatigue in patients with chronic fatigue syndrome, but there have been no trials on the effect of ALCAR for treating fatigue in multiple sclerosis (MS). To compare the efficacy of ALCAR with that of amantadine, one of the drugs most widely used to treat MS-related fatigue, 36 MS patients presenting fatigue were enrolled in a randomised, double-blind, crossover study. Patients were treated for 3 months with either amantadine (100 mg twice daily) or ALCAR (1 g twice daily). After a 3-month washout period, they crossed over to the alternative treatment for 3 months. Patients were rated at baseline and every 3 months according to the Fatigue Severity Scale (FSS), the primary endpoint of the study. Secondary outcome variables were: Fatigue Impact Scale (FIS), Beck Depression Inventory (BDI) and Social Experience Checklist (SEC). Six patients withdrew from the study because of adverse reactions (five on amantadine and</p>

		blind, crossover trial.		one on ALCAR). Statistical analysis showed significant effects of ALCAR compared with amantadine for the Fatigue Severity Scale ($p = 0.039$). There were no significant effects for any of the secondary outcome variables. The results of this study show that ALCAR is better tolerated and more effective than amantadine for the treatment of MS-related fatigue.
Torpy DJ, Bachmann AW, Gartside M, Grice JE, Harris JM, Clifton P, Easteal S, Jackson RV, Whitworth JA.	University of Queensland Department of Medicine, Greenslopes Hospital, Brisbane, Queensland, Australia. dtorpy@mail.rah.sa.gov.au	Association between chronic fatigue syndrome and the corticosteroid-binding globulin gene ALA-SER224 polymorphism.	Endocr Res. 2004 Aug;30(3):417-29.	Chronic fatigue syndrome (CFS) is characterized by idiopathic fatigue of greater than 6 months' duration with postexertional exacerbation and many other symptoms. A trend toward relative hypocortisolism is described in CFS. Twin and family studies indicate a substantial genetic etiologic component to CFS. Recently, severe corticosteroid-binding globulin (CBG) gene mutations have been associated with CFS in isolated kindreds. Human leukocyte elastase, an enzyme important in CBG catabolism at inflammatory sites, is reported to be elevated in CFS. We hypothesized that CBG gene polymorphisms may act as a genetic risk factor for CFS. A total of 248 patients with CFS defined by Centers for Disease Control criteria, and 248 controls were recruited. Sequencing and restriction enzyme testing of the CBG gene coding region allowed detection of severe CBG gene mutations and a common exon 3 polymorphism (c.825G-->T, Ala-Ser224). Plasma CBG levels were measured in 125 CFS patients and 198 controls by radioimmunoassay. Total and free (calculated and measured) cortisol levels were ascertained in single samples between 8-10 a.m. The age of onset (mid 30s) and gender ratio (2.2:1, female:male) of the patients were similar to those reported in U.S. epidemiologic studies. A trend toward a preponderance of serine224 homozygosity among the CFS patients was noted, compared with controls ($\chi^2 = 5.31$, $P = 0.07$). Immunoreactive-CBG (IR-CBG) levels were higher in Serine/Alanine (Ser/Ala) than Ala/Ala subjects and higher again in Ser/Ser subjects, this effect was strongest in controls; Ser/Ser: 46.1+/-1.8 (n = 31, $P = 0.03$) vs. Ser/Ala: 42.4+/-1.0 (n = 56, $P = 0.05$) vs. Ala/Ala: 40.8+/-1.7 microg/mL (n = 21). Despite higher CBG levels, there was a nonsignificant trend toward lower total and free plasma cortisol in serine allele positive patients, total cortisol: Ser/Ser: 13.3+/-1.4 (n = 34) vs. Ser/Ala: 14.0+/-0.7 (n = 66) vs. Ala/Ala: 15.4+/-1.0 (n = 23). Homozygosity for the serine allele of the CBG gene may predispose to CFS, perhaps due to an effect on hypothalamic-pituitary-adrenal axis function related to altered CBG-cortisol transport function or immune-cortisol interactions.
Tritt K, Nickel M, Mitterlehner F, Nickel C, Forthuber P, Leiberich P, Rother W, Loew T.	Section of Psychosomatic Medicine, University Clinic of the University Regensburg, Regensburg, Germany.	Chronic fatigue and indicators of long-term employment disability in psychosomatic inpatients.	Wien Klin Wochenschr. 2004 Mar 31;116(5-6):182-9.	The major goal of this study was to determine indicators of long-term disability for psychosomatic inpatients with chronic fatigue syndrome. To this end, a cross-sectional study was performed with a random sample of patients (n=1000, response rate: 83.9%) at a psychosomatic inpatient clinic. 51.1% of the patients (n=429) reported intensely persistent exhaustion that had no logical relation to actual exertion. 159 (37.1%) patients in this group were disabled from working and these comprised the main target group of this study. Significantly more patients in the target group worked part time, were disabled for a disproportionately long period of time (50.9% of all were disabled for more than 6 months in the previous year), and felt stressed because of conflicts with their superiors and/or colleagues (in each case, $P < 0.01$). While more frequent psychological comorbidity was not found, they reported physical complaints more often. It was not the patients fit for work who felt more burdened with chronic fatigue, but rather the employment-disabled, who were actually exposed to fewer demands. These patients had, in comparison with those fit to work, a stronger fixation on somatic complaints, inadequate perception of physical and psychic sensations, difficulties getting along with other people and in coping with a regular job (in each case, $P < 0.01$). Prospective examination of these indicators could help detect predictor variables for long-term disability in chronic fatigue. Such predictors could contribute to timely social-medical assessment and treatment.
Tryon WW, Jason L, Frankenberry E, Torres-Harding S.	Department of Psychology, Fordham University, 441 East Fordham Road, Bronx, NY 10458-5198, USA. wtryon@fordham.edu	Chronic fatigue syndrome impairs circadian rhythm of activity level.	Physiol Behav. 2004 Oct 15;82(5):849-53.	Some of the symptoms of chronic fatigue syndrome (CFS) are the same as for disrupted circadian rhythm. Activity level is frequently used to study circadian rhythm. Continuous waist activity measurements taken every minute 24 h/day for from 5 to 7 days in 10 controls and from 2 to 7 days in 8 patients with CFS yielded two primary findings: (a) lower daytime activity and (b) less regular activity-rest cycles in persons with CFS than in controls.
Turkington D, Hedwat D, Rider I, Young AH.	Royal Victoria Infirmary, Newcastle upon Tyne, UK.	Recovery from chronic fatigue syndrome with modafinil.	Hum Psychopharmacol. 2004 Jan;19(1):63-4.	PMID: 14716715 [PubMed - in process]
Unger ER, Nisenbaum R, Moldofsky H, Cesta A, Sammut C, Reyes M, Reeves WC.		Sleep assessment in a population-based study of chronic fatigue syndrome.	BMC Neurol. 2004 Apr 19;4(1):6.	Background Chronic fatigue syndrome (CFS) is a disabling condition that affects approximately 800,000 adult Americans. The pathophysiology remains unknown and there are no diagnostic markers or characteristic physical signs or laboratory abnormalities. Most CFS patients complain of unrefreshing sleep and many of the postulated etiologies of CFS affect sleep. Conversely, many sleep disorders present similarly to CFS. Few studies characterizing sleep in unselected CFS subjects have been published and none have been performed in cases identified from population-based studies. Methods. The study included 339 subjects (mean age 45.8 years, 77% female, 94.1% white) identified through telephone screen in a previously described population-based study of CFS in Wichita, Kansas. They completed questionnaires to assess fatigue and wellness and 2 self-administered sleep questionnaires. Scores for five of the six sleep factors (insomnia/hypersomnia, non-restorative sleep, excessive daytime somnolence, sleep apnea, and restlessness) in the Centre for Sleep and Chronobiology's Sleep Assessment

				Questionnaire(c) (SAQ(c)) were dichotomized based on threshold. The Epworth Sleepiness Scale score was used as a continuous variable. Results. 81.4% of subjects had an abnormality in at least one SAQ(c) sleep factor. Subjects with sleep factor abnormalities had significantly lower wellness scores but statistically unchanged fatigue severity scores compared to those without SAQ(c) abnormality. CFS subjects had significantly increased risk of abnormal scores in the non-restorative (adjusted odds ratio [OR] = 28.1; 95% confidence interval [CI]= 7.4-107.0) and restlessness (OR = 16.0; 95% CI = 4.2-61.6) SAQ(c) factors compared to non-fatigued, but not for factors of sleep apnea or excessive daytime somnolence. This is consistent with studies finding that, while fatigued, CFS subjects are not sleepy. A strong correlation (0.78) of Epworth score was found only for the excessive daytime somnolence factor. Conclusions. SAQ(c) factors describe sleep abnormalities associated with CFS and provide more information than the Epworth score. Validation of these promising results will require formal polysomnographic sleep studies.
van der Meer JW, Lamberts SW, Buchwald D.		Dr Baschetti rides/writes again. Comment on: Eur J Clin Invest. 2003 Dec;33(12):1029-31.	Eur J Clin Invest. 2004 Apr;34(4):317; author reply 318-9.	
Van Engelen BG, Kalkman JS, Schillings ML, Van Der Werf SP, Bleijenberg G, Zwarts MJ.	Neuromusculair Centrum Nijmegen, Instituut voor Neurologie, Universitair Medisch Centrum St Radboud, Postbus 9101, 6500 HB Nijmegen.	[Fatigue in neuromuscular disease] [Article in Dutch]	Ned Tijdschr Geneeskd. 2004 Jul 3;148(27):1336-41.	Chronic fatigue is a symptom of diseases such as cancer, multiple sclerosis, Parkinson's and cerebrovascular disease. Fatigue can also be present in people with no demonstrable somatic disease. If certain criteria are met, chronic-fatigue syndrome may be diagnosed in these cases. Fatigue is a multi-dimensional concept with physiological and psychological dimensions. The 'Short Fatigue Questionnaire' consisting of 4 questions is a tool to measure fatigue with a high degree of reliability and validity. Within the group of neuromuscular disorders, fatigue has been reported by patients with post-polio syndrome, myasthenia gravis, and Guillain-Barre syndrome. The percentage of neuromuscular patients suffering from severe fatigue (64%) is comparable with that of patients with multiple sclerosis, a disease in which fatigue is an acknowledged symptom. Now that reliable psychological and clinical neurophysiological techniques are available, a multidisciplinary approach to fatigue in patients with well-defined neuromuscular disorders may contribute towards the elucidation of the pathophysiological mechanisms of chronic fatigue, with the ultimate goal being to develop methods of treatment for fatigue in neuromuscular patients.
Van Hoof Elke Clin Psych		Article: Cognitive Behavioural Therapy as Cure-All for CFS	Journal of Chronic Fatigue Syndrome 2004 11 (4): 43 - 47	
Van Hoof E, Coomans D, Cluydts R, De Meirleir K.		The Fennell Phase Inventory in a Belgian Sample	Journal of Chronic Fatigue Syndrome 2004; 12(1):53-69.	The present study is a follow-up of the research conducted by Jason, Fennell et al. (1995, 1999, 2000) on a multistage theory for chronic fatigue syndrome (CFS). This multistage model is a very promising method for the evaluation of patients suffering from CFS and could facilitate the appropriate selection of various psychosocial therapies that improve the patient's ability to cope with their illness. Four predictive factors emerged with moderate to excellent reliability. A Spearman's rank correlation revealed positive correlations between our four-factor model and the three-factor model identified by Jason et al. (1999). A correlation matrix between the dimensional psychological investigation and the Fennell Phases revealed characteristics as suggested by previous research. Biological parameters varied over the different phases suggesting an important interaction between body and psyche.
Van Houdenhove B, Egle UT.	Faculty of Medicine, K.U.Leuven, Leuven, Belgium. boudewijn.vanhoudenhove@uz.kuleuven.ac.be	Fibromyalgia: a stress disorder? Piecing the biopsychosocial puzzle together.	Psychother Psychosom. 2004 Sep-Oct;73(5):267-75.	Fibromyalgia (FM) is a controversial syndrome, characterised by persistent widespread pain, abnormal pain sensitivity and additional symptoms such as fatigue and sleep disturbance. The syndrome largely overlaps with other functional somatic disorders, particularly chronic fatigue syndrome (CFS). Although the exact aetiology and pathogenesis of FM are still unknown, it has been suggested that stress may play a key role in the syndrome. This article first reviews the function of the stress response system, placing special emphasis on the relationships between adverse life experiences, stress regulation and pain-processing mechanisms, and summarising the evidence for a possible aetiopathogenetic role of stress in FM. Finally, an integrative biopsychosocial model that conceptualizes FM as a stress disorder is proposed, and the clinical and research implications of the model are discussed.
Vermeulen RC, Scholte HR.	Research Center Amsterdam, Amsterdam, Netherlands. info@cfscentrumamsterdam.nl	Exploratory open label, randomized study of acetyl- and propionylcarnitine in chronic fatigue syndrome.	Psychosom Med. 2004 Mar-Apr;66(2):276-82.	OBJECTIVES: We compared the effects of acetylcarnitine, propionylcarnitine and both compounds on the symptoms of chronic fatigue syndrome (CFS). METHODS: In an open, randomized fashion we compared 2 g/d acetyl-L-carnitine, 2 g/d propionyl-L-carnitine, and its combination in 3 groups of 30 CFS patients during 24 weeks. Effects were rated by clinical global impression of change. Secondary endpoints were the Multidimensional Fatigue Inventory, McGill Pain Questionnaire, and the Stroop attention concentration test. Scores were assessed 8 weeks before treatment; at randomization; after 8, 16, and 24 weeks of treatment; and 2 weeks later. RESULTS: Clinical global impression of change after treatment showed considerable improvement in 59% of the patients in the acetylcarnitine group and 63% in the propionylcarnitine group, but less in the acetylcarnitine plus

				propionylcarnitine group (37%). Acetylcarnitine significantly improved mental fatigue ($p = .015$) and propionylcarnitine improved general fatigue ($p = .004$). Attention concentration improved in all groups, whereas pain complaints did not decrease in any group. Two weeks after treatment, worsening of fatigue was experienced by 52%, 50%, and 37% in the acetylcarnitine, propionylcarnitine, and combined group, respectively. In the acetylcarnitine group, but not in the other groups, the changes in plasma carnitine levels correlated with clinical improvement. CONCLUSIONS: Acetylcarnitine and propionylcarnitine showed beneficial effect on fatigue and attention concentration. Less improvement was found by the combined treatment. Acetylcarnitine had main effect on mental fatigue and propionylcarnitine on general fatigue.
Vermeulen RC, Scholte HR.	CFS Research Centre Amsterdam, Waalstraat 25-31, 1078 BR Amsterdam, The Netherlands. r.w.vermeulen@cfscentr umamsterdam.nl	Chronic fatigue syndrome and sexual dysfunction.	J Psychosom Res. 2004 Feb;56(2):199-201.	OBJECTIVE: The study was undertaken to determine if ambulant female patients with the chronic fatigue syndrome (CFS) report problems with their sexual functioning. METHODS: We studied 35 female CFS patients and 36 healthy female controls. The severity of CFS was measured with a fatigue questionnaire and the presence and severity of sexual dysfunction with a questionnaire about sexual functioning. RESULTS: The mean fatigue score was 24.8 in the CFS patients and 11.9 in the controls ($P = .000$). No increase in sexual dysfunction was found in the CFS group. The control group showed negative correlations between the score of the fatigue questionnaire and the frequency of "sexual fantasies," "(desire for) sexual contact" and "satisfaction with sex life." Such correlations were absent in the CFS group. CONCLUSION: The satisfaction with sex life was similar in patients and controls. The results suggest that patients and controls have a different perception of fatigue.
Viner R, Gregorowski A, Wine C, Bladen M, Fisher D, Miller M, El Neil S.	Department of Adolescent Medicine, Great Ormond Street Hospital for Children and University College London Hospitals, London, UK. R.Viner@ich.ucl.ac.uk	Outpatient rehabilitative treatment of chronic fatigue syndrome (CFS/ME).	Arch Dis Child. 2004 Jul;89(7):615-9.	AIMS: To assess the outcome of outpatient multidisciplinary rehabilitative treatment (graded activities/exercise programme, family sessions, and supportive care) compared with supportive care alone for children and adolescents with chronic fatigue syndrome (CFS/ME). METHODS: Fifty six young people (aged 9-17 years) with CFS/ME by standard criteria were followed up for 3-24 months. All subjects received supportive care. Families additionally opted to either enter the rehabilitation programme (supportive care plus graded activities/exercise programme and family sessions) or have no additional treatment. RESULTS: Twenty two (39%) subjects had supportive care alone and 26 (46%) entered the programme. Treatment groups were comparable at baseline in terms of age, severity and duration of illness, Wellness score, and school attendance. At end of follow up, those in the programme group had significantly higher Wellness score and school attendance than those having supportive care alone. The programme significantly reduced the overall severity of illness: after the programme, 43% had complete resolution of CFS/ME compared to only 4.5% of those having supportive care alone. The presence of depressed mood and family beliefs about the aetiology of CFS/ME were not significantly associated with outcomes. CONCLUSIONS: Outpatient rehabilitative treatment offers significant potential to improve the prognosis of CFS/ME in childhood and adolescence.
Viner R, Hotopf M.	Department of Paediatrics, Royal Free and University College Medical School, Middlesex Hospital, London W1T 3AA. R.Viner@ich.ucl.ac.uk	Childhood predictors of self reported chronic fatigue syndrome/myalgic encephalomyelitis in adults: national birth cohort study.	BMJ. 2004 Oct 23;329(7472):941. Epub 2004 Oct 06. Comment in: BMJ. 2004 Oct 23;329(7472):928-9.	OBJECTIVE: To study childhood risk factors for chronic fatigue syndrome in adult life. DESIGN: Examination of data from the 1970 British birth cohort. PARTICIPANTS: 16,567 babies born 5-11 April 1970, followed up at 5, 10, 16, and 29-30 years. MAIN OUTCOME MEASURES: Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) identified by self report at age 30 years. Data from childhood from questionnaires given to parents and teachers. Maternal mental health assessed with the malaise inventory. RESULTS: 93 (0.8%, 95% confidence interval 0.7 to 1.0) of 11 261 participants reported ever having CFS/ME, and 48 (0.4%, 0.3 to 0.6) had the condition currently. Higher risk of CFS/ME was associated with having a limiting longstanding condition in childhood (odds ratio 2.3, 1.4 to 3.9), female sex (2.3, 1.4 to 2.6), and high social class in childhood (2.2, 1.4 to 3.5). Higher levels of exercise in childhood were associated with lower risk (0.5, 0.2 to 0.9). Maternal psychological disorder, psychological problems in childhood, birth weight, birth order, atopy, obesity, school absence, academic ability, and parental illness were not associated with risk of CFS/ME. CONCLUSIONS: We identified no association between maternal or child psychological distress, academic ability, parental illness, atopy, or birth order and increasing risk of lifetime CFS/ME. Sedentary behaviour increased the risk.
Vladutiu GD, Natelson BH.	Department of Pediatrics, School of Medicine & Biomedical Sciences, State University of New York at Buffalo, Buffalo, New York, USA. gdv@buffalo.edu	Association of medically unexplained fatigue with ACE insertion/deletion polymorphism in Gulf War veterans.	Muscle Nerve. 2004 Jul;30(1):38-43.	Genes associated with muscle metabolism and physical endurance were evaluated for variants that may contribute to the etiology of medically unexplained severe and chronic fatigue. Subjects included 49 Gulf War veterans and 61 nonveterans with chronic fatigue syndrome (CFS) or idiopathic chronic fatigue (ICF) and 30 veterans and 45 nonveterans who served as healthy controls. Increased risk for CFS/ICF was associated with alterations of the insertion/deletion (I/D) polymorphism in the angiotensin-converting enzyme gene within the Gulf War veteran sample only. The I allele frequency was decreased in affected versus unaffected veterans (0.15 versus 0.48; odds ratio [OR], 5.08; 95% confidence interval [CI], 1.97-13.35; $P < 0.0001$). Correspondingly, the II genotype was decreased fourfold in affected veterans (0.08 versus 0.35; OR = 5.87; 95% CI: 1.21-28.36; $P = 0.02$), and the DD genotype was increased twofold (0.78 versus 0.39; OR, 5.4; 95% CI, 1.6-18.4; $P = 0.007$). Veterans with the DD genotype were eight times more likely to develop CFS/ICF than were those with the II genotype (OR, 8.30; 95% CI, 1.50-56.09; $P = 0.009$).
Vojdani A, Thrasher JD.	Section of Neuroimmunology, Immunosciences Lab	Cellular and humoral immune abnormalities in Gulf War veterans.	Environ Health Perspect. 2004 Jun;112(8):840-6.	We examined 100 symptomatic Gulf War veterans (patients) and 100 controls for immunologic assays. The veterans and controls were compared for the percentage of T cells (CD3); B cells (CD19); helper:suppressor (CD4:CD8) ratio; natural killer (NK) cell activity; mitogenic response to phytohemagglutinin (PHA) and pokeweed mitogen (PWM); level of immune complexes; myelin

	Inc., 8693 Wilshire Boulevard, Suite 200, Beverly Hills, CA 90211, USA. drari@msn.com			basic protein (MBP) and striated and smooth muscle autoantibodies; and antibodies against Epstein-Barr virus, cytomegalovirus, herpes simplex virus type 1 (HSV-1), HSV-2, human herpes Type 6 (HHV-6), and Varicella zoster virus (VZV). The percentage of T cells in patients versus controls was not significantly different, whereas a significantly higher proportion of patients had elevated T cells compared with controls. The percentage of B cells was significantly elevated in the patients versus the controls. The NK cell (NK) activity was significantly decreased in the patients (24.8 +/- 16.5 lytic units) versus the controls (37.3 +/- 26.4 lytic units). The percentage of patients with lower than normal response to PHA and PWM was significantly different from controls. Immune complexes were significantly increased in the patients (53.1 +/- 18.6, mean +/- SD) versus controls (34.6 +/- 14.3). Autoantibody titers directed against MBP and striated or smooth muscle were significantly greater in patients versus controls. Finally, the patients had significantly greater titers of antibodies to the viruses compared with the controls (p < 0.001). These immune alterations were detected 2-8 years after participation in the Gulf War. The immune alterations are consistent with exposure to different environmental factors. We conclude that Gulf War syndrome is a multifaceted illness with immune function alterations that may be induced by various factors and are probably associated with chronic fatigue syndrome.
Vos R, Willems D, Houtepen R.	Health Ethics and Philosophy, Department of Health Care Studies, University of Maastricht, Maastricht, The Netherlands. Rein.Vos@ZW.unimaas.nl	Coordinating the norms and values of medical research, medical practice and patient worlds—the ethics of evidence based medicine in orphaned fields of medicine.	J Med Ethics. 2004 Apr;30(2):166-70.	Evidence based medicine is rightly at the core of current medicine. If patients and society put trust in medical professional competency, and on the basis of that competency delegate all kinds of responsibilities to the medical profession, medical professionals had better make sure their competency is state of the art medical science. What goes for the ethics of clinical trials goes for the ethics of medicine as a whole: anything that is scientifically doubtful is, other things being equal, ethically unacceptable. This particularly applies to so called orphaned fields of medicine, those areas where medical research is weak and diverse, where financial incentives are lacking, and where the evidence regarding the aetiology and treatment of disease is much less clear than in laboratory and hospital based medicine. Examples of such orphaned fields are physiotherapy, psychotherapy, medical psychology, and occupational health, which investigate complex syndromes such as RSI, whiplash, chronic low back pain, and chronic fatigue syndrome. It appears that the primary ethical problem in this context is the lack of attention to the orphaned fields. Although we agree that this issue deserves more attention as a matter of potential injustice, we want to argue that, in order to do justice to the interplay of heterogeneous factors that is so typical of the orphaned fields, other ethical models than justice are required. We propose the coordination model as a window through which to view the important ethical issues which relate to the communication and interaction of scientists, health care workers, and patients.
Wallman KE, Morton AR, Goodman C, Grove R, Guilfoyle AM.	School of Human Movement and Exercise Science, University of Western Australia, Stirling Highway, Nedlands, WA 6009, Australia. kwallman@cyllene.uwa.edu.au	Randomised controlled trial of graded exercise in chronic fatigue syndrome.	Med J Aust. 2004 May 3;180(9):444-8.	OBJECTIVE: To investigate whether 12 weeks of graded exercise with pacing would improve specific physiological, psychological and cognitive functions in people with chronic fatigue syndrome (CFS). DESIGN: Randomised controlled trial. SETTING: Human performance laboratory at the University of Western Australia. PARTICIPANTS: 61 patients aged between 16 and 74 years diagnosed with CFS. INTERVENTIONS: Either graded exercise with pacing (32 patients) or relaxation/flexibility therapy (29 patients) performed twice a day over 12 weeks. MAIN OUTCOME MEASURES: Changes in any of the physiological, psychological or cognitive variables assessed. RESULTS: Following the graded exercise intervention, scores were improved for resting systolic blood pressure (P = 0.018), work capacity (W.kg(-1)) (P = 0.019), net blood lactate production (P = 0.036), depression (P = 0.027) and performance on a modified Stroop Colour Word test (P = 0.029). Rating of perceived exertion scores, associated with an exercise test, was lower after graded exercise (P = 0.013). No such changes were observed in the relaxation/flexibility condition, which served as an attention-placebo control. CONCLUSIONS: Graded exercise was associated with improvements in physical work capacity, as well as in specific psychological and cognitive variables. Improvements may be associated with the abandonment of avoidance behaviours.
Wallman K, Goodman C, Morton A, Grove R, Dawson B	Department of Human Movement, University of Western Australia, Nedlands, Western Australia, Australia	Test-Retest Reliability of the Aerobic Power Index Test in Patients with Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2004; Mar;11(4):19–32.	Use of maximal aerobic exercise testing in a chronically ill population may not only deter potential subjects from participating in trials, or returning for repeat trials, but may also result in the exacerbation of symptoms related to CFS. The Aerobic Power Index represents a submaximal exercise test that forms the aerobic component of the Trilevel Fitness Profile. This incremental bike test has a predetermined termination point based on a target heart rate (THR) of 75% of age predicted heart rate maximum, making successful completion of the test more likely in chronically ill subjects. The aim of this study was to determine reliability of the Aerobic Power Index in 20 CFS subjects. Results for the 17 subjects who reached THR for both trials, demonstrated high reliability for watts per kilogram and oxygen uptake (ml·kg ⁻¹ ·min ⁻¹), as demonstrated by an intraclass correlation coefficient (ICC) of .97 and .91 respectively, while RPE resulted in moderate reliability (ICC = .87). The results of this study indicate that that the Aerobic Power Index is a reliable submaximal test for use in a CFS population.
Wallman KE, Morton AR, Goodman C, Grove R.	School of Human Movement and Exercise Science, The University of Western Australia, Crawley, Western Australia, Australia.	Physiological responses during a submaximal cycle test in chronic fatigue syndrome.	Med Sci Sports Exerc. 2004 Oct;36(10):1682-8.	INTRODUCTION/PURPOSE: Numerous studies have assessed physical function in individuals suffering from chronic fatigue syndrome (CFS) but neglected to match control subjects according to current activity levels, consequently casting doubt on reported results. The purpose of this study was to include current activity levels as one criterion for matching CFS subjects with healthy control subjects in order to more accurately assess physical function in these subjects. METHODS: Thirty-one healthy control subjects were matched to CFS subjects according to age, gender, body mass, height, and current activity levels. Physiological function was assessed weekly over a 4-wk period using a submaximal cycle test. RESULTS: Comparison of

	kwallman@cyllene.uwa.edu.au			absolute physiological results recorded at the end of each incremental work level of the exercise test showed that ratings of perceived effort (RPE) was the only variable that was significantly different between the two groups. Scores for RPE were significantly higher in CFS subjects for each incremental work level assessed. Conversely, results recorded on completion of the exercise test showed that the control group was capable of a greater power output than the CFS group as reflected by significantly higher scores for watts per kilogram ($P < 0.0005$), net lactate production ($P = 0.003$), oxygen uptake ($\text{mL} \times \text{kg}(-1) \times \text{min}(-1)$; $P < 0.0005$), respiratory exchange ratio ($P = 0.021$), and HR values as a percentage of age predicted HR(max) ($P = 0.001$). End-point RPE scores were again significantly higher in the CFS group ($P < 0.0005$). CONCLUSION: It is proposed that the reduced exercise tolerance in CFS is due to impairment in the mechanisms that constitute effort sense and/or to avoidance behaviors that result in a reluctance by these subject to exercise to full capacity.
Wang XQ, Takahashi T, Zhu SJ, Moriya J, Saegusa S, Yamakawa J, Kusaka K, Itoh T, Kanda T.	Department of General Medicine, Kanazawa Medical University, Ishikawa, Japan.	Effect of Hochu-ekki-to (TJ-41), a Japanese Herbal Medicine, on Daily Activity in a Murine Model of Chronic Fatigue Syndrome.	Evid Based Complement Alternat Med. 2004 Sep 1;1(2):203-206.	We aimed to evaluate the effect of a Japanese herbal medicine, Hochu-ekki-to (TJ-41), on daily activity in a murine model of chronic fatigue syndrome (CFS). CFS was induced by repeated injection of Brucella abortus (BA) antigen every 2 weeks. TJ-41 was orally administered to mice in a dose of 500 mg/kg/day for 1 week before injecting BA and for 4 weeks thereafter. We evaluated daily running activity in mice receiving TJ-41 as compared with that in untreated mice. Survival of both mouse groups was also monitored during the observation period. Body weight (BW), spleen weight (SW), SW/ BW ratio and expression levels of interleukin-10 (IL-10) mRNA in spleen were determined in both groups at the time of sacrifice. The daily activity was significantly higher in the treated group than in the control. Two mice in the untreated group died 2 days after the second injection of BA, whereas no mice in the group treated with TJ-41 died. The SW and SW/BW ratio were significantly lower in the treated mice than in the control. Suppressed IL-10 mRNA levels were observed in the spleens of the mice treated with TJ-41. Our data suggest that Hochu-ekki-to might possess an inhibitory effect on the marked decrease in running activity following BA injection.
Watanabe A.		Various clinical types of Q-fever disease.Comment on: Intern Med. 2004 Jan;43(1):49-54.	Intern Med. 2004 Jan;43(1):1-2.	
Watson NF, Jacobsen C, Goldberg J, Kapur V, Buchwald D.	Department of Neurology, University of Washington, Seattle 98104-2499, USA. nwatson@u.washington.edu	Subjective and objective sleepiness in monozygotic twins discordant for chronic fatigue syndrome.	Sleep. 2004 Aug 1;27(5):973-7.	STUDY OBJECTIVE: To examine the association of chronic fatigue syndrome (CFS) with measures of objective and subjective sleepiness. DESIGN: Monozygotic co-twin control study. SETTING: Academic medical center. PATIENTS AND PARTICIPANTS: Twenty monozygotic twin pairs discordant for CFS. INTERVENTIONS: N/A. MEASUREMENTS AND RESULTS: All twins completed an Epworth Sleepiness Scale (ESS), 4 Stanford Sleepiness Scales (SSS), and underwent a standard 4-nap multiple sleep latency test. We compared the ESS scores, average SSS scores, and average sleep latency in CFS and healthy twins. The CFS twins reported more sleepiness as measured by mean scores on the ESS (10.9 vs 8.2; 95% confidence interval [CI] = 0.3-5.5; $P = .03$) and the SSS (3.4 versus 2.1; 95% CI = 0.7-1.9; $P < .001$). The mean sleep latency on the Multiple Sleep Latency Test was not significantly different between the CFS and healthy twins (8.9 vs 10.0 minutes; 95% CI -4.4-1.7; $P = .33$). Mean SSS scores increased among the CFS twins and decreased among healthy twins from nap 1 to nap 4 ($P < .001$). The individual ESS scores and mean sleep latencies on the Multiple Sleep Latency Test were negatively correlated for all the twins (Pearson's $r = -0.40$; $P = .01$), with a slightly stronger association among the healthy twins (Pearson's $r = -0.42$, $P = .07$) than the CFS twins (Pearson's $r = -0.36$, $P = .15$). CONCLUSIONS: CFS twins reported significantly more subjective sleepiness than their healthy co-twins despite similar nonpathologic mean sleep latencies on the Multiple Sleep Latency Test. Patients with CFS may mistake their chronic disabling fatigue for sleepiness.
Weatherley-Jones E, Nicholl JP, Thomas KJ, Parry GJ, McKendrick MW, Green ST, Stanley PJ, Lynch SP.	Medical Care Research Unit, School of Health and Related Research, University of Sheffield, Regent Court, 30 Regent Street, Sheffield S1 4DA, UK. e.weatherley-jones@sheffield.ac.uk	A randomised, controlled, triple-blind trial of the efficacy of homeopathic treatment for chronic fatigue syndrome.	J Psychosom Res. 2004 Feb;56(2):189-97.	OBJECTIVE: There is no management regime for chronic fatigue syndrome (CFS) that has been found to be universally beneficial and no treatment can be considered a "cure". Patients with CFS may use complementary and alternative medicine (CAM). Our aim was to evaluate homeopathic treatment in reducing subjective symptoms of CFS. METHOD: Using a triple-blind design (patient and homeopath blind to group assignment and data analyst blind to group until after initial analyses to reduce the possibility of bias due to data analyst), we randomly assigned patients to homeopathic medicine or identical placebo. One hundred and three patients meeting the Oxford criteria for CFS were recruited from two specialist hospital out patient departments. Patients had monthly consultations with a professional homeopath for 6 months. Main outcome measures were scores on the subscales of the Multidimensional Fatigue Inventory (MFI) and proportions of each group attaining clinically significant improvements on each subscale. Secondary outcome measures were the Fatigue Impact Scale (FIS) and the Functional Limitations Profile (FLP). Ninety-two patients completed treatment in the trial (47 homeopathic treatment, 45 placebo). Eighty-six patients returned fully or partially completed posttreatment outcome measures (41 homeopathic treatment group who completed treatment, 2 homeopathic treatment group who did not complete treatment, 38 placebo group who completed treatment, and 5 placebo group who did not complete treatment). RESULTS: Seventeen of 103 patients withdrew from treatment

				or were lost to follow-up. Patients in the homeopathic medicine group showed significantly more improvement on the MFI general fatigue subscale (one of the primary outcome measures) and the FLP physical subscale but not on other subscales. Although group differences were not statistically significant on four out of the five MFI subscales (the primary outcome measures), more people in the homeopathic medicine group showed clinically significant improvement. More people in the homeopathic medicine group showed clinical improvement on all primary outcomes (relative risk=2.75, P=.09). CONCLUSIONS: There is weak but equivocal evidence that the effects of homeopathic medicine are superior to placebo. Results also suggest that there may be nonspecific benefits from the homeopathic consultation. Further studies are needed to determine whether these differences hold in larger samples.
White PD.		What causes chronic fatigue syndrome?	BMJ. 2004 Oct 23;329(7472):928-9.	
White PD, Thomas JM, Sullivan PF, Buchwald D.	Department of Psychological Medicine, Barts, London and Queen Mary School of Medicine and Dentistry, University of London. p.d.white@qmul.ac.uk	The nosology of sub-acute and chronic fatigue syndromes that follow infectious mononucleosis.	Psychol Med. 2004 Apr;34(3):499-507.	BACKGROUND: A previous principal components analysis of symptoms occurring after infectious mononucleosis suggested that a discrete fatigue syndrome occurs, which is independent of psychiatric disorder. This work has not been replicated and no latent class analysis of subjects has been published. METHOD: We prospectively examined a cohort of 150 American primary care patients 2 and 6 months after the onset of corroborated infectious mononucleosis. A subset of 50 subjects was studied 4 years after onset. We performed principal components analyses of both psychological and somatic symptoms and latent class analyses of subjects. RESULTS: Principal components analyses consistently delineated two fatigue factors at 2 and 6 months and one fatigue factor at 4 years. These factors were separate from a mixed anxiety and depressive factor. A four-class solution for the latent class analyses consisted of most subjects with few symptoms, a few with many symptoms, a group with predominantly mood symptoms and some subjects with fatigue symptoms. CONCLUSIONS: The symptoms of the principal factors with fatigue were similar to those previously described. Both the factors and classes were independent of an equally delineated mood factor and class. These results support the existence of two discrete chronic fatigue syndromes after infectious mononucleosis, one of which is still demonstrable 4 years after onset.
Whitehead L.	Department of Nursing and Midwifery, University of Stirling, Stirling, UK. lisa.whitehead@stir.ac.uk	Enhancing the quality of hermeneutic research: decision trail.	J Adv Nurs. 2004 Mar;45(5):512-8.	BACKGROUND: Researchers have ethical and professional obligations to produce research of a high standard. The constituents of quality in research appear to differ between authors, leaving readers unsure about which pathway to follow. This can reflect inadequate consideration of the theoretical framework guiding the study. Many papers fail to consider the theoretical underpinnings of the methodology chosen and the link between these and the methods employed. These need to be accessible to readers in order to assess the trustworthiness of the research. AIM: This paper discusses the development of trustworthiness in hermeneutic phenomenological research. DISCUSSION: Referring to a study on lived experience of Chronic Fatigue Syndrome/myalgic encephalitis, I describe the decision trail and discuss the strengths and limitations of the choices made throughout the study. CONCLUSION: The methodology focused my approach more fully on the importance of recognizing the influences that I brought to the study and the impact of these in generating the data. It highlighted the fact that the process of setting out my horizon can never be complete, the importance of analysing the data at a macro and micro level, acknowledging the evolution of the data over time, and ensuring that analysis does not move beyond the data and out of the hermeneutic circle. In seeking to make the decision trail clear to others, researchers must distill the philosophical principles of the methodology and set these out in a way that is accessible and open to scrutiny.
Whiteside A, Hansen S, Chaudhuri A.	Departments of Clinical Physics, Institute of Neurological Sciences, South Glasgow University Hospitals NHS Trust, Glasgow, UK.	Exercise lowers pain threshold in chronic fatigue syndrome.	Pain. 2004 Jun;109(3):497-9.	Post-exertional muscle pain is an important reason for disability in patients who are diagnosed to have Chronic Fatigue Syndrome (CFS). We compared changes in pain threshold in five CFS patients with five age and sex matched controls following graded exercise. Pain thresholds, measured in the skin web between thumb and index finger, increased in control subjects with exercise while it decreased in the CFS subjects. Increased perception of pain and/or fatigue after exercise may be indicative of a dysfunction of the central anti-nociceptive mechanism in CFS patients.
Winkler AS, Blair D, Marsden JT, Peters TJ, Wessely S, Cleare AJ.	Department of Medicine, Division of Psychological Medicine, GKT School of Medicine, Institute of Psychiatry, De Crespigny Park, London SE5 9RJ, UK.	Autonomic function and serum erythropoietin levels in chronic fatigue syndrome.	J Psychosom Res. 2004 Feb;56(2):179-83.	OBJECTIVE: Given previous findings, we wished to investigate whether there was evidence of autonomic dysfunction in patients with chronic fatigue syndrome, and whether this could be related to reduced erythropoietin levels and altered red blood cell indices. METHODS: We assessed autonomic function and analysed blood parameters (including erythropoietin) in 22 patients with chronic fatigue syndrome who were medication-free and without comorbid depression or anxiety. Results were compared to 23 iron-deficiency anaemia patients and 18 healthy individuals. RESULTS: Autonomic testing in patients with chronic fatigue syndrome yielded a significantly greater increase in heart rate together with a more pronounced systolic blood pressure fall on standing compared to healthy individuals. Heart rate beat-to-beat variation on deep breathing and responses to the Valsalva manoeuvre were normal. Two of 22 patients with chronic fatigue had mild normochromic normocytic anaemia with normal ferritin, vitamin B12 and folate levels. Serum erythropoietin levels were within reference range. CONCLUSION: Some autonomic dysfunction is present in chronic fatigue syndrome (CFS) patients; the explanation remains uncertain, but could relate

				to cardiovascular deconditioning. There were no major haematological, biochemical or immunological abnormalities in these patients.
Woldehiwet Z	Department of Veterinary Pathology, University of Liverpool, Veterinary Teaching Hospital, Leahurst, Neston, Wirral CH64 7TE, UK. zerai@liverpool.ac.uk	Q fever (coxiellosis): epidemiology and pathogenesis Erratum in: Res Vet Sci. 2004 Dec;77(3):269.	Res Vet Sci. 2004 Oct;77(2):93-100.	
Woolley J, Allen R, Wessely S.	Academic Department of Psychological Medicine, Guy's, King's & St Thomas's School of Medicine and Institute of Psychiatry, 103 Denmark Hill, London SE5 8AF, UK.	Alcohol use in chronic fatigue syndrome.	J Psychosom Res. 2004 Feb;56(2):203-6.	OBJECTIVE: To examine the anecdotal observation that patients with chronic fatigue syndrome develop alcohol intolerance. METHODS: A consecutive case series of 114 patients fulfilling UK criteria for chronic fatigue syndrome referred to a specialist clinic. Self-reported alcohol use pre- and postdiagnosis, fatigue symptoms and comorbidity measures were collected. RESULTS: Two-thirds reduced alcohol intake. The most common reasons were increased tiredness after drinking (67%), increased nausea (33%), exacerbated hangovers (23%) and sleep disturbance (24%). One-third of the subjects also stopped drinking because "it seemed sensible." Some had been advised to avoid alcohol, but the majority (66%) did so on the basis of personal experience. CONCLUSION: Our data supports the anecdotal belief that chronic fatigue syndrome patients reduce or cease alcohol intake. This is associated with greater impairment in employment, leisure and social domains of function, and may hint at psychopathophysiological processes in common with other conditions that result in alcohol intolerance.
Wyller VB, Wyller TB.		[Exhaustion--not fatigue] [Article in Norwegian]	Tidsskr Nor Laegeforen. 2004 Nov 4;124(21):2802; author reply 2802.	
Yamamoto S, Ouchi Y, Onoe H, Yoshikawa E, Tsukada H, Takahashi H, Iwase M, Yamaguti K, Kuratsune H, Watanabe Y.	Department of Physiology, Osaka City University Graduate School of Medicine, 1-4-3 Asahimachi, Abeno-ku, Osaka 545-8585 Positron Medical Center, Hamamatsu Medical Center, 5000 Hirakuchi, Hamakita, Shizuoka 434-0041 Department of Psychology, Tokyo Metropolitan Institute for Neuroscience, 2-6 Musashidai Fuchu, Tokyo 183-8526 Central Research Laboratory, Hamamatsu Photonics KK, 5000 Hirakuchi, Hamakita, Shizuoka 434-8601 Psychiatry, Department of Clinical Neuroscience Department of Hematology and Oncology, Osaka University Graduate School of Medicine, 2-2	Reduction of serotonin transporters of patients with chronic fatigue syndrome.	Neuroreport. 2004 Dec 3;15(17):2571-2574.	To assess the involvement of serotonin in the symptoms of chronic fatigue syndrome, we investigated the serotonergic neurotransmitter system of chronic fatigue syndrome patients by the positron emission tomography (PET). Here we show that the density of serotonin transporters (5-HTTs) in the brain, as determined by using a radiotracer, [C](+)McN5652, was significantly reduced in the rostral subdivision of the anterior cingulate as compared with that in normal volunteers. This subdivision is different from that in the dorsal anterior cingulate in which binding potential values of individual patient showed a weak negative correlation with self-reported pain score of the patients. Therefore, an alteration of serotonergic system in the rostral anterior cingulate plays a key role in pathophysiology of chronic fatigue syndrome.

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Yoshiuchi K, Quigley KS, Ohashi K, Yamamoto Y, Natelson BH.	Department of Psychiatry, University of Medicine and Dentistry of New Jersey, New Jersey Medical School, East Orange, NJ 07018, USA.	Use of time-frequency analysis to investigate temporal patterns of cardiac autonomic response during head-up tilt in chronic fatigue syndrome.	Auton Neurosci. 2004 Jun 30;113(1-2):55-62.	Although a number of studies have reported alterations in cardiac autonomic nervous system function in chronic fatigue syndrome (CFS), the results are not consistent across studies. Reasons for these discrepancies include (1) the use of a heterogeneous patient sample that included those with orthostatic postural tachycardia (POTS), a condition with an autonomic changes, and (2) the use of frequency domain techniques which require a stationary signal and averaging data across relatively long epochs. To deal with these shortcomings, we used the smoothed pseudo-Wigner-Ville transform (SPWVT) to analyze heart rate variability (HRV) and blood pressure variability (BPV) during head-up tilt (HUT) by separating CFS patients into those with and without POTS. SPWVT has the advantage of providing instantaneous information about autonomic function under nonstable physiological conditions. We studied 18 CFS patients without POTS, eight CFS patients with POTS and 25 sedentary healthy controls during supine rest and during the first 10 min after HUT. While we found significant effects of postural change in both groups for all autonomic variables, there were significant group*time interactions between CFS without POTS and controls for only instant center frequency (ICF) within the low frequency region both from HRV ($p=0.02$) and from BPV ($p=0.01$). Although the physiological meaning of ICF still remains unknown, the data suggest that even CFS patients without POTS may have a subtle underlying disturbance in autonomic function.
Zachrisson O, Colque-Navarro P, Gottfries CG, Regland B, Mollby R.	Institute of Clinical Neuroscience, SU/Molndal, 43180 Molndal, Sweden. olof.zachrisson@neuro.gu.se	Immune modulation with a staphylococcal preparation in fibromyalgia/chronic fatigue syndrome: relation between antibody levels and clinical improvement.	Eur J Clin Microbiol Infect Dis. 2004 Feb;23(2):98-105. Epub 2004 Jan 20.	The aims of this study were to evaluate the serological response to treatment with staphylococcal vaccine in fibromyalgia/chronic fatigue syndrome patients and to explore the relationship between serological response and clinical effect. Twenty-eight patients, half of whom served as controls, were recruited from a 6-month randomised trial in which repeated administration of the staphylococcal toxoid vaccine Staphypan Berna (Berna Biotech, Switzerland) was tested against placebo. Antibody status against extracellular toxins/enzymes, cell-wall components, and enterotoxins was evaluated at baseline and at endpoint. The clinical response to treatment was recorded in rating scales. In the group receiving active treatment, significant serological changes were recorded, whereas no significant changes were found in controls. Treatment led to a significantly increased capacity of serum to neutralise alpha-toxin and a significant increase in serum IgG to alpha-toxin and lipase. Furthermore, the increase in these parameters combined paralleled the improvement in clinical outcome. Thus, the greater the serological response, the greater was the clinical effect. In conclusion, this explorative study has shown that repeated administration of the Staphypan Berna vaccine in patients with fibromyalgia/chronic fatigue syndrome causes a serological response to several staphylococcal antigens, particularly to certain extracellular toxins and enzymes. The results further show that this response is related to the clinical outcome of treatment.
Zavestoski S, Brown P, McCormick S, Mayer B, D'Ottavi M, Lucove JC.	Department of Sociology, University of San Francisco, 2130 Fulton Street, San Francisco, CA 94117-1080, USA. smzavestoski@usfca.edu	Patient activism and the struggle for diagnosis: Gulf War illnesses and other medically unexplained physical symptoms in the US.	Soc Sci Med. 2004 Jan;58(1):161-75.	We examine Gulf War illnesses--which include the fatigue, joint pain, dermatitis, headaches, memory loss, blurred vision, diarrhea, and other symptoms reported by Gulf War veterans--in relation to other medically unexplained physical symptoms such as multiple chemical sensitivity, chronic fatigue syndrome, and fibromyalgia. Our intent is to examine the diagnosis negotiations involved in these mysterious diseases, by showing the different forms of legitimacy involved in such interactions. Factors involved in diagnostic legitimacy are: diagnostic legitimacy in the medical community, lay acceptance of the diagnosis, uncertainty in looking for causes, and social mobilization. We conclude by noting that research may not be able to find any cause for these diseases/conditions; hence, it may be necessary to embrace medical uncertainty, and also to accept patient experience in order to facilitate diagnosis, treatment, and recovery process. Such a change can alter patients' expectations and taken-for-granted assumptions about medicine, and perhaps in turn reduce the frequency with which dissatisfied individuals form illness groups that mobilize to challenge what they see as an unresponsive medical system.
[No authors listed]		Handbook of chronic fatigue syndrome.	Aust N Z J Psychiatry. 2004 Jun;38(6):479-480.	
[No authors listed]		L-carnitine.	Med Lett Drugs Ther. 2004 Nov 22;46(1196):95-6.	Although advertised on the Internet for weight loss, prevention of aging and enhancement of athletic and sexual performance, levocarnitine has only one well-established indication, and that is for treatment of carnitine deficiency. In clinical trials, the drug also seems to have had modest effects in some other conditions, particularly intermittent claudication and recovery after

				myocardial infarction, but more studies are needed.
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