

RESEARCH ABSTRACTS: ME/CFS

(**Note:** Emphasis in abstracts is added)

2002

Dysautonomias: clinical disorders of the autonomic nervous system.

Authors

Goldstein DS, Robertson D, Esler M, Straus SE, Eisenhofer G.

Source

Ann Intern Med 2002 Nov 5;137(9):753-63

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Author's Affiliation

Clinical Neurocardiology Section, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Building 10, Room 6N252, 10 Center Drive MSC-1620, Bethesda, MD 20892-1620, USA.

Abstract

The term dysautonomia refers to a change in autonomic nervous system function that adversely affects health. The changes range from transient, occasional episodes of neurally mediated hypotension to progressive neurodegenerative diseases; from disorders in which altered autonomic function plays a primary pathophysiologic role to disorders in which it worsens an independent pathologic state; and from mechanistically straightforward to mysterious and controversial entities. In chronic autonomic failure (pure autonomic failure, multiple system atrophy, or autonomic failure in Parkinson disease), orthostatic hypotension reflects sympathetic neurocirculatory failure from sympathetic denervation or deranged reflexive regulation of sympathetic outflows. Chronic orthostatic intolerance associated with postural tachycardia can arise from cardiac sympathetic activation after "patchy" autonomic impairment or blood volume depletion or, as highlighted in this discussion, from a primary abnormality that augments delivery of the sympathetic neurotransmitter norepinephrine to its receptors in the heart. Increased sympathetic nerve traffic to the heart and kidneys seems to occur as essential hypertension develops. Acute panic can evoke coronary spasm that is associated with sympathoneural and adrenomedullary excitation. In congestive heart failure, compensatory cardiac sympathetic activation may chronically worsen myocardial function, which rationalizes treatment with beta-adrenoceptor blockers. **A high frequency of positive results on tilt-table testing has confirmed an association between the chronic fatigue syndrome and orthostatic intolerance; however, treatment with the salt-retaining steroid fludrocortisone, which is usually beneficial in primary chronic autonomic failure, does not seem to be beneficial in the chronic fatigue syndrome.** Dysautonomias are an important subject in clinical neurocardiology.

Chronic fatigue and chronic fatigue syndrome: a co-twin control study of functional status.

Authors

Herrell R, Goldberg J, Hartman S, Belcourt M, Schmalting K, Buchwald D.

Source

Qual Life Res 2002 Aug;11(5):463-71

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Author's Affiliation

Division of Epidemiology-Biostatistics, University of Illinois at Chicago, USA.

Abstract

Chronic fatigue syndrome (CFS) and the symptom of chronic fatigue may be accompanied by substantial functional disability. A volunteer sample of twins discordant for fatigue was identified from throughout the US. Fatigued twins were classified using three increasingly stringent definitions: (1) > or = 6 months of fatigue (119 pairs); (2) CFS-like illness based on self-report of the Centers for Disease Control and Prevention CFS research definition criteria (74 pairs); and (3) CFS assessed by clinical examination (22 pairs). Twins with chronic fatigue were compared with their unaffected co-twins on the eight standard scales and two physical and mental component summary scales from the medical outcomes study short-form health survey (SF-36). **Substantial impairment was observed for fatigued twins across all levels of fatigue, while scores in the healthy twins were similar to US population values. Mean scores among fatigued twins on the physical and mental component summary scales were below 97 and 77%, respectively, of the US population scores. Diminished functional status was found across increasingly stringent classifications of fatigue and was associated with a dramatic decrement in physical functioning. The symptom of fatigue has a pronounced impact on functional status, especially in the domain of physical functioning.**

Brain regions involved in fatigue sensation: reduced acetylcarnitine uptake into the brain.

Authors

Kuratsune H, Yamaguti K, Lindh G, Evengard B, Hagberg G, Matsumura K, Iwase M, Onoe H, Takahashi M, Machii T, Kanakura Y, Kitani T, Langstrom B, Watanabe Y.

Source

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Author's Affiliation

Department of Molecular Medicine, Hematology and Oncology, Osaka University Graduate School of Medicine, C9, 2-2 Yamada-oka, Suita, Osaka 565-0871, Japan. kura@bldon.med.osaka-u.ac.jp

Abstract

Fatigue is an indispensable sense for ordering rest. However, the neuronal and molecular mechanisms of fatigue remain unclear. Chronic fatigue syndrome (CFS) with long-lasting fatigue sensation seems to be a good model for studying these mechanisms underlying fatigue sensation. Recently, we found that most patients with CFS showed a low level of serum acetylcarnitine, which well correlated with the rating score of fatigue, and that a considerable amount of acetyl moiety of serum acetylcarnitine is taken up into the brain. Here we show by metabolite analysis of the mouse brain that an acetyl moiety taken up into the brain through acetylcarnitine is mainly utilized for the biosynthesis of glutamate. When we studied the cerebral uptake of acetylcarnitine by using [2-(11)C]acetyl-L-carnitine in 8 patients with CFS and in 8 normal age- and sex-matched controls, a significant decrease was found in several regions of the brains of the patient group, namely, in the prefrontal (Brodmann's area 9/46d) and temporal (BA21 and 41) cortices, anterior cingulate (BA24 and 33), and cerebellum. **These findings suggest that the levels of biosynthesis of neurotransmitters through acetylcarnitine might be reduced in some brain regions of**

chronic fatigue patients and that this abnormality might be one of the keys to unveiling the mechanisms of the chronic fatigue sensation.

IgM serum antibodies to human cytomegalovirus nonstructural gene products p52 and CM2(UL44 and UL57) are uniquely present in a subset of patients with chronic fatigue syndrome.

Authors

Lerner MA, Beqaj SH, Deeter RG, Fitzgerald JT.

Source

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Author's Affiliation

Department of Medicine, William Beaumont Hospital, Wayne State University School of Medicine, Royal Oak, Michigan, USA. lerner@cdimed.com

Abstract

Human cytomegalovirus (HCMV) IgM serum antibodies to two nonstructural gene products UL44 and UL57 (p52 and CM2) were assayed in patients with the diagnosis of the chronic fatigue syndrome (CFS) according to criteria established by the US Centers for Disease Control and Prevention. A subset of 16 CFS patients demonstrated HCMV IgG, but no HCMV IgM serum antibodies to conformational structural HCMV antigens (designated, V). By convention, these findings are interpreted to indicate only a remote HCMV infection. However, HCMV IgM p52 and CM2 antibodies were uniquely present in these 16 CFS patients. Other CFS patients with similar HCMV (V) IgG antibodies (18 patients), non-fatigued HCMV (V) IgG-positive control patients (18 patients), random HCMV (V) IgG-positive control patients from a clinical laboratory (26 patients), and non-fatigued HCMV (V) IgG-negative control patients (15 patients) did not have HCMV, IgM p52 or CM2 serum antibodies ($p < 0.05$). Control HCMV (V) IgG-positive patients had no serum IgM HCMV (V) antibodies to conventional structural HCMV (V) antigen. Thus, 77 various control patients did not contain IgM p52 or CM2 serum antibodies. **The presence of IgM p52 and/or CM2 HCMV serum antibodies in this subset of CSF-specific patients may detect incomplete HCMV multiplication in which a part of the HCMV protein-coding content of the HCMV genome is processed, but remains unassembled. These findings suggest that the presence of HCMV IgM p52 and CM2 serum antibodies may be a specific diagnostic test for the diagnosis of a subset of CFS patients. Further, these data suggest an etiologic relationship for HCMV infection in this group of CFS patients.**

Role of fatigue in limiting physical activities in humans with neuromuscular diseases.

Authors

Miller RG

Source

Am J Phy Med Rehabil 2002 Nov;81(11 Suppl):S99-107 PubMed 12409815

Author's Affiliation

Department of Neurology, California Pacific Medical Center, San Francisco, California 94115, USA.

Abstract

New methods of examining both central and peripheral fatigue are now available. A broader understanding of the mechanisms of fatigue in healthy human subjects has begun to emerge. **The mechanisms of fatigue in patients with various neuromuscular diseases are even more complex than in healthy persons. Examples of both central and peripheral fatigue in various neuromuscular diseases and other disorders are presented, including metabolic myopathy, chronic fatigue syndrome, postpolio syndrome, and amyotrophic lateral sclerosis.**

A tender sinus does not always mean rhinosinusitis.

Authors

Naranch K, Park YJ, Repka-Ramirez MS, Velarde A, Clauw D, Baraniuk JN.

Source

Otolaryngol Head Neck Surg 2002 Nov;127(5):387-97 PubMed 12447232

Author's Affiliation

Chronic Pain and Fatigue Research Center, Division of Rheumatology, Immunology and Allergy, Georgetown University, Washington, DC 20007-2097, USA.

Abstract

BACKGROUND: Sinus tenderness has not been quantitatively assessed. **OBJECTIVE:** We sought to compare sinus and systemic tenderness in rhinosinusitis, allergic rhinitis, and chronic fatigue syndrome (CFS), and healthy (non-CFS) groups.

METHODS: Cutaneous pressures (kg/cm²) causing pain at 5 sinus and 18 systemic sites were measured in acute and chronic rhinosinusitis, active allergic rhinitis, healthy non-CFS/no rhinosinusitis, and CFS subjects.

RESULTS: Sinus thresholds differed significantly ($P \leq 10^{-11}$, ANOVA) between non-CFS/no rhinosinusitis (1.59 +/- 0.14 kg/cm², mean +/- 95% CI, n = 117), allergic rhinitis (1.19 +/- 0.31, n = 30), exacerbations of chronic rhinosinusitis (1.25 +/- 0.26, n = 25), non-CFS/chronic rhinosinusitis (1.23 +/- 0.27, n = 23), acute rhinosinusitis (1.10 +/- 0.20, n = 22), CFS/no rhinosinusitis (0.98 +/- 0.15, n = 70), and CFS/chronic rhinosinusitis (0.78 +/- 0.12, n = 56). Systemic pressure thresholds were lower for CFS (1.46 +/- 0.15) than for non-CFS (2.67 +/- 0.22, $P \leq 10^{-11}$).

CONCLUSIONS: The lower sinus thresholds of rhinosinusitis groups validated the sign of sinus tenderness. Sinus and systemic thresholds were both 44% lower in CFS than in non-CFS subjects, suggesting that systemic hyperalgesia contributed to CFS sinus tenderness and "rhinosinusitis" complaints.

Fractal analysis and recurrence quantification analysis of heart rate and pulse transit time for diagnosing chronic fatigue syndrome.

Authors

Naschitz JE, Sabo E, Naschitz S, Rosner I, Rozenbaum M, Priselac RM, Gaitini L, Zukerman E, Yeshurun D.

Source

Author's Affiliation

Department of Internal Medicine A, Bnai Zion Medical Center, Haifa 31048, P. O. Box 4940, Israel.
naschitz@tx.technion.ac.il

Abstract:

This study aimed to develop a method to distinguish between the cardiovascular reactivity in chronic fatigue syndrome (CFS) and other patient populations. Patients with CFS (n = 23), familial Mediterranean fever (n = 15), psoriatic arthritis (n = 10), generalized anxiety disorder (n = 12), neurally mediated syncope (n = 20), and healthy subjects (n = 20) were evaluated with a shortened head-up tilt test (HUTT). A 10-minute supine phase of the HUTT was followed by recording 600 cardiac cycles on tilt, i. e., 5 to 10 minutes. Beat-to-beat heart rate (HR) and pulse transit time (PTT) were acquisitioned. Data were processed by recurrence plot and fractal analysis. Fifty-two variables were calculated in each subject. On multivariate analysis, the best predictors of CFS were HR-tilt-R/L, PTT-tilt-R/L, HR-supine-DET, PTT-tilt-WAVE, and HR-tilt-SD. Based on these predictors, the 'Fractal & Recurrence Analysis-based Score' (FRAS) was calculated: $FRAS = 76.2 + 0.04 \cdot HR\text{-supine-DET} - 12.9 \cdot HR\text{-tilt-R/L} - 0.31 \cdot HR\text{-tilt-SD} - 19.27 \cdot PTT\text{-tilt-R/L} - 9.42 \cdot PTT\text{-tilt-WAVE}$. **The best cut-off differentiating CFS from the control population was FRAS = + 0.22. FRAS > + 0.22 was associated with CFS (sensitivity 70 % and specificity 88 %). The cardiovascular reactivity received mathematical expression with the aid of the FRAS. The shortened HUTT was well tolerated. The FRAS provides objective criteria which could become valuable in the assessment of CFS.**

**High prevalence of Mycoplasma infections among
European chronic fatigue syndrome patients.
Examination of four Mycoplasma species in blood
of chronic fatigue syndrome patients.**

Authors

Nijs J, Nicolson GL, De Becker P, Coomans D, De Meirleir K.

Source

FEMS Immunol Med Microbiol 2002 Nov 15;34(3):209-14

PubMed 12423773

Author's Affiliation

Department of Human Physiology, Faculty of Physical Education and Physiotherapy, Vrije Universiteit Brussel, KRO Gebouw-1, Laarbeeklaan 101, 1090 Brussel, Belgium.
jo.nijs@vub.ac.be

Abstract

Prevalence of Mycoplasma species infections in chronic fatigue syndrome (CFS) has been extensively reported in the scientific literature. However, all previous reports highlighted the presence of Mycoplasmas in American patients. In this prospective study, the presence of Mycoplasma fermentans, M. penetrans, M. pneumoniae and M. hominis in the blood of 261 European CFS patients and 36 healthy volunteers was examined using forensic polymerase chain reaction. **One hundred and seventy-nine (68.6%) patients were infected by at least one species of Mycoplasma, compared to two out of 36 (5.6%) in the control sample (P<0.001). Among Mycoplasma-infected patients, M. hominis was the most frequently observed infection (n=96; 36.8% of the overall sample), followed by M. pneumoniae and M. fermentans infections (equal frequencies; n=67; 25.7%). M. penetrans infections were not**

found. Multiple mycoplasmal infections were detected in 45 patients (17.2%). Compared to American CFS patients (*M. pneumoniae*>*M. hominis*>*M. penetrans*), a slightly different pattern of mycoplasmal infections was found in European CFS patients (*M. hominis*>*M. pneumoniae*, *M. fermentans*>*M. penetrans*).

Relative increase in choline in the occipital cortex in chronic fatigue syndrome.

Authors

Puri BK, Counsell SJ, Zaman R, Main J, Collins AG, Hajnal JV, Davey NJ.

Source

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Author's Affiliation

MRI Unit, MRC Clinical Sciences Centre, Imperial College School of Medicine, Hammersmith Hospital, London, UK. basant.puri@csc.mrc.ac.uk

Abstract

OBJECTIVE: To test the hypothesis that chronic fatigue syndrome (CFS) is associated with altered cerebral metabolites in the frontal and occipital cortices.

METHOD: Cerebral proton magnetic resonance spectroscopy (1H MRS) was carried out in eight CFS patients and eight age- and sex-matched healthy control subjects. Spectra were obtained from 20 x 20 x 20 mm³ voxels in the dominant motor and occipital cortices using a point-resolved spectroscopy pulse sequence.

RESULTS: The mean ratio of choline (Cho) to creatine (Cr) in the occipital cortex in CFS (0.97) was significantly higher than in the controls (0.76; P=0.008). No other metabolite ratios were significantly different between the two groups in either the frontal or occipital cortex. In addition, there was a loss of the normal spatial variation of Cho in CFS.

CONCLUSION: Our results suggest that there may be an abnormality of phospholipid metabolism in the brain in CFS.

Chronic fatigue syndrome: circadian rhythm and hypothalamic-pituitary-adrenal (HPA) axis impairment.

Authors

Racciatti D, Guagnano MT, Vecchiet J, De Remigis PL, Pizzigallo E, Della Vecchia R, Di Sciascio T, Merlitti D, Sensi S.

Source

Int J Immunopathol Pharmacol 2001 Jan-Apr;14(1):11-15 PubMed 12622884

Author's Affiliation

Clinic of Infectious Diseases, University of Chieti, Chieti, Italy.

Abstract

Chronic Fatigue Syndrome (CFS) is a clinical condition characterized by a persistent or relapsing debilitating fatigue at rest, lasting more than 6 months, and made worse by exercise. At the present moment, there are three potential etiopathogenic factors: immunologic, viral and neuroendocrine. The purpose of our study was to evaluate possible alterations of the hypothalamic-pituitary-adrenal (HPA) axis in our CFS patients by studying the circadian rhythms of prolactin (PRL), thyrotropic hormone (TSH), adrenocorticotrophic hormone (ACTH), and cortisol (CS). A total of 36 patients were enrolled according to the Centers for Disease Control and Prevention case-definition criteria. Twenty healthy subjects were included as controls. Blood samples were taken every 4 hours during a single 24-hour period. We performed a fluorometric enzyme immunoassay with serum PRL, cortisol and TSH, and an immunoradiometric assay with plasma ACTH. The circadian rhythms of PRL, TSH, ACTH and CS were statistically significant in both CFS and control groups. **At 24:00 and 04:00 hrs the CFS patients showed lower ACTH levels than healthy subjects ($p < 0.001$); the PRL levels were higher at 04.00 h in CFS patients than in healthy subjects.**

Utility of the blood for gene expression profiling and biomarker discovery in chronic fatigue syndrome.

Authors

Vernon SD, Unger ER, Dimulescu IM, Rajeevan M, Reeves WC.

Source

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Author's Affiliation Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA.

Abstract

Chronic fatigue syndrome (CFS) is a debilitating illness lacking consistent anatomic lesions and eluding conventional laboratory diagnosis. Demonstration of the utility of the blood for gene expression profiling and biomarker discovery would have implications into the pathophysiology of CFS. The objective of this study was to determine if gene expression profiles of peripheral blood mononuclear cells (PBMCs) could distinguish between subjects with CFS and healthy controls. Total RNA from PBMCs of five CFS cases and seventeen controls was labeled and hybridized to 1764 genes on filter arrays. Gene intensity values were analyzed by various classification algorithms and nonparametric statistical methods. **The classification algorithms grouped the majority of the CFS cases together, and distinguished them from the healthy controls. Eight genes were differentially expressed in both an age-matched case-control analysis and when comparing all CFS cases to all controls. Several of the differentially expressed genes are associated with immunologic functions (e.g., CMRF35 antigen, IL-8, HD protein) and implicate immune dysfunction in the pathophysiology of CFS. These results successfully demonstrate the utility of the blood for gene expression profiling to distinguish subjects with CFS from healthy controls and for identifying genes that could serve as CFS biomarkers.**