

Chronic Widespread Musculoskeletal Pain, Fatigue, Depression and Disordered Sleep in Chronic Post-SARS Syndrome; a case-controlled study Harvey Moldofsky and John Patcai

BMC Neurology 2011, 11:37doi:10.1186/1471-2377-11-37 Published: 24 March 2011

The long term adverse effects of Severe Acute Respiratory Syndrome (SARS), a viral disease, are poorly understood.

Methods: Sleep physiology, somatic and mood symptoms of 22 Toronto subjects, 21 of whom were healthcare workers, (19 females, 3 males, mean age 46.29 yrs.+/- 11.02) who remained unable to return to their former occupation (mean 19.8 months, range: 13 to 36 months following SARS) were compared to 7 healthy female subjects. Because of their clinical similarities to patients with fibromyalgia syndrome (FMS) these post-SARS subjects were similarly compared to 21 drug free female patients, (mean age 42.4 +/- 11.8 yrs.) who fulfilled criteria for fibromyalgia.

Results: Chronic post-SARS is characterized by persistent fatigue, diffuse myalgia, weakness, depression, and nonrestorative sleep with associated REM-related apneas/hypopneas, an elevated sleep EEG cyclical alternating pattern, and alpha EEG sleep anomaly.

Post- SARS patients had symptoms of pre and post-sleep fatigue and post sleep sleepiness that were similar to the symptoms of patients with FMS, and similar to symptoms of patients with chronic fatigue syndrome. Both post-SARS and FMS groups had sleep instability as indicated by the high sleep EEG cyclical alternating pattern rate.

The post-SARS group had a lower rating of the alpha EEG sleep anomaly as compared to the FMS patients. The post-SARS group also reported less pre-sleep and post-sleep musculoskeletal pain symptoms.

Conclusions: The clinical and sleep features of chronic post-SARS form a syndrome of chronic fatigue, pain, weakness, depression and sleep disturbance, which overlaps with the clinical and sleep features of FMS and chronic fatigue syndrome.

<http://www.biomedcentral.com/content/pdf/1471-2377-11-37.pdf>

Chronic fatigue syndrome in an ethnically diverse population: the influence of psychosocial adversity & physical inactivity

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Abstract (provisional)

Background Chronic fatigue syndrome (CFS) is a complex multi-factorial disorder.

This paper reports the prevalence of chronic fatigue & CFS in an ethnically diverse population sample, and tests whether prevalence varies by social adversity, social support, physical inactivity, anxiety, and depression.

Methods Analysis of survey data linking the Health Survey for England (1998/9) and the EMPIRIC study, undertaken in 2000, of a national population sample of 4281 people aged 16-74. Chronic fatigue (CF) and CFS were operationally defined from an interview in the EMPIRIC study, alongside questions about psychosocial risk factors. Previous illnesses were reported in the Health Survey for England during 1998/9 as was physical inactivity.

Results All ethnic minority groups had a higher prevalence of CFS when compared with the white group. The lowest prevalence was 0.8% in the white group and was highest at 3.5% in the Pakistani group (OR (odds

ratio) = 4.1, 95% CI (confidence interval)=1.6-10.4). Anxiety (OR=1.8, 1.4-2.2), depression (OR=1.4, 1.1-1.8), physical inactivity (OR=2.0, 1.1-3.8), social strain (OR=1.24, 1.04-1.48), and negative aspects of social support (OR=2.12, 1.4-3.3) were independent risk factors for CFS in the overall sample; together these risk factors explained ethnic differences in the prevalence of CFS, but no single risk factor could explain a higher prevalence in all ethnic groups.

Conclusions The prevalence of CFS, but not chronic fatigue, varies by ethnic group. Anxiety, depression, physical inactivity, social strain, and negative aspects of social support together accounted for prevalence differences of CFS in the overall sample.

Fibromyalgia: an afferent processing disorder leading to a complex pain generalized syndrome.

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Abstract

Fibromyalgia is a condition which appears to involve disordered central afferent processing.

The major symptoms of fibromyalgia include multifocal pain, fatigue, sleep disturbances, and cognitive or memory problems. Other symptoms may include psychological distress, impaired functioning, and sexual dysfunction. The pathophysiology of fibromyalgia remains uncertain but is believed to be largely central in nature.

In 1990 the American College of Rheumatology (ACR) published diagnostic research criteria for fibromyalgia. The criteria included a history of chronic and widespread pain and the presence of 11 or more out of 18 tender points. Pain was considered chronic widespread when all of the following are present: pain in the left side of the body; pain in the right side of the body; pain above the waist; pain below the waist. In addition, axial skeletal pain must be present and the duration of pain must be more than 3 months. A tender point is considered positive when pain can be elicited by pressures of 4 kg/cm² or less. For tender points to be considered positive, the patient must perceive the palpation as painful; tenderness to palpation is not sufficient.

However, over the next 20 years it became increasingly appreciated that the focus on tender points was not justified. In 2010 a similar group of investigators performed a multicenter study of 829 previously diagnosed fibromyalgia patients and controls using physician physical and interview examinations, including a widespread pain index (WPI), a measure of the number of painful body regions. Random forest and recursive partitioning analyses were used to guide the development of a case definition of fibromyalgia, to develop new preliminary ACR diagnostic criteria, and to construct a symptom severity (SS) scale.

The most important diagnostic variables were WPI and categorical scales for cognitive symptoms, un-refreshed sleep, fatigue, and number of somatic symptoms. The categorical scales were summed to create an SS scale. The investigators combined the SS scale and the WPI to recommend a new case definition of fibromyalgia: (WPI > or = 7 AND SS > or = 5).

Although there is no known cure for fibromyalgia, multidisciplinary team efforts using combined treatment approaches, including patient education, aerobic exercise, cognitive behavioral therapy, and pharmacologic therapies (serotonin norepinephrine reuptake inhibitors [e.g., duloxetine, milnacipran] and alpha 2-delta receptor ligands [e.g., pregabalin]) might improve symptoms as well as function in patients with fibromyalgia.

<http://webcache.googleusercontent.com/search?q=cache:SG7XfatbNYUJ:w...>

Metacognitions and negative emotions as predictors of symptom severity in chronic fatigue syndrome.

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Abstract

OBJECTIVE: Chronic fatigue syndrome (CFS) describes a condition that is primarily characterized by fatigue and flu-like symptoms that are not alleviated by rest. This study investigated the relationship among metacognitions, negative emotions, and symptom severity in CFS.

METHODS: A total of 96 patients who had received a diagnosis of CFS according to the Oxford Criteria completed a battery of self-report measures that consisted of the Depression Anxiety Stress Scales, the 30-Item Metacognitions Questionnaire, the Chalder Fatigue Questionnaire (CFQ), and the RAND 36-Item Short-Form Health Survey-Physical Functioning.

RESULTS: Correlation analyses showed that negative emotions and metacognitions were positively correlated with measures of symptom severity and that metacognitions were a better predictor of symptom severity than anxiety and depression. Hierarchical regression analyses indicated that (1) lack of cognitive confidence predicted both mental and physical factors of the CFQ and physical functioning independently of negative emotions and (2) beliefs about the need to control thoughts predicted the mental factor of the CFQ independently of negative emotions and lack of cognitive confidence.

CONCLUSION: The data support the potential application of the metacognitive model of psychological disorder to understanding CFS.

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Does a decrease in avoidance behavior and focusing on fatigue mediate the effect of cognitive behavior therapy for chronic fatigue syndrome?

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Abstract

OBJECTIVE: Cognitive behavior therapy (CBT) leads to a significant reduction in fatigue severity and impairment in patients with chronic fatigue syndrome (CFS). The purpose of the present study was to determine whether the effect of CBT for CFS on fatigue and impairment is mediated by a decrease in avoidance behavior and focusing on fatigue.

METHODS: For this purpose, we reanalyzed a randomized controlled trial which was previously conducted to test the efficacy of CBT for CFS.

Two hundred nineteen patients completed assessment prior and subsequent to treatment or a control group period.

RESULTS: Mediation analysis revealed that a decrease in focusing on fatigue mediated the effect of CBT for CFS on fatigue and impairment.

Avoidance of activity and avoidance of aversive stimuli were not significantly changed by treatment and were therefore excluded from mediation analysis.

CONCLUSION: A decrease in the focus on fatigue seems to contribute to the treatment effect of CBT for CFS

Chronic fatigue syndrome - A neuroimmunological model.

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Abstract

The aetiological and pathophysiological basis of chronic fatigue syndrome (CFS) remains a controversial field of inquiry in the research community. While CFS and similar disease conditions such as fibromyalgia (FM) and post-infectious encephalopathy have been the focus of intense scrutiny for the past 20 years, results of research were often contradictory and a cohesive pathological model has remained elusive. However, recent developments in understanding the unique immunophysiology of the brain may provide important clues for the development of a truly comprehensive explanation of the pathology of CFS.

We argue that CFS pathogenesis lies in the influence of peripheral inflammatory events on the brain and the unique immunophysiology of the central nervous system. There is also evidence that CFS patients have a relative immunodeficiency that predisposes to poor early control of infection that leads to chronic inflammatory responses to infectious insults.

The neurological and endocrine changes have been described in CFS patients support the view that CFS has an inflammatory pathogenesis when considered as a whole. An inflammatory model of disease also provides an explanation for the marked female sex bias associated with CFS.

This review therefore posits the hypothesis that CFS as a disease of long-term inflammatory processes of the brain. We will also provide an investigative framework that could be used to justify the use of anti-TNF biological agents as a reliable and effective treatment approach to CFS, a syndrome that to date remains frustratingly difficult for both patients and health care professionals to manage.

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Self-critical perfectionism, stress generation, and stress sensitivity in patients with chronic fatigue syndrome: relationship with severity of depression.

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Abstract

Chronic Fatigue Syndrome (CFS) is a highly disabling disorder that is part of a broader spectrum of chronic pain and fatigue disorders. Although the etiology and pathogenesis of CFS largely remain unclear, there is increasing evidence that CFS shares important pathophysiological disturbances with mood disorders in terms of disturbances in the stress response and the stress system.

From a psycho-dynamic perspective, self-critical perfectionism and related personality factors are hypothesized to explain in part impairments of the stress response in both depression and CFS.

Yet, although there is ample evidence that high levels of self-critical perfectionism are associated with stress generation and increased stress sensitivity in depression, evidence supporting this hypothesis in CFS is currently lacking.

This study therefore set out to investigate the relationship between self-critical perfectionism, the active generation of stress, stress sensitivity, and levels of depression in a sample of 57 patients diagnosed with CFS using an ecological momentary assessment approach.

Results showed, congruent with theoretical assumptions, that self-critical perfectionism was associated with the generation of daily hassles, which in turn predicted higher levels of depression.

Moreover, multilevel analyses showed that self-critical perfectionism was related to increased stress sensitivity in CFS patients over a 14-day period, and that increased stress sensitivity in turn was related to increased levels of depression.

The implications of these findings for future research and particularly for the development of psychodynamic treatment approaches of CFS and related conditions are discussed.

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Antibody Responses against Xenotropic Murine Leukemia Virus-Related Virus Envelope in a Murine Model

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Abstract

Background: Xenotropic murine leukemia virus-related virus (XMRV) was recently discovered to be the first human gammaretrovirus that is associated with chronic fatigue syndrome and prostate cancer (PC). Although a mechanism for XMRV carcinogenesis is yet to be established, this virus belongs to the family of gammaretroviruses well known for their ability to induce cancer in the infected hosts. Since its original identification XMRV has been detected in several independent investigations; however, at this time significant controversy remains regarding reports of XMRV detection/prevalence in other cohorts and cell type/tissue distribution. The potential risk of human infection, coupled with the lack of knowledge about the basic biology of XMRV, warrants further research, including investigation of adaptive immune responses. To study immunogenicity *in vivo*, we vaccinated mice with a combination of recombinant vectors expressing codon-optimized sequences of XMRV gag and env genes and virus-like particles (VLP) that had the size and morphology of live infectious XMRV.

Results: Immunization elicited Env-specific binding and neutralizing antibodies (NAb) against XMRV in mice. The peak titers for ELISA-binding antibodies and NAb were 1:1024 and 1:464, respectively; however, high ELISA-binding and NAb titers were not sustained and persisted for less than three weeks after immunizations.

Conclusions: Vaccine-induced XMRV Env antibody titers were transiently high, but their duration was short. The relatively rapid diminution in antibody levels may in part explain the differing prevalences reported for XMRV in various prostate cancer and chronic fatigue syndrome cohorts. The low level of immunogenicity observed in the present study may be characteristic of a natural XMRV infection in humans.

<http://www.plosone.org/article/info:doi/10.1371/journal.pone.0018272>

The effect of exercise cessation on non-articular tenderness measures and quality of life in well-trained athletes.

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Abstract

BACKGROUND: The term chronic multi-symptom illness (CMI) refers to a spectrum of pain disorders, such as fibromyalgia and chronic fatigue syndrome, that are characterized by unexplained chronic pain, fatigue, and cognitive and mood complaints

OBJECTIVES: To examine the hypothesis that exercise cessation is associated with symptoms similar to CMI in well-trained amateur athletes.

METHODS: The study, conducted in running and triathlon clubs in Israel, involved 26 asymptomatic healthy athletes who regularly exercise 6.75 +/- 3.65 hours a week. All athletes were instructed to refrain from physical activity for 7 days. All underwent a complete physical exam, rheumatological assessment including non-articular tenderness threshold (using dolorimeter) and tender points. In addition they completed the SF-36 quality of life questionnaire. Assessments were conducted before exercise cessation and 7 days later.

RESULTS: Seven days after sports deprivation all subjects were significantly more tender by all tender measures ($P < 0.001$) (dolorimeter thresholds and tender point count). There was also a significant reduction in the scores for physical role function ($P < 0.001$), emotional role function ($P < 0.001$) and summary subscales of the SF-36 questionnaire after exercise cessation.

CONCLUSIONS: Exercise deprivation is associated with change in non-articular tenderness threshold and reduction in quality of life scores. This may be associated with the development of chronic multi-symptom illness.

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Characterization and treatment of chronic active Epstein-Barr virus disease: a 28 year experience in the United States.

Cohen JI, Jaffe ES, Dale JK, Pittaluga S, Heslop HE, Rooney CM, Gottschalk S, Bollard CM, Rao VK, Marques A, Burbelo PD, Turk SP, Fulton R, Wayne AS, Little RF, Cairo MS, El-Mallawany NK, Fowler D, Sportes C, Bishop MR, Wilson W, Straus SE.

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Abstract Chronic active Epstein-Barr virus disease (CAEBV) is a lymphoproliferative disorder characterized by markedly elevated levels of antibody to EBV or EBV DNA in the blood and EBV RNA or protein in lymphocytes in tissues. We present our experience with CAEBV over the last 28 years including the first 8 cases treated with hematopoietic stem cell transplantation (HSCT) in the U.S.

Most cases of CAEBV have been reported from Japan. Unlike CAEBV in Japan where EBV is nearly always found in T or NK cells in tissues, EBV was usually detected in B cells in tissues from our patients. Most patients presented with lymphadenopathy and splenomegaly; fever, hepatitis, and pancytopenia were common. Most died of infection or progressive lymphoproliferation.

Unlike cases reported from Japan, our patients often showed a progressive loss of B cells, and hypogammaglobulinemia. While patients with CAEBV from Japan have normal or increased numbers of NK cells, many of our patients had reduced NK cell numbers. Although immunosuppressive agents, rituximab, autologous cytotoxic T cells, or cytotoxic chemotherapy often resulted in short term remissions, they were not curative. HSCT was often curative for CAEBV, even in patients with active lymphoproliferative disease that was unresponsive to chemotherapy.

These studies are registered at www.clinicaltrials.gov as NCT00032513 for CAEBV, NCT00062868 and NCT00058812 for EBV-specific T cell studies, and NCT00578539 for the hematopoietic stem cell transplant protocol.

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Increased plasma peroxides as a marker of oxidative stress in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS).

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Abstract

Background: There is evidence that myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is characterized by activation of immune, inflammatory, oxidative and nitrosative stress (IO&NS) pathways.

The present study was carried out in order to examine whether ME/CFS is accompanied by increased levels of plasma peroxides and serum oxidized LDL (oxLDL) antibodies, two biomarkers of oxidative stress.

Material/Methods: Blood was collected from 56 patients with ME/CFS and 37 normal volunteers. Severity of ME/CFS was measured using the Fibromyalgia and Chronic Fatigue Syndrome (FF) Rating Scale.

Results: Plasma peroxide concentrations were significantly higher in patients with ME/CFS than in normal controls. There was a trend towards significantly higher serum oxLDL antibodies in ME/CFS than in controls. Both biomarkers contributed significantly in discriminating between patients with ME/CFS and normal controls. Plasma peroxide and serum oxLDL antibody levels were both significantly related to one of the FF symptoms.

Conclusions: The results show that ME/CFS is characterized by increased oxidative stress.

No Evidence of XMRV or Related Retroviruses in a London HIV-1-Positive Patient Cohort

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Abstract [Top](#)

Background

Several studies have implicated a recently discovered gammaretrovirus, XMRV (Xenotropic murine leukaemia virus-related virus), in chronic fatigue syndrome and prostate cancer, though whether as causative agent or opportunistic infection is unclear. It has also been suggested that the virus can be found circulating amongst the general population. The discovery has been controversial, with conflicting results from attempts to reproduce the original studies.

Methodology/Principal Findings

We extracted peripheral blood DNA from a cohort of 540 HIV-1-positive patients (approximately 20% of whom have never been on anti-retroviral treatment) and determined the presence of XMRV and related viruses using TaqMan PCR. While we were able to amplify as few as 5 copies of positive control DNA, we did not find any positive samples in the patient cohort.

Conclusions/Significance

In view of these negative findings in this highly susceptible group, we conclude that it is unlikely that XMRV or related viruses are circulating at a significant level, if at all, in HIV-1-positive patients in London or in the general population.

Citation: Gray ER, Garson JA, Breuer J, Edwards S, Kellam P, et al. (2011) No Evidence of XMRV or Related Retroviruses in a London HIV-1-Positive Patient Cohort. PLoS ONE 6(3): e18096. doi:10.1371/journal.pone.0018096

Chronic fatigue syndrome: a qualitative investigation of young patient's beliefs and coping strategies.

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Abstract

Purpose. The aim of this pilot study was to explore illness beliefs and coping strategies among adolescent patients with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME), applying a qualitative methodology. Recent studies have explored the illness beliefs and coping strategies of adult patients with CFS/ME as possible contributing factors to the disease aetiology. These studies have mainly used quantitative methods, finding that patients often explain their illness as being due to physical causes, deny psychological causes and make use of passive and avoidant coping strategies.

Method. Semi-structured, in-depth interviews were conducted with nine adolescent patients with CFS/ME, thematic analysis was adapted to the material and the results were interpreted in light of theories of attribution and coping.

Results. The qualitative method allowed for more complex and nuanced accounts of illness experience. The findings showed that the adolescents differ from what has previously been reported, applying more varied and flexible illness attributions and coping mechanisms than expected.

Conclusions. The heterogeneity suggested in the results has implications. We suggest three perspectives should be taken into account, both for further research and in clinical practice: (1) individual differences; (2) a developmental perspective and (3) interactive relational focus.

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Adolescent Chronic Fatigue Syndrome: Prevalence, Incidence, and Morbidity

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OBJECTIVE To determine nationwide general practitioner (GP)-diagnosed prevalence and pediatrician–diagnosed incidence rates of adolescent chronic fatigue syndrome (CFS), and to assess CFS morbidity.

DESIGN AND SETTING We collected data from a cross-sectional national sample among GPs and prospective registration of new patients with CFS in all pediatric hospital departments in the Netherlands.

PATIENTS AND METHODS Study participants were adolescents aged 10 to 18 years. A representative sample of GPs completed questionnaires on the prevalence of CFS in their adolescent patients. Pediatric hospital departments prospectively reported new cases of CFS in adolescent patients. For every new reported case, a questionnaire was sent to the reporting pediatrician and the reported patient to assess CFS morbidity. Prevalence was estimated through the data from GP questionnaires and incidence was estimated on the basis of cases newly reported by pediatricians from January to December 2008.

RESULTS Prevalence was calculated as 111 per 100 000 adolescents and incidence as 12 per 100 000 adolescents per year. Of newly reported patients with CFS, 91% scored at or above cutoff points for severe fatigue and 93% at or above the cutoff points for physical impairment. Forty-five percent of patients with CFS reported >50% school absence during the previous 6 months.

CONCLUSIONS Clinically diagnosed incidence and prevalence rates show that adolescent CFS is uncommon compared with chronic fatigue. The primary adverse impact of CFS is extreme disability associated with considerable school absence.

<http://pediatrics.aappublications.org/cgi/content/abstract/peds.201...>

Quantitative Sensory Testing Profiles in Chronic Back Pain Are Distinct From Those in Fibromyalgia

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Abstract

OBJECTIVES: Alterations in the central nervous system leading to higher pain sensitivity have been shown in both chronic back pain

(CBP) and fibromyalgia syndrome (FMS). The aim of this study was to disclose commonalities and differences in the pathophysiology of FMS and CBP.

METHODS: We used the quantitative sensory testing protocol of the German Research Network on Neuropathic Pain to obtain comprehensive profiles of somatosensory functions. The protocol comprised thermal and mechanical detection and pain thresholds, vibration thresholds, and pain sensitivity to sharp and blunt mechanical stimuli. We studied

21 FMS patients (mean pain duration: 13.4 y), 23 CBP subjects (mean pain duration: 15.9 y), and 20 healthy controls (HCs). Each participant received the test battery on the back and on the dorsal hand (pain-free control site).

RESULTS: On the back, FMS patients showed increased thermal and mechanical pain sensitivity compared with HCs and CBP participants. On the hand dorsum, FMS patients showed higher mechanical pain sensitivity compared with CBP participants and HCs and higher cold pain sensitivity compared with HCs. CBP participants showed increased pressure pain sensitivity and lower vibration sensitivity on the back, but no significant differences on the hand dorsum compared with HCs.

DISCUSSION: FMS patients showed increased sensitivity for different pain modalities at all measured body areas, suggesting central disinhibition as a potential mechanism. CBP participants in contrast, showed localized alterations within the affected segment possibly due to peripheral sensitization.

A Chinese Herbal Decoction, Danggui Buxue Tang, Improves Chronic Fatigue Syndrome Induced by Food Restriction and Forced Swimming in Rats.

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Abstract

Danggui Buxue Tang (DBT), a Chinese medicinal decoction that contains *Radix Angelicae sinensis* (Danggui) and *Radix Astragali* (Huangqi) at a ratio of 1:5, is used commonly for treating women's ailments. The present study explored the effects of this preparation on chronic fatigue syndrome (CFS).

Rats were subjected to a combination of food restriction and forced swimming to induce CFS, and rats were gavaged once daily with either

12 or 24 g/kg DBT for 28 days. Body weights, T-cell subset counts, (3) H-TdR incorporation measurements and mRNA levels of IL-1 β , TNF- α , NF- κ B, p38MAPK and JNK were determined on days 14 and 28.

The swimming endurance capacity was measured on day 28. Rats that received DBT exhibited increased body weight and endurance capacity, corrected T cell subsets counts, increased (3) H-TdR incorporation and decreased mRNA levels of IL-1 β , TNF- α , NF- κ B, p38MAPK and JNK compared with rats that did not receive DBT.

The results indicate that DBT can ameliorate CFS through immune modulation and may act to normalize cytokines and their related signaling pathways. Copyright © 2011 John Wiley & Sons, Ltd.

Assessment of a 44 gene classifier for the evaluation of chronic fatigue syndrome from peripheral blood mononuclear cell gene expression.

Frampton D, Kerr J, Harrison TJ, Kellam P., Department of Infection, Division of Infection and Immunity, University College London, London, United Kingdom.

Abstract

Chronic fatigue syndrome (CFS) is a clinically defined illness estimated to affect millions of people worldwide causing significant morbidity and an annual cost of billions of dollars. Currently there are no laboratory-based diagnostic methods for CFS. However, differences in gene expression profiles between CFS patients and healthy persons have been reported in the literature.

Using mRNA relative quantities for 44 previously identified reporter genes taken from a large dataset comprising both CFS patients and healthy volunteers, we derived a gene profile scoring metric to accurately classify CFS and healthy samples. This metric out-performed any of the reporter genes used individually as a classifier of CFS. To determine whether the reporter genes were robust across populations, we applied this metric to classify a separate blind dataset of mRNA relative quantities from a new population of CFS patients and healthy persons with limited success.

Although the metric was able to successfully classify roughly two-thirds of both CFS and healthy samples correctly, the level of misclassification was high. We conclude many of the previously identified reporter genes are study-specific and thus cannot be used as a broad CFS diagnostic.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3068152/?tool=pubmed>

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Chronic fatigue syndrome (CFS) is a clinically defined illness estimated to affect millions of people worldwide causing significant morbidity and an annual cost of billions of dollars. Currently there are no laboratory-based diagnostic methods for CFS. However, differences in gene expression profiles between CFS patients and healthy persons have been reported in the literature.

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Antibody Responses against Xenotropic Murine Leukemia Virus-Related Virus Envelope in a Murine Model.

Makarova N, Zhao C, Zhang Y, Bhosle S, Suppiah S, Rhea JM, Kozyr N, Arnold RS, Ly H, Molinaro RJ, Parslow TG, Hunter E, Liotta D, Petros J, Blackwell JL., Emory Vaccine Center, Emory University

Abstract

BACKGROUND: Xenotropic murine leukemia virus-related virus (XMRV) was recently discovered to be the first human gammaretrovirus that is associated with chronic fatigue syndrome and prostate cancer (PC).

Although a mechanism for XMRV carcinogenesis is yet to be established, this virus belongs to the family of gammaretroviruses well known for their ability to induce cancer in the infected hosts. Since its original identification XMRV has been detected in several independent investigations; however, at this time significant controversy remains regarding reports of XMRV detection/prevalence in other cohorts and cell type/tissue distribution. The potential risk of human infection, coupled with the lack of knowledge about the basic biology of XMRV, warrants further research, including investigation of adaptive immune responses. To study immunogenicity in vivo, we vaccinated mice with a combination of recombinant vectors expressing codon-optimized sequences of XMRV gag and env genes and virus-like particles (VLP) that had the size and morphology of live infectious XMRV.

RESULTS: Immunization elicited Env-specific binding and neutralizing antibodies (NAb) against XMRV in mice. The peak titers for ELISA-binding antibodies and NAb were 1:1024 and 1:464, respectively; however, high ELISA-binding and NAb titers were not sustained and persisted for less than three weeks after immunizations.

CONCLUSIONS: Vaccine-induced XMRV Env antibody titers were transiently high, but their duration was short. The relatively rapid diminution in antibody levels may in part explain the differing prevalences reported for XMRV in various prostate cancer and chronic fatigue syndrome cohorts. The low level of immunogenicity observed in the present study may be characteristic of a natural XMRV infection in humans.

The health status of Q-fever patients after long-term follow-up.

Gabriella Morroy , Jeannette B Peters , Malou van Nieuwenhof , Hans HJ Bor , Jeannine LA Hautvast , Wim van der Hoek , Clementine J Wijkmans and Jan H Vercoulen

BMC Infectious Diseases 2011, 11:97doi:10.1186/1471-2334-11-97

Abstract (provisional)

Background In the Netherlands, from 2007 to 2009, 3,522 Q-fever cases from three outbreaks were notified. These outbreaks are the largest documented outbreaks in the world. Previous studies suggest that symptoms can persist for a long period of time, resulting in a reduced quality of life (QoL). The aim of this study is to qualify and quantify the health status of Q-fever patients after long-term follow-up.

Methods 870 Q-fever patients of the 2007 and 2008 outbreaks were mailed a questionnaire 12 to 26 months after the onset of illness. We assessed demographic data and measured health status with the Nijmegen Clinical Screening Instrument (NCSI). The NCSI consists of eight sub-domains of functional impairment, symptoms, and QoL. The NCSI scores of Q-fever patients older than 50 years were compared with patients younger than 50 years, and with norm data from healthy individuals and patients with chronic obstructive pulmonary disease.

Results The response rate was 65.7%. The long term health status of two thirds of Q-fever patients (both younger and older than 50 years) was severely affected for at least one sub-domain. Patients scores were most severely affected on the sub-domains general QoL (44.9%) and fatigue (43.5%). Hospitalization in the acute phase was significantly related to long-term behavioural impairment (OR 2.8, CI 1.5-5.1), poor health related QoL (OR 2.3, CI 1.5-4.0), and subjective symptoms (OR 1.9, CI 1.1-3.6). Lung or heart disease, depression and arthritis significantly affected the long-term health status of Q-fever patients.

Conclusions Q-fever patients present 12 to 26 months after the onset of illness with severe -clinically relevant-: subjective symptoms, functional impairment, and impaired QoL. All measured domains of the health status are impaired. Especially patients that have been hospitalized and those with chronic co-morbidity score worse. Our unique data underline that more attention is needed not only to prevent exposure to Q fever but also for the prevention and treatment of the long-term consequences of this zoonosis.

Multisensory hypersensitivity in women with fibromyalgia: implications for well being and intervention.

Wilbarger JL, Cook DB.

Abstract

OBJECTIVE: To document sensory sensitivities to nonnoxious sensory stimuli in daily life for participants with fibromyalgia (FM).

DESIGN: Descriptive study of a convenience sample using a self-report survey of sensory processing.

SETTING: Participants were recruited from the general community. The procedure took place in a research room at the University of Wisconsin-Madison.

PARTICIPANTS: Women with FM (n=27) were compared with women with rheumatoid arthritis (RA) (n=28) and healthy pain-free women (controls) (n=28) (N=83).

INTERVENTIONS: Not applicable.

MAIN OUTCOME MEASURE: A self-report measure of sensory sensitivity to stimuli encountered in daily life. Items ask participants if they are sensitive to sensations that do not seem to bother other people or avoid common activities or environments because of sensory stimuli.

RESULTS: The FM group reported significantly increased sensory sensitivities to both somatic (tactile) and nonsomatic (eg, auditory and olfactory) sensory stimuli compared with the RA and control groups. The RA and control groups did not differ in reported hypersensitivities.

CONCLUSIONS: Women with fibromyalgia reported increased sensitivities to stimuli in the environment and could experience more stress related to sensory conditions in daily life.

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SLEEP-WAKE BEHAVIOR IN CHRONIC FATIGUE SYNDROME Sleep-Wake Behavior in Chronic Fatigue Syndrome

Khairunnessa Rahman, BMedSci (Hons)¹; Alexander Burton, PhD¹; Sally Galbraith, PhD²; Andrew Lloyd, MD³; Ute Vollmer-Conna, PhD¹ ¹School of Psychiatry, University of NSW, Sydney, Australia; ²School of Mathematics and Statistics, University of NSW, Sydney, Australia; ³Inflammation and Infection Research Centre, School of Medical Sciences, University of NSW, Sydney, Australia

Study Objectives: Disturbances of the internal biological clock manifest as fatigue, poor concentration, and sleep disturbances—symptoms reminiscent of chronic fatigue syndrome (CFS) and suggestive of a role for circadian rhythm disturbance in CFS. We examined circadian patterns of activity, sleep, and cortisol secretion in patients with CFS.

Design: Case-control study, 5-day behavioral observation.

Setting: Natural setting/home environment

Participants: 15 patients with CFS and 15 healthy subjects of similar age, sex, body mass index (BMI), and activity levels.

Measurements: Self-report questionnaires were used to obtain medical history and demographic information and to assess health behaviors, somatic and psychological symptoms, and sleep quality. An actiwatch accelerometer recorded activity and sleep patterns over 5 days with concurrent activity and symptom logs. Diurnal salivary cortisol secretion was measured. Additionally, overnight heart rate monitoring and pain sensitivity assessment was undertaken.

Results: Ratings of symptoms, disability, sleep disturbance, and pain sensitivity were greater in patients with CFS. No between-group differences were found in the pattern or amount of sleep, activity, or cortisol secretion. Afternoon activity levels significantly increased evening fatigue in patients but not control subjects. Low nocturnal heart rate variability was identified as a biological correlate of unrefreshing sleep.

Conclusions: We found no evidence of circadian rhythm disturbance in CFS. However, the role of autonomic activity in the experience of unrefreshing sleep warrants further assessment. The activity symptom-relationship modelled here is of clinical significance in the approach to activity and symptom management in the treatment of CFS.

Citation: Rahman K; Burton A; Galbraith S; Lloyd A; Vollmer-Conna U. Sleep-wake behavior in chronic fatigue syndrome. SLEEP 2011;34(5):671-678.

<http://www.journalsleep.org/ViewAbstract.aspx?pid=28135>

Gut study divides people into three types Bacterial populations fall into three distinct classes that could help to personalize medicine.

Nicola Jones

Just as there are a few major blood types that divide up the world, so too, a study has found, there are just three types of gut-microbe populations. The result could help to pinpoint the causes of obesity and inflammatory bowel disease, and to personalize medicine.

"This is important. Say you want to compare ill people and healthy people; you better match them properly [by gut type]," Dusko Ehrlich told Nature at a human microbiome conference in Vancouver, Canada, in March. Ehrlich, a senior researcher on the paper published in Nature today¹, is director of the Microbial Genetics Research Unit at the National Institute for Agricultural Research in Jouy-en-Josas, France, and part of a European consortium aiming to unpick links between gut microbes and disease.

The finding of just three types of gut-microbe population was an unexpected result that fell out of the team's early analysis. The types aren't related to age, gender, nationality or diet. "What causes it? We don't know," says Ehrlich.

One possible explanation, which the team is testing, is that a person's gut-microbe make-up is determined by his or her blood type.

Alternatively, it might be determined by metabolism: there are three major chemical pathways by which people get rid of excess hydrogen gas created during food fermentation in the colon, and the gut type might be linked to those. Or, perhaps the first microbes a baby is exposed to as his or her immune system is developing determines the type.

A person's gut type might help to determine whether people can eat all they like and stay slim, whether they will experience more gut pain than others when sick and how well they can metabolize a certain drug.

It's unclear whether a person's gut type might change over time, either naturally or in response to something such as a steady diet of probiotic yoghurt...."The real question is: what is the gene set we need in our guts to be healthy?" says Finlay. That has yet to be answered.

To read the entire article:

<http://www.nature.com/news/2011/110420/full/news.2011.249.html>

JVI Accepts, published online ahead of print on 4 May 2011

J. Virol. doi:10.1128/JVI.00693-11

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Absence of XMRV and other MLV-related viruses in patients with Chronic Fatigue Syndrome

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ABSTRACT

Chronic fatigue syndrome (CFS) is a multi-system disorder characterized by prolonged and severe fatigue that is not relieved by rest. Attempts to treat CFS have been largely ineffective primarily because the etiology of the disorder is unknown. Recently CFS has been associated with xenotropic murine leukemia virus-related virus (XMRV) as well as other murine leukemia virus (MLV)-related viruses, though not all studies have found these associations. We collected blood samples from 100 CFS patients and 200 self-reported healthy volunteers from the same geographical area. We analyzed these in a blinded manner using molecular, serological and viral replication assays. We also analyzed samples from patients in the original study that reported XMRV in CFS. We did not find XMRV or related MLVs, either as viral sequences or infectious virus, nor did we find antibodies to these viruses in any of the patient samples, including those from the original study. We show that at least some of the discrepancy with previous studies is due to the presence of trace amounts of mouse DNA in the Taq polymerase enzymes used in these previous studies. Our findings do not support an association between CFS and MLV-related viruses including XMRV and off-label use of antiretrovirals for the treatment of CFS does not seem justified at present.

[Med Hypotheses](#). 2011 Apr 5. [Epub ahead of print]

Chronic fatigue syndrome - A neuroimmunological model.

[Arnett SV](#), [Alleva LM](#), [Korossy-Horwood R](#), [Clark IA](#).

Source

Research School of Biology, Australian National University, Australia.

Abstract

The aetiological and pathophysiological basis of chronic fatigue syndrome (CFS) remains a controversial field of inquiry in the research community. While CFS and similar disease conditions such as fibromyalgia (FM) and post-infectious encephalopathy have been the focus of intense scrutiny for the past 20 years, results of research were often contradictory and a cohesive pathological model has remained elusive. However, recent developments in understanding the unique immunophysiology of the brain may provide important clues for the development of a truly comprehensive explanation of the pathology of CFS. We argue that CFS pathogenesis lies in the influence of peripheral inflammatory events on the brain and the unique immunophysiology of the central nervous system. There is also evidence that CFS patients have a relative immunodeficiency that predisposes to poor early control of infection that leads to chronic inflammatory responses to infectious insults. The neurological and endocrine changes have been described in CFS patients support the view that CFS has an inflammatory pathogenesis when considered as a whole. An inflammatory model of disease also provides an explanation for the marked female sex bias associated with CFS. This review therefore posits the hypothesis that CFS as a disease of long-term inflammatory processes of the brain. We will also provide an investigative framework that could be used to justify the use of anti-TNF biological agents as a reliable and effective treatment approach to CFS, a syndrome that to date remains frustratingly difficult for both patients and health care professionals to manage.

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Sexual transmission of XMRV: a potential infection route

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Abstract

Although XMRV dissemination in humans is a matter of debate, the prostate of select patients seem to harbor XMRV, which raises questions about its potential route of transmission.

We established a model of infection in rhesus macaques inoculated with XMRV.

In spite of the intravenous inoculation, all infected macaques exhibited readily detectable XMRV signal in the reproductive tract of all 4 males and

1 female during both acute and chronic infection stages.

XMRV showed explosive growth in the acini of prostate during acute but not chronic infection.

In seminal vesicles, epididymis and testes, XMRV protein production was detected throughout infection in interstitial or epithelial cells.

In the female monkey, epithelial cells in the cervix and vagina were also positive for XMRV gag.

The ready detection of XMRV in the reproductive tract of male and female macaques infected intravenously, suggests the potential for sexual transmission for XMRV.

In conclusion, our study demonstrates XMRV protein expression in the reproductive tract of the experimentally-infected rhesus macaques at all times post infection supporting the potential for sexual transmission of this virus.

Acknowledgements

These studies were supported by Abbott Diagnostics and the NCRR support to the Yerkes NPRC DRR000165

Evidence for a Heritable Predisposition to Chronic Fatigue Syndrome

Frederick Albright , Kathleen Light , Alan Light , Lucinda Bateman and Lisa A Cannon-Albright BMC Neurology 2011, 11:62doi:10.1186/1471-2377-11-62 Published: 27 May 2011

Abstract (provisional)

Background

Chronic Fatigue Syndrome (CFS) came to attention in the 1980s, but initial investigations did not find organic causes. Now decades later, the etiology of CFS has yet to be understood, and the role of genetic predisposition in CFS remains controversial. Recent reports of CFS association with the retrovirus xenotropic murine leukemia virus-related virus (XMRV) or other murine leukemia related retroviruses (MLV) might also suggest underlying genetic implications within the host immune system.

Methods We present analyses of familial clustering of CFS in a computerized genealogical resource linking multiple generations of genealogy data with medical diagnosis data of a large Utah health care system. We compare pair-wise relatedness among cases to expected relatedness in the Utah population, and we estimate risk for CFS for first, second, and third degree relatives of CFS cases.

Results We observed significant excess relatedness of CFS cases compared to that expected in this population. Significant excess relatedness was observed for both close ($p < 0.001$) and distant relationships ($p = 0.010$). We also observed significant excess CFS relative risk among first (2.70, 95% CI: 1.56-4.66), second (2.34, 95% CI: 1.31-4.19), and third degree relatives (1.93, 95% CI: 1.21-3.07).

Conclusions These analyses provide strong support for a heritable contribution to predisposition to Chronic Fatigue Syndrome. A population of high-risk CFS pedigrees has been identified, the study of which may provide additional understanding.

<http://www.biomedcentral.com/1471-2377/11/62> fulltext- <http://www.biomedcentral.com/content/pdf/1471-2377-11-62.pdf>

XENOTROPIC MURINE LEUKEMIA VIRUS-RELATED VIRUS (XMRV) IS NOT FOUND IN PERIPHERAL BLOOD CELLS FROM TREATMENT-NAIVE HIV+ PATIENTS

Maggi Fabrizio^{1,*}, Focosi Daniele², Lanini Letizia¹, Sbranti Selenia¹, Mazzetti Paola¹, Macera Lisa¹, Davini Sara², De Donno Monica², Mariotti Maria Luciana², Antonelli Guido³, Scatena Fabrizio², Pistello

Mauro^{1,4} DOI: 10.1111/j.1469-0691.2011.03580.x

Abstract

The human pathogen xenotropic murine leukemia virus-related virus (XMRV) has been tentatively associated with prostate cancer and chronic fatigue syndrome. Unfortunately subsequent studies failed to identify the virus in various clinical settings. To determine whether XMRV circulates in humans and the relationship with its host, we searched the virus in 124 HIV infected patients who might have been exposed to XMRV, might be prone to infection due to progressive immune deficiency, and had not been treated with antiretroviral drugs yet.

Using nested polymerase chain reaction (PCR) and single step TaqMan real-time PCR, both designed on XMRV gag gene, we could not find any positive samples. These findings add to the growing amount of skepticism on XMRV.

<http://onlinelibrary.wiley.com/doi/10.1111/j.1469-0691.2011.03580.x...>

Bioinformatics. 2011 Apr 22;6(3):120-4.

Meta analysis of Chronic Fatigue Syndrome through integration of clinical, gene expression, SNP and proteomic data.

Pihur V, Datta S, Datta S.

Abstract

We start by constructing gene-gene association networks based on about 300 genes whose expression values vary between the groups of CFS patients (plus control). Connected components (modules) from these networks are further inspected for their predictive ability for symptom severity, genotypes of two single nucleotide polymorphisms (SNP) known to be associated with symptom severity, and intensity of the ten most discriminative protein features. We use two different network construction methods and choose the common genes identified in both for added validation.

Our analysis identified eleven genes which may play important roles in certain aspects of CFS or related symptoms. In particular, the gene WASF3 (aka WAVE3) possibly regulates brain cytokines involved in the mechanism of fatigue through the p38 MAPK regulatory pathway.

Further information can be found here: <http://www.somnathdatta.org/Supp/CamdaCFS/supp.htm>

Self-esteem mediates the relationship between maladaptive perfectionism and depression in chronic fatigue syndrome.

Kempke S, Luyten P, Van Houdenhove B, Goossens L, Bekaert P, Van Wambeke P., Department of Psychology, University of Leuven, Tiensestraat 102, 3000, Leuven, Belgium, stefan.kempke@psy.kuleuven.be.

Abstract

Patients with chronic fatigue syndrome (CFS) often experience depression which may negatively affect prognosis and treatment outcome. Research has shown that depression in CFS is associated with maladaptive or self-critical perfectionism. However, currently, little is known about factors that may explain this relationship, but studies in nonclinical samples suggest that low self-esteem may be an important mediator of this relationship.

The present study therefore examined whether self-esteem mediated the cross-sectional association between maladaptive perfectionism and severity of depression in 192 patients meeting Centres for Disease Control and Prevention criteria for CFS.

Patients completed self-report measures of maladaptive perfectionism, self-esteem, depression, and fatigue. Regression analyses and more direct tests of indirect effects (i.e., the Sobel test and bootstrapping) were used to test for mediation. Congruent with expectations, we found that self-esteem fully mediated the relationship between maladaptive perfectionism and depression in CFS.

Findings from this study suggest that self-esteem may explain the link between maladaptive perfectionism and depression in CFS, which may have important implications for the treatment and prevention of depression in these patients.

PMID: 21584732 [PubMed - as supplied by publisher]

Immunologic and psychosocial status in chronic fatigue syndrome.

Nas K, Cevik R, Batum S, Sarac AJ, Acar S, Kalkanli S., Departments of Physical Medicine and Rehabilitation, School of Medicine, Dicle University, Diyarbakir, Turkey. knas@dicle.edu.tr Abstract

OBJECTIVE: The aim of the study was to investigate the immunologic functions and psychosocial status in patients with chronic fatigue syndrome (CFS).

METHODS: Twenty-five patients with CFS diagnosed by the international CFS definition criteria and 20 age- and gender-matched healthy controls were recruited. Depression was assessed by Beck Depression Inventory (BDI) and health status was assessed by Nottingham Health Profile (NHP). Monoclonal antibodies (MAbs) were measured to identify the following NK cell subsets: CD3, CD4, CD8 and CD56 and cytokine measurements were performed for IL2r, IL6 and IL8 in both patients and control subjects.

RESULTS: The BDI and NHP scores of CFS group were found to be significantly higher than in the control group. The absolute numbers of CD56 cell were also significantly decreased in the patients with CFS compared with the healthy controls. There were no other significant differences of NK cell activity (CD3, CD4 and CD8) and there were significant differences in IL6 and IL2r levels between patients and controls.

There were significant correlations between serum IL-6 level and sleep, social isolation and physical ability NHP subscores, and between CD56 NK cell activity and emotional reaction NHP sub score in CFS patients.

CONCLUSION: Significantly higher ratios of psychological and physical disturbances were found in patients with CFS. Decreased CD56 NK cell activity and increased IL2r levels seem to be important immunopathologic changes in CFS. IL-6 and CD 56 NK cell activity may play an important role in sleep, physical, social, and psychological manifestations of CFS (Tab. 3, Fig. 1, Ref. 36).

<http://www.bmj.sk/2011/11204-12.pdf>

Qual Life Res. 2011 May 18. [Epub ahead of print]

Quality and acceptability of patient-reported outcome measures used in chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME): a systematic review.

Haywood KL, Staniszewska S, Chapman S., Royal College of Nursing Research Institute, School of Health and Social Studies, University of Warwick, Coventry, CV4 7AL, UK, k.l.haywood@warwick.ac.uk.

PURPOSE: To review the quality and acceptability of condition-specific, domain-specific and generic multi-item patient-reported outcome measures (PROMs) used in the assessment of adults with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME).

METHODS: Systematic literature searches were made to identify PROMs. Quality and acceptability was assessed against an appraisal framework, which captured evidence of both the thoroughness and results of evaluations: evidence of measurement (reliability, validity, responsiveness, interpretability, data quality/precision) and practical properties (feasibility, patient acceptability), and the extent of active patient involvement was sought.

RESULTS: A total of 11 CFS/ME-specific, 55 domain-specific and 11 generic measures were reviewed. With the exception of the generic SF-36, all measures had mostly limited evidence of measurement and/or practical properties. Patient involvement was poorly reported and often cursory.

CONCLUSIONS:

The quality and acceptability of reviewed PROMs is limited, and recommendations for patient-reported assessment are difficult. Significant methodological and quality issues in PROM development/evaluation were identified by the appraisal framework, which must be addressed in future research.

Clear discrepancies exist between what is measured in research and how patients define their experience of CFS/ME. Future PROM development/evaluation must seek to involve patients more collaboratively to measure outcomes of importance using relevant and credible methods of assessment.

Psychol Health. 2011 Jan 1:1-17. [Epub ahead of print]

Emotion recognition and emotional theory of mind in chronic fatigue syndrome.

Oldershaw A, Hambrook D, Rimes KA, Tchanturia K, Treasure J, Richards S, Schmidt U, Chalder T., Section of Eating Disorders, Division of Psychological Medicine and Psychiatry, Institute of Psychiatry, King's College London, London, UK.

Abstract

Background: Difficulties with social function have been reported in chronic fatigue syndrome (CFS), but underpinning factors are unknown. Emotion recognition, theory of mind (inference of another's mental state) and 'emotional' theory of mind (eToM) (inference of another's emotional state) are important social abilities, facilitating understanding of others. This study examined emotion recognition and eToM in CFS patients and their relationship to self-reported social function.

Methods: CFS patients (n = 45) and healthy controls (HCs; n = 50) completed tasks assessing emotion recognition, basic or advanced eToM (for self and other) and a self-report measure of social function.

Results: CFS participants were poorer than HCs at recognising emotion states in the faces of others and at inferring their own emotions. Lower scores on these tasks were associated with poorer self-reported daily and social function. CFS patients demonstrated good eToM and performance on these tasks did not relate to the level of social function.

Conclusions: CFS patients do not have poor eToM, nor does eToM appear to be associated with social functioning in CFS. However, this group of patients experience difficulties in emotion recognition and inferring emotions in themselves and this may impact upon social function.

Br Med Bull. 2011 May 6. [Epub ahead of print]

XMRV, prostate cancer and chronic fatigue syndrome.

Kenyon JC, Lever AM.

Source: Department of Medicine, University of Cambridge, Level 5, Addenbrooke's hospital, Hills Road, Cambridge CB0 0QQ, UK.

Abstract

Background: A new retrovirus, xenotropic murine leukaemia virus-related virus (XMRV), was identified in 2006 and an association was claimed between it and a genetic polymorphism predisposing to cancer of the prostate. In 2009 the same virus was identified in a cohort of patients with chronic fatigue syndrome (CFS). In 2010 a second related virus was identified in a separate group of CFS patients. A series of studies from disparate geographical areas have failed to substantiate this work. Most recently several papers have suggested that the detection of these viruses was explained by laboratory contamination.

Sources of data: All papers including the wording XMRV were abstracted from the NIH library of medicine database and included in the analysis. Areas of agreement XMRV is a newly described retrovirus whose nucleic acid has been identified in samples from patients with both prostate cancer and CFS.

Areas of controversy: Opinions differ as to whether the detected nucleic acid indicates infection with this virus in this disease or whether laboratory contamination of samples accounts for its presence.

Growing points An increasing number of papers now refute the association of XMRV with human disease in humans although there is some evidence of serological reactivity to the virus.

While it is unlikely that XMRV is a major cause of either prostate cancer or CFS, it can infect human cells and might yet have a role in human disease. Areas timely for developing research Further studies to either prove or disprove the disease association of the virus are ongoing.

Lower whole blood glutathione peroxidase (GPX) activity in depression, but not in myalgic encephalomyelitis / chronic fatigue syndrome: another pathway that may be associated with coronary artery disease and neuroprogression in depression

Maes M, Mihaylova I, Kubera M, Uytterhoeven M, Vrydags N, Bosmans E.

Source: Piyavate Hospital, Bangkok, Thailand, Thailand.

Abstract

BACKGROUND: Major depression and myalgic encephalomyelitis / chronic fatigue syndrome (ME/CFS) are two disorders accompanied by an upregulation of the inflammatory and oxidative and nitrosative (IO&NS) pathways and a decreased antioxidant status. Moreover, depression is accompanied by disorders in inflammatory and neuroprogressive (IN-PRO) pathways.

METHODS: This study examines whole blood glutathione peroxidase (GPX) in depression and in ME/CFS; GPX is an enzyme that reduces hydroperoxides by oxidizing glutathione and consequently protects the cells from oxidative damage.

Blood was sampled in 39 patients with depression, 40 patients with ME/CFS and 24 normal volunteers. Whole blood was analysed for GPX activity using the Ransel assay (Randox). Severity of illness was measured by means of the Hamilton Depression Rating Scale (HDRS) and the Fibromyalgia and Chronic Fatigue Syndrome Rating Scale (FF scale).

RESULTS: We found that whole blood GPX activity was significantly ($p=0.001$) lower in depressed patients than in normal controls and that there were no significant differences between ME/CFS and controls.

In depression and ME/CFS, there were significant and inverse relationships between GPX activity and the FF items, depressed mood and autonomic symptoms. In depression, there were significant and negative correlations between whole blood GPX and the HDRS score and autonomic symptoms.

DISCUSSION:

The results show that lowered whole blood GPX activity contributes to the lowered antioxidant status in depression. Since GPX activity is a predictor of neuroprogression and coronary artery disease (CAD), lowered GPX activity in depression contributes to the IN-PRO pathways and the comorbidity between depression and CAD.

Our results suggest that patients with depression would benefit from Ebselen or a supplementation with glutathione, N-Acetyl-L-Cysteine and selenium.

Metacognitive Factors in Chronic Fatigue Syndrome.

Maher-Edwards L, Fernie BA, Murphy G, Nikcevic AV, Spada MM.

Source: Fatigue Service, Royal Free Hospital, London, UK.

Abstract

Chronic fatigue syndrome (CFS), which is characterized by fatigue and flu-like symptoms that are not alleviated by rest, is a poorly understood condition and an often controversial diagnosis.

Earlier research has indicated that general metacognitions are associated with the severity of symptoms in patients with CFS. In the current study, we aimed to determine whether specific metacognitive factors are implicated in CFS.

Using the metacognitive profiling interview template we investigated the following: (1) whether patients held positive or negative metacognitions about conceptual processes; (2) what their goals with respect to engaging in these processes were; and (3) what indicated that it was appropriate to stop.

We also examined attention focus when experiencing CFS symptoms, and its advantages and disadvantages.

Results showed that patients endorsed positive and negative metacognitions pertaining to conceptual processes. The goals of engaging in these processes were to identify the cause of, and devise strategies to cope with, symptoms.

Patients were either unable to identify a stop signal for conceptual processing or identified an improvement in fatigue-related symptoms as representing the stop signal.

Finally, patients reported that their attention focus when experiencing symptoms included distraction and monitoring of symptoms.

Advantages to these strategies included symptom management, whereas disadvantages included an escalation of negative affect.

The present findings provide preliminary evidence that specific metacognitive factors may be involved in CFS.

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Brain Behav Immun. 2011 Apr 28. [Epub ahead of print]

Increased HDAC in association with decreased plasma cortisol in older adults with chronic fatigue syndrome.

Jason L, Sorenson M, Sebally K, Alkazemi D, Lerch A, Porter N, Kubow S.

Source: Department of Nursing, DePaul University, Chicago, IL, United States.

Abstract

Hypocortisolism is a frequent finding in individuals with chronic fatigue syndrome (CFS) with other research findings implying potential dysregulation of glucocorticoid signaling.

Glucocorticoid signaling is under the influence of several pathways, several of which are of interest in the study of CFS. Oxidative stress and decreased antioxidant capacity are known to disrupt the hypothalamic-pituitary-adrenal (HPA) axis (Epel et al., 2004) and the presence of histone deacetylases (HDAC) could also impact glucocorticoid signaling.

The intent of this pilot study was to investigate the relationship among oxidative stress elements, select HDAC's (2/3) and glucocorticoid receptor signaling in an elderly sample with CFS.

Findings suggest increased histone deacetylases activity, lower total antioxidant power, in the context of decreased plasma cortisol and increased plasma dehydroepiandrosterone concomitant with decreased expression of the encoding gene for the glucocorticoid receptor. These findings support the presence of HPA axis dysregulation in elderly individuals with CFS.

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Patients' hopes and expectations of a specialist chronic fatigue syndrome/ME service: a qualitative study.

McDermott C, Lynch J, Leydon GM.

Source Primary Medical Care Research Department, University of Southampton, Southampton, UK.

Abstract

Background. The 2007 National Institute for Health and Clinical Excellence guidelines on Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) recommend early management of the condition (National Institute for Health and Clinical Excellence (NICE).

Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (or Encephalopathy):

Diagnosis and Management of CFS/ME in Adults and Children. NICE Clinical Guideline 53. London: National Collaborating Centre for Primary Care, 2007) Investment by the Department of Health has expanded the number of specialist UK CFS/ME services but there has been little research on what patients hope or expect from referral.

Methods. A qualitative study exploring hopes and expectations of patients newly referred to a CFS/ME Service in the South of England.

Interviews with 20 patients were analysed using the constant comparative method. Results. Participants hoped referral to a specialist service would clarify diagnosis, give guidance and support, assist in understanding the complexity of the illness and provide hope for the future. While many participants valued the support of their GP, all viewed referral as offering a level of specialist expertise beyond that available in primary care.

Many participants expressed high levels of uncertainty about the nature of CFS/ME. While participants hoped that the service would be able to provide information and guidance, many expressed the view that more information earlier in their illness would make the waiting period less stressful and make it possible for them to do more to help themselves.

Conclusions. GP referral to a specialist service appeared to be highly valued by the participants in this study. The levels of uncertainty expressed by many patients about the nature of CFS/ME raises the issue of the role of information on CFS/ME during the early stages of the illness and suggests a need for more reassurance and positive advice during the waiting period.

Fam Pract. 2011 May 9. [Epub ahead of print]

Xenotropic Murine Leukemia Virus-related Virus-associated Chronic Fatigue Syndrome Reveals a Distinct Inflammatory Signature

VINCENT C. LOMBARDI¹, KATHRYN S. HAGEN¹, KENNETH W. HUNTER⁴, JOHN W. DIAMOND^{2†}, JULIE SMITH-GAGEN³, WEI YANG³ and JUDY A. MIKOVITS¹,
Whittemore Peterson Institute, University of Nevada, Reno

Abstract.

Background:

The recent identification of xenotropic murine leukemia virus-related virus (XMRV) in the blood of patients with chronic fatigue syndrome (CFS) establishes that a retrovirus may play a role in the pathology in this disease. Knowledge of the immune response might lead to a better understanding of the role XMRV plays in this syndrome. Our objective was to investigate the cytokine and chemokine response in XMRV-associated CFS.

Materials and Methods:

Using Luminex multi-analyte profiling technology, we measured cytokine and chemokine values in the plasma of XMRV-infected CFS patients and compared these data to those of healthy controls. Analysis was performed using the Gene Expression Pattern Analysis Suite and the Random Forest tree classification algorithm.

Results:

This study identifies a signature of 10 cytokines and chemokines which correctly identifies XMRV/CFS patients with 93% specificity and 96% sensitivity.

Conclusion:

These data show, for the first time, an immunological pattern associated with XMRV/CFS.

Psychol Med. 2011 May;41(5):1099-107. Epub 2010 Jul 21.

The pathway from glandular fever to chronic fatigue syndrome: can the cognitive behavioural model provide the map?

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Abstract

BACKGROUND: The cognitive behavioural model of chronic fatigue syndrome (CFS) suggests that the illness is caused through reciprocal interactions between physiology, cognition, emotion and behaviour. The purpose of this study was to investigate whether the psychological factors operationalized in this model could predict the onset of CFS following an acute episode of infectious mononucleosis commonly known as glandular fever (GF).

METHOD: A total of 246 patients with GF were recruited into this prospective cohort study. Standardized self-report measures of perceived stress, perfectionism, somatization, mood, illness beliefs and behaviour were completed at the time of their acute illness. Follow-up questionnaires determined the incidence of new-onset chronic fatigue (CF) at 3 months and CFS at 6 months post-infection.

RESULTS: Of the participants, 9.4% met the criteria for CF at 3 months and 7.8% met the criteria for CFS at 6 months. Logistic regression revealed that factors proposed to predispose people to CFS including anxiety, depression, somatization and perfectionism were associated with new-onset CFS. Negative illness beliefs including perceiving GF to be a serious, distressing condition, that will last a long time and is uncontrollable, and responding to symptoms in an all-or-nothing behavioural pattern were also significant predictors. All-or-nothing behaviour was the most significant predictor of CFS at 6 months.

Perceived stress and consistently limiting activity at the time of GF were not significantly associated with CFS.

CONCLUSIONS: The findings from this study provide support for the cognitive behavioural model and a good basis for developing prevention and early intervention strategies for CFS.

PMID: 20663256 [PubMed - in process]

Origins of XMRV deciphered, undermining claims for a role in human disease

Part 1 of 2 Parts

Delineation of the origin of the retrovirus known as XMRV from the genomes of laboratory mice indicates that the virus is unlikely to be responsible for either prostate cancer or chronic fatigue syndrome in humans, as has been widely published. The virus arose because of genetic recombination of two mouse viruses. Subsequent infection of lab experiments with XMRV formed the basis of the original association.

Reporting in *Science*, Vinay Pathak, Ph.D., and his research team from the National Cancer Institute (NCI), part of the National Institutes of Health, in collaboration with other researchers, described experiments that provide an understanding of when and how XMRV arose and explain the original, incorrect association. XMRV stands for xenotropic murine leukemia virus–related virus.

This study is being reported in the same issue of *Science* as another study of XMRV (Knox et al.) that finds a lack of association between the virus and CFS even in the same patients from a 2009 study. "Taken together, these results essentially close the door on XMRV as a cause of human disease," said John Coffin, Ph.D., special advisor to the NCI director, and professor at Tufts University School of Medicine, a coauthor of the paper with Pathak.

Murine leukemia viruses are retroviruses that cause cancers and other diseases in mice. They are divided into different classes, one of which is xenotropic murine leukemia viruses. Although viruses in this class cannot grow in or infect cells from most mice, in the laboratory they can infect cells from other species, including human cells.

XMRV was first reported in samples from a human prostate tumor in 2006, and has been reported to be present in 6 percent to 27 percent of human prostate cancers. Later research reported XMRV in the blood of 67 percent of people with CFS.

The assertion that XMRV is circulating in the human population has been challenged by several studies that have failed to detect XMRV in multiple sets of specimens from people with prostate cancer or CFS and healthy controls.

To try to resolve the degree of association between XMRV and human disease, Pathak, who led these studies at NCI in its Viral Mutation Section, Coffin, and their colleagues examined human prostate cancer cells which contained XMRV, as well as the tumors from which these prostate cell specimens arose after they were grafted into mice. Grafting human tumors, called xenografts, into mice is a common way to study disease when it might be unsafe to test new treatments or methods in humans.

Origins of XMRV deciphered, undermining claims for a role in human disease

Part 2 of 2 Parts

Upon careful examination in this new study, it was shown that initial prostate tumor xenografts did not contain XMRV but later tumors that had been derived from them did, demonstrating that XMRV was not present in the original human tumor as previously supposed. Instead, the virus appears to have infected tumor cells while they were in mice. In addition, the mice that were used for xenografting the prostate tumor cells contained two previously undescribed viruses, PreXMRV-1 and PreXMRV-2. Each of these viruses has a stretch of over 3,200 nucleotides, the basic building blocks of DNA, which is nearly identical to XMRV, differing by only a single nucleotide.

Genetic comparison of the PreXMRV-1 and PreXMRV-2 sequences revealed that each one has non-overlapping stretches that are nearly identical to XMRV. Pathak, Coffin, and their colleagues postulate that recombination between these viruses generated XMRV in human cells while the cells were being grown in a mouse sometime between 1993 and 1996 and infected the prostate tumor cells. Recombination between virus genomes in a cell infected by more than one virus is common.

Based on this genetic analysis, the scientists concluded that XMRV was not present in the original prostate tumor samples but arose only after they had been put into mice. The probability that an identical recombination event occurred independently is about 1 in 1 trillion, making it extremely unlikely that XMRV arose from another source. The researchers concluded that the association of XMRV with human disease is due to contamination of samples with virus originating from this recombination event.

"After the reports of XMRV in human prostate cancer, and later of XMRV in people with CFS, retrovirologists all over the world were excited to explore its role in human infection and disease. The results published today are not

what we would have expected, but due to the time and resources dedicated to the understanding of this virus by researchers at NCI and NIH as well as others, scientists can now concentrate on identifying the real causes of these diseases," said Pathak.

References: Paprotka et al. Recombinant Origin of the Retrovirus XMRV.

Online Science. May 31, 2011. DOI: 10.1126/science.1205292

Knox et al. No Evidence of Murine-like Gammaretroviruses in CFS Patients Previously Identified as XMRV-infected. Online Science. May 31, 2011.

Psychiatry Res. 2011 May 18. [Epub ahead of print]

The relationship between posttraumatic stress disorder, illness cognitions, defence styles, fatigue severity and psychological well-being in chronic fatigue syndrome.

Eglinton R, Chung MC.

Source: Independent Medical and Psychological Services, Taunton, United Kingdom.

Abstract

This study investigated firstly, the rate of PTSD and the level of psychological well-being amongst people with CFS; and secondly the extent to which illness cognitions, defence styles and PTSD symptom severity related to fatigue severity and psychological well-being.

78 participants with a diagnosis of CFS completed the Chalder Fatigue Scale, the General Health Questionnaire-28, the Posttraumatic Stress Diagnostic Scale, the Illness Cognition Questionnaire and the Defence Style Questionnaire. Fifty-nine participants were recruited from the general public to form the non-fatigued control group.

CFS participants had significantly higher levels of PTSD symptoms, lower levels of psychological well-being and more traumatic life events compared to the non-fatigued controls. Trauma exposure and PTSD severity both predicted CFS status.

However, regression analyses demonstrated no significant relationship between PTSD symptoms and fatigue severity or the degree of psychological well-being.

'Helplessness' predicted both physical and mental fatigue and psychological well-being, whilst the 'mature' defence styles predicted fatigue severity only.

The results offer support to previous research showing that the rate of traumatic life events and PTSD are significantly higher amongst the CFS population.

The lack of relationship between PTSD symptoms and fatigue severity or psychological well-being indicates that these processes may operate independently of one another, via different appraisal processes.

This study focused on fatigue severity, but it may be that the role of pain in CFS is a key element in the previously reported association between PTSD and CFS.

Resistance exercise training does not affect postexercise hypotension and wave reflection in women with fibromyalgia.

Kingsley JD, McMillan V, Figueroa A.

Source: Department of Nutrition, Food, and Exercise Sciences, 436 Sandels Building, Florida State University

Abstract

The purpose of this study was to assess the effects of resistance exercise training (RET) on aortic wave reflection and hemodynamics during recovery from acute resistance exercise in women with fibromyalgia (FM) and healthy women (HW).

Nine women with FM (aged 42 ± 5 years; mean \pm SD) and 14 HW (aged 45 ± 5 years) completed testing at baseline and after 12 weeks of whole-body RET that consisted of 3 sets of 5 exercises.

Heart rate (HR), digital blood pressure (BP, plethysmography), aortic BP, and wave reflection (radial tonometry) were assessed before and 20 min after acute leg resistance exercise. Aortic and digital diastolic blood pressure (DBP) were significantly decreased ($p < 0.05$) and aortic and digital pulse pressures (PP) were significantly increased ($p < 0.05$) after acute exercise before RET.

Acute resistance exercise had no effect on HR, wave reflection (augmentation index and reflection time), digital, or aortic systolic BP.

RET improved muscle strength without affecting acute DBP and PP responses. Acute resistance exercise produces postexercise diastolic hypotension without affecting systolic blood pressure, HR, and wave reflection responses in women with and without FM.

RET does not alter resting and postexercise hemodynamics and aortic wave reflection in premenopausal women.

The full study can be found here: http://www.nrcresearchpress.com/doi/abs/10.1139/h10-105?url_ver=Z39...

Factors Affecting Duration of Chronic Fatigue Syndrome in Pediatric Patients.

Petrov D, Marchalik D, Sosin M, Bal A.

Source: UMDNJ/Robert Wood Johnson Medical School, New Brunswick, NJ, USA.

Abstract

OBJECTIVE: To determine factors affecting duration of chronic fatigue syndrome (CFS) in pediatric patients.

METHODS: This Retrospective cohort consisted of patients with CFS at the regional referral infectious disease clinic for evaluation of fatigue in children and adolescents. Demographic, clinical, and laboratory data were analyzed to identify the impact on duration and severity of pediatric CFS.

RESULTS: A total number of 53 predominantly white (98.1%) patients with CFS, aged 9-18 years, were included in the study. Other than fatigue, headaches and sleep disturbance were the most common symptoms of pediatric CFS. Seropositive status for *Borrelia burgdorferi* (*B. burgdorferi*) and Epstein-Barr virus (EBV) was identified in 66% of the patients with the diagnosis of CFS by CDC criteria.

No association was found between the CFS symptoms, gender, or age at diagnosis and duration of fatigue symptoms. Duration of CFS was associated with high Body-Mass Index (BMI) in a regression model after adjustment for patient's age, gender, and seropositive status for *B. burgdorferi* and/or EBV (0.34 ± 0.15 , $P < 0.04$).

CONCLUSIONS: BMI is significantly associated with prolonged duration of CFS.

Gene expression alterations at baseline and following moderate exercise in patients with Chronic Fatigue Syndrome, and Fibromyalgia Syndrome.

Light AR, Bateman L, Jo D, Hughen RW, Vanhaitsma TA, White AT, Light KC.

Department of Anesthesiology, University of Utah, Salt Lake City, UT The Brain Institute, University of Utah, Salt Lake City, UT Department of Neurobiology and Anatomy, University of Utah, Salt Lake City, UT Department of Exercise and Sport Science, University of Utah, Salt Lake City, UT.

Abstract

Objectives: To determine mRNA expression differences in genes involved in signaling and modulating sensory fatigue, and muscle pain in patients with Chronic Fatigue Syndrome (CFS) and Fibromyalgia Syndrome (FM) at baseline, and following moderate exercise.

Design: Forty eight Patients with CFS-only, or CFS with comorbid FM, 18 Patients with FM that did not meet criteria for CFS, and 49 healthy Controls underwent moderate exercise (25 minutes at 70% maximum age predicted heart-rate). Visual-analogue measures of fatigue and pain were taken before, during, and after exercise. Blood samples were taken before, and 0.5, 8, 24, and 48 hours after exercise. Leukocytes were immediately isolated from blood, number coded for blind processing and analyses, and flash frozen. Using real-time, quantitative PCR, the amount of mRNA for 13 genes (relative to control genes) involved in sensory, adrenergic, and immune functions was compared between groups at baseline, and following exercise. Changes in amounts of mRNA were correlated with behavioral measures, and functional clinical assessments.

Results: No gene expression changes occurred following exercise in Controls. In 71% of CFS patients, moderate exercise increased most sensory and adrenergic receptor's and one cytokine gene's transcription for 48 hours. These post-exercise increases correlated with behavioral measures of fatigue and pain. In contrast, for the other 29% of CFS patients, adrenergic α -2A receptor's transcription was decreased at all time points after exercise; other genes were not altered. History of orthostatic intolerance was significantly more common in the α -2A decrease subgroup. FM only patients showed no post-exercise alterations in gene expression, but their pre-exercise baseline mRNA for two sensory ion channels and one cytokine were significantly higher than Controls.

Conclusions: At least two subgroups of CFS patients can be identified by gene expression changes following exercise. The larger subgroup showed increases in mRNA for sensory and adrenergic receptors and a cytokine. The smaller subgroup contained most of the CFS patients with orthostatic intolerance, showed no post-exercise increases in any gene, and was defined by decreases in mRNA for α -2A. FM only patients can be identified by baseline increases in 3 genes. Post-exercise increases for 4 genes meet published criteria as an objective biomarker for CFS, and could be useful in guiding treatment selection for different subgroups.

Immunological abnormalities as potential biomarkers in Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis

Ekua W Brenu , Mieke L van Driel , Don R Staines , Kevin J Ashton , Sandra B Ramos , James Keane , Nancy G Klimas and Sonya M Marshall-Gradisnik Journal of Translational Medicine 2011,

Abstract (provisional)

Background: Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) is characterized by severe prolonged fatigue, and decreases in cognition and other physiological functions, resulting in severe loss of quality of life, difficult clinical management and high costs to the health care system. To date there is no proven pathomechanism to satisfactorily explain this disorder. Studies have identified abnormalities in immune function but these data are inconsistent. We investigated the profile of markers of immune function (including novel markers) in CFS/ME patients.

Methods: We included 95 CFS/ME patients and 50 healthy controls. All participants were assessed on natural killer (NK) and CD8+T cell cytotoxic activities, Th1 and Th2 cytokine profile of CD4+T cells, expression of vasoactive intestinal peptide receptor 2 (VPACR2), levels of NK phenotypes (CD56bright and CD56dim) and regulatory T cells expressing FoxP3 transcription factor.

Results: Compared to healthy individuals, CFS/ME patients displayed significant increases in IL-10, IFN-gamma, TNF-alpha, CD4+CD25+ T cells, FoxP3 and VPACR2 expression. Cytotoxic activity of NK and CD8+T cells and NK phenotypes, in particular the CD56bright NK cells were significantly decreased in CFS/ME patients. Additionally granzyme A and granzyme K expression were reduced while expression levels of perforin were significantly increased in the CFS/ME population relative to the control population. These data suggest significant dysregulation of the immune system in CFS/ME patients.

Conclusions: Our study found immunological abnormalities which may serve as biomarkers in CFS/ME patients with potential for an application as a diagnostic tool.

<http://www.translational-medicine.com/content/9/1/81>

fulltext- <http://www.translational-medicine.com/content/pdf/1479-5876-9-81.pdf>

An intriguing and hitherto unexplained co-occurrence: Depression and chronic fatigue syndrome are manifestations of shared inflammatory, oxidative and nitrosative (IO&NS) pathways.

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Abstract

There is a significant 'comorbidity' between depression and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). Depressive symptoms frequently occur during the course of ME/CFS. Fatigue and somatic symptoms (F&S), like pain, muscle tension, and a flu-like malaise, are key components of depression.

At the same time, depression and ME/CFS show major clinical differences, which allow to discriminate them with a 100% accuracy.

This paper aims to review the shared pathways that underpin both disorders and the pathways that discriminate them. Numerous studies have shown that depression and ME/CFS are characterized by shared aberrations in inflammatory, oxidative and nitrosative (IO&NS) pathways, like systemic inflammation and its long-term sequels, including O&NS-induced damage to fatty acids, proteins and DNA; dysfunctional mitochondria; lowered antioxidant levels, like zinc and coenzyme Q10; autoimmune responses to neoepitopes formed by O&NS; lowered omega-3 polyunsaturated fatty acid levels; and increased translocation of gram-negative bacteria.

Some IO&NS-related pathways, like the induction of indoleamine 2-3-dioxygenase, neurodegeneration and decreased neurogenesis, are more specific to depression, whereas other pathways, like the 2'-5'

oligoadenylate synthetase/RNase L pathway, are specific to ME/CFS.

Most current animal models of depression, e.g. those induced by cytokines, are not reminiscent of human depression but reflect a mixture of depressive and F&S symptoms.

The latter symptoms, sometimes called sickness behavior, differ from depression and ME/CFS because the former is a (sub)acute response to infection-induced pro-inflammatory cytokines that aims to enhance recovery, whereas the latter are characterized by long-term sequels in multiple IO&NS pathways.

Depression and ME/CFS are not 'comorbid' disorders, but should be regarded as 'co-associated disorders' that are clinical manifestations of shared pathways.

How to explain central sensitization to patients with 'unexplained' chronic musculoskeletal pain: Practice guidelines.

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Abstract

Central sensitization provides an evidence-based explanation for many cases of 'unexplained' chronic musculoskeletal pain. Prior to commencing rehabilitation in such cases, it is crucial to change maladaptive illness perceptions, to alter maladaptive pain cognitions and to reconceptualise pain.

This can be accomplished by patient education about central sensitization and its role in chronic pain, a strategy known as pain physiology education.

Pain physiology education is indicated when: 1) the clinical picture is characterized and dominated by central sensitization; and 2) maladaptive illness perceptions are present. Both are prerequisites for commencing pain physiology education.

Face-to-face sessions of pain physiology education, in conjunction with written educational material, are effective for changing pain cognitions and improving health status in patients with various chronic musculoskeletal pain disorders. These include patients with chronic low back pain, chronic whiplash, fibromyalgia and chronic fatigue syndrome.

After biopsychosocial assessment pain physiology education comprises of a first face-to-face session explaining basic pain physiology and contrasting acute nociception versus chronic pain (Session 1). Written information about pain physiology should be provided as homework in between session 1 and 2. The second session can be used to correct misunderstandings, and to facilitate the transition from knowledge to adaptive pain coping during daily life.

Pain physiology education is a continuous process initiated during the educational sessions and continued within both the active treatment and during the longer term rehabilitation program.

Chronic fatigue syndrome in the media: a content analysis of newspaper articles.

Knudsen AK, Omenås AN, Harvey SB, Løvvik CM, Lervik LV, Mykletun A., Department of Health Promotion and Development, Faculty of Psychology, University of Bergen , Bergen , Norway.

Abstract

OBJECTIVES: Although cognitive behavioural therapy and graded exercise treatment are recognized evidence-based treatments for chronic fatigue syndrome/myalgic encephalomyelitis (ME), their use is still considered controversial by some patient groups. This debate has been reflected in the media, where many patients gather health information. The aim of this study was to examine how treatment for chronic fatigue syndrome/ME is described in the newspaper media.

DESIGN: Content analysis of newspaper articles.

SETTING: The digitalized media archive Atekst was used to identify Norwegian newspaper articles where chronic fatigue syndrome/ME was mentioned.

PARTICIPANTS: Norwegian newspaper articles published over a 20-month period, from 1 January 2008 to 31 August 2009.

MAIN OUTCOME MEASURES: Statements regarding efficiency of various types of treatment for chronic fatigue syndrome/ME and the related source of the treatment advice. Statements were categorized as being either positive or negative towards evidence-based or alternative treatment.

RESULTS: One hundred and twenty-two statements regarding treatment of chronic fatigue syndrome/ME were identified among 123 newspaper articles. The most frequent statements were positive statements towards alternative treatment Lightning Process (26.2%), negative statements towards evidence-based treatments (22.1%), and positive statements towards other alternative treatment interventions (22.1%). Only 14.8% of the statements were positive towards evidence-based treatment.

Case-subjects were the most frequently cited sources, accounting for 35.2% of the statements, followed by physicians and the Norwegian ME association.

CONCLUSIONS: Statements regarding treatment for chronic fatigue syndrome/ME in newspapers are mainly pro-alternative treatment and against evidence-based treatment. The media has great potential to influence individual choices. The unbalanced reporting of treatment options for chronic fatigue syndrome/ME in the media is potentially harmful.

An XMRV Derived Retroviral Vector as a Tool for Gene Transfer

Virology Journal 2011, 8:284 doi:10.1186/1743-422X-8-284 Daniel Cervantes-Garcia , Augusto Rojas-Martinez , David Camerini

ABSTRACT

Background: Retroviral vectors are widely used tools for gene delivery and gene therapy. They are useful for gene expression studies and genetic manipulation in vitro and in vivo.

Many retroviral vectors are derived from the mouse gammaretrovirus, murine leukemia virus (MLV). These vectors have been widely used in gene therapy clinical trials. XMRV, initially found in prostate cancer tissue, was the first human gammaretrovirus described.

Findings: We developed a new retroviral vector based on XMRV called pXC. It was developed for gene transfer to human cells and is produced by transient cotransfection of LNCaP cells with pXC and XMRV-packaging plasmids.

Conclusions: We demonstrated that pXC mediates expression of inserted transgenes in cell lines. This new vector will be a useful tool for gene transfer in human and non-human cell lines, including gene therapy studies.

PLoS One. 2011;6(5):e19953. Epub 2011 May 25.

PCR master mixes harbour murine DNA sequences. Caveat emptor!

Tuke PW, Tettmar KI, Tamuri A, Stoye JP, Tedder RS.

Source : Transfusion Microbiology Research and Development, National Transfusion Microbiology Laboratories, National Health Service Blood and Transplant, Colindale, London, United Kingdom.

Abstract

BACKGROUND: XMRV is the most recently described retrovirus to be found in Man, firstly in patients with prostate cancer (PC) and secondly in 67% of patients with chronic fatigue syndrome (CFS) and 3.7% of controls.

Both disease associations remain contentious. Indeed, a recent publication has concluded that "XMRV is unlikely to be a human pathogen". Subsequently related but different polytropic MLV (pMLV) sequences were also reported from the blood of 86.5% of patients with CFS. and 6.8% of controls. Consequently we decided to investigate blood donors for evidence of XMRV/pMLV.

METHODOLOGY/PRINCIPAL FINDINGS: Testing of cDNA prepared from the whole blood of 80 random blood donors, generated gag PCR signals from two samples (7C and 9C). These had previously tested negative for XMRV by two other PCR based techniques. To test whether the PCR mix was the source of these sequences 88 replicates of water were amplified using Invitrogen Platinum Taq (IPT) and Applied Biosystems Taq Gold LD (ABTG). Four gag sequences (2D, 3F, 7H, 12C) were generated with the IPT, a further sequence (12D) by ABTG re-amplification of an IPT first round product. Sequence comparisons revealed remarkable similarities between these sequences, endogenous MLVs and the pMLV sequences reported in patients with CFS.

CONCLUSIONS/SIGNIFICANCE: Methodologies for the detection of viruses highly homologous to endogenous murine viruses require special caution as the very reagents used in the detection process can be a source of contamination and at a level where it is not immediately apparent. It is suggested that such contamination is likely to explain the apparent presence of pMLV in CFS.

The full paper can be read here: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3102076/?tool=pubmed>

Phylogeny-directed search for murine leukemia virus - like retroviruses in vertebrate genomes, and in patients suffering from Myalgic Encephalomyelitis/Chronic Fatigue Syndrome and Prostate Cancer.

Jonas Blomberg^{1*}, Ali Sheikholvaezin¹, Amal Elfaitouri¹, Fredrik Blomberg¹, Anna Sjösten¹, Johan Mattsson Ulfstedt¹, Rüdiger Pipkorn², Clas Källander³, Christina Öhrmalm¹, Göran Sperber⁴ ¹Section of Clinical Microbiology, Department of Medical Sciences, Uppsala University ²Deutsches Krebsforschungszentrum, Im Neuenheimer Feld 280, 69120 Heidelberg, Germany ³Cavidi tech AB, Uppsala Science Park, 751 83 Uppsala, Sweden.

Abstract

Gammaretrovirus-like sequences occur in most vertebrate genomes. Murine Leukemia Virus (MLV)-like retroviruses (MLLV) are a subset, which may be pathogenic and spread cross species. Retroviruses highly similar to MLLVs (Xenotropic Murine retrovirus Related Virus; XMRV, and Human Mouse Retroviruslike RetroViruses; HMRV) reported from patients suffering from prostate cancer (PC) and myalgic encephalomyelitis/ chronic fatigue syndrome (ME/CFS) raise the possibility that also humans have been infected.

Structurally intact, potentially infectious, MLLVs occur in the genomes of some mammals, especially mouse. Mouse MLLVs contain three major groups. One, MERV G3, contained MLVs and XMRV/HMRV. Its presence in mouse DNA, and the abundance of xenotropic MLVs in biologicals, is a source of false positivity.

Theoretically, XMRV/HMRV could be one of several MLLV transspecies infections. MLLVV pathobiology and diversity indicate optimal strategies for investigating XMRV/HMRV in humans, and raise ethical concerns. The alternatives that XMRV/HMRV may give a hard to detect "stealth" infection, or that XMRV/HMRV never reached humans, have to be considered.

<http://downloads.mts.hindawi.com/MTS-Files/AV/papers/XMLV/341294.v2.pdf?AWSAccessKeyId=0CX53QQSTHRYZZQRKA02&Expires=1312617376&Signature=r70Ucvn63zC3VfUwpjMHirYLLFA%3D>

Mitochondrial enzymes discriminate between mitochondrial disorders and chronic fatigue syndrome.

Smits B, van den Heuvel L, Knoop H, Küsters B, Janssen A, Borm G, Bleijenberg G, Rodenburg R, van Engelen B.

Source: Neuromuscular Center Nijmegen, Department of Neurology, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands.

Abstract

We studied the extent of mitochondrial involvement in chronic fatigue syndrome (CFS) and investigated whether measurement of mitochondrial respiratory chain complex (RCC) activities discriminates between CFS and mitochondrial disorders.

Mitochondrial content was decreased in CFS compared to healthy controls, whereas RCC activities corrected for mitochondrial content were not.

Conversely, mitochondrial content did not discriminate between CFS and two groups of mitochondrial disorders, whereas ATP production rate and complex I, III and IV activity did, all with higher activities in CFS.

We conclude that the ATP production rate and RCC activities can reliably discriminate between mitochondrial disorders and CFS.

Prevalence of asymptomatic Celiac disease in children with Fibromyalgia: a pilot study

Taubman B, Mamula P, Sherry DD.

ABSTRACT:

BACKGROUND: The objective of this study was to prospectively determine the prevalence of asymptomatic celiac disease among children presenting with fibromyalgia. The secondary objective was to investigate if their symptoms resolved on a gluten free diet.

FINDINGS: All children seen in the Amplified Musculoskeletal Pain clinic between the ages of 12 and 17 years of age who fulfilled the 1990 American College of Rheumatology diagnostic criteria for fibromyalgia were invited to participate.

A total immunoglobulin A (IgA) level, IgA antiendomysial (EMA) and IgA anti-TTG antibodies was obtained on all study subjects. A visual analog scale for pain and a functional disability inventory were obtained on all patients. If a patient had elevated EMA or TTG a small bowel biopsy was done. Patients with celiac disease were placed on a gluten-free diet and observed to see if their symptoms resolved. 50 patients, 45 females, completed the study.

Only one patient was found to have celiac disease. On a gluten-free diet her tissue transglutaminase antibody level returned to normal but her visual analog scale scores increased and her functional disability inventory was 40 initially and 21 at follow up.

CONCLUSIONS: In this pilot, single center study at a tertiary children's hospital patients with fibromyalgia do not seem to have occult celiac disease at an increased rate over the population as a whole.

Full study can be found here: <http://www.ped-rheum.com/content/9/1/11>

Interference with work in fibromyalgia - effect of treatment with pregabalin and relation to pain response.

Straube S, Moore RA, Paine J, Derry S, Phillips CJ, Hallier E, McQuay HJ.

ABSTRACT:

BACKGROUND: Clinical trials in chronic pain often collect information about interference with work as answers to component questions of commonly used questionnaires but these data are not normally analysed separately.

METHODS: We performed a meta-analysis of individual patient data from four large trials of pregabalin for fibromyalgia lasting 8-14 weeks. We analysed data on interference with work, inferred from answers to component questions of Fibromyalgia Impact Questionnaire (FIQ), Short Form 36 Health Survey, Sheehan Disability Scale, and Multidimensional Assessment of Fatigue, including "How many days in the past week did you miss work, including housework, because of fibromyalgia?" from FIQ. Analyses were performed according to randomised treatment group (pregabalin 150-600mg daily or placebo), pain improvement (0-10 numerical pain rating scale scores at trial beginning vs. end), and end of trial pain state (100mm visual analogue pain scale [VAS]).

RESULTS: Comparing treatment group average outcomes revealed modest improvement over the duration of the trials, more so with active treatment than with placebo. For the 'work missed' question from FIQ the change for patients on placebo was from 2.2 (standard deviation [SD] 2.3) days of work lost per week at trial beginning to 1.9 (SD 2.1) days lost at trial end ($p < 0.01$). For patients on 600mg pregabalin the change was from 2.1 (SD 2.2) days to 1.6 (SD 2.0) days ($p < 0.001$). However, the change in days of work lost was substantial in patients with a good pain response: from 2.0 (SD 2.2) days to 0.97 (SD 1.6) days ($p < 0.0001$) for those experiencing $\geq 50\%$ pain improvement and from 1.9 (SD 2.2) days to 0.73 (SD 1.4) days ($p < 0.0001$) for those achieving a low level of pain at trial end (< 30 mm on the VAS). Patients achieving both $\geq 50\%$ pain improvement and a pain score < 30 mm on the VAS had the largest improvement, from 2.0 (SD 2.2) days to 0.60 (SD 1.3) days ($p < 0.0001$). Analysing answers to the other questions yielded qualitatively similar results.

CONCLUSIONS: Effective pain treatment goes along with benefit regarding work. A reduction in time off work > 1 day per week can be achieved in patients with good pain responses.

EEG Biofeedback Treatment Improves Certain Attention and Somatic Symptoms in Fibromyalgia: A Pilot Study

Caro XJ, Winter EF.

Source: David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA, USA, xjcaro@earthlink.net.

Abstract Fibromyalgia (FMS) is a chronic, painful disorder often associated with measurable deficiencies in attention. Since EEG biofeedback (EEG-BF) has been used successfully to treat attention problems, we reasoned that this modality might be helpful in the treatment of attention problems in FMS. We also speculated that improvement in central nervous system (CNS) function might be accompanied by improvement in FMS somatic symptoms.

We studied fifteen FMS patients with attention problems, demonstrated by visual and auditory continuous performance testing (CPT), while completing 40 or more EEG-BF sessions. Training consisted of a "SMR protocol" that augmented 12-15 Hz brainwaves (sensory motor rhythm; SMR), while simultaneously inhibiting 4-7 Hz brainwaves (theta) and 22-30 Hz brainwaves (high beta).

Serial measurements of pain, fatigue, psychological distress, morning stiffness, and tenderness were also obtained. Sixty-three FMS patients who received standard medical care, but who did not receive EEG-BF, served as controls.

Visual, but not auditory, attention improved significantly ($P < 0.008$). EEG-BF treated subjects also showed improvement in tenderness, pain and fatigue. Somatic symptoms did not change significantly in controls. Visual attention parameters and certain somatic features of FMS appear to improve with an EEG-BF SMR protocol. EEG-BF training in FMS deserves further study.

The functional status and well being of people with myalgic encephalomyelitis/chronic fatigue syndrome and their carers

Luis C Nacul , Eliana M Lacerda , Peter Campion , Derek Pheby , Maria DE L Drachler , Jose C Leite , Fiona Poland , Amanda Howe , Shagufta Fayyaz and Mariam Molokhia

Abstract (provisional)

Background: Diagnosis of myalgic encephalomyelitis/chronic fatigue syndrome or ME/CFS is largely based on clinical history, and exclusion of identifiable causes of chronic fatigue. Characterization of cases and the impact of interventions have been limited due to clinical heterogeneity and a lack of reliable biomarkers for diagnosis and outcome measures. People with ME/CFS (PWME) often report high levels of disability, which are difficult to measure objectively. The well being of family members and those who care for PWME are also likely to be affected. This study aimed to investigate the functional status and well being of PWME and their lay carers, and to compare them with people with other chronic conditions.

Methods: We used a cross sectional design to study 170 people aged between 18 and 64 years with well characterized ME/CFS, and 44 carers, using SF-36 v2TM. Mean physical and mental domains scores (scales and component summaries) were calculated and compared internally and externally with reference standards for the general population and for population groups with 10 chronic diseases.

Results: SF-36 scores in PWME were significantly reduced, especially within the physical domain (mean norm-based Physical Component Summary (PCS) score = 26.8), but also within the mental domain (mean norm-based score for Mental Component Summary (MCS) = 34.1). The lowest and highest scale scores were for 'Role-Physical' (mean= 25.4) and 'Mental Health' (mean=36.7) respectively. All scores were in general lower than those for the general population and diseased-specific norms for other diseases. Carers of those with ME/CFS tended to have low scores in relation to population norms, particularly within the mental domain (45.5).

Conclusions: ME/CFS is disabling and has a greater impact on functional status and well being than other chronic diseases such as cancer. The emotional burden of ME/CFS is felt by lay carers as well as by people with ME/CFS. We suggest the use of generic instruments such as SF-36, in combination of other objective outcome measurements, to describe patients and assess treatments.

>From the study- "Previous studies have shown that a considerable impact on the functional status and well-being or the quality of life of people with ME/CFS. These studies varied in relation to the methods used, including the reference population, how cases were ascertained, and how quality of life has been measured. When SF-36 was used, the scales scores were not normalized, which made comparisons difficult.

However, we have also presented our results using the standard scoring system (0-100 scores), to enable comparisons with these previous studies. While low scores were consistently found previously, they were not as low as in our study. Possible explanations, other than differences in populations and methods, include the specificity of the case definitions we used, which might have excluded cases that would have been positive if other, more complacent diagnostic criteria were used. The fact that the scores of cases meeting the Canadian criteria were consistently lower than those not meeting the criteria further suggests that diagnosis specificity is related to disease severity, and that diagnostic criteria such as the Canadian may be more appropriate for research studies investigating risk factors and disease biomarkers."

fulltext- <http://www.biomedcentral.com/cont>

The economic impact of chronic fatigue syndrome in Georgia: direct and indirect costs

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The electronic version of this article is the complete one and can be found online at: <http://www.resource-allocation.com/content/9/1/1>

Abstract

Background Chronic fatigue syndrome (CFS) is a debilitating chronic illness affecting at least 4 million people in the United States. Understanding its cost improves decisions regarding resource allocation that may be directed towards treatment and cure, and guides the evaluation of clinical and community interventions designed to reduce the burden of disease.

Methods This research estimated direct and indirect costs of CFS and the impact on educational attainment using a population-based, case-control study between September 2004 and July 2005, Georgia, USA. Participants completed a clinical evaluation to confirm CFS, identify other illnesses, and report on socioeconomic factors. We estimated the effect of CFS on direct medical costs (inpatient hospitalizations, provider visits, prescription medication spending, other medical supplies and services) and loss in productivity (employment and earnings) with a stratified sample (n = 500) from metropolitan, urban, and rural Georgia. We adjusted medical costs and earnings for confounders (age, sex, race/ethnicity, education, and geographic strata) using econometric models and weighted estimates to reflect response-rate adjusted sampling rates.

Results Individuals with CFS had mean annual direct medical costs of \$5,683. After adjusting for confounding factors, CFS accounted for \$3,286 of these costs (p < 0.01), which were driven by increased provider visits and prescription medication use. Nearly one-quarter of these expenses were paid directly out-of-pocket by those with CFS. Individuals with CFS reported mean annual household income of \$23,076. After adjustment, CFS accounted for \$8,554 annually in lost household earnings (p < 0.01). Lower educational attainment accounted for 19% of the reduction in earnings associated with CFS.

Conclusions

Study results indicate that chronic fatigue syndrome may lead to substantial increases in healthcare costs and decreases in individual earnings. Studies have estimated up to 2.5% of non-elderly adults may suffer from CFS. In Georgia, a state with roughly 5.5 million people age 18-59, illness could account for \$452 million in total healthcare expenditures and \$1.2 billion of lost productivity.

Metabolic Abnormalities in Pain-Processing Regions of Patients with Fibromyalgia: A 3T MR Spectroscopy Study.

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Abstract

BACKGROUND AND PURPOSE: A growing body of evidence suggests the involvement of the brain in FM. The purpose of this proton MRS study was to test the hypothesis that there are metabolic alterations in some brain regions processing pain (VLPFC and thalamus) in patients with FM compared with HC.

MATERIALS AND METHODS: Twelve patients with FM (30-54 years of age; mean age, 43.2 years), and 12 HC, matched for age and sex, underwent 1 session of single-voxel MRS performed on a 3T MR imaging scanner. MRS spectra were acquired with a PRESS for localization. The raw data from each spectrum was evaluated with an LCModel. T tests were used to evaluate differences of brain metabolites between groups. The Pearson correlation tested the relationship of metabolite ratios and clinical symptoms.

RESULTS: Glx/Cr and Glu/Cr ratios within the VLPFC of both sides were significantly higher in patients than in HC ($P < .01$). No significant differences of metabolites between groups were found in the thalami.

Positive correlations were found between Glu/Cr in the left thalamus and the VAS for pain ($r = 0.730$, $P = .007$) and between mIns/Cr in the right VLPFC and the VAS for pain ($r = 0.607$, $P = .037$) and the FIQ ($r = 0.719$, $P = .008$).

CONCLUSIONS: The presence of elevated Glu/Cr levels in VLPFC strengthens the opinion that a complex neurophysiologic imbalance of different brain areas involved in pain processing underlies FM. These data may be useful in the diagnosis and development of more effective pharmacologic treatments.

In the mind or in the brain? Scientific evidence for central sensitisation in chronic fatigue syndrome.

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Abstract

Eur J Clin Invest 2011 ABSTRACT: Background Central sensitisation entails several top-down and bottom-up mechanisms, all contributing to the hyperresponsiveness of the central nervous system to a variety of inputs. In the late nineties, it was first hypothesised that chronic fatigue syndrome (CFS) is characterised by hypersensitivity of the central nervous system (i.e. central sensitisation). Since then, several studies have examined central sensitisation in patients with CFS. This study provides an overview of such studies. Materials and Methods Narrative review. Results Various studies showed generalised hyperalgesia in CFS for a variety of sensory stimuli, including electrical stimulation, mechanical pressure, heat and histamine.

Various tissues are affected by generalised hyperalgesia: the skin, muscle tissue and the lungs. Generalised hyperalgesia in CFS is augmented, rather than decreased, following various types of stressors like exercise and noxious heat pain. Endogenous inhibition is not activated in response to exercise and activation of diffuse noxious inhibitory controls following noxious heat application to the skin is delayed. Conclusions The observation of central sensitisation in CFS is in line with our current understanding of CFS. The presence of central sensitisation in CFS corroborates with the presence of several psychological influences on the illness, the presence of infectious agents and immune dysfunctions and the dysfunctional hypothalamus-pituitary-adrenal axis as seen in these severely debilitated patients.

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Unraveling persistent host cell infection with *Coxiella burnetii* by quantitative proteomics.

Vranakis I, De Bock PJ, Papadioti A, Samoilis G, Tselentis Y, Gevaert K, Tsiotis G, Psaroulaki A.

Abstract

The interaction between the immune system and invading bacteria is sufficient to eradicate microorganisms for the majority of bacterial infections, but suppression of the microbicidal response leads to reactivation or chronic evolution of infections and to bacterial persistence. To identify the cellular pathways affected by bacterial persistence, we applied the MS-driven COmbined FRActional DIagonal Chromatography (COFRADIC) proteomics technique for a comparative study of protein expression in the *C. burnetii* strains Nine Mile (NM) and its respective strain (NMper) isolated from 18 months persistently infected cell cultures. In total, three different proteome comparisons were performed with the total bacterial proteome, potentially secreted bacterial proteins and the eukaryotic infected proteome being assessed. Our results revealed that among the 547 identified bacterial proteins, 53 had significantly altered levels of expression and indicated potential metabolic differences between the two strains.

Regarding differences in the secreted proteins between both strains and different modulation of the host cell machineries reflect at least large rearrangements of both bacterial and eukaryotic proteomes during the persistent model of infection when compared to the acute one and emphasizes that *C. burnetii* orchestrates a vast number of different bacterial and eukaryotic host cell processes to persist within its host.

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Chronic fatigue syndrome: study of a consecutive series of 824 cases assessed in two specialized units.

[Article in Spanish] Ruiz E, Alegre J, García Quintana AM, Aliste L, Blázquez A, Fernández de Sevilla T.

SourceServicio de Medicina Interna, Unidad de Urgencias, Hospital General Universitario Vall d'Hebron, Barcelona, España.

Abstract

BACKGROUND AND OBJECTIVE: The chronic fatigue syndrome (CFS) is a disabling disorder. Few studies are available in our area on the prevalence and characteristics of CFS. Therefore, we carried out a study of a consecutive series of 824 cases diagnosed in two specialized units.

PATIENTS AND METHODS: We evaluated all of the CFS patients seen from January 2008 to June 2010. We analyzed social and demographic data, employment status, time of clinical evolution, trigger factors and onset, Fukuda and Canadian criteria, associated comorbidities and treatment.

RESULTS: A total of 824 patients were included, 748 (91%) woman, mean age 48 ± 9 years. Average age of onset of symptoms was 35 ± 11 years, time to diagnosis 108 ± 88 month. A precipitating factor was identified in

481 (58%) patients, the onset was gradual in 517 (63%) and 515 (62.5%) were not employed. The most outstanding diagnostic criteria of Fukuda were prolonged generalized fatigue after exercise, sleep disturbance and impairments in concentration and short-term memory. The different groups of symptoms defined by the Canadian consensus showed that CFS is a homogeneous entity. Accompanying comorbidity phenomena were anxiety 691 (83%), sicca syndrome 678 (82%), fibromyalgia 450 (55%). A total of 63% of patients (520) received pharmacological treatment.

CONCLUSIONS: CFS is an illness that preferentially affects young women and results in employment absenteeism. The most relevant clinical features were prolonged generalized fatigue after exercise, neurocognitive impairment and sleep disturbance. In the evaluation of the patient, it is very important to apply the Canadian criteria and to assess comorbidity.

Multi-source synthesis of data to inform health policy

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Abstract

Objectives: To propose a new method for comparing and integrating original qualitative data with systematic reviews of quantitative and qualitative studies, demonstrated by a study of the psychosocial needs of chronic fatigue syndrome (CFS) sufferers in Québec.

Methods: A systematic literature review was performed across various databases for English and French language studies, on the psychosocial aspects of CFS. Qualitative, quantitative, and mixed method studies published between January 1994 and July 2008 were included.

Unpublished literature and reference lists of included studies were also searched. Themes identified in the literature were used to guide semi-structured interviews with seventeen CFS-sufferers, mostly recruited from a large specialist practice in Montreal. Interviews were transcribed verbatim and validated by a research assistant. Transcripts were coded using the identified themes. New codes were created when new issues arose. All themes were subsequently synthesized into overall categories using a constant comparative method.

Results: The literature search yielded thirty-one papers: twenty-eight primary studies and three systematic reviews. Twelve themes were identified and synthesized into four overall problem categories, such as "Lack of professional recognition." Interviews confirmed findings from the literature, but also revealed unidentified needs specific to CFS-sufferers in Québec. Policy recommendations were provided to address these needs.

Conclusions: Multi-Source Synthesis provides a systematic method for synthesizing data from original studies with literature findings, thereby broadening the knowledge base and the local relevance of decisions concerning specific patient populations.

Absence of evidence of Borna disease virus infection in Swedish patients with Chronic Fatigue Syndrome.

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Abstract

Chronic Fatigue Syndrome (CFS) is characterized by debilitating fatigue, somatic symptoms and cognitive impairment. An infectious basis has been proposed; candidate agents include enteroviruses, herpesviruses, retroviruses and Borna disease virus (BDV), a novel neurotropic virus associated with neuropsychiatric disorders.

Sera and peripheral blood mononuclear cells (PBMC) from Swedish CFS patients were assayed for evidence of infection using ELISA and Western immunoblot for detection of antibodies to BDV proteins N, P and gp18; and using nested reverse transcriptase polymerase chain reaction (RT-PCR) for detection of BDV N- and P-gene transcripts.

No specific immunoreactivity to BDV proteins was found in sera from 169 patients or 62 controls. No BDV N- or P-gene transcripts were found through RT-PCR analysis of PBMC from 18 patients with severe CFS. These results do not support a role for BDV in pathogenesis of CFS.

MCP-1 and IL-8 as Pain Biomarkers in Fibromyalgia: A Pilot Study.

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Abstract

Objective. Although fibromyalgia (FM) is traditionally a non-inflammatory condition, emerging data also suggest that FM has an immunologic component. Previous studies have reported that peripheral blood concentrations of two chemokines (i.e., interleukin-8 [IL-8] and monocyte chemoattractant protein-1 [MCP-1]) were elevated in FM patients compared with normal controls.

We sought to determine the longitudinal relationships of changes in the levels (picogram/mL) of IL-8 and MCP-1 with changes in the severity of FM-related pain.

Design. Secondary data analysis of a cohort of 16 FM subjects who provided blood samples at two time points: week 1 and week 12.

Setting. Urban rheumatology clinic practices.

Patients. Individuals who met the American College of Rheumatology 1990 criteria for FM. Outcome Measures. Changes from week 1 to week 12 of the following variables: Brief Pain Inventory (BPI) pain severity and plasma concentrations of IL-8 and MCP-1.

Results. Change in BPI pain severity was significantly associated with changes in IL-8 and MCP-1 plasma concentrations. Specifically, for each unit increase in the change of BPI pain severity, IL-8 increased by 2.5 pg/mL ($P = 0.03$) and MCP-1 increased by 9.4 pg/mL ($P = 0.006$). None of the covariates (i.e., body mass index, medications, severity of depression, and overall FM burden) were significantly associated with either chemokines.

Conclusion. Although preliminary, our findings raise the hypothesis that IL-8 and MCP-1 may be involved in the pathogenesis of FM. If replicated in a larger study, IL-8 and MCP-1 may assist in determining prognosis and in monitoring of treatment response.

EEG spectral coherence data distinguish chronic fatigue syndrome patients from healthy controls and depressed patients – A case control study

Previous studies suggest central nervous system involvement in chronic fatigue syndrome (CFS), yet there are no established diagnostic criteria. CFS may be difficult to differentiate from clinical depression.

The study's objective was to determine if spectral coherence, a computational derivative of spectral analysis of the electroencephalogram (EEG), could distinguish patients with CFS from healthy control subjects and not erroneously classify depressed patients as having CFS.

Methods: This is a study, conducted in an academic medical center electroencephalography laboratory, of 632 subjects: 390 healthy normal controls, 70 patients with carefully defined CFS, 24 with major depression, and 148 with general fatigue. Aside from fatigue, all patients were medically healthy by history and examination.

EEGs were obtained and spectral coherences calculated after extensive artifact removal. Principal Components Analysis identified coherence factors and corresponding factor loading patterns. Discriminant analysis determined whether spectral coherence factors could reliably discriminate CFS patients from healthy control subjects without misclassifying depression as CFS.

Results: Analysis of EEG coherence data from a large sample (n=632) of patients and healthy controls identified 40 factors explaining 55.6% total variance. Factors showed highly significant group differentiation ($p < .0004$) identifying 89.5% of unmedicated female CFS patients and 92.4% of healthy female controls.

Recursive jackknifing showed predictions were stable. A conservative 10-factor discriminant function model was subsequently applied, and also showed highly significant group discrimination ($p < .001$), accurately classifying 88.9% unmedicated males with CFS, and 82.4% unmedicated male healthy controls.

No patient with depression was classified as having CFS. The model was less accurate (73.9%) in identifying CFS patients taking psychoactive medications. Factors involving the temporal lobes were of primary importance.

Conclusions: EEG spectral coherence analysis identified unmedicated patients with CFS and healthy control subjects without misclassifying depressed patients as CFS, providing evidence that CFS patients demonstrate brain physiology that is not observed in healthy normals or patients with major depression. Studies of new CFS patients and comparison groups are required to determine the possible clinical utility of this test. The results concur with other studies finding neurological abnormalities in CFS, and implicate temporal lobe involvement in CFS pathophysiology.

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BMC Neurology 2011, 11:82

LOSS OF CAPACITY TO RECOVER FROM ACIDOSIS ON REPEAT EXERCISE IN CHRONIC FATIGUE SYNDROME – A CASE CONTROL STUDY

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European Journal of Clinical Investigation © 2011 DOI

Background: Chronic fatigue syndrome (CFS) patients frequently describe difficulties with repeat exercise. Here we explore muscle bioenergetic function in response to 3 bouts of exercise.

Methods: 18 CFS (CDC 1994) patients and 12 sedentary controls underwent assessment of maximal voluntary contraction (MVC), repeat exercise with magnetic resonance spectroscopy and cardio-respiratory fitness test to determine anaerobic threshold.

Results: CFS patients undertaking MVC fell into 2 distinct groups. 8 (45%) showed normal PCr depletion in response to exercise at 35% of MVC (PCr depletion >33%; lower 95% CI for controls). 10 CFS patients had low PCr depletion (generating abnormally low MVC values). The CFS whole group exhibited significantly reduced anaerobic threshold, heart rate, VO₂, VO₂ peak and peak work compared to controls. Resting muscle pH was similar in controls and both CFS patient groups. However, the CFS group achieving normal PCr depletion values showed increased intra-muscular acidosis compared to controls after similar work after each of the 3 exercise periods with no apparent reduction in acidosis with repeat exercise of the type reported in normal subjects. This CFS group also exhibited significant prolongation (almost 4-fold) of the time taken for pH to recover to baseline.

Conclusion: When exercising to comparable levels to normal controls CFS patients exhibit profound abnormality in bioenergetic function and response to it. Although exercise intervention is the logical treatment for patients showing acidosis any trial must exclude subjects who do not initiate exercise as they will not benefit. This potentially explains previous mixed results in CFS exercise trials.

Abnormality of circadian rhythm of serum melatonin and other biochemical parameters in fibromyalgia syndrome.

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Abstract

Fibromyalgia syndrome (FMS) is a complex chronic condition causing widespread pain and variety of other symptoms. It produces pain in the soft tissues located around joints throughout the body. FMS has unknown etiology and its pathophysiology is not fully understood.

However, abnormality in circadian rhythm of hormonal profiles and cytokines has been observed in this disorder. Moreover, there are reports of deficiency of serotonin, melatonin, cortisol and cytokines in FMS patients, which are fully regulated by circadian rhythm.

Melatonin, the primary hormone of the pineal gland regulates the body's circadian rhythm and normally its levels begin to rise in the mid-to-late evening, remain high for most of the night, and then decrease in the early morning. FMS patients have lower melatonin secretion during the hours of darkness than the healthy subjects. This may contribute to impaired sleep at night, fatigue during the day and changed pain perception.

Studies have shown blunting of normal diurnal cortisol rhythm, with elevated evening serum cortisol level in patients with FMS. Thus, due to perturbed level of cortisol secretion several symptoms of FMS may occur.

Moreover, disturbed cytokine levels have also been reported in FMS patients. Therefore, circadian rhythm can be an important factor in the pathophysiology, diagnosis and treatment of FMS.

This article explores the circadian pattern of abnormalities in FMS patients, as this may help in better understanding the role of variation in symptoms of FMS and its possible relationship with circadian variations of melatonin, cortisol, cytokines and serotonin levels.

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Reliability and validity of Short Form 36 Version 2 to measure health perceptions in a sub-group of individuals with fatigue.

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, California , USA.

Abstract:

Purpose: To determine the validity and reliability of Short Form 36 Version 2 (SF36v2) in sub-groups of individuals with fatigue.

Method: Thirty subjects participated in this study, including n=16 subjects who met case definition criteria for chronic fatigue syndrome (CFS) and n=14 non-disabled sedentary matched control subjects. SF36v2 and Multidimensional Fatigue Inventory (MFI-20) were administered before two maximal cardiopulmonary exercise tests (CPETs) administered 24 h apart and an open-ended recovery questionnaire was administered 7 days after CPET challenge. The main outcome measures were self-reported time to recover to pre-challenge functional and symptom status, frequency of post-exertional symptoms and SF36v2 sub-scale scores.

Results: Individuals with CFS demonstrated significantly lower SF36v2 and MFI-20 sub-scale scores prior to CPET. Between-group differences remained significant post-CPET, however, there were no significant group by test interaction effects. Subjects with CFS reported significantly more total symptoms ($p < 0.001$), as well as reports of fatigue ($p < 0.001$), neuroendocrine ($p < 0.001$), immune ($p < 0.01$), pain ($p < 0.01$) and sleep disturbance ($p < 0.01$) symptoms than control subjects as a result of CPET.

Many symptom counts demonstrated significant relationships with SF36v2 sub-scale scores ($p < 0.05$). SF36v2 and MFI-20 sub-scale scores demonstrated significant correlations ($p < 0.05$). Various SF36v2 sub-scale scores demonstrated significant predictive validity to identify subjects who recovered from CPET challenge within 1 day and 7 days ($p < 0.05$). Potential floor effects were observed for both questionnaires for individuals with CFS.

Conclusion: Various sub-scales of SF36v2 demonstrated adequate reliability and validity for clinical and research applications. Adequacy of sensitivity to change of SF36v2 as a result of a fatiguing stressor should be the subject of additional study.

<http://www.hindawi.com/journals/av/aip/341294.pdf>

Phylogeny-directed search for murine leukemia virus - like retroviruses in vertebrate genomes, and in patients suffering from Myalgic Encephalomyelitis/Chronic Fatigue Syndrome and Prostate Cancer.

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Abstract

Gammaretrovirus-like sequences occur in most vertebrate genomes. Murine Leukemia Virus (MLV)-like retroviruses (MLLV) are a subset, which may be pathogenic and spread cross species. Retroviruses highly similar to MLLVs (Xenotropic Murine retrovirus Related Virus; XMRV, and Human Mouse Retroviruslike RetroViruses; HMRV) reported from patients suffering from prostate cancer (PC) and myalgic encephalomyelitis/ chronic fatigue syndrome (ME/CFS) raise the possibility that also humans have been infected.

Structurally intact, potentially infectious, MLLVs occur in the genomes of some mammals, especially mouse. Mouse MLLVs contain three major groups. One, MERV G3, contained MLVs and XMRV/HMRV. Its presence in mouse DNA, and the abundance of xenotropic MLVs in biologicals, is a source of false positivity.

Theoretically, XMRV/HMRV could be one of several MLLV transspecies infections. MLLVV pathobiology and diversity indicate optimal strategies for investigating XMRV/HMRV in humans, and raise ethical concerns. The alternatives that XMRV/HMRV may give a hard to detect "stealth" infection, or that XMRV/HMRV never reached humans, have to be considered.