GULF WAR ILLNESS

Gut DNA Virome Diversity and Its Association with Host Bacteria Regulate Inflammatory Phenotype and Neuronal Immunotoxicity in Experimental Gulf War Illness.

Seth RK[1], Maqsood R[2], Mondal A[3], Bose D[4] , Kimono D[5], Holland LA[6], Janulewicz Lloyd P[7], Klimas N[8], Horner RD[9], Sullivan K[10], Lim ES[11], Chatterjee S[12,13].

Viruses. **2019 Oct 21**;11(10). pii: E968. doi: 10.3390/v11100968. PMID: 31640184.

Gulf War illness (GWI) is characterized by the persistence of inflammatory bowel disease, chronic fatigue, neuroinflammation, headache, cognitive impairment, and other medically unexplained conditions. Results using a murine model show that enteric viral populations especially bacteriophages were altered in GWI. The increased viral richness and alpha diversity correlated positively with gut bacterial dysbiosis and proinflammatory cytokines. Altered virome signature in GWI mice also had a concomitant weakening of intestinal epithelial tight junctions with a significant increase in Claudin-2 protein expression and decrease in ZO1 and Occludin mRNA expression. The altered virome signature in GWI, decreased tight junction protein level was followed by the presence an activation of innate immune responses such as increased Toll-like receptor (TLR) signaling pathways. The altered virome diversity had a positive correlation with serum IL-6, IL-1β, and IFN-γ, intestinal inflammation (IFN-γ), and decreased Brain-Derived Neurotrophic Factor (BDNF), a neurogenesis marker. The co-exposure of Gulf War chemical and antibiotic (for gut sterility) or Gulf War chemical and Ribavirin, an antiviral compound to suppress virus alteration in the gut showed significant improvement in epithelial tight junction protein, decreased intestinal-, systemic-, and neuroinflammation. These results showed that the observed enteric viral dysbiosis could activate enteric viral particle-induced innate immune response in GWI and could be a novel therapeutic target in GWI.

CHRONIC FATIGUE SYNDROME

Evidence of altered cardiac autonomic regulation in myalgic encephalomyelitis/chronic fatigue syndrome: A systematic review and meta-analysis.

Nelson MJ[1], Bahl JS[1], Buckley JD[1], Thomson RL[1,2], Davison K[1].

Medicine (Baltimore). **2019 Oct**;98(43):e17600. doi: 10.1097/MD.0000000000017600. PMID: 31651868.

BACKGROUND: Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a complex condition with no reliable diagnostic biomarkers. Studies have shown evidence of autonomic dysfunction in patients with ME/CFS, but results have been equivocal. Heart rate (HR) parameters can reflect changes in autonomic function in healthy individuals; however, this has not been thoroughly evaluated in ME/CFS.

METHODS: A systematic database search for case-control literature was performed. Meta-analysis was performed to determine differences in HR parameters between ME/CFS patients and controls.

RESULTS: Sixty-four articles were included in the systematic review. HR parameters assessed in ME/CFS patients and controls were grouped into ten categories: resting HR (RHR), maximal HR (HRmax), HR during submaximal exercise, HR response to head-up tilt testing (HRtilt), resting HR variability (HRVrest), HR variability during head-up tilt testing (HRVtilt), orthostatic HR response (HROR), HR during mental task(s) (HRmentaltask), daily average HR (HRdailyaverage), and HR recovery (HRR) Meta-analysis revealed RHR (MD±95% CI=4.14±1.38, P<.001), HRtilt (SMD±95% CI=0.92±0.24, P<.001), HROR (0.50±0.27, P<.001), and the ratio of low frequency power to high frequency power of HRVrest (0.39±0.22, P<.001) were higher in ME/CFS patients compared to controls, while HRmax (MD±95% CI=-13.81±4.15, P<.001), HR at anaerobic threshold (SMD±95% CI=-0.44±0.30, P=0.005) and the high frequency portion of HRVrest (-0.34±0.22, P=.002) were lower in ME/CFS patients.

CONCLUSIONS: The differences in HR parameters identified by the meta-analysis indicate that ME/CFS patients have altered autonomic cardiac regulation when compared to healthy controls. These alterations in HR parameters may be symptomatic of the condition.

CHRONIC FATIGUE SYNDROME (Continued)

Rethinking the Standard of Care for Myalgic Encephalomyelitis/Chronic Fatigue Syndrome.

Friedberg F[1], Sunnquist M[2], Nacul L[3,4].

J Gen Intern Med. **2019 Oct 21**. doi: 10.1007/s11606-019-05375-y. PMID: 31637650. [Epub ahead of print]

For over two decades, the standard of care for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) has been cognitive behavior therapy (CBT) and graded exercise therapy (GET). Both interventions had been recommended by the US Centers for Disease Control and the UK NICE guidelines.[1] Behavioral intervention as the clinical standard was given a considerable boost by the 5 million–pound PACE trial, a large multi-arm randomized trial of CBT and GET launched in 2007.[2] This British government–funded trial was intended to definitively answer whether such interventions were beneficial in ME/CFS. In their 2011 and 2013 publications, the PACE trial authors announced with widespread publicity that 22% of their patients had “recovered” and 59–61% had clinically improved across the CBT and GET interventions.[2, 3]

More generally, multiple literature reviews have reported that these therapies are not only effective at improving fatigue and, to a lesser extent, physical function in ME/CFS but also safe.[4,5,6] It would seem obvious then that good clinical care of these patients would include these behavioral interventions. But, a closer look at these trials has generated many concerns about their applicability to these patients. This perspective critically examines their findings and more generally discusses the behavioral intervention literature in ME/CFS. Finally, we briefly describe a pragmatic clinical approach for these often-marginalized patients.

[View the full text and references for this viewpoint article in the Journal of General Internal Medicine.]

HEADACHE and MIGRAINE

Major depression subtypes are differentially associated with migraine subtype, prevalence and severity.

Pisanu C[1,2], Lundin E[1], Preisig M[3], Gholam-Rezaee M [3], Castelao E[3], Pistis G[3], Merikangas KR[4], Glaus J[4], Squassina A[2], Del Zompo M[2], Schiöth HB[1,5], Mwinyi J[1].

Cephalalgia. **2019 Oct 24**:333102419884935. doi: 10.1177/0333102419884935. PMID: 31645113. [Epub ahead of print]

OBJECTIVE: Migraine and major depressive disorder show a high rate of comorbidity, but little is known about the associations between the subtypes of major depressive disorder and migraine. In this cross-sectional study we aimed at investigating a) the lifetime associations between the atypical, melancholic, combined and unspecified subtype of major depressive disorder and migraine with and without aura and b) the associations between major depressive disorder and its subtypes and the severity of migraine.

METHODS: A total of 446 subjects with migraine (migraine without aura: n = 294; migraine with aura: n = 152) and 2511 controls from the population-based CoLaus/PsyCoLaus study, Switzerland, were included. Associations between major depressive disorder subtypes and migraine characteristics were tested using binary logistic or linear regression.

RESULTS: Melancholic, combined and unspecified major depressive disorder were associated with increased frequency of migraine with aura, whereas only melancholic major depressive disorder was associated with increased frequency of migraine without aura. Lifetime and unspecified major depressive disorder were associated with severe migraine intensity among subjects with migraine with aura but not migraine without aura, while combined major depressive disorder was associated with higher migraine frequency independently from migraine subtype.

CONCLUSION: This study suggests that melancholic but not atypical major depressive disorder is associated with migraine and migraine subtypes. Future studies exploring pathophysiological mechanisms shared between melancholic depression and migraine are warranted.

HEADACHE and MIGRAINE (Continued)

Efficacy, Tolerability, and Safety of DFN-15 (Celecoxib Oral Solution, 25 mg/mL) in the Acute Treatment of Episodic Migraine: A Randomized, Double-Blind, Placebo-Controlled Study.

Lipton RB[1], Munjal S[2], Brand-Schieber E[2], Tepper SJ[3], Dodick DW[4].

Headache. **2019 Oct 24**. doi: 10.1111/head.13663. PMID: 31647577. [Epub ahead of print]

OBJECTIVE: The objective of this study was to evaluate the efficacy, tolerability, and safety of 120 mg DFN-15 vs placebo for the acute treatment of migraine.

BACKGROUND: Certain nonsteroidal anti-inflammatory drugs (NSAIDs) are guideline-recommended therapies for the acute treatment of migraine, but patients who use them may have issues with gastrointestinal tolerability. Celecoxib, a selective inhibitor of cyclooxygenase-2, produces analgesia similar to nonselective NSAIDs. DFN-15 is an oral, ready-made liquid solution of celecoxib being investigated for the acute treatment of migraine.

METHODS: A randomized, double-blind, placebo-controlled, efficacy, tolerability, and safety study in adults with migraine was conducted. Subjects treated a single migraine attack with 120 mg DFN-15 or placebo as soon as possible after the onset of pain of moderate to severe intensity. The 2 independent coprimary efficacy endpoints were the proportion of subjects with freedom from pain and the absence of the most bothersome symptom (MBS) at 2 hours postdose. A second double-blind treatment period followed the first, but did not contribute to the primary outcomes and will be reported elsewhere.

RESULTS: There were 622 subjects randomized (1:1) to double-blind treatment with either 120 mg DFN-15 or placebo, and 567 (91.2%) treated a migraine with study drug (n = 285 DFN-15; n = 282 placebo). Groups were balanced in demographic characteristics; the mean age was 40, and most subjects were female (87% [494/567]). At 2 hours postdose, DFN-15 was significantly superior to placebo for pain freedom (35.6% [98/275] vs 21.7% [57/263], P < .001), with an odds ratio (95% CI) of 2.00 (1.36, 2.94) and for freedom from the MBS (57.8% [134/232] vs 44.8% [104/232], P = .007), with an odds ratio (95% CI) of 1.68 (1.17, 2.43). A total of 13.3% (38/285) of DFN-15-treated subjects and 8.9% (25/282) of placebo-treated subjects reported a treatment-emergent adverse event (TEAE). Study drug-related TEAEs were reported by 9.1% (26/285) of DFN-15 subjects and 6.0% (17/282) of placebo subjects, the most common of which were dysgeusia (4.2% [12/285] vs 1.4% [4/282]) and nausea (3.2% [9/285] vs 1.8% [5/282]). No subjects treated with DFN-15 reported TEAEs that were severe or led to withdrawal, and no serious TEAEs or deaths were reported in the study.

CONCLUSIONS: DFN-15 was significantly more effective than placebo for the acute treatment of migraine, with a generally favorable tolerability and safety profile.

Predictors of episodic migraine transformation to chronic migraine: A systematic review and meta-analysis of observational cohort studies.

Xu J[1,2], Kong F[1,2], Buse DC[3].

Cephalalgia. **2019 Oct 21**:333102419883355. doi: 10.1177/0333102419883355. PMID: 31635478. [Epub ahead of print]

BACKGROUND AND PURPOSE: An estimated 2.5-3.1% of people with episodic migraine develop chronic migraine in a year. Several risk factors are associated with an increased risk for this transformation. We conducted a systematic review and meta-analysis to provide quantitative and qualitative data on predictors of this transformation.

METHODS: An electronic search was conducted for published, prospective, cohort studies that reported risk factors for chronic migraine among people with episodic migraine. Risk of bias was assessed using the Newcastle-Ottawa Quality Assessment Scale. Quality of evidence was determined according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidelines. Effect estimates were retrieved and summarized using risk ratios.

RESULTS: Of 5695 identified publications, 11 were eligible for inclusion. The pooled analysis (GRADE system) found "high" evidence for monthly headache day frequency ≥ 10 (risk ratio = 5.95), "moderate" evidence for depression (risk ratio = 1.58), monthly headache day frequency ≥ 5 (risk ratio = 3.18), and annual household income ≥ $50,000 (risk ratio = 0.65) and "very low" evidence for allodynia (risk ratio = 1.40) and medication overuse (risk ratio = 8.82) in predicting progression to chronic migraine.

CONCLUSIONS: High frequency episodic migraine and depression have high quality evidence as predictors of the transformation from episodic migraine to chronic migraine, while annual household income over $50,000 may be protective.

CHRONIC PAIN

Self-reported disability in women with fibromyalgia from a tertiary care center.

Horta-Baas G[1], Romero-Figueroa MDS[2].

Adv Rheumatol. **2019 Oct 23**;59(1):45. doi: 10.1186/s42358-019-0086-4. PMID: 31647024.

BACKGROUND: The World Health Organization Disability Assessment Schedule (WHODAS) 2.0 is a generic instrument to assess disability. Pain and psychological factors seem to play a pronounced disabling role in fibromyalgia (FM). There are few studies that investigate the factors associated with disability in patients with fibromyalgia from the patient's perspective. Information about FM disability using self-reported questionnaires is limited. This study aimed to assess the relationship between the ordinal response variable (degree of disability), and four explanatory variables: pain intensity, depression, anxiety, and alexithymia.

METHODS: One hundred fifteen women with FM were enrolled in the cross-sectional study. For the assessment of disability the WHODAS 2.0 (36-item version) was used. Univariate and multivariate (ordinal logistic regression) analyses were performed to assess the relationship between pain (Visual Analogue Scale), depression and anxiety (Hospital Anxiety and Depression Scale), alexithymia (Modified Toronto Alexithymia Scale) and disability.

RESULTS: Disability was detected by global WHODAS score in 114 patients (99%), with the corresponding percentages for mild, moderate and severe disability being 11.3, 46.96 and 40.87%, respectively. Global WHODAS score was more severe among subjects with depression (50 vs 36.4, $p < 0.001$, effect size = 0.33) and alexithymia (50 vs 33.6, $p < 0.001$, effect size = 0.38). Pain intensity mean scores for mild, moderate and severe disability were 5.0, 6.1 and 7.3, respectively ($p < 0.001$, omega-squared = 0.12). Pain intensity explained the global disability degree and its domains except for the cognitive one. Whereas, depression explained cognitive and personal relation domains. On the other hand, alexithymia explained global disability degree and all domains of WHODAS 2.0 questionnaire.

CONCLUSIONS: Most of the patients with fibromyalgia perceived themselves with moderate to severe disability. The main explanatory variables of the perceived disability were the pain intensity and psychological factors (alexithymia and depression).

The Role of Physical Activity and Sedentary Behavior in Predicting Daily Pain and Fatigue in Older Adults: a Diary Study.

Park S[1], Thøgersen-Ntoumani C[2], Veldhuijzen van Zanten JJCS[1], Ntoumanis N[2].

Ann Behav Med. **2018 Jan 5**;52(1):19-28. doi: 10.1007/s12160-017-9921-1. PMID: 28646335.

[Note: Delayed posting in PubMed—Not previously listed in RAC Research Alerts.]

Background: Little attention has been paid to within-person daily associations among light physical activity (PA), moderate-to-vigorous physical activity (MVPA), and sedentary behavior (SB) with subsequent bodily pain and fatigue. Daily reports of pain and fatigue are less likely to be affected by recall bias and to conflate days of high and low pain/ fatigue into one overall score.

Purpose: The purpose of this study was to examine daily within-person associations between pain, fatigue, and physical health and ascertain whether such associations are moderated by individual differences in these variables.

Methods: Participants were 63 community-living older adults (female n = 43, mean age = 70.98 years). Questionnaires measured typical levels of PA, SB, bodily pain, fatigue, and physical health. Subsequently, on a daily basis over a 1-week period, participants' levels of light PA, MVPA, and SB were measured using accelerometers. Participants completed a questionnaire rating their pain and fatigue at the end of each day.

Results: Multilevel modeling revealed positive within-person associations between daily light PA, dailyMVPA, and pain, as well as negative within-person associations between daily SB and pain. For individuals with higher typical levels of fatigue, there was a negative association between daily light PA, MVPA, and fatigue. For individuals with better levels of physical health, there was also a negative association between daily MVPA and fatigue. For those with higher typical levels of fatigue and better levels of physical health, there was a positive association between daily SB and fatigue. No such interaction effects were found between high levels of typical pain and PA or SB.

Conclusions: Our findings indicate that efforts to promote daily PA in older adults might be more effective for those who report high typical levels of fatigue and physical health, compared to those who report high levels of daily physical pain.

IRRITABLE BOWEL SYNDROME

Fecal microbiota transplantation in irritable bowel syndrome: A systematic review and meta-analysis.

Myneedu K[1], Deoker A[1], Schmulson MJ[2], Bashashati M[1].

United European Gastroenterol J. **2019 Oct**;7(8):1033-1041. doi: 10.1177/2050640619866990. PMCID: PMC6794695. PMID: 31662860.

Background: Modulating gut microbiota is a potential treatment for irritable bowel syndrome (IBS). This meta-analysis explored whether fecal microbiota transplantation (FMT) is successful in treating IBS.

Methods: A systematic review was performed to find trials on FMT in IBS. Ratios and relative ratios (RR) of improvement for single-arm trials (SATs) and randomized controlled trials (RCTs) were calculated, respectively. Changes in IBS Severity Scoring System (IBS-SSS) and IBS Quality of Life (IBS-QOL) instrument compared to baseline in FMT versus placebo groups were pooled.

Results: In SATs, 59.5% (95% confidence interval (CI) 49.1-69.3) of IBS patients showed significant improvement. In RCTs, there were no differences between FMT and control in improvement (RR=0.93 (95% CI 0.50-1.75)) or changes in the IBS-SSS and IBS-QOL.

Conclusions: FMT was not effective in IBS. Variations in FMT methods and patient factors may contribute to the heterogeneous results of the trials.

The Alignment of Dietary Intake and Symptom-Reporting Capture Periods in Studies Assessing Associations between Food and Functional Gastrointestinal Disorder Symptoms: A Systematic Review.

Duncanson K[1,2,3], Burrows T[4,5], Keely S[6,7], Potter M[8], Das G[9], Walker M[10,11], Talley NJ[12].

Nutrients. **2019 Oct 28**;11(11). pii: E2590. doi: 10.3390/nu11112590. PMCID: PMC6893476. PMID: 31661839.

Food ingestion is heavily implicated in inducing symptoms of irritable bowel syndrome (IBS) and functional dyspepsia (FD), which affect over one-third of adults in developed countries. The primary aim of this paper was to assess the alignment of dietary assessment and symptom-reporting capture periods in diet-related studies on IBS or FD in adults. Secondary aims were to compare the degree of alignment, validity of symptom-reporting tools and reported significant associations between food ingestion and symptoms. A five-database systematic literature search resulted in 40 included studies, from which data were extracted and collated. The food/diet and symptom capture periods matched exactly in 60% (*n* = 24/40) of studies, overlapped in 30% (*n* = 12/40) of studies and were not aligned in 10% (*n* = 4/40) of studies. Only 30% (*n* = 12/40) of studies that reported a significant association between food and global gastrointestinal symptoms used a validated symptom-reporting tool. Of the thirty (75%) studies that reported at least one significant association between individual gastrointestinal symptoms and dietary intake, only four (13%) used a validated symptom tool. Guidelines to ensure that validated symptom-reporting tools are matched with fit-for-purpose dietary assessment methods are needed to minimise discrepancies in the alignment of food and symptom tools, in order to progress functional gastrointestinal disorder research.

OTHER RESEARCH OF INTEREST

A chronological map of 308 physical and mental health conditions from 4 million individuals in the English National Health Service.

Kuan V[1,2], Denaxas S[2,3,4], Gonzalez-Izquierdo A[2,3], Direk K[2,3], Bhatti O[5,6], Husain S[7], Sutaria S[8], Hingorani M[9], Nitsch D[10], Parisinos CA[3], Lumbers RT[2,3,11], Mathur R[10], Sofat R[2,3], Casas JP[3,12], Wong ICK[13,14], Hemingway H[2,3,15,16], Hingorani AD[1,2,16].

Lancet Digit Health. **2019 May 20**;1(2):e63-e77. doi: 10.1016/S2589-7500(19)30012-3. PMCID: PMC6798263. PMID: 31650125.

Background: To effectively prevent, detect, and treat health conditions that affect people during their lifecourse, health-care professionals and researchers need to know which sections of the population are susceptible to which health conditions and at which ages. Hence, we aimed to map the course of human health by identifying the 50 most common health conditions in each decade of life and estimating the median age at first diagnosis.

Methods: We developed phenotyping algorithms and codelists for physical and mental health conditions that involve intensive use of health-care resources. Individuals older than 1 year were included in the study if their primary-care and hospital-admission records met research standards set by the Clinical Practice Research Datalink and they had been registered in a general practice in England contributing up-to-standard data for at least 1 year during the study period. We used linked records of individuals from the CALIBER platform to calculate the sex-standardised cumulative incidence for these conditions by 10-year age groups between April 1, 2010, and March 31, 2015. We also derived the median age at diagnosis and prevalence estimates stratified by age, sex, and ethnicity (black, white, south Asian) over the study period from the primary-care and secondary-care records of patients.

Findings: We developed case definitions for 308 disease phenotypes. We used records of 2 784 138 patients for the calculation of cumulative incidence and of 3 872 451 patients for the calculation of period prevalence and median age at diagnosis of these conditions. Conditions that first gained prominence at key stages of life were: atopic conditions and infections that led to hospital admission in children (<10 years); acne and menstrual disorders in the teenage years (10-19 years); mental health conditions, obesity, and migraine in individuals aged 20-29 years; soft-tissue disorders and gastro-oesophageal reflux disease in individuals aged 30-39 years; dyslipidaemia, hypertension, and erectile dysfunction in individuals aged 40-59 years; cancer, osteoarthritis, benign prostatic hyperplasia, cataract, diverticular disease, type 2 diabetes, and deafness in individuals aged 60-79 years; and atrial fibrillation, dementia, acute and chronic kidney disease, heart failure, ischaemic heart disease, anaemia, and osteoporosis in individuals aged 80 years or older. Black or south-Asian individuals were diagnosed earlier than white individuals for 258 (84%) of the 308 conditions. Bone fractures and atopic conditions were recorded earlier in male individuals, whereas female individuals were diagnosed at younger ages with nutritional anaemias, tubulointerstitial nephritis, and urinary disorders.

Interpretation: We have produced the first chronological map of human health with cumulative-incidence and period-prevalence estimates for multiple morbidities in parallel from birth to advanced age. This can guide clinicians, policy makers, and researchers on how to formulate differential diagnoses, allocate resources, and target research priorities on the basis of the knowledge of who gets which diseases when. We have published our phenotyping algorithms on the CALIBER open-access Portal which will facilitate future research by providing a curated list of reusable case definitions.

Funding: Wellcome Trust, National Institute for Health Research, Medical Research Council, Arthritis Research UK, British Heart Foundation, Cancer Research UK, Chief Scientist Office of the Scottish Government Health and Social Care Directorates, Department of Health and Social Care (England), Health and Social Care Research and Development Division (Welsh Government), Public Health Agency (Northern Ireland), Economic and Social Research Council, Engineering and Physical Sciences Research Council, National Institute for Social Care and Health Research, and The Alan Turing Institute.

OTHER RESEARCH OF INTEREST (Continued)

The association of fatigue with dispositional mindfulness: relationships by levels of depressive symptoms, sleep quality, childhood adversity, and chronic medical conditions.

Whitaker RC[1], Herman AN[2], Dearth-Wesley T[2], Hubbell K[3], Huff R[3], Heneghan LJ[3], Rowe PC[4].

Prev Med. **2019 Oct 20**:105873. doi: 10.1016/j.ypmed.2019.105873. PMID: 31644898. [Epub ahead of print]

Although mindfulness-based interventions may be effective in addressing the common symptom of fatigue, no population-based studies have examined the relationship between mindfulness and fatigue. We determined whether higher levels of dispositional mindfulness were associated with lower levels of fatigue. Cross-sectional data were obtained through the Pennsylvania Head Start Staff Wellness Survey, a 2012 web-based survey in which 2199 of 3375 (65%) eligible staff participated. The analytic sample was restricted to the 2083 female respondents with complete data on dispositional mindfulness (Cognitive and Affective Mindfulness Scale-Revised) and fatigue (Fatigue Severity Scale). We determined the mean covariate-adjusted fatigue scores in each quartile of dispositional mindfulness. This relationship was examined in the overall sample and within subgroups defined by levels of four variables: depressive symptoms, poor sleep quality, childhood adversity, and chronic medical conditions. The sample was 86% non-Hispanic White, and 61% had a bachelor's or more advanced degree. The mean (SD) Fatigue Severity Scale score was 3.3 (1.3). The adjusted mean fatigue score decreased significantly and in a graded manner across higher quartiles of mindfulness, with the adjusted fatigue score 1.4 points lower (95% confidence interval: -1.5, -1.2) among those in the highest quartile of dispositional mindfulness compared to the lowest. This significant graded relationship was present within each subgroup examined, and there was not a statistically significant interaction between dispositional mindfulness and any subgroup variable. Future trials of mindfulness-based interventions should consider assessing the outcome of fatigue in both clinical and non-clinical populations.

Fatigue in primary genetic mitochondrial disease: No rest for the weary.

Parikh S[1], Galioto R[2], Lapin B[3], Haas R[4], Hirano M[5], Koenig MK[6], Saneto RP[7], Zolkipli-Cunningham Z[8], Goldstein A[8], Karaa A[9].

Neuromuscul Disord. **2019 Sep 25**. pii: S0960-8966(19)31132-0. doi: 10.1016/j.nmd.2019.09.012. PMID: 31653361.

Rates of perceived fatigue, anxiety, depression, sleepiness and mitochondrial disease severity were assessed prospectively in 2017-2018 using established validated questionnaires in 48 adult patients with genetically confirmed primary mitochondrial disease. Fatigue was found to be very common among patients with primary mitochondrial disease, with 34 to 48 (71-100%) patients reporting fatigue depending on the measure used, and the severity of fatigue correlating with the severity of disease. Moderate-to-severe depression (10/48; 20.8%) anxiety (28/48; 58.3%) and sleep problems (16/48; 33.3%) were frequent in our patients with fatigue and these conditions were even more prevalent in those with severe fatigue. In conclusion, perceived fatigue was common in patients with primary mitochondrial disease and appeared to correlate with disease severity. Depression, anxiety and sleep disorders were more common in the cohort than those with other chronic diseases but with rates similar to that seen in multiple sclerosis. The severity of perceived fatigue correlated with an increased risk of these comorbid conditions. The Fatigue Severity Scale may more selectively measure non-anxiety/sleep-related fatigue in primary mitochondrial disease and additional testing is planned.

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