GULF WAR ILLNESS

No Updates this Week for Gulf War Illness or Chronic Multisymptom Illness.

CHRONIC FATIGUE SYNDROME

Circadian rhythm abnormalities and autonomic dysfunction in patients with Chronic Fatigue Syndrome/Myalgic Encephalomyelitis.

Cambras T[1], Castro-Marrero J[2], Zaragoza MC[2,3], Díez-Noguera A[1], Alegre J[2].

PLoS One. **2018 Jun 6**;13(6):e0198106. doi: 10.1371/journal.pone.0198106. PMCID: PMC5991397. PMID: 29874259. eCollection 2018.

Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) patients frequently show autonomic symptoms which may be associated with a hypothalamic dysfunction. This study aimed to explore circadian rhythm patterns in rest and activity and distal skin temperature (DST) and their association with self-reported outcome measures, in CFS/ME patients and healthy controls at two different times of year. Ten women who met both the 1994 CDC/Fukuda definition and 2003 Canadian criteria for CFS/ME were included in the study, along with ten healthy controls matched for age, sex and body mass index. Self-reported measures were used to assess fatigue, sleep quality, anxiety and depression, autonomic function and health-related quality of life. The ActTrust actigraph was used to record activity, DST and light intensity, with data intervals of one minute over seven consecutive days. Sleep variables were obtained through actigraphic analysis and from subjective sleep diary. The circadian variables and the spectral analysis of the rhythms were calculated. Linear regression analysis was used to evaluate the relationship between the rhythmic variables and clinical features. Recordings were taken in the same subjects in winter and summer. Results showed no differences in rhythm stability, sleep latency or number of awakenings between groups as measured with the actigraph. However, daily activity, the relative amplitude and the stability of the activity rhythm were lower in CFS/ME patients than in controls. DST was sensitive to environmental temperature and showed lower nocturnal values in CFS/ME patients than controls only in winter. A spectral analysis showed no differences in phase or amplitude of the 24h rhythm, but the power of the second harmonic (12h), revealed differences between groups (controls showed a post-lunch dip in activity and peak in DST, while CFS/ME patients did not) and correlated with clinical features. These findings suggest that circadian regulation and skin vasodilator responses may play a role in CFS/ME.

Association of T and NK Cell Phenotype With the Diagnosis of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS).

Rivas JL[1], Palencia T[1], Fernández G[2], García M [1,3].

Front Immunol. **2018 May 9**;9:1028. doi: 10.3389/fimmu.2018.01028. PMCID: PMC5954087. PMID: 29867995. eCollection 2018.

Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a pathological condition characterized by incapacitating fatigue and a combination of neurologic, immunologic, and endocrine symptoms. At present its diagnosis is based exclusively on clinical criteria. Several studies have described altered immunologic profiles; therefore, we proposed to further examine the more significant differences, particularly T and NK cell subpopulations that could be conditioned by viral infections, to discern their utility in improving the diagnosis and characterization of the patients. The study included 76 patients that fulfilled the revised Canadian Consensus Criteria (CCC 2010) for ME/CFS and 73 healthy controls, matched for age and gender. Immunophenotyping of different T cell and natural killer cell subpopulations in peripheral blood was determined by flow cytometry. ME/CFS patients showed significantly lower values of T regulatory cells ($CD4^+CD25^{++(high)}FOXP3^+$) and higher NKT-like cells ($CD3^+CD16^{+/-}CD56^+$) than the healthy individuals. Regarding NK phenotypes, NKG2C was significantly lower and NKCD69 and NKCD56 bright were significantly higher in the patients group. A classification model was generated using the more relevant cell phenotype differences (NKG2C and T regulatory cells) that was able to classify the individuals as ME/CFS patients or healthy in a 70% of cases. The observed differences in some of the subpopulations of T and NK cells between patients and healthy controls could define a distinct immunological profile that can help in the diagnostic process of ME/CFS patients, contribute to the recognition of the disease and to the search of more specific treatments. However, more studies are needed to corroborate these findings and to contribute to establish a consensus in diagnosis.

HEADACHE and MIGRAINE

DFN-02 (Sumatriptan 10 mg With a Permeation Enhancer) Nasal Spray vs Placebo in the Acute Treatment of Migraine: A Double-Blind, Placebo-Controlled Study.

Lipton RB[1,2], Munjal S[3], Brand-Schieber E[3], Rapoport AM[4].

Headache. **2018 May**;58(5):676-687. doi: 10.1111/head.13309. PMID: 29878341.

OBJECTIVE: The objective of this study was to evaluate the efficacy, safety, and tolerability of DFN-02 - a nasal spray comprising sumatriptan 10 mg and a permeation-enhancing excipient (0.2% 1-O-n-Dodecyl-β-D-Maltopyranoside [DDM]) - for the acute treatment of migraine with or without aura in adults.

BACKGROUND: Prior work has shown that DFN-02, which contains only half the recommended adult dose of sumatriptan found in the original formulation (10 mg vs 20 mg), is more rapidly absorbed than commercial nasal spray of sumatriptan, with favorable pharmacokinetic and safety profiles. The efficacy of DFN-02 in the acute treatment of migraine has not been previously assessed.

METHODS: This was a multicenter, randomized, 2-period, double-blind, placebo-controlled efficacy, safety, and tolerability phase 2 study of DFN-02. Subjects with at least a 12 month history of episodic migraine, who averaged 2-8 attacks per month, with no more than 14 headache days per month and a minimum of 48 headache-free hours between attacks, were randomized (1:1) to receive DFN-02 or a matching placebo. Subjects were instructed to treat a single migraine attack of moderate to severe pain intensity. The primary efficacy endpoint, the proportion of subjects who were pain-free at 2 hours postdose in the first double-blind treatment period, was assessed with 2 protocol prespecified primary analyses: last observation carried forward (LOCF) and observed cases (OC). Secondary efficacy endpoints at 2 hours included pain relief; absence of the most bothersome symptom (MBS) among nausea, photophobia, and phonophobia; freedom from nausea, photophobia, and phonophobia. Sustained pain freedom from 2 through 24 hours postdose was also assessed.

RESULTS: Of 107 subjects randomized, 86.9% (N = 93 [DFN-02, n = 50; placebo, n = 43]) had data in the first double-blind treatment period. The study met its primary endpoint; the proportion of subjects who were free from headache pain at 2 hours postdose, was statistically significantly higher in the DFN-02 group than in the placebo group in both prespecified primary analyses: LOCF (DFN-02, n = 21/48; placebo, n = 9/40; 43.8% vs 22.5%, P = .044) and OC (DFN-02, n = 21/48; placebo, n = 8/39; 43.8% vs 20.5%, P = .025). For secondary efficacy endpoints, at 2 hours postdose, DFN-02 was also statistically significantly superior to placebo for the proportion of subjects who had pain relief (83.3% vs 55.0%, P = .005); who were free of their MBS (70.7% vs 39.5%, P = .007); and who were free of nausea (78.3% vs 42.1%, P = .026), photophobia (71.8% vs 38.9%, P = .005), and phonophobia (78.1% vs 40.0%, P = .004). Compared with placebo, statistically significantly greater proportions of subjects who were treated with DFN-02 had sustained pain freedom from 2 through 24 hours postdose (38.9% vs 13.8%, P = .029). In total, 9.7% (9/93) of subjects reported a treatment-emergent adverse event during the study: 10.0% (5/50) of DFN-02 subjects in the first double-blind treatment period and 13.5% (5/37) of DFN-02 subjects in the second double-blind treatment period. The most common treatment-emergent adverse event with DFN-02 was dysgeusia (3/37 subjects in the second double-blind treatment period).

CONCLUSIONS: DFN-02 was shown to be effective, well tolerated, and safe in the acute treatment of episodic migraine. Additional studies are needed to confirm these preliminary results. (ClinicalTrials.gov Identifier: NCT02856802).

Efficacy of Nimodipine Plus Yufeng Ningxin Tablets for Patients with Frequent Migraine.

Mu H[1], Wang L[2].

Pharmacology. **2018 Jun 7**;102(1-2):53-57. doi: 10.1159/000489314. PMID: 29879719. [Epub ahead of print]

BACKGROUND/AIMS: To test the effects of Nimodipine plus Yufeng Ningxin tablets on frequent migraine.

METHODS: Two hundred forty-two patients with frequent migraine were divided into the control group with those consuming Flunarizine (120 cases) and the treatment group with those consuming Nimodipine plus Yufeng Ningxin tablets (122 cases). The course of frequent migraine treatment lasted 7 weeks. The number of migraine days, visual analogue scale (VAS) score, and response rate were measured.

RESULTS: There was significant difference in the cure rate as the Nimodipine plus Yufeng Ningxin tablets group compared with the Flunarizine group (78.7 vs. 21.7%; $p < 0.001$). Fewer migraine days and VAS score were observed in the treatment group when compared with the control group ($p < 0.05$). Nimodipine plus Yufeng Ningxin tablets were superior to Flunarizine in terms of the response rate at week 7 ($p < 0.05$).

CONCLUSION: Due to its high cure rate, treatment with Nimodipine plus Yufeng Ningxin tablets is recommended to control frequent migraine, and this hypothesis needs to be confirmed through further studies conducted on a more extensive population.

HEADACHE and MIGRAINE (Continued)

Comparison of Pregabalin and Sodium Valproate in Migraine Prophylaxis: A Randomized Double-Blinded Study.

Hesami O[1], Shams MR[2], Ayazkhoo L[3], Assarzadegan F[1], Safarpour Lima B[1], Delavar Kasmaei H[4], Sistanizad M[3,5].

Iran J Pharm Res. **2018 Spring**;17(2):783-789. PMCID: PMC5985194. PMID: 29881434.

Patients suffering from headache, particularly migraine type, are among the most dissatisfied patients. The aim of this study was comparing the efficacy of pregabalin with valproate sodium, in preventing migraine headache. In a randomized, double-blinded study, adult patients eligible for prophylactic treatment (*i.e.*, patients with 4-15 attacks per month in last two months) were recruited. Patients' demographic data, duration of symptoms, headache frequency (attacks per month) and intensity (based on visual analogue scale) and also drugs used to relief headache were recorded. The patients were randomly assigned to two groups; valproate sodium (200 mg two times daily) and pregabalin (50 mg two times daily). The patients were examined by neurology specialist monthly for three months and the related data were recorded. The Data were analyzed using SPSS version 21, with related statistical tests. Total number of 140 patients with recurrent migraine were entered into the study. Sixty-nine patients were assigned to group A and 71 to group B by the randomizing table. Inter-group analysis of data in two arms of the study showed that two medications were equally effective except that pregabalin was not significantly effective in reducing number of attacks during first month of therapy compared to baseline. This differences were not significant at second and third month of the study. Our study showed that pregabalin, has comparable efficacy with valproate sodium in reducing migraine frequency, intensity, and duration of attacks and could be an alternative for migraine prophylaxis.

Olfactory bulbus volume and olfactory sulcus depth in migraine patients: an MRI evaluation.

Doğan A[1], Bayar Muluk N[2,3], Şahan MH[4], Asal N[4], Inal M[4], Ergün U[5].

Eur Arch Otorhinolaryngol. **2018 Jun 6**. doi: 10.1007/s00405-018-5029-x. PMID: 29876641. [Epub ahead of print]

OBJECTIVES: To compare the measurements of olfactory bulb volume and olfactory sulcus depth in patients with migraine and a control group.

METHODS: The study included the cranial MRI (1.5 T) images of 200 adults diagnosed with migraine and a control group of 100 subjects without migraine. The control group mainly consisted of the patients with non-migraneous headache. The measurements were obtained from coronal T2-weighted images for standard olfactory bulb (OB) volume and olfactory sulcus (OS) depth.

RESULTS: The OB volume and OS depth values were lower in the migraine group than in the control group. In the migraine group, left OB volume of the males was significantly lower than those of the females. In both the migraine and control groups separately, the left-side OB volume values and the right side OS depth values were significantly greater than those of the contralateral side. There were positive correlations between right and left OB volume, and right and left OS depth values. No change was seen in OB volume and OS depth values according to gender. In older patients, a decrease was determined in the right and left OB volume, and the left-side OS depth values. There was a negative correlation between osmophobia and OB volume values. In migraine patients with osmophobia, the OB volume values were significantly decreased.

CONCLUSION: OB volume values were lower in migraine patients. When osmophobia was present, the OB volume was lower than that of the non-osmophobia migraine patients. Olfactory function monitoring with olfactory tests and olfactory volume monitoring on MRI can be recommended for all migraine patients to diagnose olfactory dysfunction earlier, especially those with osmophobia. Because their OB volume values were detected as lower than those of the migraine patients without osmophobia, it may be thought that blood flow changes and osmophobia may affect the olfactory bulb volume shrinkage in migraine patients.

CHRONIC PAIN

Pain and modifiable risk factors among weight loss seeking Veterans with overweight.

Godfrey KM[1], Bullock A[2], Dorflinger L[3], Min KM[4], Ruser C[5], Masheb RM[6].

Appetite. **2018 Jun 6**. pii: S0195-6663(18)30117-X. doi: 10.1016/j.appet.2018.06.010. PMID: 29885382. [Epub ahead of print]

OBJECTIVE: Overweight/obesity and chronic pain frequently co-occur and demonstrate a bidirectional relationship. Modifiable risk factors, such as eating behaviors and mental health symptoms, may be important to understand this relationship and improve interventions in Veterans.

DESIGN: Cross-sectional.

SETTING: Veterans Health Administration Medical Center outpatient clinic.

SUBJECTS: The sample of Veterans (N = 126) was mostly male (89.7%), White (76%), and non-Hispanic (94%) with average age of 61.9 years (SD = 8.5) and average body mass index (BMI) of 38.5 (SD = 7.5).

METHODS: Veterans referred for weight loss treatment (MOVE!) at VA Connecticut completed self-report questionnaires, and electronic medical records were reviewed.

RESULTS: Mean self-reported pain rating was 4.5 out of 10 (SD = 2.3). Moderate to severe pain was endorsed by 60% of the sample. Veterans with higher pain intensity and interference reported higher global eating disorder symptoms, emotional overeating, night eating, insomnia severity, and mental health symptoms (all p's < 0.01). However, pain intensity and interference were not associated with BMI.

What Is the Role of the Placebo Effect for Pain Relief in Neurorehabilitation? Clinical Implications From the Italian Consensus Conference on Pain in Neurorehabilitation.

Castelnuovo G[1,2], Giusti EM[1,2], Manzoni GM[1,3], Saviola D[4], Gabrielli S[5], Lacerenza M[5], Pietrabissa G[1,2], Cattivelli R[1,2], Spatola CAM[1,2], Rossi A[1], Varallo G[1], Novelli M[1], Villa V[1], Luzzati F[6], Cottini A[6], Lai C[7], Volpato E[2,8], Cavalera C[2], Pagnini F[2,9], Tesio V[10], Castelli L[10], Tavola M[11], Torta R[12], Arreghini M[13], Zanini L[13], Brunani A[13], Seitanidis I[13], Ventura G[13], Capodaglio P[13], D'Aniello GE[1,2], Scarpina F[1], Brioschi A[14], Bigoni M[14], Priano L[12,14], Mauro A[12,14], Riva G[1,2], Di Lernia D[2], Repetto C[2], Regalia C[2], Molinari E[1,2], Notaro P[15], Paolucci S[16], Sandrini G[17,18], Simpson S[19,20], Wiederhold BK[21], Gaudio S[22], Jackson JB[23], Tamburin S[24], Benedetti F[12].

Front Neurol. **2018 May 18**;9:310. doi: 10.3389/fneur.2018.00310. PMCID: PMC5968866. PMID: 29867723. eCollection 2018.

Background: It is increasingly acknowledged that the outcomes of medical treatments are influenced by the context of the clinical encounter through the mechanisms of the placebo effect. The phenomenon of placebo analgesia might be exploited to maximize the efficacy of neurorehabilitation treatments. Since its intensity varies across neurological disorders, the Italian Consensus Conference on Pain in Neurorehabilitation (ICCP) summarized the studies on this field to provide guidance on its use.

Methods: A review of the existing reviews and meta-analyses was performed to assess the magnitude of the placebo effect in disorders that may undergo neurorehabilitation treatment. The search was performed on Pubmed using placebo, pain, and the names of neurological disorders as keywords. Methodological quality was assessed using a pre-existing checklist. Data about the magnitude of the placebo effect were extracted from the included reviews and were commented in a narrative form.

Results: 11 articles were included in this review. Placebo treatments showed weak effects in central neuropathic pain (pain reduction from 0.44 to 0.66 on a 0-10 scale) and moderate effects in postherpetic neuralgia (1.16), in diabetic peripheral neuropathy (1.45), and in pain associated to HIV (1.82). Moderate effects were also found on pain due to fibromyalgia and migraine; only weak short-term effects were found in complex regional pain syndrome. Confounding variables might have influenced these results.

Clinical implications: These estimates should be interpreted with caution, but underscore that the placebo effect can be exploited in neurorehabilitation programs. It is not necessary to conceal its use from the patient. Knowledge of placebo mechanisms can be used to shape the doctor-patient relationship, to reduce the use of analgesic drugs and to train the patient to become an active agent of the therapy.

CHRONIC PAIN (Continued)

Chronic pulmonary disease is associated with pain spreading and restless legs syndrome in middle-aged women-a population-based study.

Ding Z[1], Stehlik R[1,2], Hedner J[1,3], Ulfberg J[4], Grote L[5,6,7].

Sleep Breath. **2018 Jun 4**. doi: 10.1007/s11325-018-1673-z. PMID: 29869108. [Epub ahead of print]

INTRODUCTION: Recent studies suggest an increased prevalence of chronic pain conditions and restless legs syndrome (RLS) in patients with chronic pulmonary disease (CPD). We analyzed the prevalence and risk factors for pain and RLS in a population-based sample of females with comorbid CPD.

METHOD: Questionnaire-based data from 2745 women aged 18-64 years were analyzed regarding comorbid CPD status (severe bronchitis, emphysema, asthma). Pain status was assessed according to symptoms reflecting severity (Visual Analogue Scale, VAS rating 0-10) and duration and spreading (limited spread or widespread) of pain. A diagnosis of RLS was defined by four validated diagnostic criteria. Anthropometrics and co-morbidities were assessed as covariates in univariate and multivariate analyses.

RESULTS: Widespread pain was overrepresented in women with CPD (44.6 vs. 24.6%, $p < 0.001$). The odds ratio for widespread pain in women with CPD was 1.6 (95% confidence interval (CI) 1.2-2.2, $p < 0.001$) in the fully adjusted model. Severe pain (VAS rating ≥ 7) was more prevalent in females with known CPD (28.8 vs. 15.4%, $p < 0.001$, odd ratio 1.4 (95% CI 1.0-1.9, $p = 0.029$)). The prevalence of RLS was 37.4 and 23.8% in subjects with or without CPD, respectively ($p < 0.001$). In multivariate analysis, CPD was associated with a 30% risk increase for RLS (odds ratio 1.3 (95% CI 1.0-1.7, $p = 0.04$)).

CONCLUSION: This population-based study identified CPD as an independent risk factor for severe and widespread pain as well as for RLS. Further research addressing pathophysiological mechanisms linking CPD and chronic pain conditions/RLS is warranted.

Factors Associated with Suicidal Ideation in Patients with Chronic Non-Cancer Pain.

Racine M[1], Sánchez-Rodríguez E[2], Gálan S[3], Tomé-Pires C[4], Solé E[5], Jensen MP[6], Nielson WR[7], Miró J[5], Moulin DE[8], Choinière M[1].

Pain Med. **2017 Feb 1**;18(2):283-293. doi: 10.1093/pm/pnw115. PMID: 28204732.

Objectives: This study's aim was to identify the most important general and pain-related risk factors of suicidal ideation in a large sample of patients with chronic non-cancer pain.

Methods: A total of 728 patients with chronic non-cancer pain were recruited from the waitlists of eight multidisciplinary pain clinics across Canada. Patients were assessed using self-administered questionnaires to measure demographic, pain-related (intensity, duration, interference, sleep problems), psychological (anxiety, anger, depressive symptoms including suicidal ideation), cognitive (catastrophizing, attitudes/beliefs), and health-related quality of life variables. A hierarchical logistic regression analysis was used to identify the factors that were associated with presence/absence of suicidal ideation while controlling for depressive symptoms.

Results: The results showed that being a male, longer pain duration, higher anger levels, feelings of helplessness, greater pain magnification, and being more depressed were significant independent predictor factors of suicidal ideation, while better perceived mental health was related with a lesser likelihood of suicidal ideation. Moreover, being in a relationship and believing in a medical cure for pain might be protective of suicidal ideation while being anxious may be more associated with suicidal ideation.

Conclusions: These results indicate that development of suicidal ideation is more closely related to pain chronicity and certain psychosocial factors than how severe or physically incapacitating the pain is. Many of these factors could potentially be modified by early identification of suicidal ideation and developing targeted cognitive interventions for suicidal at-risk patients. Research to examine the efficacy of these interventions for reducing suicidal ideation is warranted.

OTHER RESEARCH OF INTEREST

Military status and alcohol problems: Former soldiers may be at greater risk.

Vest BM[1], Homish DL[2], Fillo J[3], Homish GG[2].

Addict Behav. **2018 Sep**;84:139-143. doi: 10.1016/j.addbeh.2018.04.011. PMCID: PMC5975126. PMID: 29679924. Epub 2018 Apr 13.

OBJECTIVES: The goal of this study was to explore differences in alcohol problems as a function of military status (current soldier, previous soldier and civilian spouses), and the possible interaction between sex and military status. We hypothesized that 1) soldiers would be at greater risk for alcohol problems than civilian spouses, and 2) former soldiers would be at greater risk compared to current soldiers.

METHODS: Data were drawn from Operation: SAFETY, a longitudinal study examining physical and mental health among U.S. Army Reserve and National Guard soldiers and their partners. The analytic sample included male and female participants who completed both the baseline and first follow-up assessments (N = 772). Negative binomial regression models were used to examine differences between military status group on alcohol problems at follow-up, controlling for sex and alcohol consumption at baseline. Interactions between military status and sex were also examined.

RESULTS: Among current soldiers, males experienced significantly more alcohol problems compared to women (4.47, 3.46; p = 0.005). Likewise, among previous soldiers, males experienced significantly more alcohol problems compared to women (6.69, 2.92; p = 0.002). Male previous soldiers had significantly more alcohol problems compared to both male current soldiers and male civilian spouses (6.69, 4.47, p = 0.04; 6.69, 3.96; p = 0.02). Among women, there were no significant differences by military status.

CONCLUSIONS: Our results indicate that male previous soldiers are at greater risk of alcohol problems than both current soldiers and civilian spouses. Health care and service providers should consider screening and monitoring soldiers who separate from the military, as alcohol use may increase.

The association of fatigue, pain, depression and anxiety with work and activity impairment in immune mediated inflammatory diseases.

Enns MW[1,2], Bernstein CN[3], Kroeker K[4], Graff L[5], Walker JR[5], Lix LM[2,4], Hitchon CA[3], El-Gabalawy R[5,6], Fisk JD[7], Marrie RA[2,3]; CIHR Team in Defining the Burden and Managing the Effects of Psychiatric Comorbidity in Chronic Immunoinflammatory Disease.

PLoS One. **2018 Jun 7**;13(6):e0198975. doi: 10.1371/journal.pone.0198975. PMID: 29879231. eCollection 2018.

Impairment in work function is a frequent outcome in patients with chronic conditions such as immune-mediated inflammatory diseases (IMID), depression and anxiety disorders. The personal and economic costs of work impairment in these disorders are immense. Symptoms of pain, fatigue, depression and anxiety are potentially remediable forms of distress that may contribute to work impairment in chronic health conditions such as IMID. The present study evaluated the association between pain [Medical Outcomes Study Pain Effects Scale], fatigue [Daily Fatigue Impact Scale], depression and anxiety [Hospital Anxiety and Depression Scale] and work impairment [Work Productivity and Activity Impairment Scale] in four patient populations: multiple sclerosis (n = 255), inflammatory bowel disease (n = 248, rheumatoid arthritis (n = 154) and a depression and anxiety group (n = 307), using quantile regression, controlling for the effects of sociodemographic factors, physical disability, and cognitive deficits. Each of pain, depression symptoms, anxiety symptoms, and fatigue individually showed significant associations with work absenteeism, presenteeism, and general activity impairment (quantile regression standardized estimates ranging from 0.3 to 1.0). When the distress variables were entered concurrently into the regression models, fatigue was a significant predictor of work and activity impairment in all models (quantile regression standardized estimates ranging from 0.2 to 0.5). These findings have important clinical implications for understanding the determinants of work impairment and for improving work-related outcomes in chronic disease.

OTHER RESEARCH OF INTEREST (Continued)

A multi-modal MRI study of the central response to inflammation in rheumatoid arthritis.

Schrepf A[1], Kaplan CM[2], Ichesco E[2], Larkin T[2], Harte SE[2], Harris RE[2], Murray AD[3], Waiter GD[3], Clauw DJ[2], Basu N[3,4].

Nat Commun. **2018 Jun 8**;9(1):2243. doi: 10.1038/s41467-018-04648-0. PMID: 29884867.

It is unknown how chronic inflammation impacts the brain. Here, we examined whether higher levels of peripheral inflammation were associated with brain connectivity and structure in 54 rheumatoid arthritis patients using functional and structural MRI. We show that higher levels of inflammation are associated with more positive connections between the inferior parietal lobule (IPL), medial prefrontal cortex, and multiple brain networks, as well as reduced IPL grey matter, and that these patterns of connectivity predicted fatigue, pain and cognitive dysfunction. At a second scan 6 months later, some of the same patterns of connectivity were again associated with higher peripheral inflammation. A graph theoretical analysis of whole-brain functional connectivity revealed a pattern of connections spanning 49 regions, including the IPL and medial frontal cortex, that are associated with peripheral inflammation. These regions may play a critical role in transducing peripheral inflammatory signals to the central changes seen in rheumatoid arthritis.

Bilateral Vestibular Dysfunction Associated With Chronic Exposure to Military Jet Propellant Type-Eight Jet Fuel.

Fife TD[1], Robb MJA[2], Steenerson KK[3], Saha KC[1].

Front Neurol. **2018 May 16**;9:351. doi: 10.3389/fneur.2018.00351. eCollection 2018. PMCID: PMC5964212. PMID: 29867750.

We describe three patients diagnosed with bilateral vestibular dysfunction associated with the jet propellant type-eight (JP-8) fuel exposure. Chronic exposure to aromatic and aliphatic hydrocarbons, which are the main constituents of JP-8 military aircraft jet fuel, occurred over 3-5 years' duration while working on or near the flight line. Exposure to toxic hydrocarbons was substantiated by the presence of JP-8 metabolite *n*-hexane in the blood of one of the cases. The presenting symptoms were dizziness, headache, fatigue, and imbalance. Rotational chair testing confirmed bilateral vestibular dysfunction in all the three patients. Vestibular function improved over time once the exposure was removed. Bilateral vestibular dysfunction has been associated with hydrocarbon exposure in humans, but only recently has emphasis been placed specifically on the detrimental effects of JP-8 jet fuel and its numerous hydrocarbon constituents. Data are limited on the mechanism of JP-8-induced vestibular dysfunction or ototoxicity. Early recognition of JP-8 toxicity risk, cessation of exposure, and customized vestibular therapy offer the best chance for improved balance. Bilateral vestibular impairment is under-recognized in those chronically exposed to all forms of jet fuel.

Sleepiness, fatigue, anxiety and depression in Chronic Obstructive Pulmonary Disease and Obstructive Sleep Apnea - Overlap - Syndrome, before and after continuous positive airways pressure therapy.

Economou NT[1], Ilias I[2], Velentza L[1], Papachatzakis Y[1], Zarogoulidis P[3], Kallianos A[1], Trakada G[1].

PLoS One. **2018 Jun 11**;13(6):e0197342. doi: 10.1371/journal.pone.0197342. PMID: 29889828. eCollection 2018.

Patients with Chronic Obstructive Pulmonary Disease (COPD) and / or Obstructive Sleep Apnea (OSA) often complain about sleepiness, fatigue, anxiety and depression. However, common screening questionnaires, like Epworth Sleepiness Scale (ESS), Fatigue Severity Scale (FSS) and Hospital Anxiety and Depression Scale (HADS) have not been previous evaluated in patients with overlap-coexisting COPD and OSA-syndrome versus patients with OSA alone. Our study compared ESS, FSS and HADS between patients with overlap syndrome and patients with OSA, before and after treatment with Continuous Positive Airways Pressure (CPAP). We examined 38 patients with coexisting COPD and OSA versus 38 patients with OSA-only and 28 subjects without respiratory disease, serving as controls. All patients underwent pulmonary function tests (PFTs), oximetry and overnight polysomnography and completed the questionnaires, before and after 3 months of CPAP therapy. The two patient groups did not differ significantly in terms of age, Body Mass Index (BMI), neck, waist and hip circumferences, and arterial blood pressure values. They also had similar comorbidities. They differed significantly, as expected, in PFTs (Forced Vital Capacity-FVC, 2.53±0.73 vs 3.08±0.85 lt, p = 0.005, Forced Expiratory Volume in 1sec-FEV1, 1.78±0.53 vs 2.60±0.73 lt/min, p<0.001) and in daytime oximetry (94.75±2.37 vs 96.13±1.56%, p = 0.007). ESS, HADS-Anxiety and HADS-Depression scores did not differ statistically significant between these two groups, whereas overlap syndrome patients expressed significantly more fatigue (FSS) than OSA-only patients, a finding that persisted even after 3 months of CPAP therapy. We conclude that sleepiness, anxiety and depression were similar in both groups, whereas fatigue was more prominent in patients with overlap syndrome than in sleep apneic patients and did not ameliorate after treatment.

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