GULF WAR ILLNESS

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

CHRONIC FATIGUE SYNDROME

Reduced glycolytic reserve in isolated natural killer cells from Myalgic encephalomyelitis/chronic fatigue syndrome patients: A preliminary investigation.

Nguyen T[1,2], Staines D[1,2], Johnston S[1,2], Marshall-Gradisnik S[1,2].

Asian Pac J Allergy Immunol. **2018 Jul 8**. doi: 10.12932/AP-011117-0188. PMID: 29981562. [Epub ahead of print]

BACKGROUND: Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is medically unexplained post-exertional fatigue associated with significant reduction in natural killer cell (NK) cytotoxicity activity. Cytotoxic activity relies on glycolytic flux and mitochondrial respiration to fulfill energetic cellular demands. While mitochondrial dysfunction has been reported in ME/CFS patients, no previous investigation has examined the bioenergetic profile of isolated NK cells from ME/CFS patients.

OBJECTIVE: This study was to determine the metabolic function in resting NK cells from ME/CFS patients.

METHOD: Six ME/CFS patients (aged 50.33±4.95) were age and sex-matched with non-fatigued healthy controls (aged 50.00±5.04). Mitochondrial stress tests measured parameters of mitochondrial function in the NK cells including basal respiration, ATP production, proton leak, maximal respiration, spare respiratory capacity and bioenergetic health index. Glycolytic stress tests measured parameters of glycolytic function such as glycolytic reserve, glycolysis and glycolytic capacity in isolated NK cells from ME/CFS patients and healthy controls using an extracellular flux analyzer, Seahorse XFp.

RESULT: There was a significant reduction of glycolytic reserve in resting NK cells from ME/CFS patients (0.6±0.07 mpH/ min) compared with healthy control (2.25±1.3 mpH/min). Mitochondrial respiration in resting NK cells did not approach statistical significance between ME/CFS patients and healthy controls.

CONCLUSION: These findings suggest resting NK cells from ME/CFS patients have reduced ability to increase glycolytic flux to respond to high energetic demands for ATP production. Hence, the reduced glycolytic reserves we have identified in isolated resting isolated NK cells should be further investigated to assist in understanding ME/CFS pathogenesis.

Truncal ataxia or disequilibrium is an unrecognised cause of orthostatic intolerance in patients with myalgic encephalomyelitis.

Miwa K[1], Inoue Y[2].

Int J Clin Pract. **2017 Jun**;71(6). doi: 10.1111/ijcp.12967. PMID: 28613452.

No Abstract for this article. See full text in Int J Clin Pract. Article introductory paragraphs:

Chronic fatigue syndrome (CFS) causes a marked reduction in the activities of daily living and impairs the quality of life. Recently, dysfunction of the central nervous system associated with myalgic encephalomyelitis (ME) has been postulated as the main cause of CFS. Most patients with ME/CFS have orthostatic intolerance (OI) which is the primary factor restricting the daily functional capacity and in turn quality of life. OI is characterised by the inability to remain upright without severe signs and symptoms, such as hypotension, tachycardia, light-headedness, pallor, fatigue, weakness, dizziness, diminished concentration, tremulousness and nausea. Most symptoms of OI have been surmised to be related to reduced cerebral blood flow with or without impaired cerebral circulatory autoregulation, and the compensatory activation of the sympathetic nervous system. Indeed, many patients have postural orthostatic tachycardia, delayed orthostatic hypotension and neurally mediated hypotension. Also many patients have low cardiac output in association with a small left ventricle. With further progression of the disease, patients may have even sitting intolerance and finally become bedridden.

Although static balance is an essential element for the performance of daily activities as well as postural stability, the possible relation between disequilibrium and OI has never been investigated. The possible role of static or truncal ataxia in the genesis of both orthostatic and sitting intolerance was examined in patients with ME.

HEADACHE and MIGRAINE

Effect of Infusion of Calcitonin Gene-Related Peptide on Cluster Headache Attacks: A Randomized Clinical Trial.

Vollesen ALH[1], Snoer A[1], Beske RP[1], Guo S[1], Hoffmann J[2], Jensen RH[1], Ashina M[1].

JAMA Neurol. **2018 Jul 9**. doi: 10.1001/jamaneurol.2018.1675. PMID: 29987329. [Epub ahead of print]

Importance: Signaling molecule calcitonin gene-related peptide (CGRP) induces migraine attacks and anti-CGRP medications abort and prevent migraine attacks. Whether CGRP provokes cluster headache attacks is unknown.

Objective: To determine whether CGRP induces cluster headache attacks in episodic cluster headache in active phase, episodic cluster headache in remission phase, and chronic cluster headache.

Design, Setting, and Participants: A randomized, double-blind, placebo-controlled, 2-way crossover study set at the Danish Headache Center, Rigshospitalet Glostrup, in Denmark. Analyses were intent to treat. Inclusion took place from December 2015 to April 2017. Inclusion criteria were diagnosis of episodic/chronic cluster headache, patients aged 18 to 65 years, and safe contraception in women. Exclusion criteria were a history of other primary headache (except episodic tension-type headache <5 days/mo), individuals who were pregnant or nursing; cardiovascular, cerebrovascular, or psychiatric disease; and drug misuse.

Interventions: Thirty-seven patients with cluster headaches received intravenous infusion of 1.5 µg/min of CGRP or placebo over 20 minutes on 2 study days.

Main Outcomes and Measures: Difference in incidence of cluster headache-like attacks, difference in area under the curve (AUC) for headache intensity scores (0 to 90 minutes), and difference in time to peak headache between CGRP and placebo in the 3 groups.

Results: Of 91 patients assessed for eligibility, 32 patients (35.2%) were included in the analysis. The mean (SD) age was 36 (10.7) years (range, 19-60 years), and the mean weight was 78 kg (range, 53-100 kg). Twenty-seven men (84.4%) completed the study. Calcitonin gene-related peptide induced cluster headache attacks in 8 of 9 patients in the active phase (mean, 89%; 95% CI, 63-100) compared with 1 of 9 in the placebo group (mean, 11%; 95% CI, 0-37) (P = .05). In the remission phase, no patients with episodic cluster headaches reported attacks after CGRP or placebo. Calcitonin gene-related peptide-induced attacks occurred in 7 of 14 patients with chronic cluster headaches (mean, 50%; 95% CI, 20-80) compared with none after placebo (P = .02). In patients with episodic active phase, the mean AUC from 0 to 90 minutes for CGRP was 1.903 (95% CI, 0.842-2.965), and the mean AUC from 0 to 90 minutes for the placebo group was 0.343 (95% CI, 0-0.867) (P = .04). In patients with chronic cluster headache, the mean AUC from 0 to 90 minutes for CGRP was 1.214 (95% CI, 0.395-2.033), and the mean AUC from 0 to 90 minutes for the placebo group was 0.036 (95% CI, 0-0.114) (P = .01). In the remission phase, the mean AUC from 0 to 90 minutes for CGRP was 0.187 (95% CI, 0-0.571), and the mean AUC from 0 to 90 minutes for placebo was 0.019 (95% CI, 0-0.062) (P > .99).

Conclusions and Relevance: Calcitonin gene-related peptide provokes cluster headache attacks in active-phase episodic cluster headache and chronic cluster headache but not in remission-phase episodic cluster headache. These results suggest anti-CGRP drugs may be effective in cluster headache management.

Trial Registration: clinicaltrials.gov (NCT02466334).

Molecular genetic overlap between migraine and major depressive disorder.

Yang Y[1,2], Zhao H[3,4], Boomsma DI[5], Ligthart L[5], Belin AC[6], Smith GD[7], Esko T[8,9,10], Freilinger TM[11,12], Hansen TF[13], Ikram MA[14], Kallela M[15], Kubisch C[16], Paraskevi C[17], Strachan DP[18], Wessman M[19,20]; International Headache Genetics Consortium, van den Maagdenberg AMJM[21,22], Terwindt GM[21], Nyholt DR[23]. Collaborators (107)

Eur J Hum Genet. **2018 Jul 11**. doi: 10.1038/s41431-018-0150-2. PMID: 29995844. [Epub ahead of print]

Migraine and major depressive disorder (MDD) are common brain disorders that frequently co-occur. Despite epidemiological evidence that migraine and MDD share a genetic basis, their overlap at the molecular genetic level has not been thoroughly investigated. Using single-nucleotide polymorphism (SNP) and gene-based analysis of genome-wide association study (GWAS) genotype data, we found significant genetic overlap across the two disorders. LD Score regression revealed a significant SNP-based heritability for both migraine (h^2 = 12%) and MDD (h^2 = 19%), and a significant cross-disorder genetic correlation (r_G = 0.25; P = 0.04). Meta-analysis of results for 8,045,569 SNPs from a migraine GWAS (comprising 30,465 migraine cases and 143,147 control samples) and the top 10,000 SNPs from a MDD GWAS (comprising 75,607 MDD cases and 231,747 healthy controls), implicated three SNPs (rs146377178, rs672931, and rs11858956) with novel genome-wide significant association ($P_{SNP} \leq 5 \times 10^{-8}$) to migraine and MDD. Moreover, gene-based association analyses revealed significant enrichment of genes nominally associated ($P_{gene\text{-}based} \leq 0.05$) with both migraine and MDD ($P_{binomial\text{-}test}$ = 0.001). Combining results across migraine and MDD, two genes, ANKDD1B and KCNK5, produced Fisher's combined gene-based P values that surpassed the genome-wide significance threshold ($P_{Fisher's\text{-}combined} \leq 3.6 \times 10^{-6}$). Pathway analysis of genes with $P_{Fisher's\text{-}combined} \leq 1 \times 10^{-3}$ suggested several pathways, foremost neural-related pathways of

signalling and ion channel regulation, to be involved in migraine and MDD aetiology. In conclusion, our study provides strong molecular genetic support for shared genetically determined biological mechanisms underlying migraine and MDD.

HEADACHE and MIGRAINE (Continued)

Association of Tinnitus and Other Cochlear Disorders With a History of Migraines.

Hwang JH[1,2], Tsai SJ[3], Liu TC[4], Chen YC[2,5], Lai JT[6].

JAMA Otolaryngol Head Neck Surg. **2018 Jul 12**. doi: 10.1001/jamaoto.2018.0939. PMID: 30003226. [Epub ahead of print]

Importance: A headache is a symptom of a migraine, but not all patients with migraine have headaches. It is still unclear whether a migraine might increase the risk of cochlear disorders, even though a migraine does not occur concurrently with cochlear disorders.

Objective: To investigate the risk of cochlear disorders for patients with a history of migraines.

Design, Setting, and Participants: This study used claims data from the Taiwan Longitudinal Health Insurance Database 2005 to identify 1056 patients with migraines diagnosed between January 1, 1996, and December 31, 2012. A total of 4224 controls were also identified from the same database based on propensity score matching. Statistical analysis was performed from January 23, 1996, to December 28, 2012.

Main Outcomes and Measures: The incidence rate of cochlear disorders (tinnitus, sensorineural hearing impairment, and/or sudden deafness) was compared between the cohorts by use of the Kaplan-Meier method. The Cox proportional hazards regression model was also used to examine the association of cochlear disorders with migraines.

Results: Of the 1056 patients with migraines, 672 were women and 384 were men, and the mean (SD) age was 36.7 (15.3) years. Compared with the nonmigraine cohort, the crude hazard ratio for cochlear disorders in the migraine cohort was 2.83 (95% CI, 2.01-3.99), and the adjusted hazard ratio was 2.71 (95% CI, 1.86-3.93). The incidence rates of cochlear disorders were 81.4 (95% CI, 81.1-81.8) per 1 million person-years for the migraine cohort and 29.4 (95% CI, 29.2-29.7) per 1 million person-years for the nonmigraine cohort. The cumulative incidence of cochlear disorders in the migraine cohort (12.2%) was significantly higher than that in the matched nonmigraine cohort (5.5%). Subgroup analysis showed that, compared with the nonmigraine cohort, the adjusted hazard ratios in the migraine cohort were 3.30 (95% CI, 2.17-5.00) for tinnitus, 1.03 (95% CI, 0.17-6.41) for sensorineural hearing impairment, and 1.22 (95% CI, 0.53-2.83) for sudden deafness.

Conclusions and Relevance: In this population-based study, the risk of cochlear disorders, especially for tinnitus, was found to be significantly higher among patients with a history of migraines. This finding may support the presence and/or concept of "cochlear migraine."

Epidemiology of migraine in men: Results from the Chronic Migraine Epidemiology and Outcomes (CaMEO) Study.

Scher AI[1], Wang SJ[2,3], Katsarava Z[4], Buse DC[5, 6], Fanning KM[7], Adams AM[8], Lipton RB[5,6,9].

Cephalalgia. **2018 Jan 1**:333102418786266. doi: 10.1177/0333102418786266. PMID: 29996667. [Epub ahead of print]

Objective: To assess migraine epidemiology in men by examining gender differences in disease presentation, comorbidities, and prognosis.

Patients and Methods: The Chronic Migraine Epidemiology and Outcomes (CaMEO) Study is a longitudinal survey of US adults with migraine identified by web questionnaire. Data were stratified by gender, collected between September 2012-November 2013, and included sociodemographics, headache features, Migraine Disability Assessment, Migraine Symptom Severity Score, Allodynia Symptom Checklist, and comorbidities. Discrete time hazard models addressed 1-year likelihood of transition from episodic to chronic migraine headache frequency.

Results: Of the 16,789 migraine respondents, 4294 were men (25.6%). Compared to women, men were slightly older at onset of their headaches (mean 24.1 vs. 22.3 years) and had fewer headache days/month (4.3 vs. 5.3 days), slightly less severe attacks (Migraine Symptom Severity Score, 21.6 vs. 22.6), reduced frequencies of grade IV Migraine Disability Assessment scores (15.7% vs. 24.1%), allodynia (32.6% vs. 49.7%), chronic migraine (6.5% vs. 9.6%, each $p < 0.001$), and common comorbidities. Men were less likely to report consulting a doctor for their headaches and receiving a migraine diagnosis if they consulted. Men and women with episodic migraine had similar crude 1-year risk of chronic migraine onset. Controlling for known risk factors (i.e. depression, headache frequency, allodynia), men had greater likelihood of chronic migraine onset at 6, 9, and 12 months (each $p < 0.05$).

Conclusions: Findings confirmed gender differences. Men with migraine generally have less severe attacks and disability and are less likely to receive a diagnosis than women with migraine. Prognostic factors may be better understood for women than men.

CHRONIC PAIN

Yoga for Military Veterans with Chronic Low Back Pain: A Randomized Clinical Trial.

Groessl EJ[1], Liu L[2], Chang DG[3], Wetherell JL[4], Bormann JE[5], Atkinson JH[4], Baxi S[6], Schmalzl L[7].

Am J Prev Med. **2017 Nov**;53(5):599-608. doi: 10.1016/j.amepre.2017.05.019. PMID: 28735778. Epub 2017 Jul 20.

INTRODUCTION: Chronic low back pain (cLBP) is prevalent, especially among military veterans. Many cLBP treatment options have limited benefits and are accompanied by side effects. Major efforts to reduce opioid use and embrace nonpharmacological pain treatments have resulted. Research with community cLBP patients indicates that yoga can improve health outcomes and has few side effects. The benefits of yoga among military veterans were examined.

DESIGN: Participants were randomized to either yoga or delayed yoga treatment in 2013-2015. Outcomes were assessed at baseline, 6 weeks, 12 weeks, and 6 months. Intention-to-treat analyses occurred in 2016.

SETTING/PARTICIPANTS: One hundred and fifty military veterans with cLBP were recruited from a major Veterans Affairs Medical Center in California.

INTERVENTION: Yoga classes (with home practice) were led by a certified instructor twice weekly for 12 weeks, and consisted primarily of physical postures, movement, and breathing techniques.

MAIN OUTCOME MEASURES: The primary outcome was Roland-Morris Disability Questionnaire scores after 12 weeks. Pain intensity was identified as an important secondary outcome.

RESULTS: Participant characteristics were mean age 53 years, 26% were female, 35% were unemployed or disabled, and mean back pain duration was 15 years. Improvements in Roland-Morris Disability Questionnaire scores did not differ between the two groups at 12 weeks, but yoga participants had greater reductions in Roland-Morris Disability Questionnaire scores than delayed treatment participants at 6 months -2.48 (95% CI= -4.08, -0.87). Yoga participants improved more on pain intensity at 12 weeks and at 6 months. Opioid medication use declined among all participants, but group differences were not found.

CONCLUSIONS: Yoga improved health outcomes among veterans despite evidence they had fewer resources, worse health, and more challenges attending yoga sessions than community samples studied previously. The magnitude of pain intensity decline was small, but occurred in the context of reduced opioid use. The findings support wider implementation of yoga programs for veterans.

TRIAL REGISTRATION: This study is registered at www.clinicaltrials.gov NCT02524158.

The effect of pain on major cognitive impairment in older adults.

van der Leeuw G[1], Ayers E[2], Leveille SG[3], Blankenstein AH[4], van der Horst HE[4], Verghese J[2].

J Pain. **2018 Jul 9**. pii: S1526-5900(18)30328-6. doi: 10.1016/j.jpain.2018.06.009. PMID: 30004021. [Epub ahead of print]

Older adults frequently report pain; cross-sectional studies have shown that pain is associated with worse cognitive function. However, longitudinal studies are lacking. We prospectively studied 441 participants without dementia, including 285 with pain, aged 65 years and older, enrolled in the Central Control of Mobility in Aging Study, a prospective cohort study. We analyzed the longitudinal association between pain (Medical Outcomes Study pain severity scale) and major cognitive impairment (Repeatable Battery for the Assessment of Neuropsychological Status and the Trail Making Test Delta) using Cox regression analysis adjusted for age, gender, ethnicity and education. Over a mean follow-up of 2.75 years (S.D. 1.94 years) there was no difference in the risk of developing cognitive impairment between participants with pain and participants without pain. However, among those with pain, risk for developing major memory impairment was higher among those with high levels of pain, compared to those with low levels of pain (adjusted HR: 3.47, 95% CI: 1.42-8.46). The association with pain and incident impairments in attention or executive function was not significant. We did not find that pain is associated with incident cognitive impairment in general, but among older adults with pain, a high level of pain is associated with increased risk of developing incident memory impairment.

PERSPECTIVE: Our study results suggest that high levels of pain may contribute to incident memory impairment. Further research is needed to determine whether a high level of chronic pain is a modifiable risk factor for cognitive impairment in older adults.

CHRONIC PAIN (Continued)

Dynamic Pain Connectome Functional Connectivity and Oscillations Reflect Multiple Sclerosis Pain.

Bosma RL[1], Kim JA[1,2], Cheng JC[1,2], Rogachov A[1,2], Hemington KS[1,2], Osborne NR[1,2], Oh J[3], Davis KD[1,2,4].

Pain. **2018 Jul 2**. doi: 10.1097/j.pain.0000000000001332. PMID: 29994989. [Epub ahead of print]

Pain is a prevalent and debilitating symptom of multiple sclerosis (MS), yet the mechanisms underlying this pain are unknown. Previous studies have found that the functional relationships between the salience network, specifically the right temporoparietal junction a salience node (SN), and other components of the dynamic pain connectome (default mode (DMN), ascending and descending pathways) are abnormal in many chronic pain conditions. Here we use resting state fMRI and measures of static and dynamic functional connectivity (sFC, dFC), and regional BOLD variability to test the hypothesis that MS patients have abnormal DMN-SN cross-network sFC, SN-ascending and SN-descending pathways dFC, and disrupted BOLD variability in the dynamic pain connectome that relate to pain inference and neuropathic pain. Thirty-one MS patients and 31 controls completed questionnaires to characterize pain and pain interference, and underwent a resting state fMRI scan from which measures of sFC, dFC, and BOLD variability were compared. We found that 1) ~50% of our patients had neuropathic pain features, 2) abnormalities in SN-DMN sFC were driven by the mixed-neuropathic subgroup, 3) in patients with mixed-neuropathic pain, dFC measures showed that there was a striking change in how the SN was engaged with the ascending nociceptive pathway and descending modulation pathway, 4) BOLD variability was increased in the DMN, 5) the degrees of sFC and BOLD variability abnormalities were related to pain interference. We propose that abnormal SN-DMN cross-network FC and temporal dynamics within and between regions of the dynamic pain connectome reflect MS pain features.

Predictors of Postdeployment Prescription Opioid Receipt and Long-term Prescription Opioid Utilization Among Army Active Duty Soldiers.

Adams RS[1], Thomas CP[2], Ritter GA[1], Lee S[1], Saadoun M[1], Williams TV[3], Larson MJ[1].

Mil Med. **2018 Jul 11**. doi: 10.1093/milmed/usy162. PMID: 30007291. [Epub ahead of print]

Introduction: Little is known about long-term prescription opioid utilization in the Military Health System. The objectives of this study were to examine predictors of any prescription opioid receipt, and predictors of long-term opioid utilization among active duty soldiers in the year following deployment.

Materials and Methods: The analytic sample consisted of Army active duty soldiers returning from deployment to Operation Enduring Freedom, Operation Iraqi Freedom, or Operation New Dawn in fiscal years 2008-2014 (N = 540,738). The Heckman probit procedure was used to jointly examine predictors of any opioid prescription receipt and long-term opioid utilization (i.e., an episode of 90 days or longer where days-supply covered at least two-thirds of days) in the postdeployment year. Predictors were based on diagnoses and characteristics of opioid prescriptions.

Results: More than one-third of soldiers (34.8%, n = 188,211) had opioid receipt, and among those soldiers, 3.3% had long-term opioid utilization (or 1.1% of the cohort, n = 6,188). The largest magnitude predictors of long-term opioid utilization were receiving a long-acting opioid within the first 30 days of the episode, diagnoses of chronic pain (no specified source), back/neck pain, or peripheral/central nervous system pain, and severe pain score in vital records.

Conclusions: Soldiers returning from deployment were more likely to receive an opioid prescription than the overall active duty population, and 1.1% initiated a long-term opioid episode. We report a declining rate of opioid receipt and long-term opioid utilization among Army members from fiscal years 2008-2014. This study demonstrates that the most important predictors of opioid receipt were not demographic factors, but generally clinical indicators of acute pain or physical trauma.

CHRONIC PAIN (Continued)

Cumulative Childhood Adversity as a Risk Factor for Common Chronic Pain Conditions in Young Adults.

You DS[1], Albu S[2], Lisenbardt H[1], Meagher MW[1].

Pain Med. **2018 Jul 11**. doi: 10.1093/pm/pny106. PMID: 30011037. [Epub ahead of print]

Objective: Multiple and specific types of childhood adverse events are risk factors for chronic pain conditions. Although both can covary, no study has evaluated one aspect while controlling for the other. Therefore, the current study examined whether more adverse events would be a risk factor for common chronic pain conditions and pain medication use in young adults after controlling for different adversity types such as physical, emotional, and sexual traumatic events or vice versa.

Methods: This cross-sectional study recruited 3,073 undergraduates (72% female, mean age = 18.8 years, SD = 1.4 years) who completed the survey for current health status and early life traumatic events.

Results: More adverse events were associated with a 1.2-1.3-fold increase in the odds of any chronic pain, chronic back pain, headache, and dysmenorrhea with adjusting for adversity types, but they were not associated with the risk of comorbid pain conditions and use of pain medications. In contrast, specific adversity types were unrelated to chronic pain conditions when controlling for the number of adverse events.

Conclusions: Cumulative childhood adverse events may be a more relevant risk factor for chronic pain conditions than the experience of a specific type of adverse event. Clinicians and researchers need to evaluate cumulative childhood adversity when assessing its link to chronic pain.

OTHER RESEARCH OF INTEREST

Eating disorder symptoms in female veterans: The role of childhood, adult, and military trauma exposure.

Arditte Hall KA[1], Bartlett BA[2], Iverson KM[1], Mitchell KS[1].

Psychol Trauma. **2018 May**;10(3):345-351. doi: 10.1037/tra0000301. PMID: 28682107. Epub 2017 Jul 6.

OBJECTIVE: Eating disorders are understudied among female U.S. military veterans, who may be at increased risk due to their high rates of trauma exposure and trauma-related sequelae. The current study sought to examine whether different types of trauma in childhood and adulthood confer differential risk for eating disorder symptoms (EDSs) in this population.

METHOD: We analyzed survey data from a sample of female Veterans Health Administration patients (N = 186) to examine the association between 5 trauma types (i.e., childhood physical abuse, adult physical assault, childhood sexual abuse, adult sexual assault, and military-related trauma) and EDS severity.

RESULTS: Approximately 14% of the sample reported clinical levels (i.e., standardized Eating Disorder Diagnostic Scale score ≥16.5) of EDSs. Multiple traumatization was associated with increased EDSs. Adult physical assault, adult sexual assault, and military-related trauma were individually associated with more severe eating disorder symptomatology, though only military-related trauma was uniquely associated with disordered eating in the full model.

DISCUSSION: EDSs are common among female veterans, and trauma exposures are differentially associated with symptom severity. It is critical to assess for EDSs in female veterans, particularly those with a history of military-related trauma, to facilitate detection and appropriate treatment. (PsycINFO Database Record

OTHER RESEARCH OF INTEREST (Continued)

Organic solvents and MS susceptibility: Interaction with MS risk HLA genes.

Hedström AK[1], Hössjer O[2], Katsoulis M[2], Kockum I[2], Olsson T[2], Alfredsson L[2].

Neurology. **2018 Jul 3**. pii: 10.1212/WNL.0000000000005906. doi: 10.1212/WNL.0000000000005906. PMID: 9351910. [Epub ahead of print]

OBJECTIVE: We hypothesize that different sources of lung irritation may contribute to elicit an immune reaction in the lungs and subsequently lead to multiple sclerosis (MS) in people with a genetic susceptibility to the disease. We aimed to investigate the influence of exposure to organic solvents on MS risk, and a potential interaction between organic solvents and MS risk human leukocyte antigen (HLA) genes.

METHODS: Using a Swedish population-based case-control study (2,042 incident cases of MS and 2,947 controls), participants with different genotypes, smoking habits, and exposures to organic solvents were compared regarding occurrence of MS, by calculating odds ratios with 95% confidence intervals using logistic regression. A potential interaction between exposure to organic solvents and MS risk HLA genes was evaluated by calculating the attributable proportion due to interaction.

RESULTS: Overall, exposure to organic solvents increased the risk of MS (odds ratio 1.5, 95% confidence interval 1.2-1.8, p = 0.0004). Among both ever and never smokers, an interaction between organic solvents, carriage of HLA-DRB1*15, and absence of HLA-A*02 was observed with regard to MS risk, similar to the previously reported gene-environment interaction involving the same MS risk HLA genes and smoke exposure.

CONCLUSION: The mechanism linking both smoking and exposure to organic solvents to MS risk may involve lung inflammation with a proinflammatory profile. Their interaction with MS risk HLA genes argues for an action of these environmental factors on adaptive immunity, perhaps through activation of autoaggressive cells resident in the lungs subsequently attacking the CNS.

Prevalence of Prescription Medications With Depression as a Potential Adverse Effect Among Adults in the United States.

Qato DM[1,2], Ozenberger K[1], Olfson M[3].

JAMA. **2018 Jun 12**;319(22):2289-2298. doi: 10.1001/jama.2018.6741. PMID: 29896627.

Importance: Prescription medications are increasingly used among adults in the United States and many have a potential for causing depression.

Objectives: To characterize use of prescription medications with depression as a potential adverse effect and to assess associations between their use and concurrent depression.

Design, Setting, and Participants: Five 2-year cycles (2005-2006 through 2013-2014) of the National Health and Nutrition Examination Survey, representative cross-sectional surveys of US adults aged 18 years or older, were analyzed for use of medications with depression as a potential adverse effect. Multivariable logistic regression examined associations between use of these medications and concurrent depression. Analyses were performed among adults overall, excluding antidepressant users, and among adults treated with antidepressants and with hypertension.

Exposures: Prescription medications with depression as a potential adverse effect (listed in Micromedex).

Main Outcomes and Measures: Prevalence of any use and concurrent use of medications with a potential to cause depression and prevalence of depression (PHQ-9 score ≥10).

Results: The study included 26 192 adults (mean age, 46.2 years [95% CI, 45.6-46.7]; women, 51.1%) and 7.6% (95% CI, 7.1%-8.2%) reported depression. The overall estimated prevalence of use of medications with depression as an adverse effect was 37.2%, increasing from 35.0% (95% CI, 32.2%-37.9%) in the cycle years 2005 and 2006 to 38.4% (95% CI, 36.5%-40.3%) in 2013 and 2014 (P for trend = .03). An estimated 6.9% (95% CI, 6.2%-7.6%) reported use of 3 or more concurrent medications with a potential for depression as an adverse effect in 2005 and 2006 and 9.5% (95% CI, 8.4%-10.7%) reported such use in 2013 and 2014 (P for trend = .001). In adjusted analyses excluding users of antidepressants, the number of medications used with depression as possible adverse effects was associated with increased prevalence of concurrent depression. The estimated prevalence of depression was 15% for those reporting use of 3 or more medications with depression as an adverse effect vs 4.7% for those not using such medications (difference, 10.7% [95% CI, 7.2%-14.1%]). These patterns persisted in analyses restricted to adults treated with antidepressants, among hypertensive adults, and after excluding users of any psychotropic medication.

Conclusions and Relevance: In this cross-sectional survey study, use of prescription medications that have depression as a potential adverse effect was common. Use of multiple medications was associated with greater likelihood of concurrent depression.

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