GULF WAR ILLNESS

A Detoxification Intervention for Gulf War Illness: A Pilot Randomized Controlled Trial.

Kerr K[1], Morse G[2,3], Graves D[4], Zuo F[5], Lipowicz A[6], Carpenter DO[7].

Int J Environ Res Public Health. **2019 Oct 28**;16(21). pii: E4143. doi: 10.3390/ijerph16214143. PMID: 31661809.

Approximately 30% of the 700,000 US veterans of the 1990-1991 Persian Gulf War developed multiple persistent symptoms called Gulf War illness. While the etiology is uncertain, several toxic exposures including pesticides and chemical warfare agents have shown associations. There is no effective medical treatment. An intervention to enhance detoxification developed by Hubbard has improved quality of life and/or reduced body burdens in other cohorts. We evaluated its feasibility and efficacy in ill Gulf War (GW) veterans in a randomized, waitlist-controlled, pilot study at a community-based rehabilitation facility in the United States. Eligible participants (*n* = 32) were randomly assigned to the intervention (*n* = 22) or a four-week waitlist control (*n* = 10). The daily 4-6 week intervention consisted of exercise, sauna-induced sweating, crystalline nicotinic acid and other supplements. Primary outcomes included recruitment, retention and safety; and efficacy was measured via Veteran's Short Form-36 (SF-36) quality of life, McGill pain, multidimensional fatigue inventory questionnaires and neuropsychological batteries. Scoring of outcomes was blinded. All 32 completed the trial and 21 completed 3-month follow-up. Mean SF-36 physical component summary score after the intervention was 6.9 (95% CI; -0.3, 14.2) points higher compared to waitlist control and 11 of 16 quality of life, pain and fatigue measures improved, with no serious adverse events. Most improvements were retained after 3 months. The Hubbard regimen was feasible, safe and might offer relief for symptoms of GW illness.

CHRONIC FATIGUE SYNDROME

Serum agrin and talin are increased in major depression while agrin and creatine phosphokinase are associated with chronic fatigue and fibromyalgia symptoms in depression.

Al-Hakeim HK[1], Al-Issa AAR[1], Maes M[2,3,4].

Metab Brain Dis. **2019 Nov 16**. doi: 10.1007/s11011-019-00506-0. PMID: 31734845. [Epub ahead of print]

Chronic fatigue and fibromyalgia symptoms frequently occur in major depressive disorder (MDD). The pathophysiology of these symptoms may in part, be ascribed to activated immune pathways, although it is unclear whether muscular factors play a role in their onset. The aim of the present study is to examine the role of muscle proteins in major depression in association with symptoms of chronic fatigue and fibromyalgia. We measured serum levels of agrin, talin-2, titin, and creatine phosphokinase (CPK) as well as the FibroFatigue (FF), the Hamilton Depression Rating Scale (HAM-D) and the Beck Depression Inventory (BDI-II) scores in 60 MDD patients and 30 healthy controls. The results show a significant increase in agrin and talin-2 in MDD patients as compared with controls. There were highly significant correlations between agrin and HAM-D, BDI-II and FF scores. Agrin, but not talin or titin, was significantly and positively associated with all 12 items of the FF scale. We found that a large part of the variance in HAM-D (47.4%), BDI-II (43.4%) and FF (43.5%) scores was explained by the regression on agrin, smoking, female sex (positively associated) and education (inversely associated). CPK was significantly and inversely associated with the total FF score and with muscle and gastro-intestinal symptoms, fatigue, a flu-like malaise, headache and memory, autonomic and sleep disturbances. These results suggest that aberrations in neuromuscular (NMJs) and myotendinous junctions play a role in MDD and that the aberrations in NMJs coupled with lowered CPK may play a role in chronic fatigue and fibromyalgia symptoms in MDD. Moreover, the increase of agrin in MDD probably functions as part of the compensatory immune-regulatory system (CIRS).

CHRONIC FATIGUE SYNDROME (Continued)

Naltrexone Restores Impaired Transient Receptor Potential Melastatin 3 Ion Channel Function in Natural Killer Cells From Myalgic Encephalomyelitis/Chronic Fatigue Syndrome Patients.

Cabanas H[1,2,3], Muraki K[3,4], Staines D[1,2,3], Marshall-Gradisnik S[1,2,3].

Front Immunol. **2019 Oct 31**;10:2545. doi: 10.3389/fimmu.2019.02545. PMCID: PMC6834647. PMID: 31736966.

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a seriously long-term and debilitating illness of unknown cause hallmarked by chronic pain and fatigue, memory and concentration impairment, and inflammation. ME/CFS hypothesis involves impaired Transient receptor potential melastatin 3 (TRPM3) ion channel function, affecting calcium signaling and Natural killer (NK) cell functions. Currently, substances called opioids, agonists of mu (μ)-opioid receptors (μOR), are the strongest painkillers clinically available for people suffering from strong or long-lasting pain characteristic of ME/CFS. μOR have been reported to specifically inhibit TRPM3 and to be expressed in immune cells where they play an immunomodulatory and immunosuppressive role. Naltrexone hydrochloride (NTX) acts as an antagonist to the μOR thus negating the inhibitory function of this opioid receptor on TRPM3. Therefore, understanding the mechanism of action for NTX in regulating and modulating TRPM3 channel function in NK cells will provide important information for the development of effective therapeutic interventions for ME/CFS. Whole-cell patch-clamp technique was used to measure TRPM3 activity in Interleukin-2 (IL-2) stimulated and NTX-treated NK cells for 24 h on eight ME/CFS patients and 8 age- and sex-matched healthy controls, after modulation with a TRPM3-agonist, pregnenolone sulfate (PregS), NTX and a TRPM3-antagonist, ononetin. We confirmed impaired TRPM3 function in ME/CFS patients through electrophysiological investigations in IL-2 stimulated NK cells after modulation with PregS and ononetin. Importantly, TRPM3 channel activity was restored in IL-2 stimulated NK cells isolated from ME/CFS patients after incubation for 24 h with NTX. Moreover, we demonstrated that NTX does not act as an agonist by directly coupling on the TRPM3 ion channel gating. The opioid antagonist NTX has the potential to negate the inhibitory function of opioid receptors on TRPM3 in NK cells from ME/CFS patients, resulting in calcium signals remodeling, which will in turn affect cell functions, supporting the hypothesis that NTX may have potential for use as a treatment for ME/CFS. Our results demonstrate, for the first time, and based on novel patch clamp electrophysiology, potential pharmaco-therapeutic interventions in ME/CFS.

A systematic review of natural killer cells profile and cytotoxic function in myalgic encephalomyelitis/chronic fatigue syndrome.

Eaton-Fitch N[1,2], du Preez S[3,4], Cabanas H[3,5], Staines D[3,5], Marshall-Gradisnik S[3,5].

Syst Rev. **2019 Nov 14**;8(1):279. doi: 10.1186/s13643-019-1202-6. PMID: 31727160.

BACKGROUND: Compromised natural killer (NK) cell cytotoxic function is a well-documented and consistent feature of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). Other outcomes evaluated in NK cells of ME/CFS patients, however, remain equivocal. The aim of this study was to conduct a systematic review of the literature regarding NK cell phenotype, receptor expression, cytokine production and cytotoxicity in ME/CFS patients and determine the appropriateness as a model for ME/CFS.

METHODS: Medline (EBSCOHost), Scopus, EMBASE and PubMed databases were systematically searched to source relevant papers published between 1994 and March 2018. This review included studies examining NK cells' features in ME/CFS patients compared with HC following administration of specific inclusion and exclusion criteria. Secondary outcomes included genetic analysis in isolated NK cells or quality of life assessment. Quality assessment was completed using the Downs and Black checklist in addition to The Joanna Briggs Institute checklist.

RESULTS: Seventeen eligible publications were included in this review. All studies were observational case control studies. Of these, 11 investigated NK cell cytotoxicity, 14 investigated NK cell phenotype and receptor profiles, three examined NK cell cytokine production, six investigated NK cell lytic protein levels and four investigated NK cell degranulation. Impaired NK cell cytotoxicity remained the most consistent immunological report across all publications. Other outcomes investigated differed between studies.

CONCLUSION: A consistent finding among all papers included in this review was impaired NK cell cytotoxicity, suggesting that it is a reliable and appropriate cellular model for continued research in ME/CFS patients. Aberrations in NK cell lytic protein levels were also reported. Although additional research is recommended, current research provides a foundation for subsequent investigations. It is possible that NK cell abnormalities can be used to characterise a subset of ME/CFS due to the heterogeneity of both the illness itself and findings between studies investigating specific features of NK function.

CHRONIC FATIGUE SYNDROME (Continued)

Checking our blind spots: current status of research evidence summaries in ME/CFS.

Davenport TE[1,2], Stevens SR[2], VanNess JM[2,3], Stevens J[2], Snell CR[2].

Br J Sports Med. **2019 Oct**;53(19):1198. doi: 10.1136/bjsports-2018-099553. PMID: 30018122. Epub 2018 Jul 17. [Note: Delayed posting in PubMed—Not previously listed in RAC Research Alerts.]

The evidence-based practice (EBP) model hierarchically organises scientific information by level, from lowly case studies to lofty systematic reviews and clinical trials. Clinical trials best influence recommendations because they putatively have the greatest internal validity.[1] This assumption is based on sound research ethics, such as scientific competence and good faith actors, as well as observed differences in outcomes. An EBP blind spot emerges when fundamental assumptions are unmet. Based on findings of a 2018 PEDro evidence summary in *BJSM*[2] and elsewhere,[3] it now seems clear that scientific research in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) resides in a blind spot.

[View full text of this editorial in the British Journal of Sports Medicine.]

HEADACHE and MIGRAINE

Evaluation of Cardiovascular Outcomes in Adult Patients With Episodic or Chronic Migraine Treated With Galcanezumab: Data From Three Phase 3, Randomized, Double-Blind, Placebo-Controlled EVOLVE-1, EVOLVE-2, and REGAIN Studies.

Oakes TM[1], Kovacs R[2], Rosen N[3], Doty E[1], Kemmer P[1], Aurora SK[1], Camporeale A[1].

Study eval 2886 pts--Headache. **2019 Nov 13**. doi: 10.1111/head.13684. PMID: 31721185. [Epub ahead of print]

OBJECTIVE: Blood pressure (BP), pulse, electrocardiogram (ECG), and clinical cardiovascular (CV) outcomes in patients with episodic or chronic migraine treated for up to 6 months with galcanezumab compared to placebo were evaluated.

BACKGROUND: Calcitonin gene-related peptide, a potent microvascular vasodilator, has a hypothesized protective role in CV health. Increased CV risks have been reported in patients with migraine.

METHODS: In 2 similarly designed episodic migraine 6-month studies and 1 chronic migraine 3-month study, data from patients randomized (1:1:2) to subcutaneous injection of galcanezumab 120 mg/month (following initial 240 mg loading dose) or 240 mg/month or placebo were pooled. Treatment comparisons for cardiovascular treatment-emergent adverse events (CV TEAE) and categorical and mean changes in BP, pulse, and ECG were evaluated using the Cochran-Mantel-Haenszel test. Mean changes from baseline in BP, pulse, and ECG were evaluated using the analysis of covariance model.

RESULTS: Overall, among galcanezumab 120 mg (n = 705) and 240 mg (n = 730), and placebo (n = 1451) groups, the percentage of patients reporting ≥1 CV TEAE was low and was similar between the galcanezumab 120 mg (2.6%; odds ratio [OR] = 0.9; 95% confidence interval [CI]: 0.5,1.5) and galcanezumab 240 mg (3.3%; OR = 1.1; 95% CI: 0.7,1.9), and placebo (2.9%) groups. The frequency of any individual CV TEAE, broad or narrow term, was ≤1.4%. The CV-related serious adverse events that occurred in the galcanezumab 240 mg group (n = 3; acute myocardial infarction, pulmonary embolism, and transient ischemic attack) and placebo group (n = 3; pulmonary embolism, deep vein thrombosis, and myocardial infarction) were not considered treatment related. Four placebo- and 1 galcanezumab-treated patient discontinued due to a CV TEAE. Least squares mean and categorical changes from baseline in BP, pulse, and QT interval corrected using Fridericia's correction were similar across treatment groups.

CONCLUSIONS: In this 6-month treatment trial, the percentages of galcanezumab- and placebo-treated patients that reported CV TEAEs or serious adverse events were low and similar between groups with few discontinuations. Thus, no clinically meaningful treatment group differences were observed for changes in BP, pulse, or ECG parameters. Additional longer-term studies in a broader and larger cohort are required to better characterize CV safety.

HEADACHE and MIGRAINE (Continued)

Effects of Botulinum Toxin on Migraine Attack Features in Chronic Migraine: A Six-Month Open-Label Observation Study through Electronic Diary Smartphone Application.

Santoro A[1], Delussi M[2], Leone M[1], Miscio AM[1], De Rocco L[3], Leo G[3], De Tommaso M[2].

Study 34 pts, 707 migraines--Toxins (Basel). **2019 Nov 15**;11(11). pii: E668. doi: 10.3390/toxins11110668. PMID: 31731628.

OnobotulintoxinA (OBT-A) is a treatment option for Chronic Migraine (CM). It works on central sensitization and pain but its mode of action is still unknown. To observe how OBT-A treatment works on single migraine attacks, this paper covers an over-6-month observation period through self-reported smartphone application data. This was an observational, open-label cohort study conducted on 34 CM patients under OBT-A treatment, selected between December 2016 and December 2017, who agreed to download a smartphone headache diary application (Aid Diary) according to the study instructions. The analysis was conducted using the smartphone application data reports on allodynia, intensity and extension of pain, and vegetative symptoms. We analysed a total of 707 records of single migraine attacks reported by compliant users (n = 34) in real-time. OBT-A significantly reduced allodynia, the number of vegetative symptoms, pain extension and intensity in single migraine attacks. Pain intensity was correlated with pain extension. In single migraine attacks, OBT-A improved symptoms of central sensitization. This action could be exerted by modulating nociceptive transmission and reducing the burden of single migraine episodes and improving the overall quality of life.

CHRONIC PAIN

Mindfulness Training and Yoga for the Management of Chronic Non-malignant Pain: A Review of Clinical Effectiveness and Cost-effectiveness [Internet].

Editors: Lachance CC, McCormack S.

Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; **2019 Sep**. CADTH Rapid Response Reports. PMID: 31725209.

Chronic pain involves persistent or recurrent pain lasting longer than three months.[1] It is a global health issue that is common in both developed and developing countries.[2] For example, nearly one in four Canadian adults has a chronic pain condition.[3,4] Medications, such as opioids, are frequently prescribed for patients experiencing chronic non-malignant (i.e., non-cancer) pain to alleviate their symptoms. Given the side effects of their use (e.g., nausea, constipation, respiratory depression), potential for addiction and misuse, and uncertainty in their long-term effectiveness for treating chronic non-malignant pain, alternative strategies should be explored.[5] Complementary and alternative medicine therapies, such as mindfulness training and yoga, are potential treatment options for individuals who have chronic non-malignant pain.[6,7] Mindfulness is defined as the intentional and non-judgmental conscious awareness of the present moment.[7] Yoga is a mind-body practice with three main components: physical poses/postures, breathing control, and meditation/relaxation.[8] Most recently, two CADTH Rapid Response reports examined the clinical effectiveness, cost-effectiveness, and evidence-based guidelines regarding the use of mindfulness training (published in June 2019)[9] and yoga (published in July 2019)[10] for chronic pain management in adults. The report on mindfulness found insufficient evidence to draw conclusions about its potential clinical effectiveness.[9] The report on yoga found evidence from one randomized study suggesting that yoga plus conventional treatment with analgesics was effective for reducing chronic pelvic pain, while conventional treatment with analgesics alone was not.[10] No economic evaluations were identified in either report.[9,10] Notably, both reviews focused on comparing mindfulness or yoga with or without pharmacotherapy to pharmacotherapy alone (e.g., opioids, nonsteroidal anti-inflammatory drugs, acetaminophen).[9,10] To inform policy decisions, further exploration of mindfulness or yoga compared with no treatment may provide additional insight on the clinical and cost-effectiveness of these complementary and alternative medicine therapies for management of chronic non-malignant pain. The aim of this report is to summarize the evidence regarding both the clinical effectiveness and cost-effectiveness of the use of mindfulness training or yoga for the management of chronic non-malignant pain.

CHRONIC PAIN (Continued)

An Association of Serotonin with Pain Disorders and Its Modulation by Estrogens.

Paredes S[1], Cantillo S[1], Candido KD[1,2,3], Knezevic NN[1,2,3].

Int J Mol Sci. **2019 Nov 15**;20(22). pii: E5729. doi: 10.3390/ijms20225729. PMID: 31731606.

Ovarian hormones play an important role in pain perception, and are responsible, at least in part, for the pain threshold differences between the sexes. Modulation of pain and its perception are mediated by neurochemical changes in several pathways, affecting both the central and peripheral nervous systems. One of the most studied neurotransmitters related to pain disorders is serotonin. Estrogen can modify serotonin synthesis and metabolism, promoting a general increase in its tonic effects. Studies evaluating the relationship between serotonin and disorders such as irritable bowel syndrome, fibromyalgia, migraine, and other types of headache suggest a clear impact of this neurotransmitter, thereby increasing the interest in serotonin as a possible future therapeutic target. This literature review describes the importance of substances such as serotonin and ovarian hormones in pain perception and illustrates the relationship between those two, and their direct influence on the presentation of the aforementioned pain-related conditions. Additionally, we review the pathways and receptors implicated in each disorder. Finally, the objective was to stimulate future pharmacological research to experimentally evaluate the potential of serotonin modulators and ovarian hormones as therapeutic agents to regulate pain in specific subpopulations.

Role of the immune system in neuropathic pain.

Malcangio M[1].

Scand J Pain. **2019 Nov 14**. pii: /j/sjpain.ahead-of-print/sjpain-2019-0138/sjpain-2019-0138.xml. doi: 10.1515/sjpain-2019-0138. PMID: 31730538.

Background: Acute pain is a warning mechanism that exists to prevent tissue damage, however pain can outlast its protective purpose and persist beyond injury, becoming chronic. Chronic Pain is maladaptive and needs addressing as available medicines are only partially effective and cause severe side effects. There are profound differences between acute and chronic pain. Dramatic changes occur in both peripheral and central pathways resulting in the pain system being sensitised, thereby leading to exaggerated responses to noxious stimuli (hyperalgesia) and responses to non-noxious stimuli (allodynia). **Critical role for immune system cells in chronic pain:** Preclinical models of neuropathic pain provide evidence for a critical mechanistic role for immune cells in the chronicity of pain. Importantly, human imaging studies are consistent with preclinical findings, with glial activation evident in the brain of patients experiencing chronic pain. Indeed, immune cells are no longer considered to be passive bystanders in the nervous system; a consensus is emerging that, through their communication with neurons, they can both propagate and maintain disease states, including neuropathic pain. The focus of this review is on the plastic changes that occur under neuropathic pain conditions at the site of nerve injury, the dorsal root ganglia (DRG) and the dorsal horn of the spinal cord. At these sites both endothelial damage and increased neuronal activity result in recruitment of monocytes/macrophages (peripherally) and activation of microglia (centrally), which release mediators that lead to sensitisation of neurons thereby enabling positive feedback that sustains chronic pain. **Immune system reactions to peripheral nerve injuries**: At the site of peripheral nerve injury following chemotherapy treatment for cancer for example, the occurrence of endothelial activation results in recruitment of CX3C chemokine receptor 1 (CX3CR1)-expressing monocytes/macrophages, which sensitise nociceptive neurons through the release of reactive oxygen species (ROS) that activate transient receptor potential ankyrin 1 (TRPA1) channels to evoke a pain response. In the DRG, neuro-immune cross talk following peripheral nerve injury is accomplished through the release of extracellular vesicles by neurons, which are engulfed by nearby macrophages. These vesicles deliver several determinants including microRNAs (miRs), with the potential to afford long-term alterations in macrophages that impact pain mechanisms. On one hand the delivery of neuron-derived miR-21 to macrophages for example, polarises these cells towards a pro-inflammatory/pro-nociceptive phenotype; on the other hand, silencing miR-21 expression in sensory neurons prevents both development of neuropathic allodynia and recruitment of macrophages in the DRG. **Immune system mechanisms in the central nervous system**: In the dorsal horn of the spinal cord, growing evidence over the last two decades has delineated signalling pathways that mediate neuron-microglia communication such as P2X4/BDNF/GABAA, P2X7/Cathepsin S/Fractalkine/CX3CR1, and CSF-1/CSF-1R/DAP12 pathway-dependent mechanisms. **Conclusions and implications**: Definition of the modalities by which neuron and immune cells communicate at different locations of the pain pathway under neuropathic pain states constitutes innovative biology that takes the pain field in a different direction and provides opportunities for novel approaches for the treatment of chronic pain.

IRRITABLE BOWEL SYNDROME

Lactobacillus plantarum PS128 Ameliorated Visceral Hypersensitivity in Rats Through the Gut-Brain Axis.

Liu YW[1,2], Wang YP[3,4,5], Yen HF[1], Liu PY[4], Tzeng WJ[1], Tsai CF[5,6], Lin HC[5,7], Lee FY[5,7], Jeng OJ[8], Lu CL[9,10,11,12], Tsai YC[13,14].

Probiotics Antimicrob Proteins. **2019 Nov 5**. doi: 10.1007/s12602-019-09595-w. PMID: 31691208. [Epub ahead of print]

Irritable bowel syndrome (IBS) is a common functional gastrointestinal disorder characterized by abdominal pain and alterations in bowel habits. Current treatments for IBS are unsatisfactory due to its multifactorial pathogenesis involving the microbiota-gut-brain axis. Lactobacillus plantarum PS128 (PS128) was reported to exhibit neuromodulatory activity which may be beneficial for improving IBS. This study aimed to investigate the effect of PS128 on visceral hypersensitivity (VH) and the gut-brain axis using a 5-hydroxytryptophan (5-HTP)-induced VH rat model without colonic inflammation induction, mimicking the characteristics of IBS. Male Sprague-Dawley rats were administered with PS128 (10^9 CFU in 0.2 mL saline/rat/day) or saline (0.2 mL saline/rat/day) for 14 days. Colorectal distension (CRD) with simultaneous electromyography recording was performed 30 min before and 30 min after the 5-HTP injection. Levels of neuropeptides and neurotrophins were analyzed. PS128 significantly reduced VH induced by the 5-HTP injection and CRD. Neurotransmitter protein levels, substance P, CGRP, BDNF, and NGF, were decreased in the dorsal root ganglion but increased in the spinal cord in response to the 5-HTP injection; PS128 reversed these changes. The hypothalamic-pituitary-adrenal axis was modulated by PS128 with decreased corticosterone concentration in serum and the expression of mineralocorticoid receptors in the amygdala. Oral administration of PS128 inhibited 5-HTP-induced VH during CRD. The ameliorative effect on VH suggests the potential application of PS128 for IBS.

OTHER RESEARCH OF INTEREST

Military Sexual Trauma in Older Women Veterans: Prevalence and Comorbidities.

Gibson CJ[1,2], Maguen S[3,4], Xia F[5], Barnes DE[3,4,6], Peltz CB[5], Yaffe K[3,4,6,7].

J Gen Intern Med. **2019 Nov 11**. doi: 10.1007/s11606-019-05342-7. PMID: 31713042. [Epub ahead of print]

BACKGROUND: Recent attention has highlighted the common occurrence and health consequences of military sexual trauma (MST) in younger women veterans. However, almost nothing is known about MST in older veterans.

OBJECTIVE: To describe MST among older women veterans, including prevalence and common comorbidities.

DESIGN: Cross-sectional observational study, using data from national Department of Veterans Affairs medical records.

PARTICIPANTS: Population-based sample of women Veterans aged 55+ with at least one documented MST screen response and at least one clinical encounter in fiscal years 2005-2015.

MAIN MEASURES: MST screen: medical diagnoses (diabetes, hypertension, hyperlipidemia, myocardial infarction, cerebrovascular disease, congestive heart failure, obesity, chronic pain conditions, back pain, dementia, insomnia, sleep apnea, menopause symptoms) and mental health diagnoses (anxiety, depression, posttraumatic stress disorder, tobacco use, alcohol use disorder, substance use disorder, opioid use disorder, suicidal ideation) from International Classification of Diseases, Ninth Revision Clinical Modification codes in the medical record.

KEY RESULTS: In this cohort of older women veterans (n = 70,864, mean age 65.8 ± 10.4 years), 13% had a positive MST screen. In multivariable regression analyses adjusted for age, race/ethnicity, and marital status, MST was strongly associated with most mental health diagnoses, particularly posttraumatic stress disorder (OR 7.25, 95% CI 6.84-7.68), depression (OR 2.39, 95% CI 2.28-2.50), and suicidal ideation (OR 2.42, 95% CI 2.08-2.82). MST was also associated with multiple medical conditions, particularly sleep disorders (insomnia OR 1.61, 95% CI 1.43-1.82; sleep apnea OR 1.48, 95% CI 1.37-1.61) and pain (chronic pain OR 1.58, 95% CI 1.50-1.67; back pain OR 1.40, 95% CI 1.34-1.47).

CONCLUSIONS: A history of MST is common among older women veterans and associated with a range of medical and mental health diagnoses. These findings call attention to the need for additional research in this understudied population, and the importance of trauma-informed care approaches for women across the lifespan.

OTHER RESEARCH OF INTEREST (Continued)

Heritability of the fibromyalgia phenotype varies by age.

Dutta D[1], Brummett CM[2,3], Moser SE[2], Fritsche LG[4,5], Tsodikov A[4], Lee S[4,5], Clauw DJ[2,6], Scott LJ[4,5].

Arthritis Rheumatol. **2019 Nov 17**. doi: 10.1002/art.41171. PMID: 31736264. [Epub ahead of print]

OBJECTIVES: Many studies suggest a strong familial component to fibromyalgia (FM). However, these studies have nearly all been confined to individuals with "primary" FM, i.e. FM without any other accompanying disorder. The current 2011-16 criteria for diagnosing FM construct a score using a combination of the number of painful body sites and the severity of somatic symptoms (FM-score). We estimated the genetic heritability of FM-score across sex and age groups to identify subgroups of individuals with greater heritability, which may help in the design of future genetic studies.

METHODS: We collected data on 26,749 individuals of European ancestry undergoing elective surgery at the University of Michigan (Michigan Genomics Initiative study, MGI). We estimated the SNP-based heritability of FM-score by age and sex categories using genome-wide association study (GWAS) data and a linear mixed model.

RESULTS: Overall, FM-score had an estimated heritability of 13.9% (SE=2.9%). Estimated FM-score heritability was highest in individuals ≤ 50 years of age (23.5%; SE=7.9%) and lowest in individuals >60 years (7.3%; SE=8.1%). These patterns remained the same when we analyzed FM as a case-control phenotype. Even through women had approximately 30% higher average FM-score than males across age categories, FM-score heritability did not differ significantly by sex.

CONCLUSION: Younger individuals appear to have a much stronger genetic component to the FM-score than older individuals. Older individuals may be more likely to have what previously had been called "secondary FM." Regardless of the cause, these results have implications for future genetic studies of FM and associated conditions.

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