GULF WAR ILLNESS

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

CHRONIC FATIGUE SYNDROME

Autonomic dysfunction in myalgic encephalomyelitis and chronic fatigue syndrome: comparing self-report and objective measures.

Kemp J[1], Sunnquist M[2], Jason LA[1], Newton JL[3] .

Clin Auton Res. **2019 May 21**. doi: 10.1007/s10286-019-00615-x. PMID: 31115729. [Epub ahead of print]

Letter to the Editor:

Myalgic encephalomyelitis (ME) and chronic fatigue syndrome (CFS) have debilitating impacts on affected individuals. Core symptoms include post-exertional malaise, neurocognitive challenges, and sleep dysfunction [1]. Additionally, a significant minority of patients experience autonomic symptoms, including orthostatic intolerance, gastrointestinal disturbances, and circulation issues [2].

Several case definitions for ME and CFS require the presence of autonomic dysfunction for diagnosis [2], while other researchers have proposed an “autonomic dysfunction” subtype of ME and CFS [3]. Identifying the appropriate measures of autonomic symptomatology for individuals with ME and CFS will further contribute to understanding the role of the autonomic system in this illness.

Heart rate variability (HRV), a measure of the variation in time between heart beats, has been utilized as an objective measurement of autonomic functioning in ME and CFS research, and some researchers have suggested that HRV could be utilized as a “potential bedside diagnostic tool” for ME and CFS [4]. HRV can be divided into two major components, the low-frequency (LF) component, indicative of sympathetic dominance, and the high-frequency (HF) component, indicative of parasympathetic dominance. In addition, the LF to HF ratio is considered to be an indicator of sympatho-vagal balance [5].

As objective measures can be costly and time-intensive, some researchers utilize self-report measures of autonomic symptoms. Previous research has compared results from the self-report Composite Autonomic Symptom Scale (COMPASS) [6] and HRV and found a significant negative correlation between LF-HRV and COMPASS scores [7]. The aim of the study reported here was to extend upon this body of literature by examining the association between HRV and autonomic items from another self-report measure, the DePaul Symptom Questionnaire (DSQ) [8].

[Full text with references for this editorial excerpt continues in Clinical Autonomic Research.]

HEADACHE and MIGRAINE

Early onset of effect of onabotulinumtoxinA for chronic migraine treatment: Analysis of PREEMPT data.

Dodick DW[1], Silberstein SD[2], Lipton RB[3], DeGryse RE[4] , Adams AM[4], Diener HC[5].

Cephalalgia. **2019 May 21**:333102418825382. doi: 10.1177/0333102418825382. PMID: 31112399. [Epub ahead of print]

BACKGROUND: The Phase 3 REsearch Evaluating Migraine Prophylaxis Therapy (PREEMPT) trials demonstrated efficacy/tolerability of onabotulinumtoxinA for headache prevention in adults with chronic migraine. This post hoc analysis assessed time of onset of onabotulinumtoxinA after the first treatment in total and responder populations and consistency weekly through five treatment cycles.

METHODS: In the 24-week, double-blind, placebo-controlled phase of PREEMPT, individuals were randomized 1:1 to onabotulinumtoxinA (155-195 U) or placebo every 12 weeks for two cycles. The primary pooled efficacy variable was change in headache days per 28 days at week 24. We assessed change in headache and migraine/probable migraine (hereafter migraine) days/week compared with baseline week 4.

RESULTS: Baseline mean (SD) headache days/week (week 4 of baseline) for onabotulinumtoxinA (n = 688) and placebo (n = 696) were similar (4.8 [1.6] vs. 4.8 [1.6] days/week, respectively), as were migraine days/week (4.6 [1.7] vs. 4.6 [1.7] days/week). The effect of onabotulinumtoxinA on change in headache and migraine days/week was significantly greater than placebo at week 1, persisting from week 3 after the first treatment (-1.6 [2.2] vs. -1.1 [2.2] headache days/week [$p < 0.001$] and -1.6 [2.2] vs. -1.1 [2.2] migraine days/week [$p < 0.001$]). Headache and migraine days decreased in onabotulinumtoxinA responders beginning 1 week after treatment 1.

CONCLUSIONS: Treatment with onabotulinumtoxinA is associated with significant reductions in headache and migraine days/week at week 1, persisting after week 3, compared with placebo. Combined with earlier reports showing onabotulinumtoxinA treatment results in a persistent and progressive reduction in headache days over 56 weeks, it is suggested peak benefit may require multiple treatments.

TRIAL REGISTRATION NUMBER: **ClinicalTrials.gov**: **NCT00156910** and **NCT00168428**.

CHRONIC PAIN

Percutaneous Peripheral Nerve Stimulation for the Treatment of Chronic Pain Following Amputation.

Cohen SP[1], Gilmore CA[2], Rauck RL[2], Lester DD[3], Trainer RJ[3], Phan T[3], Kapural L[2], North JM[2], Crosby ND[4], Boggs JW[4].

Mil Med. **2019 May 21**. pii: usz114. doi: 10.1093/milmed/usz114. PMID: 31111898. [Epub ahead of print]

INTRODUCTION: Chronic pain and reduced function are significant problems for Military Service members and Veterans following amputation. Peripheral nerve stimulation (PNS) is a promising therapy, but PNS systems have traditionally been limited by invasiveness and complications. Recently, a novel percutaneous PNS system was developed to reduce the risk of complications and enable delivery of stimulation without surgery.

MATERIALS AND METHODS: Percutaneous PNS was evaluated to determine if stimulation provides relief from residual and phantom limb pain following lower-extremity amputation. PNS leads were implanted percutaneously to deliver stimulation to the femoral and/or sciatic nerves. Patients received stimulation for up to 60 days followed by withdrawal of the leads.

RESULTS: A review of recent studies and clinical reports found that a majority of patients (18/24, 75%) reported substantial (≥50%) clinically relevant relief of chronic post-amputation pain following up to 60 days of percutaneous PNS. Reductions in pain were frequently associated with reductions in disability and pain interference.

CONCLUSIONS: Percutaneous PNS can durably reduce pain, thereby enabling improvements in quality of life, function, and rehabilitation in individuals with residual or phantom limb pain following amputation. Percutaneous PNS may have additional benefit for Military Service members and Veterans with post-surgical or post-traumatic pain.

CHRONIC PAIN (Continued)

The Relation of Self-Compassion to Functioning among Adults with Chronic Pain.

Edwards KA[1], Pielech M[1], Hickman J[2], Ashworth J[2], Sowden G[2], Vowles KE[1,2].

Eur J Pain. **2019 May 21**. doi: 10.1002/ejp.1429. PMID: 31115099. [Epub ahead of print]

Previous research has shown that self-compassion is associated with improved functioning and health outcomes among multiple chronic illnesses. However, the role of self-compassion in chronic pain-related functioning is understudied. The present study sought to understand the association between self-compassion and important measures of functioning within a sample of patients with chronic pain. Treatment-seeking individuals (N= 343 with chronic pain) that were mostly White (97.9%) and female (71%) completed a battery of assessments that included the Self-Compassion Scale (SCS), as well as measures of pain-related fear, depression, disability, pain acceptance, success in valued activity, and use of pain coping strategies. Cross-sectional multiple regression analyses that controlled for age, sex, pain intensity, and pain duration, revealed that self-compassion accounted for a significant and unique amount of variance in all measures of functioning (r^2 range: .07 - .32, all $p < .001$). Beta weights indicated that higher self-compassion was associated with lower pain-related fear, depression, and disability, as well as greater pain acceptance, success in valued activities, and utilization of pain coping strategies. These findings suggest that self-compassion may be a relevant adaptive process in those with chronic pain. Targeted interventions to improve self-compassion in those with chronic pain may be useful. SIGNIFICANCE: Self-compassion is associated with better functioning across multiple general and pain-specific outcomes, with the strongest associations among measures related to psychological functioning and valued living. These findings indicate that self-compassion may be an adaptive process that could minimize the negative impact of chronic pain on important areas of life.

IRRITABLE BOWEL SYNDROME

The Role of Dietary Energy and Macronutrients Intake in Prevalence of Irritable Bowel Syndromes.

Zhang JJ[1], Ma H[1], Zhu JZ[2], Lu C[1], Yu CH[1], Li YM[1].

Biomed Res Int. **2019 May 16**;2019:8967306. doi: 10.1155/2019/8967306. PMCID: PMC6541956. PMID: 3122362.3 eCollection 2019.

Background: Irritable bowel syndrome (IBS) is a chronic gastrointestinal disorder characterized by abdominal pain and altered bowel habits in the absence of any detectable organic illnesses. Interest in the effect of dietary opponents to the IBS pathogenesis has been increased in recent years. This study aims to review previous studies to determine the relationship between IBS prevalence in community and dietary energy and macronutrients intakes according to the national nutrition surveys.

Methods: A literature search was conducted in PubMed and EMBASE to September, 2018, to identify population-based studies that reported the prevalence of IBS. Daily energy intake, daily carbohydrates, and protein and fat percent contribution to energy intake (%) were obtained from study population-based national nutrition survey. The correlations of prevalence of IBS and dietary intakes were obtained by Spearman coefficient or Pearson coefficient.

Results: Global prevalence of IBS was 11.7%. There was no correlation between overall prevalence of IBS of individual countries and national energy intake (P = 0.785), protein proportion (P = 0.063), carbohydrates proportion (P = 0.505), or fat proportion (P = 0.384) according to the years when the studies were conducted. No correlations were detected between dietary intake and male or female IBS prevalence. Interestingly, protein proportion was positively correlated with the prevalence of IBS in Rome III criteria (r = 0.569).

Conclusion: Our findings demonstrate that dietary energy and macronutrients intake do not play a direct role in prevalence of IBS. However, IBS diagnostic criteria seem to have a bias on the correlation between prevalence of IBS and dietary intake. Further studies are needed to confirm the correlation between prevalence of IBS and specific dietary intake.

IRRITABLE BOWEL SYNDROME (Continued)

Emerging evidence that irritable bowel syndrome & functional dyspepsia are microbial diseases.

Talley NJ[1], Walker MM[2].

Indian J Med Res. **2019 Apr**;149(4):437-440. doi: 10.4103/ijmr.IJMR_84_19. PMCID: PMC6676832. PMID: 31411166.

Conventionally, functional gastrointestinal disorders (FGIDs) as classified by the Rome IV Criteria refer to a group of chronic conditions categorized by gut symptoms that arise via multiple pathophysiological processes, conceptualized as disorders of gut-brain interactions[1]. Gastrointestinal (GI) symptoms in inflammatory bowel disease and gastric or colon cancer also arise through gut-brain interactions (no brain, no pain), so in this sense, FGIDs are not unique. Gut pathology is considered to be absent in the FGIDs, and the underlying aetiology is accepted to be unknown[1]. However, emerging evidence is challenging the current paradigm there is no pathology and no known aetiology. In particular, a microbial pathogenesis may be more important than has been previously appreciated. While there are 33 adult and 20 paediatric FGIDs classified in Rome IV[1], among the most prevalent are the irritable bowel syndrome (IBS), characterized by abdominal pain, bowel dysfunction and often bloating and functional dyspepsia (FD), characterized by early satiety, postprandial fullness or epigastric pain[2,3]. Here we discuss the emerging evidence that microbes and inflammation play an aetiopathogenic role in IBS and FD.

Psychological co-morbidity is common in FGIDs; however, the available evidence confirms that this association is largely not explained by healthcare-seeking behaviour but instead is an intimate characteristic of the disorder in a majority of cases[4]. Recently, prospective epidemiological studies have suggested that about 50 per cent of patients with an FGID have a brain-gut-driven condition, where psychological symptoms are followed at a later time by the new onset of gut symptoms, suggesting that there may be a more dominant brain to gut pathway[5]. On the other hand, in the remaining 50 per cent of cases, gut symptoms begin first followed by new-onset psychological alterations, indicating a gut-to-brain-driven disease process rather than a primary brain disorder[5]. This is further supported by a strong link between immune activation (*e.g.* through increased tumour necrosis factor alpha levels) and the severity of psychological co-morbidities present in these disorders[2,3,5,6]. If the gut is key to the onset of many with FGIDs, identifying the disease pathways may permit treatments that target cure rather than present management which is directed at symptom control, as the gut is more accessible than the brain and the gut microenvironment can be locally manipulated….

[Full text with figures and references for this article excerpt continues in the Indian Journal of Medical Research.]

OTHER RESEARCH OF INTEREST

The Department of Defense Birth and Infant Health Research Program: Assessing the Reproductive Health of U.S. Active-Duty Women.

Khodr ZG[1,2], Bukowinski AT[1,2], Hall C[1,2], Gumbs GR[1,2], Wells NY[2], Conlin AMS[1,2].

Semin Reprod Med. 2018 Nov;36(6):351-360. doi: 10.1055/s-0039-1678751. PMID: 31003250. **Epub 2019 Apr 19**.

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

As the percentage of women serving in the active-duty military continues to grow, and as their roles continue to expand, the importance of monitoring reproductive health in the military community increases. The Department of Defense Birth and Infant Health Research (BIHR) program conducts ongoing epidemiologic studies to assess potential increased risks for adverse reproductive and infant health outcomes in the military population. Military personnel endure unique physical and mental demands as a part of their occupational duties (e.g., extensive preventive care, numerous trainings, and deployments), which require special consideration as parental exposures in reproductive health research that cannot be well assessed in the general population. From 2003 to 2014, the BIHR program captured 250,604 pregnancies among approximately 2.4 million active-duty women of reproductive age when limited to non-cadet Army, Air Force, Navy, and Marine Corps personnel. Approximately 15,000 live births occurred each year, and the live birth rate ranged from 76.9 per 1,000 in 2003 to 71.0 per 1,000 in 2014. Safety of military-unique preventive measures, environmental exposures, and occupational hazards in pregnancy are summarized herein. Reproductive health is important to our service members and their families, and optimizing the health of military families ultimately contributes to force readiness.

OTHER RESEARCH OF INTEREST (Continued)

Impact of Deployment on Reproductive Health in U.S. Active-Duty Servicewomen and Veterans.

Gawron LM[1,2], Mohanty AF[1,3], Kaiser JE[2], Gundlapalli AV[1,3,4].

Semin Reprod Med. 2018 Nov;36(6):361-370. doi: 10.1055/s-0039-1678749. PMCID: PMC6597167. PMID: 31003251. **Epub 2019 Apr 19**.

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

Reproductive-age women are a fast-growing component of active-duty military personnel who experience deployment and combat more frequently than previous service-era women Veterans. With the expansion of the number of women and their roles, the United States Departments of Defense and Veterans Affairs have prioritized development and integration of reproductive services into their health systems. Thus, understanding associations between deployments or combat exposures and short- or long-term adverse reproductive health outcomes is imperative for policy and programmatic development. Servicewomen and women Veterans may access reproductive services across civilian and military or Veteran systems and providers, increasing the need for awareness and communication regarding deployment experiences with a broad array of providers. An example is the high prevalence of military sexual trauma reported by women Veterans and the associated mental health diagnoses that may lead to a lifetime of high risk-coping behaviors that increase reproductive health risks, such as sexually transmitted infections, unintended pregnancies, and others. Care coordination models that integrate reproductive healthcare needs, especially during vulnerable times such as at the time of military separation and in the immediate postdeployment phase, may identify risk factors for early intervention with the potential to mitigate lifelong risks.

Associations Between Trauma-Related Rumination and Symptoms of Posttraumatic Stress and Depression in Treatment-Seeking Female Veterans.

Arditte Hall KA[1,2,3], Davison EH[1,2,3], Galovski TE[1,2,3], Vasterling JJ[1,2,3], Pineles SL[1,2,3].

J Trauma Stress. **2019 Apr**;32(2):260-268. doi: 10.1002/jts.22385. PMID: 31009555.

Trauma-related rumination is a cognitive style characterized by repetitive negative thinking about the causes, consequences, and implications of a traumatic experience. Frequent trauma-related rumination has been linked to posttraumatic stress disorder (PTSD) and depression in civilian samples but has yet to be examined among military veterans. This study extended previous research by examining trauma-related rumination in female veterans who presented to a Veterans Affairs women's trauma recovery clinic (N = 91). The study had two main aims: (a) to examine associations between trauma-related rumination and specific PTSD symptoms, adjusting for the overlap between trauma-related rumination and other relevant cognitive factors, such as intrusive trauma memories and self-blame cognitions; and (b) to assess associations between trauma-related rumination, PTSD, and depression, adjusting for symptom comorbidity. At intake, patients completed a semistructured interview and self-report questionnaires. Primary diagnoses were confirmed via medical record review. Trauma-related rumination was common, with more than 80% of patients reporting at least sometimes engaging in this cognitive style in the past week. After adjusting for other relevant cognitive factors, trauma-related rumination was significantly associated with several specific PTSD symptoms, r_p s = .33-.48. Additionally, the severity of trauma-related rumination was associated with overall PTSD symptom severity, even after adjusting for comorbid depression symptoms, r_p^2 = .35. In contrast, the association between trauma-related rumination and depressive symptom severity was not significant after adjusting for comorbid PTSD symptoms, r_p^2 = .008. These results highlight trauma-related rumination as a unique contributing factor to the complex clinical presentation for a subset of trauma-exposed veterans.

OTHER RESEARCH OF INTEREST (Continued)

Lower Sexual Satisfaction and Function Mediate the Association of Assault Military Sexual Trauma and Relationship Satisfaction in Partnered Female Service Members/Veterans.

Blais RK[1].

Fam Process. **2019 Apr 30**. doi: 10.1111/famp.12449. PMID: 31041829. [Epub ahead of print]

Little is known about the association of military sexual trauma (MST) and relationship satisfaction among partnered female service members/veterans (SM/Vs). Extant civilian literature shows a strong association between sexual trauma and poorer relationship outcomes, and theory suggests that sexual function and satisfaction may mediate this association. Given that as many as 40% of female SM/Vs report MST and roughly half of female veterans are partnered and in their peak sexual years, it is critical to understand the association of MST, relationship satisfaction, sexual function, and sexual satisfaction in this population. Female SM/Vs (N = 817) completed a demographic inventory, self-report measures of MST, relationship satisfaction, sexual function, and sexual satisfaction. One hundred fifty-one (18.48%) participants did not experience MST. Three hundred eighty-eight (47.49%) reported that they experienced harassment-only MST, and 278 (34.03%) reported assault MST. At the bivariate level, lower relationship satisfaction was associated with lower sexual function and satisfaction with large effect sizes. Assault MST was associated with lower relationship satisfaction and sexual function and satisfaction with small-to-medium effect sizes. No differences in relationship satisfaction, sexual satisfaction, and function between those with harassment-only and no MST were observed. Mediation analyses demonstrated that lower sexual function and satisfaction mediated the association of assault MST and relationship satisfaction. Couples' therapy offered to SM/Vs with MST should screen for type of MST, sexual function, and satisfaction. Addressing the sequelae of MST and increasing sexual function and satisfaction in these partnerships may be critical treatment targets.

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