GULF WAR ILLNESS

Autoimmune/inflammatory syndrome induced by mineral oil: a health problem.

Vera-Lastra O[1,2], Medina G[3,4], Cruz-Domínguez MP[3,4], Ramírez GM[5], Blancas RBP[5], Amaro ALP[3,4], Martínez AV[5], Delgado JS[6], Jara LJ[3,4].

Clin Rheumatol. **2018 Apr 4**. doi: 10.1007/s10067-018-4078-2. [Epub ahead of print]

Autoimmune/inflammatory syndrome induced by adjuvant (ASIA) includes the following conditions: siliconosis, Gulf War syndrome, macrophagic myofasciitis syndrome, and post-vaccination phenomena. Afterward, other syndromes have been recognized, such as in ASIA by mineral oil (ASIA-MO). These conditions are triggered by adjuvants and they are the result of the interplay of genetic and environmental factors. ASIA-MO is defined as the infiltration of oily type modeling substances for cosmetic purposes. It has been reported in many countries and used surreptitiously. Pathogenesis of ASIA-MO is not clear, but is characterized by chronic granulomatous inflammation, like the pristane model in mice, with increase of proinflammatory cytokines: type I interferons (IFNα and IFNß), systemic lupus erythematosus (SLE), and erosive arthritis. In humans, an increase of interleukin 1 (IL-1) has been found. Clinical spectrum of ASIA-MO is heterogeneous, varying from mild to severe and being local and systemic. The systemic manifestations can be non-specific and specific, meeting criteria for any autoimmune disease (AID), i.e., SLE, rheumatoid arthritis, and systemic sclerosis, among others. The areas of the body where the mineral oil is mostly applied include the following: buttocks (38-72%), breasts (12-16%), lower extremities (18-22%), and face (6-10%). The penis augmentation is also common. Treatment is focused on local and systemic manifestations and requires medical and surgical management representing a challenge for the physician.

CHRONIC FATIGUE SYNDROME

Circulating extracellular vesicles as potential biomarkers in chronic fatigue syndrome/myalgic encephalomyelitis: an exploratory pilot study.

Castro-Marrero J[1], Serrano-Pertierra E[2], Oliveira-Rodríguez M[2], Zaragozá MC[1,3], Martínez-Martínez A[1], Blanco-López MDC[2], Alegre J[1].

J Extracell Vesicles. **2018 Mar 22**;7(1):1453730. doi: 10.1080/20013078.2018.1453730. PMCID: PMC5912186. eCollection 2018.

Chronic Fatigue Syndrome (CFS), also known as Myalgic Encephalomyelitis (ME) is an acquired, complex and multisystem condition of unknown etiology, no established diagnostic lab tests and no universally FDA-approved drugs for treatment. CFS/ME is characterised by unexplicable disabling fatigue and is often also associated with numerous core symptoms. A growing body of evidence suggests that extracellular vesicles (EVs) play a role in cell-to-cell communication, and are involved in both physiological and pathological processes. To date, no data on EV biology in CFS/ME are as yet available. The aim of this study was to isolate and characterise blood-derived EVs in CFS/ME. Blood samples were collected from 10 Spanish CFS/ME patients and 5 matched healthy controls (HCs), and EVs were isolated from the serum using a polymer-based method. Their protein cargo, size distribution and concentration were measured by Western blot and nanoparticle tracking analysis. Furthermore, EVs were detected using a lateral flow immunoassay based on biomarkers CD9 and CD63. We found that the amount of EV-enriched fraction was significantly higher in CFS/ME subjects than in HCs ($p = 0.007$) and that EVs were significantly smaller in CFS/ME patients ($p = 0.014$). Circulating EVs could be an emerging tool for biomedical research in CFS/ME. These findings provide preliminary evidence that blood-derived EVs may distinguish CFS/ME patients from HCs. This will allow offer new opportunities and also may open a new door to identifying novel potential biomarkers and therapeutic approaches for the condition.

CHRONIC FATIGUE SYNDROME (Continued)

Integration of DNA methylation & health scores identifies subtypes in myalgic encephalomyelitis/chronic fatigue syndrome.

de Vega WC[1,2], Erdman L[3,4], Vernon SD[5], Goldenberg A[3,4], McGowan PO[1,2,6,7].

Epigenomics. **2018 Apr 25**. doi: 10.2217/epi-2017-0150. PMID: 29692205. [Epub ahead of print]

AIM: To identify subtypes in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) based on DNA methylation profiles and health scores.

METHODS: DNA methylome profiles in immune cells were integrated with symptomatology from 70 women with ME/CFS using similarity network fusion to identify subtypes.

RESULTS: We discovered four ME/CFS subtypes associated with DNA methylation modifications in 1939 CpG sites, three RAND-36 categories and five DePaul Symptom Questionnaire measures. Methylation patterns of immune response genes and differences in physical functioning and postexertional malaise differentiated the subtypes.

CONCLUSION: ME/CFS subtypes are associated with specific DNA methylation differences and health symptomatology and provide additional evidence of the potential relevance of metabolic and immune differences in ME/CFS with respect to specific symptoms.

HEADACHE and MIGRAINE

Improving research through NINDS Headache Common Data Elements.

Oshinsky ML[1], Tanveer S[2]; NINDS Version 2.0 Headache Common Data Elements Working Group.

Cephalalgia. **2018 Jan 1**:333102418773076. doi: 10.1177/0333102418773076. PMID: 29688036. [Epub ahead of print]

To the Editor: Historically, comparing data across studies has been challenging due to variations in data collection tools (1). Headache clinical research has much to gain by accepting and adopting standardized instruments and case report forms.

The updated National Institute of Neurological Disorders and Stroke (NINDS) Headache Common Data Elements (CDE) aim to promote the efficiency of clinical research studies, improve the quality of clinical data, increase the feasibility of data sharing and interoperability, significantly reduce study start-up time and, lastly, support new investigators by providing standardized case report forms and instruments recommendations (2).

The Headache Version 2.0 CDEs include five (5) working group summary documents, 26 Case Report Forms (CRFs), and 41 instrument recommendations. A CDE details report, describing additional information such as definitions, accompanies each CRF. CDE recommendations are classified according to the strength of the recommendation. The four classification categories are as follows: Core, Supplemental-Highly Recommended, Supplemental, and Exploratory (3).

Full text of editorial with references continues on-line in SAGE journals Cephalalgia.

MiR-30a relieves migraine by degrading CALCA.

Zhai Y[1], Zhu YY.

Eur Rev Med Pharmacol Sci. **2018 Apr**;22(7):2022-2028. doi: 10.26355/eurrev_201804_14731. PMID: 29687858.

OBJECTIVE: To investigate both the relationship and underlying mechanism between miR-30a and migraine.

PATIENTS AND METHODS: Peripheral blood samples were collected from migraine patients and healthy people to extract RNA for quantitative Real-time PCR (qRT-PCR). The relationship between mRNA expressions and patient data was analyzed by t-test. Target genes of miR-30a were predicted by the TargetScan. The binding of miR-30a to the target gene was verified by dual fluorescein reporter assay. The protein expression of calcitonin/alpha-CGRP gene (CALCA), the miR-30a target gene, was detected by Western blot.

RESULTS: Expression levels of miR-30a in peripheral blood of migraine patients were significantly lower than those of healthy controls detected by qRT-PCR, and the methylation level of miR-30a in promoter region was remarkably increased. In addition, expression levels of miR-30a were significantly decreased in patients with bilateral seizures, persistent pain and high pain index. CALCA was found to be the target gene of miR-30a via bioinformatics analysis. We verified that miR-30a degrades CALCA by dual-luciferase reporter assay. Western blot results showed that overexpression of miR-30a down-regulated the CALCA expression, and knockdown of miR-30a upregulated the CALCA expression.

CONCLUSIONS: Expression levels of miR-30a are significantly decreased in migraine patients and can relieve migraine through the degradation of CALCA.

CHRONIC PAIN

Pain Intensity, Disability, and Quality of Life in Patients with Chronic Low Back Pain: Does Age Matter?

Wettstein M[1,2], Eich W[1], Bieber C[1], Tesarz J[1].

Pain Med. **2018 Apr 25**. doi: 10.1093/pm/pny062. PMID: 29701812. [Epub ahead of print]

Objective: Nonspecific chronic low back pain (CLBP) is a frequent medical condition among middle-aged and older adults. Its detrimental consequences for functional ability and quality of life are well known. However, less is known about associations of chronological age with disability and well-being among CLBP patients. Coping with pain may be harder with advancing age due to additional age-associated losses of physical, sensory, and other resources, resulting in higher disability and lower quality of life. Alternatively, older patients may feel less impaired and report higher quality of life than younger patients because the experience of chronic pain may be better anticipated and more "normative" in old age.

Methods: We investigated an age-heterogeneous sample of 228 CLBP patients (mean age = 59.1 years, SD = 10.2 years, range 41-82 years). Our outcomes were pain intensity, pain disability (as assessed by self-reported activity restrictions and performance-based tests), and measures of quality of life (health-related quality of life: SF-12 physical and mental health; well-being: anxiety, depression, perceived control over life, affective distress).

Results: Although older patients had higher performance-based disability, they scored higher on mental health and on most measures of well-being than younger patients.

Conclusions: Our findings provide evidence for a "paradoxical" pattern of age effects in CLBP patients and are thus in line with other studies based on nonclinical samples: Although disability in CLBP patients increases with advancing age, indicators of quality of life are equal or even higher in older patients.

A population-based examination of the co-occurrence and functional correlates of chronic pain and generalized anxiety disorder.

Csupak B[1], Sommer JL[2], Jacobsohn E[1], El-Gabalawy R[3].

J Anxiety Disord. **2018 Apr 17**. pii: S0887-6185(18)30047-1. doi: 10.1016/j.janxdis.2018.04.005. PMID: 29703452. [Epub ahead of print]

OBJECTIVES: This study aimed to: 1) Establish the prevalence of co-occurring chronic pain conditions (i.e., arthritis, back pain, and migraines) and generalized anxiety disorder (GAD), and 2) Examine levels of pain severity, disability, and work absenteeism among comorbid chronic pain conditions and GAD.

METHODS: Data were analyzed from the 2012 Canadian Community Health Survey-Mental Health (CCHS-MH; N = 25,113). Chi-square analyses assessed whether significant differences existed in pain severity in those with comorbid chronic pain and GAD versus pain conditions alone. Multivariable regressions examined the association between comorbid chronic pain and GAD with functional outcomes.

RESULTS: The weighted prevalence of GAD among those with chronic migraines, arthritis and back pain was 6.9%, 4.4%, and 6.1% respectively, compared to 2.6% among the entire sample. Severity of pain was increased among those with comorbid chronic pain and GAD compared with chronic pain conditions alone. Migraine was the only pain condition that was significantly associated with disability in our most stringent adjustment model. After controlling for other psychiatric disorders, comorbid GAD and chronic pain was not associated with work absenteeism.

CONCLUSION: Chronic pain is common among the Canadian population and is associated with substantial disability. Results demonstrated that GAD is prevalent among chronic pain conditions, and comorbidity is associated with greater pain severity. GAD in the context of migraines, in particular, may represent an important treatment target to reduce disability.

CHRONIC PAIN (Continued)

Effects of a 12-Week Digital Care Program for Chronic Knee Pain on Pain, Mobility, and Surgery Risk: Randomized Controlled Trial.

Mecklenburg G[#1], Smittenaar P[#1], Erhart-Hledik JC[2], Perez DA[1], Hunter S[1].

J Med Internet Res. **2018 Apr 25**;20(4):e156. doi: 10.2196/jmir.9667. PMID: 29695370.

BACKGROUND: Chronic knee pain, most commonly caused by knee osteoarthritis, is a prevalent condition which in most cases can be effectively treated through conservative, non-surgical care involving exercise therapy, education, psychosocial support, and weight loss. However, most people living with chronic knee pain do not receive adequate care, leading to unnecessary use of opiates and surgical procedures.

OBJECTIVE: Assess the efficacy of a remotely delivered digital care program for chronic knee pain.

METHODS: We enrolled 162 participants into a randomized controlled trial between January and March 2017. Participants were recruited from participating employers using questionnaires for self-assessment of their knee pain, and randomized into treatment (n=101) and control (n=61) groups. Participants in the treatment group were enrolled in the Hinge Health digital care program for chronic knee pain. This is a remotely delivered, home-based 12-week intervention that includes sensor-guided exercise therapy, education, cognitive behavioral therapy, weight loss, and psychosocial support through a personal coach and team-based interactions. The control group received three education pieces regarding self-care for chronic knee pain. Both groups had access to treatment-as-usual. The primary outcome was the Knee Injury and Osteoarthritis Outcome Score (KOOS) Pain subscale and KOOS Physical Function Shortform (KOOS-PS). Secondary outcomes were visual analog scales (VAS) for pain and stiffness respectively, surgery intent, and self-reported understanding of the condition and treatment options. Outcome measures were analyzed by intention to treat (excluding 7 control participants who received the digital care program due to administrative error) and per protocol.

RESULTS: In an intent-to-treat analysis the digital care program group had a significantly greater reduction in KOOS Pain compared to the control group at the end of the program (greater reduction of 7.7, 95% CI 3.0 to 12.3, P=.002), as well as a significantly greater improvement in physical function (7.2, 95% CI 3.0 to 11.5, P=.001). This was also reflected in the secondary outcomes VAS pain (12.3, 95% CI 5.4 to 19.1, P<.001) and VAS stiffness (13.4, 95% CI 5.6 to 21.1, P=.001). Participants' self-reported likelihood (from 0% to 100%) of having surgery also reduced more strongly in the digital care program group compared to the control group over the next 1 year (-9.4 percentage points, pp, 95% CI -16.6 to -2.2, P=.01), 2 years (-11.3 pp, 95% CI -20.1 to -2.5, P=.01), and 5 years (-14.6 pp, 95% CI -23.6 to -5.5, P=.002). Interest in surgery (from 0 to 10) also reduced more so in the digital care program compared to control group (-1.0, 95% CI -1.7 to -0.2, P=.01). Participants' understanding of the condition and treatment options (on a scale from 0 to 4) increased more substantially for participants in the digital care program than those in the control group (0.9, 95% CI 0.6 to 1.3, P<.001). In an analysis on participants that completed the intervention (per protocol analysis) all primary and secondary outcomes remained significant at greater effect magnitudes compared to intention to treat, with those completing the program showing a 61% (95% CI 48 to 74) reduction in VAS pain compared to 21% (95% CI 5 to 38) in the control group (P<.001). Accounting for the cost of administering the program, we estimate net cost savings on surgery alone of US $4340 over 1 year and $7900 over 5 years for those participants completing the digital care program compared to those in the control group receiving treatment-as-usual. In an exploratory subgroup analysis including only participants exhibiting clinical symptoms of osteoarthritis the program proved equally effective.

CONCLUSIONS: This trial provides strong evidence that a comprehensive 12-week digital care program for chronic knee pain, including osteoarthritis, yields significantly improved outcomes for pain, physical function, stiffness, surgery risk, and understanding of the condition, compared to a control group.

TRIAL REGISTRATION: International Standard Randomized Controlled Trial Number (ISRCTN) 13307390; http://www.isrctn.com/ISRCTN13307390 (Archived by WebCite at http://www.webcitation.org/6ycwjGL73).

OTHER RESEARCH OF INTEREST

Disability Rating, Age at Death, and Cause of Death in U.S. Veterans with Service-Connected Conditions.

Maynard C[1,2], Trivedi R[3,4], Nelson K[1,2,5], Fihn SD[1,2,5,6].

Mil Med. **2018 Mar 26**. doi: 10.1093/milmed/usy040. PMID: 29590473. [Epub ahead of print]

Introduction: The association between disability and cause of death in Veterans with service-connected disabilities has not been studied. The objective of this study was to compare age at death, military service and disability characteristics, including disability rating, and cause of death by year of birth. We also examined cause of death for specific service-connected conditions.

Materials and methods: This study used information from the VETSNET file, which is a snapshot of selected items from the Veterans Benefits Administration corporate database. We also used the National Death Index (NDI) for Veterans which is part of the VA Suicide Data Repository. In VETSNET, there were 758,324 Veterans who had a service-connected condition and died between the years 2004 and 2014. Using the scrambled social security number to link the two files resulted in 605,493 (80%) deceased Veterans. Age at death, sex, and underlying cause of death were obtained from the NDI for Veterans and military service characteristics and types of disability were acquired from VETSNET. We constructed age categories corresponding to period of service; birth years 1938 and earlier corresponded to Korea and World War II ("oldest"), birth years 1939-1957 to the Vietnam era ("middle"), and birth years 1958 and later to post Vietnam, Gulf War, and the more recent conflicts in Iraq and Afghanistan ("youngest").

Results: Sixty-two percent were in the oldest age category, 34% in the middle group, and 4% in the youngest one. The overall age at death was 75 ± 13 yr. Only 1.6% of decedents were women; among women 25% were in the youngest age group, while among men only 4% were in the youngest group. Most decedents were enlisted personnel, and 60% served in the U.S. Army. Nearly 61% had a disability rating of >50% and for the middle age group 54% had a disability rating of 100%. The most common service-connected conditions were tinnitus, hearing loss, and post-traumatic stress disorder (PTSD). In the oldest group, nearly half of deaths were due to cancer or cardiovascular conditions and <2% were due to external causes. In the youngest group, cardiovascular disease and cancer accounted for about 1/3 of deaths, whereas external causes or deaths due to accidents, suicide, or assault accounted for nearly 33% of deaths. For Veterans with service-connected PTSD or major depression; 6.5% of deaths were due to external causes whereas for Veterans without these conditions, only 3.1% were due to external causes.

Conclusion: The finding of premature death due to external causes in the youngest age group as well as the finding of higher proportions of external causes in those with PTSD or major depression should be of great concern to those who care for Veterans.

Health Status of Gulf War and Era Veterans Serving in the US Military in 2000.

Porter B[1], Long K, Rull RP, Dursa EK; Millennium Cohort Study Team.

J Occup Environ Med. **2018 Jan 24**. doi: 10.1097/JOM.0000000000001280. PMID: 29370011. [Epub ahead of print]

OBJECTIVE: This research describes Gulf War and era veterans enrolled in the Millennium Cohort Study, who were sampled from US military personnel serving in 2000, and compares Health characteristics of this sample to a Department of Veterans' Affairs study sampled from the complete population.

METHODS: Demographics characteristics of this sample were described. Self-reported health characteristics were compared between the two studies.

RESULTS: Gulf War and era veterans in the Millennium Cohort were generally healthier than in the VA study; they had fewer medical conditions and mental health disorders and better self-reported health. In both studies, Gulf War veterans had poorer health outcomes than era veterans.

CONCLUSION: The Millennium Cohort Study is a unique resource for examining the long-term health effects of Gulf War deployment, particularly comparing deployed and nondeployed personnel and examining illnesses with long latencies.

OTHER RESEARCH OF INTEREST (Continued)

Physical health conditions associated with full and subthreshold PTSD in U.S. military veterans: Results from the National Health and Resilience in Veterans Study.

El-Gabalawy R[1], Blaney C[2], Tsai J[3], Sumner JA[4], Pietrzak RH[3].

J Affect Disord. **2018 Feb**;227:849-853. doi: 10.1016/j.jad.2017.11.058. PMID: 29689700. Epub 2017 Nov 15.

BACKGROUND: While both full and subthreshold posttraumatic stress disorder (PTSD) may be linked to physical conditions, contemporary population-based data on these associations in military veterans are scarce. Further, little is known about how component aspects of PTSD, which is a heterogeneous disorder, may relate to physical conditions in this population.

METHODS: Data were analyzed from a population-based sample of 3157 U.S. military veterans who participated in the 2011 National Health and Resilience in Veterans Study. Multiple logistic regression analyses evaluated associations between full and subthreshold PTSD, and physical conditions.

RESULTS: A total 6.1% of the sample met screening criteria for full PTSD and 9.0% for subthreshold PTSD. Both full and subthreshold PTSD were associated with increased odds of sleep disorder (adjusted odds ratio [AOR] = 3.52 and 2.10, respectively) and respiratory conditions (AOR = 2.60 and 1.87, respectively). Full PTSD was additionally associated with increased odds of osteoporosis or osteopenia (AOR = 2.72) and migraine (AOR = 1.91), while subthreshold PTSD only was associated with increased odds of diabetes (AOR = 1.42). Analyses of PTSD symptom clusters revealed that all of these associations were primarily driven by dysphoric arousal symptoms, which are characterized by sleep difficulties, anger/irritability, and concentration problems.

LIMITATIONS: The study used self-report measures for health conditions and DSM-IV diagnostic criteria for PTSD.

CONCLUSION: Results of this study provide a characterization of physical conditions associated with full and subthreshold PTSD in U.S. military veterans. They highlight the potential importance of PTSD dysphoric arousal in risk models of certain physical conditions in this population.

Veteran-centred content in medical education.

Ross PT[1], Lypson ML[1,2].

Clin Teach. **2018 Mar 30**. doi: 10.1111/tct.12775. PMID: 29600591. [Epub ahead of print]

BACKGROUND: Veterans have unique experiences that warrant special consideration in health care. Unfortunately, training in veteran-centred care has not been a clear focus of medical education, and only a very small proportion of medical schools include military cultural competency in their curricula.

METHODS: We conducted an 80-minute focus group with six US veterans. Open-ended questions were used to elicit their perceptions of the health care that they receive, and how it can be improved. The audio-recording was transcribed verbatim and coded for thematic content. A phenomenological analytic approach was used to analyse the 31-page transcript and arrive at the final themes.

RESULTS: Former service members from various periods of conflict (e.g. World War II, Vietnam, Persian Gulf) offered key insights about how to improve veterans' health care experiences. Veterans suggested that consideration of their previous military service would improve care. They lamented that the lack of military consciousness is a barrier to care. Finally, they suggested that clinicians pay close attention to the transition from service member to civilian, as reintegration to civilian life is a critical life experience. Training in veteran-centred care has not been a clear focus of medical education DISCUSSION: Veteran-centred care ensures optimal health care through ease of access to services, and through positive patient-provider interactions. Being aware of military culture can help providers to contextualise veterans' experiences and beliefs about health care seeking and illness management, particularly for invisible wounds of war, including traumatic brain injury (TBI) and post-traumatic stress disorder (PTSD).

OTHER RESEARCH OF INTEREST (Continued)

Genome-wide association analyses identify 44 risk variants and refine the genetic architecture of major depression.

Wray NR[1,2] plus 160 et al.

Nat Genet. **2018 Apr 26**. doi: 10.1038/s41588-018-0090-3. PMID: 29700475. [Epub ahead of print]

Major depressive disorder (MDD) is a common illness accompanied by considerable morbidity, mortality, costs, and heightened risk of suicide. We conducted a genome-wide association meta-analysis based in 135,458 cases and 344,901 controls and identified 44 independent and significant loci. The genetic findings were associated with clinical features of major depression and implicated brain regions exhibiting anatomical differences in cases. Targets of antidepressant medications and genes involved in gene splicing were enriched for smaller association signal. We found important relationships of genetic risk for major depression with educational attainment, body mass, and schizophrenia: lower educational attainment and higher body mass were putatively causal, whereas major depression and schizophrenia reflected a partly shared biological etiology. All humans carry lesser or greater numbers of genetic risk factors for major depression. These findings help refine the basis of major depression and imply that a continuous measure of risk underlies the clinical phenotype.

Motor Unit Number Estimate and Isometric Hand Grip Strength in Military Veterans with or Without Muscular Complaints: Reference Values for Longitudinal Follow-up.

Li M[1,2,3], Yao W[1,2], Sundahl C[3].

Mil Med. **2018 Mar 26**. doi: 10.1093/milmed/usy025. PMID: 29590409. [Epub ahead of print]

Introduction: It remains unclear if Gulf War (GW) veterans have a higher risk of developing motor neuron disorder. We intended to establish baseline neurophysiological values, including thenar motor unit number estimate (MUNE) and isometric hand grip (IHG) strength, to compare future follow-ups of deployed GW veterans with or without muscular complaints.

Materials and Methods: We evaluated 19 GW veterans with self-reported weakness, cramps, or excessive muscle fatigue (Ill-19) and compared them with 18 controls without such muscular complaints (C-18). We performed MUNE on hand thenar muscles using adapted multipoint stimulation method for Ill-19 and 15 controls (C-15). We measured IHG strength (maximum force, endurance, and fatigue level) on Ill-19 and C-18 with a hand dynamometer. We performed nerve conduction studies on all study participants to determine which subjects had mild carpal tunnel syndrome (CTS). We compared the MUNE and IHG strength measures between Ill group and controls and between those with CTS and those without CTS.

Results: We obtained thenar MUNE of Ill-19 (95% CI of mean: 143-215; mean age: 46 yr) and compared it with that of C-15 (95% CI of mean: 161-230; mean age: 45 yr), and 95% of CI of mean among IHG strength variables (maximum force: 324-381 Newton; endurance: 32-42 s; fatigue level: 24%-33%) compared with C-18 (maximum force: 349-408 Newton; endurance: 35-46 s; fatigue level: 21%-27%). There was no significant difference in either MUNE or IHG strength between Ill-19 group and controls. The MUNE and IHG maximum forces were significantly lower in those with CTS compared with those without CTS. As a surrogate of mild CTS, the median versus ulnar distal sensory latency on nerve conduction study was only weakly associated with MUNE, maximum force, and fatigue level, respectively.

Conclusion: To our knowledge, no published study on MUNE reference values of military veteran population has been available. The quantifiable values of both thenar MUNE and IHG strength of military veterans serve as baselines for our longitudinal follow-up of motor neuron function of deployed troops. These reference values are also useful for other laboratories to study veterans' motor system with or without mild CTS.

OTHER RESEARCH OF INTEREST (Continued)

Prediction of Persistent Post-Concussion Symptoms Following Mild Traumatic Brain Injury.

Cnossen MC[1], van der Naalt J[2,3], Spikman JM[4], Nieboer D[5], Yue JK[6,7], Winkler EA[8], Manley G[9], von Steinbuechel N[10], Polinder S[11], Steyerberg EW[12] , Lingsma H[13,14].

J Neurotrauma. **2018 Apr 25**. doi: 10.1089/neu.2017.5486. PMID: 29690799. [Epub ahead of print]

Persistent post-concussion symptoms (PPCS) occur frequently after mild traumatic brain injury (mTBI). The identification of patients at risk for poor outcome remains challenging since valid prediction models are missing. The objectives of the current study were to assess the quality and clinical value of prediction models for PPCS, and to develop a new model based on the synthesis of existing models and addition of complaints at emergency department (ED). MTBI patients (Glasgow Coma Scale score 13-15) were prospectively recruited from three Dutch level I trauma centers between 2013-2015 in the UPFRONT study. PPCS were assessed using the Head Injury Severity Checklist at six-month post-injury. Two prediction models (Stulemeijer 2008; Cnossen 2017) were examined for calibration and discrimination. The final model comprised variables of existing models with the addition of headache, nausea/vomiting and neck pain at ED, using logistic regression and bootstrap validation. Overall 591 patients (mean age 51years, 41% female) were included; 241 (41%) developed PPCS. Existing models performed poorly at external validation (AUC: 0.57-0.64). The newly developed model included female sex (OR 1.48, 95%CI [1.01-2.18]), neck pain (OR 2.58,[1.39-4.78]), two-week post-concussion symptoms (OR 4.89,[3.19-7.49]) and two-week posttraumatic stress (OR 2.98,[1.88-4.73]) as significant predictors. Discrimination of this model was adequate (AUC after bootstrap validation: 0.75). Existing prediction models for PPCS perform poorly. A new model performs reasonably with predictive factors already discernible at ED warranting further external validation. Prediction research in mTBI should be improved by standardizing definitions and data collection and by using sound methodology.

Effects of Milk vs Dark Chocolate Consumption on Visual Acuity and Contrast Sensitivity Within 2 Hours: A Randomized Clinical Trial.

Rabin JC[1], Karunathilake N[1], Patrizi K[1].

JAMA Ophthalmol. **2018 Apr 26**. doi: 10.1001/jamaophthalmol.2018.0978. PMID: 29710322. [Epub ahead of print]

Importance: Consumption of dark chocolate can improve blood flow, mood, and cognition in the short term, but little

Objective: To compare the short-term effects of consumption of dark chocolate with those of milk chocolate on visual acuity and large- and small-letter contrast sensitivity.

Design: A randomized, single-masked crossover design was used to assess short-term visual performance after consumption of a dark or a milk chocolate bar. Thirty participants without pathologic eye disease each consumed dark and milk chocolate in separate sessions, and within-participant paired comparisons were used to assess outcomes. Testing was conducted at the Rosenberg School of Optometry from June 25 to August 15, 2017.

Main Outcomes and Measures: Visual acuity (in logMAR units) and large- and small-letter contrast sensitivity (in the log of the inverse of the minimum detectable contrast [logCS units]) were measured 1.75 hours after consumption of dark and milk chocolate bars.

Results: Among the 30 participants (9 men and 21 women; mean [SD] age, 26 [5] years), small-letter contrast sensitivity was significantly higher after consumption of dark chocolate (mean [SE], 1.45 [0.04] logCS) vs milk chocolate (mean [SE], 1.30 [0.05] logCS; mean improvement, 0.15 logCS [95% CI, 0.08-0.22 logCS]; P < .001). Large-letter contrast sensitivity was slightly higher after consumption of dark chocolate (mean [SE], 2.05 [0.02] logCS) vs milk chocolate (mean [SE], 2.00 [0.02] logCS; mean improvement, 0.05 logCS [95% CI, 0.00-0.10 logCS]; P = .07). Visual acuity improved slightly after consumption of dark chocolate (mean [SE], -0.22 [0.01] logMAR; visual acuity, approximately 20/12) and milk chocolate (mean [SE], -0.18 [0.01] logMAR; visual acuity, approximately 20/15; mean improvement, 0.04 logMAR [95% CI, 0.02-0.06 logMAR]; P = .05). Composite scores combining results from all tests showed significant improvement after consumption of dark compared with milk chocolate (mean improvement, 0.20 log U [95% CI, 0.10-0.30 log U]; P < .001).

Conclusions and Relevance: Contrast sensitivity and visual acuity were significantly higher 2 hours after consumption of a dark chocolate bar compared with a milk chocolate bar, but the duration of these effects and their influence in real-world performance await further testing.

Trial Registration: clinicaltrials.gov Identifier: **NCT03326934**.

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