GULF WAR ILLNESS

Depleted Uranium and Human Health.

Faa A[1], Gerosa C[1], Fanni D[1], Floris G[2], Eyken PV[3], Lachowicz JI[4], Nurchi VM[4].

Curr Med Chem. **2018**;25(1):49-64. doi: 10.2174/0929867324666170426102343. PMID: 28462701.

Depleted uranium (DU) is generally considered an emerging pollutant, first extensively introduced into environment in the early nineties in Iraq, during the military operation called "Desert Storm". DU has been hypothesized to represent a hazardous element both for soldiers exposed as well as for the inhabitants of the polluted areas in the war zones. In this review, the possible consequences on human health of DU released in the environment are critically analyzed. In the first part, the chemical properties of DU and the principal civil and military uses are summarized. A concise analysis of the mechanisms underlying absorption, blood transport, tissue distribution and excretion of DU in the human body is the subject of the second part of this article. The following sections deal with pathological condition putatively associated with overexposure to DU. Developmental and birth defects, the Persian Gulf syndrome, and kidney diseases that have been associated to DU are the arguments treated in the third section. Finally, data regarding DU exposure and cancer insurgence will be critically analyzed, including leukemia/lymphoma, lung cancer, uterine cervix cancer, breast cancer, bladder cancer and testicular cancer. The aim of the authors is to give a contribution to the debate on DU and its effects on human health and disease.

KEYWORDS: Depleted uranium; Persian Gulf syndrome; desert storm; uranium chemical properties; uranium metabolism; uranium toxicity

CHRONIC FATIGUE SYNDROME

A Systematic Review of Probiotic Interventions for Gastrointestinal Symptoms and Irritable Bowel Syndrome in Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME).

Corbitt M[1], Campagnolo N[2,3], Staines D[2,3], Marshall-Gradisnik S[2,3].

Probiotics Antimicrob Proteins. **2018 Feb 20**. doi: 10.1007/s12602-018-9397-8. [Epub ahead of print]

Gastrointestinal (GI) symptoms and irritable bowel (IB) symptoms have been associated with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME). The aim of this study was to conduct a systematic review of these symptoms in CFS/ME, along with any evidence for probiotics as treatment. Pubmed, Scopus, Medline (EBSCOHost) and EMBASE databases were searched to source relevant studies for CFS/ME. The review included any studies examining GI symptoms, irritable bowel syndrome (IBS) and/or probiotic use. Studies were required to report criteria for CFS/ME and study design, intervention and outcome measures. Quality assessment was also completed to summarise the level of evidence available. A total of 3381 publications were returned using our search terms. Twenty-five studies were included in the review. Randomised control trials were the predominant study type (n = 24). Most of the studies identified examined the effect of probiotic supplementation on the improvement of IB symptoms in IBS patients, or IB symptoms in CFS/ME patients, as well as some other significant secondary outcomes (e.g. quality of life, other gastrointestinal symptoms, psychological symptoms). The level of evidence identified for the use of probiotics in IBS was excellent in quality; however, the evidence available for the use of probiotic interventions in CFS/ME was poor and limited. There is currently insufficient evidence for the use of probiotics in CFS/ME patients, despite probiotic interventions being useful in IBS. The studies pertaining to probiotic interventions in CFS/ME patients were limited and of poor quality overall. Standardisation of protocols and methodology in these studies is required.

HEADACHE and MIGRAINE

Medication overuse headache following repeated morphine, but not [INCREMENT]9-tetrahydrocannabinol administration in the female rat.

Kandasamy R[1], Dawson CT[2], Hilgendorf TN[2], Morgan MM[1,3,2].

Behav Pharmacol. **2018 Feb 16**. doi: 10.1097/FBP.0000000000000382. PMID: 29462111. [Epub ahead of print]

The potential of [INCREMENT]-tetrahydrocannabinol (THC) as a treatment for migraine depends on antinociceptive efficacy with repeated administration. Although morphine has good antinociceptive efficacy, repeated administration causes medication overuse headache (MOH) - a condition in which the intensity/frequency of migraine increases. The present study compared the effect of repeated morphine or THC administration on the magnitude and duration of migraine-like pain induced by a microinjection of allyl isothiocyanate (AITC) onto the dura mater of female rats. Acute administration of THC or morphine prevented AITC-induced depression of wheel running. This antinociception was maintained in rats treated repeatedly with THC, but not following repeated administration of morphine. Moreover, repeated morphine, but not THC administration, extended the duration of AITC-induced depression of wheel running. These data indicate that tolerance and MOH develop rapidly to morphine administration. The lack of tolerance and MOH to THC indicates that THC may be an especially effective long-term treatment against migraine.

Vulnerability to Infarction During Cerebral Ischemia in Migraine Sufferers.

Pezzini A[1], Busto G[2], Zedde M[2], Gamba M[2], Zini A[2], Poli L[2], Caria F[2], De Giuli V[2], Simone AM[2], Pascarella R[2], Padovani A[2], Padroni M[2], Gasparotti R[2], Colagrande S[2], Fainardi E[2].

Stroke. **2018 Feb 19**. pii: STROKEAHA.118.020554. doi: 10.1161/STROKEAHA.118.020554. PMID: 29459398. [Epub ahead of print]

BACKGROUND AND PURPOSE: Cerebral hyperexcitability in migraine experiencers might sensitize brain tissue to ischemia. We investigated whether a personal history of migraine is associated with vulnerability to brain ischemia in humans.

METHODS: Multicenter cohort study of patients with acute ischemic stroke who underwent a brain computed tomography perfusion and were scheduled to undergo reperfusion therapy. In a case-control design, we compared the proportion of subjects with no-mismatch, the volume of penumbra salvaged, as well as the final infarct size in a group of patients with migraine and a group of patients with no history of migraine.

RESULTS: We included 61 patients with migraine (34 [55.7%] men; mean age, 52.2±15.1 years; migraine without aura/migraine with aura, 44/17) and 61 patients with no history of migraine. The proportion of no-mismatch among migraineurs was significantly higher than among nonmigraineurs (17 [27.9%] versus 7 [11.5%]; *P*=0.039) and was more prominent among patients with migraine with aura (6 [35.3%]; *P*=0.030) while it was nonsignificantly increased in patients with migraine without aura (11 [25.0%]; *P*=0.114). Migraine, especially migraine with aura, was independently associated with a no-mismatch pattern (odds ratio, 2.65; 95% CI, 0.95-7.41 for migraine; odds ratio, 5.54; 95% CI, 1.28-23.99 for migraine with aura), and there was a linear decrease of the proportion of patients with migraine with aura with increasing quartiles of mismatch volumes. Patients with migraine with aura had also smaller volumes of salvaged penumbra (9.8±41.2 mL) compared with patients with migraine without aura (36.4±54.1 mL) and patients with no migraine (45.1±55.0 mL; *P*=0.056). Conversely, there was no difference in final infarct size among the 3 migraine subgroups (*P*=0.312).

CONCLUSIONS: Migraine is likely to increase individual vulnerability to ischemic stroke during the process of acute brain ischemia and might represent, therefore, a potential new therapeutic target against occurrence and progression of the ischemic damage.

HEADACHE and MIGRAINE (Continued)

Diamine oxidase (DAO) supplement reduces headache in episodic migraine patients with DAO deficiency: A randomized double-blind trial.

Izquierdo-Casas J[1], Comas-Basté O[2], Latorre-Moratalla ML[2], Lorente-Gascón M[3], Duelo A[4], Soler-Singla L[1], Vidal-Carou MC[5].

Clin Nutr. **2018 Feb 15**. pii: S0261-5614(18)30014-1. doi: 10.1016/j.clnu.2018.01.013. PMID: 29475774. [Epub ahead of print]

BACKGROUND & AIMS: Histamine intolerance is a disorder in the homeostasis of histamine due to a reduced intestinal degradation of this amine, mainly caused by a deficiency in the enzyme diamine oxidase (DAO). Among histamine related symptoms, headache is one of the most recorded. Current clinical strategies for the treatment of the symptomatology related to this disorder are based on the exclusion of foods with histamine or other bioactive amines and/or exogenous DAO supplementation. The aim of this study was to assess the efficacy of a food supplement consisting of DAO enzyme as a preventive treatment of migraine in patients with DAO deficiency through a randomized double-blind trial.

METHODS: 100 patients with confirmed episodic migraine according to current International Headache Society (IHS) criteria and DAO deficiency (levels below 80 HDU/ml) were randomized in two groups. One group received DAO enzyme supplementation and the other received placebo for one month. Clinical outcomes assessed were duration and number of attacks, perception of pain intensity and adverse effects during treatment. The use of triptans was also recorded.

RESULTS: Great variability was found in the duration of migraine attacks reported by placebo and DAO groups. A significant reduction ($p = 0.0217$) in hours of pain was achieved in patients treated with DAO supplement, with mean durations of 6.14 (±3.06) and 4.76 (±2.68) hours before and after treatment, respectively. A smaller reduction without statistical signification was also observed for this outcome in the placebo group, from 7.53 (±4.24) to 6.68 (±4.42) hours. Only in DAO group, a decrease in the percentage of patients taking triptans was observed. The number of attacks and the scores of pain intensity showed a similar reduction in both groups. No adverse effects were registered in patients treated with DAO enzyme.

CONCLUSIONS: Migrainous patients supplemented with DAO enzyme during one month significantly reduced the duration of their migraine attacks by 1.4 h. No statistically significant reduction was found in placebo group before and after treatment. The reduction of pain hours observed in placebo group (0.9 h) could explain the lack of significant differences between both study groups. One month of DAO supplementation has demonstrated a positive trend in the improvement of migraine but more studies with a longer treatment period are needed to better assess the efficacy of DAO supplementation.

CLINICAL TRIAL REGISTRATION NUMBER: ISRCTN10091019; www.isrctn.org.

Calcitonin gene-related peptide (receptor) antibodies: an exciting avenue for migraine treatment.

MaassenVanDenBrink A[1], Terwindt GM[2], van den Maagdenberg AMJM[3,4]. EDITORIAL REVIEW

Genome Med. **2018 Feb 22**;10(1):10. doi: 10.1186/s13073-018-0524-7. PMID: 29471874. Link to full text in Genome Med.

Specific prophylactic migraine treatments are urgently needed because of the unmet needs of many migraine patients. Antibodies targeting calcitonin gene-related peptide (CGRP) or its receptor have recently shown efficacy in episodic and chronic migraine and will be available soon.

CHRONIC PAIN

Literacy-Adapted Cognitive Behavioral Therapy Versus Education for Chronic Pain at Low-Income Clinics: A Randomized Controlled Trial.

Thorn BE[1], Eyer JC[1], Van Dyke BP[1], Torres CA[1], Burns JW[2], Kim M[3], Newman AK[1], Campbell LC[4], Anderson B[5], Block PR[1], Bobrow BJ[6], Brooks R[7], Burton TT[7], Cheavens JS[3], DeMonte CM[8], DeMonte WD[9], Edwards CS[7], Jeong M[10], Mulla MM[1], Penn T[11], Smith LJ[12], Tucker DH[7].

Ann Intern Med. **2018 Feb 27**. doi: 10.7326/M17-0972. PMID: 29482213. [Epub ahead of print]

Background: Chronic pain is common and challenging to treat. Although cognitive behavioral therapy (CBT) is efficacious, its benefit in disadvantaged populations is largely unknown.

Objective: To evaluate the efficacy of literacy-adapted and simplified group CBT versus group pain education (EDU) versus usual care.

Design: Randomized controlled trial. (ClinicalTrials.gov: NCT01967342).

Setting: Community health centers serving low-income patients in Alabama.

Patients: Adults (aged 19 to 71 years) with mixed chronic pain.

Interventions: CBT and EDU delivered in 10 weekly 90-minute group sessions.

Measurements: Self-reported, postintervention pain intensity (primary outcome) and physical function and depression (secondary outcomes).

Results: 290 participants were enrolled (70.7% of whom were women, 66.9% minority group members, 72.4% at or below the poverty level, and 35.8% reading below the fifth grade level); 241 (83.1%) participated in posttreatment assessments. Linear mixed models included all randomly assigned participants. Members of the CBT and EDU groups had larger decreases in pain intensity scores between baseline and posttreatment than participants receiving usual care (estimated differences in change scores-CBT: -0.80 [95% CI -1.48 to -0.11]; P = 0.022; EDU: -0.57 [CI, -1.04 to -0.10]; P = 0.018). At 6-month follow-up, treatment gains were not maintained in the CBT group but were still present in the EDU group. With regard to physical function, participants in the CBT and EDU interventions had greater posttreatment improvement than those receiving usual care, and this progress was maintained at 6-month follow-up. Changes in depression (secondary outcome) did not differ between either the CBT or EDU group and the usual care group.

Limitations: Participants represented a single health care system. Self-selection bias may have been present.

Conclusion: Simplified group CBT and EDU interventions delivered at low-income clinics significantly improved pain and physical function compared with usual care.

Primary Funding Source: Patient-Centered Outcomes Research Institute.

Glial cell type-specific changes in spinal dipeptidyl peptidase 4 expression and effects of its inhibitors in inflammatory and neuropatic pain.

Király K[1], Kozsurek M[2], Lukácsi E[2], Barta B[2], Alpár A[2], Balázsa T[2], Fekete C[3], Szabon J[3], Helyes Z[4,5], Bölcskei K[4], Tékus V[4], Tóth ZE[2], Pap K[6], Gerber G[2], Puskár Z[7].

Sci Rep. **2018 Feb 22**;8(1):3490. doi: 10.1038/s41598-018-21799-8. PMID: 29472575.

Altered pain sensations such as hyperalgesia and allodynia are characteristic features of various pain states, and remain difficult to treat. We have shown previously that spinal application of dipeptidyl peptidase 4 (DPP4) inhibitors induces strong antihyperalgesic effect during inflammatory pain. In this study we observed low level of DPP4 mRNA in the rat spinal dorsal horn in physiological conditions, which did not change significantly either in carrageenan-induced inflammatory or partial nerve ligation-generated neuropathic states. In naïve animals, microglia and astrocytes expressed DPP4 protein with one and two orders of magnitude higher than neurons, respectively. DPP4 significantly increased in astrocytes during inflammation and in microglia in neuropathy. Intrathecal application of two DPP4 inhibitors tripeptide isoleucin-prolin-isoleucin (IPI) and the antidiabetic drug vildagliptin resulted in robust opioid-dependent antihyperalgesic effect during inflammation, and milder but significant opioid-independent antihyperalgesic action in the neuropathic model. The opioid-mediated antihyperalgesic effect of IPI was exclusively related to mu-opioid receptors, while vildagliptin affected mainly delta-receptor activity, although mu- and kappa-receptors were also involved. None of the inhibitors influenced allodynia. Our results suggest pathology and glia-type specific changes of DPP4 activity in the spinal cord, which contribute to the development and maintenance of hyperalgesia and interact with endogenous opioid systems.

CHRONIC PAIN (Continued)

Genetic Variation in P2rx7 and Pain Tolerance.

Kambur O[1,2,3], Kaunisto MA[4], Winsvold BS[5], Wilsgaard T[6], Stubhaug A[1,2], Zwart JA[2,5], Kalso E[7], Nielsen CS[1,8].

Pain. **2018 Feb 20**. doi: 10.1097/j.pain.0000000000001188. PMID: 29470314. [Epub ahead of print]

P2X7 is a non-selective cation channel activated by extracellular ATP. P2X7 activation contributes to the pro-inflammatory response to injury or bacterial invasion and mediates apoptosis. Recently, P2X7 function has been linked to chronic inflammatory and neuropathic pain. P2X7 may contribute to pain modulation both by effects on peripheral tissue injury underlying clinical pain states, and through alterations in central nervous system processing, as suggested by animal models. To further test its role in pain sensitivity, we examined whether variation within the P2RX7 gene, which encodes the P2X7 receptor, was associated with experimentally induced pain in human patients. Experimental pain was assessed in Tromsø 6, a longitudinal and crosssectional population based study (N=3016), and the BrePainGen cohort, consisting of patients who underwent breast cancer surgery (N=831). For both cohorts, experimental pain intensity and tolerance were assessed with the cold pressor test. In addition, multi-site chronic pain was assessed in Tromsø 6 and pain intensity one week after surgery was assessed in BrePainGen. We tested whether the single nucleotide polymorphism (SNP) rs7958311, previously implicated in clinical pain, was associated with experimental and clinical pain phenotypes. In addition, we examined effects of SNPs rs208294 and rs208296, for which previous results have been equivocal. Rs7958311 was associated with experimental pain intensity in the meta-analysis of both cohorts. Significant associations were also found for multi-site pain and postoperative pain. Our results strengthen the existing evidence and suggest that P2X7 and genetic variation in the P2RX7-gene may be involved in the modulation of human pain sensitivity. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Medical Cannabis for the Treatment of Fibromyalgia.

Habib G, Artul S.

J Clin Rheumatol. **2018 Feb 14**. doi: 10.1097/RHU.0000000000000702. PMID: 29461346. [Epub ahead of print]

BACKGROUND: Fibromyalgia is a chronic pain syndrome, characterized by chronic musculoskeletal pain, fatigue, and mood disturbances. There are nearly no data on the effect of medical cannabis (MC) treatment on patients with fibromyalgia.

METHODS: Data were obtained from the registries of 2 hospitals in Israel (Laniado Hospital and Nazareth Hospital) on patients with a diagnosis of fibromyalgia who were treated with MC. After obtaining patient consent, demographic, clinical, and laboratory parameters were documented. All the patients also completed the Revised Fibromyalgia Impact Questionnaire regarding the period before and after MC treatment.

RESULTS: Thirty patients were identified, and 26 patients were included in the study. There were 19 female patients (73%), and the mean age of the study group was 37.8 ± 7.6 years. The mean dosage of MC was 26 ± 8.3 g per month, and the mean duration of MC use was 10.4 ± 11.3 months. After commencing MC treatment, all the patients reported a significant improvement in every parameter on the questionnaire, and 13 patients (50%) stopped taking any other medications for fibromyalgia. Eight patients (30%) experienced very mild adverse effects.

CONCLUSIONS: Medical cannabis treatment had a significant favorable effect on patients with fibromyalgia, with few adverse effects.

CHRONIC PAIN (Continued)

Opioid-related genetic polymorphisms do not influence postoperative opioid requirement: A prospective observational study.

Aubrun F[1], Zahr N, Langeron O, Boccheciampe N, Cozic N, Belin L, Hulot JS, Khiami F, Riou B.

Eur J Anaesthesiol. **2018 Feb 22**. doi: 10.1097/EJA.0000000000000793. PMID: 29474345. [Epub ahead of print]

BACKGROUND: Among the various factors that may influence the pharmacological response to opioids, genetic polymorphisms [single nucleotide polymorphisms (SNP)] have generated some interest.

OBJECTIVES: To examine the influence on morphine dose requirements and adverse events in the postoperative period of four SNP [opioid receptor mu1 (OPRM1), ATP-binding cassette subfamily B, member 1 (ABCB1) ex-21 and ex-26, catechol-o-methyltransferase (COMT)] in candidate genes involved in morphine pharmacodynamics and pharmacokinetics.

DESIGN: A single centre prospective study.

SETTING: University Hospital, Paris, France, from 2 January 2007 to 15 November 2011.

PATIENTS: A total of 438 white adults scheduled for major orthopaedic surgery (spine, hip and knee) under general anaesthesia. The main exclusion criteria were receiving opioids for chronic pain, nonopioid drugs within 2 days prior to surgery, pregnancy, renal insufficiency, sleep apnoea obstruction syndrome, morbid obesity, severe hepatic impairment, cognitive dysfunction.

INTERVENTIONS: Assays of plasma concentrations of morphine and metabolites (morphine 3-glucuronide and morphine 6-glucuronide) were performed and common polymorphisms in four candidate genes [OPRM1 A118G rs1799971; P-glycoprotein (ABCB1) T3435C (rs1045642) and G2677T/A (rs2032582); COMT Val 158 Met (rs4680)] were analysed.Morphine was titrated by staff in the postanaesthesia care unit (PACU) and in the ward patient-controlled intravenous analgesia was used for 24 h.

MAIN OUTCOME MEASURES: The dose of morphine required to achieve pain relief and the influence of SNP in genes involved in morphine pharmacodynamics and kinetics on morphine dose requirements. Secondary endpoints were the concentrations of morphine, morphine 6-glucuronide and morphine 3-gluguronide, the proportion of patients requiring a rescue analgesic and the proportion of morphine-related adverse events.

RESULTS: A total of 404 patients completed the study to final analysis. The mean±SD morphine dose to achieve pain relief was 15.8±8.8 mg in the PACU and 22.7±18.6 mg during patient-controlled intravenous administration. Morphine-related adverse events were observed in 37%. There was no relationship between any genetic polymorphisms and morphine dose, morphine 3-gluguronide and morphine 6-glucuronide concentration, morphine-related adverse events or pain level. In the PACU only, P-glycoprotein polymorphisms (ex-21; ex-26) were significantly associated with morphine concentration but the prediction of the model was poor (R=0.04)
CONCLUSION: No major relationship has been demonstrated between SNP of OPRM1, ABCB1, COMT and morphine requirement, pain level or adverse effects in the postoperative period.
TRIAL REGISTRATION: **NCT00822549 (www.clinicaltrials.gov).**

OTHER RESEARCH OF INTEREST

The Association Between Toxic Exposures and Chronic Multisymptom Illness in Veterans of the Wars of Iraq and Afghanistan.

DeBeer BB[1], Davidson D, Meyer EC, Kimbrel NA, Gulliver SB, Morissette SB.

J Occup Environ Med. **2017 Jan**;59(1):54-60. doi: 10.1097/JOM.0000000000000922. PMCID: PMC5556390. PMID: 28045798.

OBJECTIVE: The purpose of this study was to determine if post-9/11 veterans deployed to the Iraq and Afghanistan conflicts experienced toxic exposures and whether they are related to symptoms of chronic multisymptom illness (CMI).

METHODS: Data from 224 post-9/11 veterans who self-reported exposure to hazards in theater were analyzed using hierarchical regression.

RESULTS: Of the sample, 97.2% endorsed experiencing one or more potentially toxic exposure. In a regression model, toxic exposures and CMI symptoms were significantly associated above and beyond covariates. Follow-up analyses revealed that pesticide exposures, but not smoke inhalation was associated with CMI symptoms.

CONCLUSIONS: These findings suggest that toxic exposures were common among military personnel deployed to the most recent conflicts, and appear to be associated with CMI symptoms. Additional research on the impact of toxic exposures on returning Iraq and Afghanistan Veterans' health is needed.

OTHER RESEARCH OF INTEREST (Continued)

Psychotic experiences and general medical conditions: a cross-national analysis based on 28 002 respondents from 16 countries in the WHO World Mental Health Surveys.

Scott KM[1], Saha S[2], Lim CCW[2], Aguilar-Gaxiola S[3], Al-Hamzawi A[4], Alonso J[5], Benjet C[6], Bromet EJ[7], Bruffaerts R[8], Caldas-de-Almeida JM[9], de Girolamo G[10], de Jonge P[11], Degenhardt L[12], Florescu S[13], Gureje O[14], Haro JM[15], Hu C[16], Karam EG[17], Kovess-Masfety V[18], Lee S[19], Lepine JP[20], Mneimneh Z[21], Navarro-Mateu F[22], Piazza M[23], Posada-Villa J[24], Sampson NA[25], Stagnaro JC[26], Kessler RC[25], McGrath JJ[2].

Psychol Med. **2018 Feb 26**:1-10. doi: 10.1017/S0033291718000363. PMID: 29478433. [Epub ahead of print]

BACKGROUND: Previous work has identified associations between psychotic experiences (PEs) and general medical conditions (GMCs), but their temporal direction remains unclear as does the extent to which they are independent of comorbid mental disorders.

METHODS: In total, 28 002 adults in 16 countries from the WHO World Mental Health (WMH) Surveys were assessed for PEs, GMCs and 21 Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) mental disorders. Discrete-time survival analyses were used to estimate the associations between PEs and GMCs with various adjustments.

RESULTS: After adjustment for comorbid mental disorders, temporally prior PEs were significantly associated with subsequent onset of 8/12 GMCs (arthritis, back or neck pain, frequent or severe headache, other chronic pain, heart disease, high blood pressure, diabetes and peptic ulcer) with odds ratios (ORs) ranging from 1.3 [95% confidence interval (CI) 1.1-1.5] to 1.9 (95% CI 1.4-2.4). In contrast, only three GMCs (frequent or severe headache, other chronic pain and asthma) were significantly associated with subsequent onset of PEs after adjustment for comorbid GMCs and mental disorders, with ORs ranging from 1.5 (95% CI 1.2-1.9) to 1.7 (95% CI 1.2-2.4).

CONCLUSIONS: PEs were associated with the subsequent onset of a wide range of GMCs, independent of comorbid mental disorders. There were also associations between some medical conditions (particularly those involving chronic pain) and subsequent PEs. Although these findings will need to be confirmed in prospective studies, clinicians should be aware that psychotic symptoms may be risk markers for a wide range of adverse health outcomes. Whether PEs are causal risk factors will require further research.

Editors: National Academies of Sciences, Engineering, and Medicine; Health and Medicine Division; Board on Health Sciences Policy; Forum on Neuroscience and Nervous System Disorders.

Source: Washington (DC): National Academies Press (US); **2017 Sep**. **The National Academies Collection: Reports funded by National Institutes of Health.**

Citation: National Academies of Sciences, Engineering, and Medicine. 2018. *Biomarkers of neuroinflammation: Proceedings of a workshop*. Washington, DC: The National Academies Press. doi: https://doi.org/10.17226/24854. PMID: 28921942. Full text link to Proceedings of a Workshop.

Excerpt: Neuroinflammation is a burgeoning area of interest in academia and biopharma, with a broadly acknowledged role in many central nervous system (CNS) disorders. However, there is little agreement on the pathophysiological mechanisms that underlie the manifestations of neuroinflammation in the CNS compartment and how neuroinflammation operates as a driver and also as a consequence of disease in the brain. Moreover, another unclear area is how to translate increased understanding of the mechanisms that underlie neuroinflammation and its manifestations in the CNS to therapeutics.

To address these gaps in understanding mechanisms and how to translate that understanding into therapeutics, the Forum on Neuroscience and Nervous System Disorders of the National Academies of Sciences, Engineering, and Medicine convened a workshop on March 20-21, 2017, bringing together key leaders in the field from industry, academia, and governmental agencies to explore the role and mechanisms of neuroinflammation in a variety of CNS diseases. The workshop also considered strategies to advance the identification and validation of biomarkers of neuroinflammation that could accelerate development of therapies, bringing much-needed treatments to patients with disorders ranging from neuroinflammatory diseases such as multiple sclerosis (MS) to neuropsychiatric disorders such as depression. This publication summarizes the presentations and discussions from the workshop.

OTHER RESEARCH OF INTEREST (Continued)

General Medical, Mental Health, and Demographic Risk Factors Associated With Suicide by Firearm Compared With Other Means.

Boggs JM[1], Beck A[1], Hubley S[1], Peterson EL [1], Hu Y[1], Williams LK[1], Prabhakar D[1], Rossom RC[1], Lynch FL[1], Lu CY[1], Waitzfelder BE[1], Owen-Smith AA[1], Simon GE[1], Ahmedani BK[1].

Psychiatr Serv. **2018 Feb** 15:appips201700237. doi: 10.1176/appi.ps.201700237. PMID: 29446332. [Epub ahead of print].

OBJECTIVE: Mitigation of suicide risk by reducing access to lethal means, such as firearms and potentially lethal medications, is a highly recommended practice. To better understand groups of patients at risk of suicide in medical settings, the authors compared demographic and clinical risk factors between patients who died by suicide by using firearms or other means with matched patients who did not die by suicide (control group).

METHODS: In a case-control study in 2016 from eight health care systems within the Mental Health Research Network, 2,674 suicide cases from 2010-2013 were matched to a control group (N=267,400). The association between suicide by firearm or other means and medical record information on demographic characteristics, general medical disorders, and mental disorders was assessed.

RESULTS: The odds of having a mental disorder were higher among cases of suicide involving a method other than a firearm. Fourteen general medical disorders were associated with statistically significant (p<.001) greater odds of suicide by firearm, including traumatic brain injury (TBI) (odds ratio [OR]=23.53), epilepsy (OR=3.17), psychogenic pain (OR=2.82), migraine (OR=2.35), and stroke (OR=2.20). Fifteen general medical disorders were associated with statistically significant (p<.001) greater odds of suicide by other means, with particularly high odds for TBI (OR=7.74), epilepsy (OR=3.28), HIV/AIDS (OR=6.03), and migraine (OR=3.17).

CONCLUSIONS: Medical providers should consider targeting suicide risk screening for patients with any mental disorder, TBI, epilepsy, HIV, psychogenic pain, stroke, and migraine. When suicide risk is detected, counseling on reducing access to lethal means should include both firearms and other means for at-risk groups.

Bibliometric analysis of military trauma publications: 2000-2016.

Vickers ML[1], Coorey CP[1], Milinovich GJ[1], Eriksson L[2], Assoum M[3], Reade MC[1,4].

J R Army Med Corps. **2018 Jan 13**. pii: jramc-2017-000858. doi: 10.1136/jramc-2017-000858. PMID: 29331949. [Epub ahead of print]

INTRODUCTION: Bibliometric tools can be used to identify the authors, topics and research institutions that have made the greatest impact in a field of medicine. The aim of this research was to analyse military trauma publications over the last 16 years of armed conflict in order to highlight the most important lessons that have translated into civilian practice and military doctrine as well as identify emerging areas of importance.

METHODS: A systematic search of research published between January 2000 and December 2016 was conducted using the Thompson Reuters Web of Science database. Both primary evidence and review publications were included. Results were categorised according to relevance and topic and the 30 most cited publications were reviewed in full. The h-index, impact factors, citation counts and citation analysis were used to evaluate results.

RESULTS: A plateau in the number of annual publications on military trauma was found, as was a shift away from publications on wound and mortality epidemiology to publications on traumatic brain injury (TBI), neurosurgery or blast injury to the head. Extensive collaboration networks exist between highly contributing authors and institutions, but less collaboration between authors from different countries. The USA produced the majority of recent publications, followed by the UK, Germany and Israel.

CONCLUSIONS: In recent years, the number of publications on TBI, neurosurgery or blast injury to the head has increased. It is likely that the lessons of recent conflicts will continue to influence civilian medical practice, particularly regarding the long-term effects of blast-related TBI.

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