

The Journal of Pain

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Volume 22, Number 8, August 2021

REVIEW ARTICLES

879 Pain Catastrophizing, Opioid Misuse, Opioid Use, and Opioid Dose in People With Chronic Musculoskeletal Pain: A Systematic Review

Javier Martinez-Calderon, Mar Flores-Cortes, Jose Miguel Morales-Asencio, and Alejandro Luque-Suarez

This article sought to analyze the cross-sectional and longitudinal association between pain catastrophizing and opioid misuse, opioid use, and opioid dose in people with chronic musculoskeletal pain. For this systematic review, CINAHL, Embase, PsycINFO, PubMed, manual searches, and grey literature were searched from inception to May 2020. This article shows that pain catastrophizing seems to be associated with opioid misuse in people with chronic musculoskeletal pain. The overall certainty of the evidence was judged to be very low, thus, these results should be interpreted with caution.

892 AAAPT Diagnostic Criteria for Acute Thoracic Surgery Pain

Emine Ozgur Bayman, Michele Curatolo, Siamak Rahman, and Timothy J. Brennan

Patients undergoing thoracic surgery experience particular challenges for acute pain management. Availability of standardized diagnostic criteria for identification of acute pain after thoracotomy and video assisted thoracic surgery (VATS) would provide a foundation for evidence-based management and facilitate future research. The Analgesic, Anesthetic, and Addiction Clinical Trial Translations, Innovations, Opportunities, and Networks (ACTION) public-private partnership with the US Food and Drug Administration (FDA), the American Pain Society (APS), and the American Academy of Pain Medicine (AAPM) formed the ACTION-APS-AAPM Pain Taxonomy (AAAPT) initiative to address absence of acute pain diagnostic criteria. This multidisciplinary working group used available studies and expert opinion to characterize acute pain after thoracotomy and VATS. The resulting diagnostic criteria will serve as the starting point for subsequent empirically validated criteria, as discussed in this article.

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ON THE COVER

Chemotherapy-induced Peripheral Neuropathy is a common, difficult-to-treat, and dose-limiting side effect associated with Oxaliplatin (OXA) treatment. In this study, the authors evaluated the effect of three antioxidants - namely N-acetylcysteine, α -lipoic acid and vitamin E - upon nociceptive parameters and antitumor efficacy of OXA in a tumor bearing Swiss mice model. The results report preventive and therapeutic efficacy of orally administered antioxidants (N-acetylcysteine, α -lipoic acid and Vitamin-E) for alleviating oxaliplatin-induced peripheral neuropathy in tumor-bearing mice. Antioxidants anti-nociceptive effects are associated with inhibition of ROS-dependent neuroinflammation, and occur at no detriment of OXA antitumor activity, therefore indicating a translational potential of these compounds. See Agnes, et al, Page 996.

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ORIGINAL REPORTS

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Does Cognitive Functioning Predict Chronic Pain in Older Adult? Results From the CoLaus|PsyCoLaus Longitudinal Study

Isabelle Rouch, Jean-Michel Dorey, Marie-Pierre F. Strippoli, Mehdi Gholam, Pedro Marques-Vidal, Bernard Laurent, Armin von Gunten, and Martin Preisig

Chronic pain (CP) and cognitive impairment are common in the elderly. CP was found to be associated with cognitive impairment in many cross-sectional studies. However, their cross-sectional design precluded inference on temporality. This study aimed to assess the association between cognitive functioning and the occurrence of CP in elderly community dwellers. The findings show that presence of inhibitory deficits is associated with a higher risk of developing subsequent CP in older adults. In the presence of painful events, a cognitive assessment should be recommended to identify frail patients and to manage them carefully.

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Fibromyalgia Patients Are Not Only Hypersensitive to Painful Stimuli But Also to Acoustic Stimuli

Roland Staud, Melyssa M. Godfrey, and Michael E. Robinson

Fibromyalgia (FM) is a chronic widespread pain syndrome associated with hypersensitivity to nociceptive stimuli. This increased sensitivity has been associated with central sensitization of dorsal horn neurons. Increasing evidence, however, suggests that the mechanisms of FM hypersensitivity not only affect pain but include light, smell, and sound. Researchers hypothesized that supraspinal augmentation of sensory input, including sound, represent a hallmark of FM and tested 23 FM patients and 28 healthy controls for sensory augmentation of nociceptive and non-nociceptive sensations. Conclusions show that FM patients are also sensitive to innocuous stimuli like sound, suggesting that brain mechanisms may be responsible for the increased sensitivity of FM patients.

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The Psychological Functioning in the COVID-19 Pandemic and Its Association With Psychological Flexibility and Broader Functioning in People With Chronic Pain

Lin Yu, Kitty Kioskli and Lance M. McCracken

People with chronic pain may be particularly vulnerable to the impact of the COVID-19 pandemic, and psychological flexibility may protect them. This study investigated psychological functioning in the context of COVID-19, including fear and avoidance – specifically, its association with daily functioning and the role of psychological flexibility, among people with chronic pain. Responses from 555 adults with chronic pain were collected through a cross-sectional online survey. The authors report that COVID-19-related fear and avoidance correlated with pain, pain-related disability, depression, and work and social adjustment. Pandemic-related fear, avoidance and interference were significant predictors of some measures of daily functioning beyond demographics and pain.

940 **Spa Therapy for the Treatment of Fibromyalgia: An Open, Randomized Multicenter Trial**

Caroline Maindet, Aurore Maire, Céline Vermorel, Claire Cracowski, Carole Rolland, Romain Forestier, Alexa Comte, Christian-François Roques, Eric Serra, and Jean-Luc Bosson

Fibromyalgia (FM) is a common chronic pain pathology. An open, randomized clinical trial of patients with FM comparing an immediate versus delayed 18-day spa therapy in five spa therapy care facilities in France enrolled 220 patients. Randomization was in blocks of four, stratified by center, severity of fibromyalgia and previous spa therapy. Patients in the intervention group showed improvement in pain, fatigue, and symptom severity (secondary outcomes). The results showed a clinically significant improvement at 6 months for those who received immediate therapy, which was maintained up to 12 months. These demonstrate the benefit of spa treatment in patients with fibromyalgia.

952 **Medial Prefrontal High-Definition Transcranial Direct Current Stimulation to Improve Pain Modulation in Chronic Low Back Pain: A Pilot Randomized Double-blinded Placebo-Controlled Crossover Trial**

Megan E. McPhee and Thomas Graven-Nielsen

Chronic low back pain is highly disabling, but often without identifiable source. Focus has been on impaired anti-nociceptive mechanisms contributing to pain maintenance, though methods of targeting this impairment remain limited. This study used active versus sham medial prefrontal cortex (mPFC) high-definition transcranial direct current stimulation (HD-tDCS) for three-consecutive days to improve descending pain inhibitory function. The findings show that *mPFC* HD-tDCS did not alter pain, psychological nor psychophysical outcomes, though correlational analysis suggested response may depend on baseline pain inhibitory efficacy, with best potential effects in patients with severe impairments in descending pain inhibitory mechanisms. Future work should focus on appropriate patient selection and optimizing stimulation targeting.

968 **P2X4R Contributes to Central Disinhibition Via TNF- α /TNFR1/GABA_AR Pathway in Post-stroke Pain Rats**

Jiajie Lu, Xiaoning Guo, Manyun Yan, Xiaqing Yuan, Shujun Chen, Yiqing Wang, Juehua Zhu, Shicun Huang, Haitao Shen, Haiying Li, Qun Xue, Qi Fang, Jianqiang Ni, Lei Gan, Hongru Zhao, Haifeng Lu, and Gang Chen

Central post-stroke pain (CPSP) is a disabling condition in stroke patients. It is a type of neuropathic pain for which the mechanism and relevant drug pathways remain unknown. Inflammatory response and central disinhibition have been suggested recently. This team's previous research has shown targeting P2X4R may be effective in the treatment of CPSP, but the downstream pathway of the P2X4R has not been studied. In this study, researchers found the increase in TNF- α level and endocytosis of surface GABA_AR in CPSP, and these effects were inhibited by blocking P2X4R. These findings suggest that modulation of P2X4R-TNF- α /TNFR1-GABA_AR signaling could provide a new therapeutic strategy to treat CPSP.

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Pain Catastrophizing Mediates and Moderates the Link Between Acute Pain and Working Memory

Philip M. Procento, Kevin L. Rand, Jesse C. Stewart, and Adam T. Hirsh

The bidirectional relationship between pain and working memory (WM) deficits is well documented but poorly understood. Pain catastrophizing – exaggerated, negative cognitive and emotional responses toward pain – may contribute to WM deficits by occupying finite, shared cognitive resources. This study assessed the role of pain catastrophizing as both a state-level process and trait-level disposition in the link between acute pain and WM. Participants in the pain group (versus control group) who reported a greater trait-level tendency to catastrophize about pain experienced greater state-level catastrophizing about pain during the ischemic task, which led to worse verbal and non-verbal WM performance. The results raise the possibility that interventions that reduce catastrophizing may lead to improved cognitive function among people with pain.

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Antioxidants Improve Oxaliplatin-Induced Peripheral Neuropathy in Tumor-Bearing Mice Model: Role of Spinal Cord Oxidative Stress and Inflammation

Jonathan Paulo Agnes, Vitória Wibbelt dos Santos, Raquel Nascimento das Neves, Rosângela Mayer Gonçalves, Marina Delgobo, Carolina Saibro Girardi, Débora Denardin Lückemeyer, Marcella de Amorim Ferreira, Sérgio José Macedo-Júnior, Samantha Cristiane Lopes, Fernando Spiller, Daniel Pens Gelain, José Cláudio Fonseca Moreira, Rui Daniel Prediger, Juliano Ferreira, and Alfeu Zanotto-Filho

Chemotherapy-Induced Peripheral Neuropathy is a common, difficult-to-treat, and dose-limiting side effect associated with Oxaliplatin (OXA) treatment. In this study, the authors evaluated the effect of three antioxidants – namely N-acetylcysteine, α -lipoic acid and vitamin E – upon nociceptive parameters and antitumor efficacy of OXA in a tumor bearing Swiss mice model. The results report preventive and therapeutic efficacy of orally administrated antioxidants (N-acetylcysteine, α -lipoic-acid and Vitamin-E) for alleviating oxaliplatin-induced peripheral neuropathy in tumor-bearing mice. Antioxidants' anti-nociceptive effects are associated with inhibition of ROS-dependent neuroinflammation, and occur at no detriment of OXA antitumor activity, therefore indicating a translational potential of these compounds

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