

The Journal of Pain

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Volume 22, Number 10, October 2021

FOCUS ARTICLE

1129 Shifting the National Consciousness about Pain Treatment: The Critical Need for a National Public Education Campaign

Diana J. Burgess, Donna Vallone, Matthew J. Bair, Marianne S. Matthias, Brent C. Taylor, and Stephanie L. Taylor

The failure of past practices and policies related to opioid prescribing for chronic pain has led federal agencies and professional organizations to recommend multimodal approaches that prioritize evidence-based nonpharmacological pain treatments (NPT). These approaches hold great promise for reducing the burden of chronic pain and reducing opioid use. Unfortunately, NPT approaches are underutilized due to an array of interrelated barriers, including the public's attitudes and beliefs about chronic pain and its treatment. Despite these dual crises of chronic pain and opioid use in the US, there has never been a concerted effort to broadly educate the American public about these issues and NPT pain management options.

REVIEW ARTICLE

1134 Prevalence and Interference of Chronic Pain Among People With Hemophilia: A Systematic Review and Meta-Analysis

Ana Cristina Paredes, Pedro Teixeira, Armando Almeida, and Patrícia Ribeiro Pinto

Chronic pain is a common condition among people with hemophilia, associated with joint deterioration due to repeated joint bleeds. This systematic review and meta-analysis aimed to determine the prevalence of chronic pain due to haemophilia and to analyze its interference in the lives of patients. A systematic search was performed using PubMed, EMBASE, Web of Science and SciElo. This review revealed a wide range of hemophilia-related chronic pain across studies, varying methodologies and sample characteristics. Research in the hemophilia field should clearly distinguish between acute and chronic pain and provide complete characterization of study samples. Pain is a central issue in the lives of people with hemophilia, posing a significant challenge for healthcare providers.

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ON THE COVER

Chronic pain is a major health care problem. A better mechanistic understanding and new treatment approaches are urgently needed. In the brain, pain has been associated with neural oscillations at alpha and gamma frequencies, which can be targeted using transcranial alternating current stimulation (tACS). This work investigated the potential of tACS to modulate pain and pain-related autonomic activity in an experimental model of chronic pain in 29 healthy participants. This research applied tACS to modulate experimental pain in healthy participants. However, results show that tACS did not modulate pain, autonomic responses, or EEG oscillations. These findings help to shape future tACS studies for the treatment of pain. See May, et al, Page 1256.

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ORIGINAL REPORTS

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The Persistent Pain Transcriptome: Identification of Cells and Molecules Activated by Hyperalgesia

Matthew R. Sapiro, Jenny J. Kim, Amelia J. Loydpierson, Dragan Maric Taichi Goto, Fernando A. Vazquez, Mary K. Dougherty, Radhika Narasimhan, Wallis T. Muhly, Michael J. Iadarola, and Andrew J. Mannes

During persistent pain, the dorsal spinal cord responds to painful inputs from the site of injury, but the molecular modulatory processes have not been comprehensively examined. Using transcriptomics and multiplex in situ hybridization, the authors identified the most highly regulated receptors and signaling molecules in rat dorsal spinal cord in peripheral inflammatory and post-surgical incisional pain models. The deadly impact of the opioid crisis and the need to replace morphine and other opioids in clinical practice is well recognized. Embedded within this research is the goal of obtaining knowledge from transcriptomics to search for non-opioid analgesic targets. Developing such analgesics would address unmet clinical needs.

1180

Predictors of Sickness Absence in a Clinical Population With Chronic Pain

Riccardo LoMartire, Örjan Dahlström, Mathilda Björk, Linda Vixner Paolo Frumento, Lea Constan, Björn Gerdle, and Björn Olov Äng

Chronic pain-related sickness absence is an enormous socioeconomic burden globally. Optimized interventions are reliant on a lucid understanding of the distribution of social insurance benefits and their predictors. This register-based observational study analyzed data for a 7-year period for interdisciplinary treatment at specialist clinics. Patients were divided into three classes characterized by low sickness absence, sick leave, and disability pension, with eight predictors of class membership being identified. Sickness absence history was the strongest predictor of future sickness absence. Predictors of future sickness absence are also identified that should be considered when adapting IDT programs to the patient's needs.

1195

Specialized Pro-resolving Mediators Reduce Pro-nociceptive Inflammatory Mediator Production in Models of Localized Provoked Vulvodynia

Megan L. Falsetta, Ronald W. Wood, Mitchell A. Linder, Adrienne D. Bonham, Kenneth V. Honn, Krishna Rao Maddipati, Richard P. Phipps, Constantine G. Haidaris, and David C. Foster

Localized provoked vulvodynia (LPV) is the most common cause of chronic dyspareunia in premenopausal women, characterized by pain with light touch to the vulvar vestibule surrounding the vaginal opening. The devastating impact of LPV includes sexual dysfunction, infertility, depression, and even suicide. Yet, its etiology is unclear. No effective medical therapy exists; surgical removal of the painful vestibule is the last resort. The authors applied knowledge of more recently discovered vulvodynia disease mechanisms to screen novel therapeutics, and identified several specialized pro-resolving mediators as likely potent and safe for treating LPV with potential for broader application.

1210 Adverse Childhood Experiences (ACEs) and Internalizing Mental Health, Pain, and Quality of Life in Youth With Chronic Pain: A Longitudinal Examination

Sarah Nelson, Jaimie K. Beveridge, Richelle Mychasiuk, and Melanie Noel

The aims of this longitudinal study were twofold: 1) Identify categories of adverse childhood experiences (ACEs), such as neglect, abuse, household dysfunction in childhood. These increase risk for internalizing mental health problems, pain-related impairment, and poorer quality of life; and 2) Examine the moderating role of posttraumatic stress symptoms (PTSS) in these associations, in a clinical sample of youth with chronic pain. This study found that the risk of poorer outcomes imposed by ACEs at baseline remains longitudinally and that PTSS moderates the relationship between ACEs and anxiety and depressive symptoms, in youth with chronic pain. These results underscore the importance of assessing for ACEs and PTSS alongside chronic pain in youth.

1221 When Do We Not Face Our Fears? Investigating the Boundary Conditions of Costly Pain-Related Avoidance Generalization

Eveliina Glogan, Kristof Vandael, Rena Gatzounis, and Ann Meulders

Excessive generalization of fear and avoidance are hallmark symptoms of chronic pain disability, yet research focusing on the mechanisms underlying avoidance, specifically, is scarce. Two experiments investigated the boundary conditions of costly pain-related avoidance in healthy participants who learned to avoid pain by performing increasingly effortful arm-movements using a robot-arm. This research demonstrates generalization of instrumentally acquired avoidance in healthy people under conditions of uncertainty. Results suggest that targeting pain-related uncertainty may be a useful tool for clinicians adopting a psychological approach to treating excessive pain-related avoidance in chronic pain.

1233 Yoga, Eurythmy Therapy and Standard Physiotherapy (YES-Trial) for Patients With Chronic Non-specific Low Back Pain: A Three-Armed Randomized Controlled Trial

Andreas Michalsen, Michael Jeitler, Christian S. Kessler, Nico Steckhan, Sibylle Robens, Thomas Ostermann, Farid I. Kandil, Josephin Stankewitz, Bettina Berger, Sonny Jung, Matthias Kröz, and Arndt Büssing

This research aimed to evaluate the effects of yoga and eurythmy therapy compared to conventional physiotherapy exercises in patients with chronic low back pain. In a three-armed, multicentre, randomized controlled trial, patients with chronic low back pain were treated for 8 weeks in group sessions (75 minutes once per week). Results show that, compared with the gold standard of conventional physiotherapeutic exercises, eurythmy therapy and yoga therapy lead to comparable symptomatic improvements in patients with chronic low back pain. However, the within-group effect sizes were small to moderate and did not reach clinical meaningfulness on patients' physical disability.

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Should Exercises be Painful or not? Effects on Clinical and Experimental Pain in Individuals with Shoulder Pain

M Balasch-Bernat, E Lluch, HB Vaegter, and L Dueñas

Exercise can reduce pain, however the effect of painful vs non-painful exercises is uncertain. The primary aim of this randomized crossover study was to compare the effect of painful vs nonpainful isometric shoulder exercises on pain intensity after exercise in individuals with rotator cuff-related shoulder pain. Secondary exploratory aims were to describe the effects on pressure pain thresholds (PPTs), conditioned pain modulation (CPM) and muscle strength. Results indicate that both painful and non-painful isometric exercises caused a moderate but relatively short-lasting increase in shoulder pain in individuals with rotator cuff-related shoulder pain.

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Modulating Brain Rhythms of Pain Using Transcranial Alternating Current Stimulation (tACS) - A Sham-Controlled Study in Healthy Human Participants

Elisabeth S. May, Vanessa D. Hohn, Moritz M. Nickel, Laura Tiemann, Cristina Gil Ávila, Henrik Heitmann, Paul Sauseng, and Markus Ploner

Chronic pain is a major health care problem. A better mechanistic understanding and new treatment approaches are urgently needed. In the brain, pain has been associated with neural oscillations at alpha and gamma frequencies, which can be targeted using transcranial alternating current stimulation (tACS). This work investigated the potential of tACS to modulate pain and pain-related autonomic activity in an experimental model of chronic pain in 29 healthy participants. However, results show that tACS did not modulate pain, autonomic responses, or EEG oscillations. These findings help to shape future tACS studies for the treatment of pain.

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Sexually Dimorphic Role of Toll-like Receptor 4 (TLR4) in High Molecular Weight Hyaluronan (HMWH)-induced Anti-hyperalgesia

Ivan J.M. Bonet, Dionéia Araldi, Paul G. Green, and Jon D. Levine

Hyaluronan, a negatively charged linear disaccharide polymer, is an integral component of the extracellular matrix that plays a role in several physiological processes. High molecular weight hyaluronan (HMWH) has been used extensively to treat osteoarthritis pain and has been shown to have anti-inflammatory and immunosuppressive effects. This research tested the hypothesis that, in the setting of inflammation, HMWH acts at TLR4 to attenuate hyperalgesia. The study found that the attenuation of prostaglandin E2 (PGE2)-induced hyperalgesia by HMWH was attenuated by a TLR4 antagonist (NBP2-26245), but only in male and ovariectomized female rats. The role of TLR4 in anti-hyperalgesia induced by HMWH is a sexually dimorphic, TLR4 dependent inhibition of inflammatory hyperalgesia that provides a novel molecular target for the treatment of inflammatory pain.

1283 Differential Activation of Colonic Afferents and Dorsal Horn Neurons Underlie Stress-Induced and Comorbid Visceral Hypersensitivity in Female Rats

Dong-Yuan Cao, Bo Hu, Yang Xue, Shelby Hanson, Dean Dessem, Susan G. Dorsey, and Richard J. Traub

Chronic Overlapping Pain Conditions, including irritable bowel syndrome (IBS) and temporomandibular disorder (TMD), represent a group of idiopathic pain conditions that likely have peripheral and central mechanisms contributing to their pathology, but are poorly understood. These conditions are exacerbated by stress and have a female predominance. The presence of one condition predicts the presence or development of additional conditions, making this a significant pain management problem. Experiments were performed on cycling adult female Sprague-Dawley rats, seeking to determine if the duration and magnitude of peripheral sensitization and spinal central sensitization differs between restraint stress-induced visceral hypersensitivity (SIH) and chronic comorbid pain hypersensitivity (CPH). Results show that the diverse nature of peripheral organs hinders a clear understanding of underlying mechanisms accounting for the comorbidity. This study highlights a mismatch between the condition-dependent behavior and peripheral and spinal mechanisms that contribute to visceral pain hypersensitivity.

1294 Local and Systemic Expression Pattern of MMP-2 and MMP-9 in Complex Regional Pain Syndrome

Fabiola Escolano-Lozano, Eva Gries, Tanja Schlereth, Violeta Dimova, Panoraia Baka, Eva Vlckova, Simone König, and Frank Birklein

Matrix metalloproteinases (MMP) are endopeptidases which contribute to trauma reaction after tissue injury. MMPs play an important role in neuropathic pain and mechanical allodynia but also in inflammation and edema in various tissues. These proteins seem to be significantly involved in bone repair after fracture and wound healing, while they are also upregulated in chronic wounds. This study compared concentrations of these enzymes in skin and serum of patients with complex regional pain syndrome (CRPS), other pain diseases and healthy subjects. Findings describe an upregulation of MMPs, and results provide evidence that MMP-2 and -9 play a key role in CRPS pathophysiology.

The Moderating Role of Attention Control in the Relationship Between Pain Catastrophizing and Negatively-Biased Pain Memories in Youth With Chronic Pain

Aline Wauters, Melanie Noel, Dimitri M.L. Van Ryckeghem, Sabine Soltani, and Tine Vervoort

The role of attention control in understanding the development of negatively-biased pain memories, as well as its moderating role in the relationship between pain catastrophizing and negatively-biased pain memories, was examined in this study. Youth with chronic pain performed a cold pressor task (CPT) and completed self-report measures of state/trait pain catastrophizing and attention control, with the latter comprising both attention focusing and attention shifting. Two weeks after the CPT, pain-related memories were elicited via telephone, allowing for computation of pain and anxiety memory bias indices. Results showed no main effects of attention control and pain catastrophizing on pain memories. However, both components of attention control (ie, attention focusing and attention shifting) moderated the impact of pain catastrophizing on memory bias, with opposite interaction effects. Findings underscore the importance of targeting differential components of attention control and can inform intervention efforts to minimize the development of negatively biased pain memories in youth with chronic pain.

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