

The Journal of Pain

Table of Contents

Volume 22, Number 4, April 2021

FOCUS ARTICLES

359 I. Indices of Pain Intensity Derived From Ecological Momentary Assessments: Rationale and Stakeholder Preferences

Arthur A. Stone, Joan E. Broderick, Roberta E. Goldman, Doerte U. Junghaenel, Alicia Bolton, Marcella May, and Stefan Schneider

Pain assessment that fully represents patients' pain experiences is essential for chronic pain research and management. The traditional primary outcome measure has been a patient's average pain intensity over a time period. In this series of three articles, the authors examine whether pain assessment can be enhanced by considering additional outcome measures capturing temporal aspects of pain, such as pain maxima, duration, and variability. Ecological momentary assessments make the assessment of such indices readily available. In this first article, the rationale for considering additional pain indices derived from ecological momentary assessment is discussed, and the authors examine which are most important to stakeholders. This research suggests that multiple temporal aspects of pain intensity are important. This should be considered when evaluating the efficacy of pain management.

The Journal of Pain will publish appropriate images on the journal cover. Selected figures may accompany a submitted manuscript (authors should make a note in the covering letter), or images may be submitted individually. Please present your art for consideration. Visit <http://ees.elsevier.com/jpain> to upload your materials.

ON THE COVER

Effective treatment of neuropathic pain is lacking, largely due to an incomplete understanding of the pathogenesis. In this study, three main experiments were designed to investigate the mechanism of anti-nociception induced by intrathecally administered endothelin-1 in neuropathic pain. Findings show that inducing spinal GABAergic neuronal HDAC5 nuclear exportation may be a novel therapeutic approach for managing neuropathic pain. Characterizing the anti-nociceptive effect of ET-1 and investigating the associated epigenetic mechanisms in animal models may lead to the development of new therapeutic strategies and targets for treating neuropathic pain, the authors conclude. See Gu, et al, Page 454.

USASP

US ASSOCIATION FOR THE STUDY OF PAIN

371

II. Indices of Pain Intensity Derived From Ecological Momentary Assessments and Their Relationships With Patient Functioning: An Individual Patient Data Meta-analysis

Stefan Schneider, Doerte U. Junghaenel, Joan E. Broderick, Masakatsu Ono, Marcella May, and Arthur A. Stone

Pain intensity is a complex and dynamic experience. A focus on assessing patients' average pain levels may miss important aspects of pain. In this second of three articles investigating alternative indices of pain intensity derived from Ecological Momentary Assessments (EMA), the authors examine the indices' associations with physical and psychosocial functioning. EMA data from 10 studies were reanalyzed to construct indices of Average Pain, Maximum Pain, Minimum Pain, Pain Variability, Time in High Pain, Time in Low Pain, Pain after Wake-up. Three sets of individual patient data meta-analyses examined the test-retest reliability of the pain indices; factors such as physical functioning, fatigue, depression, mental health, and social functioning; and the incremental validity of alternative indices above Average Pain. The authors conclude that utilizing EMA for the assessment of Maximum Pain, Pain Variability, and Time in High Pain may provide an enhanced window into the relationships between pain and patients' physical and psychosocial functioning.

386

III. Detecting Treatment Effects in Clinical Trials With Different Indices of Pain Intensity Derived From Ecological Momentary Assessment

Stefan Schneider, Doerte U. Junghaenel, Masakatsu Ono, Joan E. Broderick, and Arthur A. Stone

Pain intensity represents the primary outcome in most pain clinical trials. Identifying methods to measure aspects of pain that are most sensitive to treatment may facilitate discovery of effective interventions. In this third of three articles examining alternative indices of pain intensity derived from ecological momentary assessments (EMA), the authors compare treatment effects based on Average Pain, Maximum Pain, Minimum Pain, Pain Variability, Time in High Pain, Time in Low Pain, and Pain After Wake-Up. Findings show that alternative summary measures of pain intensity derived from EMA may broaden the scope of outcomes useful in pain clinical trials. In this analysis of a pharmacological treatment for fibromyalgia, most pain summary measures indicated similar effects.

REVIEW ARTICLE**400****Investigating the True Effect of Psychological Variables Measured Prior to Arthroplastic Surgery on Postsurgical Outcomes: A P-Curve Analysis**

Nils Georg Niederstrasser and Stephanie Cook

Patients' presurgical psychological profiles have been posited to predict pain and function following arthroplastic surgery of the hip and knee. Nevertheless, findings are conflicting, and this may be rooted in biased reporting that makes the determination of evidential value difficult. This ambiguity may have negative consequences for researchers and governmental agencies, as these rely on findings to accurately reflect reality. P-Curve analyses were used to establish the presence of evidential value and selective reporting in a sample of 26 studies examining presurgical psychological predictors on outcomes. The examined studies indicate there is evidential value for the effect of depression on pain intensity and function, anxiety on pain intensity and function, pain catastrophizing on pain intensity, as well as the combined effects of all psychological predictors on pain intensity and function. There were no signs that any results were influenced by biased reporting. The results highlight the importance of patients' psychological profiles in predicting surgical outcomes, which represent a promising avenue for future treatment approaches.

ORIGINAL REPORTS**415****Prior Pain Exposure and Mere Possession of a Placebo Analgesic Predict Placebo Analgesia: Findings From a Randomized, Double-Blinded, Controlled Trial**

Victoria Wai-lan Yeung and Andrew L Geers

A recent study found that merely possessing a placebo analgesic reduces pain. The current study tested for a possible moderator of this effect. Specifically, does the mere possession of a placebo analgesic affect pain for individuals with and without immediate prior experience with the pain task? Healthy participants were randomized to a prior pain condition or without a prior pain condition. The authors found a significant prior pain experience and possession status interaction effect on placebo analgesia. The impact of expectancy and emotion on the underlying process are discussed. This work offers a novel perspective on the time course of placebo effect, and provides practical implications on potential pain intervention for clinicians and paradigm design for researchers of placebo study.

432

Assessment of Chronic Pain Management in the Treatment of Opioid Use Disorder: Gaps in Care and Implications for Treatment Outcomes

Matthew S. Ellis, Zachary Kasper, and Theodore Cicero

Chronic pain is a significant comorbid condition among individuals with opioid use disorder (OUD). However, due to conflicting perceptions of responsibility, structural barriers, and a lack of widely applied standards of care, it is unclear what the landscape of chronic pain management looks like in addiction medicine. Using a national opioid surveillance system, the authors analyzed survey data from new entrants to 225 OUD treatment centers from 2013 to 2018, as well as an online survey among a subset of respondents. This article concludes that chronic pain is commonly reported, yet not managed by many OUD treatment programs, increasing the likelihood of opioid relapse. In order to improve low retention and success rates among OUD patients, interdisciplinary collaboration, evidence-based policies or processes for quality pain management in addiction care need to be prioritized.

440

Analgesic Effects of Topical Amitriptyline in Patients With Chemotherapy-Induced Peripheral Neuropathy: Mechanistic Insights From Studies in Mice

Anne-Laure Genevois, Jérôme Ruel, Virginie Penalba, Séverine Hatton, Camille Petitfils, Myriam Ducrocq, Paola Principe, Gilles Dietrich, Céline Greco, and Patrick Delmas

Oral amitriptyline hydrochloride (amitriptyline) is ineffective against some forms of chronic pain and is often associated with dose-limiting adverse events. This work evaluated the potential effectiveness of high-dose topical amitriptyline in a preliminary case series of chemotherapy-induced peripheral neuropathy patients, and investigated whether local or systemic adverse events associated with the use of amitriptyline were present in these patients. The authors also investigated the mechanism of action of topically administered amitriptyline in mice. Preliminary results suggest that topical amitriptyline could provide effective pain relief for chemotherapy-induced peripheral neuropathy patients without any systemic or local adverse events. Investigation of the mechanism of this analgesic action in mice revealed that this activity was mediated through local inhibition of nociceptor Nav channels.

454 **Central Endothelin-1 Confers Analgesia by Triggering Spinal Neuronal Histone Deacetylase 5 (HDAC5) Nuclear Exclusion in Peripheral Neuropathic Pain in Mice**

Pan Gu, Tingting Fan, Stanley Sau Ching Wong, Zhiqiang Pan, Wai Lydia Tai, Sookja Kim Chung, and Chi Wai Cheung

Effective treatment of neuropathic pain is lacking, largely due to an incomplete understanding of the pathogenesis. In this study, three main experiments were designed to investigate the mechanism of anti-nociception induced by intrathecally administered endothelin-1 in neuropathic pain. Findings show that inducing spinal GABAergic neuronal HDAC5 nuclear exportation may be a novel therapeutic approach for managing neuropathic pain. Characterizing the anti-nociceptive effect of ET-1 and investigating the associated epigenetic mechanisms in animal models may lead to the development of new therapeutic strategies and targets for treating neuropathic pain, the authors conclude.

Instructions to Authors is available online at <http://www.jpain.org/authorinfo>. **A Mandatory Submission Form (http://cdn.elsevier.com/promis_misc/YJPAI_mandatory_submission_form.docx) must accompany all submissions.** This form should be downloaded, signed, and emailed to jpain@jpain.us.