

The Journal of Pain

Table of Contents

Volume 11, Number 8, August 2010

Critical Review

701 The Determination and Application of Fixed-Dose Analgesic Combinations for Treating Multimodal Pain

Robert B. Raffa, Joseph V. Pergolizzi Jr, and Ronald J. Tallarida

When the pathophysiology of a medical condition is multi-modal—related to multiple physiological causes or mediated by multiple pathways—the optimal strategy can be to use a drug or a combination of drugs that contribute multiple mechanisms to the therapeutic endpoint. This Critical Review article examines the medical relevance of the quantitative evaluation of drug combinations, using pain and combinations of analgesics as specific examples.

Original Reports

710 A Principal Components Analysis of Negative Affect-Related Constructs Relevant to Pain: Evidence for a Three Component Structure

Charlotte Mounce, Edmund Keogh, and Christopher Eccleston

This article explores the relationships between various negative-affect pain-related measures and discusses the results from a principal components analysis. The findings show that some questionnaires may measure the same latent construct. A method could be developed to measure the core components more concisely for both clinical and research purposes, the authors report.

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ON THE COVER

The anatomy and physiology of pain transmission. See Raffa, et al, page 701.

718

Peripheral Acid-Sensing Ion Channels and P2X Receptors Contribute to Mechanical Allodynia in a Rodent Thrombus-Induced Ischemic Pain Model

Hyoung-Sig Seo, Dae-Hyun Roh, Seo-Yeon Yoon, Suk-Yun Kang, Ji-Young Moon, Hyun-Woo Kim, Ho-Jae Han, Jin Mo Chung, Alvin J. Beitz, and Jang-Hern Lee

The authors previously established a thrombus-induced ischemic pain (TIIP) model in the rat, which mimics the pathophysiology of ischemic pain in peripheral arterial disease (PAD) patients. Since ischemia induces acidosis and ATP release, one goal was to investigate the role of acid-sensing ion channels (ASICs), transient receptor potential vanilloid-1 receptors, and P2X receptors in the maintenance of ischemia-induced mechanical allodynia. Results show that peripheral ASICs and P2X receptors are involved in the maintenance of TIIP. This provides mechanistic information that may be useful for the management of the chronic ischemic pain observed in human patients with PAD.

728

Comparison of the Cold Pressor Test and Contact Thermode-Delivered Cold Stimuli for the Assessment of Cold Pain Sensitivity

Ruth Ruscheweyh, Frederike Stumpfenhorst, Stefan Knecht, and Martin Marziniak

Sensitivity to suprathreshold cold pain stimuli is an important part of comprehensive pain sensitivity testing and can be assessed by the cold pressor test or using a contact thermode-based device. This article compares 2 methods of cold pain assessment in humans and analyzes their relationship to heat and pinprick pain. This may help researchers select the appropriate cold pain test, and may promote the understanding of communalities and differences between different pain modalities.

737

Changes in the Spatiotemporal Expression of Local and Referred Pain Following Repeated Intramuscular Injections of Hypertonic Saline: A Longitudinal Study

Troy K. Rubin, Luke A. Henderson, and Vaughan G. Macefield

Intramuscular injection of hypertonic saline produces a dull ache in the muscle belly but also refers into distal structures. The authors previously observed that the pattern of pain referral alters during painful stimuli separated by a week. This research tested the hypothesis that the intensity and area of pain exhibits plasticity when an identical noxious stimulus is delivered to the same site over sequential trials. Findings show that weekly injections into tibialis anterior cause decreases in local pain but increases in referred pain, suggesting central changes in processing noxious inputs.

746 **The Adequacy of Chronic Pain Management Prior to Presenting at a Tertiary Care Pain Center: The Role of Patient Socio-Demographic Characteristics**

Carmen R. Green and Tamera Hart-Johnson

Most patients seeking treatment for pain receive initial care in a primary care setting. This study examined the adequacy of pain management prior to specialty pain care and showed blacks and women had less adequate pain care at the referral stage. These findings indicate variability in chronic pain care and the need for research focusing on whether these disparities persist with specialized pain care.

755 **Parental Responses to Pain in High Catastrophizing Children: The Moderating Effect of Child Attachment**

Tine Vervoort, Liesbet Goubert, and Geert Crombez

This research found preliminary evidence for the moderating impact of child attachment in understanding patterns of parental responses related to pain catastrophizing. For less securely attached children, higher levels of catastrophizing were associated with more negative parental responses. For more securely attached children, higher levels of catastrophizing were associated with more positive responses. Further investigation relating to catastrophizing and attachment may offer a better comprehension of the interpersonal nature of pain catastrophizing.

764 **Exercise Alters Pain Sensitivity in Gulf War Veterans With Chronic Musculoskeletal Pain**

Dane B. Cook, Aaron J. Stegner, and Laura D. Ellingson

Veterans of the first Gulf War (GVs) have reported numerous symptoms with no apparent explanation. A primary complaint is chronic musculoskeletal pain (CMP). CMP symptoms in GVs are similar to those reported by fibromyalgia (FM) patients, but have not received equivalent attention. CMP research suggests that acute exercise may exacerbate pain while chronic exercise can reduce pain and improve other symptoms. Results indicate that similar abnormalities in central nervous system processing of nociceptive information documented in FM may also be occurring in GVs with CMP.

773

Evaluating a Sham-Controlled Sensory-Testing Protocol for Nonverbal Adults With Neurodevelopmental Disorders: Self-Injury and Gender Effects

Frank J. Symons, Vicki Harper, Satomi K. Shinde, Jamie Clary, and James W. Bodfish

Ambiguous or blunted responses to sensory and painful stimuli among individuals with severe intellectual disabilities and co-morbid communicative impairments put them at risk for misinterpretation of their pain. This work investigated a sham-controlled sensory testing protocol as a way to guard against observer bias during non-verbal behavioral recording for individuals with intellectual disabilities. A novel application of a modified approach to quantitative sensory testing for non-verbal adults with intellectual and developmental disabilities is presented.

782

The Relationship of Changes in Pain Quality to Pain Interference and Sleep Quality

Mark P. Jensen, Errol M. Gould, Timothy W. Victor, Arnold R. Gammaioni, Richard E. White, and Bradley S. Galer

Pain is a complex multidimensional experience that includes overall intensity, unpleasantness, location, and quality. Most research focuses only on the intensity and affective components of pain. This study sought to address this gap by examining, in a sample of patients with carpal tunnel syndrome, the associations between pain quality and 2 domains of patient functioning: pain interference and sleep quality. Results indicate that measures of pain quality contributed to the prediction of pain interference and sleep quality over and above the effects of global pain intensity and unpleasantness.

789

Pain-Related Anxiety as a Mediator of the Effects of Mindfulness on Physical and Psychosocial Functioning in Chronic Pain Patients in Korea

Sungkun Cho, Elaine M. Heiby, Lance M. McCracken, Sun-Mi Lee, and Dong-Eon Moon

Mindfulness involves reducing potential influences from aversive cognitions, sensations, and emotions on behavior. It may influence the experience of pain-related anxiety and enhance other aspects of physical and psychosocial functioning. The purpose of this study was to investigate a potential mediating role of pain-related anxiety between mindfulness and physical and psychosocial functioning in chronic pain patients.

Commentary

798

Central Sensitization Versus Synaptic Long-Term Potentiation (LTP): A Critical Comment

Jürgen Sandkühler

Letters to the Editor

801

Synaptic Plasticity and Central Sensitization: Author Reply

Alban Latremoliere and Clifford J. Woolf

804

The Integration of Emotion and Reason in Caregiver Pain Assessment

Simon van Rysewyk