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Critical Review

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Clinical Pain in Schizophrenia: A Systematic Review

Gwenda Engels, Anneke L. Francke, Berno van Meijel,
Johanna G. Douma, Heidi de Kam, Wubbien Wesselink,
Wim Houtjes, and Erik J. A. Scherder

Studies about clinical pain in schizophrenia are rare. Conclusions on pain sensitivity in people with schizophrenia are primarily based on experimental pain studies. This review attempts to assess clinical pain, that is, everyday pain without experimental manipulation. People with schizophrenia appear to have a diminished prevalence of pain. However, it was found that this applies to pain with an apparent medical cause, such as headache after lumbar puncture. For less severe situations, prevalence and intensity of pain appear to be comparable between people with schizophrenia and controls. Knowledge about pain in schizophrenia is important for adequate treatment in clinical practice.

ON THE COVER

Despite accumulating evidence of the clinical effectiveness of acupuncture, its mechanism remains largely unclear. It is assumed that molecular signaling around the acupuncture needled area is essential for initiating the effect of acupuncture. Results from this study show that extracellular signal-regulated kinase phosphorylation following acupuncture needling is a biochemical hallmark initiating the effect of acupuncture including analgesia. See Park et al, page 535.

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Original Reports

468 **Effect of Estrogen Depletion on Pain Sensitivity in Aromatase Inhibitor–Treated Women With Early-Stage Breast Cancer**

N. Lynn Henry, Anna Conlon, Kelley M. Kidwell, Kent Griffith, Jeffrey B. Smerage, Anne F. Schott, Daniel F. Hayes, David A. Williams, Daniel J. Clauw, and Steven E. Harte

Despite positive oncologic benefits in the treatment of breast cancer, aromatase inhibitors (AIs) can negatively impact quality of life, which can lead to decreased adherence to therapy. The etiology may be due in part to estrogen deprivation. This article presents findings of the effect of estrogen deprivation on objective measures of pain sensitivity. In postmenopausal women, medication-induced estrogen depletion did not result in an identifiable change in pressure pain threshold or conditioned pain modulation. Impaired conditioned pain modulation may be associated with chemotherapy.

476 **Racial Bias in Pain Perception and Response: Experimental Examination of Automatic and Deliberate Processes**

Vani A. Mathur, Jennifer A. Richeson, Judith A. Paice, Michael Muzyka, and Joan Y. Chiao

Racial disparities in pain treatment pose a significant public problem. Prior studies have demonstrated that clinicians and nonclinicians are less perceptive of, and suggest less treatment for, pain in African Americans. These authors investigated the effects of explicit/implicit patient race presentation, patient race, and perceiver race on pain perception and response. African American and European American participants rated pain perception, empathy, helping motivation, and treatment suggestion in response to vignettes about patients' pain. Vignettes were accompanied by a rapid (implicit) or static (explicit) presentation of an African or European American patient's face. Results suggest that known disparities in pain treatment may be largely due to automatic rather than deliberate biases. Biases were not associated with traditional implicit measures of racial attitudes, suggesting that biases in pain perception and response may be independent of general prejudice.

485 **Activation of Cutaneous Immune Responses in Complex Regional Pain Syndrome**

Frank Birklein, Peter D. Drummond, Wenwu Li, Tanja Schlereth, Nahid Albrecht, Philip M. Finch, Linda F. Dawson, J. David Clark, and Wade S. Kingery

Complex regional pain syndrome (CRPS) is a painful, disabling, and often chronic condition with an estimated 50,000 new cases in the U.S. each year. The current investigation used CRPS patient skin biopsies to determine whether keratinocyte and mast cell proliferation occur in CRPS skin, and to identify the cellular source of the up-regulated TNF- α , IL-6, and tryptase observed in CRPS experimental skin blister fluid. The results of this study support the hypotheses that CRPS involves activation of the innate immune system, with keratinocyte and mast cell activation and proliferation, inflammatory mediator release, and pain.

496 Monocytes/Macrophages Control Resolution of Transient Inflammatory Pain

Hanneke L. D. M. Willemen, Niels Eijkelkamp, Anibal Garza Carbajal, Huijing Wang, Matthias Mack, Jitske Zijlstra, Cobi J. Heijnen, and Annemieke Kavelaars

Many Americans suffer from chronic pain. One limitation for developing novel interventions is the limited understanding of the neurobiological pathways leading to transition from acute to chronic pain. This work reports that IL-10-producing monocytes/macrophages promote resolution of transient inflammatory hyperalgesia, and that reduced monocyte/macrophage G-protein-coupled receptor kinase 2 (GRK2) impairs resolution of hyperalgesia and reduces IL-10 production. The authors propose that low GRK2 expression and/or impaired IL-10 production by monocytes/macrophages represent peripheral biomarkers for the risk of developing chronic pain after inflammation.

507 Association of Chronic Widespread Pain With Objectively Measured Physical Activity in Adults: Findings From the National Health and Nutrition Examination Survey

Elizabeth J. Dansie, Dennis C. Turk, Kathryn R. Martin, Dane R. Van Domelen, and Kushang V. Patel

Chronic widespread pain (CWP), the core feature of fibromyalgia, is a potentially debilitating disorder that is commonly associated with pain hypersensitivity. Many people with CWP have reduced cardiorespiratory fitness and lead predominately sedentary lifestyles. Using objective measurement of physical activity in a nationally representative sample, results from this research show that adults with CWP participate in less activity than individuals without chronic pain. Findings indicate that clinicians should emphasize the importance of increasing physical activity in patients with CWP.

516 Contribution of Chemokine CCL2/CCR2 Signaling in the Dorsal Root Ganglion and Spinal Cord to the Maintenance of Neuropathic Pain in a Rat Model of Lumbar Disc Herniation

Xiang Zhu, Su Cao, Ming-Di Zhu, Jin-Qian Liu, Jun-Jie Chen, and Yong-Jing Gao

Lumbar disc herniation (LDH) is a major cause of sciatica, but the underlying mechanisms are not well understood. Chemokine CCL2 has been implicated to play a vital role in the neuroinflammation and central sensitization after spinal nerve ligation. This work investigated the expression and the role of CCL2 and its receptor CCR2 in LDH-induced pain. Findings show that CCL2/CCR2 in the dorsal root ganglion and spinal cord is involved in the maintenance of LDH-induced pain. Targeting CCL2/CCR2 signaling may be a potential treatment for chronic radicular neuropathic pain.

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The Interplay of Pain-Related Self-Efficacy and Fear on Functional Outcomes Among Youth With Headache

Elizabeth Carpino, Sharon Segal, Deirdre Logan,
Alyssa Lebel, and Laura E. Simons

Headaches are a persistent problem in youth and adolescents. Pain-related self-efficacy is an important resiliency factor impacting the influence of pain-related fear on functional disability and impacting school functioning in youth with headache. The findings of this work indicate that one's confidence in the ability to function despite pain and fear avoidance contributes to pain-related outcomes in youth with chronic headache. Enhancing self-efficacy may be a key mechanism for improving behavioral outcomes. Clinicians can reduce pain-related fear and enhance pain-related self-efficacy through interventions that encourage accomplishment and self-confidence.

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From Peripheral to Central: The Role of ERK Signaling Pathway in Acupuncture Analgesia

Ji-Yeun Park, Jongbae J. Park, Songhee Jeon,
Ah-Reum Doo, Seung-Nam Kim, Hyangsook Lee,
Younbyoung Chae, William Maixner, Hyejung Lee, and
Hi-Joon Park

Despite accumulating evidence of the clinical effectiveness of acupuncture, its mechanism remains largely unclear. It is assumed that molecular signaling around the acupuncture needled area is essential for initiating the effect of acupuncture. To determine possible bio-candidates involved in the mechanisms of acupuncture and to investigate the role of such bio-candidates in its effects, this research carried out 2 experiments. Results show that extracellular signal-regulated kinase phosphorylation following acupuncture needling is a biochemical hallmark initiating the effect of acupuncture including analgesia.

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Internalized Stigma in People Living With Chronic Pain

Olivia C. Waugh, Donald G. Byrne, and Michael K. Nicholas

Although persistent pain occurs in a sociocultural context, the influence of personal devaluation and invalidation is often neglected. As such, the present study sought to consider whether individuals' experience, perception, or anticipation of negative social reactions to their pain may become internalized and affect the self. To examine this issue, 92 adults with chronic pain responded to a questionnaire exploring the presence of internalized stigma and its association with a range of psychological consequences. In conclusion, this report shows that internalized stigma is strongly associated with indicators of patient outcome. It presents an area for future work with the aim to improve our understanding and treatment of people living with pain.

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The Influence of Patient Sex, Provider Sex, and Sexist Attitudes on Pain Treatment Decisions

Adam T. Hirsh, Nicole A. Hollingshead, Marianne S. Matthias, Matthew J. Bair, and Kurt Kroenke

There is conflicting evidence of sex/gender disparities in pain management. Some studies have found that women receive less aggressive treatment than men, whereas others found reversed or comparable treatment patterns between genders. Research suggests that patient sex, provider sex, and providers' sexist attitudes interact to influence pain care; however, few empirical studies have examined these influences. This analysis investigated sex differences in pain treatment and the extent to which providers' sexist attitudes were associated with these differences. The results show that patient and provider sex, but not providers' sexist attitudes, influence pain care. These findings may inform efforts to raise awareness of sex/gender differences in pain care and reduce disparities.

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Reduction of Bodily Pain in Response to an Online Positive Activities Intervention

Leslie R. M. Hausmann, Acacia Parks, Ada O. Youk, and C. Kent Kwok

This research tested whether completing positive activities in one's daily life produces long-term reductions in self-reported bodily pain in a randomized controlled trial of an online positive activities intervention. Participants recruited via the Web were randomly assigned to complete 0, 2, 4, or 6 positive activities administered online over a 6-week period. Results show that positive activities can decrease reported levels of bodily pain. Moreover, this study demonstrates that these activities can be administered over the internet, a potential avenue for broadly disseminating health interventions at relatively low cost and with high sustainability.

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