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MIND-BODY ROUNDUP

OSHER CENTER FOR INTEGRATIVE MEDICINE
HARVARD MEDICAL SCHOOL AND BRIGHAM AND WOMEN'S HOSPITAL

Minding the Mind-Body Literature

This is the first in a series of regular columns coauthored by researchers associated with the Osher Center for Integrative Medicine, jointly based at Harvard Medical School and Brigham and Women's Hospital. In the column, three researchers associated with the Harvard Osher Center will each summarize a top recent publication from the burgeoning mind-body literature and provide commentary on why they chose to shine a light on it. While from time to time other researchers from the Center may participate, the core team are Peter Wayne, director of research for the Center and Executive Editor, JACM; JACM associate editors Gloria Yeh, MD, MPH, director, research fellowship in integrative medicine at Harvard Medical School; and Darshan Mehta, MD, MPH, medical director, the Benson-Henry Institute. We are pleased and honored to bring you this column. We welcome your substantive responses. – John Weeks, Editor-in-Chief, *JACM*

T'ai Chi Is Effective for Knee Osteoarthritis and the Grief It Causes

Peter M. Wayne, PhD
Director of Research, Osher Center for Integrative Medicine
Division of Preventive Medicine
Associate Professor of Medicine
Harvard Medical School and Brigham and Women's Hospital

Osteoarthritis (OA) of the knees is a major public health problem and a leading cause of long-term pain and disability. Like other chronic pain conditions, knee OA can become a significant barrier to physical and social activity, leading to declines in self-efficacy and emotional well-being. No effective medical treatments for OA currently exist. Nonsteroidal anti-inflammatory drugs and acetaminophen are commonly used to treat OA pain but sometimes have only limited efficacy and are associated with potentially serious adverse effects. Knee-specific physical therapy produces moderate short-term benefits for pain and physical functioning, but its long-term effectiveness and broader impact on psychological well-being are NOT known. Prior pilot studies suggested that *t'ai chi*—a multicomponent traditional Chinese mind–body practice—could positively affect both OA pain and disability as well as psychological well-being, but these potential benefits have not been confirmed in larger-scale trials with active controls.

In an elegantly designed and rigorously conducted comparative effectiveness trial supported by the National Center for Complementary and Integrative Health (NCCIH)/National Institutes of Health (NIH), Dr. Chenchen Wang

and colleagues from Tufts University School of Medicine compared *t'ai chi* with standard physical therapy for patients with knee OA. A total of 204 ethnically diverse participants with symptomatic and radiographic knee OA (mean age, 60 years; 70% women; 53% white) were randomly assigned to *t'ai chi* (two times per week for 12 weeks) or standard physical therapy (two times per week for 6 weeks, followed by 6 weeks of monitored home exercise). Both the *t'ai chi* and physical therapy programs were based on well-developed and previously tested protocols and were delivered by multiple experienced practitioners. Outcomes were assessed at baseline and 12, 24, and 52 weeks. The primary outcome was Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score at 12 weeks. Secondary outcomes included physical function, depression, medication use, and quality of life.

At 12 weeks, the WOMAC score was substantially reduced in both groups (*t'ai chi*, 167 points [95% confidence interval (CI), 145–190 points]; physical therapy, 143 points [95% CI, 119–167 points]). The between-group difference was not significant but favored *t'ai chi*. Both groups also showed similar clinically significant improvement in most secondary outcomes, and the benefits were maintained up to 52 weeks. Of note, the *t'ai chi* group had significantly greater improvements in depression. No serious adverse events occurred.

This study is important for several reasons. First, and somewhat surprisingly, it represents the first large-scale trial with more than 100 participants per study group evaluating *t'ai chi* for pain. Second, the findings support that *t'ai chi* is at least as good as the current gold standard of physical therapy for treating OA, making it a sound alternative or complementary treatment option. Follow-up studies are needed to evaluate its relative cost-effectiveness, which is likely to be favorable given that instructions are typically provided in a group setting. Finally, it is noteworthy that along with improved pain and function, *t'ai chi* but not PT reduced levels of depression. A growing body of research supports comorbidities of depression with chronic pain, and these findings suggest that the more holistic nature of *t'ai chi*, which targets physical as well as cognitive and affective processes, may afford unique advantages. Future studies should probe these multisystems effects because it is likely that changes in bottom-up physical and top-down mental processes are highly interdependent and reciprocally mediate one another—making mind–body therapies such as *t'ai chi* uniquely effective treatment options for complex chronic pain conditions.

Citation: Wang C, Schmid CH, Iversen MD, et al. Comparative effectiveness of tai chi versus physical therapy for knee osteoarthritis: a randomized trial. Ann Intern Med 2016;165:77–86.

Mindfulness and Pathways of Pain Control: Opportunity Knocks

Gloria Yeh, MD, MPH
Director, Research Fellowship in Integrative Medicine
Director of Mind-Body Research
Division of General Medicine and Primary Care
Beth Israel Deaconess Medical Center
Harvard Medical School

While many studies show mindfulness meditation reduces pain across a wide spectrum of disorders, mechanistic pathways are not clearly understood. Among the most studied of the endogenous modulatory systems mediating the perception of pain is the endogenous opioidergic system. Zeidan et al. conducted a randomized, double-blind, four-group study using a 2×2 factorial experimental pain paradigm to investigate involvement of the opioidergic system in mindfulness meditation–related analgesia. Investigators measured behavioral pain responses to noxious heat stimuli in healthy human volunteers during mindfulness meditation or no meditation (control at rest) and with intravenous administration of the opioid antagonist naloxone or without naloxone (saline administration). Those randomly assigned to the meditation groups underwent four 20-minute sessions of mindfulness training across 4 separate days; the control groups attended time-matched audio book listening sessions. After successful completion of the trainings, participants came in for an experimental testing session.

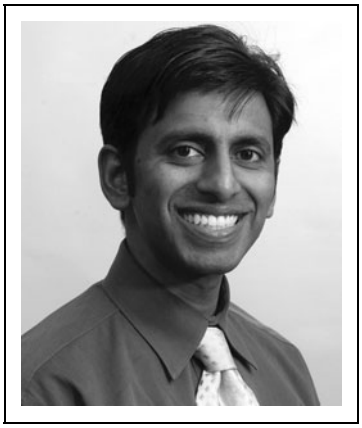
Results showed that mindfulness meditation with saline administration significantly reduced ($p = 0.001$) pain intensity (−21% vs. 21%) and unpleasantness ratings (−36% vs. −18%) compared with the control group. Meditation with naloxone administration also significantly reduced pain (−24%) and unpleasantness (−33%), with no significant differences when compared with meditation with saline. Similarly, meditation with naloxone significantly reduced

pain compared with both control saline and control naloxone groups. The observation that the naloxone failed to inhibit pain reduction with meditation demonstrates that mindfulness meditation does not rely on endogenous opioidergic mechanisms to reduce pain.

It is well known that endogenous opioids are involved in the cognitive inhibition of pain; however, this provocative study by Zeidan et al. underscores that other important mechanisms are at play. In fact, recent lines of evidence have converged to better elucidate that mindfulness meditative analgesia is mediated by multiple unique psychological and neural processes and that modulation of the contextual appraisal of pain is an important component. Also pivotal are the findings that the neural pathways and activation of prefrontal and cingulate cortices appear to be distinct from those seen with placebo analgesia. Now more than ever, this type of mechanistic information may be critical to inform practice and policy as we move forward toward implementation, choosing which therapies to best use and for which patients, when along the disease spectrum to use them, and how to do this in the most effective and cost-effective way. With the current national conversation on the devastating and costly opioid epidemic, the potential role of integrative pain management has received much attention. With the understanding that meditative analgesia is not necessarily dependent on the opioid system, there may be an opportunity for mindfulness-based therapies to help decrease or prevent opioid use/misuse because mindfulness may address pain reduction through unique mechanisms without cross-tolerance with opioid medications. Within this context, there may be potential for meditative therapies that are relatively accessible to have even farther-reaching public health implications.

Citation: Zeidan F, Adler-Neal AL, Wells RE, et al. Mindfulness-meditation-based pain relief is not mediated by endogenous opioids. J Neurosci 2016;36:3391–3397.

Mind–Body Approach to Low Back Pain: A "No-Brainer" or "All-Brainer," Depending on How You Look at It



Darshan Mehta, MD
Medical Director, Benson-Henry Institute for Mind Body Medicine
Massachusetts General Hospital
Associate Director of Education
Osher Center for Integrative Medicine
Harvard Medical School and Brigham and Women's Hospital

It is estimated that nearly 40% of adults will be affected by low back pain (LBP) over the course of their lifetime. It is the leading cause of disability in the United States. Recent guidelines from the Centers for Disease Control and Prevention recommended that physicians use nonpharmacologic approaches in the management of LBP, especially to avert the opioid epidemic that has been particularly well documented in the United States. Behavioral interventions, such as cognitive-behavioral therapy (CBT), have been shown to be effective in the treatment of LBP, among other pain conditions. More recently, there has also been an interest in multimodal mind–body interventions, such as mindfulness-based stress reduction (MBSR), in the treatment and management of LBP. However, to date, there have been no head-to-head comparison between these nonpharmacologic strategies in LBP treatment.

Cherkin and colleagues' beautiful randomized prospective study, supported by NCCIH/NIH, compared CBT to MBSR to usual care. A total of 342 patients (mean age, 49 years; 66% women; 83% white) were randomly assigned to the three arms, with mean duration of reported back pain of just over 7 years. Both the CBT and MBSR arms were manualized, with the CBT arm delivered by 4 licensed PhD-level psychologists and the MBSR arm delivered by 8 experienced practitioners. Outcomes were reported at baseline and 4, 8, 26, and 52 weeks; the primary outcome was the percentage of individuals with a clinically meaningful (>30%) improvement on the modified Roland Disability Questionnaire and self-reported back pain bothersomeness at 26 weeks.

Just less than two thirds of participants reported clinically meaningful improvement in both the MBSR (61%) and CBT (58%) arms compared with usual care (44%). On pain bothersomeness, just under half reported clinically meaningful improvements in the MBSR (44%) and CBT (45%) groups, compared with 27% in the usual care group. Of particular note, the MBSR group continued to have statistically significant findings on these metrics at 52 weeks,

although this was a secondary outcome of the study. Additionally, these results are even more astounding, given that just half of participants in the MBSR group and 57% in the CBT group attended at least 6 group sessions; moreover, only one fourth attended the optional 6-hour MBSR retreat. This suggests a ''real-life'' dimension to the study—even a ''suboptimal'' participation had a clinically meaningful outcome.

This powerful study demonstrates that MBSR is an acceptable option in the treatment of chronic LBP. While it is important to understand the mediators and ''dose-response'' of the interventions, the clinical utility should be underscored. Both patients and providers have greater choices in the management of these conditions, and the side effect profile (which should not be ignored) probably pales in comparison to that commonly encountered through pharmacologic management. One hopes that these studies do include cost and healthcare utilization metrics, as ballooning costs of healthcare, especially around LBP, loom on the horizon.

Citation: Cherkin DC, Sherman KJ, Balderson BH, et al. Effect of mindfulness-based stress reduction vs cognitive behavioral therapy or usual care on back pain and functional limitations in adults with chronic low back pain: a randomized clinical trial. JAMA 2016;315:1240–1249.

Address correspondence to:
Peter M. Wayne, PhD
Harvard Medical School
Osher Center for Integrative Medicine
Division of Preventive Medicine
Brigham and Women's Hospital
and Harvard Medical School
900 Commonwealth Avenue, 3rd Floor
Boston, MA 02215

E-mail: pwayne@partners.org