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Complementary And Integrative Approaches For Pain Management

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Educational Objectives

1) Describe the mechanisms underlying several mind and body therapies for pain relief.
2) Address how mind and body practices can translate into clinical care.
3) Explain how therapies can be matched to individual patients.

Introduction

Many people around the world use health care approaches that were developed outside conventional allopathic medicine. More than 30% of adults in the United States, with similar numbers in Europe, utilize complementary health approaches [20,47]. Chronic pain, particularly musculoskeletal pain, is one of the most common reasons for individuals to use complementary health care approaches. It is estimated that more than 40% of individuals with chronic musculoskeletal pain try some form of complementary therapy [21].

Complementary approaches include a multitude of modalities and products. These are sometimes broken down into two broad categories—natural products and mind and body practices. This distinction is artificial since there is a mind and body component in the use of natural products. Nevertheless, natural products include a wide variety of products, including herbs (botanicals), vitamins and minerals, and probiotics, and it was estimated in 2012 that 17% of Americans used at least one of these products [20]. Mind and body approaches also include a wide selection of procedures, including yoga, tai chi, meditation, hypnotherapy, cognitive-behavioral therapy, massage therapy, acupuncture, movement therapies, and arthrodial manipulation. One commonly used mind and body approach is yoga and related disciplines, such as tai chi, with 10% of Americans practicing these disciplines. Another modality that is used by 15–40% of Americans is manual therapy, practiced in various forms by chiropractors, osteopaths, physical therapists, and massage therapists [23]. Of note, in the United States, 95% of spinal manipulative therapy is performed by chiropractors. Cognitive-behavioral therapy is less used, perhaps because of limited accessibility and affordability, but it has proven effectiveness for treating chronic pain [62,64,66,81].

Chronic pain has become a health crisis in the United States and around the world. It is estimated that the prevalence of chronic pain (defined as chronic, recurrent, or long-lasting pain continuing for at least 6 months) is more than 30% in women and more than 25% in men [39]. Pain is most commonly treated using pharmacotherapy, but with

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the growing opioid epidemic, it is important to examine the use of nonpharmacological therapies to treat pain.

Rather than giving an overview of all complementary practices, this course will focus on three nonpharmacological approaches to treating chronic pain that have shown significant clinical effects—cognitive-behavioral therapies, manual therapies, and yoga therapy—and discuss mechanisms that may underlie their effectiveness.

Cognitive-Behavioral Therapies

Current interest in chronic pain stems from its prevalence, difficulty of treatment, and increasing recognition of the biopsychosocial factors involved in the experience of pain. Musculoskeletal conditions are a leading cause of disability in individuals of working age [2]. Chronic pain is difficult to treat effectively, as medical and surgical interventions produce only variable results. Furthermore, pain continues to be inadequately controlled [53], despite the fact that the patients with chronic pain syndromes often receive high doses of opioids regardless of the risk for adverse events. Therefore there is a need to optimize nonpharmacological treatment strategies for the management of chronic, nonmalignant pain [61].

In response to this need for effective, side-effect-free treatment, behavioral interventions such as cognitive-behavioral therapy (CBT) have been developed. The CBT approach is based on the assumption that pain is not a single sensation but has many dimensions. The gate control theory of pain postulated that psychological factors play an integral role in the pain experience [58,59]. One of the contributions of the gate control theory has been its emphasis on the central nervous system as an essential component in nociceptive processing and perception. The gate control theory provides the conceptual framework for integration of the sensory, affective, and cognitive dimensions of pain. Since 1965 many studies show that these three dimensions of pain do not simply occur in parallel but rather overlap as neurophysiological processes. Furthermore, most modern pain theories maintain that the experience of pain should be considered as a complex sensory and emotional experience. Thus it is reasonable to expect that a psychological intervention such as CBT, which teaches patients to understand and control sensory, emotional, and cognitive aspects of pain, could alter responses to both pain and emotionally provocative stimuli.

Emotions and Pain

For decades scientists have explored the context and meaning of pain and its emotional dimensions [10]. The notion of suffering from pain corresponds to the negative emotions associated with the pain experience. Extending the gating control theory of pain, Price proposed a four-stage model of pain processing consisting of: (1) an initial sensory-discriminative stage with the perceived intensity of pain perception; (2) an immediate affective response, called immediate pain unpleasantness; (3) longer-term cognitive processes that relate to the meaning that pain represents, also called extended pain affect, or suffering; (4) overt behavioral expressions of pain [74]. As the “immediate pain unpleasantness” is usually associated with an acute pain and the “extended pain affect” (suffering) with chronic pain, there is an evidence of a reciprocal interaction of current and later stages of pain processing [75]. A number of brain imaging studies support the distinction often drawn in the pain literature between the sensory aspect of pain processing and the affective one [17]. In short, many studies demonstrate that patients suffering from chronic pain display emotional dysregulation [3,44,69,78,83,84] and indicate that the emotional dysregulation exacerbates chronic pain [19,50,57,76,85,87,88,91]. The theoretical and clinical findings point to the important empirical question: How do emotions influence pain?

Cognitive Factors in Chronic Pain

As mentioned above, the experience of chronic pain is multifactorial: sensory, emotional, and cognitive. Physiological phenomena usually underlie the experience of pain. Coexisting physiological and cognitive factors act at peripheral and central levels to modulate the experience of pain [32]. Cognitive factors such as patients’ beliefs, attitudes, expectations, self-efficacy, and catastrophizing self-statements are also related to pain, activity level, disability, and response to treatment [30,33]. In addition, the context in which pain occurs significantly affects both the experience and the expression of pain, such as interpersonal relationships, financial problems, and one’s work situation [95]. These referenced studies demonstrate the importance of a patient’s ability to use healthy cognitive regulation strategies to moderate the experience of pain.

Catastrophizing and Neural Responses to Pain

Pain catastrophizing, or the tendency to ruminate upon and magnify pain sensations and to feel helpless in the face of pain, is recognized as one of the most consistent psychological predictors of the pain experience [34,41,43,89]. The influence of catastrophizing on pain can be substantial. Catastrophizing has been suggested to augment pain perception through enhanced emotional response to pain and heightened attention to painful stimuli. Studies suggest that catastrophizing increases pain-related fear, which in turn increases attention to the stimulus [24,25,71]. There is also evidence that catastrophizing is positively associated with affective pain ratings, which in turn may lead to higher overall evaluations of the experience of pain [35,36,80]. Studies suggest that pain catastrophizing, independent of the influence of depression, is significantly associated with increased activity in brain areas related to anticipation of pain, attention to pain, emotional aspects of pain, and motor control. These results support the hypothesis that catastrophizing influences pain perception through altering attention and anticipation, and by heightening emotional responses to pain. We conducted an investigation that documented that psychotherapeutic approaches such as CBT can reverse the brain's abnormal responses in patients with musculoskeletal pain [81,86].

Group CBT for Management of Chronic Pain

There is considerable evidence that group CBT offers significant therapeutic benefits to patients with persistent pain [7,8,99]. McCracken and Turk [55] conclude that "BT-CBT for chronic pain reduces patients' pain, distress, and pain behavior, and improves their daily functioning." Morley et al. [62] concluded that patients participating in behavioral therapy and cognitive-behavioral therapy (BT-CBT) treatments demonstrated greater improvement in pain experience, pain behavior, and use of positive coping strategies. Keefe's work documents that systematic training in pain coping skills training (a form of CBT) represents a particularly valuable addition to chronic pain management [22,45]. Pain coping skills training protocols are based on the rationale that cognitive and behavioral factors such as coping strategies, beliefs, and expectations can have a major impact on pain and disability [92]. These protocols have two major components. First, patients are taught about interrelationships among thoughts, feelings, and behavior to help them reconceptualize pain and enhance their ability to exercise greater control over maladaptive thoughts, feelings, and behavior. Second, patients are trained in a variety of cognitive and behavioral techniques designed to enhance their ability to cope with pain. These techniques include training in relaxation, pacing of daily activities, goal setting, cognitive restructuring, and problem solving. Patients are given home practice assignments designed to help them apply coping skills in a wide variety of situations. Coping skills training protocols emphasize the importance of regular coping skills practice in the development and maintenance of effective pain control. Controlled studies have shown that, after completing coping skills training, many chronic pain patients report significant reductions in pain and stress and improvements in psychological disability, physical and mental health, self-efficacy, and coping [15,42,43,63,66,70].

Details of Group Cognitive-Behavioral Therapy

This section describes a CBT intervention designed to (1) decrease maladaptive coping skills such as catastrophizing, and (2) enhance patients' ability to use attention diversion and changes in activity to control and decrease pain by increasing their use of potentially adaptive strategies. Coping strategies are described as skills that can be mastered through practice. Patients meet in 90-minute group sessions held weekly for 11 weeks. CBT therapists utilize three general methods to achieve the above therapeutic goals:

1) Changing Cognitions (Cognitive Restructuring)

Cognitive restructuring [9] is used to help patients recognize the relationships between thoughts, feelings, and behavior. These techniques teach patients to identify irrational, maladaptive thoughts and to replace them with alternative, rational coping thoughts. A self-instructional training intervention [92] is used to help patients utilize calming self-statements when dealing with severe pain.

2) Attention Diversion Methods

Patients are taught three attention diversion methods: relaxation, imagery, and distraction. Relaxation training involves concentrating on muscle tension signals and using them as cues to relax. Brief relaxation methods (mini-practices) are used to teach patients how to apply relaxation during daily activities. Imagery is described as an adjunct to relaxation [77]. Distraction techniques include focusing on physical or auditory stimuli [90].

3) Controlling Pain by Changing Activity Patterns

Activity-rest cycling [38,40] and pleasant activity scheduling [51] are used to reduce pain and enable patients to pace themselves and increase their activity level. In activity-rest cycling, patients identify activities in which they overexert themselves (e.g., housework or shopping), and learn to break them up into periods of activity and rest (e.g., 45 minutes of housework followed by 10 minutes of rest). Patients identify pleasant activities they enjoy such as visiting friends, going to a movie, or reading; they learn to set and record weekly activity goals.

We were able to conclude from our studies that (1) CBT improves the ability to decrease pain and reduce opioid medication use [63,65,66]; (2) CBT modifies the dysfunctional brain function associated with chronic pain [86]; and (3) CBT can partially reversed gray matter atrophy associated with chronic pain [81].

These results add to mounting evidence that CBT can be a valuable treatment option for chronic pain, and that treating pain can partially reverse abnormalities in brain function and structure associated with chronic pain.

Manual Therapy Approaches to Pain

Therapeutic touch may have been the first form of health care. Touch seems to be the best therapy to take advantage of the "meaning response," defined as the value that the patient places on an interaction with a caregiver [60]. It is not surprising that manual therapies have flourished in every society.

Manual therapies are those applied primarily using the hands of the practitioner, and can be categorized in a somewhat overlapping spectrum, from light touch to deep pressure and joint manipulation or mobilization. Most involve some type of palpation, which is usually used diagnostically as well as often being part of the treatment. Collectively, manual therapies may be the most frequent treatment type for patients with pain, but the treatments are not specifically directed at pain as a symptom. Rather, the therapies are directed at proposed pathophysiologies, which are claimed to be detectable by the practitioner, who then works toward correcting the underlying problem with the belief that the pain will subside. However, most proposed pathophysiologies have not yet been shown to exist, which may not allow for testing the mechanisms of action of the manual therapies in a scientifically rigorous way. This problem is compounded by our general lack of knowledge about peripheral pain mechanisms, especially when non-cutaneous structures (muscles, nerves, and other soft tissues) are concerned. Finally, the training to perform manual therapy is not homogeneous, often differing by country and region for a given discipline. Thus, there are a number of challenges to understanding manual therapies, most of which stem from a relative lack of research. And finally, research approaches are more difficult because of the strong nonspecific effects and meaning responses that all forms of therapeutic touch share. Even acupuncture practice can be considered to be included in manual therapy, as the practice involves therapeutic touch.

We will use the treatment of low back pain to better understand these concepts. Besides injuries and pathologies that can be imaged, the proposed pathologies for low back pain include intra-articular adhesions, fascial or capsular thickening or loss of elasticity, muscle tightness or shortness, ligamentous shortness or contracture, and altered neural control of any or all of the structures. There is no strong evidence supporting any of these proposed pathophysiologies. Manual treatment options for back pain include spinal joint manipulation, various forms of deep tissue massage directed at fascia and muscles, muscle stretching, methods thought to alter neural control (usually involving reflex mechanisms), and many other approaches. Most of these treatments are not applied in isolation, depending on the training, experience, and licensing of the practitioner. For instance, chiropractors perform many soft-tissue therapies with the goal of augmenting the spinal manipulation they may also perform. There are thousands of studies and almost as many meta-analyses in support of spinal manipulation and soft tissue mobilization (massage) for back pain. Individual studies usually support moderate clinical effects of these treatments, with spinal manipulation often but not always outperforming other approaches and sham treatments [31,79,101]. The disparate results of these studies seem to be more a function of study design rather than of the topic being studied. One consistent concern is that pain as an outcome is strongly subject to nonspecific effects or meaning responses. Another pervasive problem with studying "nonspecific back pain" is the nonhomogeneous presentation of patients [37,67], which is likely to indicate varied basic pathophysiology and would be predicted to dilute any treatment effect. If we understood and could detect pathophysiologies, that is, increase our diagnostic acumen, we could better determine which treatments work best for which diagnoses.

Although challenging, research into manual therapy is not impossible, but it has not been sufficient to support the efficacy of most forms of manual therapies, let alone their mechanisms. We have recently studied soft-tissue mobilization for the prevention of two common pathologies that are often painful: work-related musculoskeletal/repetitive motion disorders, and postoperative peritoneal adhesions. In both cases, we essentially performed clinical trials using existing animal models that closely match human clinical presentations. The hypotheses for these investigations were based entirely on clinical observations that arose out of multidisciplinary collaboration. These two lines of investigation will be used as examples as to how mechanistic preclinical research can be performed.

Work-Related Musculoskeletal Disorders

In a line of research spearheaded by Mary Barbe and Ann Barr [5], rats are trained to repetitively perform a task, specifically, to pull a bar to receive a food reward. Force, speed, and force profiles of the task are among the performance metrics measured, and numerous behavioral and histological outcomes are tested. This model is interesting in that the rats perform the task entirely voluntarily. The resultant pathophysiologies have been well documented and are consistent with those seen in people who perform similar tasks [29]. The rats are essentially patients, and therefore can enter what can be referred to as "preclinical trials."

Our first experiment to test the efficacy of manual therapy involved designing a combination of therapies that is consistent with what a chiropractor or an advanced massage therapist, physical therapist, or osteopath might perform [1,14]. Because the documented pathophysiologies involve all structures of the forearm and hand, including vascular changes in the skin, the treatment included light mobilization, skin rolling, deeper digital pressure, wrist joint mobilization, and general extension or stretching of the upper limb. Our goal was to observe if our treatment would alter the pathophysiological changes that are documented to occur in this model. We also sought to begin the treatment at the time when signs and symptoms appear, with the attempt to duplicate the time where patients may present to their provider. A video of the treatment has been published [14].

Our early results have been striking. We have learned that these forms of manual therapy, at least when combined, have preventive and protective effects on all parameters, including symptoms of pain and nociception and performance, as well as affecting the fibrotic changes that are found throughout the upper limb after many weeks of performing the tasks. We are working toward determining which treatment types are most effective, and also whether the pathologies that develop can be reversed when treatment begins later on, further into the progression of the disorder.

Postoperative Peritoneal Adhesions

Postoperative peritoneal adhesions are a ubiquitous side effect of peritoneal surgery, and up to 10% of patients will suffer symptoms secondary to adhesions, including pain [12,68]. There remains no acceptably effective treatment for established adhesions, and investigators agree that prevention is the best goal. A manual therapy method referred to as "visceral manipulation" has been practiced in most cultures for centuries [28,46]. As is the case with most manual therapies, there are many forms of this practice. While some practitioners palpate the abdominal contents looking for what they believe is restricted motion, other practitioners use very light touch to palpate the proposed rhythms of organs, for which there is no evidence for their existence [6]. The approach is touted to have effects on digestive and reproductive function, and to reduce abdominal and pelvic pain. However, there has been almost no research on the efficacy or mechanisms of this approach, other than the known benefits of massage as a treatment for constipation [27].

Using modifications of accepted models of postoperative adhesions (cecal abrasion), we tested the prediction that manual therapy designed to mobilize the gastrointestinal system would prevent or treat postoperative adhesions. We were able to conclude that this approach is a possible preventive of the subtype of adhesions that are most likely to cause clinical symptoms [13], but more research on mechanisms of pain was indicated by our studies. We were not able to demonstrate consistent effects on treating the adhesions once they have formed. In fact, the treatment had little effect if started 3 days after the surgery, corresponding with the regeneration of the mesothelium and early collagen proliferation. It is important to point out we did not have a measure of pain in these experiments. In fact, the rats displayed no behavior consistent with pain at any point during the experiments, including during the treatments, which were initiated within hours of the surgery.

Mechanism of action and efficacy are independent factors. If effective, even only by multiple anecdotes, a given treatment should not be discounted. A good example is the use and development of aspirin, where the only evidence of efficacy was folklore for millennia [93,102]. After a chemical modification and increased apparent efficacy, the use of the drug increased, but there was no research related to efficacy for many decades. The mechanism of action of aspirin was not understood until the middle of the 20th century. On this timeline, research into the efficacy and mechanisms of manual therapies is essentially a century behind. It is essential to perform efficacy trials for therapies that are in common use. If these therapies are effective, understanding the mechanisms at play might be advantageous, since they may guide modifications of the treatments to enhance their efficacy.

Much research is needed to support the underlying pathophysiologies in painful syndromes that affect the musculoskeletal system. Mechanistic research is possible, but there is currently a dearth of appropriate models. At this point, the only way to know if a particular manual therapy will work for a specific patient with pain is to try a course of therapy. As with other practitioners, the best way to find a practitioner is by word of mouth, and patients should accept that it might take a few attempts to find an appropriate clinical "fit."

Yoga Therapy

Yoga practice involves both physical and mental training. Currently, several types of yoga are practiced in western societies, and most of them incorporate the practice of physical postures (termed *asana* in Sanskrit), breathing exercises (*pranayama*), concentration exercises that focus the attention (*dharana*), and meditation (*dhyana*).

A number of studies have found yoga practice to be both beneficial and safe for alleviating different chronic pain conditions (reviewed by [54,105]). These studies have often assumed that the therapeutic effects of yoga stem from its effect on the musculoskeletal system, such as increasing strength and flexibility. However, yoga also involves focused attention; it improves mood and reduces depression [49,82,104]. Both attentional and emotional factors influence pain perception [56,95,103]. Furthermore, yoga practitioners are encouraged to adopt an emotionally detached observation of the present moment, and, accordingly, yoga can improve mindfulness scores [16], which are also associated with improved pain tolerance [48]. The emotional and cognitive tools developed in yoga practice could potentially alter people's relationship with pain, particularly by strengthening their control over their affective reaction to pain. We investigated possible the neuroanatomical underpinnings of the beneficial effects of yoga using sensory testing and magnetic resonance imaging (MRI) techniques, and found that yoga practitioners tolerated pain more than twice as long as matched control subjects [98]. The yoga practitioners also had more gray matter than healthy controls in multiple brain regions, and these increases correlate with the duration and intensity of yoga practice, suggesting a possible causative relationship between yoga practice and increased brain gray matter [97]. The increased gray matter in yoga practitioners contrasts with findings from chronic pain patients, who have less gray matter than healthy controls (reviewed in [18]). For yoga practitioners, the gray matter increase in the insular cortex correlated with both pain tolerance and years of yoga experience, suggesting a possible causal relationship between yoga and insular size. Yoga practitioners also had increased left intrainsular white matter integrity, consistent with a strengthened insular integration of nociceptive input and parasympathetic autonomic regulation. Yoga practitioners, as opposed to controls, used cognitive strategies involving parasympathetic activation and interoceptive awareness to tolerate pain, which could have led to use-dependent hypertrophy of the insular cortex. Together, these findings suggest that in addition to increasing strength and flexibility, yoga may reduce pain through changes in brain anatomy and connectivity.

Integrative Therapies—Which Ones Are Best for Which Patients?

Although there are many differences among mind-body therapies, there are some commonalities in the way they affect in individual's psychological state. Many therapies provide a means to distract an individual from chronic pain. Further, a belief in the effectiveness of the therapy can alter an individual's mood state, as well as create an expectation-related placebo analgesia.

Human brain imaging studies examining the effects of distraction on pain processing find that when a person focuses on pain, the pain-evoked activity in several cortical areas, including the primary somatosensory cortex, insula, and anterior cingulate cortex, is stronger than when a person is distracted from the pain [4,17,52,73,94,96]. However, some of these studies used distracting stimuli that also alter arousal or emotional state, so that the modulatory effects could be due to either attentional or emotional factors. Studies that manipulated attention while controlling for emotional state found that pain-evoked activity was modulated by attentional direction only in the insula and primary somatosensory cortex [17,96], which is consistent with the role of these regions in pain sensation.

Neuroimaging studies also reveal that negative emotional states produced by looking at emotional faces, listening to unpleasant music, or smelling unpleasant odors alter pain-evoked cortical activation. However, in contrast to the predominant attention-evoked modulation in the somatosensory cortex, the brain region showing the most consistent emotion-related modulation is the anterior cingulate cortex (ACC) [72,73,96]. The modulation of activity in the ACC is consistent with evidence that this region is particularly important for pain unpleasantness.

Anticipation of the relief of pain is a primary contributor to placebo analgesia [11] and could contribute to the effectiveness of both conventional and complementary therapies for pain relief. Brain imaging studies of expectation-related placebo analgesia find that immediately preceding the presentation of a noxious stimulus, when an individual receives a placebo "analgesic" and is expecting a reduction in pain, there is activation of pain-modulatory circuity in the brain (ACC–frontal cortex–periaqueductal gray pathway) [26,100]). Interestingly, this circuitry involves similar brain regions to those that are activated when a positive emotional state reduces pain.

So, how to choose a "complementary" therapy for pain management? Since there are probably many similarities among therapies in the neural mechanisms underlying pain reduction, probably the most important factor in choosing a therapy is whether the individual likes the therapy and will continue its use. A therapy that is distracting from the pain, improves the person's mood state, and creates expectations of pain relief should maximize the engagement of endogenous pain-relieving circuitry in the brain.

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