

## Integrative and Behavioral Approaches to the Treatment of Cancer-Related Neuropathic Pain

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### ABSTRACT

**Integrative oncology is the synthesis of mainstream cancer care and evidence-based complementary therapies. Complementary strategies include massage therapies, acupuncture, fitness, and mind–body techniques, which take advantage of the reciprocal relationship between the mind and body. Neuropathic pain—and pain more generally—is part of a complex process involving the whole physical and psychosocial being, therefore re-**

**quiring an integrative management approach. Several studies have demonstrated, for example, that social context plays an important role in the perception of pain and that a patient’s coping strategies can influence the persistence of pain. In this article, we briefly describe research illustrating the promise of integrative approaches for the treatment of cancer-related neuropathic pain. *The Oncologist* 2010;15(suppl 2):19–23**

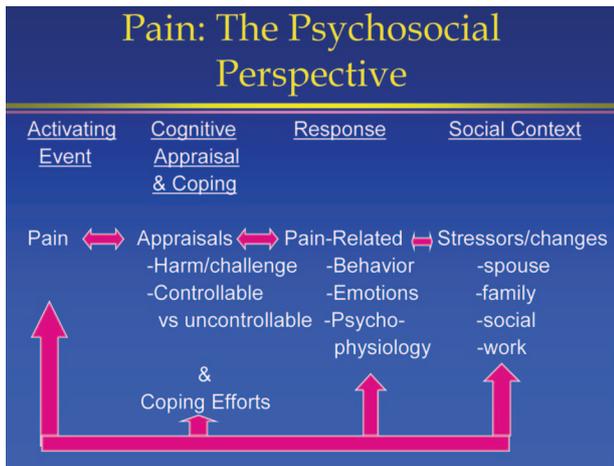
### INTRODUCTION

Neuropathic pain is defined as pain arising as a direct consequence of a lesion or disease affecting the somatosensory system [1]. It is generally understood that cancer patients experience neuropathic pain as a result of a number of distinct mechanisms ranging from physical nerve compression caused by the tumor itself to neurotoxicity of chemotherapeutic regimens, and that the signs and symptoms of neuropathic pain vary greatly among patients. Currently, there are no agents approved by the U.S. Food and Drug Administration for the treatment of neuropathic pain specifically associated with cancer or its treatment, and the

agents that are used in the clinic have relatively low success rates [2–4]. Increasingly, researchers are focusing on better methods to assess and define discrete aspects of neuropathic pain in an effort to develop more targeted therapeutics.

Although the dissection of neuropathic pain down to its precise symptomatic and mechanistic components is an important element in discovering novel molecular and interventional therapies, less emphasis is placed on the equally important view that neuropathic pain—and pain more generally—is part of a complex process involving the whole physical and psychosocial being. Therefore, it requires an

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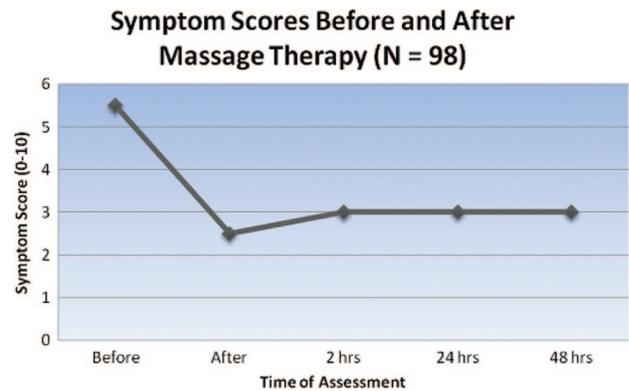


**Figure 1.** The perception of pain is influenced by several psychosocial factors.

integrative approach to patient management. In our experience, patients cannot always readily distinguish between neuropathic pain and other signs of neuropathic distress such as tingling, pressure, and burning. However, in an integrative approach, the perceptual elements that comprise this distress may be less important than the larger context of the patient's experience and perceptions.

Pain is not, as Descartes illustrated centuries ago, a simple matter of a single neural pathway relaying information about a stimulus in the body to the brain. Rather, the experience of pain is a result of the complex processing of information relayed to the brain from the sensory periphery and other aspects of sensorimotor, cognitive, and emotional processing (Fig. 1). Even the patient's own coping strategies can influence the persistence of pain. Several studies have demonstrated that cancer patients who engage in pain catastrophizing (ruminating about pain and feeling helpless about managing pain) are more likely to experience intense pain [5]. Thus, psychological and behavioral strategies that address psychosocial factors, particularly for the increasing numbers of cancer survivors who continue to experience pain even after their cancer is at bay, offer promising treatment avenues that can be integrated into a comprehensive pain management program for cancer patients.

Integrative oncology is the synthesis of mainstream cancer care and evidence-based complementary therapies. Whereas so-called "alternative" therapies are typically biologically invasive, promoted to displace mainstream care, and costly [6]; in contrast, complementary treatments are noninvasive, safe, inexpensive ways to address refractory symptoms alongside mainstream care. Complementary strategies include massage therapies, acupuncture, fitness (nutrition and physical activity), and mind-body



**Figure 2.** Massage therapy reduces pain and other symptoms in cancer patients over many hours.

techniques such as music therapy, meditation, and self-hypnosis, which take advantage of the reciprocal relationship between the mind and body. Integrative medicine also includes the study of herbs and other dietary supplements. In this article, we briefly describe research illustrating the promise of three approaches for the treatment of cancer-related neuropathic pain: massage therapy, acupuncture, and psychological/behavioral interventions.

### MASSAGE THERAPY

Massage therapy, defined as the manipulation of soft tissue areas of the body, is increasingly offered to cancer patients in the clinical setting. Its benefits include reductions in pain, anxiety, nausea, and fatigue. The National Comprehensive Cancer Network recommends the use of massage therapy in its treatment guidelines for refractory cancer pain [7]. At Memorial Sloan-Kettering Cancer Center (MSKCC), massage therapy has been an important component of the Integrative Medicine Service since 1999. Cassileth and Vickers [8] at MSKCC conducted a study of 1,290 cancer patients, measuring scores on a 10-point scale for a variety of symptoms including pain, fatigue, stress, nausea, and depression. Perhaps not unexpectedly, there was an immediate 50% drop in these symptom scores after massage therapy, and the drop in symptom score was sustained for a 48-hour follow-up period in a subset of 98 patients examined longer term (Fig. 2). Investigators therefore initiated a three-arm week-long randomized clinical trial to evaluate the persistence of benefits from massage therapy. The study is closed and data are under analysis.

Massage therapy, like other relaxation therapies such as meditation, yoga, and tai chi, is based on a reciprocal relationship in every human being between the body and the mind. Calming the body automatically calms the mind; calming the mind causes the body to relax. This is an im-

portant intrinsic relationship that we consciously take advantage of in caring for cancer patients and the multiple levels of distress they experience.

### ACUPUNCTURE

Acupuncture derives from techniques that began 3,000–5,000 years ago, first with needles made of locally available materials, such as slivers of wood, bone, or stone [9]. The ancient belief was that the body consisted of six vertical channels on each side of the body. Through these channels was said to flow the “vital life force,” sometimes referred to as chi. Illness was considered the result of blocked chi. Modern medical practitioners no longer think in terms of a life force to describe the effects of acupuncture, but there is no question that acupuncture’s effects are real.

The modern acupuncture needle is much thinner than a typical hospital needle, measuring approximately the width of a human hair, and is painlessly inserted only a few millimeters into the skin. Many have questioned whether the benefits of acupuncture are attributable to placebo effects. However, the benefits of acupuncture have been documented in animals, children, and adults at greater than the 20%–30% placebo-based effects that are usually observed in chronic pain studies [10–12]. Furthermore, randomized trials in which control acupuncture needles retract into a handle much like a stage knife and do not enter the skin demonstrate the benefits of acupuncture for a range of cancer-induced symptoms. These include dyspnea in advanced cancer [13], post-thoracotomy pain [14], hot flashes in breast cancer [15], pain dysfunction and xerostomia after neck dissection [16]. Physiological measures such as blood oxygen level dependent (BOLD) signal changes in functional magnetic resonance imaging have also been observed with acupuncture [17]. Currently, the Radiation Therapy Oncology Group is running a phase II/III clinical trial comparing acupuncture-like transcutaneous electrical nerve stimulation with pilocarpine in the treatment of radiation-induced xerostomia.

Although the underlying mechanisms are not fully understood, acupuncture appears to stimulate the parasympathetic cholinergic system, increasing the release of calcitonin gene-related peptide (CGRP), neuropeptide Y (NPY), and vasoactive intestinal polypeptide (VIP) in saliva during *and* after acupuncture [18]. Acupuncture can also activate parts of the brain involved in the gustatory reflex and salivation [17]. One study has shown that collagen fibers wind around the acupuncture needle to form a whorl-like pattern, causing fibroblasts further away to alter their morphology, resulting in a change in tissue impedance and electrical current that could account for altered neural trans-

mission in pain pathways [19]. Undoubtedly, much more work will be required to completely understand the mechanisms by which acupuncture reduces neuropathic pain.

### PSYCHOLOGICAL AND BEHAVIORAL INTERVENTIONS

Psychological and behavioral interventions for pain consist of two basic components: (a) education regarding how psychological factors (i.e., thoughts, feelings, and behaviors) can influence and be influenced by pain; and (b) structured training in one or more cognitive (e.g., imagery, hypnosis, restructuring of overly negative thoughts, distraction strategies) or behavioral (e.g., activity pacing, behavioral goal setting, progressive relaxation training) pain coping skills. There is growing evidence that psychological interventions may be effective for cancer-related pain [20].

Although these interventions have not been systematically studied in cancer patients specifically for the treatment of neuropathic pain, recent work in other patient populations experiencing chronic pain suggests their promise. Below are three examples that operate at different levels in the psychosocial cascade associated with the experience of chronic pain.

Self-hypnosis is taught to patients experiencing chronic pain as a means to induce relaxation and analgesia. Self-hypnosis is defined as an intervention in which a hypnotist teaches a person how to use an induction (an invitation to focus awareness) and one or more specific suggestions (e.g., suggestions for relaxation, changing thoughts, acceptance, increasing activity, etc.) to modify their pain. The use of the term hypnosis does not imply that a person enters a special mental state. Guided imagery involves a trainer/therapist teaching a person how to use specific self-generated images (e.g., relaxing in the sun on a beach) to foster pain management. The focus of progressive relaxation training is on systematically tensing and relaxing major muscle groups in order to achieve deep body relaxation. In a recent study of the effectiveness of hypnosis, 37 patients with spinal cord injury and resulting persistent pain were randomized to 10 sessions of either a standard relaxation technique involving electromyography biofeedback or a protocol for self-hypnosis [21]. Both interventions produced immediate and significant reductions in pain; however, only self-hypnosis was effective in decreasing pain over the long-term course of treatment (3 months).

The use of mirror therapy, another behavioral intervention, also suggests interesting avenues for modification of cognitive processing. Mirror therapy has been applied to amputees experiencing phantom limb pain, in which it is theorized that the false interpretation of signals by the so-

matosensory system as cramping pain in the missing limb can be corrected by “tricking” the brain with corresponding visual inputs of a freely moving limb. In mirror therapy, the patient views his or her intact limb in reflection, such that it appears to be the missing limb. Although the literature is not entirely consistent in its conclusions as to the efficacy of mirror therapy, in one compelling study, 22 lower limb amputees were randomly assigned to one of three conditions: training with the reflected image, training with a covered mirror, or training by mentally visualizing the missing limb only. Training with mirror therapy for 15 minutes daily over 4 weeks gave pain relief to 100% of the subjects, as compared with 17% and 33% of the subjects in the other two conditions [22].

Cognitive restructuring to alter pain appraisals and coping has also been shown to decrease pain. In a study of 18 subjects with disabling persistent pain due to spinal cord injury, amputation, multiple sclerosis, or cerebral palsy, cognitive restructuring was compared with an education-only control [23]. The key elements of the cognitive restructuring protocol included recognizing negative cognitions such as “I will never be able to cope” in response to a pain flare, challenging those negative cognitions and developing coping self-statements such as “This is tough, but I have coped with it before and there are things I can do to cope or deal with it.” The researchers found that cognitive restructuring

led to greater decreases in pain than did the education-only control.

## CONCLUSIONS

Neuropathic pain or sensory dysfunction is a chronic, often debilitating condition that affects an increasing number of cancer patients. Many factors appear to play a role in the experience of pain, and we must recognize that these factors can help us understand how patients adjust to pain. Further assessment will develop and refine new interventions that contribute to pain management.

The advantage of complementary approaches such as massage therapy, acupuncture, and mind–body therapies such as meditation and self-hypnosis is that they are inexpensive, safe, noninvasive, and absent of side effects, in contrast to pharmaceuticals administered for pain management. Evidence for the efficacy of these approaches continues to accumulate. Furthermore, these techniques should be especially welcome in light of current and pending health care realities, especially increasing costs and the decreasing availability of physicians.

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