

Stress-induced Physiologic Changes as a Basis for the Biopsychosocial Model of Chronic Musculoskeletal Pain

A New Theory?

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Objectives: (1) To integrate the scientific literatures of the biopsychosocial model of chronic musculoskeletal pain and of stress-induced physiologic wound and muscle changes, and (2) to propose a clinical assessment and treatment model that incorporates this dual literature into the management of chronic musculoskeletal pain.

Methods: English language literature search from January 1990 to February 2008 using the MEDLINE and PsycINFO databases and the keywords “wound healing,” “musculoskeletal injury,” “skeletal muscle injury,” “psychological,” “social,” “stress,” “anxiety,” and “pain.”

Results: An illustrative case report is introduced. Review of the scientific literature revealed that psychologic stress is associated with slower or delayed wound healing in stressed older adults, restrained mice, socially isolated hamsters, adults with leg wounds, and surgical patients. One study showed that expressive writing positively affected the healing of a small skin puncture. Psychosocial stress affected aspects of muscle activity and spinal loading. Slaughter studies demonstrated that high preslaughter stress in pigs negatively affected postslaughter meat quality. A clinical model for the treatment of selected patients with painful musculoskeletal symptoms is offered.

Discussion: Important links exist between psychologic and social factors and recovery from insults to the “soft tissues.” Identifiable biochemical and physiologic processes mediate this relationship. It is time to rethink and refine views of the role of psychologic and social factors in musculoskeletal illness, chronicity, and pain.

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Musculoskeletal injury, subsequent experience of chronic pain, and resultant disability are widespread in industrialized nations.¹ Activity limitation related to chronic pain or discomfort may represent the most common form of disability among people of working age (15 to 64 y),² and chronic pain from musculoskeletal injury has reverberating negative effects on patients and their family members.^{3–5} Musculoskeletal problems account for a major component of lack of return to work in industrial economies,^{2,6–11} and it is evident that society loses productivity and often becomes responsible for the financial support of the disabled person and his or her medical care and rehabilitation.

Numerous physical, physiologic, biochemical, and immunologic factors contribute to the response to a musculoskeletal injury, to the development of a particular musculoskeletal disease, and to the perpetuation of a chronic painful state. Psychologic and social factors have also been shown to play a significant role in the experience, clinical presentation, and chronicity of pain.^{12–16} Reflecting these multiple and interacting determinants, a biopsychosocial model for the clinical presentation and assessment of low back pain and disability and other musculoskeletal disorders has frequently been described in the literature.^{17,18}

The concept of “clinical red flags”—key signs and symptoms that indicate to the clinician that a case of back pain may be more serious than routine back pain with respect to intensity, potential for development of chronicity or spread of musculoskeletal impairments, or diagnosis of a significant comorbid condition—is used by many physicians in their practices. A related approach, referred to as “clinical yellow flags,” evaluates 4 groups of risk factors that are suggestive of the development of chronic musculoskeletal pain.¹⁹ These factors include psychologic and behavioral parameters—beliefs, coping strategies, distress, illness behavior, and willingness to change—that are predictors of chronicity subsequent to the development of a musculoskeletal problem.

Assessment of such yellow flags is based on questions in the form of interview prompts, designed for use by general practitioners in the office at the time of initial presentation. These questions serve as a means for determining which patients with acute musculoskeletal-related symptoms are likely to experience chronic pain. Helliwell and Taylor²⁰ and Main and Williams²¹ refer to these yellow flags as risk factors and obstacles or barriers to recovery. They have been shown to have clinically significant prognostic value and may be used to trigger early interventions designed to prevent progression from acute to chronic pain.²²

Although the scientific literature is replete with articles concerning the role of psychologic (eg, stress/anxiety and depression) and social factors in the development of chronic musculoskeletal pain,^{18,23–25} a unifying integration of this literature exploring possible pathophysiologic mechanisms that may mediate these well established but poorly understood “mind-body” relationships seems to be missing. Gatchel and colleagues¹⁸ discuss the significant role of negative mood in patients with chronic pain “because it is likely to influence treatment motivation and compliance with treatment recommendations.” The role of anxiety or negative emotion in producing increased autonomic and central nervous system responses is briefly mentioned, but the potential direct or indirect effect of mood state on the body’s soft tissues is not. We routinely invoke explanations about mood and recovery from musculoskeletal injury in our practices to explain to patients and to other practitioners why recovery from a particular soft tissue injury may differ from one person to the next, but it remains for such accounts to be formally stated and their empirical support integrated. The objective of this paper is to consider current scientific literature that explores the pathophysiologic relationship between wound healing and muscle activity and the moderating effects of psychologic and social factors on this process. We suggest that clinicians who understand and exploit such a psychophysiologic approach to the management of musculoskeletal injury will provide themselves and their patients with an effective treatment modality, one that is based on biomedical considerations and on human behavior, the unique social environment of the patient, his or her phenomenology, and an appreciation of clinical and existential factors.

On a more pragmatic basis, in this paper we suggest that the recovery from a wound is analogous in significant respects to recovery from a musculoskeletal injury, and we apply findings from wound recovery research in the context of our analysis. We briefly describe the phases of wound healing in animals and humans, summarize effects of psychologic and social factors on wound healing and immunologic/biologic systems, and review epidemiologic literature relevant to the relationship of psychosocial factors and musculoskeletal injury recovery. We then present a clinical assessment and treatment model that incorporates findings from this literature in a biopsychosocial approach to the management of musculoskeletal injury. We have successfully used this model to treat

selected patients who have sustained a musculoskeletal injury or are experiencing painful musculoskeletal symptoms. This approach incorporates evidence linking psychologic and social factors and the experience of injury in patients experiencing pain in their muscles, ligaments, and other soft tissues. We believe that it has the potential to improve treatment and patient outcomes in this medical domain.

LITERATURE SEARCH

We performed a search of the English language literature from January 1990 to February 2008 using the MEDLINE and PsycINFO databases and the keywords “wound healing,” “musculoskeletal injury,” “skeletal muscle injury,” “psychological,” “social,” “stress,” “anxiety,” and “pain.” The search identified over 200 human and animal studies, of which we retained the 45 that explored the pathophysiologic relationship between wound healing and muscle activity and the moderating effects of psychologic and social factors on this process.

ILLUSTRATIVE CASE REPORT

The following case report illustrates a number of issues relevant to our discussion. A 54-year-old otherwise healthy woman had noted nonradicular right low back pain. The occasionally incapacitating pain had commenced after she performed specific exercises about 5 years earlier. A complete oncologic evaluation was negative. On physical examination, she had tenderness on palpation of the right upper buttock and paralumbar musculature. The neurologic examination was normal. Diagnoses of myofascial pain or musculoligamentous injury of the right paralumbar and gluteal muscles and low back strain/sprain were made.

The woman’s husband had died 4½ years earlier and she continued to grieve this loss. Conflict existed between her and her adult daughter, who was still living at home.

WOUND-HEALING PHASES

Research on acute wounds in animal models has shown that wounds heal in 4 phases: hemostasis (phase 1), inflammation (phase 2), proliferation or granulation (phase 3), and remodeling or maturation (phase 4).²⁶ It is believed that chronic wounds (wounds that have prolonged healing times) also go through these basic phases. Some authors combine the first 2 phases.²⁷

After incurring a soft tissue or musculoligamentous injury, most patients eventually progress to a state of “healing” in which various tests, including standard radiography and nuclear medicine images, are normal. Local tenderness may be the only physical finding. For the purposes of this paper, we assume that perpetuation of pain is because of factors related to deficits in phase 3 (proliferation or granulation) or 4 (remodeling or maturation) of wound healing, to some type of central process, distant from the wound site per se, to particular psychologic and social factors, or a combination of these. The following literature review elucidates roles that

psychologic and social factors may play during and after wound healing.

EFFECT OF PSYCHOLOGIC AND SOCIAL FACTORS ON WOUND HEALING

Kiecolt-Glaser and colleagues²⁸ demonstrated slower wound healing in stressed older adults. Their research on marital stress and wound healing showed that healing took 2 days longer in couples who exhibited high levels of hostility than in couples whose hostility seemed low.²⁹ These investigators also noted that wounds took a day longer to heal after marital arguments than after initial supportive positive discussion. Mucosal wound healing in dental students was found to be impaired by the stress associated with major school examinations.³⁰ Gouin and colleagues³¹ reported that anger delayed healing of standardized blister wounds on the nondominant forearm of community dwellers. Finally, skin wounds of older adults (mean age 61 y) healed on an average of 10 days faster in those who exercised than in those who did not exercise.³² The authors were somewhat surprised to find a sharp increase in cortisol levels in the exercise group. This hormone is typically boosted by stress, and other studies have suggested that exercise may lower stress levels.^{33,34} The authors suggested that the increase in cortisol levels may represent a biologic pathway by which exercise helps wounds heal.³² Alternatively, humoral, endocrine, or other factors induced by exercise may produce the improvement, or people who exercise may heal faster owing to other factors such as generally better health and better wound self-care. Studies to date have been observational and researches applying stress in a randomized controlled fashion to human participants with an existing or experimentally induced wound have not been identified.

A set of immunologic hormones, proinflammatory cytokines, are involved in the early stages of wound healing.²⁷ Laboratory studies have shown that the concentration of these cytokines in experimental wounds is affected by the degree of self-rated stress that participants report at the time of cytokine measurement, such that high levels of stress are associated with lower levels of the proinflammatory cytokines that are involved in wound healing.³⁵⁻⁴³ This association may be explained by the higher levels of cortisol commonly associated with stress. When cortisol levels increase, immune response is suppressed. Cortisol either reduces the number of neutrophils that rush to the wound site or lessens the concentration of the cytokines necessary for healing. In this fashion, stress modulates immune response, lowers cytokine levels, and delays wound healing.

Padgett and colleagues⁴⁴ compared cutaneous wound healing in 6 restraint stress (RST) and 6 control mice. The former were placed in centrifuge tubes for 3 cycles of restraint, followed by dorsal application of a 3.5-mm sterile punch wound and 5 subsequent cycles of restraint; the control mice were wounded, but not restrained. In the RST mice, reduced inflammation

surrounding the wounds was observed 1, 3, and 5 days after wound infliction; the reduction in inflammation and delayed healing correlated with increased serum corticosterone levels. Administration of a glucocorticoid receptor antagonist to the RST mice (which would have served to reduce serum corticosterone levels and permit more normal immune response and proinflammatory cytokine levels) resulted in healing rates comparable with those of the control animals. On average, wounds healed 3.1 days sooner in the control mice than in the RST mice, but this difference was statistically eliminated with the administration of glucocorticoid receptor antagonist. Reepithelialization was complete within 14 days in the control group, but took 16 days in the RST animals. Stress seemed to affect only the first stage of wound repair; once healing began, wound recovery was comparable in stressed and control animals. French and colleagues⁴⁵ reported similar stress/wound healing findings in tree lizards.

Padgett and colleagues⁴⁴ indicated that the experience of stress launches a cascade of events that constrict blood vessels and deprive the tissues of oxygen. These investigators hypothesized that hyperbaric oxygen therapy may reverse delays in healing not because it relieves stress per se, but rather, because it helps to rectify tissue oxygen deficits and thus, facilitates wound healing. To test this hypothesis, they measured in a mouse model levels of expression of the gene for inducible nitric oxide synthase, an enzyme that makes nitric oxide.⁴⁶ Nitric oxide is critically involved in wound healing by increasing blood flow and the delivery of oxygen and by attacking bacteria. If oxygen levels fall, the gene's activity increases. The investigators found that when the animals were stressed, expression of the gene increased, presumably to help make more nitric oxide. But when the animals received hyperbaric oxygen, gene expression returned to normal levels, which suggested that the nitric oxide levels necessary for healing had been restored by the increased tissue oxygen levels. This evidence is consistent with a link between stress, blood vessel constriction and oxygen deprivation, and delayed healing.

In wound healing by second intention, closure is accomplished through 2 distinct physiologic processes, contraction and reepithelialization. Horan and colleagues⁴⁷ found that wound contraction was decreased by more than 45% in RST mice. Stress was noted to impair contraction as early as day 1 postwounding, and this trend continued through day 5. Fibroblast migration and differentiation were delayed through day 7 postwounding. In related research, Rojas and coworkers⁴⁸ found that stress impairs bacterial clearance during wound healing in mice, resulting in a significant increase in the incidence of opportunistic infection and possible delay in wound healing.

Previous studies have shown that behavioral stress delays wound healing and impairs proinflammatory cytokine gene expression in a glucocorticoid-dependent fashion,⁴⁹ and other data demonstrate that androstenediol can attenuate many of the anti-inflammatory

influences of glucocorticoids.⁵⁰ In this connection, Mikhli and coworkers⁵¹ performed a study to determine whether treatment of RST mice with androstenediol would prevent the suppression of proinflammatory cytokine gene expression and restore healing to control levels. They found that RST mice had delayed healing of a punch wound compared with control mice deprived of food and water. RST mice showed significantly decreased interleukin-1 β expression 24 hours after being wounded. However, treatment with androstenediol prevented stress-induced delay in healing: wounds in androstenediol-treated RST animals had closed by 51.6% within 24 hours, compared with 37.5% in untreated RST animals. In addition, androstenediol treatment prevented the stress-induced suppression of interleukin-1 β gene expression. The authors concluded that androstenediol may provide a pharmacologic approach to block the anti-inflammatory effects of behavioral stress, and thus, may provide a therapy to improve healing.

Detillion and colleagues⁵² conducted a series of experiments in hamsters to learn how social interaction may affect wound healing and to better understand the mechanisms by which it may do so. During a 3-week study, female Siberian hamsters were housed with a sibling or were isolated. All animals received small minor skin wounds at the backs of their necks. The wounds healed nearly twice as fast in the hamsters paired with a sibling as in the socially isolated hamsters. Hamsters paired with a sibling also produced less cortisol. The investigators also treated a group of socially isolated hamsters with oxytocin, a hormone released during social contact and associated with social bonding in monogamous animals. Oxytocin treatment seemed to attenuate the effects of stress on wound healing, as the treated animals healed about 25% faster than the untreated animals. These findings are suggestive of a role for cortisol and oxytocin as biochemical mediators of the relationship between social interaction, social isolation, and facilitated or delayed wound healing. Similar findings were reported by Martin and colleagues⁵³ in a study comparing monogamous and polygynous mice.

In a study of 53 adults being treated for leg wounds, delayed wound healing was 4 times more common in patients who scored in the upper 50% of the Hospital Anxiety and Depression Scale as in patients who scored in the lower 50%.⁵⁴ Wound healing was delayed in 15 of 16 patients with anxiety and in all 13 patients with depression. The investigators postulated that psychologic factors may have both direct and indirect effects on the rate of wound healing. Depression is associated with widespread impairment of both cellular and humoral immunity,⁵⁵ which may delay wound healing. They also suggested that depressed individuals may not take care of themselves as well as those without depression, and that a poor appetite and an irregular sleep schedule, which often accompany depression, may interfere with the normal functioning of the immune system. The authors did not, however, discuss potential confounding variables, such as the prevalence of diabetes and smoking in their partici-

pants or the possible role of differential wound severity. The limits to inference of causal direction in an observational study must also be considered. Depressive symptoms predicted the speed of oral mucosal wound healing in a group of undergraduate students as well.⁵⁶

In a randomized study, Weinman and colleagues⁵⁵ examined the effect of expressive writing on wound healing. Eighteen participants were instructed to write about the most upsetting experience they had had, describing how they had felt, and 18 others to write about trivial things, such as how they spent their free time. Both groups spent 20 minutes a day writing for 3 days. After the writing exercise, a small skin puncture was created on the participants' upper arms, and the wounds were examined 2 weeks later. Participants who had written about emotional experiences had smaller wounds and healed more quickly than those who wrote about emotionally trivial experiences. Exploratory analyses also showed that participants with wounds that healed more slowly had higher levels of stress and psychologic distress. One interpretation of these findings is that expressing emotions in writing creates lower stress levels reflected in the biochemical environment of a participant's body and facilitates wound healing.

Ebrecht and colleagues⁵⁷ conducted a study among 24 nonsmoking men to evaluate whether perceived stress and cortisol levels predict the speed of wound healing. A significant negative correlation was observed between speed of healing of a standard 4-mm punch biopsy and scores on both the Perceived Stress Scale and the General Health Questionnaire at the time of biopsy. Area under the morning cortisol response curve was negatively correlated with speed of wound healing, which indicated a clear elevation in the morning cortisol slope of those whose wounds were slowest to heal. The slow-healing group showed higher stress levels, lower trait optimism, and higher cortisol levels after awakening than the fast-healing group. None of the health behaviors investigated (alcohol consumption, exercise, healthy eating, and sleep) were correlated with speed of healing at any point. In a paper by Levenstein and colleagues,⁵⁸ anxiety was associated with poor duodenal ulcer healing, even when smoking was accounted for.

Psychologic stress has been shown to be associated with slower surgical wound healing and impaired overall recovery from surgery.^{59–64} There is also randomized trial evidence that preoperative psychologic interventions can have significant positive effects on various components of postoperative recovery.⁶⁵ More recently, an observational study showed that patients' expectations have a fairly clear relationship with recovery from minor surgical procedures, as assessed by symptom severity, return to work, and quality of healing.⁶⁶

In an observational study, Broadbent and coworkers⁶⁷ administered a standardized questionnaire assessing psychologic stress and worry to 47 adults undergoing routine inguinal hernia repair surgery. The authors concluded that psychologic stress slows wound healing by impairing the inflammatory response and matrix

degradation processes in the wound immediately after surgery.

Finally, in a randomized controlled research, Holden-Lund⁶⁸ assigned 24 patients undergoing cholecystectomy to either relaxation with guided imagery or control (quiet period) conditions and then assessed 3 indexes of recovery: state anxiety, urinary cortisol levels, and wound inflammatory responses. Analysis of variance showed that the relaxation group demonstrated significantly less state anxiety, lower cortisol levels 1 day after surgery, and less surgical wound erythema than the control group.

EFFECT OF PSYCHOLOGIC AND SOCIAL FACTORS ON MUSCLE ACTIVITY

Marras and coworkers⁶⁹ studied the effects of psychosocial stress on muscle activity and spine loading in a laboratory setting. They had 25 participants perform sagittally symmetric lifts under stressful and nonstressful conditions, and used trunk muscle activity, kinematics, and kinetics to evaluate 3-dimensional spine loading by means of an electromyogram-assisted biomechanical model. Participants' personality traits were assessed at baseline with the Myers-Briggs type Indicator Personality Inventory. Reaction to stress was confirmed by means of the Spielberger State-Trait Anxiety Inventory and blood pressure readings. The investigators found that experimentally induced psychosocial stress increased spine compression and lateral shear in some, but not all, participants. Differences in muscle coactivation accounted for these stress reactions. Sex also influenced spine loading, as anterior-posterior shear forces increased in response to stress in women but decreased in men. A relationship between psychosocial stress and spine loading, moderated by participant's sex, was therefore identified. More work is needed to link pain and muscle activity.

In a related report, Waersted⁷⁰ discussed current knowledge on low-level, long-lasting work-related muscle activity, focusing on the shoulder and upper part of the trapezius and on mental, rather than biomechanical, reasons for the muscle activation. Muscle activity without an obvious biomechanical purpose, or nonbiomechanical muscle activity, has low-level variability and low second-to-second variability, resembling a static muscle contraction. It is suggested that 3 aspects of the participant-task interrelation may be of importance in the generation of such muscle activity: the mental effort demanded by the task itself (mental load), the participant's attitude and emotional state while working at the task (emotional load), and the trait characteristics of the participant, influencing his or her readiness both to be aroused in a given situation and to respond with neuromuscular activation when aroused.

SLAUGHTER STUDIES

Commercial meat producers are concerned about effects of stress on meat quality. Stress before slaughter is

known to cause undesirable effects on the end quality of meat, such as pale, soft, exudative meat and dark, firm, dry meat.⁷¹ Hambrecht and colleagues⁷² studied how preslaughter handling affects pork quality and glycolytic potential in muscles differing in fibre type composition. High preslaughter stress decreased muscle glycogen in both the longissimus muscle and the supraspinatus muscle, but the decrease was greater in the former. Lactate concentrations during the first 135 minutes postmortem were increased only in the longissimus. Increases in ultimate pH and decreases in redness were greater in the serratus ventralis, whereas increases in electrical conductivity were greatest in the longissimus. Longer and rougher transportation was considered a stressor, and in general, negatively affected the post-slaughter quality of both muscle types compared with muscle from nonstressed pigs.

BACK TO OUR CASE

We counseled the woman that her back pain emanated from injured or affected "muscles and ligaments." Myofascial pain involving paralumbar and gluteal musculature was another relevant diagnosis. The pain was not felt to be because of problems with joints, nerves, or bones. Optimal treatment was facetiously explained to be "muscle ligament transplantation," that is, removing the offending tissue and replacing it with a healthier group of tissues. This method of treatment was noted to occur with other organ systems such as the heart, kidney, or liver.

We explained to the patient that because it was not possible to actually replace the painful tissue, an approach aimed at both healing and removing deleterious influences was necessary. These influences include poor diet, smoking (which may compromise optimal blood flow), lack of exercise, and ergonomic problems (Fig. 1). The patient was told that in any individual, a physical insult together with common psychologic and social concerns, such as stress, anxiety, financial worry, a history of sexual or physical abuse, marital conflict, or the loss of a loved one, is known to exacerbate the experience of muscle and ligament pain and delay healing (Fig. 2). Such psychologic and social challenges, the physician noted, could also lead directly to the experience of muscle and ligament pain. Possible mechanisms of this phenomenon were explained to include chronic muscle contraction and the stress/autonomic response, which affects sweating, cardiovascular function, and wound healing in different animal and human populations.

Like many people, the patient had never considered the possibility that psychologic or social factors could actually contribute to her pain syndrome. On a subsequent visit, however, and with further reflection, she realized that when conflict with her daughter arose or when she was mourning the loss of her husband, her back pain would dramatically escalate. By keeping a suggested diary, she gradually started to recognize numerous triggers that prolonged the pain, and with the help of a

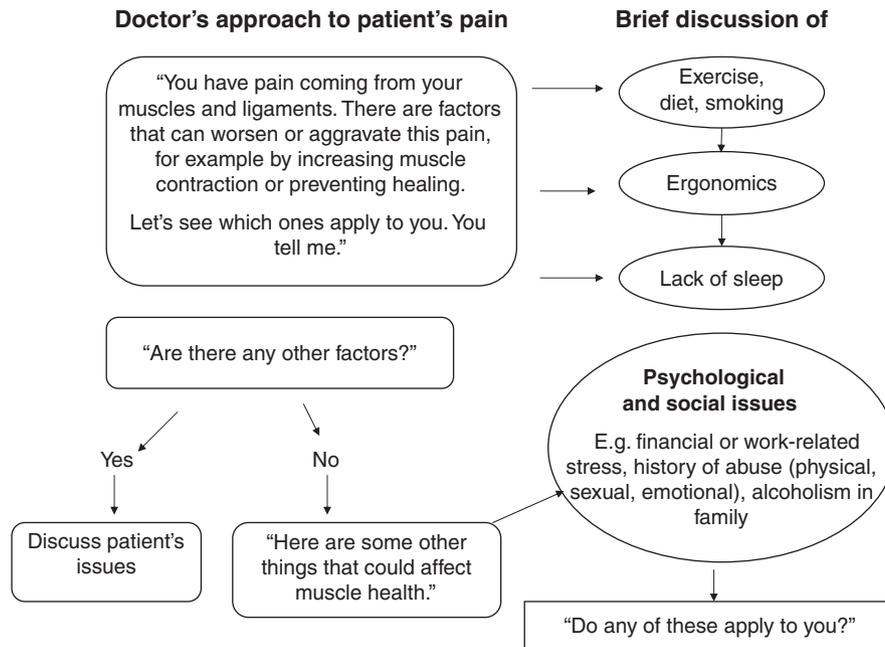


FIGURE 1. Clinical model for the treatment of selected patients who have sustained a musculoskeletal injury or are experiencing painful musculoskeletal symptoms. The model integrates psychologic and social factors with other treatments.

psychotherapist she was able to better control her responses to stress, with subsequent less frequent and less intense episodes of pain. Fewer physician visits and decreased analgesic consumption were other sequelae of her new knowledge of psychosocial influences.

DISCUSSION

Our review of animal and human studies on wound healing and musculoskeletal function reveals that there are important links between psychologic and social factors and recovery from insults to the so called "soft tissues"

Musculoskeletal Injury and Psychosocial Factors Model: Possible Interactions

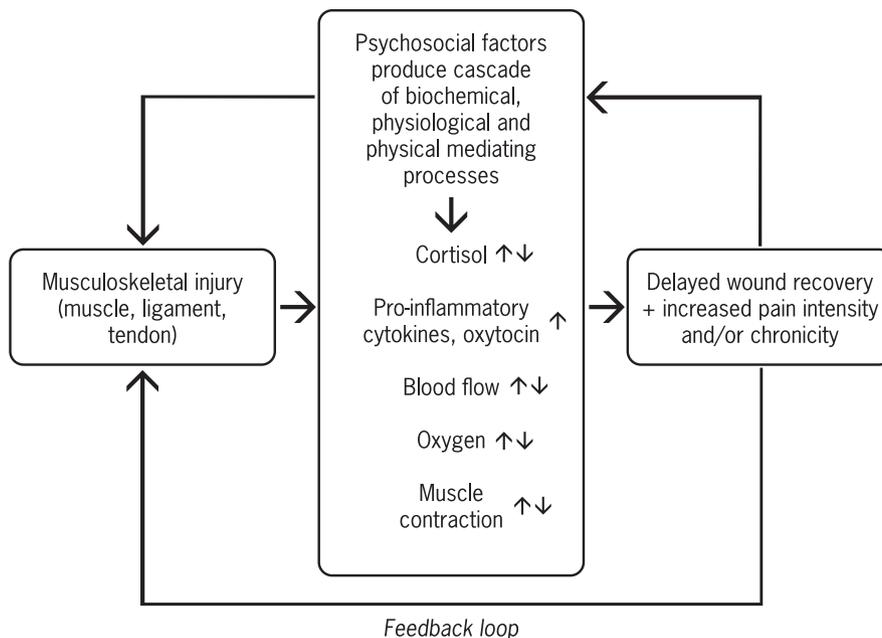


FIGURE 2. Proposed interrelation of musculoskeletal injury, psychologic factors, and wound recovery.

(muscles, ligaments, skin, and subcutaneous tissues), and that there seem to be identifiable biochemical mediators of the relationship between the 2. Although this may not seem to be a unique concept, the effort to specify the nature of these biochemical mediators represents an essential first step, with substantial ramifications for better understanding of this linkage and for translation into therapeutic interventions and more sophisticated and better focused research. The studies cited are suggestive and obviously not definitive, but they clearly provide a basis and a direction for rigorous further research to clarify the biochemical, physiologic, and behavioral mechanisms that mediate between psychologic and social factors and the experience of musculoskeletal syndromes and chronicity or recovery from them. The unifying theme emerging from this analysis is that psychologic, behavioral, social, and environmental factors can have profound effects, via specified and yet-to-be specified biologic mechanisms, on tissue healing, muscle contraction, and even the microscopic and macroscopic quality of skeletal muscle tissue.

In the practice of musculoskeletal medicine, psychologic, environmental, social, and accessibility factors are generally relegated to secondary roles. More often than not, they at times are regarded as nuisances rather than legitimate etiologic and consequential factors, and rarely are considered as triggers for a cascade of biochemical, physiologic, and behavioral events that contribute to pain experience (or recovery), chronicity (or remission), and disability (or rehabilitation). Although it is acknowledged that “patients’ beliefs, distress, and coping strategies...must be an integral part of management” to avoid pain-related disability and chronicity,²¹ the possible effect of psychologic factors on recovery from tissue injury is rarely formally recognized. These psychologic factors must be as seen as etiologic—alongside the physiologic soft tissue injury—and consequently, must be an integral part of the therapeutic focus. The identification of specific mechanisms of action of these factors has not been the subject of definitive research guided by clearly articulated models of the complexity of the relationships involved. We believe that acknowledgment of this link must be introduced in musculoskeletal medicine to stimulate conduct of the basic science and clinical translation of results into improved patient care in this field. Although cardiovascular medicine has adopted similar principles (eg, stress reduction exercises have been shown to play a role in reducing thickening of the arterial intimal lining because of atherosclerosis), musculoskeletal and pain medicine lags behind. This is likely because of 2 reasons. First, cardiovascular medicine has several tests, such as those describing the heart’s vessels and cardiac output, which can clearly objectify what the particular problem is to begin with (eg, a blocked or narrowed vessel of the heart, an impairment of heart muscle function). Musculoskeletal medicine, particularly when dealing with pain issues, has fewer imaging and functional modalities at its disposal, and therefore, the etiology of the pain is more elusive.

Second, champions of “mind-body medicine,” such as the popular Dr Dean Ornish,⁷³ focus more on the benefits of lifestyle changes such as stress reduction to cardiovascular health than to musculoskeletal health. It is hoped that this will change in the future.

What links the research we have considered is an underlying focus on the identification of specific processes that may mediate the relationship of psychologic and social factors, musculoskeletal injury, and the experience of pain, chronicity, and recovery. It seems clear that the interplay of the fields of psychology, immunology, and physiology will be a cornerstone in advancing the understanding of the role of psychologic and social factors as contributors to clinical end points critical in this field.

We have included a set of suggestions as to how the clinician can introduce some of these concepts to patients (Fig. 1). This is where the cited research extends into the pain management aspect of the clinician’s practice. Nothing upsets a patient more than the physician’s implication that “the problem is in your head.” In reality, “the problem” of many musculoskeletal injuries is likely in the muscles, ligaments, and multiple neural pathways, but, yes, also in psychologic and social problems or issues that produce a cascade of biochemical and physiologic events that can modify, delay, or worsen the healing and recovery process.

It is hoped that this clinical review article will stimulate medical and psychologic clinical and research communities to rethink and refine views of the role of psychologic and social factors in musculoskeletal illness chronicity, pain, and recovery. To the physician, we stress: do not abandon patients by appearing uninterested in their psychologic problems and then implying that the chronic painful symptom is wholly psychologic. The mind and the soft tissues are linked by some well-established biochemical and physiologic processes. To the psychologist or mental health worker, we assert: emphasize to the patient not only the power of the mind to cope better with the injury, but also that the adoption of healthier coping and the resolution of germane personal issues of the past and present have the potential to actually change tissue health and promote recovery at numerous biologic levels. Recognize the intrinsic and biologically mediated relationship between psychosocial factors and wound recovery, and your outlook when seeing these patients will change forever. The yellow flags wave for improvement in treatment, not as a sign to run away as fast as possible from the problem.

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