# Psychological Influences on Surgical Recovery

## *Perspectives From Psychoneuroimmunology*

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*Greater fear or distress prior to surgery is associated with a slower and more complicated postoperative recovery. Although anxiety presumably interferes with recuperation through both behavioral and physiological mechanisms, the pathways have been unclear. Recent work in psychoneuroimmunology (PNI) has demonstrated that stress delays wound healing. In addition, a second line of research has illustrated the adverse effects of pain on endocrine and immune function. A biobehavioral model is described that is based on these and other data; it suggests a number of routes through which psychological and behavioral responses can influence surgery and postsurgical outcomes. Clinical and research implications are highlighted.*

Surgery is a threatening experience, with multiple stressful components—concerns about one's physical condition, admission to a hospital, anticipation of painful procedures, worries about survival and recovery, and separation from family. Accordingly, it is not surprising that even operations that physicians consider "minor" can provoke strong emotional reactions in patients (Johnston, 1988). If these psychological responses are sufficiently intense, they can have important consequences: The weight of the evidence suggests that greater distress or anxiety prior to surgery is associated with a slower and more complicated postoperative recovery (Johnston & Wallace, 1990; Mathews & Ridgeway, 1981). Moreover, researchers who have assessed the impact of psychosocial interventions administered before surgery have generally demonstrated positive effects on postsurgical psychological and physical function (see reviews by Contrada, Leventhal, & Anderson, 1994; Devine, 1992; Johnston & Vögele, 1993; Johnston & Wallace, 1990; Mumford, Schlesinger, & Glass, 1982; Suls & Wan, 1989).

Although anxiety presumably interferes with recovery through both behavioral and physiological mechanisms, the pathways for such effects have been unclear. Recent work in psychoneuroimmunology (PNI) has provided evidence that stress delays wound repair (Kiecolt-Glaser, Marucha, Malarkey, Mercado, & Glaser, 1995; Marucha, Kiecolt-Glaser, & Favagehi, 1998; Padgett, Marucha, & Sheridan, 1998). In addition, a second line of research has illustrated the adverse effects of pain on immune and endocrine function (Liebeskind, 1991). Thus, viewing the psychological literature on postsurgical recovery within a PNI context suggests a new conceptual framework, illustrated in Figure 1.

The model suggests that psychological variables could influence wound healing, a key variable in short-term postsurgical recovery, through several pathways: (a) Emotions have direct effects on "stress" hormones, and they, in turn, can modulate immune function. (b) The patient's emotional response to surgery can influence the type and amount of anesthetic, and anesthetics vary in their effects on the immune and endocrine systems. (c) Certain health behaviors may dictate differences in choice of anesthetic (e.g., alcohol intake), or extent of surgery (e.g., obesity). In addition, health habits such as smoking that are themselves stress-responsive can have direct deleterious consequences for immune function and wound healing. (d) Individuals who are more anxious are also more likely to experience greater postsurgical pain, and pain can down-regulate immune function. Thus, immune function, already poorer as a consequence of presurgical stress, could decline even further.

After providing a brief overview of key events in wound healing, we discuss the model's components and paths. Literature addressing psychological influences on recovery from surgery is viewed within the context of our framework. Underscoring fundamental methodological concerns that emerge as a consequence of our conceptualization, we suggest that researchers need to consider each of the pathways to maximize the signal-to-noise ratio. We end by highlighting clinical issues and applications.

*Editor's note.* Cynthia D. Belar served as action editor for this article.

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Work on this article was supported in part by National Institutes of Health Grants K02 MH01467 and R37 MH42096.

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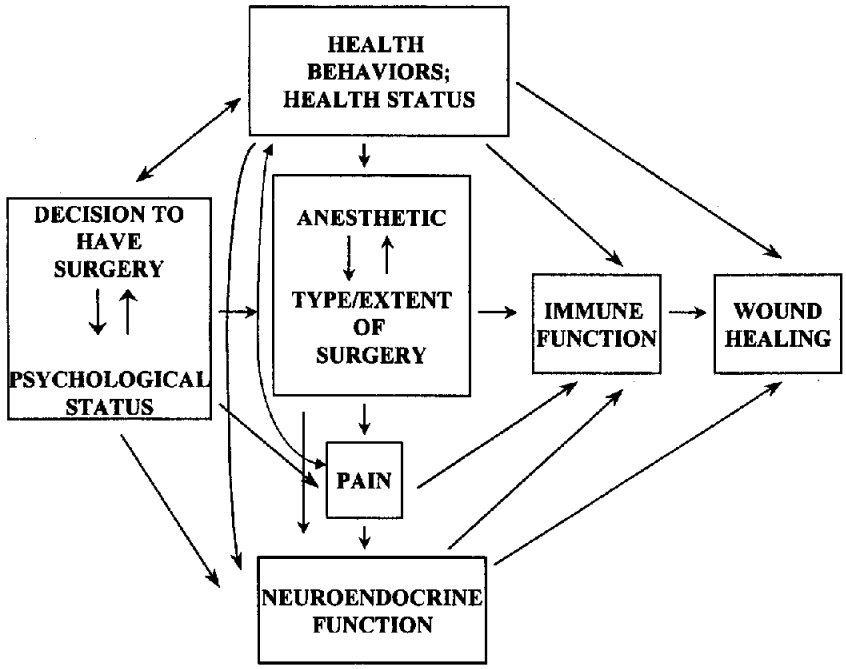
 0003-066X/98/$2.00
Vol. 53, No. 11, 1209–1218

**Figure 1**
*A Biobehavioral Model of the Psychological, Behavioral, and Biological Pathways That Influence Wound Healing: The Central Short-Term Outcome in Recovery From Surgery*




*Note.* This figure is intended to illustrate our conceptual framework for understanding the complex relationships among relevant domains rather than providing a formal testable model. For simplicity, most paths are described as moving in one causal direction, and all possible connections are not illustrated (e.g., psychological variables such as stress and appraisal may influence the relationship between extent of surgery and immune function). Psychological appraisals of the resulting physical stressor may modulate immune function and wound healing. In addition, direct connections between the central nervous system (CNS) and immune function are also possible, through direct CNS innervation of lymphoid tissue (Felten & Felten, 1991).

## Wound Healing: Immune and Neuroendocrine Influences

Wound repair progresses through several overlapping stages (Hübner et al., 1996). In the initial inflammatory stage, vasoconstriction and blood coagulation are followed by platelet activation and the release of platelet-derived growth factors (Van De Kerkhof, Van Bergen, Spruijt, & Kuiper, 1994). The factors act as chemoattractants for the migration of phagocytes (neutrophils and monocytes) to the site, starting the proliferative phase that involves the recruitment and replication of cells necessary for tissue regeneration and capillary regrowth. Wound remodeling, the final step, may continue for weeks or months. The healing process is a cascade, and success in the later stages of wound repair is highly dependent on initial events (Hübner et al., 1996).

Immune function plays a key role early in this cascade. Proinflammatory cytokines such as interleukin 1 (IL-1) and tumor necrosis factor (TNF) are essential to this effort; they help to protect a person from infection and prepare injured tissue for repair by enhancing phagocytic cell recruitment and activation (Lowry, 1993). Furthermore, cytokines released by recruited cells regulate the ability of fibroblasts and epithelial cells to remodel the damaged tissue (Lowry, 1993).

A number of hormones and neuropeptides can influence this immunological cascade (Hübner et al., 1996; Zwilling, 1994). For example, mice treated with glucocorticoids showed impairments in the induction of IL-1 and TNF, as well as defects in wound repair (Hübner et al., 1996). Human studies have also demonstrated that stress-induced elevations in glucocorticoids can transiently suppress both IL-1 and TNF production (DeRijk et al., 1997). Accordingly, dysregulation of glucocorticoid secretion provides one obvious mechanism by which stress can alter wound healing.

In contrast to the generally negative effects of glucocorticoids, growth hormone (GH) can enhance wound healing (Veldhuis & Iranmanesh, 1996). GH serves as a macrophage activator (Zwilling, 1994); among its activities, it stimulates monocyte migration. GH also amplifies superoxide anion generation and bacterial killing by macrophages, influential mechanisms for protection from infection after wounding (Zwilling, 1994).

Although acute stressors can provoke transient increases in GH (Kiecolt-Glaser, Malarkey, Cacioppo, &

Glaser, 1994), deep sleep is the normal stimulus for release of much of our daily GH release (Veldhuis & Iranmanesh, 1996); thus, stressors that modify the architecture of sleep can also lessen GH secretion. Moreover, aging decreases GH secretion, and this steep decline may be further accelerated by a chronic stressor (Veldhuis & Iranmanesh, 1996; Malarkey et al., 1996). Although only a few of the paths have been highlighted here, it is obvious that stress-related alterations in the hypothalamic-pituitary-adrenal (HPA) axis can have important repercussions for the wound-healing cascade.

## Stress and Wound Healing

Considerable data from animal and human studies have demonstrated that stress can alter multiple aspects of immune function (Glaser & Kiecolt-Glaser, 1994). For example, family members who provide care for a relative with Alzheimer's disease are typically more distressed than well-matched controls; a number of studies suggest that caregivers also have poorer immune function (Kiecolt-Glaser et al., 1994; Kiecolt-Glaser, Glaser, Gravenstein, Malarkey, & Sheridan, 1996). Consistent with these differences in immune function, further work showed that caregivers took an average of 9 days or 24% longer than controls to completely heal a small, standardized wound. Importantly, photographic data demonstrated that the largest differences in wound size were most apparent early in the process.

Analyses of the production of IL-1$\beta$ in response to lipopolysaccharide (LPS) stimulation showed that caregivers' peripheral blood leukocytes (PBLs) produced less than those of controls (Kiecolt-Glaser et al., 1995). IL-1$\beta$ produced early after tissue injury can regulate the production, release, and activation of metalloproteinases, which are important in the destruction and remodeling of the wound; IL-1 also regulates fibroblast chemotaxis and production of collagen (Lowry, 1993). Moreover, IL-1 stimulates production of other cytokines important for wound healing, including IL-2, IL-6, and IL-8 (Lowry, 1993). Accordingly, these IL-1$\beta$ data provide evidence of one immunological mechanism that may underlie caregivers' deficits in wound repair.

A subsequent study confirmed and extended the data obtained with caregivers. Mice subjected to restraint stress healed a punch biopsy wound an average of 27% more slowly than unstressed mice (Padgett et al., 1998). In addition, analysis of the dermal and epidermal layers surrounding wounds revealed less cellular infiltration in restraint-stressed mice than controls one to three days after wounding. To test the hypothesis that the delayed wound healing in restrained mice reflected HPA activation, Padgett et al. (1998) assessed serum corticosterone; levels in the stressed group averaged 162.5 ng/ml, compared with 35.7 ng/ml in the controls. Blocking glucocorticoid receptors in restraint-stressed animals with RU40555 resulted in healing rates comparable to control animals. Accordingly, these data provided good evidence that disruption of neuroendocrine homeostasis modulates wound healing.

Further research assessed the impact of a brief commonplace stressor, academic examinations, on alterations in mucosal wound repair. Prior work has demonstrated that medical students' cellular immune responses during examinations were poorer than those measured in the same individuals during lower stress periods (Kiecolt-Glaser & Glaser, 1991); thus, we were interested in whether the distress associated with exams would modulate mucosal wound healing among a group of 11 dental students (Marucha et al., 1998). Wounds placed three days before a major test healed an average of 40% more slowly than those made during summer vacation, and the differences were quite reliable: No student healed as rapidly during this stressful period as during vacation, and no student produced as much IL-1. Although this study demonstrated differences in mucosal wounds, the critical early events in the wound healing process are virtually identical for oral and dermal wounds (Wikesjö, Nilveus, & Selvig, 1992). These data confirmed and extended our prior findings in several important ways.

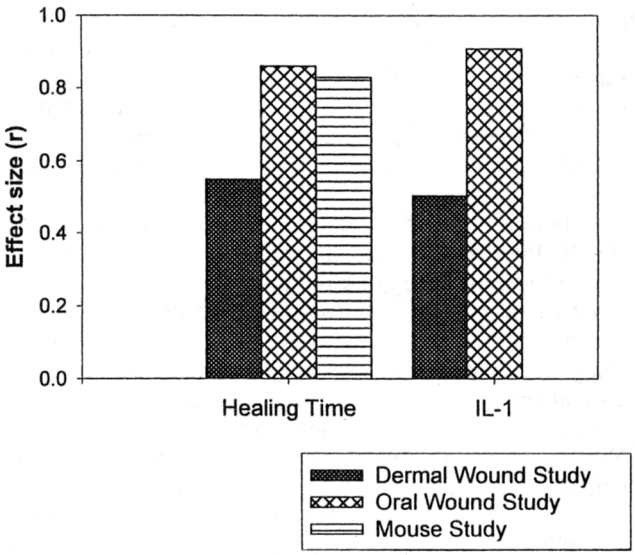
Perhaps the most notable finding was the demonstration of how a relatively mild stressor impacted wound repair. Like most professional students, these dental students were experts at taking tests—they had long histories of performing well under these very conditions. The fact that something as transient, predictable, and relatively benign as examination stress can have significant consequences for wound healing suggests that other everyday stressors may produce similar deficits in wound repair.

It is clear that each of the three studies that assessed the repair of standardized wounds found marked stress-related reductions in healing, with delays from 24% to 40%. Figure 2 shows effect sizes for these studies, using a simple correlation as a measure of the relationship between stress and two key outcome variables, healing time and production of IL-1. Unquestionably, the effects are not just statistically significant, but large in a substantive sense. Of interest is the fact that the effect sizes for IL-1 and wound healing parallel each other within the two human studies, consistent with the importance of early events in the immunological cascade for subsequent healing (as described earlier, greater stress is associated with lower IL-1 levels, but correlations are shown as positive to simplify the figure). In addition, the effect sizes for wound healing were largest and almost identical in the two paradigms that afforded the greatest control over extraneous influences, that is, the Padgett et al. (1998) study in which mice had been randomly assigned to treatment groups, and the within-subject design whereby each student served as his or her own control (Marucha et al., 1998). These stress-related deficits in wound repair have broad implications for surgical recovery.

## Pain: Influences on Neuroendocrine and Immune Function

The impact of painful stress on neuroendocrine and immune function has been studied both in laboratory ani-

**Figure 2**
*Effect Sizes for Three Studies That Employed a Standardized Wound (Kiecolt-Glaser et al., 1995; Marucha et al., 1998; Padgett et al., 1998)*




*Note.* IL-1 = interleukin 1. In each case a simple correlation expresses the relationship between stress and two key outcome variables, healing time and IL-1; stress is associated with longer healing times and lower IL-1 production.

mals and humans. Animal models of painful stress include acute stimuli that do not cause tissue damage such as footshock and tailshock (e.g., Pezzone, Dohanics, & Rabin, 1994). Such painful stressors have been shown to suppress natural killer cell activity (NKCA), lymphocyte proliferative responses to mitogens, specific antibody production, and mixed lymphocyte reaction (Liebeskind, 1991). Several reports of stress-induced immune suppression that also incorporated neuroendocrine measures demonstrated elevated plasma beta-endorphin (Sacerdote, Manfredi, Bianchi, & Panerai, 1994) and corticosterone levels (Pezzone et al., 1994).

The neuroendocrine and immune consequences of tissue-damaging stimuli such as surgery have been well documented in both animals and humans. Postoperative elevations in plasma levels of epinephrine, cortisol, and beta-endorphin reflect sympathetic nervous system (SNS) and HPA axis activation (e.g., Salomaki, Leppaluoto, Laitinen, Vuolteenaho, & Nuutinen, 1993). Immune suppression during surgery is evidenced by suppression of NKCA (e.g., Pollock, Lotzova, & Stanford, 1991), lymphocyte proliferative responses to mitogens, and changes in lymphocyte populations (Tonnessen, Brinklov, Christensen, Olesen, & Madsen, 1987). Further supporting the connections among the SNS, the HPA axis, and the immune system, coincidental surgery-induced changes in these systems also have been demonstrated (Koltun et al., 1996).

The above mentioned findings cannot confirm the role of pain per se in these neuroendocrine and immune consequences of painful stress; however, there is evidence to support such a suggestion. First, several studies have shown that anesthetic techniques that block transmission of nociceptive impulses either locally (Pasqualucci et al., 1994) or at the level of the spinal cord (Koltun et al., 1996) also significantly reduce neuroendocrine or immune responses affected by surgery. Moreover, when Pasqualucci et al. (1994) assessed visual analog scale (VAS) pain scores, they found that the local anesthetic infiltration group also exhibited significantly lower pain scores as well. Second, two prospective studies found that, compared with inhalational anesthesia, epidural anesthesia was associated with a significant reduction in the incidence of postoperative infections, a biologically significant immune outcome (Cuschieri, Morran, Howie, & McArdle, 1985; Yeager, Glass, Neff, & Brinck-Johnsen, 1987). Cuschieri et al. (1985) also documented significantly lower postoperative VAS pain scores in the epidural group. Third, narcotic anesthesia has been shown to suppress the hormonal response to surgery (Lacoumenta et al., 1987). Fourth, effective postoperative pain management with systemic opioids has been associated with reductions in plasma cortisol levels (Moller, Dinesen, Sondergard, Knigge, & Kehlet, 1988). Finally, it was recently shown that providing analgesic doses of morphine in rats significantly attenuates surgery-induced increases in the metastasis of a tumor cell line that is controlled by natural killer cells, providing further evidence of the potential negative immune consequences of pain with implications for the whole organism (Page, Ben-Eliyahu, & Liebeskind, 1994; Page, McDonald, & Ben-Eliyahu, in press).

The inflammatory response is an important mechanism to consider for its contributions to pain, immunity, and the initiation of wound healing. Tissue damage from surgical procedures causes the local release of factors including substance P, bradykinin, prostaglandins, and histamine. Cytokines such as IL-1 are released from indigenous tissue cells and early recruited cells, such as the neutrophil (Hübner et al., 1996). Together, these factors initiate the inflammatory response marked by vasodilation, increased capillary permeability, and the sensitization of peripheral afferent nerve fibers. In addition to its immune-related roles, IL-1 contributes to local hyperalgesia (Schweizer, Feige, Fontana, Muller, & Dinarello, 1988), as well as a systemic hyperalgesic state and illness symptoms such as fever and malaise (Watkins et al., 1995). The sensitization of nociceptive fibers manifests as a decrease in the threshold necessary to initiate nociceptive impulse transmission, resulting in hyperalgesia (Woolf, 1994). Prostaglandin E participates in the local sensitization of nociceptive fibers (Martin, Basbaum, Kwiat, Goetzl, & Levine, 1987), as well as in the suppression of NKCA (Leung, 1989). Faist et al. (1990) showed that inhibiting prostaglandin synthesis with indomethacin treatment reversed surgery-induced depression of postop-

erative delayed type hypersensitivity responses and lymphocyte proliferation and also resulted in a significant reduction in the incidence of infection.

It is clear that pain, like other stressors, adversely affects immune function; anesthetics that block transmission of nociceptive impulses are also associated with better immune function, as well as reductions in postoperative infections. As will be discussed shortly, more anxious patients experience greater postsurgical pain (Johnston, 1988). Thus, more distressed individuals could ultimately be doubly disadvantaged: Immune function, already poorer as a consequence of presurgical stress, could decline even further as a consequence of enhanced postsurgical pain.

## Health Status and Health Behaviors

Aging is associated with an increased risk for surgery. Immune function declines with age, particularly functional aspects of the cellular immune response (Verhoef, 1990); these age-related declines are related to infectious complications, one factor in the increased surgical mortality in the elderly (Thomas & Ritchie, 1995). Moreover, age and distress appear to interact to promote immune down-regulation: Older adults show greater immunological impairments related to stress or depression than younger adults (Herbert & Cohen, 1993; Kiecolt-Glaser, Glaser, et al., 1996).

Some evidence suggests that surgical stress may also interact with both age and psychological stress to heighten risk for older adults. In work from Linn and Jensen (1983), older and younger adults did not differ immunologically prior to elective surgery for hernia repair; however, the former had significantly lower proliferative responses to two mitogens five days after the operation. In a related study, Linn, Linn, and Jensen (1983) divided older and younger patients on the basis of their preoperative anxiety; high anxious older patients had significantly more complications than the other three groups. Thus, morbidity and mortality following surgery are already substantially greater among older adults (Thomas & Ritchie, 1995); further suppression of the immune response by psychological stress may put older adults at even greater risk.

Key behavioral risk factors for surgery include smoking, alcohol and drug abuse, and nutrition (Kehlet, 1997). It is important to note that heightened distress is associated with riskier behavior on all of these dimensions (Steptoe, Wardle, Pollard, Canaan, & Davies, 1996), and each of these health habits can alter wound healing through their effects on immune function; additional paths for influence include effects on anesthetic choices and changes in levels of stress hormones. Moreover, these behaviors interact with one another; for example, heavy alcohol use is linked to poorer nutrition (Benveniste & Thut, 1981).

In addition to nutrition, other consequences of preoperative alcohol abuse include alcohol-related immunosuppression, subclinical cardiac dysfunction, and amplified endocrine changes in response to surgery (Kehlet, 1997). Alcohol also appears to retard wound healing directly via delays in cell migration and deposition of collagen at the wound site (Benveniste & Thut, 1981). Furthermore, individuals who are depressed or anxious are more likely to self-medicate with alcohol or other drugs, and alcohol abuse can potentiate distress (Grunberg & Baum, 1985).

Smoking, another surgical risk behavior, diminishes proliferation of fibroblasts and macrophages, reduces blood flow to the skin through vasoconstriction, and can inhibit enzyme systems for oxidative metabolism and oxygen transport (Silverstein, 1992). In addition to demonstrably slower healing, smokers have higher rates of postoperative infections, perhaps related to the fact that nicotine and other toxins in cigarette smoke depress both primary and secondary immune responses by reducing the chemotactic and phagocytic activities of leukocytes (Silverstein, 1992).

Distressed individuals are more likely to experience sleep and appetite disturbances. As noted earlier, deep sleep is associated with secretion of GH, a hormone that facilitates wound healing, and fragmented sleep results in reduced GH secretion; even partial sleep loss one night results in elevated cortisol levels the next evening (Leproult, Copinschi, Buxton, & Cauter, 1997). Postoperative sleep is typically disturbed as a function of the physiological stress of surgery, pain, opioid use, noise, and awakenings from monitoring and nursing procedures (Kehlet, 1997). Thus, postsurgical sleep deprivation may itself be a significant stressor (Johnston, 1988), and distress may exacerbate or prolong sleep difficulties through such mechanisms as intensified pain sensitivity.

Certainly, individuals who experience greater pain are likely to modify other health behaviors besides sleep in response to this stressor. In addition, some health behaviors may in turn influence pain perception, for example, smoking is associated with greater pain tolerance (Lane, Lefebvre, Rose, & Keefe, 1995).

The assessment of health behaviors is an important component of PNI studies (Kiecolt-Glaser & Glaser, 1988). Moreover, the surgical literature provides clear evidence for the importance of certain health habits for recovery (Kehlet, 1997). Accordingly, the assessment of key risk factors (e.g., smoking and alcohol and drug use) would seem to be an important component of psychological studies addressing surgical recovery—and yet such data are frequently omitted. For example, few studies mention any assessment of smoking in the analysis of outcomes. Similarly, few researchers have systematically discussed relevant indexes of preoperative health status, even though many postsurgical outcomes of interest are undoubtedly colored by chronic health problems such as diabetes. Our model suggests that the assessment of health behavior should be an important component of studies addressing behavioral influences on postsurgical morbidity.

## Psychological Influences on Surgical Recovery

Conceptualizing surgery as a short-term stressor, considerable research has focused on how patients' emotional responses influence postoperative recovery. In general, high preoperative fear or stress is predictive of a variety of poorer outcomes, including greater pain, longer hospital stays, more postoperative complications, and poorer treatment compliance (Johnston, 1988; Mathews & Ridgeway, 1981).

Some of the postoperative repercussions of distress may be mediated through variables such as anesthetic intake; highly anxious patients require more anesthesia than those who are less distressed (Abbott & Abbott, 1995; Gil, 1984; Johnston, 1988; Markland & Hardy, 1993). As one consequence, endocrinological and immunological changes secondary to anesthesia could be greater among more fearful individuals. In addition, Abbott and Abbott (1995) noted that the side effects of various anesthetics, muscle relaxants, and narcotics may include a number of the postoperative behaviors that are sometimes used as outcome measures (e.g., vomiting, nausea, headache, and pain at the incisional site). Higher doses could presumably increase the severity of symptoms.

Across a number of studies, greater self-reported anxiety and stress are typically related to more severe postoperative pain (Johnston, 1988; Mathews & Ridgeway, 1981). In addition to direct effects on endocrine and immune function, the greater pain sensitivity of more anxious patients may also have further consequences for recovery because of differences in compliance. For example, breathing exercises can reduce the risk of pneumonia, and ambulation decreases the risk of phlebitis and may improve wound healing (Kehlet, 1997). However, individuals who are more distressed may be more cautious about following recommendations for walking, coughing, or deep breathing because of pain (Mathews & Ridgeway, 1981).

Linn, Linn, and Klimas (1988) assessed the relevance of differences in preoperative pain tolerance and stress to postoperative immune function; physiological responses to a cold pressor test were measured the day before surgery in 24 men undergoing hernia repair. After controlling for preoperative immunological values (as well as age and social support), lymphocytes from men who reported more recent stressful life events had lower proliferative responses to phytohemagglutinin (PHA). In addition, high responders to the cold pressor stress (i.e., a lower pain threshold) had significantly lower proliferative responses to pokeweed mitogen after surgery; they also required more pain medication and had more complications.

Personality variables may moderate postsurgical outcomes via their influences on stress, mood, and coping (Mathews & Ridgeway, 1981). In an excellent study that assessed the effect of dispositional optimism on recovery from coronary artery bypass surgery, initial analyses showed that optimism was unrelated to severity of disease or to other relevant medical variables (Scheier et al., 1989). Subsequent analyses controlled for extensiveness of surgery, severity of disease, and a triad of risk factors (smoking, hypertension, high cholesterol) before assessing the contribution of optimism to various recovery indexes. Given the rigor of these efforts, the findings are of particular note: Compared with pessimistic men, optimistic men fared better on perioperative physiological indexes—they began walking faster after surgery, and rehabilitation staff rated them as showing a more favorable physical recovery.

Research from another population has provided evidence of possible mechanisms that may underlie optimists' enhanced postoperative recuperation. Among law students in their first year of study, optimism was associated with more positive moods, coping, and differences in response to stress, and these differences appeared to mediate optimists' better immune function during examinations (Segerstrom, Taylor, Kemeny, & Fahey, 1998).

The optimism data are consistent with evidence that interventions that alter appraisal, coping, and/or mood may also modulate immune and endocrine function, thereby enhancing surgical recovery (Kiecolt-Glaser et al., 1985; Kiecolt-Glaser & Glaser, 1992; Manyande et al., 1995). In fact, intervention studies provide some of the best evidence for the role of psychological factors in surgical recovery. In one of the earliest of such studies (Egbert, Battit, Welch, & Barlett, 1964), anesthesiologists paid brief visits to patients the night before surgery to provide information about typical postsurgical physical sensations and to teach them a relaxation technique designed to reduce pain. Those patients who received this additional visit left the hospital an average of 2.7 days earlier and required roughly half as much morphine as individuals receiving routine care. Among the more than 200 treatment studies that have followed Egbert et al.'s (1964) work (see reviews by Contrada et al., 1994; Devine, 1992; Gil, 1984; Johnston & Vögele, 1993; Johnston & Wallace, 1990; Mumford et al., 1982; Suls & Wan, 1989), beneficial outcomes have included decreased anxiety and stress, reductions in hospital stay, fewer postoperative complications, better treatment compliance, less pain and lower use of analgesics, and alterations in physiological indexes (primarily cardiovascular and respiratory measures).[1] Several studies have suggested that presurgical psychological status can influence physiological responses during the surgery itself (Abbott & Abbott, 1995; Greene, Zeichner, Roberts, Callahan, & Granados, 1989; Markland & Hardy, 1993; Scheier et al., 1989) as well as speed of physical recovery (time to open

[1] Because most surgical wounds are sutured, direct assessments of healing are not possible. In addition, although infection is a highly relevant complication within our PNI context, it usually occurs at base rates too low to be useful for research purposes.

eyes) following the discontinuation of anesthesia (Liu, Barry, & Weinman, 1994).

A meta-analysis by Johnston and Vögele (1993) addressed relationships between the major types of interventions (procedural intervention, sensory information, behavioral instruction, cognitive intervention, relaxation, hypnosis, or emotion-focused intervention) and eight outcome variables (negative affect, pain, pain medication, length of stay, behavioral and clinical indexes of recovery, physiological indexes, and satisfaction). Using both published and unpublished studies, they concluded that each of the eight outcomes showed significant benefit. Among the interventions, procedural information and behavioral instruction produced the most ubiquitous improvements across all eight outcomes, whereas relaxation studies showed benefits for all indexes except behavioral recovery.

Summarizing results from several meta-analyses of presurgical intervention studies, Contrada et al. (1994) argued that the association between surgical preparation and outcome is clinically meaningful. Depending on the meta-analysis, two thirds to three quarters of intervention patients had better outcomes than controls, and the size of the improvement was 20% to 28%. Moreover, the effect sizes for interventions with two or three content categories (information, coping skills training, and psychosocial support) were larger than those that had only a single thrust (Contrada et al., 1994).

In contrast to their efficacy, most presurgical interventions have been remarkably brief. For example, the psychoeducational treatments included in Devine's (1992) meta-analysis took 7 to 90 minutes, with a median length of 30 minutes; the great majority were limited to a single session. Moreover, delivery was frequently not individualized; some studies used a group format, whereas others relied on such low-cost alternatives as booklets, manuals, audiotapes, and videotapes. Nonetheless, 79% to 84% of the studies showed beneficial effects (depending on the outcome) for pain, psychological distress, and various indexes of recovery. In fact, 79% of the studies showed that these interventions were associated with a shorter length of hospital stay: Compared with controls, treatment patients spent an average of 1.5 fewer days in the hospital.

Indeed, positive effects are not limited to formal interventions; one study suggested that even small environmental differences may be beneficial. Hospital records of gall bladder surgery from 1972 to 1981 were examined to determine whether assignment to a room with a view from a window made a difference (Ulrich, 1984). Consistent with studies that have documented the utility of distraction or attention redirection as a coping strategy to reduce distress and pain (Gil, 1984), comparisons of well-matched patient pairs showed that those with a view had shorter hospital stays (7.96 vs. 8.70 days) and that they took fewer potent analgesics than those without a view.

How do such modest interventions produce such differences? Recall the magnitude of the effect sizes for stress and wound healing (Figure 2); those data suggest that even treatments that have relatively small consequences for psychological distress could translate into faster repair through the direct and indirect routes suggested by our model.

The positive effects of interventions are even more striking in view of the significant limitations of many studies. These have included heterogeneity in patient groups, in surgical and anesthetic procedures, and in the types of outcomes assessed; failure to assess and control for patients' prior experience with surgery or other invasive medical procedures; differential treatment of comparison groups on variables other than those being manipulated; and the absence of manipulation checks to demonstrate that interventions were delivered in a uniform manner, or that patients actually acquired or utilized new skills or implemented cognitive or behavioral strategies (see critiques by Anderson & Masur, 1983; Gil, 1984; Johnston & Vögele, 1993; Ludwick-Rosenthal & Neufield, 1988). In addition, we suggest that many of the published studies may also have underestimated effect sizes because they failed to consider relevant health behaviors that can make sizable contributions to error variance.

In the same vein, differences in pain and analgesic use should also be assessed. Our model highlights the importance of effective pain control, particularly in the immediate postoperative period. As discussed earlier, the healing process is a cascade, with success in the later stages of wound repair highly dependent on initial events (Hübner et al., 1996); it is important to note that effective postoperative pain management with systemic opioids has been associated with reductions in plasma cortisol, a hormone strongly associated with poorer wound healing (Moller et al., 1988). Although most of the researchers studying psychological influences on postsurgical outcomes have conceptualized pain as an outcome, it also contributes to the process: Poorly controlled acute pain could retard wound healing and prolong the recovery period (Liebeskind, 1991; Page et al., 1994, in press).

## Implications for Research and Practice

In the United States, 80% of all surgeries are considered "elective" in the sense that the patient can choose when to have the operation (Sobel & Ornstein, 1996). Early assessment of psychological predictors of outcome provides the opportunity to identify those patients who might be at greater risk (e.g., Block, 1996). However, to provide maximally effective interventions, further information about the impact of individual differences in coping style and level of anticipatory anxiety would be valuable. For example, "monitors," patients with a vigilant coping style, scan for threat-relevant cues, whereas "blunters" rely more on avoidant coping (Miller, 1992). The two groups appear to show better adjustment in health-related contexts when interventions are tailored to their coping

style. Monitors fare better with voluminous sensory and procedural information; blunters show the opposite response (Miller, 1992; Prokop, Bradley, Burish, Anderson, & Fox, 1991). Such data are particularly important precisely because there is less opportunity to provide care for patients following surgery (Deardorff & Reeves, 1997).

As a consequence of technical advances, many surgeries are less invasive than in the past and thus are now performed on an outpatient basis, or with a greatly reduced hospital stay (Macho & Gable, 1994). In addition, managed care guidelines are increasingly constraining the length of hospitalization. With any extended convalescence at home, family members play more prominent roles. The self-regulatory model proposed by Contrada et al. (1994) provides guidance regarding intervention content that explicitly addresses the patient, the patient's spouse or partner, and the patient–partner relationship. In this context, the demands that at-home recuperation may place on family members who provide care should not be overlooked, and neither should the potential toll for caregivers (see also Kiecolt-Glaser et al., 1994).

Our knowledge of how psychological interventions are actually translated into faster physical recovery is limited by the range of measures used in most studies. Despite the fact that reduction of anxiety or stress is a goal of many of the interventions, the kinds of outcomes assessed do not typically include data from each of the relevant domains: self-report, behavioral, and physiological. Although the addition of endocrine and immune measures both pre- and postoperatively would be worthwhile for psychological studies, appending psychological measures to biologically oriented studies would also be quite valuable. For example, researchers who used an indwelling catheter to collect blood samples every 20 minutes for 24 hours found that presurgical patients showed remarkable increases in cortisol secretion as they were being prepared preoperatively (body shaving, wash, and enema), with values that spiked 6.9 to 10.5 standard deviations above the mean for control patients for that time of day (Czeisler et al., 1976). The interdisciplinary study of such phenomena could amplify our understanding of psychological and behavioral influences on health.

Indeed, surgery offers an attractive paradigm for examining the responses of patients to a distinctive naturalistic stressor (Johnston, 1988). One innovative study addressed social comparison and affiliation under threat among coronary-bypass patients (Kulik, Mahler, & Moore, 1996). The men were assigned preoperatively to a room alone, or they shared a semiprivate room with a roommate who was either cardiac or noncardiac, and either preoperative or postoperative. Those patients assigned a postoperative roommate were less anxious before surgery. In addition, those who either roomed with a cardiac patient or a postoperative patient walked more after their operation, and had shorter hospital stays. The no-roommate patients had the slowest recoveries.

The Kulik et al. (1996) data illustrate an important theme in this literature: Whatever their content, many presurgical interventions may benefit recovery in part because they provide additional interpersonal support during a stressful time (Contrada et al., 1994; Johnston, 1988). There is certainly ample evidence that social support can moderate the effects of psychological stress; in addition, a number of studies have shown relationships between social support and dimensions of autonomic, endocrine, and immune function, with family ties appearing to be a key source of support related to physiological functioning (Kiecolt-Glaser, Newton, et al., 1996; Uchino, Cacioppo, & Kiecolt-Glaser, 1996). Consistent with this literature, male coronary bypass patients who received greater spousal support used less pain medication, had a more rapid discharge from the surgical intensive care unit, and spent fewer total days in the hospital (Kulik & Mahler, 1989).

Indeed, one factor that should spur research in this arena is its obvious and immediate practical applicability. Compared with the costs of hospitalization, psychological interventions are clearly cost-effective (Contrada et al., 1994; Devine, 1992; Mumford et al., 1982).

As described earlier, dental students took an average of 40% longer to heal a small, standardized wound made prior to examinations, compared with an identical wound made during vacation (Marucha et al., 1998). In contrast to the relatively mild and predictable stress of academic examinations, surgery is a high-stakes stressor, with possible consequences that include death, pain, disfigurement, economic losses, alterations in social roles, and uncertainty about both the outcome and the time course for recovery (Contrada et al., 1994). Given the multiple threats embodied in an approaching surgery, it is not surprising that patients may display marked elevations in anxiety for at least six days prior to surgery, with clearly heightened distress persisting for five to six days afterward, dropping back to normal levels only after a period of weeks (Johnston, 1980). Stressors that are perceived as unpredictable and uncontrollable can continue to be associated with elevated stress hormones (Baum, Cohen, & Hall, 1993). The ability to "unwind" after stressful encounters, that is, quicker return to one's neuroendocrine baseline, influences the total burden that stressors place on an individual (Frankenhaeuser, 1986). Accordingly, interventions that promote early adaptation can produce substantial benefits for mental and physical health.

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