Cognitive Processing, Discovery of Meaning, CD4 Decline, and AIDS-Related Mortality Among Bereaved HIV-Seropositive Men

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This study investigated whether finding meaning in response to an HIV-related stressor was associated with changes in immune status and health. Forty HIV-seropositive men who had recently experienced an AIDS-related bereavement completed interviews assessing cognitive processing and finding meaning after the loss and provided blood samples for a 2- to 3-year follow-up. AIDS-related mortality over an extended follow-up was determined from death certificates. As predicted, men who engaged in cognitive processing were more likely to find meaning from the loss. Furthermore, men who found meaning showed less rapid declines in CD4 T cell levels and lower rates of AIDS-related mortality (all $p_{\rm S} < .05$), independent of health status at baseline, health behaviors, and other potential confounds. These results suggest that positive responses to stressful events, specifically the discovery of meaning, may be linked to positive immunologic and health outcomes.

The ways in which individuals respond to stressful life events may influence their immune status and, potentially, their physical health. A growing number of studies in the field of psychoneuroimmunology have found that exposure to stressful experiences is associated with changes in the human immune system (for review, see Cohen & Herbert, 1996; Kemeny, Solomon, Morley, & Herbert, 1992). It has been hypothesized that these immune changes are related to cognitive and emotional responses elicited by the stressor (e.g., Cohen & Herbert, 1996). However, studies have generally failed to assess the associations between particular ways of responding to a stressor, both positive and negative, and immune outcomes. In addition, few studies have examined the health consequences of immune changes associated with stressful experiences and the psychological responses they provoke.

One important way of responding to a stressful experience

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There is emerging evidence suggesting that cognitive processing may be associated with physical well-being following a stressful experience. Experimentally induced disclosure of thoughts and feelings about a past stressor has been associated with fewer health center visits (Pennebaker & Beall, 1986; Pennebaker, Colder, & Sharp, 1990), positive changes in indexes of autonomic activity (Pennebaker, Hughes, & O'Heeron, 1987), and positive changes in the immune system (Esterling, Antoni, Fletcher, Margulies, & Schneiderman, 1994; Pennebaker, Kiecolt-Glaser, & Glaser, 1988; Petrie, Booth, Pennebaker, Davison, & Thomas, 1995). Disclosure can be seen as a behavior that promotes cognitive processing as it often triggers active consideration of the stressful experience as well as one's thoughts and feelings about it.

The process of thinking about a stressful event may lead to a number of different psychological outcomes, such as regaining a sense of mastery over one's life or regaining one's self-esteem. One potentially important cognitive outcome of this process is the ability to find meaning. Finding meaning is thought to be one way that individuals integrate victimizing events into their belief systems and reestablish a positive view of the world (Janoff-Bulman & Frieze, 1983). Indeed, some authors have argued

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that finding meaning is a central component of psychological recovery from traumatic events (Taylor, 1983). Examples of finding meaning include a rearrangement of life's priorities, an enhanced sense of living in the present, deeper communication with loved ones, and a greater appreciation for the fragility and preciousness of life (Taylor, 1983; Yalom, 1980).

The ability to find meaning from a traumatic experience has been demonstrated in a number of different groups (e.g., Affleck, Tennen, Croog, & Levine, 1987; Schwartzberg, 1993; Taylor, 1983; Thompson, 1991) and is typically associated with better psychological adjustment (e.g., Mendola et al., 1990; Thompson, 1991). We were able to locate only one study that addressed the association between finding meaning and physical health outcomes. Affleck et al. (1987) found that heart attack patients who perceived benefits from their first attack (e.g., changes in philosophy of life and values) were less likely to have a subsequent attack and exhibited less morbidity over an 8-year follow-up. The effects of finding meaning on specific physiological systems, including the immune system, and on mortality have yet to be examined.

The present study was designed to determine whether cognitive processing and the discovery of meaning predicted changes in immune status and survival in a sample of HIV-seropositive men who had recently been bereaved of a close friend or partner to AIDS. We evaluated immune changes in this group by assessing changes in CD4 helper-inducer T lymphocytes, which have been closely tied to disease progression among HIV-infected individuals (e.g., Fahey et al., 1990). We hypothesized that men who engaged in cognitive processing following the death of their friend or lover would be more likely to find meaning from the bereavement experience. Further, we hypothesized that the discovery of meaning would be associated with positive changes in CD4 T cell levels over a 2- to 3-year follow-up period and with a lower rate of AIDS-related mortality over an extended follow-up. Both cognitive processing and the discovery of meaning were assessed from semistructured interviews of psychological responses to the loss.

Method

Participants

Participants were recruited from the Los Angeles site of the Multicenter AIDS Cohort Study (MACS), a multisite longitudinal research study of the epidemiology and natural history of HIV infection and AIDS in gay and bisexual men (see Detels et al., 1988, and Kaslow et al., 1987). Between 1984 and 1985, 1,637 HIV-positive and HIV-negative men without AIDS were enrolled in the MACS. In 1987, 798 MACS participants were recruited into the Natural History of AIDS Psychosocial Study (NHAPS; see Kemeny et al., 1994; Taylor et al., 1992). This study was designed to examine the effects of psychosocial factors on psychological adjustment, behavior, and health among men confronting the AIDS epidemic.

For the present study, 40 NHAPS participants were selected who met the following criteria: (a) participated in a semistructured bereavement interview following the loss of a close friend or partner to AIDS, (b) HIV seropositive for at least 2 years prior to the interview, (c) no AIDS diagnosis at time of interview, and (d) CD4 T lymphocyte values available for at least 2 years following the bereavement. Mean age of these participants was 39.5 years (range = 27-50), 98% were Caucasian, and 65% had at least a college degree. This group of participants is demographically similar to the MACS and the NHAPS samples.

Procedure

Every 6 months, MACS participants were examined for signs and symptoms of AIDS and interviewed for information on factors that may contribute to seroconversion or HIV progression (e.g., sexual behavior and drug use). In addition, blood samples were drawn at each MACS visit. NHAPS participants were mailed a questionnaire packet before each MACS visit that included both standardized psychological questionnaires and AIDS-specific questionnaires developed by the NHAPS. NHAPS participants who had lost a close friend or partner to AIDS within the previous year were identified from their NHAPS questionnaires. These participants were invited to participate in semistructured bereavement interviews that assessed their psychological responses to the loss. On average, the interviews were completed 8 months following the bereavement (range = 4 days to 18 months). The interviews were audiotaped and transcribed.

Measures

Information on the context of the bereavement and psychological responses to the loss was obtained from the bereavement interviews. CD4 T lymphocyte values were obtained from the MACS blood samples drawn within 1 year of postbereavement and then at 6-month intervals over a 2- to 3-year follow-up period (mean number of blood draws = 6). Information on psychosocial adjustment, health status, and health behaviors over the follow-up period was obtained from MACS interviews and NHAPS questionnaires completed between the first and last blood draws. Psychological traits were assessed from NHAPS questionnaires completed at entry into the NHAPS (prior to the bereavement). AIDS-related mortality information was based on death certificate searches routinely conducted by the MACS through February 1996.

Measures of Bereavement Context and Psychological Responses to Bereavement

Bereavement status and nature of relationship to the deceased. Information on the nature of each participant's relationship with his deceased friend or lover and the number of other AIDS-related losses experienced in the previous year was obtained from the bereavement interviews.

Grief. The Texas Inventory of Grief (Faschingbauer, DeVaul, & Zisook, 1977), a 13-item inventory assessing current feelings of grief in response to a particular loss, was completed by all participants following the bereavement interview. This scale has acceptable psychometric properties and is widely used in bereavement research.

Cognitive processing and the discovery of meaning. We assessed cognitive processing and the discovery of meaning from transcripts of the bereavement interviews using a coding system developed for this study. The definitions of cognitive processing and the discovery of meaning were developed on the basis of a review of the theoretical and empirical literature relevant to these constructs. *Cognitive processing* was defined in this coding scheme as deliberate, effortful, or long-lasting thinking about the death. All statements that reflected active or deliberate thinking about the death were coded as cognitive processing. These statements included trying to accept the reality of the death, thinking about the person who died or one's relationship with that person, thinking about one's own mortality or illness, thinking about one's actions toward the person before their death, and thinking about one's own life.

Discovery of meaning was defined in this coding system as a major shift in values, prioritics, or perspectives in response to the loss. All statements reflecting a significant change in one of these domains were coded as discovery of meaning. These included a greater appreciation for loved ones, an enhanced sense of living in the present, a perception of life as fragile and precious, a commitment to enjoying life, and an enhanced sense of spirituality or faith. In addition, new personal growth goals, increased self-understanding, and fewer interpersonal fears were coded as discovery of meaning. Examples of both cognitive processing and discovery of meaning statements coded from the bereavement interviews are shown in Table 1.

Cognitive processing and discovery of meaning were treated as dichotomous variables in all analyses. Participants were classified as low in cognitive processing if they had zero or one cognitive processing statement and as high in cognitive processing if they had two or more cognitive processing statements. (A no-yes classification was not used for this variable because only one participant had zero cognitive processing codes.) Participants were classified as "no" on discovery of meaning if they had zero discovery of meaning statements and as "yes" on discovery of meaning if they had one or more discovery of meaning statements. The reliability of these classifications was determined by an independent coder. Interrater agreement for a subsample of 20 interviews was acceptable for both cognitive processing ($\kappa = .67$, p < .01) and discovery of meaning ($\kappa = .60$, p < .01).

Measures of Psychological States and Traits

Depression. We assessed depression using the Center for Epidemiological Studies Depression scale, a reliable and valid 20-item scale designed by Radloff (1977) to assess depressive symptomatology in the general population. We calculated mean levels of depression over the 2to 3-year follow-up period by summing depression scores at each visit and dividing by the total number of scores available.

Negative affectivity. We assessed negative affectivity using the Bendig (1956) short form of the Taylor Manifest Anxiety Scale (TMAS). This 20-item scale correlates highly with other measures of trait anxiety, depression, and neuroticism and can be considered an alternate measure of the negative affectivity construct (Watson & Clark, 1984). The TMAS was completed by participants at the time of their initial enrollment in the NHAPS, prior to the bereavement about which they were interviewed.

Measures of HIV-Related Symptoms and Health Behaviors

HIV-related symptoms. At each MACS interview, participants were asked whether or not they had experienced the following six HIV-related symptoms over the past 6 months: (a) weight loss of at least 10 pounds (4.5 kg) unrelated to dieting, (b) diarrhea that lasted 2 weeks, (c) night sweats that lasted 2 weeks, (d) fever higher than 100 °F that lasted for 2 weeks, (e) shingles or herpes zoster, and (f) candida, thrush, or white patches in the throat or mouth. We calculated the total number of HIV-related symptoms experienced in the 6 months prior to the interview by summing the number of these symptoms endorsed at the first postbereavement MACS visit.

Health behaviors. Health behaviors that may influence immune function and HIV progression were assessed from MACS interviews and NHAPS questionnaires. At each MACS visit, participants were asked about use of AZT (yes or no), use of recreational drugs, including amphetamines (yes or no), nitrite inhalants (yes or no), or marijuana (yes or no), and frequency of alcohol consumption in the past 6 months. The interview also assessed whether participants had engaged in unprotected anal-receptive sex in the past 6 months (yes or no), as this may relate to the number of HIV strains contracted, as well as exposure to other STDs. In each NHAPS questionnaire, participants were asked about amount of exercise (number of days of aerobic and anaerobic exercise) and sleep (average number of hours [per night]) in the past week. Each of these behaviors was assessed over the 2- to 3-year followup period.

Measure of CD4 T Lymphocyte Levels

Blood was drawn at each MACS visit, and levels of CD4 T lymphocytes were determined by two-color (Leu3+ Leu4+) flow cytometry on whole blood (see Giorgi et al., 1990). CD4 levels are reported as absolute number of CD4 T lymphocytes per cubic millimeter of peripheral blood. We calculated CD4 slopes using simple linear regression.

Table 1

Sample Cognitive Processing and Discovery of Meaning Statements

Category	Definition	Example
Cognitive processing	Deliberate, effortful, or long-lasting	"I think in a spiritual way, I tried to understand it."
	thinking about the death	"I keep thinking about what the lessons are for me, what can I learn." "I've been thinking more about what I'm doing, dealing with myself and what I want to accomplish."
		"I'm muddling through my own feelings of what could have been, what was, and what is, and I'm more thinking of my future."
		"I'll think about (him), as a person, as a friend. More importantly, I think about him as a life."
Discovery of meaning	Major shift in values, priorities, or perspectives in response to the loss	"What (his) death did was snap a certain value thing into my behavior which is 'Listen, you don't know how long you've got. You just lost another one. Spend more time with the people that mean something to you.' "
		"In one way I suppose that his passing influenced me to believe more strongly about the quality of life and living life in a satisfying way as much as possible."
		"I certainly appreciated more the friends that I have and became much closer with them."
		"I would say that (his) death lit up my faith."
		" partially because of what I saw (him) do and the fact that he didn't seem to be willing to take the risk that was necessary, I continue to show up and take those risks."

Table 2	
Characteristics of Sample,	Bereavement Context,
and Responses to the Loss	

Characteristic	% of sample	М	SD	Range
Age (years)	_	39.5	5.7	27-50
Race				
White, non-Hispanic	98			
White, Hispanic	2			
Education				
High school graduate	35			
College graduate and above	65			
Deceased was one of closest friends	56			
Deceased was a confidante	76			
No. of months knew deceased		100.1	68.4	6-288
No. of AIDS-related losses in				
previous year		2.0	1.7	1-8
Ability to function affected by				
death	45			
Sleep compromised by death	36			

Measure of AIDS-Related Mortality

Cause and date of death information was based on death certificate searches conducted by the MACS. All deaths that occurred in this sample were AIDS related. The present analyses were based on death certificates available through February 1996 (length of follow-up from bereavement through February 1996: M = 7.40, SD = 1.35).

Results

Nature of Relationship and Psychological Responses to Bereavement

Characteristics of the sample, the bereavement context, and psychological responses to the loss are reported in Table 2. Typically, the participants lost a confidante whom they had known for many years and whose death impacted their ability to function in everyday life. Table 3 reports descriptive statistics for potential psychosocial and biobehavioral confounds in the

Table 3

two cognitive processing (high or low) and discovery of meaning (yes or no) groups. Cognitive processing was associated with fewer HIV-related symptoms at the beginning of the followup period, F(1, 35) = 5.98, MSE = 0.20, p < 0.05. Neither cognitive processing nor the discovery of meaning was significantly associated with grief, depression at the beginning of the follow-up period, partner status (i.e., whether or not the participant had a partner following the bereavement), the type of loss that had been experienced (i.e., close friend or partner), CD4 level at the beginning of the follow-up period, or negative affectivity (all ps > .10 in chi-square analyses and one-way analyses of variance).

Cognitive Processing and Discovery of Meaning

More than half of the participants (26, or 65%) had engaged in active, deliberate, or long-lasting thinking about the death and were classified as high in cognitive processing. A lesser number (16, or 40%) reported making shifts in their values, priorities, or perspectives in response to the loss and were classified as finding meaning from the bereavement. Cognitive processing was significantly associated with the discovery of meaning, $\chi^2(1, N = 40) = 5.93$, p = .01. Among those men who reported finding meaning, almost all were classified as high in cognitive processing (14 out of 16). These results indicate that men who engaged in active or deliberate thinking about the death were more likely to report positive shifts in their values or priorities in response to the loss. On the other hand, a significant number of participants who were classified as high in cognitive processing did not find meaning from the bereavement (12 out of 26), indicating that cognitive processing was not always associated with the discovery of meaning from the death.

Cognitive Processing, Discovery of Meaning, CD4 Slope, and AIDS-Related Mortality

On average, CD4 T lymphocyte levels declined over the 2to 3-year follow-up period (mean CD4 slope = -36.14, SD =77.18), consistent with previous studies of CD4 loss in HIV-

61

468 (276)

0.25 (0.53)

	Cognitive processing		Discovery of meaning	
Variable	High	Low	Yes	No
Grief	38 (9)	35 (7)	38 (8)	36 (9)
Depression	7 (6)	11 (10)	7 (6)	10 (9)
Negative affectivity	6 (4)	6 (4)	6 (4)	6 (4)
% whose relationship with		• •		
deceased was close friend	77	93	81	83

62

479 (316)

0.46 (0.66)^a

38

461 (180)

0.15 (0.38)

46

458 (193)

0.08(0.28)

Mean Levels (and Standard Deviations) of Psychosocial and Biobehavioral Variables for Cognitive Processing and Discovery of Meaning Groups

 $^{*}F(1, 35) = 5.98, MSE = 0.20, p < .05.$

% with intimate partner at time

No. of HIV-related symptoms at

beginning of follow-up

of bereavement CD4 T lymphocyte level at beginning of follow-up

seropositive individuals (e.g., Detels et al., 1988). High levels of cognitive processing were associated with a marginal decrease in the rate of CD4 decline ($\beta = 0.30, R^2 = .09, p < .09$.06). Discovery of meaning was associated with a significant decrease in the rate of CD4 decline, such that men who found meaning from the loss of their friend or partner showed significantly less rapid decreases in CD4 levels than men who did not find meaning ($\beta = 0.45$, $R^2 = .20$, p < .01). Simultaneous regression analyses showed that finding meaning remained a significant predictor of CD4 slope despite controlling for cognitive processing ($\beta = 0.40, p < .05$), whereas cognitive processing was no longer associated with CD4 slope after controlling for the discovery of meaning ($\beta = 0.15, p > .30$). Thus, cognitive processing appeared to be associated with changes in CD4 slope only to the extent that it led to the discovery of meaning from the bereavement. The relationship between cognitive processing, discovery of meaning, and CD4 slope is illustrated in Figure 1.

Discovery of meaning was also associated with a lower rate of AIDS-related mortality, $\chi^2(1, N = 40) = 4.0, p < .05$. Fifteen of the 40 participants in this study died of AIDS-related causes; only 3 of these men reported finding meaning from the death of their friend or partner, whereas 13 of the 25 survivors did find meaning from the loss. The association between cognitive processing and mortality was not significant, $\chi^2(1, N = 40) = 1.44, p > .20$.

We next assessed whether the relationship between the discovery of meaning and mortality might be explained by differences in CD4 slope among men who did and did not find meaning from the bereavement. Consistent with previous research, CD4 slope was independently associated with survival, F(1,38) = 29.53, MSE = 0.08, p < .0001. After controlling for CD4 slope levels, we found that discovery of meaning was no

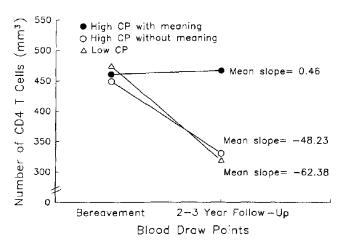


Figure 1. Mean CD4 slopes for participants categorized as high in cognitive processing (CP) who found meaning from the bereavement (n = 14), those categorized as high in CP who did not find meaning (n = 12), and those categorized as low in CP (n = 14). The high CP with meaning group had a significantly higher mean CD4 slope than either of the other two groups, which were not significantly different from each other, F(2, 37) = 3.47, p < .05. Slopes represent the mean number of CD4 cells lost per year in the 2- to 3-year follow-up period.

longer a significant predictor of mortality, Cochran-Mantel-Haenszel (CMH) general association statistic (1, N = 40) = 0.31, p > .55. Based on criteria for mediation established by Baron and Kenny (1986), these results suggest that the lower rate of AIDS-related mortality in participants who found meaning from the bereavement may be attributed to the less rapid decline in CD4 T lymphocytes evidenced in this group.¹

Potential Psychosocial and Biobehavioral Mediators

We considered a number of psychosocial and biobehavioral characteristics that have been associated with immune status in previous research or that may influence one's ability to find meaning following a bereavement experience. These included age, two measures of HIV-related health assessed at the beginning of the follow-up period (number of HIV-related symptoms and number of CD4 T cells at the beginning of the follow-up period), behavioral variables assessed over the 2- to 3-year follow-up period (sleep, exercise, unprotected anal-receptive intercourse, cigarette smoking, alcohol consumption, use of AZT, and use of recreational drugs), and depressive symptomatology assessed over the 2- to 3-year follow-up. Of these variables, none were significantly associated with the discovery of meaning, and only use of AZT was significantly associated with CD4 slope and with mortality. Discovery of meaning remained a significant predictor of both CD4 slope ($\beta = .44, R^2 = .19$, p < .01)² and AIDS-related mortality, CMH general association statistic $(1, N = 40) = 3.92, p < .05, {}^{3}$ after controlling for use of AZT.

Discussion

In this study of HIV-seropositive men recently bereaved of a close friend or partner to AIDS, we found that nearly two thirds thought about the death and its implications for their own lives in some deliberate, effortful, or long-lasting way, referred to here as cognitive processing. Those men who engaged in cognitive processing were more likely to discover meaning from the be-reavement experience, as reflected by shifts in their values, priorities, and perspectives (e.g., Taylor, 1983). The discovery of meaning was associated with positive changes in a key immuno-

¹ It could be argued that considering CD4 slope as a mediator of the association between finding meaning and mortality is misleading, given the strong association between CD4 decline and mortality among HIV-positive individuals. However, although these variables are closely related, recent data indicate that CD4 decline does not account for all, or even the majority of, variance in AIDS-related mortality. Studies have found considerable variability in survival among individuals with very low CD4 T cell levels (e.g., Sabin et al., 1997; Spino, Kahn, Dolin, & Phair, 1997), and other important biological factors have been identified that may be even stronger predictors of mortality among HIV-positive individuals (e.g., Liu et al., 1997; Mellors et al., 1996).

² Discovery of meaning remained a significant predictor of CD4 slope after controlling for all of the potential mediators assessed in a series of hierarchical regression analyses.

³ An additional analysis was conducted to control for the length of the follow-up period (from bereavement to February 1996). The association between discovery of meaning and AIDS-related mortality remained significant after stratifying the data by length of follow-up.

logical marker of HIV progression, CD4 T lymphocyte decline. Participants who both engaged in cognitive processing and found meaning from the death showed no mean decline in CD4 T cells over the 2- to 3-year follow-up period, a pattern that has been characterized as a CD4 plateau in previous research with HIVseropositive gay men (Detels et al., 1988). In contrast, participants who engaged in cognitive processing but did not find meaning and those who did not engage in cognitive processing lost an average of approximately 119 and 155 CD4 T cells, respectively, over the follow-up, a rate of decline that could be characterized as moderate to fast on the basis of a long-term follow-up study of CD4 decline among HIV-positive individuals (Munoz et al., 1995).

More important, the discovery of meaning was associated with a lower rate of AIDS-related mortality over a 4- to 9-year follow-up period. Previous research has supported the importance of finding meaning for psychological adjustment following a stressful life event (e.g., Mendola, Tennen, Affleck, McCann, & Fitzgerald, 1990; Thompson, 1991) and has suggested that finding meaning in response to a life-threatening illness may have beneficial effects on physical health (Affleck et al., 1987). However, ours is the first study to show an association between finding meaning and mortality and the first to report an association between meaning and physical health indexes that does not appear to be mediated by health behaviors or other potential confounds, at least as assessed in this report. These findings suggest that HIV-positive men who are prompted by the death of a loved one to make major shifts in their own values and priorities, emphasizing such things as close relationships, living each day to the fullest, and personal growth, may show physiological benefits, including a lower rate of mortality.

How does one reach a new perspective on life following a traumatic event? This question has been largely unaddressed in previous research, although possible determinants of more general positive outcomes have been discussed (e.g., Schaefer & Moos, 1992). Our findings suggest that cognitive processing may be one route through which individuals find meaning from a stressful experience. Actively thinking about a past trauma can be a difficult and painful process, provoking short-term increases in negative mood (e.g., Pennebaker et al., 1988; Petrie et al., 1995) and in certain measures of autonomic activity (Hughes, Uhlmann, & Pennebaker, 1994). However, this process may be required to reach a positive cognitive outcome following the event, inspiring changes in attitudes and values that would not otherwise be considered.

The results of the present study highlight the importance of distinguishing between the process of responding to a stressful experience and the cognitive outcomes of those responses. Almost one half of the men in this sample who engaged in cognitive processing did not report finding meaning from the bereavement; for some of these men, processing may have led to other positive cognitive outcomes, such as acceptance of the loss. For others, cognitive processing may have led to more negative cognitive outcomes, such as depressive rumination (extended focus on negative feelings and the causes and consequences of those feelings; Nolen-Hoeksema, 1991), recurrent, intrusive, and disruptive thoughts about the experience (Silver, Boon, & Stones, 1983), or "shattered meaning" (an inability to find any meaning in the death or in the impact of AIDS on the gay community

as a whole; Schwartzberg, 1993). Thus, one way of responding to a stressor may lead to a diversity of cognitive outcomes, each of which may have a different effect on psychological adjustment, immune function, and physical health.

Physiological mediators linking discovery of meaning and CD4 T cell levels were not assessed in this report. Potential mechanisms through which psychological factors may influence the immune system include central nervous system control of the autonomic nervous system and of hormone and neuropeptide production. In particular, both activation of the sympathetic nervous system (SNS) and production of glucocorticoids from adrenal cortical cells via stimulation of the hypothalamic-pituitary-adrenal (HPA) axis are known to be influenced by psychological stimuli, particularly stress, and have demonstrated effects on immune function. Finding meaning may buffer stressrelated changes in the SNS, the HPA axis, or both, or may have direct beneficial effects on these systems. It is possible that any meaning-related changes in SNS activation or glucocorticoid production could lead to enhanced preservation of CD4 T cell populations among HIV-infected individuals because of the effect of these systems on cytokine production, leukocyte traffic, and CD4-programmed cell death (see Cole & Kemeny, 1997, for review of possible neuroimmune mechanisms in HIV). For example, recent experimental data indicates that products of SNS activation (i.e., norepinephrine) can accelerate HIV replication in vitro through suppression of immunoregulatory cytokines (Cole, Korin, Fahey, & Zack, 1998). However, the understanding of the psychobiology of positive states is extremely limited, and it is possible that the immunological effects of positive psychological factors, such as finding meaning, may be mediated by other hormonal or neuropeptide systems not considered here.

The primary limitation of the present study is the small sample size. Thus, these findings must be considered preliminary and should be interpreted with caution. In addition, the participants were almost exclusively White and well-educated men, potentially limiting the generalizability of the findings. Perhaps HIV-infected individuals who do not have the financial and social resources that these men possess may not have the luxury to think about bereavement in the same way or may be less likely to derive meaning from stressful past experiences. The immune and health correlates of these variables may also differ in a larger or more diverse sample or among patients with other types of diseases. In addition, although we considered a number of potential mediators and confounding variables, it is possible that the relationships observed may have been influenced by these or by other psychosocial and biobehavioral characteristics that were not assessed. Another potential limitation is the approach to assessing cognitive processing and finding meaning, which has not been empirically validated in other studies. Finally, causality cannot be addressed unambiguously in a nonexperimental study, but in this case the prospective longitudinal design reduces the plausibility of the reverse direction of causality.

To date, most research in psychoneuroimmunology has focused on negative states, including stress, depression, and loneliness. However, exposure to stressful life events does not invariably end in depression and despair; it may also act as a catalyst for a reevaluation of one's goals and priorities and a reexamination of one's sense of self. In the psychological literature, there is an increasing recognition of the positive outcomes that may result from stressful events, including finding new meaning in life, developing new coping skills, and enhancing one's social resources (e.g., O'Leary & Ickovics, 1995; Schaefer & Moos, 1992). The results of this study suggest that these positive states, specifically finding meaning, may be associated with positive immunologic and health outcomes following exposure to stress.

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