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Perceived Stress and Cellular Immunity: When Coping Counts

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This cross-sectional study investigated whether active and avoidance coping methods were differentially related to immune function depending on stress level. Perceived stress and coping method were assessed in 173 healthy older adults and related to the number and percentage of CD3+, CD4+, and CD8+ T lymphocytes as well as the proliferative response of peripheral blood leukocytes to phytohemagluttinin (PHA) and concanavalin A (Con A). Both active and avoidance coping significantly interacted with perceived stress on proliferative responses to both mitogens. Higher levels of active coping were significantly related to a more vigorous proliferative response to PHA and Con A, particularly at high stress levels. At low stress levels, active coping was not significantly related to proliferative responses, whereas avoidance coping was significantly associated with a greater proliferative response to Con A. These results suggest that the relationships between certain coping methods and immune function depend on perceived stress level.

KEY WORDS: psychoneuroimmunology; psychoimmunology; avoidance; aging.

INTRODUCTION

Coping styles, defined as the cognitive and behavioral efforts to manage external and internal demands that are appraised as taxing or exceeding an individual's resources (Lazarus and Folkman, 1984), are likely to differ

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among individuals, even when they are faced with a similar stressful situation. These differences may be accounted for by different appraisals of the situation or by preferences for different coping styles. Evidence suggests that preferred coping style is influenced by situational (Folkman and Lazarus, 1980) and dispositional factors (Carver *et al.*, 1989). Nevertheless, different coping styles may, in turn, influence the person's ability to eliminate or reduce the source of stress and its emotional impact.

One categorization of coping style that appears to distinguish successful from unsuccessful coping is active versus avoidance coping methods (Billings and Moos, 1981). Active coping may include an active cognitive component, which results in positive reappraisal of the situation, or an active behavioral component, which results in action that eliminates or reduces the source of stress. Thus, active coping methods include coping efforts that others have referred to as problem-focused, which are directed at altering the person–environment relationship, and emotion-focused, which are efforts directed at regulating the emotional response to the situation (Billings and Moos, 1981; Folkman and Lazarus, 1980; Goodkin *et al.*, 1992a). Problem-focused coping has been associated with less depression, fewer physical symptoms (Nakano, 1991), improved quality of life (Swindells *et al.*, 1999) and, in one study, better immune function (McNaughton *et al.*, 1990). Emotion-focused coping has been linked to anxiety, depression, emotional and physical distress (Compas *et al.*, 1996; Nyamathi *et al.*, 1992), and poorer quality of life (Swindells *et al.*, 1999). However, in some chronic stress conditions, both problem- and emotion-focused coping appeared to have positive benefits on health and well-being (Ingledew *et al.*, 1997; McQueeney *et al.*, 1997), while avoidance coping had negative effects (Ingledew *et al.*, 1997). Thus, the effects of coping may not depend as much on whether problem- or emotion-focused coping styles are used, but rather if active or avoidance methods are used, particularly in situations of chronic stress.

As part of our sample included chronically stressed individuals (caregivers), coping was categorized on the basis of coping method, rather than coping focus. Furthermore, the categorization of active versus avoidance coping has been used in other studies on health and immune measures, which are of interest in this study. For example, persons who actively coped with certain kinds of life events were more likely to have better mental health and immune function (Billings and Moos, 1981; Esterling *et al.*, 1993; Goodkin *et al.*, 1992a,b, 1996; Lackner *et al.*, 1993; Molassiotis *et al.*, 1997). Conversely, avoidance coping, exemplified by denial and disengagement, generally had effects opposite to those of active coping, being associated with increased distress, poorer mental health (Aldwin and Revenson, 1987; Carver *et al.*, 1993; Folkman and Lazarus, 1986; Stanton and Snider, 1993; Stephens *et al.*, 1988), and poorer immune function (Goodkin *et al.*, 1992b).

In addition to these main effects of coping, coping can also interact with measures of psychological distress, thus moderating the negative effects of stressful events. For example, active coping interacted with depression, such that life events were more likely to be associated with depression if active coping was low, but not when active coping was high (Billings and Moos, 1981; Finney *et al.*, 1984). In another study, problem-based (active) coping buffered the effects of financial strain on periodontal disease (Genco *et al.*, 1999). Thus, the effects of stress appear to depend to some extent on coping method. Conversely, the positive or negative effects of coping methods appear to depend on the context of stress, being more evident in high stress conditions.

Although significant interactions of stress with coping on mental and physical health have been noted (Aldwin and Revenson, 1987; Billings and Moos, 1981; Nakano, 1991), their interaction on immune measures is largely unknown. This is somewhat surprising as interactions of stress and coping on physical health would presumably depend to some extent on immune competence. However, detection of significant interactions may have been obscured because of small sample sizes, specialized populations (i.e., HIV positive or younger adults), a limited number of immune measures studied, or restricted ranges of critical variables. To create more favorable conditions in which to observe significant interactions of stress and coping on certain aspects of immune function, we measured the number and percentage of CD3+ (total T), CD4+ (T helper), and CD8+ (T suppressor/cytotoxic) lymphocytes and the ability of these cells to respond to two mitogens in a large sample of healthy older adults who had a broad range of perceived stress.

Caring for a family member with a progressive dementia-related disorder, such as Alzheimer's disease, has been conceptualized as a model of chronic stress. Indeed, caregivers report greater distress and depression, reduced social support, and poorer mental health than do noncaregivers (Bodnar and Kiecolt-Glaser, 1994; Cohen and Eisdorfer, 1988; Dura *et al.*, 1990; Kiecolt-Glaser *et al.*, 1991; Redinbaugh *et al.*, 1995). Furthermore, following disease onset, modal survival time for Alzheimer patients is about 8 years (Heston *et al.*, 1981). During this time, progressively greater demands are placed on the caregiver as the patient has increasing needs for supportive care (Heckler, 1985). Thus, the burden of caregiving is significant and escalates over time. Furthermore, the detrimental psychological and immunological effects of caregiving may persist for long periods in former caregivers (Bodnar and Kiecolt-Glaser, 1994; Esterling *et al.*, 1996). By including former and current caregivers in our sample, we extended the range and variability of perceived stress scores, thus allowing us to adequately assess the effects of coping in low and high stress conditions.

As mentioned, previous studies have found active coping to moderate the effects of stress on mental and physical health. In contrast, avoidance coping may magnify these effects. We hypothesized similar relationships regarding stress and coping, with several immune markers as dependent measures. Specifically, we expected active coping to be positively associated and avoidance coping negatively associated with the immune measures, most notably in participants who report high levels of stress.

METHODS

Participants

Participants were part of a longitudinal study on chronic stress, immune function, and health. Family caregivers of dementia patients were recruited from three local dementia evaluation centers, neurologists' referrals, the city's Alzheimer's Disease and Related Disorders Association (ADRDA) support groups, the monthly ADRDA newsletter, respite care programs, and governmental caregiver support programs. Comparison participants were recruited through newspaper advertisements, church groups, notices posted in senior citizen centers, and referrals from other participants.

To minimize the potential confounding influence of health behaviors on immune function, we excluded participants who were taking immunosuppressive medication or had a health problem with an immunological component such as cancer, recent surgery, or hormonal disorder ($n = 17$), smoked ($n = 26$, range 1–14 packs/day), consumed more than 10 alcoholic drinks in the past week ($n = 7$, range 14–28 drinks), or drank more than 10 caffeinated drinks in the past 48 h ($n = 5$, range 12–32 drinks). Thus, 55 participants were excluded based on these health criteria (11 former caregivers, 22 current caregivers, and 22 comparison participants). One former caregiver did not complete the perceived stress measure and 2 former caregivers and 1 comparison did not fully complete the coping measure. Because of missing immune data, 17 additional participants (2 former caregivers, 7 current caregivers, and 8 comparison participants) were excluded. However, the participants that were excluded due to missing immune data did not significantly differ from the rest of the sample on demographic factors, health behaviors, perceived stress, or coping. Thus, data from a total of 34 former caregivers, 61 current caregivers, and 78 comparison participants ($N = 173$) were used for analyses.

Because there were no significant differences on demographic factors between groups, except for sleep, we report them for the sample as a whole. The average age of our sample was 62.4 years (SD = 13.8), with females comprising approximately 75% of the sample. The majority of participants

had completed at least some college (70%) and nearly all were Caucasian (93%). Median yearly income was in the range of $20,000–$29,999. Other health variables measured included body mass (mean 25.3 kg/m^2, SD = 4.3), exercise (3.2 h/week, SD = 4.0), and sleep. Over the three nights prior to participation in the study, comparison participants slept an average of 0.3 h (SD = 1.8) less than usual, former caregivers slept 1.0 h (SD = 1.8) less, and current caregivers slept 1.4 h (SD = 2.7) less than usual. Of the 61 current caregivers, 18 (30%) were providing in-home care, while the rest were providing care outside of the home. Former caregivers had not been providing care for an average of 20.9 months (SD = 11.6).

Psychological Measures

Participants completed the 10-item Perceived Stress Scale (PSS-10; Cohen and Williamson, 1988), which measured the degree to which individuals perceived their daily life during the past month as uncontrollable, unpredictable, and overloading. This scale does not specifically ask about any particular stressful situation (such as caregiving). The PSS-10 has a single factor and has adequate reliability (Cohen and Williamson, 1988). Higher scores on the PSS-10 represent higher levels of perceived stress. Cronbach's alpha in the current sample was 0.91.

Dispositional coping style was measured with the 53-item Coping Orientation to Problems Experienced (COPE; Carver *et al.*, 1989). Individual items were rated on a scale from 1 (*I usually don't do this at all*) to 4 (*I usually do this a lot*). The COPE has 13 subscales, each with four items, and 1 subscale (alcohol/drug use) with only one item. A second-order principle components factor analysis, with varimax oblique rotation, was performed on the 13 four-item COPE subscales in our sample. Three factors, with minimum eigenvalues of 1, accounted for 54% of the total variance. Each of the coping subscales had coefficients of at least 0.60 on their respective factor. The first factor was labeled "active" and, similar to previous findings (Carver *et al.*, 1989; Goodkin *et al.*, 1992a; Segerstrom *et al.*, 1998), consisted of planning (coming up with strategies to best handle the problem), suppression of competing activities (deferring from activities or thoughts that would detract from dealing with the stressor), active coping (taking direct action to eliminate or circumvent the stressor), restraint coping (waiting for the appropriate opportunity to act), acceptance (accepting the reality of the situation), and positive reinterpretation and growth (viewing the stressor in more positive terms). Although turning to religion was also associated with the active coping factor, Carver *et al.* (1989) suggest that turning to religion could be used for a wide variety of reasons, thus making it difficult to know whether

it was used in an active or avoidant manner. Therefore, it was not included in the active coping factor. The second factor was labeled "social support," and included seeking social support for instrumental and emotional reasons and focusing on venting of emotion. Although social support is an important factor in health, this factor measured the amount of social support sought, not necessarily received, and is not further discussed. We labeled the third factor "avoidance," which included denial (refusing to accept the reality of the stressor), mental disengagement (doing activities that take their mind off the situation), and behavioral disengagement (giving up). Composite active and avoidance coping scales were calculated as the mean of the individual 4-item subscales that comprised them, thus potentially ranging from 4 to 16. Cronbach alphas for the active and avoidance coping scales were 0.88 and 0.72, respectively.

Immunological Assays

Prior to the completion of the psychological interviews, blood was drawn between 8 and 10 A.M. to control for diurnal variations. Peripheral blood leukocytes (PBLs) from 50 cc of heparin-treated blood were separated using Hypaque-Ficoll density gradients, washed two times with Mg- and Ca-free buffer, counted in a Coulter Counter, then used as described.

For enumerative analyses, mononuclear cells were obtained and then resuspended in RPMI 1640 media supplemented with 5% heat-inactivated fetal bovine serum. 1.0×10^6 cells were aliquoted to 10×75 mm^2 snap-cap tube(s) for reaction with monoclonal antibodies (MAbs). MAbs were conjugated with either fluorescent isothiocyanate (FITC) or phycoerythrin (PE) fluorochromes and paired for dual color analyses with reagents and isotype controls from Coulter to identify the percent of CD3+ (total T), CD4+ (T helper) and CD8+ (T suppressor/cytotoxic) T-lymphocytes. Absolute numbers of CD3+, CD4+, and CD8+ cells were calculated by multiplying these percentages by the total lymphocyte count obtained from a complete blood count and differential performed by the Clinical Immunology Laboratory at the Ohio State University Hospital.

The mitogens phytohemagluttinin (PHA) and concanavalin A (Con A), which stimulate proliferation of T cells, were used at a final concentration of 2.5, 5.0, 10.0, and 20.0 μg/mL in complete RPMI 1640 media supplemented with 5% fetal bovine serum. All assays were performed in triplicate and complete medium was used for background controls. One-tenth milliliter of mitogen was added to 1×10^5 lymphocytes (in 0.1 mL complete medium) in 96 well plates, and incubated at 37°C in 5% CO_2 for 60 h. Fifty microliters of tritiated thymidine (10 uCi/mL, specific activity 83 Ci/mM) were added to each well and the plates incubated at 37°C in 5% CO_2 for 4 h. Cells were

harvested onto FG/A filters. Radioactivity was recorded in counts per minute (cpm) using a Beckman LS7000 scintillation counter. Following tests for normality, proliferation data were log-transformed. Data are expressed as the log of the difference between stimulated and unstimulated samples, measured in counts per minute ($\log_{10}$. cpm) and averaged across concentration.

Statistical Procedures

SAS v8.0 (SAS Institute, Cary, NC) was used to perform all statistical procedures. Predictor variables were centered and standardized prior to use in hierarchical regression models, as recommended (Aiken and West, 1991). Separate hierarchical regressions were run with each immune measure as the dependent variable. Preliminary correlational analyses were conducted to determine if health behaviors or demographic factors were significantly related to immune function, in which case they were included as control variables in subsequent regression analyses. Age, the only variable to meet such criteria, was entered first in each regression equation. Following age, we entered perceived stress, coping method (active or avoidance), and the stress by coping interaction term.

Because the stress by coping interaction term was, in some cases, significant, we conducted further analyses to sufficiently describe the pattern of the interaction. One option would have been to categorize perceived stress scores into high, medium, and low levels and then test the relationship between coping method and immune function at each level of stress. However, categorization of PSS scores would have reduced statistical power (Finney *et al.*, 1984). Instead, we used the statistical procedures recommend by Aiken and West (1991) to describe the interaction of two continuous variables (stress and coping). To do this, simple regression equations of coping method on immune function were plotted with the value for perceived stress held constant at three selected values: the mean PSS-10 score, 1 SD above the mean, and 1 SD below the mean. This resulted in three regression lines that revealed the relationship between coping method and immune function at these specific values of perceived stress. Results were determined to be significant at $p < 0.05$.

RESULTS

Stress, Coping, and Immune Function

Of primary interest, significant interactions between perceived stress and both coping methods were found on proliferation of PBLs to the mitogens PHA and Con A (ps < 0.05, see Table I), indicating that the relationship

Table I. Hierarchical Regression Summary for Stress and Coping on Proliferative Measures

	Cumulative R^2	Increase R^2	t	p
PHA[a]				
Age	0.06	0.06	−3.27	0.001
PSS-10	0.07	0.01	−1.21	ns
Active	0.09	0.02	2.02	0.04
Active × PSS-10	0.12	0.03	2.49	0.01
Age	0.06	0.06	−3.27	0.001
PSS-10	0.07	0.01	−1.21	ns
Avoid	0.07	0.00	−0.15	ns
Avoid × PSS-10	0.09	0.02	−2.20	0.03
Con A[b]				
Age	0.01	0.01	−0.97	ns
PSS-10	0.01	0.00	0.21	ns
Active	0.01	0.00	0.16	ns
Active × PSS-10	0.05	0.05	2.89	0.004
Age	0.01	0.01	−0.97	ns
PSS-10	0.01	0.00	0.21	ns
Avoid	0.01	0.00	0.70	ns
Avoid × PSS-10	0.05	0.04	−2.67	0.008

Note. PSS-10 = Perceived Stress Scale. Avoid = Avoidance coping.
[a]Full model: for active, $F(4, 172) = 5.80$, $p < 0.001$; for avoidance, $F(4, 172) = 4.31$, $p < 0.01$.
[b]Full model: for active, $F(4, 172) = 2.36$, $p = 0.06$; for avoidance, $F(4, 172) = 2.17$, $p = 0.07$.

between coping and proliferation to mitogen depended on stress level. Further analyses and plotting of the interactions revealed that, in general, active and avoidance coping were more strongly associated with proliferation to PHA and Con A in participants reporting high, but not medium or low stress levels.

Figures 1 and 2 illustrate the significant interactions between perceived stress and each method of coping on proliferation of PBLs to PHA at three different levels of perceived stress: 1 SD below the PSS-10 mean (7.5; low), the PSS-10 mean (14.5; medium), and 1 SD above the PSS-10 mean (21.5; high). Standardized beta weights and their significance, calculated according to the recommendation of Aiken and West (1991), are shown next to each regression line. At a low level of perceived stress, active coping was not significantly related to the proliferative response to PHA (see Fig. 1). However, at a high level of perceived stress, active coping exhibited a significant positive relationship with the proliferative response to PHA ($b = 0.13$, $p = 0.002$).

Although the interaction between perceived stress and avoidance coping was significant (see Table I), the slopes of the simple regression lines in Fig. 2 at 1 SD above and below the PSS-10 mean were not significantly different from zero (ps > 0.05). Only by selecting more extreme PSS-10 values did the

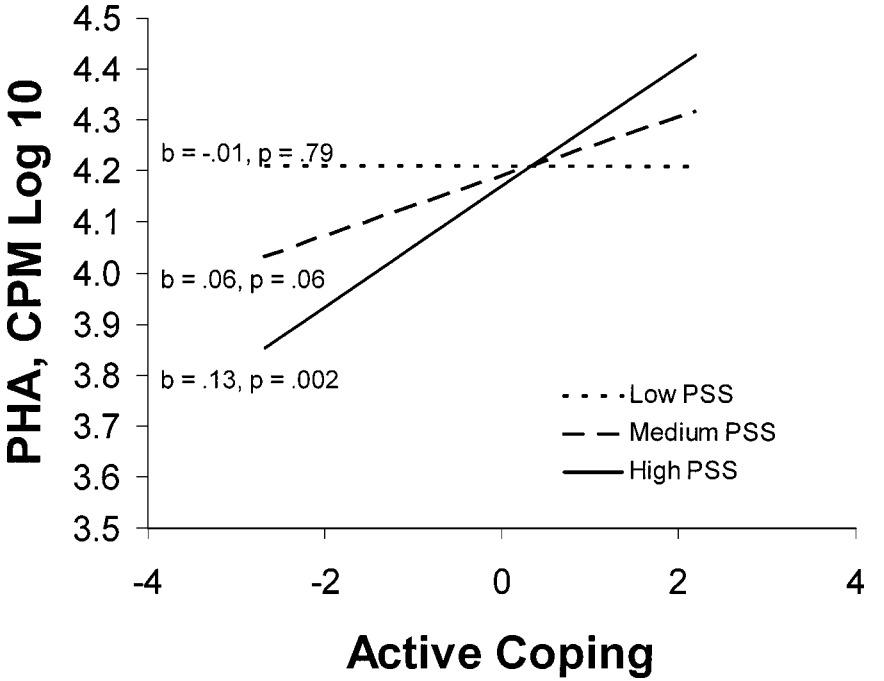

Fig. 1. Simple slopes of active coping on proliferation to PHA at low (1 SD below the mean), medium (mean), and high (1 SD above the mean) levels of perceived stress. Abscissa represents standardized active coping scores.

tests of simple slopes achieve significance (2 SD above the mean, $b = -0.16$, $p = 0.04$; 2 SD below the mean, $b = 0.16$, $p = 0.05$).

Figures 3 and 4 represent the interactions once again between stress and coping method, but with Con A rather than PHA as the dependent variable. Similar to findings with PHA, higher levels of active coping were significantly associated with a greater proliferative response to Con A ($b = 0.13$, $p = 0.04$), see Fig. 3. At low levels of perceived stress, this relationship was in the opposite direction, but was not significant ($b = -0.13$, $p = 0.06$). Similar to findings with PHA, avoidance coping was not significantly associated with the proliferative response to Con A at high stress levels, ($b = -0.10$, $p = 0.15$). However, at low levels of perceived stress, avoidance coping was significantly associated with greater proliferation to Con A ($b = 0.19$, $p = 0.01$).

Investigation of the individual coping subscales that comprised the active and avoidance factors revealed significant interactions between stress and coping style on cell proliferation in response to both Con A and PHA. Of the active coping subscales, significant interaction terms were found for positive

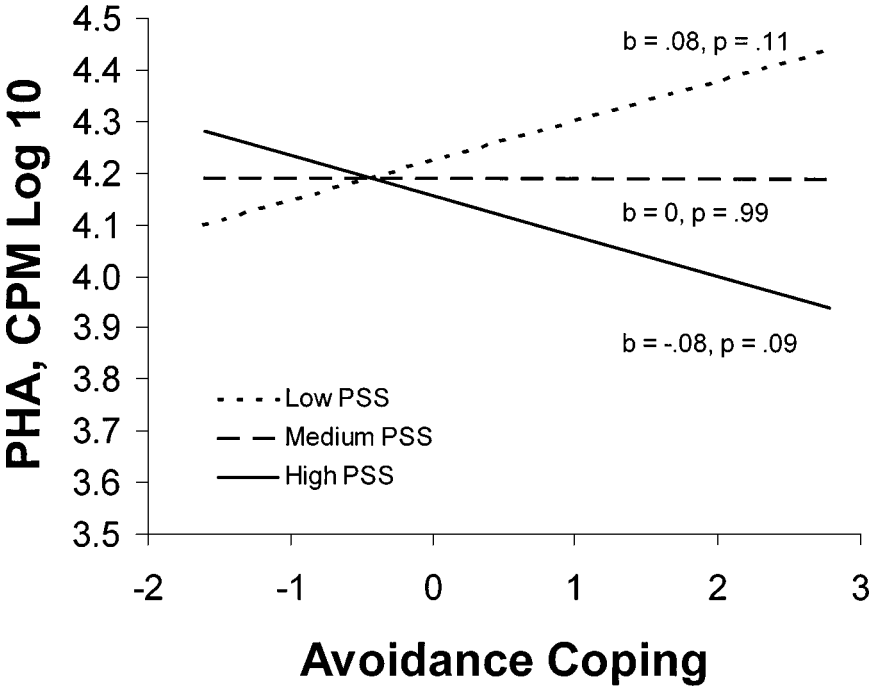

Fig. 2. Simple slopes of avoidance coping on proliferation to PHA at low (1 SD below the mean), medium (mean), and high (1 SD above the mean) levels of perceived stress. Abscissa represents standardized avoidance coping scores.

reinterpretation and growth, active coping, and planning (ps < 0.02). Of the avoidance subscales, the interaction of perceived stress with behavioral disengagement was the only one that achieved significance ($p < 0.0002$). Plotting of the interactions revealed similar patterns to that of the composite coping factors.

Regarding quantitative immune measures, none of the regression models with CD3+, CD4+, and CD8+ cell numbers or percentages, or the CD4+/CD8+ ratio as the dependent variable were significant. This was true regardless of coping method. Thus, the differences in the response of PBLs to both mitogens were not related to the number of cells, but rather reflect an alteration in cell function.

Stress and Coping

Correlations between coping method and perceived stress were in the expected direction. Active coping was negatively correlated with PSS-10

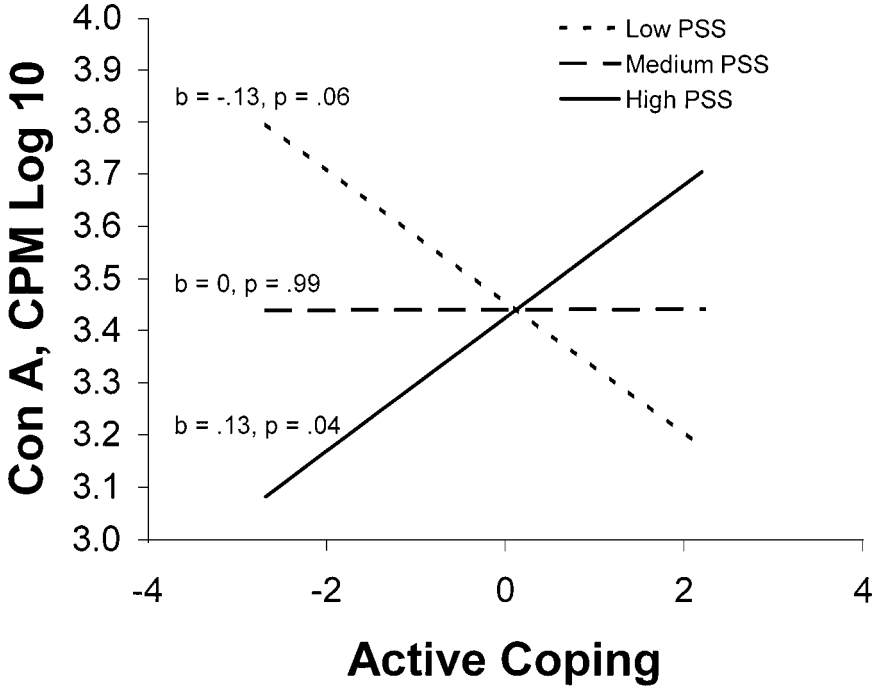

Fig. 3. Simple slopes of active coping on proliferation to Con A at low (1 SD below the mean), medium (mean), and high (1 SD above the mean) levels of perceived stress. Abscissa represents standardized active coping scores.

scores, $r = -0.25$, $p < 0.001$, whereas avoidance coping was positively correlated with PSS-10 scores, $r = 0.20$, $p < 0.01$. Active and avoidance coping were not significantly related to each other, $r = -0.04$, $p > 0.64$. On average, active coping (12.17, SD = 1.68) was used a greater amount than avoidance coping (6.69, SD = 1.67).

Demographics and Health Related Behaviors

As mentioned in the statistical procedures, age was included as a control variable in the regression analyses. Age was weakly, but negatively related to the percent of CD3+ cells, $r = -0.19$, $p = 0.01$, as well as proliferation to PHA, $r = -0.24$, $p < 0.01$ (see also Table I). Including other demographic or health-related behaviors such as sex, education, race, income, body mass, exercise, sleep, or alcohol and caffeine use in the regression analyses did not significantly affect the stress by coping interactions.

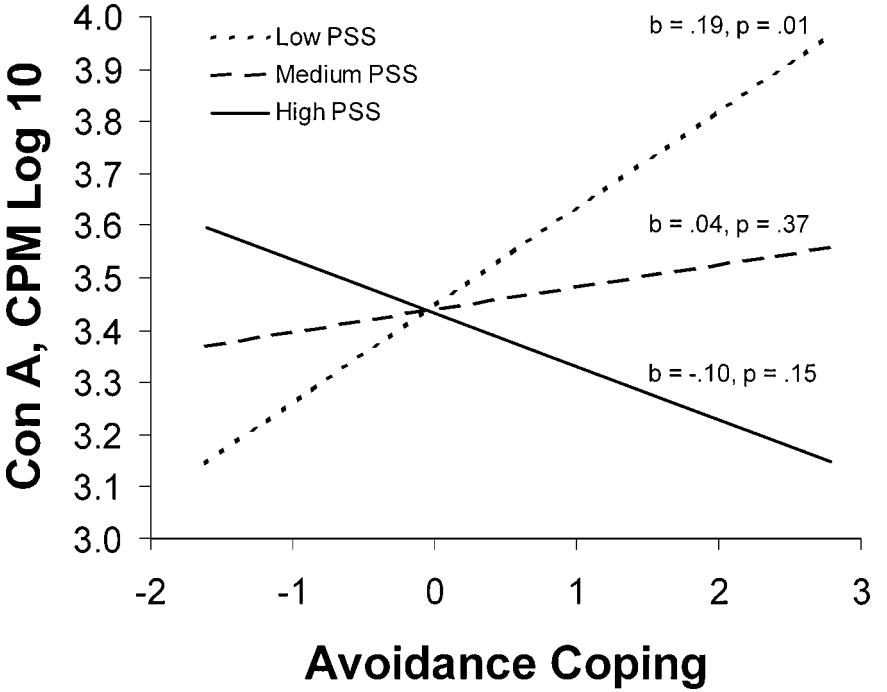

Fig. 4. Simple slopes of avoidance coping on proliferation to Con A at low (1 SD below the mean), medium (mean), and high (1 SD above the mean) levels of perceived stress. Abscissa represents standardized avoidance coping scores.

As anticipated, adding 34 former caregivers and 61 current caregivers to our sample of 78 comparison participants extended the distribution of perceived stress, which enabled us to sufficiently test the effects of coping on immune function at various stress levels. This was supported by a significant group difference on average PSS-10 scores, $F(2, 170) = 8.61$, $p < 0.0001$, with former and current caregivers reporting greater perceived stress than comparison participants, while reporting comparable amounts of active and avoidance coping, Fs < 1.40, ps > 0.05, and immune function (Fs < 1.17, ps > 0.05); see Table II.

DISCUSSION

Active and avoidance coping were related to the proliferative response of PBLs to two mitogens, and the magnitude and direction of these relationships depended on levels of perceived stress. After controlling for age and

Table II. Group Means and Standard Deviations of Stress, Coping, and Immune Measures

Dependent measures	Former caregivers ($N = 34$)		Current caregivers ($N = 61$)		Comparisons ($N = 78$)	
	Mean	SD	Mean	SD	Mean	SD
PSS-10	15.24	7.44	16.93	6.93	12.21	6.34
Active coping	12.51	1.62	11.92	1.64	12.21	1.73
Avoidance coping	6.65	1.34	6.63	1.62	6.75	1.85
% T_H (Helper) cells	43.27	12.53	43.93	11.14	44.98	9.66
Number T_H cells	795.28	430.56	785.91	369.95	821.69	373.64
% T_S (Suppressor/Cytotoxic)	19.11	10.32	20.65	8.09	19.39	7.21
Number T_S	322.30	154.28	380.19	246.63	350.49	167.77
% $CD3^+$ cells	56.43	12.40	60.15	15.15	57.32	11.63
Number $CD3^+$ cells	1022.14	467.12	1090.92	529.50	1054.81	492.73
T_H/T_S ratio	2.84	1.60	2.59	1.55	2.81	1.75
Mean log (PHA) cpm	4.22	0.30	4.18	0.47	4.15	0.41
Mean log (Con A) cpm	3.47	0.52	3.41	0.69	3.39	0.60

Note. PSS-10 = Perceived Stress Scale.

perceived stress, active coping was a significant predictor of greater proliferation to both mitogens at high stress levels, but not at moderate or low stress levels. At low levels of stress, active coping was not significantly related to proliferative responses to PHA or Con A. These findings confirm that active coping can have positive effects on immune function and, more importantly, reveal that active coping is more likely to have positive effects at high stress levels.

Avoidance coping, generally considered maladaptive, was less likely to be significantly associated with proliferation to mitogen, even though the interaction between perceived stress and avoidance coping was significant. Post hoc regression analyses generally did not find significance for the simple slopes (Figs. 2 and 4) at commonly used values (1 SD away from the mean). Unexpectedly, at low levels of stress, avoidance coping was significantly related to greater proliferation to Con A. This suggests there may be situations where avoidance coping is adaptive. Findings with avoidance coping should be interpreted cautiously though, as avoidance coping was used much less than active coping, as found in other studies (Billings and Moos, 1981; Carver and Scheier, 1994), and was composed of fewer subscales. This limited variability could bias the direction and magnitude of these relationships.

We found, as others have (Carver *et al.*, 1989; Segerstrom *et al.*, 1998), that the different coping methods were weakly correlated, suggesting that they are relatively independent. Thus, the positive effects of active coping could mask some of the negative effects of avoidance coping if they occur together, which they sometimes do (Holahan and Moos, 1987). However,

the benefit of any given coping method depends on numerous other factors as well such as control (Brosschot *et al.*, 1998; Laudenslager *et al.*, 1983; Reynaert *et al.*, 1995), perceived effectiveness of coping (Ntoumanis and Biddle, 1998; Zautra *et al.*, 1989), and, as demonstrated in the present study, stress level.

Perceived stress is generally associated with poorer cellular immunity (Kiecolt-Glaser and Glaser, 1995), yet this relationship also likely depends on the amount and type of coping employed. From another perspective, perceived stress is what sets the context in which other factors such as coping style can have positive or negative effects, with the direction of the relationship between coping method and immune function changing across the spectrum of perceived stress. This change of direction is much like that observed between age and height at various developmental stages. Age and height are positively related during childhood, unrelated during middle adulthood, and then negatively related during late adulthood. Further research is needed to characterize how the relationship between coping and immune function varies with stress level as well as other factors.

Several limitations of this study should be noted. Although these findings provide important direction for additional research, the practical magnitude of the interactions may be limited, as the full regression model R^2s ranged from 5 to 12% with the interaction terms accounting for 3–5%. If anything, this illustrates the complexity of factors that are involved in psychological influences on immune function. Yet these findings are important, as they add to the literature on coping and immune function, an area that requires further exploration. One other limitation in the application of these findings is that our perceived stress and coping measures did not refer to a specific stressor (such as caregiving), and, therefore, any inferences about the specific application to caregiving would not be justified.

Of interest, it was not the enumerative measures of immune system that were significantly related to coping method, but rather the functional measures. This suggests first, that the number or percentage of cells does not necessarily correlate with their function, and second, that multiple measures of immune function are required to capture the complexity of changes in the immune system.

These findings provide new evidence for the moderating effects of coping on stress–immune relationships, extending findings that have predominantly been observed in studies measuring mental or physical health. In addition, discovery of the positive effects of active coping on the immune measures complements the existing coping literature that has largely focused on the negative rather than positive effects of different coping styles (Carver and Scheier, 1994). Methodological factors that likely contributed to the discovery of these interactive effects include conducting both enumerative and

functional immunological assays, and using a large sample that had a broad range of perceived stress.

Similar to others (Bender *et al.*, 1986; Murasko *et al.*, 1987), we found trends indicating poorer cellular immunity with increasing age. Thus, the positive or negative relationships between coping method and immune function may be particularly relevant for older adults, as a decline in cellular immunity engenders a greater risk of morbidity and mortality in this population (Murasko *et al.*, 1990; Wayne *et al.*, 1990).

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