workers has importance in the field of industrial health.

There are limitations to this study. First, subjects of the present study were from just one industrial company, so there are some limitations in the ability to generalize from this outcome. Secondly, this study did not control factors like employees' working conditions, work positions, personalities, marital status etc. Especially in the area of job stress, Johnson(21)'s Demand-Control-Support model, which was amended by Karasek(22)'s Job demand-control model with the addition of social support as an important factor for the job stress model is broadly used, as in the study done by Olstad(23). However, in this study, social support was not regarded. Studies that regard these factors are required for the future. In addition, this research did not regard diagnoses of PTSD by psychiatrists. Also, because this research was done in a Japanese company in which proportion of male workers was rather high, the number of female subjects was not as large as the males, and this may be of some influence. However, we enrolled into the study all subjects who took the health check within the studied period, and there were no refusals to respond to our questionnaire. Finally the design of this study was retrospective and cross sectional. Prospective and longitudinal study is also necessary.

With its large number of subjects, this research showed past traumatic life events influence on later strains, by using the JCQ for the first time in addition to depression and anxiety. Because strain could be regarded as an index of stress tolerance in this study, the experience of past trauma effects later stress sensitivity, with those two factors having an interaction among themselves and with stress responses like depression and anxiety. This indicates that stress tolerance is an important factor when mental responses after traumatic stress are considered. The need for further research that overcomes the limitations of this study is indicated.

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Positive coping up- and down-regulates T cell immunity dependent on stress levels.

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Abstracts

Background: Specific coping styles have been shown to modulate stress-induced immune alterations and influence actual health outcomes. This study examined the effects of stressors and coping styles on human T cell immunity by a cross-sectional design.

Methods: Seventy-one men (18-60 years old) were asked to fill a self-administered questionnaire for evaluating quantitative workload, mental demand, and coping styles. The numbers of T cell subpopulations, interferon-gamma (IFN-γ) and interleukin-4 (IL-4) after stimulation with phytohemaglutinin were measured.

Results: Positive and negative coping were negatively related with IL-4 and the number of CD4+ cells, respectively. Positive coping had significant interactions with mental demand for the number of CD8+ cells, IFN-γ, IL-4, and IFN-γ/IL-4. Among men reporting high mental demand, positive coping was related with increased IFN-γ and IFN-γ/IL-4. Among men reporting low mental demand, positive coping was related with decreased number of CD8+ cells, IFN-γ and IL-4. Analyses adjusting for the numbers of CD3+ and CD8+ cells revealed that the interactions of positive coping by mental demand for cytokine levels were attributable to the changes in T cell functions rather than those in T cell subpopulations.

Conclusions: Positive coping was involved in stress-induced changes in numerical and functional measures of T cell immunity. From the perspectives of immunology, optimal stress characteristics were determined by one's own coping styles. Our finding suggests that it is important to consider the interactive effects of the complexity of work and the individual coping style in stress management.

Keywords: stress, coping, cellular immunity, psychoneuroimmunology

Introduction

Progress in psychoneuroimmunology (PNI) has revealed that psychological stress has an impact on the immune system [1, 2]. It is recognized that chronic stress leads to a down-regulation of immune functions and increases susceptibility to and progression of infectious diseases and other immune-related disorders.

Human PNI studies investigating the effect of psychological stress on immune functions have produced inconsistent results [3, 4]. The results from PNI studies in animal model cannot always be replicated in human studies [3]. Kiecolt-Glaser JK et al. showed that immune reactivity to stressors have a considerable variability across human subjects [5]. The discrepancies from human PNI studies may be due to the variety of ways in which people cope with stressors.

Specific coping strategies (active coping, escape-avoidance coping, repression, concealment, control, and type C) have been shown to modulate immune functions among patients with AIDS, depression, and cancer and influence actual health outcomes [4, 6-8]. The results from these studies are generally consistent.

There are a limited number of studies on the mediating role of coping in stress-induced immune alterations among healthy subjects [9-11]. Stowell JR et al. showed that at a higher stress level, active coping enhances proliferative response to phytohemaglutinin (PHA) and concanavalin A (Con A) whereas at a low stress level, avoidance coping is related to a greater proliferative response to Con A [9]. Futterman AD et al. observed that escape-avoidance coping is related with the reduction in percentage of T cells and of CD4+ cells and the increase in percentage of B cells [10]. The above results suggest that positive coping is protective toward or enhances cellular immunity in a stressful situation whereas negative coping has an adverse effect.

To our knowledge, the previous studies on healthy subjects did not elucidate the effect of coping styles on cytokine productions with respect to stressors, though T cell and its cytokine productions have been shown to be labile to stress [12]. Considering the changes in cellular immunity observed in these studies, it is highly expected that coping would influence cytokine levels through its interactive effects with stressors on stress response.

In the present study, we investigated the effect of coping styles on stressor-induced changes in T cell subpopulations, interferon-gamma (IFN-γ) and interleukin-4 (IL-4) after stimulation with PHA in male workers at a fire station by a cross-sectional design.

Methods

Participants

We provided a questionnaire to 71 non-smoking male workers (18-60 years

old) at a fire station and obtained blood samples from them. The study was performed with written informed consent and was approved by the ethics committee at National Center of Neurology and Psychiatry.

Among the 71 subjects, 38 men were firefighters, 17 men were paramedics, and 16 men were rescue crews. There was no significant difference in psychological and immunological measures among the three groups except that firefighters had significantly higher IL-4 than paramedics and rescue crews (data not shown). All the subjects were 24h-shiftworkers, but no one worked the day before venipuncture. Thus the differences of shift work do not exist among these subjects. Although this study did not address the long-term effect of toxic exposures on immune functions, we considered that it matters little if we supposed that the subjects did not undergo the immediate effect at the time of venipucture. In this study, types of job, shiftwork, and toxic exposures were not entered into data analysis.

Stress questionnaire

The quantitative workload and the mental demand scale were derived from the Japanese version of the National Institute for Occupational Safety and Health (NIOSH, USA) Generic Job Stress Questionnaire (GJSQ) [13, 14].

The quantitative workload scale consisted of 4 items with 5 alternatives designed to evaluate the perceived workload that the respondent has to deal with in the course of his daily work. The scale was scored as described previously [15, 16].

The mental demand scale consists of 5 items with 4 alternatives evaluating the degree to which concentration or mental work is required when the subject accomplishes his work. The scale was scored as described previously [17, 18].

Coping questionnaire

Coping was measured with the responses to stress scale derived from the Japanese version of the Stress and Coping Inventory (SCI) [19, 20]. The scale lists 25 cognitive and behavioral strategies that the respondents use to deal with a stressful encounter. Subjects respond on a 0-3 point Likert scale how often they use the coping strategies in a stressful situation. A factor analysis of the pretested sample suggested 2 subscales that clustered around positive coping and negative coping. The scale demonstrated significant test-retest reliability and adequate internal consistency [20]. In this study, the coefficient alphas were 0.87 and 0.74 for positive and negative coping, respectively.

Immunological assays

Lymphocyte subpopulation

Blood samples were collected in heparinized tubes (Becton-Dickinson, New Jersey, USA) at 10:00 am in the morning and stored at room temperature for no longer than 4 h before the assays. The total numbers of WBC and leukocyte differential counts were determined by a Coulter counter (Beckman Coulter, Inc, Fullerton, CA, USA). Lymphocyte

subsets were determined by flowcytometry analysis (EPICS XL, Beckman Coulter, Inc, Fullerton, CA, USA) using a standard procedure. Enumeration by flowcytometry included the following cells: T cells (CD3/fluorescein isothyocyanate (FITC)) and two types of T cell subsets (CD4/FITC, CD8/phycoerythrin (PE)). All antibodies were purchased from Beckman Coulter, Inc, (Fullerton, CA, USA).

Cytokine assay

For determination of IFN-γ and IL-4, a whole blood assay was applied [21]. Blood was drawn into syringes pretreated with heparin (Beckton-Dickson, NJ, USA) at 10 am and stored at room temperature for no longer than 4h before the assays. Aliquots of 50 μl of blood were resuspended under laminar airflow in 400 μl of RPMI 1640 medium containing 2 mM glutamine, 100 U/ml penicillin and 100 U/ml streptomycin. For stimulation of IFN-γ and IL-4, 2.5 μg of PHA (Sigma-Aldrich Japan, Tokyo) was added, dissolved in 50 μl of a medium containing 50% RPMI and 50% sterile water (final concentration, 5 μg/ml). At the end and in the beginning of each measurement, an unstimulated control was included to exclude contaminations of blood and reagents. The samples were incubated for 48 h at 37 degrees of Celsius thermometer with 5% carbon dioxide in humidified air. The supernatants were harvested and stored at –80 degrees of Celsius thermometer until assay. The samples were thawed only once and all cytokine levels were measured in duplicate by ELISA kits (Human Immunoassay ELISA kit, BioSource International, Camarillo, CA), according to the manufacturer's instructions.

Statistical analysis

Before data analysis, immunological data were log transformed because of their skewed distribution (table 1). Pearson's correlation analysis was performed to assess the associations among stress, coping, and immune functions. A median split divided the sample into relatively low- and high-stress and coping groups. Psychological factors were then included in a general linear model to evaluate the effect of stress and coping on immune functions. The analyses were performed separately on each of the two stress types. Positive coping x negative coping and three-way interactions were excluded from the model. Significant interactions were followed by analyses of covariance (ANCOVAs). A p value < 0.05 was considered to indicate statistical significance. All tests were two-tailed.

Results

Table 2 summarizes correlations among psychological variables. Quantitative workload was significantly positively correlated with positive coping. Mental demand had no correlations with coping.

As shown in Table 3, stressors were not related with T cell immunity. Negative coping had a significantly negative correlation with the number of CD4+

cells and a marginally significant correlation with the number of CD3+ cells. Elderly men had a higher IL-4 and a lower IFN-γ/IL-4 ratio.

ANCOVA evaluating the effect of quantitative workload and coping adjusting for age showed that quantitative workload had no main effect on immune functions (table 4). Positive coping had a tendency to decrease IL-4 but it failed to reach significance [Means (SD) of ln IL-4: low positive coping = 3.70 (1.01); high positive coping = 3.17 (0.93)]. Negative coping significantly decreased the number of CD4+ cells [Means (SD) of ln CD4+: low negative coping = 6.73 (0.29); high positive coping = 6.57 (0.28)]. There is no significant interaction between quantitative workload and coping.

ANCOVA adjusting for age revealed no significant main effect of mental demand on T cell immunity (table 5). Positive coping significantly decreased IL-4. Negative coping is marginally related with a decrease in the number of CD4+ cells. There were significant interactive effects of mental demand and positive coping on the number of CD8+ cells, IFN-γ, IL-4, and IFN-γ/IL-4.

To identify the sources of the interactions, post-hoc analyses were performed (figure 1). Four comparisons (high/low mental demand x high/low positive coping) were made for CD8+, IFN-γ, IL-4, and IFN-γ/IL-4, respectively. ANCOVAs adjusting for age revealed that positive coping increased IFN-γ and IFN-γ/IL-4 at a higher level of mental demand and decreased CD8+, IFN-γ and IL-4 at a lower level of mental demand. Among men with a higher use of positive coping, mental demand increased IFN-γ and IL-4. Among men with a lower use of positive coping, mental demand decreased CD8+, IFN-γ and IFN-γ/IL-4.

To examine whether the mental demand x positive coping interactions for PHA-stimulated IFN-γ and IL-4 productions were attributable to the fluctuations in the number of T cells or in T cell functions, additional ANCOVAs were performed. Figure 2 shows that there were significant interactive effects of mental demand and positive coping on the productions of IFN-γ and IL-4 (pg) per 1 x 10^3 CD3+ cells. Figure 3 shows that the interactions for IFN-γ, IL-4, and IFN-γ/IL-4 remained significant after adjusting for age and the number of CD8+ cells except that positive coping was marginally related with increased IFN-γ/IL-4 at a higher level of mental demand. As shown in table 5, there was no significant interaction between mental demand and positive coping for the number of CD 3+ cells. These results suggest that the interactions for IFN-γ and IL-4 were influenced by the changes in T cell functions rather than by the changes in T cell numbers.

Table 1. Descriptive Statistics of Psychological and Immunological Variables.

Variable	N	Mean	(SD)	Range
Age	7139.57		(11.60)	18 -60
Quantitative workload	7111.67		(3.85)	5 20
Mental demand	7114.82		(2.09)	10 -20
Positive coping	7135.11		(7.98)	15 -50
Negative coping	7115.82		(3.95)	8 -26
CD3+ (/μl)[a]	711380.24		(413.44)	795.98-2557.65
CD4+ (/μl)[a]	71805.95		(245.28)	345.35-1619.75
CD8+ (/μl)[a]	71574.29		(252.86)	217.11-1528.10
IFN-γ (pg/ml)[a]	702055.89		(2007.43)	20 -9358
IL-4 (pg/ml)[a]	7049.58		(55.73)	3.8 -360.7
IFN-γ / IL-4[a]	7064.33		(82.62)	2.07 -492.52

[a] Means (SD) of immunological data before log transformation are indicated.

Table 2. Pearson's Correlation Coefficients Exploring the Relationships among Psychological Variables.

	Age		Quantitative workload		Mental demand	
Variable	r	p	r	p	r	p
Age	1	—	-0.156	n.s.[a]	-0.159	n.s.
Quantitative workload			1	—	0.483	p<0.0001
Mental demand					1	—
Positive coping						
Negative coping						

[a] n.s. = not significant

(Table 2. continued)

	Positive coping		Negative coping	
Variable	r	p	r	p
Age	-0.396	p<0.001	-0.233	0.046
Quantitative workload	0.244	0.038	0.036	n.s.
Mental demand	0.180	n.s.	-0.021	n.s.
Positive coping	1	—	0.154	n.s.
Negative coping			1	—

Table 3. Pearson's Correlation Coefficients Exploring the Relationships between Psychological and Immunological Variables.

	ln CD3+ (/μl)		ln CD4+ (/μl)		ln CD8+ (/μl)	
Variable	r	p	r	p	r	p
Age	-0.159	n.s.[a]	0.074	n.s.	-0.359	0.002
Quantitative workload	0.045	n.s.	0.019	n.s.	0.075	n.s.
Mental demand	-0.094	n.s.	-0.121	n.s.	-0.037	n.s.
Positive coping	-0.034	n.s.	-0.193	n.s.	0.140	n.s.
Negative coping	-0.229	0.058	-0.345	0.004	-0.031	n.s.

[a] n.s. = not significant

(Table 3. continued)

	ln IFN-γ (pg/ml)		ln IL-4 (pg/ml)		ln (IFN-γ / IL-4)	
Variable	r	p	r	p	r	p
Age	-0.090	n.s.	0.281	0.019	-0.341	0.004
Quantitative workload	0.034	n.s.	-0.075	n.s.	0.103	n.s.
Mental demand	-0.016	n.s.	0.020	n.s.	-0.036	n.s.
Positive coping	-0.017	n.s.	-0.209	n.s.	0.159	n.s.
Negative coping	-0.088	n.s.	-0.195	n.s.	0.064	n.s.

Table 4. ANCOVA for the Effects of Quantitative Workload and Coping Strategies on Immunological Variables.

	ln CD3+ (/μl)		ln CD4+ (/μl)		ln CD8+ (/μl)	
Variable	F(1,61)	p	F(1,61)	p	F(1,61)	p
Age	1.111	n.s.[a]	0.241	n.s.	6.644	0.012
Quantitative workload	0.043	n.s.	0.035	n.s.	0.002	n.s.
Positive coping	0.228	n.s.	0.237	n.s.	0.125	n.s.
Negative coping	2.195	n.s.	4.037	0.049	0.500	n.s.
Quantitative workload × Positive coping	0.518	n.s.	0.089	n.s.	0.582	n.s.
Quantitative workload × Negative coping	0.141	n.s.	0.094	n.s.	0.283	n.s.

[a] n.s. = not significant

(Table 4. continued)

	ln IFN-γ (pg/ml)		ln IL-4 (pg/ml)		ln (IFN-γ / IL-4)	
Variable	F(1,59)	p	F(1,59)	p	F(1,59)	p
Age	0.468	n.s.	3.300	n.s.	5.853	0.019
Quantitative workload	2.311	n.s.	0.733	n.s.	1.292	n.s.
Positive coping	1.761	n.s.	2.905	0.094	0.027	n.s.
Negative coping	0.375	n.s.	0.908	n.s.	0.005	n.s.
Quantitative workload × Positive coping	3.612	n.s.	0.332	n.s.	3.418	n.s.
Quantitative workload × Negative coping	0.083	n.s.	2.931	n.s.	3.385	n.s.

Table 5. ANCOVA for the Effects of Mental demand and Coping Strategies on Immunological Variables.

	ln CD3+ (/μl)		ln CD4+ (/μl)		ln CD8+ (/μl)	
Variable	F(1,62)	p	F(1,62)	p	F(1,62)	p
Age	2.222	n.s.[a]	0.086	n.s.	9.483	0.003
Mental demand	3.276	n.s.	2.481	n.s.	2.175	n.s.
Positive coping	0.565	n.s.	0.505	n.s.	0.308	n.s.
Negative coping	1.533	n.s.	3.893	0.053	0.111	n.s.
Mental demand × Positive coping	3.930	n.s.	0.893	n.s.	5.381	0.024
Mental demand × Negative coping	1.082	n.s.	0.634	n.s.	0.762	n.s.

[a] n.s. = not significant

	ln IFN-γ (pg/ml)		ln IL-4 (pg/ml)		ln (IFN-γ / IL-4)	
Variable	F(1,60)	p	F(1,60)	p	F(1,60)	p
Age	0.334	n.s.	4.825	0.032	6.520	0.013
Mental demand	0.167	n.s.	1.910	n.s.	0.504	n.s.
Positive coping	0.891	n.s.	4.005	p<0.050	0.383	n.s.
Negative coping	0.226	n.s.	0.541	n.s.	0.006	n.s.
Mental demand × Positive coping	15.743	p<0.0001	4.821	0.032	7.427	0.008
Mental demand × Negative coping	0.045	n.s.	0.444	n.s.	0.106	n.s.

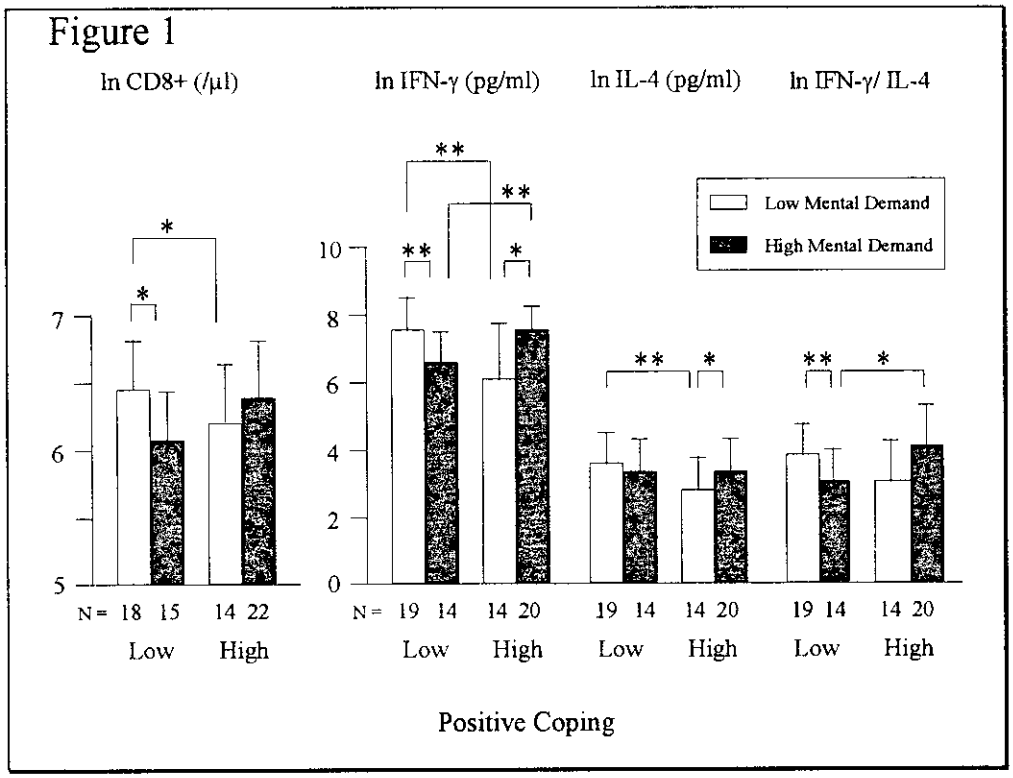

Figure 1.
Means (SD) of ln CD8+, ln IFN-γ, ln IL-4, and ln IFN-γ/IL-4 as a function of mental demand and positive coping. The main effect of mental demand and positive coping on immune functions was analyzed separately by ANCOVA adjusting for age. * $p < 0.05$, ** $p < 0.01$.
(CD8+) At a lower stress level: $F (1, 29) = 4.308$, $p = 0.046$. At a higher stress level: $F (1, 34) = 1.836$, $p = 0.184$. At a lower level of positive coping: $F (1, 30) = 7.044$, $p = 0.013$. At a higher level of positive coping: $F (1, 33) = 0.201$, $p = 0.657$.
(IFN-γ) At a lower stress level: $F (1, 30) = 9.619$, $p = 0.004$. At a higher stress level: $F (1, 31) = 11.563$, $p = 0.002$. At a lower level of positive coping: $F (1, 30) = 9.571$, $p = 0.004$. At a higher level of positive coping: $F (1, 31) = 6.594$, $p = 0.015$.
(IL-4) At a lower stress level: $F (1, 30) = 9.072$, $p = 0.005$. At a higher stress level: $F (1, 31) = 0.277$, $p = 0.602$. At a lower level of positive coping: $F (1, 30) = 0.237$, $p = 0.630$. At a higher level of positive coping: $F (1, 31) = 6.763$, $p = 0.014$.
(IFN-γ/IL-4) At a lower stress level: $F (1, 30) = 2.391$, $p = 0.132$. At a higher stress level: $F (1, 31) = 5.929$, $p = 0.021$. At a lower level of positive coping: $F (1, 30) = 7.491$, $p < 0.01$. At a higher level of positive coping: $F (1, 31) = 1.416$, $p = 0.243$.

Figure 2

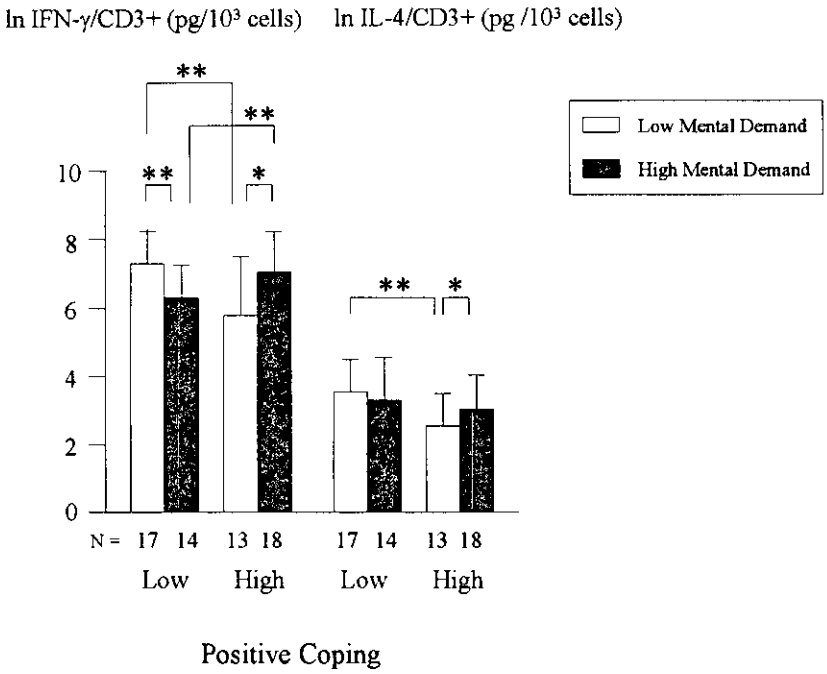

Figure 2.
Means (SD) of ln [IFN-γ/CD3 (pg/10^3cells) and ln [IL-4/10^3CD3+ (pg/10^3cells)] as a function of mental demand and positive coping. The main effect of mental demand and positive coping on immune functions was analyzed separately by ANCOVA adjusting for age. * $p < 0.05$, ** $p < 0.01$.
(IFN-γ) At a lower stress level: $F(1, 27) = 11.462$, $p = 0.002$. At a higher stress level: $F(1, 29) = 10.293$, $p = 0.003$. At a lower level of positive coping: $F(1, 28) = 10.808$, $p = 0.003$. At a higher level of positive coping: $F(1, 28) = 6.224$, $p = 0.019$.
(IL-4) At a lower stress level: $F(1, 27) = 9.046$, $p = 0.006$. At a higher stress level: $F(1, 29) = 0.376$, $p = 0.544$. At a lower level of positive coping: $F(1, 28) = 0.007$, $p = 0.935$. At a higher level of positive coping: $F(1, 28) = 7.515$, $p = 0.011$.

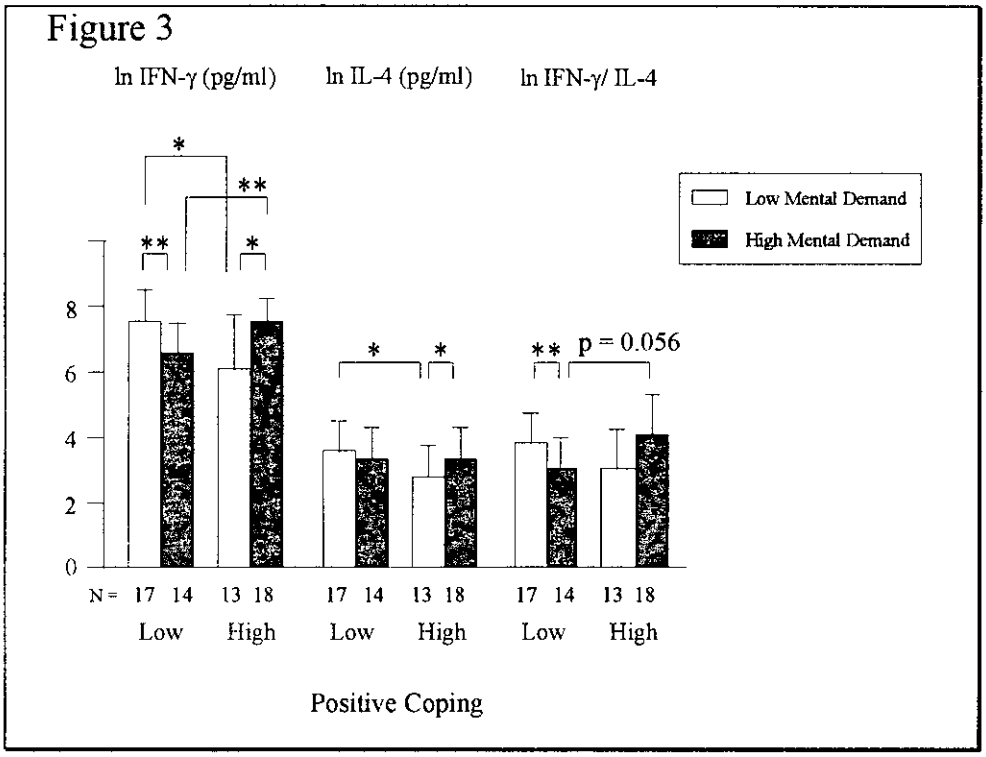

Figure 3.
Means (SD) of ln IFN-γ, ln IL-4, and ln IFN-γ/IL-4 as a function of mental demand and positive coping. The main effect of mental demand and positive coping on immune functions was analyzed separately by ANCOVA adjusting for age and the number of CD8+ cells. * $p < 0.05$, ** $p < 0.01$.
(IFN-γ) At a lower stress level: $F(1, 26) = 6.653$, $p = 0.016$. At a higher stress level: $F(1, 28) = 8.855$, $p = 0.006$. At a lower level of positive coping: $F(1, 27) = 8.513$, $p = 0.007$. At a higher level of positive coping: $F(1, 27) = 5.489$, $p = 0.027$.
(IL-4) At a lower stress level: $F(1, 26) = 5.278$, $p = 0.030$. At a higher stress level: $F(1, 28) = 0.328$, $p = 0.571$. At a lower level of positive coping: $F(1, 27) = 0.050$, $p = 0.825$. At a higher level of positive coping: $F(1, 27) = 6.089$, $p = 0.020$.
(IFN-γ/IL-4) At a lower stress level: $F(1, 26) = 1.042$, $p = 0.317$. At a higher stress level: $F(1, 28) = 3.981$, $p = 0.056$. At a lower level of positive coping: $F(1, 27) = 9.190$, $p = 0.005$. At a higher level of positive coping: $F(1, 27) = 0.565$, $p = 0.459$.

Discussion

The present study indicated that positive coping is involved in stress-induced changes in the number of CD8+ cells, PHA-stimulated IFN-γ and IL-4 productions, and IFN-γ/IL-4 ratio. Positive coping was related with the reduced IL-4 but had no main effect on the number of CD8+ cells or IFN-γ. The results suggest that positive coping not only has a direct effect on immune functions in itself but up- and down-regulates immune functions dependent on stress levels.

At a higher level of mental demand, men with high positive coping demonstrated a higher level of IFN-γ than men with low positive coping. IFN-γ in men with high positive coping was enhanced whereas IFN-γ in men with low positive coping was suppressed in a stressful encounter. The effects of positive coping on the number of CD8+ cells, IL-4, and IFN-γ/IL-4 were less clear than IFN-γ though the effects were exerted in the same direction. There is a possibility that a limitation in sample size made a partial contribution to the results. Fawzy FI et al. showed that a structured psychiatric intervention for patients with malignant melanoma (health education, enhancement of problem-solving skills, stress management, and psychological support) effectively reduces psychological distress and enhances active-behavioral coping [22]. They also found increases in the percentage of large granular lymphocytes and natural killer (NK) cells, an increase in NK cytotoxic activity, and a small decrease in the percentage of CD4+ cells [23]. These results suggest that positive coping enhances cellular immunity in a stressful situation.

Previous studies showed that the sympathetic nervous system (SNS) and the hypothalamic-pituitary-adrenocortical (HPA) axis play an important role in stress-coping responses [4]. Subjects with a low level of instrumental coping demonstrated an increased SNS and HPA response to a laboratory stressor [24]. A prolonged over-activation of the SNS and the HPA axis may lead to a down-regulation of immune functions.

At a lower level of mental demand, men with high positive coping had lower CD8+ cells, IFN-γ and IL-4 than those with low positive coping. Similar responses were observed in the previous study [9]. Positive coping may operate as a maladaptive strategy in a non-stressful situation. In what ways do given forms of coping affect biological responses to various levels of stressors? The importance of this issue warrants further investigations.

The mental demand scale used in the present study assesses whether individuals appraise their work as complex or not. Our results indicate that men with a greater use of positive coping demonstrate enhanced immune functions when they make an effort to manage a complex mental task. In contrast, their immune functions are suppressed when they are accomplishing a simple and monotonous task to which they feel does not need a special attention to be paid. Coping seems to play a less important

role in immune responses to the quantity than to the complexity of work. As cytokine productions from T cells in non-smoking subjects could be regarded as a surrogate for health outcomes like NK cell activity, it is possible to hypothesize that optimal stress characteristics are determined by one's own coping style. Lazarus RS et al. showed that people use various forms of coping in virtually every type of stressor [25]. Among the subjects in the present study, coping was not significantly correlated with mental demand. It may be assumed that they did not necessarily adjust themselves physiologically to the demands of the complexity of their work. Our hypothesis emphasizes that it is important to assign the workers to a mental work that will be fit for their coping patterns. Otherwise, although it is difficult, it would be also important to give workers the appropriate education about coping skills enabling to adapt themselves to the complexities of the allotted works.

Escape-avoidance coping is known to reduce the percentage of CD4+ cells among individuals in a stressful situation such as family members of patients undergoing bone marrow transplantation [10]. The relationship between negative coping and a reduction of the number of CD4+ cells presented here coincides with the results from the previous studies. Our results, however, failed to reveal a significant interaction between stress and negative coping for immune functions that was seen in the previous report [9]. The inconsistency of the results may be partly explained by the difference in the coping inventories. Stowell JR et al. used escape-avoidance coping as a modulator in immune reactivity to a stressor [9]. A factor analysis for the coping inventory from the Japanese version of SCI extracted two subscales (positive and negative coping) [20]. In addition to escape-avoidance, negative coping used in the present study may include other forms of coping, some of which can provoke similar physiological responses that were seen in the case of positive coping. It is likely that heterogeneity of the construct of negative coping compared to that of positive coping resulted in not finding out a significant interaction for the immune system that may exist in reality.

Neither quantitative workload nor mental demand had a main effect on immune functions. Types and duration of stressors are known to have differential effects on T cell immunity. Many studies revealed that acute stress enhances T helper1 (Th1)–derived cytokine productions [26, 27]. Li T et al. showed that repeated restraint stress suppresses Th1 responses [28]. Quantitative workload and mental demand are chronic and trivial stressors. Pike JL et al. showed that although chronic life stress can exaggerate the reactivity of the sympathetic, neuroendocrine, and immune systems to an acute stressor, chronic stress does not affect the baseline measures before acute psychological challenge [29]. The effect of the two stressors used here may be too small to alter immune functions in themselves.

This study did not concern the chronic effects of toxic exposure and shiftwork that have been shown to lead to significant health outcomes [30-33]. Although toxin-induced immune changes have not been elucidated in firefighters, experimental studies on humans have showed that disrupted sleep and circadian rhythm alter immune functions [21, 34]. The long-term effects of these possible confounders on immune functions should be assessed in future studies.

In contrast to CD4+ cells, CD8+ cells had no linear relationship with coping but were sensitive to the interactive effects of the stressor and coping. Although the directions of the interactive effects on cytokine productions were the same as CD8+ cells, the results suggest that the interactions for cytokine productions were influenced mainly by the changes in T cell functions and partially by that in the number of CD8+ cells. Studies that elucidate the underling mechanisms and verify these interactive effects in other populations will be needed.

The cross-sectional design of the present study does not allow for any causal interpretation. The results, however, put forward a notion that it is important to take into account the interactive effects of the complexity of an assigned work and the individual coping style in stress management.

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