J Occup Health 2010; 52: 31–38

Journal of Occupational Health

Relationship of Job Satisfaction, Psychological Distress and Stress-Related Biological Parameters among Healthy Nurses: A Longitudinal Study

Monica AMATI[1], Marco TOMASETTI[1], Marida CIUCCARELLI[1], Laura MARIOTTI[1], Lucia Miria TARQUINI[1], Massimo BRACCI[1], Maurizio BALDASSARI[2], Cristian BALDUCCI[3], Renata ALLEVA[4], Battista BORGHI[4], Eugenio MOCCHEGIANI[5], Alfredo COPERTARO[6] and Lory SANTARELLI[1]

[1]Department of Molecular Pathology and Innovative Therapies, Clinic of Occupational Medicine, Polytechnic University of Marche, [2]Occupational Medicine, Hospital University of Ancona, [3]Department of Cognitive and Education Sciences, University of Trento, [4]Department of Anaesthesiology, IRCCS Orthopaedic Institute Rizzoli, [5]Immunolgy Center, Section of Nutrigenomics and Immunosenenscence, Res. Dept. INRCA and [6]Healthcare Workers Service, Regional Health Administration, Loreto Hospital, Italy

Abstract: Relationship of Job Satisfaction, Psychological Distress and Stress-Related Biological Parameters among Healthy Nurses: A Longitudinal Study: Monica AMATI, *et al*. Department of Molecular Pathology and Innovative Therapies, Clinic of Occupational Medicine, Polytechnic University of Marche, Italy—Objective: To examine the relationship between job satisfaction, psychological distress, psychosocial processes and stress-related biological factors, and to evaluate whether over time changes of work satisfaction could affect the immunological-inflammatory status of workers. **Methods:** One hundred and one nurses were enrolled at the Clinic of Occupational Medicine, Polytechnic University of Marche, Ancona, Italy. Perceived job satisfaction, psychological distress, and social support were assessed every 4 mo over a 1-yr period using 4 self-reported questionnaires. T lymphocytes CD3, $CD4^+$, $CD8^+$, $CD8^+$-$CD57^+$, B lymphocyte $CD19^+$, NK cells $CD56^+$, and NK cell activity were determined. **Results:** Job satisfaction was associated with reduced psychological distress and was characterized by low cell numbers of $CD8^+$ suppressor T cells, $CD8^+$-$CD57^+$ activated T cells, $CD56^+$ NK cells and low IL-6 levels. Over time changes in psychological parameters were related to changes in the immunological-inflammatory variables. Subjects who increased their job satisfaction showed a reduced psychological stress associated with reduced number of $CD8^+$-$CD57^+$ activated T cells and inflammatory cytokines. **Conclusions:** Job (dis)satisfaction is related with psychological mechanisms in stress affecting cellular immune function.
(J Occup Health 2010; 52: 31–38)

Key words: Cytokines, Immunological parameters, Job satisfaction, Lymphocytes, Nurses, Psychological stress

Received Mar 13, 2009; Accepted Oct 30, 2009
Published online in J-STAGE Dec 22, 2009
Correspondence to: M. Amati, Department of Molecular Pathology and Innovative Therapies, Clinic of Occupational Medicine, Polytechnic University of Marche, via Tronto 10/A Torrette 60020, Ancona, Italy (e-mail: m.amati@univpm.it)

Increased psychological stress at work has been reported in several studies[1–3]. The impact of job stress on health outcome has been extensively studied[4, 5]. Three psychosocial factors are considered to be important for the health and well-being of workers—job demands, job control, and social support—based on the hypothesis that the combination of increased job demands and reduced freedom to make job decisions (low control or low decision latitude) is related to poor health outcome[5]. It was found that increased psychosocial strain, increased reporting of job stress and lack of social support were all related to an enhancement of clinical symptoms[6]. Support from other people plays an influential role in health and well-being. The relationship between social support and mental health has been shown to vary with the type of mental health problem and source of support[7]. Poor mental health status associated with decreased job satisfaction has been found among Japanese teachers[8].

Work-related stress is reported to alter immunological parameters[9–11]. Endresen *et al.*[10] showed that, in nurses, job stress was positively correlated with serum IgA concentrations but inversely correlated with IgM concentrations. Inverse correlations between job demand and $CD4^+$ T lymphocytes and between job control and $CD4^+$ and $CD8^+$ T lymphocytes in male shift workers has previously been observed[12]. In a previous study of Japanese blue-collar workers exposed to lead , job strain was inversely correlated with $CD4^+CD29^+$ T (helper-inducer) lymphocytes, whereas job control was positively correlated with $CD4^+CD29^+$ T lymphocyte[11]. Furthermore, it was found that nurses' NK cell activity was low during the night shift[13], while it was reported that a low percentage of $CD56^+$ NK cells had a significant correlation with both long work and short sleep among male Japanese engineers[14]. Interaction between psychological distress and immunologic factors are relevant to a variety of diseases including inflammatory diseases[15], cardiovascular disease[16], infections, and tumors[17]. Based on the hypothesis that overwork and job stress would result in a poor levels of immune variables, first we examined the relationship between job satisfaction, psychological distress, psychosocial processes and stress-related biological factors; then, we evaluated whether over time changes of the work satisfaction could affect the immunological-inflammatory status of workers shifting them towards an immune-risk phenotype.

Materials and Methods

Participants

From November 2004 to February 2007, 115 nurses who were working at the Surgery and Anesthesiology and Resuscitation Unit of the Public Hospital of Loreto (Ancona) and the Hospital University of Ancona (Ancona), Italy, were enrolled at the Clinic of Occupational Medicine, Polytechnic University of Marche, Ancona, Italy. The workers were invited by letter and underwent a clinical examination for medical surveillance. The research protocol was approved by the Ethical Committee of the Polytechnic University of Marche, Ancona, Italy. All participants were fully informed of the procedure of the study and 101 subjects (88%) provided their informed consent for participation. The inclusion criteria were <65 yr old with at least 2-yr of service. Nurses affected by major mental disorders (schizophrenia, psychosis) and with other diseases (inflammatory, rheumatic, autoimmune and endocrinal diseases) and subjects under pharmacological therapies were excluded from the study. The participants were interviewed by trained personnel and answered a detailed questionnaire about alcohol drinking, smoking, current job, shift work, and occupational tasks. All workers underwent a clinical examination and filled in 4 self-reported questionnaires related to job satisfaction, degree of psychological distress, and social support at home. The participants were asked to return their completed questionnaires within a week. Venous blood samples and the questionnaires were collected at the baseline (T1), 4th (T2), 8th (T3) and 12th (T4) mo.

Psychometric assessments

A questionnaire on socio-demographic variables was used for all participants.

1) Assessment of job satisfaction

The research questionnaire Healthcare Job Satisfaction Scale (HJSS) was used. The questionnaire has a 19-item instrument specifically developed to measure job satisfaction among nurses. Conflict with other nursing staff, nursing role conflict, conflict with physicians or autonomy, conflict with death or dying, quantitative work load, qualitative work load and conflict with patients were evaluated. The 19 items were assigned scores from 0 to 10, with 10 indicating greater job satisfaction[18].

2) Assessment of degree of psychological distress

Psychological distress was evaluated by the mean of two scales, the Perceived Stress Scale (PSS) and the General Health Questionnaire (GHQ-12). The PSS includes a 14-item questionnaire which measures perception of stress, feelings and thoughts during the past month. The PSS assesses the degree to which subjects perceive their lives as unpredictable, uncontrollable and with burden overload and includes direct inquiries about current levels of experienced stress. Scores range from 0 to 40[19]. A score of 40 indicates greater perceived stress. The GHQ is a well-established scale for the evaluation of psychological distress in general population samples. In relation to diagnosed mental disorders, the GHQ has shown good clinical validity[20–22]. The 12 items are scored on a 12-point scale, with higher scores indicating greater psychological stress. The GHQ has been recommended in large epidemiological studies because of its excellent screening performance and the briefness of the scale[21]. Scores range from 0 to 12.

3) Assessment of social support

Social support was assessed using the Multidimensional Scale of Perceived Social Support (MSPSS)[23]. This scale consists of 12 items, each scored on a Likert Scale from 1 (disagree very strongly) to 7 (agree very strongly). Addition of the 12-item scores provides a total score for overall social support. The reliability and validity of the MSPSS have been established in a variety of adolescent samples from different ethnic groups[24–26]. Scores range from 0–84. Higher scores correspond to greater social support.

4) Blood sampling and immunological analysis

Blood samples were taken from subjects between 8:00 and 9:00 a.m. at the Clinic Occupational Medicine before starting the daytime shift, and immunological analysis was performed within 1 h of blood collection. Heparin was used as an anticoagulant to collect venous blood from subjects for measuring leukocyte counts and for immunofluorescence staining. Plasma samples were collected from blood tubes and stored at –80°C for biochemical analysis. All samples were transported and handled at room temperature (i.e. 15 to 20°C).

5) Lymphocytes subpopulations

Circulating numbers of lymphocytes, T cell subsets, B cells, and natural killer (NK) cells were assessed in heparinized whole blood using dual-color fluorescence analysis. Blood was stained using monoclonal antibodies (Becton Dickinson, San Jose, CA) labeled with either fluorescein isothiocyanate (FITC) or phycoerythrin (PE) to quantify $CD3^+$ (T cells), $CD4^+$ (helper T cells), $CD8^+$ (suppressor/cytotoxic T cells), $CD8^+$-$CD57^+$ (activated T cells), $CD19^+$ (B cells), and $CD56^+$ (NK cells). Mouse IgG1 and mouse IgG2a were used as negative controls. Absolute numbers of cells were calculated from a total leukocyte blood count.

Briefly, 100 μl of blood sample were incubated with each pair of monoclonal antibodies for 15 min in darkness. All antibodies were used at optimal dilutions. After incubation, 2 m*l* of FACS Lysing Solution (Becton Dickinson) was added to each sample and the samples were mixed gently and incubated for 10 min in the dark to lyse the erythrocytes. Samples were centrifuged at 1,000 rpm for 5 min and the supernatant was aspirated. The pelleted cells were resuspended in 2 m*l* of PBS. After recentrifugation, the pelleted cells were resuspended in 0.5 m*l* of PBS and then subjected to immunofluorescence analysis on a flowcytometer (FACScan, Becton Dickinson). The lymphocyte subpopulations were expressed as number/m*l*.

6) NK cell activity

For cytotoxicity assays, the K562 tumor cell line was used as the target. NK T cell cytotoxicity was assayed using a fluorometric method as previously described[27]. K562 tumor target cells (1×10^6) were labeled with 15 μM calcein-AM (Molecular Probe, Eugene, OR) for 30 min at 37°C and washed 2 times with cold complete medium. Labeled target cells (5×10^3/50 μl) and varying numbers of cryopreserved and thawed effector cells (from 5×10^6 to 5×10^3 PBMC/100 μl) were incubated in triplicate in V-bottom 96-well plates (Effector/Target E/T ratios from 50/1 to 1/1). After incubation at 37°C in 5% CO_2 for 4 h, 75 μl of each supernatant were harvested and transferred to new plates. Then, 100 m*l* of 1% Triton X-100 in 0.05 M borate buffer, pH 9.0, was added to each well. The plate was kept for 20 h at 4°C to allow for solubilization and then read for fluorescence with a dual-scanning microplate spectrofluorometer (Spectramax Gemini–Molecular Devices, Sunnyvale, CA). The proportion of specific lyses was calculated as follows: Specific lyses=Fmed-Fexp/Fmed, where F is the fluorescence of solubilized cells after the supernatant has been removed, med=F from target cells incubated in CM medium alone, and exp=F from target cells incubated with effector cells. Results are expressed as Lytic Units (LU $20/10^7$ cells).

7) Cytokine assay

The IL-1β, IL-6, INFγ and TNFα levels were assessed in plasma, by using a multiplex sandwich ELISA kit (SearchLight, Pierce Biotechnology, Rockford, IL, USA), according to the manufacturer's instructions. Results are expressed as pg/m*l*.

Statistical analysis

Continuous variables are given as mean ± SD and categorical variables as number of subjects. Analysis of covariance (ANCOVA) with repeated measures was used to evaluate differences among the T1, T2, T3, T4 time points adjusted for age, body mass index and time in current job. Posthoc comparisons were carried out using the Scheffe test to evaluate the differences between baseline (T1) and follow-up (T2, T3, T4).

Relationships between psychometric indicators (job satisfaction, degree of stress, psychological distress, social support) and immunological-inflammatory parameters (lymphocyte T subpopulations, B lymphocytes, NK cells, NK cell activity, plasma levels of inflammatory cytokines) were examined by Pearson's correlation analysis.

To evaluate the over the time variation of the biological parameters in relation to psychological changes, the individual changes of the psychometric score at T4 with respect to the baseline time T1 (T4–T1) were determined. Thus, for each psychological test (HJSS, PSS, GHQ-12, MSPSS), three groups were determined: subjects who showed no psychological changes ($\Delta T=0$), subjects who had an increased psychological score ($\Delta T>0$), and subjects who showed a decrease of psychological score ($\Delta T<0$). Then, for each biological variable the variation with respect to baseline (unchanged psychological score) was determined. One way ANOVA and the posthoc Scheffe test were used to evaluate the differences between groups.

The significance level for all statistical analyses was set at a probability of less than 0.05 (two-tailed test). All data in this study were analyzed by statistical software Statistical Package for Social Sciences version 15 (SPSS Inc, Chicago, IL) and by Statview Macintosh.

Results

One hundred one nurses who were working at the

Surgery and Anesthesiology and Resuscitation Unit, were repeatedly enrolled into the study every 4 mo over a 1-yr period. They were aged 36.7 ± 7.5 yr and were mainly female (74%) and most of them were shift workers (73%). Sixty percent of subjects were smokers and 65% of them drank at least 2 glasses/day of alcoholic drinks (Table 1). Immunological parameters, inflammatory cytokines, and psychometric scores of the study population at the baseline (T1), and at 4 (T2), 8 (T3), 12 (T4) mo follow-up are summarized in Table 2.

Table 1. Demographic characteristics of recruited subjects

Characteristics	Mean ± SD	Min–Max
Age (yr)	36.7 ± 7.5	24.0–58.0
Sex (M/F)	26/75	–
Body max index (BMI)	22.6 ± 3.6	21.2–25.8
Smoking (yes/no)	60/41	–
Drinking (yes/no)	66/35	–
Shift work (yes/no)	74/27	–
Time in current job (yr)	11.2 ± 8.3	1.0–32.0

N=101. Continuous variables are expressed as mean ± SD and as Min-Max range, categorical variables as number of subjects.

Table 3 shows Pearson's correlation between psychometric parameters and stress-related immunological and inflammatory variables evaluated at baseline (T1). Subjects with high job satisfaction showed low PSS and GHQ-12 scores, corresponding to a low degree of psychological distress. An inverse correlation was also observed between the social support (MSPSS) and for both the psychometric tests used to evaluate the degree of stress (PSS and GHQ-12). Subjects with psychological distress showed a decrease of $CD4^+$ helper T cells with an increase in the number of $CD8^+$ suppressor T cells. The $CD4^+/CD8^+$ ratio inversely correlated with the GHQ-12 scores. In these subjects a positive correlation was observed between psychological distress scores and the number of $CD8^+$-$CD57^+$ activated T lymphocytes and to a lesser extend with $CD56^+$ NK cells. Job satisfaction and social support did not affect the $CD4^+$ helper T cell and $CD8^+$ suppressor T cell status, whereas an inverse correlation was found with the number of $CD56^+$ NK cells and with $CD8^+$-$CD57^+$ activated T lymphocytes. In addition, subjects with a high social support score also showed low NK cell activity. None of the psychometric tests correlated with the number of $CD19^+$ B lymphocytes. By analysis of inflammatory

Table 2. Psychological and immunological-inflammatory parameters at the different time points

Characteristics	T1	T2	T3	T4
Immunological parameters				
Total lymphocytes (n°/ml × 10^3)	2.12 ± 0.70	2.18 ± 0.73	2.39 ± 0.71	2.30 ± 0.58
$CD19^+$ B cells (n°/ml × 10^3)	0.27 ± 0.14	0.28 ± 0.15	0.32 ± 0.17*	0.30 ± 0.14*
$CD3^+$ T cells (n°/ml × 10^3)	1.68 ± 0.48	1.71 ± 0.50	1.88 ± 0.54	1.76 ± 0.46
$CD4^+$ T cells (n°/ml × 10^3)	1.07 ± 0.36	1.12 ± 0.37	1.24 ± 0.41*	1.18 ± 0.36*
$CD8^+$ T cells (n°/ml × 10^3)	0.61 ± 0.23	0.61 ± 0.22	0.64 ± 0.23	0.59 ± 0.18
$CD8^+$-$CD57^+$ T cells (n°/ml × 10^3)	0.12 ± 0.12	0.14 ± 0.13	0.16 ± 0.12**	0.16 ± 0.14**
$CD56^+$ NK cells (n°/ml × 10^3)	0.23 ± 0.13	0.23 ± 0.12	0.23 ± 0.11	0.21 ± 0.13
NK activity (U lysis/cells × 10^3)	93.45 ± 37.10	63.94 ± 48.81**	117.50 ± 140.94	95.49 ± 48.78
Inflammatory parameters				
IL-1β (pg/ml)	7.64 ± 32.88	12.48 ± 12.35**	5.75 ± 19.58	1.99 ± 5.65
IL-6 (pg/ml)	6.21 ± 20.18	3.30 ± 4.37	6.40 ± 12.07	8.03 ± 19.83**
INFγ (pg/ml)	7.44 ± 26.10	20.20 ± 18.09**	8.10 ± 24.00	8.69 ± 17.41
TNFα (pg/ml)	30.80 ± 89.56	21.75 ± 48.41	32.12 ± 72.71	30.30 ± 111.20
Psychological parameters				
HJSS (score 0–10)	7.20 ± 1.16	6.83 ± 1.33*	6.64 ± 1.43*	6.67 ± 1.51*
PSS (score 0–40)	14.52 ± 6.12	14.94 ± 7.52	16.53 ± 8.10	16.2 ± 8.00
GHQ-12 (score 0–12)	2.01 ± 2.59	2.55 ± 3.39	2.61 ± 3.28	2.46 ± 3.34
MSPSS (score 0–84)	63.60 ± 12.94	63.10 ± 13.83	63.31 ± 12.43	64.70 ± 12.88

N=101. Psychological and immunological-inflammatory parameters of subjects at the baseline time (T1), and at 4 (T2), 8 (T3), 12 (T4) mo follow-up. Results are expressed as mean ± SD and differences among the time points adjusted for age, body mass index and time in current job were evaluated by ANCOVA repeated measures and the significance determined by the *post hoc* Scheffe test. T1 vs T2, T3, T4 and $p<0.05$ was considered statistically significant. *: $p<0.05$; **: $p<0.001$.

Table 3. Correlations between psychometric parameters and immunological-inflammatory variables

	HJSS	PSS	GHQ-12	MSPSS
Psychometric variables				
HJSS	–	**–0.435**	**–0.235**	0.122
PSS	**–0.435**	–	**0.680**	**–0.389**
GHQ-12	**–0.235**	**0.680**	–	–0.172
Immunological variables				
Total lymphocytes (n°/m*l*)	–0.113	**0.161**	**0.175**	**–0.194**
$CD19^+$ B cells (n°/m*l*)	–0.083	0.071	0.083	–0.046
$CD3^+$ T cells (n°/m*l*)	–0.086	0.096	0.094	–0.120
$CD4^+$ T cells (n°/m*l*)	–0.059	0.002	**–0.161**	–0.127
$CD8^+$ T cells (n°/m*l*)	–0.096	**0.212**	**0.244**	–0.144
$CD4^+/CD8^+$ ratio	0.027	–0.087	–0.134	0.150
$CD8^+$-$CD57^+$T cells (n°/m*l*)	**–0.176**	**0.298**	**0.201**	**–0.187**
$CD56^+$ NK cells (n°/m*l*)	**–0.172**	**0.138**	0.092	**–0.234**
NK activity (U lysis/cells)	–0.035	0.150	0.101	**–0.184**
Inflammatory variables				
IL-1β (pg/m*l*)	–0.124	0.119	–0.027	0.089
IL-6 (pg/m*l*)	**–0.149**	0.043	0.023	0.096
INFγ (pg/m*l*)	–0.026	0.022	–0.033	0.093
TNFα (pg/m*l*)	–0.120	–0.015	0.079	–0.076

N=101. Pearson's correlation coefficient analysis obtained from data collected at the baseline time (T1). The $p<0.05$ was considered statistically significant and significant correlations are shown in bold.

cytokines, it was observed that job-satisfied subjects showed low blood levels of IL-6.

The psychological status variation was evaluated by calculating the changes of the psychometric score at T4 with respect to the baseline T1, and for each psychological test (HJSS, PSS, GHQ-12, MSPSS), three groups were determined: subjects who showed no psychological changes ($\Delta T=0$), subjects who had an increased psychological score ($\Delta T>0$), and subjects who showed a decrease of psychological score ($\Delta T<0$). Then, for each biological variable the variation with respect to baseline (unchanged psychological score) was determined. As shown in Fig. 1, the number of $CD8^+$ T cells and $CD8^+$-$CD57^+$ T lymphocytes was found to be increased in subjects that showed an increased state of distress. A high number of $CD8^+$-$CD57^+$ T lymphocytes was associated with higher levels of IL-1β and IL-6 was observed in subjects whose job satisfaction declined over time. In addition, the levels of TNFα best reflected the changes of psychological stress, increasing in association with increased distress status.

Discussion

Good reliability was found among the psychological tests used. Subjects with high values of PSS and GHQ-12, which estimate psychological distress, showed low scores of job satisfaction and social support (Table 3). The study population showed a low-to-medium level of self-perception of stress. Job satisfaction was associated with a better psychological status. The subjects with high scores of social support and job satisfaction showed low scores on PSS and GHQ-12 (Table 3). Psychological distress is associated with an immune-risk phenotype: elevated levels of total lymphocytes, increased $CD8^+$ suppressor T cells, $CD8^+$-$CD57^+$ activated T cells and $CD56^+$ NK cells, reduced $CD4^+$ helper T cells, and a low $CD4^+/CD8^+$ ratio. Conversely, high job satisfaction and social relationships evaluated by the HJSS and MSPSS tests were associated with lower levels of $CD8^+$-$CD57^+$ activated T cells and $CD56^+$ NK cells, and reduced plasma content of IL-6. High social support appeared to be associated with a reduction in $CD8^+$-$CD57^+$ T cells, suggesting a role for social support in protecting against immune deficiency during times of stress.

Among indices of immune function, $CD57^+$ T cells are of particular importance. Reactive microenvironment infiltrated predominantly with $CD57^+$ T cells is associated with a significantly higher frequency of adverse manifestations; $CD57^+$ T rosettes occur around neoplastic cells[28]. A growing body of evidence points toward CD57 as a marker of general immune dysfunction. CD57 antigen is normally expressed only by a minority of human $CD8^+$ T-cell lymphocytes (16%), but its expression increases during chronic immune activation and with increasing age[29]. The percentage of $CD8^+$-$CD57^+$ cells increases in different clinical conditions, such as

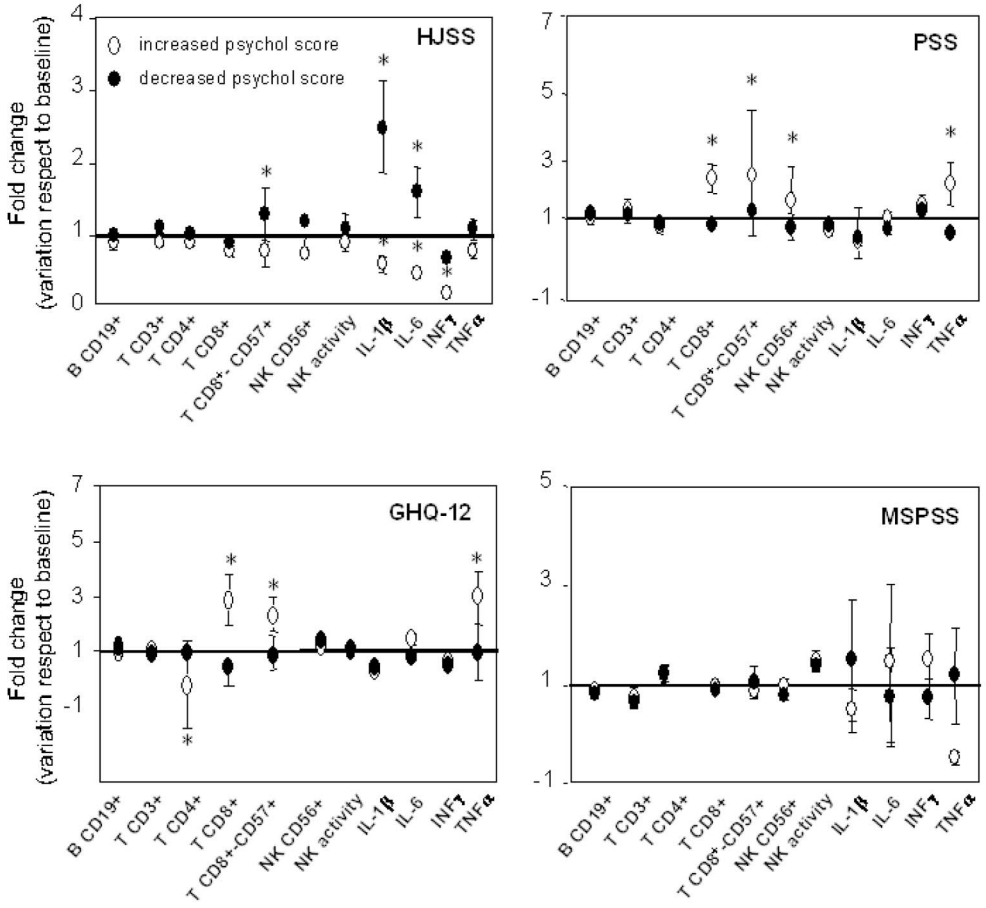

Fig. 1. Fold change of the immunological-inflammatory parameters at 12 months' follow-up with respect to the baseline value. The psychological status variation was evaluated by calculating the individual changes of the psychometric score at T4 with respect to the baseline time T1. For each psychometric test (HJSS, PSS, GHQ-12, MSPSS), three groups were determined: subjects who showed no psychological changes (line), subjects who had an increased psychological score (○), and subjects who showed a decrease of psychological score (●). Then, for each biological variable the variation with respect to baseline was determined. Results are represented as mean ± SD of fold change with respect to unchanged values (baseline). One way ANOVA and the posthoc Scheffe test were used to evaluate the differences between groups, $p<0.05$ was considered statistically significant. *: Increased psychological score group and decreased psychological score group vs. unchanged psychological score group.

infections associated with immune dysfunction including AIDS[30], tuberculosis[31], B19 virus infection[32], and cytomegalovirus disease[33]. Also, the expression of CD57 renders cells susceptible to activation-induced cell death by apoptosis. Therefore, CD57 seems to be a good candidate as a marker of lymphocyte dysfunction.

NK cell subsets and NK cell activity are known to be important in the host defense against viral diseases and they appear to play a significant role in protection against neoplastic growth[34]. Studies concerning the effects of psychological stress on immune function have mainly dealt with depression or life events. Long-lasting life stress is associated with reduced NK cell activity[35]. In the occupational health field, cell activity and the proportion or numbers of NK cells were shown to decrease with a depersonalization score on the Maslach Burnout Inventory (MBI) among office workers[36]. A decrease in these indices is associated with the level of job stress[37], or overwork[38]. Some authors have shown that perceived job stress, particularly quantitative work load, reduces NK cell activity through a decrease in NK cell number[39]. However, stressors have also been shown to increase the number of circulating NK cells[40, 41]. In our study, job satisfaction and high social support were

associated with reduced NK $CD56^+$ cells, whereas a higher NK $CD56^+$ cell number was found in subjects with a higher perceived stress (Table 3). It seems that pronounced inter-individual variations exist with respect to stressor-provoked alterations of circulating lymphocytes. The levels of NK cells may be dependent upon the reactivity of the individuals being tested and their recent stressor history[40]. Moreover, it has been observed that levels of circulating NK cells are high in depressed patients. Depression has been associated with increased perception of day-to-day stressors. It has been reported that the use of inappropriate emotion-focused coping was associated with an increased number of NK cells, whereas the more adaptive problem-focused coping style was accompanied by lower levels of circulating NK cells[42]. Given that mild stressors may increase circulating NK cells, it is conceivable that an increased number of NK cells is observed in subjects with low job satisfaction, high perceived stress and low social support.

High social support appeared to induce a reduction in $CD8^+$-$CD57^+$ T cells, thus suggesting a role for social support in protecting against immune deficiency during times of stress.

Over time changes in the psychological parameters have been related to changes in biochemical-immunological variables (Fig. 1). Subjects who increased their job satisfaction showed a reduced level of inflammatory cytokines, such as IL-1β, IL-6, and $CD8^+$-$CD57^+$ activated T cells. The follow-up analysis supports the hypothesis that immunological-inflammatory changes with respect to job satisfaction and psychological distress. These immune alterations may have relevance for susceptibility to diseases.

Although a small population was analyzed, we showed that perceived job stress is associated with the psychological status and social relationships of the workers. The data suggest that job (dis)satisfaction and psychological mechanisms in stress affect cellular immune function, shifting workers towards an immune-risk phenotype.

Acknowledgments: We thank Dr Elettra Pignotti, IRCCS Orthopaedic Institute "Rizzoli", Bologna, Italy, for the statistical and analysis and data interpretation.

References

1) del Valle JF, López M, Bravo A. Job stress and burnout in residential child care workers in Spain. Psicothema 2007; 19: 610–5.
2) Virtanen M, Vahtera J, Pentti J, Honkonen T, Elovainio M, Kivimäki M. Job strain and psychologic distress influence on sickness absence among Finnish employees. Am J Prev Med 2007; 33: 182–7.
3) Tomei G, Rosati MV, Martini A, et al. Assessment of subjective stress in video display terminal workers. Ind Health 2006; 44: 291–5.
4) Nomura K, Nakao M, Sato M, Ishikawa H, Yano E. The association of the reporting of somatic symptoms with job stress and active coping among Japanese white-collar workers. J Occup Health 2007; 49: 370–5.
5) Karasek R, Baker D, Marxer F, Ahlbom A, Theorell T. Job decision latitude, job demands, and cardiovascular disease: A prospective study of Swedish men. Am J Public health 1981; 71: 694–705.
6) Marcus M, Gerr F. Upper extremity musculoskeletal symptoms among female office workers: Associations with video display terminal use and occupational psychological stressors. Am J Ind Med 1996; 29: 161–70.
7) Stice E, Ragan J, Randall P. Prospective relations between social support and depression: Differential direction of effects for parent and peer support? J Abnorm Psychol 2004;113:155–9.
8) Nagai M, Tsuchiya KJ, Toulopoulou T, Takei N. Poor mental health associated with job dissatisfaction among school teachers in Japan. J Occup Health 2007; 49: 515–22.
9) Henningsen GM, Hurrell JJ Jr, Baker F, et al. Measurement of salivary immunoglobulin A as an immunologic biomarker of job stress. Scand J Work Environ Health 1992; 18: 133–6.
10) Endresen IM, Vernes R, Ursin H, Tonder O. Psychological stress-factors and concentration of immunoglobulins and complement components in Norwegian nurses. Work Stress 1987; 1: 365–75.
11) Kawakami N, Tanigawa T, Araki S, et al. Effects of job strain on helper-inducer (CD4+CD29+) and suppressor-inducer (CD4+CD45RA+) T cells in Japanese blue-collar workers. Psychother Psychosom 1997; 66: 192–8.
12) Meijiman TF, van Dormolen M, Herber RFM, Rogen H, Kuioer S. Job strain, neuroendocrine activation, and immune status. In: Sauter SL, Murphy LR, editors. Organizational Risk Factors for Job Stress. Washington, DC: American Psychological Association; 1995. p.113–26.
13) Kobayashi F, Furui H, Akamatsu Y, Watanabe T, Horibe H. Changes in psychophysiological functions during night shift in nurses. Influence of changing from a full-day to a half-day work shift before night duty. Int Arch Occup Environ Health 1997; 69: 83–90.
14) Yasuda A, Iwasaki K, Sasaki T, Oka T, Hisanaga N. Lower percentage of CD56+ cells associated with long working hours. Ind Health 2001; 39: 221–3.
15) Miller GE, Cohen S, Ritchey AK. Chronic psychological stress and the regulation of pro-inflammatory cytokines: A glucocorticoid-resistance model. Health Psychol 2002; 21: 531–41.
16) Hamer M, Molloy GJ, Stamatakis E. Psychological distress as a risk factor for cardiovascular events: Pathophysiological and behavioral mechanisms. J Am Coll Cardiol 2008; 52: 2163–5.
17) Tiersma ES, van der Lee ML, Garssen B, et al. Psychosocial factors and the course of cervical intra-epithelial neoplasia: A prospective study. Gynecol

Oncol 2005; 97: 879–86.
18) Gigantesco A, Picardi A, Chiaia E, Balbi A, Morosini P. Job satisfaction among mental health professionals in Rome, Italy. Community Ment Health J 2003; 39: 349–55.
19) Picardi A, Battisti F, Tarsitani L, Baldassari M, Copertaro A, Mocchegiani E, Biondi M. Attachment security and immunity in healthy women. Psychosom Med 2007; 69: 40–6.
20) Goldberg D, Williams P. A user's guide to the General Health Questionnaire. Berkshire: NEER-Nelson Publishing; 1988.
21) Holi MM, Marttunen M, Aalberg V. Comparison of the GHQ-36, the GHQ-12 and the SCL-90 as psychiatric screening instruments in the Finnish population. Nord J Psychiatry 2003; 57: 233–8.
22) Goldberg DP, Gater R, Sartorius N, et al. The validity of two versions of the GHQ in the WHO study of mental illness in general health care. Psychol Med 1997; 27: 191–7.
23) Dahlem NW, Zimet GD, Walker RR. The Multidimensional Scale of Perceived Social Support: A confirmation study. J Clin Psychol 1991; 47: 756–1.
24) Canty-Mitchell J, Zimet GD. Psychometric properties of the Multidimensional Scale of Perceived Social Support in urban adolescents. Am J Community Psychol 2000; 28: 391–400.
25) Clara IP, Cox BJ, Enns MW, Murray LT, Torgrudc LJ. Confirmatory factor analysis of the multidimensional scale of perceived social support in clinically distressed and student samples. J Pers Assess 2003; 81: 265–70.
26) Chou KL. Assessing Chinese adolescents' social support: The multidimensional scale of perceived social support. Personality Individual Differences 2000; 28: 299–307.
27) Neri S, Mariani E, Meneghetti A, Cattini L, Facchini A. Calcein-acetyoxymethyl cytotoxicity assay: Standardization of a method allowing additional analysis on recovered effector cells and supernatants. Clin Diagn Lab Immunol 2001; 8: 1131–5.
28) Atayar C, van den Berg A, Blokzijl T, et al. Hodgkin lymphoma associated T-cells exhibit a transcription factor profile consistent with distinct lymphoid compartments. J Clin Pathol 2007; 60: 1092–7.
29) Tarazona R, DelaRosa O, Alonso C, et al. Increased expression of NK cell markers on T lymphocytes in aging and chronic activation of the immune system reflects the accumulation of effector/senescent T cells. Mech Ageing Dev 2000; 121: 77–88.
30) Stites DP, Casavant CH, McHugh TM, et al. Flow cytometric analysis of lymphocyte phenotypes in AIDS using monoclonal antibodies and simultaneous dual immunofluorescence. Clin Immunol Immunopathol 1986; 38: 161–77.
31) Sada-Ovalle I, Torre-Bouscoulet L, Valdez-Vázquez R, Martínez-Cairo S, Zenteno E, Lascurain R. Characterization of a cytotoxic CD57+ T cell subset from patients with pulmonary tuberculosis. Clin Immunol 2006; 121: 314–23.
32) Isa A, Kasprowicz V, Norbeck O, et al. Prolonged activation of virus-specific CD8+ T cells after acute B19 infection. PLOS Medicine 2005; 2: e343.
33) He XH, Zha QB, Liu Y, Xu LH, Chi XY. High frequencies of cytomegalovirus pp65(495–503)-specific CD8 (+) T cells in healthy young and elderly Chinese donors: Characterization of their phenotype and TCR Vbeta usage. J Clin Immunol 2006; 26: 417–29.
34) Herberman RB, Ortaldo JR. Natural Killer cells: Their role in defences against diseases. Science 1981; 214: 24–30.
35) Kawamura N, Kim Y, Asukai N. Suppression of cellular immunity in men with a past history of posttraumatic stress disorder. Am J Psychiatry 2001; 158: 484–6.
36) Nakamura H, Nagase H, Yoshida M, Ogino K. Natural killer (NK) cell activity and NK cell subsets in workers with a tendency of burnout. J Psychosom Res 1999; 46: 569–78.
37) De Gucht V, Fischler B, Demanet C. Immune dysfunction associated with chronic professional stress in nurses. Psychiatry Res 1999; 85: 105–11.
38) Yasuda A, Iwasaki K, Sasaki T, Oka T, Hisanaga N. Lower percentage of CD56+ cells associated with long working hours. Ind Health 2001; 39: 221–3.
39) Morikawa Y, Kitaoka-Higashiguchi K, Tanimoto C, et al. A cross-sectional study on the relationship of job stress with natural killer cell activity and natural killer cell subsets among healthy nurses. J Occup Health 2005; 47: 378–83.
40) Brosschot JF, Benschop RJ, Godaert GL, et al. Influence of life stress on immunological reactivity to mild psychological stress. Psychosom Med 1994; 56: 216–24.
41) Marsland AL, Manuck SB, Fazzari TV, Stewart CJ, Rabin BS. Stability of individual differences in cellular immune responses to acute psychological stress. Psychosom Med 1995; 57: 295–8.
42) Ravindran AV, Griffiths J, Merali Z, Anisman H. Variations of lymphocyte subsets associated with stress in depressive populations. Psychoneuroendocrinology 1996; 21: 659–71.