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Short Communication

Job satisfaction is associated with elevated natural killer cell immunity among healthy white-collar employees

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ABSTRACT

Although the association of job satisfaction with health has been well documented, little is known about the biological mechanisms underlying this relationship. This study investigates the association of job satisfaction with cell-mediated immunity among Japanese white-collar daytime workers. A total of 306 healthy full-time employees (141 women and 165 men), aged 22–69 (mean 36) years, provided a blood sample for the measurement of circulating immune (natural killer (NK), B, and total T) cells and NK cell cytotoxicity (NKCC) and completed a questionnaire survey during April to June 2002. Job satisfaction was measured by a 4-item scale from the Japanese version of the generic job stress questionnaire with higher scores indicating greater satisfaction. Analyses were done separately for women and men using a hierarchical multiple linear regression model controlling for multiple confounders. The results revealed that greater job satisfaction was positively correlated with NKCC ($\beta = .207$; $p = .029$) and the number of NK ($CD3^-CD56^+$) cells ($\beta = .261$; $p = .008$) in women. In men, job satisfaction was marginally correlated with NKCC ($\beta = .165$; $p = .050$) but was not correlated with the number of NK ($CD3^-CD56^+$) cells ($\beta = .142$; $p = .107$). Job satisfaction did not correlate with numbers of T ($CD3^+CD56^-$) and B ($CD19^+$) cells in both women and men. Our findings suggest an independent association between job satisfaction and NK cells but the association seems to be stronger in women than in men. Although the results provide a support for the biological plausibility of the job satisfaction-health relationship, additional research is required to determine whether greater job satisfaction contributes to recovery/maintenance of NK cell immunity and host defense over time.

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1. Introduction

Job satisfaction, defined as the degree of pleasure a worker derives from his/her job, has been one of the most widely studied constructs in the work and organizational literature for several decades (Spector, 1997). Studies suggest that job satisfaction is determined by a number of work environment characteristics such as relationships with colleagues and managers, income level, chances of promotion and advancement, level of interest in the job, independence at work, job stability and security, work stressors, and fairness/justice at work (Fischer and Sousa-Poza, 2009; Spector, 1997). Job satisfaction is also influenced by personal factors such as gender, age, education, health behaviors, personality traits, and genetic components (Spector, 1997). Some previous studies revealed that levels of job satisfaction in industrialized countries have declined in the past decades because of changes in employment conditions such as globalization, flexible employment, higher mobility, and deep economic recessions (Sousa-Poza and Sousa-Poza, 2000). As job satisfaction captures both micro-level daily interactions on the job and macro-level factors related to selection into a job, it is often used as a summary measure of workers' health and well-being in occupational health research (de Castro et al., 2008).

To date, a number of studies have reported a link between job satisfaction and health. A comprehensive meta-analysis based on 485 studies of job satisfaction and health reported that workers with low levels of satisfaction were more likely to experience anxiety ($\rho = .420$), burnout ($\rho = .478$), depression ($\rho = .428$), low self-esteem ($\rho = .429$), subjective physical illness ($\rho = .287$), and cardiovascular disease ($\rho = .121$), indicating that job satisfaction is an important predictor of psychological and physical health (Faragher et al., 2005). Reduced job satisfaction is also associated with common infection (Mohren et al., 2005) and sickness absence (Munch-Hansen et al., 2008), in which the immune response may play a key role.

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Although the connection between job satisfaction and health appears to be close, a major weakness in research of the job satisfaction-health relationship is that most studies rely on self-reports rather than objective health measures, which limits discovery of the biological mechanism(s). To date, only a handful of studies have attempted to examine the psychoimmunologic mechanism of job satisfaction. A study of Norwegian female nurses ($n = 34$) found that a sum of facet-specific job satisfaction consisting of comfort, challenge, financial rewards, relations with coworkers, and resource adequacy and promotions, significantly associated with decreased circulating immunoglobulin (Ig) A and complement component C3 but not with IgG or IgM (Endresen et al., 1987). A large cohort study in Israel (917 men and 622 women) reported that facet-specific job satisfaction was inversely correlated with C-reactive protein (CRP) in men ($B = -.20$, $p < .05$) but not in women ($B = -.10$, $p > .05$) (Shirom et al., 2006). In contrast, global job satisfaction was inversely correlated with serum interleukin (IL)-6 in women but not in men in a sample of Swedish working people (141 women and 102 men) (Theorell et al., 2000). A recent prospective study on job stress and immunity among nurses (75 women and 26 men) found that those who experienced a decrease in job satisfaction over a 1-year period had increased levels of IL-1β, IL-6, and $CD8^+CD57^+$ T cells, and a decreased level of interferon (IFN)-γ (Amati et al., 2010). Taken together, these studies suggest that greater job satisfaction may have a positive impact on immune outcomes but the findings are not always congruent when studies are compared to each other. The inconsistent findings may partly be attributable to the fact that some essential confounders including age, sex, lifestyle and biological factors were not considered (Amati et al., 2010; Endresen et al., 1987; Theorell et al., 2000), which may have significant impact on results. In addition, it is not clear whether job satisfaction is associated solely with humoral/inflammatory markers or also with cellular immune measures such as natural killer cell cytotoxicity (NKCC) and circulating lymphocytes and whether the association differs by sex. Clearly, more effort is needed to explore the psychoimmunologic basis of job satisfaction.

Our study was intended to fill a gap in the current knowledge about the psychoimmunologic mechanisms of job satisfaction by assessing cellular immune parameters. We measured NKCC and circulating NK ($CD3^-CD56^+$) cells together with B ($CD19^+$) and total T ($CD3^+CD56^-$) cells among 404 white-collar employees. We selected these immune markers because reduction of NKCC and circulating NK and T cells are reported to be associated with poor working conditions including job stress (Bargellini et al., 2000; Boscolo et al., 2009; Cohen et al., 2007; Di Donato et al., 2006; Miyazaki et al., 2003; Morikawa et al., 2005; Nakata et al., 2000a, 2002; Okamoto et al., 2008), and these markers are frequently used in human psychoimmunologic studies (Segerstrom and Miller, 2004). Our *a priori* hypothesis is that lowered job satisfaction is associated with selected immune markers in the direction of reduced immune functioning.

2. Methods

2.1. Subjects and procedure

The study design was cross-sectional and data were collected with a self-administered questionnaire at a pharmaceutical company and a trading company in Japan. The study was conducted as a part of occupational health examinations conducted during April through June 2002. All employees in both companies were full-time, white-collar, daytime Japanese workers. A total of 643 employees were initially recruited for this study. The survey questionnaire, including purpose, instruction, and informed consent was given to a total of 626 employees (17 employees could not be reached because they were out due to sickness (mostly because of psychiatric illnesses) or maternity leave). Four hundred and four employees agreed to participate in the questionnaire survey and blood test, and replied with a signed consent form (response rate 64.5%). Of these 404 employees, 37 were excluded because of missing data for one of the study parameters. An additional 61 employees reporting physical/mental disorders were excluded (see 'Covariates' section for detail), which resulted in a sample size of 306 participants (141 women and 165 men). Participants were not exposed to hazardous chemicals that could affect immunological outcomes.

The study protocol was reviewed and approved by the Institutional Review Board of the National Institute of Occupational Safety and Health, Japan and by the Ethical Committee of the Kyushu University.

2.2. Measures

2.2.1. Job satisfaction

Job satisfaction was assessed by a 4-item scale included in the Japanese version of the generic job stress questionnaire (GJSQ) (Nakata et al., 2007) developed by the US National Institute for Occupational Safety and Health (NIOSH) (Hurrell and McLaney, 1988). Items and responses for the scale are as follows:

(1) Knowing what you know now, if you had to decide all over again whether to take the type of job you now have, what would you decide (**JSQ1**)? I would...
(1) decide definitely not to take this type of job, (2) have some second thoughts, (3) decide without hesitation to take the same job

(2) If you were free right now to go into any type of job you wanted, what would your choice be (**JSQ2**)? I would...
(1) not want to work, (2) take a different job, (3) take the same job

(3) If a friend of yours told you he/she was interested in working in a job like yours, what would you tell him/her (**JSQ3**)? I would...
(1) advise against it, (2) have doubts about recommending it, (3) strongly recommend it

(4) All in all, how satisfied would you say you are with your job (**JSQ4**)?
(1) not at all satisfied, (2) not too satisfied, (3) somewhat satisfied, (4) very satisfied

Each item response number corresponds to its item score. The total job satisfaction score was calculated by adding the scores of JSQ1 to JSQ4. The Cronbach's alpha value for this scale was 0.68, which is considered to be an acceptable level for job satisfaction measures (van Saane et al., 2003). The test–retest stability over 1 year with a subsample ($n = 124$) of the current study was high ($r = .586$, $p < .001$). Validity was estimated by calculating the correlations between job satisfaction and the covariates, and the relationships were in the expected direction indicating a high convergent validity (Table 1).

2.2.2. Preparation of blood samples

Fasting blood samples were collected between 9.00 and 11.00 a.m. from participants to control for diurnal variations. Ethylenediaminetetraacetic acid dipotassium (2K-EDTA) was used as an anticoagulant to collect 2 ml of venous blood from subjects for measurement of leukocytes counts and immunofluorescence staining. Similarly, 5 ml heparinized venous blood was collected to measure NKCC. All samples were transported and handled at room

Table 1

Characteristics of study participants and intercorrelations[a] among selected variables stratified by sex (upper diagonal is men and lower diagonal is women).

Variable	Women (n = 141)			Men (n = 165)			p[b]	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15	
	Mean	SD	Range	Mean	SD	Range		r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p
1. Job satisfaction[c,d]	9.3	1.4	5–12	9.6	1.6	5–13	*.038*			−.129	*.098*	.133	*.089*	.056	*.472*	−.011	*.892*	−.018	*.815*	.053	*.500*	.285	*<.001*	−.203	*.009*	−.378	*<.001*	.006	*.934*	.103	*.189*	.152	*.051*	.015	*.848*	.069	*.376*
2. Work hours/day	8.9	1.4	7–13	10.3	1.7	7–15	*<.001*	−.102	*.299*			−.240	*.002*	.102	*.193*	−.074	*.342*	−.049	*.528*	−.044	*.571*	−.388	*<.001*	.015	*.853*	.085	*.277*	.130	*.095*	.007	*.926*	−.124	*.113*	−.022	*.784*	−.134	*.085*
3. Age (in years)[g]	33.4	8.8	22–58	38.3	11.3	23–69	*<.001*	−.002	*.983*	−.127	*.133*			−.170	*.029*	.001	*.994*	.176	*.024*	.131	*.094*	.248	*.001*	−.247	*.001*	−.033	*.672*	.052	*.504*	.066	*.402*	.079	*.316*	.062	*.431*	.041	*.598*
4. Education (in years)	14.7	1.7	12–21	16.0	1.3	12–21	*<.001*	.116	*.169*	.100	*.239*	−.619	*<.001*			.017	*.827*	−.069	*.381*	−.018	*.817*	.040	*.613*	.026	*.741*	−.172	*.028*	−.032	*.685*	.009	*.912*	.025	*.752*	−.077	*.325*	−.083	*.289*
5. Smoking (number of cigarettes smoked/day)	2.3	5.9	0–40	8.7	11.7	0–60	*<.001*	−.114	*.178*	−.014	*.872*	−.099	*.244*	−.124	*.143*			.243	*.002*	−.058	*.457*	.149	*.056*	−.017	*.826*	.008	*.923*	.014	*.854*	−.042	*.595*	−.064	*.418*	.279	*<.001*	.360	*<.001*
6. Alcohol consumption (g ethanol/week)	41.7	69.6	0–403	149.7	138.5	0–805	*<.001*	.088	*.920*	.194	*.021*	−.619	*.045*	.136	*.107*	.203	*.016*			.041	*.605*	.143	*.066*	−.219	*.005*	−.080	*.309*	−.077	*.324*	.086	*.270*	.032	*.684*	.075	*.335*	−.026	*.736*
7. Leisure-time physical activity (METs/week)	5.1	9.1	0–52.5	5.9	9.4	0–46.8	*.487*	−.011	*.987*	−.041	*.631*	.045	*.600*	−.011	*.894*	.017	*.841*	.108	*.204*			.101	*.198*	.027	*.727*	−.143	*.068*	.102	*.190*	−.019	*.804*	−.063	*.423*	.027	*.734*	.041	*.603*
8. Subjective sleep sufficiency[d,e]	2.3	0.8	1–4	2.4	0.7	1–4	*.544*	.145	*.086*	−.184	*.029*	−.062	*.467*	−.012	*.885*	.048	*.571*	−.024	*.777*	.018	*.829*			−.289	*<.001*	−.198	*.011*	.013	*.868*	−.090	*.248*	.051	*.512*	.055	*.480*	.191	*.014*
9. Depressive symptoms (CES-D Scale score)[f,g]	14.2	6.6	0–36	12.3	5.5	0–34	*.007*	−.237	*.005*	.123	*.146*	−.289	*.001*	.170	*.044*	.023	*.787*	.021	*.803*	−.013	*.880*	−.019	*.822*			.194	*.012*	−.029	*.710*	−.014	*.862*	−.155	*.046*	−.070	*.372*	.009	*.907*
10. Interpersonal (intragroup) conflict at work[f]	19.8	6.0	8–40	18.8	4.9	8–33	*.100*	−.252	*.003*	.065	*.443*	.020	*.815*	−.016	*.849*	−.047	*.582*	−.030	*.721*	−.093	*.274*	−.071	*.400*	.168	*.046*			−.052	*.503*	−.043	*.581*	−.101	*.195*	.014	*.855*	.005	*.951*
11. BMI (kg/height (m)^2)[g]	19.9	2.2	15.4–28.9	23.3	2.8	17.2–32.8	*<.001*	.121	*.153*	.038	*.651*	.405	*<.001*	−.215	*.010*	−.045	*.597*	.012	*.889*	.046	*.590*	−.014	*.865*	−.085	*.318*	−.009	*.913*			.118	*.132*	.145	*.063*	.164	*.035*	.056	*.473*
12. NKCC (% cytotoxicity)[g]	37.3	16.7	4–74	49.9	16.8	5–77	*<.001*	.203	*.016*	−.057	*.503*	.124	*.142*	.057	*.500*	−.058	*.494*	−.068	*.421*	.045	*.597*	.118	*.162*	−.110	*.193*	.010	*.902*	.104	*.218*			.488	*<.001*	−.108	*.166*	−.133	*.087*
13. NK ($CD3^-CD56^+$) cells (cells/mm^3)[g]	239	141	38–765	320	212	64–1438	*<.001*	.189	*.025*	−.084	*.322*	.078	*.358*	−.077	*.361*	.111	*.191*	−.006	*.947*	−.003	*.972*	.065	*.441*	−.117	*.169*	−.032	*.710*	.030	*.724*	.484	*<.001*			.133	*.088*	−.019	*.804*
14. B ($CD19^+$) cells (cells/mm^3)[g]	222	113	25–911	238	141	18–736	*.260*	.061	*.475*	.046	*.589*	.280	*.001*	−.091	*.281*	−.042	*.623*	.004	*.961*	.074	*.382*	.006	*.939*	−.086	*.312*	−.116	*.172*	.270	*.001*	−.049	*.565*	.017	*.838*			.250	*.001*
15. Total T ($CD3^+CD56^-$) cells (cells/mm^3)[g]	1192	284	586–2017	1172	419	353–3208	*.624*	−.042	*.620*	.149	*.077*	−.023	*.785*	−.033	*.695*	−.007	*.932*	.141	*.094*	.079	*.353*	−.074	*.384*	.019	*.824*	.013	*.878*	.146	*.085*	−.344	*<.001*	−.227	*.007*	.293	*<.001*		

[a] Pearson product-moment correlation coefficients.

[b] p Value derived from Student's t test or Welch's test (compared between women and men).

[c] Sum of JSQ1 to JSQ4 (possible range 4–13).

[d] Positively oriented.

[e] Subjective sleep sufficiency (1 = very insufficient, 2 = somewhat insufficient, 3 = fairly sufficient, 4 = very sufficient).

[f] Negatively oriented.

[g] Although log-transformed values were used to approximate normal distribution in statistical analyses, mean values, SDs, and ranges are presented without log transformation to allow comparison with other studies.

temperature (i.e., 15–20 °C). Immunofluorescence staining analysis and measurement of NKCC were conducted within 24 and 12 h of blood collection, respectively. We determined counts of total leukocytes and total lymphocytes by an automated cell counter (Coulter Counter SP-VI, Coulter Electronics, Hialeah, Florida, USA), and lymphocyte subpopulations by flow cytometry analysis (EPICS XL, Beckman Coulter Inc, California, USA), as described in detail elsewhere (Nakata et al., 2000a, 2002).

2.2.3. Cell surface-marker analysis

The following sets of monoclonal antibodies were used to perform four-color direct immunofluorescence surface-marker analysis: anti-CD45-FITC/anti-CD56$^-$RD1/anti-CD19-ECD/anti-CD-3$^-$PC5. A combination of Mouse IgG1-FITC/Mouse IgG1-RD1/Mouse IgG1-ECD/Mouse IgG1-PC5 was used as the negative control. All monoclonal antibodies were purchased from Beckman Coulter Inc, USA. We calculated the number in each lymphocyte subset by multiplying lymphocyte counts by the percentage of positive cells in each category, as determined by flow cytometer.

With regard to immunoprotective roles of selected lymphocytes, T and B cells bear central roles in cellular and humoral immunity; subsets of T ($CD4^+$ and $CD8^+$) cells control production of immunoglobulins from B cells and secretion of cytokines. NK cells are large granular cells possessing killer activity against certain tumor cells and virus-infected cells without prior sensitization. Although interpretation of changes in number of lymphocyte subsets needs great care, an excessive increase of T cells is known to be associated with systemic inflammation, whereas a persistent decrease of T cells is related to immunodeficiency and psychological disorders such as depression (Herbert and Cohen, 1993; Westermann and Pabst, 1990). Similarly, an extreme decrease of B cells is associated with suppression in production of immunoglobulins, while a decrease of NK cells is associated with reduced effectiveness in killing infected and cancerous cells (Whiteside and Herberman, 1994).

2.2.4. Cytotoxicity assay

A standard 4-h Chromium-51 (^{51}Cr) release assay was used to determine NKCC (Pross et al., 1981). K562 was used as target cells and labeled with [^{51}Cr]-sodium chromate (New England Nuclear, Boston, Mass., USA) at 37 °C for an hour, washed and re-suspended at 2×10^5/ml in Roswell Park Memorial Institute (RPMI)-1640 medium containing 10% Fetal Calf Serum, 2 mM glutamine, 100 U/ml penicillin and 100 U/ml streptomycin. Labeled target cells were incubated with effector cells at an effector/target [E/T] cell ratio of 20:1 in U-bottomed 96-well plates at 37 °C for 4 h. Radioactivity in the supernatant was determined by a gamma counter. The assay was performed in quadruplicate. The percentage of specific lysis as cytotoxicity was determined according to the following formula: percentage of specific lysis = [(mean experimental cpm release − mean spontaneous cpm release)/(mean maximal cpm release − mean spontaneous cpm release)].

Reduced NKCC is a significant prognostic indicator of poor lifestyle practices and infection among healthy individuals. People under poor lifestyle practices such as smoking and no habitual exercise exhibited 15–20% decrease of NKCC than those with good lifestyle counterparts (i.e., nonsmoking or regular habitual exercise) (Kusaka et al., 1992). Also, according to several prospective studies, healthy subjects with persistently low NKCC exhibited a higher risk for developing infections within 6–12 months (Levy et al., 1991; Ogata et al., 2001).

2.2.5. Covariates

Covariates included age (in years), education (in years), smoking (number of cigarettes smoked per day), alcohol consumption (g ethanol per week), leisure-time physical activity, subjective sleep sufficiency, depressive symptoms, interpersonal (intragroup) conflict at work, height, weight, occupational grade (managerial or non-managerial), company type (pharmaceutical or trading), typical work hours per day including overtime, self-reported illness, and medication usage. Alcohol consumption was estimated by asking the usual amount of alcoholic drinks consumed per day and the number of occasions in a week that alcoholic drinks were consumed. We converted gross liquor consumption into net ethanol intake. We assessed leisure-time physical activity by calculating the energy expenditure of habitual physical exercise. We asked frequency, type, and length of physical exercise per month and converted these data to metabolic equivalents (METs). Estimated METs were assigned to the physical activities according to their mean intensity levels. One MET corresponds to an energy expenditure of approximately 1 kcal/kg/hr. Weekly leisure-time physical activity was calculated from this questionnaire. Validity and test–retest reliability were previously confirmed (Suzuki et al., 1998). Subjective sleep sufficiency was determined by a single question (Nakata et al., 2000b): do you think your daily sleep is sufficient? Response options were: (1) very insufficient, (2) somewhat insufficient, (3) fairly sufficient, or (4) very sufficient. Depressive symptoms were measured by a Japanese version of the Center for Epidemiologic Studies Depression scale (CES-D) (Shima et al., 1985). The 20-item depressive symptom scale measures the level of depressive symptoms experienced in the past week (Radloff, 1977). The internal consistency of the CES-D scale for the study sample was 0.84. Interpersonal (intragroup) conflict at work was assessed by an 8-item scale included in the GJSQ (Hurrell and McLaney, 1988; Nakata et al., 2007), which measures how much the worker feels the relationships within their working group are harmonious, cooperative, and supportive (possible range, 8–40). Items are rated on a five-point scale ranging from 1 (disagree strongly) to 5 (strongly agree). Examples of these items include "There is harmony within my group" and "In our group, we have lots of bickering over who should do what." A higher score indicates higher conflict within the working group. The internal consistency of this scale was 0.83. Information on height (m) and weight (kg) were obtained to assess body mass index (BMI), calculated as weight in kilograms divided by the square of height in meters. For self-reported illness, participants were asked if they had been diagnosed or treated for any of the following symptoms or disorders at the time of the study: hypertension, diabetes mellitus, menopausal disorder, depression, asthma, allergies, cancer, cardiovascular disease, arrhythmia, angina pectoris, liver disease, cerebrovascular disease, hyperlipidemia, hyperthyroidism, gastric/duodenal ulcer, autonomic imbalance, or other diseases. If the subjects reported 'other diseases,' they were asked to specify the condition. As a result, participants with the following symptoms or disorders were identified; hypertension ($n = 18$), diabetes mellitus ($n = 6$), menopausal disorder ($n = 3$), depression ($n = 4$), asthma ($n = 2$), severe allergies ($n = 12$), liver diseases ($n = 2$), gastric/duodenal ulcer ($n = 4$), autoimmune disorders ($n = 2$), hyperlipidemia ($n = 13$), autonomic imbalance ($n = 2$), and the common cold ($n = 10$); no other symptoms/disorders (including cancer) were reported from the participants. In order to eliminate the potential effects of health status on immune parameters, we excluded from the analyses all participants who reported the above disorders as well as women who reported pregnancy ($n = 61$). We also obtained data on the use of the following medications; aspirin ($n = 38$), β-blockers ($n = 2$), acetaminophen (included in pain killers, $n = 30$), corticosteroids ($n = 1$), antidepressants ($n = 2$), and anxiolytic drugs ($n = 1$). All participants with self-reported illnesses as described above were eliminated, leaving only aspirin ($n = 35$) and acetaminophen ($n = 30$) users in the subsequent analyses.

2.3. Statistical analyses

All immune markers and variables (age, BMI, and CES-D scale score) with skewed distributions were logarithmically transformed to achieve a more normal distribution in values. The difference between women and men was assessed by the Student's *t* test or Welch's test (Table 1). Since there were significant differences in variables by sex and given the fact that the affective response and immune reaction to stress differ by sex (Edwards et al., 2006; Shirom et al., 2006), subsequent analyses were carried out separately for women and men. Intercorrelations between continuous variables were tested by Pearson product-moment correlation coefficient.

Hierarchical multiple linear regression analysis was performed to test the relationship between immune markers (dependent variables) and job satisfaction and covariates (independent variables). In step 1, we entered job satisfaction, age, education, smoking, alcohol consumption, physical activity, subjective sleep sufficiency, BMI, use of aspirin, and use of acetaminophen (Model 1); Model 1 was then adjusted for depressive symptoms and interpersonal (intragroup) conflict at work (Model 2), and finally adjusted for occupational factors (occupational grade, company type, and work hours) (Model 3). To test an inverse directionality (immune markers predicting job satisfaction), we switched dependent and independent variables while controlling for all covariates.

The independent variables of medication usage, occupational grade, and company type were treated as categorical variables while the remaining variables were treated as continuous variables. The covariates were selected based on their possible associations with job satisfaction and immunity in previous studies (Shirom et al., 2006; Theorell et al., 2000). The significance level for all statistical analyses was $P < 0.05$ (two-tailed test). We analyzed the data using the Statistical Package for the Social Sciences version 15.0 (SPSS, Inc., Chicago, IL, USA).

3. Results

3.1. Sample characteristics

Characteristics of the study participants and the differences between women and men are shown in Table 1. As shown in this table, most variables measured in this sample differed by sex. Job satisfaction score, work hours, years of education, cigarettes smoked per day, alcohol consumption, BMI, and CES-D scale score in women were significantly lower than those of men. NK ($CD3^-CD56^+$) cells and NKCC were significantly lower in women than in men, while total T ($CD3^+CD56^-$) and B ($CD19^+$) cells were comparable between both sexes.

3.2. Association between covariates and immune markers

Intercorrelations among dependent/independent variables are shown in Table 1. The table is presented with men in the upper diagonal and women in the lower diagonal. A positive relationship between job satisfaction and NK ($CD3^-CD56^+$) cells was found in both women and men, while job satisfaction correlated with NKCC only in women. Work hours was marginally but inversely correlated with total T ($CD3^+CD56^-$) cells in men, while positively correlated with total T ($CD3^+CD56^-$) cells in women. In men, the number of cigarettes smoked per day was positively correlated with T ($CD3^+CD56^-$) and B ($CD19^+$) cells, sleep sufficiency was positively correlated with total T ($CD3^+CD56^-$) cells, and BMI was positively correlated with B ($CD19^+$) cells. In women, age and BMI were positively correlated with B ($CD19^+$) cells while total T ($CD3^+CD56^-$) cells marginally correlated with alcohol consumption and BMI. In this sample, education, alcohol consumption, and interpersonal conflict at work did not correlate with immune markers in either sex.

3.3. Relationship between job satisfaction and immune markers

Relationships between job satisfaction and immune markers are shown in Table 2a. The results of the hierarchical multiple linear regression analysis revealed that greater job satisfaction positively correlated with NK ($CD3^-CD56^+$) cells and NKCC in women. In men, job satisfaction was marginally ($p = .05$) correlated with NKCC but not with NK ($CD3^-CD56^+$) cells. In both women and men, job satisfaction did not show significant associations with numbers of total T ($CD3^+CD56^-$) or B ($CD19^+$) cells.

Additional analyses with immune markers as predictors of job satisfaction showed that NKCC and NK ($CD3^-CD56^+$) cell counts were moderate predictors of job satisfaction in women but NKCC was a weak predictor of job satisfaction in men (Table 2b).

4. Discussion

This study examined the cross-sectional association between job satisfaction and cell-mediated immunity in a sample of 306 healthy white-collar Japanese daytime employees. Findings from this study suggest that job satisfaction shows a dose-dependent relationship with NK cell markers and the relationship seems to be stronger in women than in men. Our finding provides some support for the biological plausibility of the well-established link between job satisfaction and health and well-being. However, additional research is needed to determine whether greater job satisfaction contributes to recovery/maintenance of NK cell immunity and host defense over time. Our findings, in conjunction with previously reported

Table 2a
Summary of hierarchical multiple linear regression analysis for the association between job satisfaction[a] and immune markers stratified by sex ($n = 141$ for women and $n = 165$ for men).

Immune marker (dependent variable)	Model 1[b]				Model 2[c]				Model 3[d]			
	Women		Men		Women		Men		Women		Men	
	β[e]	p	β[e]	p	β[e]	p	β[e]	p	β[e]	p	β[e]	p
Lg NKCC (% cytotoxicity)	.181	.040	.148	.062	.198	.038	.156	.072	.207	.029	.165	.050
Lg NK ($CD3^-CD56^+$) cells (cells/mm^3)	.250	.006	.152	.061	.257	.009	.131	.135	.261	.008	.142	.107
Lg B ($CD19^+$) cells (cells/mm^3)	.077	.363	−.015	.847	.066	.481	−.033	.709	.070	.499	−.031	.725
Lg Total T ($CD3^+CD56^-$) cells (cells/mm^3)	−.052	.568	.012	.878	−.051	.605	.023	.793	−.043	.669	.020	.817

[a] Positively oriented.
[b] Adjusted for age, education, smoking, alcohol consumption, physical activity, subjective sleep sufficiency, BMI, use of aspirin, and use of acetaminophen.
[c] Adjusted for age, education, smoking, alcohol consumption, physical activity, subjective sleep sufficiency, BMI, use of aspirin, use of acetaminophen, depressive symptoms (CES-D scale score), and intragroup conflict score.
[d] Adjusted for age, education, smoking, alcohol consumption, physical activity, subjective sleep sufficiency, depressive symptoms, BMI, use of aspirin, use of acetaminophen, depressive symptoms (CES-D scale score), intragroup conflict score, work hours, occupational grade, and company type.
[e] Standardized regression coefficients for each variable's unique contribution.

Table 2b
Multiple linear regression analyses with job satisfaction[a] as a dependent variable and immune markers and covariates as independent variables stratified by sex (n = 141 for women and n = 165 for men).

Job satisfaction (dependent variable)	Women		Men		Women		Men	
	β[b]	p	β[b]	p	β[b]	p	β[b]	p
Lg NKCC (% cytotoxicity)[c]	.198	.032	.162	.050				
Lg NK ($CD3^-CD56^+$) cells (cells/mm^3)[c]					.227	.007	.129	.108
Lg B ($CD19^+$) cells (cells/mm^3)	.007	.936	−.003	.975	−.012	.891	−.040	.623
Lg Total T ($CD3^+CD56^-$) cells (cells/mm^3)	.008	.934	.040	.625	.003	.971	.031	.702
Lg Age (years)	−.173	.205	.083	.414	−.168	.211	.094	.359
Education (years)	−.170	.344	−.054	.540	−.162	.358	−.056	.532
Smoking (numbers of cigarettes smoked/day)	−.174	.040	−.014	.884	−.202	.018	−.001	.990
Alcohol consumption (g ethanol/week)	.084	.332	−.109	.188	.076	.379	−.107	.198
Leisure−time physical activity (METs/week)	−.038	.633	−.027	.726	−.027	.730	−.016	.837
Subjective sleep sufficiency[d]	.156	.091	.205	.022	.171	.060	.187	.035
Lg BMI (kg/height $(m)^2$)	.104	.202	−.064	.421	.120	.135	−.060	.453
Use of aspirin (dummy variable, reference = no)	−.101	.226	−.072	.350	−.072	.384	−.063	.412
Use of acetaminophen (dummy variable, reference = no)	−.117	.178	.087	.273	−.133	.124	.086	.283
Lg Depressive symptoms (CES-D Scale score)	−.164	.059	−.050	.540	−.167	.051	−.028	.735
Interpersonal (intragroup) conflict at work	−.281	.001	−.386	<.001	−.272	.001	−.380	<.001
Occupational grade (dummy variable, reference = non-managerial)	.054	.513	.032	.749	.066	.417	.024	.811
Company type (dummy variable, reference = pharmaceutical)	−.083	.423	−.065	.473	−.072	.477	−.034	.699
Work hours/day (including overtime)	−.094	.276	.035	.678	−.074	.384	.038	.651
R^2	*.289*		*.253*		*.304*		*.246*	
Adjusted R^2	*.177*		*.154*		*.201*		*.146*	
F	*2.568*		*2.548*		*2.938*		*2.459*	
p Value	*.001*		*.001*		*<.001*		*.001*	

[a] Positively oriented.
[b] Standardized regression coefficients for each variable's unique contribution.
[c] NKCC and NK ($CD3^-CD56^+$) cells were separately integrated due to a high collenearity between the two.
[d] Subjective sleep sufficiency (1 = very insufficient, 2 = somewhat insufficient, 3 = fairly sufficient, 4 = very sufficient).

findings (Amati et al., 2010; Shirom et al., 2006; Theorell et al., 2000), indicate that job satisfaction may have the potency to result in a switch away from T helper 2 (Th2) immune response towards Th1 response as indicated by increased NK cell immunity and IFN-γ secretion, and reduced IL-6 and CRP secretion.

We found a consistent association between job satisfaction and NK cell markers, independent of a broad range of confounders. This finding is relevant to the epidemiological evidence that workers with reduced job satisfaction report a higher prevalence of common infection (Mohren et al., 2005) because NK cells appear to play a major role in killing virally infected cells (Whiteside and Herberman, 1994). Common infection is an important occupational health problem because it is the major cause of sickness absence in the workforce; the Whitehall II study indicated that respiratory disorders and gastroenteritis accounted for 50–60% of all spells of absence (Feeney et al., 1998). Results of the Maastricht cohort study suggested that workers who rated their level of job satisfaction as 'not good/moderate' had a 36% increased risk of being absent from work due to common infections compared to those reporting a 'good' satisfaction level (Mohren et al., 2005). The finding indicates that reduced job satisfaction may promote acquisition of infection or reactivation of latent infection (Glaser et al., 1999), which can result in increased sickness absence. Maintaining or regaining an appropriately higher level of NK cell immunity may have a protective effect on infection-related disorders.

The association between job satisfaction and NK cells may also relate to inflammatory disorders such as cardiovascular disease (CVD) because infection and chronic inflammation have been suggested as possible mediating mechanisms (Clays et al., 2005). Since job satisfaction represents a subjective evaluation of the working conditions as a whole and is relatively stable across time (Dormann and Zapf, 2001), its association with NK cells may persist unless employees cannot change working conditions causing job dissatisfaction. In this regard, employees with lowered job satisfaction coupled with reduced NK cell immunity may be more susceptibility to ubiquitous infectious agents such as *Cytomegalovirus*, *Helicobacter pylori,* and *Chlamydia pneumonia* which has been suggested both as a source of chronic inflammation and a potential risk factor of CVD in seroepidemiological studies (Gattone et al., 2001; Pasceri et al., 1998). Although the chronic infection-CVD relationship has yet to reach an universal agreement (Danesh et al., 2000), our result still opens a possibility that reduced job satisfaction increases susceptibility to infection by attenuating NK cell immunity, which may consequently contribute to inflammatory activity and hence to the development of CVD. Clearly, more evidence is needed to confirm this speculation.

No significant association between job satisfaction and total T ($CD3^+CD56^-$) or B ($CD19^+$) cells was found in this study. A recent study also reported a similar finding that job satisfaction does not correlate with numbers of T ($CD3^+$) or B ($CD19^+$) cells (Amati et al., 2010). There is a chance that function of T and B cells as represented by a proliferative response to mitogenic stimulation may be associated with job satisfaction but we conclude that the quantity of circulating T and B cells is not associated with job satisfaction.

Limited evidence is available which focused on the interaction of sex differences with work conditions on NK cells. Most studies examined men or women only (Boscolo et al., 2009; Morikawa et al., 2005; Nakata et al., 2000a) or both sexes combined (Amati et al., 2010; Cohen et al., 2007; Okamoto et al., 2008). A study which examined the effects of occupational stress on cell-mediated immune response in university/museum employees reported that those working under higher stress conditions had significantly lower NKCC than their lower stress counterparts but the effect was similar in both sexes (Di Donato et al., 2006). Although our analysis found a stronger association between job satisfaction and NK cells in women than in men, it seems contextual rather than biological with regard to sex differences of NK cell-related outcomes at this stage.

Although our study design was cross-sectional in nature, we assumed that job satisfaction predicts levels of NK cell immunity. However, it is also conceivable that immunologically healthier (in this case higher NK cell immunity) participants may express higher job satisfaction levels than those with poor NK cell immune

response. To test this alternative hypothesis, we adopted job satisfaction as a dependent variable and immune markers as independent variables in a hierarchical multiple linear regression analysis (Table 2b). We found that the opposite directionality is also true indicating a possibility that job satisfaction and NK cell response may have a reciprocal relationship. However, additional data is necessary to explore this possibility in a prospective study design.

This study has strengths and limitations that should be considered for the interpretation of the results. The study used a well-established measure of job satisfaction and controlled for a broad array of potential confounders with a large and relatively homogenous sample, i.e., white-collar healthy daytime Japanese employees working full-time, analyzed separately by sex. This way, the perception of job satisfaction within participants could be conceptually equivalent and the results may be at least generalized to this specific population. Limitations include the following. First, participants were employees from specific occupations and are not representative of the entire Japanese workforce or workers of other racial/ethnic groups. Second, we did not collect data on facets of job satisfaction that capture specific dimensions of job satisfaction. Measuring both global and facet job satisfaction could help us understand the relationship between job satisfaction and immunity in more detail. Third, the study was cross-sectional in nature; thus no causal interpretations can be made. Fourth, we could not control for menstrual phase or oral contraceptive use in women, which might have affected immunologic outcomes. Fifth, data on illness medical records were collected through self-report rather than medical diagnosis, which may introduce recall/reporting bias. Sixth, we did not measure cellular and inflammatory immune measures simultaneously, which limit the interpretation of our findings. Finally, although we adjusted for a variety of confounders, we could not exclude the possibility that unadjusted factors, i.e., personality traits, genetic components, anxiety, other work-related factors, and concurrent life stressors such as marital discord, work-family conflict, interpersonal difficulties outside work, health problems, financial difficulties, as well as unknown third factor(s) which could affect both the dependent and independent variables may explain the present findings.

With these limitations in mind, this study suggested that job satisfaction shows a dose-dependent relationship with NK cell immunity, which provides some support for the psychoimmunologic plausibility of a job satisfaction-health relationship. Because the effect sizes between job satisfaction and NK cells observed in this study ($.131 \leqslant |r| \leqslant .261$) were comparable or even greater than that of the meta-analytic association of chronic stress with NKCC ($|r| = .12$) and NK cell numbers ($|r| = .14$) (Segerstrom and Miller, 2004), examination of NK cell markers in relation to job satisfaction may be a promising approach in occupational health psychoimmunology. Future studies should test mechanistic causal associations between job satisfaction, NK cells, inflammatory markers, and long-term health including immune-mediated susceptibility to the common cold and/or reactivation of latent viruses that, together, could contribute to absenteeism and lost productivity in the workplace.

5. Disclaimer

The findings and conclusions in this report are those of the author(s) and do not necessarily represent the views of the National Institute for Occupational Safety and Health, USA.

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