phenomenon. However, this study opens a new door to explore brain neurocircuit in the processing and control of visceral perception.

In this study, reasonable pain reduction was associated with a decrease in CEP amplitude. In many studies, great care is taken to prevent subjective factors from causing bias. However, for visceral perception during hypnotic modulation only few objective measures have been reported. Previous studies on CEP following gastrointestinal stimulation have showed that recording of CEP is a reliable and reproducible method for studying gastrointestinal sensory pathways.[15,16] In addition, Our previous studies have shown that as stimulation intensity and sensory perception increase, the latency of CEP components shortens and their amplitude increases.[17–19] This phenomenon is common across all evoked potential modalities and reflects the recruitment of an increasing number of afferents with faster conduction velocity.[25] The fact that analgesic suggestion reduced CEP amplitude with a concomitant decrease in subjective sensations to rectal stimulation provides evidence of the high inducibility of adaptive modulation of visceral perception via a functional module of the brain. On the other hand, hyperalgesic suggestion induced changes in subjective ratings of perception which well correlated with CEP changes. However, all CEP components did not always change significantly. These results suggest that the hyperalgesic effect on verbal responses was more dependent on the cortico-cortical modulation rather than the activations of afferent pathways.[26]

Previous studies of evoked potentials in other sensory systems have shown that an increase in evoked potential amplitude can occur either due to an increase in excitability of the afferent pathways or via an inhibition of the descending pain inhibitory system.[27,28] Previous studies examining brain activity during pain modulation by suggestion-induced expectation confirm that increased activity were found in brain areas controlling descending inhibitory systems, but may not in brain areas receiving ascending nociceptive input.[3] The descending pain modulatory system is well characterized as anatomical network that enables us to regulate nociceptive processing (largely within the dorsal horn) in various circumstances and produce either facilitation (pronociception) or inhibition (antinociception).[25] Signals of EEG can well document this type of inhibitory control in humans.[29–31] In our study, analgesic suggestion may have induced a certain expectation of decreased pain and probably induced increased activity of the inhibition components of the descending pain modulatory system, as well as top–down pain control. Such change would allow reduction in CEP P1–N2 amplitude but not delay in CEP latencies. Our findings provide the first evidence that hypnotic modulation can alter visceral perception by changing electrophysiological properties in time-window of 200–300 ms following visceral stimulation in the human brain.

In this study, the modulatory effects of analgesic suggestion on brain processing of visceral perception were proved to be at least in part dependent on histaminergic neurons. This is a great advantage of this study because identification of the controlling molecule of suggestion and pain will produce further understanding of the central control of pain. Peripheral histamine is involved in stimulation of nociceptive fibres.[10–13] Clinically, antihistamines are empirically administered to expect augmented antinociception in para-anaesthetic medication. On the other hands, central histamine has both analgesic[12,32–34] and algesic[11,13,35,36] effects. It has emerged that central histamine plays an important role in antinociception.[37] The evidence supporting antinociceptive (but not pronociceptive) action of central histamine can be summarized as follows: (i) histamine, when applied into the cerebral ventricles or PAG, has an analgesic effect in several paradigms including the tail-flic and hot-plate tests;[12,32–33] and (ii) H_1 and/or H_2 receptor antagonists block central histamine-mediated antinociception. Both H_1 and H_2 receptor antagonists when applied intracerebrovenricularly or into the PAG, have been shown to block central histamine-induced antinociception.[32–34] The descending histaminergic neurons originate from the hypothalamus and terminate at the PAG and the dorsal horn of the spinal cord.[9] In addition, in human brain, the highest H_1R binding sites are in the limbic system and the cerebral cortex (especially prefrontal, temporal and cingulate regions).[38] The descending influences from prefrontal cortex that elicit inhibition of nociceptive transmission are being identified in different behavioural circumstances; such as during hypnotic or placebo suggestions. In this study, administration of H_1R antagonist to the healthy subjects clearly reversed analgesic suggestion-induced reduction in P1 amplitude and subjective visceral pain. Therefore, during hypnotic suggestion in human, the H_1R blockage might inhibit the descending inhibitory control via deactivation of histamine neurons in fronto-cingulate regions.

In this study, the H_1R blockage resulted in the overall shortening of CEP latencies. Attenuation of the endogenous components of CEP results in the overall shortening of CEP latencies.[31] The highest histamine H_1 binding sites are in the limbic system and the

cerebral cortex.[38] Therefore, in human brain, the H_1R blockage might attenuate the endogenous components of CEP via deactivation of histamine neurons in cerebral cortical regions.

In conclusion, we could prove the hypothesis that hypnotic suggestion modulates brain processing of visceroafferent signals recorded by CEP. We have also shown in this study that blockage of the H_1 reduces analgesic effects of hypnotic suggestion in healthy normal subjects.

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Marital status and non-small cell lung cancer survival: the Lung Cancer Database Project in Japan

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Abstract

***Objective*: Previous studies have suggested that marital status is associated with survival from lung cancer; however, its association is not conclusive. The association between marital status and survival in Japanese patients with non-small cell lung cancer (NSCLC) was prospectively investigated.**

***Methods*: Between July 1999 and July 2004, a total of 1230 NSCLC patients were enrolled. The baseline survey consisted of the collection of clinical information and various demographic data, including marital status. A Cox regression model was used to estimate the hazards ratio (HR) of all-cause mortality adjustments for age, BMI, education level, performance status, histology type, clinical stage, smoking status, choice of definitive treatment, and depression.**

***Results*: The multivariable adjusted HR of male widowed patients versus male married patients was 1.7 (95% confidence interval = 1.2 – 2.5, $p = 0.005$). However, no significant increased risk of death in female widowed patients compared with female married patients was observed (HR = 0.7, 95% confidence interval = 0.5 – 1.1, $p = 0.15$). With regard to separated/divorced and single patients no significant increased risk of death in male and/or female compared with married patients was observed.**

***Conclusions*: The present data suggest that male widowed patients with NSCLC have a higher mortality rate than male married patients with NSCLC, after controlling for various factors.**

Keywords: marital status; non-small cell lung cancer; prospective study; survival

Introduction

Lung cancer is among the most common forms of cancer and is the most common cause of cancer-related death in the world [1,2]. Many studies have suggested that marital status is associated with survival from lung cancer; however, its association is not conclusive. Having a spouse die can significantly increase a person's risk of death; this 'widow/widower effect' is especially pronounced in men [3–6]. Therefore, the association between marital status and lung cancer survival should be clarified according to sex and subdivided marital status, such as married, widowed, separated/divorced, or single. However, only two studies have examined the association between marital status and lung cancer survival according to sex and subdivided marital status [7,8]. One study suggested that separated/divorced, single, and widowed patients had a higher risk of death compared with married patients, for both sexes [7]. The other one found no association between marital status and survival among divorced and widowed patients [8]. However, these studies were limited by small sample sizes [8] and a lack of differentiation between small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) [7,8].

Possible associations between marital status and survival from lung cancer may be mediated by several factors. An unmarried status has been associated with an increased frequency of unhealthy life-style behaviors (especially with regard to smoking habits), maladjustment to the cancer diagnosis (especially among subjects who continue smoking even after they have been diagnosed as having cancer), psychological reactions (especially depression), delays in seeking treatment (more

advanced stages at the time of cancer diagnosis), and a lower likelihood of receiving definitive treatment [9–18]. However, previous studies did not consider these variables and did not clarify the effects of each factor on the associations between marital status and sex-specific survival from NSCLC.

In this prospective study, we investigated the influence of marital status on survival in patients with NSCLC in Japan. We were able to evaluate survival according to each sex and marital status in view of potential confounding factors and to clarify the effects of each modifying factor, such as smoking habits, psychological reactions, delays in seeking treatment, and likelihood of receiving definitive treatment, on the associations between marital status and survival. If several intermediate factors are provided, the physician could suggest possible means of improving the prognosis to their patients.

Methods

Participants

The design of this study, which was included as part of The Lung Cancer Database Project in Japan, has been reported in detail elsewhere [19]. Briefly, consecutive newly diagnosed lung cancer patients were invited to participate in the study, which was conducted at the Thoracic Oncology Division, National Cancer Center Hospital East, Kashiwa, Japan. Patients were included in the database study if they met all of the following criteria: informed of their lung cancer diagnosis; newly diagnosed patients with primary lung cancer; physically capable of completing the questionnaires; absence of cognitive impairment, such as dementia and delirium; ability to provide written consent; and no problems regarding the patients' participation in this project, as judged by their physicians.

In total, the project was explained to 2506 patients, and 2036 (81.3%) patients with newly diagnosed, untreated primary lung cancer were admitted during the project enrolment period. A total of 470 cases were ineligible for the following reasons: could not be contacted (49 cases), lung cancer diagnosis not confirmed at the time of admission (175 cases), non-lung cancer (120 cases), poor physical state (77 cases), refusal to participate in the project (43 cases), treated for lung cancer at another hospital (5 cases), and not yet informed of the diagnosis (1 case). For 40 of the 2036 patients, written informed consent could not be confirmed, and one patient withdrew consent during the follow-up period. Finally, the analyzed cohort consisted of 1995 patients.

As a result, the analytic cohort consisted of 1995 patients who were enrolled in the study between July 1999 and July 2004. The study protocol was approved by the institutional review board of the National Cancer Center, Japan. Each patient was fully informed of the purpose of the study before obtaining written consent and prior to participation in the study.

Exposure data

The patients completed the questionnaires during the waiting period prior to admission, and the questionnaires were collected after the patients were admitted. Questionnaires on demographic data and health habits (excluding the questionnaires on psychological factors) were distributed to all patients who had been registered by July 2004. Questionnaires on psychological factors were distributed only to patients who had registered by July 2003.

Demographic factors (age at cancer diagnosis, sex, education level, marital status, body mass index [BMI], smoking status, past history of cancer) and medical information (histology, clinical stage, PS, and first treatment) were obtained from the self-administered questionnaires and the patients' medical charts. PS was assessed by each attending physician using the Eastern Cooperative Oncology Group criteria [20].

To examine patient characteristics associated with variations in best-treatment practices, we defined, *a priori*, the minimally recommended initial therapies for each cancer stage at the time of diagnosis. As a practical matter, therapy for lung cancer is mainly decided, which take into account not only clinical stage but also age, comorbid illness, organopathy, and physical status. For the purposes of this analysis, the determination of the recommended therapies was based on pertinent information from medical literature published before 2004, including both randomized trials and meta-analyses of randomized trials, as well as the definitions of accepted therapy reflected in the Japan Lung Cancer Society clinical practice guidelines for the treatment of lung cancer, published in 2005 [21]. For tumor-node metastasis system stages I, II, and IIIA N0-1 surgical resection was considered the recommended initial therapy. For stage IIIA N2 patients, combination chemoradiotherapy was defined as the recommended therapy. For stage IIIB patients, combination chemoradiotherapy or chemotherapy alone was defined as the recommended therapy. For patients with stage IV disease, chemotherapy alone was considered the recommended therapy.

Depression symptoms were evaluated using the depression subscale of the Hospital Anxiety and Depression Scale (HADS) [22]. The HADS has

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been used as a reliable and valid method of screening for depression in patients with cancer. Each item is rated on a scale of 0–3, with higher scores denoting a greater mood disturbance. The reliability and validity of the Japanese version of this questionnaire has been established in Japanese cancer patients [23]. The present study used a cutoff point of four out of five [23].

Follow-up

In order to follow up the subjects for vital status, confirmation was made by medical records, normal postal mail, and municipality registration data. The survival of subjects was followed from July 1999 to December 2004. The psychological questionnaire was only distributed to the patients who had registered by July 2003. In this study, we analyzed the subject who answered psychological questionnaire. Out of the remaining 1995 patients, 414 patients were excluded from the analysis because of lack of psychological questionnaires. A total of 351 cases were excluded from the analysis for the following reasons: double cancer (188 cases) or SCLC (163 cases). Finally, 1230 patients were included in the subsequent analyses.

The person-months of follow-up were counted for each subject from the date of enrollment in the study until death or the end of the study period (December 2004), whichever occurred first, and a total of 31 508 person-months (median, 24 months; range, 0–67 months) were accrued. During the follow-up period, 716 deaths from all causes were identified.

Statistical analysis

All statistical analyses were performed according to sex. Standard descriptive statistics were used to characterize the marital status. Thus, marital status was categorized into married, widowed, separated/divorced, and single. Intergroup comparisons of categorical and continuous variables were performed using chi-square tests and one-way analyses of variance, respectively. Hazard ratios (HRs) were computed as the number of deaths from all causes among the subjects in each marital status category versus the number of deaths from all causes among the respective reference category (married patients). A Cox proportional-hazards regression analysis was conducted to adjust for age at the time of cancer diagnosis, BMI in kg/m^2 (<18.5, >18.5, or unknown), education level (college/university or higher, or not), PS (0, 1, or 2–4) histological type (adenocarcinoma, squamous carcinoma, large, or other), smoking status (never-smoker, ex-smoker, or current smoker), clinical stage (IA–IIB, IIIA–IIIB, or IV), HADS depression score (<5, $\geqslant 5$, or unknown), and choice of cancer treatment (definitive treatment or non-definitive treatment) using the SAS PHREG procedure included in the SAS version 8.2 statistical software package (Cary, NC, USA). The assumption of proportional hazards was verified graphically. In all the statistical evaluations, p-values of less than or equal to 0.05 were considered to denote a significant difference. All p-values were two-tailed.

In secondary analyses, we also conducted stratified analyses to examine factors that markedly modified the associations between marital status and survival, such as smoking status, clinical stage, HADS-depression, or definitive treatment.

Results

The mean age of the subjects was 63.9 years, and the percentage of men was 70%. The proportions of married, widowed, separated/divorced, and single patients were 84, 9, 4, and 3%, respectively. The mean age differed significantly according to marital status for both male and female patients (Table 1). Moreover, the smoking status also differed significantly according to marital status for both male and female patients. In women, BMI, histology, and definitive treatment differed significantly according to marital status. No significant associations between marital status and any other variables were seen.

According to the univariate Cox proportional-hazards regression analyses, six demographic or clinical variables were significantly associated with increased HRs of lung cancer survival for male and female subjects versus their respective reference categories: BMI (<18.5), smoking status (ex-smoker and current smoker), clinical stage (IIIA–IIIB or IV), PS (1 or 2–4), histology type (squamous cell carcinoma or large cell carcinoma), definitive treatment (non-definitive), and HADS depression score ($\geqslant 5$) (Table 2).

Table 3 shows the HRs for lung cancer survival according to marital status. A univariate Cox proportional-hazards regression analysis showed no significant association between survival and marital status for male and female subjects (Table 3). These findings remained basically unchanged even after multivariate adjustments for age, BMI, education level, PS, histology type, clinical stage, smoking status, choice of definitive treatment, and HADS depression score. For male patients, however, a multivariate Cox proportional-hazards regression analysis showed a significant association between survival and marital status. The multivariable adjusted HRs of widowed, separated/divorced, and single patients versus married patients were 1.7 (95% confidence interval (CI), 1.2–2.5; $p = 0.005$), 1.1 (0.7–1.7; $p = 0.72$), and 0.9 (0.5–1.5; $p = 0.61$), respectively.

Table 1. Demographic, medical, and psychological characteristics in NSCLC patients to marital status

	Male				Female			
	Marital status				Marital status			
	Married	Widowed	Separate/ divorced	Single	Married	Widowed	Separate/ divorced	Single
No. of subjects	774	41	26	24	262	72	19	12
Demographic characteristics								
Mean age in years (SD)	64.3 (8.9)	70.5 (8.3)	62.7 (8.4)	50.0 (10.1)	61.9 (9.3)	69.6 (8.2)	59.6 (8.1)	59.7 (14.6)
Body mass index (kg/m^2) (%)								
<18.5	11	10	12	8	8	3	26	25
$\geqslant 18.5$	88	90	85	92	91	96	74	75
Unknown	1	0	4	0	1	1	0	0
Duration of education (%)								
>15 yr	23	20	27	29	6	4	0	17
$\leqslant 15$ yr	77	78	73	71	94	96	100	83
Unknown	1	2	0	0	0	0	0	0
Smoking status (%)								
Never-smoker	4	0	0	25	76	71	42	58
Ex-smoker	33	44	23	4	7	11	16	8
Current smoker	62	56	77	71	17	18	42	33
Medical characteristics								
Clinical stage[a] (%)								
IA–IIB	44	44	38	25	57	71	53	50
IIIA–IIIB	29	39	42	29	18	10	26	8
IV	27	17	19	46	25	19	21	42
Performance status[b] (%)								
0	39	39	27	21	56	63	47	50
1	55	59	65	79	39	36	42	42
2–4	6	2	8	0	5	1	11	8
Histology type (%)								
Adenocarcinoma	57	49	62	67	86	88	68	75
Squamous cell carcinoma	28	44	35	25	8	6	26	17
Large cell carcinoma	12	7	0	8	6	7	5	0
Other	3	0	4	0	1	0	0	4
Definitive treatment (%)								
Definite	85	85	73	83	91	94	74	83
Non-definitive	15	15	27	17	9	6	26	17
Psychological characteristics								
HADS depression (%)								
<5	42	37	23	54	43	44	47	50
$\geqslant 5$	53	51	69	38	54	51	47	42
Unknown	5	12	8	8	3	4	5	8

[a] Defined by TNM classification: International Union Against Cancer.
[b] Defined by Eastern Cooperative Oncology Group (ECOG).

For female patients, however, a multivariate Cox proportional-hazards regression analysis showed no significant association between survival and marital status. The multivariable HRs of widowed, separated/divorced, and single patients versus married patients were 0.7 (0.5–1.1; $p = 0.15$), 0.5 (0.3–1.1; $p = 0.10$), and 1.2 (0.5–2.7; $p = 0.71$), respectively.

In addition, we conducted an effect modification analysis to assess the effects of clinical stage, smoking status, choice of definitive treatment, and HADS depression score on the relationship between marital status and survival in male widowed patients. All of these factors had no significant effect on the association between male widowed patients and survival ($p > 0.05$ for all variables).

No survival differences were seen between married and unmarried (including widowed, separated/divorced, and single) patients. The multivariable adjusted HR of unmarried patients versus married patients was 1.0 (0.8–1.2; $p = 0.91$).

Discussion

In this prospective study conducted in Japan, a significant association was found between marital status and survival in male patients with NSCLC. Male widowed patients had a higher mortality risk

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Table 2. Results of univariate analysis for survival from lung cancer

	Male				Female			
	No. of subjects	Person-months median (range)	Cases	Univariate HR (95% CI)	No. of subjects	Person-months median (range)	Cases	Univariate HR (95% CI)
No. of subjects	865	21.6 (0.6–66.3)	548		365	26.8 (0.5–66.7)	168	
Demographic characteristics								
Age								
<49	58	20.5 (0.9–64.4)	38	1.0 (referent)	30	25.7 (1.8–56.7)	16	1.0 (referent)
50–59	193	21.8 (1.7–65.7)	125	1.0 (0.7–1.5)	95	28.1 (2.9–66.1)	42	0.7 (0.4–1.3)
60–69	350	20.7 (0.8–65.9)	221	1.0 (0.7–1.5)	136	28.2 (1.9–66.7)	63	0.8 (0.4–1.3)
70<	264	22.1 (0.6–66.3)	164	0.9 (0.7–1.4)	104	26.7 (0.5–63.7)	47	0.8 (0.4–1.4)
Body mass index (kg/m^2)								
⩾18.5	765	22.1 (0.6–66.3)	469	1.0 (referent)	330	27.3 (0.5–66.7)	146	1.0 (referent)
<18.5	93	14.4 (0.8–66.3)	73	1.6 (1.2–2.0)	31	18.6 (3.7–62.8)	20	1.9 (1.2–3.0)
Unknown	7	15.7 (5.6–58.6)	6	1.6 (0.7–3.6)	4	25.7 (11.7–30.7)	2	1.4 (0.3–5.5)
Duration of education								
>15 yr	197	20.3 (0.9–65.8)	122	1.0 (referent)	22	29.3 (3.4–45.2)	6	1.0 (referent)
⩽15 yr	661	21.9 (0.8–66.3)	423	0.9 (0.8–1.2)	343	26.7 (0.5–66.7)	162	1.8 (0.8–4.0)
Unknown	7	29.7 (0.6–63.9)	3	0.7 (0.2–2.3)	0	—	0	—
Smoking status								
Never-smoker	39	28.4 (2.4–63.9)	18	1.0 (referent)	265	28.3 (0.9–66.7)	110	10 (referent)
Ex-smoker	283	21.3 (0.8–66.3)	179	1.6 (0.9–2.6)	34	26.7 (0.5–54.8)	15	1.1 (0.7–1.9)
Current smoker	543	20.3 (0.6–66.3)	351	1.7 (1.1–2.8)	66	22.1 (1.8–63.6)	43	2.0 (1.4–2.9)
Medical characteristics								
Clinical stage[a]								
IA, IB, IIA, IIB	371	34.2 (3.1–66.3)	121	1.0 (referent)	216	35.2 (0.9–66.7)	45	1.0 (referent)
IIIA, IIIB	259	16.1 (0.6–65.9)	201	4.1 (3.3–5.2)	61	23.1 (3.2–65.6)	46	6.1 (4.0–9.3)
IV	235	8.0 (0.8–63.8)	226	9.8 (7.8–12.3)	88	11.3 (0.5–62.1)	77	12.0 (8.2–17.7)
Performance status[b] (%)								
0	336	29.7 (3.1–66.3)	140	1.0 (referent)	207	33.9 (0.9–66.7)	51	1.0 (referent)
1	482	15.6 (0.8–66.3)	363	2.8 (2.3–3.4)	141	21.5 (2.4–66.1)	100	4.2 (2.9–5.9)
2–4	47	4.1 (0.6–25.2)	45	12.7 (8.9–17.9)	17	5.7 (0.5–23.2)	17	28.9 (16.1–52.0)
Histology type								
Adenocarcinoma	490	23.0 (0.6–66.3)	306	1.0 (referent)	309	27.9 (0.5–66.7)	130	1.0 (referent)
Squamous cell carcinoma	252	20.7 (0.9–66.3)	157	0.9 (0.8–1.2)	32	24.9 (3.4–60.8)	23	2.2 (1.4–3.4)
Large cell carcinoma	99	14.6 (1.4–65.8)	72	1.4 (1.0–1.8)	21	22.5 (2.9–61.9)	14	1.8 (1.0–3.1)
Other	24	29.0 (2.8–65.6)	13	0.8 (0.4–1.3)	3	29.7 (22.9–57.6)	1	0.7 (0.1–4.8)
Definitive treatment								
Definitive	733	23.0 (0.8–66.3)	445	1.0 (referent)	331	27.9 (0.9–66.7)	140	1.0 (referent)
Non-definitive	132	10.1 (0.6–65.9)	103	1.9 (1.5–2.3)	34	12.9 (0.5–56.7)	28	3.2 (2.1–4.8)
Psychological characteristics								
HADS depression								
<5	452	23.5 (0.9–66.3)	265	1.0 (referent)	189	28.7 (0.9–66.7)	71	1.0 (referent)
⩾5	364	16.7 (0.8–65.9)	251	1.3 (1.1–1.6)	163	25.1 (0.5–66.1)	89	1.7 (1.2–2.4)
Unknown	49	24.4 (0.6–60.6)	32	1.1 (0.8–1.6)	13	38.6 (4.9–60.9)	8	1.6 (0.8–3.4)

[a] Defined by TNM classification: International Union Against Cancer.
[b] Defined by Eastern Cooperative Oncology Group (ECOG)

than male married patients. Our study had some methodological advantages over previous studies in that we were able to take into account differences in sex and marital status as well as potential modifying factors, such as smoking status, psychological variables, choice of definitive treatment, and disease stage at the time of diagnosis. The present study indicates that these potential modifying factors did not participate in association between marital status and survival in male patients with NSCLC. Further examinations are needed to clarify the details of this association.

Of the three studies that examined the association between marital status and lung cancer survival according to sex and subdivided marital status [7,8]. Kravdal [7] followed up SCLC and NSCLC patients (number of patients were not specified) and documented 15 882 deaths in males and 3944 deaths in females. Single female patients had a higher risk of death than married patients. Lastly, Kvikstad *et al.* [8] followed up 333 female married, divorced, and widowed cases of SCLC and NSCLC for 6 years, revealing 268 deaths. No significant associations were found between marital

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Table 3. Hazard ratios (HR) of cancer survival according to the marital status

	Male				Female				Total			
	Married	Widowed	Separate/ divorced	Single	Married	Widowed	Separate/ divorced	Single	Married	Widowed	Separate/ divorced	Single
No. of subjects	774	41	26	24	262	72	19	12	1036	113	45	36
Person-months of follow-up	21.8 (0.6–66.3)	17.0 (2.5–57.9)	23.7 (0.9–65.9)	19.1 (3.0–65.1)	26.5 (0.5–66.7)	30.5 (4.4–63.6)	28.1 (5.9–62.2)	23.6 (5.2–50.2)	23.6 (0.5–66.7)	25.9 (2.5–63.6)	27.2 (0.9–65.9)	21.0 (3.0–65.1)
No. of death from all causes	481	31	20	16	121	31	9	7	602	62	29	23
Unadjusted HR	1.0 (referent)	1.4 (0.9–1.9)	1.3 (0.8–2.0)	1.1 (0.7–1.9)	1.0 (referent)	0.9 (0.6–1.3)	0.9 (0.5–1.8)	1.8 (0.9–3.4)	1.0 (referent)	0.9 (0.7–1.1)	1.1 (0.7–1.5)	1.2 (0.8–1.8)
p-Value		0.08	0.26	0.62		0.45	0.84	0.23		0.32	0.77	0.39
Multivariable adjusted HR1	1.0 (referent)	1.4 (0.9–2.1)	1.1 (0.7–1.7)	1.1 (0.7–1.9)	1.0 (referent)	0.8 (0.5–1.3)	0.7 (0.3–1.4)	1.8 (0.8–3.9)	1.0 (referent)	0.9 (0.7–1.3)	0.9 (0.6–1.3)	1.2 (0.8–1.8)
p-Value		0.06	0.81	0.69		0.43	0.27	0.17		0.81	0.57	0.52
Multivariable adjusted HR2	1.0 (referent)	1.7 (1.2–2.5)	1.1 (0.7–1.7)	0.9 (0.5–1.5)	1.0 (referent)	0.7 (0.5–1.1)	0.5 (0.3–1.1)	1.2 (0.5–2.7)	1.0 (referent)	1.1 (0.9–1.5)	0.9 (0.6–1.3)	0.9 (0.6–1.4)
p-Value		0.005	0.72	0.61		0.15	0.10	0.71		0.41	0.42	0.65

HR1: age, BMI, education, PS, and histology type adjusted.
HR2: age, BMI, education, PS, histology type, smoke stage, definitive treatment, and HADS-depression adjusted.

status and survival among female divorced and widowed patients. The present study showed no significant association between marital status and survival when male and female patients were examined as a single group. On the other hand, when the subjects were divided into male and female patients, only the male widowed patients had a higher mortality risk than the male married patients. Having a spouse die significantly increases a person's risk of death in the general population, and this 'widow/widower effect' is especially pronounced in men [3–6]. In the present study, the findings for male patients with NSCLC are consistent with these previous results.

Possible associations between marital status and survival may be mediated by several factors. An unmarried status has been associated with an increased frequency of smoking, depression, advanced disease stage at the time of diagnosis, and a lower likelihood of receiving definitive treatment [9–13,15–18]. Previous studies did not consider possible modifying factors' effects to examine differences in sex and marital status [7,8]. Therefore, it is not clarified why single, separate/divorced, and widowed patients have a higher mortality compared with married patients. This is the first study to examine differences in sex and subdivided marital status as well as the effects of potential modifying factors, such as smoking status, psychological variables, choice of definitive treatment, and disease stage at the time of diagnosis, on the association between marital status and survival from NSCLC. In the present study, smoking status, disease stage at the time of diagnosis, choice of definitive treatment, and the HAD depression score did not have a significant modifying effect on the relationship between male widowed patients and survival. Thus, smoking status, disease stage at the time of diagnosis, choice of definitive treatment, and the HAD depression score might not have a major impact on the association between marital status and survival. However, an unmarried status has been associated with an increased chance of the patient continuing to smoke even after a diagnosis of cancer has been made [12]. The continuation of smoking even after a diagnosis of cancer has been made is known to be significantly associated with survival [12,14]. In this study, we could not evaluate this association because information on smoking continuation after cancer diagnosis was not available.

Our study had several limitations. First, the study was performed at a single National Cancer Center. Whether our results can be generalized to reflect other institutions remains unclear. Thus, further studies performed at multiple institutions are necessary to clarify the prognostic effects of marital status on the survival of lung cancer patients. Second, in this study the subjects were only NSCLC patients. Histological classification of

the lung cancers in our database at the National Cancer Center Hospital East (NCCHE), Japan, revealed that small cell carcinomas were much less common (11%) than NSCLC (89%); other reports have suggested that these cancers account for nearly 80 and 20% of all lung cancers, respectively [24]. Moreover, NSCLC and SCLC differ in terms of their prognosis as well as the therapeutic strategies employed [25]. Therefore, we clarified the association between marital status and survival using a homogeneous group, focusing only on NSCLC patients. Third, data on unhealthy lifestyle behaviors after a cancer diagnosis had been made were unavailable. An unmarried status has been associated with an increased frequency of maladjustment to the cancer diagnosis (especially among subjects who continue to smoke even after they have been diagnosed as having cancer) [12]. There is some possibility that the association between marital status and survival may be mediated by this factor. If data on unhealthy lifestyle behaviors after cancer diagnosis were made available, then the mechanism responsible for the association between marital status and survival could be clarified, and the physician could suggest possible means to improve the prognosis to their cancer patients.

In conclusion, our data indicated that marital status might influence survival among male widowed NSCLC patients in Japan. The present results indicate that potential modifying factors, such as smoking status, disease stage at the time of diagnosis, choice of definitive treatment, and the HAD depression score, did not participate in association between marital status and survival in male patients with NSCLC. Further research on marital status and survival in male patients with NSCLC within the potential modifying factors such as continued smoking and including a large population is needed to clarify the details of this association.

Conflict of interest

None of the authors have any conflict of interest with any aspect of submitting this article for publication.

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Personality and body mass index: A cross-sectional analysis from the Miyagi Cohort Study

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Abstract

Objective: Obesity is an increasingly prevalent public health problem worldwide, and is associated with a higher risk of developing various noncommunicable diseases. To further examine the association between personality and overweight, obesity, or underweight, we conducted a cross-sectional analysis in Japan. We hypothesized that extraversion and psychoticism would have a positive association with overweight, and that neuroticism and lie would have an inverse association with overweight, whereas the association between personality and underweight would be the reverse image of overweight. **Methods:** In 1990, 30,722 subjects (40–64 years of age) completed a self-administered questionnaire including body weight and height and the Japanese version of the Eysenck Personality Questionnaire-Revised Short Form. Multivariate logistic regression analysis was used to calculate odds ratios for overweight [body mass index (BMI)≥25.0 kg/m^2] or underweight (BMI<18.5) relative to each category on the personality subscale. **Results:** In men and women, extraversion and psychoticism had positive associations with overweight, whereas neuroticism had an inverse association. Lie had an inverse association with overweight in men. In men and women, only extraversion had an inverse association with underweight and neuroticism had a positive association with underweight. **Conclusion:** Our findings indicate that personality is associated with both overweight and underweight. These results may provide clues to devising more effective measures for preventing overweight, obesity, or underweight or for weight control intervention.

Keywords: Adults; Japanese; Overweight; Personality; Underweight

Introduction

Obesity is an increasingly prevalent public health problem worldwide, and is associated with a higher risk of developing various noncommunicable diseases [1,2]. In Japan, the proportion of individuals who are overweight [body mass index (BMI)≥25.0] has been increasing in men of all ages and in elderly women, whereas the proportion of underweight (BMI<18.5) individuals has been increasing in women aged 20–49 years [3].

There have been a number of studies of interventions for preventing or controlling excess weight or obesity [4,5]. These interventions included physical activity, dietary pattern, pharmacological or behavioral therapy, or a variety of their combinations [5]. In practical terms, such obesity treatment programs may produce a wide range of responses

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in terms of both the magnitude and rate of weight changes due to differences in physiological and psychological factors among individuals [6]. A previous study has suggested that psychological aspects should be considered in weight loss strategies for obesity management [7]. Jonsson et al. [7] found that some psychological aspects were able to predict weight loss outcome 1 year after the end of their treatment in 28 obese patients.

Although consideration of personality in interventions for weight control is of potential importance, the psychological correlates and causes of overweight or obesity remain unclear [8]. To date, three reported cross-sectional studies have examined the association between the subscales of the Eysenck Personality Questionnaire (EPQ) and obesity. In the four subscales of EPQ, extraversion represents sociability, liveliness, and surgency; neuroticism represents emotional instability and anxiousness; psychoticism represents tough-mindedness, aggressiveness, coldness, and egocentricity; and lie represents unsophisticated dissimulation and social naivety or conformity [9]. Among previous studies, two found a positive association between extraversion and obesity [10,11], but Faith et al. [12] reported an inverse association in women and a positive association in men. With regard to the association between neuroticism and obesity, one study found an inverse association [10], one found no association [11], and one found a positive association in women and no association in men [12]. Only one study referred to the association between psychoticism and obesity, and reported a positive association in men but no association in women [12]. In contrast, two studies reported no association between the subscales of EPQ (extraversion and neuroticism) and underweight [13,14]. Furthermore, all of these studies were conducted in Western countries, and there is no report from Asian countries, where the prevalence of overweight, obesity, or underweight differs considerably from that in Western populations.

To further examine the association between personality and overweight, obesity, or underweight, we conducted a cross-sectional analysis in Japan. We hypothesized that extraversion and psychoticism would have a positive association with overweight and that neuroticism and lie would have an inverse association with overweight, whereas the association between personality and underweight would be the reverse image of overweight. Such a population would provide an opportunity to examine the association between personality and overweight as well as underweight.

Research methods and procedures

Study population

We analyzed cross-sectional data from a baseline survey conducted for the Miyagi Cohort Study. We have already reported the design of this prospective cohort study in detail elsewhere [15]. Briefly, we delivered two self-administered questionnaires to all 51,921 residents aged 40–64 years living in 14 municipalities of Miyagi Prefecture in rural northern Japan from June through August 1990. The first questionnaire asked about various health-related habits, and the second was the Japanese version of the EPQ-Revised (EPQ-R) Short Form [16]. The questionnaires were delivered to, and collected at, the subjects' residences by members of health promotion committees appointed by the municipal governments. The response rate for the first questionnaire was 91.7% (n=47,605), and that for the second questionnaire among the respondents to the first was 87.0% (n=41,424). We considered the return of self-administered questionnaires signed by the subjects to imply their consent to participate in the study. The study protocol was approved by the Institutional Review Board of Tohoku University Graduate School of Medicine.

Of the 41,424 subjects who responded to the two questionnaires, we excluded 54 subjects who responded "yes" or "no" to each of the 48 items and 8600 subjects for whom responses to any of the 48 items in the EPQ-R were missing. We further excluded 1133 subjects who had incomplete responses for body weight or height information. Because Nakaya et al. [17] reported that a neurotic tendency among subjects with a prevalence of cancer may have been a consequence, rather than a cause, of having been diagnosed with cancer, 915 subjects who had entered a history of cancer, stroke, or myocardial infarction in the self-reported questionnaire were further excluded. Finally, 30,722 subjects were used for the final analysis.

Measurement

Personality was measured using the Japanese version of the EPQ-R Short Form, one of a series of personality inventories developed by Eysenck and Eysenck [18]. The EPQ-R Short Form has 48 questions with dichotomized responses (yes or no); there are 12 questions for each of the four personality subscales (extraversion, neuroticism, psychoticism, and lie). Scores on each subscale range from 0 to 12, with higher scores indicating a greater tendency to possess the personality trait represented by each subscale. Extraversion represents sociability, liveliness, and surgency; neuroticism represents emotional instability and anxiousness; psychoticism represents tough-mindedness, aggressiveness, coldness, and egocentricity; and lie represents unsophisticated dissimulation and social naivety or conformity [9]. Several Eysenck's personality questionnaires have been translated into Japanese [16,19,20]. In previous work, Hosokawa and Ohyama [16] developed the Japanese version of the EPQ-R and examined its reproducibility and validity among 329 college students and 253 adults. Cronbach's α coefficient, a measure of internal consistency, was greater than .70 for all subscales except psychoticism (.42 for college students and .48 for adults). Test–retest reliability coefficients of the four subscales over a 6-month period ranged from .70 to .85, indicating substantial

Table 1
Characteristics of study subjects according to the highest and lowest of four categories of each of four personality subscales

Characteristics/ Personality subscales[a]	Extraversion		*P* values[b]	Neuroticism		*P* values[b]	Psychoticism		*P* values[b]	Lie		*P* values[b]
Men												
Category	≤3	≥9		≤2	≥8		≤2	≥5		≤4	≥9	
Number of subjects	4387	3497		3244	4083		3397	5210		3239	4673	
Age (years), mean (S.D.)	50.7 (7.6)	50.9 (7.5)	.004	51.3 (7.6)	50.5 (7.5)	<.0001	52.5 (7.7)	49.6 (7.3)	<.0001	48.0 (6.9)	53.6 (7.4)	<.0001
Height (cm), mean (S.D.)	164.2 (6.2)	164.7 (6.1)	.001	164.4 (6.2)	164.4 (6.3)	.96	163.9 (6.1)	164.8 (6.2)	<.0001	165.4 (6.0)	163.7 (6.3)	<.0001
Weight (kg), mean (S.D.)	62.6 (8.6)	65.2 (8.9)	<.0001	64.6 (8.7)	63.2 (8.8)	<.0001	63.2 (8.5)	64.3 (9.0)	<.0001	64.8 (8.7)	63.0 (8.6)	<.0001
BMI (kg/m^2), mean (S.D.)	23.2 (2.8)	24.0 (2.8)	<.0001	23.9 (2.7)	23.4 (2.8)	<.0001	23.5 (2.7)	23.7 (2.8)	.01	23.7 (2.8)	23.5 (2.8)	.01
Age >55 years old, %	34.6	36.7	.002	38.6	34.4	.001	45.3	28.6	<.0001	20.8	51.8	<.0001
BMI≥25.0 kg/m^2, %	23.7	33.6	<.0001	30.7	26.2	.0002	25.9	28.9	.01	29.1	26.7	.06
BMI>18.5 kg/m^2, %	3.0	1.5	<.0001	1.5	3.0	<.0001	2.2	2.0	.35	2.0	2.2	.61
Education, up to 19 years of age, %	82.0	79.7	.003	79.9	82.1	.16	80.4	81.7	.41	81.5	80.8	.009
Living with spouse, %	86.7	91.7	<.0001	88.8	88.9	.008	89.6	87.9	.053	90.5	87.1	<.0001
History of diseases[c], %	49.5	42.6	<.0001	37.1	52.8	<.0001	49.5	43.7	<.0001	46.0	45.9	.78
Never smoker, %	20.6	17.8	.01	18.8	19.4	.51	22.5	16.0	<.0001	15.9	22.8	<.0001
Never drinker, %	19.3	11.9	<.0001	15.9	14.5	.18	16.3	14.8	.28	13.5	17.7	<.0001
Walking ≥1 h/day, %	38.4	43.6	<.0001	43.3	38.5	.003	40.6	40.5	.11	38.4	43.8	<.0001
Physical activity, ≥5 h/week, %	19.3	34.9	<.0001	30.6	23.4	<.0001	29.6	24.9	<.0001	25.8	27.7	<.0001
Women												
Category	≤3	≥8		≤3	≥9		≤1	≥4		≤5	≥10	
Number of subjects	4741	4255		4155	3243		2472	5149		2886	3540	
Age (years), mean (S.D.)	51.0 (7.5)	51.4 (7.4)	.01	51.8 (7.4)	50.8 (7.4)	<.0001	51.5 (7.6)	50.7 (7.3)	<.0001	47.8 (6.7)	54.4 (6.7)	<.0001
Height (cm), mean (S.D.)	152.2 (5.2)	153.2 (5.3)	<.0001	152.6 (5.1)	152.6 (5.5)	.94	152.6 (4.9)	152.7 (5.3)	.60	153.6 (5.2)	151.8 (5.1)	<.0001
Weight (kg), mean (S.D.)	54.0 (7.6)	56.4 (7.8)	<.0001	56.2 (7.7)	54.2 (7.6)	<.0001	54.6 (7.5)	55.2 (7.8)	<.0001	55.4 (7.8)	54.8 (7.5)	.004
BMI (kg/m^2), mean (S.D.)	23.3 (3.0)	24.0 (3.1)	<.0001	24.1 (3.1)	23.3 (3.1)	<.0001	23.4 (3.0)	23.7 (3.1)	<.0001	23.5 (3.0)	23.8 (3.1)	<.0001
Age >55 years old, %	36.2	38.6	.03	40.8	36.0	.14	39.4	34.2	<.0001	19.5	55.0	<.0001
BMI>25.0 kg/m^2, %	26.5	34.5	<.0001	35.8	26.1	<.0001	26.8	30.8	<.0001	27.5	30.7	.0003
BMI>18.5 kg/m^2, %	3.5	2.0	.0002	1.8	3.8	<.0001	2.8	2.6	.29	3.1	2.7	.41
Education, up to 19 years of age, %	82.4	81.4	.06	82.2	82.1	.12	83.3	81.4	.09	78.6	85.2	<.0001
Living with spouse, %	79.2	81.0	.36	80.3	78.9	.21	82.2	79.3	.01	83.8	76.1	<.0001
History of diseases[c], %	39.8	35.8	<.0001	31.4	45.1	<.0001	38.9	36.3	.17	36.2	39.5	.003
Never smoker, %	74.0	69.1	<.0001	72.6	70.0	.02	75.1	69.3	<.0001	75.0	70.0	<.0001
Never drinker, %	65.8	53.0	<.0001	60.0	57.7	.002	63.9	55.7	<.0001	54.8	63.2	<.0001
Walking ≥1 h/day, %	38.6	44.0	<.0001	43.4	39.9	.0001	42.8	40.3	.08	39.4	45.6	<.0001
Physical activity, ≥5 h/week, %	13.3	27.4	<.0001	23.4	16.0	<.0001	20.6	18.0	.006	17.6	23.1	<.0001

[a] Each personality subscale (scored on a scale of 0–12) was divided into four categories approximately equal in size, on the basis of the score in the population by sex. Consequently, different personality subscales have different cutoff scores by sex.
[b] Continuous variables were analyzed by ANOVA, and categorical variables were analyzed by chi-square test.
[c] History of hypertension, renal diseases, liver diseases, gallstone diseases, diabetes mellitus, peptic ulcers, or tuberculosis.

stability. Confirmatory factor analysis supported the original theoretical structure of the four scales proposed by Eysenck and Eysenck [18].

The baseline survey included questions on self-reports of body weight and body height, and BMI was calculated as the weight divided by the square of the height (kg/m^2). We grouped subjects into the following three categories: underweight (BMI<18.5), normal (BMI=18.5–24.9), and overweight (BMI≥25.0), based on the proposal by the World Health Organization in which BMI values of 18.5–24.9 and ≥25.0 are defined as normal and overweight or preobese, respectively [1,21].

We evaluated the validity of self-reported body weight and body height. Among the study subjects, 7153 individuals

Table 2
ORs and 95% CIs for overweight (BMI≥25.0 Kg/m^2) according to personality subscales

Personality subscale	Men					Women				
	Category [a]				P for trend [b]	Category [a]				P for trend [b]
	1 (referent)	2	3	4		1 (referent)	2	3	4	
Extraversion	≤3	4–5	6–8	≥9		≤3	4–5	6–7	≥8	
No. of cases/ No. of subjects	1040/4387	822/3148	1213/4192	1174/3497		1258/4741	1082/3469	921/3033	1467/4255	
Crude OR (95% CI)	1.00	1.14 (1.03–1.26)	1.31 (1.19–1.44)	1.63 (1.47–1.80)	<.0001	1.00	1.26 (1.14–1.38)	1.21 (1.09–1.34)	1.46 (1.33–1.59)	<.0001
Age-adjusted OR (95% CI)	1.00	1.14 (1.03–1.27)	1.32 (1.20–1.45)	1.63 (1.48–1.80)	<.0001	1.00	1.24 (1.13–1.37)	1.19 (1.08–1.32)	1.45 (1.32–1.58)	<.0001
Multivariable OR[c] (95% CI)	1.00	1.17 (1.05–1.30)	1.37 (1.25–1.52)	1.73 (1.56–1.91)	<.0001	1.00	1.27 (1.15–1.40)	1.23 (1.11–1.37)	1.53 (1.39–1.68)	<.0001
Neuroticism	≤2	3–4	5–7	≥8		≤3	4–5	6–8	≥9	
No. of cases/ No. of subjects	995/3244	903/3169	1280/4728	1071/4083		1488/4155	1035/3361	1358/4739	847/3243	
Crude OR (95% CI)	1.00	0.90 (0.81–1.003)	0.84 (0.76–0.93)	0.80 (0.73–0.89)	<.0001	1.00	0.80 (0.72–0.88)	0.72 (0.66–0.79)	0.63 (0.57–0.70)	<.0001
Age-adjusted OR (95% CI)	1.00	0.90 (0.81–1.001)	0.84 (0.76–0.92)	0.80 (0.72–0.88)	<.0001	1.00	0.80 (0.73–0.89)	0.73 (0.67–0.80)	0.65 (0.59–0.72)	<.0001
Multivariable OR[c] (95% CI)	1.00	0.88 (0.79–0.98)	0.81 (0.73–0.90)	0.76 (0.68–0.84)	<.0001	1.00	0.79 (0.72–0.87)	0.70 (0.64–0.77)	0.61 (0.55–0.67)	<.0001
Psychoticism	≤2	3	4	≥5		≤1	2	3	≥4	
No. of cases/ No. of subjects	880/3397	918/3349	948/3268	1503/5210		662/2472	1171/3846	1307/4031	1588/5149	
Crude OR (95% CI)	1.00	1.08 (0.97–1.20)	1.17 (1.05–1.30)	1.16 (1.05–1.28)	.007	1.00	1.20 (1.07–1.34)	1.31 (1.18–1.47)	1.22 (1.10–1.36)	.002
Age-adjusted OR (95% CI)	1.00	1.07 (0.96–1.20)	1.16 (1.04–1.29)	1.14 (1.03–1.25)	.03	1.00	1.19 (1.06–1.33)	1.32 (1.18–1.47)	1.26 (1.13–1.40)	.0001
Multivariable OR[c] (95% CI)	1.00	1.11 (0.99–1.23)	1.21 (1.09–1.35)	1.21 (1.09–1.33)	.0006	1.00	1.20 (1.07–1.34)	1.32 (1.18–1.48)	1.28 (1.14–1.42)	<.0001
Lie	≤4	5–6	7–8	≥9		≤5	6–7	8–9	≥10	
No. of cases/ No. of subjects	942/3239	927/3206	1132/4106	1248/4673		793/2886	1203/3947	1645/5125	1087/3540	
Crude OR (95% CI)	1.00	0.99 (0.89–1.11)	0.93 (0.84–1.03)	0.89 (0.80–0.98)	.002	1.00	1.15 (1.04–1.29)	1.35 (1.13–1.38)	1.17 (1.05–1.30)	.005
Age-adjusted OR (95% CI)	1.00	1.003 (0.90–1.12)	0.95 (0.86–1.05)	0.92 (0.83–1.02)	.02	1.00	1.08 (0.97–1.20)	1.08 (0.97–1.20)	0.94 (0.84–1.05)	.37
Multivariable OR[c] (95% CI)	1.00	0.99 (0.89–1.10)	0.94 (0.84–1.04)	0.90 (0.81–0.998)	.007	1.00	1.08 (0.97–1.20)	1.07 (0.97–1.19)	0.93 (0.83–1.05)	.29

[a] Each personality subscale (scored on a scale of 0–12) was divided into four categories approximately equal in size, on the basis of the score in the population by sex. Consequently, different personality subscales have different cutoff scores.

[b] *P* values for trend were calculated by treating scores of each personality subscales as continuous variables.

[c] Adjusted for age (in years); education (up to 19 years of age or 19 years or older); marital status at baseline (whether or not living with spouse); history of hypertension, renal diseases, liver diseases, gallstone diseases, diabetes mellitus, peptic ulcers, or tuberculosis; cigarette smoking (never smoked, smoked in the past, or currently smoking); alcohol consumption (never drank alcohol, drank in the past, or currently drinking); walking time per day (less than 30 min, from 30 min to 1 h, or more than 1 h); physical activity time per week (less than 1 h, 1–2 h, 3–4 h, or more than 5 h); and job type (service-type job, farmer and manufacturing, or others).

had their body height and weight measured during health examinations provided by local governments in 1990. The Pearson's correlation coefficient (r) between self-reported and measured values was .97 for body weight, .85 for body height, and .91 for BMI. Thus, self-reported height and weight at the time of the baseline questionnaire were sufficiently valid. The questions included the following data: age, education, marital status, history of diseases, cigarette smoking, alcohol consumption, walking time per day, physical activity time per week, and job type.

Statistical methods

Each personality subscale was divided into four categories by sex to obtain even-sized quartiles as closely as possible. We used multivariate logistic regression analysis

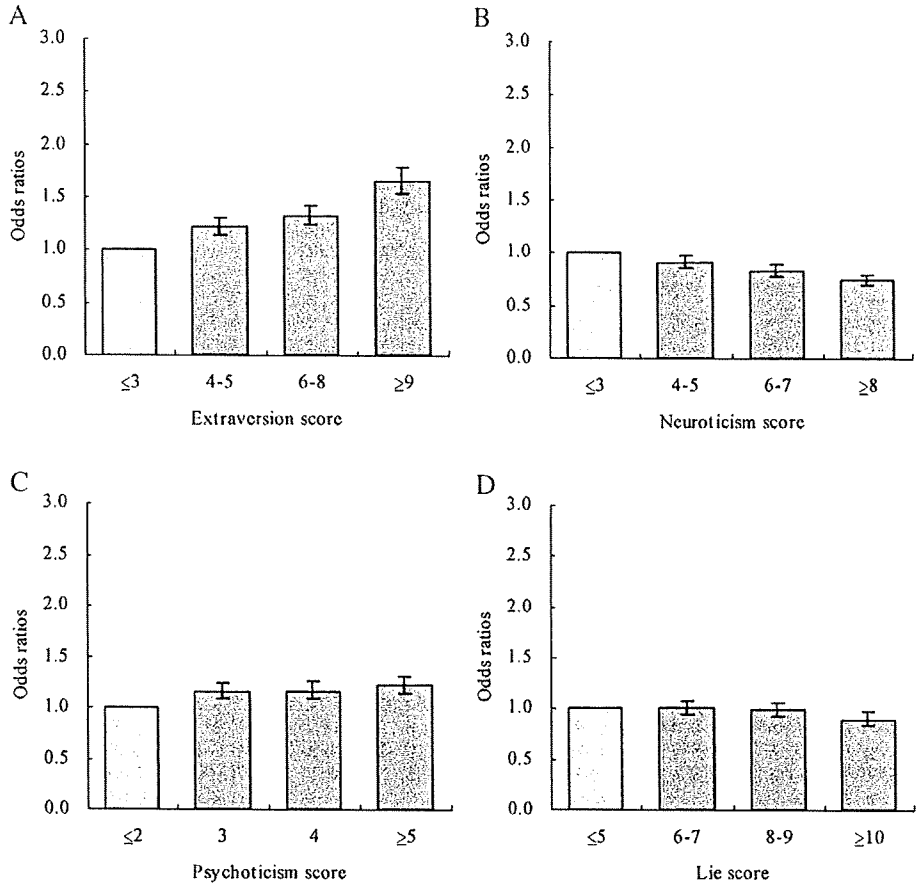

Fig. 1. ORs and 95% CIs for overweight (BMI≥25.0 kg/m^2) according to extraversion (A), neuroticism (B), psychoticism (C), and lie (D).

to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for overweight or underweight relative to each category of a personality subscale, with the lowest category treated as the reference group. Trend tests were performed by treating personality subscales as continuous variables.

In these analyses, we regarded the following data as covariates: age (continuous variable); education (up to 19 years of age or 19 years or older); marital status (whether or not living with spouse); history of hypertension, renal diseases, liver diseases, gallstone diseases, diabetes mellitus, peptic ulcers, or tuberculosis; cigarette smoking (never smoked, smoked in the past, or currently smoking); alcohol consumption (never drank alcohol, drank in the past, or currently drinking); walking time per day (less than 30 min, from 30 min to 1 h, or more than 1 h); physical activity time per week (less than 1 h, 1–2 h, 3–4 h, or more than 5 h); and job type (service-type job, farmer and manufacturing, or others).

We examined in detail potential confounding and effect modification by age and other covariates on the associations between personality scales and overweight or underweight. No statistically significant interaction was observed between personality and other confounding factors for overweight or underweight on a multiplicative scale (data not shown).

All statistical analyses were performed using SAS software, version 9.1 [22]. All the statistical tests reported were two sided. Differences at $P<.05$ were accepted as statistically significant.

Results

The subjects' characteristics according to the highest and the lowest categories (i.e., approximate quartiles) of each personality subscale are shown in Table 1. Subjects in the highest category of extraversion were less likely to have never smoked ($P=.01$ in men, $P<.0001$ in women), to have never drank ($P<.0001$ in men and women), or to have a history of diseases ($P<.0001$ in men and women) and were more likely to walk ($P<.0001$ in men and women) and to engage in exercise ($P<.0001$ in men and women) than those in the lowest category. Subjects in the highest category of neuroticism were less likely to walk ($P=.0003$ in men, $P=.0001$ in women) or to engage in exercise ($P<.0001$ in men and women) and were more likely to have a history of

Table 3
ORs and 95% CIs for underweight (BMI<18.5 Kg/m^2) according to personality subscales

Personality subscale	Men					Women				
	Category[a]				P for trend[b]	Category[a]				P for trend[b]
	1 (referent)	2	3	4		1 (referent)	2	3	4	
Extraversion	≤3	4–5	6–8	≥9		≤3	4–5	6–7	≥8	
No. of cases/ No. of subjects	133/4387	65/3148	62/4192	53/3497		164/4741	82/3469	79/3033	86/4255	
Crude OR (95% CI)	1.00	0.68 (0.50–0.91)	0.48 (0.35–0.65)	0.49 (0.36–0.68)	<.0001	1.00	0.68 (0.52–0.88)	0.75 (0.57–0.98)	0.58 (0.44–0.75)	<.0001
Age-adjusted OR (95% CI)	1.00	0.66 (0.49–0.90)	0.47 (0.35–0.64)	0.49 (0.35–0.67)	<.0001	1.00	0.68 (0.52–0.89)	0.75 (0.57–0.99)	0.58 (0.44–0.75)	<.0001
Multivariable OR[c] (95% CI)	1.00	0.69 (0.51–0.93)	0.49 (0.36–0.67)	0.51 (0.37–0.71)	<.0001	1.00	0.69 (0.53–0.90)	0.76 (0.58–1.004)	0.57 (0.44–0.75)	<.0001
Neuroticism	≤2	3–4	5–7	≥8		≤3	4–5	6–8	≥9	
No. of cases/ No. of subjects	47/3244	44/3169	100/4728	122/4083		73/4155	92/3361	124/4739	122/3243	
Crude OR (95% CI)	1.00	0.96 (0.63–1.45)	1.47 (1.04–2.08)	2.10 (1.49–2.94)	<.0001	1.00	1.57 (1.15–2.15)	1.50 (1.12–2.01)	2.19 (1.63–2.93)	<.0001
Age-adjusted OR (95% CI)	1.00	0.96 (0.64–1.46)	1.38 (1.05–2.11)	2.15 (1.53–3.03)	<.0001	1.00	1.57 (1.15–2.14)	1.49 (1.12–2.00)	2.17 (1.62–2.91)	<.0001
Multivariable OR[c] (95% CI)	1.00	0.98 (0.65–1.49)	1.49 (1.05–2.12)	2.19 (1.55–3.09)	<.0001	1.00	1.56 (1.14–2.13)	1.50 (1.12–2.01)	2.15 (1.60–2.90)	.0001
Psychoticism	≤2	3	4	≥5		≤1	2	3	≥4	
No. of cases/ No. of subjects	74/3397	79/3349	58/3268	102/5210		68/2472	115/3846	92/4031	136/5149	
Crude OR (95% CI)	1.00	1.09 (0.79–1.50)	0.81 (0.57–1.15)	0.90 (0.66–1.21)	.93	1.00	1.09 (0.80–1.48)	0.83 (0.60–1.14)	0.96 (0.71–1.29)	.71
Age-adjusted OR (95% CI)	1.00	1.11 (0.81–1.53)	0.85 (0.60–1.20)	0.98 (0.72–1.33)	.60	1.00	1.09 (0.81–1.48)	0.82 (0.60–1.14)	0.95 (0.71–1.28)	.77
Multivariable OR[c] (95% CI)	1.00	1.06 (0.77–1.47)	0.82 (0.58–1.17)	0.90 (0.66–1.23)	.96	1.00	1.09 (0.80–1.48)	0.82 (0.60–1.13)	0.91 (0.67–1.22)	.91
Lie	≤4	5–6	7–8	≥9		≤5	6–7	8–9	≥10	
No. of cases/ No. of subjects	66/3239	68/3206	75/4106	104/4673		89/2886	102/3947	126/5125	94/3540	
Crude OR (95% CI)	1.00	1.04 (0.74–1.47)	0.90 (0.64–1.25)	1.09 (0.80–1.49)	.89	1.00	0.83 (0.63–1.11)	0.79 (0.60–1.04)	0.86 (0.64–1.15)	.08
Age-adjusted OR (95% CI)	1.00	0.99 (0.70–1.39)	0.80 (0.57–1.13)	0.92 (0.66–1.27)	.30	1.00	0.85 (0.64–1.14)	0.82 (0.62–1.09)	0.91 (0.67–1.24)	.19
Multivariable OR[c] (95% CI)	1.00	1.02 (0.72–1.44)	0.85 (0.60–1.19)	0.97 (0.70–1.34)	.46	1.00	0.88 (0.66–1.17)	0.86 (0.65–1.14)	0.97 (0.71–1.32)	.39

[a] Each personality subscale (scored on a scale of 0–12) was divided into four categories approximately equal in size, on the basis of the score in the population by sex. Consequently, different personality subscales have different cutoff scores.

[b] *P* values for trend were calculated by treating scores of each personality subscales as continuous variables.

[c] Adjusted for age (in years); education (up to 19 years of age or 19 years or older); marital status at baseline (whether or not living with spouse); history of hypertension, renal diseases, liver diseases, gallstone diseases, diabetes mellitus, peptic ulcers, or tuberculosis; cigarette smoking (never smoked, smoked in the past, or currently smoking); alcohol consumption (never drank alcohol, drank in the past, or currently drinking); walking time per day (less than 30 min, from 30 min to 1 h, or more than 1 h); physical activity time per week (less than 1 h, 1–2 h, 3–4 h, or more than 5 h); and job type (service-type job, farmer and manufacturing, or others).

diseases (*P*<.0001 in men and women) than those in the lowest category. Subjects in the highest category of psychoticism were younger than those in the lowest category (*P*<.0001 in men and women) and were less likely to have never smoked (*P*<.0001 in men and women) or to have never drank (women only; *P*<.0001). Subjects in the highest category of the lie scales were older than those in the lowest category (*P*<.0001 in men and women) and were less likely to live with their spouse (*P*<.0001 in men and women) and were more likely to have never smoked (men only; *P*<.0001), to have never drank alcohol (*P*<.0001 in men and women), to walk (*P*<.0001 in men and women), to engage in exercise (*P*<.0001 in men and women), and to have attended school up to 19 years of age (women only; *P*<.0001).

In men and women, extraversion and psychoticism had a statistically significant positive association with overweight, whereas neuroticism had an inverse association. In men, lie had an inverse association with overweight (Table 2; Fig. 1).

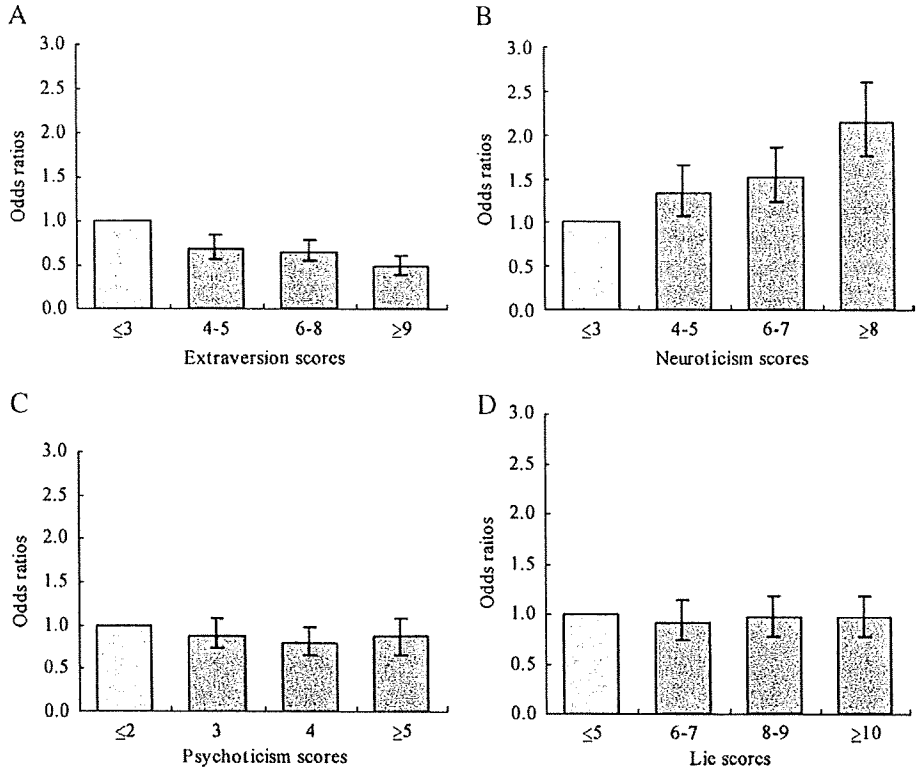

Fig. 2. ORs and 95% CIs for underweight (BMI≥18.5 kg/m^2) according to extraversion (A), neuroticism (B), psychoticism (C), and lie (D).

In men and women in the highest category of each personality subscale compared with the lowest category, multivariate ORs (95% CIs) were 1.73 (1.56–1.91) and 1.53 (1.39–1.68) for extraversion, 0.76 (0.68–0.84) and 0.61 (0.55–0.67) for neuroticism, and 1.21 (1.09–1.33) and 1.28 (1.14–1.42) for psychoticism, respectively. In the highest category of lie compared with the lowest category, the multivariate OR (95% CI) was 0.90 (0.81–0.998) in men. In men and women, multivariate analysis with the exclusion of subjects who were underweight showed similar results (data not shown).

In men and women, extraversion had a statistically significant inverse association with underweight and neuroticism had a positive association (Table 3; Fig. 2). In men and women, in the highest category of each personality subscale compared with the lowest category, multivariate ORs (95% CIs) were 0.51 (0.37–0.71) and 0.57 (0.44–0.75) for extraversion and 2.19 (1.55–3.09) and 2.15 (1.60–2.90) for neuroticism, respectively. In men and women, multivariate analysis with the exclusion of subjects who were overweight showed similar results (data not shown).

Discussion

In this population-based cross-sectional analysis conducted in Japan, we found that extraversion and psychoticism had a positive association and that neuroticism had an inverse association with overweight in men and women, respectively. To compare with the lowest category of each subscale, we increased the ORs for overweight to 73% and 53% in the highest category of extraversion and to 21% and 28% in the highest category of psychoticism and decreased the ORs to 23% and 39% in the highest category of neuroticism in men and women, respectively. In men, lie had an inverse association with overweight. To compare with the lowest category of lie, we decreased the OR for overweight in the highest category to 10%. In contrast, we found that extraversion had an inverse association, that neuroticism had a positive association with underweight, and that psychoticism and lie had no association with underweight, in men and women, respectively. To compare with the lowest category of each subscales, we decreased the ORs for underweight to 49% and 43% in the highest category of extraversion and increased the ORs to 119% and 115% in the highest category of neuroticism in men and women, respectively. The associations between the four categories of the Eysenck personality subscale and overweight or underweight were approximated an inverse association. In men and women, extraversion had a positive association with overweight and an inverse association with underweight, neuroticism had an inverse association with overweight and a positive association with underweight, and psychoticism was associated only with overweight. In men, lie had a positive association with overweight. To our knowledge, this is the first report to examine the association

of personality with overweight or underweight in an Asian country, where relatively large proportions of the population are overweight and underweight.

Our results were consistent with those of Kittel et al.'s [10] but inconsistent with those of other previous studies [11–14]. Our analyses of methodological advantages may provide clues for interpreting the discrepancies among previous studies on personality and overweight, obesity, or underweight. Of four inconsistent studies, Hallstrom and Noppa [11] compared 77 obese and 718 nonobese women aged 38–54 in a general population and reported that higher scores of extraversion were associated with obesity, whereas no association was observed between neuroticism and obesity. Slof et al. [13] and Mazzeo et al. [14] also reported no association between extraversion, neuroticism, and underweight with sample sizes of 891 and 1073, respectively. Our sample size was 30,722 and revealed statistically significant positive or inverse associations, suggesting that the null results of previous studies may have been due to lack of power. Faith et al. [12] examined 3826 men and 4063 women aged 30–50 years in the United Kingdom and reported that increased extraversion and psychoticism scores were related to higher BMI in men and that increased neuroticism scores and decreased extraversion scores were related to higher BMI in women. The findings in men were consistent with our results. Although we could not explain the discrepancy in women, Faith et al.'s and our results were extremely different. In this study, we compared the baseline characteristics between men and women: Men were younger and were more likely to have a history of diseases, to smoke, to drink, and to engage in exercise than women. Men and women were analyzed separately because of such gender differences in baseline characteristics. Although Faith et al. [12] obtained results that differed between men and women, our results were almost the same for both sexes. We were unable to explain these differences between previous studies and our results regarding the difference in baseline characteristics between men and women.

Our study had several methodological strengths. First, this was a population-based study with a large sample size of 30,722 subjects. However, the large sample size increased the possibility of the type I error. Our results showed a great difference between the reference category and other categories, and P values for trends were sufficiently small to allow discussion of the results. For example, when comparing with the lowest category of each subscale, the ORs for overweight were increased to 73% and 53% in the highest category of extraversion, in men and women, respectively. If there was a possibility of type I error, this might be disregarded. Second, extensive control for potentially confounding variables such as age, education, marital status, history of diseases, cigarette smoking, alcohol consumption, walking time per day, physical activity per week, and job type was considered. We compared the baseline characteristics between excluded subjects and included subjects: Excluded subjects were older and more likely to be men (50% vs. 45.1%, in included subjects and excluded subjects, respectively) and more likely to have missed answers in education, marital status, cigarette smoking, alcohol consumption, walking time per day, physical activity time per week, and job type than included subjects. However, we consider it unlikely that the association between personality and overweight or underweight was substantially distorted by the effect of excluding these subjects. Finally, this study used the validated Japanese version of the personality questionnaire developed by Eysenck and Eysenck [16,18]. Several models of personality structure view traits as biologically based and temperamental dimensions of individual differences [23,24]. Eysenck proposed broad factors—extraversion, neuroticism, psychoticism, and lie—which he viewed as a sufficient model (or "paradigm") of personality [23–25]. Several Eysenck's personality questionnaires have been translated into Japanese [16,19,20] and have been applied in various research and clinical settings [26–29]. These studies have indicated that Eysenck's personality theory is as applicable to Japanese individuals as it is to Western individuals.

Several methodological limitations, however, should also be considered when interpreting our results. First, our study had a cross-sectional design, and therefore, no temporal relationship between personality and being overweight or underweight can be inferred. Second, we used self-reported height and weight to calculate BMI. Thus, the measurement of BMI probably underestimated the true BMI of overweight or underweight subjects, and this might have led to conservative estimates of the association between personality and overweight or underweight. Third, we obtained data for persons aged 40 years or older. Thus, it is uncertain whether our findings of the association between personality and overweight or underweight would also apply to adolescents or children whose body builds tend to differ from those of middle-age or older individuals.

Personality dimensions are associated with some genetic and physiological mechanisms. Some personality traits were associated with varying levels of dopamine and serotonin [30–40]. In addition, serotonin has a suppressive effect on food intake and body weight [41–43], and availability of the dopamine receptor is decreased in obese individuals in proportion to their BMI [44]. The relationships of personality with these genetic or physiological factors might affect body composition.

Obesity and excess body weight is now a worldwide problem, and evidence is now emerging to suggest that it is increasing at an alarming rate [2]. However, few countries have effectively addressed this issue. Factors associated with being overweight or obese are diverse, and our data indicate that personality trait is one of these factors. For example, our data suggested that people with a high level of extraversion might be more prone to obesity than those with a low level of extraversion. Such personality traits should be taken into account when planning interventions for overweight, obese, or underweight people, and different intervention programs

need to be designed for each personality trait in a public health policy or clinical work. For example, if a person is found to have a high score for extraversion or psychoticism, or a low score for neuroticism, then awareness of the risk of being overweight or obese should be promoted, whereas if a person is found to have a high score for neuroticism and a low score for extraversion, then awareness of the risk of being underweight should be promoted.

In conclusion, this cross-sectional analysis of a middle-aged Japanese population has demonstrated that personality traits have a statistically significant association with overweight and underweight. Extraversion, neuroticism, and psychoticism are associated with overweight, lie is associated with overweight in men, and extraversion and neuroticism are associated with underweight. These results may provide clues to devising more effective measures for preventing overweight, obesity, or underweight or for weight control intervention.

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