Table 2
Subjective evaluation

	Zolpidem		Placebo		Paired t/Wilcoxon signed-ranks t	Interaction	Drug main	Time main
	Mean	S.E.M.	Mean	S.E.M.	t/z	Drug × time F	Effect F	Effect F
Total sleep time (TST) (min)	447.43	9.16	395.00	12.58	3.31[*]			
Sleep latency (SL) (min)	19.00	4.86	50.71	13.56	−2.58[*]			
Number of awakenings (n)	1.57	0.53	2.57	0.61	−1.15			
The minutes from awakening to getting out of the bed (min)	10.86	3.62	14.29	4.14	−0.77			
Depth of sleep	3.57	0.37	3.14	0.34	−0.76			
Mood of awakening	2.86	0.26	3.14	0.34	−0.71			
Stanford sleepiness scale (SSS)	2.54	0.28	2.52	0.29		1.25	0.04	6.49[**]
Alertness (VAS)	70.76	9.42	75.17	7.78		0.65	3.53	5.53[**]
Well-being (VAS)	70.72	25.43	76.38	16.51		0.41	8.34[**]	3.04[**]
Fatigue (VAS)	62.39	9.33	64.54	8.05		0.94	1.34	2.64[**]

TST and the following five evaluations were asked at the time of getting up in the next morning. The scale's extreme depth of sleep and mood of awakening were "deep (5)–light (1)", "good (5)–bad (1)". SSS and VAS were asked every hour from 7:00 to 22:00 h and were analyzed by repeated-measures ANOVA with a grouping factor (placebo vs. drug group). The scale's of VAS extremes were "very alert–very drowsy", "very good–very bad" and "very tired–very rested". TST was 53 min longer in the zolpidem group. The time of SL was 32 min shorter in the zolpidem group compared with the placebo group. SSS, alertness, well-being and fatigue showed significant main effects of time. The well-being showed a significant main effect of drug ($F = 8.34$, $p = 0.001$).

[*] $p < 0.05$.
[**] $p < 0.01$.

(10 mg), temazepam (30 mg, $T_{1/2} = 5.3$ h, $\omega1 = \omega2$) and for placebo administration, no significant differences between CFF scores were observed. These results suggest that effects on the CFF of hypnotics may be varied depending on the compound and their half lives and dosage (Smith and Misiak, 1976; Mizuki et al., 1987; Bensimon et al., 1990; Berlin et al., 1993).

Several researchers also reported effects of zolpidem on the CFF. Richens et al. (1993) studied rebound insomnia following cessation of zolpidem and showed that the data of CFF was not significantly different at 9 and 11 h after administration. Bensimon et al. (1990) reported that 20 mg of zolpidem administration brought significantly higher score of CFF than that of flunitrazepam 2 mg ($T_{1/2} = 21.5$ h, ωRS: non-selective) at 10 h after administration. However, they did not check the significant differences in CFF between zolpidem and placebo administrations. Berlin et al. (1993) reported that the score of the CFF at 1.5 h after zolpidem treatment (10 mg) was significantly lower compared to that with placebo treatment but was recovered to the same level as placebo at 4 h after administration. Interestingly, 6–8 h after administration, the score with zolpidem treatment was higher than that with placebo, although the difference was not significant. Improvements of CFF in later hours in this study as well as those in the following morning might be due to the hyperarousal state withdrawal from the zolpidem administration, though hyperarousal was not detected by visual analog scales in our study.

As previously demonstrated by nocturnal polysomnographic study (10 mg, zolpidem) in normal healthy adults (Uchimura et al., 2006), and meta-analysis study with objective and/or subjective evaluations (Nowell et al., 1997), the results of our subjective sleep evaluations also suggest that zolpidem (10 mg) significantly shortened sleep latency and prolonged total sleep time. Therefore, the refreshment of the good nocturnal sleep

due to hypnotic administration may also likely contribute to the enhancement of CFF.

Several researchers studied the residual effects of zolpidem. The withdrawal symptoms of zolpidem abuse, such as tremor, agitation, anxiety and seizure were reported (Madrak and Rosenberg, 2001; Roger et al., 1993) to be the same as withdrawal symptoms of benzodiazepines (Chouinard, 2004). Roger et al. (1993) reported "diurnal agitation" as the residual effects of regularly used zolpidem in the elderly people with insomnia. Although none of the subjects claimed any of these side effects, the score of well-being is better in the placebo group than zolpidem group. The functional significance of this result is not known at this moment, and one study rather reported that well-being was enhanced by continuous zolpidem (5 or 10 mg) administration with healthy volunteers who do shifted night work (Hart et al., 2003). Our subjects never took a hypnotic before the enrolment of this study, and they may have felt anxious with subjective feeling if they received hypnotic the night before. As we described before, zolpidem is considered free from residual effects, such as on mood, anxiety, and malaise (Terzano et al., 2003; Bensimon et al., 1990; Allain et al., 2003), consistent with the results that no subjects reported fatigue nor any other side effects.

The limitation of this study are (i) this experiment was conducted in home condition without polysomnography, (ii) the assessment of nocturnal sleep was made only based on subjective scales.

In conclusion, zolpidem has a hypnotic activity without disturbing psychomotor and physical performance on the following day when given to healthy adults. Zolpidem (and other short half-life hyponotics) may therefore be used in healthy subjects, including athletes, to adjust their extrinsic sleep disturbances and their consecutive psychomotor and physical impairments.

Acknowledgements

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Original Article

Use of alcohol and hypnotic medication as aids to sleep among the Japanese general population

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Abstract

Objective: The present study was conducted to clarify the prevalence of the use of alcohol and hypnotic medication as sleep aids, and associated factors, in the general population in Japan.

Methods: The survey was conducted in June 2000, using self-administered questionnaires, targeting a population that was selected randomly from among 300 communities throughout Japan. A total of 18,205 responses indicating alcohol use and 16,804 responses indicating hypnotic medication use were analyzed.

Results: The prevalence of alcohol use as a sleep aid one or more times per week was 48.3% among men and 18.3% among women. The prevalence of the use of hypnotic medication one or more times per week was 4.3% among men and 5.9% among women. The prevalence of alcohol used as a sleep aid increased gradually for men and women up to age 55–59 years and 40–44 years, respectively, and then declined with increasing age thereafter. The prevalence of the use of hypnotic medication among both men and women showed a trend toward a gradual increase with age. The use of alcohol as a sleep aid was associated with "difficulty maintaining sleep," but no such problem was associated with the use of hypnotic medication.

Conclusions: Alcohol is a more popular sleep aid than hypnotic medication. The factors associated with the use of alcohol and of hypnotic medication are different.

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Keywords: Sleep; Alcohol; Hypnotic medication; Japan; Epidemiology; Prevalence; Insomnia

1. Introduction

Sleep disturbances have come to be viewed as an important public health problem, as it has become clear that they are risk factors for various physical and mental disorders as well as industrial and traffic accidents. In various countries, nationwide epidemiological studies on sleep have been conducted, using samples represent-

ing the general population [1–13]. In those studies, the prevalence of insomnia was reported to be 5–48%, although it should be noted that the methods for evaluating insomnia differ from study to study. Insomnia is, thus, recognized as a common problem in modern industrialized countries, including Japan.

It is important for the future promotion of sleep hygiene to clarify the prevalence of substance use as aids to sleep among the general population, as well as associated factors. So far, two research groups in the United States have conducted studies on substances used as

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sleep aids and reported that the use of alcohol was significant among men and the use of hypnotic medication was significant among women [6,14,15]. In Japan, Doi et al. [8] reported that the prevalence of hypnotic medication use three times or more per week was 3.4% among men and 5.4% among women, and Liu et al. [9] reported that 6.3% of the general population regularly used hypnotic medication or alcohol as a sleep aid. Soldatos et al. [16] conducted cross-national comparisons on sleep habits in 10 countries, including Japan, and reported the prevalence of the use of hypnotic medication in Japan to be the second lowest among them (15.3%), while the prevalence of alcohol use as a sleep aid in Japan was the highest (30.3%) among those countries.

The prevalence of the use of substances as sleep aids, and their associated factors, however, has not been completely investigated in Japan. In the study by Doi et al., no question about the use of alcohol as a sleep aid appeared on the questionnaire. In the study by Liu et al., because only one question was used for the evaluation of both alcohol and hypnotic medication use, the prevalence of each was not calculated. In the study by Soldatos et al., the samples used were not representative of the general population because data were collected at public booths on the street and at railway stations or by internet polls.

In the present study, therefore, we examined the prevalence of the use of each alcohol and hypnotic medication as sleep aids, as well as their associated factors, using samples truly representative of the general population in Japan.

2. Methods

2.1. Selection of subjects

The present study was part of a national survey (Active Survey of Health and Welfare) organized by the Statistics and Information Department of the Ministry of Health, Labor, and Welfare of Japan. Its aim was to collect basic information on health and welfare, and included questions concerning symptoms of depression and sleep. The survey was conducted through health centers across Japan.

Subjects were recruited from 300 census precincts in Japan, selected randomly from among 824,000 precincts matched for equal population size. Each census precinct was numbered from north to south, and 300 precincts were selected by choosing precinct numbers at certain intervals. As a result, survey precincts were sampled from all over the country. A health center with jurisdiction for each precinct was designated, and investigators were sent from those health centers to visit all of the households in the area to distribute the questionnaires, which were collected a few days later. The survey target-

ed all those aged 12 years or more in the 300 sampled precincts and was conducted simultaneously throughout Japan in June 2000. Oral informed consent to participate was obtained from the subjects, whose privacy was protected in accordance with Declaration of Helsinki guidelines.

2.2. Measures

A self-administered questionnaire was devised by two of the authors together with an appropriate official of the Ministry of Health, Labor, and Welfare. This questionnaire consisted of 44 items, including (i) sociodemographic information such as age, gender, and size of the community; (ii) general health status; (iii) physical and psychological complaints; (iv) information on mental stress; (v) sleep habits and sleep problems; and (vi) the Japanese version of the Center for Epidemiologic Studies Depression Scale (CES-D) [17].

The CES-D, which is a 20-item inventory designed specifically to assess symptoms of depression in the general population, was used to screen for current depressive states during the period of one week leading up to the survey. This questionnaire is adequately reliable and valid for use in a general population. The CES-D yields an item score (range: 0–3) and a sum of the 20-item scores (range: 0–60). Higher scores indicate increasing severity of symptoms of depression. Although this scale is designed to screen, but not diagnose, major depression, a score of 16 or higher is highly suggestive of symptoms of depression. Shima et al. developed the Japanese version of the CES-D, examined its reliability and validity, and recommended that the cutoff point be set at 16, as with the United States version of the CES-D [18].

The following eight questions about sleep experienced during the previous month were included in the questionnaire:

1. Do you have difficulty falling asleep? (yes/no): difficulty initiating sleep (DIS).
2. Do you wake up frequently at night? (yes/no): difficulty maintaining sleep (DMS).
3. Do you wake up too early in the morning? (yes/no): early morning awakening (EMA).
4. Is your sleep interrupted by your snoring or dyspnea? (yes/no): interruption of sleep by snoring or dyspnea (ISSD).
5. Do you feel disagreeable sensations in your legs after you go to bed? (yes/no): disagreeable sensations in legs (DSL).
6. Do you fall asleep when you must not sleep (for example, when you are driving a car)? (yes/no): excessive daytime sleepiness (EDS).
7. Do you get sufficient rest from sleep? (very sufficient/sufficient/insufficient/very insufficient): subjective sleep sufficiency.

8. How many hours do you sleep on average?: sleep duration.

The following two questions about the use of alcohol and hypnotic medication as sleep aids during the previous month were included in the questionnaire:

Do you drink alcoholic beverages to obtain enough sleep?

Do you take medicine, such as a hypnotic, to obtain enough sleep?

One of the four options ("none," "once or twice per month," "once or twice per week," or "three times or more per week") was to be selected regarding use of alcohol and hypnotic medication. In the statistical analysis, these four optional categories were regrouped, if required, into two categories: the former two categories and the latter two (i.e., "once or more per week" and "less than once per week").

2.3. Statistical analysis

Questionnaires were returned by 32,729 subjects. Data from the following respondents were excluded from the analyses: (i) those who submitted blank answer forms ($n = 707$); (ii) those under 20 years of age, because the study was aimed at adults ($n = 3086$); (iii) those who did not respond to the questions on gender or age ($n = 222$); and (iv) those who neglected to answer six or more questions on the CES-D questionnaire ($n = 4028$).

For the statistical analysis, firstly, the prevalence of each alcohol and hypnotic medication used as a sleep aid was calculated by gender and by age class. Next, the prevalence of each alcohol and hypnotic medication used as sleep aids one or more times per week was then calculated separately by sleep problems, sleep duration, and subjective sleep sufficiency. χ^2 tests were conducted to examine relationships between each of these items and alcohol or hypnotic medication use. Finally, logistic regression analyses were conducted to examine the factors associated with use of alcohol and of hypnotic medication one or more times per week.

3. Results

Out of 24,686 subjects, the number of valid responses for questions about the use of alcohol as a sleep aid was 18,205 (73.7%), and 16,804 (68.1%) for questions about the use of hypnotic medication.

The breakdown of responses to the questions on the use of alcohol as a sleep aid and the use of hypnotic medication are given in Table 1. The prevalence of

Table 1
Prevalences (%) of alcohol and hypnotic medication use as aids to sleep by sex and age class

Substance use	Sex	Age class	None	1 or 2 times per month	1 or 2 times per week	3 times or more per week	N
Alcohol							
	Male	20–29	55.8	15.1	13.0	16.1	1806
		30–39	46.1	9.1	11.5	33.3	1839
		40–49	35.0	7.3	10.0	47.7	1814
		50–59	32.5	5.9	11.2	50.3	1834
		60–69	40.0	7.1	8.6	44.3	1097
		70-	55.5	5.8	8.7	30.1	589
		Total	42.9	8.8	10.9	37.4	8979
	Female	20–29	73.1	13.2	8.4	5.3	1969
		30–39	69.9	10.2	9.3	10.5	1981
		40–49	64.8	9.5	10.0	15.7	1819
		50–59	68.8	10.1	8.6	12.5	1677
		60–69	78.1	8.2	6.0	7.8	939
		70-	87.5	3.6	4.2	4.8	841
		Total	71.8	9.9	8.3	10.0	9226
Hypnotic medication							
	Male	20–29	98.6	0.5	0.2	0.6	1690
		30–39	97.2	0.8	0.6	1.4	1660
		40–49	96.8	1.3	0.9	1.1	1516
		50–59	94.1	1.4	1.4	3.1	1467
		60–69	86.4	3.6	3.7	6.3	898
		70-	76.1	4.9	3.4	15.6	552
		Total	94.1	1.6	1.3	3.0	7783
	Female	20–29	97.5	1.1	0.5	0.9	1924
		30–39	97.1	1.3	0.4	1.3	1881
		40–49	95.2	1.6	1.1	2.1	1710
		50–59	89.0	4.4	3.0	3.6	1587
		60–69	79.4	6.6	5.9	8.1	979
		70-	73.8	7.3	4.3	14.6	940
		Total	91.1	3.1	2.0	3.9	9021

alcohol use "one or more times per week" among men was 48.3% (95% confidence interval (CI): 47.3–49.3%), and among women was 18.3% (95% CI: 17.5–19.1%); the prevalence among men was significantly higher than among women (P < 0.01). The prevalence of the use of hypnotic medication "once or more per week" among men was 4.3% (95% CI: 3.8–4.8%) and that among women was 5.9% (95% CI: 5.4–6.4%); the prevalence among women was significantly higher than among men (P < 0.01). The prevalence of both alcohol and hyp-

notic medication use one or more times per week was 1.5% (95% CI: 1.2–1.8%) among men and 0.8% (95% CI: 0.6–1.0%) among women.

To better comprehend the trend associated with age, we stratified the subjects into five-year age classes, and the prevalence of the use of alcohol and of hypnotic medication as a sleep aid one or more times per week was calculated by gender for each five-year age class. The results for men are shown in Fig. 1, and those for women in Fig. 2. The prevalence of alcohol use as a
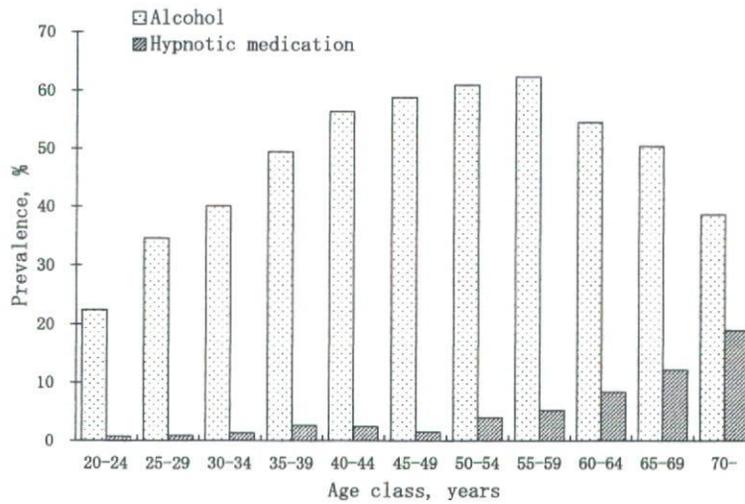

Fig. 1. The prevalence of the use of alcohol and hypnotic medication as sleep aids among Japanese males. *Note.* The prevalence of the use of alcohol as a sleep aid one or more times per week and the use of hypnotic medication one or more times per week was calculated for each five-year age class.
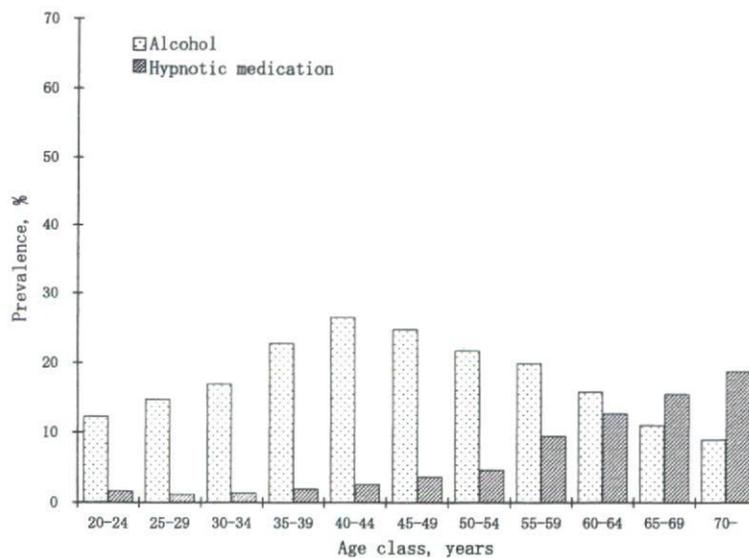

Fig. 2. The prevalence of the use of alcohol and hypnotic medication as sleep aids among Japanese females. *Note.* The prevalence of the use of alcohol as a sleep aid one or more times per week and use of hypnotic medication one or more times per week was calculated for each five-year age class.

sleep aid among men and women increased stepwise until the age class of 55–59 years and 40–44 years, respectively, and decreased stepwise thereafter. The prevalence of hypnotic medication use among both men and women increased stepwise with age.

Associations between the prevalence of alcohol use as a sleep aid one or more times per week and the different sleep items, the 95% CIs, and results of the χ^2 tests are given in Table 2. A significant association was recognized between alcohol use as a sleep aid and DIS for women but not for men. Significant associations were recognized between alcohol use as a sleep aid and DMS, EMA, ISSD, and depressive states, for both men and women.

Associations between the prevalence of the use of hypnotic medication one or more times per week and the different sleep items, 95% CIs, and results of the χ^2 tests are given in Table 3. Significant associations were recognized between all sleep items, except EDS, and the use of hypnotic medication for both men and women. The prevalence of hypnotic medication use was higher among those having shorter sleep duration, and it decreased as

sleep duration became longer. However, the trend turned toward increase when sleep duration exceeded 8 h.

The results of a logistic regression analysis, alcohol use as a sleep aid one or more times per week as a response variable, are given in Table 4. The odds ratios were highest for men in their 50 s and for women in their 40 s. The sleep items that showed significant associations between alcohol use as a sleep aid for both men and women were DMS and depressive states.

The results of a logistic regression analysis, using hypnotic medication one or more times per week as a response variable, are given in Table 5. The odds ratios regarding hypnotic medication use were significantly higher for those in higher age classes, those with DIS, those with 8 h or more of sleep duration, and those with subjective sleep insufficiency. Among the sleep items, the odds ratios for DIS were highest for both men and women.

4. Discussion

In this study, a significant association was shown between the prevalence of alcohol use as a sleep aid

Table 2

Prevalence (%) of alcohol use as an aid to sleep once or more per week by sleep item

	Male N	%	95% CI	P-value	Female N	%	95% CI	P-value
Difficulty initiating sleep				0.14				<0.01
No	7594	47.9	46.8–49.0		7328	17.1	16.2–18.0	
Yes	1385	50.1	47.5–52.7		1898	23.0	21.1–24.9	
Difficulty maintaining sleep				<0.01				<0.01
No	7320	46.5	45.4–47.6		7012	17.1	16.2–18.0	
Yes	1659	55.9	53.5–58.3		2214	22.1	20.4–23.8	
Early morning awakening				<0.01				0.04
No	6607	44.6	43.4–45.8		7464	17.9	17.0–18.8	
Yes	2372	58.5	56.5–60.5		1762	20.0	18.1–21.9	
Interruption of sleep by snoring or dyspnea				<0.01				0.01
No	8719	48.0	47.0–49.0		9068	18.2	17.4–19.0	
Yes	260	58.8	52.8–64.8		158	25.9	19.1–32.7	
Disagreeable sensations in legs				0.08				<0.01
No	8749	48.1	47.1–49.1		8911	18.0	17.2–18.8	
Yes	230	53.9	47.5–60.3		315	25.1	20.3–29.9	
Excessive daytime sleepiness				0.02				0.70
No	8681	48.5	47.4–49.6		8971	18.3	17.5–19.1	
Yes	298	41.6	36.0–47.2		255	19.2	14.4–24.0	
Depressive status (CES-D> = 16)				<0.01				<0.01
No	6558	46.4	45.2–47.6		6316	16.5	15.6–17.4	
Yes	2421	53.4	51.4–55.4		2910	22.1	20.6–23.6	
Sleep duration(h)				<0.01				<0.01
<5	221	42.1	35.6–48.6		246	22.4	17.2–27.6	
5 ⩽ <6	997	45.8	42.7–48.9		1086	19.9	17.5–22.3	
6 ⩽ <7	2720	47.2	45.3–49.1		3108	19.6	18.2–21.0	
7 ⩽ <8	2745	48.7	46.8–50.6		2774	18.1	16.7–19.5	
8 ⩽ <9	1749	51.8	49.5–54.1		1520	16.2	14.3–18.1	
9 ⩽ <10	280	49.3	43.4–55.2		231	12.6	8.3–16.9	
10≦	170	38.8	31.5–46.1		175	9.7	4.9–13.5	
Subject sleep sufficiency				0.04				<0.01
Very sufficient	1709	45.3	42.9–47.7		1487	13.4	11.7–15.1	
Sufficient	4177	49.2	47.7–50.7		4348	17.4	16.3–18.5	
Insufficient	2568	48.5	46.6–50.4		2888	21.3	19.8–22.8	
Very insufficient	469	50.1	45.6–54.6		454	23.8	19.9–27.7	

P-values were calculated by χ^2 test. CI: confidence interval CES-D; the Center for Epidemiologic Studies Depression Scale.

Table 3
Prevalence (%) of hypnotic medication use once or more per week by sleep item

	Male N	%	95% CI	P-value	Female N	%	95% CI	P-value
Difficulty initiating sleep				<0.01				<0.01
No	6515	2.3	1.9–2.7		7064	3.0	2.6–3.4	
Yes	1268	14.6	12.7–16.5		1957	16.2	14.6–17.8	
Difficulty maintaining sleep				<0.01				<0.01
No	6369	3.0	2.6–3.4		6826	4.1	3.6–4.6	
Yes	1414	10.5	8.9–12.1		2195	11.3	10.0–12.6	
Early morning awakening				<0.01				<0.01
No	5794	3.1	2.7–3.5		7252	4.5	4.0–5.0	
Yes	1989	7.8	6.6–9.0		1769	11.5	10.0–13.0	
Interruption of sleep by snoring or dyspnea				<0.01				0.03
No	7562	4.2	3.7–4.7		8872	5.8	5.3–6.3	
Yes	221	9.0	5.2–12.8		149	10.1	5.3–14.9	
Disagreeable sensations in legs				<0.01				<0.01
No	7579	4.1	3.7–4.5		8718	5.6	5.1–6.1	
Yes	204	12.3	7.8–16.8		303	14.2	10.3–18.1	
Excessive daytime sleepiness				0.67				0.17
No	7514	4.3	3.8–4.8		8781	5.8	5.3–6.3	
Yes	269	4.8	2.2–7.4		240	7.9	4.5–11.3	
Depressive status (CES-D$>$ = 16)				<0.01				<0.01
No	5680	1.9	1.5–2.3		6127	3.0	2.6–3.4	
Yes	2103	10.7	9.4–12.0		2894	12.0	10.8–13.2	
Sleep duration(h)				<0.01				<0.01
<5	198	7.6	3.9–11.3		248	14.5	10.1–18.9	
5 ≤ <6	872	4.7	3.3–6.1		1055	7.1	5.6–8.6	
6 ≤ <7	2395	3.2	2.5–3.9		3004	4.6	3.9–5.3	
7 ≤ <8	2382	2.9	2.2–3.6		2697	3.9	3.2–4.6	
8 ≤ <9	1470	4.8	3.7–5.9		1501	6.9	5.6–8.2	
9 ≤ <10	237	12.7	8.5–16.9		233	9.9	6.1–13.7	
10≤	162	15.4	9.8–21.0		184	16.3	11.0–21.6	
Subject sleep sufficiency				<0.01				<0.01
Very sufficient	1448	1.9	1.2–2.6		1459	3.5	2.6–4.4	
Sufficient	3587	3.8	3.2–4.4		4255	4.7	4.1–5.3	
Insufficient	2282	6.1	5.1–7.1		2809	7.2	6.2–8.2	
Very insufficient	417	7.7	5.1–10.3		446	14.1	10.9–17.3	

P-values were calculated by χ^2 test. CI: confidence interval CES-D; the Center for Epidemiologic Studies Depression Scale.

and DMS for both men and women. As this is a cross-sectional survey, the causal relationship between these two factors cannot be determined, but it would be natural to interpret it as "drinking alcohol in order to promote good sleep actually led to difficulty in maintaining sleep," rather than "drinking alcohol because they could not maintain sleep." Previous physiological studies have pointed out that alcohol tends to shorten sleep latency, reduce rapid eye movement (REM) sleep, and increase non-REM sleep, which makes alcohol immediately rewarding as a hypnotic [19–21]. Alcohol, however, is metabolized relatively rapidly and its hypnotic effect does not last long [22]. As a consequence, withdrawal tends to occur in the last half of the night and produces shallow or disrupted sleep [23,24]. Sleep may also be interrupted by gastric irritation, headache, and a full bladder. The results of our study support these findings of previous physiological studies in light of epidemiological evidence. It is suggested that the likelihood that alcohol used with the intent of promoting good sleep instead hinders the mainte-

nance of sleep. The results of our study also suggest that alcohol, which does not have a good hypnotic effect, is more commonly used than hypnotic medications among adults in general, except elderly women, in Japan. This is a serious problem for sleep hygiene in Japan. It is important in future public health activities to inform the Japanese populace that, contrary to popular belief, alcohol works negatively for obtaining good sleep. Moreover, it has been indicated that tolerance to and dependence on alcohol is more easily developed than for hypnotics, and that alcohol produces side effects, such as liver disease, more easily than hypnotics [19,25–27]. The public must be informed of those findings as rationales against using alcohol as a sleep aid.

A significant association was indicated between the use of hypnotic medications and DIS for both men and women. Among other covariates used, DIS indicated the highest adjusted odds ratio. This result concurs with the corresponding result of a study of Americans [14]. Thus, the results of the study presented here, carried out on a sample closely representing the general

Table 4
The results of a logistic regression analysis for alcohol use as an aid to sleep once or more per week

	Male			Female		
	AOR	95% CI	P-value	AOR	95% CI	P-value
Age class			<0.01			<0.01
20–29	0.52	0.45–0.60		0.64	0.54–0.76	
30–39	1.00			1.00		
40–49	1.60	1.40–1.83		1.43	1.22–1.67	
50–59	1.81	1.58–2.07		1.06	0.90–1.25	
60–69	1.25	1.07–1.47		0.61	0.49–0.76	
70	0.67	0.54–0.82		0.39	0.30–0.52	
Size of community			0.49			0.05
City of 500,000 people or more	1.00			1.00		
City of 150,000 to less than 500,000 people	1.07	0.94–1.21		0.87	0.75–1.02	
City of 50,000 to less than 150,000 people	1.02	0.89–1.17		0.85	0.72–1.00	
City of less than 50,000 people, suburban districts	1.09	0.96–1.24		0.80	0.69–0.94	
Difficulty initiating sleep			0.76			<0.01
No	1.00			1.00		
Yes	1.02	0.90–1.16		1.31	1.15–1.50	
Difficulty maintaining sleep			<0.01			<0.01
No	1.00			1.00		
Yes	1.22	1.08–1.38		1.21	1.07–1.38	
Early morning awakening			<0.01			0.11
No	1.00			1.00		
Yes	1.41	1.27–1.56		1.12	0.97–1.29	
Interruption of sleep by snoring or dyspnea			0.04			0.12
No	1.00			1.00		
Yes	1.31	1.01–1.71		1.35	0.93–1.95	
Disagreeable sensations in legs			0.65			0.10
No	1.00			1.00		
Yes	1.07	0.81–1.41		1.26	0.96–1.66	
Excessive daytime sleepiness			0.03			0.66
No	1.00			1.00		
Yes	0.76	0.60–0.98		0.93	0.67–1.29	
Depressive status (CES-D> = 16)			<0.01			<0.01
No	1.00			1.00		
Yes	1.29	1.16–1.43		1.27	1.12–1.43	
Sleep duration (h)			0.03			0.91
<5	0.85	0.63–1.15		1.02	0.73–1.43	
5 ≤ <6	0.98	0.84–1.15		0.94	0.79–1.13	
6 ≤ <7	1.00			1.00		
7 ≤ <8	1.04	0.93–1.16		1.02	0.89–1.17	
8 ≤ <9	1.24	1.08–1.41		1.02	0.89–1.17	
9 ≤ <10	1.15	0.89–1.50		0.93	0.61–1.41	
10≤	0.94	0.67–1.33		0.75	0.44–1.28	
Subject sleep sufficiency			0.13			0.28
Very sufficient	0.88	0.78–1.00		0.90	0.75–1.07	
Sufficient	1.00			1.00		
Insufficient	0.99	0.89–1.17		1.08	0.95–1.24	
Very insufficient	1.13	0.96–1.24		1.10	0.85–1.43	

AOR, adjusted odds ratio; CI, confidence interval; CES-D, the Center for Epidemiologic Studies Depression Scale.

population in Japan, suggest that DIS is also a strong motive for hypnotic medication use in Japan. Different from the case of alcohol use as a sleep aid, it is interesting that no association was recognized between the use of hypnotic medications and DMS.

In this study, a significant association was recognized between the use of hypnotic medication and EMA. Data on hypnotics prescribed in a hospital affiliated with a medical college showed that ultra-short-, short-, inter-mediate-, and long-acting hypnotics account for

14.1%, 41.5%, 28.9%, and 15.5%, respectively, of those prescribed [28]. One of the reasons for the association between the use of hypnotic medication and EMA is that such ultra-short- and short-acting hypnotics are commonly used in Japan.

In the present study, an independent association was indicated between depressive status and the use of hypnotic medication even when many items were taken as covariates for the logistic model. This result can be explained by inferring that antidepressants may have

Table 5
The results of a logistic regression analysis for hypnotic medication use once or more per week

	Male			Female		
	AOR	95% CI	P-value	AOR	95% CI	P-value
Age class			<0.01			<0.01
20–29	0.37	0.19–0.71		0.70	0.41–1.21	
30–39	1.00			1.00		
40–49	0.97	0.57–1.65		2.21	1.39–3.51	
50–59	2.44	1.55–3.86		4.18	2.74–6.40	
60–69	6.16	3.90–9.74		9.10	5.96–13.90	
70	11.25	7.01–18.08		12.64	8.24–19.40	
Size of community			0.55			<0.01
City of 500,000 people or more	1.00			1.00		
City of 150,000 to less than 500,000 people	0.84	0.59–1.19		0.67	0.51–0.89	
City of 50,000 to less than 150,000 people	0.83	0.56–1.21		0.61	0.45–0.83	
City of less than 50,000 people, suburban districts	0.78	0.55–1.10		0.58	0.44–0.76	
Difficulty initiating sleep			<0.01			<0.01
No	1.00			1.00		
Yes	4.75	3.62–6.22		4.04	3.26–5.02	
Difficulty maintaining sleep			0.94			0.24
No	1.00			1.00		
Yes	0.99	0.75–1.30		1.14	0.92–1.41	
Early morning awakening			0.01			<0.01
No	1.00			1.00		
Yes	1.44	1.11–1.87		1.39	1.12–1.72	
Interruption of sleep by snoring or dyspnea			0.22			0.30
No	1.00			1.00		
Yes	1.44	0.81–2.56		0.72	0.38–1.35	
Disagreeable sensations in legs			0.33			0.71
No	1.00			1.00		
Yes	1.30	0.77–2.18		1.08	0.72–1.61	
Excessive daytime sleepiness			0.92			0.35
No	1.00			1.00		
Yes	0.97	0.48–1.92		1.32	0.74–2.35	
Depressive status (CES-D $\geq$ =16)			<0.01			<0.01
No	1.00			1.00		
Yes	3.51	2.67–4.60		2.56	2.05–3.18	
Sleep duration (h)			<0.01			0.01
<5	1.30	0.65–2.60		1.16	0.71–1.89	
$5 \leqslant <6$	1.16	0.74–1.80		0.98	0.70–1.36	
$6 \leqslant <7$	1.00			1.00		
$7 \leqslant <8$	1.05	0.73–1.51		1.11	0.84–1.48	
$8 \leqslant <9$	1.59	1.08–2.33		1.75	1.28–2.39	
$9 \leqslant <10$	3.34	1.94–5.73		1.61	0.92–2.79	
$10\leqslant$	2.85	1.56–5.22		2.20	1.30–3.73	
Subject sleep sufficiency			<0.01			<0.01
Very sufficient	0.52	0.33–0.82		0.76	0.53–1.08	
Sufficient	1.00			1.00		
Insufficient	1.48	1.09–2.01		1.43	1.12–1.83	
Very insufficient	1.70	1.00–2.90		2.83	1.87–4.26	

AOR, adjusted odds ratio; CI, confidence interval; CES-D, the Center for Epidemiologic Studies Depression Scale.

been included among the hypnotic medications in our survey, which made depressive status a factor strongly associated with hypnotic medication use. In effect, it is known that antidepressants such as amitryptyline, mianserin, and trazodone, have hypnotic properties [29–31], and these antidepressants are frequently used in Japan [32,33]. Unfortunately, a question on the types of hypnotics used was not included in the study questionnaire. It may be difficult for the general population to specify the types of hypnotics they use.

There are some limitations to this study. First, this is a cross-sectional study, and so causal relationships could not be determined, even for items between which an association was indicated. Second, while in previous studies in the United States data on how hypnotic medications were obtained were classified as either "over-the-counter (OTC)" or "by prescription,"[14,15] in the present study this classification was not made during data collection. In Japan, it is inferred that very few subjects obtained hypnotic medication through means other

than prescription. Third, objective data could not be used for the present evaluation of sleep disturbances. However, some studies have reported that self-reported data on sleep status do concur, to a certain extent, with physiological data [34,35]. Fourth, the respondents who neglected to answer six or more questions out of 20 in the CES-D questionnaire were excluded from the analysis. A non-response bias regarding CES-D may have been generated. Finally, in the questions on alcohol use as a sleep aid, nothing on types and volume of alcohol taken was included. If the volume of alcohol consumed as a sleep aid had been calculated from such data, our study results could be compared with results of other studies to be performed in Japan and overseas in the future. Furthermore, questions on sociodemographic factors, such as working status, size of family, education, and income, were not included in the questionnaire. Those factors could possibly influence the habits of alcohol use as a sleep aid and hypnotic medication use. In future studies, questions on the above-mentioned points, which were not included in this study, must be included in questionnaires in order to improve studies on the use of alcohol and hypnotic medication as sleep aids.

Acknowledgments

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Sleep Findings in Young Adult Patients with Posttraumatic Stress Disorder

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Background: Laboratory sleep studies in posttraumatic stress disorder (PTSD) have not provided consistent evidence of sleep disturbance, despite apparent sleep complaints. Most of these studies have investigated middle-aged chronic PTSD subjects with a high prevalence of comorbidities such as substance dependence and/or personality disorder.

Methods: Ten young adult PTSD patients (aged 23.4 ± 6.1 years) without comorbidities of substance dependence and/or personality disorder underwent 2-night polysomnographic recordings. These sleep measures were compared with those of normal control subjects and were correlated with PTSD symptoms.

Results: Posttraumatic stress disorder patients demonstrated significantly poorer sleep, reduced sleep efficiency caused by increased wake time after sleep onset, and increased awakening from rapid eye movement (REM) sleep (REM interruption). We found significant positive correlations between the severity of trauma-related nightmare complaints and the percentage of REM interruption, as well as wake time after sleep onset.

Conclusions: The results indicate that trauma-related nightmares are an important factor resulting in increased REM interruptions and wake time after sleep onset in PTSD.

Impaired sleep is a common complaint among patients with posttraumatic stress disorder (PTSD). However, laboratory sleep studies of PTSD have not provided consistent evidence of sleep disturbances. Most studies have tested middle-aged chronic PTSD subjects typically decades after the traumatic events, except for a handful of studies that were conducted during the immediate aftermath of trauma (Lavie 2001). There are likely a number of factors affecting sleep when PTSD persists for many years. Possible factors considered to explain the discrepancies of objective findings may include differences of 1) the amount of time since the trauma, 2) the age of subjects, 3) the source of the trauma, 4) the acuity of the trauma, 5) many comorbid psychiatric disorders, 6) comorbidities of substance dependence, and 7) the administration of psychotropic medications.

Therefore, we investigated young adult and drug-naïve or drug-free PTSD patients without comorbidities of substance dependence and/or personality disorders, although we could not exclude patients with concomitant major depressive disorder due to its high prevalence. We tested polysomnographic recordings within 1 to 3.5 years after the trauma in these patients and correlated sleep measures with PTSD symptoms.

Methods and Materials

Ten PTSD patients were recruited from the inpatient unit and outpatient clinic in the Department of Neuropsychiatry, Kurume University Hospital. The diagnoses of all patients were confirmed

as PTSD according to the Structured Clinical Interview for DSM-IV (SCID) (American Psychiatric Association 1994) criteria and by exceeding the cutoff value of 50 for the Clinician-Administered PTSD Scale (CAPS) (Blake *et al.* 1995). Subjects with comorbidities of substance dependence and/or personality disorders and those who could not be kept off psychotropic medication for at least 2 weeks prior to this study were excluded. Table 1 shows the background of all PTSD patients. Six of 10 patients had never been treated with any psychotropic medications. Four patients (patients 3, 5, 6, and 8) had been receiving a selective serotonin reuptake inhibitor (SSRI) or benzodiazepines and were required to undergo a washout period of at least 2 weeks.

Control data were obtained from 10 age- and sex-matched healthy subjects. The control subjects were recruited from medical school students and through newspaper advertisements. Their average age was 24.4 ± 9.7 years, which did not significantly differ from that of the PTSD patients. All patients and control subjects were free of physical diseases and other sleep disorders. Written informed consent was obtained from both groups.

All subjects underwent 2 consecutive nights of standard polysomnographic study. They went to bed at their chosen time, and all woke up naturally without an alarm. The records were hand-scored in 20-second epochs according to the criteria of Rechtschaffen and Kales (1968) by a technician blind to the subject's identity.

The extracted sleep measures included indices of sleep initiation and maintenance, sleep architecture, and rapid eye movement (REM) latency, REM interruption (minutes), percentage of REM interruption (%), and REM density. Rapid eye movement periods were determined according to the recently reported procedure (Mellman *et al.* 2002). For each REM period, we determined REM interruptions by summing the intrusive wake times during the REM period and adding the subsequent wake time to the last epoch of REM period before emerging to more than 2 minutes of non-REM sleep. However, if final awakening was derived from the final REM period, the subsequent wake time was not included as REM interruptions. Rapid

Table 1. Background of PTSD Subjects

Case	Age (years)	Sex	Nature of Trauma	Time Since Trauma (months)	Concurrent Diagnoses	Trauma-Related Nightmare	Total Score in CAPS
1	18	M	Sea accident	8	MDD, PD	+	96
2	18	M	Sea accident	8	MDD	−	78
3	19	M	Sea accident	21	MDD	+	77
4	25	F	Vehicle crash	3	MDD	+	84
5	36	F	Vehicle crash	40	—	+	83
6	19	F	Vehicle crash	19	MDD	+	107
7	23	M	Vehicle crash	3	—	−	60
8	31	F	Vehicle crash	39	MDD	+	108
9	25	F	Rape survivor	10	MDD, PD	+	66
10	23	M	Fire accident	4	MDD	+	83
Mean	23.4			15.4			84.4
SD	6.1			14.1			17.1

CAPS, Clinician-Administered PTSD Scale; F, female; M, male; MDD, major depressive disorder; PD, panic disorder; PTSD, posttraumatic stress disorder.

eye movement interruption was calculated as the sum of REM interruptions for each REM period and the percentage of REM interruption was defined as (REM interruption [min]/total REM time [min] + REM interruptions [min]) × 100. Rapid eye movement density was determined by calculating the percentage of 2-second intervals containing at least one horizontal eye movement.

Sleep measures from the second night in both groups were compared by Mann-Whitney *U* test, with .05 as the level of significance. Furthermore, sleep measures were correlated with the total score and subscale scores in CAPS by Spearman rank correlation, with .05 as the level of significance. Multiplicity controlling experimental-wise *p*-value was not applied, since the correlation analysis was performed in an exploratory manner.

Results

The average bedtime of the PTSD subjects (11:01 PM) did not significantly differ from that of the control subjects (10:56 PM). Table 2 shows the comparison of sleep data between both groups. Rapid eye movement interruption and the percentage of REM interruption in the PTSD group was significantly increased compared with the control group. The PTSD group demon-strated significantly reduced sleep efficiency caused by increased wake time after sleep onset. The percentage of slow-wave sleep (SWS) in the PTSD group was significantly decreased compared with the control group. An apnea-hypopnea index in the PTSD group did not significantly differ from the control group (.93 and 1.23 events per hour).

Table 3 shows the correlations between the total score and subscale scores in CAPS and polysomnographic data. There were significant positive correlations between the nightmare score (Criterion B-2) and the percentage of REM interruption, as well as wake time after sleep onset ($R = .82$, $p = .0142$ and $R = .71$, $p = .0358$, respectively). There were significant negative correlations between the nightmare score (Criterion B-2) and sleep latency. In addition, there was a significant negative correlation between the avoidance of stimuli (Criterion C) and total sleep time.

Discussion

The presence of repeated nightmares in PTSD has been hypothesized as a dysfunction of REM sleep mechanisms (Ross *et al.* 1989) and several studies have reported elevated REM sleep phasic events such as greater REM density and motor activity

Table 2. Comparison of Sleep Data Between PTSD and Control Groups

Measurement	PTSD Group (n = 10) Mean	PTSD Group (n = 10) SD	Control Group (n = 10) Mean	Control Group (n = 10) SD	Analysis p Value
Total Sleep Time (min)	450.3	76.0	466.7	72.4	n.s.
Sleep Efficiency (%)	85.5	2.5	94.9	2.1	.0002
Sleep Latency (min)	25.6	21.0	12.9	7.5	n.s.
Waking Time After Sleep Onset (min)	35.9	19.7	11.1	6.6	.0041
Number of Arousals	22.7	10.1	12.1	7.3	.0280
Stage 1 Sleep (%)	11.6	5.7	6.8	2.8	n.s.
Stage 2 Sleep (%)	52.5	10.2	50.6	8.2	n.s.
Stage 3 and 4 Sleep (%)	7.9	7.4	18.1	7.9	.0041
REM Sleep (%)	20.7	4.6	22.7	4.9	n.s.
REM Latency (min)	88.8	37.3	92.5	46.0	n.s.
REM Density (%)	30.8	9.0	25.6	7.0	n.s.
REM Interruption (min)	12.8	12.1	2.3	1.8	.0354
Percentage of REM Interruptions (%)	10.6	8.1	2.2	1.8	.0247

Analysis, Mann-Whitney *U* Test.
n.s., nonsignificant; PTSD, posttraumatic stress disorder; REM, rapid eye movement.

Table 3. Correlations Between the Total Score and Subscale Scores in CAPS and Polysomnographic Data

	TST (min)	SE (%)	SL (min)	WASO (min)	Number Arousals	%SWS (%)	REM Density (%)	Percentage of REM Interruptions (%)
Total Score in CAPS	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Re-experiencing (Criterion B)	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Nightmare (Criterion B-2)	n.s.	n.s.	$-.78$ ($p = .014$)	$.71$ ($p = .036$)	n.s.	n.s.	n.s.	$.82$ ($p = .014$)
Avoidance of Stimuli (Criterion C)	$-.65$ ($p = .049$)	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Hyperarousal (Criterion D)	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Difficulty Initiating and Maintaining Sleep (Criterion D-1)	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.

The correlation coefficient and *p* value by Spearman's rank correlation are shown.
CAPS, Clinician-Administered PTSD Scale; n.s., nonsignificant; REM, rapid eye movement; SE, sleep efficiency; SL, sleep latency; SWS, slow wave sleep; TST, total sleep time; WASO, wake-time-after-sleep-onset.

during REM sleep in chronic combat-related PTSD patients (Mellman *et al.* 1997; Ross *et al.* 1994a, 1994b).

One of the most notable findings in this study is the observation of REM interruption in PTSD patients, replicating the results of two recent studies (Breslau *et al.* 2004; Mellman *et al.* 2002). Mellman *et al.* (2002) tested prospective polysomnographic recordings in 21 injured subjects within a month of injury and found a more fragmented pattern of REM sleep in subjects developing PTSD by calculating the average duration of continuous REM sleep. Breslau *et al.* (2004) compared polysomnographic measures between 71 lifetime PTSD subjects and 212 control subjects in a community sample and reported increased brief arousal from REM sleep in PTSD subjects by calculating the rate per hour of shifts to stage 1 sleep and waking from REM sleep.

Another noteworthy observation is the significant positive correlation between the severity of trauma-related nightmares and the percentage of REM interruptions, as well as wake time after sleep onset. Adapting the REM sleep measures in the aforementioned studies (Breslau *et al.* 2004; Mellman *et al.* 2002) to our small sample, we could not find significant correlations between the nightmare score and those measures. Therefore, it may be important that the measurements of fragmented REM sleep should include not only intrusive wake times during the REM period but also the subsequent wake time to REM period to understand the relationships between nightmares and REM mechanisms in PTSD.

We do not have sufficient explanation for the negative correlations between trauma-related nightmares and sleep latency, but they may be in part related to prior observations that nightmares are rarely observed in the sleep laboratory (Fisher *et al.* 1970; Hartmann 1984) and the "guarded environment" may facilitate sleep initiation for patients with frequent nightmares. Regarding the negative correlations between the avoidance of stimuli and total sleep time, we speculate that avoidance symptoms may result in decreased going out into the sun and consequently produce reduced total sleep time.

Generally, our PTSD patients demonstrated unequivocal sleep maintenance impairments, along with decreased slow-wave sleep. These results diverge from most previous studies (Hurwitz *et al.* 1998; Klein *et al.* 2002; Ross *et al.* 1994a, 1994b). These different findings may be mainly due to the high sleep efficiency (94.9%) of the control group in this study; however, in fact, we found significant improvements of these sleep measures, along with the amelioration of PTSD symptoms after psychotropic medication (unpublished data).

Our PTSD subjects were young adult and drug-naïve or drug-free PTSD patients without history of substance dependence; therefore, they may be vulnerable to PTSD-related sleep disturbances. They demonstrated no evidence of sleep apnea, although several previous studies tested middle-aged patients with chronic PTSD and reported a high incidence of sleep-related breathing disorders (Krakow *et al.* 2001). These different findings may result from differences of the age of subjects among studies.

Finally, confidence in these findings is tempered by several study limitations. The first limitation is the modest sample size in this study. The second limitation is the high comorbidity (80%) of major depressive disorder (MDD); therefore, we could not determine particularly whether the decreased percentage of SWS was derived from PTSD or concomitant MDD. Other limitations include the differences in the amount of time since the trauma and trauma characteristics. Despite these limitations, our findings suggest that trauma-related nightmares may be an important factor resulting in REM interruptions and wake time after sleep onset in PTSD. Attempts to test these findings under controlled conditions in larger samples may further advance the understanding of the relationship between sleep and PTSD.

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Regular Article

Factors influencing subjective sleepiness in patients with obstructive sleep apnea syndrome

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Abstract   The aim of the present paper was to clarify the factors influencing subjective daytime sleepiness in patients with obstructive sleep apnea syndrome (OSAS). Subjects included 230 adult male OSAS patients aged 20–73 years. Single and multiple linear regression analyses were performed to estimate the association between the Epworth Sleepiness Scale (ESS) and the following variables: Minnesota Multiphasic Personality Inventory (MMPI), Self-Rating Depression Scale (SDS), age, body mass index (BMI), sleep duration during the preceding month and apnea–hypopnea index (AHI). Single linear regression analysis showed that age had a negative association with ESS score, while BMI, AHI, SDS, hypochondriasis (Hs), hysteria, psychopathic deviant, psychasthenia, schizophrenia and hypomania on the MMPI had a positive association with ESS score. However, the other remaining parameters such as nocturnal sleep duration during the preceding month, depression, masculinity–femininity, paranoia, social introversion on the MMPI had no statistical association with ESS score. Multiple linear regression analysis with stepwise elimination method was applied to choose the significant factors associated with ESS. It was found that three variables including age, AHI and Hs scores were independent factors influencing ESS score. The R^2 for the model was 0.14, suggesting that these factors account for 14% of possible variance of subjective daytime sleepiness of OSAS patients. These results suggest that subjective daytime sleepiness in patients with OSAS may be influenced not only by the severity of respiratory disorder indices but also by certain personality characteristics affecting Hs score and by age.

Key words   aging, Minnesota Multiphasic Personality Inventory, obstructive sleep apnea, personality characteristics, sleepiness.

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is characterized by repetitive episodes of complete or partial pharyngeal obstruction during sleep. The disorder is accompanied by frequent arousals at the termination of apnea and/or hypopnea, resulting in the occurrence of excessive daytime sleepiness.[1] The severity of OSAS is based on two parameters: level of daytime sleepiness and apnea–hypopnea index per hour (AHI).[2] The Epworth Sleepiness Scale (ESS) is a convenient tool for measuring subjective daytime sleepiness and has been widely used in clinical settings.[3,4] However, it has been reported that correlation between ESS and AHI is weak,[5–8] and that subjective sleepiness was reported only in 46% of the participants with moderate to severe sleep-disordered breathing.[9]

The following three factors could be presumed to influence subjective daytime sleepiness in patients with OSAS: (i) sleep fragmentation caused by respiratory events during sleep;[10–12] (ii) sleep debt brought about by shortening of nocturnal sleep duration;[9,13,14] and (iii) perceptive characteristics of daytime sleepiness

affected by one's personality or mental state.[8,15] Moreover, other factors such as biological aging[11] and obesity[16] have been reported to affect one's subjective daytime sleepiness.

Some previous studies investigated the influence of mental state on subjective daytime sleepiness using self-rating scales such as the Symptom Checklist 90 (SCL-90), the Profile of Mood States (POMS) or the Beck Depression Inventory (BDI). However, there is no previous research focusing on the relationship between subjective daytime sleepiness and personality characteristics.

To clarify factors influencing subjective daytime sleepiness of OSAS patients, we performed a study focusing on the relationship between ESS and descriptive variables including personality characteristics manifested by Minnesota Multiphasic Personality Inventory (MMPI) parameters.

METHODS

Subjects

The ethics committee of Ohta Sleep Disorder Center approved the present study, and written informed consent was obtained from all participants prior to taking part in the investigation.

Subjects included 367 adult male patients who were referred to the outpatient clinic of the Ohta Sleep Disorder Center from January 2002 through December 2003. They were referred for suspicion of OSAS due to habitual snoring, existence of nocturnal apnea witnessed by their family members and/or excessive daytime sleepiness. Through routine clinical interviews we accumulated data on background variables such as age, body mass index (BMI), general health information, current usage of drugs and alcohol and past history of disease that related to the occurrence of OSAS. None of the subjects had current or previous cerebral, cardiovascular, pulmonary, or psychiatric disease, dementia, a history of alcohol or drug abuse, or regular usage of hypnotics. Other sleep disorders such as primary hypersomnia or parasomnias were also completely ruled out by sleep disorder expert physicians. The reports of subjective mean length of nocturnal sleep for the preceding month were divided into four grades: 0, X > 7 h; 1, 7 ≥ X > 6 h; 2, 6 ≥ X > 5 h; 3, X ≤ 5 hours) based on the results of the Pittsburgh Sleep Quality Index.[17]

To assess personality characteristics, we used the authorized Japanese version of the MMPI, and to ascertain the existence of depressive state we used the authorized Japanese version of the Self-Rating Depression Scale (SDS). All subjects completed every questionnaire. The MMPI contains 550 items that yield 10 clinical scales covering a large variety of psychiatric symptoms and personality features.[18] According to standardized criteria,[19] we analyzed T-scores of the following 10 clinical scales as variables: hypochondriasis (Hs); depression (D); hysteria (Hy); psychopathic deviant (Pd); masculinity–femininity (Mf); paranoia (Pa); psychasthenia (Pt); schizophrenia (Sc); hypomania (Ma); and social introversion (Si). The SDS consisted of 20 items that correspond to various clinical symptoms associated with depression. Scores on the SDS have been widely used to assess the presence of a depressive state in various medical conditions as well as in the general population.[20]

Standard polysomnogram (PSG) recordings were made using the standard package of Alice 4 (Respironics, Pittsburgh, PA, USA). Electroencephalogram (EEG), electro-oculogram, chin and bilateral anterior tibialis surface electromyogram, electrocardiogram, airflow through the nose and mouth by thermistor, thoracoabdominal movement, and oxyhemoglobin saturation (SpO_2) on pulse oximetry were performed. The analysis of PSG data was done using the standard criteria of Rechtschaffen and Kales,[21] and the EEG arousals were scored using the American Sleep Disorders Academy guidelines.[22] An apnea event was defined as the cessation of airflow through the nose and mouth lasting ≥10 s during PSG. Hypopnea was defined as a decrease in airflow of ≥50% associated with an oxygen saturation of ≥3% below the preceding baseline value and/or with an arousal.[2] AHI was calculated as the total number of apnea and hypopnea events per hour of sleep.

After collecting the aforementioned information, we excluded 137 subjects as follows: (i) subjects with AHI <5/h (n = 10); (ii) subjects who took some psychotropic drugs that may affect sleepiness at the examination (n = 40); (iii) subjects who had <70% sleep efficiency on the PSG (n = 52); and (iv) subjects who had periodic limb movements ≥15/h because this might elevate subjective daytime sleepiness (n = 35).[23] Thus, 230 patients were enrolled in this cross-sectional study.

Statistical analysis

In order to ascertain the multicolinearity among 10 clinical items of MMPI, Spearman's rank correlation coefficient was calculated. Single and multiple linear regression analyses were performed to estimate the relationship between ESS score and the following variables: MMPI, SDS, AHI, age, BMI and nocturnal sleep duration during the preceding month. All analyses were performed using SPSS version 12.0J (SPSS, Chicago, IL, USA). A stepwise approach was per-

formed in a backward elimination manner, which began by including all explanatory variables in the model. Variables were dropped one at a time and the equation was assessed at each step. The procedure was repeated until a satisfactory model was achieved. The process was continued until all the remaining variables had $P < 0.05$.

RESULTS

Demographic variables and clinical characteristics of subjects are shown in Table 1. The study population consisted of patients with a mean age of 46.4 ± 11.8 years and a median age of 45.0 years. BMI was 26.5 ± 4.3 kg/m², and 138 of the subjects (60.0%) had a BMI exceeding the cut off for normal range among the Japanese population (i.e. 25 kg/m²).[24] Of the subjects, 192 (83.5%) reported getting 5–7 h of nocturnal sleep during the preceding month. The ESS was 8.1 ± 4.2 and 55 of the subjects (22.9%) had a score >10, which was considered to be pathologically sleepy.[3,11] The mean AHI was 42.8 ± 26.4/h, and the median value was 39.3.

Table 1. Descriptive variables of OSAS subjects

Variables	Mean ± SD	Range
Age (years)	46.4 ± 11.8	20–73
BMI (kg/m²)	26.5 ± 4.3	18.2–44.6
Sleep duration during the preceding month (0/1/2/3†)	1.5 ± 0.8 26/82/110/120–3	
ESS score	8.1 ± 4.2	0–22
AHI (/h)	42.8 ± 26.4	5.0–107.9
Sleep efficiency (%)	83.3 ± 7.5	70.0–97.9
SDS score	36.9 ± 7.7	21–66
MMPI items		
L (Lie)	51.1 ± 10.1	36–86
F (Frequency)	50.1 ± 9.9	33–109
K (Defensiveness)	52.8 ± 10.1	26–74
Hypochondriasis (Hs)	58.7 ± 13.1	28–96
Depression (D)	54.3 ± 12.0	31–95
Hysteria (Hy)	56.6 ± 13.1	22–98
Psychopathic deviate (Pd)	52.8 ± 9.9	31–86
Masculinity-femininity (Mf)	50.2 ± 8.5	26–78
Paranoia (Pa)	52.2 ± 9.4	30–90
Psychasthenia (Pt)	52.3 ± 10.8	30–93
Schizophrenia (Sc)	52.8 ± 10.6	29–88
Hypomania (Ma)	48.2 ± 8.7	28–75
Social introversion (Si)	49.0 ± 10.4	26–74

† 0: X > 7 h; 1: 7 ≥ X > 6 h; 2: 6 ≥ X > 5 h; 3: 5 ≥ X hours.
AHI, apnea–hypopnea index; BMI, body mass index; ESS, Epworth Sleepiness Scale; MMPI, Minnesota Multiphasic Personality Inventory; OSAS, obstructive sleep apnea syndrome; SDS, Self-Rating Depression Scale.

On the MMPI the pattern of mean validity scores Lie (L), Frequency (F) and Defensiveness (K) indicated that the subjects generally responded to items in an honest manner (mean L: 51.1 ± 10.1), without any bias such as "faking severity" (mean F: 50.1 ± 9.9) or "denial of distress" (mean K: 52.8 ± 10.1). The scale with the highest ranked absolute magnitude was Hs, which averaged 58.7 ± 13.1. The second highest item was Hy (mean, 56.6 ± 13.1). But the means of all other T-scores for the MMPI items were within normal range (45–70), indicating that the subjects did not have definite pathological abnormalities with regards to psychological parameters.

A correlation matrix for the 10 personality characteristics on the MMPI is shown in Table 2. There were several statistically clear and significant correlations ($r \geq 0.5$) among many MMPI variables: Hs vs D, Hy, Pd, Pt and Sc; D vs Pt, Sc and Si; Hy vs Pd and Pt, Pd vs Pt and Sc, and Pt vs Sc.

As for the results of SDS, the mean score was 36.9 ± 7.7, and the values for all the subjects remained within normal limits.[25]

To assess the association of each variable with ESS score, single linear regression analysis with 95% confidence intervals was applied. Age had negative association with ESS score (Pearson correlation coefficient, $r = -0.245$, $P < 0.001$), while BMI ($r = 0.165$, $P = 0.012$), AHI ($r = 0.199$, $P = 0.002$), SDS ($r = 0.169$, $P = 0.010$), Hs ($r = 0.212$, $P = 0.001$), Hy ($r = 0.177$, $P = 0.007$), Pd ($r = 0.133$, $P = 0.044$), Pt ($r = 0.227$, $P = 0.001$), Sc ($r = 0.228$, $P < 0.001$) and Ma ($r = 0.163$, $P = 0.014$) on MMPI had a positive association with ESS score. However, the other remaining parameters such as nocturnal sleep duration during the preceding month, D, Mf, Pa, Si on MMPI had no statistical association with ESS score (Table 3). Next, multiple linear regression analysis with stepwise elimination was applied to choose the significant factors associated with ESS. Considering the results of correlation matrix among items on the MMPI, we selected five items (Hs, Mf, Pa, Ma and Si). The analysis showed that three variables including age, AHI and Hs scores were independent factors influencing ESS score (Table 4). The R^2 for the model was 0.14, suggesting that these factors account for 14% of possible variance of subjective daytime sleepiness of OSAS patients.

DISCUSSION

The present study showed that subjective daytime sleepiness in patients with OSAS was influenced by AHI and age as well as by characteristics of personality. The positive correlation between AHI and ESS was consistent with several previous studies,[3,4,9,11,26] indicating that

Table 2. Correlation matrix among T-scores for each item on the MMPI

	Hs	D	Hy	Pd	Mf	Pa	Pt	Sc	Ma	Si
Hs	1.000									
D	0.552**	1.000								
Hy	0.778**	0.425**	1.000							
Pd	0.566**	0.396**	0.568**	1.000						
Mf	0.128	0.291**	0.201*	0.188*	1.000					
Pa	0.269**	0.150	0.358**	0.398**	0.341**	1.000				
Pt	0.625**	0.665**	0.544**	0.510**	0.315**	0.342**	1.000			
Sc	0.592**	0.530**	0.494**	0.565**	0.262**	0.374**	0.744**	1.000		
Ma	−0.077	−0.204*	−0.018	0.127*	0.027	0.184*	0.003	0.159	1.000	
Si	0.177*	0.618**	−0.041	−0.004	0.178*	0.004	0.405**	0.288**	−0.263**	1.000

Spearman's rank correlation coefficient * $P < 0.01$; ** $P < 0.001$.

D, Depression; Hs, Hypochondriasis; Hy, Hysteria; Ma, Hypomania; Mf, Masculinity–femininity; MMPI, Minnesota Multiphasic Personality Inventory; Pa, Paranoia; Pd, Psychopathic deviate; Pt, Psychasthenia; Sc, Schizophrenia; Si, Social introversion.

Table 3. Correlation coefficient between clinical variables and ESS score

Variables	Pearson correlation coefficient	P
Age (years)	−0.245	<0.001
BMI (kg/m²)	0.165	0.012
Sleep duration during the preceding month	0.090	0.174
AHI (/h)	0.199	0.002
SDS score	0.169	0.010
MMPI items		
Hypochondriasis (Hs)	0.212	0.001
Depression (D)	0.108	0.103
Hysteria (Hy)	0.177	0.007
Psychopathic deviate (Pd)	0.133	0.044
Masculinity-femininity (Mf)	0.003	0.958
Paranoia (Pa)	0.077	0.245
Psychasthenia (Pt)	0.227	0.001
Schizophrenia (Sc)	0.228	<0.001
Hypomania (Ma)	0.163	0.014
Social introversion (Si)	0.094	0.155

AHI, apnea–hypopnea index; BMI, body mass index; MMPI, Minnesota Multiphasic Personality Inventory; SDS, Self-Rating Depression Scale.

sleep fragmentation brought about by frequent respiratory events during sleep would play an important role on the occurrence of subjective daytime sleepiness.

Although Johns showed that age did not influence ESS in patients with OSAS,[4] the present results indicated that there was a negative correlation between age and ESS. This result was in line with epidemiological results of both the Sleep Heart Health Study[11] and the Penn state cohort study.[27] Moreover, in clinical settings it has been demonstrated that the severity of OSAS decreased with advancing age.[28] Krieger *et al.* also reported that respiratory effort in response to upper airway occlusion decreased with increasing age.[29] This finding suggested that a smaller respiratory effort leads to the lesser degree of both fatigue and daytime sleepiness in elderly OSAS subjects compared to younger subjects. Moreover, it was reported that the deteriorating effects of sleep loss on psychomotor performance was smaller in the elderly compared to a younger population.[30] These physiological characteristics and the aforementioned characteristics of OSAS itself in the elderly were thought to contribute to the prevention of sleepiness in the daytime.

The relationship between ESS and obesity has been debatable. In the present study BMI was not significantly correlated with ESS. This finding indicated that the potential confounding between AHI and BMI may have reduced the contribution of BMI in the final equation.

Furthermore, sleep duration during the preceding month was not significantly correlated with ESS in the present study. This finding is different to that of Kapur *et al.*[9] in which sleep duration was significantly correlated with subjective sleepiness in patients with OSAS. However, we speculate that subjective daytime sleepiness in patients with OSAS is directly affected by individual differences in the demand for and length of habitual sleep.[31]

Previous studies indicated that depressive symptoms were highly prevalent among OSAS patients,[32–34] and the relationship between subjective level of sleepiness and depressive symptoms should be clarified. But in the present study the values of SDS in all the subjects