sleep/wake parameters. Video games may stimulate children by exposing their eyes to bright light and causing excitement at bedtime, which may alter their circadian rhythms (Higuchi, Motohashi, Liu, & Maeda, 2005).

Although use of the Internet was less prevalent than television viewing and playing video games among elementary school children, the rate of Internet use before bedtime increased with advancing age, and its use seemed to affect sleep/wake parameters. A recent report indicated that 67.9% of 6- to 12-year-old children and 93.0% of 13- to 19-year-old adolescents used the Internet during the past year (Japanese Ministry of Internal Affairs and Communication, 2007). It could be speculated that the negative effect on sleep/wake parameters is more prominent among junior and senior high school students. A previous report found that television viewing, computer game playing, and Internet use all have a negative impact on self-reported sleep/wake parameters in adolescents (Van den Bulck, 2004).

A recent lifestyle survey of children in Japan showed that elementary school children often use cell phones not only for telephone calls but also for e-mail transmissions and Internet access (Benesse Educational Research and Development Center, 2005). Furthermore, television programs can be viewed free of charge on most popular cell phones currently sold in Japan. This means that children, just by having a cell phone, may talk on the telephone, surf the Internet, send e-mail, and even watch television. We should advise parents to keep these advanced cell phones away from children before bedtime.

After-school activity, including extra schooling, is another factor affecting children's sleep. Pressure to enter a better junior or senior high school is a general trend in Japan, China, Korea, and other Asian countries. Children are urged to stay up late to prepare for exams. Usually, extra school classes for senior students end later in the evening. Our study indicated that the later time to come home from school significantly affects sleep/wake parameters. Health care professionals and educators should be aware that late after-school activities may disturb sleep.

One of the limitations in our study was that the sample was from one elementary school. Thus, our findings may not be generalizable to all school children in Japan. However, we chose an elementary school that was located neither in an urban area nor rural area so that we could reduce regional or socioeconomic bias. In addition, we selected a public elementary school that all except a few children in the area must attend. Therefore, we assumed that sampling bias due to regional or socioeconomic factors was minimal. It may be important to survey urban and rural areas of Japan to see if there are significant geographic differences in sleep habits.

Another limitation was that psychometric data were not received; demographic details such as family size, number of siblings, number of rooms, and parental education were not asked about; and the frequency and duration of bedtime activities were not quantified. However, our findings may be useful in educating parents and healthcare practitioners to encourage children to have better sleep.

CONCLUSION

Activities before bedtime, televisions and cell phones in the bedroom, and after-school activities were shown to affect the sleep/wake schedule, although the effects remained small. To improve children's nocturnal sleep, children and parents should avoid factors (especially playing video games and using the Internet before bedtime) that potentially affect the sleep/wake schedule. Televisions, cell phones, and computers should not be taken into the bedroom, and after-school activities that delay bedtime and shorten sleep duration should be limited.

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Original Article

Clinical significance and correlates of behaviorally induced insufficient sleep syndrome

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Abstract

Background and purpose: The aim of this study was to investigate the demographic variables and clinical characteristics of behaviorally induced insufficient sleep syndrome (BIISS) and to compare it with the other major hypersomnia disorders.
Patients and methods: One-thousand two-hundred forty-three consecutive patients referred to the outpatient clinic for complaint of excessive daytime sleepiness (EDS) were retrospectively investigated.
Results: The rate of BIISS in patients with EDS was 7.1%, predominant in males. The mean age of initial visit was younger than that for obstructive sleep apnea syndrome (OSAS), while the mean age of onset of symptoms was older than that for idiopathic hypersomnia, narcolepsy, and circadian rhythm sleep disorders. The mean Epworth sleepiness scale (ESS) score before treatment was lower than that for narcolepsy but higher than that for both OSAS and circadian rhythm sleep disorders. Twenty-two percent of BIISS cases reported having accidents or near-miss accidents during the five-year period preceding the investigation, and this group showed higher ESS scores than the group without accidents.
Conclusions: Our findings showed that an unignorably large number of people suffer from BIISS, and that people with severe cases of the disorder are at high risk for getting into an accident. Characteristics and demographic information could be helpful for making a differential diagnosis of BIISS.

Keywords: BIISS; Excessive daytime sleepiness; Prevalence; Clinical settings; Accident; Hypersomnia

1. Introduction

Chronic insufficient sleep or sleep loss is a common problem in modern industrial societies. The current length of sleep time for the working population is about one hour shorter than it was 40–50 years ago, which leads to a substantially less rested feeling in the morning [1]. Japanese workers have been presumed to be a risk group in whom nocturnal sleep is restricted due to extensive overtime work and long commuting times [2]. This type of schedule may result in the accumulation of chronic sleep debt [3].

The prevalence rates of excessive daytime sleepiness (EDS) were 13.3% for women and 7.2% for men in a sample of Japanese employees [4]. Some patients who complain of EDS and of repeated episodes of falling asleep during the day have neither a sleep disorder nor a medication use disorder; instead they are chronically

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sleep-deprived [3]. A considerable number of people liquidate sleep debt or compensate for chronically inadequate sleep by extending their sleep time on weekends or during vacations [5].

Sleep loss and EDS may have serious consequences, including traffic and industrial accidents, decreases in productivity and performance, and interpersonal problems [6–8]. In spite of these adverse consequences, the prevalence of behaviorally induced insufficient sleep syndrome (BIISS) as defined in the International Classification of Sleep Disorders-2nd edition (ICSD-2) has not been well ascertained, particularly in Japan.

The first aim of the present study was to estimate the prevalence of BIISS in a clinical setting. The frequency of traffic and industrial accidents or near-miss accidents in BIISS patients and their relationship to subjective daytime sleepiness measured by the Epworth sleepiness scale (ESS) [9] were also investigated. Our second aim was to investigate the clinical characteristics of BIISS, which could be helpful for making a differential diagnosis of the disorder.

2. Methods

One-thousand two-hundred forty-three consecutive patients, referred to the outpatient clinic of the Japan Somnology Center over the course of one year (May 2003–April 2004) for complaint of EDS, were retrospectively investigated. We reviewed the diagnoses using a systematic evaluation including interviews, polysomnographic (PSG) findings, multiple sleep latency test (MSLT) results, sleep logs, and treatment outcomes. When assessing BIISS, the following ICSD-2 criteria [10] were used: (1) complaint of EDS, (2) shorter habitual sleep episodes than expected from age-adjusted normative data, (3) longer sleep schedules on weekends or vacations than usual, and (4) no disorder or substance use associated with sleepiness. Circadian rhythm sleep disorder was ruled out by asking patients to keep a sleep log. Mental disorder and substance use disorder were also ruled out by psychiatrists with expertise in sleep disorders. BIISS was diagnosed in subjects whose subjective symptoms were clearly improved by extending sleep length. After extending nocturnal sleep by about 2 h for two weeks and checking it with a sleep log, PSG and MSLT were performed in order to differentiate BIISS from narcolepsy, idiopathic hypersomnia, and other secondary hypersomnias. We also excluded patients who were long sleepers and those suspected to have chronic fatigue syndrome [11]. In all cases, the final diagnosis was made when at least two clinicians were in complete agreement. There were 88 well-defined BIISS cases of 1243 consecutive patients with complaints of EDS.

We retrospectively investigated the demographic variables, age at onset of EDS, and severity of subjective sleepiness before treatment, estimated by ESS scores, and compared these variables with other hypersomnias. Based on patients' self-reported answers, we also investigated whether BIISS patients had been involved in either an accident or a near-miss accident due to sleepiness while driving and/or working during the five-year period preceding the investigation. ESS scores for the group with a history of accidents or near-miss accidents and for the group without such a history were compared.

The difference between sleep length on weekdays and on weekends, based on retrospective self-report has been accepted as an index which estimates sleep debt [10]. Both sleep debt and subjective sleepiness were compared in each group and examined in relationship to the usual sleep time on weekdays.

To acquire information for the differential diagnosis of BIISS from other hypersomnias, we compared descriptive variables such as mean age at the initial visit to our outpatient clinic, mean age at the onset of the symptoms, ESS score before treatment, BMI, and weekday sleep-length.

The data were statistically analyzed using Stat View statistical software (Abacus Concepts, Inc.). A two-tailed *t*-test was used to compare ESS scores between the group having had a sleep-related accident and the group who had not. The relationship between sleep debt and the usual sleep-length on weekdays, as well as the distribution of ESS scores, and the comparison of variables among the five groups with major hypersomnias were separately conducted by a one-way analysis of variance (ANOVA). Bonferroni/Dunn tests were used for post-hoc comparisons. The statistical significance was defined as $p < 0.05$.

3. Results

The demographics of the 88 individuals diagnosed with BIISS in our sample are as follows: the male-to-female ratio was 7:3, with a mean age of 30.2 ± 7.3 years old (range: 17–52 years old); the mean age of onset of the symptoms was 28.6 ± 7.5 years old. The average educational level was 15.3 years; 68% graduated from junior college, college or graduate school. In addition, 90.6% were employed and had worked for a mean of 7.0 ± 7.2 years (range: 1–30 years) in their current job.

Patients diagnosed with BIISS reported sleeping an average of 5.5 ± 0.8 h (range: 4–7 h) during weeknights and 7.9 ± 1.6 h (range: 4–12 h) on weekends. The difference in sleep length between weekday and weekend was 2.4 ± 1.6 h (range: 0–7.5 h). The mean ESS score before treatment was 13.6 ± 3.4 (range: 7–23).

At least one accident or near-miss due to sleepiness on the job or while driving was reported by 22.1% of BIISS patients. The group who had been involved in an accident or near-miss showed significantly higher

ESS scores (15.5 ± 3.8) compared to the group who had not been involved in a sleep-related accident (13.0 ± 3.1; $p < 0.01$) (Fig. 1).

The relationship between sleep debt and subjective sleepiness as measured by the ESS for the weekday sleep-length groups is presented in Fig. 2. Sleep debt was significantly more in the group with 5–6 h of nocturnal sleep-length on weekdays compared to the groups with 7–8 or 6–7 h ($F(3, 84) = 3.6$, $p < 0.05$; $p < 0.01$, $p < 0.05$, respectively). However, there was no significant difference in ESS scores among the weekday sleep-length groups ($F(3, 82) = 1.5$, ns).

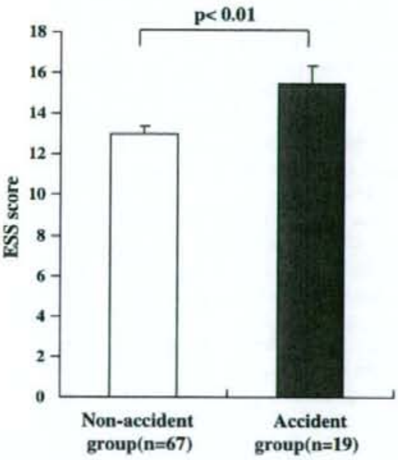

Fig. 1. The comparison of ESS scores between the accident group and the non-accident group.

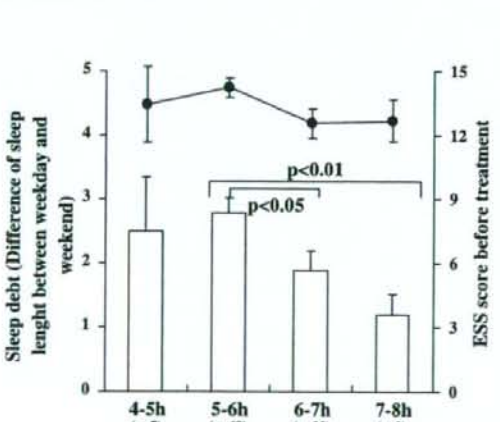

Fig. 2. The relationship between both sleep debt and subjective sleepiness as measured on ESS among the weekday sleep-length groups.

Table 1 shows the final diagnostic categories and breakdown of the 1243 patients complaining of EDS. BIISS (7.1%) ranked fourth among EDS-related diagnoses in our patient population. Obstructive sleep apnea syndrome (OSAS) was the most frequent diagnosis (34.7%), followed by idiopathic hypersomnia (10.9%) and narcolepsy (8.8%). Less frequent diagnoses associated with EDS included circadian rhythm sleep disorder (6.1%), sleep disorder associated with mental disorder (4.3%), and periodic limb movement disorder (2.7%). All subjects underwent nocturnal PSG, and 11 of 431 patients with OSAS underwent MSLT. PSG and clinical interview were used to diagnose patients who had idiopathic hypersomnia with long sleep time ($n = 89$), and patients with idiopathic hypersomnia without long sleep time were diagnosed by PSG and MSLT ($n = 47$). Fifty-seven patients were diagnosed with narcolepsy with cataplexy, after confirmation of EDS, cataplexy, and sleep onset REM period (SOREMP) by PSG. Fifty-two patients with EDS, hypnagogic hallucination and sleep paralysis underwent both PSG and MSLT and were diagnosed with narcolepsy without cataplexy. BIISS was diagnosed when we confirmed a disappearance of EDS after prolongation of nocturnal sleep duration ($n = 87$), except for one patient for whom a diagnosis of BIISS was made using both MSLT and PSG.

Background and clinical variables were compared among the five most frequent diagnostic groups of patients with EDS (Table 2). There was a significant difference in age at the time of the initial visit to our outpatient clinic ($F(4) = 94.3$, $p < 0.0001$). A post-hoc test revealed that the BIISS patients were younger than

Table 1
Diagnoses of the 1243 patients with excessive daytime sleepiness

Diagnosis	*n*	%
Obstructive sleep apnea syndrome	431	34.7
Idiopathic hypersomnia	136	10.9
Narcolepsy	109	8.8
Behaviorally induced insufficient sleep syndrome	88	7.1
Circadian rhythm sleep disorders	76	6.1
Sleep disorders associated with mental disorders	54	4.3
Periodic limb movement disorder or restless legs syndrome	33	2.7
Insomnia	30	2.4
Parasomnias	14	1.1
Long sleeper	12	1.0
Recurrent hypersomnia	3	0.2
More than two diseases causative	69	5.6
for daytime sleepiness	25	2.0
(of which ISS + other hypersomnia)		
Undiagnosed	188	15.1

Undiagnosed, patients who did not have a confirmed diagnosis due to interruption of the diagnostic examination or treatment, or patients in whom two clinicians did not completely agree on the final diagnosis.

Table 2
Comparison of the descriptive variables among the five groups with major hypersomnia disorders

	Mean age of initial visit		Mean age of symptoms-onset[a]		ESS score of the initial visit		BMI		Sleep length of weekday	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Behaviorally induced insufficient sleep syndrome	30.2	7.3	28.6	7.5	13.6	3.4	22.2	2.8	5.5	0.8
Sleep apnea syndrome	45.1	12.1***	–	–	12.5	3.6**	27.4	4.9***	6.1	1.0***
Idiopathic hypersomnia	31.4	9.0	19.2	7.3***	14.3	3.0	21.8	3.1	6.3	1.1***
Narcolepsy	31.0	13.3	17.2	7.5***	15.7	3.0***	23.4	4.1*	6.4	1.3***
Circadian rhythm sleep disorders	27.7	8.1	18.9	6.4***	12.4	3.7*	21.9	3.8	7.8	2.3***

Result with post-hoc test (compared with BIISS). *$p < 0.05$; **$p < 0.01$; ***$p < 0.0001$.
Mean sleep latency of MSLT, sleep apnea syndrome 6.50 min, idiopathic hypersomnia 5.25 min, narcolepsy 2.15 min.
[a] We exclude obstructive sleep apnea syndrome from this analysis because of the data is unknown in the population with this syndrome.

patients with OSAS at the initial visit ($p < 0.0001$). Age of onset was compared among the four groups, excluding the group with OSAS because a lack of subjective awareness of apnea made it difficult to identify the onset of this syndrome [12]. Results showed a significant difference in the ages of onset among the groups ($F(3) = 33.1$, $p < 0.0001$). Post-hoc tests revealed that the onset age for BIISS was older than that for idiopathic hypersomnia, narcolepsy, and circadian rhythm sleep disorders ($p < 0.0001$, respectively). The ESS scores before treatment also showed a significant difference among the groups ($F(4) = 23.2$, $p < 0.0001$). The group with BIISS had lower scores than the group with narcolepsy ($p < 0.0001$) but higher scores than the groups with OSAS ($p < 0.01$) and circadian rhythm sleep disorder ($p < 0.05$). There was a significant difference in body mass index (BMI) among the groups ($F(4) = 76.2$, $p < 0.0001$); the mean BMI for BIISS patients was 22.2 ± 2.8 kg/m^2, which was smaller than for patients with OSAS ($p < 0.0001$) and narcolepsy ($p < 0.05$). The sleep length on weekdays in the BIISS group was shorter than that in the other patient groups with EDS ($F(4) = 40.7$, $p < 0.0001$).

4. Discussion

In this study, BIISS was the diagnosis for 7.1% of patients who came to our sleep disorders clinic with a complaint of EDS. This frequency is similar to previous studies conducted in the United States [3,10]. BIISS was the fourth most prevalent diagnosis among patients with EDS in our results. OSAS, idiopathic hypersomnia, and narcolepsy were more frequent than BIISS, while the frequency of circadian rhythm sleep disorder and periodic limb movement disorder was lower. Our findings strongly impress that there is a noticeable large number of patients who were not aware that their sleep duration was insufficient.

A population-based study of 12,000 adults conducted by Hublin et al. showed that the prevalence of BIISS in Finland was 20.4% [13]. In a survey using a randomly drawn sample from the general adult population of Japan, 28.7% of adults reported short nocturnal sleep duration (less than 6 h) and 23.1% had a feeling of insufficient sleep [8]. Although these results indicate a high frequency of sleep loss among the general population, the number of people with insufficient sleep who consult medical facilities is clearly low. The reason for this discrepancy could be that most of the people with insufficient sleep are aware that their EDS derives from chronic sleep debt, and they try independently to improve their sleep-curtailed lifestyle.

The male-to-female ratio among the previous studies was inconsistent [13,14]. The gender differences in the prevalence between the studies can be explained largely by differences in methodology, definition of BIISS, or living circumstances of the subject population. Hublin et al. reported that the prevalence of patients with BIISS was higher in women than in men [13]. However, the result of the present study, which used the ICSD-2 for diagnosis, showed that BIISS was much more common among men than women. This finding was quite similar to the finding of Roehrs et al. [14]. It has been reported that women are more likely to be aware of sleepiness [15], and it is plausible that this characteristic might lead women to cope with their sleepiness by taking naps as self-treatment. Most of the BIISS patients were at slightly less than 30 years of mean age and had spent an average of 7 years in their present job. It has been reported that a very large number of Japanese workers feel that they have a heavy workload, which leads to an increase in their sleep-related problems [16]. Our findings raise the possibility that an increase in the demand for long work hours leads to a reduction of nocturnal sleep-length, which contributes to the development of BIISS among employees in this generation.

There was a significant difference between sleep length on weekdays and sleep debt. The group with a 5- to 6-h weekday sleep-length had a significantly greater sleep debt than the groups with a 6- to 7- and 7- to 8-h weekday sleep-length. The ESS score did not relate to usual sleep-length on weekdays for BIISS-afflicted patients. This finding could imply, as reported by Papp et al. [17], that not only the amount of sleep debt but also individual sensitivity to insufficient sleep may affect levels of daytime sleepiness.

BIISS can be associated with significant decrements in daytime performance, particularly with tasks that require close attention and vigilance [18]. Excessive sleepiness undoubtedly increases the risk of accidents [19,20]. In our findings, 22% of the patients with BIISS reported having accidents or near misses. Because our study grouped traffic- and job-related accidents together, the prevalence of traffic accidents alone could not be determined. However, we strongly suspect that the incidence of traffic accidents due to sleepiness is higher than that of the general population, in which the rate of traffic accidents remains under 3% [21]. Moreover, the group of patients reporting these adverse events showed higher ESS scores than the other patients. This finding leads us to emphasize that severe BIISS should not be overlooked, as in the cases of severe OSAS [22,23]. BIISS should be managed by prolonging nocturnal sleep or taking an appropriate daytime nap [24].

Since people with BIISS referred to sleep disorder centers usually complain of excessive sleepiness, the precise differential diagnosis of BIISS from other hypersomnias such as OSAS, idiopathic hypersomnia, and circadian rhythm sleep disorders is necessary. However, it is sometimes difficult to distinguish BIISS from other hypersomnias [3]. Our results show not only a clear reduction of weekday sleep-length, but also some other important clinical characteristics. First, the age at the initial visit of BIISS patients was about 30 years old, and that is clearly younger than that for OSAS, which typically develops in middle age [25]. Second, the BMI among BIISS patients was within the normal range, while patients with OSAS tend to be obese, as is generally known [25]. Third, the onset age for BIISS was higher than that for idiopathic hypersomnia, narcolepsy, and circadian rhythm sleep disorders, all of which usually appear in adolescence or early adulthood [26]. Finally, BIISS yielded a lower ESS score than narcolepsy but significantly higher scores than OSAS or circadian rhythm sleep disorders. This finding suggests that subjective sleepiness could become more serious in patients with BIISS than in patients with OSAS.

This study has some limitations. Only patients visiting the outpatient clinic of a single sleep disorders center were included. The differences and similarities between these outpatients and individuals with BIISS in the general population should be examined in a future study. Information regarding accidents and near misses was collected only by self-report, and it is possible that some patients did not give accurate answers to all of the questions. We were unable to obtain accident or near-miss data in the other groups with hypersomnia. Comparison of ESS scores between BIISS patients with a history of accidents and other groups with hypersomnia would be useful to understand the clinical significance of BIISS. Moreover, the calculation of sleep debt should be reconsidered, given that many individuals with insufficient sleep on weekdays do not compensate for their lack of sleep on weekends.

In conclusion, we want to emphasize that a large number of people suffer from BIISS and that the disorder can cause accidents or near misses. Our findings show the clinical significance and characteristics of BIISS that could be helpful for identifying patients with BIISS in clinical settings. Further study will be necessary for verifying the validity of these characteristics as a diagnostic tool.

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Movement Disorders
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Prevalence of Restless Legs Syndrome in a Rural Community in Japan

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Abstract: To assess the prevalence and clinical significance of restless legs syndrome (RLS) in a Japanese population, we carried out a community-based survey in a rural area of Japan. We sent questionnaires requesting information on demographics, the Center for Epidemiological Studies Depression scale, the Short Form-8, the Pittsburgh Sleep Quality Index, the National Institutes of Health/International RLS Study Group (IRLSSG) consensus questionnaire, and the IRLSSG severity scale for RLS (IRLS) to 5,528 eligible adult residents in the town of Daisen in the Tottori prefecture of Japan. Next, we performed telephone interviews to identify subjects with probable RLS. Of the 2,812 subjects (51.1%) who gave complete answers on the IRLSSG questionnaire, 50 (1.8%) were judged as RLS positive. The prevalence of RLS was significantly higher in women than in men, and significantly lower in individuals 60 years of age or older. Multiple logistic regression analysis revealed that the existence of RLS was significantly associated with depression, lowered mental quality of life, and sleep disturbances. The prevalence of RLS in adult Japanese populations may be lower than that reported in Caucasian populations. However, in a group of Japanese subjects, RLS had a significant impact on daytime functioning as well as subjective sleep quality. © 2008 Movement Disorder Society

Key words: gender; questionnaire; depression; quality of life; sleep disturbance

Restless legs syndrome (RLS) is diagnosed using the diagnostic criteria of the International RLS Study Group (IRLSSG), which consists of the following four items: (1) an urge to move the legs, usually accompanied or caused by an uncomfortable sensation in the legs; (2) beginning or worsening of symptoms during periods of rest or inactivity; (3) partial or total relief of symptoms by movement; and (4) symptoms that are worse in the evening or night than during the day, or that occur only in the evening or night.[1] In western countries, the prevalence of RLS has been reported to range from 5 to 15%,[2–4] but the prevalence of RLS in the general Asian population has not been well-elucidated using authorized questionnaires.[5–7] RLS is thought to play a role in the occurrence of insomnia[8,9] and depression,[4,10] as well as in decreased quality of life.[4,8,11] However, the influence of RLS on daytime functioning and sleep disturbances among individuals in an Asian population has not been investigated.

To clarify these issues, we performed a community-based cross-sectional study on the prevalence of RLS and its effect on mood, quality of life, and subjective sleep disturbances in a rural area of Japan.

SUBJECTS AND METHODS

The ethics committee of Tottori University approved this study, and all subjects gave written informed consent. This survey was performed from November 2005 to January 2006 in the town of Daisen in the Tottori prefecture of Japan. In 2004, the total population was 6,643 and there were 5,528 residents who were 20 years of age or older (mean age, 55.2 years; 2,521 men and 3,007 women).

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Epidemiological data on residents 20 years of age or older were collected using a questionnaire. The questionnaire contained items on demographics, mood, physical and mental condition, sleep condition, and the existence of RLS. We used the 12-item version of the Center for Epidemiological Studies Depression scale (CES-D)[12] for estimating mood status, the Short Form-8 (SF-8)[13] for assessing quality of life, and the Pittsburgh Sleep Quality Index (PSQI)[14] for determining sleep disturbances in the subjects. Based on the total scores on the CES-D, we divided participants into three categories: 0 to 11 as a minimal depressive state, 12 to 20 as a somewhat elevated depressive state, and 21 to 36 as a very elevated depressive state.[12] For the SF-8, calculations were made according to standard methods,[15] and the scale consisted of domains including general health, physical function, role physical, body pain, vitality, social function, mental health, and role emotional. The physical component summary score (PCS) of the SF-8 was evaluated as an index of physical quality of life, and the mental component summary score (MCS) was evaluated as an index of mental quality of life. General population averages for these scores were set at 50 points. If subjects had a score below 50 points, this indicated a deteriorated QOL.[15] For the PSQI, the scale included the following seven components: sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleep medications, and daytime dysfunction. Subjects with more than 5.5 points for their total PSQI score were defined as having sleep disturbances.[14]

We used the Japanese version of the RLS questionnaire, with particular consideration placed on questions for epidemiological studies of RLS that were recommended by the RLS Diagnosis and Epidemiology Workshop at the National Institutes of Health (NIH), in collaboration with members of the IRLSSG.[1] This NIH/IRLSSG consensus questionnaire consisted of the following four items: (1) whether the subjects had unpleasant leg sensations and an urge to move their legs, (2) whether these uncomfortable feelings occurred only or mainly at rest and if they improved with movement (i.e., moving the legs, rubbing the legs, walking around), (3) whether these uncomfortable feelings worsened in the evening or were worse at night than in the morning, and (4) how often the uncomfortable feeling occurred, i.e., less than once a year, at least once a month, at least twice a month, two or more times per week, four or more times per week, or six or more times per week. Subjects fulfilling items 1, 2, and 3, and experiencing RLS symptoms at least one time per year, as judged by the answer to item 4, were regarded as possible RLS subjects.

Subjects who fulfilled more than two items of the questionnaire were contacted by a board-certified sleep disorder expert neurologist within 3 months after the survey to conduct 15- to 20-min detailed telephone interviews to confirm the diagnosis of RLS. In this study, the telephone interviews, which focused on the four essential criteria items for RLS, were made by a single neurologist who specialized in sleep disorders. On the basis of these interviews, we determined whether a subject met the four essential diagnostic criteria for RLS. We then divided the subjects into four subgroups according to the relationship between the results of the questionnaire survey and the results of the telephone interviews. The 3-RLS group gave positive answers to all three questionnaire items and were positively diagnosed with RLS by telephone interview; the 3-not RLS group gave positive answers to all three questionnaire items, but were negatively diagnosed with RLS by telephone interview; the 2-RLS group gave positive answers to two questionnaire items and were positively diagnosed with RLS by telephone interview, and the 2-not RLS group gave positive answers to two questionnaire items and were negatively diagnosed with RLS by telephone interview. We compared the age and gender distributions for each of these groups.

We administered the IRLSSG severity rating scale (IRLS)[16] to RLS-positive subjects. Subjects with IRLS scores less than 10 were categorized as mild; 11 to 20 as moderate, 21 to 30 as severe, and 31 or higher as very severe.[16]

We estimated the prevalence of RLS among our survey population and the severity of the disorder among RLS-positive subjects, as well as the influence of RLS on mood, quality of life, and subjective sleep disturbances. A Chi-squared test was employed to compare the categorical variables. A Mann-Whitney U test and an analysis of variance (ANOVA) followed by the Scheffe post hoc test were utilized to assess statistical differences of continuous variables.

The factors associated with depression (CES-D; cut off value ≥ 12), quality of life (PCS, MCS; cut off value <50), and subjective sleep disturbance (PSQI; cut off value ≥ 5.5) were examined with the aid of a series of logistic regression analyses. In these analyses, we used gender, age group (cut off at 60 years old), and the existence of RLS as explanatory variables. All variables were initially examined in univariate models. To control for confounding factors and to determine the main correlates, we performed multivariate logistic regression analyses for all variables that showed a significant correlation in the univariate models. Statistical

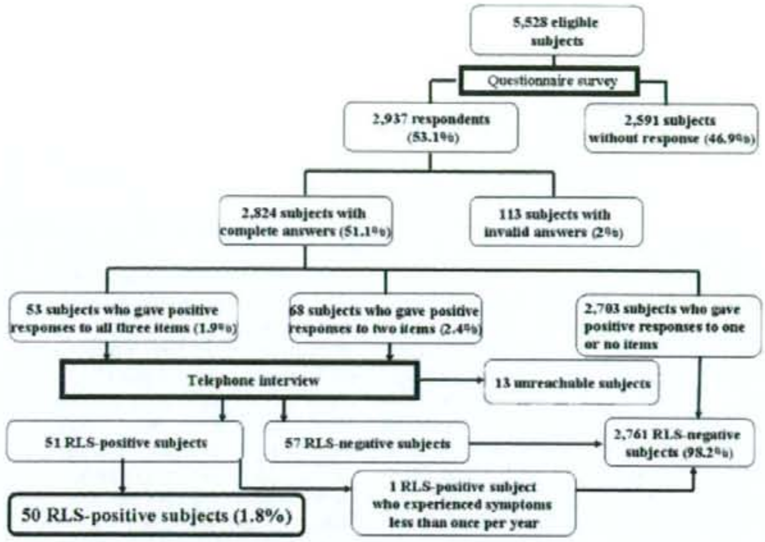

FIG. 1. Schematic of RLS diagnostic process.

tests of the regression estimating odds ratios (ORs) were based on Wald statistics. The odds ratios and their 95% confidence intervals (CIs) were presented to show the association. Correlation coefficients were estimated with the Spearman's rank test. Statistical significance was set at $P < 0.05$. These statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS, ver. 11.5J, 2002; SPSS, Tokyo, Japan).

RESULTS

Of the 5,528 eligible subjects, 2,937 (53.1%) subjects responded to our questionnaire. After we excluded 113 invalid answers, the results of 2,824 (51.1%) subjects were analyzed. The subjects evaluated consisted of 1,223 men and 1,601 women, with ages ranging from 20 to 97 years. The mean age and percentage of men and women subjects who responded [52.9 ± 17.8 years, 1223 men (48.5%) and 1601 women (53.2%), $P = 0.001$] was slightly different from those of subjects who did not respond or whose answers were invalid [50.1 ± 20.3 years, 1298 men (51.5%) and 1406 women (46.8%), $P = 0.001$]. On the questionnaire survey, 53 subjects had items 1, 2 and 3 of the NIH/IRLSSG consensus questionnaire, and 68 subjects had two of the above items of the questionnaire. Detailed telephone interviews were conducted with those 121 subjects, with the exception of 13 subjects to whom we could not contact via telephone.

Based on the telephone interviews, 51 subjects were RLS positive. However, one subject experienced RLS symptoms less than once a year. Thus, we estimated the at least yearly prevalence of RLS in this population was 1.8% (50/2811) (see Fig. 1).

All subjects who received a positive diagnosis of RLS by telephone interview answered item 4 on the frequency of RLS symptoms, with the exception of one person. On the basis of the answers to this item, the proportion of subjects divided by the frequency of symptoms was as follows: at least one time a year but less than one time per month.10 (20.4%); one time per month, 6 (12.3%); 2 to 4 times per month, 15 (30.6%); 2 to 3 times per week, 8 (16.3%); 4 to 5 times per week, 5 (10.2%); 6 to 7 times per week, 5 (10.2%). As a result, we estimated that the weekly prevalence of the disorder was at least 36.7% in RLS-affected subjects.

We determined the proportion of subjects who appeared to have RLS based on both the questionnaire surveys and telephone interviews. Except for the 13 subjects who could not be reached by telephone, 47 subjects gave positive responses to all three items, and 61 subjects gave positive responses to two items. The

TABLE 1. *Characteristics of RLS-positive and RLS-negative groups based on results of questionnaires and telephone interview diagnoses*

		Questionnaire responses		
		Positive for three items	Positive for two items	Total
Telephone interview diagnoses	RLS+	3-RLS group (n = 32) M:F = 6:26 Age:50.3 ± 16.7 years	2-RLS group[a] (n = 19) M:F = 9:10 Age:40.6 ± 19.5 years	RLS positive (n = 51) M:F = 15:36
	RLS−	3-not RLS group[a] (n = 15) M:F = 6:9 Age:62.7 ± 15.6 years	2-not RLS group[a] (n = 42) M:F = 11:31 Age:59.5 ± 20.2 years	RLS negative (n = 57) M:F = 17:40
	Unknown	n = 6, M:F = 2:4	n = 7, M:F = 3:4	n = 13, M:F = 5:8
	Total	n = 53, M:F = 14:39	n = 68, M:F = 23:45	n = 121, M:F = 37:84

RLS: restless legs syndrome; M:F = male:female.
3-RLS group: subjects with positive response to three items diagnosed with RLS by telephone interviews.
3-not RLS group: subjects with positive responses to three items not diagnosed with RLS by telephone interviews.
2-RLS group: subjects with positive response to two items diagnosed with RLS by telephone interviews.
2-not RLS: subjects with positive responses to two items not diagnosed with RLS by telephone interviews.
Unknown: subjects unable to be contacted by telephone.
[a]Four groups had significant differences in age. The 3-not RLS and 2-not RLS groups were significantly older than the 2-RLS group. Ages are expressed as the mean ± SD.

proportion of subjects in the 3-RLS group was 32 of 47 (68.1%), and in the 3-not RLS group was 15 of 47 (31.9%). During telephone interviews, it was determined that 9 of 15 subjects in the 3-not RLS group had misidentified a sense of dysesthesia and/or paresthesia in their lower limbs as an RLS-like sensation. Among the other remaining subjects, 4 subjects had neuralgia, one had leg swelling, and one had itching. The proportion of subjects in the 2-RLS group was 19 of 61 (31.1%), and that in the 2-not RLS group was 42 of 61 (68.9%).

Among the 4 subgroups, significant differences in age were noted by ANOVA [$F(3,107)$, $P = 0.001$] (Table 1). A post hoc test revealed that the subjects in the 3-not RLS groups and 2-not RLS group were significantly older than those in the 2-RLS group ($P = 0.01$, 0.005, respectively). However, there was no difference in gender distribution among the 4 groups (Table 1).

Among the subjects with valid answers to the questionnaires, the proportion of RLS-positive women (2.3%) was significantly higher than that of men (1.2%) ($P = 0.043$). The age distribution of the RLS-positive subjects is shown in Figure. 2. The proportion of RLS-positive subjects, estimated at 2.7% in individuals with 20 to 59 years of age, was significantly higher that that in individuals with 60 years of age or older (0.8%; $P = 0.001$). The proportion of RLS-positive subjects varied significantly among the 10-year age groups (chi squared test, $P = 0.003$) (see Fig. 2).

When descriptive variables were compared between RLS-positive and RLS-negative subjects, the former

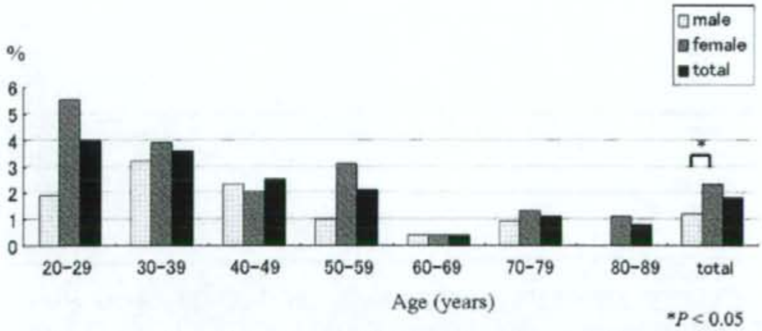

FIG. 2. Prevalence of RLS by gender and age. The prevalence of RLS differed significantly among the 10-year age groups (chi square test, $P = 0.003$). For all subjects, the prevalence was significantly higher in women than in men ($P < 0.05$).

TABLE 2. *Comparison of descriptive variables between RLS-positive and RLS-negative subjects*

	RLS-positive subjects (n = 50)	RLS-negative subjects (n = 2761)	Significance
Age (yr)[a]	46.7 ± 18.2	57.6 ± 17.7	$P = 0.001$
Gender (M/F)[b]	15/35	1207/1565	$P = 0.043$
CES-D (points)[a]	11.7 ± 6.3	8.6 ± 4.9	$P = 0.001$
Distribution of CES-D categories[b]			$P = 0.001$
minimal	29 (56.8)	1991 (71.9)	
somewhat elevated	16 (31.4)	554 (20)	
very elevated	6 (11.8)	65 (2.3)	
SF-8			
PCS[a]	47.4 ± 6.7	47.5 ± 7.4	*ns*
MCS[a]	46.5 ± 7.0	49.8 ± 6.6	$P = 0.001$
PSQI[a]	6.02 ± 2.26	4.13 ± 2.73	$P = 0.001$

RLS: restless legs syndrome, M/F: male/female, CES-D: Center for Epidemiological Studies Depression Scale, SF-8: Short Form-8, PCS: Physical Component Summary score, MCS: Mental Component Summary score, PSQI: Pittsburgh Sleep Quality Index, *ns*: not significant.

[a]Values are expressed as mean ± SD.

[b]Data are presented as number of subjects, with percentages in parantheses.

group was significantly younger than the latter group ($P = 0.001$) (Table 2). The RLS-positive group had significantly higher CES-D scores compared with the RLS-negative group ($P < 0.001$), and contained significantly larger numbers of subjects with somewhat or very elevated CES-D scores ($P < 0.001$). Moreover, MCS summary scores on the SF-8 were significantly lower, and PSQI total scores were significantly higher in the RLS-positive group than those in the RLS-negative group ($P = 0.001$). On the other hand, PCS summary scores on the SF-8 were quite similar between the two groups. With regard to the domains of the SF-8, the RLS-positive group had significantly lower scores for bodily pain ($P = 0.011$), general health ($P = 0.011$), vitality ($P = 0.011$), and mental health ($P = 0.001$) compared with the RLS-negative group. As for the components of the PSQI, the RLS-positive group had significantly higher scores for quality of sleep ($P = 0.001$), sleep latency ($P = 0.007$), sleep duration ($P = 0.048$), sleep disturbance ($P = 0.001$), and daytime dysfunction ($P = 0.001$) than the RLS-negative group.

Multivariate logistic regression analysis revealed that a somewhat or very evaluated score of CES-D was significantly associated with the existence of RLS (OR = 2.32, 95%CI: 2.03–2.61). Regarding quality of life, lowering of the MCS was significantly associated with being women (OR = 1.26, 95%CI: 1.18–1.34), being elderly (OR = 1.36, 95%CI: 1.09–1.44), and the existence of RLS (OR = 2.18, 95%CI: 1.88–2.48), but only age appeared as an associated factor for lowering of the PCS. Subjective sleep disturbances were significantly associated with being elderly (OR = 1.53, 95%CI: 1.44–1.62) and the existence of RLS (OR = 4.79, 95%CI: 4.50–5.08) (Table 3).

TABLE 3. *Univariate and multivariate logistic regression analysis on factors associated with restless legs syndrome (RLS)*

Factor	Univariate Relative Risk (95% CI)	*P*	Multivariate Relative Risk (95%CI)	*P*
Depression[a]				
Gender		ns		ns
Age		ns		ns
RLS	2.44 (2.16 – 2.73)	0.002	2.32 (2.03 – 2.61)	0.003
Decreased physical quality of life[b]				
Gender	1.18 (1.10 – 1.26)	0.034		ns
Age	4.20 (4.12 – 4.29)	0.001	4.24 (4.16 – 4.32)	0.001
RLS		ns		ns
Decreased mental quality of life[c]				
Gender	1.25 (1.18 – 1.33)	0.004	1.26 (1.18 – 1.34)	0.003
Age	1.37 (1.29 – 1.45)	0.001	1.36 (1.09 – 1.44)	0.001
RLS	2.43 (2.13 – 2.73)	0.003	2.18 (1.88 – 2.48)	0.01
Sleep disturbance[d]				
Gender		ns		ns
Age	1.47 (1.38 – 1.56)	0.001	1.53 (1.44 – 1.62)	0.001
RLS	4.28 (3.99 – 4.57)	0.001	4.79 (4.50 – 5.08)	0.001

[a]Depression was defined as less than 12 points on the Center for Epidemiologic Studies Depression Scale.

[b]Decreased physical quality of life was defined as less than median values (49.21) for the physical component score.

[c]Decreased mental quality of life was defined as less than 50 points for the mental component score.

[d]Sleep disturbance was defined as more than 5.5 points on the Pittsburgh Sleep Quality Index. *ns*: not significant. A *P*-value < 0.05 was considered statistically significant. CI: confidence interval.

Among the 50 subjects who were identified with RLS by telephone interviews, 37 completed and returned the IRLS. The mean score on the IRLS was 12.8 ± 6.8. Thirteen subjects (35.1%) were categorized as mild, 19 (51.3%) were categorized as moderate, and 5 (13.5%) were categorized as severe. No subject had a score of 30 or more. The IRLS showed a slight positive correlation with the PSQI, especially in subjects who experienced symptoms at least once per month ($r = 0.411$, $P = 0.03$).

DISCUSSION

The prevalence of RLS estimated from the results of telephone interviews was 1.8%. Of the 13 subjects that could not be reached for the telephone interview there were 6 subjects who fulfilled all three of the RLS questionnaire items and 7 subjects with two positive items. When calculating whether subjects were positive for RLS according to the results of both questionnaires and telephone interviews (3-RLS group: 32 RLS of 47 subjects with three positive items; 2-RLS group: 19 RLS of 61 subjects with two positive items), 4 of 6 subjects with three positive items and 2 of 7 subjects with two positive items were speculated to be RLS positive. With the addition of these subjects, the prevalence of RLS in this study population was estimated at 2.0% (56 of 2824 subjects). These findings suggested that the prevalence of RLS in Japanese individuals was lower than the previously reported prevalence in Caucasian subjects.[2–4] However, the prevalence found in this study was clearly higher than that found in a population in Singapore,[5] and was not negligible.

In this study, the prevalence of RLS was significantly lower in the elderly subjects (60 years of age or older) than in the younger subjects. Although this finding differed from results obtained in western populations,[17] the prevalence of RLS-positive subjects in the elderly population in our study was quite consistent with that reported by Mizuno et al.[7] A report on a Turkish population[11] also indicated no age contribution to the occurrence of RLS. Taken together, these findings suggest that the prevalence of RLS in an Asian population does not increase with advancing age.

On the basis of the results of the questionnaire and detailed telephone interviews, it appears possible that elderly persons are likely to misidentify sensory symptoms such as dysesthesia or paresthesia as RLS. This may contribute to the high prevalence of RLS determined among elderly populations in epidemiological surveys using questionnaires.[18] Our results also revealed that the prevalence of RLS was apparently higher in women than in men. This finding is consistent with results from studies on western populations.[4,7,11,12,17] Although we could not obtain IRLS responses from about 25% of our RLS-positive subjects, the total scores on the IRLS were much lower in our RLS-positive subjects compared with those from the United States, with total scores of 23.8 ± 6.8.[19] This finding suggests that RLS in the Japanese population may be milder than that in western populations.

It is commonly accepted that many patients with RLS in the clinical setting suffer from insomnia.[4,9] In our study, the total score on the PSQI was significantly higher in the RLS-positive group. Also, multiple logistic regression analysis showed a significant association between the existence of subjective sleep disturbances and the existence of RLS. Moreover, the increased severity of RLS manifested on the IRLS seemed to correlate positively with the PSQI score, especially among the subjects who experienced symptoms at least once per month.

Regarding the SF-8, the MCS summary scores deteriorated significantly in subjects with probable RLS while the PCS summary scores in this group did not differ from those in the group without RLS. Moreover, multiple logistic regression analysis revealed that the existence of RLS was significantly associated with deterioration in mental quality of life but not physical quality of life. This finding is different from that in the previous reports in which both mental and physical health had deteriorated in RLS sufferers.[8,11] However, the severity of RLS in the subjects in these reports was clearly higher than that of our RLS-positive subjects. When this difference is taken into consideration, it is possible that in our RLS-positive subjects, the physical quality of life was well maintained due to the mild severity of the disorder. Another possibility is that RLS symptoms did not affect physical function directly, as reported by Rothdach et al.[4]

As for depressive symptoms, the RLS-positive subjects in our study had higher CES-D scores, which was similar to previous reports.[4,10] Moreover, multiple logistic regression analysis showed that the existence of RLS was significantly associated with depression. Taking these findings into consideration, we can assert that RLS has an impact not only on the occurrence of subjective sleep disturbances but also on daytime dysfunction, in spite of the mild severity of the disorder in this study.

This study suffers from several limitations. Firstly, the rural community studied may not be representative of the general Japanese population, and a larger, randomized sample is needed to ascertain the real prevalence of RLS. Secondly, our study might include responder bias such that subjects with leg discomfort or sleep disturbances are more likely to respond to the questionnaire. Thirdly, we made a probable diagnosis of RLS based on telephone interviews, but did not conduct face-to-face interviews with the subjects. However, the prevalence of RLS estimated by the telephone interviews[20,21] was consistent with that made by face-to-face interviews in previous studies.[8,9,17] Therefore, the probable diagnosis made by telephone interviews in this study was thought to be similar to reality. Fourthly, we interviewed the subjects who responded as having two or more of the RLS symptom items, but we could not interview the participants answering only one item positively or the participants answering all three questions negatively due to a lack of response. For this reason, we must consider the possibility that RLS-positive subjects who responded as having one positive item or no positive items on the questionnaire were overlooked. If we interviewed randomly selected subjects in these groups, we could calculate the rate of subjects with false negative results. Considering this issue, the prevalence of RLS in our study population could be a little higher than 1.8%. Therefore, we propose that the prevalence of RLS in Japanese subjects with at least yearly symptoms might be ~2%.

CONCLUSION

In summary, our results support the finding that the prevalence of RLS in Japanese populations is lower than that in Caucasian populations.[2–4,8–10,17,18] The occurrence of RLS in Japan subjects appears to be predominant in women, and is independent of increasing age. Although the severity of RLS in our subjects was mild, the disorder seemed to be associated with depressive symptoms, a disturbed quality of life, and subjective sleep disturbances.

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SCIENTIFIC INVESTIGATIONS

Health-Related Quality of Life Among Drug-Naïve Patients with Narcolepsy with Cataplexy, Narcolepsy Without Cataplexy, and Idiopathic Hypersomnia Without Long Sleep Time

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Objective: To evaluate the health-related quality life (HRQOL) of drug-naïve patients with narcolepsy with cataplexy (NA with CA), narcolepsy without cataplexy (NA without CA) and idiopathic hypersomnia without long sleep time (IHS without LST), and to explore the factors influencing the HRQOL. Factors associated with the occurrence of automobile accidents are also discussed.

Methods: A total of 137 consecutive drug naïve patients who met the criteria of the 2nd edition of the *International Classification of Sleep Disorders* (NA with CA, n = 28; NA without CA, n = 27; IHS without LST, n = 82) were enrolled. The patients were asked to fill out questionnaires, including the SF-36, Epworth Sleepiness Scale (ESS), sociodemographic variables, and items regarding driving habits and the experiences related to automobile accidents.

Results: All 3 diagnostic groups had significantly lower scores in most SF-36 domains compared with Japanese normative data. Significant differences among the 3 diagnostic groups were not observed. Specific factors in SF-36 domains were not found with multiple linear regression analyses, while disease duration was positively correlated with mental health among all subjects. Among the patients reporting driving habits, ESS score (≥16) was positively associated with the experience of automobile accidents.

Conclusions: Our results indicated that HRQOL decreases in drug-naïve patients with hypersomnia, but neither disease category nor severity of the disorder appears as an associated factor. Increased severity of hypersomnia, however, was thought to play an important role in the occurrence of automobile accidents.

Keywords: Narcolepsy, idiopathic hypersomnia without long sleep time, health-related quality of life, SF-36, automobile accidents

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Hypersomnia, a complaint of excessive daytime sleep or sleepiness, affects 9% to 17% of the general population,[1-4] with an impact on the functions of daily life. Some previous studies provided the data suggesting that patients with narcolepsy suffer from severe limitations and difficulties in everyday life activities (school, job, interpersonal relationships, and social activities).[5,6] Studies using the 36-item short from (SF-36) showed that health-related quality of life (HRQOL) among patients with hypersomnias of central origin, especially narcolepsy, decreases in comparison to the general population.[7-11]

In the 2nd edition of the *International Classification of Sleep Disorders* (ICSD-2),[12] narcolepsy was classified into 2 categories focusing on the existence of cataplexy (i.e., narcolepsy with cataplexy [NA with CA] and without cataplexy [NA without CA]). Idiopathic hypersomnia without long sleep time (IHS without LST), also known as NREM narcolepsy or essential hypersomnia, manifesting hypersomnolence similar to narcolepsy without REM sleep abnormality, was also classified as an independent category. Most studies related to HRQOL in patients with hypersomnia have been done on narcoleptic patients with and without psychostimulant medication, and no study has been conducted focusing on untreated patients in the above 3 diagnostic groups[7-11] Moreover, conclusive information about the association between clinical backgrounds and the impairment of HRQOL in these drug-naïve patients has not been obtained.

Excessive daytime sleepiness (EDS) while driving or performing other activities that require constant alertness is dangerous. Narcolepsy has marked effects on daytime performance and has been associated with an increased risk of automobile accidents, as well as accidents on the job and at home.[13,14] However, a relationship between the subjective severity of sleepiness and the occurrence of automobile accidents in the drug-naïve patients has not been elucidated.

The aims of the present study were as follows: (1) to evaluate HRQOL of drug-naive patients with NA with CA, NA without

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CA, and IHS without LST; (2) to explore the factors influencing HRQOL; and (3) to clarify the association between clinical background factors including severity of sleepiness and occurrence of automobile accidents.

METHODS

The present study was approved by the local ethics committee of the Japan Somnology Center. Informed consent was obtained from all the patients who participated in the study.

Participants

Among patients ≥ 20 years who visited the outpatient clinic of the Japan Somnology Center seeking medical assistance, 137 consecutive drug-naïve patients with a diagnosis of NA with CA (n = 28), NA without CA (n = 27), or IHS without LST (n = 82) who met the criteria of ICSD-2[12] were enrolled between May 2003 and October 2004. Because of an insufficient number of patients, IHS with LST was not targeted in the present study. All subjects with NA without CA and IHS without LST underwent overnight polysomnography followed by a standard multiple sleep latency test (MSLT).[15] Among the subjects with NA with CA, 7 did not undergo MSLT, but each had a history of typical cataplexy and clear sleep onset REM periods during overnight polysomnography. The 21 remaining subjects with NA with CA and all the subjects with NA without CA had ≥ 2 SOREMP and < 8 min mean sleep latency on MSLT. All subjects with IHS without LST showed ≤ 8 min of mean sleep latency and 0-1 SOREMP on MSLT. Diagnoses were made according to the above criteria by at least 2 board-certified sleep disorder expert psychiatrists. Patients with comorbidities of other sleep disorders (e.g., obstructive sleep apnea syndrome, periodic limb movement disorder, circadian rhythm sleep disorders), psychiatric disorders (including mood disorders) and other major medical illnesses, and patients taking sedatives habitually were completely excluded from this study.

Measures

The participants were asked to fill out a questionnaire that included an instrument assessing dimensions of HRQOL, an instrument evaluating subjective sleepiness, questions regarding sociodemographic variables, and items regarding driving habits and the experiences of automobile accidents. Additional clinical information including demographic variables was also obtained from the participants' medical records.

Medical Outcomes Study Short Form-36 Version 1.2

HRQOL was assessed by using the Japanese version of the Short Form-36 health survey questionnaire (SF-36, Ver. 1.2), a self-administered questionnaire that has been widely used and validated on Japanese general population.[16-18] The questionnaire comprises 36 questions divided into the following 8 domains representing different aspects of HRQOL.

1. *Physical functioning (PF),* the subject's ability to deal with the physical requirement of life, such as attending to personal needs, walking, and flexibility.
2. *Role limitations due to physical problems (RP),* the extent to which physical capabilities limit activity.
3. *Role limitations due to emotional problems (RE)* the extent, if any, to which emotional factors interfere with work or other activities.
4. *Social functioning (SF),* the extent to which physical health or emotional problems have interfered with family, friends, and other social interactions during the previous 4 weeks.
5. *Mental health (MH),* feelings of anxiety and depression.
6. *Energy/vitality (VT),* feelings of pep, energy, and fatigue.
7. *Bodily pain (BP),* perceived amount of pain experienced during the previous 4 weeks and the extent to which that pain interfered with normal work activities.
8. *General health perceptions (GH),* general health in terms of personal perception.

Epworth Sleepiness Scale

Subjective sleepiness was assessed at the time of the first visit, using the Epworth Sleepiness Scale (ESS),[19] a widely accepted self-completion questionnaire, previously validated on both the Japanese general population and patients with hypersomnia.[20] Participants were asked about the possibility of falling asleep in 8 specific situations that are commonly encountered in daily life (0 = would never doze; 3 = high chance of dozing). The ESS score is the sum of 8 item-scores and can range from 0 to 24.[19] The severity of subjective sleepiness was defined by the ESS score: normal (ESS score < 11), mild (≥ 11, < 16) and severe (≥ 16).[21-23]

Sociodemographic Variables, Automobile Accidents, and Clinical Information

Sociodemographic variables included marital status, numbers of family members in the household, educational status, and occupation. Questions about driver's license, driving habit, and the experience of automobile accidents were embedded: "Have you ever been involved in automobile accidents or near-miss incidents while driving during the last 5 years?" Clinical information including age, gender, age at onset of hypersomnia, and length of its morbidity was also obtained.

Statistical Analysis

Demographic, sociodemographic and clinical variables were compared among three diagnostic groups (NA with CA, NA without CA, and IHS without LST). One-way analysis of variance (ANOVA) was used for the comparison of the continuous variables among the 3 diagnostic groups, and the chi-squared test was employed for categorical variables.

The scores of 8 subscales of the SF-36 were converted into Japanese norm-based score according to their gender and age (standardized t score transformation with a mean of 50 ± 10).[18] Scores below 50 indicate that health status is below average compared to the general Japanese population. This method enables comparison of the magnitude of impact among the 8 subscales, which reflects the recommendation of Japanese Manual of SF-36.[18] The scores of all subjects were compared with those

Table 1—Descriptive Variables Including Main Demographic and Clinical Features and Prevalence of Automobile Accidents in Each Diagnostic Group

characteristics	Overall	NA with CA	NA without CA	IHS without LST	p value
Number of participants	137	28	27	82	
Gender (%)					
Male	48.2	35.7	37.0	56.1	n.s.
Female	51.8	64.3	63.0	49.3	
Age (years)					
Mean ± SD	31.2 ± 9.2	33.2 ± 13.0	28.6 ± 8.6	31.4 ± 7.6	n.s.
Median (range)	28 (20-61)	28.5 (21-61)	26 (20-57)	29 (21-59)	
Age at onset (years)					
Mean ± SD	18.6 ± 6.7	18.8 ± 7.0	17.8 ± 4.2	18.8 ± 7.2	n.s.
Median (range)	18 (8-55)	18 (10-38)	18 (11-27)	17 (8-55)	
Disease duration (years)					
Mean ± SD	12.6 ± 8.5	14.4 ± 12.3	11.0 ± 8.7	12.5 ± 6.6	n.s.
Median (range)	11 (1-50)	11.5 (2-50)	8.5 (2-39)	12 (1-29)	
Marital status (%)					
Married	26.3	17.9	11.1	34.1	0.033
Not married	73.7	82.1	88.9	65.9	
Number of family menbers (%)					
≥ 1	60.6	75.0	40.7	62.2	n.s.
0	32.8	21.4	48.1	31.7	
missing	6.6	3.6	11.1	6.1	
Education (%)					
Junior high school	17.5	25.0	25.9	12.2	n.s.
Vocational school	19.0	14.3	18.5	20.7	
College or higher	59.1	57.1	55.6	61.0	
missing	4.4	3.6	0	6.1	
Occupation (%)					
Employed (full time)	64.7	60.7	55.6	68.3	n.s.
Employed (part time)	11.0	14.3	22.2	6.1	
Housewives	7.4	10.7	7.4	6.1	
Students	15.4	14.3	11.1	17.1	
missing	1.5	0	3.7	2.4	
Mean sleep latency on MSLT (Mean ± SD)	3.1 ± 2.1 (n = 130)	1.7 ± 1.6 (n = 21)	2.6 ± 2.7 (n = 27)	3.6 ± 1.8[a] (n = 82)	< 0.001
ESS score					
Mean ± SD	14.8 ± 3.3	16.9 ± 2.8	14.5 ± 2.7b	14.1 ± 3.3C	< 0.001
0-10 (%)	9.5	0.0	7.4	13.4	
11-15 (%)	46.0	32.1	55.6	47.6	0.037
16-24 (%)	44.5	67.9	37.0	39.0	
N of having driving licence and driving habit	80	16	14	50	
Trouble while driving (%) automobile accidents or near-miss incidents	55.0	75.0	50.0	50.0	n.s.

NA, narcolepsy; CA, cataplexy; IHS, idiopathic hypersomnia; LST, long sleep time; MSLT, multiple sleep latency test; ESS, Epworth Sleepiness Scale; n.s. not siginificant. a) versus NA with CA, $p < 0.001$, Scheffe's test. b) versus NA with CA, $p = 0.017$, Scheffe's test. c) versus NA with CA, $p < 0.001$, Scheffe's test.

of the national normative scores among each diagnostic group by using Welch's test. Multiple linear regression analyses were performed to identify the factors associated with HRQOL as measured by the SF-36 scores among each diagnostic group. Gender (female/male), age, disease duration, and the ESS score were set as the independent variables.

After evaluating the rates of the patients with experiences of automobile accidents or near-miss incidents, multiple logistic regression analyses were performed to explore the factors associated with the occurrence of these accidents or near-miss incidents among the subject patients. The dependent variable was the experience of the occurrence of these accidents or near-miss incidents, which were dichotomized for analysis (accident or near-miss incident / none). The independent variables were gender, age, disease duration, the diagnostic group, and the ESS score (normal / mild / severe).

Multiple linear regression analysis was performed to clarify the contribution of single covariates, including the experience of automobile accidents or near-miss incidents, to the SF-36 scales score among the subject patients having usual driving habits. Gender, age, disease duration, the diagnostic group, ESS score, and the experience of automobile accidents or near-miss incidents were set as the independent variables. Four participants who did not have a driver's license, 49 without usual driving habits, 2

Table 2—SF-36 Profiles of the Patients with Hypersomina by Diagnostic Groups in Comparisons with National-Norm Socres

no.	overall n = 137		NA with CA n = 28		NA without CA n = 27		IHS without LST n = 82	
Subscale	Scale Scores§	p value†	Scale Scores§	p value†	Scale Scores§	p value†	Scale Scores§	p value†
PF	51.2 (8.4)	0.023	53.4 (6.1)	0.008	51.4 (5.7)	n.s.	50.5 (9.7)	n.s.
RP	36.1 (24.5)	< 0.001	38.7 (23.6)	0.020	33.0 (28.4)	0.004	36.2 (23.6)	< 0.001
BP	51.0 (11.1)	n.s.	53.9 (9.1)	0.036	53.0 (9.7)	n.s.	49.4 (12.0)	n.s.
GH	47.3 (10.8)	0.004	47.9 (8.2)	n.s.	49.0 (12.6)	n.s.	46.5 (10.9)	0.009
VT	43.8 (9.7)	< 0.001	45.7 (9.4)	0.026	44.0 (9.6)	0.003	43.1 (9.9)	< 0.001
SF	43.9 (12.6)	< 0.001	43.1 (12.0)	0.006	45.3 (12.7)	n.s.	43.7 (12.9)	< 0.001
RE	36.5 (22.6)	< 0.001	39.9 (25.6)	n.s.	33.4 (22.3)	0.001	36.4 (21.7)	< 0.001
MH	44.6 (10.6)	< 0.001	45.3 (11.6)	0.046	45.3 (11.1)	0.034	44.2 (10.1)	< 0.001

NA, narcolepsy; CA, cataplexy; IHS, idiopathic hypersomnia; LST, long sleep time. PF, physical health; RP, role physical; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role emotional; MH, mental health; and n.s., not siginificant. §; Scale scores are made acording to norm-based scoring (standardized t score transformation with a mean of 50 ± 10), and parenthesis indicate standard deviation. †; vs national-norm scores.

who did not answer the question about the experience of accidents, and 2 who did not answer the item about a driver's license were excluded from the analysis about the accidents. As a result, 80 current drivers were included in the accident analyses.

RESULTS

The descriptive variables for the main demographic and clinical features of the patients in each diagnostic group are shown in Table 1. Of 137 participants, 51.8% were female. The age range was 20 years to 61 years, with a median of 28 years. Demographic and clinical variables did not differ statistically among the 3 diagnostic groups except for marital status, the mean sleep latency on MSLT, and the ESS scores. Residual analysis revealed that the rates of married patients were significantly higher in IHS without LST ($p < 0.01$), and were significantly lower in NA without CA ($p < 0.05$). ANOVA showed that the mean sleep latency on MSLT differed significantly among the 3 diagnostic groups ($F_{2,127} = 8.44$, $p < 0.001$). Scheffe's post hoc test revealed that the mean sleep latency in the NA with CA group was significantly shorter than that of IHS without LST ($p = 0.001$). ANOVA also showed that the ESS scores differed significantly among the 3 diagnostic groups ($F_{2,134} = 7.53$, $p < 0.001$). Scheffe's post hoc test revealed that the ESS scores in the NA with CA group were significantly higher than that of the other 2 groups (NA with CA vs. NA without CA, $p = 0.012$; NA with CA vs. IHS without LST, $p < 0.001$). Residual analysis revealed that the rates of patients with ESS scores between 16 from 24 were significantly higher in NA with CA ($p < 0.01$).

Comparison of Short Form-36 with Normative Data

As a total group, the patients had significantly lower SF-36 scores in all domains except PF and BP scales than age- and gender-matched Japanese normative data.

Although the scores of all 8 subscales of the SF-36 did not differ statistically among the 3 diagnostic groups, RP, VT, and MH were significantly lower in all these diagnostic groups than normative data. The SF was significantly lower in both the patients with NA with CA and IHS without LST; RE was significantly lower in both the patients with NA without CA and IHS without LST; and GH was significantly lower in the patients with IHS without LST. In contrast, PF and BP were significantly higher in the patient group with NA with CA in comparison to normative data (Table 2).

Factors Influencing the HRQOL

Multiple linear regression analyses showed that only disease duration was positively correlated with the ME among the total subjects ($\beta = 0.248$, $p = 0.048$, $R^2 = 0.037$). In patients with NA with CA, a negative association between the RP and ESS scores was found in multiple linear regression analyses ($\beta = -0.504$, $p = 0.024$, $R^2 = 0.225$). In patients with NA without CA, MH was positively associated with disease duration and being male ($\beta = 0.960$, $p = 0.007$, $\beta = -0.404$, $p = 0.017$, respectively, $R^2 = 0.551$) (Table 3).

Automobile Accident Rates and Factors Associated with Automobile Accidents

Of the 80 current drivers, 44 patients (55.0%) had experienced at least one accident or near-miss incident during the preceding 5 years (Table 1). Table 4 shows the results of the logistic regression analysis. Only ESS scores were significantly associated with increased experience of automobile accident or near-miss incident (severe; OR = 14.63, 95% CI: 1.97 to 108.67). However, the experience of automobile accidents or near-miss incidents was not associated with any SF-36 scale scores among the subject current drivers with hypersomnia.

DISCUSSION

Several studies have revealed that physical and mental components of HRQOL is decreased among the patients with insomnia[24-27] and among those with sleep apnea.[28-30] However, only a few studies have reported on HROQL of drug-naïve patients with hypersomnia, with comparison to the general population by diagnostic groups.[9,10] Vignatelli et al. found that drug-naïve patients with narcolepsy (newly diagnosed narcolepsy group) showed significantly lower scores in all subscales of SF-36 except for BP, when compared with scores of the general Italian population. Beusterien et al. also assessed SF-36 in a group of patients positive for narcolepsy based on the criteria of the 1st edition of *ICSD*