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ORIGINAL ARTICLE

Psychological characteristics and the efficacy of hospitalization treatment on delayed sleep phase syndrome patients with school refusal

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Abstract

The study investigated the efficacy of the treatment of patients with delayed sleep phase syndrome (DSPS) through hospitalization, given social cues and their psychological characteristics, using a picture-frustration study. The participants were 22 DSPS patients with school refusal during adolescence, consisting of 13 boys and 9 girls (mean age ± *SD* = 16.0 ± 1.4, range = 13–18). Over 90% of the DSPS patients with school refusal showed improvements in their sleep–wake rhythm (S–W) just after hospitalization. Over 50% of them maintained their improved S–W after discharge and attended school. The picture-frustration study for DSPS patients with school refusal, especially in patients who showed no improvement in their S–W and school refusal after discharge, showed low aggression, low expression of their dissatisfaction, high suppression of their emotion, low social interest and high self-criticism. Patients who did not show improvement in their S–W through hospitalization have psychological problems such as those mentioned above. They may therefore need to take psychological intervention such as self-assertion training.

Key words: delayed sleep phase syndrome, picture-frustration study, psychological characteristics, school refusal.

INTRODUCTION

Delayed sleep phase syndrome (DSPS) patients have a difficulty in falling asleep at a socially acceptable time of night and an inability to be easily aroused in the morning. Most studies reported that the onset of DSPS is in adolescence[1–4] and, in some cases, in childhood.[1,4] Patients with DSPS in adolescents and childhood are not able to get up early in the morning, which leads to poor school performance. Recently, social life seems to be night-shifted and people stay up late, eating, watching television and surfing the Internet. These life changes may produce problems with our biological clock.

School refusal has become a social problem and has been given attention in child and adolescent psychiatry.[5] Although the term, school refusal is used only for those who do not attend school, school refusal can lead to many psychiatric problems. Some adolescents and children with school refusal had neurosis, psychosis, behavior disorders, and emotional disorders and some of them may have DSPS. Tomoda *et al.*[6] reported that some adolescents and children with school refusal had sleep–

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wake rhythm (S–W) problems, such as DSPS and non-24 sleep–wake rhythm disorder. In this way, studies have suggested that there is a relationship between DSPS and school refusal.[3,6–8] The psychological characteristics of DSPS are a tendency to neurosis with high anxiety and depression, and low social adjustment.[9] Further, most DSPS patients have little self-assertion, and are characterized by self-criticism and passivity. They also have problems in coping with stress.[10] Although studies have been carried out on the psychological characteristics of DSPS patients, few studies have been done on adolescents with DSPS and school refusal.

In our study, we investigated the psychological characteristics of DSPS patients with school refusal who were hospitalized at the department of psychiatry. Because we sometimes see DSPS patients with school refusal who are not able to express affection properly and have problems in coping, we focused on their coping styles. In addition, we compared the psychological characteristics of those patients who showed improvement of their S–W through the hospitalization to those who did not improve. Furthermore, we also compared the psychological characteristics of patients whose school refusal decreased after hospitalization with those who had had not improved in this respect. The hospitalization treatment attempted to improve DSPS by giving the patients time cues such as interventions by nurses in the morning, and evaluated the efficacy of their treatment by the improvement of their S–W and the decrease in their school refusal.

METHODS

Participants

The participants were 22 patients consisting of 13 boys and 9 girls (mean age ± *SD* = 16.0 ± 1.4). Their diagnosis was delayed sleep phase syndrome, according to DSM-IV criteria by psychiatrists (OY, JM, SK, MO), and they continued to refuse to attend school for over a month or attended school only a few days a month. They were hospitalized to improve their S–W at the department of psychiatry in the hospital attached to Shiga University of Medical Science from March to October, 2003. We analyzed 21 patients for the efficacy of their treatment in being given time cues through hospitalization.

Procedures

The Rosenzweig picture-frustration study (P-F study) was administered to all participants[11] immediately after hospitalization and they were given social time cues. However, we were not able and were not able to check the school attendance of one of participants after discharge and six of 21 did not fully complete the Rosenzweig picture-frustration study (P-F study) and were omitted from the final analysis.

Hospitalization treatment

All participants were given social time cues during hospitalization with a scheduled lights-on time, a morning wake-up call by nurses, three meal times and a lights-off time. They participated in group therapy in the mornings, 5 days a week. Social time cues were set by nurses calling them to wake up and opening the curtains at 6.00 hours every morning and so on. The patients who were not affected by the social time cues received light treatment. Of the 22 patients, 14 received light treatment (see Table 1).

Effectiveness of treatment

We evaluated the effects of treatments based on the patients' sleep conditions and school attendance after discharge, using their medical records. We checked the improvement of sleep conditions based on the following criteria: (i) patients were able to get up within 60 min of their wake-up time, according to the hospital schedule during hospitalization; (ii) their improved S–W was maintained for three months after discharge; (iii) they were able to get up on time to attend school for about three months after discharge; and (iv) they attended school more than 70% of school days after discharge, we considered their school refusal behavior had improved in the patients who improved in these four categories. However, because we were not able to contact one patient after discharge and were thus not able to check his school attendance situation, we finally analyzed 21 patients for the efficacy of their treatment of given time cues through hospitalization.

The picture-frustration study

The P-F study consists of 24 frustration situations and measures the three directions of aggression and the three types of aggression. The patients were asked to describe in conversation what they imagined after being presented with each frustration situation picture. The conversations were analyzed according to the direction ("extraggression," such as the expression of aggression, "intraggression," such as self-criticism and

Table 1 Demographic data and treatment process for each patient

			Before hospitalization				After hospitalization			
Patients	Age	Sex	Mean of sleep onset time (h)	Mean of wake-up time (h)	School attendance†	Light therapy	Mean of sleep onset time (h)	Mean of wake-up time (h)	Impact of S–W rhythm on school attendance	School attendance‡
1	16	B	02.00	14.00	1	+	20.00	07.00	Yes	○
2	18	B	00.00	10.00	1	+	23.00	07.00	Yes	○
3	16	G	13.00	13.00	3	+	11.00	07.50	No	×
4	18	G	02.00	14.00	2	–	00.00	06.00	Yes	○
5	17	B	14.00	02.00	1	+	23.00	06.00	Yes	○
6	15	B	05.00	15.00	2	–	00.00	06.50	No	×
7	18	B	14.00	02.00	1	+	23.00	08.00	No	×
8	16	B	06.00	14.00	1	–	23.00	07.00	Yes	×
9	17	B	01.00	10.00	1	–	22.00–23.00	06.00–07.00	Yes	×
10	17	B	00.00	09.00	4	+	00.00	08.00	No	×
11	15	B	Irregular	Irregular	2	–	23.00	07.00	Yes	×
12	15	B	01.00	10.00	4	–	00.00	07.00	Yes	○
13	16	B	01.00	12.00	3	–	23.00	06.00	Yes	○
14	15	B	12.00	23.00	3	+	00.00	07.50	No	○
15	15	G	02.00	10.00	1	+	23–0	07.00	Yes	○
16	17	G	00.00	11.00	4	+	23.00	08.00–12.00	No	×
17	17	G	00.00	12.00	4	+	22.00	09.00	No	×
18	14	G	23.00–00.00	10.00	1	–	23.00	7–10	No	–
19	13	G	04.00	14.00	1	+	22.00	07.00	No	○
20	18	G	03.00	11.00	1	+	23.00	07.00	Yes	○
21	16	G	03.00	11.00	3	+	23.00	08.00	No	○
22	17	B	02.00	12.00	3	+	00.00	07.50	Yes	○

†1, total absence from school over one month; 2, attending school several times a month; 3, attending school several times a week; and 4, attending school late. No patient was able to attend school more than 70% of the school days. ○ shows a 70% or more rate of school attendance; "×" shows an under 70%. rate of school attendance B, boy; G, girl, S–W, sleep–wake.

"imaggression," such as self-deception or suppression) and the type of aggression. These include "obstacle-dominance," such as the emphasis on obstructions, "ego-defense" and "need-persistence," such as the request or high need to solve the problems. These were then classified into nine categories ("extrapeditive," such as the expression of compliant or disappointment, "extrapunitive" such as aggression towards others or self-assertion, "extrapersitive," such as demanding support from others, "intropeditive," such as the suppression of compliance or disappointment, "intropunitive," such as self-blame or self-criticism, "intropersistive" such as solving problems by oneself, "impeditive," such as the slight expression of compliance or disappointment, "impunitive" such as blaming nobody and "impersistive," such as waiting for the time to pass. This test also rates group conformity (GCR). GCR scale reflects the extent of social adjustment.

Data analysis

Firstly, we calculated the frequencies of S–W improvement before and after discharge, and the frequencies of school refusal improvement after discharge on our evaluation criteria (see "effectiveness of treatment" below). As we were not able to check one patient's situation after discharge, we finally analyzed 21 patients for the efficacy of their treatment in being given time cues through hospitalization.

Secondly, we analyzed the psychological characteristics of 15 patients who completed the P-F study. We calculated each mean score of three directions, three types and nine categories of the P-F study. We also conducted a one-way analysis of variance per group (improvement vs non-improvement in S–W leading to school attendance after discharge) for each of the three directions, three types, and nine categories. Finally, we conducted a one-way analysis of variance per group (improvement vs those whose school attendance did not improve) for each of the three directions, three types and nine categories.

RESULTS

The efficacy of treatment on hospitalization

Table 1 shows the demographic data, sleep conditions and school attendance before and after hospitalization for each patient. Next, we calculated the frequencies of improved S–W before hospitalization treatment and after discharge, and the frequency of improved school attendance after discharge. All patients got up within 60 min of wake-up on hospitalization schedule and maintained the improved S–W after discharge. Twelve of those patients maintained their improved S–W after discharge and 12 had actually attended school more than 70% of the school days. Finally, the frequency of improved S–W and school attendance after discharge was seen in 57.1% of the patients.

Psychological characteristics

We calculated three direction scores, three type scores, and nine category scores of the P-F study based on Hayashi's methods in a revised Japanese version.[12] The mean GCR of the DSPS patients was 54.1%, and the mean GCR of healthy adolescents was 58%. Tables 2 and 3 show DSPS patients' scores for the three directions, three types, and nine categories. Compared to the distribution of healthy adolescents, on the extr-aggression response, 13 DSPS patients' scores were low; on the imaggression response and on the ego-defence response, 14 and 10 DSPS patients' scores were high, respectively (see Table 2). As Table 3 shows, compared to the distribution of healthy adolescents, on the impunitive response, 15 DSPS patients' scores were high, and on the extrapunitive response, 13 DSPS patients' scores were low.

Table 4 shows each mean score of the nine categories of patients' improved and unimproved S–W, respectively. As a result of a one-way analysis of variance per group (improved and unimproved S–W leading to school attendance after discharge, respectively,) patients with non-improvement S–W after discharge had a higher mean score on the impeditive response than patients with improved S–W after discharge ($F_{113} = 4.09$, $P < 0.10$). Although no significant differences were found, the mean score of patients whose S–W showed no improvement were higher on the impunitive and intropunitive responses than of those whose S–W did improve. The mean scores of patients whose S–W did not improve was much lower on the extrapeditive response and extrapunitive response than patients whose S–W did improve (Table 4).

On the other hand, as a result of a one-way analysis of variance per group (those whose school attendance improved vs those whose attendance showed no improvement), patients whose school attendance did not improve had a higher mean score on the impeditive response than patients whose school attendance did ($F_{113} = 3.25$, $P < 0.10$). The mean scores of patients

Table 2 Delayed sleep phase syndrome patients' scores, mean scores and SDs for the three directions and three types in a picture-frustration study, compared to the mean scores and SDs of healthy adolescents

	Three directions			Three types		
Patients	Obstacle-dominance	Ego-defense	Need-persistence	Extr-aggression	Intr-aggression	Im-aggression
1	–	–	–	–	–	–
2	7.0	14.0	3.0	15.0	3.0	6.0
3	7.5	8.5	8.0	8.5	7.5	8.0
4	–	–	–	–	–	–
5	–	–	–	–	–	–
6	5.0	16.0	3.0	0.0	10.0	14.0
7	–	–	–	–	–	–
8	5.5	9.5	7.0	3.5	7.0	11.5
9	5.5	12.5	6.0	12.5	5.5	6.0
10	6.5	12.5	5.0	7.5	9.0	7.5
11	–	–	–	–	–	–
12	5.5	12.0	7.5	5.5	8.5	10.0
13	2.5	14.0	7.5	9.0	6.5	8.5
14	6.0	11.0	6.0	2.0	12.0	9.0
15	9.5	10.0	4.5	10.0	6.0	8.0
16	5.0	13.5	5.5	3.5	10.0	10.5
17	6.5	12.0	5.5	5.5	7.5	11.0
18	4.0	13.0	7.0	4.0	11.0	9.0
19	–	–	–	–	–	–
20	4.0	13.5	6.5	3.0	10.0	11.0
21	4.5	1.0	8.5	5.5	5.0	13.5
22	7.0	10.0	7.0	5.5	10.0	8.5
Mean	5.83	11.33	6.03	6.43	7.83	9.53
SD	1.64	3.49	1.66	4.04	2.4	2.41
Healthy adolescents						
Mean	6.73	11.08	5.52	9.08	7.68	7.28
SD	2.44	2.52	2.72	3.04	1.84	2.16

whose school attendance did not improve were lower on the extrapeditive and extrapunitive responses than those of healthy adolescents. The former was lower than patients with whose attendance improved on the extrapunitive score. Patients whose attendance at school did not improve had a higher mean score on the impunitive and intropunitive responses than patients whose attendance improved (see Table 5).

DISCUSSION

Our objectives were to investigate the efficacy of the hospitalization treatment with giving time cues to DSPS patients and their psychological characteristics using the P-F study. All patients showed an improvement of their S–W through their treatment during hospitalization, and after discharge, and 57% of patients showed an improvement of their S–W and attended school after their discharge. This was after they had received social cues to synchronize their circadian rhythm during hospitalization. As Shirayama *et al.*[13] report, the patients who lose only the social cues are able to improve their S–W and school refusal behavior after only a change in their environment. It is essential that DSPS patients regulate their life environments and time schedules.

We investigated the psychological characteristics of the DSPS patients. As noted above, our results showed that the extraggression scores of the DSPS patients were low and their imaggression scores were high. That is, we found that DSPS patients were less aggressive and less assertive, and tended to compromise and repress their emotions and thinking, compared to healthy

Table 3 Delayed sleep phase syndrome patients' scores, mean scores, and SDs for the nine categories in a picture-frustration study compared to the mean scores and SDs of healthy adolescents

Patients	Extra-peditive	Extra-punitive	Extra-persitive	Intro-peditive	Intro-punitive	Intro-persistive	Im-peditive	Im-punitive	Im-persistive
1	–	–	–	–	–	–	–	–	–
2	3.0	10.0	2.0	3.0	0.0	0.0	1.0	4.0	1.0
3	4.0	2.0	2.5	2.5	3.0	7.5	1.0	4.5	2.5
4	–	–	–	–	–	–	–	–	–
5	–	–	–	–	–	–	–	–	–
6	0.0	0.0	0.0	3.0	6.0	1.0	2.0	10.0	2.0
7	–	–	–	–	–	–	–	–	–
8	3.5	0.0	0.0	0.0	4.5	2.5	2.0	5.0	4.5
9	4.0	5.5	3.0	1.5	2.0	2.0	0.0	5.0	1.0
10	2.0	4.5	1.0	2.0	3.0	4.0	2.5	5.0	0.0
11	–	–	–	–	–	–	–	–	–
12	1.5	1.0	3.0	1.5	4.5	2.5	1.5	6.5	10.0
13	1.0	5.5	2.5	0.0	2.5	4.0	1.5	6.0	1.0
14	2.0	0.0	0.0	3.0	6.0	3.0	1.0	5.0	3.0
15	5.5	4.0	0.5	3.0	3.0	0.0	1.0	3.0	4.0
16	1.5	0.5	1.5	2.0	6.0	2.0	1.5	13.5	5.5
17	0.0	2.5	3.0	2.5	3.5	1.5	4.0	6.0	1.0
18	1.0	2.5	0.5	2.5	4.5	4.0	0.5	6.0	2.5
19	–	–	–	–	–	–	–	–	–
20	1.5	1.0	0.5	2.0	5.0	3.0	0.5	7.5	3.0
21	1.0	3.0	1.5	0.5	2.5	2.0	3.0	5.5	5.0
22	2.0	3.0	0.5	3.0	2.5	4.5	2.0	4.5	2.0
Mean	2.17	2.83	1.44	2.00	3.60	2.63	1.63	6.07	3.03
SD	1.55	2.76	1.16	1.08	1.71	1.89	1.01	2.62	2.53
Healthy adolescents									
Mean	3.12	4.55	1.37	2.08	3.10	2.42	1.42	3.32	2.45
SD	1.83	2.52	1.15	1.25	1.43	1.65	1.10	1.53	1.43

Table 4 Mean scores and SD for the nine categories in a picture-frustration study on patients with improved and unimproved sleep–wake rhythms

	Patients with improved sleep–wake rhythm ($n = 8$)		Patients with unimproved sleep–wake rhythm ($n = 7$)		
	Mean	SD	Mean	SD	*F*-values
Extrapeditive	2.75	1.54	1.50	1.38	2.71
Extrapunitive	3.75	3.27	1.79	1.70	2.03
Extrapersitive	1.50	1.25	1.36	1.14	0.05
Intropeditive	1.75	1.25	2.21	0.86	0.68
Intropunitive	3.00	1.65	4.29	1.63	2.30
Intropersistive	2.31	1.65	3.00	2.22	0.47
Impeditive	1.19	0.70	2.14	1.11	4.09*
Impunitive	5.19	1.44	7.07	3.38	2.07
Impersistive	3.31	3.03	2.71	2.00	0.20

*$P < 0.10$. Patients with improved sleep–wake rhythm are those getting up on time to attend school after discharge.

Table 5 Mean scores and SD for the nine categories, in a picture-frustration study on patients with improved and unimproved school refusal behavior

	Patients with improved school refusal behavior ($n = 9$)		Patients with unimproved school refusal behavior ($n = 6$)		
	Mean	SD	Mean	SD	*F*-values
Extrapeditive	2.39	1.52	1.83	1.69	0.44
Extrapunitive	3.67	3.07	1.58	1.77	2.23
Extrapersitive	1.50	1.17	1.33	1.25	0.07
Intropeditive	1.94	1.16	2.00	1.05	0.01
Intropunitive	3.11	1.80	4.33	1.77	1.96
Intropersistive	2.33	1.56	3.08	2.40	0.55
Impeditive	1.28	0.87	2.17	1.03	3.25*
Impunitive	5.22	1.35	7.33	3.63	2.59
Impersistive	3.33	2.87	2.58	2.08	0.30

*$P < 0.10$.

adolescents. Although no significance difference was found, the patients with non-improved S–W had a lower extrapunitive mean score than those with improved S–W and healthy adolescents. The former were higher on the impunitive mean score than the latter. The psychological characteristics of these DSPS patients included a low expression of aggression, high emotional suppression and low social interest. As a result, they tended to withdraw from society. These results support the findings of Shirayama *et al.*[13] that DSPS patients had low levels of general activity and were defensive and inhibited. Their difficulty in waking up early in the morning might cause hopelessness, helplessness, and social withdrawal, as has been proposed.[10,14] As a result, DSPS patients may lose the social cues for synchronizing their circadian rhythm. As Yamadera *et al.*[15] (2003) showed, over 50% of DSPS patients had low social ability and some DSPS patients had high levels of anxiety, depression and neuroticism. Our results also suggest that DSPS patients have psychological problems as described above.

We compared the psychological characteristics between patients with improved S–W and who attended school and those who did not attend school after discharge, and we compared patients whose school attendance improved and those whose school attendance did not. Our results show that, compared with than healthy adolescents and patients who did improve, patients whose S–W and whose school attendance did not improve were (i) higher on the impeditive,-impunitive, and intropunitive mean scores; and (ii) had lower extrapeditive and extrapunitive mean scores. These results suggest that such patients tended to suppress their emotions or have low social interest. They had a high level of self-criticism, they seldom complained and they showed little aggression. They also showed lower levels of general activity and tended to withdraw from society more than patients whose S–W and school attendance improved after discharge. However, as this study has some problems, in that our sample is small and no statistical significance has been found, further work in this area is needed.

In summary, all DSPS patients with school refusal behavior had improved S–Ws after hospitalization and, after discharge, over 50% of them were able to attend school. We suggest that if DSPS patients are given social time cues during hospitalization, about half of them may continue to have improved S–Ws that allow them to attend school after discharge.

The psychological characteristics for DSPS patients with school refusal, especially in patients who did not have improved S–W and school refusal behavior after discharge were low levels of aggression, low expression of their dissatisfaction, high suppression of their emotion, low social interest and high self-criticism. This may indicate that psychological intervention such as a self-assertion training is needed in such cases.

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Narcolepsy Without Cataplexy: 2 Subtypes Based on CSF Hypocretin-1/Orexin-A Findings

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Study Objectives: Cerebrospinal fluid (CSF) hypocretin-1 levels and their relationship with the clinical characteristics of narcolepsy without cataplexy have not been well elucidated. Our aim was to examine whether clinical characteristics vary with CSF hypocretin-1 levels among narcoleptic patients without cataplexy.

Design: Clinical features, variables on the multiple sleep latency test, and results of HLA typing were correlated with CSF hypocretin-1 levels.

Setting: University-based sleep laboratories and a sleep disorders center.

Patients: Seventeen patients (5 male, 12 female) who fulfilled the diagnostic criteria of narcolepsy without cataplexy according to the International Classification of Sleep Disorders.

Inerventions: Patients underwent lumbar puncture for CSF sampling.

Measurements and Results: Five patients showed a markedly decreased CSF hypocretin-1 level, whereas the remaining 12 patients showed almost normal levels. The mean rapid eye movement (REM) latency was significantly shorter and the age at onset was significantly earlier in the low CSF hypocretin-1 group compared with the normal CSF hypocretin-1 group. HLA-DR2 was positive in all of the patients with low CSF hypocretin-1, whereas only 33.3% of patients with normal CSF hypocretin-1 were DR2 positive.

Conclusions: Some narcoleptic patients without cataplexy have low CSF hypocretin-1 levels. In patients who have narcolepsy without cataplexy, short mean REM latency, younger age at onset, and HLA-DR2 are associated with CSF hypocretin-1 deficiency. Markedly decreased CSF hypocretin-1 levels could be a significant marker for identifying subgroups of narcolepsy patients without cataplexy.

Keywords: Narcolepsy without cataplexy, cerebrospinal fluid hypocretin-1,HLA-DR2

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INTRODUCTION

NARCOLEPSY IS A DISORDER CHARACTERIZED BY EXCESSIVE DAYTIME SLEEPINESS, CATAPLEXY, AND UNUSUAL RAPID TRANSITIONS FROM THE AWAKE state to rapid eye movement (REM) sleep. In the first edition of the International Classification of Sleep Disorders (ICSD),[1] the diagnosis of narcolepsy had dual essential criteria: (1) narcolepsy with cataplexy, defined as hypersomnia that persists more than 3 months plus episodes of cataplexy, and (2) narcolepsy without cataplexy, defined as hypersomnia manifested as shortened sleep latency with narcolepsy-related symptoms, such as sleep paralysis, hypnagogic hallucination or sleep disruption, plus a sleep-onset REM period (SOREMP) on nocturnal polysomnography (PSG) or 2 or more SOREMPs on the multiple sleep latency test (MSLT) examination.[1] Recently, the ICSD was revised to its second edition (ICSD-2) in which narcolepsy with cataplexy and narcolepsy without cataplexy are separetely defined.[2] The diagnosis of narcolepsy with cataplexy is easy when patients show typical cataplexy. However, the diagnosis of narcolepsy without cataplexy must be made with PSG followed by an MSLT, and it can be diagnosed only when 2 or more SOREMPs on the MSLT are observed.[2]

Hypocretin/orexin is a hypothalamic neuropeptide involved in sleep-wake regulation and energy homeostasis.[3,4] It has recently been shown that hypocretin deficiency is closely related to the pathogenesis of human narcolepsy and that the hypocretin-1/orexin-A level in cerebrospinal fluid (CSF) is markedly decreased in most patients with narcolepsy with cataplexy.[5-7] However, studies on narcolepsy without cataplexy have been carried out in only a small number of patients, and the results have been controversial.[6-12]

With regard to HLA typing, DR2, DRB1*1501 (a subtype of DR2), and DQB1*0602 (a subtype of DQ1) have been shown to be strongly associated with narcolepsy with cataplexy.[13-15] In contrast, narcolepsy without cataplexy is less associated with HLA types than is narcolepsy with cataplexy.[16] These previous results on CSF hypocretin-1 levels and HLA suggest that narcolepsy without cataplexy might be a heterogeneous clinical syndrome, whereas narcolepsy with cataplexy forms a uniform entity. However, systematic investigation regarding CSF hypocretin-1 and its relationship to both clinical parameters and HLA types among patients having narcolepsy without cataplexy has been limited.

The aim of the present study was thus to examine the CSF hypocretin-1 levels in patients who had narcolepsy without cataplexy and to clarify the CSF hypocretin-1 level correlation with clinical characteristics and findings on the MSLT as well as HLA types.

METHODS

Seventeen patients who had narcolepsy without cataplexy (5

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male, 12 female) were included in the study. Our series included 5 patients whose CSF hypocretin-1 levels were reported by Kanbayashi and colleagues. [6] However, those investigators were focusing mainly on the difference between narcolepsy and idiopathic hypersomnia. Thus, the purpose of that report was entirely different from that of the present study.

In this study, the ICSD-1 was used for the diagnosis of narcolepsy. The diagnosis of narcolepsy without cataplexy was made according to the second essential criterion of narcolepsy, which is used for patients not presenting with cataplexy, in the ICSD-1 as follows[1]: (1) excessive daytime sleepiness, (2) REM-related symptoms such as hypnagogic hallucinations and sleep paralysis, and (3) sleep latency of less than 10 minutes plus 1 or more SOREMPs on PSG or a mean sleep latency of less than 5 minutes plus 2 or more SOREMPs out of 4 or 5 sessions on the MSLT. Except for 1 patient who showed a typical SOREMP on PSG and only 1 SOREMP on the MSLT, all of the other patients fulfilled the ICSD-2 criteria of narcolepsy without cataplexy, ie, a mean sleep latency of less than 8 minutes and 2 or more SOREMPs.[2] Cataplexy was defined as the sudden loss of bilateral muscle tone provoked by strong emotion,[1,2] and its absence was confirmed based on clinical interview by board-certified sleep specialists. Because mild hypotonus may be overlooked not only by examiners, but also by patients themselves, possible cataplexy episodes, including even mild sensations of weakness, were carefully evaluated and excluded. Patients were also confirmed to have no other sleep disorders, such as obstructive sleep apnea syndrome, restless legs syndrome, or periodic limb movement disorder, which could cause excessive daytime sleepiness.

Physical and neurologic examinations were normal in all patients. A family history of narcolepsy was not noted in any of the patients. None of the patients was medicated with either central nervous system stimulants or tricyclic antidepressants when enrolled. Clinical profiles such as age, age at clinical onset, duration of illness, and usual length of nocturnal sleep time at the time of evaluation are shown in Tables 1 and 2. HLA markers for narcolepsy were also examined. HLA DR2 was screened in all patients, and a detailed HLA analysis of DQB1*0602 was made in 5 patients.

PSG, including 4 channels of scalp electroencephalogram (C_3, C_4, O_1, O_2), electrooculogram, chin electromyogram, electrocardiogram, nasal/oral airflow, chest/abdominal respiratory effort, snoring, and anterior tibialis electromyogram, were recorded for all patients. After confirming that the nocturnal PSG fulfilled the conditions of at least 7 hours of nocturnal sleep and a sleep efficiency of 80% or more, we conducted the MSLT using a standard protocol in all patients.[17] Sleep stages were scored according to the standard criteria.[18] Sleep onset on the MSLT was defined as either the appearance of 3 consecutive 30-second epochs of stage 1 or an epoch of any other sleep stages including REM sleep. A SOREMP was defined as the appearance of an epoch of REM sleep either during the first 20 minutes on nocturnal PSG or during the first 15 minutes of the MSLT. Regarding the MSLT variables, sleep propensity (manifested as mean sleep latency) and REM propensity (estimated as both the percentage of naps with SOREMPs and the mean REM latency) in 4 or 5 sessions of the MSLT were analyzed. Subjective excessive daytime sleepiness was scored by the Epworth Sleepiness Scale.[19]

CSF was examined after written informed consent was obtained. The CSF was kept frozen (-80° C) prior to the hypocretin-1 measurement. CSF hypocretin-1 levels were measured by a commercially available radioimmunoassay kit (Phoenix Pharmaceuticals, Belmont, Calif). Considering that a CSF hypocretin-1 level below 110 pg/mL is diagnostic for narcolepsy with cataplexy,[7] our patients were divided into low (< 110 pg/mL) and normal (> 110 pg/mL) groups. Although a CSF hypocretin-1 level of more than 200 pg/mL is considered a normal value,[7] we included 1 patient with mildly decreased hypocretin-1 levels (110-200 pg/mL) in the normal group to compare the clinical characteristics between the 2 groups.

Table 1—Demographic, Duration of Morbidity, HLA types, CSF Hypocretin-1 and MSLT Findings of the Subjects

Demographics			Narcolepsy characteristics			MSLT findings		
Patient No.	Sex	Age	Disease duration	Hypocretin-1, pg/mL	HLA DR2 (DQB1*0602)	Mean sleep latency, min	SOREMP (%SOREMP)	Mean REM latency, min
1	F	16	3	<40	+	3.1	3/5 (60)	2.5
2	M	17	5	<40	+	0.9	4/4 (100)	2.6
3	F	31	25	<40	+	1.0	4/4 (100)	2.0
4	F	50	35	51	+	3.4	1/5 (20)*	4.0
5	F	28	15	53	+	2.1	4/4 (100)	5.2
6	F	25	8	187	-	1.5	2/5 (40)	12.0
7	F	45	26	204	+ (+)	0.1	4/4 (100)	8.2
8	F	16	1	236	-	4.5	2/5 (40)	6.5
9	F	22	4	263	- (-)	2.2	2/4 (50)	3.9
10	M	26	3	265	-	3.5	2/5 (40)	9.5
11	F	28	9	278	+ (-)	4.8	2/4 (50)	4.1
12	F	23	5	285	- (-)	2.3	2/4 (50)	2.0
13	F	40	24	285	-	4.4	2/5 (40)	8.3
14	M	16	0.5	288	-	5.0	4/4 (100)	12.4
15	F	33	14	329	-	4.3	2/5 (40)	10.5
16	M	33	18	356	+ (-)	5.0	3/4 (75)	7.7
17	M	20	4	475	+	4.8	2/5 (40)	4.7

*The patient who had 1 sleep-onset rapid eye movement (REM) periods (SOREMP) on the Multiple Sleep Latency Test had a SOREMP on polysomnography. CSF refers to cerebrospinal fluid; MSLT, Multiple Sleep Latency Test;SOREMP, sleep-onset REM periods; %SOREMP, percentage of naps with SOREMPs((number of SOREMPs / number of MSLT sessions) x 100).

Table 2—Clinical Characteristics and Sleep Parameters in Patients Who Have Narcolepsy Without Cataplexy With Low CSF Hypocretin-1 Levels and Those With Normal Levels

	Low CSF hypocretin-1	Normal CSF hypocretin-1	p Value
Number of patients	5	12	
Sex	M 1, F 4	M 4, F 8	
Age, y	28.4 ± 13.8 (16-50)	27.4 ± 9.1 (16-45)	> .99
Age at onset, y	11.8 ± 3.4 (6-15)	17.6 ± 2.4 (15-23)	.0023
Disease duration, y	16.6 ± 13.5 (3-35)	9.7 ± 8.8 (0.5-26)	.29
Clinical symptoms			
Initial symptom			
Hypersomnia	4 (80.0)	11 (91.6%)	.49
Hypnagogic hallucination	1 (20.0)	1 (8.3%)	.49
REM-related symptoms			
Sleep paralysis	3 (60.0)	5 (41.7)	.49
Hypnagogic hallucination	3 (60.0)	9 (75.0)	.53
Usual length of night sleep, h	6.7 ± 1.0	7.1 ± 1.1	.52
ESS score	16.5 ± 3.7	15.5 ± 3.8	.66
MSLT parameters			
Mean sleep latency, min	2.1 ± 1.2	3.5 ± 1.6	.05
Mean REM latency, min	3.3 ± 1.3	7.5 ± 3.3	.0233
% SOREMP, %	76.0 ± 35.8	55.4 ± 23.1	.18
CSF hypocretin-1, pg/mL	44.8 ± 6.6	287.6 ± 75.4	.0015
Positive HLA-DR2	5 (100.0)	4 (33.3)	.012

Data are presented as number with range or percentages in parentheses or as mean ±SD. CSF refers to cerebrospinal fluid; ESS, Epworth Sleepiness Scale, MSLT,Multiple Sleep Latency Test; SOREMP, sleep-onset REM periods; %SOREMP,percentage of naps with SOREMPs.

Those parameters described above were compared between the 2 groups. Statistical analysis was carried out using the χ^2 test and the Mann-Whitney test with StatView (version 5) software. A p value of less than .05 was considered significant.

RESULTS

Demographics, characteristics of narcoleptic symptoms, and MSLT findings on each patient are shown in Table 1. CSF hypocretin-1 levels were undetectably low (< 40 pg/mL) in 3 patients and markedly decreased in 2 patients (51, 53 pg/mL). These 5 patients comprised the low group. Eleven patients who had CSF hypocretin-1 levels of more than 200 pg/mL and a patient with a level of 187 pg/mL (patient 6) comprised the normal group.[7] The CSF hypocretin-1 level in the normal group ranged from 187 to 475 pg/mL, with a mean of 287.6 ± 75.4 pg/mL.

Comparison of clinical parameters and MSLT results between the 2 groups is shown in Table 2. Age at onset of hypersomnia ranged from 6 to 15 years (mean 11.8 ± 3.4 years) in the low group, whereas the normal group developed hypersomnia at ages of 15 to 23 years (mean 17.6 ± 2.4 years); the age of onset was significantly younger in the low group. Duration of disease ranged from 3 to 35 years in the low group and from 0.5 to 26 years in the normal group, and the values were not significantly different between the 2 groups. One patient in the low group and 3 in the normal group had a disease duration of 3 years or less. Mean usual length of night sleep time ranged from 5.5 to 8.0 hours in the low group and from 6.0 to 9.5 hours in the normal group, showing no statistical difference between the 2 groups. The Epworth Sleepiness Scale score was more than 11 points in all patients and did not differ between the 2 groups.

Mean sleep latency on the MSLT examination ranged from 0.9 to 3.4 minutes in the low group and from 0.1 to 5.0 minutes in the normal group, showing no statistical difference between the 2 groups. The number of SOREMPs out of 4 or 5 MSLT sessions ranged from 1 to 4 in the low group and from 2 to 4 in the normal group. The patient with only 1 SOREMP on the MSLT showed a sleep latency of 3.5 minutes and a REM latency of 4 minutes on PSG carried out before the MSLT. The percentage of naps with SOREMPs on MSLT did not show any statistical difference between the 2 groups. However, mean REM latency ranged from 2.0 to 5.2 minutes (mean 3.3 ± 1.3 minutes) in the low group and from 2.0 to 12.4 minutes (mean 7.5 ± 3.3 minutes) in the normal group, showing that the REM latency was significantly shorter in the low group. HLA-DR2 was positive in 9 patients. The CSF hypocretin-1 levels and their association with positive and negative results of HLA-DR2 are shown in the Figure. All of the patients in the low group were DR2 positive, whereas DR2 was positive in only 33.3% (4 cases) in the normal group. However, comparison of clinical parameters and MSLT results between the patients divided by positive or negative HLA-DR2 showed no statistical difference. Detailed HLA analysis was carried out for 5 patients in the normal group. Only 1 was DQB1*0602 positive; thus, at least 10 out of 12 patients (83.3%) with normal CSF hypocretin-1 levels were determined to be HLA-DQB1*0602 negative.

DISCUSSION

In this study, we investigated the CSF hypocretin-1 levels in patients with well-characterized narcolepsy without cataplexy. Previous reports on the relationship between HLA profile and CSF hypocretin-1 levels in both narcolepsy with and without cataplexy are summarized in Table 3. Except for the report by Ebrahim et al showing that CSF hypocretin-1 level was markedly decreased in all the narcoleptic patients without cataplexy but not as deficient as in patients with narcolepsy with cataplexy, [8] decreased CSF hypocretin-1 levels were seen in fewer than 15% of the patients of narcolepsy without cataplexy. [6,7,9-12] In the present study, levels of CSF hypocretin-1 were markedly decreased in approximately one third of the patients who had narcolepsy without cataplexy, and the rate was higher than expected.

Considering that our patients were generally young, it is possible that patients with narcolepsy with cataplexy in the early stages of disease prior to the development of cataplexy may have been included in our patient population, leading to the higher rate of the patients with low CSF hypocretin-1. Generally, cataplexy develops within several months after the onset of hypersomnia in most patients with narcolepsy.[20] In the present study, the clinical states and CSF hypocretin-1 levels were examined at least 3 years after the onset of hypersomnia in all of the patients with de-

Table 3—Summary of the Previous Reports on CSF hypocretin-1 Levels in Various Narcolepsy Subgroups

Group of patients	HLA	Patients, no.	Patients with decreased hypocretin-1[a]
Mignot et al(2002)[7]			
Narcolepsy with typical cataplexy	DQB1*0602 (+):93%[b]	101	88/101 (87%)
Narcolepsy with atypical cataplexy	DQB1*0602 (+):35%[b]	29	5/29 (17%)
HLA negative narcolepsy/ cataplexy	DQB1*0602 (-)	7	2/7 (29%)
Narcolepsy without cataplexy	DQB1*0602 (+):56%[b]	20	3/20 (15%)
Hong et al (2002)[12]			
Narcolepsy with typical cataplexy	DQB1*0602 (+)	17	5/5 (100%)
Narcolepsy with atypical cataplexy	DQB1*0602 (+)	1	1/1 (100%)
	DQB1*0602 (-)	2	N/A
Kanbayashi et al (2002)[6]			
Narcolepsy with cataplexy	DR2 (+)	9	9/9 (100%)
	DR2 (-)	2	0/2 (0%)
Narcolepsy without cataplexy	DR2 (+)	3	0/3 (0%)
	DR2 (-)	2	0/2 (0%)
Krahn et al (2002)[9]			
Narcolepsy with cataplexy	DQB1*0602 (+)	16	12/13 (92%)
	DQB1*0602 (-)	4	0/4 (0%)
Narcolepsy without cataplexy	DQB1*0602 (+)	3	0/3 (0%)
	DQB1*0602 (-)	6	0/6 (0%)
Ebrahim et al (2003)[8]			
Narcolepsy with cataplexy	DQB1*0602 (+)	14	10/10 (100%)
Narcolepsy without cataplexy	DQB1*0602 (+)	3	3/3 (100%)
	DQB1*0602 (-)	1	1/1 (100%)
Bassetti et al (2003)[11]			
Narcolepsy with cataplexy	DQB1*0602 (+)	3	3/3 (100%)
	DQB1*0602 (-)	1	0/1 (0%)
Narcolepsy without cataplexy	DQB1*0602 (+)	2	0/2 (0%)
	DQB1*0602 (-)	2	0/2 (0%)
Dauvilliers et al (2003)[10]			
Narcolepsy with cataplexy	DQB1*0602 (+)	25	23/25 (92%)
	DQB1*0602 (-)	1	0/1 (0%)
Narcolepsy without cataplexy	DQB1*0602 (+)	8	1/8 (13%)
	DQB1*0602 (-)	1	0/1 (0%)
Oka et al. (this study)			
Narcolepsy without cataplexy	DR2 (+)	9	5/9 (56%)
	DR2 (-)	8	0/8 (0%)

CSF refers to cerebrospinal fluid.
[a]Hypocretin-1 values of 110 pg/mL or less were used as the cutoff value.
[b]Percentage of patients with positive DQB1*0602.

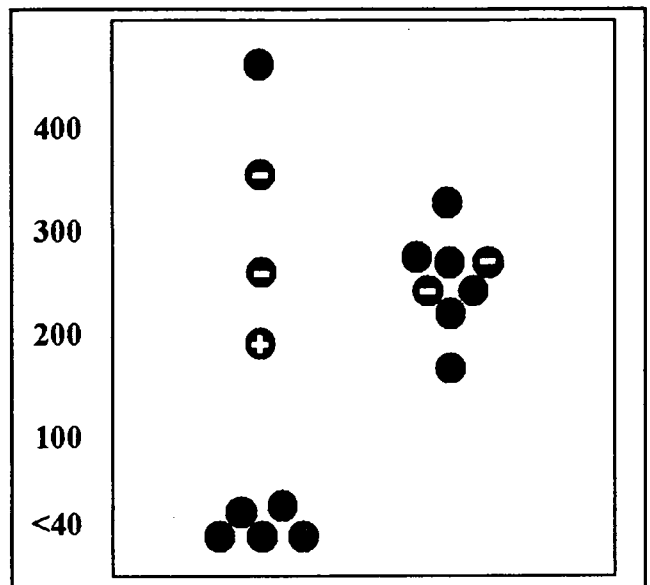

Figure 1—Hypocretin-1 levels in the cerebrospinal fluid (CSF) and HLA typing in patients who have narcolepsy without cataplexy: a comparison between HLA-DR2 (+) and DR2 (–). Symbols of "+" and "–" within in the circle indicate the results of subtype analysis of HLA DQB1*0602 as positive and negative, respectively.

creased CSF hypocretin-1, whereas the examination was carried out within 3 years after the onset of excessive daytime sleepiness in 3 patients out of 12 in the normal group. Especially in the low group, the onset of hypersomnia was more than 10 years before the present evaluation in 3 patients, and 1 of them developed hypersomnia 35 years before. Therefore, it is rather unlikely that they would develop cataplexy in the future. As another option, we should consider the possibility that mild cataplexy might have been overlooked. However, since all of the clinical interviews and examinations were made carefully by board-certified sleep specialists in our study, this possibility is also unlikely. Therefore, our patients were judged as having true narcolepsy without cataplexy, and we would like to emphasize that a certain number of narcoleptic patients without cataplexy show markedly decreased CSF hypocretin-1 levels.

Because hypocretin-1 deficiency has been commonly recognized in patients with narcolepsy with cataplexy, a strong association between the mechanism of cataplexy and hypocretin-1 deficiency has been assumed.[5,6] However, the present results indicate that lowered CSF hypocretin-1 levels could also be recognized in patients with narcolepsy without cataplexy. This finding is compatible with the report in which patients with secondary hypersomnia due to a neurologic disorder showed both SOREMPs on the MSLT and decreased CSF hypocretin-1 level but did not develop cataplexy throughout the clinical course.[21]

Among the clinical variables, the MSLT in the low group showed a shorter REM latency than in the normal group, whereas percentage of naps with SOREMPs and severity of excessive daytime sleepiness, as manifested on both mean sleep latency on the MSLT and the Epworth Sleepiness Scale, did not show any difference between the 2 groups. This finding indicates that REM propensity is partially increased in the low group, leading to the speculation that the degree of REM pathology is somewhat stronger in the low group compared with the normal group. In addition, the onset of excessive daytime sleepiness was earlier in the low group than in the normal group. Although the reason for this phenomenon is unknown, the result seems to be in line with that of an earlier report in which narcolepsy symptoms were more severe in patients with early-onset than those with late-onset disease.[20]

One of the most striking findings in our study was that HLA-DR2 was positive in all of the patients in the low group, whereas all of the patients with negative HLA-DR2 had normal CSF hypocretin-1 values. As indicated in Table 3, among the previously reported patients with narcolepsy with cataplexy, the CSF

hypocretin-1 level was low in most of the patients with HLA-DQB1*0602 [8-12] or DR2.[6] On the other hand, the CSF hypocretin-1 level was mostly normal in those who were HLA-DQB1*0602 [7,9-11] or DR2 negative.[6] These results corroborate the idea that there could exist a strong relationship between HLA profile and CSF hypocretin-1 level in narcolepsy with cataplexy.[9] Young and colleagues reported that HLA DQB1*0602 positivity in patients with narcolepsy without cataplexy was associated with decreased CSF hypocretin-1 levels,[22] and our results were in line with their findings. We speculate that a similar relationship between the HLA profile and the CSF hypocretin-1 level could also exist in narcolepsy without cataplexy.

Although detailed HLA analysis including HLA-DQB1*0602 was carried out in only 5 patients in the present study, at least 83.3% of patients with normal hypocretin-1 levels were regarded to be HLA-DQB1*0602 negative. Moreover, REM pathology on the MSLT and the disease onset were significantly different between the low group and the normal group. Taken together with the difference in the profile of both HLA and hypocretin-1, narcolepsy without cataplexy could be a heterogeneous group, and patients who have narcolepsy without cataplexy who also have normal CSF hypocretin-1 levels may have a different pathophysiologic mechanism from that of patients with typical narcolepsy with cataplexy.

In conclusion, some patients who have narcolepsy without cataplexy have low CSF hypocretin-1 levels, and they are more likely to have an early clinical onset, shorter mean REM latency, and positive HLA status. Thus, CSF hypocretin-1 levels may become a useful clue in distinguishing subgroups of patients who have narcolepsy without cataplexy, reflecting different pathophysiologic mechanisms.

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Insomnia Among Japanese Adolescents: A Nationwide Representative Survey

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Study Objectives: Although a number of previous studies have examined the prevalence of insomnia among adolescents, there have been very few nationwide studies. The objectives of this nationwide study were to clarify the prevalence of insomnia, its symptoms, and associated factors among Japanese adolescents.

Design and Setting: This study was designed as a cross-sectional sampling survey. The targets were junior and senior high schools throughout Japan. Sample schools were selected by cluster sampling. Self-reported anonymous questionnaires were sent to schools for all students to fill out.

Participants: A total of 103,650 adolescents responded, and 102,451 questionnaires were subjected to analysis.

Intervention: N/A

Measurements and Results: The prevalence of difficulty initiating sleep, difficulty maintaining sleep, and early morning awakening was 14.8%, 11.3%, and 5.5%, respectively. Insomnia was defined as the presence of one or more of these three symptoms. The prevalence of insomnia was 23.5%. Multivariate analyses revealed that, among junior high school students, male sex, poor mental health, skipping breakfast, drinking alcohol, smoking, not participating in extracurricular activities, and late bedtime had significantly higher odds ratios for insomnia. Among senior high school students, the same characteristics were associated with a significantly higher odds ratio for insomnia, as was the additional factor of having no intent to study at university.

Conclusion: Insomnia in Japanese adolescents is common and associated with multiple factors. The results of this study suggest the need for comprehensive program to prevent insomnia in Japanese adolescents.

Keywords: Insomnia; adolescents; Japan

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INTRODUCTION

INSOMNIA IS A RISK FACTOR FOR ASSOCIATED WITH VARIOUS PHYSICAL AND MENTAL DISORDERS, AS WELL AS INDUSTRIAL AND TRAFFIC ACCIDENTS; INSOMNIA is therefore considered to be a serious public health issue. Nationwide epidemiological studies of sleep have been conducted in various countries using samples representative of the general population.[1,2] Methods used for evaluating insomnia differed among these studies; the prevalence of insomnia among adults was reported to be between 5% and 48%.

In industrialized countries, insomnia is recognized to be a common problem. In Japan, a study conducted in 1997 on a general adult population comprising 3,030 subjects revealed that the prevalence of insomnia was 21.4%.[3]

Adolescence is a time of social as well as biological transition; therefore, sleep disturbance among adolescents must be discussed separately from that among adults. Since it is known that insomnia affects the future somatic, interpersonal, and psychological functioning of adolescents,[4] it is expected to be a serious school health problem. Some epidemiological studies of insomnia among adolescents overseas have been reported. Ohayon et al., in a study of 1,125 adolescents sampled from 4 European countries (France, Great Britain, Germany, and Italy), reported that 25.7% of the adolescents had one or more of the following insomnia symptoms: difficulty initiating sleep (DIS), difficulty maintaining sleep (DMS), early morning awakening (EMA), or nonrestorative sleep.[5] A study conducted in the United States on 5,423 adolescents reported that 34.0% of the subjects had experienced DIS, DMA, or EMA often or daily in the prior two weeks.[6] In Asia, Liu et al. in a study of 1,365 Chinese adolescents reported that the prevalence of insomnia was 16.9% and that the factors associated with insomnia were greater age, lack of habitual physical exercise, poor physical health, self-selected diet, longer distance from home to school, and life stresses.[7] These studies are meaningful because they have clarified the prevalence of insomnia among adolescents in each country. However, the studies were limited by relatively small sample sizes and poor representative sampling.

In Japan, a representative epidemiological study of sleep disturbance among adolescents was conducted for the first time in 2000.[8] The study reported that factors such as female sex, not eating breakfast, smoking, drinking alcohol, and psychological stress were associated with sleep disturbances such as short sleep duration and subjective sleep insufficiency. However, the questionnaire used in that study assessed only one symptom of insomnia. In a self-reported study on sleep, it is usual to evaluate insomnia using the following three symptoms: DIS, DMA, and EMA.[5-7,9-13] In the survey conducted in 2000, questions on DMS

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and EMA were not posed. Therefore, in this study, questions on all three of these insomnia symptoms were included in the questionnaire. The aim of this study was to clarify the prevalence of insomnia and its associated factors among Japanese adolescents.

METHODS

Subjects and Sampling

We have previously conducted two cross-sectional nationwide surveys (1996 and 2000) on lifestyle habits such as drinking alcohol, smoking, eating, and sleeping among Japanese adolescents.[8,14-18] This study was the third such survey.

For this study, of the 11,060 junior high schools and 4,627 senior high schools registered in Japan in May 2003, 131 junior high schools (selection rate: 1.2%) and 109 senior high schools (selection rate: 1.9%) were sampled. A single-stage cluster sampling method was employed with the probability of sampling proportional to the number of current students. All students enrolled in the sampled schools were subjects of this study. The sample size was determined by referring to the response rates and confidence intervals (CIs) based on variance of results obtained from the two previous studies.

In the Japanese education system, children enter primary school at the age of 6 years and leave after 6 years of study. They then enter junior high school for 3 years of study, followed by 3 years of study at senior high school. Primary and junior high school education is compulsory. In this report, the first to third years of junior high school are called the 7th to 9th grades, and the first to third years of senior high school are called the 10th to 12th grades.

Survey Procedure

We sent a letter to the principal of each selected school, asking for cooperation in our survey, along with the same number of questionnaires and envelopes as the number of students enrolled at the school. At schools that agreed to participate in our survey, each class teacher distributed the questionnaires to the students. To protect the privacy of respondents and to obtain candid responses, it was clearly stated on the questionnaire that completed questionnaires would not be seen by the teachers. After filling in the anonymous questionnaire, each student was asked to seal the questionnaire in the provided envelope with an adhesive flap. Collection and delivery of the questionnaires were entrusted to the teachers, who were instructed to follow the guidelines for conducting the survey. The teachers collected and sent the sealed envelopes back to the National Institute of Public Health without opening them. The survey period was from December 2004 to the end of January 2005. This survey was approved by the Ethics Committee of the National Institute of Public Health.

Measures

The major areas that were included in the questionnaire were: (1) lifestyle, including drinking and smoking behavior; (2) sleep status, including insomnia symptoms and bedtime; (3) mental health status; and (4) personal data. The following three questions about insomnia symptoms experienced during the previous month were embedded in the questionnaire:

1. "Do you have difficulty falling asleep at night?" (DIS)
2. "Do you wake up during the night after you have gone to sleep?" (DMS)
3. "Do you wake up too early in the morning and have difficulty getting back to sleep?" (EMA)

Each question had five possible replies: "never," "seldom," "sometimes," "often," and "always." "Often" and "always" were taken as an affirmative answer to the question. The presence of DIS, DMS, or EMA was defined when an affirmative answer to question 1, 2, or 3 was obtained, respectively. Insomnia was defined as being present when an affirmative answer was obtained for any of the three questions.

The demographic variables were: sex, grade, type of school (junior high school/senior high school), and intention to study at university (yes/no). The questions related to lifestyle were whether the student ate breakfast (daily/occasionally/never), and whether he/she participated in extracurricular activities (participating actively/ participating but not actively/not participating).

A question "How many days did you smoke in the past one month?" was included in the questionnaire. If the response to this question was one day or more, then it was defined as "smoking." Similarly, a question "How many days did you consume alcoholic beverages in the past one month?" was asked, and if the response was one day or more, then it was defined as "drinking alcohol."

The Japanese version of the 12-item General Health Questionnaire (GHQ12-J) was used to evaluate mental health status.[19,20] The GHQ12-J is a widely used, self-administered questionnaire that was designed as a screening tool for mental illness. It assesses 12 symptoms of psychiatric disorders during the previous month. Every item on the GHQ12-J describes a symptom and has four possible replies: the two answers that indicate the absence of the symptom are given a score of "0", and the two that indicate the presence of the symptom receive a "1." The overall score on the scale will thus fall into a range of 0-12, and it follows that the higher the total score, the poorer the state of mental health. The GHQ was originally applied to adult populations and subsequently used and validated for adolescents as well.[21-23] In the present study, any participant whose total GHQ12-J score was ≥ 4 points was considered to be a person with poor mental health, as assessed by most previous studies.[23-25]

Statistical Analyses

First, the prevalences of DIS, DMS, EMA, and insomnia, and the 95% CIs were calculated. Then, the prevalences of DIS, DMS, EMA, and insomnia with regard to sex and grade were calculated. Finally, multivariate logistic regression analyses were performed to examine the factors associated with insomnia symptoms. The analyses were conducted separately for the junior and senior high school students since the results might provide the basis for future educational planning at each level. All analyses were performed using SPSS 11.5 for Windows.

RESULTS

Response Rates

Replies were obtained from 92 of the 131 junior high schools (school response rate: 70.2%) and 87 of the 109 senior high schools (school response rate: 79.8%; combined junior and senior high school response rate: 74.6%). A total of 103,650 envelopes were collected. The student response rate as a proportion of enrolled students in the sampled schools was 88.4% in the junior

high schools, 86.3% in the senior high schools, and 87.1% as a whole. Accordingly, the overall response rate was 60.7% in the junior high schools, 67.7% in the senior high schools, and 64.8% as a whole. Of the collected questionnaires, 1,199 were excluded because the sex or grade was not specified, or the answers were inconsistent. The data of the remaining 102,451 questionnaires were analyzed.

Prevalence of Insomnia and Insomnia Symptoms

The responses to the questions on the three insomnia-related symptoms with regard to sex and grade are shown in Tables 1 to 3. The prevalence (and 95% CI) of DIS, DMA, and EMA were 14.8% (14.6%-15.0%), 11.3% (11.1%-11.5%), and 5.5% (5.4%-5.6%), respectively. The prevalence of DIS was the highest. The prevalence (and 95% CI) of DIS among males was 14.4% (14.1%-14.7%) and among females was 15.3% (15.0%-15.6%). Thus, the prevalence of DIS was significantly higher among females ($P < .01$). The prevalence (and 95% CI) of DMS among males was 11.0% (10.7%-11.3%) and among females was 11.7% (11.4%-12.0%). Thus, the prevalence of DMS was also significantly higher among females ($P < .01$). The prevalence (and 95% CI) of EMA among males was 5.7% (5.5%-5.9%) and among females was 5.2% (5.0%-5.4%); in this case, the prevalence was

Table 1—Prevalence of Difficulty Initiating Sleep Among Japanese Adolescents*

	Never	Seldom	Sometimes	Often	Always	Uncertain	N
Male							
Junior high school							
7th grade	38.2	19.5	27.6	6.8	4.5	3.4	6917
8th grade	36.0	18.7	29.2	7.7	5.2	3.1	6845
9th grade	32.1	16.3	32.7	10.1	6.3	2.4	6917
Senior high school							
10th grade	34.9	19.2	30.1	8.9	5.1	1.8	12235
11th grade	32.7	19.2	31.7	9.4	5.1	1.8	12241
12th grade	32.5	18.5	30.8	10.1	6.3	1.8	10843
Total	34.2	18.7	30.5	9.0	5.4	2.2	55998
Female							
Junior high school							
7th grade	30.9	21.8	32.5	7.8	5.4	1.6	6229
8th grade	29.4	19.4	34.2	9.2	6.2	1.6	6234
9th grade	28.2	16.1	35.9	10.5	8.1	1.2	6243
Senior high school							
10th grade	32.8	18.8	32.9	8.8	5.5	1.1	9580
11th grade	30.4	18.9	34.1	9.8	5.4	1.3	9289
12th grade	29.9	18.4	34.7	10.3	5.5	1.2	8878
Total	30.4	18.9	34.0	9.4	5.9	1.3	46453

*Data expressed as percentage of the analyzed subjects.

Table 2—Prevalence of Difficulty Maintaining Sleep Among Japanese Adolescents*

	Never	Seldom	Sometimes	Often	Always	Uncertain	N
Male							
Junior high school							
7th grade	38.5	20.0	28.5	6.1	3.5	3.4	6917
8th grade	40.3	18.0	28.1	6.6	4.0	3.0	6845
9th grade	42.5	17.7	26.9	7.0	3.6	2.2	6917
Senior high school							
10th grade	41.2	17.9	27.9	7.4	3.8	1.7	12235
11th grade	39.8	18.7	27.8	8.0	3.9	1.8	12241
12th grade	42.4	18.0	26.9	7.3	3.7	1.8	10843
Total	40.8	18.3	27.7	7.2	3.8	2.2	55998
Female							
Junior high school							
7th grade	38.0	20.1	30.1	6.4	3.8	1.6	6229
8th grade	37.7	19.9	30.5	6.7	3.8	1.5	6234
9th grade	41.1	17.8	28.5	7.2	4.2	1.1	6243
Senior high school							
10th grade	40.5	17.7	29.0	7.6	4.2	1.0	9580
11th grade	37.8	17.5	30.6	8.1	4.6	1.3	9289
12th grade	37.5	17.2	31.6	8.0	4.6	1.2	8878
Total	38.8	18.2	30.1	7.4	4.3	1.3	46453

*Data expressed as percentage of the analyzed subjects.

Table 3—Prevalence of Early Morning Awakening Among Japanese Adolescents*

	Never	Seldom	Sometimes	Often	Always	Uncertain	N
Male							
Junior high school							
7th grade	67.0	14.0	12.4	3.1	2.9	0.6	6917
8th grade	68.0	13.4	11.6	3.5	3.0	0.6	6845
9th grade	70.0	12.1	11.1	3.1	3.0	0.7	6917
Senior high school							
10th grade	68.5	14.0	10.9	3.6	2.4	0.5	12235
11th grade	68.2	14.7	11.3	3.2	2.1	0.5	12241
12th grade	69.5	14.0	10.8	3.1	2.1	0.6	10843
Total	68.6	13.9	11.3	3.3	2.5	0.6	55998
Female							
Junior high school							
7th grade	66.7	15.7	12.1	2.8	2.3	0.4	6229
8th grade	67.9	14.7	11.9	3.0	2.1	0.4	6234
9th grade	68.2	14.4	11.4	3.3	2.2	0.4	6243
Senior high school							
10th grade	67.6	14.9	12.0	3.4	1.8	0.4	9580
11th grade	66.0	16.2	12.2	3.3	1.9	0.4	9289
12th grade	66.4	15.4	12.6	3.3	1.9	0.4	8878
Total	67.0	15.3	12.1	3.2	2.0	0.4	46453

*Data expressed as percentage of the analyzed subjects.

significantly higher among males (P< .01).

The prevalence of insomnia in relation to sex and grade is shown in Table 4. The prevalence (and 95% CI) of insomnia was 23.5% (23.2%-23.8%) in the total sample: 23.3% (22.9%-23.7%) among males, and 23.7% (23.3%-24.1%) among females. No statistically significant difference was observed between males and females (P = .47). Among both males and females, the prevalence of DIS and insomnia increased gradually from the 7th to 9th grade, decreased in the 10th grade, and then gradually increased again toward the 12th grade.

Table 4—Prevalence of Insomnia Among Japanese Adolescents*

	Without insomnia	With insomnia	Uncertain	N
Male				
Junior high school				
7th grade	76.1	20.3	3.6	6917
8th grade	74.7	22.1	3.3	6845
9th grade	72.8	24.6	2.5	6917
Senior high school				
10th grade	74.5	23.5	2.0	12235
11th grade	74.3	23.7	2.0	12241
12th grade	73.4	24.6	2.1	10843
Total	74.3	23.3	2.4	55998
Female				
Junior high school				
7th grade	77.2	21.0	1.7	6229
8th grade	75.5	22.7	1.7	6234
9th grade	72.5	26.1	1.4	6243
Senior high school				
10th grade	75.7	23.0	1.2	9580
11th grade	74.0	24.5	1.5	9289
12th grade	73.9	24.7	1.4	8878
Total	74.8	23.7	1.5	46453

*Data expressed as percentage of the analyzed subjects.

Logistic Regression Analyses

The results of logistic regression analyses using the data for junior and senior high school students are shown in Tables 5 and 6, respectively. Four logistic models that use DIS, DMS, EMA, and insomnia as response variables were created. As covariates, 9 items that are shown in Tables 5 and 6 were used in common.

The adjusted odds ratios (AORs) for EMA and insomnia among male junior high school students and AORs for DIS, EMA, and insomnia among male senior high school students were significantly higher than among their female counterparts. With regard to EMA among junior and senior high school students, AORs were found to be significantly higher as grades became lower.

Among junior high school students, AOR for DIS was higher, and AOR for EMA was lower among students who intended to study at university than among those who did not. However, among senior high school students, AORs for all response variables were significantly lower among students who intended to study at university than among those who did not.

Among both junior and senior high school students, AORs for all response variables were significantly higher among those who had been evaluated as having poor mental health, those who skipped breakfast, those who drank alcohol, and those who smoked than among subjects who did not have these features. AORs for insomnia were significantly lower among those who participated in extracurricular activity than among those who did not.

Among both junior and senior high school students, AORs for DIS and insomnia were significantly higher among those whose bedtime was after 00:00 than among those whose bedtime was before or at 00:00. On the contrary, AORs for DMS were significantly low among senior high school students whose bedtime was after 00:00.

Table 5—Logistic Regression Results for Prediction of Insomnia and Symptoms of Insomnia Among Japanese Junior High School Students

		DIS			DMS			EMA			Insomnia		
	N	AOR	95%CI	P value	AOR	95%CI	P value	AOR	95%CI	P value	AOR	95%CI	P value
Sex				.69			.58			<.01			<.01
Male	20030	1.00			1.00			1.00			1.00		
Female	18401	1.01	0.95-1.08		0.93	0.87-1.00		0.71	0.65-0.78		0.91	0.86-0.96	
Junior high school				.55			.10			<.01			.72
7th grade	12788	1.00			1.00			1.00			1.00		
8th grade	12746	1.02	0.94-1.11		0.98	0.89-1.06		0.93	0.82-1.04		0.99	0.93-1.06	
9th grade	12897	1.05	0.96-1.14		0.91	0.83-0.99		0.79	0.70-0.90		0.97	0.91-1.04	
Intention to study at university				.02			.74			<.01			.50
No	33679	1.00			1.00			1.00			1.00		
Yes	4525	1.12	1.02-1.23		0.98	0.88-1.10		0.73	0.62-0.86		1.03	0.95-1.11	
Poor mental health (GHQ score ≥4)				<.01			<.01			<.01			<.01
No	22963	1.00			1.00			1.00			1.00		
Yes	14379	2.96	2.78-3.16		2.35	2.19-2.52		3.05	2.76-3.36		2.74	2.60-2.89	
Eating breakfast				<.01			<.01			<.01			<.01
Daily	31104	1.00			1.00			1.00			1.00		
Occasional	3668	1.43	1.30-1.57		1.47	1.33-1.63		1.58	1.38-1.81		1.48	1.37-1.61	
Never	2009	1.86	1.66-2.08		1.88	1.66-2.14		2.21	1.89-2.57		1.89	1.70-2.09	
Drinking alcohol				<.01			<.01			<.01			<.01
No	30416	1.00			1.00			1.00			1.00		
Yes	7771	1.39	1.30-1.50		1.34	1.23-1.46		1.46	1.31-1.63		1.39	1.30-1.48	
Smoking				<.01			<.01			<.01			<.01
No	36333	1.00			1.00			1.00			1.00		
Yes	1662	1.44	1.26-1.64		1.65	1.44-1.90		1.79	1.51-2.11		1.62	1.44-1.82	
Participating in extracurricular activities				<.01			<.01			<.01			<.01
No	7730	1.00			1.00			1.00			1.00		
Yes	30251	0.88	0.81-0.95		0.86	0.78-0.93		0.80	0.71-0.90		0.87	0.81-0.93	
Bedtime				<.01			.10			.06			<.01
Before or at 00:00	25786	1.00			1.00			1.00			1.00		
After 00:00	12454	1.83	1.71-1.95		1.07	0.99-1.15		1.11	1.00-1.23		1.41	1.33-1.50	

Abbreviations: DIS, difficulty initiating sleep; DMS, difficulty maintaining sleep; EMA, early morning awakening; AOR, adjusted odds ratio; CI, confidence interval; GHQ, general health questionnaire.
Subjects with missing data were excluded from the analysis.

DISCUSSION

The results of this study appear to be representative of the study population for three reasons: (1) the subject schools were selected randomly from among those nationwide; (2) the number of analyzed cases exceeded 100,000; and (3) the rate of response to the questionnaires was acceptably high. Epidemiological studies of insomnia among adolescents have already been conducted in Western countries. However, to our knowledge, none of these previous studies involved such a large sample size or were as representative as our present study.

A uniform definition of insomnia was not followed in the previous epidemiological studies of adolescents. However, in many investigations, three insomnia symptoms – DIS, DMS, and EMA – were studied, and insomnia was evaluated and examined by using a combination of these symptoms.[5-7,9-13] In this study, a subject was considered to have insomnia if he/she had experienced one or more of these three insomnia symptoms in the past month. This definition of insomnia was adopted when our questionnaire was compiled to allow comparison between our study and the previous studies that had targeted either the general adult population of Japan[3] or Chinese adolescents.[7] The prevalence of insomnia observed among the adolescents in our study (23.5%) appears to be similar to that observed among the general adult population of Japan (21.4%). However, the prevalence of DIS, DMS, and EMS among the adolescents was 14.8%, 11.3%, and 5.5%, respectively, and differed from the values observed among the general adult population (8.3%, 15.0%, and 8.0%, respectively).[3] Among all the insomnia symptoms, the prevalence of DIS was the highest among the adolescents, and was much higher than that observed among Japanese adults. Thus, DIS may be a form of sleep disturbance among Japanese adolescents that requires special attention. As it is known that the prevalence of DMS and EMA increases with age,[3,26] the low prevalence of DMS and EMA in adolescents as compared to adults is not surprising. The prevalence of insomnia, DIS, DMS, and EMA among Chinese adolescents was reported to be 16.9%, 10.8%, 6.3%, and 2.1%, respectively[7]; thus the corresponding values for Japanese adolescents were higher.

We observed that the prevalence of both DIS and DMS was higher among females, whereas that of EMA was significantly higher among males. As a study conducted in 2000 targeting the general adult population of Japan revealed a similar result,[26] this may be a common characteristic feature among both Japanese adults and adolescents. Although there was no significant sex-based difference in the prevalence of insomnia, a significantly high AOR for insomnia among males was revealed by multivariate analysis. Some confounding factors may account for this observation; one of these may be mental health status. In this study,

Table 6—Logistic Regression Results for Prediction of Insomnia and Symptoms of Insomnia Among Japanese Senior High School Students

		DIS			DMS			EMA			Insomnia		
	N	AOR	95%CI	P value	AOR	95%CI	P value	AOR	95%CI	P value	AOR	95%CI	P value
Sex				.02			.15			<.01			.02
Male	34608	1.00			1.00			1.00			1.00		
Female	27371	0.95	0.90-0.99		1.04	0.99-1.10		0.90	0.84-0.97		0.95	0.91-0.99	
Senior high school				.32			.05			<.01			.21
10th grade	21458	1.00			1.00			1.00			1.00		
11th grade	21144	0.98	0.92-1.04		1.07	1.00-1.13		0.86	0.79-0.94		0.99	0.95-1.04	
12th grade	19377	0.95	0.90-1.01		0.99	0.93-1.06		0.83	0.75-0.91		0.96	0.91-1.01	
Intention to study at university				<.01			<.01			<.01			<.01
No	25224	1.00			1.00			1.00			1.00		
Yes	36561	0.77	0.73-0.81		0.76	0.72-0.80		0.72	0.67-0.78		0.75	0.72-0.78	
Poor mental health (GHQ score ≥4)				<.01			<.01			<.01			<.01
No	31802	1.00			1.00			1.00			1.00		
Yes	28963	2.68	2.55-2.82		2.13	2.02-2.25		2.47	2.28-2.67		2.41	2.31-2.51	
Eating breakfast				<.01			<.01			<.01			<.01
Daily	47268	1.00			1.00			1.00			1.00		
Occasional	6788	1.40	1.30-1.50		1.34	1.24-1.45		1.38	1.24-1.53		1.38	1.30-1.46	
Never	5001	1.79	1.66-1.93		1.66	1.53-1.80		1.80	1.61-2.01		1.75	1.64-1.87	
Drinking alcohol				<.01			<.01			<.01			<.01
No	39854	1.00			1.00			1.00			1.00		
Yes	21869	1.20	1.14-1.26		1.20	1.13-1.27		1.21	1.12-1.31		1.22	1.17-1.27	
Smoking				<.01			<.01			<.01			<.01
No	53577	1.00			1.00			1.00			1.00		
Yes	7721	1.46	1.36-1.56		1.41	1.30-1.52		1.57	1.41-1.74		1.48	1.39-1.57	
Participating in extracurricular activities				<.01			.17			.07			<.01
No	25120	1.00			1.00			1.00			1.00		
Yes	36586	0.83	0.79-0.87		0.96	0.91-1.02		0.93	0.86-1.01		0.90	0.86-0.93	
Bedtime				<.01			<.01			.06			<.01
Before or at 00:00	26681	1.00			1.00			1.00			1.00		
After 00:00	35168	1.81	1.72-1.91		0.81	0.76-0.85		0.93	0.86-1.00		1.17	1.12-1.22	

Abbreviations: DIS, difficulty initiating sleep; DMS, difficulty maintaining sleep; EMA, early morning awakening; AOR, adjusted odds ratio; CI, confidence interval; GHQ general health questionnaire.
Subjects with missing data were excluded from the analysis.

GHQ scores were used as covariates to evaluate mental health status. GHQ scores tended to be higher among female than among male participants. In addition, participants whose GHQ scores were higher tended to have insomnia symptoms. Therefore, if an analysis is conducted without adjusting for GHQ scores, any association between males and the prevalence of insomnia may not be conspicuous. In a previous survey we conducted on sleep disturbances among Japanese adolescents,[8] we did not place sufficient emphasis on mental health status; therefore, females were observed to be at higher risk of all forms of sleep disturbance that were examined. However, as revealed in the present study, if an analysis is conducted with adjustment for GHQ scores, males appear to have a significantly higher risk of insomnia than females.

In this study, when insomnia was used as a response variable, no significant association was recognized between insomnia and school grade. However, when each insomnia symptom was used as a response variable, interesting results were obtained. AOR for EMA among both junior and senior high school students decreased as the grade advanced. Few studies have reported the associations between each insomnia symptom and the school grade or age of adolescents. Among Chinese adolescents, the prevalence of DIS and EMA was reported to increase with age.[7] This was not consistent with our findings. The social factors affecting students may differ according to school grade, however specifying the social factors that affect students is beyond the scope of this study. In any event, it must be recognized that students of different grades have different levels of risk for symptoms of insomnia. Further studies of this issue are required in the future.

This study recognized a strong association between poor mental health status and insomnia, and all insomnia symptoms, among both junior and senior high school students. In Japan, Tagaya et al. reported in a community study targeting senior high school students that an association was recognized between short sleep duration and poor mental health.[27] Also, many studies overseas reported that an association was observed between adolescents' mental health status and sleep disturbance.[4,9,12,28-33] The present study supports the findings of the previous ones, and is also meaningful for two reasons: (1) we used the GHQ, which is employed worldwide, for evaluation of mental health status, and (2) representative samples were selected. Our findings further suggest the importance of mental health care for adolescents in the context of sleep hygiene.

Many studies conducted in Japan and overseas have reported associations between various sleep disorders and smoking cigarettes or drinking alcohol among adolescents.[7,8,11,12,30,32,34] Only two studies, however, have investigated the association of insomnia with these two factors.[7,12] In our study, smoking and drinking alcohol were considered to be independent risk factors for insom-