Table 1
The factor loadings in exploratory factor analysis of the Japanese version of the Ford Insomnia Response to Stress Test among the healthy subjects, the insomnia patients, and the previous results of the participants in the study with the original version of the Ford Insomnia Response to Stress Test.

Items	Healthy subjects (n = 161)	Insomnia patients (n = 177)	Drake et al. [18] (n = 104)[a]
3. After a stressful experience in the evening	0.92	0.85	0.73
2. After a stressful experience during the day	0.89	0.85	0.40
4. After getting bad news during the day	0.76	0.77	0.73
6. After having a bad day at work	0.74	0.70	0.68
7. After an argument	0.68	0.69	0.76
1. Before an important meeting the next day	0.63	0.51	0.56
8. Before having to speak in public	0.58	0.48	0.42
5. After watching a frightening movie or television show	0.48	0.40	0.48
9. Before going on vacation the next day	0.22	0.21	0.51

[a] Participants were from a general population-based sample other than individuals with notable sleep-disordered breathing. Instructions of the Ford Insomnia Response to Stress Test were as follows: "When you experience the following situations, how likely is it for you to have difficulty sleeping? Circle an answer even if you have not experienced these situations recently."

Table 2
Comparison of variables between the subjects with low scores and high scores on the Japanese version of the Ford Insomnia Response to Stress Test.

Subjects and variables	Total subjects	Subjects with low scores on the FIRST-J	Subjects with high scores on the FIRST-J	P value (low FIRST-J vs high FIRST-J)	Effect size (95% CI)	
Healthy subjects						
Demographics						
Age (y)	51.5 ± 9.4	53.2 ± 8.4	49.7 ± 10.2	<.05[a]	d = 0.38	(0.07–0.69)
Gender (women, %)	32.9	18.3	48.1	<.01[b]	φ = 0.31	(0.16–0.45)
Measures						
FIRST	18.6 ± 5.6	14.0 ± 2.6	23.5 ± 3.3	<.01[a]	d = 3.20	(2.74–3.66)
PSQI	4.3 ± 2.2	3.9 ± 2.2	4.7 ± 2.1	<.05[b]	d = 0.47	(0.02–0.66)
AIS	2.9 ± 2.1	2.4 ± 1.9	3.4 ± 2.1	<.01[a]	d = 0.50	(0.19–0.81)
STAI	41.6 ± 10.4	38.2 ± 9.5	44.9 ± 10.3	<.01[a]	d = 0.68	(0.36–1.00)
Insomnia patients						
Demographics						
Age (y)	46.8 ± 15.8	46.0 ± 16.9	47.0 ± 15.5	ns[a]	d = 0.06	(−0.43 to 0.30)
Gender (women, %)	57.1	52.2	62.1	ns[b]	φ = 0.09	(−0.06 to 0.23)
Measures						
FIRST	24.0 ± 5.9	15.4 ± 2.7	26.3 ± 4.2	<.01[a]	d = 2.78	(2.21–3.36)
PSQI	13.0 ± 2.8	13.1 ± 3.0	12.9 ± 2.8	ns[a]	d = 0.07	(−0.36 to 0.50)
AIS	12.4 ± 2.8	12.7 ± 4.5	12.3 ± 3.8	ns[a]	d = 0.10	(−0.48 to 0.68)
STAI	48.2 ± 10.48	43.1 ± 9.4	49.6 ± 10.8	<.01[a]	d = 0.62	(0.20–1.03)

Abbreviations: FIRST-J, Japanese version of the Ford Insomnia Response to Stress Test; CI, confidence interval; y, years; PSQI, Pittsburgh Sleep Quality Index; AIS, Athens Insomnia Scale; STAI, State-Trait Anxiety Inventory (items for trait); ns, not significant.

[a] Unpaired test.

[b] χ^2 test, ranges of sample size depending on the number of missing data are the following: 155–161 in the healthy subjects, 131–176 in the insomnia patients, 76–82 in the healthy subjects with low scores on the FIRST-J, 72–79 in the healthy subjects with high scores on the FIRST-J, 29–37 in the insomnia patients with low scores on the FIRST-J, and 102–140 in the insomnia patients with high scores on the FIRST-J.

original version, the FIRST-J was confirmed to have adequate internal consistency with a high Cronbach α coefficient among the study population. Exploratory factor analysis also revealed that the FIRST-J had a single-factor structure closely resembling that of the original version, though the factor loading of item 9 (before going on vacation next day) was lower than the value of the original version. However, considering the lack of influence of item 9 on correlations between the FIRST-J and the measures for insomnia severity or anxiety, we believe that removal of item 9 is not necessary for comparison of the total score of the FIRST between the original version and the Japanese version. Although the reason for the low factor loading of item 9 remains unclear, this difference could possibly be due to cultural or racial differences between participants in Japan and in the United States, where the original version of the FIRST was developed. This speculation is supported by the fact that the influence of a positive emotion-related stressor such as a vacation is likely to be reflected by cultural or racial differences [40,41].

Two cognitive processes, rumination after experiencing a particular stressor and worry before experiencing a particular stressor, reportedly influenced the insomnia mechanism [42]. Our study revealed that the influence of the former was stronger than that of the latter: items in the FIRST-J associated with rumination (items 2, 3, 4, 5, and 7) showed higher factor loadings than those associated with worry (items 1, 8, and 9), which is consistent with the report by Carney et al. [42]. However, factor analysis showed no 2-factor structure. Rumination- and worry-associated items were clearly distinguishable. In our study, the scores of the PSQI and AIS for the healthy participants with high FIRST-J scores were significantly higher than those for participants with low FIRST-J scores, which is consistent with the results of the original version using n-PSG measures [18]. This finding indicates that the FIRST-J has adequate discriminant validity.

Our results of the FIRST-J score positively correlating with the score of the STAI in both the healthy participants and the insomnia patients indicate that sleep reactivity is related with trait anxiety, which is known as a factor determining vulnerability to insomnia [3,26]. Correlation also was found between the score of the FIRST-J and those of the PSQI or the AIS in the healthy participants. However, no significant correlation was found between the FIRST-J and these measures in the insomnia patients, which might indicate that sleep reactivity is related with vulnerability to insomnia, but it does not play a major role as a process aggravating insomnia. Among the healthy participants, significant differences were found

Table 3
Correlations between scores of the Japanese version of the Ford Insomnia Response to Stress Test and the other measures in the healthy subjects and the insomnia patients.

			STAI	PSQI	AIS
Healthy subjects[a]	Not adjusted	FIRST-J	.44**	.22**	.30**
		FIRST-J without item 9	.44**	.23**	.29**
	After controlling for age and gender	FIRST-J	.47**	.20*	.26**
		FIRST-J without item 9	.47**	.21*	.23**
Insomnia patients[b]	Not adjusted	FIRST-J	.39**	.03	.05
		FIRST-J without item 9	.39**	.02	.07
	After controlling for age and gender	FIRST-J	.45**	.04	.06
		FIRST-J without item 9	.43**	.04	.07

Abbreviations: FIRST-J, Japanese version of Ford Insomnia Response to Stress Test; STAI, State-Trait Anxiety Inventory (items for trait); PSQI, Pittsburgh Sleep Quality Index; AIS, Athens Insomnia Scale.
Parentheses indicate 95% confidence interval.
[a] Sample sizes range from 131 to 172 depending on the number of missing data.
[b] Sample sizes range from 151 to 161 depending on the number of missing data.
** $P < .01$.
* $P < .01$.

in age and gender between the groups with high and low FIRST-J scores. However, no significant differences were found in these variables between the groups with high and low FIRST-J scores in the insomnia patients. Regarding gender differences, our result was consistent with a report of a previous study described by Drake et al. [18]. The higher rate of women in the high-scoring FIRST-J group might be one factor for the predominant female prevalence of insomnia. Regarding age, Drake et al. [18] reported that high-scoring FIRST participants were older than those who were low scoring, though the healthy participants with high FIRST-J scores were younger than those with low scores in our study. The reason for this inconsistency is unclear. However, neither age nor gender had a notable influence on correlation between sleep reactivity and insomnia severity or anxiety.

As also shown in results of an earlier study [27], our study revealed that the insomnia patients had a significantly higher FIRST-J score than the healthy participants. The participants with high FIRST-J scores also included a greater number of participants with insomnia. These results support the idea that sleep reactivity is associated with vulnerability to insomnia.

Our study has some limitations. First, only self-rating scales were used for evaluating insomnia. Further study should be conducted using n-PSG measures, not only for screening other sleep disorders but also for drawing conclusions about the relation between sleep reactivity and insomnia. Second, no assessment of stress manipulation was performed in our study. An earlier study [21] showed that participants with high FIRST-J scores were more likely to feel daily stress that negatively affected their sleep, and thus further study should be undertaken to explore the relation between sleep reactivity and stress manipulation. Third, the test–retest reliability of the FIRST-J was not validated in our study. Fourth, our study was conducted with a cross-sectional design. Prospective research should be made to clarify the significance of sleep reactivity on the development of insomnia. Fifth, current participants with insomnia might not be representative of the general insomnia population, as they were recruited from outpatients of a single sleep disorders clinic.

5. Conclusion

The FIRST-J has satisfactory validity and internal consistency similar to the original version. Considering that FIRST-J was associated with severity of insomnia in the healthy participants but not in the insomnia patients, the measure is expected to become an important trait marker for insomnia in Japanese individuals.

Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2013.09.022.

Acknowledgments

Our study was supported by a Grant-in-Aid for Young Scientists (B) (22730574) from the Japan Society for the Promotion of Science.

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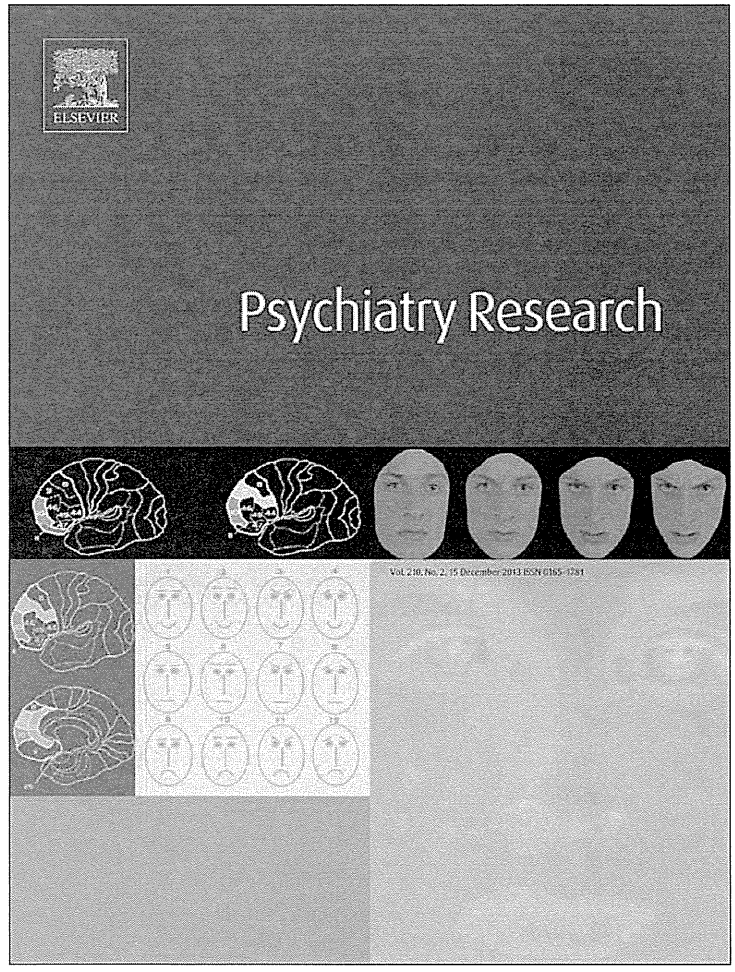

Psychiatry Research 210 (2013) 515–521

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Cognitive behavioural therapy with behavioural analysis for pharmacological treatment-resistant chronic insomnia

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ARTICLE INFO

Article history:
Received 8 August 2012
Received in revised form
3 June 2013
Accepted 15 June 2013

Keywords:
Cognitive behavioural therapy
Behavioural analysis
Insomnia
Hypnotics
Treatment-resistant

ABSTRACT

This study aimed to determine whether (1) cognitive behavioural therapy with behavioural analysis for insomnia (CBTi-BA) is more effective for insomnia and co-morbid depressive symptoms than treatment as usual (TAU) and (2) whether CBTi-BA promotes earlier reduction of the daily dose of hypnotic medication in chronic insomnia resistant to pharmacological treatment. A total of 63 patients with chronic insomnia aged 20–77 years who already received hypnotic medication regularly were assigned to two interventions: combined therapy or TAU alone. The subjects provided demographic information and completed self-rating scales for insomnia and depressive symptoms. After treatment, the combined therapy group showed significant decreases in the symptoms of both insomnia and depression and significant reductions in the daily dose of hypnotic medication compared with the group receiving TAU alone. In the combined therapy group, 71% of the participants reported a reduction in insomnia to normal levels and 79% succeeded in decreasing the daily dose of hypnotics to 50% or less of the baseline dose. These results revealed that CBTi-BA can reduce insomnia and depressive symptoms as well as the daily dose of hypnotic medication in patients with chronic insomnia resistant to pharmacological treatment.

1. Introduction

Nearly 20% of the general adult population has been reported to have insomnia (Mellinger et al., 1985; Ancoli-Israel and Roth, 1999; Kim et al., 2000). Additionally, 10–15% of the insomniac population shows a chronic course (Mellinger et al., 1985; Ford and Kamerow, 1989; Ohayon, 2002). Chronic morbidity of insomnia is often associated with the development, treatment resistance or relapse of depression (Ford and Kamerow, 1989; Buysse et al., 2008; Okajima et al., 2012). Pharmacotherapy and cognitive behavioural therapy for insomnia (CBTi) are the most often prescribed treatments for insomnia. Among these, pharmacotherapy is commonly used but is disadvantageous in that insomnia symptoms are frequently observed to recur shortly after discontinuation of the treatment. Pharmacotherapy is also associated with side effects such as cognitive impairment and an increased risk of injury due to falls in older adults (Hindmarch, 1991). Recently, the U.S. Food and Drug Administration (FDA), 2013 recommended that doses of hypnotics should be reduced because blood levels in some patients (women in particular) may be sufficiently high the morning after use to impair activities that require alertness, such as driving (FDA, 2013). Furthermore, long-term use of hypnotic medication increases patients' risk of developing a tolerance to the medication and/or becoming dependent on the usual dose (Soldatos et al., 1999; Griffiths and Johnson, 2005). Moreover, a considerable number of patients are known to be resistant to pharmacotherapy (Morgan et al., 2003).

CBTi is effective for improving insomnia symptoms in 70–80% of patients (Morin, Hauri et al., 1999) and possesses a long-term preventive effect on symptom recurrence (Morin, Colecchi et al., 1999). The treatment has also been expected to promote the reduction of and withdrawal from sleep medication use (Morin et al., 2004; Soeffing et al., 2008; Morin et al., 2009). However, only a few studies explored the efficacy of CBTi in patients with pharmacological treatment-resistant chronic insomnia; conclusive evidence on its effectiveness is yet to be produced (Morgan et al., 2003; Morin et al., 2004; Belleville et al., 2007; Soeffing et al., 2008). In particular, existing research differs on whether CBTi is helpful for reducing the daily dosage of hypnotic medications. Soeffing et al. (2008) reported that the dosage of hypnotics was decreased when CBTi was coadministered in hypnotics-dependent

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0165-1781/$ - see front matter © 2013 Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.psychres.2013.06.028

older adults, but that there were no significant differences in the dosage between the groups with CBTi and placebo control at the end of the treatment period. By contrast, Morgan et al. (2003) reported that the frequency of medication use in insomnia treatment significantly differed between CBTi groups and control groups at both the end of treatment and follow-up. In their study, however, only 47% of the patients in the CBTi groups succeeded in decreasing the dose of hypnotics to 50% or less of baseline dosages, and only 29% in the CBTi group succeeded in discontinuation of medication at the end of the treatment. Therefore, the effectiveness of traditional CBTi is believed to be limited with regard to the reduction of the use of hypnotics in patients with chronic insomnia resistant to pharmacological treatment (Morin and Espie, 2004).

The inclusion criteria for participants in these previous studies were the use of hypnotics at least three nights per week (percentage of the participants who used hypnotics continuously and nightly between the CBTi group and control group was 59% and 56%, respectively) (Morgan et al., 2003). The proportion of participants who used two or more types of hypnotics was relatively low (i.e., the CBTi group and control group, 21% and 16%, respectively) (Belleville et al., 2007). However, most patients in clinical settings use hypnotics almost every night, and a larger percentage of them take two or more types of hypnotics.

Why has the effectiveness of traditional CBTi been limited in such patients? One possible reason for this phenomenon is the issue of instruction, including psychoeducation and sleep hygiene, in CBTi. In general, the provision of instructions to patients seems to be favourable, as interventions with instructional control have been shown to be effective (Galizio, 1979; Lowe, 1979). However, an instructional control intervention does not derive from basic behavioural principles and is not a specific behavioural intervention method, possibly forming rigid behavioural repertoires that are less sensitive to the actual contingencies (Hayes, 1989). In this regard, focussing on the actual contingencies could be necessary to guide patients from inflexible behavioural repertoires (e.g., taking the same dose of hypnotics every night) to more flexible ones (e.g., taking the same dose of hypnotics if needed or practising dose tapering).

Currently, the importance of the practice of behavioural or functional analysis (Ramnero and Törneke, 2008), such as behavioural activation treatment (Martell et al., 2001) and acceptance and commitment therapy (Hayes et al., 1999), has been accepted among the 'third wave' behaviour therapies (Kanter et al., 2008). Behavioural or functional analysis seeks to examine the actual contingencies among antecedent behaviour (e.g., sleep-related behaviour) and subsequent consequences. In CBTi sessions with behavioural or functional analysis, the therapist and the patient discuss the influence of the patient's problem behaviours on short-term and long-term consequences as well as alternative behaviours that can maintain the effectiveness of the treatment over time. Thereafter, patients are instructed to test the behaviours in daily life. This method has been shown to be more effective than traditional cognitive therapy for depression (Dimidjian et al., 2006). Kanter et al. (2008) emphasised that treatment focussing on reinforcement contingencies (i.e., behavioural analysis) is more effective than treatment based on the provision of instructions (i.e., CBTi). Ghaderi (2006) compared the efficacy of CBT with behavioural analysis and traditional CBT for bulimia nervosa and showed that the proportion of subjects who responded to treatment was higher in the group receiving CBT with behavioural analysis than the group receiving traditional CBT alone. Therefore, it can be expected that CBTi with additional behavioural analysis would be more effective for pharmacological treatment-resistant chronic insomnia than traditional CBTi.

Earlier studies have shown considerable heterogeneity in the characteristics of participants between clinical- and research-based studies (i.e., patients who are referred for treatment as opposed to participants recruited mainly by media advertisement) (e.g., Stepanski et al., 1989; Martin and Ancoli-Israel, 2002; Davidson et al., 2009). For example, clinical patients are more likely to suffer from not only severe nocturnal insomnia symptoms but also daytime dysfunction, including higher levels of anxiety and depression; further, they are more likely to fail to respond to treatment with hypnotics (Davidson et al., 2009). Therefore, it is preferable to conduct studies in clinical settings to clarify whether CBTi is effective for patients with pharmacological treatment-resistant insomnia. However, only a few studies have been conducted with this patient population (Morgan et al., 2003).

Against this background, the present study evaluates the effectiveness of CBTi with behavioural analysis (CBTi-BA) for patients with pharmacological treatment-resistant chronic insomnia in a clinical setting. The goal was to clarify the following issues: (1) whether CBTi-BA is more effective in treating insomnia and comorbid depressive symptoms than treatment as usual (TAU) and (2) whether CBTi-BA can promote a reduction in the daily dose of hypnotic medications used in treatment.

2. Methods

2.1. Participants

Eligible participants of this study were patients of the Yoyogi Sleep Disorder Center presenting between October 2008 and October 2010 seeking treatment for chronic insomnia unresponsive to prior pharmacological therapies, who were 20 years of age or older and met the criteria of insomnia according to the second edition of the International Classification of Sleep Disorders (American Academy of Sleep Medicine, 2005). Most of the patients had been referred by local psychiatrists or general practitioners. Participants' disturbed sleep met all the following additional criteria: (1) difficulties in initiating and/or maintaining sleep, defined as subjective sleep-onset latency and/or waking after sleep onset >30 min at least three nights per week (Lichstein et al., 2003); (2) insomnia morbidity for over 6 months (Lichstein et al., 2003); (3) a score of 6 or greater for insomnia as measured by the Pittsburgh Sleep Quality Index (PSQI; Doi et al., 2000); and (4) nightly use of hypnotic medication for a minimum of the preceding 3 months (Morin et al., 2004; Belleville et al., 2007). Exclusion criteria were (1) insomnia due to medical or psychiatric disorders (American Psychiatric Association, 2000) or pharmaceutical causes and (2) the existence of other sleep disorders such as obstructive sleep apnoea syndrome, restless leg syndrome, periodic limb movement disorder or circadian rhythm sleep disorders. In order to exclude patients with these sleep disorders, eligible patients underwent nocturnal polysomnography and/or provided self-report sleep logs for more than 2 weeks, if necessary.

2.2. Procedure

This study was performed as an open trial with a quasi-experimental design. After the diagnoses were made by board-certified sleep disorder specialist physicians, participants were assigned to TAU alone or combined therapy (CBTi-BA plus TAU) according to the patients' choice. Instruments as indicated below were administered to the patients in both intervention groups during the first visit. The same questionnaires were also administered to the combined therapy group immediately after the sixth session (mean (standard deviation, S.D.)=2.43 (0.62) months) and to the TAU group after at least 2 months of biweekly or monthly TAU sessions (mean (S.D.)=2.32 (0.49) months). This study was approved by the ethical review board of the Neuropsychiatric Research Institute, Japan; written informed consent was obtained from all participants.

2.3. Measures

2.3.1. PSQI

This well-validated instrument is composed of four open-ended questions and 19 self-rated items (four-point scale) assessing subjective sleep disturbances over a 1-month period (Buysse et al., 1989; Doi et al., 2000). Questions focus on the following seven components: sleep quality (C1), sleep latency (C2), sleep duration (C3), sleep efficiency (C4), other sleep disturbances (C5), medication use (C6) and daytime dysfunction (C7). The PSQI was used as an initial eligibility screening measure for subjects in this study; it was also used to detect changes in subjective sleep disturbance over the course of treatment. Scores were compared between the groups. Pathology is indicated by a score of 5.5 points or greater (Buysse et al., 1989; Doi et al., 2000).

2.3.2. Athens Insomnia Scale (AIS)

The Athens Insomnia Scale (AIS) is a self-rated inventory consisting of eight items (Soldatos et al., 2000, 2003; Okajima et al., in press): the first five items assess difficulty in sleep initiation, awakening during the night, early morning awakening, total sleep time and overall quality of sleep, while the last three items pertain to the daytime consequences of insomnia, such as problems with the sense of well-being, overall functioning and sleepiness during the day. Responses are made on a four-point scale that ranges from 0 (no problem at all) to 3 (very serious problem). Participants were requested to rate each item as positive (i.e., to choose among rating options 1, 2 and 3) when they had experienced sleep difficulty at least thrice weekly during the previous month as defined by the International Statistical Classification of Diseases and Related Health Problems 10th revision (ICD-10) criteria for insomnia (World Health Organization, 1992). The scale was used as a measure of outcomes to document concomitant change in insomnia symptoms over the course of treatment. With this instrument, pathology is determined by a score of 6 points or greater (Soldatos et al., 2003; Okajima et al., in press).

2.3.3. Self-rating Depression Scale (SDS)

We used the Self-rating Depression Scale (SDS) (Zung, 1965) for estimating the severity of depressive symptoms with a four-point scale (1=a little of the time, 2=some of the time, 3=a good part of the time and 4=most of the time). The SDS is a self-rated inventory consisting of 20 items. We used total SDS scores to measure depression. Patients with a total SDS score of 50 points or higher were rated as showing definite depressive symptoms during the preceding 1 month (Barrett et al., 1978). As SDS also addresses insomnia, the total score of SDS after removing this item was also calculated.

2.4. Sleep diaries

All participants completed sleep diaries every morning for 2 weeks at baseline. Participants assigned to the combined therapy group were asked to continue their sleep diaries all through the treatment period so as to practise the sleep-scheduling technique.

2.5. Treatment condition

After completing the baseline assessment, the patients were assigned to the treatment group they had selected: TAU alone or combined therapy.

2.5.1. CBTi with behavioural analysis

The patients receiving CBTi-BA attended six biweekly individual treatment sessions, each 50 min in length. The first session began after the intake interview and case formulation based on the functional analysis. The CBTi was administered according to a manualised multicomponent approach consisting of several modules introduced at different stages in the treatment process (Morin and Espie, 2004; Edinger and Carney, 2008). The treatment components of CBTi-BA include sleep education and sleep hygiene (session 2), progressive muscle relaxation (session 3), sleep scheduling (consists of sleep restriction and stimulus control, sessions 4 and 5), coping with worry (session 6) and an explanation of medication tapering (Morin and Espie, 2004) based on principles of behavioural analysis (Ramnero and Törneke, 2008). The procedures discussed for tapering medication were addressed on a case-by-case basis because the sleep-related problem behaviour and timing appropriate for tapering differed from person to person. The therapist explained how to taper the medication and discussed the potential risk of rebound insomnia. The therapy sessions were facilitated by a clinical psychologist and behaviour therapist (I.O.). On the basis of the principles of behavioural analysis, a therapist explained to each patient the contingency between antecedent sleep-related behaviour and subsequent short- and long-term consequences and discussed the relationship between problematic sleep-related behaviour (e.g., patient taking additional hypnotic medications when he/she could not fall asleep) and short-term consequences (e.g., the patient could get some relief) as well as long-term consequences (e.g., possibly becoming dependent upon the medication). Subsequently, the therapist and the patients discussed alternative behaviours (e.g., get out of bed and perform the progressive muscle relaxation exercise) more likely to result in a long-term favourable outcome (e.g., sleeping without additional use of hypnotics). The patients followed these instructions between sessions, tracking their results according to the aforementioned procedures.

2.5.2. Treatment as usual

The TAU group followed the standard clinical treatment protocol, under which sleep disorder specialist physicians offered appointments to prescribe or to discontinue prescriptions during at least 2 months of the treatment period. The patients allocated to TAU received no treatment other than pharmacological therapy and information about tapering their medication. Patients in this group also received no counselling from clinical psychologists on coping with insomnia.

2.6. Data management and statistical analysis

The sample size of this study was determined on the basis of a power analysis using data from one previous study on tapering hypnotics with or without CBTi (Belleville et al., 2007). Data on sleep efficiency, a commonly used subjective sleep parameter, were used for the power analysis because the PSQI or AIS had not been used in the Belleville et al. (2007) study. A comparison between patients seeking to taper hypnotic use with and without CBTi yielded an effect size of 0.70 for sleep efficiency. With a sample size of 34 individuals per treatment group during the 6-week treatment, under a two-tailed analysis of variance (ANOVA, α=0.05), power to detect effect size was estimated at 80% (Cohen, 1988).

Descriptive and inferential statistics were computed using Statistical Package for the Social Sciences (SPSS) version 19.0 (IBM Inc., Tokyo, Japan). Two-sample *t*-tests or χ^2 tests were used to examine demographic and clinical variables: age, duration of hypnotic medication use, duration of insomnia morbidity, daily dose of hypnotics and the PSQI, AIS and SDS scores at baseline. Daily doses of hypnotics were calculated as lormetazepam equivalent. A 2 × 2 (group × time) repeated-measures ANOVA with Bonferroni-corrected *post hoc* comparisons and effect sizes (Cohen's *d*) was used to investigate differences between the interventions (combined therapy group vs. TAU group) in terms of treatment effects as measured by the change in scores (difference in values between the 'end' point and baseline data of each scale). Typically, values of 0.2 or below reflect a generally small effect size, around 0.5 reflect a moderate effect size and 0.8 and above reflect a large effect size (Cohen, 1988). In addition, a Spearman correlation analysis was conducted to examine the relationship between the change in insomnia symptoms and that in depressive symptoms.

The rate of patients' normalisation between the two treatments was examined by calculating the proportion of the participants who showed a decrease in AIS score to 5 or less (Soldatos et al., 2003; Okajima et al., 2012) for insomnia symptoms and a total SDS score of 49 or less (Barrett et al., 1978) for depressive symptoms at the 'end' point. In addition, we calculated the proportion of the participants who were able to reduce their daily dose of hypnotic medication to 50% or less of the dose at baseline and those who were able to cease the medication at the end of the treatment, as in a previous study (Morgan et al., 2003). To evaluate the outcomes in more detail, we investigated the difference between the combined therapy and TAU alone in terms of the number needed to treat (NNT; McQuay and Moore, 1997), which is the number of patients who need to be treated with a particular treatment (e.g., combined therapy), to obtain a normalised patient for a treatment period. An NNT of 2 or 3 indicates favourable effectiveness of treatment (McQuay and Moore, 1997).

3. Results

3.1. Baseline characteristics

A total of 68 patients completed the study (each group: n=34). In the TAU group, however, three patients answered at least one of the above-indicated scales incompletely, and scales were not obtained from two patients at the end of the treatment. Therefore, the total number of samples sufficient for analysis was 63 (combined therapy: n=34; TAU: n=29). Age, gender, duration of insomnia morbidity, duration of hypnotic medication use, scores of self-rating measures (PSQI, AIS and SDS) and the daily dose of hypnotic medications (lormetazepam dose equivalents) did not differ significantly between the two groups at baseline (Table 1). Ten patients (29%) in the combined therapy group and eight (28%) in the TAU group scored 50 points or higher on the SDS, qualifying as having depression at baseline. No significant difference was found between the two treatment groups in terms of the proportion of patients scoring as depressed.

The proportions of patients using hypnotics of different half-life categories were as follows: 18% used ultra-short-acting type (zolpidem, zopiclone or triazolam); 27%, short-intermediate-acting type (brotizolam, triazolam, lormetazepam, flunitrazepam, estazolam or nitrazepam); and 3% long-acting type (fludiazepam or quazepam). None used antidepressants. As many as 33 (52%) were taking two or more kinds of hypnotics. There was no significant difference between the two treatment groups in terms of the proportion of patients in each hypnotic category (Table 1).

3.2. Outcome measures

Means and standard deviations for clinical measures at baseline and at the end of the treatment are presented in Table 2.

Table 1
The baseline Characteristics of patients completing the treatment period.

	Total	Combined therapy[a] $n=34$	TAU alone, $n=29$	t or χ^2 values (d.f.)	p-value
Gender (M/F)	21/42	10/24	11/18	χ^2 (1)=0.51	0.48
Age, year (Mean, S.D.)	46.51 (15.55)	49. 35 (14.71)	43.17 (16.08)	t (61)=1.59	0.12
Duration of insomnia morbidity, year (Mean, S.D.)	7.45 (9.31)	8.72 (10.94)	5.84 (6.55)	t (57)=1.19	0.24
Duration of hypnotic medication use, year (Mean, S.D.)	3.91 (4.81)	4.58 (5.55)	2.88 (3.23)	t (49)=1.24	0.20
PSQI (Mean, S.D.)	13.05 (2.96)	13.59 (3.25)	12.45 (2.52)	t (59)=1.53	0.13
AIS (Mean, S.D.)	11.53 (4.08)	11.56 (4.83)	11.50 (3.01)	t (60)=0.06	0.96
SDS (Mean, S.D.)	45.00 (7.30)	44.73 (7.83)	45.33 (6.73)	t (60)=−0.32	0.75
Type of medication used for insomnia, n (%)					
Ultra-short-acting hypnotics alone	11 (18)	7 (21)	4 (14)	χ^2 (1)=0.50	0.48
Short or intermediate-acting hypnotics alone	17 (27)	10 (29)	7 (24)	χ^2 (1)=0.22	0.64
Long-acting hypnotics alone	2 (3)	1 (3)	1 (3)	χ^2 (1)=0.01	0.91
Antidepressant alone	0 (0)	0 (0)	0 (0)		
Two or more kinds of drugs, n (%)	33 (52)	16 (47)	17 (59)	χ^2 (1)=0.84	0.36

AIS=Athens Insomnia Scale. F=female. M=male. PSQI=Pittsburgh Sleep Quality Index. S.D. = standard deviation. SDS=Self-rating Depression Scale. TAU=treatment as usual.

[a] Combined therapy means cognitive behavioral therapy with behavioral analysis for insomnia (CBTi-BA) plus TAU.

Table 2
The changes in clinical symptom measures in each intervention group.

	Combined therapy[a], Mean (S.D.)		TAU alone, Mean (S.D.)		Effect sizes (d)[b] (95% CI)
	Baseline	End-of-treatment	Baseline	End-of-treatment	
Total score of PSQI	13.59 (3.25)	8.10 (2.95)	12.45 (2.52)	11.17 (3.23)	1.25 (0.71–1.79)
C1, sleep quality	2.21 (0.81)	1.06 (0.42)	2.21 (0.41)	1.69 (0.71)	0.73 (0.22–1.24)
C2, sleep latency	2.35 (0.81)	1.21 (0.91)	2.34 (0.94)	2.00 (0.96)	0.79 (0.28–1.30)
C3, sleep duration	2.03 (0.85)	1.67 (0.74)	1.90 (1.05)	1.62 (1.02)	0.08 (−0.42–0.58)
C4, habitual sleep efficiency	1.38 (1.29)	0.44 (0.76)	1.07 (1.28)	0.93 (1.22)	0.62 (0.11–1.13)
C5, sleep disturbance	1.25 (0.51)	0.81 (0.54)	1.03 (0.42)	0.97 (0.42)	0.64 (0.13–1.15)
C6, use of sleeping medication	2.79 (0.60)	2.00 (1.30)	2.31 (1.10)	2.62 (0.94)	0.97 (0.45–1.49)
C7, daytime dysfunction	1.52 (0.76)	0.88 (0.78)	1.59 (0.91)	1.35 (0.94)	0.58 (0.07–1.09)
Total score of AIS	11.56 (4.83)	4.74 (3.06)	11.50 (3.01)	8.71 (4.59)	0.92 (0.40–1.44)
Total score of SDS	44.73 (7.83)	39.41 (8.40)	45.33 (6.73)	44.90 (5.89)	0.70 (0.19–1.21)
Total score of SDS after excluding item for insomnia	41.41 (7.44)	37.55 (8.02)	41.83 (6.92)	42.29 (5.91)	0.59 (0.08–1.10)

Note. AIS = Athens Insomnia Scale. PSQI=Pittsburgh Sleep Quality Index. S.D. = standard deviation. SDS=Self-rating Depression Scale.TAU = treatment as usual. d=Cohen's effect size (Cohen, 1988). 95% CI=95% Confidence Interval.

[a] Combined therapy means cognitive behavioral therapy with behavioral analysis for insomnia (CBTi-BA) plus TAU.
[b] Effect sizes were calculated by using the difference in the scores between the baseline and the end of the treatment.

Significant group × time effects were obtained for the PSQI ($F_{1,58}=22.91$, $P<0.01$), AIS ($F_{1,60}=16.61$, $P<0.01$) and SDS ($F_{1,60}=8.51$, $P<0.01$) self-rating measures. *Post hoc* comparisons showed that the PSQI and the AIS scores significantly decreased at the end of the treatment in both treatment groups ($P<0.01$, respectively) but that the SDS score significantly decreased at the end of the treatment in only the combined therapy group ($P<0.01$). The reduction in the scores of all these scales at the end of treatment was significantly larger in the combined therapy group than in the TAU group ($P<0.01$). A similar reduction of the SDS score was also shown after excluding the item score for insomnia with two-way repeated measures ANOVA ($F_{1,60}=5.39$, $P<0.01$) and *post hoc* analysis ($P<0.01$). The effect sizes (d) were 1.25 for the PSQI, 0.92 for the AIS, 0.70 for the SDS and 0.59 for the SDS without the insomnia item (Table 2).

Significant group × time interaction effects were also obtained for the PSQI subscales – sleep quality (C1; $F_{1,61}=8.32$, $P<0.01$), sleep latency (C2; $F_{1,61}=10.10$, $P<0.01$), habitual sleep efficiency (C4; $F_{1,59}=5.78$, $P=0.02$), sleep disturbance (C5; $F_{1,59}=6.18$, $P=0.02$), use of sleep medication (C6; $F_{1,60}=14.37$, $P<0.01$) and daytime dysfunction (C7; $F_{1,60}=4.99$, $P=0.03$). *Post hoc* comparisons showed that the score for sleep quality was significantly decreased at the end of the treatment in both intervention groups. However, the scores of the other scales were significantly decreased at the end of the treatment only in the combined therapy group ($P<0.01$, respectively). In addition, decreases in the scores for sleep quality, sleep latency, use of sleeping medication and daytime dysfunction at the end of treatment were significantly larger in the combined therapy group than in the TAU group ($P<0.01$, respectively). Not an interaction effect, but a significant main effect of time was obtained for sleep duration (C3; $F_{1,59}=5.78$, $P=0.02$). The effect sizes (d) were 0.73 for sleep quality, 0.79 for sleep latency, 0.08 for sleep duration, 0.62 for habitual sleep efficiency, 0.64 for sleep disturbance, 0.97 for use of sleep medication and 0.58 for daytime dysfunction (Table 2).

3.3. *The dose of hypnotic medications*

The average lormetazepam equivalent dose of hypnotic medication per night changed from 1.70 mg (S.D.=1.28) at baseline to 0.54 mg (S.D.=0.61) at the end of the treatment in the combined therapy group and from 1.33 mg (S.D.=0.88) to 1.25 mg (S.D.=1.07) in the TAU group (Fig. 1). A significant group × time effect was obtained for the change in the nightly dose of hypnotics ($F_{1,61}=19.32$, $P=0.01$). *Post hoc* comparison showed that a significant decrease in the nightly dose of hypnotics at the end of the treatment was observed in only the combined therapy group ($P<0.01$) and that the decrease in the dosage in this group was significantly larger than that in the TAU group ($P<0.01$). The effect size (d) was 1.10 (95% confidence interval (CI): 0.57–1.63).

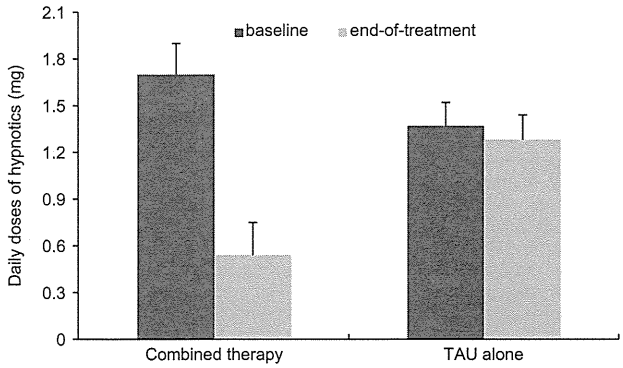

Fig. 1. The change in nightly dosage of hypnotics in each group. Values are expressed as lormetazepam-equivalent doses.

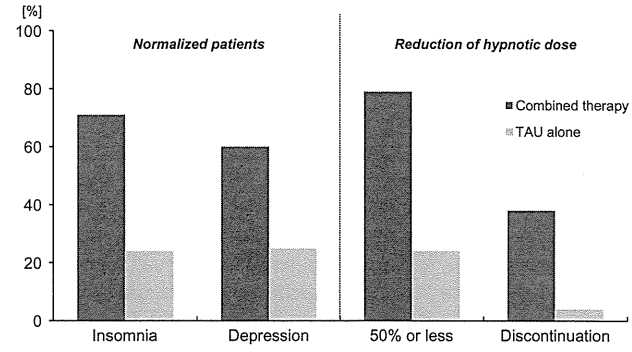

Fig. 2. The proportion of normalized patients and reduction in dosage of hypnotics at the end of the treatment.

3.4. Correlation between the changes in scores of insomnia and depression

There was a significant and strong positive correlation between the changes in the scores of the PSQI and the AIS from the baseline to the end of treatment ($r=0.71$, 95% CI: 0.50–0.84, $P<0.01$). There were also weak but significant correlations between the changes in the scores of the SDS and the PSQI ($r=0.33$, 95% CI: 0.01–0.59, $P<0.01$) and between those of the SDS and the AIS ($r=0.40$, 95% CI: 0.09–0.64, $P<0.01$). An almost similar result was obtained for the relationship between SDS and PSQI or AIS after excluding the insomnia item score from the total score of SDS ($r=0.31$, 95% CI: 0.07–0.52, $P<0.05$; $r=0.36$, 95% CI: 0.04–0.61, $P<0.01$, respectively).

3.5. Outcome for normalised patients and dose reduction of hypnotics

At the end of the treatment, 24 patients (71%) in the combined therapy group and seven patients (24%) in the TAU group showed an AIS score of 5 or less; and NNT was 2.2 (95% CI; 1.5–4.1). Regarding depression, six out of 10 patients (60%) in the combined therapy group and two out of eight patients (25%) in the TAU group scored 49 or less on the SDS; and NNT was 2.9 (95% CI; 1.3–13.0). Regarding hypnotic medication, 27 patients (79%) in the combined therapy group succeeded in tapering the daily dose to 50% or less of baseline, while only six patients (24%) in the TAU group had that same outcome. In addition, 13 patients (38%) in the former group were able to discontinue the medication, while only one patient (4%) in the latter group had that same outcome. NNT was 1.8 (95% CI: 1.3–2.9) for 50% or more of the dose reduction of hypnotics and 2.9 (95% CI: 1.9–6.2) for the cessation of medication (Fig. 2).

3.6. Post hoc power analysis

We conducted a power analysis using the sample size of this study and obtained sufficient effect sizes for the PSQI ($d=1.25$), the AIS ($d=0.92$) and the decrease in the nightly dose of hypnotics ($d=1.05$). With a sample size of 34 in the combined therapy group and 29 in the TAU group ($\alpha=0.01$, two-tailed), power ($1-\beta$) was estimated at 0.99, 0.83 and 0.93, respectively.

4. Discussion

This study was the first to compare the efficacy of combined therapy with CBTi-BA plus TAU and TAU alone in patients with chronic insomnia who had not obtained sufficient improvement after a course of regular pharmacological treatment in a clinical setting. We found that the combined therapy was more effective for both insomnia and depressive symptoms at the end of treatment than TAU alone.

Although the total scores of the PSQI and the AIS were significantly reduced at the end of treatment even in the TAU group, the effect of combined therapy on these measures was clearly superior to that of TAU alone because the effect sizes (d) were large. However, different from the other variables' effect on the PSQI, superiority of the effect of CBTi-BA was not observed for the sleep duration (C3) subscale. With regard to this phenomenon, a previous meta-analytic study (Smith et al., 2002) revealed that hypnotic medication was superior in terms of improvement in sleep duration compared to CBTi. Given this, the fact that patients in both treatment groups received pharmacotherapy during the study period might contribute to the lack of difference in effect on sleep duration between the two groups. In addition, considering that CBTi may increase total sleep time as measured at the follow-up appointment but not at the end of the treatment (Okajima et al., 2011), the result at the follow-up might become different from that at the end of the treatment, if we evaluated the PSQI at the follow-up appointment.

The present findings that symptoms of depression were significantly improved only in the combined therapy group support the results of previous studies (Mimeault and Morin, 1999; Zavesicka et al., 2008). In the present study, mean baseline scores of the SDS in both treatment groups were approximately 45 points. Given that the pathological cut-off level of the SDS is estimated at 50 points (Barrett et al., 1978), the mean scores of the participants corresponded to non-pathological or mild degree designations. However, we found significant and positive correlations between the score of PSQI or the AIS and that of the SDS. Thus, CBTi-BA might improve depressive symptoms through reducing insomnia symptoms as previously reported in research on eszopiclone (Fava et al., 2006).

Normalisation of insomnia symptoms was achieved in 71% of the patients treated with the combined therapy (NNT=2.2). Moreover, 79% of patients in this group succeeded in decreasing the dose of hypnotics to 50% or less of baseline dosage (NNT=1.8) and 38% of CBTi-BA-treated patients were able to discontinue the medication (NNT=2.9). The rates of tapering and/or discontinuation of hypnotic medications in the present study are higher than those reported in previous studies (Morgan et al., 2003). The reason behind this phenomenon is unclear. However, considering that long-term use of hypnotics may raise the risk of developing both tolerance and dose dependence with drugs of this kind (Soldatos et al., 1999; Griffiths and Johnson, 2005) and that physical quality of life (QOL) is likely to be deteriorated in patients using sleep medication irrespective of insomnia symptoms (Sasai et al., 2010; Komada et al., 2011), the use of CBTi-BA to support

attempts to taper off hypnotics would be beneficial for long-term pharmacologically treated patients with insomnia.

Our study has several limitations. First, the present study was conducted as a quasi-experimentally designed open trial and not as a randomised controlled trial (RCT). Although there was no significant difference in descriptive variables between the two intervention groups at the baseline, the selection bias or placebo effect could not be negligible (Kazdin, 2003). In addition, the role of motivation to discontinue hypnotic medication was not evaluated; it would therefore be desirable to evaluate patients' motivations in future research. Furthermore, we did not directly compare the effectiveness between CBTi-BA and the traditional CBTi. It is necessary to conduct an RCT to compare the effectiveness directly between CBTi-BA and traditional CBTi for patients with pharmacological treatment-resistant chronic insomnia.

Second, our study did not have any patients with severe depression, mainly because we excluded patients with straightforward mood disorders. Although CBTi has reportedly been effective for treating symptoms of depression in primary insomnia and for both insomnia and moderate depressive symptoms in major depressive disorders (Manber et al., 2008; Okajima et al., 2011; Watanabe et al., 2011), further research on the effectiveness of CBTi-BA in patients with pharmacological treatment-resistant chronic insomnia and at least minor co-morbid depression is warranted.

Finally, the number of participants was relatively small and all the participants were drawn from one clinical location. Therefore, the participants of our study might not be representative of all patients with pharmacological treatment-resistant chronic insomnia.

In summary, the results of the present study revealed that CBTi-BA in a clinical setting is highly effective for improving both insomnia and depressive symptoms as well as for reducing the daily dose of hypnotics in patients with treatment-resistant chronic insomnia. Future research should be conducted to evaluate the long-term effects of CBTi-BA on patients of this type, focussing in particular on the preventive effect against the relapse of insomnia symptoms.

Disclosure statement

None of the authors has any conflicts of interest for this study.

Acknowledgement

This work was supported by JSPS KAKENHI Grant Number 22730574.

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Psychiatry and Clinical Neurosciences 2013; **67**: 420–425 doi:10.1111/pcn.12073

Regular Article

Development and validation of the Japanese version of the Athens Insomnia Scale

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Aim: The aim of this study was to develop and validate a Japanese version of the Athens Insomnia Scale (AIS-J).

Methods: The AIS-J was created using a back-translation design. A total of 477 outpatients with chronic insomnia and 163 individuals from the general community were recruited. Participants were asked to complete the AIS-J along with two other insomnia scales – Japanese versions of the Pittsburgh Sleep Quality Index and the Insomnia Severity Index.

Results: The AIS-J consisted of a two-factor structure: 'nocturnal sleep problem' (items 1–5) and 'daytime dysfunction' (items 6–8). Internal consistency coefficients ranged from 0.78 to 0.88. Correlations between the AIS-J and the aforementioned authorized scales were 0.81 and 0.85, respectively. Scores on the AIS-J were significantly higher for the insomnia group than for the control group. The AIS-J cut-off value for identifying pathological insomnia was estimated at 6 points or more, and the AIS-J-nocturnal cut-off value was estimated at 4 points or more.

Conclusions: The AIS-J has sufficient validity and diagnostic utility.

Key words: Athens Insomnia Scale, insomnia, Japanese, reliability, validation.

IT IS ESTIMATED that insomnia symptoms are prevalent in approximately one-fifth of the general adult population.[1] In several population-based studies, 25–35% of subjects experience occasional or mild insomnia,[2,3] and in 10–15% of these subjects, insomnia follows a chronic course.[3–5] There are several insomnia-related, self-rating scales currently available for evaluating subjective insomnia. Among these, the Pittsburgh Sleep Quality Index (PSQI),[6–8] the Insomnia Severity Index (ISI),[9–11] and the Athens Insomnia Scale (AIS)[12–14] are commonly used, authorized insomnia symptom questionnaires. All three scales have been shown to have appropriate diagnostic utility and include a set of items for evaluating both nocturnal sleep disturbance and daytime dysfunction. In regard to the specific characteristics of each scale, the item for frequency of sleep medication use is set only in the PSQI,[8] while the ISI is capable of categorizing insomnia severity as follows: absence of insomnia (0–7), sub-threshold insomnia (8–14), moderate insomnia (15–21), and severe insomnia (22–28).[11] The AIS was created to assess the severity of insomnia on the basis of the ICD-10[15] diagnostic criteria for insomnia.[12] However, the PSQI has somewhat more items than the AIS and ISI (19, 8, and 7 items, respectively) and scoring points for each item is not easy in the PSQI. When we calculated the 'sleep duration (C3)' score, for example, an answer to question 4 (actual sleep time at night during the past month) filled out by a respondent, we had to transform the scores into a range from 0 (>7 h) to 3 (<5 h). On the contrary, the total AIS or ISI scores can

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Received 7 August 2012; revised 26 March 2013; accepted 29 March 2013.

be calculated simply by summing all item scores. In the ISI, it is doubtful whether patients' self-rating of insomnia severity ratings for each symptom, between 0 (*none*) and 4 (*very severe*), is adequate. However, the AIS estimates nocturnal and daytime sleep problems that occur at least three times a week on the basis of ICD-10 criteria,[15] and the total score is calculated as a sum of all scores according to items that have been self-checked by subjects. Therefore, the state of insomnia seems to be more easily clarified by the AIS than with the PSQI and the ISI. While the AIS can be regarded as a highly useful instrument in both clinical and research settings, a well-validated Japanese version of the scale has not yet been established. Therefore, this study aims to develop and validate a Japanese version of the AIS (AIS-J).

METHODS

Participants

The study sample comprised 640 individuals (52.0% men and 58.0% women) with a mean age of 48.8 ± 15.5 years. The sample included 477 outpatients with chronic insomnia who fulfilled the criteria of the second edition of the International Classification of Sleep Disorders.[16] All outpatients visited our sleep clinic seeking treatment for their sleep disorders (224 men, 253 women; mean age 47.9 ± 16.8 years). Of these outpatients, 112 patients were confirmed to have comorbid sleep disorders based on the results of a polysomnography and sleep logs (30 patients had sleep apnea and 27 had delayed sleep phase syndrome) or psychiatric disorders (45 had a depressive disorder and 10 had an anxiety disorder) that met the diagnostic criteria of the 10th revision of the International Classification of Diseases.[17] All the diagnoses were made by sleep disorder expert psychiatrists. The control group consisted of 163 individuals who scored less than 6 points on the Japanese version of the PSQI (PSQI-J)[18] (109 men, 54 women; mean age 51.3 ± 10.1 years). All control subjects were working in a private company and had never visited any psychiatric hospital or sleep clinic.

Measures

AIS-J

The original AIS is a self-rating inventory consisting of eight items.[12,19] The first five assess difficulty in sleep initiation, awakening during the night, early morning awakening, total sleep duration, and overall quality of sleep. The last three items pertain to the daytime consequences of insomnia (i.e., problems with sense of well-being, overall functioning, and sleepiness during the day). The following two versions of the original AIS were validated: the total version of the scale (AIS-8) and the five-item version for nocturnal sleep problems (AIS-5). Each item of the AIS is rated on a 4-point scale (i.e., 0 = no problem at all, 1 = slightly problematic, 2 = markedly problematic, and 3 = extremely problematic). Respondents are required to rate their subjective judgment of symptom-positivity (1, 2, and 3) if they have experienced sleep difficulties at least three times per week during the preceding month (consistent with the ICD-10 criteria for insomnia[15]). The total score cut-off for identifying pathological insomnia in the original AIS version has been previously determined as 6 points.[19]

PSQI-J

The PSQI-J is composed of four open-ended questions and 19 self-rated items (with a 4-point scale) that assess subjective sleep disturbances over a 1-month period. This scale is already well validated.[8] The specific domains of focus are sleep quality (C1), sleep latency (C2), sleep duration (C3), sleep efficiency (C4), other sleep disturbances (C5), medication use (C6), and daytime dysfunction (C7).[8] Internal consistency for the PSQI-J is high ($\alpha = 0.77$).[18]

Japanese version of the ISI

The Japanese version of the ISI (ISI-J), developed by Morin *et al.*,[11] has been used in many clinical research studies, especially those concerning the effectiveness of cognitive behavioral therapy. The ISI-J is a self-rating inventory consisting of seven items. It is designed to assess the perceived severity of insomnia symptoms (initial, middle, terminal), the degree of dissatisfaction regarding sleep, how sleep interference affects daytime functioning, the noticeability of any impairments, and the level of concern caused by sleep problems. Each item is rated on a 5-point scale from 0 to 4. The usual period for which responses are sought covers the 2 weeks immediately before the assessment. Internal consistency for the Japanese version of the ISI-J is also high ($\alpha = 0.84$).[20]

Procedure

A back-translation procedure was used to ensure equivalence between the original English version and the Japanese translated version. This consisted of first translating the scale from English into Japanese and then from Japanese back into English and finally evaluating the level of agreement between the two English versions (original and back-translated). Physicians, clinical psychologists, and a native speaker with extensive knowledge of both Japanese and English language carried out the process. No substantial differences were pointed out by the author of the original AIS[12] after comparing the two English versions. Thus, the proposed Japanese version of the AIS was confirmed to be acceptable. This study was conducted after receiving the approval of the ethical review board of the Neuropsychiatric Research Institute, Japan, and written informed consent was obtained from all the participants.

Statistical analysis

All statistical analyses were conducted using SPSS version 19.0 for Windows (IBM, Tokyo, Japan). Factorial validity for the AIS-J was evaluated using an exploratory factor analysis utilizing a maximum likelihood solution method with promax rotation. Factors were determined by setting eigenvalues to be greater than or equal to 1. Internal consistency for the AIS-J was evaluated using Cronbach's alpha. Concurrent validity was evaluated using a correlation analysis between insomnia-related scales (PSQI-J and ISI-J). In addition, we compared differences in AIS-J scores, including total score as well as scores for nocturnal symptoms and daytime dysfunction between the total insomnia patients and the controls and between the controls and patients with primary or secondary insomnia by using an unpaired two-tailed *t*-test or an ANOVA.

A receiver–operator curve (ROC)[21] was plotted and the mean (95% confidence interval [CI]) area under the curve (AUC) was used to estimate an AIS-J cut-off score for distinguishing pathological insomnia from a normal condition. When the tangent line slope of the ROC (computed using SPSS) is statistically equal to 1 (i.e., AUC = 0.5), then the ROC curve is considered inaccurate for prediction purposes. The predictive ability of a variable was classified with reference to the AUC (excellent = 0.9–1.0, good = 0.8–0.9, fair = 0.7–0.8, poor = 0.6–0.7, or non-discriminative = 0.5–0.6).[22] The best cut-off value for pathological insomnia was determined on the basis of sensitivity, specificity, positive likelihood ratio (LR+), and negative likelihood ratio (LR–). In accordance with the authorized method, the cut-off score was assessed as adequate when LR+ was 2.0 or higher and LR– was 0.5 or less.[23]

In the study, the significance level was set at $P < 0.05$.

RESULTS

Factor structure (construct validity)

The exploratory factor analysis shows that the AIS-J consists of a two-factor structure: 'nocturnal sleep problem' (AIS-J-nocturnal, items 1–5) and 'daytime dysfunction' (AIS-J-daytime, items 6–8). The correlation coefficient (r) between factors was 0.62 (Table 1).

Internal consistency

Cronbach's alpha values for factor 1, factor 2 and the total score were high ($\alpha = 0.85$, 0.78, and 0.88, respectively).

Table 1. Results of exploratory factor analysis of the AIS-J

	Factor loadings	
Items	Factor I	Factor II
AIS-J 2: *Awakenings during the night*	0.87	−0.08
AIS-J 3: *Final awakening*	0.85	−0.18
AIS-J 4: *Total sleep duration*	0.62	0.14
AIS-J 5: *Sleep quality*	0.60	0.27
AIS-J 1: *Sleep induction*	0.33	0.28
AIS-J 7: *Functioning capacity during the day*	−0.05	0.94
AIS-J 6: *Well-being during the day*	0.06	0.85
AIS-J 8: *Sleepiness during the day*	−0.08	0.45
Factor correlation	I	II
I	1.00	0.62
II		1.00

AIS-J, Japanese version of the Athens Insomnia Scale.

Table 2. Comparison of the AIS-J between the groups

	Control group			Insomnia group			Comparison between the groups
	Total ($n = 163$)	Male ($n = 109$)	Female ($n = 54$)	Total ($n = 477$)	Male ($n = 244$)	Female ($n = 253$)	t-value, d.f., P-value
AIS-J-total	2.64 (2.02)	2.51 (2.11)	2.89 (1.83)	11.81 (4.50)	11.69 (4.62)	11.91 (4.42)	37.32,623, $P = 0.00$
Nocturnal	1.63 (1.42)	1.51 (1.44)	1.87 (1.36)	8.12 (3.00)	7.84 (3.05)	8.34 (2.98)	29.59,316, $P = 0.00$
Daytime	1.01 (0.87)	1.00 (0.91)	1.02 (0.79)	3.65 (1.95)	3.65 (1.89)	6.34 (2.01)	18.46,332, $P = 0.00$

Note. Values are expressed as mean (SD). AIS-J, Japanese version of the Athens Insomnia Scale.

Concurrent validity

The correlation analysis showed a significantly high correlation between the AIS-J and the PSQI-J ($r = 0.81$, 95%CI: 0.78–0.84) and between the AIS-J and the ISI-J ($r = 0.85$, 95%CI: 0.82–0.87).

Also, we analyzed the correlation among the scales in each of the insomnia subgroups (primary insomnia, depression, and anxiety disorder). It showed a significantly medium correlation between the AIS-J and the PSQI-J ($r = 0.57$, 95%CI: 0.48–0.65) and between the AIS-J and the ISI-J ($r = 0.58$, 95%CI: 0.46–0.68) in patients with primary insomnia, but significant correlations were not found in patients with depression or those with anxiety disorder.

Comparison of scores between insomnia and control groups

Means and standard deviations for the scale scores of both the insomnia group and the control group are presented in Table 2. There were significant differences for all the scales in terms of total score, nocturnal sleep problem score, and daytime dysfunction score (Table 2). Scores for all scales were significantly higher for the total insomnia patients than the controls. In addition, the comparisons among the four groups (controls, primary insomnia, depression, and anxiety disorder) showed that AIS-J scores for all the insomnia subgroups were significantly higher than those for the controls (AIS-J-total, $F_{3,639} = 204.80$; AIS-J-nocturnal, $F_{3,635} = 195.57$; and AIS-J-daytime, $F_{3,638} = 85.89$, respectively), and that the daytime dysfunction score was significantly higher for both the depression and anxiety disorder groups than the primary insomnia group (Fig. 1).

AIS-J cut-off score for distinguishing pathological insomnia from a normal condition

ROC analysis showed that the AUC was 0.96 (95%CI: 0.95–0.98). The cut-off value of the AIS-J total for insomnia (primary and secondary insomnia) was

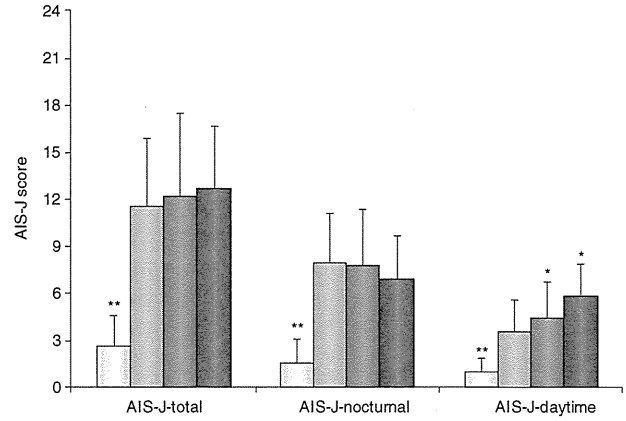

Figure 1. Comparison of the Japanese version of the Athens Insomnia Scale (AIS-J; total, nocturnal, and daytime scores) among the subgroups.**The scores were significantly lower for the control group than the insomnia subgroups ($P < 0.05$).*AIS-J daytime score was significantly higher for both the depression and anxiety disorder groups than the primary insomnia group ($P < 0.05$). □, Healthy control; ▨, insomnia; ■, depression; ■, anxiety disorder.

Table 3. Cut-off point for the AIS-J, estimated with receiver–operator curve

	AUC (95%CI)	Cut-off score	Sensitivity	Specificity	LR+	LR–
AIS-J-total	0.96	4.5	0.95	0.87	7.02	0.06
	(0.95–0.98)	5.5	0.92	0.93	13.62	0.09
		6.5	0.90	0.98	36.46	0.11
AIS-J-nocturnal	0.97	2.5	0.97	0.80	4.88	0.04
	(0.95–0.98)	3.5	0.93	0.94	16.73	0.07
		4.5	0.89	0.97	28.82	0.11

AIS-J, Japanese version of the Athens Insomnia Scale; AUC, area under the curve; CI, confidence interval; LR+, positive likelihood ratio. LR–, negative likelihood ratio.

estimated at 5.5 points. The cut-off value had a sensitivity of 92% and a specificity of 93% (Table 3). Furthermore, the cut-off value of the AIS-J-nocturnal was estimated at 3.5 points (Table 3). When limited to primary insomnia, the same cut-off values were observed (AIS-J-total: AUC = 0.97, 95%CI: 0.95–0.99, sensitivity = 0.93, specificity = 0.93, LR+ = 13.78, and LR– = 0.08; AIS-J-nocturnal: AUC = 0.97, 95%CI: 0.95–0.99, sensitivity = 0.94, specificity = 0.94, LR+ = 16.88, and LR– = 0.07).

DISCUSSION

The present study aimed to develop a Japanese version of the AIS and to examine the scale's reliability and validity. The results show that the AIS-J consists of a two-factor structure (nocturnal sleep problem and daytime dysfunction). This finding is consistent with the concepts surrounding an insomnia diagnosis on ICSD-2.[16] In a report by Soldatos *et al.*,[12] the AIS-5 was conceptually grouped into nocturnal sleep difficulty but factor analysis was not conducted. In the present study, the five items included in the 'nocturnal sleep problem' factor were consistent with those of the AIS-5.[12] However, the factor loading on sleep induction (item 1) was smaller than that of other items and the value for the original version, which was 0.74.[12] The reason for this observation is unclear.

In addition, we confirmed that the AIS-J has a high internal consistency (nocturnal sleep problem factor: $\alpha = 0.83$, AIS-J-total: $\alpha = 0.86$) similar to that of the original scale (AIS-5: $\alpha = 0.79$ and AIS-8: $\alpha = 0.86$).[12] Thus, the results of this study support previous findings that show the AIS-J has sufficient internal consistency.

With regard to concurrent and construct validity, the AIS-J shows a high correlation with alternative authorized scales that measure insomnia symptoms. This result is compatible with a previous report that showed the AIS is both positively and highly correlated with the PSQI-J ($r = 0.82$) in an Asian population.[24]

The ROC curve analysis reveals that the cut-off AIS-J score for determining pathological insomnia was 5.5, and this is almost the same as the cut-off score for the original AIS.[19] Therefore, pathological insomnia can be diagnosed if a person scores 6 points or higher on the AIS-J. In addition, the cut-off score of the AIS-J-nocturnal (5-item version) was 3.5, and this short version would be helpful when conducting large-scale epidemiological surveys. The *t*-test result also supports the AIS-J as having a satisfactory ability to discriminate between pathological insomnia and non-pathological sleep status. These results suggest that the AIS-J has a high validity and that the scale is adequate for assessing insomnia symptoms.

There are some limitations to this study. First, test–retest reliability was not conducted for this study. Second, all the participants were middle-aged. Therefore, an examination of whether the same results would be obtained from a population sample that includes all generations is necessary. Finally, as in previous studies,[12,25] sample participants who were recruited from the community did not undergo a face-to-face assessment to clarify whether they had concomitant sleep disorders; these participants were merely those who had not received previous treatment for sleep or psychiatric disorders and produced normal PSQI-J scores. Nonetheless, this study shows that the AIS-J has high validity, and as the scale is both convenient to administer and has a high accuracy, the AIS-J can be expected to have high utility not only in epidemiological research but also for clinical evaluation.

The AIS-J is an adequate self-rating measure both for diagnosing insomnia and for assessing insomnia severity. This scale is expected to be highly useful in a variety of clinical and research settings where there is a requirement for sleep problems to be quantified.

ACKNOWLEDGMENTS

None of the authors has any conflicts of interest concerning this study. This work was supported by JSPS KAKENHI Grant Number 22730574.

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Sleep Breath (2013) 17:589–595
DOI 10.1007/s11325-012-0725-z

ORIGINAL ARTICLE

Validity of sheet-type portable monitoring device for screening obstructive sleep apnea syndrome

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Received: 24 February 2012 / Revised: 21 May 2012 / Accepted: 23 May 2012 / Published online: 16 June 2012

Abstract
Purpose The SD-101 is a non-restrictive sheet-like medical device that measures sleep-disordered breathing using pressure sensors that can detect the gravitational alterations in the body that accompany respiratory movement. One report has described that the screening specificity of the SD-101 for mild to moderate obstructive sleep apnea syndrome (OSAS) is relatively low. The present study examines whether the accuracy of the SD-101 for OSAS screening is improved by simultaneously measuring percutaneous oxygen saturation (SpO_2).

Methods Sixty consecutive individuals with suspected OSAS consented to undergo overnight polysomnography (PSG) together with simultaneous measurements of SD-101 and SpO_2 at our laboratory.
Results The apnea–hypopnea index (AHI) determined from PSG and the respiratory disturbance index determined from SD-101 measurements significantly correlated (SD-101 alone: $r=0.871$, $p<0.0001$; SD-101 with SpO_2: $r=0.965$, $p<0.0001$). Bland–Altman plots showed a smaller dispersion for the SD-101 with SpO_2 than for the SD-101 alone. The SD-101 with SpO_2 detected an AHI of >15 on PSG with a sensitivity and specificity of 96.9 and 90.5 % compared with 87.5 and of 85.7 %, respectively, of the SD-101 alone.
Conclusions Simultaneously measuring SpO_2 improved the accuracy of the SD-101 for OSAS screening. Furthermore, this modality appears to offer high sensitivity and specificity for detecting even moderately severe OSAS.

Keywords Obstructive sleep apnea syndrome · Oximetry · Sheet-like monitoring device · Polysomnography · Validation

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Introduction

The reported prevalence of obstructive sleep apnea syndrome (OSAS) is 4 and 2 % among adult men and women, respectively [1]. However, recent studies have shown a higher prevalence of the disorder [2, 3], and one study found a 22.3 % prevalence of moderate to severe sleep-disordered breathing (SDB; respiratory disturbance index [RDI]≥15) among a working population of Japanese males [4]. Since OSAS is associated with an elevated risk of hypertension [5, 6], nocturnal arrhythmia [7], cardiovascular disease [8], and stroke [9], early diagnosis and treatment of the disorder are important [10]. Attended in-laboratory polysomnography

(PSG) with subsequent manual scoring of the data is the gold standard test for a diagnosis of OSAS. However, PSG is costly and laborious and therefore difficult to conduct on all patients with suspected OSAS. Consequently, as a convenient screening tool for OSAS, portable monitoring (PM) devices enabling the measurement of respiratory disorder variables at home have been widely applied.

Sheet-like SD-101 is several millimeters thick and contains 162 membrane-type pressure sensors that can detect the gravitational alterations in the body that accompany respiratory movements [11]. The SD-101 converts changes in pressure distribution into waveforms and analyzes the resulting breathing patterns. Unlike general PM devices, this sensor avoids the discomfort imposed on examinees associated with attached nasal, oral air flow or snore sensors, and chest/abdominal belts for sensing respiratory movements. Therefore, this method has the advantage for OSAS screening insofar as an examinee simply sleeps on a bed sheet without physical restraint or invasiveness. The concept of the SD-101 system is similar to that of the static charge-sensitive bed (SCSB) [12], which is a sheet-type diagnostic device that has been in use since the 1990s. This device can perform noninvasive ballistocardiography and monitor heart rate and respiration by sensing micromovements of the body as changes in static volume on two metal plates placed under a mattress. However, the SCSB differs from the SD-101 in that respiratory movement is detected from the low-frequency band of heart rate variability.

One report has suggested that the diagnostic accuracy of the SD-101 for OSAS screening is fair, although its ability to differentiate patients with mild to moderate OSAS from normal individuals was relatively low in that study [13]. The original version of the SD-101 can detect only the cessation or a decrease in respiratory movement and cannot measure the oxygen desaturation accompanying respiratory events. Therefore, this method might not accurately detect hypopnea events [11, 13]. Considering this inadequacy, a newer version of the SD-101 including oxygen saturation (SpO_2) monitoring is under development. If the accuracy of the SD-101 with SpO_2 monitoring is sufficiently high, this device might become an important tool for screening OSAS among elderly individuals (particularly those with dementia), patients with mental disorders, and others who cannot tolerate examinations such as PSG or the standard PM described above, in which sensors are directly attached to the body.

The present study compares the validity of simultaneous SD-101 with SpO_2 monitoring to that of the SD-101 alone for OSAS screening during in-laboratory PSG.

Methods

This study proceeded after obtaining approval from both the Institutional Review Board of Neuropsychiatric Research Institute and Fujita Health University. We enrolled 60 consecutive patients (men, 53; women, 7; age, 50.0±13.5 years; BMI, 25.5±3.3 kg/m^2) who attended the outpatient clinic of the Japan Somnology Center or that of the Respiratory Medicine, Department of Internal Medicine of Fujita Health University between September 2008 and September 2009 with suspected OSAS based on information about habitual snoring or episodes of apnea witnessed by family members. All of them consented to the collection of simultaneous measurements using the SD-101 with SpO_2 during in-laboratory PSG. We explained the purpose of the study to these patients, and all of them provided written informed consent to participate. Patients who had already been treated for OSAS, those with electrical implants such as cardiac pacemakers who might have been at risk of electrical interference, and those whose body weight was outside the mechanically measurable range (<15 or >200 kg) [11] were excluded from the study.

Clinical technologists attached PSG sensors to the participants on the evening of the examination, then allowed them to sleep on beds with the SD-101 and simultaneously recorded PSG and SD-101 data.

The PSG devices were either an Alice 3 or an Alice 5 (Respironics, Inc., Murrysville, PA, USA), both of which generated electroencephalograms (C3-A2, C4-A1, O1-A2, O2-A1), left and right electrooculograpms, submental electromyograms, and electrocardiograms and measured nasal airflow using nasal pressure sensors (Alice 5) and thermistors (Alice 3), respiratory chest/abdominal efforts using piezosensors, snoring sounds, SpO_2, and body position. Sleep stages were scored manually every 30 s per epoch according to the criteria of Rechtchaffen and Kales [14]; arousals were scored according to the ASDA Arousal Criteria [15]. Episodes of apnea/hypopnea were determined based on the AASM Chicago criteria of a reduction in airflow amplitude of >50 % from baseline persisting for ≥10 s in the presence of arousal and/or oxygen desaturation of at least 3 % [16].

The SD-101 can detect and collect information about respiration via 162 force-sensing resistors (FSRs) positioned at 4-cm intervals on a bed pad [11, 13]. The FSRs comprise a film device with a polymeric membrane in which electrical resistance decreases with increasing force. This device can thus measure changes in pressure [17]. The diaphragm of an examinee lying on the sensor sheet moves while breathing and pressure changes are recognized by the FSRs under the person. Specifically, the lungs expand and contract, and thoracic-specific gravity decreases and increases during aspiration and exhalation, respectively. These physiological changes create minor changes in pressure that are detected by the SD-101 through the FSRs on the sensor sheet at a sampling frequency of 10 Hz. The changes in pressure reflected on FSRs are automatically selected and averaged to generate a respiratory waveform after the signal noise is

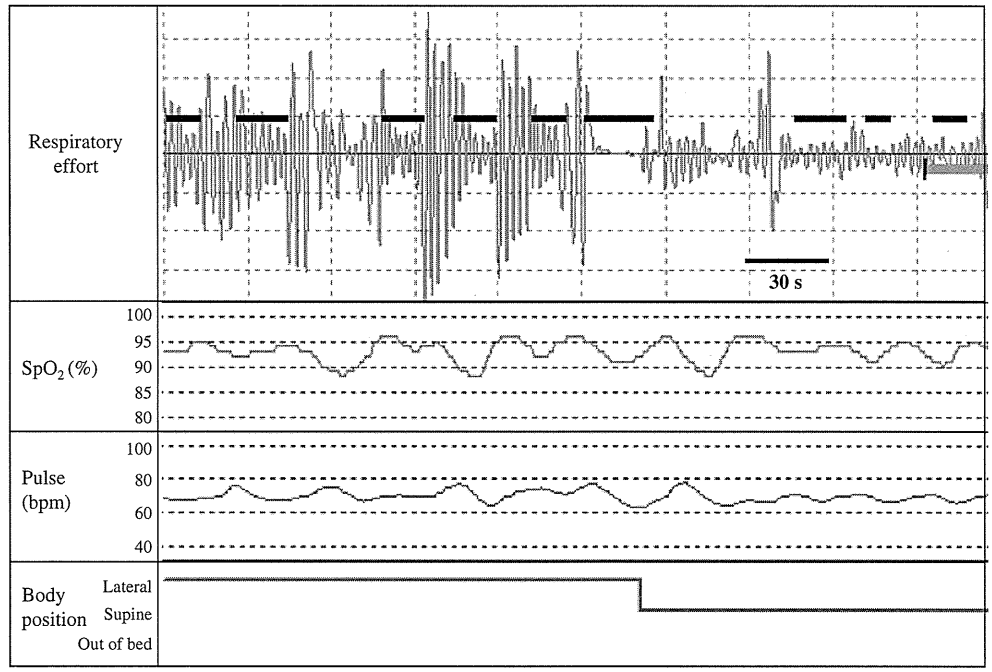

Fig. 1 Traces of 5-min data from SD-101 system

digitally filtered out (Fig. 1). Furthermore, the device automatically detects body position by assessing the area of the body in contact with the sheet from the pressure distribution. Values for SpO_2 were simultaneously recorded with the respiratory waveform, and SpO_2 data obtained by pulse oximetry using an SX Module SX-2007 (Kenzmedico Co. Ltd., Saitama, Japan) were retrieved as an external input and stored on a compact flash card. The SD-101 alone can automatically judge events of apnea or hypopnea [11]. However, during the manual scoring of respiratory events on SD-101 with SpO_2 by a single technician who was blinded to respiratory events (apnea or hypopnea), these were defined as a ≥50 % decrease in respiratory effort waveforms lasting >10 s or a ≥30 % decrease in respiratory effort waveforms lasting >10 s associated with a ≥3 % decrease in SpO_2 from the preceding baseline value.

The attending technician who performed the PSG and SD-101 analyses was blinded to the patients' information to prevent bias, affecting the results. We defined the apnea–hypopnea index (AHI) for PSGs as the total number of apnea or hypopnea events divided by total sleep time (TST) and the RDI from SD-101 as respiratory events divided by time in bed (TIB), respectively, because TST could not be estimated from the SD-101 data.

To evaluate the validity of the SD-101, we firstly calculated the correlation between RDI obtained from SD-101 and AHI obtained from PSG using Pearson's correlation analysis. Bland–Altman plots were then generated to assess agreement between the PSG and SD-101 results [18]. We also estimated the area under the receiver operating characteristic (ROC) curves (AUC) with RDI on the SD-101 system [19]. We then determined the optimal RDI values at cutoff AHI of 5 and 15 episodes per hour by calculating the sensitivity, specificity, positive and negative predictive values, as well as false-negative and false-positive values to establish the screening accuracy of the SD-101. Data were analyzed using SPSS11.5 (SPSS Japan, Inc., Tokyo, Japan); $p<0.05$ was considered to indicate statistical significance.

Results

We concurrently measured PSG and SD-101 in 60 patients, but excluded seven because SpO_2 data from six of them

Table 1 Demographic and polysomnographic parameters of the participants (n=53)

Variable	Value	Range
Gender (male/female)	46:7	
Age (years)	50.1±13.8	24–80
Body mass index (kg/m^2)	25.3±3.4	19.6–34.2
Epworth sleepiness scale (ESS)	9.9±3.4	1–21
AHI (episodes per hour)	24.5±21.2	0–70.1
RDI (episodes per hour)	22.6±17.7	1.0–66.8
3 % Desaturation index (episodes per hour)	13.8±14.5	0–50.5
Arousal index (episodes per hour)	24.7±16.8	0.5–69.7
Time in bed (min)	501.6±29.5	453–579
Total sleep time (min)	412.8±76.9	158–527
Sleep efficiency (%)	81.7±14.2	35.2–98.5

Continuous variables are expressed as the means±SD

AHI apnea–hypopnea index, *RDI* respiratory disturbance index