雑誌

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Enomoto M, Tsutsui T, Higashino S, Otaga M, Higuchi S, Aritake S, Hida A, Tamura M, Matsuura M, Kaneita Y, Takahashi K, Mishima K	Sleep-related Problems and Use of Hypnotics in Inpatients of Acute Hospital Wards.	General Hospital Psychiatry	32	276-283	2010
Kaji T, Mishima K, Kitamura S, Enomoto M, Nagase Y, Li L, Kaneita Y, Ohida T, Nishikawa T, Uchiyama M	Relationship between late-life depression and life stressors: Large-scale cross-sectional study of a representative sample of the Japanese general population.	Psychiatry Clin Neurosci	64	426-434	2010
Abe Y, Mishima K, Kaneita Y, Li L, Ohida T, Nishikawa T, Uchiyama M	Stress coping behaviors and sleep hygiene practices in a sample of Japanese adults with insomnia.	Sleep and Biological Rhythms	9	35-45	2011
Furihata R, Uchiyama M, Takahashi S, Konno C, Suzuki M, Osaki K, Kaneita Y, Ohida T	Self-help behaviors for sleep and depression: A Japanese nationwide general population survey.	Journal of Affective Disorders	130	75-82	2011
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ORIGINAL ARTICLE

Newly developed waist actigraphy and its sleep/wake scoring algorithm

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Abstract

The purpose of this study was to formulate an algorithm for assessing sleep/waking from activity intensities measured with a waist-worn actigraphy, the Lifecorder PLUS (LC; Suzuken Co. Ltd., Nagoya, Japan), and to test the validity of the algorithm. The study consisted of 31 healthy subjects (M/F = 20/11, mean age 31.7 years) who underwent one night of simultaneous measurement of activity intensity by LC and polysomnography (PSG). A sleep(S)/wake(W) scoring algorithm based on a linear model was determined through discriminant analysis of activity intensities measured by LC over a total of 235 h and 56 min and the corresponding PSG-based S/W data. The formulated S/W scoring algorithm was then used to score S/W during the monitoring epochs (2 min each, 7078 epochs in total) for each subject. The mean agreement rate with the corresponding PSG-based S/W data was 86.9%, with a mean sensitivity (sleep detection) of 89.4% and mean specificity (wakefulness detection) of 58.2%. The agreement rates for the individual stages of sleep were 60.6% for Stage 1, 89.3% for Stage 2, 99.2% for Stage 3 + 4, and 90.1% for Stage REM. These results demonstrate that sleep/wake activity in young to middle-aged healthy subjects can be assessed with a reliability comparable to that of conventional actigraphy through LC waist actigraphy and the optimal S/W scoring algorithm.

Key words: actigraphy, polysomnography, sleep/wake scoring algorithm, sleep-waking, waist-worn.

INTRODUCTION

An actigraphy is a small lightweight device for non-invasive and continuous monitoring of human rest/activity (sleep/wake) cycles.[1,2] The most commonly used actigraphy in current sleep research is a unit that is worn on the non-dominant wrist like a wristwatch for continuous measurement of forearm motor activity. The actigraphy unit generally consists of a piezoelectric accelerometer and a memory for storing the measured values for a specific time epoch, typically from 1 s to several minutes.

Algorithms using the activity level measured by the actigraphy to determine whether the person wearing the unit is awake or asleep during the time epoch have been developed for use with individual actigraphy units.[3–5] Studies to date investigating the agreement rate of polysomnography (PSG) and various actigraphy units in

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healthy adults have reported a very high agreement rate of 85 to 96% between the two methods with use of the optimal specific sleep/wake scoring algorithm.[3–7]

Although actigraphy is suitable for assessment of sleep/wake activity during a specific time epoch, it cannot be used independently for confirmation or diagnosis of sleep disturbances because, contrary to PSG, it does not allow for collection of data on electrooculogram (EOG), electromyogram (EMG), electrocardiogram (ECG), and breathing function during sleep.[7] On the other hand, it has a distinct advantage over PSG in that it allows for continuous recording of rest/activity (sleep/wake state) over long periods of time outside of the sleep lab with minimal disruption to the subject's normal life. It is therefore commonly used in human sleep physiology research and clinical studies in patients with insomnia and circadian rhythm sleep disorders.[6] Future beneficial applications of actigraphy include sleep disturbance screening in a large number of subjects and evaluation of the effectiveness and side effects of drug and non-drug therapies requiring continuous assessment of sleep/wake activity. Inexpensive multipurpose devices providing a favorable cost–benefit balance in the clinical setting are, however, necessary to realize these new potential applications. There have been a few previous studies that assessed sleep/wake activity using an actigraphy placed on the trunk[8,9] and the head[10] because the current mainstream wrist-worn actigraphy unit cannot be readily used in individuals with upper dystaxia, individuals with involuntary movement such as finger tremors, and children and dementia patients who may inadvertently interfere with the device. Most are also not waterproof and cannot thus readily be used in individuals whose work involves handling of water. So actigraphy units that can be worn on body sites other than the wrist, such as the trunk, are still needed.

We therefore focused our research on an inexpensive activity monitor that is worn around the waist to measure activity as a new actigraphy option in sleep research and sleep medicine. In our study, data obtained from healthy adults was used to formulate an algorithm to score sleep/waking measured by waist actigraphy and test the validity of the algorithm.

METHODS

Features of waist actigraphy

An inexpensive activity monitor that is worn around the waist (Lifecorder PLUS [LC]; Suzuken Co. Ltd., Nagoya, Japan; ¥14800 = €100 = $128) was used to measure activity level during sleep. The LC was originally developed for measurement of daytime physical-activity level and has been used for the assessment of physical-activity-related energy expenditure.[11,12] The LC measures acceleration along the longitudinal axis every 4 s with an internal piezoelectric accelerometer and classifies the intensity into 11 levels from 0 to 9 (0, 0.5, 1, 2, 3, 4, 5, 6, 7, 8, 9) every 2 min.[11] Level 0 (corresponding to <0.06 G) denotes immobility and Levels 0.5 to 9 (corresponding to ≥0.06 G) denote subtle to strong movements. The cut-off point of activity intensity (the acceleration value) for each level is not provided by the manufacturer. It is possible to continuously record the activity intensity level with the time information for at least 2 months. After the completion of measurement, the recorded activity intensity data can be downloaded to a personal computer through a USB cable. The scoring algorithm was formulated from these data.

Experimental subjects

The study consisted of 31 healthy adults (20 males and 11 females with a mean age of 31.6 ± 10.4 years). Monitoring was performed by the Sleep Electroencephalography Lab at Aoki Hospital and the Sleep/Biological Rhythm Monitoring Unit of the National Institute of Mental Health of the National Center of Neurology and Psychiatry. Subjects underwent simultaneous continuous monitoring of intensity of physical movement during sleep by PSG and LC. The study was approved by the ethics committee of the National Center of Neurology and Psychiatry. Subjects were informed of the purposes and methods of the study and gave written consent to participate in the investigation.

PSG and LC recordings

The PSG consisted of measurement of a standard electroencephalogram (C3-A2, C4-A1, O1-A2, O2-A1), EOG, chin EMG, ECG, breathing function, and tibialis anterior EMG data every 30 s. The Polymate 1524 (TEAC Corporation, Tokyo, Japan) and Comet PSG (Grass-Technologies, RI, USA) were used for the PSG. The sleep stage (Stage 1, Stage 2, Stage 3 + 4, Stage REM or Stage wake) was then determined every 30 s according to the rules of Rechtschaffen and Kales.[13] Four consecutive 30-s intervals of sleep stage data were used to assess sleep/wake state every 2 min to correspond with the intervals with LC data. When four consecutive data contained two or more of Stage wake, the data set was classified as wake (W_{PSG}) according to the definition

adopted the previous studies.[14–16] All other data sets were classified as sleep (S_{PSG}). Furthermore, S_{PSG} was subclassified as Stage REM, Stage 1, Stage 2, or Stage 3 + 4, according to the most frequent sleep stage in the data set (e.g. when S_{PSG} contained two or more Stage 1 data, it was classified as Stage 1). However, when S_{PSG} contained two of two different stages, the priority order (Stage REM → Stage 1 → Stage 2 → Stage 3 + 4) was used (e.g. when S_{PSG} contained two Stage 1 and two Stage REM, it was classified as Stage REM).

Formulation of an algorithm for assessing sleep/waking

A S/W scoring algorithm for LC was newly formulated by the discriminant analysis. The data used for the development were the datasets of S_{PSG} (=0) and W_{PSG} (=1) corresponding to the LC exercise intensities obtained from 7078 epochs obtained from 31 subjects on 31 nights over a total of 235 h and 56 min.

Taking the S/W algorithm for the present actigraphy into account, we assume the five-dimension linear model that incorporates the exercise intensities during 10 min with the center of the time epoch of interest. The activity intensities 4 min before the scored epoch, 2 min before the scored epoch, during the scored epoch, 2 min after the scored epoch, and 4 min after the scored epoch were represented by x_1, x_2, x_3, x_4, and x_5, respectively. A linear discriminant function was given as the following equation for an arbitrary set of weight coefficients of a_1, a_2, a_3, a_4, and a_5.

$$z = a_1x_1 + a_2x_2 + a_3x_3 + a_4x_4 + a_5x_5$$

Where the variable of z can be used as the discriminant score to classify a set of activity intensities into the stage of S_{LC} or W_{LC}.

The above discriminant function was determined by the discriminant analysis. Supposing that the LC activity intensity in sleeping status and in waking status are categorized in class 1 and 2, respectively, and the number of the datasets in each class is set to n_1 and n_2, the i-th ($i = 1$ to n_k) variable in class k ($k = 1, 2$), $z_i^{(k)}$ is given as

$$z_i^{(k)} = a_1x_{1i}^{(k)} + a_2x_{2i}^{(k)} + a_3x_{3i}^{(k)} + a_4x_{4i}^{(k)} + a_5x_{5i}^{(k)}.$$

The variation of $\{z_i^{(k)}\}$ is represented by the total sum of squares, S_T, which can be decomposed to the between sum of squares, S_B, and the within sum of the squares, S_W ($S_T = S_B + S_W$).

$$S_T = \sum_{k=1}^{2}\sum_{i=1}^{n_k}(z_i^{(k)} - \bar{z})^2$$

$$S_B = \sum_{k=1}^{2} n_k(\bar{z}^{(k)} - \bar{z})^2$$

$$S_W = \sum_{k=1}^{2}\sum_{i=1}^{n_k}(z_i^{(k)} - \bar{z}^{(k)})^2.$$

Since the better discriminability between the two classes using z is equivalent to the increase of the ratio of correlation, $\eta^2 = S_B / S_T$, the set of weight coefficients, $\hat{a}_1$, $\hat{a}_2$, $\hat{a}_3$, $\hat{a}_4$, $\hat{a}_5$, that gives the maximum η^2 can be calculated by the following equations:

$$\begin{bmatrix} s_{11} & s_{12} & s_{13} & s_{14} & s_{15} \\ s_{21} & s_{22} & s_{23} & s_{24} & s_{25} \\ s_{31} & s_{32} & s_{33} & s_{34} & s_{35} \\ s_{41} & s_{42} & s_{43} & s_{44} & s_{45} \\ s_{51} & s_{52} & s_{53} & s_{54} & s_{55} \end{bmatrix} \begin{bmatrix} \hat{a}_1 \\ \hat{a}_2 \\ \hat{a}_3 \\ \hat{a}_4 \\ \hat{a}_5 \end{bmatrix} = \begin{bmatrix} \bar{x}_1^{(1)} - \bar{x}_1^{(2)} \\ \bar{x}_2^{(1)} - \bar{x}_2^{(2)} \\ \bar{x}_3^{(1)} - \bar{x}_3^{(2)} \\ \bar{x}_4^{(1)} - \bar{x}_4^{(2)} \\ \bar{x}_5^{(1)} - \bar{x}_5^{(2)} \end{bmatrix}.$$

Where $\bar{x}_j^{(k)}$ is the average of the j-th variable in class k, $s_{jj'}$ is the within covariance between the j-th and j'-th variables. They are evaluated by

$$\bar{x}_j^{(k)} = \frac{1}{n_k}\sum_{i=1}^{n_k} x_{ji}^{(k)}$$

$$s_{jj'} = \frac{1}{n_1 + n_2 - 2}\sum_{k=1}^{2}\sum_{i=1}^{n_k}(x_{ji}^{(k)} - \bar{x}_j^{(k)})(x_{j'i}^{(k)} - \bar{x}_{j'}^{(k)}).$$

S/W agreement rate

The S/W scoring algorithm was used to determine the S_{LC}/W_{LC} state from the activity intensity data in a total of 7078 epochs in the 31 subjects, and the agreement rate with the corresponding S_{PSG}/W_{PSG} results was calculated by subject and sleep stage. The agreement rate with the PSG-based sleep epochs (sensitivity) and agreement rate with the PSG-based wakefulness epochs (specificity) were also calculated by subject. SPSS version 11.5 was used for the statistical analysis (SPSS Japan Inc., Tokyo, Japan). Results were expressed as mean ± SD.

RESULTS

S/W scoring algorithm

The following S/W scoring algorithm was derived from the results of discriminant analysis of the activity

Table 1 Sleep parameters scored by polysomnography (PSG) and Lifecorder (LC) data

Sleep parameters	PSG	LC	Significance
Sleep efficiency (%)	90.2 ± 9.6 (61.8–99.1)	86.8 ± 11.1 (44.1–100.0)	$t(60) = 1.26$, $P = 0.21$
Total sleep time (min)	406.6 ± 78.9 (179.3–587.0)	376.3 ± 76.3 (208.0–586.0)	$t(60) = 1.53$, $P = 0.13$
Wake after sleep onset (min)	45.2 ± 48.3 (3.67–232.7)	59.9 ± 68.5 (0–388.0)	$t(60) = 0.98$, $P = 0.33$

Table 2 Decision parameters of S/W prediction algorithm for the Lifecorder

			Number of epochs
Agreement rates (%)	Overall	86.9 ± 8.9	7078
	Stage W	58.2 ± 30.4	819
	Stage 1	60.6 ± 26.2	427
	Stage 2	89.3 ± 10.6	3694
	Stage 3 + 4	99.2 ± 2.1	838
	Stage REM	90.1 ± 17.5	1300
Sensitivity (%)		89.4 ± 10.6	
Specificity (%)		58.2 ± 30.4	
Percentage of S_{PSG} epochs misscored as W_{LC} (%)		10.6 ± 10.6	
Percentage of W_{PSG} epochs misscored as S_{LC} (%)		41.8 ± 30.4	

S, sleep; W, wakefulness.

intensity data and PSG-based sleep/wake data from the total 7078 epochs obtained from 31 subjects:

$$z = 0.635x_1 + 0.427x_2 + 0.701x_3 + 0.805x_4 + 0.718x_5$$

where $z \geq 1$ indicates wakefulness (W_{LC}) and $z < 1$ indicates sleep (S_{LC}).

The linear discriminant function was transformed in advance by using linearity of the discriminant function in such a way that the threshold (z) becomes 1. Here, x_1, x_2, x_3, x_4, and x_5, indicate the activity intensity 4 min before the scored epoch, 2 min before the scored epoch, during the scored epoch, 2 min after the scored epoch, and 4 min after the scored epoch.

Validity of the S/W scoring algorithm

The sleep parameters derived from PSG and the LC activity intensity data are shown in Table 1. Sleep efficiency, total sleep time, and wakefulness after sleep onset were each derived from PSG and the LC activity intensity data (Table 1). No statistically significant differences were observed between PSG and the LC in any of the sleep parameters.

Table 2 shows the sleep/wake agreement rates between the LC and PSG, and the sensitivity and specificity of the LC. The overall agreement rate between the LC and PSG in the 31 subjects was 86.9 ± 8.9%. By sleep stage, the Stage 1 agreement rate was low at approximately 60%, but the Stage 2, Stage REM, and Stage 3 + 4 agreement rates were high at approximately 90% for Stage 2 and Stage REM and close to 100% for Stage 3 + 4.

The S/W scoring algorithm had a mean sensitivity (S detection) of 89.4 ± 10.6% and a mean specificity (W detection) of 58.2 ± 30.4%. In other words, 10.6 ± 10.6% of S_{PSG} were misscored as W_{LC} and 41.8 ± 30.4% of W_{PSG} were misscored as S_{LC}.

Activity intensity distribution before and after the scored epoch

Figure 1 shows the mean activity intensity recorded by the LC for nine consecutive epochs (18 min) centered at the W_{PSG} epoch (averaged for a total of W_{PSG} 819 epochs obtained from 31 subjects). The mean activity intensity recorded by the LC peaked just after the W_{PSG} epoch.

DISCUSSION

In the study, an S/W scoring algorithm for the LC was formulated through linear-based discriminant analysis of the corresponding longitudinal "PSG-based sleep/wake state" and "LC-recorded activity intensity" data in 7078 epoch recordings in 31 subjects over a total of

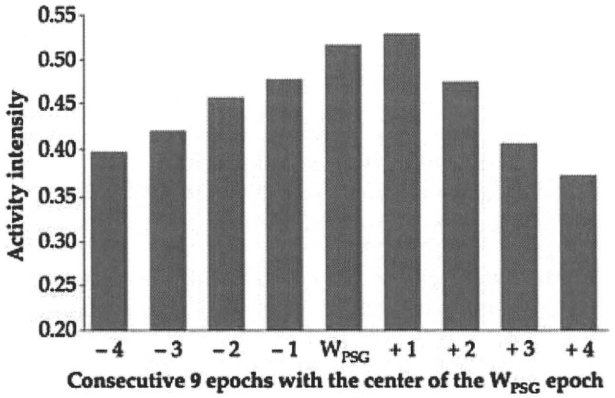

Figure 1 Activity intensity distribution before and after the scored epoch. The mean activity intensity recorded by the Lifecorder (LC) for nine consecutive epochs (18 min) centered at the W_{PSG} epoch. Vertical bars indicate the activity intensity. The mean activity intensity bars formed an inverted U-shape and peaked just after the W_{PSG} epoch.

235 h and 56 min. Comparison of the S/W activity determined from the LC data through the S/W scoring algorithm and the comparable activity determined from the PSG data through the rules of Rechtschaffen and Kales showed a mean agreement rate of approximately 87% in the 31 subjects. This rate is comparable to the 85 to 96% agreement rates obtained with conventional actigraphy units and their S/W scoring algorithms.[3–7] The LC and its S/W scoring algorithm yielded a high agreement rate of 90% or greater for Stage 2 and Stage 3 + 4 deep sleep and REM sleep, as well as an approximately 60% agreement rate for W_{PSG}, which is higher than that yielded by conventional algorithms. In order to examine the superiority of the five-dimensional model over the three-, seven-, or nine-dimensional models, we assumed linear models which incorporate the activity intensities during intervals of 6, 14, and 18 min centered at the time epoch of interest. The total agreement rates of the algorithms for the three-, five-seven-, and nine-dimensional models were 82.9%, 86.9% 86.0%, and 87.3%, respectively. Finally, we adopted the algorithm of the five-dimensional model since the agreement rate appeared to become saturated for models with more than five-dimensions. These findings show that when used with the S/W scoring algorithm developed in the study, the LC is a useful sleep assessment device with equivalent S/W identification capacity to conventional actigraphy systems.

Silent awakeness has been generally difficult to detect through actigraphic S/W assessment, in which it may be misscored as sleep, resulting in a pattern of overassessment of total sleep time and sleep efficiency compared to PSG-based assessment.[4,16,17] The LC and the S/W scoring algorithm derived in this study did not, however, result in a pattern of over-identification of S_{LC}, but contrarily yielded lower total sleep time and sleep efficiency values than the S_{PSG}/W_{PSG} assessment (Table 1). The specificity of the S/W scoring algorithm for the LC (58.2%) is in fact higher than that for conventional actigraphy units and their S/W scoring algorithms (40.6 *vs* 44%),[4,17] demonstrating that the S/W scoring algorithm for the LC developed in the study allows for more accurate identification of W_{LC}.

The S/W detection algorithm for wrist actigraphy used in a previous study assigned the highest weighting coefficient to the scored epoch.[4] However, in the S/W scoring algorithm for the LC, the highest weighting coefficient was assigned to the period immediately following the scored epoch. In fact, the mean activity intensity recorded by the LC peaked just after the W_{PSG} epoch (Fig. 1), and the delayed increase in truncal movement after awakening characterized the highest weighting coefficient assigned immediately after the scored epoch.

The LC is worn on the trunk while the conventional actigraphies used to be worn on the non-dominant wrist.[3–7] This may be related to the high specificity of the LC and its S/W scoring algorithm. The different application sites mean that S/W activity is assessed through different types of movement during sleep, either extremity or trunk movement (which are often independent),[18,19] which may produce the differences in assessment noted above. The LC and its S/W scoring algorithm investigated in the current study may more accurately detect silent awakeness due to the sensitivity to small movements of the torso during sleep and a resulting higher composite variable z value.

There are several issues that require further exploration with respect to use of the LC as a novel option for sleep assessment. First, the time epoch of S/W scoring algorithms for conventional actigraphy is often 1 min or less.[3,5,14] The time epoch for the LC used in this study is 2 min, leading to the assumption that devices with higher temporal resolution may result in higher agreement rates. Although it is more expensive (¥37 000 = €230 = $350), there is an LC that is programmable to 4-s time epochs. It would therefore be of merit to formulate an S/W scoring algorithm for this LC to determine whether it yields a higher agreement rate. Second, the S/W scoring algorithm formulated in the study uses the data from the scored time epoch as well as the data from the two epochs (4-min interval) immediately prior

and immediately after to scoring S/W. This means that activity intensity data prior to onset of sleep will be included in the scoring formula for the scored time epoch unless at least 4 min have passed from the onset of sleep on PSG. This complicates detection of differences in sleep latency of the order of several minutes. Accordingly, sleep latency was not analyzed in this study. This perhaps poses a constraint to the use of the LC in studies and tests requiring accurate evaluation of sleep latency. It is expected that development of LCs with higher temporal resolution and their S/W scoring algorithms will solve this issue.

In the current study, an S/W scoring algorithm for the LC was formulated from the data of young to middle-aged healthy adults and the validity of the algorithm was tested. Other potential useful applications of the inexpensive LC include sleep disorder screening in a large number of individuals. In the future, it will be necessary to determine whether the high agreement rates can also be obtained when the LC and its S/W scoring algorithm are used to assess sleep/wake activity in subjects from different age groups, including children and the elderly, and in patients with common sleep disorders, such as insomnia and sleep respiratory disturbances.

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REFERENCES

1 Kupfer DJ, Foster FG. Sleep and activity in a psychotic depression. *J. Nerv. Ment. Dis.* 1973; **156:** 341–8.
2 Kripke DF, Mullaney DJ, Messin S, Wyborney VG. Wrist actigraphic measures of sleep and ryhthms. *Electroencephalogr. Clin. Neurophysiol* 1978; **44:** 674–6.
3 Webster JB, Kripke DF, Messin S, Mullaney DJ, Wyborney G. An activity-based sleep monitor system for ambulatory use. *Sleep* 1982; **5:** 389–99.
4 Cole RJ, Kripke DF, Gruen W, Mullaney DJ, Gillin JC. Automatic sleep/wake identification from wrist activity. *Sleep* 1992; **15:** 461–9.
5 Jean-Louis G, Kripke DF, Cole RJ, Assmus JD, Langer RD. Sleep detection with an accelerometer actigraph: comparisons with polysomnography. *Physiol. Behav.* 2001; **72:** 21–8.
6 Ancoli-Israel S, Cole R, Alessi C, Chambers M, Moorcroft W, Pollak CP. The role of actigraphy in the study of sleep and circadian rhythms. *Sleep* 2003; **26:** 342–92.
7 Acebo C, Lebourgeois MK. Actigraphy. *Respir. Care Clin. N. Am.* 2006; **12:** 23–30.
8 Kochersberger G, McConnell E, Kuchibhatla MN, Pieper C. The reliability, validity, and stability of a measure of physical activity in the elderly. *Arch. Phys. Med. Rehabil.* 1996; **77:** 793–5.
9 Paavonen EJ, Fjallberg M, Steenari MR, Aronen ET. Actigraph placement and sleep estimation in children. *Sleep* 2002; **25:** 235–7.
10 Spivak E, Oksenberg A, Catz A. The feasibility of sleep assessment by actigraph in patients with tetraplegia. *Spinal Cord.* 2007; **45:** 765–70.
11 Kumahara H, Schutz Y, Ayabe M *et al.* The use of uniaxial accelerometry for the assessment of physical-activity-related energy expenditure: a validation study against whole-body indirect calorimetry. *Br. J. Nutr.* 2004; **91:** 235–43.
12 Saito N, Yamamoto T, Sugiura Y, Shimizu S, Shimizu M. Lifecorder: a new device for the long-term monitoring of motor activities for Parkinson's disease. *Intern. Med.* 2004; **43:** 685–92.
13 Rechtschaffen A. A manual of standardized terminology, technique and scoring system for sleep stages of human subjects. Los Angeles, CA: Brain Information Service/ Brain Research Institute, UCLA. 1968.
14 Sadeh A, Sharkey KM, Carskadon MA. Activity-based sleep-wake identification: an empirical test of methodological issues. *Sleep* 1994; **17:** 201–7.
15 Lotjonen J, Korhonen I, Hirvonen K, Eskelinen S, Myllymaki M, Partinen M. Automatic sleep-wake and nap analysis with a new wrist worn online activity monitoring device vivago WristCare. *Sleep* 2003; **26:** 86–90.
16 Paquet J, Kawinska A, Carrier J. Wake detection capacity of actigraphy during sleep. *Sleep* 2007; **30:** 1362–9.
17 de Souza L, Benedito-Silva AA, Pires ML, Poyares D, Tufik S, Calil HM. Further validation of actigraphy for sleep studies. *Sleep* 2003; **26:** 81–5.
18 Van Hilten JJ, Middelkoop HA, Kuiper SI, Kramer CG, Roos RA. Where to record motor activity: an evaluation of commonly used sites of placement for activity monitors. *Electroencephalogr. Clin. Neurophysiol.* 1993; **89:** 359–62.
19 Middelkoop HA, van Dam EM, Smilde-van den Doel DA, Van Dijk G. 45-hour continuous quintuple-site actimetry: relations between trunk and limb movements and effects of circadian sleep-wake rhythmicity. *Psychophysiology* 1997; **34:** 199–203.

Association between Depression and Insomnia Subtypes: A Longitudinal Study on the Elderly in Japan

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Study Objective: To examine the association between depression and three subtypes of insomnia, namely, difficulty initiating sleep (DIS), early morning awakening (EMA), and difficulty maintaining sleep (DMS).

Design: Cross-sectional and longitudinal study.

Setting: Community dwellers in Japan.

Participants: Nationally representative samples of adults aged 65 and over (total N = 4,997) were selected by a multistage stratified random sampling method in 1999 and were interviewed face-to-face in 1999, 2001, 2003, and 2006. Those who responded to the 3rd survey conducted in 2003 and the 4th survey conducted in 2006 were used in this study.

Measurement and Results: Depression was evaluated according to the 11-item short form of the CES-D scale at 2 points in time. Insomnia subtypes were assessed by self-reported measures. A logistic regression was employed to examine the association between insomnia subtypes and the presence of depression, controlling for relevant factors. A cross-sectional analysis based on the 2003 data demonstrated statistically significant odds ratios (ORs) for DIS and EMA. In the longitudinal study, DIS at the time of the 3rd survey was found to be significantly related to the presence of depression at the time of the 4th survey, with an odds ratio (95%CI) of 1.592 (1.012 to 2.504). EMA (OR 1.070; 95% CI, 0.664 to 1.723) and DMS (OR 1.215; 95% CI, 0.860 to 1.716), however, were not found to be significantly related to the presence of depression.

Conclusion: The longitudinal study revealed a statistically significant relationship, controlling for other relevant factors, between DIS and the presence of depression three years later, but not between EMA or DMS and depression. Based on our findings, we recommend that the association between insomnia subtypes and depression be studied longitudinally in clinical settings.

Keywords: Depression, insomnia subtypes, longitudinal study, elderly Japanese

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DEPRESSION IS SUSPECTED TO BE STRONGLY ASSOCIATED WITH SLEEPING DIFFICULTIES. THE WHO STUDY ON GLOBAL BURDEN OF DISEASES PREDICTED depression would be the second greatest Burden of Disease in 2020 in developed countries.[1] These countries therefore urgently need to address the issue of depression. Depression is prevalent among the aged, and it is known that its prevalence rises after the age of 50 among Japanese people.[2]

It is reported that insomnia can be a precursor or risk factor in depression and that depression could result in insomnia. Thus, the two diseases apparently have a bidirectional relationship.[3] Furthermore, insomnia is listed as a major diagnostic feature of depression in the Diagnostic and Statistical Manual of Mental Disorders, 4th Ed (DSM-IV), attesting to the close association of the two diseases.[4]

This problem has attracted many researchers, and various epidemiological studies have thus far been carried out. In their pioneering longitudinal study, Ford and Kamerow[5] reported that those who complained of insomnia at the baseline showed a high risk of developing major depression after one year (odds ratio [OR]: 39.8), while those relieved of insomnia by the time of a second survey showed a much lower risk (OR: 1.6). Breslau et al.[6] observed young adults longitudinally for three years and found that those with a history of insomnia at the baseline had a relative risk of 4.0 of developing major depression by a second examination. Chang et al.[7] conducted a long-term cohort study in which they followed college graduates up to 45 years. They reported that insomnia in young people could result in the risk of developing depression for at least 30 years. All these studies have confirmed the importance of insomnia as a risk factor of depression and the need for early detection and treatment of insomnia. Riemann and Voderholzer[8] reviewed eight longitudinal studies (including the three studies mentioned above) conducted before 2000, which examined the relationship between depression and insomnia. In their review, they listed two other studies dealing with that relationship among those aged ≥ 65 years.[9,10] More recently, epidemiological longitudinal studies of the association between insomnia and depression were conducted in various populations: among those ≥ 18 years old in the UK,[11] those ≥ 30 years old in Norway,[12] young adults in Switzerland,[13] the general population in Sweden,[14] and those ≥ 65 years old in South Korea.[15] All of these studies, again, indicate the effect of insomnia on depression for different populations. These reports, however, did not examine the relationship of depression to the different insomnia subtypes: difficulty initiating sleep (DIS), early morning awakening (EMA), and difficulty maintaining sleep (DMS).

A commentary on this article appears in this issue on page 1585.

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Hartz et al.[16] examined risk factors for insomnia subtypes by using a cross-sectional survey and concluded that every insomnia subtype is strongly associated with depressive symptoms. Rodin et al.[17] stated EMA was more closely related to depression than three other sleep problems, including difficulty falling asleep. Although Rodin et al. collected longitudinal data to examine the relationship between sleep disturbances and depression, their analyses of the relationship were basically cross-sectional in nature. Their analyses suggested that "in the same subject, a decrease in depression is associated with a corresponding decrease in early morning awakening."

Nevertheless, two recent large-scale epidemiological studies in Japan yielded quite different results concerning the relationship between depression and subtypes of insomnia. Using the CES-D to elucidate the relationship of depression to insomnia, Kaneita et al. evaluated 24,686 people (aged ≥ 20 years) throughout Japan for depression.[2] Sukegawa et al. studied 2,023 residents aged ≥ 65 years in one city using the Geriatric Depression Scale and Pittsburgh Sleep Quality Index.[18] These studies, both of which used questionnaire surveys based on self-rated responses, reported that the closest connection to depression was found not with EMA or DMS, but with DIS. Being cross-sectional studies, however, they could not adequately explore the causal relationship between insomnia subtypes and the presence of depression. We therefore, employed a longitudinal survey on elderly Japanese to examine the temporal association between insomnia subtypes and the presence of depression three years later.

PARTICIPANTS AND METHODS

Selection of Participants

Nihon University has been conducting a nationally representative longitudinal survey on elderly Japanese since 1999 (Nihon University Japanese Longitudinal Study of Aging: NUJLSOA).[19] Six thousand seven hundred elderly Japanese aged ≥ 65 years were sampled by a multistage stratified sampling method in conformity with the population composition at the time. Four thousand nine hundred ninety-seven participants gave informed consent (74.6% retrieval). They were visited and interviewed by well-trained interviewers. Participants aged ≥ 75 years were oversampled by a factor of 2 so that the data for this age group could be analyzed in detail. All the numbers reported in the results are weighted values.

The survey was repeated on the same cohort in 2001, 2003, and 2006, with sample refreshing in 2001 and 2003 for those aged 65 and 66. The present study was based on the 2003 data (number of participants excluding proxy respondents: 4,028) consisting of 1,765 males (45.0%) and 2,263 females (55.0%). All of these participants were included in our cross-sectional studies. Of those, 3,065 without depression in 2003 were included in our longitudinal analyses. We excluded those who had died by the time the 4th survey was conducted in 2006 and those whose responses to the interview were in any way incomplete. The present study employs surveys conducted in 2003 and 2006 because questions on sleep disturbances were only first introduced in the survey conducted in 2003 as a module and kept in the survey conducted in 2006.

Measures

The relationship between the presence of depression and insomnia subtypes was examined by controlling for sleep related, sociodemographic, and health-related factors in the multivariate analyses in our study. Depression, a dependent variable of our study, was evaluated by means of the 11-item short form of the Center for Epidemiological Studies Depression (CES-D) Scale, which had been proposed by Kohout et al.[20] from the 20-item standard form CES-D, developed by Radloff.[21] The time frame of the CES-D is over the previous one week. Shima et al.[22] have confirmed the reliability and validity of the Japanese version of the 20-item standard form, for which they proposed 16 as a reasonable cut-off point. The cut-off point, reliability, and validity of the Japanese version of the 11-item CES-D scale used in this study has been examined and reported by Yokoyama et al.[23] The cut-off point for the 11-item CES-D scale was estimated at 7, equivalent to the cut-off point of 16 for the Japanese version of the standard 20-item CES-D scale. In the present study, those with a score ≥ 7 were defined as having depression.

Sleeping problems, including three insomnia symptoms, were measured by self-reported responses to 5 questions utilized by previous studies.[24-26] The five questions used in the survey are the following:

1) Difficulty initiating sleep (DIS): "Do you have difficulty falling asleep at night?"
2) Early morning awakening (EMA): "Do you wake up too early in the morning and have difficulty getting back to sleep?"
3) Difficulty maintaining sleep (DMS): "Do you wake up during the night after you have gone to sleep?"
4) Excessive daytime sleepiness (EDS): "Do you feel excessively sleepy during the daytime?"[27]
5) Discomfort feeling in the legs (DFL): "Is your sleep interrupted by an itchiness (creeping sensation) or burning sensation in your legs after you go to bed at night?"[28,29]

There are five response categories for these questions: 1, never; 2, seldom; 3, sometimes; 4, often; and 5, always. Those who responded 1 to 3 to the questions were regarded as not having the particular sleeping problem, and those who responded 4 and 5 as having the particular sleeping problem. Insomnia (ANY as a variable name in the tables) was defined, according to a previous study,[25] as the condition that resulted in the participant reporting the presence of at least one of the symptoms: DIS, DMS, and EMA.

In addition, two more sleep related variables were controlled for in this study. Subjective sleep sufficiency was examined with the question: "When you wake up in the morning, how often do you feel that you have had a good night's rest?" Response categories to this question are the same as those for insomnia symptoms. Those who responded "never" and "seldom" were regarded as having had insufficient sleep, and those who chose one of the three other responses as having had sufficient sleep. This question is the flip side of the question on non-restorative sleep.

Sleep duration was evaluated by the self-reported response to the question: "How many hours do you sleep a day on average?" The responses were classified into 5 categories (< 6 h; ≥ 6 to < 7 h; ≥ 7 to < 8 h; ≥ 8 to < 9 h; ≥ 9 h) and analyzed. Kaneita et al.[2] showed the effect of sleep duration on depression as taking on a U-shape, with the bottom at about 7 hours.

Sociodemographic factors including age, gender, educational history, and present place of residence (rural vs. urban dwellers) were controlled for as in most of the previous studies examining the relationship between depression and insomnia. This is because studies have shown that the prevalence of depression and insomnia increases as age increases, and tends to be higher for females.[2,15,16] Many previous studies of the relationship between insomnia and depression have also controlled for educational history[2,15,16] and current place of residence.[15]

For analyses, age was treated as a categorical variable. Four dummy variables were created for each 5-year age group: that is 70-74, 75-79, 80-84, and ≥ 85. Those aged 65-69 were the reference age group. Educational history was classified into two groups (junior high school or less, and high school or more). The present place of residence was subdivided into two groups, urban and rural, the former denoting cities and towns, and the latter referring to areas engaged in farming, forestry, and fishing.

Three health-related factors were also controlled for in the present study. Previous studies have indicated a higher prevalence of depression among those with psychological stress,[7] poor self-rated health,[30] and activities of daily living (ADL) difficulties.[31,32] Participants were asked if they had psychological stress in their daily life. This required either a "yes" or "no" answer.

Participants were asked about their self-rated health with the question: "How do you rate your present general health condition: 1 excellent; 2 good; 3 fair; 4 poor; 5 very poor?" Their responses were grouped into 3 categories: 1 and 2 as good, 3 as fair, and 4 and 5 as poor.[33] Two dummy variables were created for good and poor, and fair was treated as the reference group in the analyses.

For ADL, participants were asked if the following seven activities were difficult or not difficult to perform: bathing, eating, dressing, getting in and out of bed or chairs, walking inside the house, going outside, and using a toilet. Participants with at least one difficulty were classified as having difficulty.

The study procedure was approved by the Ethics Committee of Nihon University.

Statistical Analyses

First, we computed Pearson correlation coefficient among the three insomnia symptoms (i.e., DIS, EMA, and DMS) in order to examine the relationship among them. The correlation was computed for all the participants, including those without depression at the time of the 3rd survey conducted in 2003.

We examined statistically the association of insomnia with the presence of depression. Comparison was made by using the mean CES-D scores computed for those who were identified as having depression and those who were not. Comparisons of 2 categories were performed with the unpaired Student *t*-test, and comparisons of ≥ 3 categories were performed with one-way ANOVA and the Tukey method of multiple comparison.

The relationship between depression and insomnia symptoms was analyzed on the basis of univariate and multivariate logistic regressions. The cross-sectional study using data from the 3rd survey of NUJLSOA (2003) was conducted by a series of logistic regression analyses. The longitudinal study was conducted only on those without depression in 2003. Insomnia variables in 2003 were then regressed on the presence of depression in 2006, controlling for age, gender, educational history, place of residence, sleep duration, EDS, DFL, subjective sleep sufficiency, psychological stress, self-rated health, and ADL.

Table 1— Comparison of age groups between present study and census data

	Age (y)				
	65-69	70-74	75-79	80-84	85+
Present study in 2003					
Total (%)	32.8	25.2	19.5	13.9	8.7
Men (%)	34.7	27.8	19.0	11.7	6.8
Women (%)	31.2	23.1	19.8	15.6	10.3
Census data in 2000					
Total (%)	32.3	26.8	18.9	11.8	10.1

Values given are percentage in age group. All the numbers listed in Table 1 and onward are weighted so they resemble the extracted values from the population composition and not integers.

The 11-item CES-D scale includes the question on whether sleep was restless. In analyzing the relationship between depression and sleeping problems, a possible bias, especially for cross-sectional analyses, may be introduced by including the sleep-related question in the CES-D scale. We therefore conducted additional analyses with the 10-item CES-D scale, excluding this question. By applying a regression equation, following the method of Kohout et al.,[20] the cut-off point for the 10-item CES-D scale was estimated at 6.5. Because the cut-off points have to be an integer number, scores of 6 and 7 were used to evaluate the relationship between insomnia subtypes and the presence of depression. To evaluate possible biases, both the cross-sectional and longitudinal study were repeated for the presence of depression defined by the 10-item short form of the CES-D scale with the cut-off points of 6 and 7 in order, but excluding the sleep item question.

Statistical analyses were performed with SAS 9.1.[34] The statistical level of significance was $P < 0.05$ (two-sided tests).

RESULTS

Demographic Characteristics

Table 1 compares the age-bracketed proportional composition of elderly Japanese in the third survey conducted in 2003 and in the census data of 2000. The proportional composition at the baseline was similar to that in the census data in all age brackets except for the ≥ 85 bracket, where data used for this study were slightly lower. The average age and standard deviation (minimum to maximum) for the participants were 73.1 ± 6.4 (65 to 99) for 2003 and 75.7 ± 6.1 (67 to 103) for 2006.

Correlation among Insomnia Subtypes

Correlation coefficients among the 3 insomnia subtypes are shown in Table 2. Numbers in the upper triangle correspond to all participants and numbers in the lower triangle correspond to those without depression in the third survey conducted in 2003. The correlation was relatively higher for all the participants of the survey compared to those without depression. In all cases, the Pearson correlation coefficients are < 0.4, and the

Table 2—Pearson correlation coefficient among insomnia subtypes: 2003

Insomnia subtype	DIS	EMA	DMS
DIS	-	0.383*	0.309*
EMA	0.282*	-	0.358*
DMS	0.248*	0.321*	-

Numbers in the upper triangle are based on all participants (N ≅ 4,000). Numbers in the lower triangle are based on participants without depression (N ≅ 3,050). DIS refers to difficulty initiating sleep; EMA, early morning awakening; DMS, difficulty maintaining sleep. *Statistically significant at 0.01 level.

relationship among the 3 insomnia subtypes is considered to be relatively weak.

Prevalence of Insomnia Symptoms and Depression

Table 3 compares participants' attributes. When estimated by means of the 11-item short form CES-D scale, the presence of depression among elderly Japanese (≥ 65 years) stood at 13.8%, as shown in the first line of Table 3. Overall prevalence of insomnia (ANY) for the sample was 27.8%. The prevalence of insomnia subtypes from highest to lowest is as follows: DMS (22.9%); EMA (11.5%); DIS (11.1%). Prevalence of sleep disturbances was 8.1% for EDS and 3.7% for DFL. Overall, 16.8% of elderly Japanese reported subjective insufficient sleep.

The prevalence of depression in the insomnia symptom groups was: DIS (34.8%); EMA (29.1%); and DMS (20.2%). Each insomnia symptom had significantly different average CES-D scores. DIS had the highest average "yes" responses. Elderly Japanese with EDS, DFL, and subjective insufficient sleep seemed to report a relatively higher prevalence of depression: 28.1%, 24.4%, and 23.3%, respectively.

Relationship between Insomnia Symptoms and Depression

Table 4 shows results of the cross-sectional and longitudinal study on the relationship between insomnia (defined as having any one of the insomnia subtypes) and depression in both univariate and multivariate analyses, thereby allowing a comparison of results from previously conducted studies. For multivariate analyses, sleep related, sociodemographic, and health-related factors were controlled. In the cross-sectional study, insomnia (ANY) was statistically significantly related to the presence of depression in both univariate (OR: 2.217 with 95% CI 1.832 to 2.682) and multivariate analyses (aOR: 1.272 with 95% CI 1.000 to 1.618). However, in the longitudinal study, insomnia (ANY) was significant only at 0.1 level in the multivariate analysis (aOR: 1.293 with 95% CI 0.959 to 1.744), while controlling for sleep related, sociodemographic, and health related factors.

Table 5 illustrates the results of the cross-sectional study involving all participants of the third survey. Using a univariate analysis, all insomnia symptoms were found to be significantly related to the presence of depression. The multivariate analysis, on the other hand, demonstrated that only DIS and EMA had a significant relationship to the presence of depression, after controlling for age, gender, educational history, place of residence, sleep duration, EDS, DFL, subjective sleep sufficiency, psychological stress, self-rated health, and ADL. The adjusted odds ratios (95% CI) were 2.020 (1.455 to 2.805) and 1.441 (1.025 to 2.026), respectively.

Table 6 represents the results of the longitudinal study of those without depression in 2003. The presence of depression in 2006 in the participants who had not been suffering from the disease at the time of the 3rd survey was regarded as the response variable and insomnia symptoms as the explanatory variables, after controlling for sleep related, sociodemographic, and health-related factors. DIS, EMA, and DMS were all shown to be significantly related to depression in the univariate analysis; but in the multivariate analysis DIS was the only symptom with a significant relationship to the presence of depression, with an adjusted odds ratio (95% CI) of 1.592 (1.012 to 2.504).

It is worth mentioning that the results indicate that gender, stress, and self-rated health among the control variables had statistically significant effects on the presence of depression. The effect of psychological stress was substantively about the same as DIS with an adjusted odds ratio (95% CI) of 1.553 (1.125 to 2.145). Those who reported their health as poor at the baseline survey were more likely to have depression in the following survey with an adjusted odds ratio (95% CI) of 2.517 (1.778 to 3.562).

In addition, we examined the relationship between the presence of depression and the insomnia subtypes by controlling for the baseline participants' CES-D scores that vary from 0 to 6 with other control variables. The result of this analysis (not shown) differed slightly from the result shown in Table 6. The adjusted odds ratios (95% CI) for DIS, EMA, and DMS were 1.509 (0.957 to 2.381), 1.023 (0.634 to 1.651), and 1.206 (0.853 to 1.706), respectively. Although the significance level of the effect of DIS on depression was slightly affected by controlling for the CES-D score at baseline, the general tendency of the effect of insomnia subtypes was not affected.

Comparison of the Sleep-Item-Excluded 10-Item CES-D Scale with the 11-Item CES-D Scale

The results of the cross-sectional and longitudinal analyses were re-examined based on the 10-item CES-D scale, which, excluding the sleep item, is the 11-item short form of CES-D with 2 different cut-off points (6 and 7). As shown in Table 7, the adjusted odds ratios in the cross-sectional analyses (95% CI) were 1.819 (1.327 to 2.493) for DIS with the cut-off point of 6, and 1.721 (1.214 to 2.439) with the cut-off point of 7. For EMA, the adjusted odds ratios (95% CI) were 1.262 (0.910 to 1.748) with the cut-off point of 6, and 1.476 (1.030 to 2.114) with the cut-off point of 7. In the longitudinal analyses, the adjusted odds ratios (95% CI) were 1.659 (1.047 to 2.629) for DIS with the cut-off point of 6, and 1.444 (0.936 to 2.227) with the cut-off point of 7. Although there are slight differences between the 10-item scale and the 11-item scale, the general tendency appears to be similar.

From the cross-sectional analyses, DIS and EMA appeared to be associated with the presence of depression. Only DIS, however, demonstrated a significant relationship to the development of depression with the cut-off point of 6 when the sleep item was removed from the 11-item short form of the CES-D Scale.

Table 3—Sample distribution, prevalence of depression and mean CES-D scores by categories of sample attributes and self-reported responses, and results of statistical test for mean CES-D scores among categories in 2003

Baseline items in 2003 Category	Percentage of category (%)	Prevalence of depression* (%)	11-item short forms of the CES-D score (mean ± SD)	Statistical test for mean CES-D scores#
Total	100.0	13.8	4.1 ± 2.7	
Age (year)				
65-69	32.8	10.2	3.8[a] ± 2.7	P <= 0.001[#1]
70-74	25.2	13.9	4.2 ± 3.0	
75-79	19.5	15.9	4.3[b] ± 2.9	
80-84	13.9	19.3	4.4[c] ± 2.2	
85+	8.7	15.9	4.4[d] ± 2.1	
Gender				
Women	55.0	16.0	4.2 ± 2.8	P = 0.006
Men	45.0	11.1	4.0 ± 2.5	
Sleep duration (h)				
< 6	10.7	21.2	4.7[a] ± 3.4	P < 0.001[#2]
≥ 6 to 7	19.7	13.1	4.0[b] ± 5.0	
≥ 7 to 8	23.9	10.7	3.8[c] ± 2.5	
≥ 8 to 9	29.8	12.0	3.9[d] ± 2.5	
≥ 9	15.9	18.0	4.5[e] ± 2.7	
Educational history				
Junior high school	55.4	15.9	4.3 ± 2.6	P < 0.001
More than high school	44.6	11.3	3.9 ± 2.8	
Place of residence				
Urban	68.0	13.9	4.2 ± 2.4	P = 0.037
Rural	32.0	13.8	4.0 ± 2.8	
Sleep disturbance				
Any ins: Yes	27.8	21.0	4.8 ± 3.2	P < 0.001
No	72.2	10.7	3.8 ± 2.4	
DIS: Yes	11.1	34.8	6.0 ± 3.7	P < 0.001
No	88.9	11.2	3.9 ± 2.4	
EMA: Yes	11.5	29.1	5.7 ± 3.6	P < 0.001
No	88.5	11.9	3.9 ± 2.5	
DMS: Yes	22.9	20.2	4.8 ± 3.2	P < 0.001
No	77.1	11.9	3.9 ± 2.5	
EDS: Yes	8.1	28.1	5.2 ± 3.9	P < 0.001
No	91.9	12.6	4.0 ± 2.5	
DFL: Yes	3.7	24.4	5.3 ± 3.5	P < 0.001
No	96.3	13.4	4.0 ± 2.6	
Subjective sleep sufficiency				
Insufficient	16.8	23.3	5.0 ± 3.2	P < 0.001
Sufficient	83.2	11.7	3.9 ± 2.5	
Psychological stress				
Yes	25.1	32.9	5.7 ± 3.5	P < 0.001
No	74.9	7.4	3.6 ± 2.1	
Self-rated health				
Good	31.9	5.6	3.3[a] ± 2.1	P < 0.001[#3]
Fair	40.3	10.1	3.9[b] ± 2.3	
Poor	27.8	32.5	5.7[c] ± 3.3	
Activity of daily living (ADL)				
Any	12.7	35.9	6.0 ± 3.3	P < 0.001
None	87.3	11.8	3.9 ± 2.5	

*Calculation of prevalence (%) was conducted by 11-item Short Forms of CES-D (cut-off point = 7). #Comparisons of 2 categories were performed with unpaired Student *t*-test; and comparison of ≥ 3 categories were performed with one way ANOVA and Tukey method of multiple comparison [#1]Statistically significant pairs among the age groups were [a] and [b], [a] and [c], [a] and [d], [a] and [e]. [#2]Statistically significant pairs among the sleep durations were [a] and [b], [a] and [c], [d] and [e], [c] and [e]. [#3]Statistically significant pairs among the categories of self-rated health were [a] and [b], [a] and [c], [b] and [c]. Any ins refers to any of DIS, EMA or DMS; DIS, difficulty initiating sleep; EMA, early morning awakening; DMS, difficulty maintaining sleep; EDS, excessive daily sleepiness; DFL, discomfort feeling in the legs.

Table 4—Association between depression and ANY insomnia subtypes by univariate and multivariate analyses in the cross-sectional study and longitudinal study[a]

	Univariate logistic regression analysis					
Baseline items in 2003	**Cross-sectional study in 2003**			**Longitudinal study from 2003 to 2006**		
Category	**OR[b]**	**95% CI**	**P-value**	**OR[b]**	**95% CI**	**P-value**
Sleep disturbance						
ANY ins: Yes	2.217	1.832 to 2.682	< 0.001	1.460	1.111 to 1.918	0.007
No	1.000	referent		1.000	referent	
	Multivariate logistic regression analysis					
Baseline items in 2003	**Cross-sectional study in 2003**			**Longitudinal study from 2003 to 2006**		
Category	**aOR[c]**	**95% CI**	**P-value**	**aOR[c]**	**95% CI**	**P-value**
Age (y)						
65-69	1.000	referent		1.000	referent	
70-74	1.358	1.005 to 1.836	0.046	1.252	0.894 to 1.753	0.191
75-79	1.626	1.183 to 2.235	0.003	1.020	0.688 to 1.511	0.922
80-84	2.008	1.399 to 2.883	0.000	1.394	0.876 to 2.218	0.161
85+	1.609	0.959 to 2.700	0.072	1.384	0.654 to 2.928	0.396
Gender						
Women	1.361	1.076 to 1.722	< 0.001	1.298	0.979 to 1.720	0.070
Men	1.000	referent		1.000	referent	
Educational history						
Junior high school	0.864	0.742 to 1.005	0.059	0.924	0.777 to 1.098	0.368
More than high school	1.000	referent		1.000	referent	
Place of residence						
Urban	1.073	0.804 to 1.374	0.577	1.000	0.743 to 1.346	0.999
Rural	1.000	referent		1.000	referent	
Sleep duration (h)						
< 6	1.337	0.905 to 1.973	0.144	0.875	0.508 to 1.505	0.629
≥ 6 to 7	1.015	0.722 to 1.428	0.932	1.259	0.851 to 1.865	0.249
≥ 7 to 8	1.000	referent		1.000	referent	
≥ 8 to 9	1.083	0.783 to 1.497	0.631	1.218	0.842 to 1.764	0.295
≥ 9	1.289	0.884 to 1.877	0.187	1.126	0.693 to 1.828	0.632
Sleep disturbance						
ANY ins: Yes	1.272	1.000 to 1.618	< 0.001	1.293	0.959 to 1.744	0.092
No	1.000	referent		1.000	referent	
EDS: Yes	1.418	1.008 to 1.995	0.045	0.850	0.497 to 1.453	0.551
No	1.000	referent		1.000	referent	
DFL: Yes	0.853	0.506 to 1.439	0.551	1.096	0.494 to 2.429	0.822
No	1.000	referent				
Subjective sleep sufficiency						
Insufficient	1.867	1.426 to 2.444	< 0.001	1.045	0.711 to 1.536	0.822
Sufficient	1.000	referent		1.000	referent	
Psychological stress						
Yes	5.357	4.246 to 6.758	< 0.001	1.633	1.187 to 2.246	0.003
No	1.000	referent		1.000	referent	
Self-rated health						
Good	0.671	0.491 to 0.918	0.013	0.824	0.597 to 1.137	0.239
Fair	1.000	referent		1.000	referent	
Poor	2.917	2.254 to 3.774	< 0.001	2.533	1.793 to 3.579	< 0.001
Activity of daily living (ADL)						
Any	1.496	1.053 to 2.124	0.024	1.251	0.691 to 2.262	0.460
None	1.000	referent		1.000	referent	

[a]The cross-sectional study was conducted on baseline subjects in 2003; the longitudinal study was conducted on subjects who participated in both the 2003 and 2006 surveys. [b]Crude odds ratio due to univariate logistic regression analysis. [c]Adjusted odds ratio due to multivariate logistic regression analysis. ANY ins refers to any of difficulty initiating sleep, early morning awakening, or difficulty maintaining sleep; EDS, excessive daytime sleepiness; DFL, discomfort feeling in the legs; 95%CI, 95% confidence interval.

DISCUSSION

An important feature of this study is that it was designed longitudinally so that the relationship between insomnia symptoms and depression could be examined in temporal order. A second feature is that we differentiated among the diverse components of insomnia, namely, DIS, EMA, and DMS. The study indicated that DIS had a statistically significant relationship to developing depression three years later, while EMA and DMS did not. As far as we know, there have been no reports, based on longitudinal studies of elderly Japanese, on this relationship. Our findings thus provide an important reference point for further studies on the association between insomnia subtypes and depression.

A sizable literature supports insomnia as a risk factor for depression. Yet, insomnia is a composite pathological entity consisting of such various symptoms as DIS, EMA, and DMS, and it has not been established which of these contribute to the development of depression. On the basis of the survey results on the Japanese general population in 2000, Kaneita et al.[2] reported that DIS, EMA, and DMS were related independently to depression. Although their investigation enabled us to understand the significance and separate correlation between these symptoms and depression, because of the cross-sectional nature of the data, their study could not assess the direction of effect between each symptom and the presence of depression. Our current study takes us one step further towards understanding the relationship between the presence of depression and subtypes of insomnia.

Previous studies on depression using cross-sectional data have attached more importance to EMA than DIS.[3,35] Although in our own univariate and multivariate cross-sectional analyses a significant relationship was found between EMA and the presence of depression, no statistically significant relationship between them was found in our multivariate longitudinal analysis. In the present investigation we adjusted for these associated phenomena by employing multivariate analysis; otherwise it might have been possible

for EMA to present a seemingly high correlation. To elucidate the relationship between insomnia symptoms and depression, it appears essential to design longitudinal studies with due attention to the adjustment of associative factors. As a result, we found a statistically significant relationship between DIS and the presence of depression, but not between EMA and depression. In addition, we found a statistically and substantively significant effect of psychological stress and poor self-rated health on the presence of depression. These relationships may need to be studied further using longitudinal data.

Our findings, moreover, may shed light on the bidirectional relationship between insomnia and depression. Buysse et al.,[13] using a longitudinal cohort study of young adults, expressed the bidirectional relationship between insomnia and depression in temporal order without specifying particular insomnia subtypes. They stated that "insomnia predicted future MDE (major depressive episodes) and that MDE tended to predict future insomnia." Based on our study, DIS seems to precede the presence of depression. Rodin et al.[17] followed 196 subjects aged 62 and over for three years and indicated that depression is related to sleep disturbance, particularly EMA. EMA possibly arose as a result of depression. If one were to examine, using longitudinal data, the relationship between depression and insomnia as a composite measure that includes DIS and EMA, one might find a bidirectional relationship between depression and insomnia. If this relationship between DIS, depression, and EMA holds in the cross-sectional studies, we should observe the significant association both between DIS and depression, and depression and EMA, as observed in the present study. However, the results from the cross-sectional studies may be misleading. In the future, we plan to study the relationship between the presence of depression and EMA in the opposite direction, as examined by Rodin et al.[17]

Although our study produced different results from those of previous studies, it is quite difficult to compare

Table 5—Association between depression and insomnia subtypes in the cross-sectional study[a]

	Logistic regression analyses					
Baseline items in 2003	**Univariate analysis**			**Multivariate analysis**		
Category	**OR[b]**	**95% CI**	**P-value**	**aOR[c]**	**95% CI**	**P-value**
Age (year)						
65-69	1.000	referent		1.000	referent	
70-74	1.423	1.101 to 1.838	0.006	1.359	1.001 to 1.844	0.049
75-79	1.675	1.282 to 2.189	< 0.001	1.620	1.174 to 2.235	0.003
80-84	2.121	1.584 to 2.841	< 0.001	1.986	1.375 to 2.867	< 0.001
85+	1.673	1.117 to 2.508	0.013	1.516	0.889 to 2.583	0.126
Gender						
Women	1.526	1.257 to 1.853	< 0.001	1.327	1.047 to 1.681	0.019
Men	1.000	referent		1.000	referent	
Educational history						
Junior high school	0.669	0.552 to 0.811	< 0.001	0.790	0.622 to 1.004	0.054
More than high school	1.000	referent		1.000	referent	
Place of residence						
Urban	0.987	0.807 to 1.208	0.898	1.066	0.830 to 1.370	0.616
Rural	1.000	referent		1.000	referent	
Sleep duration (h)						
< 6	2.238	1.628 to 3.075	< 0.001	1.162	0.776 to 1.742	0.466
≥ 6 to 7	1.261	0.939 to 1.693	0.124	0.944	0.667 to 1.337	0.747
≥ 7 to 8	1.000			1.000	referent	
≥ 8 to 9	1.132	0.858 to 1.495	0.380	1.098	0.792 to 1.521	0.575
≥ 9	1.823	1.337 to 2.487	<0.001	1.349	0.923 to 1.972	0.122
Sleep disturbance						
DIS: Yes	4.208	3.329 to 5.319	< 0.001	2.020	1.455 to 2.805	< 0.001
No	1.000	referent		1.000	referent	
EMA: Yes	3.049	2.403 to 3.870	< 0.001	1.441	1.025 to 2.026	0.036
No	1.000	referent		1.000	referent	
DMS: Yes	1.869	1.525 to 2.289	< 0.001	0.819	0.613 to 1.094	0.176
No	1.000	referent		1.000	referent	
EDS: Yes	2.716	2.064 to 3.574	< 0.001	1.319	0.929 to 1.875	0.122
No	1.000	referent		1.000	referent	
DFL: Yes	2.131	1.465 to 3.101	< 0.001	0.788	0.463 to 1.342	0.381
No	1.000	referent		1.000	referent	
Subjective sleep sufficiency						
Insufficient	2.290	1.839 to 2.852	< 0.001	1.758	1.335 to 2.315	< 0.001
Sufficient	1.000	referent		1.000	referent	
Psychological stress						
Yes	6.104	4.997 to 7.455	< 0.001	5.169	4.088 to 6.537	< 0.001
No	1.000	referent		1.000	referent	
Self-rated health						
Good	0.531	0.397 to 0.709	< 0.001	0.664	0.485 to 0.910	0.011
Fair	1.000	referent		1.000	referent	
Poor	4.270	3.435 to 5.307	< 0.001	2.187	3.688 to 3.231	< 0.001
Activities of daily living (ADL)						
Any	4.180	3.211 to 5.443	< 0.001	1.419	0.991 to 2.032	0.056
None	1.000	referent		1.000	referent	

[a]The cross-sectional study was conducted on baseline subjects in 2003. [b]Crude odds ratio due to univariate logistic regression analysis. [c]Adjusted odds ratio due to multivariate logistic regression analysis. The logistic regression analysis was conducted as a response variable of CES-D (Score ≥ 7) by the short form. DIS refers to difficulty initiating sleep; EMA, early morning awakening; DMS, difficulty maintaining sleep; EDS, Exceesive daytime sleepiness; DFL, discomfort feeling in the legs; 95%CI, 95% confidence interval.

Table 6—Association between depression and insomnia subtypes in the longitudinal study (2003-2006)[a] for subjects without depression in 2003

Baseline items in 2003	Logistic regression analyses					
	Univariate analysis			Multivariate analysis		
Category	OR[b]	95% CI	P-value	aOR[c]	95% CI	P-value
Age (y)						
65-69	1.000	referent		1.000	referent	
70-74	1.333	0.966 to 1.840	0.081	1.219	0.869 to 1.711	0.252
75-79	1.144	0.788 to 1.660	0.480	1.006	0.677 to 1.493	0.978
80-84	1.728	1.131 to 2.640	0.012	1.347	0.841 to 2.157	0.215
85+	1.657	0.851 to 3.224	0.137	1.344	0.634 to 2.849	0.441
Gender						
Women	1.253	0.966 to 1.627	0.090	1.327	1.000 to 1.761	0.050
Men	1.000	referent		1.000	referent	
Educational history						
Junior high school	0.874	0.675 to 1.131	0.306	0.906	0.680 to 1.206	0.499
More than high school	1.000	referent		1.000	referent	
Place of residence						
Urban	0.948	0.721 to 1.246	0.700	0.968	0.718 to 1.305	0.832
Rural	1.000	referent		1.000	referent	
Sleep duration (h)						
< 6	1.147	0.694 to 1.894	0.593	0.849	0.487 to 1.481	0.564
≥ 6 to 7	1.378	0.948 to 2.004	0.093	1.227	0.824 to 1.828	0.314
≥ 7 to 8	1.000	referent		1.000	referent	
≥ 8 to 9	1.246	0.878 to 1.770	0.219	1.218	0.839 to 1.767	0.300
≥ 9	1.319	0.840 to 2.073	0.229	1.175	0.722 to 1.912	0.517
Sleep disturbances						
DIS: Yes	2.042	1.391 to 2.997	< 0.001	1.592	1.012 to 2.504	0.044
No	1.000	referent		1.000	referent	
EMA: Yes	1.541	1.030 to 2.306	0.035	1.070	0.664 to 1.723	0.782
No	1.000	referent		1.000	referent	
DMS: Yes	1.432	1.066 to 1.925	0.017	1.215	0.860 to 1.716	0.269
No	1.000	referent		1.000	referent	
EDS: Yes	1.401	0.869 to 2.260	0.166	0.819	0.477 to 1.408	0.471
No	1.000	referent		1.000	referent	
DFL: Yes	2.120	1.125 to 3.995	0.020	0.990	0.440 to 2.230	0.981
No	1.000	referent		1.000	referent	
Subjective sleep sufficiency						
Insufficient	1.093	0.760 to 1.573	0.631	1.051	0.713 to 1.547	0.803
Sufficient	1.000	referent		1.000	referent	
Psychological stress						
Yes	1.846	1.375 to 2.479	< 0.001	1.553	1.125 to 2.145	0.008
No	1.000	referent		1.000	referent	
Self-rated health						
Good	0.745	0.546 to 1.016	0.063	0.794	0.574 to 1.099	0.164
Fair	1.000	referent		1.000	referent	
Poor	2.589	1.881 to 3.563	< 0.001	2.517	1.778 to 3.562	< 0.001
Activity of daily living (ADL)						
Any	2.223	1.312 to 3.766	0.003	1.207	0.664 to 2.193	0.538
None	1.000	referent		1.000	referent	

[a]The longitudinal study was conducted on subjects participating in the 2003 and 2006 surveys, with the former serving as the baseline. [b]Crude odds ratio due to univariate logistic regression analysis. [c]Adjusted odds ratio due to multivariate logistic regression analysis, the logistic regression analysis was conducted as a response variable of CES-D (score ≥ 7) by Shorter Form in 2006.
DIS refers to difficulty initiating sleep; EMA, early morning awakening; DMS, difficulty maintaining sleep; EDS, excessive daytime sleepiness; DFL, discomfort feeling in the legs; 95%CI, 95% confidence interval.

studies on the relationship between insomnia and depression because the definition, criteria, and measures of insomnia and depression were different for each study. One plausible reason why we had different results is that our criteria for insomnia symptoms were less strict and, therefore, individuals with transient and minor sleep disturbances may have been included. More specifically, it may have caused a relative increase in sleep maintenance complaints among the elderly population. As a result, minor transient insomniacs may have diluted the clinical sample of sleep maintenance insomniacs, possibly reducing the specificity of this particular symptom for predicting later presence of depression.

Insomnia, which is defined rather loosely in our study, could be another concern for our longitudinal study. As mentioned before, questions on insomnia subtypes used in the study relied on self-reports without reference to time. Our findings were not particularly robust, and odds ratios in our results were relatively low compared to ones found in previous longitudinal studies. In order to examine the effect of changes in definitions of insomnia, we have run another model for a longitudinal study with more strict criteria for insomnia subtypes. We defined presence of insomnia subtypes only for those who answered "always" (we included both "often" and "always" in our present study because of obtaining stable estimates). Adjusted odds ratios (95% CI) for DIS increased from 1.592 (1.012 to 2.504) to 2.086 (1.091 to 3.989) with a significance level of 0.026. This indicates that to examine the relationship between DIS and depression in the longitudinal study may be warranted. In any case, given that epidemiological data on the relationship between insomnia subtypes and the development of depression are relatively scarce, it is hoped that many more longitudinal studies on this subject will be carried out and more knowledge accumulated.

Study Limitations

This study has a few limitations. First, our study participants were limited to those aged 65 and older.

Studies with the general population should be conducted to see whether our conclusions apply to the population at large.

Second, we evaluated depression using only the CES-D scale. Neither the DSM-IV[4] nor the ICD-10[36] are applicable to a community-based survey, and, therefore, could not be employed to diagnose clinically the subjects of our study. Many epidemiological studies have, in fact, relied on the CES-D scale, as its reliability and validity have been sufficiently established. Nevertheless, given that comparing disease prevalence among regions is problematic[37] and that clinical diagnoses and CES-D scale evaluations of depression do not always agree,[38] the use of other diagnostic methods should be considered in the future.

Third, because at the time of the baseline survey we did not ask participants whether they had ever had depression before, we may be examining the relationship between insomnia subtypes and recurrence of depression rather than between insomnia subtypes and initial onset of depression.

Fourth, as is commonly found in epidemiological work, we did not have objective data on disturbed sleep. While it is desirable to obtain objective data, it is very difficult to conduct such studies on a community scale. More objective and yet simple epidemiological research techniques should be developed. In addition, we did not make an insomnia diagnosis using established criteria. We simply used endorsement of specific insomnia subtypes which did not include a time frame or frequency. Moreover, because of the data limitation, we did not utilize daytime impairment/dysfunction as required by most current insomnia nosologies.

Fifth, the association between insomnia symptoms and the presence of depression was evaluated only at two points in the three-year period. No specific information on depression was obtained regarding when during the three years the condition developed, nor how long the condition lasted. In addition, three years may be too long to observe the association between insomnia symptoms and depression. Although, as in the present study, several longitudinal studies on sleep disorder have evaluated results using information from two study points, the number of observation points chosen and the duration of the study should receive careful consideration in future studies.

Lastly, we should point out the possibility of non-response bias in our study. Because a longitudinal study is destined to lose participants by death and lost-to-follow-up, only those who have managed to maintain health tend to be surveyed in the follow-up. In addition, proxy responses and non response to CES-D questions tend to increase as participants age. In order for the study of precursor symptoms and risk factors of insomnia to be meaningful, due attention in future studies should be given to the upper age limit in studies.

Despite these limitations, we hope that our study results will contribute to the future progress of mental health care and the solution of sleeping problems. If our findings are found to be true by clinical research, DIS subtype is possibly a better predictor of depression than overall insomnia severity. By understanding better the relationship between depression and insomnia subtypes, we may have a chance to lower the prevalence of depression among older adults in Japan.

Table 7—Comparison of adjusted odds ratios (95% CI) of 10-item CES-D scale and 11-item CES-D scale based on multivariate analyses of the association of insomnia subtypes with depression in cross-sectional and longitudinal study

	10-item CES-D Scale				11-item CES-D Scale*	
	Cut-off point = 6		Cut-off point = 7		Cut-off point = 7	
	Cross-sectional study					
Insomnia Subtypes	aOR#	95%CI	aOR	95%CI	aOR	95%CI
DIS	1.819	(1.327 to 2.493)	1.721	(1.214 to 2.439)	2.020	(1.455 to 2.805)
EMA	1.262	(0.910 to 1.748)	1.476	(1.030 to 2.114)	1.441	(1.025 to 2.026)
DMS	0.874	(0.669 to 1.142)	0.899	(0.662 to 1220)	0.819	(0.613 to 1.094)
	Longitudinal study					
	aOR	95%CI	aOR	95%CI	aOR	95%CI
DIS	1.659	(1.047 to 2.629)	1.444	(0.936 to 2.227)	1.592	(1.012 to 2.504)
EMA	1.242	(0.773 to 1.993)	1.153	(0.735 to 1.808)	1.070	(0.664 to 1.723)
DMS	1.304	(0.916 to 1.854)	1.263	(0.905 To 1.763)	1.215	(0.860 to 1.716)

*Results were taken from Table 5 for the cross-sectional study and from Table 6 for the longitudinal study. #aOR: adjusted odds ratio and 95%CI; 95% confidence interval. Logistic regression analysis was conducted by controlling for age, gender, educational history, place of residence, sleep duration, excessive day time sleepiness, discomfort feeling in the legs, subjective sleep sufficiency, psychological stress, self-rated health, and activities of daily living. DIS refers to difficulty initiating sleep; EMA, early morning awakening; DMS, difficulty maintaining sleep.

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REFERENCES

1. Murray CJL, Lopez AD, eds. The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020. Cambridge, MA, Harvard School of Public Health on behalf of World Health Organization and the World Bank, 1996 (Global Burden of Disease and Injury Series, Vol. I).
2. Kaneita Y, Ohida T, Uchiyama M, et al. The relationship between depression and sleep disturbances: a Japanese nationwide general population survey. J Clin Psychiatry 2006; 67:196-203.
3. Lustberg L, Reynolds CF. Depression and insomnia: questions of cause and effect. Sleep Med Rev 2000;4:253-62.

4. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, 4th ed. Washington, DC: American Psychiatric Association, 1994.
5. Ford DE, Kamerow DB. Epidemiologic study of sleep disturbances and psychiatric disorders. An opportunity for prevention? JAMA 1989;262:1479-84.
6. Breslau N, Roth T, Rosenthal L, et al. Sleep disturbance and psychiatric disorders: a longitudinal epidemiological study of young adult. Biol Psychiatry 1996;39:411-8.
7. Chang PP, Ford DE, Mead LA, et al. Insomnia in young men and subsequent depression: the Johns Hopkins precursors study. Am J Epidemiol 1997;146:105-14.
8. Riemann D, Voderholzer U. Primary insomnia: a risk factor to develop depression? J Affect Disord 2003;76:255-9.
9. Brabbins CJ, Dewey ME, Copeland RM, et al. Insomnia in the elderly: prevalence, gender differences and relationship with morbidity and mortality. Int J Geriatr Psychiatry 1993;8:473-80.
10. Foley DJ, Monjan A, Simonsick EM, et al. Incidence and remission of insomnia among elderly adults: an epidemiological study of 6800 persons over 3 years. Sleep 1999;22(Suppl2):366-72.
11. Morphy H, Dunn KM, Lewis M, Boardman HF, Croft PR. Epidemiology of insomnia: a longitudinal study in a UK population. Sleep 2007;30:274-80.
12. Neckelmann D, Mykletun A, Dahl AA. Chronic Insomnia as a risk factor for developing anxiety and depression. Sleep 2007;30:873-80.
13. Buysse DJ, Angst JA, Gamma A, et al. Prevalence, course, and comorbidity of insomnia and depression in young adults. Sleep 2008; 31:473-80.
14. Jansson-Frojmark M, Lindblom K. A bidirectional relationship between anxiety and depression, and insomnia? A prospective study in the general population. J Psychosom Res 2008; 64:443-9.
15. Kim JM, Stewart R, Kim SW, et al. Insomnia, depression, and physical disorders in late life: a 2-year longitudinal community study in Korea. Sleep 2009;32:1221-8.
16. Hartz AJ, Daly JM, Kohatsu ND, et al. Risk factors for insomnia in a rural population. Ann Epidemiol 2007;17: 940-7.
17. Rodin J, McAvay G, Timko C. A longitudinal study of depressed mood and sleep disturbances in elderly adults. J Gerontol 1988;43:45-53.
18. Sukegawa T, Itoga M, Seno H, et al. Sleep disturbance and depression in the elderly in Japan. Psychiatry Clin Neurosci 2003; 57:265-70.
19. Saito Y. A survey on health and lifestyle. Report series No.1. The Nihon University Center for Information Networking 2000. (in Japanese)
20. Kohout FJ, Berkman LF, Evans DA, Huntley JC. Two shorter forms of the CES-D depression symptom index. J Aging Health 1993;5:179-93.
21. Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. Appl Psychol Meas 1977;1:385-401.
22. Shima S, Shikano T, Kitamura T, Asai M. New self-rating scales for depression. SEISHIN IGAKU 1985; 27:717-723. (in Japanese)
23. Yokoyama E, Kaneita Y, Saito Y, et al. Cut-off point for the 11-item shorter form of the CES-D Depression Scale. Nihon Univ. J Med 2008;50:123-32.
24. Kim K,Uchiyama M,Okawa M,Liu X, Ogihara R. An epidemiological study of insomnia among the Japanese general population. Sleep 2000;23:41-7.
25. Liu X, Uchiyama M, Kim K, et al. Sleep loss and daytime sleepiness in the general adult population of Japan. Psychiatr Res 2000;93:1-11.
26. Ohida T, Osaki Y, Doi Y, et al. An epidemiologic study of self-reported sleep problems among Japanese adolescents. Sleep 2004;27:975-85.
27. Kaneita Y, Ohida T, Uchiyama M, et al. Excessive daytime sleepiness among Japanese general population. J Epidemiol 2005;15:1-8.
28. Suzuki K, Ohida T, Sone T, et al. The prevalence of restless legs syndrome among pregnant women in Japan and the relationship between restless legs syndrome and sleep problems. Sleep 2003; 26:673-7.
29. Ekbom KA. Restless legs. Acta Med Scand 1945; 158 (Suppl):4-122.
30 Roberts RE, Kaplan GA, Shema SJ, et al. Prevalence and correlates of depression in an aging cohort: the Alameda county study. J Gerontol B Psychol Sci Soc Sci 1997; 52B:S252-8.
31. Livingston G, Blizard B, Mann A. Does sleep disturbance predict depression in elderly people? A study in inner London. Br J Gen Pract 1993;43:445-8.
32. Roberts RE, Shema SJ, Kaplan GA, Strawbridge WJ. Sleep complaints and depression in an aging cohort: A prospective perspective. Am J Psychiatry 2000;157:81-88.
33. Idler EL, Benyamini Y. Self-rated health and mortality. A review of twenty-seven community studies. J Health Soc Behav 1997; 38: 21-37.
34. SAS Institute Inc. SAS User's Guide: Statistics, Version 9.1. 2004. Cary, NC. USA.
35. Reynolds CF, Hoch CC, Kuper DJ et al. Bedside differentiation of depression pseudodementia from dementia. Am J Psychiatry 1988;145:1099-103.
36. World Health Organization. International Classification of Disease and Related Health Problems 10th Revision, 1992.
37. Mackinnon A, MaCallum J, Anderson I. The Center for Epidemiological Studies Depression Scale in older samples in Indonesia, North Korea, Myanmar, Sri Lanka, and Thailand. J Gerontol B Psychol Sci Soc Sci 1998;53:343-52.
38. Katona C, Livingstone G. Impact of screening of old people with physical illness for depression? Lancet 2000;356:91-2.

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Sleep-related problems and use of hypnotics in inpatients of acute hospital wards

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Abstract

Objective: Although sleep disorders are highly prevalent among patients with physical disorders, only limited information is available about the actual status of sleep-related problems in inpatients of acute hospital wards. We conducted a multicenter cross-sectional observational survey investigating the prevalence of sleep disorders and use of hypnotic-sedative drugs among inpatients of acute wards in 44 general hospitals in Japan.

Method: Questionnaire-, actigraph- and observation-based sleep evaluations were simultaneously performed in 557 adult inpatients [mean age 72.8±12.8 (S.D.) years] of acute wards during a one-month period in July 2007.

Results: Of the 421 patients with data available, 22.3% had at least one of the following sleep disorders: sleep apnea syndrome, restless legs syndrome, periodic limb movement disorder and nocturnal behavior disorder. Similarly, 62.7% had insomnia, 6.9% had severe daytime sleepiness and 12.8% had other sleep-related symptoms. Only 13.8% were free of any sleep-related problem. Although 33.7% of insomnia patients were taking hypnotic-sedative drugs, 65.2% of them complained of residual insomnia symptoms.

Conclusion: The findings obtained in this study have revealed the remarkably high prevalence of sleep-related problems experienced by inpatients of acute hospital wards in Japan. Proper diagnosis of sleep disorders should be made among patients with physical disorders.

Keywords: Sleep disorders; Insomnia; Acute hospital wards; Physical illness; Hypnotic use

1. Introduction

Sleep disorders, including insomnia, sleep apnea syndrome (SAS), restless legs syndrome (RLS) and periodic limb movement disorder (PLMD), are highly prevalent and particularly common in elderly patients with physical disorders. Sleep disorders reduce patients' quality of life (QOL) by causing symptoms such as daytime sleepiness and cognitive impairment and may also exacerbate underlying disorders by inhibiting respiratory, cardiovascular and

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metabolic functions. In one study of older patients in a skilled-care geriatric hospital in Japan, the presence of insomnia was associated with a higher risk of mortality during the 2-year follow-up period [1].

The prevalence of these sleep disorders increases with age [2], and the high incidence of physical disorders among the elderly population is a contributing factor. Previous epidemiologic studies have revealed that the prevalence of insomnia among the general population is 10.2–48.0% [3–6], and insomnia frequently occurs in association with chronic pain disorders, respiratory diseases and neurological diseases [7]. SAS, RLS or PLMD also frequently coexists with various physical diseases including hypertension [8], ischemic heart disease [9,10], chronic kidney failure [11], iron-deficiency anemia [12] and neurological diseases such as Parkinson's disease [13]. It is also noteworthy that medications used for the treatment of sleep disorders may worsen physical disorders; for example, most standard hypnotics benzodiazepines cause *sleep apnea* by reducing the muscle tone of the upper respiratory tract during sleep [14].

The fact that physical and sleep disorders can coexist at a high frequency should always be taken into account when making an accurate diagnosis and developing a treatment strategy that provides a favorable risk-benefit balance. Nevertheless, we currently have only limited information about the actual status of sleep-related problems experienced by inpatients of acute hospital wards. Thus, the objectives of the present study were to investigate the breakdown and prevalence of sleep disorders and use of hypnotic-sedative drugs in acute ward inpatients and to identify problems in the clinical practice of sleep medicine.

2. Methods

2.1. Subjects and method

Study subjects who were 20 years of age or more were randomly selected from among the inpatients of acute hospital wards, excluding psychiatric and tuberculosis wards, of 44 general hospitals in Japan. The patients' identities were coded at each hospital ward, and then patients were randomly sampled. The investigation was carried out among 557 subjects [316 males, 241 females; mean age, 72.8±12.8 (S.D.) years; range 22–96 years] who had provided informed consent or whose family member had provided informed consent, simultaneously at all hospitals during a period of 1 month in July 2007. Each patient's primary disorder was classified according to the International Classification of Diseases and Related Health Problems Version 10 (*ICD-10*) (Table 1). The ethics committee at each research site approved the present study.

2.2. Investigation methods

The investigation was conducted over 2 days for each patient to check his or her sleep condition and details of treatment. The investigation consisted of subjective sleep evaluation using a self-administered questionnaire (Table 2), objective sleep evaluation by actigraphy, observational sleep evaluation by nursing staff and a survey of medication use as recorded in the medical records.

The questionnaire was designed to identify the presence of insomnia, SAS, RLS, PLMD, nocturnal behavior disorder (NBD), daytime sleepiness and nocturnal sleep-related symptoms. In the questionnaire, Q1–Q6 were completed by the patients, and Q7 and Q8 were completed by medical staff. Although NBD can be further divided into nocturnal delirium, REM sleep behavior disorder, behavioral and psychological symptoms of dementia and other symptoms, these disorders were not distinguished in view of the primary objective of the present study and technical restrictions.

For objective sleep evaluation, subjects were asked to wear an actigraph [Lifecorder PLUS (LC), Suzuken, Nagoya, Japan] [15] on their waist for two consecutive days for continuous recording of the intensity of activity. Total sleep time (TST; the sum of all sleep time during time in bed), total wake time (TWT; the sum of all wake time during time in bed) and sleep efficiency (SE; the percentage of TST relative to time in bed) were then calculated from the LC data. Time in bed (TIB) was defined as the time during

Table 1
Illness identified in enrolled patients

System organ/disease class	Total	SAS, RLS, PLMD and NBD	Insomnia			Good Sleep
	557 (100%)	94 (100%)	Improved 31 (100%)	Untreated 175 (100%)	Not-Improved 58 (100%)	63 (100%)
Diseases of the circulatory system	140 (25.1)	20 (21.3)	7 (22.6)	44 (25.1)	9 (15.5)	15 (23.8)
Neoplasms	127 (22.8)	19 (20.2)	5 (16.1)	47 (26.9)	26 (44.8)	8 (12.7)
Diseases of the respiratory system	68 (12.2)	11 (11.7)	3 (9.7)	17 (9.7)	8 (13.8)	9 (14.3)
Diseases of the digestive system	62 (11.1)	13 (13.8)	2 (6.5)	21 (12.0)	7 (12.1)	8 (12.7)
Diseases of the nervous system	45 (8.1)	11 (11.7)	2 (6.5)	9 (5.1)	3 (5.2)	5 (7.9)
Diseases of the genitourinary system	16 (2.9)	4 (4.3)	1 (3.2)	5 (2.9)	1 (1.7)	3 (4.9)
Diseases of the musculoskeletal system and connective tissue	14 (2.5)	2 (2.1)	1 (3.2)	7 (4.0)	0 (0.0)	3 (4.9)
Certain infectious and parasitic diseases	8 (1.4)	0 (0.0)	1 (3.2)	3 (1.7)	1 (1.7)	0 (0.0)
Other diseases	77 (13.8)	14 (14.9)	9 (29.0)	22 (12.6)	3 (5.2)	12 (19.0)

SAS; sleep apnea syndrome, RLS; restless legs syndrome, PLMD; periodic limb movement disorder, NBD; nocturnal behavior disorder.