メキシレチン

関連キーワード:
抗不整脈薬

併用情報	一般名	臨床症状・対処	機序 ・ 危険因子
注意	フルボキサミン	メキシチレンの血中濃度↑ メキシチレンを減量するなどして注意して使用する。	メキシチレンの血中濃度↑or 半減期↑or AUC↑

併用薬剤名

メチルフェニデート

併用情報	一般名	臨床症状・対処	機序 ・ 危険因子
注意	イミプラミン	イミプラミンの作用↑	イミプラミンの肝代謝↓、血中濃度↑
注意	クロミプラミン	クロミプラミンの血中濃度↑	代謝↓
注意	フェノバルビタール	フェノバルビタールの血中濃度↑ 減量するなど注意すること。	メチルフェニデートが肝代謝を抑制すると考えられている。
注意	マプロチリン	三環系抗うつ剤(イミプラミン)で作用↑	代謝↓
注意	ロフェプラミン	他の三環系抗うつ薬(イミプラミン)で作用↑の報告がある。	代謝↓、血中濃度↑

併用薬剤名

ピロカルピン

関連キーワード:
コリン作動薬

併用情報	一般名	臨床症状・対処	機序 ・ 危険因子
注意	スルピリド	内分泌機能調節異常又は錐体外路症状	相加作用
注意	ゾテピン	内分泌機能調節異常又は錐体外路症状	相加作用
注意	チアプリド	内分泌機能調節異常又は錐体外路症状	相加作用
注意	チミペロン	内分泌機能調節異常又は錐体外路症状	相加作用
注意	デカン酸フルフェナジン	内分泌機能調節異常又は錐体外路症状	相加作用
注意	トリフロペラジン	内分泌機能調節異常又は錐体外路症状	相加作用
注意	ピモジド	内分泌機能調節異常又は錐体外路症状	相加作用
注意	フルフェナジン	内分泌機能調節異常又は錐体外路症状	相加作用

注意	プロクロルペラジン	内分泌機能調節異常又は錐体外路症状観察を十分に行い，慎重に投与する。	相加作用
注意	プロペリシアジン	内分泌機能調節異常又は錐体外路症状観察を十分に行い，慎重に投与する。	相加作用
注意	ブロムペリドール	内分泌機能調節異常又は錐体外路症状	相加作用
注意	ペルフェナジン	内分泌機能調節異常又は錐体外路症状	相加作用
注意	ペロスピロン	内分泌機能調節異常又は錐体外路症状	相加作用
注意	モサプラミン	内分泌機能調節異常又は錐体外路症状	相加作用
注意	レボメプロマジン	内分泌機能調節異常又は錐体外路症状	相加作用

併用薬剤名

メトプロロール

関連キーワード:
降圧薬
抗不整脈薬

併用情報	一般名	臨床症状・対処	機序 ・ 危険因子
注意	パロキセチン	重度の血圧低下が報告されている。	メトプロロールの(S)-体及び(R)-体のT1/2↑、AUC↑

併用薬剤名

薬物代謝酵素(主にCYP3A4)を誘導する薬剤

例)
カルバマゼピン
リファンピシン　　など

関連キーワード:
CYP3A4 阻害作用を有する薬剤

併用情報	一般名	臨床症状・対処	機序 ・ 危険因子
注意	デカン酸ハロペリドール	デカン酸ハロペリドールの作用↓	薬物代謝酵素誘導作用により，デカン酸ハロペリドールの血中濃度↓
注意	ハロペリドール	ハロペリドールの作用↓	薬物代謝酵素誘導作用により，ハロペリドールの血中濃度↓

併用薬剤名
四環系抗うつ薬 例） マプロチリン　　など

併用情報	一般名	臨床症状・対処	機序 ・ 危険因子
注意	フルタゾラム	併用中のフルタゾラムを急速に減量又は中止すると痙攣発作が起こるおそれがある。	フルタゾラムの抗痙攣作用が、四環系抗うつ剤による痙攣発作の発現を抑えている可能性がある。
注意	フェノバルビタール	(1)相互に作用↑ (2)これらの抗うつ剤の血中濃度↓ 減量するなど注意すること。	(1)相加作用 (2)フェノバルビタールの肝薬物代謝酵素誘導作用による。
注意	ロフラゼプ酸エチル	併用中のロフラゼプ酸エチルを急速に減量又は中止すると痙攣発作が起こるおそれがある。	ロフラゼプ酸エチルの抗痙攣作用が、四環系抗うつ剤による痙攣発作の発現を抑えている可能性がある。

併用薬剤名
リスペリドン 関連キーワード: 抗精神病薬 抗ドパミン作用を有する薬剤 非定型抗精神病薬

併用情報	一般名	臨床症状・対処	機序 ・ 危険因子
注意	パロキセチン	悪性症候群があらわれるおそれあり。過鎮静、錐体外路症状等。	リスペリドン及び活性代謝物の血中濃度↑
注意	マプロチリン	マプロチリンの血中濃度↑	リスペリドンによってマプロチリンの代謝が阻害され、マプロチリンの血中濃度↑

併用薬剤名
リトナビル 関連キーワード: CYP3A4 阻害作用を有する薬剤 HIV プロテアーゼ阻害剤 抗 HIV 薬

併用情報	一般名	臨床症状・対処	機序 ・ 危険因子
注意	アミトリプチリン	アミトリプチリンの作用↑	CYP3A4阻害作用によりアミトリプチリンの代謝↓により血中濃度↑
注意	アルプラゾラム	中枢神経抑制作用↑	アルプラゾラムの代謝↓で、AUC↑、クリアランス↑、半減期↑
禁忌	エスタゾラム	過度の鎮静や呼吸抑制等	CYPに対する競合的阻害により 、エスタゾラムの血中濃度↑
禁忌	クアゼパム	過度の鎮静や呼吸抑制	リトナビルのチトクロームP450に対する競合的阻害作用により，併用した場合，クアゼパムの血中濃度が大幅に上昇することが予測される.
禁忌	クロラゼプ酸二カリウム	過度の鎮静や呼吸抑制	CYP3A阻害により，クロラゼプ酸二カリウムの代謝↓血中濃度↑
禁忌	ジアゼパム	過度の鎮静や呼吸抑制等	CYP阻害により、ジアゼパムの血中濃度↑
注意	トラゾドン	トラゾドンの血中濃度↑ トラゾドンを減量するなど用量に注意すること。	トラゾドンの代謝↓
禁忌	トリアゾラム	トリアゾラムの作用↑及び作用時間↑	どちらもCYP3A4で代謝されるため、トリアゾラムの代謝↓血中濃度↑
禁忌	ピモジド	QT延長、心室性不整脈等	代謝阻害により、ピモジドの血中濃度↑
禁忌	フルラゼパム	過度の鎮静や呼吸抑制	CYPに対する競合的阻害作用により、フルラゼパムの血中濃度↑
禁忌	ミダゾラム	過度の鎮静や呼吸抑制	CYP3A4阻害により、ミダゾラムの血中濃度↑

併用薬剤名

利尿薬

例）
チアジド系降圧利尿薬　　など

関連キーワード:
降圧薬

併用情報	一般名	臨床症状・対処	機序 ・ 危険因子
注意	バルビタール	起立性低血圧↑ 減量するなど注意する。	機序は不明
注意	フェノバルビタール	起立性低血圧が増強されることがある。 減量するなど注意すること。	機序は不明であるが、高用量のフェノバルビタールは血圧を低下させることがある。

併用薬剤名
リネゾリド

併用情報	一般名	臨床症状・対処	機序 ・ 危険因子
注意	パロキセチン	セロトニン症候群等のセロトニン作用による症状があらわれることがある。これらの薬物を併用する際には観察を十分に行うこと。	相加作用

併用薬剤名
リファンピシン 関連キーワード: CYP1A2 誘導作用を有する薬剤 CYP3A4 誘導作用を有する薬剤 肝酵素誘導作用をもつ薬剤

併用情報	一般名	臨床症状・対処	機序 ・ 危険因子
注意	イミプラミン	イミプラミンの血中濃度↓	肝酵素誘導作用による。
注意	オランザピン	オランザピンの作用↓	CYP1A2 誘導作用により、オランザピンのクリアランス↑、血中濃度↓
注意	クエチアピン	クエチアピンの作用↓	CYP3A4 の誘導により、クエチアピンのクリアランス↑(外国人でクリアランスが約 5 倍↑、Cmax が 66%↓、AUC が 80%↓)
注意	クロミプラミン	クロミプラミンの血中濃度↓	肝酵素誘導作用による。
注意	ゾピクロン	ゾピクロンの作用↓	CPY3A4 誘導により、ゾピクロンの代謝↑
注意	ゾルピデム	ゾルピデムの作用↓	CYP3A4 の誘導によりゾルピデムの代謝↑、血中濃度↓
注意	デカン酸ハロペリドール	デカン酸ハロペリドールの作用↓	薬物代謝酵素誘導作用により, デカン酸ハロペリドールの血中濃度↓
注意	トリアゾラム	トリアゾラムの作用↓	トリアゾラムの代謝↑
注意	ノルトリプチリン	ノルトリプチリンの作用↓	ノルトリプチリンの代謝↑
注意	パロキセチン	パロキセチンの作用↓	パロキセチンの血中濃度↓
注意	ハロペリドール	ハロペリドールの作用↓	薬物代謝酵素誘導作用により, ハロペリドールの血中濃度↓
注意	ミダゾラム	ミダゾラムの作用↓	酵素誘導により、ミダゾラムの代謝↑
注意	ロフェプラミン	他の三環系抗うつ薬(イミプラミン)の血中濃度↓の報告がある。	肝薬物代謝酵素誘導作用によるロフェプラミンの代謝促進で血中濃度↓

併用薬剤名
レボドパ製剤 関連キーワード: 抗パーキンソン病薬 ドパミン作動薬

併用情報	一般名	臨床症状・対処	機序 ・ 危険因子
注意	オランザピン	相互に作用↓	拮抗作用
注意	カルピプラミン	相互に作用↓	拮抗作用
注意	クロカプラミン	相互に作用↓	拮抗作用
注意	クロルプロマジン	相互に作用↓	拮抗作用
注意	スルトプリド	相互に作用↓	拮抗作用
注意	スルピリド	相互に作用↓	拮抗作用
注意	スルピリド	相互に作用↓	拮抗作用
注意	ゾテピン	相互に作用↓	拮抗作用
注意	チアプリド	相互に作用↓	拮抗作用
注意	チミペロン	相互に作用↓	拮抗作用
注意	デカン酸ハロペリドール	相互に作用↓	拮抗作用
注意	デカン酸フルフェナジン	相互に作用↓	拮抗作用
注意	トリフロペラジン	相互に作用↓	拮抗作用
注意	ハロペリドール	相互に作用↓	拮抗作用
注意	ピモジド	相互に作用↓	拮抗作用
注意	フルフェナジン	相互に作用↓	拮抗作用
注意	プロクロルペラジン	相互に作用↓ 投与量を調節するなど慎重に投与する。	拮抗作用
注意	プロペリシアジン	相互に作用↓ 投与量を調節するなど慎重に投与する。	拮抗作用
注意	ブロムペリドール	ドパミン作動薬の作用↓	拮抗作用
注意	ペルフェナジン	相互に作用↓	拮抗作用
注意	ペロスピロン	相互に作用↓	拮抗作用
注意	モサプラミン	相互に作用↓	拮抗作用
注意	レボメプロマジン	相互に作用↓	拮抗作用

併用薬剤名
レボメプロマジン 関連キーワード: 抗精神病薬 フェノチアジン系薬剤

併用情報	一般名	臨床症状・対処	機序 ・ 危険因子
注意	イミプラミン	抗コリン作用↑ 中枢神経抑制作用↑	相加作用

注意	クロミプラミン	抗コリン作用↑ 中枢神経抑制作用↑	相加作用
注意	マプロチリン	鎮静、抗コリン作用↑	相加作用

併用薬剤名
ワルファリン 関連キーワード: クマリン系抗凝血薬 止血・血液凝固を阻害する薬剤 出血傾向が増強する薬剤

併用情報	一般名	臨床症状・対処	機序・危険因子
注意	アミトリプチリン	クマリン系抗凝固薬の作用↑	アミトリプチリンの肝薬物代謝酵素阻害作用により、クマリン系抗凝固薬の代謝↓
注意	イミプラミン	クマリン系抗凝血剤の血中濃度半減期↑	機序不明。他の三環系抗うつ薬(ノルトリプチリン)で報告あり。
注意	クロミプラミン	クマリン系抗凝血剤の血中濃度半減期↑	機序不明。他の三環系抗うつ剤(ノルトリプチリン)で報告あり。
注意	セルトラリン	ワルファリンのプロトロンビン反応時間↑(AUCが8%増)の報告あり。セルトラリンの投与を開始もしくは中止する場合は、プロトロンビン時間を慎重にモニターすること。	機序不明
注意	セルトラリン	異常出血(鼻出血、胃腸出血、血尿等)注意して投与する。	SSRIによって血小板凝集能が阻害される。
注意	トラゾドン	プロトロンビン時間↓	機序不明
注意	トリクロホスナトリウム	クマリン系抗凝血剤の作用↑ 通常より頻回にプロトロンビン値の測定を行うなど慎重に投与する。	トリクロホスナトリウムの主代謝産物であるトリクロル酢酸が血漿蛋白結合部位からワルファリンを遊離置換し、遊離型ワルファリン濃度を増加させる。
注意	ノルトリプチリン	クマリン系抗凝血剤の血中濃度半減期↑	ワルファリンの肝代謝↓
注意	バルビタール	クマリン系抗凝血剤の作用↓ 通常より頻回に血液凝固時間の測定を行い、クマリン系抗凝血剤の量を調整する。	バルビタールの肝薬物代謝酵素誘導作用によって、半減期↓
注意	パロキセチン	他の抗うつ剤でクマリン系抗凝固薬の作用↑	パロキセチンとの相互作用は認められていない。
注意	パロキセチン	出血傾向↑	相加作用
注意	フェノバルビタール	クマリン系抗凝血剤の作用↓ 通常より頻回に血液凝固時間の測定を行い、クマリン系抗凝血剤の用量を調整する。	フェノバルビタールの肝薬物代謝酵素誘導作用による。
注意	フルボキサミン	ワルファリンの血中濃度↑ or 半減期↑ or AUC↑ プロトロンビン時間を測定し、ワルファリンの用量を調節するなど、注意して投与すること。	ワルファリンの代謝↓

注意	フルボキサミン	皮膚の異常出血(斑状出血、紫斑等)、出血症状(胃腸出血等)	SSRI の血小板凝集阻害が相加され、出血傾向↑
注意	ペントバルビタール	抗凝血作用↓ 頻回にプロトロンビン値の測定を行い、ワルファリンカリウムの用量を調節する。	ワルファリンカリウムの代謝↑、半減期↓、クリアランス↑
注意	ペントバルビタール	抗凝血作用↓ 頻回にプロトロンビン値の測定を行い、ワルファリンカリウムの用量を調節する。	ワルファリンカリウムの代謝↑、半減期↓、クリアランス↑
注意	抱水クロラール	クマリン系抗凝固剤の作用↑ 通常より頻回にプロトロンビン値の測定を行うなど慎重に投与する。	抱水クロラールは血漿たん白に結合したクマリン系抗凝固血剤を遊離させる。
注意	マプロチリン	クマリン系抗凝血剤の血中濃度半減期↑	機序不明。他の三環系抗うつ薬(ノルトリプチリン)で報告がある。

Ⅲ．研究成果の刊行に関する一覧表

雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Enomoto M, Endo T, Higuchi S, Miura N, Nakano Y, Kohtoh S, Taguchi Y, Suenaga K, Aritake S, Matsuura M, Mishima K	Newly Developed Waist Actigraphy and its Sleep/Wake Scoring Algorithm.	Sleep and Biological Rhythms	7	17-22	2009
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 and Clinical Neurosciences	10	1440-1819	2010
Nagase Y, Uchiyama M, Kaneita Y, Li L, Mishima K, Nishikawa T, Ohida T	Coping Strategies and Their Correlates with Depression in the Japanese General Population.	Psychiatry Res	168 (1)	57-66	2009
Kaneita Y, Uchiyama M, Takemura S, Yokoyama E, Miyake T, Harano S, Asai T, Tsutsui T, Kaneko A, Nakamura H, Ohida T	Use of alcohol and hypnotic medication as aids to sleep among the Japanese general population.	Sleep Medicine	8	723-732	2009

Ⅳ. 研究成果の刊行物・別刷

Sleep and Biological Rhythms 2009; 7: 17–22 doi:10.1111/j.1479-8425.2008.00377.x

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 electro-oculogram (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

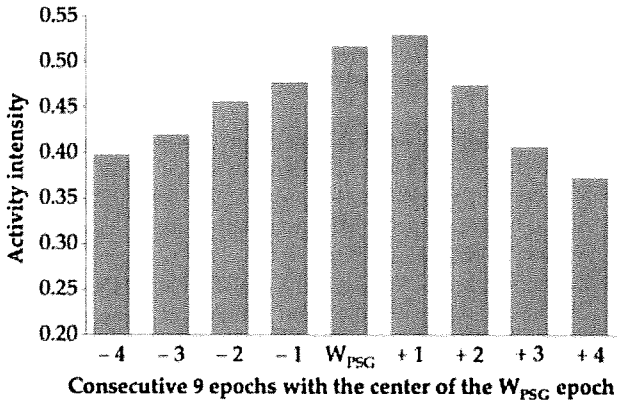

Figure 1 Activity intensity distribution before and after the scored epoch. The mean activity intensity recorded by the Lifecorder (LC) for nine consecutive epochs (18 min) centered at the W_{PSG} epoch. Vertical bars indicate the activity intensity. The mean activity intensity bars formed an inverted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

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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.

Table 2
Question items and percentages of respondents in the analyzed 421 inpatients

Items		1)	2)	3)	4)
Q1. How long did it take from light off until you went to sleep?					
1) less than 15 minutes 2) 15-29 minutes 3) 30-59 minutes 4) more than 60 minutes		50.4	20.4	14.5	14.7
Q2. How many times did you awake during last night?					
1) none 2) 1-2 times 3) 3-4 times 4) more than 5 times		21.4	35.9	24.9	17.8
Q3. What time did you get up this morning (h:min)?		22.6*	77.4		
Q4. Did you get up in the morning unrefreshed or nonrestored?					
1) good 2) fair 3) insufficient 4) poor		38.7	37.1	19.2	5.0
Q5. Do you have daytime sleepiness?**					
1) none 2)some 3) moderate 4) severe		22.8	22.8	47.5	6.9
Q6. Did you experience any of the following symptoms during last night (completed by a patient)					
Q6-a creeping sensation or restless discomfort in the limbs	1) yes 2) no	5.9	94.1		
Q6-b legs or arms jerk	1) yes 2) no	2.4	97.6		
Q6-c hot flash	1) yes 2) no	4.8	95.2		
Q6-d night sweat	1) yes 2) no	6.9	93.1		
Q6-e palpitation	1) yes 2) no	1.2	98.8		
Q6-f anxiety or panic	1) yes 2) no	1.0	99.0		
Q6-g sleep paralysis	1) yes 2) no	0.0	100.0		
Q6-h nightmare	1) yes 2) no	3.1	96.9		
Q7. Did the patient experience any of the following symptoms during last night (completed by nursing staffs)					
Q7-a loud snoring, or apnea lasting for 10 seconds or longer	1) yes 2) no	10.0	90.0		
Q7-b periodic legs or arms jerk	1) yes 2) no	2.1	97.9		
Q7-c sleep-talking, delirium or abnormal behaviors such as wandering	1) yes 2) no	6.9	93.1		
Q8. Whether or not the patient took any hypnotic-sedative drug(s) for treatment of insomnia within the past one week and the name of the drug(s) if any (completed by nursing staffs)					
1) yes 2) no Name of drugs [ ]		27.6	72.4		

* Patients who woke up 30 minutes or earlier than the desired time without falling asleep again (Q3).
** answered at 2 pm.

which patients were supposed to be in bed as specified by each hospital ward, and specifically the time from "lights out" to the time at which patients were expected to wake. Mean TIB was approximately between 9 p.m. and 6 a.m. Observations by the nursing staffs on each of the wards confirmed that the patients were in bed during TIB on the evenings of the study.

For the observational sleep evaluations, several nursing staffs alternated in order to record continuously the subjects' sleep states. Opening and closing of eyes, breathing, movement and any unusual behavior of the subjects were observed and recorded at a distance so as to not disturb the subjects.

2.3. Differential diagnosis of sleep disorders

The diagnostic flow for the patients included in the investigation is shown in Fig. 1. Some of the preselected subjects (n=136) were either excluded from data analyses or could not participate due to reasons such as sudden change in physical condition such as fever, severe dementia, consciousness disturbance due to organic brain damages, need for emergency examination, hospital transfer or discharge or due to missing data on their amount of physical activity. As a result, a total of 421 patients comprised the analysis population [228 males, 193 females; mean age, 72.5±12.6 (S.D.) years; range 22-96 years]. The number of respondents for each question item is shown in Table 2.

Patients were initially examined for the presence of SAS (positive answer to Q7-a), RLS (positive answer to Q6-a), PLMD (positive answer to Q6-b or Q7-b) or NBD (positive answer to Q7-c). Those who were NOT diagnosed with SAS, RLS, PLMD or NBD were subsequently examined for the presence of insomnia. Patients were judged as having insomnia when the subjective sleep investigation indicated the presence of any one of the following:

i. Disturbances of initiating sleep (DIS): Q1, the answer indicates 30 min or more.
ii. Disturbances of maintaining sleep (DMS): Q2, the answer indicates three times or more.
iii. Early morning awakening (EMA): Q3, the answer indicates wake time 30 minutes or earlier than the desired time without falling asleep again.
iv. Non-restorative sleep (NRS): Q4, the answer indicates insufficient or poor sleep.