A Novel Adaptive Wrist Actigraphy Algorithm for Sleep-Wake Assessment in Sleep Apnea Patients

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Study Objectives: Current actigraphic algorithms are relatively less accurate in detecting sleep and wake in sleep apnea patients than in people without sleep apnea. In the current study, we attempted to validate a novel automatic algorithm, which was developed for actigraphic studies in normal subjects and patients with obstructive sleep apnea by comparing it on an epoch-by-epoch basis to standard polysomnography.

Design: Prospective cohort study.

Setting: Multicenter, university hospital, sleep laboratories.

Participants: A total of 228 subjects from 3 different sleep centers (Skara, Boston, Haifa) participated.

Intervention and Measurements: Simultaneous recording of polysomnography and Watch_PAT100, an ambulatory device that contains a built-in actigraph. The automatic sleep/wake algorithm is based on both the quantification of motion (magnitude and duration) and the various periodic movement patterns, such as those occurring in patients with moderate to severe obstructive sleep apnea.

Results: The overall sensitivity and specificity to identify sleep was 89% and 69%, respectively. The agreement ranged from 86% in the normal subjects to 86%, 84%, and 80% in the patients with mild, moderate, and severe obstructive sleep apnea, respectively. There was a tight agreement between actigraphy and polysomnography in determining sleep efficiency (78.4 ± 9.9 vs $78.8 \pm 13.4\%$), total sleep time (690 ± 152 vs 690 ± 154 epochs), and sleep latency (56.8 ± 31.4 vs 43.3 ± 45.4 epochs). While for most individuals the difference between the polysomnography and actigraphy was relatively small, for some there was a substantial disagreement.

Conclusions: We conclude that this actigraphy algorithm provides a reasonably accurate estimation of sleep and wakefulness in normal subjects and patients with obstructive sleep apnea on an epoch-by-epoch basis. This simple method for assessment of total sleep time may provide a useful tool for the accurate quantification of obstructive sleep apnea in the home environment.

Key Words: Actigraph, polysomnograph, Watch_PAT 100, Sleep/wake

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INTRODUCTION

ACTIGRAPHIC METHODOLOGY, INCLUDING AUTOMATED ANALYSIS TOOLS, HAS BEEN UTILIZED FOR THE CLINICAL DETECTION OF SLEEP AND WAKEFULNESS. Most previous validation studies, initially reviewed by the American Academy of Sleep Medicine (AASM) in 1995[1] and again in 2003,[2] have compared actigraphic data with those obtained from simultaneous polysomnography (PSG) recordings.

Comparative data were primarily generated from groups of normal healthy volunteers,[3-11] children,[9,12] insomniacs,[13,14] and nursing home residents,[15] as well as mixed groups of normal controls and patients with sleep-disordered breathing.[16-18] The accuracy of actigraphy in determining sleep and wake was reasonably high in the normal subjects, with values differing by up to 30 minutes for sleep latency and 1 hour for total sleep time.[3,4,16] Differences were larger in insomniacs.[13] In addition, on a minute-by-minute analysis, Sadeh et al[18] found a 78% to 90% agreement between actigraphic and PSG recordings in a mixed sample of subjects. The correlation between actigraphy- and PSG-based sleep-efficiency indexes in this study were high in normal children and adults (0.81 and 0.9, respectively), but fairly low (0.63) in patients with obstructive sleep apnea (OSA).[18] However, 1 extensive study monitoring patients for a week by both PSG and actigraphy found low predictive values and an overestimation of sleep.[8] The American Sleep Disorders Association practice parameters[19] recommend actigraphy for the assessment of primary insomnia and circadian rhythm disorders but not for sleep-disordered breathing. These recommendations were further supported in a recent review by Ancoli-Israel et al[2], developed under the auspices of the AASM.

The high prevalence of OSA,[20] as well as high costs for PSG recordings, have sparked a search for simple ambulatory sleep-monitoring systems.[21-29] However, the accuracy of such systems relies on the reasonably high validity of a concomitant sleep-time assessment. Therefore, ambulatory cardiorespiratory systems, without the capability to identify sleep, are frequently not sufficiently accurate.[27-29] On the other hand, ambulatory systems that record both sleep and cardiorespiratory parameters (ambulatory

PSG) are often cumbersome.[24,30,31] The purpose of the present study was to perform an epoch-by-epoch validation of an algorithm developed specifically for sleep/wake estimation based on actigraphic monitoring of sleep apnea patients.

METHODS

Overview of Study Design

The study consisted of 228 subjects recruited to 3 different sleep centers (100 from Haifa, Israel; 71 from Skara, Sweden; and 57 from Boston, USA). All participants underwent a full-night PSG study with simultaneous recording with a Watch_PAT100 system (WP100, Itamar Medical, Caesarea, Israel), which has an embedded actigraphy module. In the Boston and Haifa cohorts, the PSG-WP100 studies were conducted in the sleep laboratory, whereas, in Skara, the participants were studied at home with both PSG and WP100. In the Skara patients, electrodes and sensors were hooked up in the laboratory, standard calibrations were run by an experienced research nurse, signals were visualized on the screen, and sensor positions were modified to optimize signal quality and secured by tape and net. Participants were asked to go home and use the event button (lights off/on) for timing indications. The following morning, the equipment was removed by the nurses, and the data stored in the memory card downloaded to the computer using the PSG Somnologica software (Medcare, Reykjavik, Iceland). Fewer than 4% of the records were unusable. PSG data were manually scored by experienced polysomnography technicians blinded to the actigraphy data. Scoring in each site was performed by 1 experienced PSG technologist. Actigraphic signals were automatically scored using a sleep/wakefulness analysis software (ASWA) embedded in the zzzPAT package (Itamar Medical, Caesarea, Israel). Following analyses, data from the 2 monitoring systems were synchronized and compared on an epoch-by-epoch basis.

Study Subjects

This was a 3-center study based on separate cohorts. Haifa recruited 17 normal volunteers via advertising and 83 randomly selected patients from a cohort referred to the sleep laboratory for a diagnostic sleep recording due to suspected OSA. Boston recruited 57 patients referred to the sleep laboratory for suspected OSA (randomly selected subjects who indicated an interest in participating in research on a questionnaire). Skara recruited 71 subjects randomly drawn from a population-based cohort of 348 subjects undergoing ambulatory PSG studies. This study population included normotensive subjects (random population sample) and patients with hypertension (seen in the local primary care center). The study was approved by the local institutional review boards in all institutes, and signed informed consent was obtained from each participant prior to study inclusion.

The 228 subjects were stratified into 4 subgroups based on the PSG findings. Subjects were allocated to different respiratory disturbance index (RDI) classes (see PSG recording) according to the following definition: (1) RDI < 10, normal range; (2) 10 = RDI < 20, mild OSA; (3) 20 = RDI < 40, moderate OSA; and (4) RDI = 40, severe OSA. Age, sex, body mass index, and PSG-based RDI for all subjects in each of the 4 subgroups as well as for all subjects are given in Table 1.

PSG Recording

Overnight PSGs were performed according to standard laboratory protocol using electroencephalogram, electrooculogram, submental and bilateral anterior tibialis electromyogram, electrocardiogram, nasal-oral airflow (thermistors and nasal pressure), chest and abdominal wall motion (piezoelectrodes or belts), body position, and arterial oxygen saturation. The Embla systems (Flaga, Reykjavik, Iceland) were used in the Skara and Haifa cohorts, whereas the Alice III system (Respironics, Pittsburgh, Penn, USA) was applied in Boston. Sleep was staged according to standard criteria.[33] Respiratory events were scored according to the AASM guidelines for measurement in clinical research,[34] and the RDI was calculated as the number of respiratory events divided by the actual time of sleep (determined by the PSG).

Actigraphy

Each participant was equipped with a WP100 device worn on the nondominant hand during sleep. The device incorporated an embedded actigraph module (AMI, Ambulatory Monitoring Inc, New York, USA). It also contained an oxygen-saturation sensor and peripheral arterial tonometer (signals were not utilized in the study). Data were recorded onto a flash memory card (for off-line automatic analysis) within the WP100, which was specially developed for unattended home sleep studies of patients with suspected OSA.[32]

The actigraph used in this application is a single-axis (perpendicular to the device's x-y plane) beam sensitive to movement linked with a piezoelectric transducer, sampled at 100 Hz. The device includes an analog band-pass Butterworth filter (0.16 to 2.5 Hz). Although the signal is filtered at a low-frequency band, the amplitude of the signal at medium frequency (17-25 Hz) is

Table 1—Demographic, Clinical, and Sleep Data

Level of OSA severity	No.	Age, y	Men/women, no.	BMI, kg/m²	RDI, events/h
Normal	38	38.6 ± 15.5†	25/13	23.6 ± 3.5	6.3 ± 2.4
Mild	54	47.2 ± 14.9*†	41/13	29.4 ± 5.4*	14.4 ± 3.0
Moderate	83	50.7 ± 11.9*†	59/24	30.3 ± 6.3*	28.9 ± 6.1
Severe	53	55.0 ± 10.9*	38/15	32.3 ± 6.3*	65.8 ± 17.2
All	228	48.8 ± 14.0	163/65	29.4 ± 6.3	30.3 ± 23.1

* $P < .05$ (vs Normal)
† $P < .05$ (vs Severe)
OSA refers to obstructive sleep apnea, BMI, body mass index, RDI, respiratory disturbance index.

sufficiently high. The sampled signal was digitized using a 12-bit unipolar data-acquisition system that was part of the WP100.

PSG-WP100 Synchronization

The PSG and the WP100 were synchronized using a continuous synchronization bilevel signal generated by the WP100 and recorded on both devices. This signal was later processed by a specifically designed algorithm to achieve minimal synchronization error. The error was in the order of that generated by computer internal clock differences. This error was identified and taken into account during the comparison process.

Automatic Sleep/Wake Analysis

The ASWA algorithm has several steps that eventually provide an automatically generated adaptive decision-making process that differentiates between sleep and wake for each 30-second epoch:

A. Determination of the typical background movement activity of the patient throughout the night, which is provided by a function termed here as Σ. The function Σ describes the density of small background movements based on the observation that the actigraphic signal is more spiky, saturated, and entropic during wakefulness while having an overall denser, lower amplitude, and/or periodic patterns during sleep.

B. The actigraphic signal is filtered with a digital band-pass filter between 2 and 2.5 Hz, using a multirate filtering. The out-

come of this process is regarded as the "amount of motion activity" in the signal and is termed here as the *Energy* of the signal. The Energy is processed in 2 ways, as described in the following steps C and D.

C. For each 30-second epoch, values of Energy below an adaptive threshold determined using Σ (computed in A) are disregarded, and the remaining Energy is integrated using a symmetrical weighted sliding window (Hanning) of 5 minutes' duration. The window is centered by this epoch, and thus this summation provides the level of movement activity in the surroundings of the selected epoch. The result is termed here the *Integrated Local Movement*. ASWA defines a wake epoch by comparing the integrated local movement to a threshold, which is individually adapted using Σ.

D. For each 30-second epoch, the algorithm also searches for periodicity[35] in the Energy signal within a 10-minute symmetrical window. If the algorithm detects periodicity within a range of 12 to 90 seconds (such as expected during periodic apneic events), this epoch is declared a sleep state, overruling the decision made in step C. Figure 1 shows an example of periodicity in the Energy signal of a patient with severe OSA.

The ASWA was developed based on a training set of 36 subjects studied prior to the current validation study.

Data Analysis

Sleep and wakefulness were blindly determined by the sleep technologist in 30-second epochs for the PSG and automatically
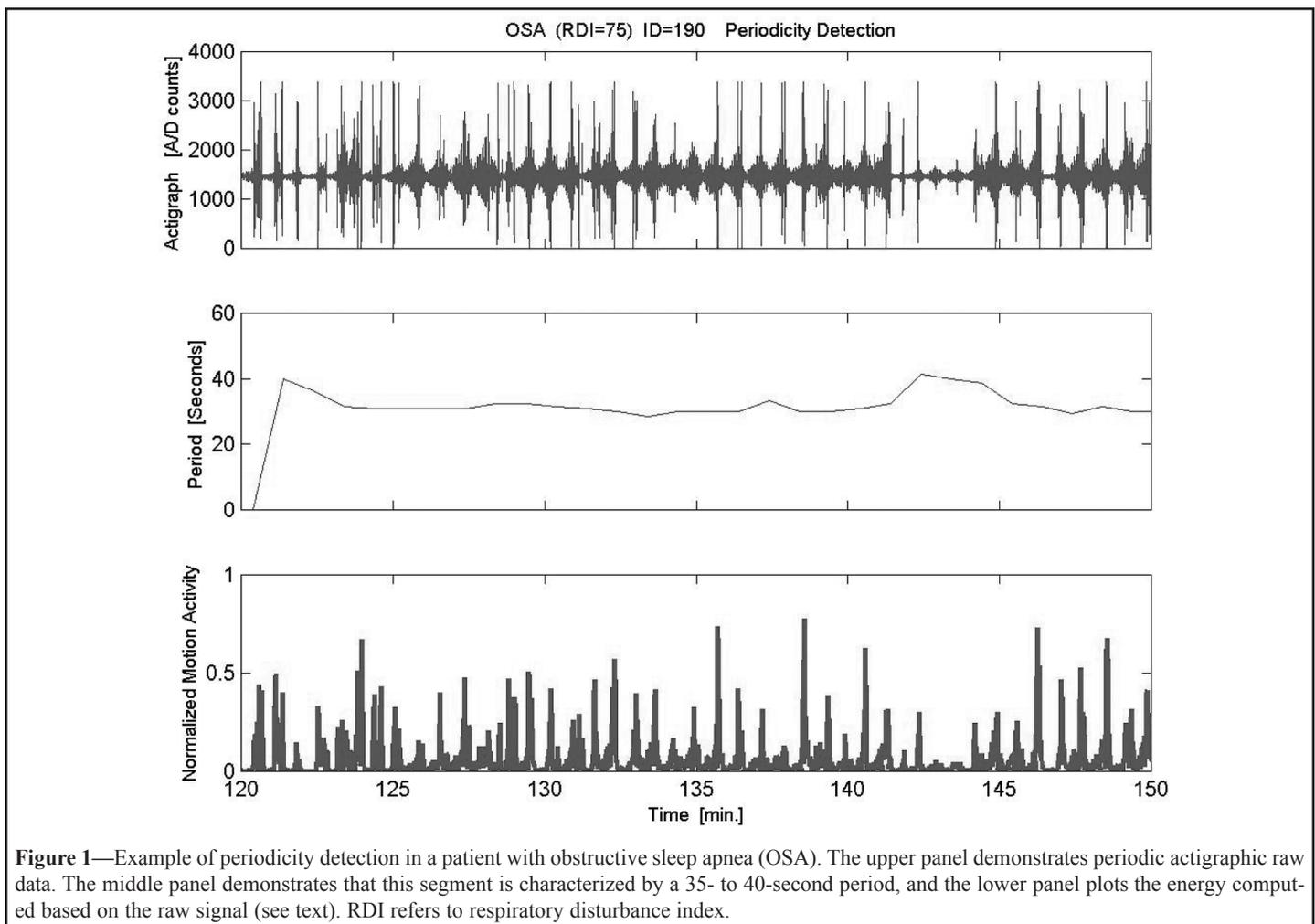

Figure 1—Example of periodicity detection in a patient with obstructive sleep apnea (OSA). The upper panel demonstrates periodic actigraphic raw data. The middle panel demonstrates that this segment is characterized by a 35- to 40-second period, and the lower panel plots the energy computed based on the raw signal (see text). RDI refers to respiratory disturbance index.

by the ASWA from the actigraphic signal (zzzPAT software, Itamar, Caesarea, Israel). For each individual, the ASWA sensitivity to detect a sleep epoch, as well as the specificity and agreement, were analyzed using the PSG scoring as the gold standard. In addition, the general sleep parameters—sleep latency, total sleep time, and sleep efficiency were determined. Comparisons between the subgroups were performed by either analysis of variance or paired t test. All values are presented as means ± SD with $P < .05$ being considered statistically significant.

RESULTS

Age and body mass index tended to be higher as severity of OSA increased (Table 1). Sensitivity, specificity, and agreement for each apnea-severity group are presented in Table 2. In general, there was a high agreement between the actigraphy-based ASWA and the PSG scoring in the various OSA severity groups (Figure 2). Agreement tended to decrease as the severity of OSA increased. Sensitivity of the ASWA to identify sleep showed a

similar trend, with the values ranging from 90.7% in the normal group to 85.3% in the severe apneics. Specificity was less affected by OSA severity and was similar in all groups, ranging between 68% and 71%. The sensitivity, specificity, and agreement values did not differ systematically between the various data-collecting sites (Table 3).

Comparisons of sleep efficiency, total sleep time, and sleep latency between PSG and actigraphy in the various groups showed no significant difference between the 2 methods for the sleep efficiency and total sleep time (Table 4). However, the actigraphy method tended to consistently overestimate sleep latency in comparison with PSG. While this trend was nonsignificant in normal controls (62.2 ± 33.2 vs 51.2 ± 2.6 epochs) and in severe apneics (59.1 ± 35.2 vs 48.6 ± 57.0 epochs), significant differences were observed in mild apneics (54.4 ± 27.1 vs 37.8 ± 38.8 epochs, $t = 2.86$, $P = .006$), moderate apneics (54.4 ± 30.8 vs 39.9 ± 36.7 epochs, $t = 3.35$, $P = .001$), as well as for the entire group (43.3 ± 45.4 vs 56.8 ± 31.4 epochs, $t = 4.34$, $P = .0001$). When considering the distribution of individual differences in these measures (Figure 3), it should be noted that, for most individuals, the difference between the PSG and actigraphy was relatively small, although for some there was a substantial disagreement up to a maximum of 37% in sleep efficiency, 200 minutes for total sleep time, and 160 minutes for sleep latency.

Table 2—Sensitivity, Specificity and Agreement in Groups with the Various Severities of Obstructive Sleep Apnea, Based on an Epoch-By-Epoch Comparison

Level of OSA severity	No.	Sensitivity, %	Specificity, %	Agreement, %
Normal	38	90.73 ± 6.39	69.12± 18.38	86.07 ± 5.47
Mild	54	90.40 ± 5.49	70.45 ±15.42	85.86 ± 5.49
Moderate	83	89.07 ± 6.13	68.15 ± 17.2	84.39 ± 5.48
Severe	53	85.25 ± 8.72	70.76 ± 17.5	79.86 ± 8.10
All	228	88.77 ± 6.87	69.45 ±17.01	83.96 ± 6.81

OSA refers to obstructive sleep apnea.

Table 3—Sensitivity, Specificity and Agreement at the 3 Study Sites, Based on an Epoch-By-Epoch Comparison

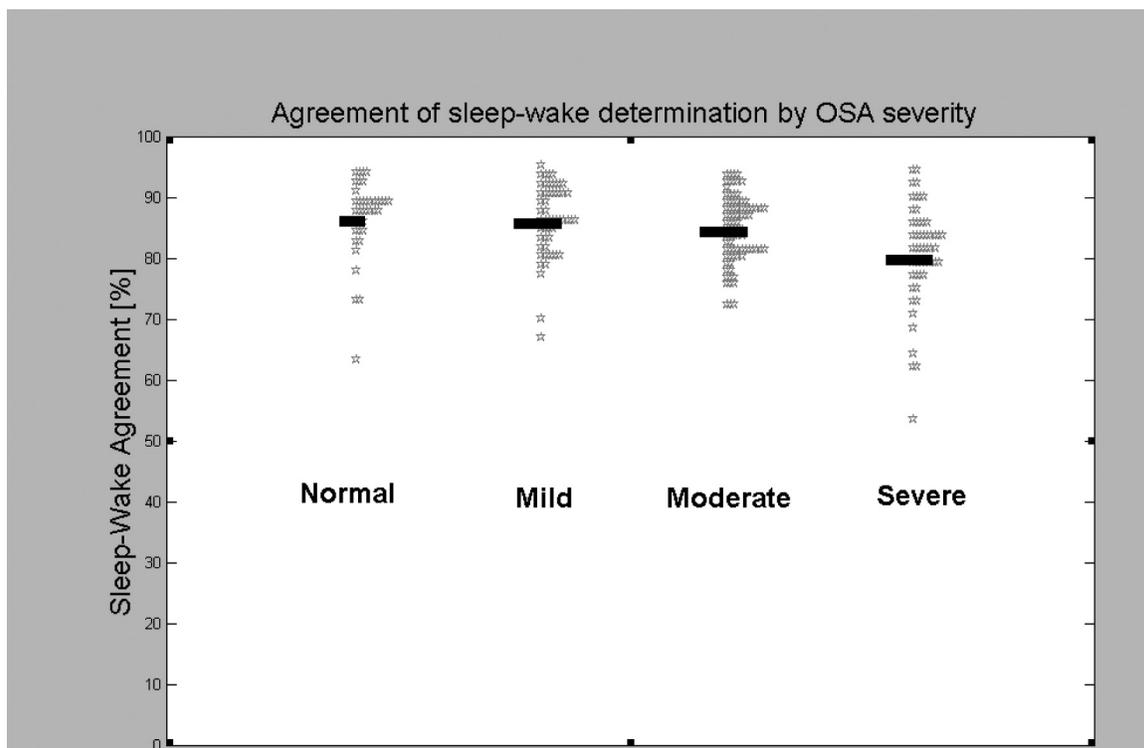| Study site	No.	Sensitivity, %	Specificity, %	Agreement, %
Haifa	100	87.13 ± 7.19	74.35 ± 17.50	84.02 ± 6.32
Skara	71	90.72 ± 5.92	65.61 ± 16.16	84.28 ± 6.29
Boston	57	89.23 ± 6.80	65.67 ± 15.13	83.48 ± 8.23
All	228	88.77 ± 6.87	69.45 ± 17.01	83.96 ± 6.81

Figure 2—Agreement of sleep-wake determination by severity of obstructive sleep apnea (OSA). Horizontal bars indicate the mean agreement within each group. Agreement tended to decrease as the severity of OSA increased.

DISCUSSION

This study has demonstrated that actigraphy may be used to accurately identify sleep and wakefulness on an epoch-by-epoch basis in patients with OSA. The ASWA algorithm was reasonably stable across the 3 study sites, variable settings, and a wide range of severities of sleep-disordered breathing. Importantly, the ability of the ASWA algorithm to accurately identify sleep and wakefulness permits a WP100-based calculation of the RDI using total sleep time rather than total recording time.

Several previous studies evaluated actigraphic algorithms for the detection of sleep and wakefulness. However, most studies focused on normal subjects and insomniacs (including patients with circadian rhythm abnormalities) rather than patients with sleep apnea. It is evident that the movements associated with sleep apnea-induced arousals may impair the accuracy of actigraphic algorithms.[17,18,36] Considering that the standard scoring method is based on an epoch-by-epoch analysis (30 seconds),

comparing actigraphy and PSG using 30-second epochs appears to be rational. In fact, a recent study comparing actigraphy with PSG on an epoch-by-epoch basis reported an 80% agreement.[6] However, that study was limited to recordings in normal subjects, and no patients with OSA were included. The high agreement in the present study therefore supports a reasonable robustness of the algorithm when the composition of the study group is taken into account.

Simple and portable instruments for sleep/wake assessment may prove to be highly useful in clinical diagnostic routines. For instance, in patients with insomnia or circadian rhythm disorders, it may prove more appropriate to measure sleep in the natural home environment rather than in the sleep laboratory. This need justifies the substantial recent effort to develop accurate and reliable actigraphy algorithms for sleep detection in the home environment. Several studies have utilized actigraphy to diagnose OSA with disappointing results.[21,30,37] The purpose of the present study was not to diagnose OSA by actigraphy. It was, rather, to

Table 4—Sleep Indexes in the Groups with the Various Severities of Obstructive Sleep Apnea

Level of OSA severity	Sleep Efficiency, %		Total Sleep Time, epochs		Sleep Latency, epochs	
	PSG	ASWA	PSG	ASWA	PSG	ASWA
Normal	79.2 ± 14.9	79.6 ± 11.6	666 ± 175	670 ± 177	51.2 ± 52.6	62.2 ± 33.2
Mild	80.7 ± 12.2	80.6 ± 8.4	707 ± 134	707 ± 121	37.8 ± 38.8	54.4 ± 27.1*
Moderate	80.0 ± 12.1	79.4 ± 9.2	702 ± 152	702 ± 158	39.9 ± 36.7	54.4 ± 30.8*
Severe	74.7 ± 14.9	73.6 ± 9.8	673 ± 162	667 ± 152	48.6 ± 57.0	59.1 ± 35.2
All	78.8 ± 13.4	78.4 ± 9.9	690 ± 154	690 ± 152	43.3 ± 45.4	56.8 ± 31.4*

*$P < .05$ polysomnography (PSG) vs automatic sleep-wake analysis (ASWA). OSA refers to obstructive sleep apnea.
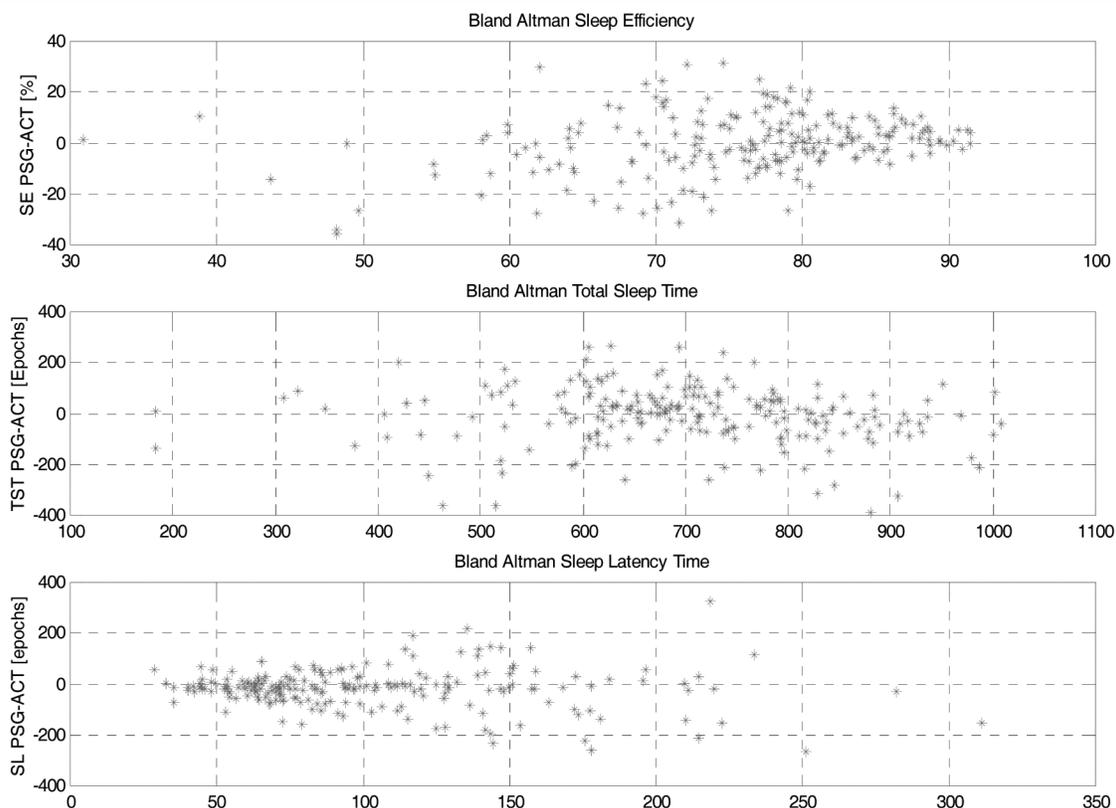

Figure 3—Bland-Altman comparisons of sleep efficiency (SE), total sleep time (TST) and sleep latency (SL) between polysomnography (PSG) and actigraphy scoring. The y-axis in each plot shows the difference between the 2 methods, and the x-axis, the average of their score. The units for the upper panel (both axes) are percentages, and for the 2 lower panels are epochs.

validate an algorithm for accurate estimation of sleep and wakefulness in patients with OSA, in order to provide this quantitative measure as adjunct information for accurate calculation of RDI. Most ambulatory devices that have attempted to diagnose OSA in the home environment have the disadvantage of not distinguishing wakefulness from sleep in determining RDI.[25,38-40] This affected mainly the diagnosis of mild and moderate cases. A previous attempt adding actigraphy to a portable apnea-detecting system[41] was unsuccessful, as no specific algorithm for sleep/wake detection in the OSA population was developed. Consequently, sensitivity and predictive values were low, especially in the cases with severe OSA. In order to overcome such limitations and improve accuracy, the ASWA used the characteristic rhythmicity of actigraphic movements seen in apneic patients. The recently published AASM practice parameter on actigraphic usage recommended that actigraphy should not be applied alone for OSA diagnosis, but it may provide a useful adjunct to portable OSA testing.[36] The current study supports this recommendation.

In this study, the agreement between the actigraphy and PSG tended to be less accurate in severe apnea cases (86.1% agreement in the normal group versus 79.9% in the severe OSA group). The reduced accuracy in severe cases may be attributed to greater movement intensity in such patients. Indeed, Middelkoop et al[37] reported a decrease in the duration of periods with no movements as the severity of apnea increased. From a clinical point of view, the reduced accuracy in sleep/wake detection in the severe subgroup is likely to have little impact on clinical diagnostic procedures, as these patients with severe OSA generally are easy to identify.

Total sleep time and sleep efficiency were generally quite similar for the 2 methods, although for certain individuals the differences between the 2 methods were substantial. The largest disagreement occurred in 3 individuals in whom the ASWA consistently overscored sleep compared to the PSG. Sleep latencies, however, showed a greater discrepancy (Table 4, Figure 3). It appears that the ASWA tended to identify sleep onset later than did the PSG (longer sleep latencies). On the other hand, it subsequently missed some wake periods that were misclassified as sleep. Overestimation of sleep time appears to be a general limitation of actigraphy, since most studies report actigraphy to overscore sleep.[1,2,8,42]

The present study has several limitations. First, patients did not wear the actigraph alone on their wrist, rather, it was a part of the WP100 device. This should be kept in mind, since the whole device is heavier than a typical actigraph and, therefore, may have affected movements during sleep and consequently the accuracy of the algorithm tested. This limitation is important if the algorithm is to be applied to a stand-alone actigraph. Second, the study population did not include children or patients with specific movement or neurologic disorders. These subgroups need to be targeted in future validation studies. Third, signals for comparison need to be aligned. The epoch-by-epoch comparison between the systems was based on time locking of the actigraphy epochs with those of the PSG. Although this may generate a technical problem, the current study used a repetitive synchronization process by feeding a continuous signal generated by the WP100 to the PSG system throughout the night. This procedure prevented the 2 measures from drifting apart over the course of the night. Finally, the ASWA scoring of the actigraphy in this study relied

solely on objective measures. As has been suggested in previous studies, subjective reports or estimations may help the clinician in interpreting actigraphic data. It is plausible that if subjective reports had been used in this study, some of the individual differences between the PSG and actigraphy could have been explained or reduced.

Despite these limitations, we believe this study shows that actigraphy can accurately identify sleep and wakefulness on an epoch-by-epoch basis, in both normal subjects and patients with OSA within a wide range of severity. Actigraphy, therefore, may be utilized as a useful adjunct in ambulatory systems aimed at diagnosing OSA in the home environment.

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