

Detecting REM sleep from the finger: an automatic REM sleep algorithm based on peripheral arterial tone (PAT) and actigraphy

Sarah Herscovici¹, Avivit Pe'er¹, Surik Papyan¹ and Peretz Lavie²

¹ Itamar Medical Ltd., Cesarea, Israel

² Sleep Laboratory, Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel

E-mail: plavie@tx.technion.ac.il

Received 8 June 2006, accepted for publication 13 November 2006

Published 12 December 2006

Online at stacks.iop.org/PM/28/129

Abstract

Scoring of REM sleep based on polysomnographic recordings is a laborious and time-consuming process. The growing number of ambulatory devices designed for cost-effective home-based diagnostic sleep recordings necessitates the development of a reliable automatic REM sleep detection algorithm that is not based on the traditional electroencephalographic, electrooculographic and electromyographic recordings trio. This paper presents an automatic REM detection algorithm based on the peripheral arterial tone (PAT) signal and actigraphy which are recorded with an ambulatory wrist-worn device (Watch-PAT100). The PAT signal is a measure of the pulsatile volume changes at the finger tip reflecting sympathetic tone variations. The algorithm was developed using a training set of 30 patients recorded simultaneously with polysomnography and Watch-PAT100. Sleep records were divided into 5 min intervals and two time series were constructed from the PAT amplitudes and PAT-derived inter-pulse periods in each interval. A prediction function based on 16 features extracted from the above time series that determines the likelihood of detecting a REM epoch was developed. The coefficients of the prediction function were determined using a genetic algorithm (GA) optimizing process tuned to maximize a price function depending on the sensitivity, specificity and agreement of the algorithm in comparison with the gold standard of polysomnographic manual scoring. Based on a separate validation set of 30 patients overall sensitivity, specificity and agreement of the automatic algorithm to identify standard 30 s epochs of REM sleep were 78%, 92%, 89%, respectively. Deploying this REM detection algorithm in a wrist worn device could be very useful for unattended ambulatory sleep monitoring.

The innovative method of optimization using a genetic algorithm has been proven to yield robust results in the validation set.

Keywords: peripheral arterial tonometry, REM sleep, sleep apnea, genetic algorithm

Introduction

Since the discovery of rapid eye movement (REM) sleep by Aserinsky and Kleitman (1953) its identification has been based on simultaneous recordings of electro-oculogram (EOG), electromyogram (EMG) and electroencephalogram (EEG). Rechtschaffen and Kales's classic manual (Rechtschaffen and Kales 1968) provides a distinct list of criteria by which REM sleep is identified and scored based on simultaneous changes in these electrophysiological recordings. As manual scoring of REM sleep is a laborious time-consuming process, attempts have been made to construct automatic REM detection algorithm based on EEG analysis (Grozinger *et al* 1997, Haustein *et al* 1986, Sforza and Vandi 1996) occurrence of eye movements (Ktonas and Smith 1978, Tsuji *et al* 2000, Boukadoum and Ktonas 1988) or on a combination of eye movements and EEG, or on eye movements and head movements (Helfand *et al* 1986, Mamelak and Hobson 1989). The recently developed technologies for ambulatory sleep recordings which mostly rely on a relatively small number of physiological channels further emphasize the need for a cost effective method to identify and score REM periods. Ambulatory devices, mostly designed to allow a diagnosis of breathing disorders in sleep, that is the most prevalent sleep disorder, do not provide information on sleep-wake states nor on REM sleep. This information is valuable for determining patients' sleep quality, the integrity of the sleep cycle and the severity of the sleep disorder.

Recently, we have reported that the continuous measurement of the peripheral arterial tone (PAT) signal from the fingertip during sleep provides a sensitive surrogate signal of changes in sympathetic tone. Thus, arousal events during sleep, or stressful events during wakefulness, cause profound transient attenuations in the PAT signal, indicating peripheral vasoconstriction (Schnall *et al* 1999, Iani *et al* 2004). This new methodology has been described in this journal previously (Penzel *et al* 2004). Rapid eye movement sleep is closely associated with increased sympathetic tone (Brandenberger *et al* 2001, Somers *et al* 1993, Berlad *et al* 1993), and is associated with a sustained attenuation of the PAT signal (Lavie *et al* 2000). Moreover, episodic vasoconstrictions associated with the occurrence of rapid eye movements are superimposed on this attenuation (Likhtik and Lavie 2001). The observations that the amplitude of the PAT signal and its variability during REM sleep are uniquely different in comparison with NON-REM sleep (Lavie *et al* 2000, Likhtik and Lavie 2001, Dvir *et al* 2002) prompted us to develop an automatic REM scoring algorithm based on these features and on actigraphic sleep-wake detection. The actigraphic method for sleep-wake differentiation is based on wrist movements rather than electroencephalographic recordings, and its reliability and validity have been reported previously (Hedner *et al* 2004). So far, none of the cardio-respiratory ambulatory devices incorporated any objective documentation of sleep-wake states, and rather rely on approximating sleep time from lights off and lights on times. This algorithm, developed using genetic algorithm (GA) optimization tools (Goldberg 1989, Holland 1992, Koza 1992), is described in the present paper.

Methods

The PAT signal

The PAT signal was recorded using the WP_100 (Itamar Medical Caesarea, Ltd), a wrist-mounted device simultaneously with polysomnographic (PSG) data both registered in a time-synchronized manner in the sleep laboratory. The WP_100 device was described in detail previously (Bar *et al* 2003, Pittman *et al* 2004). Briefly, it is comprised of a battery-powered, forearm-mounted console unit placed just above the wrist, and two finger-mounted probes: PAT probe and pulse oximetry. The PAT probe applies a uniform pressure field over the distal two phalanges of the finger, including the fingertip, which unloads arterial wall tension and inhibits distal venous pooling and distension—potential sources of veno-arterial mediated vasoconstriction reflex. The PAT probe measures the pulsatile variations in blood volume in the finger. This unit provides the power supply, first-level signal processing, data acquisition, and storage functions required for monitoring the pulse oximetry and PAT signals. In addition, data from an embedded actigraph are continuously recorded. All three signals are recorded at a sample rate of 100 Hz and stored on a removable flash disk throughout the study. A fourth signal, pulse rate, is derived from the PAT signal waveform.

Standard in-laboratory overnight PSG was performed using a computerized polysomnography system (Embla, Flaga Medical, Reykjavik, Iceland), with the following channels: EEG (C3-A2 and O2-A1), EOG (right and left), chin EMG, arterial oxygen saturation, nasal airflow (pressure canula), ECG, chest and abdominal wall motion (respiratory effort belts), bilateral tibialis EMG, body position, and auxiliary channel with a synchronizing signal from the WP_100 device. The PSG recordings were scored manually for sleep stages and respiratory events (apnea/hypopnea/RERA) according to the American Academy of Sleep Medicine criteria (American Academy of Sleep Medicine Task Force 1999). A respiratory event was defined as an airflow amplitude reduction of >50% from the baseline lasting at least 10 s, or having a less significant reduction in the airflow amplitude, but coupled with arousal or oxygen desaturation of at least 4% or arousal coupled with flow limitation in the airflow signal. The PSG-respiratory disturbances index (RDI) was calculated as the number of respiratory events per hour of sleep. The scorer had no access to the WP_100 data or results while scoring the PSG data and vice versa. The overnight sleep studies were considered acceptable for data analysis if none of the following rejection criteria occurred: (1) PSG-related rejection (PSG actual sleep time <1.5 h, technical failure of synchronizing the PSG to the WP_100, or poor quality of PSG recording); and (2) WP_100-related rejection (WP_100 valid sleep time <1.5 h).

The automatic REM detection algorithm (ARDA)

Each WP_100 sleep record was divided into 5 min sliding windows with 30 s increments. For each interval, two time series were constructed based on the amplitudes and inter-pulse periods derived from the PAT signal. A set of 16 features was extracted from the two time series: the average PAT amplitude, the average inter pulse period (IPP), the scaling exponents of a detrended fractal analysis (DFA) of the PAT amplitude and the IPP (Dvir *et al* 2002, Bunde *et al* 2000, Peng *et al* 1995) various spectral components and the ratios of the high-to-low frequency peaks of the spectral density functions derived from the PAT amplitude and IPP. Subsequently, the likelihood of detecting a 30 s epoch defined as 'sleep' by the actigraph algorithm as being a REM sleep epoch, was constructed using a 16-term prediction function based on the above features. The validation of the actigraph algorithm to identify sleep and waking was reported previously (Hedner *et al* 2004).

The following prediction function was used:

$$\begin{aligned} \text{Pr(REM)} = & k_1 * \text{Amp} + k_2 * \text{IPPDFA} + k_3 * \text{AmpDFA} + k_4 * \text{SpectComp11} \\ & + k_5 * \text{SpectComp21} + k_6 * \text{IPP} + k_7 * \text{ADP} + k_8 * \text{ULFIPP} + k_9 * \text{VLFIPP} \\ & + k_{10} * \text{LFIPP} + k_{11} * \text{HFIPP} + k_{12} * \text{ULFAmp} + k_{13} * \text{VLFamp} + k_{14} * \text{LFAmp} \\ & + k_{15} * \text{HFAmp} + k_{16} \end{aligned}$$

where Amp is the mean of the PAT signal amplitude, IPP is the PAT derived inter-pulse period, IPPDFA is the scaling DFA exponent based on the IPP, AmpDFA is the scaling DFA exponent of the amplitude, SpectComp11 is the ratio of the low to high spectral density of the amplitude, SpectComp21 is the ratio of the low to high spectral density of the IPP, ADP is a weighting factor to account for the increased amount of REM sleep in the last third of the sleep period, LF is the low frequency spectral density, ULF is the ultra low frequency spectral density, VLF is the very low frequency spectral density and HF the high frequency spectral density.

The frequency ranges for the spectral densities are: from 0.4 to 0.15 Hz (HF), from 0.15 to 0.04 Hz (LF), from 0.04 to 0.015 Hz (VLF) and from 0.015 to 0.005 Hz (ULF), which correspond to the respiratory, baro-receptors, thermoregulation and hormonal ranges, respectively (Burgess *et al* 2004). Even though the physiologic origins of ULF in heart rate variability are obscure there is evidence that it may be related to physical activity and transitions from sleep to wake and wake to sleep (Roach *et al* 2004).

A sleep epoch was determined as REM if $\text{Pr(REM)} \geq \text{threshold}$; otherwise the determination was an epoch of non-REM sleep. The values of the coefficients (K_1 – K_{16}) and the threshold were determined using genetic algorithms (GA). In addition, the following heuristic rules were applied: (i) the first 45 min after sleep onset, as defined by the actigraphic sleep–wake algorithm, were considered as a non-REM period. (ii) Short stand alone REM segments of less than 5 min were considered non-REM periods. (iii) Epochs of 2 min or less of non-REM in between 2 periods of REM were considered as REM and could overrule the actigraphic sleep–wake algorithm. The reason for applying the 45 min rule is that except for narcolepsy and depression, REM sleep during habitual sleep seldom occurs within the first 45 min after sleep onset. Thus, declaring the first 45 min of sleep as NONREM sleep sacrifices small number of REM periods but at the same time allowed us to improve the accuracy of ARDA considerably.

Genetic algorithms

The GA was used to optimize the values of the K_i coefficients maximizing the best score for a defined price function. The GA is best used when the search space is large, complex, not intuitively understood and there is no precise mathematical model to describe the link between the variables but rather some weak indications. In such cases classical gradient optimization methods can easily obtain local optima of the price function but might give poor performance on another set derived from the same population. GA, by analogy, considers the optimal solution as a genotype (the set of K_i) with several genes (each of the K_s), having a set of possible values (Goldberg 1989). Genetic algorithms simulate an initial population, randomly chosen, and in an iterative way compute the value of the population performance according to the pre-defined price function. In each cycle of testing all the competing links between the genes define a generation. Then, it simulates repeatably the population changes until reaching a genome that performs best (Goldberg 1989, Holland 1992, Koza 1992). The number of generations required is strongly dependant on the initial population chosen and the time it takes depends on computing resources. In our case ~100 generations were needed.

Table 1. Demographic data of the training (T, N = 30) and validation (V, N = 30) sets.

RDI	Gender M/F		Age		BMI		RDI/PSG	
	T	V	T	V	T	V	T	V
RDI ≤ 20	5/5	8/2	39.1 ± 15.3	40 ± 15.3	25.9 ± 6.9	27.5 ± 5.6	10.4 ± 6.1	7.2 ± 5.2
20 < RDI < 40	8/2	9/1	47.9 ± 14.7	53.5 ± 7.5	29.1 ± 5.8	30.9 ± 6.0	28.3 ± 6.8	29.0 ± 5.0
RDI ≥ 40	8/2	10/0	53.3 ± 11.5	51.5 ± 14.7	29.8 ± 4.3	32.0 ± 4.2	57.1 ± 16.9	58.3 ± 17.6

BMI: body mass index, RDI: respiratory disturbance index (number of apneas plus hypopneas divided by hours of sleep).

The strength of GA stems from the implicitly parallel search for the solution space with a population of candidate solutions (K_i) that is manipulated in repeated iterative simulations. The candidate solutions represent every possible behaviour of the price function.

Training and validation sets

The algorithm was optimized using a training set of 30 subjects, all referred for whole night polysomnography due to suspected sleep apnea syndrome. To allow a wide range of obstructive sleep apnea (OSA) severities the training set comprised of 10 patients with mild or no OSA (RDI < 20, m/f : 5/5, age: 39.1 ± 15.3, BMI: 25.9 ± 6.9), 10 patients with moderate OSA (20 < RDI < 40, m/f : 8/2, age: 47.9 ± 14.7, BMI: 29.1 ± 5.8) and 10 patients with severe OSA (RDI > 40, m/f : 8/2 age: 53.3 ± 11.5, BMI: 29.8 ± 4.3). None of the subjects had previously undergone a PSG study or was treated for sleep apnea. The exclusion criteria for the study were as follows: permanent pacemaker, nonsinus cardiac arrhythmias, severe lung disease, finger deformity that precludes adequate probe application, use of α -adrenergic receptor blockers less than 24 h from the study or use of short acting nitrates less than 3 h from the study or unwillingness to sign an informed consent. The study protocol was approved by the Ethics Committee of the RAMBAM Medical Centre, and subjects gave their written informed consent prior to participation. The reason for selecting a training set of patients with sleep-disordered breathing is that 80–85% of all patients are referred to diagnostic sleep recordings because of suspected sleep apnea. Furthermore, in these patients the PAT signal is affected by the apneic events which could potentially mask the REM-related changes in the signal, thus it is of particular importance to determine the validity of ARDA in these patients.

The validation set comprised 30 patients meeting the same inclusion and exclusion criteria stratified as the training set.

Results

Table 1 presents the demographic data of the training set stratified to the three sleep apnea severity groups. The group comprised 21 men and 9 women, with an average age, BMI and RDI of 46.8 ± 14.78 years, 28.81 ± 5.8 kg m⁻² and 31.9 ± 22.3 events h⁻¹, who slept for 344.5 ± 50.9 min as determined by PSG. Table 2 presents the manually and automatically scored REM data for the training and validation sets. The training set showed a close agreement between the manual and automatic scoring with respect to total minutes (67.9 ± 29.9 versus 71.0 ± 34.3 min; $r = 0.68$, $p < 0.0003$) and percentage of REM sleep (19.4 ± 6.8 versus 20.3 ± 8.4%; $r = 0.57$, $p < 0.0009$). There was a moderate agreement, however, with respect to the total number of REM periods (3.3 ± 1.3 versus 3.5 ± 1.3; $r = 0.33$, $p < 0.06$). Table 3 presents a 3 × 3 states matrix of Wake/REM/NREM epochs as determined by PSG and the sleep–wake

Table 2. REM data obtained by manual and automatic analysis for the training (T) and validation (V) sets and the correlations between them.

	REM dur (min)		REM (%)		Number of REM	
	T	V	T	V	T	V
Manual scoring	67.9 ± 29.9	71.9 ± 26.5	19.4 ± 6.8	19.9 ± 5.9	3.3 ± 1.3	3.4 ± 1.2
Automatic scoring	71.0 ± 34.3	67.8 ± 34.7	20.3 ± 8.4	19.9 ± 8.8	3.5 ± 1.3	3.3 ± 1.6
Correlation	0.68	0.65	0.57	0.58	0.33	0.34
	$P < 0.0003$	$p < 0.0003$	$P < 0.0009$	$p < 0.0009$	$P < 0.06$	$p < 0.06$

REM dur: REM duration; REM (%): percentage of REM sleep.

Table 3. A 3 × 3 states matrix of the training set as determined by the sleep–wake and ARDA Watch-PAT algorithms in comparison with PSG.

PAT	PSG		
	Wake	Sleep non-REM	REM sleep
Wake	3242	1648	188
Sleep non-REM	1316	13 526	874
REM sleep	361	1441	3001

Sensitivity, specificity and agreement for the detection of a REM epoch are calculated for epochs defined as sleep (shaded).

actigraphic algorithm and ARDA for the training set. Epochs in each state were accumulated across all subjects. The overall sensitivity, specificity and agreement of ARDA to detect PSG scored REM epochs were calculated only on epochs detected as sleep by both the PSG and the sleep–wake algorithm. These were 77.5%, 90% and 88%, respectively. When calculated only on epochs scored as sleep by the Watch-PAT sleep–wake algorithm, or separately for the three subgroups, there were small and insignificant differences.

The validation set was similar to the training set. It comprised of 27 men and 3 women, with an average age, BMI and RDI of 48.4 ± 13.9 years, $30.1 \pm 5.4 \text{ kg m}^{-2}$ and $34.8 \pm 27.8 \text{ events h}^{-1}$ respectively, who slept for $355.5 \pm 47.5 \text{ min}$. Similarly to the training set, there was a close agreement between the manual and automatic scoring for REM duration (71.9 ± 26.5 versus $67.8 \pm 34.7 \text{ min}$; $r = 0.65$, $p < 0.0003$) and REM percentages (19.9 ± 5.9 versus $19.9 \pm 8.8\%$; $r = 0.58$, $p < 0.0009$), and a moderate agreement for the number of REM periods (3.4 ± 1.2 versus 3.3 ± 1.6 ; $r = 0.34$, $p < 0.06$). This close agreement is demonstrated in figures 1 and 2 that depict the wake, non-REM and REM states scored manually from the PSG records, and as determined automatically by the actigraphic sleep–wake and REM detection algorithms, for two patients of different OSA severities from the validation set. ARDA sensitivity, specificity and agreement in detecting REM epochs, calculated as in the training group, were 78%, 92% and 89%, respectively (table 4). As in the training set, analysis of the sleep epochs as determined by the Watch-PAT sleep–wake algorithm, or by groups of apnea severity did not reveal meaningful differences. Figure 3 depicts the Bland–Altman of % REM showing a well-balanced agreement between the PSG and ARDA over the whole range with insignificant under-scoring in the low range and an over-scoring in the high range.

Finally, we analysed the detection accuracy of ARDA in the validation group with the receiving-operating characteristic curve (ROC). The area under the curve was 88% which indicates a very good accuracy (figure 4).

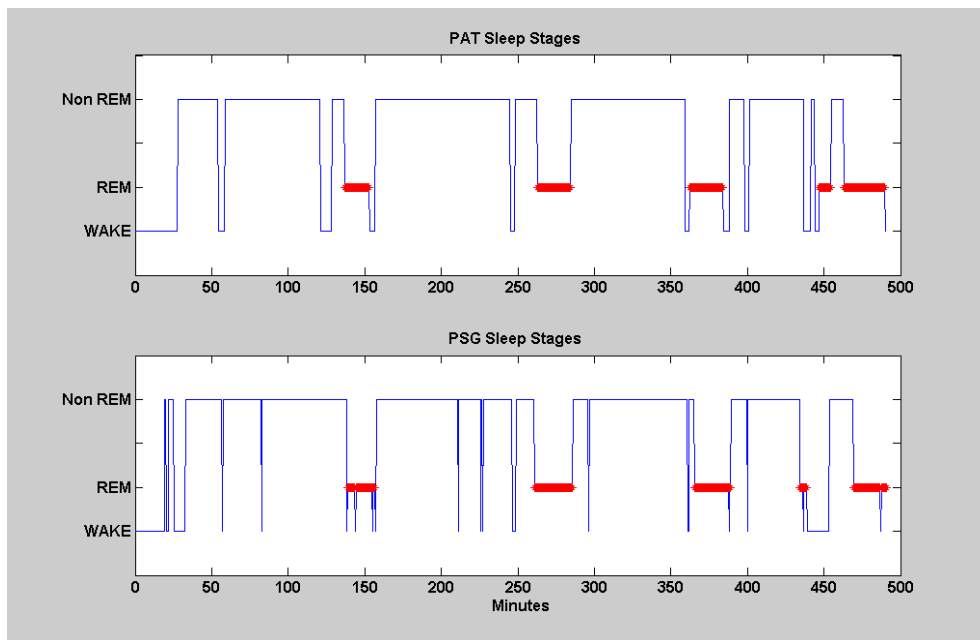


Figure 1. A graph describing minutes of 'wake', 'NONREM sleep' and 'REM sleep' scored manually from the polysomnographic records and by the automatic sleep-wake and REM detection algorithms, in a patient from the group with mild-normal sleep apnea group.

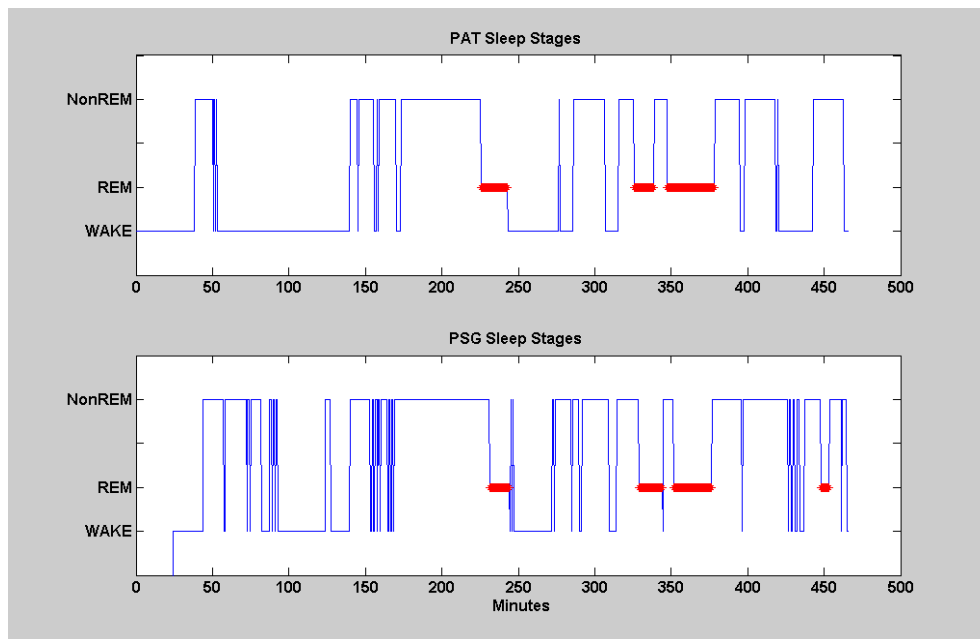


Figure 2. A graph describing minutes of 'wake', 'NONREM sleep' and 'REM sleep' scored manually from the polysomnographic records and by the automatic sleep-wake and REM detection algorithms, in a patient from the group with moderate sleep apnea.

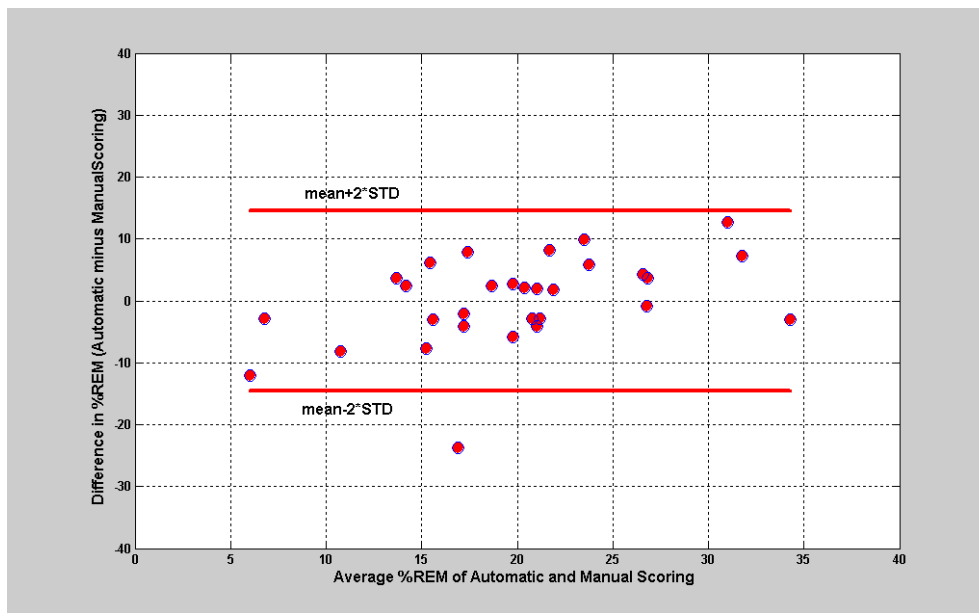


Figure 3. A graph describing the Bland–Altman of error in % REM detection versus mean value of % REM from the polysomnography (PSG) and the automatic REM detection algorithm (ARDA). Error in % REM = ARDA % REM – PSG % REM.

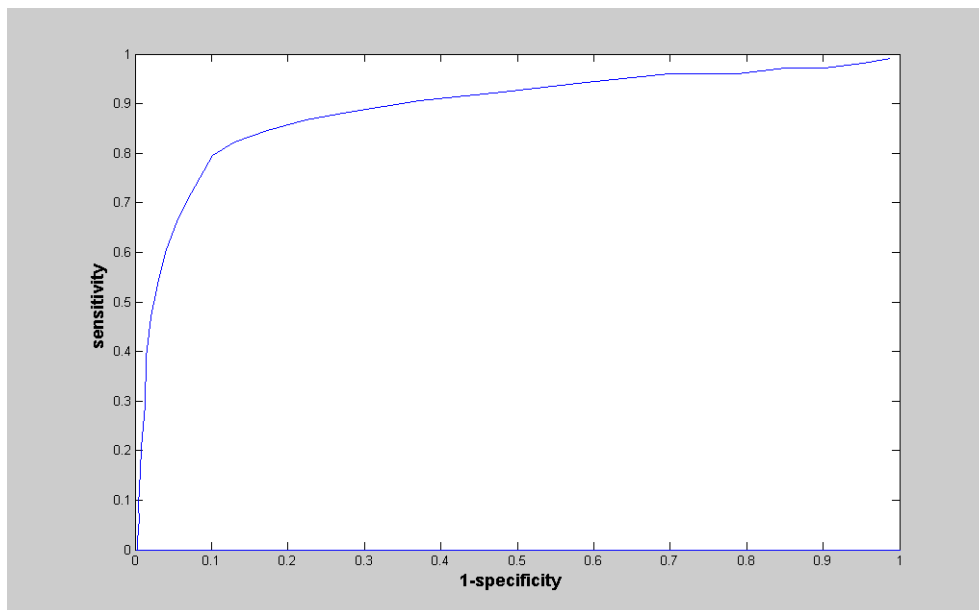


Figure 4. Receiver-operating characteristic curve showing the sensitivity and 1-specificity of each of the observed values of the ARDA scores. The area under the curve is 88%.

Table 4. A 3×3 states matrix of the validation set as determined by the sleep-wake and ARDA Watch-PAT algorithms in comparison with PSG.

PAT	PSG		
	Wake	Sleep non-REM	REM sleep
Wake	3275	1995	242
Sleep non-REM	933	13 659	862
REM sleep	167	1134	3061

Sensitivity, specificity and agreement for the detection of a REM epoch are calculated for epochs defined as sleep (shaded).

Discussion

The present paper describes a novel method to identify REM sleep that is based on a single recording channel of the finger's peripheral arterial tone and actigraphy. The rationale of using the peripheral tone in the finger relies on the well-documented association between REM sleep and sympathetic activation shown by several researchers using a variety of methodologies. These include analysis of heart rate variability by spectral analysis or Poincare plots of R-R intervals (Berlad *et al* 1993, Roach *et al* 2004, Trinder *et al* 2001, Charloux *et al* 2002), electrophysiological recordings from the peroneal nerve (Somers *et al* 1993), lumbar sympathetic nerve activity (Miki *et al* 2004) and measurements of pre-ejection period and blood pressure (Sei and Morita 1999). Furthermore, there is evidence that there is strong coupling between the REM related sympathetic activation and adrenocorticotrophic and electroencephalographic ultradian cycles (Gronfier *et al* 1999, Brandenberger *et al* 1998).

Using a newly designed finger probe to measure the peripheral arterial tone, Lavie *et al* (2000) demonstrated that REM sleep is associated with a characteristic increase in peripheral tone manifested as robust vasoconstriction in the fingers' arterioles. The attenuation in the PAT signal amplitude was associated with increased variability that was closely linked with the occurrence of rapid eye movements (Likhtik and Lavie 2001). Thus, bursts of rapid eye movements were temporally related to phasic vasoconstrictions superimposed on the tonic attenuation of the PAT signal throughout the REM period. The temporal pattern of the fluctuations in the amplitude of the PAT signal was distinctly different from that observed in non-REM sleep, as revealed by a detrended fractal analysis (Dvir *et al* 2002).

In view of the unique characteristics of the PAT signal during REM sleep, the ARDA comprised features extracted from variations in the amplitude of the PAT signal and from variations in the PAT-derived inter-pulse period as a surrogate of heart rate variability. Thus, the basic elements of the algorithm included the amplitude of the PAT signal, and features reflecting the pattern of variability in the PAT amplitude based on spectral analysis and detrended fractal analysis (DFA). As the variability in the amplitude of the PAT signal during REM sleep reflects the occurrence of rapid eye movements that were shown to follow periodic pattern (Lavie 1979, Krynicki 1975), we expected to find low frequencies in variations in the PAT amplitude in addition to higher magnitudes of the fractal exponents as shown by Dvir *et al* (2002). The rest of the components were derived from the spectral analysis of the inter-pulse interval time series relying on previous results demonstrating that heart rate variability during REM sleep is characterized by an increased power density in the low-frequency end of the spectrum and decreased power density in the high-frequency range. We also incorporated a weighting element that gives more weight to REM occurring towards the end of the sleep

period to account for the nonsymmetrical distribution of REM sleep during the night (Agnew and Webb 1968). Removing the asymmetric weighting index from the prediction equation degraded the sensitivity of ARDA by 4.8%, only in patients with RDI < 20. This effect was smaller in the entire sample (−1.8%). Thus, the probability of an epoch of sleep to be defined as REM by the ARDA was high if there was a simultaneous occurrence of amplitude attenuation, increase of spectral power density in the low relative to the high frequencies of the spectral range calculated from the amplitude and inter-pulse period time series, and increase in the DFA exponent.

Considering that a single channel of information was utilized and that sleep–wake determination was solely based on actigraphy rather than on polysomnography, the algorithm was reasonably accurate with 78% sensitivity and 92% specificity in an independent validation set. Similar results were obtained whether we analysed sleep epochs scored jointly by PSG and the Watch-PAT sleep–wake algorithm, or by the Watch-PAT algorithm alone. Moreover, ARDA performed equally well in patients with different ages and sleep apnea severities. As the resumption of breathing in sleep apnea patients is associated with intense sympathetic activation and peripheral vasoconstriction, the fact that the algorithm performed equally well in patients with severe as well as mild sleep apnea suggests that its performance was minimally affected by the added variability in the amplitude of the PAT signal due to the apnea events.

As could be expected, however, presence of sleep apnea in these patients greatly influenced the relative amount of REM sleep. Percentage and minutes of REM sleep and the number of REM periods as determined by ARDA were all negatively correlated with the severity of sleep apnea as indexed by RDI (−0.43, $p < 0.01$; −0.41, $p < 0.02$ and −0.38, $p < 0.04$, respectively). This is congruent with the relationship between manually determined percentages of REM sleep and RDI calculated across 10 000 PSG records of sleep apnea patients investigated in our laboratory (−0.22, $p < 0.000 01$) (unpublished observations).

The very close accuracy of the ARDA in the training and validation sets suggests a robust algorithm. This robustness was achieved due to the use of a novel optimization method—the GA, which was shown to yield similarly robust results in other studies (Goldberg 1989, Holland 1992, Koza 1992). The Bland–Altman slight asymmetry can be attributed to either a few outliers or the fact that the optimization price function was solely based on epoch-to-epoch agreement and sensitivity and specificity, and did not include % REM as a factor. It might be that including this factor in the price function could have corrected this asymmetry but probably on the account of reducing the accuracy as projected in the agreement.

Breathing disorders in sleep is the most prevalent sleep disorder affecting at least 2% of women and 4% of men in the general population (Ball *et al* 1997, Young *et al* 1993, 1997), most of them are yet undiagnosed (Young *et al* 1997). The ambulatory Watch-PAT 100 device, which records and stores the PAT signal, is intended for home monitoring of sleep apnea patients that can greatly facilitate patient diagnosis and treatment. Adding the ARDA to the Watch-PAT 100 device can provide an important tool to assess sleep structure in addition to apneas and sleep–wake detection.

It should be emphasized, however, that ARDA is not intended to replace PSG. The performance of the ARDA is limited by its inability to detect sleep onset REM periods, or REM periods occurring within 45 min of sleep onset. Thus, this algorithm cannot be used in patients with known changes in the REM–nonREM cycle such as with endogenous depression (Kupfer *et al* 1976) or narcolepsy (Dement *et al* 1966). In order to detect altered REM–NONREM cycles, ARDA should be modified to remove the restriction of not allowing the occurrence of REM sleep during the first 45 min after sleep onset, which should be an interesting future research agenda.

In spite of this limitation, the convenience of obtaining information on REM sleep using an unattended and simple-to-operate hand-mounted device may add clinically important information in the diagnosis and follow-up of sleep apnea patients. Such information may be valuable in assessing the effect of breathing disorders in sleep on sleep structure and identifying patients with REM-related sleep apnea. Furthermore, as post-treatment increase in REM sleep is associated with subjective improvement in sleep quality (Verma *et al* 2001), this added feature of the Watch_PAT 100 will be useful in evaluating the efficacy of treatment in sleep apnea patients.

References

- Agnew H W Jr and Webb W B 1968 The displacement of stages 4 and REM sleep with a full night of sleep *Psychophysiology* **5** 142–8
- American Academy of Sleep Medicine Task Force 1999 Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force *Sleep* **22** 667–89
- Aserinsky E and Kleitman N 1953 Regularly occurring periods of eye motility and concurrent phenomena during sleep *Science* **118** 273–4
- Ball E M, Simon R D Jr, Tall A A, Banks M A, Nino-Murcia G and Dement W C 1997 Diagnosis and treatment of sleep apnea within the community. The Walla Walla project *Arch. Intern. Med.* **157** 419–24
- Bar A, Pillar G, Dvir I, Sheffy J, Schnall R P and Lavie P 2003 Evaluation of portable device based on peripheral arterial tone for unattended home sleep studies *Chest* **123** 695–703
- Berlad I, Shlitner A, Ben-Haim S and Lavie P 1993 Power spectrum analysis and heart rate variability in stage 4 and REM sleep: evidence for state-specific changes in autonomic dominance *J. Sleep Res.* **2** 88–90
- Boukadoum A M and Ktonas P Y 1988 Non-random patterns of REM occurrences during REM sleep in normal human subjects: an automated second-order study using Markovian modelling *Electroencephalogr. Clin. Neurophysiol.* **70** 404–16
- Brandenberger G, Charloux A, Gronfier C and Otzenberger H 1998 Ultradian rhythms in hydromineral hormones *Horm. Res.* **49** 131–5
- Brandenberger G, Ehrhart J, Piquard F and Simon C 2001 Inverse coupling between ultradian oscillations in delta wave activity and heart rate variability during sleep *Clin. Neurophysiol.* **12** 992–6
- Bunde A, Havlin S, Kantel J W, Penzel T, Peter J-H and Voigt K 2000 Correlated and uncorrelated regions in heart-rate fluctuations during sleep *Phys. Rev. Lett.* **85** 3736–9
- Burgess H J, Penev P D, Schneider R and Van Cauter E 2004 Estimating cardiac autonomic activity during sleep: impedance cardiography, spectral analysis, and Poincare plots *Clin. Neurophysiol.* **115** 19–28
- Charloux A, Piquard F, Ehrhart J, Mettauier B, Geny B, Simon C and Brandenberger G 2002 Time-courses in renin and blood pressure during sleep in humans *J. Sleep Res.* **11** 73–9
- Dement W, Rechtschaffen R and Gulevich G 1966 The nature of the narcoleptic sleep attack *Neurology* **16** 18–33
- Dvir I, Adler Y, Freimark D and Lavie P 2002 Evidence for fractal correlation properties in variations of peripheral arterial tone during REM sleep *Am. J. Physiol. Heart Circ. Physiol.* **283** H434–H439
- Goldberg D E 1989 *Genetic Algorithms in Search, Optimization and Machine Learning* (Reading, MA: Addison-Wesley)
- Gronfier C, Simon C, Piquard F, Ehrhart J and Brandenberger G 1999 Neuroendocrine processes underlying ultradian sleep regulation in man *J. Clin. Endocrinol. Metab.* **84** 2686–90
- Grozinger M, Wolf C, Uhl T, Schnaffer C and Roschke J 1997 Online detection of REM sleep based on the comprehensive evaluation of short adjacent EEG segments by artificial neural networks *Prog. Neuropsychopharmacol. Biol. Psychiatry* **21** 951–63
- Haustein W, Pilcher J, Klink J and Schulz H 1986 Automatic analysis overcomes limitations of sleep stage scoring *Electroencephalogr. Clin. Neurophysiol.* **64** 364–74
- Hedner J, Pillar G, Pittman S D, Zou D, Grote L and White D P 2004 A novel adaptive wrist actigraphy algorithm for sleep–wake assessment in sleep apnea patients *Sleep* **27** 1560–6
- Helfand R, Lavie P and Hobson A J 1986 REM/NONREM discrimination via ocular and limb monitoring: correlation with polygraphic data and development of a REM state algorithm *Psychophysiology* **23** 334–9
- Holland J H 1992 *Adaptation in Natural and Artificial Systems* (Cambridge, MA: MIT Press)
- Iani C, Gopher D and Lavie P 2004 Effects of task difficulty and invested mental effort on peripheral vasoconstriction *Psychophysiology* **41** 789–98

- Koza JR 1992 *Genetic Programming: on the Programming of Computers by Means of Natural Selection* (Cambridge, MA: MIT Press)
- Krynicky V 1975 Time trends and periodic cycles in REM sleep eye movements *Electroencephalogr. Clin. Neurophysiol.* **39** 507–13
- Ktonas P Y and Smith J R 1978 Automatic REM detection: modifications on an existing system and preliminary normative data *Int. J. Biomed. Comput.* **9** 445–64
- Kupfer D J, Foster F G and Reich L 1976 EEG sleep changes as predictors in depression *Am. J. Psychiatry* **33** 622–6
- Lavie P 1979 Rapid eye movements in REM sleep—more evidence for a periodic organization *Electroencephalogr. Clin. Neurophysiol.* **46** 683–8
- Lavie P, Schnall R P, Sheffy J and Shlitner A 2000 Peripheral vasoconstriction during REM sleep detected by a new plethysmographic method *Nature Med.* **6** 606
- Likhtik E and Lavie P 2001 REM-related peripheral vasoconstriction—association with rapid eye movement density *Sleep* (Suppl) **24** A78 (abstract)
- Mamelak A and Hobson A J 1989 Nightcap: a home-based sleep monitoring system *Sleep* **12** 157–66
- Miki K, Oda M, Kamijyo N, Kawahara K and Yoshimoto M 2004 Lumbar sympathetic nerve activity and hindquarter blood flow during REM sleep in rats *J. Physiol.* (Pt 1) **557** 261–71
- Peng C K, Havlin S, Stanley H E and Goldberger A L 1995 Quantification of scaling exponents and crossover phenomena in non-stationary heartbeat time series *Chaos* **5** 82–7
- Penzel T, Kesper K, Pinnow I, Becker H F and Vogelmeier C 2004 Peripheral arterial tonometry, oximetry and actigraphy for ambulatory recording of sleep apnea *Physiol. Meas.* **25** 1025–36
- Pittman S D, Ayas N T, MacDonald M M, Malhotra A, Fogel R B and White D P 2004 Using a wrist-worn device based on peripheral arterial tonometry to diagnose obstructive sleep apnea: in-laboratory and ambulatory validation *Sleep* **27** 923–33
- Rechtschaffen A and Kales A 1968 *A Manual of Standardized Terminology, Techniques, and Scoring System for Sleep Stages of Human Subjects* (Washington, DC: Public Health Service, US Government Printing Office)
- Roach D, Wilson W, Ritchie D and Sheldon R 2004 Dissection of long-term heart rate variability. Controlled induction of prognostic measures by activity in the laboratory *J. Am. Coll. Cardiol.* **43** 2271–7
- Sayers B M 1973 Analysis of heart rate variability *Ergonomics* **16** 17–32
- Schnall R P, Shlitner A, Sheffy J, Kedar R and Lavie P 1999 Periodic, profound peripheral vasoconstriction: a new marker of obstructive sleep apnea *Sleep* **22** 939–46
- Sei H and Morita Y 1999 Why does arterial blood pressure rise actively during REM sleep? *J. Med. Invest.* **46** 11–7
- Sforza E and Vandi S 1996 Automatic Oxford-Medilog 9200 sleep staging scoring: comparison with visual analysis *J. Clin. Neurophysiol.* **3** 227–33
- Somers V K, Dyken M E, Mark A L and Abboud F M 1993 Sympathetic-nerve activity during sleep in normal subjects *N. Engl. J. Med.* **328** 303–7
- Trinder J, Kleiman J, Carrington M, Smith S, Breen S, Tan N and Kim Y 2001 Autonomic activity during human sleep as a function of time and sleep stage *J. Sleep Res.* **10** 253–64
- Tsuji Y, Satoh H, Itoh N, Sekiguchi Y and Nagasawa K 2000 Automatic detection of rapid eye movements by discrete wavelet transform *Psychiatry Clin. Neurosci.* **54** 276–7
- Verma A, Radtke R A, Van Landingham K E, King J H and Husain A M 2001 Slow wave sleep rebound and REM rebound following the first night of treatment with CPAP for sleep apnea: correlation with subjective improvement in sleep quality *Sleep Med.* **2** 215–23
- Young T, Evans L, Finn L and Palta M 1997 Estimation of the clinically diagnosed proportion of sleep apnea syndrome in middle-aged men and women *Sleep* **20** 705–6
- Young T, Palta M, Dempsey J, Skatrud J, Weber S and Badr S 1993 The occurrence of sleep-disordered breathing among middle-aged adults *N. Engl. J. Med.* **328** 1230–5