Sleep Breathing Flow Characteristics as a Sign for the Detection of Wakefulness in Patients with Sleep Apnea

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Key Words

Sleep apnea-hypopnea syndrome · Airflow waveform morphology · Sleep efficiency

Abstract

Background: To improve the performance of simplified sleep studies, it is essential to properly estimate the sleep time. **Objectives:** Our aim is to estimate sleep efficiency on the basis of flow breathing signal characteristics. **Methods:** Twenty subjects with sleep apnea-hypopnea syndrome diagnosed by polysomnography were studied. A characteristic pattern of flow signal defined our criteria for wakefulness and sleep. Sleep was analyzed in 2 different runs: (1) in the usual manner (neurological and respiratory variables), and (2) only the nasal cannula flow signal was displayed on the computer screen and the sleep and wakefulness periods were scored according to our criteria. At the end of the scoring process, all the signals were displayed on the screen to analyze the concordance. **Results:** Three thousand and sixty-nine screens were analyzed. The polysomnography sleep efficiency measured was 80.8%. The estimated sleep efficiency measured by nasal prongs was 78.9%. The detection

and concordance of wakefulness had a sensitivity of 58.7%, a specificity of 96.4%, a positive predictive value of 81.3% and a negative predictive value of 89.6%. **Conclusions:** Our criteria for sleep and wakefulness based on airflow waveform morphology are a helpful parameter for estimating sleep efficiency in a simplified sleep study.

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Introduction

Sleep apnea-hypopnea syndrome (SAHS) is a common health problem [1, 2]. Polysomnography (PSG) is the recommended method for diagnosis [3] but requires expertise and is time consuming and expensive. Increasing awareness of SAHS in the media and in medical circles [4], in addition to the growing evidence of SAHS comorbidity [5] and even mortality [6], has exponentially in-

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creased the number of patients requiring evaluation. However, this growth in demand has not been accompanied by improvements in the approach to this problem [7]. Therefore, there is a growing interest in alternative diagnostic methods and approaches. One approach that could be helpful is the performance of simple sleep studies using respiratory variables that can be used both in a laboratory and at home and would provide an accurate diagnosis at a much lower cost [8–10].

However, simplified respiratory systems have limitations, such as the lack of electroencephalogram channels, and thus the inability to assess sleep architecture or staging, or to calculate total sleep time. The latter is particularly important because it may dramatically change the apnea-hypopnea index in patients who present a low sleep efficiency [11]. Improving the performance of simplified studies is essential to any attempt to estimate sleep time. Our aim in the present study is to ascertain whether it is possible to estimate the sleep time study by analyzing the flow breathing signal characteristics.

Methods and Materials

Study Subjects

The study population consisted of 20 consecutive subjects (mean age 50 ± 13 years, 17 males, 3 females, body mass index 28.6 ± 4.5) with a suspicion of SAHS, referred from the outpatient clinic of the Hospital Clinic in Barcelona to undergo a PSG in the sleep laboratory. Informed consent was obtained from all subjects, and the study protocol was approved by the Ethics Committee of our Hospital.

Sleep Study

PSG was performed in the usual manner [12]. Briefly, the registered variables were electroencephalogram, chin electromyogram, electro-oculogram, tibial electromyogram, arterial oxygen saturation, flow measured by linearized nasal prongs, waveform, thermistor, and rib cage and abdominal motion. Sleep staging was performed manually, using the criteria of the American Academy of Sleep Medicine scoring rules [3]. An apnea was defined as the absence of airflow for ≥ 10 s. Hypopnea was defined as any discernible reduction in the amplitude of the airflow signal ending in an arousal and/or association with a 3% desaturation, with a duration of at least 10 s.

Wakefulness Criteria Using the Flow Signal

We examined 200 wakefulness epochs from other PSG studies beforehand in order to define our criteria for wakefulness and sleep, based on the airflow waveform morphology shown and defined in figure 1.

Study Design

After PSG, 2 different scoring passes were undertaken to analyze the results. In the first, the neurological and respiratory vari-

ables were assessed following the abovementioned classical method. The neurological variables were scored for periods of 30 s. The respiratory variables were scored for periods of 3 min, although not on the flow channel; they were scored on a new, specially created dirt-free channel. In the second respiratory scoring pass, only the nasal prong signal was displayed on the computer screen (6 epochs). Wakefulness or sleep periods were marked on the flow signal, following our criteria shown in figure 1. The scoring was performed blind to the full PSG. At the end of the scoring process, all the signals were displayed on the screen to analyze the concordance. To this end, the following process was followed: (1) the screen showed epochs of 3 min. The scored sleep phases (W, N1, N2, N3 or rapid eye movement) were displayed on the top of the screen while the flow signal periods of wakefulness were indicated by lines under the flow signal. (2) For the purpose of our study, we assumed that when over half the screen was scored as wakefulness or sleep on the neurological or the flow signal, then all the 3-min periods would be considered as wakefulness or sleep. The short respiratory periods with wakefulness criteria, consisting of ≤ 5 irregular breaths, were not counted because they were considered to be probable respiratory arousals.

Data Analysis

The PSG and probe concordance between sleep and wakefulness stages was measured by 2×2 tables. The sensitivity, specificity, positive and negative predictive values were all calculated.

Results

Mean total bed time was 7.7 ± 0.6 h. After the performance of PSG, the mean apnea-hypopnea index was 25.6 ± 17 and the mean CT90 was 4%. Table 1 shows the main results of the patients' sleep characteristics (stages, sleep time and sleep efficiency), while the bed time was used to estimate the sleep efficiency from the flow signal.

Three thousand and sixty-nine screens were analyzed. The PSG scoring showed 653 screens positive to wakefulness and 2,416 screens positive to the sleep stage. Sleep time measured by PSG was 6.2 ± 1.0 h, and sleep efficiency was $80.8 \pm 10.9\%$. When using the nasal flow scoring, 471 screens were considered as wakefulness and 2,598 as sleep. The sleep time estimated by means of the nasal flow signal was 6.1 ± 1.0 h, and the estimated sleep efficiency was $78.9 \pm 11.8\%$. Concordance of the wakefulness period between PSG and nasal prongs was observed on 383 screens (58.7%), and concordance in sleep periods on 2,328 screens (96.4%). The detection and concordance of wakefulness with the previously described criteria had a sensitivity of 0.59 and a specificity of 0.96. To identify wakefulness, the mean positive predictive value was 81% and the mean negative predictive value was 90%.

Fig. 1. Sleep and wakefulness flow characteristics. The flow signal was assessed in arbitrary units on nasal prongs.

Discussion

Our results show that the visual airflow waveform morphology is a helpful parameter for identifying wakefulness on the evidence of the high positive predictive value obtained in this study. Furthermore, the higher negative predictive value results in an estimate of sleep efficiency with little probability of error in a simplified sleep study using the previously described criteria for sleep. We believe that a method based on the character-

istics of the flow breathing signal can help us to optimize the results obtained in a simplified sleep study.

Previous studies have investigated the variability of breathing during both wakefulness and sleep but they tended to focus on the breathing pattern within each of these 2 states [13]. Further studies have observed that respiratory variability is diminished during sleep, when compared with wakefulness [14]. However, there is an absence of studies in which the breathing patterns of wakefulness have been applied during sleep to improve the

Table 1. Characteristics of the patients studied

Patient No.	PSG sleep stage					PSG		Flow signal by nasal probe	
	N1 %	N2 %	N3 %	REM %	bed time, h	sleep time, h	sleep efficiency, %	estimated sleep time, h	estimated sleep efficiency, %
1	8.4	47.3	16.9	27.4	7.6	5.9	77.6	5.5	72.4
2	14.7	59.4	7.0	18.8	8.5	6.3	74.1	5.9	69.4
3	4.8	58.4	19.3	17.5	7.7	6.8	88.3	5.9	76.6
4	3.1	73.0	0.0	23.9	6.9	5.4	78.3	5.3	76.8
5	6.6	67.3	14.3	11.8	6.9	3.0	43.5	2.9	42.0
6	18.5	65.8	0.0	15.6	7.3	5.4	74.0	5.1	69.9
7	13.7	56.1	11.3	18.9	7.9	6.0	75.9	5.8	73.4
8	4.5	56.2	18.4	20.9	8.4	7.4	88.1	7.2	85.7
9	26.6	37.3	11.9	24.3	8.7	7.7	88.5	7.4	85.1
10	2.7	44.6	29.0	23.7	7.8	6.9	88.5	6.6	84.6
11	10.6	36.5	27.4	25.5	7.1	6.1	85.9	6.2	87.3
12	25.3	24.8	0.7	49.2	8.2	6.9	84.1	7.1	86.6
13	8.0	66.5	14.8	10.8	7.6	6.6	86.8	6.7	88.2
14	3.0	46.9	23.9	26.2	6.9	6.7	97.1	6.7	97.1
15	64.1	28.8	6.7	0.0	7.1	5.3	74.6	5.5	77.5
16	14.8	47.5	17.1	0.0	7.8	6.2	79.5	6.3	80.8
17	32.1	22.0	2.6	43.3	7.5	5.6	74.7	5.0	66.7
18	15.1	66.9	3.5	14.6	7.8	6.7	85.9	6.8	87.2
19	6.7	53.5	17.7	22.2	7.3	6.5	89.0	6.6	90.4
20	16.2	75.6	7.4	0.7	8.5	7.0	82.4	6.9	81.2
Mean	15.0	51.7	12.5	19.8	7.7	6.2	80.8	6.1	78.9

outcomes of a sleep study. Furthermore, there are many sleep apnea monitoring devices equipped with software that enable us to undertake an automated analysis of data, but such analyses result in an underestimate of the respiratory disturbance index, in comparison with visual analysis [15]. Our study follows the same lines as the one recently published by the Rapoport group [16], but this was performed on continuous positive airway pressure (CPAP) treatment, and our study was performed during a diagnosis procedure. Ayappa et al. [16] identified periods of irregular/chaotic breathing defined as sequences of 3 or more breaths with irregular amplitude and frequency. Each study analyzed was scored by 2–5 scorers who separately assessed the interscorer agreement in a second pass. The agreement between the sleep stages and the flow signal for wakefulness were analyzed during a 30-second epoch screen, and agreement for wakefulness (true positive event) was defined as the majority of the breaths in the identified irregular respiration event that occurred during an epoch being scored as wakefulness by electroencephalogram. The runs of 4 or more consecutive epochs scored as wakefulness were thus defined as wakefulness. Based on this design, the authors developed

an automated algorithm for detection of irregular respiration on the basis of the analysis of individual breaths. This artificial neural network was then validated in subjects undergoing a CPAP titration. The identification of a transition from sleep to wakefulness in an autotitration with a CPAP device previously modified to include this algorithm triggered rapid drops from the instantaneously delivered pressure to the minimum pressure. This resulted in a lower mean CPAP during an arousal or in response to wakefulness, echoing the frequent reaction of sleep technicians in this situation. In fact, our criteria of wakefulness, based on the airflow waveform morphology, and those described by Ayappa et al. [16] were comparable, albeit with different targets: diagnosis of SAHS on the one hand and titration of CPAP on the other. Thus, the only difference in the method described lies in the analysis of the concordance of wakefulness between PSG and the flow signal by nasal probe. In our study, the breathing pattern for sleep and wakefulness was scored on a 3-min epoch screen instead of a 30-second epoch screen because we analyzed the flow signal on a 3-min screen for the diagnosis of SAHS in a simplified sleep study. In addition, the aim of this study was not to de-

velop an automated mechanism to detect wakefulness in a sleep study, but rather to improve the accuracy of simplified sleep studies with practical criteria for estimating sleep efficiency in these cases.

However, in the present study, some considerations and limitations need to be pointed out: (1) mistakes can arise in the rapid eye movement state, where the breathing pattern is typically irregular, or in studies where the respiratory signal is suboptimal on account of nasal obstruction or breathing through the mouth; (2) periods of wakefulness, in which the patient is relaxed and respiration is regular, could result in lower sensitivity; (3) additional studies are required to assess variability between different scorers. This is especially important in scorers

who are not fully qualified sleep physicians and who, at least in some countries (such as ours), use simplified systems [10]. Finally, (4) comparisons with automatic scoring performed by sleep devices are also required.

In conclusion, the criteria for sleep and wakefulness based on airflow waveform morphology that we have described could be a good parameter for estimating sleep efficiency in a simplified sleep study. Their application would produce findings that can enhance the diagnosis of SAHS and optimize the performance of simplified sleep studies, although we still need to obtain more data from larger numbers of patients, particularly those with a mild-moderate condition or those with associated comorbidity.

References

- 1 Young T, Palta M, Dempsey J, et al: The occurrence of sleep-disordered breathing among middle-aged adults. *N Engl J Med* 1993;328:1230–1235.
- 2 Durán J, Esnaola S, Rubio R, et al: Obstructive sleep apnea-hypopnea and related clinical features in a population-based sample of subjects aged 30 to 70 years. *Am J Respir Crit Care Med* 2001;163:685–689.
- 3 Iber C, Ancoli-Israel S, Cheson AL, Quan SF: AASM Manual for the Scoring of Sleep and Associated Events. Westchester, American Academy of Sleep Medicine, 2007.
- 4 Young T, Peppard PE, Gottlieb DJ: Epidemiology of obstructive sleep apnea: a population health perspective. *Am J Respir Crit Care Med* 2002;165:1217–1239.
- 5 Bradley TD, Floras JS: Obstructive sleep apnoea and its cardiovascular consequences. *Lancet* 2009;373:82–93.
- 6 Young T, Finn L, Peppard PE, Szklo-Coxe M, Austin D, Nieto FJ, Stubbs R, Hla KM: Sleep disordered breathing and mortality: eighteen-year follow-up of the Wisconsin sleep cohort. *Sleep* 2008;31:1071–1078.
- 7 Li Y, Chongsuvivatwong V, Geater A, Liu A: Are biomarker levels a good follow-up tool for evaluating obstructive sleep apnea syndrome treatments? *Respiration* 2008;76:317–323.
- 8 Parra O, García-Escasans N, Montserrat JM, et al: Should patients with sleep apnoea/hypopnoea be diagnosed and managed on the basis of home sleep studies? *Eur Respir J* 1997;10:1720–1724.
- 9 Mulgrew A, Nurit F, Najib A, et al: Diagnosis and initial management of obstructive sleep apnea without polysomnography. A randomized validation study. *Ann Intern Med* 2007;146:157–166.
- 10 Hernández L, Torrella M, Roger N, Lluell A, Ballester E, Quinto L, Serrano M, Masa F, Montserrat JM: Management of sleep apnea: concordance between nonreference and reference centers. *Chest* 2007;132:1853–1857.
- 11 Aarab G, Lobbezoo F, Hamburger HL, Naeije M: Variability in the apnea-hypopnea index and its consequences for diagnosis and therapy evaluation. *Respiration* 2009;77:32–37.
- 12 Rechtschaffen A, Kales A: A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects. NIH Publication. Washington, US Government Printing Office, 1968, p 204.
- 13 Bruce EN: Chemoreflex and vagal afferent mechanisms enhance breath to breath variability of breathing. *Respir Physiol* 1997;110:237–244.
- 14 Busha BF, Stella MH: State and chemical drive modulate respiratory variability. *J Appl Physiol* 2002;93:685–696.
- 15 Fietze I, Glos M, Röttig J, et al: Automated analysis of data is inferior to visual analysis of ambulatory sleep apnea monitoring. *Respiration* 2002;69:235–241.
- 16 Ayappa I, Norman RG, Whiting D, Tsai AH, Anderson F, Donnelly E, Silberstein DJ, Rapoport DM: Irregular respiration as a marker of wakefulness during titration of CPAP. *Sleep* 2009;32:99–104.