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Spectral analysis of electroencephalogram and oximetric signals in obstructive sleep apnea diagnosis

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Abstract— **This study assessed the hypothesis that blood oxygen saturation (SaO_2) and electroencephalogram (EEG) recordings could provide complementary information in the diagnosis of the obstructive sleep apnea (OSA) syndrome. We studied 148 patients suspected of suffering from OSA. Classical spectral parameters based on the relative power in specified frequency bands ($A_{f\text{-}band}$) or peak amplitudes (PA) were used to characterize the frequency content of SaO_2 and EEG recordings. Additionally, the median frequency (MF) and the spectral entropy (SE) were applied to obtain further spectral information. We applied a forward stepwise logistic regression (LR) procedure with crossvalidation leave-one-out to obtain the optimum spectral feature set. Two features from the oximetric spectral analysis (PA and MFsat) and three features from the EEG spectral analysis (A_{delta}, A_{alpha} and SEeeg) were automatically selected. 91.0% sensitivity, 83.3% specificity and 88.5% accuracy were obtained. These results suggest that MF and SE could provide additional information to classical frequency characteristics commonly used in OSA diagnosis. Additionally, nocturnal SaO_2 and EEG recordings during the whole night could provide complementary information to help in the detection of OSA syndrome.**

I. Introduction

OBSTRUCTIVE sleep apnea (OSA) syndrome is a major sleep-related breathing disorder, affecting 1 to 5% of adult men and 2% of women in western countries [1]. OSA is characterized by repetitive reduction or cessation of airflow due to partial or complete airway obstruction, leading to hypoxemia, bradycardia, arousals and fragmented sleep [2]. OSA is associated with hypertension, cardiovascular and cerebrovascular diseases and several neurobehavioral morbidities, which are of potentially great public health and economic importance [1,3]. The gold standard diagnostic method for a definitive diagnosis of OSA syndrome is overnight polysomnography (PSG). However, its relative high cost and complexity limit its capacity as a diagnostic test for OSA [4]. The main alternatives to PSG are aimed to reduce the number of recordings to be analyzed. Blood oxygen saturation (SaO_2), electrocardiogram (ECG) and electroencephalogram (EEG) have been widely used. Oxygen desaturation indexes and the cumulative time spent below a specified saturation level are generally provided by oximetry equipments [5,6]. Spectral features from classical frequency analysis are also commonly applied [7,8]. Changes in heart rate variability due to apneic episodes have been widely investigated to help in OSA diagnosis [9]. Electroencephalographic analysis also involves a great amount of studies related to OSA. Sleep related breathing disorders are linked to significant changes in sleep EEG [10]. Cortical arousals induced by apneas and hypopneas are thought to be the major contributing cause of sleep fragmentation and excessive daytime sleepiness [11]. However, quantitative EEG changes also occur when no visually discernible arousal activity is present [10].

Power spectral density (PSD) estimation has been widely used to analyze SaO_2 and EEG. Visual inspection of the PSD function from SaO_2 recordings was applied for diagnostic purposes [7,8]. On the other hand, EEG-based studies focused on the detection of arousals at the end of apnea events [11, 12]. Other researchers assessed differences in the power spectrum distribution between sleep and wakefulness EEG [13,14]. A positive correlation was found between EEG slowing during wakefulness (spectral power increase in the slow frequency bands delta and theta) and oxygen desaturations during the night [13]. In the present study, we analyzed the spectral content of SaO_2 and EEG recordings using the median frequency (MF) and the spectral entropy (SE), in order to obtain additional information to that provided by conventional methods. MF represents a simple way to characterize the spectral content of biomedical signals [15]. It is defined as the spectral component that contains half the PSD power. SE is an irregularity measure widely applied to quantize the degree of flatness in the power spectrum of biomedical signals [15,16].

In the present study, we hypothesized that apnea events affect oximetric and electroencephalographic recordings in a different way. Hence, combined SaO_2 and EEG spectral analyses by means of logistic regression (LR) could provide complementary information to help in OSA diagnosis. Furthermore, we assessed the diagnostic ability of MF and SE to test if they provided additional information to that obtained from classical frequency measures commonly used in OSA diagnosis.

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II. SIGNALS AND SUBJECTS

The population studied consisted of 148 patients (115 males and 33 females) with a mean ± standard deviation (SD) age of 52.9 ± 13.5 years. All subjects were suspected of suffering from OSA because of daytime hypersomnolence, loud snoring, nocturnal choking and awakenings or apneic events reported by the subject or a bedmate. Table I summarizes the demographic and clinical data of the population under study.

Overnight conventional polysomnographies (PSG) were carried out from midnight to 08:00 AM in the Sleep Unit of Hospital Universitario Pío del Río Hortega of Valladolid, Spain. The Review Board on Human Studies approved the protocol, and each subject gave his or her informed consent to participate in the study. Patients were continuously monitored using a polygraph (Alice 5, Respironics, Philips Healthcare, The Netherlands) and included EEG, electro-oculogram, chin electromyogram, airflow, ECG, measurement of chest wall movement and oximetry. Apnea was defined as the absence of airflow for more than 10 s, and hypopnea was defined as a decrease in respiratory flow of at least 50%, accompanied by a ≥ 4% decrease in the saturation of hemoglobin. The average apnea-hypopnea index (AHI) was computed for hourly periods of sleep. An AHI of 10 or more events per hour was considered as diagnostic of OSA.

In the present study, the SaO_2 profile and the EEG pattern in the central lead C3–A2 at the apex of the cranium from PSG were processed. SaO_2 and EEG were simultaneously recorded, with 1 Hz and 100 Hz sampling frequencies, respectively. Oximetric recordings were scanned to remove artifacts and drops to zero due to poor contact from the finger probe. EEG signals were processed offline with a 0.1 – 50 Hz digital bandpass filter. Additionally, high frequency artifacts usually generated by muscle activity were removed using a median-based adaptive threshold.

TABLE I
DEMOGRAPHIC AND CLINICAL FEATURES OF THE DATA SET

	All subjects	OSA positive	OSA negative
Subjects (n)	148	100 (67.6%)	48 (32.4%)
Age (years)	52.9 ± 13.5	55.2 ± 14.5	47.8 ± 9.4
Males (%)	77.7	83.0	66.7
BMI (kg/m^2)	29.8 ± 5.6	30.8 ± 5.0	27.3 ± 6.3
Time recorded (h)	7.2 ± 0.4	7.2 ± 0.4	7.2 ± 0.4
AHI (n/h)		40.9 ± 27.6	4.1 ± 2.4

Data are presented as mean ± SD or n (%). BMI: body mass index; AHI: apnea-hypopnea index.

III. METHODS

A. Common spectral features from SaO_2 and EEG

The power spectral density (PSD) of each SaO_2 and EEG recording was computed applying the widely known Welch's method [17]: every sleep recording was divided into overlapping segments, a smooth time weighting was applied and the modified periodogram of each windowed segment was computed by means of the discrete Fourier transform (DFT). Finally, all DFTs were averaged to obtain the PSD estimate. In this study, 512-sample Hanning window with 50% overlap was applied. 1024-sample DFTs were used to compute SaO_2 power spectrum, whereas 2048-sample DFTs were applied to analyze EEG. These parameters ensured the performance of the PSD estimate. The following spectral features were derived from each SaO_2 and EEG PSD:

1. Peak amplitude (PA) in the apnea frequency band [7]. It is the local maximum of the SaO_2 spectral content in the frequency range from 0.014 Hz to 0.033 Hz.
2. Relative power (A_r) in the apnea frequency band [7]. It is the ratio of the area enclosed under the PSD function in the frequency range from 0.014 Hz to 0.033 Hz to the total power of each SaO_2 signal.
3. The relative power in the EEG classical frequency bands 0.5–3.8 Hz (A_{delta}), 3.9–7.8 Hz (A_{theta}), 7.9–12.6 Hz (A_{alpha}) and 12.7–29.2 Hz (A_{beta}) [14]. The absolute band power as a fraction of the total EEG power.

B. Median frequency (MF) and spectral entropy (SE)

The spectral content of each SaO_2 and EEG recording was also parameterized using MF and SE measures.

1. MF provides a simple means of summarizing the whole spectral content of the PSD. It is defined as the spectral component which comprises 50% of the total signal power [15]:

$$0.5\sum_{0.1Hz}^{50Hz} PSD(f) = \sum_{0.1Hz}^{MF} PSD(f). \quad (1)$$

   MFsat and MFeeg were the median frequencies of each SaO_2 and EEG recording, respectively.
2. SE is a disorder quantifier related to the flatness of the PSD. Each signal frequency component in the PSD was firstly normalized to obtain a probability distribution:

$$p_j \leftarrow \frac{p_j}{\sum_j p_j}. \quad (2)$$

   SE is subsequently computed based on the Shannon's entropy [16]:

$$SE = -\sum_j p_j \ln(p_j). \quad (3)$$

   SEsat and SEeeg were the spectral entropies of each SaO_2 and EEG recording, respectively.

C. Statistical analysis

The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to assess the normal distribution of the variables involved in the study. Homocedasticity was assessed by means of the Levene's test. Statistical differences were evaluated by means of the nonparametric Mann-Whitney U test.

Receiver operating characteristics (ROC) analyses with crossvalidation leave-one-out were applied to test the diagnostic ability of each feature individually. Forward stepwise logistic regression (LR) was applied to investigate feature significance: the procedure selected the strongest variables in the data set in terms of statistical significant

differences between the groups under study. Additionally, a LR procedure with crossvalidation leave-one-out was applied to assess the optimum feature set.

IV. Results

Figs. 1 and 2 depict the normalized average PSD functions from the OSA positive and OSA negative groups for the SaO_2 and EEG recordings, respectively. PA, A_r, MFsat and SEsat spectral features were derived from each SaO_2 signal. Similarly, A_{delta}, A_{theta}, A_{alpha}, A_{beta}, MFeeg and SEeeg frequency measures were computed for each EEG pattern.

Table II shows the average (mean ± SD) values for the spectral features under study from the OSA positive and OSA negative groups. The frequency measures involved in the study did not match the normality hypothesis. Patients in the OSA positive group had significantly higher ($p << 0.05$) PA and A_r than non OSA subjects. Fig. 1 clearly shows an increase in the apnea frequency range from 0.014 Hz to 0.033 Hz, which agrees with these measures. Additionally, OSA positive patients presented significantly higher ($p << 0.05$) MFsat and SEsat than OSA negative subjects. Fig. 1 shows that 50% spectral power is reached at higher frequencies in the normalized PSD function from the OSA positive group due to the power increase in the apnea frequency region. In the same way, spectral power in the normalized PSD function from the OSA negative group is condensed into very low frequencies due to the absence of the peak in the apnea interest frequency region, leading to lower MF and SE.

Fig. 2 shows a power increase in the very low frequency components (EEG slowing in the 0.1 – 0.8 Hz band) corresponding to the OSA positive group. However, electroencephalographic activity of non OSA subjects during the night is presented in a broader band, leading to higher spectral power in the common frequency bands. Thus, sleep EEG recordings during the whole night from OSA negative subjects had average A_{delta}, A_{theta}, A_{alpha} and A_{beta} significantly higher ($p < 0.05$) than OSA positive subjects. Significant differences decreased as frequency increased. Additionally, MFeeg and SEeeg were significantly higher ($p < 0.05$) in the OSA negative than in the OSA positive group. Fig. 2 shows that the average PSD function from the OSA negative group presented a broader spectral content (lower peakedness) than the OSA positive one, leading to higher MF and SE.

All the spectral features were used as independent variables in the step forward LR procedure. Two spectral features from oximetry (PA and MFsat) and three spectral features from EEG (A_{delta}, A_{alpha} and SEeeg) were automatically selected. Table III summarizes the diagnostic results from each spectral feature individually and applying LR with a crossvalidation leave-one-out procedure. A_r provided the highest accuracy from oximetry (85.0% sensitivity, 87.5% specificity and 85.8% accuracy), while A_{delta} reached the best diagnostic results from EEG spectral analysis (67.0% sensitivity, 64.6% specificity and 66.2% accuracy). Finally, the LR procedure with the automatically selected optimum feature set improved the diagnostic ability of each single feature, with 91.0% sensitivity, 83.3% specificity and 88.5% accuracy.

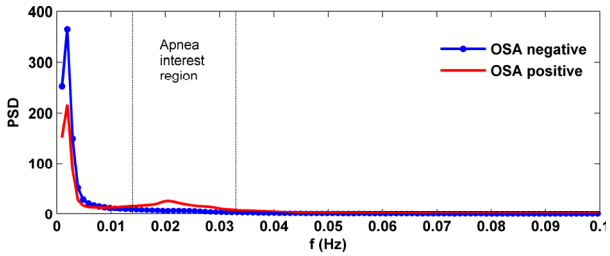

Fig. 1. Normalized average PSDs for the SaO_2 recordings from the OSA positive and OSA negative groups.

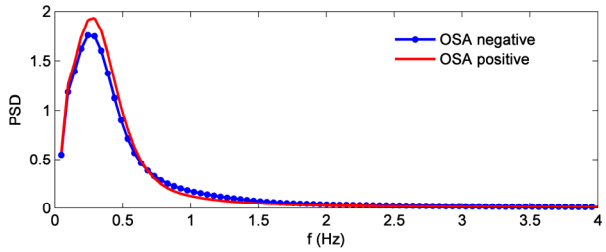

Fig. 2. Normalized average PSDs in the delta frequency band for the EEG recordings from the OSA positive and OSA negative groups.

V. Discussion and Conclusions

This study investigated the relationship between periodic changes in the SaO_2 profile and in the EEG pattern due to apnea events during the night. Spectral analysis was applied to assess the diagnostic ability of both signals in the diagnosis of OSA syndrome. MF, SE and classical spectral features from oximetry (PA and A_r) and EEG (A_{delta}, A_{theta}, A_{alpha} and A_{beta}) were computed. SaO_2 recordings from OSA positive patients presented a broader spectrum with an increase in the frequency range from 0.014 to 0.033 Hz, leading to significantly higher ($p << 0.05$) PA, A_r, MFsat and SEsat than non OSA subjects. Additionally, PSD of EEG recordings in the central lead C3–A2 from the OSA positive group showed higher peakedness in the very low frequencies, whereas OSA negative subjects showed a broader spectral content, leading to significantly higher ($p < 0.05$) MFeeg, SEeeg and relative power in the classical bands than OSA positive patients. Nonconventional MF and SE frequency measures agreed with classical oximetric and electroencephalographic spectral features. A step forward LR procedure was applied to obtain an optimum spectral feature set: two spectral features from oximetry (PA and MFsat) and three spectral features from EEG (A_{delta}, A_{alpha} and SEeeg) were automatically selected. Crossvalidation leave-one-out was applied to assess our methodology. The LR analysis achieved 91.0% sensitivity, 83.3% specificity and 88.5% accuracy, improving the diagnostic ability of each spectral feature individually. Our results suggest that spectral analysis of SaO_2 and EEG recordings could provide useful and complementary information to help in OSA diagnosis.

To our knowledge, this is the first study assessing the

TABLE II
AVERAGE VALUE FOR EACH FEATURE FROM THE GROUPS UNDER STUDY

	OSA negative	OSA positive	*p*-value
PA	2.584 ± 0.810	4.841 ± 1.536	$4.72\ 10^{-16}$
A_r	0.199 ± 0.193	4.334 ± 9.516	$6.48\ 10^{-17}$
MFsat	0.002 ± 0.002	0.010 ± 0.007	$5.92\ 10^{-13}$
SEsat	0.450 ± 0.079	0.544 ± 0.061	$4.63\ 10^{-11}$
A_{delta}	0.384 ± 0.111	0.313 ± 0.105	$1.56\ 10^{-4}$
A_{theta}	0.042 ± 0.030	0.034 ± 0.032	$1.18\ 10^{-2}$
A_{alpha}	0.038 ± 0.034	0.032 ± 0.037	$4.83\ 10^{-2}$
A_{beta}	0.033 ± 0.027	0.027 ± 0.024	$8.84\ 10^{-2}$
MFeeg	0.570 ± 0.325	0.468 ± 0.326	$6.61\ 10^{-3}$
SEeeg	0.595 ± 0. 950	0.551 ± 0.103	$5.21\ 10^{-3}$

Data are presented as mean ± SD.

TABLE III
RESULTS FROM THE DIAGNOSTIC ASSESSMENT OF EACH FEATURE INDIVIDUALLY AND APPLYING LR ANALYSIS

	Se	Sp	Ac
PA	84.0	83.3	83.8
A_r	85.0	87.5	85.8
MFsat	81.0	75.0	79.1
SEsat	79.0	75.0	77.7
A_{delta}	67.0	64.6	66.2
A_{theta}	58.0	62.5	59.5
A_{alpha}	50.0	66.7	55.4
A_{beta}	55.0	58.3	56.1
MFeeg	44.0	79.2	55.4
SEeeg	56.0	68.8	60.1
LR (PA,MFsat,A_{delta},A_{alpha},SEeeg)	91.0	83.3	88.5

Se: Sensitivity (%); Sp: Specificity (%); Ac: Accuracy (%).

diagnostic ability of combined oximetric and electroencephalographic spectral analyses by means of LR to help in the detection of OSA syndrome. Previous studies focused on single SaO_2 frequency analysis [7,8]: 90% sensitivity and 82% specificity were reached by visual inspection of the SaO_2 spectral pattern, whereas the diagnostic performance decreased using the automatically derived PA and A_r spectral characteristics. In the present study, SE and MF provides a different point of view, rather than the relative power and the peak amplitude from classical Fourier analysis. On the other hand, EEG spectral analysis has been mainly focused on the detection of arousals, evaluating changes in EEG before and after apnea events [11, 12]. Other researchers assessed differences in the power spectrum distribution between sleep and wakefulness EEG [13,14]. A positive correlation was found between EEG slowing during wakefulness and oxygen desaturations during the night [13].

We should take into account some limitations. The population under study could be larger and OSA positive patients were predominant. Further work is required to test the performance of our methodology and the state-of-the-art methods [9–14] using the same database. Furthermore, the analysis of additional sleep-related breathing disorders and other groups of especial interest, such as patients with lung diseases and young snorers, could be interesting.

In summary, we found that apnea events during the night could derive changes in the electrical activity of the brain not reflected in the SaO_2 profile, and viceversa. Thus, combined spectral analysis of SaO_2 and EEG recordings could provide complementary information to help in OSA diagnosis. Finally, MF and SE frequency measures could provide useful information to that obtained from classical spectral features based on relative power and peak amplitudes in common frequency bands.

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