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Diagnosis of pediatric obstructive sleep apnea: Preliminary findings using automatic analysis of airflow and oximetry recordings obtained at patients' home

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ABSTRACT

The obstructive sleep apnea syndrome (OSAS) greatly affects both the health and the quality of life of children. Therefore, an early diagnosis is crucial to avoid their severe consequences. However, the standard diagnostic test (polysomnography, PSG) is time-demanding, complex, and costly. We aim at assessing a new methodology for the pediatric OSAS diagnosis to reduce these drawbacks. Airflow (AF) and oxygen saturation (SpO_2) at-home recordings from 50 children were automatically processed. Information from the spectrum of AF was evaluated, as well as combined with 3% oxygen desaturation index (ODI3) through a logistic regression model. A bootstrap methodology was conducted to validate the results. OSAS significantly increased the spectral content of AF at two abnormal frequency bands below (BW1) and above (BW2) the normal respiratory range. These novel bands are consistent with the occurrence of apneic events and the posterior respiratory overexertion, respectively. The spectral information from BW1 and BW2 showed complementarity both between them and with ODI3. A logistic regression model built with 3 AF spectral features (2 from BW1 and 1 from BW2) and ODI3 achieved (mean and 95% confidence interval): 85.9% sensitivity [64.5–98.7]; 87.4% specificity [70.2–98.6]; 86.3% accuracy [74.9–95.4]; 0.947 area under the receiver-operating characteristics curve [0.826–1]; 88.4% positive predictive value [72.3–98.5]; and 85.8% negative predictive value [65.8–98.5]. The combination of the spectral information from two novel AF bands with the ODI3 from SpO_2 is useful for the diagnosis of OSAS in children.

1. Introduction

Obstructive sleep apnea syndrome (OSAS) is a disorder characterized by recurrent episodes of apnea (complete absence of airflow) and hypopnea (significant reduction of airflow) during sleep [1]. Apneic events lead to oxygen desaturations and arousals which prevent patients from resting while sleeping, disrupting both their health and quality of life. OSAS can affect both adults and children. Common symptoms in children include overnight snoring and sleep difficulties [2], which may derive in other daytime symptoms and illnesses such as cognitive and behavioral irregularities, abnormal growth, and cardiovascular risks [3,4]. Moreover, pediatric OSAS is known to be underdiagnosed [5], and the scientific literature reports up to 6% of children affected [3]. This indicates the high prevalence of the disease which, in turn, leads to an intensive use of the healthcare services [6].

Abbreviations: Acc, accuracy; AF, airflow; AHI, apnea-hypopnea index; AROC, area under the receiver-operating characteristics curve; ECG, electrocardiogram; IQR, interquartile range; LR, logistic regression; *MA*, maximum amplitude of the power spectral density; *mA*, minimum amplitude of the power spectral density; M_{f1}-M_{f4}, first to fourth statistical moments of the power spectral density; NPV, negative predictive value; ODI, oxygen desaturation index; OSAS, obstructive sleep apnea syndrome; PPV, positive predictive value; PSD, power spectral density; PSG, polysomnography; RP, respiratory polygraphy; Se, sensitivity; SLR, stepwise logistic regression; Sp, specificity; SpO_2, oxygen saturation of the blood.

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OSAS in children is diagnosed by means of nocturnal polysomnography (PSG) test, which acts as the "gold standard" [2]. PSG requires recording a wide range of physiological signals from patients overnight, including electroencephalogram (EEG), electrocardiogram (ECG), electromyogram (EMG), electrooculogram (EOG), thoracic and abdominal respiration movements, oxygen saturation (SpO_2), and airflow (AF) [1]. Hence, the necessary acquisition equipment is both complex and costly [6]. OSAS diagnosis is established according to the apnea-hypopnea index (AHI), which estimates the number of apneic events per hour of sleep time. To derive AHI, the physiological recordings need to be examined. Consequently, PSG is also time-consuming [7]. Furthermore, the equipment involved in PSG is often not well tolerated by children [8], interfering with their sleep routine.

To overcome these drawbacks a number of alternatives have been studied. One common approach is the use of a reduced set of signals from PSG to compute different estimations of AHI. In this regard, the respiratory disturbance index obtained from respiratory polygraphy (RP) was successfully assessed in an in-lab study with children involving 6 signals [9]: SpO_2, AF, heart rate, chest movements, body position, and snoring. The oxygen desaturation index (ODI), in combination with common symptoms, has been also recently evaluated as an alternative to PSG in pediatric patients [10]. On the other hand, the automatic analysis of physiological signals has been also proposed. In this sense, features from photoplethysmography time series have shown their usefulness in OSAS detection in children [11]. Moreover, studies conducting an automatic processing of the SpO_2 and ECG signals have been successfully performed in the context of adult and pediatric OSAS [12–16].

In this paper, a new method for OSAS diagnosis in children is assessed. Our methodology is based on the only use of spectral data from single-channel AF and the 3% ODI (ODI3), both of them obtained at patient's home. The main objective is to evaluate the diagnostic usefulness of eventual differences in the AF spectrum of OSAS patients (OSAS-positive) and no-OSAS subjects (OSAS-negative) in combination with ODI3. As stated above, ODI3 is a commonly used parameter in OSAS studies. Moreover, the study of AF is a straightforward choice since apneas and hypopneas are defined on the basis of its amplitude variations [17]. Additionally, the recurrence of apneic events naturally leads to the study of AF in the frequency domain. Recent works have shown that OSAS modifies the spectral content of AF recordings from adults at certain frequencies, and that the information contained in such frequencies is useful in OSAS detection [18,19]. However, no studies have been found applying a similar analysis to AF recordings from children. According to the above mentioned, we pose the following research questions:

i. How does OSAS modify the spectral information of airflow recordings from children?
ii. Are these changes useful to distinguish OSAS in children from at-home recordings?
iii. Is the airflow spectral information complementary to the classic oxygen desaturation index in pediatric OSAS detection?

To answer them, we conduct an exploratory analysis of the power spectral density (PSD) of the AF recordings. We look for spectral bands of interest showing differences in OSAS-positive and OSAS-negative subjects, as well as their characterization. The single diagnostic performance of both the AF spectral features and the ODI3 are assessed. We also evaluate their usefulness and complementarity through logistic regression models. Our hypothesis is that the joint use of spectral information contained in single-channel AF and ODI3 could be useful to diagnose OSAS in children.

Table 1
Demographic and clinical data.

Features	All	OSAS-positive	OSAS-negative
# Subjects	50	26	24
Age* (years)	5.3 ± 2.5	5.4 ± 2.7	5.2 ± 2.4
Male (%)	54.0	61.5	45.8
BMI+ (kg/m^2)	16.5 ± 2.5	16.9 ± 3.0	16.1 ± 1.7
Recording Time (h)	8.9 ± 0.8	8.8 ± 1.0	9.0 ± 0.5
AHI (e/h)	9.9 ± 13.8	17.9 ± 15.4	1.3 ± 0.8

BMI: body mass index; AHI: apnea hypopnea index.
* p-value = 0.76.
+ p-value = 0.94.

2. Methods and materials

2.1. Subjects and signals under study

This study involved AF and SpO_2 recordings from 50 children ranging 3–13 years old (24 OSAS-negative and 26 OSAS-positive). All of them were referred to the unit of respiratory sleep disorders of the University Hospital of Burgos (Spain), due to clinical suspicion of OSAS (snoring and/or witnessed breathing pauses). Those children suffering from serious chronic medical or psychiatric co-morbidities, those who required urgent treatment, and those with symptoms suggestive of sleep disorders other than OSAS (e.g., parasomnias, narcolepsy, or periodic leg movements), were excluded. AF and SpO_2 were acquired during a polygraphy test performed at patients' home through an eXim Apnea polygraph (Bitmed®, Sibel S.A., Barcelona, Spain). The sensor used to obtain AF was a thermistor and the sample rate was 100 Hz. SpO_2 was recorded through an oximeter at the same sample rate. The physicians used the AHI derived from PSG to establish OSAS. For the overnight PSG, the Deltamed Coherence® 3NT Polysomnograph, version 3.0 system (Diagniscan, S.A. ACH – Werfen Company; Paris, France) was used, recording EEG, right and left EOG, tibial and submental (leg and chin) EMG, ECG, AF by thermistor and nasal cannula, chest-abdomen movements with bands, body position, SpO_2 (Nellcor Puritan Bennett – NPB-290®), snoring, and a continuous transcutaneous recording of carbon dioxide ($PtcCO_2$). The American Academy of Sleep Medicine (AASM) criteria were used to evaluate sleep states and respiratory events [17]. The median time between PSG and RP was 14 days ([6,25], interquartile range, IQR). Apneas were scored after complete cessation of AF, as defined by the American Academy of Sleep Medicine [17]. Hypopneas were defined after a 50% reduction of AF accompanied by a 3% decrease in SpO_2 [17]. Amplitude cessations and reductions of AF required lasting 2 missed cycles in order to be considered as apneas or hypopneas, respectively [17]. An obstructive AHI threshold of 3 events/h was used to distinguish OSAS-positive from OSAS-negative subjects [20]. ODI3 was estimated as the number of desaturations (at least 3%) per hour of recording. The interruption of the oronasal flow secondary to movements was not accounted for either the PSG or the RP. An uninterpretable AF signal was defined as no AF during 30 s of normal respiration, while respiratory motion signals and SpO_2 remained unchanged. Data were excluded from analysis if >60% of the AF was uninterpretable. The Ethics Committee of the University Hospital of Burgos accepted the protocol (approval #CEIC 936) and an informed consent was obtained for each subject. Table 1 summarizes clinical and demographical data from the subjects under study. No statistical significant differences in body mass index or age were found between groups (p-value $\gg 0.01$).

2.2. Power spectral density of airflow

We computed the PSD of each AF recording to explore eventual differences between the spectral information of OSAS-positive and