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SCIENTIFIC INVESTIGATIONS

Automated Screening of Children With Obstructive Sleep Apnea Using Nocturnal Oximetry: An Alternative to Respiratory Polygraphy in Unattended Settings

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Study Objectives: Nocturnal oximetry has become known as a simple, readily available, and potentially useful diagnostic tool of childhood obstructive sleep apnea (OSA). However, at-home respiratory polygraphy (HRP) remains the preferred alternative to polysomnography (PSG) in unattended settings. The aim of this study was twofold: (1) to design and assess a novel methodology for pediatric OSA screening based on automated analysis of at-home oxyhemoglobin saturation (SpO_2), and (2) to compare its diagnostic performance with HRP.

Methods: SpO_2 recordings were parameterized by means of time, frequency, and conventional oximetric measures. Logistic regression models were optimized using genetic algorithms (GAs) for three cutoffs for OSA: 1, 3, and 5 events/h. The diagnostic performance of logistic regression models, manual obstructive apnea-hypopnea index (OAHI) from HRP, and the conventional oxygen desaturation index ≥ 3% (ODI3) were assessed.

Results: For a cutoff of 1 event/h, the optimal logistic regression model significantly outperformed both conventional HRP-derived ODI3 and OAHI: 85.5% accuracy (HRP 74.6%; ODI3 65.9%) and 0.97 area under the receiver operating characteristics curve (AUC) (HRP 0.78; ODI3 0.75) were reached. For a cutoff of 3 events/h, the logistic regression model achieved 83.4% accuracy (HRP 85.0%; ODI3 74.5%) and 0.96 AUC (HRP 0.93; ODI3 0.85) whereas using a cutoff of 5 events/h, oximetry reached 82.8% accuracy (HRP 85.1%; ODI3 76.7) and 0.97 AUC (HRP 0.95; ODI3 0.84).

Conclusions: Automated analysis of at-home SpO_2 recordings provide accurate detection of children with high pretest probability of OSA. Thus, unsupervised nocturnal oximetry may enable a simple and effective alternative to HRP and PSG in unattended settings.

Keywords: at-home respiratory polygraphy, automated pattern recognition, blood oxygen saturation, genetic algorithms, nocturnal oximetry

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INTRODUCTION

Pediatric obstructive sleep apnea (OSA) has been recognized as a highly prevalent sleep-related disorder. It may lead to long-term adverse consequences in neurocognitive development, behavioral development, cardiovascular function, metabolic function, overall health, and quality of life.[1,2] This disorder also contributes to increasing health care use and the associated costs thereof.[3] In-laboratory nocturnal polysomnography (PSG) is the current recommended test to reach a definitive diagnosis of OSA.[2,4] However, in most countries the availability of pediatric sleep laboratories is limited, and the generalized implementation of PSG cannot match clinical needs.[4,5] Moreover, PSG effectiveness and utility as the gold standard for young children and infants is problematic because of the inconvenience it imposes for both parents and children who need to spend the entire night in a sleep laboratory. In addition, high aversion to PSG has been observed in children when multiple sensors are attached.[4,6]

Accordingly, the major question is whether simplified techniques may be explored to increase accurate and effective OSA diagnoses. There are growing research efforts in the development of and validation of cost-effective diagnostic methodologies, which include history and physical examination, sleep quality questionnaires, nocturnal oximetry, respiratory polygraphy (RP), daytime (nap) PSG, and ambulatory PSG.[2,4,7–11] The American Academy of Pediatrics reported in 2012 that these methods are helpful when patients test positive for OSA, but

BRIEF SUMMARY

Current Knowledge/Study Rationale: Increasing accessibility to the diagnosis of childhood obstructive sleep apnea (OSA) by means of simplified as well as effective techniques is a challenging task. Unattended nocturnal oximetry has been recognized as a potentially useful tool even if well-validated algorithms are still sorely needed.

Study Impact: We show that automated analysis of at-home blood oxygen saturation (SpO_2) from nocturnal oximetry is a reliable and accurate alternative to home-based respiratory polygraphy in the identification of OSA in children with high pretest probability. Therefore, unattended oximetry could be an essential approach in order to develop abbreviated diagnostic tools for childhood OSA.

Table 1—Demographic and clinical characteristics and polygraphic indices of the pediatric population under study.

Measure	
Subjects, n	50
Age (years), median [IQR]	4 [4, 6]
Males, n (%)	27 (54.0)
BMI (kg/m^2), median [IQR]	16.42 [15.00, 17.53]
Recording time (h), median [IQR]	9.05 [8.40, 9.27]
$OAHI_{PSG}$ (events/h), median [IQR]	3.56 [1.21, 17.28]
$OAHI_{HRP}$ (events/h), median [IQR]	5.15 [1.27, 9.79]
$ODI3_{HRP}$ (events/h), median [IQR]	1.89 [0.84, 6.03]
Prevalence	
$OAHI_{PSG} \geq 1$ (events/h), n (%)	40 (80)
$OAHI_{PSG} \geq 3$ (events/h), n (%)	26 (52)
$OAHI_{PSG} \geq 5$ (events/h), n (%)	22 (44)

BMI = body mass index, IQR = interquartile range, $OAHI_{PSG}$ = obstructive apnea-hypopnea index from in-laboratory polysomnography, $OAHI_{HRP}$ = obstructive apnea-hypopnea index from at-home respiratory polygraphy, $ODI3_{HRP}$ = oxygen desaturation index of 3% from at-home respiratory polygraphy.

have a poor predictive value if results are negative.[2] More recently published guidelines for the diagnosis and management of childhood OSA still point out the importance of conducting an objective diagnostic test in every symptomatic child, *de facto* highlighting that further research is still needed to effectively simplify pediatric OSA diagnosis.[11]

Despite robust published evidence showing that the apnea-hypopnea index is inherently underestimated,[12] RP is rapidly becoming a widely implemented alternative to PSG in clinical settings.[8,9,11] Furthermore, ambulatory RP at home (HRP) has been suggested as a valid approach in low resource settings when in-laboratory PSG is not available.[11] A recent study demonstrated the feasibility of HRP to evaluate children with OSA at home.[13] Nocturnal oximetry has long been proposed as a screening tool for pediatric OSA in high-risk patients due to its reliability, simplicity, and suitability for children.[14–16] Recent systematic reviews have reported that oximetry can provide essential information about OSA when PSG is not accessible.[11,17] Most available studies have analyzed the blood oxygen saturation (SpO_2) profiles that were recorded during attended in-laboratory PSG.[14,18–21] However, there is still little evidence supporting the reliability of unattended oximetry. Further research is needed to compare the diagnostic performance of the two principal simplified diagnostic approaches: oximetry and HRP. In the current study, we hypothesized that single-channel SpO_2 from nocturnal oximetry will provide an equal alternative to HRP in the diagnosis of childhood OSA when recorded at home without supervision of trained personnel.

Well-validated algorithms for the interpretation of oximetric recordings are essential to achieve both high positive and negative predictive values, especially for low cutoffs such as the ones traditionally employed in the PSG-based diagnosis of pediatric OSA.[17] Signal processing techniques provide useful tools to gain not only insights into the pathological mechanisms influencing biological recordings, but also to improve the diagnostic ability of single-channel recordings when searching for simplified approaches. In this study, we propose to apply genetic algorithms (GAs) in order to compose an optimum model derived from oximetry data in childhood OSA diagnosis. GAs are optimization procedures from the field of evolutionary computation that are able to construct optimum models composed of the most relevant features characterizing the problem under study.[22] Previous studies have assessed the usefulness and applicability of GAs in the context of OSA diagnosis in adults.[23,24]

The aims of this study were twofold. The first was to exhaustively characterize at-home SpO_2 recordings and to compose models aimed at classifying children showing high-risk for OSA. The second aim was to further assess our methodology by comparing our results with manual scoring from HRP and conventional oxygen desaturation index ≥ 3% (ODI3). To achieve these goals, automated pattern recognition techniques were applied in order to improve diagnostic ability of SpO_2 as a single screening tool for OSA in children.

METHODS

Patients

A total of 50 children (27 boys and 23 girls) ranging in age from 3 to 13 years and referred to the Respiratory Sleep Disorders Unit of the University Hospital of Burgos in Spain for clinical suspicion of OSA comprised the population under study. The sample was representative of the clinical population commonly referred to our sleep unit. Patients were recruited regardless of the severity of their symptoms. In order to avoid potential bias linked with the inclusion process, only those children who arrived to the sleep unit on the days of the week selected using a random sequence participated in the study. **Table 1** summarizes the demographic and clinical data of the cohort. All patients underwent in-laboratory PSG because of habitual snoring and/or witnessed breathing pauses during sleep reported by their parents or caretakers. Exclusion criteria were the following: serious chronic medical and/or psychiatric additional conditions, symptoms indicative of sleep disorders other than OSA, and the need for urgent interventions. Children did not receive intranasal steroids, oral montelukast, or other pharmacological treatment for symptoms before they were recruited into the study. The Ethical Review Committee of the hospital approved the protocol (#CEIC 936), and informed consent to participate in the study was obtained prior to the enrollment.

Sleep Studies

Sleep studies consisted of unattended HRP at children's home and a subsequent (18.2 ± 20.0 days after) in-laboratory PSG. HRP was carried out using a polygraph eXim Apnea Polygraph (Bitmed, Sibel S.A., Barcelona, Spain). The following channels were recorded: oronasal flow (thermistor) and pressure (nasal cannula), chest and abdominal effort (impedance plethysmography), body position, snoring, and heart rate and SpO_2 by means of pulse oximetry.

In-hospital supervised PSG was carried out from 10:00 PM to 8:00 AM using a digital polysomnograph Deltamed Coherence 3NT version 3.0 (Diagniscan, S.A.U., Group Werfen, Paris, France). The following signals were recorded: electroencephalography, right and left electrooculography, tibia and submental electromyogram, electrocardiogram, airflow (thermistor and nasal cannula), chest and abdominal movements (effort bands), oximetry, continuous transcutaneous carbon dioxide, snoring, and body position.

HRP and PSG were scored manually by the same independent investigators, who were blinded to the goals of the study. The American Academy of Sleep Medicine criteria were used to perform sleep staging and quantify cardiorespiratory events.[25] Apneas were defined as the absence of oronasal airflow lasting at least two respiratory cycles, whereas hypopneas were defined as decreases greater than or equal to 50% in the amplitude of the nasal pressure or alternative signal for more than two respiratory cycles, accompanied by a desaturation ≥ 3% or an arousal. The obstructive apnea-hypopnea index (OAHI) was defined as the number of obstructive apneas and hypopneas per hour of sleep in the PSG ($OAHI_{PSG}$) and per recorded hour in the HRP ($OAHI_{HRP}$), respectively. The $OAHI_{PSG}$ was used as the gold standard for OSA diagnosis. In this study, the following common OAHI cutoff points were assessed[2,4]: 1, 3, and 5 events/h. **Table 1** shows OSA prevalence in the cohort according to these cutoffs, as well as the averaged respiratory indices from PSG, HRP, and oximetry of the population under study.

SpO_2 recordings from HRP were originally recorded at a sampling rate of 100 Hz. Each recording was then saved to a separate file and subsequently processed offline by means of the proposed automated algorithms.

Oximetry Signal Processing

Unattended SpO_2 recordings from HRP were used to perform automated binary classification of children showing symptoms of sleep apnea as OSA-negative or OSA-positive according to PSG. The following signal processing stages were implemented: (1) feature extraction, using conventional oximetric indices and measures from time and frequency domain analyses; (2) feature selection, by means of GAs; and (3) feature classification, by means of binary logistic regression.

Feature extraction

This stage is aimed at obtaining as much information as possible from the SpO_2 signal. To achieve this, three complementary analyses were conducted to exhaustively characterize the influence of recurrent apneic events on the overnight SpO_2 profile: (1) statistical moments and nonlinear measures in time domain, (2) statistical moments and spectral measures in frequency domain, and (3) conventional oximetric indices. Up to 18 features composed our initial feature set. Recent studies have shown the usefulness of these automated methods in the context of childhood OSA diagnosis from supervised in-laboratory pulse oximetry and airflow signals.[21,26] In the current study, a comprehensive analysis of input parameters and frequency bands was carried out to properly characterize the influence of OSA in SpO_2 unattended recordings at home.

First-to-fourth–order statistical moments (*M1–M4*) were applied to characterize the data histogram in the time domain. SpO_2 data from children without OSA is expected to be concentrated in a nonpathological limited region, whereas recurrent desaturations, typical of OSA, would change data distribution toward lower values. Mean (*M1t*), variance (*M2t*), skewness (*M3t*), and kurtosis (*M4t*) were applied to quantify central tendency, dispersion, asymmetry, and peakedness of the data histogram, respectively.[27] Nonlinear methods are able to derive additional and complementary information from biomedical recordings. Hence, sample entropy (*SampEn*) and central tendency measure (*CTM*) were used in this study to quantify irregularity and variability of SpO_2 recordings, respectively.[28–31]

Features from the frequency domain provide information about the duration and the repetitive nature of apneic events. The power spectral density was computed using the well-known Welch method, which is suitable for nonstationary signals.[26,31] Next, a comprehensive analysis was conducted to properly derive a frequency region in the power spectrum related to the recurrence of desaturations in children. In order to obtain such a frequency band of interest, we searched for statistical significant differences in the power spectral density amplitude between OSA-positive and OSA-negative children for every single frequency component.[26] Mean (*M1fb*), variance (*M2fb*), skewness (*M3fb*), and kurtosis (*M4fb*) were applied to quantify central tendency, dispersion, asymmetry, and peakedness of the power spectrum in the band of interest, respectively. In addition, other conventional spectral measures were also derived from this frequency band: maximum (*PAb*) and minimum (*MAb*) amplitudes and the signal relative power (*RPb*).[26]

Finally, conventional oximetric indices commonly used in clinical practice were also included in the study. The ODI3, the minimum (minSat) and average (AvgSat) saturation, and the cumulative time spent below 90% (CT90) and 95% (CT95) saturation were computed.

Feature selection and classification

GAs are optimization procedures derived from evolutionary computation with ability to efficiently inspect the search space of variables or parameters that govern a model.[22,32] GAs encode a potential solution as a chromosome-like data structure and apply genetic operations (crossover and mutation) to make the population evolve iteratively in order to reach the optimal solution.[33] At each iteration, a particular group of chromosomes (parents) are selected from the entire population to generate the offspring, which will replace chromosomes in the new population.[22] The iterative optimization process is carried out in cycles called generations.

In this study, GAs were applied for feature selection to obtain the optimum input feature subset to a binary classifier in terms of classification performance.[23,24] Therefore, an individual or chromosome from the population is just a combination of features (ie, a feature subset from the initial oximetric feature space composed of 18 features). A two-symbol binary codification was used to encode each feature subset or individual in the population, where the *k*-th bit denotes the absence (0) or the presence (1) of the *k*-th feature. Each individual has *p*

bits, where p is the number of features in the original set.[34] The classification accuracy of a binary logistic regression model was the performance metric used to drive parent selection. A bootstrapping approach was applied to compute the accuracy of each individual across the entire iteration process in order to deal with overfitting.[35] In the current study, probability of crossover (P_c) values ranging from .5 to .9 and probability of mutation (P_m) values ranging from .01 to .09 were used to introduce variations into the offspring along 100 generations.[23,24,33,34] The elite or percentage of the best individuals in the old population preserved after each generation were also varied between zero and 25%.[23,24] For each cutoff point for childhood OSA (1, 3, and 5 events/h), the optimum feature subset from the last generation was selected in terms of diagnostic performance.

Logistic regression was used for binary classification, where input patterns are classified into one of two mutually exclusive classes (OSA-negative versus OSA-positive). Logistic regression classifiers assign an input vector to the class with the maximum a posteriori probability according to a probability density for the response variable modeled by a Bernoulli distribution.[36] The maximum likelihood criterion is used to optimize coefficients of the independent input features in the logistic model.[36]

Statistical analyses

IBM SPSS Statistics version 20 (Chicago, Illinois) was used to perform statistical analyses. Normality and homoscedasticity analyses revealed that oximetric features derived from the population under study were not normally distributed and variances were unequal. Therefore, descriptive analysis of features was presented in terms of their median and interquartile range. In addition, the nonparametric Mann-Whitney U test was applied to search for statistical significant differences between OSA-negative and OSA-positive groups. A value of $P < .05$ was considered significant.

Matlab R2015a (The MathWorks Inc., Natick, Massachusetts, United States) was used to implement feature extraction, selection, and classification stages. Diagnostic performance was assessed by means of sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio (LR+), negative likelihood ratio (LR−), accuracy, and area under the receiver operating characteristics curve (AUC). A bootstrapping approach was carried out in order to ensure the statistical validity of our results because it is particularly useful to estimate statistics in small-sized datasets. The number of bootstrap samples was set to 1,000 because it ensures a proper estimation of the 95% confidence interval (95% CI).[26]

RESULTS

Optimization of the Frequency Band of Interest and Nonlinear Measures

Figure 1A, **1C**, and **1E** show the averaged power spectrum of OSA-negative and OSA-positive groups for each cutoff point under study. OSA-positive children showed greater spectral power than OSA-negative children in a very low frequency band (< 0.1 Hz) linked with the recurrence and duration of OSA typical desaturations, which agrees with previous studies.[21] Furthermore, **Figure 1B**, **1D**, and **1F** show the P value versus frequency plots to define quantitatively the band of interest. In order to retain a single frequency band regardless of the threshold for positive OSA, the broader region showing significant statistical differences between OSA groups common to all the cutoffs were selected: 0.02136–0.03357 Hz.

Input parameter optimization of nonlinear methods was also carried out in terms of significant statistical differences between OSA-negative and OSA-positive groups. Regarding *SampEn* optimization, the recommended $m = 1$ and 2 and $r = 0.1$, 0.15, 0.2, and 0.25 times the standard deviation (SD) of the time series were assessed.[28] No significant differences were reached for OAHI = 1 event/h (all values of $P > .1$) whereas the greatest differences ($P < .05$) for OAHI = 3 and 5 events/h were obtained using $m = 1$ and $r = 0.1$ SD. Thus, *SampEn* was computed using $m = 1$ and $r = 0.1$ SD for all the cutoffs. Regarding *CTM*, the greatest significant differences were achieved using rho = 1.1 for all cutoffs under study. Therefore, we finally obtained a single initial feature set independent of the diagnostic threshold for OSA, which demonstrates the consistency of the proposed methodology.

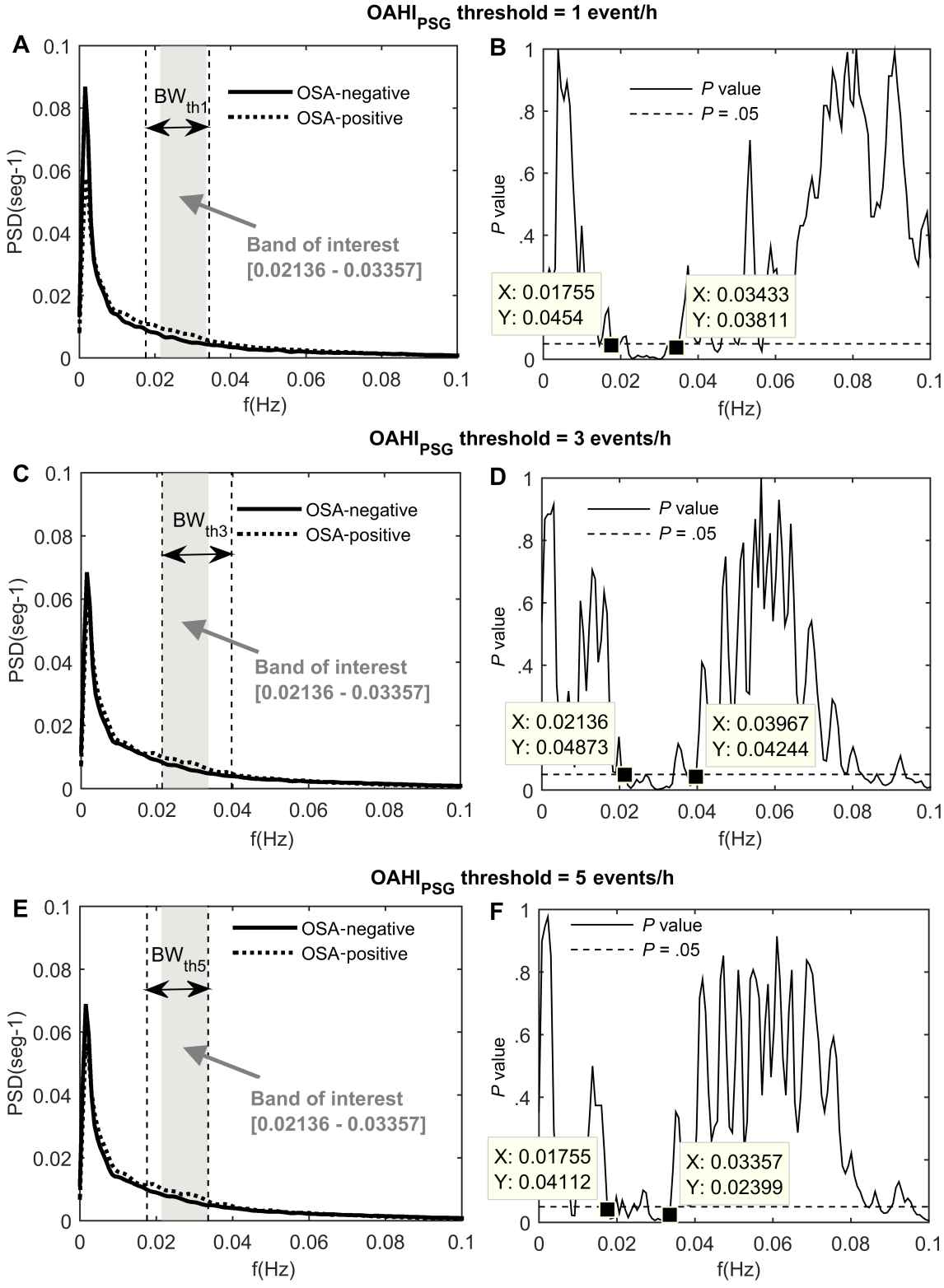
Feature Extraction

Table 2 shows the median and interquartile range of every feature involved in the study for each cutoff. Regarding features in the time domain, OSA-positive children showed overall lower *M1t* (central tendency), higher *M2t* (dispersion), higher (less negative) *M3t* (asymmetry), lower *M4t* (peakedness), higher *SampEn* (irregularity), and lower *CTM* (higher variability) than OSA-negative children for all the cutoffs. Using a clinical threshold for OSA of 1 event/h, just the *CTM* achieved significant statistical differences in the time domain. For cutoffs 3 and 5 events/h *M2t*, *M4t*, *SampEn*, and *CTM* reached significant differences. Regarding features in the frequency domain, OSA-positive children showed significantly higher ($P < .05$) *M1f* (mean spectral power), *PAb* (maximum amplitude), *RPb* (relative power), and *MAb* (minimum amplitude) in the frequency band of interest than OSA-negative children for all cutoffs under study. Finally, conventional oximetric indices showed an irregular behavior using different clinical thresholds for OSA. Only *ODI3* achieved significant statistical differences between OSA-positive and OSA-negative children for all cutoffs. Similarly, OSA-positive children showed significantly higher *CT95* than OSA-negative when using 3 and 5 events/h as cutoffs for OSA.

Feature Selection and Classification

GAs automatically selected an optimum feature subset for each clinical threshold for positive OSA. **Table 3** shows the variables included in the proposed optimum feature subsets. A total of six variables were automatically selected for cutoffs equal to 1 event/h (*M1t*, *M2t*, *M3t*, *M4t*, *M3fb*, *RPb*) and 3 events/h (*M1t*, *M2t*, *M4fb*, *PAb*, *RPb*, and *ODI3*), whereas seven features comprised the optimum set for a cutoff equal to 5 events/h (*M3t*, *M4fb*, *PAb*, *MAb*, *RPb*, *SampEn*, *ODI3*). It is noteworthy that all the proposed signal processing approaches (time, spectral, and conventional indices) were represented in these optimum subsets. **Table 4** summarizes the diagnostic performance of the

Figure 1—Averaged power spectral density functions of the OSA-negative and the OSA-positive groups from the whole population under study and *P* value versus frequency plots looking for significant statistical differences between groups ($P < .05$) for each cutoff.



(A,B) OAHI$_{PSG}$ ≥ 1 event/h. **(C,D)** OAHI$_{PSG}$ ≥ 3 events/h. **(E,F)** OAHI$_{PSG}$ ≥ 5 events/h. The region between dashed lines in figures from the left panels represent the frequency region in which significant differences were achieved for each particular cutoff (BW$_{thx}$), the gray region shows the single frequency band of interest. BW$_{thx}$ = spectral band of interest reaching statistical significant differences for the specified particular cutoff, OAHI$_{PSG}$ = obstructive apnea-hypopnea index from in-laboratory polysomnography, OSA = obstructive sleep apnea, PSD = power spectral density.

Table 2—Median and interquartile range for the whole obstructive sleep apnea–negative and obstructive sleep apnea–positive groups according to the different cutoffs under study for every oximetric feature in the original feature space.

	Cutoff $OAHI_{PSG}$ = 1 event/h			Cutoff $OAHI_{PSG}$ = 3 events/h			Cutoff $OAHI_{PSG}$ = 5 events/h		
	OSAn	OSAp	*P*	OSAn	OSAp	*P*	OSAn	OSAp	*P*
Time Domain									
M1t	97.3 [96.7, 97.6]	97.5 [96.8, 97.9]	.536	97.5 [97.1, 98.0]	97.3 [96.6, 97.7]	.171	97.5 [97.0, 98.0]	97.3 [96.5, 97.7]	.261
M2t	0.29 [0.18, 0.43]	0.49 [0.27, 0.76]	.163	0.30 [0.18, 0.48]	0.57 [0.40, 1.20]	< .05	0.32 [0.18, 0.59]	0.54 [0.40, 1.20]	< .05
M3t	−2.49 [−3.32, −1.44]	−1.68 [−2.30, −0.97]	.118	−2.14 [−3.31, −1.18]	−1.57 [−2.11, −0.87]	.073	−1.99 [−3.19, −1.16]	−1.57 [−2.11, −0.90]	.194
M4t	91.3 [42.3, 154.9]	41.0 [15.0, 102.9]	.083	88.1 [34.1, 156.5]	29.8 [8.0, 72.6]	< .05	70.5 [31.2, 146.3]	29.8 [6.3, 72.6]	< .05
SampEn ($\times 10^{-4}$)	8.75 [6.46, 10.5]	11.11 [7.79, 16.50]	.118	8.88 [6.07, 11.11]	13.61 [9.99, 17.56]	< .05	9.30 [6.43, 12.88]	12.39 [9.99, 19.25]	< .05
CTM ($\times 10^{-4}$)	9999.93 [9999.86, 9999.95]	9999.82 [9999.57, 9999.91]	< .05	9999.94 [999987, 9999.96]	9999.68 [9999.43, 9999.82]	< .05	9999.93 [9999.83, 9999.96]	9999.72 [9999.41, 9999.82]	< .05
Frequency Domain									
M1fb ($\times 10^{-2}$)	0.63 [0.56, 0.68]	0.77 [0.67, 0.89]	< .05	0.67 [0.62, 0.74]	0.78 [0.69, 0.92]	< .05	0.68 [0.62, 0.77]	0.78 [0.69, 0.92]	< .05
M2fb ($\times 10^{-6}$)	1.41 [0.72, 2.13]	2.25 [1.08, 3.48]	.057	1.71 [1.17, 2.37]	2.42 [1.00, 5.56]	.218	1.71 [1.02, 2.37]	2.74 [1.12, 5.56]	.120
M3fb	0.55 [030, 1.22]	0.30 [−0.17, 0.68]	.136	0.41 [0.27, 0.73]	0.15 [−0.22, 0.78]	.210	0.38 [0.12, 0.59]	0.21 [−0.25, 0.78]	.500
M4fb	−0.71 [−0.99, 1.78]	−0.67 [−1.23, −0.11]	.654	−0.82 [−1.28, −0.12]	−0.57 [−1.22, 0.06]	.749	−0.85 [−1.35, −0.24]	−0.42 [−1.19, 0.13]	.333
PAb ($\times 10^{-2}$)	0.92 [0.67, 0.99]	1.05 [0.93, 1.22]	< .05	0.95 [0.83, 1.05]	1.07 [0.93, 1.27]	< .05	0.96 [0.83, 1.05]	1.12 [0.93, 1.27]	< .05
MAb ($\times 10^{-2}$)	0.45 [0.39, 0.53]	0.53 [0.47, 0.63]	< .05	0.49 [0.42, 0.54]	0.56 [0.50, 0.67]	< .05	0.49 [0.42, 0.56]	0.56 [0.50, 0.67]	< .05
RPb	0.11 [0.10, 0.12]	0.13 [0.11, 0.15]	< .05	0.11 [0.11, 0.13]	0.13 [0.12, 0.16]	< .05	0.12 [0.11, 0.13]	0.13 [0.12, 0.16]	< .05
Conventional Indices									
ODI3	0.91 [0.34, 1.67]	2.73 [0.93, 6.76]	< .05	0.87 [0.45, 1.92]	5.90 [1.82, 9.08]	< .05	1.04 [0.52, 2.18]	6.1 [1.95, 9.55]	< .05
MinSat	91.5 [90.0, 92.0]	90.0 [88.0, 92.0]	.282	91.0 [90.0, 92.0]	89.0 [87.0, 90.0]	< .05	91.0 [88.5, 92.0]	89.5 [87.0, 90.0]	.052
AvgSat	97.0 [96.0, 98.0]	97.0 [96.4, 98.0]	.804	97.0 [97.0, 98.0]	97.0 [96.0, 97.7]	.212	97.0 [97.0, 98.0]	97.0 [96.0, 97.7]	.255
CT90	0 [-, -]	0.0 [0.0, 0.2]	.260	0 [-, -]	0.05 [0.0, 0.69]	< .05	0.0 [0.0, 0.07]	0.02 [0.0, 0.69]	.120
CT95	0.34 [0.11, 0.77]	0.98 [0.23, 3.73]	.139	0.36 [0.08, 1.17]	1.62 [0.57, 7.18]	< .05	0.42 [0.08, 1.41]	1.41 [0.57, 7.18]	< .05

Values presented as median [interquartile range]. *AvgSat* = average saturation, *CT90, CT95* = cumulative time with a saturation below 90% and 95%, respectively, *CTM* = central tendency measure, *M1t–M4t* = mean (M1), variance (M2), skewness (M3), and kurtosis (M4) in the time domain, *M1fb–M4fb* = mean (M1), variance (M2), skewness (M3), and kurtosis (M4) in frequency band of interest, *MAb* = minimum amplitude in frequency band of interest, *MinSat* = minimum saturation, $OAHI_{PSG}$ = obstructive apnea-hypopnea index from in-laboratory polysomnography, *ODI3* = oxygen desaturation index greater than or equal to 3%, OSA = obstructive sleep apnea, OSAn = OSA-negative group, OSAp = OSA-positive group, *P* = *P* value from the Mann-Whitney nonparametric test, *PAb* = peak amplitude in frequency band of interest, *RPb* = relative power in frequency band of interest, *SampEn* = sample entropy.

Table 3—Optimum feature subsets from the genetic algorithms-based feature selection approach for each cutoff for childhood obstructive sleep apnea under study.

Cutoff	No. of Variables	Optimum Features
$OAHI_{PSG}$ = 1 event/h	6	*M1t*, *M2t*, *M3t*, *M4t*, *M3fb*, *RPb*
$OAHI_{PSG}$ = 3 events/h	6	*M1t*, *M2t*, *M4fb*, *PAb*, *RPb*, *ODI3*
$OAHI_{PSG}$ = 5 events/h	7	*M3t*, *M4fb*, *PAb*, *MAb*, *RPb*, *SampEn*, *ODI3*

M1t–M4t = mean (M1), variance (M2), skewness (M3), and kurtosis (M4) in the time domain, *M3fb, M4fb* = skewness (M3) and kurtosis (M4) in frequency band of interest, *MAb* = minimum amplitude in frequency band of interest, $OAHI_{PSG}$ = obstructive apnea-hypopnea index from in-laboratory polysomnography, *ODI3* = oxygen desaturation index greater than or equal to 3%, OSA = obstructive sleep apnea, *PAb* = peak amplitude in frequency band of interest, *RPb* = relative power in frequency band of interest, *SampEn* = sample entropy.

logistic regression models composed of these optimal subsets, as well as the performance achieved by the manual OAHI from HRP and the conventional ODI3 alone. Our approach was the most accurate when a cutoff of 1 event/h was used to diagnose childhood OSA. The optimum logistic regression model from GAs achieved 85.5% accuracy (95% CI: 66.4–96.6), which significantly outperformed both the OAHI from HRP (74.6% accuracy, 95% CI: 57.0–88.9) and the conventional ODI3 (65.9% accuracy, 95% CI: 47.5–83.0). When the clinical threshold for positive OSA is increased to 3 events/h, our approach reached 83.4% accuracy (95% CI: 64.2–96.8), which again significantly outperformed the single ODI3 (74.5% accuracy, 95% CI: 58.5–88.7) and almost equaled the manual OAHI from conventional HRP (85.0% accuracy, 95% CI: 71.6–95.5). Finally, the optimum logistic regression model for a cutoff of 5 events/h achieved 82.8% accuracy (95% CI: 64.5–96.3), which is still higher than that obtained with ODI3 (76.7% accuracy, 95% CI: 59.2–90.9) but slightly lower than the performance reached with HRP (85.1% accuracy, 95% CI: 71.6–95.9). It is important to note that our proposal always reached higher LR+ and AUC than HRP and ODI3 whatever the cutoff.

DISCUSSION

In this study, the diagnostic performance of an automated simplified method based on unattended oximetry was assessed as

Table 4—Diagnostic performance using a bootstrap approach of each logistic regression model composed of optimum feature subsets from genetic algorithm feature selection.

Cutoff $OAHI_{PSG}$ = 1 event/h								
	Se (%)	**Sp (%)**	**PPV (%)**	**NPV (%)**	**LR+**	**LR−**	**Accuracy (%)**	**AUC**
$LR_{HOX}(6)$	89.6 (63.8, 100)	71.5 (28.3, 100)	92.5 (78.2, 100)	66.8 (16.6, 100)	4.37 (1.88, 8.23)	0.18 (0.00, 0.64)	85.5 (66.4, 96.6)	0.97 (0.89, 1.00)
$OAHI_{HRP}$	71.3 (52.5, 90.4)	88.2 (43.8, 100)	96.1 (80.2, 100)	43.4 (17.5, 72.7)	3.62 (1.64, 7.07)	0.35 (0.12, 0.78)	74.6 (57.0, 88.9)	0.78 (0.63, 0.91)
$ODI3_{HRP}$	64.3 (39.6, 92.3)	73.1 (21.0, 100)	91.6 (74.7, 100)	33.8 (7.4, 64.0)	2.28 (1.02, 5.13)	0.52 (0.18, 1.06)	65.9 (47.5, 83.0)	0.75 (0.58, 0.90)
Cutoff $OAHI_{PSG}$ = 3 events/h								
	Se (%)	**Sp (%)**	**PPV (%)**	**NPV (%)**	**LR+**	**LR−**	**Accuracy (%)**	**AUC**
$LR_{HOX}(6)$	82.9 (56.5, 100)	84.4 (51.5, 100)	86.2 (61.3, 100)	82.2 (57.4, 100)	7.40 (2.39, 15.78)	0.22 (0.00, 0.64)	83.4 (64.2, 96.8)	0.96 (0.88, 1.00)
$OAHI_{HRP}$	86.1 (59.8, 100)	84.2 (59.6, 100)	86.1 (65.2, 100)	85.6 (63.3, 100)	6.70 (2.39, 14.96)	0.16 (0.00, 0.42)	85.0 (71.6, 95.5)	0.93 (0.86, 0.98)
$ODI3_{HRP}$	71.8 (43.6, 98.2)	77.6 (38.5, 100)	79.7 (53.4, 100)	72.8 (49.2, 97.4)	3.93 (1.47, 11.81)	0.36 (0.03, 0.72)	74.5 (58.5, 88.7)	0.85 (0.73, 0.94)
Cutoff $OAHI_{PSG}$ = 5 events/h								
	Se (%)	**Sp (%)**	**PPV (%)**	**NPV (%)**	**LR+**	**LR−**	**Accuracy (%)**	**AUC**
$LR_{HOX}(7)$	82.2 (54.1, 100)	83.6 (55.7, 100)	80.8 (52.8, 100)	85.9 (62.7, 100)	8.48 (2.35, 17.48)	0.23 (0.00, 0.64)	82.8 (64.5, 96.3)	0.97 (0.89, 1.00)
$OAHI_{HRP}$	83.6 (58.8, 100)	86.4 (59.2, 100)	84.5 (57.2, 100)	87.8 (71.5, 100)	7.04 (2.31, 17.16)	0.19 (0.00, 0.44)	85.1 (71.6, 95.9)	0.95 (0.87, 0.99)
$ODI3_{HRP}$	72.7 (45.9, 97.3)	79.9 (45.9, 100)	76.7 (47.4, 100)	79.4 (61.4, 97.9)	4.80 (1.55, 14.81)	0.34 (0.03, 0.68)	76.7 (59.2, 90.9)	0.84 (0.71, 0.95)

Values are presented as median (95% CI). AUC = area under the receiver operating characteristic curve, LR+ = positive likelihood ratio, LR− negative likelihood ratio, LR_{HOX} = logistic regression model from at-home oximetry, NPV = negative predictive value, $OAHI_{PSG}$ = obstructive apnea-hypopnea index from in-laboratory polysomnography, $OAHI_{HRP}$ = obstructive apnea-hypopnea index from at-home respiratory polygraphy, $ODI3_{HRP}$ = oxygen desaturation index of 3% from at-home respiratory polygraphy, PPV = positive predictive value, Se = sensitivity, Sp = specificity.

a single tool for diagnosis of childhood OSA. Single-channel SpO_2 recordings from at-home oximetry were automatically analyzed. In-hospital complete PSG was used as the gold standard and three common clinical cutoff points for childhood OSA (OAHI of 1, 3, and 5 events/h) were employed to assess the consistency of the proposed methodology. Additionally, two indices from alternative simplified techniques, commonly proposed for OSA detection when in-laboratory PSG is not available, were analyzed for comparison purposes: manual OAHI from HRP and conventional ODI3 from oximetry.

In our aim to maximize the diagnostic ability of oximetry, a wide initial feature set was composed. As expected, spectral and nonlinear features, as well as ODI3, exhibited statistically significant differences between OSA-positive and OSA-negative children, which agrees with previous studies.[21,26] Then, automatic feature selection was accomplished by means of GAs in order to exhaustively analyze the feature space and obtain the optimum feature subset for each cutoff. We found that a proper selection of variables provided complementary information that improves the diagnostic ability of oximetry. It is noteworthy that these optimum feature subsets showed a consistent composition when considering contiguous cutoffs for childhood OSA: optimum subsets using cutoffs equal to 1 and 3 events/h share 50% of features (*M1t*, *M2t*, and *RPb*) whereas subsets from cutoffs equal to 3 and 5 events/h share even more than 50% (*M4fb*, *PAb*, *RPb*, and *ODI3*). In addition, *RPb* was included in all of the optimum feature subsets, which demonstrates the relevancy and consistency of the frequency band of interest identified in this study.

Using the GAs-derived optimum subsets, our logistic regression models from unattended oximetry significantly outperformed the conventional ODI3 in terms of accuracy and AUC for all the cutoffs. Furthermore, our proposed models reached similar accuracy and higher AUC than HRP for cutoffs equal to 3 events/h (83.4% vs. 85.0% accuracy and 0.96 vs. 0.93 AUC) and 5 events/h (82.8% vs. 85.1% accuracy and 0.97 vs. 0.95 AUC) and even outperformed manual scoring of HRP using a low cutoff equal to 1 event/h (85.5% vs. 74.6% accuracy and 0.97 vs. 0.78 AUC). It is noteworthy that manual rather than automated scoring of HRP is considered the preferred alternative to PSG when PSG is not available. Conversely, our proposed methodological approach is fully automated, which would markedly reduce the workload of specialized technicians, and improve consistency. Finally, it is important to point out that all the optimum models from oximetry reached higher LR+ than HRP and single ODI3 whatever the OAHI cutoff selected, which is an essential characteristic for screening tests. This is particularly relevant in the context of pediatric OSA because children are referred to the sleep unit because of existing symptoms of OSA.

Overall, we observed that the higher the cutoff, the lower the performance of our automated logistic regression models from unattended oximetry. In contrast, using conventional manual OAHI and ODI3, the performance of these approaches increased when the cutoff moved from 1 to 5 events/h. It is important to highlight that conventional ODI3 showed the common imbalance of unattended oximetry, with higher specificity due to underestimation of the severity of the disease, whereas automated logistic regression models showed higher sensitivity than specificity for a clinical threshold of 1 event/h for positive OSA and balanced sensitivity and specificity pairs for cutoffs equal to 3 and 5 events/h. Thus, the maximum benefit of our automated methodology in terms of simplicity and screening capability can be achieved when using lower cutoffs for positive OSA. Because most sleep laboratories use the cutoff of 1 event/h during interpretation of PSG,[2] the features that came to the forefront in our automated approaches in unattended oximetry further stress the unique superiority afforded by the proposed methodology.

Several diagnostic alternatives to PSG have been proposed to expand the accessibility of children to diagnosis and treatment in a timely manner. Quite similar to in-laboratory PSG in terms of percentage of successful recordings, unattended PSG at home has shown similar success rates among school-aged children, but much greater inconsistencies in younger children.[2] Similarly, nap-based PSG studies report high specificity but low sensitivity.[2,13] Although simple and not intrusive, clinical history and sleep quality questionnaires lack the required diagnostic accuracy, precluding their use as a routine diagnostic tool for OSA in children.[4,11,13] However, RP-based approaches have become increasingly accepted as an effective diagnostic method when carried out in a clinical setting both in adults and children.[11,37] Furthermore, ambulatory HRP has been considered a feasible means of diagnosing OSA when PSG is not available, according to a recent report of the European Respiratory Society.[11] Alonso-Álvarez et al. recently illustrated the effectiveness of HRP for OSA diagnosis in an unsupervised setting.[13] Similarly, nocturnal oximetry has become known as a simple, low-cost, and less intrusive alternative to PSG, RP, or HRP to help in childhood OSA diagnosis.[14,17] In the current study, our results suggest that automated analysis of single-channel SpO_2 from unattended oximetry may be as accurate as HRP in the diagnosis of OSA.

This is an obvious departure from previous perceptions regarding oximetry. Indeed, oximetry has been characterized as achieving high specificity but low sensitivity.[2] Nevertheless, several studies have shown the usefulness and effectiveness of common oximetric indices based on the number of overnight desaturations in the context of pediatric OSA, such as the ODI[19,20,38] and, more recently, the quantification of clusters of desaturations.[18,39] Only a few studies have been carried out at home.[38,39] In such unattended settings, both the McGill oximetry score and the ODI $\geq$ 4% (ODI4) achieved high night-to-night agreement (mean difference 0.32, limits of agreement −8.00 to 8.64 events/h).[38,39] Regarding the diagnostic performance, ODI4 achieved poor performance (67% sensitivity and 60% specificity) for detecting moderate OSA (OAHI $\geq$ 5 events/h).[38] Our proposal based on unsupervised oximetry clearly outperformed the results reported in this study. Recent approaches analyze the pulse rate (PR) signal from pulse oximetry[40] or combine data derived from the SpO_2 signal with other sources of information to improve diagnostic ability, such as the PR signal from the own pulse oximetry recording[21] or the airflow signal.[26] In the study by Sahadan et al.,[40] PR increases of 15 bpm (PRI-15) from ambulatory pulse oximetry were scored automatically. This PR-derived index reached a sensitivity ranging 16% to 39% and specificity ranging 79% to 97% for an OSA cutoff $\geq$ 1 event/h. In the study by Garde et al., time, spectral and conventional measures from both SpO_2 and PR recordings obtained by means of a pulse oximeter sensor attached to a smartphone were combined using a linear classifier.[21] These investigators reported 88.4% sensitivity and 83.6% specificity for an apnea-hypopnea index cutoff of 5 events/h. Although a portable device was used, all recordings were carried out in the hospital. Finally, in a recent study by our own group, ODI3 from oximetry was combined with spectral measures from the airflow signal using a logistic regression model.[26] All of the recordings were obtained during unattended HRP. A sensitivity of 85.9%, a specificity of 87.4%, and an accuracy of 86.3% were reached for a cutoff of 3 events/h.

Some limitations should be taken into account. First, the population cohort evaluated herein should be expanded in order to draw more generalizable conclusions. A larger dataset would allow a better optimization of the feature space using GAs because this feature selection method maximizes its usefulness when working with high-dimensional spaces and a large number of instances. Nevertheless, in order to address this issue, a bootstrapping approach was carried out both for feature selection and classification. This procedure is known to provide good estimates from small datasets. Similarly, a wider dataset would provide a better optimization of all input parameters from nonlinear and spectral features, including the frequency band of interest for childhood OSA. However, our results revealed quite consistent features and a frequency band linked with recurrent desaturations characteristic of OSA. An additional drawback that could affect our results may reside in undesirable differences related to potential temporal changes of the disease. As such, the time interval between in-hospital PSG and at-home RP was set to be lower than 2 months, a time frame that is clearly shorter than the actual waiting times for a pediatric sleep study in our sleep unit. Nevertheless, even this shorter interval could lead to potential differences between the reference OAHI and oximetry from in-laboratory PSG and OAHI and oximetry from RP at a patient's home due to the widely known night-to-night variability of OSA.

The main goal for assessing abbreviated test for pediatric OSA simply based on oximetry is to use portable oximeters at a patient's home instead of complete PSG or RP equipment. In the current investigation, we analyzed SpO_2 recordings from unattended RP recordings. Therefore, potential differences between oximetric profiles from overnight RP and from a portable standalone device could influence our results. Sampling rates, resolution, and averaging time settings may impose significant influence on the collected data and this could affect time response and reproducibility of SpO_2.[21,41] Notwithstanding, previous studies demonstrated that our approach could be easily optimized for any technical setting in order to achieve a high diagnostic performance.[24,42] In addition, current high-performance oximeters already match technical characteristics of in-hospital equipment overcoming previous limitations of portable devices due to restrictions in memory storage capability and battery life. Finally, the proposed methodology presented herein aims to confirm or discard the presence of OSA (ie, to perform binary classification). Although three commonly used OAHI cutoff points in clinical practice were assessed for positive OSA (1, 3, and 5 events/h), it would be very useful to couple the current novel approach to develop and implement a pattern recognition methodology aimed at classifying patients in the four common categories of severity (no disease, mild, moderate, and severe) or estimating the actual PSG-derived OAHI of each patient under study.

CONCLUSIONS

To the best of our knowledge, this is the first study comparing the diagnostic performance of unattended oximetry and HRP

as alternatives to standard in-laboratory PSG in the context of childhood OSA. Automated analysis of single-channel at-home SpO_2 recordings is recognized as a useful and a reliable alternative to manual scoring of HRP in the detection of children with high clinical suspicion of OSA, particularly when using low OAHI cutoff points for a positive diagnosis of the disease. Furthermore, our optimum logistic regression models significantly outperformed conventional ODI3 for all the cutoffs under study using the same dataset. Therefore, our results suggest that automated processing of the SpO_2 signal could be an essential approach in order to develop abbreviated and accurate diagnostic tools for childhood OSA in unsupervised settings.

ABBREVIATIONS

AUC, receiver operating characteristics curve
AvgSat, average saturation
BMI, body mass index
BW_{thx}, spectral band of interest for the specified particular cutoff
CT90, cumulative time spent below a saturation of 90%
CT95, cumulative time spent below a saturation of 95%
CTM, central tendency measure
GAs, genetic algorithms
HRP, at-home respiratory polygraphy
IQR, interquartile range
LR+, positive likelihood ratio
LR−, negative likelihood ratio
LR_{HOX}, logistic regression model from at-home oximetry
M1–M4, first-to-fourth order statistical moments
M1fb, mean of the power spectrum in the band of interest
M2fb, variance of the power spectrum in the band of interest
M3fb, skewness of the power spectrum in the band of interest
M4fb, kurtosis of the power spectrum in the band of interest
M1t, mean in the time domain
M2t, variance in the time domain
M3t, skewness in the time domain
M4t, kurtosis in the time domain
MAb, minimum of the power spectrum in the band of interest
minSat, minimum saturation
NPV, negative predictive value
OAHI, obstructive apnea-hypopnea index
$OAHI_{HRP}$, obstructive apneas and hypopneas per recorded hour in the HRP
$OAHI_{PSG}$, obstructive apneas and hypopneas per hour of sleep in the PSG
ODI3, oxygen desaturation index ≥ 3%
ODI4, oxygen desaturation index ≥ 4%
$ODI3_{HRP}$, Oxygen desaturation index of 3% from at-home respiratory polygraphy
OSA, obstructive sleep apnea
OSAn, OSA-negative group
OSAp, OSA-positive group
PAb, maximum of the power spectrum in the band of interest
P_c, probability of crossover
P_m, probability of mutation
PPV, positive predictive value
PSD, power spectral density
PSG, polysomnography
ROC, receiver operating characteristics
RP, respiratory polygraphy
RPb, signal relative power in the band of interest
SampEn, sample entropy
SD, standard deviation
Se, sensitivity
Sp, specificity
SpO_2, oxyhemoglobin saturation

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