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Apnea and hypopnea characterization using esophageal pressure, respiratory inductance plethysmography, and suprasternal pressure: a comparative study

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Abstract

Objectives To determine if recording of suprasternal pressure (SSP) can classify apneas and hypopneas as reliably as respiratory inductance plethysmography (RIP) belts and to compare the two methods to classification with esophageal pressure (Pes), the reference method for assessing respiratory effort.

Methods In addition to polysomnographic recordings that included Pes, SSP was recorded. Recordings from 32 patients (25 males, mean age 66.7 ± 15.3 years, and mean BMI 30.1 ± 4.5 kg/m^2) were used to compare the classification of detected apneas and hypopneas by three methods of respiratory effort evaluation (Pes, RIP belts, and SSP). Signals were analyzed randomly and independently from each other. All recordings were analyzed according to AASM guidelines.

Results Using Pes as a reference for apnea characterization, the Cohen kappa (κ) was 0.93 for SSP and 0.87 for the RIP. The sensitivity/specificity of SSP was 97.0%/96.9% for obstructive, 93.9%/98.3% for central, and 94.9%/97.9% for mixed apneas. The sensitivity/specificity of the RIP was 97.4%/91.9% for obstructive, 87.5%/97.9% for central, and 85.6%/96.6% for mixed apneas. For hypopnea characterization using the Pes as a reference, κ was 0.92 for SSP and 0.86 for the RIP. The sensitivity/specificity of SSP was 99.7%/97.6% for obstructive and 97.6%/99.7% for central. The sensitivity/specificity of the RIP was 99.8%/81.1% for obstructive and 81.1%/99.8% for central.

Conclusions These results confirm the excellent agreement in the detection of respiratory effort between SSP, RIP belts, and Pes signals. Thus, we conclude that apnea and hypopnea characterization in adults with SSP is a reliable method.

Keywords Respiratory effort · Polysomnography · Sleep apnea characterization · Suprasternal pressure

Introduction

Accurate and reliable classification of apneas and hypopneas as obstructive or central is important, since these events result from different pathophysiological mechanisms and lead to different therapeutic strategies. To distinguish between obstructive and central sleep apnea syndrome (SAS), evaluation of inspiratory effort during sleep is required. Esophageal pressure (Pes) is the reference method for the evaluation of respiratory efforts [1]. However, this method is invasive, is not well tolerated by many patients, and can affect the quality of sleep [2–4]. Therefore, respiratory inductance plethysmography (RIP) belts have been established as an indirect method for the evaluation of respiratory efforts for routine sleep studies [1]. During an apnea, the presence of RIP movements at the respiratory frequency indicates respiratory effort and the event is classified as obstructive. In addition, an increase in respiratory effort against a collapsed airway may result in an out of phase or a paradoxical RIP signals. Central apneas are characterized by the absence of RIP movements with, occasionally, cardiogenic oscillations seen on the signals [5, 6]. Obstructive hypopnea classification is based on identification

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of flattening of inspiratory airflow, and/or snoring, and/or RIP signal paradoxical movement. If none are present, a hypopnea is classified as central [1]. However, the reliability of the RIP signals depends on accurate placement and stability of the thoracoabdominal belts which is not always guaranteed. Thus, there are circumstances where RIP belts could lead to misclassification of respiratory events [7, 8].

Tracheal sounds (TS), recorded at the sternal notch, result from vibrations of the tracheal walls and not regular acoustic noises [9–12]. This characteristic can be used not only to detect tracheal breathing sounds but also to record suprasternal pressure (SSP), an adequate substitute for assessing respiratory effort [13–15]. The SSP is a non-audible signal with low frequencies that can also be recorded by TS sensors. This signal corresponds to the pressure variations induced by respiratory efforts. The patient's respiratory effort causes variations in pharyngeal pressure that cause pressure changes in the TS sensor chamber. These pressure variations are measured by movements of the skin in contact with the sensor at the sternal notch.

Our study aimed to evaluate the use of the SSP for the classification of apneas and hypopneas. Comparison with gold standard measurements for the visual assessment of respiratory effort in adults during sleep was performed. The results of the SSP signal classification were compared with those obtained with Pes signal and RIP belt movements.

Material and methods

Patients

The study included 32 patients (27 male), between 18 and 80 years old, admitted to the Charité hospital sleep laboratory for a diagnostic study or for a control PSG. Eighteen patients were recruited at the Charité Virchow campus clinic and 14 patients at the Charité Mitte campus clinic. The study was approved (DRKS-ID: DRKS00012795) by the local Ethics Committee of the Charité university hospital in Berlin. Exclusion criteria were excessive alcohol consumption or drug use, use of any medication that could impact sleep, the presence of any non-OSA sleep disorder, clinically unstable respiratory disease, and inability to read and understand the consent statement. Age, height, weight, and neck circumference of the patients were recorded.

Data acquisition

After signing written consent for participation in the study, patients underwent PSG recordings using the *SOMNOscreen plus* system (SOMNOmedics GmbH, Randersacker, Germany). Recorded data included all electrophysiological signals for sleep evaluation as well as airflow by thermistor and nasal pressure (NP), RIP belts, pulse oximetry, body position, limb movements, actigraphy, and light. In addition to the laboratory routine, Pes signal (Gaeltec, Isle of Sky, Scotland) and TS and SSP signals using the *CID-LXe* polygraph with the PneaVoX® technology (CIDELEC, Angers, France) were recorded. The PneaVoX® sensor was correctly placed on the skin at 1 cm right above the sternal notch using a double-sided ring tape and then secured in place using an extra adhesive tape on the top of the sensor. A well-sealed contact surface of the sensor is an essential element to obtain good-quality SSP signals. A Y-piece connector was used to join the nasal cannula to both systems so that the SOMNOscreen and the *CID-LXe* systems could share the same NP signal. Thus, accurate synchronization of the separate recordings was made possible.

All respiratory signals from the SOMNOscreen system were imported in the European Data Format (EDF) into MATLAB. The imported signals were resampled, filtered, and synchronized with the PneaVoX signals (TS and SSP) using the shared NP signal. The processed signals were then exported to the CIDELEC system. A new anonymized polygraph file combining all respiratory signals from both systems was created for each patient. Sections where respiratory signals used for our scoring were missing or of poor quality and sections where the used signals could not be synchronized were not validated. Synchronized recordings were then visualized and scored using the CIDELEC software.

Apneas were defined according to AASM criteria using the oronasal airflow [1]. Visual monitoring of excursions in the Pes signal, RIP belts signals, or the SSP signal was used to detect the presence of respiratory effort. Based on the absence or presence of respiratory efforts, each of these sensors used separately allowed the classification of apneas as central, obstructive, or mixed and of hypopneas as obstructive or central, in the absence of snoring and flattening of the nasal flow.

The SSP sensor used in our study, the PneaVoX®, is a stethoscope-like transducer combining an acoustic sensor and a pressure sensor inserted inside a 28-mm-diameter and 15-mm-thick shielding case. The transducer's contact surface with the skin contains a 2-mm-thick cuff designed to ensure an airtight cavity between the skin and the transducer. A band-pass filter at a low frequency range between 0.02 and 20 Hz is used to extract the SSP from the PneaVoX recorded raw signal. The patient's respiratory effort causes variations of pharyngeal pressure, which induce pressure variations in the sensor chamber. These variations are measured by a piezoelectric sensor sensitive to skin movements. Thus, the presence or absence of SSP variations, at the respiratory frequency, can be used as a surrogate marker of respiratory effort to characterize apneas. Figure 1 shows a mixed apnea where respiratory effort is absent at the beginning of the event and resumes before the event finishes. In the absence of effort, the SSP signal, like the RIP signal, can sometimes be limited to high-frequency cardiogenic oscillations.

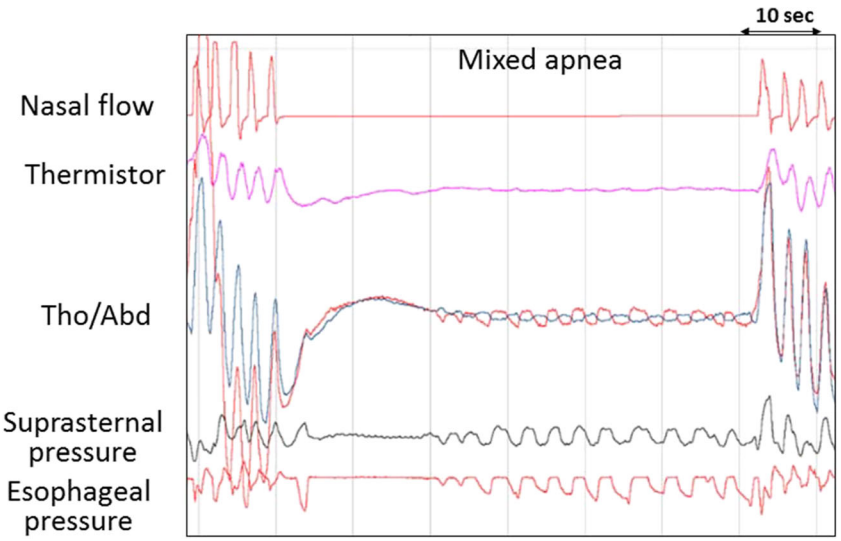

Fig. 1 Example of a mixed apnea where respiratory effort is absent at the beginning of the event and resumes before the event ends. The respiratory effort is detected on the Pes signal, the SSP signal, and the RIP signals where a paradoxical movement between the thorax and the abdomen is noticed. Tho/Abd, thoracic and abdominal signals measured using respiratory inductance plethysmography

Data analysis

Characterization was performed on each apnea detected using AASM recommendations [1]. Respiratory effort was evaluated using each of the following signals separately and in random order: Pes, RIP belts, and SSP signals. Only one signal was displayed at a time and analyzed while the other two signals were masked. The three classifications of apneas were then compared.

Using AASM recommendations, hypopneas were characterized as obstructive based on identification of flattening of inspiratory airflow, snoring, or a reduction in respiratory effort followed by a progressive increase of effort until the end of the event (Fig. 2a). In the absence of these obstruction criteria, hypopneas were scored as central (Fig. 2b). The respiratory effort evaluation was scored randomly three times using the Pes, SSP, and RIP signals separately. The SSP and RIP characterizations were compared with the Pes characterization.

Statistical analysis

Statistical analysis was performed using MATLAB R2016a software (MathWorks, MA, USA). Values are presented as mean ± standard deviation. Cohen's kappa, sensitivity, and specificity, as well as positive predictive value (PPV) and negative predictive value (NPV) for respiratory event characterization, were calculated for all patients using Pes as a reference signal.

Results

Patients

Thirty-five recordings from a group of 32 patients (five women) were examined. Three patients with heart failure were recorded on two consecutive nights with and without their pacemakers active. However, Pes measurement failed in two recordings and only 33 recordings were used. The mean unvalidated recording time for all patients was 20.5 ± 35.7 min and the mean validated recording time was 438.4 ± 68.2 min.

Patients had a mean age of 66.7 ± 15.3 years, a mean BMI of 30.1 ± 4.6 kg/m^2, and a mean neck circumference of 42.8 ± 4.1 cm. The AHI was 36.1 ± 25.1/h with a mean TST of 317.4 ± 77.5 min. Mild SAS (5 ≤ AHI < 15/h) was scored in 5 recordings, 10 were scored as moderate SAS (15 ≤ AHI < 30/h), and 18 were scored as severe SAS (AHI ≥ 30/h).

Apnea characterization

A total number of 4925 apneas were scored in all patients first based on AASM criteria and then characterized using each sensor separately. Using Pes, 2537 were considered obstructive, 1389 were central, and 999 were mixed. Using RIP belts, 2653 apneas were classified as obstructive, 1287 as central, and 985 as mixed. Using SSP, 2531 were classified as obstructive, 1365 as central, and 1029 as mixed. Table 1 shows apnea classification comparison of SSP with Pes, RIP with Pes, and SSP with RIP. The Cohen kappa (κ) statistics were 0.93 (95% confidence interval 0.92 to 0.94) for SSP with Pes, 0.87 (95% confidence interval 0.86 to 0.88) for RIP with Pes, and 0.90 (95% confidence interval 0.88 to 0.91) for SSP with RIP.

Comparing SSP with Pes, 2460 of 2536 (97.0%) obstructive, 1305 of 1390 (93.9%) central, and 948 of 999 (94.9%) mixed apneas were correctly classified. Comparing RIP with Pes, 2470 of 2536 (97.4%) obstructive, 1216 of 1390 (87.5%) central, and 855 of 999 (85.6%) mixed were correctly classified. The sensitivity and specificity of SSP and RIP compared with Pes and SSP compared with RIP are summarized in Table 2.

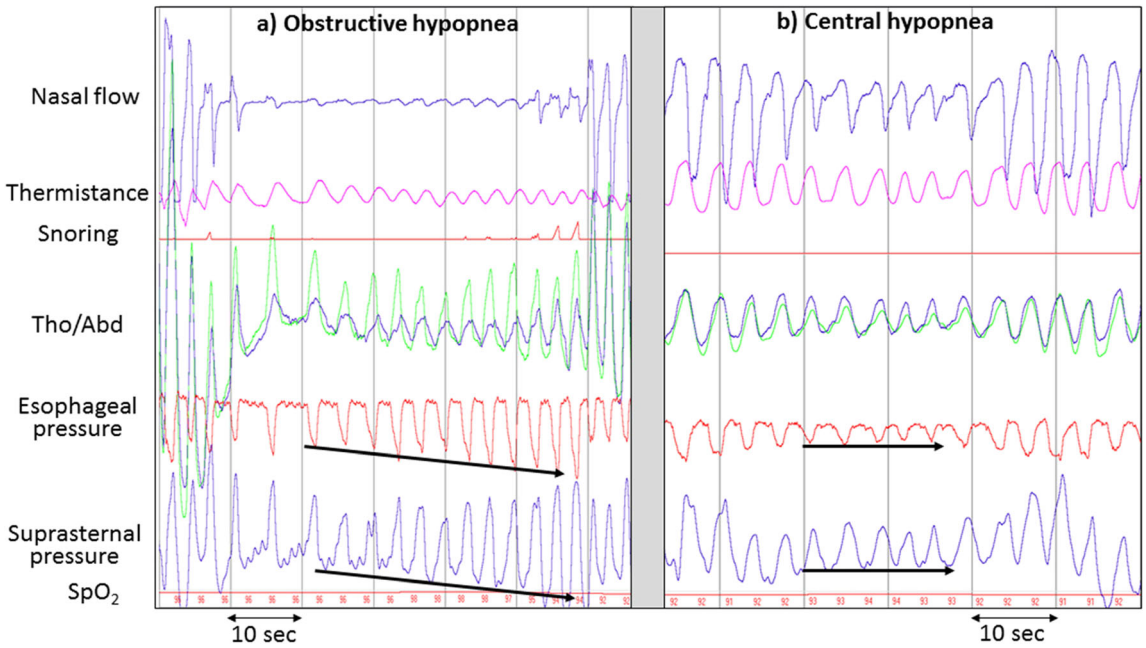

Fig. 2 Example of an obstructive hypopnea (**a**) compared with a central hypopnea (**b**). The obstructive hypopnea is presented with flattening of inspiratory airflow, snoring, and a reduction in respiratory effort followed by a progressive increase of effort, in both the esophageal pressure (Pes) and the suprasternal pressure (SSP) signals, until the end of the event. During central hypopnea, there is absence of snoring and flow limitation. Although the respiratory effort is seen on both the SSP and Pes signals, it is diminished and does not increase throughout the event

Figure 3 shows the strength of the linear association between SSP and Pes characterizations and between RIP and Pes characterizations for the three types of apneas for all patients. The coefficients of determination R^2 for SSP vs. Pes were 0.99, 0.99, and 0.99 for obstructive, central, and mixed apneas, respectively. The coefficients of determination R^2 for RIP vs. Pes were slightly lower with 0.98, 0.98, and 0.94 for obstructive, central, and mixed apneas, respectively.

Table 1 Comparison of apnea characterization of SSP with Pes, RIP with Pes, and SSP with RIP. *RIP*, respiratory inductance plethysmography; *SSP*, suprasternal pressure; *Pes*, esophageal pressure; *OA*, obstructive apnea; *MA*, mixed apnea; *CA*, central apnea

	All patients ($n = 34$)		Pes	
		OA	CA	MA
SSP	OA	2460	32	39
	CA	48	1305	12
	MA	29	52	948
		Pes		
		OA	CA	MA
RIP	OA	2470	81	102
	CA	29	1216	42
	MA	38	92	855
		RIP		
		OA	CA	MA
SSP	OA	2494	21	16
	CA	82	1216	42
	MA	77	49	903

Hypopnea characterization

For hypopneas, 2121 events were detected and then characterized using three different methods as described earlier. Using the Pes reference method, 2074 (97.8%) hypopneas were obstructive and 47 (2.2%) were central. Using SSP, 2079 (98.0%) hypopneas were obstructive and 42 (2.0%) were central. Using the RIP, 2068 (97.5%) hypopneas were obstructive and 53 (2.5%) were central. Cohen's kappa comparing SSP with the Pes was 0.92 (95% confidence interval 0.86 to 0.98). The sensitivity, specificity, PPV, and NPV of SSP for obstructive hypopnea characterization were 99.7%, 97.6%, 99.9%, and 87.2% respectively. For central hypopnea, they were 97.6%, 99.7%, 87.2%, and 99.9% respectively. Comparing the RIP with the Pes, κ was 0.86 (95% confidence interval 0.78 to 0.93). The sensitivity, specificity, PPV, and NPV of SSP for obstructive hypopnea characterization were 99.8%, 81.1%, 99.5%, and 91.5% respectively. For central hypopnea, they were 81.1%, 99.8%, 91.5%, and 99.5% respectively. Table 3 shows hypopnea classification comparison of SSP with Pes and RIP with Pes.

Table 2 Sensitivity and specificity of apnea characterization of SSP and RIP compared with Pes and SSP compared with RIP. *RIP*, respiratory inductance plethysmography; *SSP*, suprasternal pressure; *Pes*, esophageal pressure; *OA*, obstructive apnea; *MA*, mixed apnea; *CA*, central apnea

	SSP vs Pes		RIP vs Pes		SSP vs RIP	
All patients ($n = 34$)	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
OA	96.96	96.94	97.36	91.88	94.01	98.28
CA	93.95	98.27	87.54	97.91	94.56	95.83
MA	94.89	97.89	85.59	96.59	91.68	96.72

Discussion

Characterization of apneas and hypopneas using the SSP and using the RIP signals was compared with the gold standard using Pes. Provided that the scorer is familiar with the signals, the SSP is a reliable method to characterize apneas and hypopneas. Furthermore, a combination of the SSP and the RIP methods will result in a more accurate classification of respiratory events; thus, the two methods are complementary.

For the detection of respiratory efforts and the classification of events as obstructive or central, esophageal manometry is considered the reference method [1]. However, this invasive method may modify pharyngeal airway dynamics [16], may induce poor-quality sleep [2–4], and is therefore rarely used in routine clinical practice. As an alternative to Pes monitoring, the AASM recommends the use of RIP signals [1]. However, displacement of the belts due to body movements during recording at night could make the measurements less reliable. In

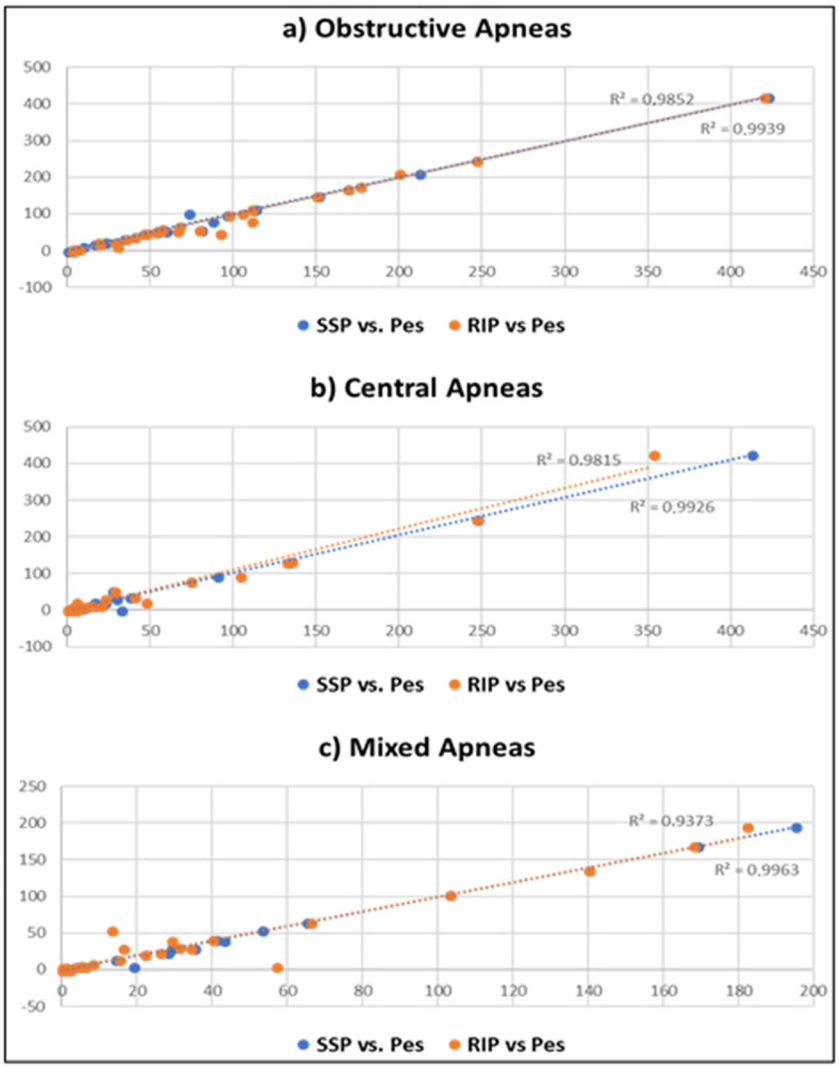

Fig. 3 Strength of the linear association between the SSP and Pes characterizations and between RIP and Pes characterizations for **a** obstructive apneas, **b** central apneas, and **c** mixed apneas in all patients. RIP, respiratory inductance plethysmography; SSP, suprasternal pressure; Pes, esophageal pressure

Table 3 Hypopnea classification comparison of SSP with Pes and RIP with Pes. *RIP*, respiratory inductance plethysmography, *SSP*, suprasternal pressure; *Pes*, esophageal pressure; *OH*, obstructive hypopnea;*CH*, central hypopnea; *PPV*, positive predictive value; *NPV*, negative predictive value

	All patients ($n = 33$)	SSP		RIP	
		OH	CH	OH	CH
Pes	OH	2073	1	2064	10
	CH	6	41	4	43
	Sensitivity (%)	99.71	97.62	99.81	81.13
	PPV (%)	99.95	87.23	99.52	91.49
	Specificity (%)	97.62	99.71	81.13	99.81
	NPV (%)	87.23	99.95	91.49	99.52

addition, it has been shown that up to one-third of apneas characterized as central with the RIP belts were reclassified as obstructive or mixed with Pes or with a diaphragmatic surface EMG [7, 8]. Calibration of RIP signals could improve RIP accuracy for detection of respiratory effort [17]. However, even calibrated RIP may not detect weak respiratory effort in some patients and results in misclassification of obstructive apneas as central [18].

Our results show that SSP accurately characterized all three types of apneas in comparison to Pes ($\kappa = 0.93$) and to RIP ($\kappa = 0.87$) methods, with high degree of sensitivity and specificity. On the other hand, compared with the Pes method, the RIP method scored slightly lower ($\kappa = 0.90$) with lower sensitivity for the characterization of central and mixed apneas, and a high sensitivity for obstructive events. However, the specificity of the RIP method was very high for both obstructive and central events. These results confirm that SSP is a reliable signal for the classification of apneas in clinical practice [13–15].

In a study using visual scoring, Meslier et al. showed good agreement between SSP and Pes signals for the classification of 3261 apneas in 26 adult patients [15]. While this study compared the SSP method with the gold standard Pes, there was no comparison between the SSP and the RIP characterization methods. Based on this study and on the fact that the SSP is widely used in France, the French clinical practice recommendations included in 2010 the measurement of SSP for the classification of apneas (Evidence Level 3) [19]. In a recent study, Amaddeo et al. compared the same tracheal sound sensor used in this study with sensors recommended by the AASM (oronasal thermal sensor and RIP belts). Detection and characterization of sleep apnea were performed in 20 children and showed good sensitivity and specificity for obstructive and central apneas. Moreover, the quality of the TS signal allowed analysis during 97% of the recording time, whereas it was only 65% for the nasal cannula and 87% for the thermistor [13]. In another recent study, we showed that SSP assessment of respiratory effort reliably distinguishes between obstructive and central hypopneas as well as between obstructive, mixed, and central apneas relative to the reference methods. However, the Pes evaluation was only performed on a subgroup of 9 patients out of the 34 used patients [14].

In this study, we scored more apneas as central with the SSP (1365) and with the Pes (1389) than with the RIP (1287). Although the difference is small, these results differ from two previous studies in which RIP belts overestimated the characterization of central apneas. Furthermore, a small percentage of apneas were scored as obstructive or mixed with the SSP (4.4%) or the RIP (5.5%) but central with the Pes. On the other hand, some apneas were scored as central with the RIP (5%) and obstructive or mixed with SSP and Pes (Fig. 4). This was also true for the SSP where 2.4% were scored as central while respiratory effort was seen on the Pes. Discrepancies in the scoring were mainly seen in 3 patients for RIP and 2 other patients for SSP. There was no particular anthropometric feature observed in these patients.

These results confirm findings in recent studies [13, 14]. Analyzing RIP belt technology from different systems (CID 102, EMBLA N7000, and SOMNOscreen), results show that RIP belts, at least in these three systems, can misclassify central events for obstructive and vice versa. This is also seen on the SSP with fewer misclassifications. However, in the absence of Pes, the use of the SSP in addition to the RIP could confirm the respiratory effort status and make the classification of apnea more reliable.

Our results also showed excellent characterization of hypopneas by SSP ($\kappa = 0.92$) in comparison with Pes. However, the RIP method scored slightly lower ($\kappa = 0.86$) than the SSP and had lower sensitivity for obstructive hypopneas and lower specificity for central hypopneas. This lower performance of the RIP is probably due to the fact that in the absence of snoring and airflow flattening in the airflow signal, obstructive hypopneas were scored when there was evidence of even a slight degree of paradoxical breathing. Furthermore, it is possible for a hypopnea to be obstructive and still exhibit in-phase thoracic and abdominal movements as if the detected hypopnea was central. In such cases, there must be other evidence of upper airway obstruction, and in the absence of airflow flattening or snoring, the SSP could help scoring an event as an obstructive hypopnea.

One limitation of our study is that the data were only analyzed by one scorer and we did not explore interscorer variability. However, interscorer variability in the scoring of sleep apnea/hypopnea events is mainly caused by how well trained the scoring technicians are and how familiar are they with the selected signals to be scored and the presentation of the traces in the used software. The amplification of the recorded signals as well as the use of digital filtering could, for instance, affects the quality and the reliability of the scoring and obstructive events could mistakenly be scored as central events or vice

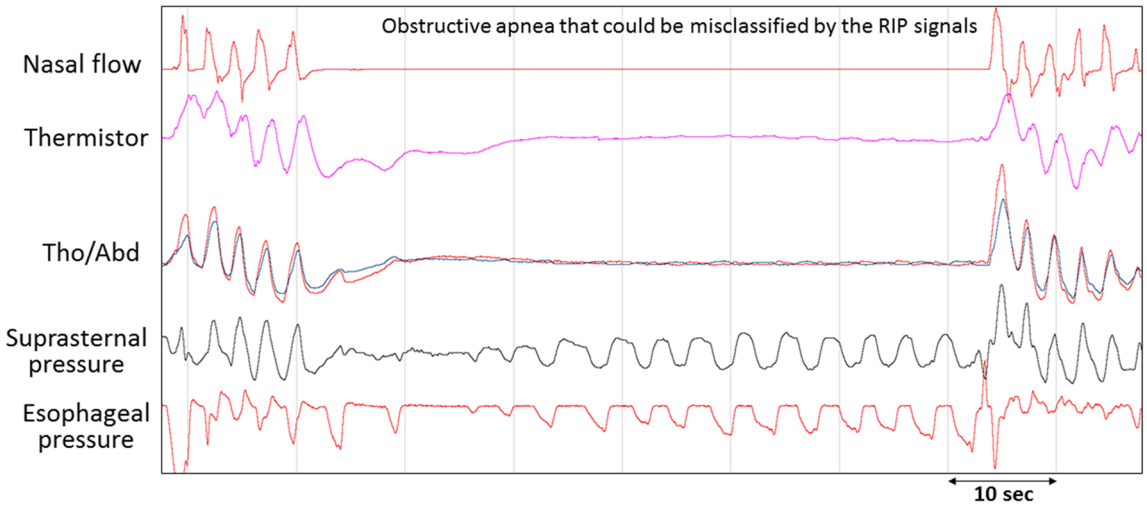

Fig. 4 Example of an apnea that could be misclassified by the RIP signals as central while it is clearly identified as obstructive on both the esophageal pressure and the suprasternal pressure signals. RIP, respiratory inductance plethysmography

versa. The lack of consensus of how long the central part of a mixed apnea should last is another problem that can affect interscorer variability. Differentiating between mixed and obstructive apneas depends sometimes on the criteria set by the scorers but this misclassification does not impact the detection of respiratory effort. Another limitation is that the central hypopneas scored in our study only represent about 2% of the total number of detected hypopneas. The differentiation of central and obstructive hypopneas is mostly settled during periodic breathing; otherwise, central hypopneas are very difficult to score even in the presence of esophageal pressure. Thus, the multiplicity of signals that can confirm the central aspect of hypopneas could help solve this issue. Finally, while SSP signal showed a high degree of stability, it was not analyzed in different sleep stages, particularly during REM sleep where ventilatory instability could affect respiratory event characterization.

Conclusions

In conclusion, based on visual characterization of apneas and hypopneas performed on 7046 events using three different methods, we confirm the excellent agreement in the detection of respiratory effort between SSP, RIP belts, and Pes signals. Misclassification of one sensor could be corrected with the presence of a second sensor. Thus, in the absence of Pes, associating the SSP with RIP belts increases the reliability of respiratory event characterization during PSG. In addition, the SSP sensor used in this study proved to be of high applicability. Unlike the RIP belts, once installed properly, it is not susceptible to move or be displaced during sleep and it does not disturb sleep. However, prospective evaluation in home recording and in specific group of patients, such as obese patients, pregnant women, and children, is needed to establish a larger clinical utility of this approach.

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Compliance with ethical standards

The study was approved (DRKS-ID: DRKS00012795) by the local Ethics Committee of the Charité university hospital in Berlin.

Conflict of interest Thomas Penzel has received research grants from Heinen & Löwenstein, Itamar, Philips/Respironics, Resmed, and Somnodent. He received speaker fees and travel support from Bayer, Itamar, Inspire, Somnodent, UCB, and Weinmann. He is a shareholder of Advanced Sleep Research GmbH, The Siestagroup GmbH, and Somnico GmbH. He was supported by the project no. LQ1605 from the National Program of Sustainability II (MEYS CR) and by the project FNUSA-ICRC no. CZ.1.05/1.1.00/02.0123 (OP VaVpI). Ingo Fietze has received research grants from Actelion, Eisai, Heinen & Löwenstein, Jazz Pharmaceuticals, Philips/Respironics, Resmed, Somnodent, UCB, and Vanda.

At the time the study was performed, AbdelKebir Sabil was fully employed by CIDELEC.

All other authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

Abbreviations AASM, American Academy of Sleep Medicine; AHI, Apnea Hypopnea Index; AI, Apnea Index; BMI, body mass index; EDF, European Data Format; EMG, electromyogram; SAS, sleep apnea syndrome; Pes, esophageal pressure; NP, nasal pressure; PSG, polysomnography; RIP, respiratory inductance plethysmography; SSP, suprasternal pressure; TST, total sleep time

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