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Screening of obstructive sleep apnea syndrome by the deep breathing technique

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ABSTRACT

Study Objectives: Obstructive sleep apnea syndrome (OSAS) is associated with alterations in heart rate variability (HRV) in relation to chronic autonomic dysfunction. We tested the ability of the deep breathing technique -a simple way to evaluate HRV- to identify OSAS patients.
Methods: Consecutive patients referred for suspected OSAS (without obesity, diabetes and heart diseases) were included. They underwent a measure of HRV at rest, and of heart rate (HR) oscillations during expiration vs. inspiration ($DeltaHR_{DB}$) when breathing deeply at the resonant frequency of six cycles per minute (deep breathing technique) while sitting awake, followed by a night-time polysomnography. We measured $DeltaHR_{DB}$ and performed temporal and spectral HRV analysis.
Results: Of 31 included subjects (77% male), 14 had mild to moderate OSAS (apnea/hypopnea index, AHI median [IQR]: 18 [12]), and 17 had no OSAS. The conventional HRV analysis did not reveal any difference between the groups with vs. without OSAS. However, the $DeltaHR_{DB}$ was lower in subjects with than without OSAS. Lower $DeltaHR_{DB}$ correlated with higher AHI, arousal index, and desaturation degree. A $DeltaHR_{DB}$ below 11 bpm predicted OSAS with a sensitivity of 100% and specificity of 86%.
Conclusions: The deep breathing technique accurately identifies a reduction in cardiac changes in patients with mild to moderate OSAS. It could be used as a simple screening tool to select patients for polysomnography.
Keywords: obstructive sleep apnea; screening; deep breathing; heart rate variability

BRIEF SUMMARY

Current Knowledge/Study Rationale: Obstructive sleep apnea syndrome (OSAS) can lead to cardiovascular diseases. OSAS is associated with alterations in heart rate variability (HRV), in relation to chronic autonomic dysfunction. Because of this close relationship, we made assumptions that HRV could be used as a marker of OSAS.
Study Impact: Maximal changes in heart rate during the Deep Breathing (DB) technique ($DeltaHR_{DB}$) inferior to 11 bpm most likely identify OSAS. Therefore, it is possible to discriminate OSAS subjects before polysomnography using DB.

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is characterized by repetitive upper airway obstructions during sleep, resulting in intermittent hypoxia, autonomic fluctuation, and sleep fragmentation. Polysomnography is the gold standard test for OSAS diagnosis [1], but it is expensive and not easily accessible. Simple screening tools may help select patients with a higher probability of OSAS.

OSAS has revealed itself as a leading, though largely treatable, cause of several cardiovascular disease entities, including hypertension, diabetes mellitus, heart failure or cardiac arrhythmias[2–5]. In particular, OSAS is associated with chronic autonomic dysfunction [6]. Heart rate variability (HRV) is a reliable measure of autonomic cardiovascular modulation [7], which integrates sympathetic and parasympathetic effects on the heart [8]. Previous studies have shown an alteration in HRV in OSAS patients using conventional HRV analyses (which include temporal and spectral frequency-domain analyses of the cardiac beat-to-beat intervals), at night (during polysomnographic recordings [9,10]), but also during wakefulness conditions [11–13]. These results suggest that HRV might be exploited to pre-identify subjects for a suspicion of OSAS before polysomnographic recordings. However, first, these usual analyses requires expertise for off-line calculation (Fourier transformation for the obtention of spectral densities for example), and second, if a trend for reduced vagal HRV in OSAS is generally found with these analyses, a significant decrease is not always obtained [14,15]. Another possibility to estimate vagal HRV is the use of the deep breathing technique, during which the examiner can instantly evaluate the oscillations of heart rate (HR) between inspiration and expiration while breathing deeply at the resonant frequency of six per minute (the amplitude of the oscillations reflecting the vagal reactivity and the baroreflex sensitivity [16]). In addition to be easier and faster, this technique seems to be more sensitive than usual tests to evidence autonomic modifications in OSAS patients [17,18]. Thus, our aim was to compare the ability of temporal and frequential analyses of HRV at rest one one hand, and the calculation of maximal cardiac changes during the deep breathing technique on the other hand, to pre-identify OSAS by the presence of autonomic differences in patients with no established cardiovascular disorders. Subjects included in this study were sent to our service because of suspected OSAS but were otherwise healthy (with no known comorbidities which could have altered the autonomic balance independently of OSAS).

METHODS

Study design

Our study was a non-interventional, prospective trial, which took place in the Sleep Disorders Unit at the Pitié-Salpêtrière Hospital of the APHP-Sorbonne University, in Paris, France. The database and statistical analysis were managed within this department and the respiratory neurophysiology unit UMRS1158, of INSERM and Sorbonne University, Paris, France. The study was approved by the ethics committee CPP Sud-Est IV.

Subjects and protocol

We prospectively included subjects if they met the following criteria: i) men and women, aged 18 to 80 years old; ii) referred for suspected OSAS; and iii) accepting to take part in the study. To minimize the risk of recruiting subjects with autonomic dysfunction not due to OSAS, we excluded subjects with any condition or disease known to interfere with the autonomic nervous system, including obesity (body mass index, BMI > 30 kg/m^2), diabetes, systemic arterial hypertension, arrythmias, heart failure, renal failure, stroke, neurodegenerative disorder, or daily use of beta-blockers, selective serotonin reuptake inhibitors, and anticholinergics. All participants underwent an electrocardiogram (EKG) in order to detect any rhythm disorder that might interfere with the HRV analysis, and its detection led to excluding them from the study.

After checking eligibility, subjects read the information note and gave their consent to participate in the study. For each subject, we measured body weight, height, resting heart and respiratory rates, blood

pressure, temperature, and transcutaneous oxygen saturation, and we collected the Epworth Sleepiness Scale (ESS). Nurses set up the polysomnography equipment (Grael HD PSG/EEG system, Compumedics, Australia): 3 electroencephalogram (EEG) leads (F3/A2, C3/A2, O1/A2); right and left electrooculogram; electromyogram (EMG) of the chin muscle for sleep stage assessment; right and left tibialis anterior EMG for periodic leg movement monitoring; nasal pressure and oral thermistor for oro-nasal flow assessment; thoracic and abdominal respiratory inductance plethysmography belts for evaluation of respiratory efforts and for detection of thoraco-abdominal asynchronism or paradox; pulse-oximetry; 1-lead EKG.

A trained physician, blinded to the HRV analysis and to the deep breathing technique, scored sleep stages, arousals, periodic leg movements and respiratory events, according to standard rules [19,20]. According to the international criteria, we defined OSAS as an AHI equal to or greater than 5 in association with at least one of the following: i) a complaint of sleepiness, nonrestorative sleep, fatigue or insomnia symptoms; ii) the patient wakes with breath holding, gasping, or choking; iii) the bed partner reports habitual snoring, breathing interruptions, or both during the patient's sleep; iv) the patient has hypertension, a mood disorder, cognitive dysfunction, coronary artery disease, stroke, congestive heart failure, or type 2 diabetes mellitus; or an AHI equal to or greater than 15, with or without signs or symptoms [21].

HRV analysis

All HRV analyses were performed blinded to OSAS status. In the evening before starting the polysomnography recording, EKG recordings were performed in patients placed in a sitting position. Spike 2 software version 6.0, CED, England, was used to import and analyze EKG waveform data offline [22]. R-R interval (RRI) duration was calculated for the analysis of HRV, and HR was derived from the RRI and displayed as the mean frequency per minute. A period of spontaneous breathing during 3 minutes allowed temporal and frequential HRV analyses.

Temporal (time domain) analysis

The standard deviation of all R–R intervals (SDNN) reflects all the cyclic components responsible for variability during recording [23], and the root mean square of successive differences (r-MSSD) reflects the short-term HRV [24]. The Poincaré plot analysis is a geometrical method for the assessment of the HRV dynamics [25,26]. A Poincaré plot is a diagram in which each R-R interval is plotted as a function of the previous one. The width of the Poincaré scattergram, i.e. the dispersion of the points perpendicular to the bisector, reflects the short-term variance (SD1)[27]. The length of the scattergram, i.e. the dispersion of the points along the bisector, evaluates the long-term variance (SD2), and is considered to be a combination of sympathetic and parasympathetic vagal activities [28]. Normalized values of SD1 (SD1nu = SD1/(SD1+SD2)) and SD2 (SD2nu = SD2/(SD1+SD2)) were also calculated, because they are commonly used as specific markers of vagal and sympathetic activities, respectively [29].

Spectral (frequency domain) analysis

Power spectra from R-R intervals were obtained by the Fourier transform (size 128, Hanning window, giving results with frequencies from 0 to 0.5 Hz and a frequency resolution of 0.007 Hz). Low- (LF) and high-frequency (HF) powers were within the ranges of 0.04–0.14 Hz and 0.14–0.40 Hz, respectively [30]. LF and HF powers are commonly expressed in normalized (LFnu = LF/(HF+LF); HFnu = HF/(LF+HF)) values, and reflect long- and short-term variance, respectively [31,32].

Deep breathing

Following spontaneous breathing, and still in a sitting position, the subjects were told to breathe through the nose at the rate of six cycles/min, during 3 minutes, without taking pauses between breaths [33]. To help the subjects adapt their breathing rate, they were asked to follow a hand-made animation, with the apparition of 5 inward and 5 outward arrows lasting 1 second each (symbolizing 5-second inspiration and 5-second expiration, respectively), with a click tone at the start of the 5-second inspiration or 5-second expiration. This was supported by verbal signals from the examiner (**Figure 1**). Cardiac oscillations

during deep breathing are regular and of high amplitude in healthy subjects because of higher vagus nerve efficiency compared to that during spontaneous breathing [34]. Five seconds for each inspiration and expiration allows the synchronization of all the parameters that influence the heart rate. The amplitude of heart rate changes during inspiration vs expiration provides an estimate of the parasympathetic activity. From the 3 minute recording, we calculated $DeltaHR_{DB}$ as the mean of the 5 largest differences between maximal HR at the peak inspiration flow and minimal HR at the peak expiration flow [35] (**Figure 1** bottom).

Statistical analysis

The analysis was performed using RStudio software version 1.3.1093 and MATLAB (R2021a). The quantitative variables were expressed as the median [IQR], while the qualitative variables were expressed as a number and a percentage. Univariate comparisons between the groups were made using Wilcoxon's non-parametric test for quantitative variables, and Fisher's test for qualitative variables. Correlations between the different variables were assessed by Spearman's nonparametric correlation coefficient conditionally to age and BMI, i.e. using partial correlation coefficients. The results were considered significant for $p<0.05$. We established the receiver-operator curve (ROC) for discrimination between subjects with and without OSAS using $DeltaHR_{DB}$. We evaluated its discriminatory power by the area under the ROC curve (AUC), and determined the Youden's point (the point maximizing the sum of sensitivity+specificity).

RESULTS

Characteristics of subjects

A total of 31 subjects were included in a 6-month period. They were mainly middle-aged males of normal weight (**Table 1**). One third was sleepy, according to the ESS. 17 subjects belonged to the group without OSAS (defined as AHI < 5) and 14 to the group with OSAS (AHI ≥ 5). BMI but not age was higher in OSAS group. The two groups did not differ in terms of sleepiness and OSAS symptoms frequency, except for snoring, which was more frequent in the OSAS group.

As expected by the grouping method, the respiratory measures (AHI, duration of apneas and hypopneas) and arousal index were higher, and oxygen desaturation was more profound in the OSAS group (**Table 2**). No other differences in the sleep structure were found.

Concerning HRV data during spontaneous breathing (**Table 3**), no significant difference was found in terms of HR or RR between groups. Neither sympathetic temporal (SD2/SD1 and SD2nu) nor frequential (LF/HF and LFnu) markers of sympathetic activity [30], differed between OSAS and non-OSAS groups. In the same manner, neither temporal nor frequential HRV analyses showed any difference between groups concerning parasympathetic parameters (r-MSSD, SD1nu or HFnu) [30]. Only the cardiac oscillation amplitude during deep breathing ($DeltaHR_{DB}$, **Table 3** and **Figure 2**), which reflects the parasympathetic activity, was lower in subjects with than without OSAS.

Correlation between $DeltaHR_{DB}$ and AHI

As BMI and age influence AHI and $DeltaHR_{DB}$, the correlation analysis was adjusted for BMI and age. Lower $DeltaHR_{DB}$ correlated with higher AHI ($rs= -0.52$, $p<0.001$, **Figure 3**), as well as with higher oxygen desaturation index (ODI, $rs= -0.48$, $p=0.009$), cumulative apnea/hypopnea time ($rs= –0.51$, $p=0.004$), mean apnea/hypopnea duration ($rs= –0.5$, $p=0.005$), arousal index ($rs= –0.42$, $p=0.022$), but not with time with $SpO_2<90\%$ ($rs= –0.13$, $p=0.050$). No significant correlation was found between $DeltaHR_{DB}$ and sleep efficacy ($rs=0.14$, $p=0.49$) as well as ESS scores ($rs=0.04$, $p=0.86$).

$DeltaHR_{DB}$ ROC curve for predicting OSAS

In **Figure 4**, the performance of $DeltaHR_{DB}$ as a predictor for OSAS is determined by a ROC curve. The AUC equals 0.979 (CI 0.932-1.000), and a $DeltaHR_{DB}$ lower than 11 bpm corresponds to a sensitivity of 100% and a specificity of 86% for predicting an AHI≥5.

DISCUSSION

We found that a $DeltaHR_{DB}$ lower than 11 bpm predicted abnormal AHI (≥5) with a 100% sensitivity and a 86% specificity in young, nonobese subjects without cardiac, neurological or renal diseases, referred for suspicion of OSAS. Lower $DeltaHR_{DB}$ correlated with higher AHI, arousal index, and oxygen desaturation.

In OSAS, the big breath and arousal following the apnea are associated with a sudden increase of cardiac output, increased chemoreflex and activation of pulmonary stretch receptors [36], leading to intermittent sympathetic activation and increased blood pressure, all of which are reversed using CPAP [37]. Awake patients with severe OSAS have increased LF/HF and LFnu, two indexes of sympathetic activity [11,12]. We found that neither LFnu nor LF/HF were significantly different between non-OSAS and OSAS patients in our study. Using temporal HRV analysis, we found that SD2 (a reflection of both sympathetic and vagal activities, see Methods), but not SD2nu nor SD2/SD1 (markers of sympathetic activities), was reduced in OSAS compared to non-OSAS subjects. Therefore, we could not conclude that our sample of mild and moderate OSAS patients had characterized sympathetic hyperactivity based on Poincare analyses. As mentioned above, our population was relatively young and had low AHI, no comorbid obesity or cardiac disease, plus a reduced size (potential lack of power), which may explain the absence of a significant increase in sympathetic activity among the subjects. Thus, this autonomic change may occur only in older and more symptomatic patients, and may not be taken as a tool for pre-identification of suspected OSAS.

A reduction of vagal parasympathetic activity is also associated with sympathetic hyperactivation in OSAS subjects [38].

Vagal reduction in the general population can be evidenced by pupillometry [39]. In this direction, OSAS subjects present a slight parasympathetic-mediated pupil constriction dysfunction [40]. Vagal indicators (HFnu, r-MSSD) [41,42] were lower in subjects with severe OSAS than in controls during sleep [9,43,44] and in patients with moderate to severe OSAS during wakefulness [11,12]. In our study, HF was reduced in OSAS patients. However, neither HFnu, nor r-MSSD, SD1 and SD1nu were significantly different between non-OSAS and OSAS subjects. Thus, it was difficult to conclude that a pre-identification of suspicion of OSAS based on vagal alteration is possible with usual HRV analysis. Few studies have evaluated vagal HRV in OSAS patients using the evaluation of cardiac changes to respiration. Jung et al. estimated vagal HRV with the maximal cardiac change during a breath-hold session, and found that it was reduced in severe OSAS [45]. Others showed that adults and children with OSAS had lower cardiac changes in the deep breathing test [17,46,47]. Importantly, this test was even more sensitive than usual HRV analyses to show differences between OSAS and non-OSAS subjects [17,18,48]. One study was unable to find similar results [14], but it is important to note that the authors analysed only four cycles of inspiration and expiration (that is very short considering that the patient has to adapt his breathing). In our study, using 3-min Deep Breahting, we found that $DeltaHR_{DB}$ was drastically reduced in individuals identified later (after polysomnographic recordings) as suffering from OSAS. Usual HRV vagal markers and the amplitude of cardiac changes during the deep breathing test decreases with age in healthy people [49,50], because the baroreflex cardiac response decreases in people over 50 [51,52]. In the same manner, obesity is an independent factor of autonomic dysfunction [53]. Our population presented no difference in age, and even though BMI was greater in OSAS subjects, we did not include any obese subjects in the study. So, the reduction in HRV parameters observed in our population is most likely due to OSAS. To note, our population of subjects was classified as mild and moderate based on AHI in polysomnographic recordings. Because no severe OSAS was among our subjects, we cannot infer (even it is likely) whether low $DeltaHR_{DB}$ would also detect severe OSAS.

We performed correlations between $DeltaHR_{DB}$ and AHI, as well as with sleep parameters, conditionally on BMI and age. $DeltaHR_{DB}$ decreased when AHI, arousals, cumulative and mean apnea/hypopnea indexes, and oxygen desaturation index increased, supporting that lower $DeltaHR_{DB}$ is associated with OSAS. According to the AUC, the performance of the $DeltaHR_{DB}$ for the diagnosis of OSAS in subjects free of other potential causes of autonomic dysfunction allowed us to establish a threshold of 11 bpm to obtain a sensitivity of 100% and a specificity of 86% in the detection of OSAS (defined by AHI≥5). The absence of autonomic dysfunction ($DeltaHR_{DB}$ equal or above 11 bpm) in some (2 out of 14, with moderate OSAS) subjects may indicate that the disease does not yet have any progressive systemic complications, implying a better prognosis in terms of cardiovascular complication risk.

Altogether, these results show that 1) performing $DeltaHR_{DB}$ analysis before polysomnography in subjects with suspicion of OSAS is a straightforward and sensitive tool to determine HRV alteration even in subjects with mild and moderate OSAS, and 2) that it is possible to discriminate subjects before polysomnography based on a $DeltaHR_{DB}$ threshold level.

Clinical implications and limits to the study

According to our findings, the deep breathing technique enabled us to discriminate subjects when referred to the hospital for suspected OSAS. We estimate here that only subjects with a $DeltaHR_{DB}$ <11 bpm should undergo polysomnographic recordings and may need cardiac care management.

This is a single-center study, with a small number of patients, which reduces the ability to generalize our results. A larger prospective study will be required to confirm the predictive validity of HRV for OSAS diagnosis and to refine the threshold value. Plus, the exclusion of patients with comorbid obesity, diabetes, cardiac and neurological problems, limit the scope of our results to a young, non-obese population which does not correspond to the typical population referred for OSAS. But we estimated that a study on this type of population was a pre-requisite to obtain a $DeltaHR_{DB}$ threshold to discriminate OSAS based on their autonomic alteration.

The Deep Breathing technique measuring $DeltaHR_{DB}$ is now available via simple smartphone applications that can be performed alone, without the help of a care professional. Whether our findings, made in best conditions of measures (using EKG, a physician supervision and a professional analysis) can be extended to these applications, remains to be demonstrated.

Low vagal HRV is associated with an increased risk of sudden death in subjects recovering from an acute myocardial infarction [54]. Moderate and severe OSAS often need cardiac management, and are at risk for sudden death [55]. Our results show that mild OSAS subjects are as likely to be at risk as those with moderate OSAS. Mild to moderate OSAS may impact the systemic autonomic system, and cardiovascular adverse outcomes could progress in an insidious and subclinical way. Our study sample is weakly representative of subjects usually seen in sleep centers for suspected OSAS. But we chose on purpose to exclude subjects with obesity and cardiovascular diseases, to ascertain that these comorbidities would not interfere with HRV analysis. $DeltaHR_{DB}$ could help clinicians to justify a specific management, or at least a more regular follow-up (in particular at the cardiovascular level) of these young, otherwise healthy and sparsely symptomatic subjects, who may be more reluctant to be treated because they do not consider themselves sick. Further studies will be needed to evaluate the occurrence of cardiovascular outcomes in OSAS patients with altered $DeltaHR_{DB}$.

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ABBREVIATIONS

AHI	apnea-hypopnea index
AUC	area under the curve
BMI	body mass index
$DeltaHR_{DB}$	maximal changes in HR during Deep Breathing
ESS	Epworth Sleepiness Scale
ODI	oxygen desaturation index
EEG	electroencephalogram
EKG	electrocardiogram
EMG	electromyogram
HF	high frequency
HR	heart rate
HRV	heart rate variability
LF	low frequency
OSAS	obstructive sleep apnea syndrome
r-MSSD	root mean square of successive differences
ROC	receiver-operator curve
SD1	transversal poincare standard deviation
SD2	longitudinal poincare standard deviation
SDNN	standard deviation of all R-R intervals
REM	rapid eye movement
SpO_2<90%	time with SpO_2<90%
TST	total sleep time

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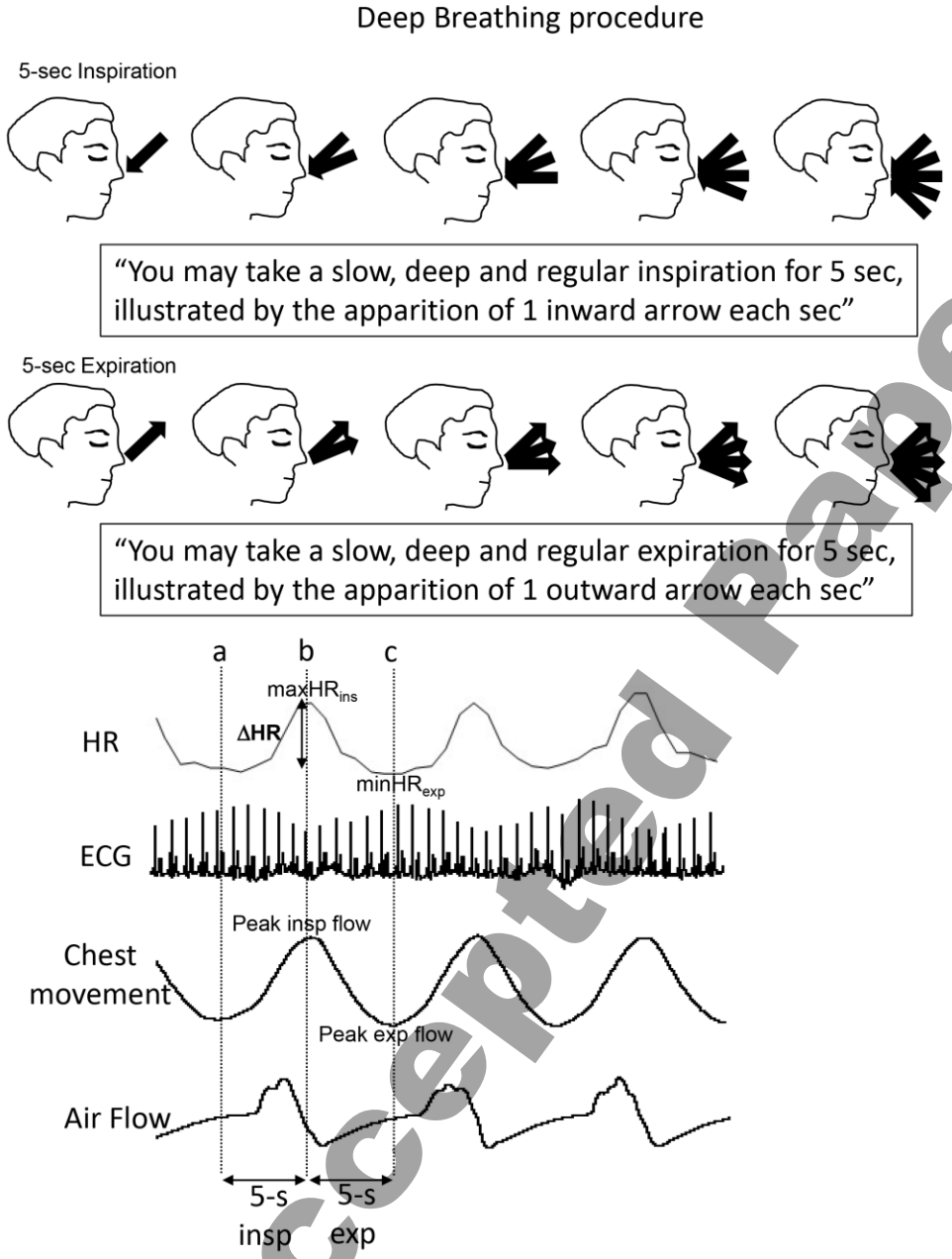
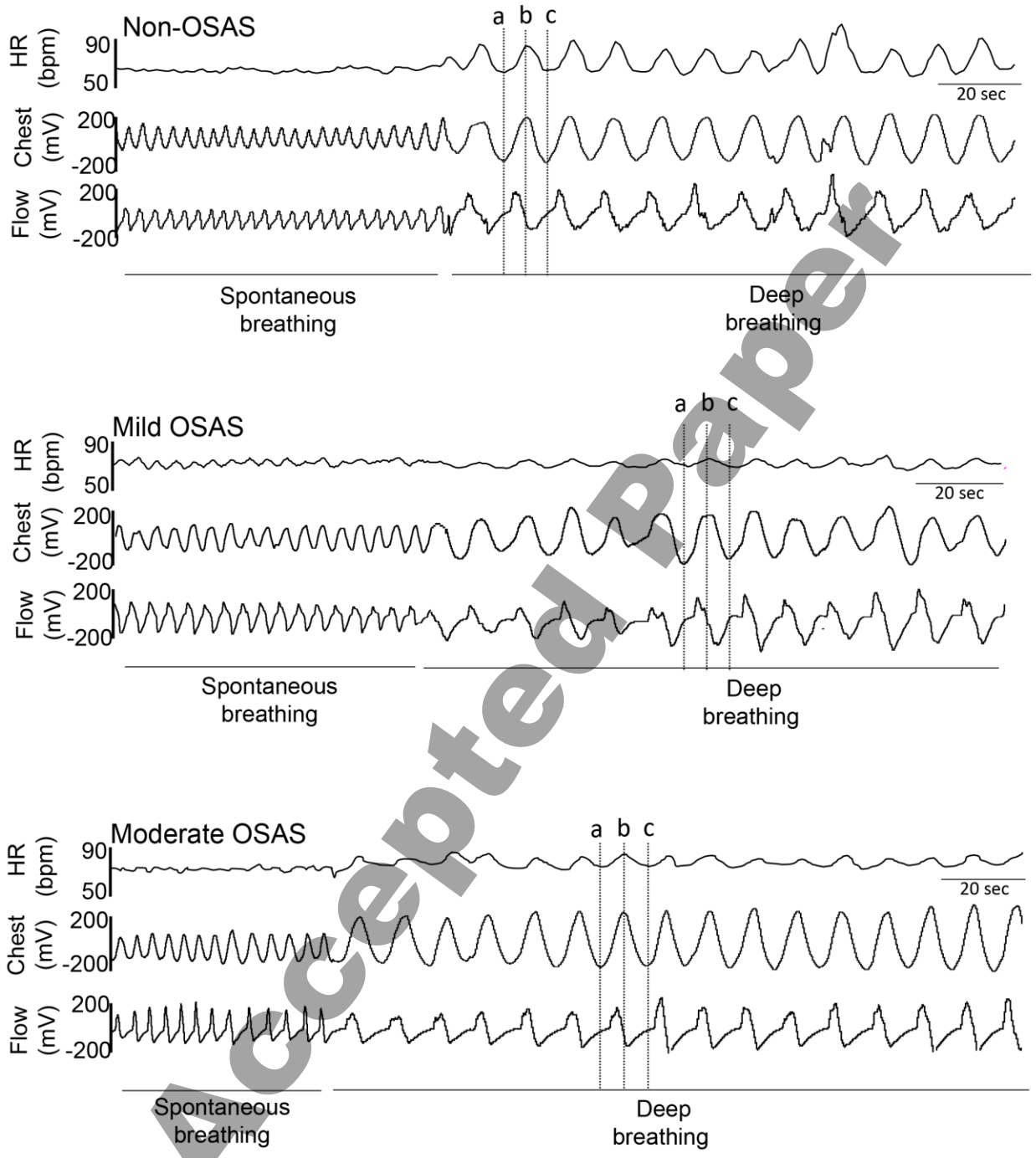
Figure 1—Hand-made animation used for the deep breathing test.



Top: Subjects were asked to breathe as indicated by the animation, showing the apparition of incoming arrows every second during 5 s (inspiration) immediately followed the apparition of outcoming arrows every second during 5 s (expiration). Verbal instructions (in the boxes) are also given to help the subject to follow the procedure.

Bottom: Examples of nasal air flow, Chest movement, ECG, and heart rate (HR) recordings during Deep Breathing. Lines show the 5-sec inspiration (5-sec insp, between lines "a" and "b"), and 5-sec expiration (5-sec exp, between lines "b" and "c") during 1 breathing cycle (10 sec in total). Inspiration begins when the thoracic signal starts to increase (see the synchronized increase in HR), and expiration begins when the thoracic signal starts to decrease (see the synchronized decrease in HR). DeltaHR_{DB} was calculated during Deep Breathing as the mean of the 5 largest differences (DHR) between maximal HR at the peak inspiratory flow (maxHR_{ins}) and minimal HR at the peak expiratory flow (minHR_{exp}).

Figure 2—HRV during deep breathing.

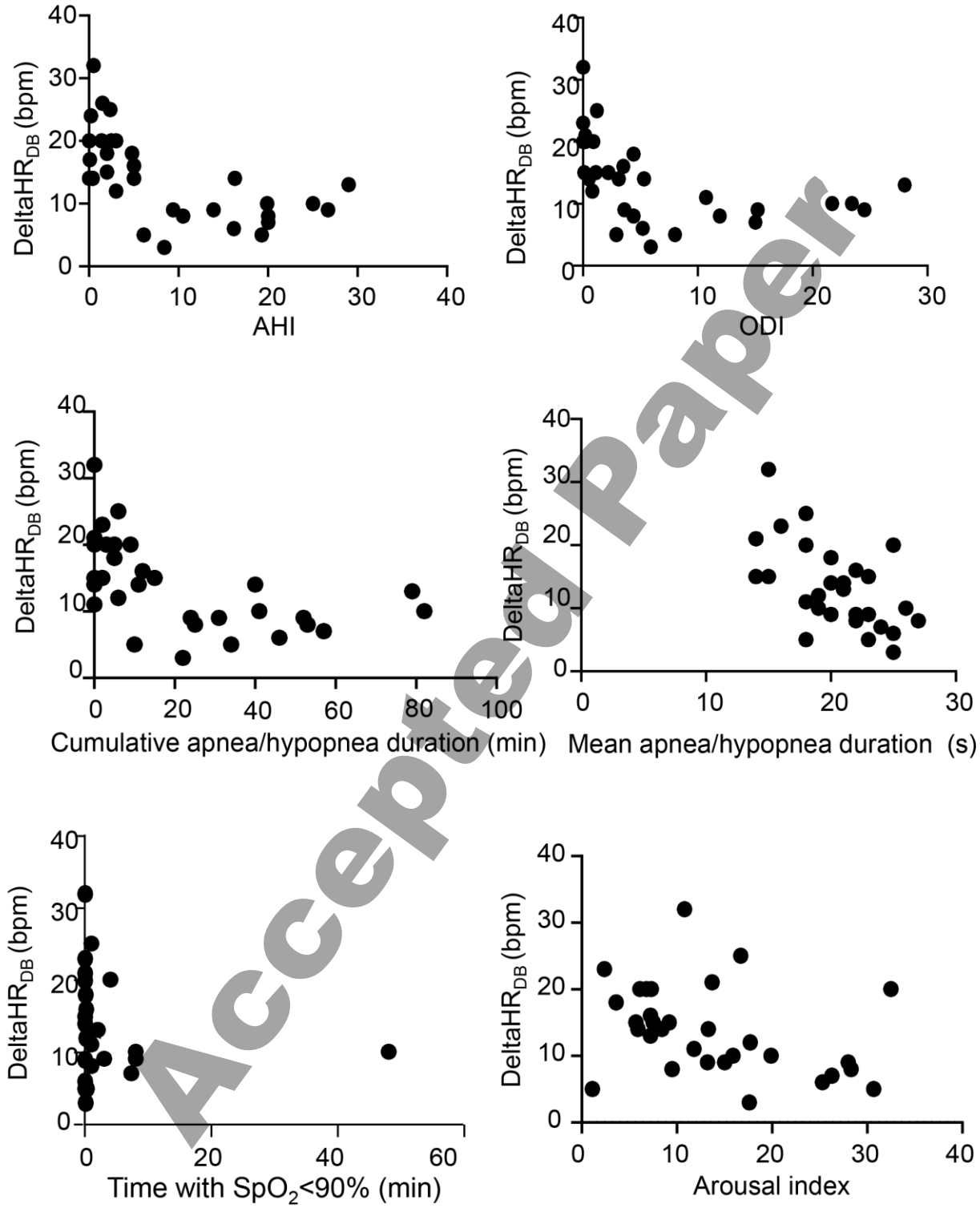


Representative tracings showing nasal air flow (Flow) and Chest movement tracings, as well as heart rate (HR) oscillations, during spontaneous and deep breathing in subjects identified as non-OSAS and mild or moderate OSAS after polysomnography.

No evidence of respiratory alteration was seen during wakefulness between the three groups, but the amplitude of oscillations during deep breathing is higher in both mild and moderate OSAS than non-OSAS subjects.

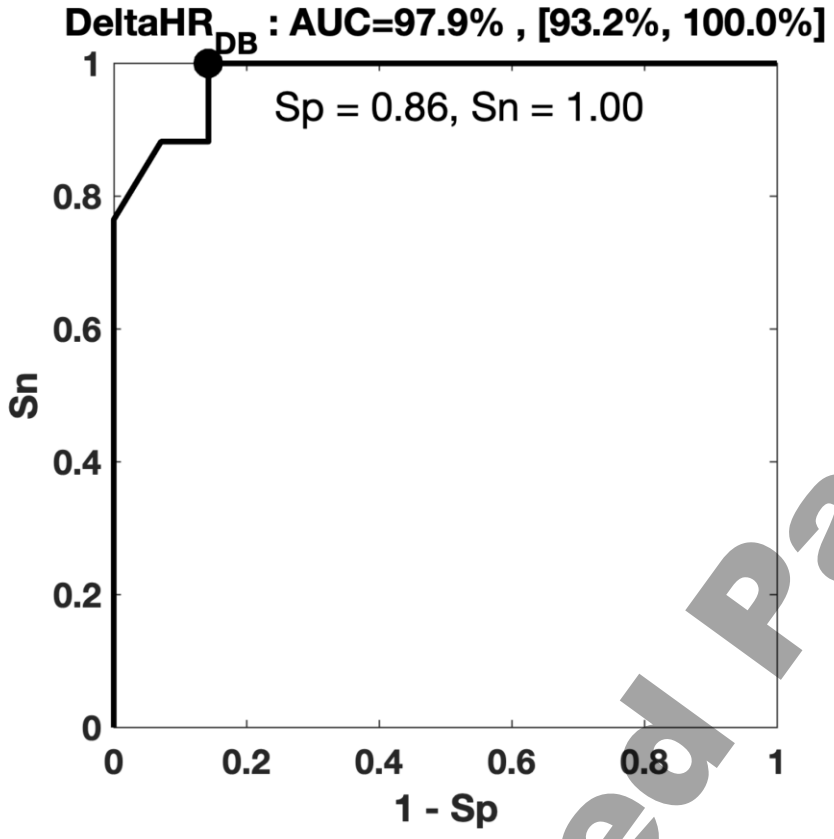
The description of lines a, b and c is given Figure 1.

Figure 3—Relations between $DeltaHR_{DB}$ and polysomnographic parameters.



Negative correlations between $DeltaHR_{DB}$ and ODI, time with SpO_2<90%, mean and cumulative duration time of apnea-hypopnea, and arousal index.

Figure 4—ROC curve analysis for $DeltaHR_{DB}$ for predicting OSAS.



The prediction performance of $DeltaHR_{DB}$ were assessed for clinically significant OSAS (AH≥5). Sp denotes the specificity (1 – Sp is hence the false positive rate), Sn the sensitivity (the true positive rate), and AUC the area under the ROC curve. The point corresponds to Youden's optimum (i.e. maximizing Sp+Sn).

Table 1—Demographics and clinical characteristics of study subjects.

	Overall (n=31)	**Without OSAS (n=17)**	**With OSAS (n=14)**	***P***
Male	24 (77)	11 (65)	13 (93)	0.071
Age (years)	50 [24]	44 [22]	55 [31]	0.099
Body mass index (kg/m^2)	24.3 [5.8]	23 [4.2]	26.5 [4.8]	0.002
Sleepiness				
Epworth Sleepiness Score, ESS	9 [6]	11 [9]	9 [4]	0.300
ESS >10	10 (32)	7 (41)	3 (21)	0.260
Symptoms				
Snoring	26 (84)	12 (71)	14 (100)	0.032
Abrupt awakenings with gasping	11 (36)	6 (35)	5 (36)	1.000
Nocturia	8 (26)	4 (24)	4 (29)	0.773
Morning headache	9 (29)	7 (41)	2 (14)	0.112

Values are the median and [interquartile range], and n (%).

Table 2—Polysomnography parameters.

	Overall (n=31)	**Without OSAS (n=17)**	**With OSAS (n=14)**	***P***
Total sleep time, TST (min)	400 [97]	410 [110]	396 [82]	0.597
Sleep efficiency (%)	86 [11]	86 [13]	86 [11]	0.589
Difference in sleep stages N1-N2 (% TST)	54 [9]	55 [13]	54 [7]	0.766
Sleep stage N3 (%TST)	22 [11]	21 [13]	25 [13]	0.968
Rapid eye movement sleep, REM (%TST)	23 [6]	23 [7]	21 [5]	0.766
Arousal index (per hour)	12 [11]	8 [8]	17 [18]	0.024
Apnea-hypopnea index, AHI (per hour)	5 [15]	2 [3]	18 [12]	<0.001
Mean apnea-hypopnea duration (s)	20 [5]	18 [6]	23 [4]	<0.001
Cumulative apnea-hypopnea time (min)	11 [38]	3 [8]	40 [29]	<0.001
Oxygen desaturation index, ODI (per hour)	4 [10]	1 [3]	10 [17]	<0.001
Time with SpO_2<90%, $TSpO_2$<90 (min)	0 [1]	0 [0]	1 [7]	0.016

Values are the median and [interquartile range].

Table 3—HRV parameters during spontaneous and deep breathing.

	Overall (n=31)	**Without OSAS (n=17)**	**With OSAS (n=14)**	***P***
Spontaneous Breathing				
Respiratory rate (cpm)	14 [5.25]	14 [0.5]	15 [5.5]	0.161
Heart rate (HR) (bpm)	70 [12]	72 [12]	68 [16]	0.303
SD2 (ms)	66 [46]	85 [29]	51 [26]	0.012
SD1 (ms)	52 [50]	62 [33]	29 [47]	0.071
Poincaré (ms^2)	12164 [15368]	15824 [9414]	6668 [13376]	0.077
SD2/SD1	1.37 [1.64]	1.33 [1.06]	2.33 [2.29]	0.246
SD2nu	57.09 [20]	57.09 [15.59]	63.1 [24.08]	0.444
SD1nu	42.91 [20]	42.91 [15.59]	36.9 [24.08]	0.444
SDNN	33.66 [26.62]	36.12 [34.85]	32.1 [12.63]	0.118
r-MSSD	23.6 [39.7]	23.57 [38.39]	24 [43.6]	0.922
LF (ms^2)	3.8 [3.7]	4 [5.35]	3.15 [4.8]	0.691
HF (ms^2)	2.0 [7.3]	3.5 [10.8]	1.3 [3.02]	0.037
LF+HF (ms^2)	6.3 [13.8]	8 [13.4]	4.1 [6.67]	0.095
LF/HF	1.35 [1.94]	1.15 [1.19]	2.16 [3.93]	0.052
LFnu	57.58 [42.59]	53.49 [32.4]	68.33 [35.18]	0.177
HFnu	41.67 [46.23]	46.51 [32.4]	31.67 [35.18]	0.177
Deep Breathing				
$DeltaHR_{DB}$ (bpm)	14 [11]	18 [6]	9 [4]	<0.001

Values are the median and [interquartile range].