

Detection of obstructive sleep apnea by analysis of phase angle using the forced oscillation signal

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Abstract

Pharyngeal collapse in patients with obstructive sleep apnea syndrome (OSAS) is linked to decreased upper airway muscle activity. We hypothesised that decreased muscle activity causes decreased stiffness of the upper airway wall and assumed that a decrease in wall stiffness would result in a change point (CP) of the morphology of phase angle time series $\phi(t)$ obtained by forced oscillation technique (FOT). We developed an algorithm to detect CPs in $\phi(t)$ and investigated $\phi(t)$ data measured in parallel to all-night polysomnography in seven patients. A total of 2724 CPs were detected by algorithm. The CPs were marked on the polysomnograms and compared with polysomnogram scoring performed jointly by three sleep expert physicians. A total of 791 (67%) of the 1172 hand-scored respiratory events showed a CP in $\phi(t)$ within a time interval of 8 sec before and 6 sec after the marked onset. A total of 672 (57%) respiratory events were detected at an earlier time by algorithm, and 119 (10%) were algorithmically detected later. The average detection time by the CP algorithm was 4.0 ± 1.1 sec earlier than the manual scoring. We conjecture that a CP in $\phi(t)$ indicates a change in upper airway collapsibility and that $\phi(t)$ might be a potentially useful parameter for detection of impending upper airway obstruction. © 2000 Elsevier Science B.V. All rights reserved.

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1. Introduction

Obstructive sleep apnea syndrome (OSAS) is usually due to pharyngeal narrowing or collapse during sleep. It is associated with a variety of potential neurocognitive deficits as well as vascu-

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lar disease (Sériès et al., 1994; Deegan and McNicholas, 1995; Strohl and Redline, 1996). Pathophysiologically, OSAS has been linked to: (a) sleep-induced decrease in upper airway dilator muscle activity; (b) decrease or complete cessation of superior pharyngeal constrictor activity; (c) an anatomically small pharyngeal airway; (d) relatively thick lateral pharyngeal walls; and (e) an increase of the total volume of parapharyngeal fatty tissue (Schwab et al., 1995; Mezzanotte et al., 1996; Schwartz et al., 1996; Kuna and Smickley, 1997).

The sleep-induced decrease in both upper airway dilator muscle activity and the superior pharyngeal constrictor activity results in slackening of muscles surrounding the pharynx and characterise the onset of an obstructive respiratory event (Remmers et al., 1978). Thus, for detection of the onset of respiratory events a signal is required which reflects upper airway muscle activity, because the sleep-induced decrease in muscle activity precedes an obstructive sleep apnea (OSA).

Earlier studies using the forced oscillation technique (FOT) have shown that this is a valuable tool for quantitatively assessing airway impedance in OSAS patients (Navajas et al., 1996; Rühle, 1996; Farré et al., 1997; Reisch et al., 1998, 1999). FOT noninvasively measures airway impedance (Z) which reflects upper airway patency. These studies suggested that the absolute value (modulus) ($|Z|$) positively correlates with the degree of upper airway obstruction.

We hypothesised that decreased upper airway muscle activity causes a decrease of upper airway wall stiffness leading to upper airway collapse. In a previous study using a mechanical model of the upper airways we demonstrated that the phase angle $\phi(t)$ of the oscillatory impedance measured with a stiff upper airway wall (low wall compliance) significantly differed from the phase angle measured with a more elastic upper airway wall (high wall compliance) even at low degrees of obstruction (Reisch et al., 1998). A mathematical simulation study has indicated that increasing upper airway wall stiffness prior to pharyngeal collapse can lead to a change in the morphology of $\phi(t)$ (Reisch et al., 1999).

We have developed a computer algorithm to detect change points (CPs) in the morphology of $\phi(t)$. The purpose of our study was to investigate the relationship between the change points algorithmically detected in $\phi(t)$ and the onset of respiratory events obtained by manual polysomnogram scoring.

2. Methods

2.1. Subjects

We investigated the phase angle data of seven patients (six males, one female) who underwent a full-night polysomnography in an accredited sleep laboratory (Hospital Ambrock, Hagen, Ger-

Table 1
Patient demographics and respiratory events prospectively scored by three sleep specialists

Subject	Sex	Age (year)	BMI (kg/m ²) ^a	Sleep time (h) ^b	Hypopneas	Obstructive apneas	Mixed apneas	Central apneas
1	M	43	32.1	5.4	4	31	238	28
2	M	36	25	6.2	55	1	5	0
3	M	22	21.8	6.7	71	6	81	4
4	F	40	24	6.3	13	6	14	0
5	M	54	36.5	6	229	3	93	3
6	M	49	33.1	6.6	66	11	24	17
7	M	54	26.6	5.7	139	5	23	2
Total					577	63	478	54

^a BMI, body mass index (weight/height² of the subject).

^b Sleep time, time of sleep during night.

many). For the patients' demographics, see Table 1. Median patient weight was 112% (range 88–150%) of ideal body weight (Geigy, 1970), the mean body mass index (BMI) was 28.4 kg m⁻². Mean patient age was 42.6 years. No subject had signs or symptoms of nasal deformity, allergic rhinitis, or upper airway infections and none was receiving any medication at the time of the study.

The study protocol was approved by the Ethics Review Board of the Hospital of Ambrock, Hagen.

2.2. Sleep studies

Standard polysomnography (Brainlab, Schwarzer, Munich, Germany) was performed measuring surface electroencephalogram (EEG) C4-A1, submental electromyogram (EMG), left and right electrooculogram (EOG), anterior tibial EMG, oxyhemoglobin saturation (s) by finger pulse oximetry (Schwarzer, Munich, Germany), nasal airflow with a thermistor, as well as inspiratory and expiratory CO₂ concentration by an infrared absorption sensor (Normocap, Datex, Helsinki, Finland). The respiratory effort and pattern were monitored by thoracic and abdominal strain gauges, and respiratory sounds by a microphone. In addition, the esophageal pressure (P_{es}) was measured in four patients using a catheter with a tip manometer (Gaeltec, Novotronic, Bonn, Germany).

Polysomnographic parameters were recorded on paper at a speed of 1 cm/sec (Schwarzer, Munich, Germany). The patients' usual bedtime was between 22:30 and 23:30 h; the studies were terminated at 6:00 h.

Sleep was staged manually according to standard criteria (Rechtschaffen and Kales, 1968). Respiratory events were classified jointly by three staff physicians specialised in sleep medicine at Ambrock Hospital. They negotiated any differences until they agreed on event classification.

The following criteria were used for apnea classification: (a) hypopneas (H) were defined as episodes of airflow reduction lasting for more than 10 sec, with the thermistor signal reduced to less than 70% and the thorax signal to less than 30% compared with the preceding breaths; (b)

obstructive apneas (OA) were defined as episodes of airflow cessation lasting longer than 10 sec associated with paradoxical movement of the chest and abdomen; (c) apneas were classified as central (CA) when there was no air flow and no respiratory movement of chest and abdomen for 10 sec at least; (d) mixed apneas (MA) were defined as events with an obstructive followed by a central component with airflow cessation of more than 10 sec. For all types of apnea, it was required that an oxygen desaturation of 4% was reached. Furthermore, esophageal pressure swings were visible to the scoring staff physicians.

Onset and classification of respiratory events were marked on the polysomnograms. For details on respiratory events see Table 1.

The manually obtained apnea–hypopnea index (AHI) was 22.8 (apneas/h) on average, varying for the seven subjects between 5 and 47.1. In total, 577 hypopneas, 63 obstructive apneas, 478 mixed apneas and 54 central apneas were detected by the staff physicians.

2.3. Forced oscillation technique (FOT)

Forced oscillation technique (FOT) measurement was performed in parallel to the polysomnography using a prototype device (Weinmann, Hamburg, Germany) (Rühle et al., 1997). It consists in superimposing a sinusoidal pressure oscillation of small amplitude on the respiratory flow of spontaneously breathing patients. The oscillations are recorded as pressure and flow signals, and then processed in order to calculate the airway impedance $Z(t)$ by its absolute value $|Z|$ and its phase angle ϕ ($Z = |Z| e^{j\phi}$; $j = (-1)^{1/2}$). The theory behind the FOT has been described in detail previously (DuBois et al., 1956; Michaelson et al., 1975; Lãndsér et al., 1976; Horowitz et al., 1983; Cauberghs and Van de Woestijne, 1984; Peslin and Fredberg, 1986).

In our set-up, the sinusoidal signal generator is a micro membrane pump of 0.8 ml cubic capacity (NMP 30; KNF, Freiburg, Germany). It is connected to a nasal CPAP mask in parallel with a conventional CPAP set-up (Somnotron 2, Weinmann, Hamburg, Germany). The signal generator is driven in the voltage regulated mode at a

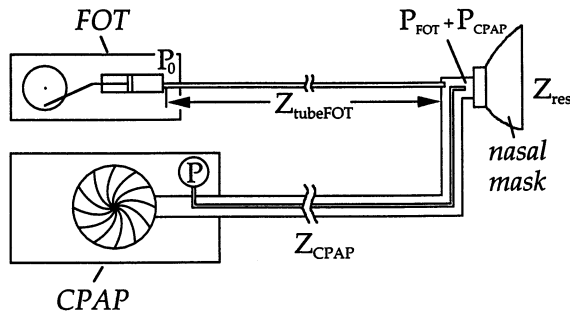


Fig. 1. Patient set-up using FOT. CPAP, continuous airway pressure generator; FOT, sinusoidal pressure generator; Z_{CPAP} , impedance (20 Hz) of the CPAP device; Z_{res} , impedance of the respiratory system; $Z_{tubeFOT}$, impedance (20 Hz) of the FOT device connection tube; P_0 , forcing pressure of the FOT pump; P_{FOT} , P_{CPAP} , pressures in the nasal mask; P , pressure transducer measuring P_{FOT} and P_{CPAP} .

constant frequency of 20 Hz. The set-up is described in detail elsewhere (Reisch et al., 1998).

CPAP pressure and FOT signal are obtained by measuring the pressure inside the nasal CPAP mask by means of a catheter which was connected to a piezoresistive transducer (176PC/14, Honeywell, Freeport, Ireland). The FOT set-up is depicted in Fig. 1. The DC-component of the measured pressure signal is the adjusted CPAP level (P_{CPAP}) which is kept at a constant level throughout the respiratory cycle by a feedback control loop. In order to isolate the forced oscillation components (P_{FOT}), the pressure signal is band-pass filtered (Butterworth 4-poles, 20 Hz).

In this experimental set-up, the FOT device measured a total impedance Z_{tot} consisting of the impedances of the FOT-tube ($Z_{tubeFOT}$), the CPAP-device (Z_{CPAP}) implicating the impedance of the device and the tube which connects the CPAP device with the nasal mask, and the respiratory system (Z_{res}) of the patient. Z_{CPAP} also includes an outlet which represents a considerably high resistance at 20 Hz., but a considerably low one at low frequencies allowing virtually normal breathing for the patient. Since $Z_{tubeFOT}$ and Z_{CPAP} are constant, the total impedance Z_{tot} depends on the impedance of the respiratory system Z_{res} and can be expressed by the pressure P_{FOT} . Thus, the absolute value of the impedance of the respiratory system ($|Z_{res}|$) corresponds to the mea-

sured pressure ($|P_{FOT}|$). The phase angle (ϕ) of the airway impedance is obtained from a trigger signal generated by the FOT pump and two consecutive pressure measurements (Reisch et al., 1998). No additional flow measurement is required (Van de Woestijne et al., 1981). In our set-up, the use of two pressure measurements instead of one pressure and one flow measurement results in a constant offset in the $\phi(t)$ time series only which is not relevant for CP detection. From the 12-bit D/A-converter of the FOT device $|P_{FOT}|$ and ϕ are given in unipolar voltage units ranging from 0 to 5 V. They are sampled at a rate of 10 Hz. $|P_{FOT}|$ and ϕ were recorded on the polysomnographic tracings in addition to the standard signals and stored on computer disk for off-line analysis. The absolute value of the FOT signal as a substitute for the mouth flow was used for the polysomnogram scoring but not the phase angle signals.

Both, $|Z_{res}|$ and ϕ , exhibit periodic behaviour during the breathing cycle which is mainly due to changes of cross-sectional area, length and mechanical parameters like wall-stiffness, inertance and resistance of lower and upper airways. All these parameters are influenced by changes in lung volume and in the activity of muscles surrounding the airways during inspiration and expiration.

In order to apply the FOT, a basic CPAP level of 3 cmH₂O was required to achieve sufficient airflow and to reduce humidity in the tube system (Rühle et al., 1997).

2.4. Computer algorithm

We developed a computer algorithm for automatic detection of three characteristic changes in the morphology of $\phi(t)$: (a) change in baseline of the time series, (b) change in the amplitude of the time series, and (c) change in the periodicity of the time series. Possible reasons for these changes and their relation to upper airway wall properties are discussed in detail elsewhere (Reisch et al., 1999). The computer algorithm continuously analyses the morphology of $\phi(t)$ by calculating a feature value for each of the three possible morphology changes. A refractory time of 20 sec after each CP detection avoided multiple detection of the same

respiratory event onset. For a detailed description of the algorithm, see Appendix A.

2.5. Study design

The CPs in the morphology of $\phi(t)$ detected by algorithm were marked in the polysomnograms in addition to the manual scoring. The CPs were then compared with the onset markers of the manual polysomnographic scorings performed by the three sleep expert physicians of the Ambrock Hospital. A CP algorithmically detected was defined to detect the same respiratory event onset if detection of the CP fell into a range of 8 sec before and 6 sec after the marked respiratory event onset. The definition of this time interval is based on (1) our experience that the variability interval of a manually scored respiratory event onset is ~ 6 sec; and (2) the hypothesis that $\phi(t)$ allows for event detection even before upper airway obstruction is heralded by any other changes.

2.6. Statistical analysis

The following parameters were used for statistical analysis to compare the CPs detected by algorithmical analysis of $\phi(t)$ with the onset markers of the manual polysomnogram scorings: (a) sensitivity (sens) is the rate of respiratory events scored by the physicians at which a CP in the morphology of $\phi(t)$ was detected within the defined time interval; (b) the percentage of scored respiratory events with a CP algorithmically detected before (earl_dec) the manual onset marker (within the time interval); and (c) the percentage of scored respiratory events at which a CP in $\phi(t)$ was detected after (late_dec) the original onset marker of the physicians. (d) The mean time difference (MTD \pm SEM) is the mean value of the lag between the CPs of $\phi(t)$ determined by algorithm within the time interval and the respiratory event onsets as evaluated by the staff physicians. Positive values indicate a respiratory event onset detection by algorithm later than the manual onset marker by the staff physicians.

To test whether manual onset time markers differed from those detected algorithmically the mean time differences (MTD) were analysed using

the Student *t*-test; $P < 0.05$ was accepted as statistically significant.

3. Results

A total of 1172 respiratory events were detected manually by the three staff physicians. 791 change points were detected algorithmically using changes in the morphology of the phase angle time series. Fig. 2 shows an example of a change in the morphology of $\phi(t)$ at the beginning of a respiratory event. The change in the morphology of $\phi(t)$ occurs 10 sec before the onset of the respiratory event determined by the staff physicians (vertical line).

Table 2 shows the comparison between manually scored and algorithmically detected onsets of respiratory events (hypopneas, obstructive apneas, mixed apneas, central apneas) with respect to sensitivity and onset detection time. 61% (352 of 577) of the hypopneas, 67% (42 of 63) of the obstructive apneas, 75% (358 of 478) of the mixed apneas, and 72% (39 of 54) of the central apneas showed a CP in the phase angle time series within the time interval around the manually scored onset. In 52% (300) of the hypopneas, in 62% (39) of the obstructive apneas, in 63% (301) of the mixed apneas, and in 52% (28) of the central apneas the CP occurs before the onset determined by the staff physicians. 9% (52) of the hypopneas, 5% (3) of the obstructive apneas, 12% (57) of the mixed apneas, and 17% (9) of the central apneas showed a CP in $\phi(t)$ later than the manual onset marker. The average mean time difference (MTD) ranged from -2.7 ± 0.5 sec for central apneas to -5.3 ± 0.3 sec for obstructive apneas.

In total, 67% (791 of 1172) of the respiratory events showed a CP in the phase angle time series within the time interval around the manually scored onset of a respiratory event. 57% (672) of the respiratory events were detected earlier by algorithm compared with manual scoring, and 10% (119) of the respiratory events showed a CP in $\phi(t)$ later than the manual onset marker. The average mean time difference (MTD) of the detected respiratory events was -4.0 ± 1.1 sec (Table 3).

Table 2
Comparison between manually scored and algorithmically detected onsets of respiratory events

Subject		1	2	3	4	5	6	7	Mean \pm SEM ^a
Hypopneas	Sens (%) / quantity	75/3	78/43	52/36	53/7	66/152	66/44	48/67	61/352
	Earl_dec (%)	50	54	40	30	62	59	36	52
	Late_dec (%)	25	23	8	23	4	7	11	9
	MTD ^a (sec)	-3.4 ± 2.0^c	-2.7 ± 0.8	-4.3 ± 0.4^d	-1.8 ± 1.9	-5.2 ± 0.2^c	-4.8 ± 0.5^c	-3.8 ± 0.5^c	-3.6 ± 0.3
Obstructive apneas	Sens (%) / quantity	74/23	100/1	33/2	83/5	33/1	54/6	80/4	67/42
	Earl_dec (%)	71	100	33	83	33	45	60	62
	Late_dec (%)	3	0	0	0	0	9	20	5
	MTD ^a (sec)	-5.6 ± 0.6^c	n.d. ^b	n.d. ^b	-6.2 ± 1.0^c	n.d. ^b	-5.3 ± 1.3^c	-3.8 ± 2.1^c	-5.3 ± 0.3^c
Mixed apneas	Sens (%) / quantity	84/201	100/5	60/49	36/5	73/68	75/18	52/12	75/358
	Earl_dec (%)	76	80	47	14	68	33	48	63
	Late_dec (%)	8	20	13	21	6	42	4	12
	MTD ^a (sec)	-5.1 ± 0.2^c	-3.8 ± 2.1	-2.9 ± 0.6	-3.2 ± 2.1	-5.3 ± 0.2^c	-1.1 ± 1.1	-4.7 ± 0.8^c	-4.0 ± 0.3^c
Central apneas	Sens (%) / quantity	86/24	$-/-^f$	25/1	$-/-$	33/1	71/12	50/1	72/39
	Earl_dec (%)	82	–	0	–	0	47	50	53
	Late_dec (%)	4	–	25	–	33	24	0	18
	MTD ^a (sec)	-5.7 ± 0.5^c	–	n.d. ^b	–	n.d. ^b	-3.1 ± 0.9	n.d. ^b	-2.7 ± 0.5^c

^a Mean \pm SEM.

^b n.d., not defined because no value or single value.

^c Significantly different from the original time marker, $P < 0.05$.

^d Significantly different from the original time marker, $P < 0.01$.

^e Significantly different from the original time marker, $P < 0.001$.

^f –, no apnea manually scored.

Table 3
Comparison between manually scored and algorithmically detected onsets of respiratory events

	Subject	1	2	3	4	5	6	7	Mean
Respiratory events	AHI ^a (h) ⁻¹	39	9	23	5	47	14	23	23
	Sens (%) / Quantity	83/251	80/49	54/88	51/17	67/222	67/80	50/84	67/791
	Earl_dec (%)	75	57	42	33	63	50	38	57
	Late_dec (%)	8	23	8	18	4	17	12	10
	MTD (sec)	-5.4 ± 0.2 ^c	-2.9 ± 0.7	-3.2 ± 0.4	-2.9 ± 1.2	-5.3 ± 0.2 ^c	-4.4 ± 0.4 ^b	-3.9 ± 0.3 ^b	-4.0 ± 1.1

^a AHI, Apnea/hypopnea index.

^b Significantly different from the original time marker, $P < 0.05$.

^c Significantly different from the original time marker, $P < 0.001$.

Table 3 shows the comparison between manually scored and algorithmically detected onsets of respiratory events with respect to apnea/hypopnea index (AHI) of the patients.

Applying only two of the three features led to a decrease of the over-all classification rate below 38%.

4. Discussion

In patients with OSAS the upper airway muscle tone decreases before respiratory event (Remmers et al., 1978; Mezzanotte et al., 1996; Schwartz et al., 1996). Since decreased muscle activity is assumed to be related to a change in upper airway wall compliance, we speculated that it would result in a change in the morphology of the FOT phase angle time series. In a simulation study using a mathematical model of the human respiratory system we

were able to show that decreasing upper airway wall-stiffness prior to a collapse leads to significant and characteristic changes in the morphology of the FOT phase angle $\phi(t)$ (Reisch et al., 1999). This gives evidence that the $\phi(t)$ signal carries information about upper airway collapsibility. However, a final confirmation would require a visual inspection by endoscope together with FOT measurements which is planned for future investigations.

The purpose of this study was to investigate whether changes in the morphology of the FOT phase angle time series $\phi(t)$ could be suitable as indicator of obstructive respiratory events. We developed a computer algorithm to detect CPs in $\phi(t)$. The detection time points of the CPs were marked on the polysomnograms which were recorded in parallel with the FOT measurement. The CPs were then compared with manual polysomnogram scorings performed by three staff physicians.

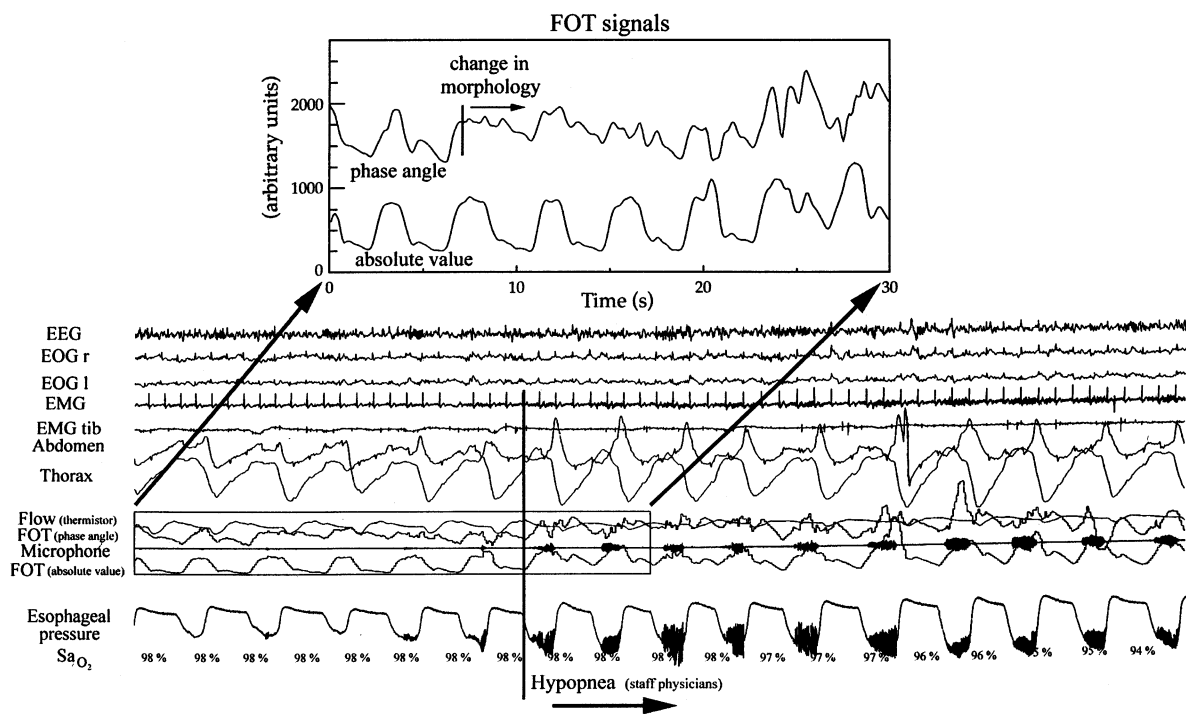


Fig. 2. A 60 sec polysomnogram segment showing changes in the morphology of the measured parameters at the onset of a respiratory event. The onset time (vertical line) and the classification (hypopnea) marked by the staff physicians are depicted in the diagram. A 30 sec segment of the FOT signals is enlarged to show the change in the morphology of the phase angle time series at the beginning of the respiratory event.

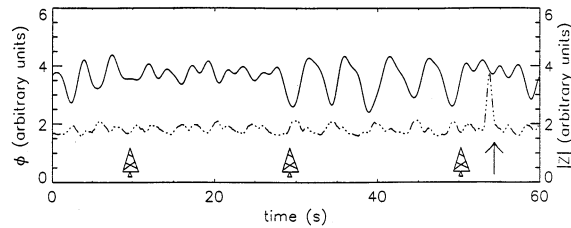


Fig. 3. A 60 sec segment of the phase angle ϕ (upper tracing; solid) and the absolute value $|Z|$ (lower tracing; chain-dotted) of an over-night FOT measurement. Three changes in the morphology of $\phi(t)$ are observed ($t=9, 29$ and 50 sec) (\blacktriangle). Upper short airway obstruction is identified by a sharp increase of $|Z|$ ($t=54$ sec) (\uparrow). $\phi(t)$ is low-pass filtered (Butterworth 6-poles, 0.5 Hz). $|Z|$ and ϕ are given in arbitrary units of the D/A-converter.

Comparing the CPs in $\phi(t)$ with manually scored respiratory event onsets, 67% of the manually detected onsets coincided with the algorithmically detected CPs, which means that a CP was detected in a range of 8 sec before and 6 sec after the marked respiratory event onset. However, the comparison of the different onset markers is only based on one time window, and the matching rate depends on the length of this time window. Changing this window to e.g. 4 sec before and 4 sec after the marked respiratory event onset would reduce the correspondence to less than 60%. An increase of the time interval to 10 sec before and 6 sec after the marked onset would improve the correspondence to over 70%. Thus, one single time interval is not sufficient to compare both methods the more so as no unbiased reasons exist how large it has to be chosen.

The algorithm detected more than twice the number of respiratory events (2724) which were manually detected (1172). One reason for this could be the high sensitivity of the FOT phase angle on changes in upper airway wall stiffness compared to polysomnographic parameters. A change of the upper airway wall stiffness does not inevitably lead to upper airway obstruction. In this case or in the case of short-term obstructions of the upper airways not exceeding 10 sec, a CP in $\phi(t)$ is detected algorithmically. These respiratory events would not be classified as sleep related disordered breathing patterns according to conventional criteria, but, however, may indicate a

physiological phenomenon. Thus, the interpretation of the phase angle data is different from common polysomnographic analysis. An example is presented in Fig. 3. The data displayed in Fig. 3 can be interpreted as follows: the upper airway muscle activity was reduced in preparation of an obstructive respiratory event which caused a change in the morphology of $\phi(t)$ at $t=9$ sec (\blacktriangle), but the decrease in upper airway wall stiffness was not sufficient to induce an airway collapse. 20 sec later a second change in the morphology of $\phi(t)$ at $t=29$ sec (\blacktriangle) can be observed. This could be interpreted as to the latter CP indicates the reversal to normal muscle tone. At $t=50$ sec (\blacktriangle), it can be assumed that the upper airway wall stiffness decreased again, followed by upper airway obstruction this time. The upper airway obstruction can be identified by the increase of $|Z(t)|$ at $t=54$ sec (\uparrow).

But the high number of CPs is also a result of the termination of respiratory events. Termination of respiratory events are correlated with an increase in upper airway wall stiffness which also cause CPs in the morphology of $\phi(t)$. From the mere change in the morphology in $\phi(t)$ it is not possible to decide whether the upper airway wall stiffness increases or decreases. Accordingly, more than one detected change in the morphology of the phase angle time series might be linked to the same respiratory event.

A CP only indicates a change of the upper airway wall state. It does not indicate the collapse of the upper airways but rather the increased tendency to collapse, i.e. an increase in collapsibility. Only partial or total airway occlusion leads to physiological symptoms like flow limitation which are observable with polysomnographic parameters usually recorded. Thus, the results should not be interpreted such as that the remaining 33% of manually detected respiratory events did not cause a change in morphology of $\phi(t)$ at their beginning. The decrease in airway wall stiffness preparing for an upper airway collapse can occur more than 8 sec earlier than the collapse itself. CPs in $\phi(t)$ were found up to 30 sec earlier than upper airway obstructions.

Recapitulating, the algorithm introduced here can only detect changes in the upper airway wall

state. Neither a classification of respiratory events can be performed nor their duration can be determined on the basis of the $\phi(t)$ analysis. Thus, the algorithmical analysis of $\phi(t)$ provides an overall index of onset of respiratory events.

CPs in $\phi(t)$, however, do not only reflect a change in upper airway wall stiffness. Central apneas were taken into the analysis since the cessation of respiratory movement leads to change in the morphology of the phase angle time series similar to CPs caused by changes in airway wall stiffness. During central apnea with open airways, geometry, size, and mechanical properties of the respiratory system do not change anymore. Consequently, the fluctuation in $\phi(t)$ that can be observed in normal tidal breathing discontinues. Analysing $\phi(t)$ exclusively, it is therefore not distinguishable whether the CP is caused by either the onset of a central apnea or a change in upper airway wall stiffness.

Furthermore, air leaks at the nasal mask can not be completely avoided. The impedance measured by FOT is affected by the impedance of a leak which is placed in parallel with the patient's airway. The leak, therefore, has a similar effect on the upper airway shunt than upper airway wall compliance. However, air leaks can be recognised by a disproportional decrease of $|Z(t)|$.

If our FOT frequency (20 Hz) would have been chosen lower, the results obtained in this study would still be the same. As recently shown by Farré et al. (1997), Fig. 2, the impedance data obtained for different FOT frequencies in the range 5–20 Hz differ by a scaling constant only. Since relative changes in the morphology of the phase angle time series are detected by our algorithm, a scaling constant would not change the results.

In summary, we developed a computer algorithm to scan time series of FOT phase angle data to detect changes in their morphology. Using a single time interval 67% of respiratory event onsets manually detected by the staff physicians matched with CPs in the FOT phase angle time series detected by algorithm. The results indicate that the phase angle ϕ of a FOT measurement could be a parameter suited to detect possible

changes in upper airway collapsibility. Thus, $\phi(t)$ might be a potentially useful tool for detection of impending upper airway obstruction.

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Appendix A. Computer algorithm for change point (CP) detection in the morphology of $\phi(t)$

A.1. Feature values

The onset of a respiratory event leads to at least one of three characteristic changes in the morphology of $\phi(t)$: (a) change in baseline; (b) change in the amplitude; and (c) change in the periodicity of the time series.

(a) A change in the baseline of a time series can be detected by comparing the means of two consecutive data segments (window 1 and window 2). The difference taken between the means has to be normalised to the variance of the data framed-up by the two windows thereby. This procedure is analogous to the 't-test', which compares the means of two data sets with respect to their variances (Cox and Hinkley, 1994). We used a similar test with robust estimators for mean and variance to calculate a feature value (F_1) indicating baseline changes in the phase angle time series:

$$F_1 = \frac{\text{Med}_{\text{window 1}} - \text{Med}_{\text{window 2}}}{\sqrt{(\text{MAD}_{\text{window 1}})^2 + (\text{MAD}_{\text{window 2}})^2}} \quad (1)$$

Med denotes the median and MAD the median of the absolute deviation from the median of the data framed-up by the two windows, respectively. A change in the mean of the phase angle data is highlighted with the right pair of windows depicted in Fig. 4.

(b) A change in the amplitude of a time series can be analysed by comparing the variance of two consecutive segments of data. This procedure is analogous to the ‘ F -test’, which compares variances (Cox and Hinkley, 1994). We used this test with robust variance estimators to calculate a feature value (F_2) indicating a change in amplitude of the phase angle time series. The logarithm was taken to obtain a symmetrical distribution of the feature values. For further details see Johnson and Kotz (1970) or Hartung and Elpelt (1992).

$$F_2 = \log_{10} \frac{(\text{MAD}_{\text{window 2}})^2}{(\text{MAD}_{\text{window 1}})^2} \quad (2)$$

MAD denotes the median of the absolute deviation from the median of the data framed-up by the two windows. A change in the amplitude of $\phi(t)$ is highlighted with the left and right pair of windows depicted in Fig. 4.

(c) Assuming $\phi(t)$ to be both periodic and stationary, the future trend of the curve could be accurately predicted based on its periodicity in the past. If a change in the periodicity appears in the future trend of the time series, the prediction of the trend will fail. A simple way to predict the data in the future is done by finding those segments in the past of the time series that match the data recorded actually. The data segment which

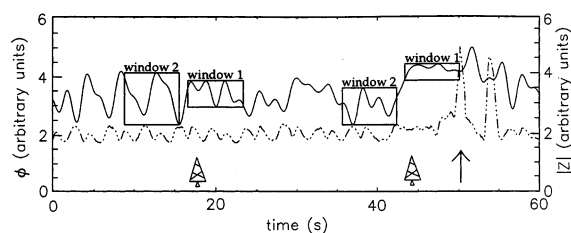


Fig. 4. A 60 sec segment of the phase angle ϕ (upper tracing; solid) and the absolute value $|Z|$ (lower tracing; chain-dotted) of an over-night FOT measurement. A change in the morphology of $\phi(t)$ can be observed at $t = 17$ sec (\blacktriangle). It is characterised by both an increase in frequency and a decrease in amplitude of $\phi(t)$. A change in baseline and amplitude of $\phi(t)$ can be observed at $t = 44$ sec (\blacktriangle) followed by an increase of $|Z|$ at $t = 50$ sec (\uparrow) indicating an upper airway obstruction. Data windows depicted in the diagram represent the data windows of the algorithm (Appendix A). $\phi(t)$ is low-pass filtered (Butterworth 6-poles, 0.5 Hz). $|Z|$ and ϕ are given in arbitrary units of the D/A-converter.

most closely matches the data actually recorded is called ‘nearest neighbour’. The prediction of the future is then performed by the values that follow the ‘nearest neighbour’. Time series prediction is discussed in detail elsewhere (Lorenz, 1963; Kostelich and Lathrop, 1993). The feature value (F_3) is then calculated from the normalised mean-squared error (NMSE) between the true time series and the predicted time series (Gershenfeld and Weigend, 1993). NMSE is an indicator for the prediction accuracy. The NMSE is normalised to the variance of the measured time series. We predicted the data framed by window 1, and used the median of the absolute deviation from the median as variance estimator.

$$F_3 = \frac{1}{\text{MAD}_{\text{window 1}}} \sqrt{\sum_{i=1}^N (x_i - \hat{x}_i)^2} \quad (3)$$

x_i is the value of the i th data point framed by window 1, and is the corresponding predicted value.

For quiet spontaneous breathing, the three features are linear independent and normal distributed.

A.2. Change point detection

Since changes in the morphology of $\phi(t)$ are mostly combinations of the three basic morphology changes the three calculated feature values have to be combined for CP detection. Therefore, the mean and the variance for each feature were obtained from a learning set which contains time series segments with quiet spontaneous breathing recorded. The features F_1 , F_2 , and F_3 calculated for the actually investigated data segments were scaled to zero mean and unit variance (F_1^* , F_2^* , F_3^*). A combination of the three normalised features were compared with a threshold for change point detection.

$$(F_1^*)^2 + (F_2^*)^2 + (F_3^*)^2 \geq \text{threshold} \quad (4)$$

The algorithm was applied to a learning set and evaluated on a test set, respectively, to obtain the ideal length of the two windows, of the gap between the two windows, of the interval for the nearest neighbour search, and the detection

threshold. Each set contained 250 time series segments of 800 data points (80 sec) including either quiet breathing or a respiratory event. After optimisation, the length of the two windows was set to 65 data points (6.5 sec), the gap between the windows to ten data points, and the interval of the nearest neighbour search (past) to 116 data points. Detection threshold was set to 30.

A.3. Filtering

The data segments were low-pass filtered (Butterworth 6-poles, 0.5 Hz) before calculating the features values.

A.4. Calculation step

The calculation of the feature values was repeated after 20 data points (2 sec).

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