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New Rule-Based Algorithm for Real-Time Detecting Sleep Apnea and Hypopnea Events Using a Nasal Pressure Signal

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Abstract We developed a rule-based algorithm for automatic real-time detection of sleep apnea and hypopnea events using a nasal pressure signal. Our basic premise was that the performance of our new algorithm using the nasal pressure signal would be comparable to that using other sensors as well as manual annotation labeled by a technician on polysomnography study. We investigated fifty patients with sleep apnea-hypopnea syndrome (age: 56.8 ± 10.5 years, apnea-hypopnea index (AHI): 36.2 ± 18.1/h) during full night PSG recordings at the sleep center. The algorithm was comprised of pre-processing with a median filter, amplitude computation and apnea-hypopnea detection parts. We evaluated the performance of the algorithm a confusion matric for each event and statistical analyses for AHI. Our evaluation achieved a good performance, with a sensitivity of 86.4 %, and a positive predictive value of 84.5 % for detection of apnea and hypopnea regardless of AHI severity. Our results indicated a high correlation with the manually labeled apnea-hypopnea events during PSG, with a correlation coefficient of $r = 0.94$ ($p < 0.0001$) and a mean difference of −2.9 ± 11.6 per hour. The proposed new algorithm could provide significant clinical and computational insights to design a PSG analysis system and a continuous positive airway pressure (CPAP) device for screening sleep quality related in patients with sleep apnea-hypopnea syndrome.

Keywords Real-time detection · Apnea · Hypopnea · Nasal pressure signal

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Introduction

Diagnosis of sleep apnea and hypopnea syndrome (SAHS) is clinically significant, but SAHS is underdiagnosed disorder [1, 2]. The SAHS may cause daytime hypersomnolence or fatigue, decreased ability to concentrate, depression and ultimately impaired quality of life [1, 3, 4]. The SAHS is also related to cardiovascular disease, metabolic dysfunction, neurocognitive dysfunction and sudden-cardiac death [1, 5].

Polysomnography (PSG) is considered the gold standard for diagnosis of SAHS [3, 6]. However, PSG is a labor-intensive, time-consuming, expensive and technically complex process that also requires specialized equipment since it requires manual annotation by an expert technician at a sleep clinic during night [7]. Moreover, manual annotation is subjective because it depends upon technicians, and is also a boring task, as noted in several studies [8]. Thus, PSG is inefficient for monitoring or detecting apnea and hypopnea in portable monitoring devices for home-healthcare.

Several methods have been proposed as an alternative to PSG for automatic detection of apnea-hypopnea through the analysis of minimum channel. Although methods using biosignals such as electrocardiogram (ECG), electroencephalogram (EEG), oxygen saturation (SpO_2) and respiratory-related acoustic signals may successfully monitor or detect apnea and hypopnea [7, 9–16], they rely on indirect respiratory

monitoring and thus require an additional sensor that can measure ECG, EEG, SpO_2 and acoustic signals. Another proposed method for apnea and hypopnea detection focuses on directly measuring respiratory signals based on nasal airflow using a pressure transducer or thermal sensor and measuring respiratory effort using inductance plethysmography (thoracic and abdominal signals) [17–25]. Among these detection methods, the nasal pressure signal recorded by a pressure transducer may more accurately reflect respiratory airflow than other sensors due to its high sensitivity, and thus may identify cases of SDB missed by other sensors [26–30]. Several studies have employed nasal pressure sensors for the aforementioned reasons even though utilization of the nasal pressure transducer may feel uncomfortable. However, only a few studies have evaluated these methods, and most of them may not to provide methods or algorithms for apnea-hypopnea detection since they depend on the summary data calculated from the portable device [21–25]. Moreover, although existing commercial PSG software programs offer automatic apnea-hypopnea analysis, a concrete method is unavailable and some controls have to be adjusted for each patient with SAHS.

In this study, we developed an algorithm for automatic and real-time detection of apnea and hypopnea events using a single-channel nasal pressure signal without the need for other kinds of signals, which may be utilized in all patients regardless of SAHS severity. In particular, the algorithm tries to conform to the guidelines of the American Academy of Sleep Medicine (AASM) [31], and minimizes signal distortion through the use of some filtering. The basic premise of our study is that the performance of a real-time algorithm based on nasal pressure signals should be comparable to that of other sensors as well as data obtained through events manually labeled by technicians. Validation of our assumptions and method will support the use of the proposed algorithm in low-cost portable PSG systems or CPAP systems in a patient's own home for objective annotation of SAHS.

Methods

Study populations and data acquisition

Fifty patients with SAHS underwent a full-night PSG study at the sleep center of the Samsung Medical Center (Seoul, Republic of Korea). This study was approved by the Institutional Review Board of Samsung Medical Center, and all patients provided written consent to participate. Table 1 presents demographic information of the study population.

Nasal pressure signals were measured using a pressure transducer with a nasal cannula (1,420,002, Embla System Inc., USA) during full-night PSG recordings. The nasal cannula used for measuring airflow was attached to a "Y" tube and an end of tube was connected to a PSG recording system. A recording system (N7000, Embla System Inc., USA) and sleep diagnostic software (RemLogic 2.0, Embla System Inc., USA) was used for PSG recordings and manual annotation, respectively. The nasal pressure signal was sampled at 200 Hz with 16-bit resolution. The fundamental unit of nasal pressure used in the software was the mbar (1000 mbar ≈ 1019.716 cmH_2O).

Structure of the automatic method

The automatic real-time method consisted of pre-processing, amplitude computation from peak/trough point detection, and detection of apnea and hypopnea events. Figure 1 summarizes the structure of the method.

Pre-processing

The raw nasal pressure signal was inverted by multiplying by '-1' and preprocessed with a 51st order median filter (x_{med}) to reduce unwanted background spike noise and snoring-related noise.

Amplitude computation from peak/trough point detection

Peak/trough points were detected from the median filtered signal in order to compute the real-time amplitude of the signal. All local peak/trough points were detected and all final peak/trough points were decided according to the following rules:

$$\text{select } p^{(\mathrm{p})}[i] \text{ when } d_{t\_p}[i] > 0.50 \text{ (sec.)} \tag{1}$$

$$\text{select } p^{(\mathrm{t})}[i] \text{ when } d_{p\_t}[i] > 0.25 \text{ (sec.)} \text{ and } p^{(\mathrm{p})}[i]-p^{(\mathrm{t})}[i] > 0.0085 \text{ (mbar)} \tag{2}$$

where i is the sequence index of the final decided point, $p^{(p)}$ refers to peak points, $p^{(\mathrm{t})}$ refers to trough points, d_{t_p} is the time duration from trough to peak point and d_{p_t} is the time duration from peak to trough point. Each number (0.50, 0.25, and 0.0085) was selected empirically in order to decide the peak/trough points. The amplitude (A) was calculated at the trough points from the computed peak/trough points as follows:

$$A[i] = p^{(\mathrm{p})}[i]-p^{(\mathrm{t})}[i] \tag{3}$$

This amplitude was used to compute the baseline of the signals for apnea and hypopnea event decisions. The symbols used in this process are illustrated in Fig. 1.

Apnea and hypopnea detection

An algorithm for apnea and hypopnea detection based on amplitude at the trough points was performed on the

Table 1 Detailed demographic information. The ranges for age, BMI, and AHI are given as the mean ± standard deviation

Severity	Mild (5 ≤ AHI < 15)	Moderate (15 ≤ AHI < 30)	Severe (AHI ≥ 30)	Overall
Patients [female/male]	5 [1/4]	20 [4/16]	25 [2/23]	50 [7/43]
Age (years)	59.4 ± 9.3	58.6 ± 11.4	54.8 ± 10.1	56.8 ± 10.5
BMI (kg/m^2)	24.1 ± 1.7	26.1 ± 4.0	26.9 ± 3.3	26.3 ± 3.5
AHI (/hour)	12.9 ± 1.9	23.8 ± 3.7	50.8 ± 14.0	36.2 ± 18.1

median-filtered nasal pressure signal (x_{med}). As mentioned above, the algorithm was designed to conform to AASM guidelines as much as possible. Table 2 summarizes the rules for the detection process of apnea and hypopnea events and the rules described as below:

Rule 1: [whether the current point is a trough point] If $x_{med}[n]$ is a trough point, Part 1 was employed, otherwise, Part 2 was selected. Part 1 consisted of computing the mean amplitude ($A_{mean}[j]$) from $A[i]$ and deciding whether or not the current state represents hypopnea. In Part 1, the A_{mean} was computed only when Rule 2 was satisfied. The parameter j was enumerated only when the A_{mean} was computed. Part 2 was aimed at deciding whether the current state was apnea, hypopnea or nothing. In Part 2, if the current state was both apnea and hypopnea, the state was decided as apnea.

Initialization: Since the $A_{mean}[j]$ was computed using the six most recent amplitudes satisfying Rule 2, initialization was required until a minimum of 6 amplitudes (*thres_count_amp* = 6) were computed. In the initialization process, the mean amplitudes were computed even when Rule 2 was unsatisfied. A user may adjust the minimum amplitudes using the threshold parameter *thres_count_amp*.

Rule 2: [condition to compute mean amplitude] The $A_{mean}[j]$ was computed only when $A[i]$ was bigger than ($A_{mean}[j]$. *thres_hypop*). The parameter *thres_hypop* is a threshold used to decide hypopnea. In this study, *thres_hypop* was set to 0.5 (50 %) according to the AASM guidelines for hypopnea scoring.

Rule 3: [whether the current point is in a hypopnea section] Hypopnea states were decided by a count number for hypopnea detection (*count_h*). Specifically, whether or not the current state was hypopnea was decided based on whether *count_h* was longer than a certain period (*thres_duration*). The *thres_duration* was set to 2200 (11 s × 200 samples).

Rule 4: [adjustment to compute mean amplitude] When an abrupt change of the amplitude was generated after the hypopnea event was terminated (*end_hyp* = 1), the mean amplitude computation was put on hold during *count_skip*. The *count_skip* was counted four times after termination of the hypopnea event or until $A[i]$ was smaller than $A_{mean}[j]$. If the abrupt change of the amplitude ($A[i]$) was bigger than *thres_amp_over* of $A_{mean}[j]$ without termination of

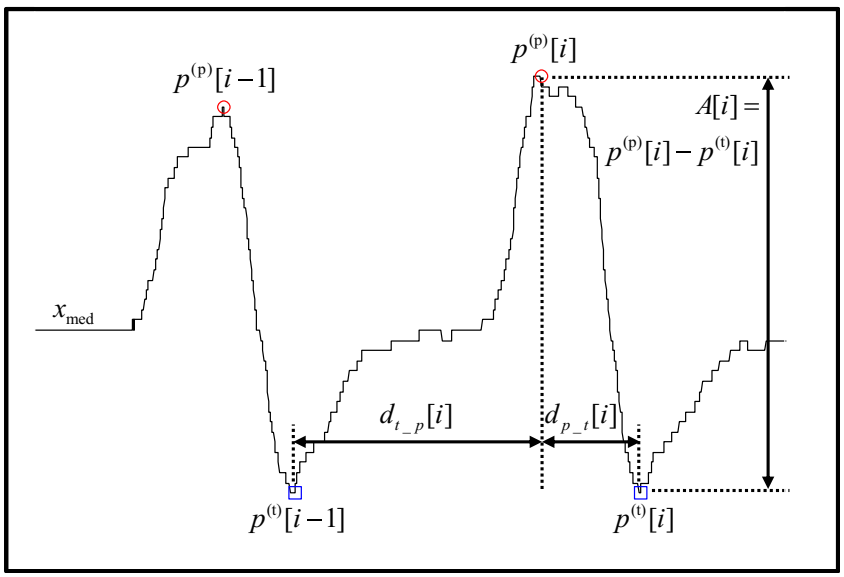

Fig. 1 Filtered nasal pressure signal and amplitude computation

Table 2 Rules for the detection process for apnea and hypopnea events

Input: x_{med}, *thres_hypop*, *thres_count_amp*, *thres_duration*, *thres_amp_over*

Output: y_{apnea}, y_{hypop}

Algorithm:

A. **Rule 1**: whether the current point is in a trough

IF $x_{med}[n]$ is trough point, THEN go to [Part 1]

OTHERWISE go to [Part 2]

B. **Initialization**

Computation of initial $A_{mean}[j]$ using $A[i]$ within *thres_count_amp*

C. **Rule 2**: computation of mean amplitude

IF $A[i] > A_{mean}[j] \cdot thres\_hypop$, THEN compute the mean amplitude

D. **Rule 3**: whether the current point is in a hypopnea section

IF $count\_h \geq thres\_duration$, THEN decide the end-point of hypopnea event

E. **Rule 4**: adjustment of mean amplitude computation

i. IF hypopnea events is terminated ($end\_hyp = 1$) & $A[i] < A_{mean}[j]$,

THEN skip the mean amplitude computation

ii. IF $A[i] > A_{mean}[j] \cdot thres\_amp\_over$, THEN adjust the mean amplitude

F. **Rule 5**: whether the current point is in an apnea section

IF $|x_{med}[n] - value\_temp| < A_{mean}(j) \cdot 0.1$ & $count\_a \geq thres\_duration$,

THEN decide the end-point of the apnea event

the hypopnea event, the mean amplitude was rescaled. The parameter *thres_amp_over* may be adjusted by the user. In this study, *thres_amp_over* was set as 1.3 (130 %).

Rule 5: [whether the current point is in an apnea section] The apnea state was decided by the absolute value of ($x_{med}[n] - value\_temp$) and count number for apnea detection (*count_a*). The parameter *count_a* was reset to 0 at the trough point and increased by 1 on each loop. The parameter *value_temp* is the value of $x_{med}[n]$ when the parameter *count_amp* was 500 (2.5 s × 200 samples). The current state was considered to be apnea or not according to whether *count_a* was longer than *thres_duration*. If the current state was apnea and the state at the latest loop was hypopnea, the hypopnea state was reset to a non-hypopnea state.

Figure 2 shows a flow chart for detection based on the rules described above. Information omitted in Fig. 2 is highlighted by 18 grey arrows (A1 to A18) and a detailed description of this information is presented as an algorithm in the Appendix.

Performance evaluation and statistical analysis

Apnea and hypopnea events were manually annotated by an experienced clinical technician and a referring clinician reviewed and confirmed the annotated events as described in the AASM guidelines [31]. In short, an apnea was annotated when the respiratory flow signal was reduced above 90 % compared to baseline for at least 10 s and a hypopnea was annotated when the nasal pressure signal dropped by more than 50 % of the baseline value for at least 10 s with a desaturation greater than 3 % from the pre-event baseline of oxygen saturation.

Confusion matrix

Performance evaluation was examined using sensitivity and positive predictive value (PPV) as follows:

$$\text{Sensitivity for event } p = \frac{N_{pp}}{\sum_q N_{pq}} \times 100\ (\%) \tag{4}$$

$$PPV\ for\ event\ p = \frac{N_{pp}}{\sum_p N_{pq}} \times 100(\%) \tag{5}$$

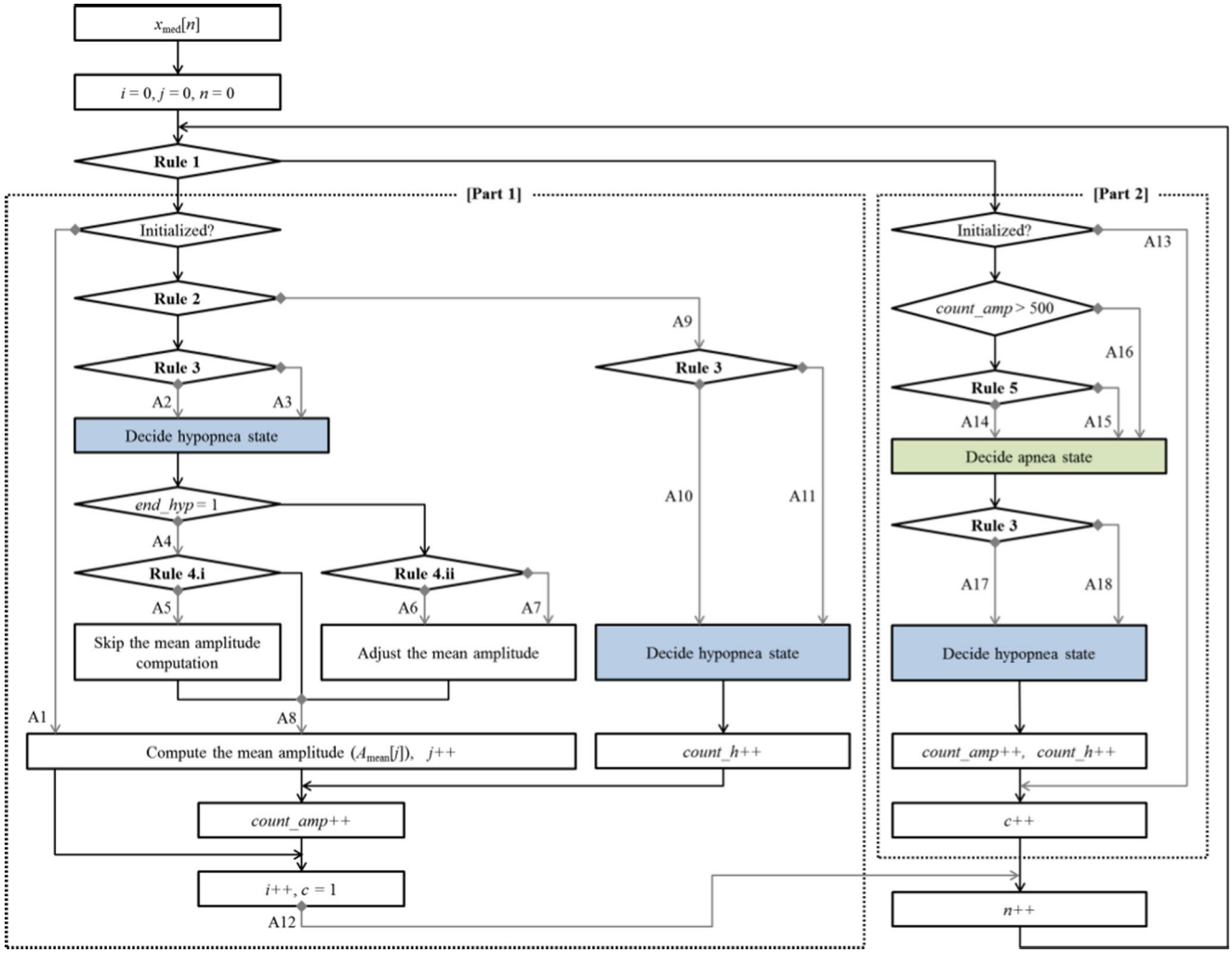

Fig. 2 Flow chart for detection of apnea and hypopnea events

$$\text{Sensitivity for all} = \frac{\text{TP}}{\text{TP} + \text{FN}} \times 100\ (\%) \tag{6}$$

$$\text{PPV for all} = \frac{\text{TP}}{\text{TP} + \text{FP}} \times 100\ (\%) \tag{7}$$

where N is the number of generated events, p and q are the number of annotated and detected events (1: apnea, 2: hypopnea and 3: normal), respectively (for example, N_{13}: the event is annotated as apnea, but is detected as normal), true positive (TP) represents the number of correctly detected apnea-hypopnea (AH) events, false negative (FN) indicates the number of missed AH events, and false positive (FP) refers to the number of incorrectly annotated AH events. Thus, sensitivity reflected the ability to correctly identify events and PPV revealed whether or not the detected events were correct. Since the non-apnea and non-hypopnea events were not countable events, the specificity and negative predictive values that require the true negative value couldn't be defined.

Statistics for apnea-hypopnea index (AHI)

Correlation statistics were employed using Pearson's correlation coefficient and linear regression equation to assess the linear relationship between AHI annotated by a technician and those measured by our proposed algorithm. Statistical significance was considered at $p < 0.01$.

A Bland-Altman plot, based on a graphical method for comparing two different methods, was used to analyze the agreement between annotated and measured AHI [32]. The differences for the Bland-Altman plot are presented as the mean ± 1.96 × standard deviation (SD) (95 % limits of agreement).

Results

Table 3 shows the results for the apnea and hypopnea detection algorithm using a single-channel nasal pressure signal. While the sensitivity and PPV for apnea events detection was high (88.5 % and 88.1 %), those for hypopnea event

Table 3 Results for the apnea and hypopnea detection algorithm

Severity	Mild (5 ≤ AHI < 15)	Moderate (15 ≤ AHI < 30)	Severe (AHI ≥ 30)	Overall
Apnea – Sensitivity (%)	88.2	87.4	88.8	88.5
Apnea – PPV (%)	85.6	87.4	88.3	88.1
Hypopnea – Sensitivity (%)	70.2	73.7	64.5	68.1
Hypopnea – PPV (%)	69.3	65.0	66.0	65.7
Both – Sensitivity (%)	80.7	83.5	87.9	86.4
Both – PPV (%)	79.2	76.2	88.5	84.5

detection were relatively low (68.1 % and 65.7 %) and those for detection of both events were high (86.4 % and 84.5 %) irrespective of AHI severity. With respect to AHI severity, the sensitivity and PPV for severe groups (87.9 % and 88.5 %) was relatively higher than those for other groups (80.7 to 83.5 % and 76.2 to 79.2 %).

Figure 3 presents a scatter plot and Bland-Altman plot for the AHI results annotated by a technician and those measured by our algorithm. The mean of the annotated AHI was 36.2 ± 18.1 events per hour and that of the measured AHI was 39.1 ± 17.0 events per hour. Figure 3(a) shows that there was a good correlation ($r = 0.94$) between the algorithm and technician-measured AHI results indicating a statistically significant relationship ($p << 0.0001$). Figure 3(a) also shows the tendency of the proposed algorithm to slightly overestimate AHI, since the best regression line crossed the y-axis at the 6.997 index. Figure 3(b) illustrates good agreement across a whole range of AHI severity except one overestimated AHI and two underestimated AHIs (mean difference: −2.9, 95 % limits of agreement: −14.5 to 8.8).

Discussion

The aim of this study was to provide a new algorithm for real-time detection of apnea and hypopnea event from a nasal pressure signal without any other kinds of signals, which was designed to conform to AASM guidelines. The algorithm consisted of simple filter, uncomplicated computation and several rules with experimental thresholds. Since the algorithm was designed to be applicable to the PSG analysis software or CPAP device systems that can monitor apnea and hypopnea automatically without supervision and post-processing such as manual annotation. As anticipated, the proposed algorithm provided overall good performance in comparison with the events annotated by technicians, and the results were summarized in Table 3 and Fig. 3.

The performance of the automatic algorithm was comparable to that of manual annotation by technicians except for detection of hypopnea events. Performance for hypopnea detection was relatively lower than that for apnea detection regardless of AHI severity (Table 3). This was thought to be related to the hypopnea detection criteria, which, unlike the apnea detection criteria, included oxygen desaturation-related rules in the AASM guidelines. The AASM guidelines for hypopnea event detection require oxygen saturation trends that can identify desaturation. However, since the algorithm did not include oxygen saturation information, false detection of hypopnea events may be generated and thus algorithm may have led to overestimation hypopnea events compared with events annotated by the technician in the case of hypopnea without desaturation (Fig. 4). Interestingly, despite this possibility for overestimation, the performance for detecting merged AH events was good, which we ascribed to the fact

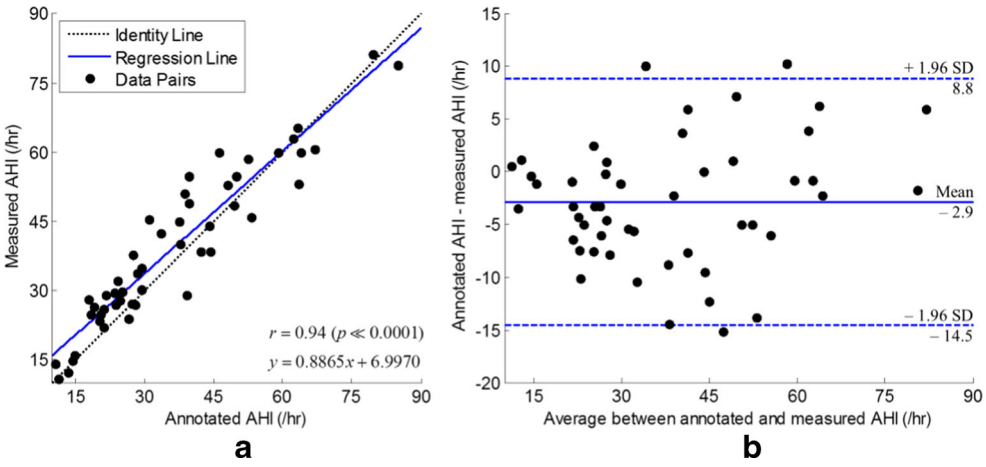

Fig. 3 Statistics analysis: (**a**) Scatter plot of the correlation and (**b**) Bland-Altman plot of AHI annotated by a technician and measured by the proposed algorithm.

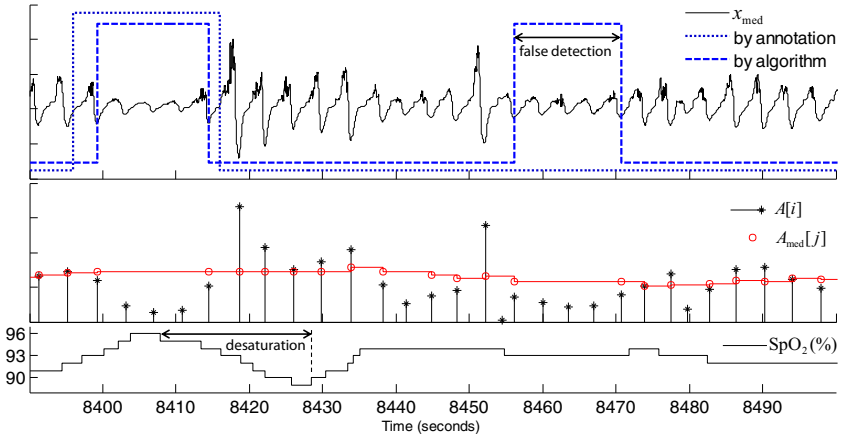

Fig. 4 Example of hypopnea detection using our proposed algorithm

that a number of real apnea events were detected as hypopnea rather than as normal, and likewise that many real hypopnea events were detected as apnea and not as normal. With respect to AHI severity, the reason that the performance of severe groups was relatively higher than other groups was attributed to patients with mild to moderate SAHS having more hypopnea events than apnea events. Based on the scatter plot for the correlation analysis (Fig. 3), we found that the AHI measured our proposed algorithm was closely correlated with the results annotated by the technician, although the results of the algorithm were slightly overestimated.

The overall performance of our algorithm was comparable to that of other algorithms in the literature employing a nasal pressure signal. In addition, the Bland-Altman plot indicated that the limits of agreement between our algorithm were narrower compared with other algorithms. Wong et al. [24] evaluated a commercial nasal pressure monitor for sleep apnea detection, and found that the mean difference of the AHI between the monitor and the PSG was 1.8 events per hour (limits of agreement: −32.4 to 36.0). Likewise, Rofail et al. [21] studied the single-channel nasal pressure monitoring based on a same device that Wong et al. used for home-based SAHS diagnosis, and found a mean difference of −4.9 events per hour (limits of agreement: −32.7 to 23.0). Erman et al. [25] employed another commercial device based on a nasal pressure transducer for screening sleep apnea, and reported a correlation coefficient of 0.89 between AHI from the device and AHI from PSG. De Almeida et al. [23] utilized another commercial device based on pressure transducer in order to identify patients with sleep apnea, and similar to the other studies reported a correlation coefficient of 0.81 and a mean difference of 27.4 events per hour (limits of agreement: 0.8 to 54.0). Lastly, Grover et al. [22] assessed the accuracy of a nasal pressure-based portable monitoring device to detect SAHS, and reported a correlation coefficient of 0.77 and a mean difference of 2.6 events per hour (limits of agreement: −37.2 to 42.4). Although these studies described the ability to automatically determine apnea-hypopnea severity, they didn't offer a concrete method for apnea-hypopnea detection. Furthermore, the performance of some of these studies was poorer than our results, with most failing to provide performance results for each apnea and hypopnea event.

Even though the results of this study demonstrate that our algorithm based on a single-channel nasal pressure signal is suitable for real-time apnea and hypopnea detection in PSG or CPAP system, several limitations remain. We only detected apnea or hypopnea events without classification between obstructive and central apneic events; however, we are planning to examine additional algorithms that may distinguish between apneic events. For applying our algorithm to the CPAP system, this study invites further research to collect data in patients who wear CPAP mask. In addition, because we employed the nasal pressure signal, the signal quality may have been poor for breaths taken through the mouth, which may have weakened our results. In the future, our algorithm will be applied to the oro-nasal pressure signal in order to better evaluate its performance. Finally, the results of this study were underpowered for mild severe groups because of the small study population. Thus, we look forward to conducting this type of study with larger populations of mild severe groups in the future in order to better generalize our results.

In conclusion, we developed the algorithm for real-time automatic detection of sleep apnea and hypopnea events using a nasal pressure signal. The algorithm doesn't need any other kinds of physical or physiological signals so that it may be embedded in a low-cost portable PSG system or the CPAP system even it could be applied to the patients regardless of SAHS severity. The algorithm also would be useful for sleep technicians, since they may adjust some thresholds in the algorithm to annotate apnea-hypopnea events according to their preferred criteria in the AASM guidelines. Importantly, the algorithm may provide a low computational cost because it does not require the same complex processing common to other studies. In addition, since we recently developed a method for

automatic snoring detection from a nasal pressure signal [33], our single channel-based algorithm should be more valuable for screening SAHS by combining the snoring detection method, especially in portable PSG or CPAP systems.

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Appendix

Pseudo-code for apnea and hypopnea detection algorithm

Input: x_{med}, *thres_hypop*, *thres_count_amp*, *thres_duration*, *thres_amp_over*

Output: y_{apnea}, y_{hypop}

Algorithm:

```
1.  i = 0,  j = 0,  c = 0 and N is a length of x_med
2.  for (n = 0 to N – 1) {
3.    if (x_med[n] is trough point) {
4.      if (j < thres_count_amp) {
5.        j++;  A_temp[j] = A[i];  A_mean[j] = mean(A_temp[1 to j]);
6.        y_hypop[n] = 0;  y_apnea[n] = 0; }
7.      else {
8.        if (A[i] > A_mean[j] · thres_hypop) {
9.          if (count_h ≥ thres_duration · sr) {
10.           if (y_hypop[n – 1] = 0) {
11.             y_hypop[(n – thres_duration · sr + 1) to n – 1] = 1;
12.             y_hypop[n] = 0;  count_skip = 0;  count_over_amp = 0; }
13.           else {
14.             if (count_h > thres_hypop_over) {
15.               y_hypop[(n – count_h + 1) to n] = 0;  end_hyp = 0; }
16.             else
17.               if (count_h ≤ thres_duration_end · sr) {
18.                 y_hypop[(n – count_h + 1) to n] = 0;  end_hyp = 0; }
19.               else { y_hypop[n] = 0;  end_hyp = 1; }
20.             }
21.           }
22.         }
23.         else { y_hypop[n] = y_hypop[n – 1]; }
24.         if (end_hyp = 1) {
25.           count_skip++;
26.           if (count_skip ≥ 4  or  A[i] < A_mean[j]) {
27.             count_skip = 0;  end_hyp = 0;
28.             A_temp[1 to (thres_count_amp – 1)] = A_temp[2 to thres_count_amp];
29.             A_temp[thres_count_amp] = A[i]; }
30.         }
31.         else {
32.           if (A[i] > A_mean[j] · thres_amp_over) {
33.             count_over_amp++;
34.             if (count_over_amp < 3) {
35.               A_temp[1 to (thres_count_amp – 1)] = A_temp[2 to thres_count_amp];
36.               A_temp[thres_count_amp] = A_mean[j] · thres_amp_over; }
37.             else {
38.               A_temp[1 to (thres_count_amp – 1)] = A_temp[2 to thres_count_amp];
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39.                         A_temp[thres_count_amp] = (A_mean[j] · 3 + A[i] · 2) / 5; }
40.                 }
41.                 else {
42.                     count_over_amp = 0;
43.                     A_temp[1 to (thres_count_amp – 1)]] = A_temp[2 to thres_count_amp];
44.                     A_temp[thres_count_amp] = A[i]; }
45.             }
46.             j++;    A_mean[j] = mean(A_temp[(j – 7) to j]);
47.             A_mean_dur = count_h;    count_h = 1;    count_amp = 0;
48.         }
49.         else {
50.             if (count_a < thres_duration · sr) { count_amp = 0; }
51.             if (count_h ≥ thres_duration · sr) {
52.                 if (y_hypop[n – 1] = 0) {
53.                     y_hypop[(n – thres_duration · sr + 1) to n] = 1;
54.                     count_skip = 0;    count_over_amp = 0; }
55.                 else {
56.                     if ((x_med[n] – x_med[n – c]) > A_mean[j] · thres_amp) {
57.                         y_hypop[n] = 0;    count_h = 0;    end_hyp = 1; }
58.                     else { y_hypop[n] = y_hypop[n – 1]; }
59.                 }
60.             }
61.             else {
62.                 if ((x_med[n] – x_med[n – c]) > A_mean[j] · thres_amp) {
63.                     y_hypop[n] = 0;    count_h = 0; }
64.                 else { y_hypop[n] = y_hypop[n – 1]; }
65.             }
66.             count_h++;
67.         }
68.         count_amp++;
69.     }
70.     i++;    c = 1;    y_apnea[n] = y_apnea[n – 1];
71. }
72. else {
73.     if (j < thres_count_amp) { y_hypop[n] = 0;    y_apnea[n] = 0; }
74.     else {
75.         if (count_amp = 500) {
76.             value_temp = x_med[n];    count_a = 500;    y_apnea[n] = 0; }
77.         else if (count_amp > 500) {
78.             if (|x_med[n] – value_temp| < A_mean(j) · 0.1) {
79.                 count_a++;
80.                 if (count_a > thres_duration · sr) {
81.                     if (y_apnea[n – 1] = 0) {
82.                         y_apnea[(n – count_a) to n] = 1;
```

```
83.                             y_hypop[(n – count_h) to n] = 0; }
84.                         else {
85.                             y_apnea[n] = 1;     y_hypop[n] = 0;
86.                             count_h = 0;     count_skip =0;     count_over_amp = 0; }
87.                     else { y_apnea[n] = 0; }
88.                 }
89.                 else {
90.                     if (y_apnea[n – 1] = 1) { end_hyp = 1 }
91.                     count_a = 0;     count_amp = 0;     y_apnea[n] = 0; }
92.                 }
93.             else { y_apnea[n] = y_apnea[n – 1]; }
94.             if (count_h ≥ thres_duration · sr) {
95.                 if (y_hypop[n – 1] = 0) {
96.                     if (y_hypop[n – (thres_duration · sr + 1)] = 1) {
97.                         y_hypop[(n – thres_duration · sr) to n] = 1
98.                         if (n – count_h = (n at A_mean[j])) {
99.                             count_h = count_h + A_mean_dur;     j– –; }
100.                    }
101.                    else { y_hypop[(n – thres_duration · sr + 1) to n] = 1; }
102.                    count_skip =0;     count_over_amp = 0;
103.                }
104.                else {
105.                    if ((x_med[n] – x_med[n – c]) > A_mean[j] · thres_amp) {
106.                        y_hypop[n] = 0;     count_h = 0;     end_hyp = 1; }
107.                    else {
108.                        if (count_h > thres_hypop_over) { // Line 364
109.                            y_hypop[(n – count_h + 1) to n] = 0;
110.                            A_temp[1 to (thres_count_amp – 3)] = A_temp[4 to thres_count_amp];
111.                            A_temp[(thres_count_amp – 3) to (thres_count_amp)]=A[(i–3) to (i–1)];
112.                            j++;     A_mean[j] = mean(A_temp[(j – 7) to j]);
113.                            A_mean_dur = count_h;     count_h = 0; }
114.                        else { y_hypop[n] = y_hypop[n – 1] }
115.                    }
116.                }
117.            }
118.            else {
119.                if ((x_med[n] – x_med[n – c]) > A_mean[j] · thres_amp) {
120.                    y_hypop[n] = 0;    count_h = 0;
121.                    if (y_hypop[n – 1] = 1) {end_hyp = 1; }
122.                }
123.                else { y_hypop[n] = y_hypop[n – 1]; }
124.            }
125.            count_amp++;     count_h++;
126.        }
```

```
127.        c++;
128.    }
129. }
```

Matching with grey arrows in Fig. 2:

A1: Line no. 5 to 6
A2: Line no. 10 to 22
A3: Line no. 23
A4: Line no. 25
A5: Line no. 27 to 29
A6: Line no. 33 to 39
A7: Line no. 42 to 44
A8: Line no. 46 to 47
A9: Line no. 50
A10: Line no. 52 to 59
A11: Line no. 62 to 64
A12: Line no. 70
A13: Line no. 73
A14: Line no. 79 to 87
A15: Line no. 90 to 91
A16: Line no. 76 and 93
A17: Line no. 95 to 116
A18: Line no. 119 to 123
Rule 1: Line no.3
Initialization: Line no. 4
Rule 2: Line no. 8
Rule 3: Line no. 51 and no. 94
Rule 4.i: Line no. 26
Rule 4.ii: Line no. 32
Rule 5: Line no. 75

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