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Periodic breathing during ascent to extreme altitude quantified by spectral analysis of the respiratory volume signal

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***Abstract*— High altitude periodic breathing (PB) shares some common pathophysiologic aspects with sleep apnea, Cheyne-Stokes respiration and PB in heart failure patients. Methods that allow quantifying instabilities of respiratory control provide valuable insights in physiologic mechanisms and help to identify therapeutic targets. Under the hypothesis that high altitude PB appears even during physical activity and can be identified in comparison to visual analysis in conditions of low SNR, this study aims to identify PB by characterizing the respiratory pattern through the respiratory volume signal. A number of spectral parameters are extracted from the power spectral density (PSD) of the volume signal, derived from respiratory inductive plethysmography and evaluated through a linear discriminant analysis. A dataset of 34 healthy mountaineers ascending to Mt. Muztagh Ata, China (7,546 m) visually labeled as PB and non periodic breathing (nPB) is analyzed. All climbing periods within all the ascents are considered (total climbing periods: 371 nPB and 40 PB). The best crossvalidated result classifying PB and nPB is obtained with *Pm* (power of the modulation frequency band) and *R* (ratio between modulation and respiration power) with an accuracy of 80.3% and area under the receiver operating characteristic curve of 84.5%. Comparing the subjects from 1_{st} and 2_{nd} ascents (at the same altitudes but the latter more acclimatized) the effect of acclimatization is evaluated. SaO_2 and periodic breathing cycles significantly increased with acclimatization (p-value < 0.05). Higher *Pm* and higher respiratory frequencies are observed at lower SaO_2, through a significant negative correlation (p-value < 0.01). Higher *Pm* is observed at climbing periods visually labeled as *PB* with > 5 periodic breathing cycles through a significant positive correlation (p-value < 0.01). Our data demonstrate that quantification of the respiratory volume signal using spectral analysis is suitable to identify effects of hypobaric hypoxia on control of breathing.**

I. INTRODUCTION

High altitude periodic breathing in healthy subjects exposed to hypobaric hypoxia shares some common pathophysiologic aspects with the sleep apnea syndromes [1]. Ventilatory control disorders such as the obstructive and central sleep apnea syndromes and Cheyne-Stokes respiration in severe heart failure, are common and may lead to significant impairment of quality of life, morbidity and even mortality [2], [3] and [4]. The study of high altitude periodic breathing (PB) may therefore not only promote the understanding of this condition, but may also give valuable insights into mechanisms and therapeutic targets in other disorders of ventilatory control. Exposure to hypobaric hypoxia at altitude induces a chemoreceptor-mediated increase in ventilation that mitigates hypoxemia but is associated with hypocapnia [5]. The resulting decrease in the CO_2 reserve, in conjunction with the increased ventilator sensitivity to hypoxia and hypercapnia leads to ventilatory control instability [6] which promotes high altitude PB, one of the causes of high altitude insomnia. High altitude PB has been thought to occur predominantly or exclusively at rest and during sleep when the wakefulness drive to breathe is reduced and ventilation is controlled by autonomic chemical feed-back control. However, preliminary observations suggest that PB occurs during wakefulness and even during physical exercise at high altitude [7].

Investigation of PB during exercise has been hampered in the past by technical and physiological reasons. For example, a poor signal to noise ratio of respiratory signals during physical activity, the effects of the measurement apparatus that increases dead-space and alters the breathing pattern [8], and cortical influences overriding autonomic rhythms of breathing as well as cardio-pulmonary interactions may all impair the identification and quantification of PB by conventional visual inspection. PB detection by visual analysis is not only difficult but very tedious and time-consuming. In order to detect respiratory oscillations, parameters derived from time frequency characterization of the envelope of the respiratory flow signal, acquired at rest using a pneumotachograph, have been successfully used to identify PB patterns and Cheyne Stokes respiration in heart failure patients [9]. Time-varying modulation of the respiratory flow envelope signal has provided accurate results in the characterization of the temporal evolution of the respiratory pattern [10]. Correntropy function, an innovative similarity measure which contains information on both, statistical distribution and time structure of the signal improved the results obtained with linear techniques [11]. However, in that database the respiratory flow signal of heart failure patients at rest was acquired using

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a pneumotachograph, not the volume signal derived from chest wall recordings without airway instrumentation.

The effects of progressive sustained and nocturnal intermittent hypoxemia on ventilation and breathing pattern during exercise at very high altitude might provide further insight into determinants of respiratory control. We hypothesize that PB appears even during physical activity (i.e., during climbing in the field) and it can be identified in comparison to visual analysis in conditions of low signal to noise ratio through the respiratory volume signal, derived unobtrusively from inductance sonsors placed around the chest wall. The aim of the present work is therefore to detect PB by characterizing respiratory volume signal in a dataset of 34 mountaineers ascending to Mt. Muztagh Ata, China (7,546 m). These daytime volume signals have been obtained during a Swiss medical research expedition while climbing and data on nocturnal ventilation have been published [12]. This respiratory pattern characterization might improve the automatic detection of PB and serve as indicator of a subject's condition at high altitude.

II. Datasets

The protocol of the expedition have been more extensively described in [12]. 36 healthy mountaineers (median age 46 and 7 women (range, 26-65 years)) participating in a Swiss medical research expedition to Mount Muztagh Ata, China, 7,546 m. Subjects climbed from 3,750 m to the summit at 7,546 m, within 19-20 days. Ventilation was recorded during climbing in the field from base camp to successive high camps and to the summit. Daily recordings lasting for 6-8 h were obtained by a portable, calibrated, respiratory inductive plethysmograph (LifeShirt, VivoMetrics, CA, USA) incorporating pulse oximetry, ECG and accelerometers. The device has been extensively validated in previous studies at the University of Zurich and provides accurate estimates of tidal volume and ventilation at rest and during exercise from elastic inductance sensors placed around the rib cage and the abomen [2], [12] and [13]. Continuous barometric recordings were also obtained. During stays at successive high camps, data were downloaded and saved in a computer.

a) Signal calibration: Inductive plethysmographic rib cage and abdominal volume signals were calibrated by the qualitative diagnostic calibration technique during natural breathing [14]. The absolute gain of the inductive plethysmographic sum signal was calibrated by the fixed volume calibration method based on several runs of 5-10 breaths during which subjects were breathing into a bag of known volume (i.e., 0.8 L) before and after each climb.

b) Protocol: Climbers were randomly assigned to one of two groups ascending with different protocols, but the total duration of the trip was 5 weeks for both [12]. Baseline evaluation was performed in Zurich (490 m) within 4 weeks before departure. Starting from Subash (3,730 m, 1_{st} Ascent), located at the base of Mt. Muztagh Ata, climbers followed two different ascent protocols as reported previously [12]. The subjects from 1_{st} ascent and 2_{nd} ascent started and finished at the same altitude but only the subjects from 2_{nd} ascent spend some days at that altitude before starting the ascent, so they were more acclimatized. Therefore, to evaluate the effect of the acclimatization in healthy mountaineers only these two ascents are compared.

III. Data Analysis

Using written protocols and accelerometer signals, periods of continuous climbing (usually lasting for about 1 h each, in total 6-9 h per day) and rest periods between climbs are identified visually. Only the climbing periods which all the mountaineers from each group start and finish climbing at the same time are selected. PB cycles were visually scored as previously described in detail [12]. Briefly, a PB cycle was defined as a transient reduction of the inductive plethysmographic sum volume signal to less than 50% of the preceding 2-minute baseline for > 5 sec if it was was part of a waxing and waning pattern of ventilation with at least 3 successive periods of hyperventilation alternating with central apneas/hypopneas. The mean number of PB per hour, defined as periodic breathing index (*PBI*) was computed.

A. Respiratory volume signal characterization

In the frequency domain, the respiratory pattern is characterized by some parameters derived from two different PSD frequency bands centered either around the respiratory frequency (Δfr : the respiratory frequency bandwidth) or the modulation frequency (Δfm: the modulation frequency bandwidth). In order to provide a better frequency resolution and to avoid the problem of leakage a parametric power spectral estimation is performed through autoregressive modeling. The optimum model order is selected for each subject according to the minimum description length criterion proposed by Rissanen. Table I describes the spectral parameters. The power and slope of the modulation frequency band reflect the strength of periodicity in ventilation.

TABLE I
Parameter Description

Parameter	**Description**
Pm	Power of the modulation frequency band
Pr	Power of the respiratory frequency band
fm	Modulation frequency peak
fr	Respiratory frequency peak
Sm	Slope in the modulation frequency band
Sr	Slope in the respiratory frequency band
R	Ratio between modulation and respiratory power P_M/P_R

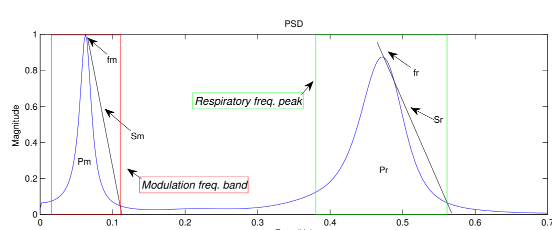

Fig. 1. Parameters extracted from the PSD of the respiratory volume signal.

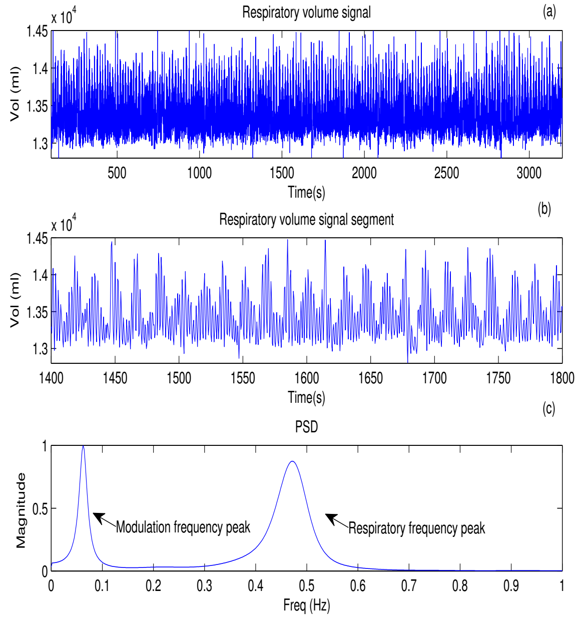

Fig. 2. (a) The respiratory volume signal (a period of continuous climbing) of a healthy mountaineer with periodic breathing (PB), (b) a respiratory volume signal segment, (c) PSD of the respiratory volume signal.

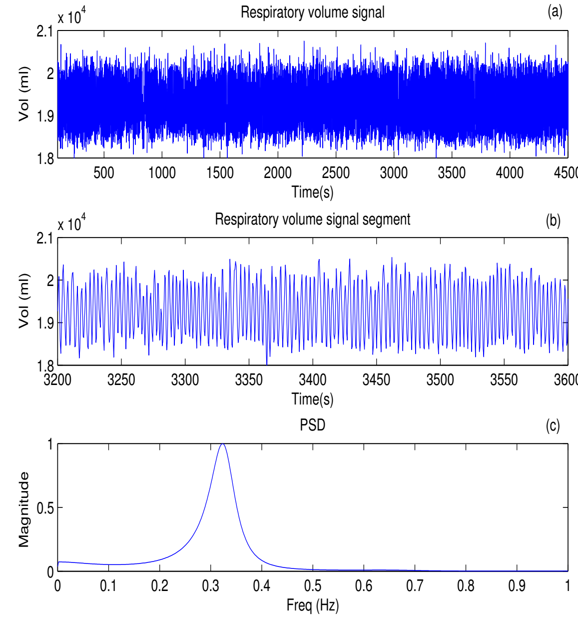

Fig. 3. (a) The respiratory volume signal (a period of continuous climbing) of a healthy mountaineer without periodic breathing (nPB), (b) a respiratory volume signal segment, (c) PSD of the respiratory volume signal.

The modulation frequency of PB patterns during exercise ranges typically from 0.01 to 0.2 Hz, and the modulation frequency peak (fm) is located in this band, $\Delta fm = 0.1Hz$. The respiratory frequency peak (fr) is tracked in the band from 0.2 to 1 Hz, $\Delta fr = 0.2Hz$. The respiratory and modulation frequency peaks ((fr and fm), the individual powers and slopes of the two frequency bands Pm, Sm and Pr, Sr and their ratio $R = Pm/Pr$ constitute the seven spectral parameters, which are investigated in this study, see Fig.1.

IV. Results

A. Illustration of the method

Figures 2 and 3 illustrate the performance of our method applied to a subject with and without periodic breathing (PB and nPB), respectively. From Fig. 2, it is clear that the periodicity is also reflected in frequency domain through the modulation frequency peak. No obvious periodicity is observed in Fig. 3 with no clear modulation frequency peak (0.01Hz is the median of the modulation frequency (fm) in nPB subjects). Respiratory frequency peak is clearly shown in both subjects.

B. Performance Evaluation

Considering all climbing periods within all the ascents (previously classified visually as 371 nPB and 40 PB climbing periods), the accuracy of the spectral parameters characterizing the breathing pattern, is evaluated classifying PB versus nPB periods. Table II presents the mean and the standard deviation of the statistically significant parameters classifying PB versus nPB patterns, evaluated by the U-Mann-Whitney test (p-value < 0.0005). The power of the modulation frequency band and the ratio R are higher in PB subjects due to the periodicity, than in nPB subjects. Modulation frequency is higher as well in subjects with PB.

TABLE II

PB vs. nPB ($\mu \pm \sigma$)

	PB	nPB
Pm	0.18 ± 0.09	0.10 ± 0.08
fm	0.06 ± 0.02	0.04 ± 0.05
R	0.41 ± 0.38	0.28 ± 0.42

Table III shows the accuracy, sensitivity and specificity of the statistically significant parameters linearly classifying PB and nPB using leave one out crossvalidation. The best result with an accuracy of 80.3% is obtained using jointly two parameters Pm and R. Fig. 4 presents the receiver operating characteristic (ROC) curve and the area under the ROC (AUC) for the three individual classification tasks, and the classification using Pm and R.

TABLE III

PB vs. nPB

	Accuracy	Sensitivity	Sensitivity
Pm	78.4%	65.0%	79.8%
fm	73.5%	85.0%	72.2%
R	75.9%	50.0%	78.7%
Pm, R	80.3%	70.0%	75.9%

C. Acclimatization and PB

The subjects from 1_{st} and 2_{nd} ascent started and finished at the same altitude but only the subjects from 2_{nd} ascent spent some days at that altitude before starting the ascent,

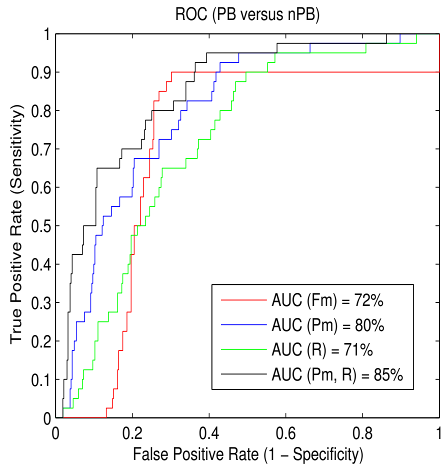

Fig. 4. ROC curves obtained with the significant parameters (Pm, fm, R and $Pm+R$).

so they were more acclimatized. To evaluate the effect of the acclimatization in healthy mountaineers, Table IV shows the statistically significant parameters comparing 1_{st} and 2_{nd} ascent (mean and standard deviation of SaO_2 and Pm and interquartile range of PBI), using the U-Mann-Whitney test. It can be observed that both SaO_2 and PBI increase with acclimatization. No significant differences are found in spectral parameters that reflect PB but it is possible to see the increasing tendency of Pm with acclimatization.

TABLE IV

1_{st} ASCENT VS. 2_{st} ASCENT ($\mu \pm \sigma$)

	1_{st} **Ascent**	2_{st} **Ascent**	p**-value**
SaO_2	72.9 ± 5.3	76.2 ± 5.0	< 0.0005
$IQR(PBI)$	7	24	< 0.05
Pm	0.096 ± 0.06	0.115 ± 0.10	n.s.

Considering 1_{st} and 2_{nd} ascents at similar altitudes, the correlations between SaO_2, visual labels of PB, and the spectral parameters that characterize respiratory pattern are studied. Higher power of the modulation frequency band and higher respiratory frequencies have been observed at lower SaO_2. Significant negative correlation (p-value < 0.01) between SaO_2 and, Pm and fr proves this relationship. Higher power of the modulation frequency band has been observed at climbing periods visually labeled as PB with $PBI > 5$. Significant positive correlation (p-value < 0.01) between visual labels of PB, and Pm, reflects this relationship.

V. CONCLUSIONS

The respiratory pattern characterization through the analysis of the respiratory volume signal is proposed to detect and quantify high altitude periodic breathing (PB). A dataset of 34 healthy mountaineers ascending to Mt. Muztagh Ata, China (7,546 m) has been analyzed. The effect of acclimatization is evaluated comparing subjects at same altitudes from two different ascents. The spectral parameters that characterize the respiratory pattern have been studied for the detection of periodic breathing. The power of the modulation band and the ratio between modulation and respiration power provided the best classification result with an accuracy of 80.3%. SaO_2 and PBI significantly increased in more acclimatized subjects. Higher power of the modulation frequency band and higher respiratory frequencies were observed at lower SaO_2. Higher modulation power was found at climbing periods visually labeled as PB with $PBI > 5$.

As a preliminary study, these results allow considering the characterization of the respiratory volume signal in terms of spectral content, as a promising tool to characterize the respiratory pattern and identify periodic breathing, without the limitations of observer bias. Further analysis of the database should be done including respiratory and cardiac information.

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