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Heart rate variability and arterial oxygen saturation response during extreme normobaric hypoxia

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ABSTRACT

The primary purpose of this study was to assess the response of autonomic cardiac activity and changes in the arterial oxygen saturation (SpO_2) during normobaric hypoxia and subsequent recovery. Heart rate variability (HRV) and SpO_2 were monitored in a supine position during hypoxia ($FiO_2 = 9.6\%$) for 10 min, and normoxic recovery in 29 subjects. Spectral analysis of HRV quantified the autonomic cardiac activity by means of low frequency (LF) (0.05–0.15 Hz) and high frequency (HF) (0.15–0.50 Hz) power transformed by natural logarithm (Ln). Based on the SpO_2 response to hypoxia, the subjects were divided into Resistant (RG, $SpO_2 = 80.8 \pm 7.0\%$) or Sensitive (SG, $SpO_2 = 67.2 \pm 2.9\%$) group. The SpO_2 and vagal activity (LnHF) significantly decreased during hypoxia in both groups. A withdrawal in vagal activity was significantly greater in SG compared to RG. Moreover, only in SG, a relative increase in sympathetic modulation (Ln LF/HF) during hypoxia occurred. Correlations ($r = -0.461$, and $r = 0.595$, both $P < 0.05$) between ΔSpO_2 (delta) and ΔLn LF/HF, and ΔLnHF were found. Based on results, it seems that SpO_2 level could be an important factor that influences the autonomic cardiac response in hypoxia.

1. Introduction

Repeated exposure to a simulated altitude has been proposed as a pre-acclimatization strategy for elite athletes before ascending to a high altitude (>4000 m) (Millet et al., 2010; Wilber, 2007). Researchers in the former Soviet Union were pioneers in altitude simulation and experimented with the discontinuous inhalation of a hypoxic gas mixture at rest more than 60 years ago. This approach was referred to as intermittent hypoxic training (IHT) and intended to stimulate adaptation in aviators (Serebrovskaya, 2002). To date, a large body of studies have shown that the response to hypoxia-induced stress is associated with autonomic nervous system (ANS) activity (Akselrod et al., 2001; Al Haddad et al., 2012; Bobyleva and Glazachev, 2007; Buchheit et al., 2004; Hainsworth et al., 2007; Povea et al., 2005; Schmitt et al., 2006).

The spectral analysis (SA) of R–R intervals to assess heart rate variability (HRV) is commonly accepted as a non-invasive method for monitoring the ANS activity (Akselrod et al., 1981), especially parasympathetic (vagal) cardiac outflow (Aubert et al., 2003). Vagal activity, which is mirrored by the high-frequency power (HF) of R–R intervals (0.15–0.50 Hz), is associated with respiratory modulated fluctuation of heart rate (HR) that causes a phenomenon known as respiratory sinus arrhythmia (RSA) (Yasuma and Hayano, 2004). Low-frequency power (LF) (0.05–0.15 Hz) is considered to reflect baroreflex activity together with both sympathetic and vagal outflow (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996) whereas LF expressed in normalized units (LFnu) reflects the sympathetic activity (Roche et al., 2002).

Acute exposure to hypoxic conditions induces a progressive decline in arterial oxygen saturation (SpO_2), causing an immediate compensatory response of the cardiorespiratory system to supply adequate oxygen to vital tissues (Rowell et al., 1989). Homeostatic adjustments to systemic hypoxia display a complex stress-regulated response, which is primarily mediated by a central command mechanism (Mazzeo, 2008) and changes in ANS function (Hainsworth et al., 2007). The hypoxia-induced increase in resting HR seems to result from a decrease in vagal outflow and an increase in relative sympathetic activity (Cornolo et al., 2004; Iwasaki et al., 2006; Povea et al., 2005; Roche et al., 2002; Serebrovskaya, 2002).

Former studies demonstrated that a preserved HRV in hypoxia was associated with i) a better adaptation response to IHT (Povea et al., 2005); ii) the ability to withstand hypoxia expressed as the time until

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the loss of consciousness occurs (Akselrod et al., 2001); and iii) a reduced risk of acute mountain sickness (AMS) development (Mazzuero, 2001). To the best of our knowledge, only one study reported that subjects who present with an initial higher resting HRV in normoxia manifested a slower decline in the SpO_2 during acute hypoxia (Akselrod et al., 2001). If this finding could be confirmed, the determination of HRV under normoxic conditions would allow the prediction of the SpO_2 response to hypoxia, which would contribute to the identification of AMS-prone subjects without the use of hypoxia (Karinen et al., 2010).

Although the HRV response in relation to SpO_2 dynamics during acute hypoxia has previously been investigated (Ito et al., 2006; Saito et al., 2005), a relationship between vagal activity and the SpO_2 response to acute normobaric hypoxia has not yet been established. Therefore, this study focused on both the cardiac vagal activity and the SpO_2 response assessment to normobaric hypoxia (~6200 m) and during the subsequent period of recovery under normoxic conditions. We hypothesized that basal HRV levels in normoxia would predict the SpO_2 response during hypoxic exposure. In addition, we assessed the correlation between vagal cardiac activity and the SpO_2 response to hypoxia to identify how hypoxia affects the autonomic function in relation to SpO_2 dynamics. Finally, we investigated the response of the autonomic cardiac regulation during normoxic recovery following hypoxia-induced disturbances in HRV.

2. Materials and methods

2.1. Subjects

The study included 29 healthy, moderately active, non-smoking, male, sports science students (age: 26.0 ± 4.9 yrs, weight: 77.6 ± 8.5 kg and height: 179.7 ± 5.6 cm). The inclusion criteria of this study were the following. The subjects had not been exposed to hypoxia for at least the previous two years and were non-smokers and were not on any medication or dietary supplements. They underwent preliminary medical screening to identify cardiovascular (resting ECG and blood pressure monitoring), and pulmonary (vital capacity test) conditions that would exclude them from the study. The exclusion criteria included pathological changes in cardiac rhythm, hypertension, smoking and acute respiratory diseases. The study was performed in accordance with the ethical guidelines outlined in the Declaration of Helsinki and was approved by the Ethics Committee of the Faculty of Physical Culture, Palacký University. All of the subjects participating in the study were volunteers and had given their written informed consent.

2.2. Experimental protocol

The subjects were required to avoid eating, drinking coffee, tea and/or any substance affecting the ANS activity for at least 2 h before the experiment. In addition, they were asked to avoid vigorous physical activity and alcohol for 48 h before the experiment. The experiment was performed between 8:00 and 11:00 a.m. in a laboratory where the ambient temperature ranged from 22 to 24 °C. During the experiment, each subject rested quietly in a supine position and was shielded against acoustic and visual disturbances. It is well known that the decrease in breathing frequency and increase in tidal volume (V_T) are positively related with an increase in the HRV–HF component (Brown et al., 1993; Hirsch and Bishop, 1981). On the other hand, while the breathing frequency is located below 0.15 Hz (9 breaths/min), an artificial increase in LF power (LF/HF ratio) may lead to misinterpretation of accurate autonomic status (Kolisko et al., 2004; Sasaki and Maruyama, 2014). Therefore, we decided to let each subject follow a regular breathing rhythm in reference to an audible signal (12 breaths/min, 0.2 Hz) played by a CD player as was previously reported (Ito et al., 2006; Roche et al., 2002). In addition, recently Sasaki and Maruyama (2014) demonstrated that breathing frequency had a greater influence on HF component with V_T since no significant correlation between HF and V_T was found.

The experimental design proceeded as follows (Fig. 1): The subjects first breathed ambient air for 7 min without a breathing mask. A breathing mask was then fitted, and the subject breathed air with a reduced O_2 concentration for 10 min. Finally, the mask was removed, and the subject breathed ambient air for a further 7 min.

The normobaric hypoxia condition equal to the altitude of 6200 m ($FiO_2 = 9.6\%$) has been widely used in the literature for intermittent hypoxic exposure (Millet et al., 2010). This condition was created using a MAG-10 system (Higher Peak, Boston, MA, USA), which simulated the lower O_2 pressure found at high altitudes by lowering the percentage of O_2 in the air. Subjects breathed air with a reduced O_2 concentration via the mask from a non-rebreathing circuit with a bag acting as a reservoir.

Oxygen saturation and ECG signal were recorded continuously throughout the experimental protocol. However, three phases were defined to further process the data as follows (Fig. 1): the preliminary phase started 1 min after the start of the protocol and lasted 6 min. The hypoxia phase started 5 min after the mask fitting and lasted 5 min. The recovery phase started 1 min after the mask removal and lasted 6 min. A pause of 1 min in the measurement of the ECG record was used to reach the steady state condition for the preliminary and recovery phases, respectively.

2.3. Oxygen saturation measurement

The SpO_2 was continuously measured using a Nonin Avant 4000 pulse oximeter (Nonin Medical, Minneapolis, MN, USA) set on the right index finger. The SpO_2 was measured at a sampling frequency of 1.0 Hz, and the average value over each phase was calculated for subsequent statistical analysis. The change in SpO_2 between the Hypoxia phase and Preliminary phase was calculated as follows $\Delta SpO_2 = SpO_{2\,\text{Hypoxia}} - SpO_{2\,\text{Preliminary}}$.

2.4. Heart rate variability analysis

To determine the HR and HRV variables, the ECG signal was measured at a sampling frequency of 1000 Hz using a VarCor PF7 diagnostic device (DIMEA Group, Olomouc, Czech Republic). The ECG record was examined, and all premature ventricular contractions, missing beats, and any artefacts were manually filtered. A set of 300 artefact-free subsequent R–R intervals was obtained from each phase.

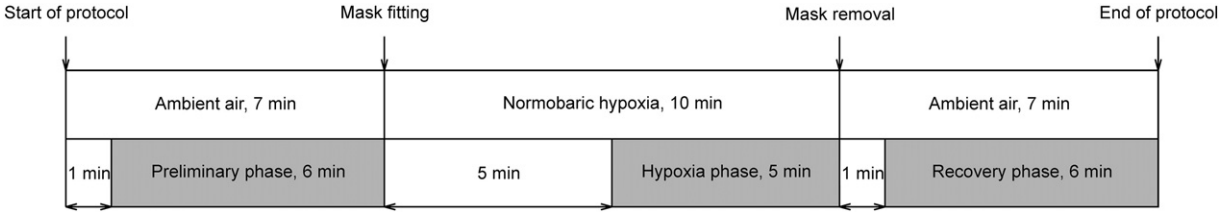

Fig. 1. Course of experimental protocol and depiction of the Preliminary, Hypoxia, and Recovery measurement phases.