

THE ACUTE EFFECTS OF INHALING DIFFERENT CONCENTRATIONS OF OXYGEN ON HEART RATE VARIABILITY AFTER EXHAUSTIVE EXERCISE

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The purpose of this study was to investigate the effects of inhaling different percentages of oxygen (O₂) after maximal exercise on heart rate variability (HRV). Eight active college males (age, 19.9 ± 1.5 years; height, 177.8 ± 6.3 cm; weight, 76.2 ± 12.7 kg) volunteered to participate in this study. Each subject inhaled normobaric 21% O₂ (NO), 12% O₂ (LO), and 60% O₂ (HO) for 40 minutes in random balanced order after exhaustive exercise on a treadmill. The beat-to-beat HRV was measured at the 10th (post-10, from 10 to 20 minutes after exercise) and 30th minutes (post-30, from 30 to 40 minutes after exercise) after maximal exercise for subsequent analysis. Time and frequency domain analyses of HRV were performed to determine the effect of inhaling different percentages of O₂ on autonomic function. The results indicated that heart rate at post-30 minutes was significantly lower in the HO group than in the LO group ($p < 0.05$). The time domain indices of the RR interval at post-30 minutes was significantly lower in the LO than in the HO group ($p < 0.05$). There were no significant differences, either at post-10 or post-30 minutes, with regard to the time domain indices among the three treatments. The natural log of high-frequency (HF) powers and the coefficient of component variance of HF powers at hyperoxia were significantly higher than at hypoxia, but there were no significant differences between hyperoxia and normoxia. In conclusion, these results demonstrated that the inhalation of the gas mixture with 60% O₂ after exhaustive exercise, compared with hypoxia, increased the vagal modulation of the autonomic nervous system on the heart and improved physiologic recovery after intense exercise.

Keywords: hyperoxia, hypoxia, maximal exercise, recovery

Introduction

Heart rate variability (HRV) has been recognized as a powerful tool for the estimation of autonomic nervous

regulation of the heart (Challapalli et al. 1999; Task Force of European Society of Cardiology and North American Society of Pacing and Electrophysiology 1996; Malliani et al. 1991). The relationship between sympathetic and parasympathetic tones can be evaluated by power spectral analysis in which the total variability of RR intervals (time duration between two consecutive R waves of the electrocardiogram) is divided into very low-, low-, and high-frequency bands and each band is quantified.

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Previous studies suggested that high-frequency power (HF, 0.15–0.40 Hz) could be mediated by the parasympathetic nervous system (PNS) and respiration (Warren et al. 1997; Pomeranz et al. 1985), and that low-frequency power (LF, 0.04–0.15 Hz) reflected both the sympathetic nervous system (SNS) and PNS activities (Arai et al. 1989; Pagani et al. 1986; Akselrod et al. 1985). The role of very low-frequency power (VLF, < 0.04 Hz) is unclear (Aubert et al. 2003). The ratio of LF and HF powers (LF:HF) is thought to reflect sympathovagal balance (Task Force of European Society of Cardiology and North American Society of Pacing and Electrophysiology 1996). Furthermore, powers in the LF and HF bands can also be expressed in normalized units, i.e. LFNU and HFNU, which are defined as relative power (Aubert et al. 2003). The relative power and the central frequency of these components are not fixed but may vary in relation to the autonomic modulation of the heart (Kamath & Fallen 1993).

Many studies have shown that HRV could reflect the effects of the hypoxic or hyperoxic conditions on the modulation of the autonomic nervous system (ANS) during passive rest situations. Buchheit et al. (2004) found that hypoxia induced a significant decrease in HRV and suggested a vagal control withdrawal in a hypoxic environment. Our previous study also indicated that the time domain analysis of HRV could validly reflect the effects of real moderate altitude environment on the modulation of the ANS (Cheng et al. 2005). Lund et al. (1999) suggested that normobaric hyperoxia and hyperbaric hyperoxia increased parasympathetic influence in the regulation of the heart in healthy individuals. Lund et al. (2000) performed the hyperbaric hyperoxia (100% O₂ at 2.5 atmospheric pressures) on professional divers, causing marked increases in HF power and HFNU at rest compared with hyperbaric normoxia.

Physiologic recovery from strenuous exercise is an important key to maintaining the quality and quantity of training sessions and competitions in athletes. Oxygen naturally plays a crucial role in recovery from injury and physiologic fatigue, specifically during hyperbaric oxygen treatment, when more oxygen is dissolved in the plasma of the pulmonary vein via the alveoli that would improve recovery from injury and fatigue (Ishii et al. 2005). Cole et al. (1999) suggested that vagal reactivation, an important cardiodeceleration mechanism immediately after

exercise, plays an important role in avoiding excessive cardiac strain. Some researchers have suggested that a delay in this reactivation holds poor prognostic value. Paterson (1996) indicated that altered cardiac autonomic state in favor of increased SNS and reduced PNS influences have been implicated in the development of dangerous arrhythmias during and after exercise. However, there were no data to show whether the hypoxic or hyperoxic environment would affect autonomic nervous function during the recovery phase. Therefore, we hypothesized that the intervention of higher than normal oxygen level might improve PNS and attenuate SNS activities during the recovery phase, and *vice versa*, the hypoxia condition might prohibit physiologic recovery from intense exercise. The purpose of this study was to evaluate the influences of normobaric hyperoxia (60% O₂), normobaric normoxia (21% O₂) and normobaric hypoxia (12% O₂) on the modulation of ANS on the heart in healthy subjects during the recovery period.

Methods

Participants

Eight healthy males volunteered to participate in this study. All subjects completed a medical history and health questionnaire and provided written informed consent before participating in the experimental procedures. Subjects were asked to avoid smoking and drinking beverages containing alcohol or caffeine 24 hours before the experimental procedures and none of them were taking any medication known to affect cardiovascular function. The protocol used in this study was reviewed and approved by an institutional committee to protect the human rights of the participants.

Experimental design

All subjects completed three experimental treatments which were separated by at least 48 hours in random balanced order. The three experimental trials included normobaric normoxic (NO, 21% O₂), normobaric hypoxic (LO, 12% O₂), and normobaric hyperoxic (HO, 60% O₂) circumstances. The laboratory temperature was controlled between 23°C and 25°C. The hypoxic gas mixtures (12% O₂) were mixed from 21% oxygen and 100% nitrogen by researchers and the hyperoxic gas mixtures

were manufactured by a factory (Air Products San Fu Co. Ltd., Taipei, Taiwan). The treatment gas mixtures were prepared in a big air bag before exercise tests, and then the subjects were asked to breath via a mask (8900 series Nasal & Mouth Breathing Mask; Hans Rudolph Inc., Kansas City, MO, USA) for 40 minutes immediately followed by the incremental running exercise. Appropriate oxygen delivery was controlled through the ventilator and the mask. Inhaled gas samples were analyzed using an oxygen analyzer (OM-25AE MAXTEC®; Maxtex Inc., Salt Lake City, UT, USA). During the recovery phase, each subject adopted the static rest in an upright sitting position.

Incremental exercise test

A brief warm-up on a treadmill was performed by all participants before the incremental exercise test. Each subject completed three incremental treadmill exercises until volitional exhaustion was reached. The tests were separated by at least 2 days. Oxygen consumption was simultaneously analyzed by a semi-automated open-circuit spirometry system (Vmax 29 Cardiopulmonary Exercise Testing Instrument; Sensormedics, Yorba Linda, CA, USA). Exercise began at an initial running speed of 2.0 m s^{-1} for 5 minutes, followed by increments of 0.5 m s^{-1} every 5 minutes until volitional exhaustion was achieved. Three of the following criteria had to be met to ensure that each participant achieved a maximal effort: (1) failure of heart rate to increase with an increase in intensity; (2) plateau of oxygen uptake with increased workload; (3) respiratory exchange ratio > 1.1 ; (4) ventilation volume $> 100 \text{ L min}^{-1}$; and (5) rating of perceived exertion > 17 on the 6–20 scale (McConnell 1988).

HRV analysis

The heart rates were continuously measured by a Polar heart rate monitor (Polar S810i™; Polar Electro Inc., Oy, Finland) before, during and after the incremental exercise. The heart rate data were measured by at least 10 minutes at the 10th (post-10, from 10 to 20 minutes after exercise) and 30th (post-30, from 30 to 40 minutes after exercise) minute after incremental exercise, and the data were transferred via Polar infrared rays (Polar IR Interface; Polar Electro Inc.) to a personal computer for further analysis.

Before processing, the heart rate signals were automatically corrected by the Polar Precision Performance

SW 3.0 package software for ectopic and missed beats, and then the modified heart rate data were transformed to ASCII files. Non-stationary signals or periods with more than 15% correction were excluded in this study. In other words, if the corrected signals exceeded 15% of the total heart rate record duration, the data were excluded in the following statistical analysis. In this study, however, only one subject's data needed to be modified up to 13.5% and the others ranged from 0.1% to 3.6%. The electrocardiogram was subsequently plotted as a tachogram of heart period, which was evaluated for the RR mean, standard deviation of all normal RR intervals (SDNN), and the square root of the mean squared successive differences between adjacent RR intervals (RMSSD). The waveform was then resampled at 4.0 Hz, and the spectral power was derived via a 1024-point linear fast Fourier transformation with a Hamming window. The power spectrum was then analyzed for LF (0.05–0.15 Hz) and HF (0.15–0.40 Hz) powers. The time domain and frequency domain analyses of RR intervals were performed by the analytic software (AcqKnowledge® version 3.7.2; BIOPAC Systems Inc., Santa Barbara, CA, USA). Sympathovagal balance was estimated by dividing the power of the LF band by that of the HF band (Pagani et al. 1986). Because the raw values of LF and HF did not follow the normal distribution, natural log (ln) transformation was applied (lnLF, lnHF, and lnLF:lnHF). LF and HF were further normalized, LFNU: $\text{LF}/(\text{LF} + \text{HF}) \times 100$ and HFNU: $\text{HF}/(\text{LF} + \text{HF}) \times 100$ (Parekh & Lee 2005; Pichon et al. 2004; Carter et al. 2003). Lastly, the coefficient of component variance (CCV) of LF- and HF-power (Hayano et al. 1990) was also calculated using the following formula: $\text{CCV}_A (\%) = 100 \times (\text{power of component A})^{1/2}/(\text{RR mean})$.

SpO₂ analysis

The portable monitor (OxiMax® NPB-40 handheld pulse oximeter; Nellcor Puritan Bennett LLC, Pleasanton, CA, USA) was utilized to measure the arterial blood oxygen saturation (SpO₂), and the SpO₂ probe was set on the right forefinger of subjects during the recovery phase. Before and after maximal exercise, all subjects were asked to rest quietly in a sitting position, and were advised to breathe regularly without intermittent deep breaths. The SpO₂ data were collected before and after the incremental exercises for further analysis.

Statistical analysis

All data were expressed as mean \pm standard deviation (SD). The differences between mean values were tested by repeated measures one-way analysis of variance (ANOVA). In the presence of a significant F value, *post hoc* comparisons of means were provided by Tukey's range test. Statistical significance was denoted by a p value < 0.05 .

Results

Physical characteristics

Physical characteristics of the subjects are presented in the Table. $\dot{V}O_{2\max}$ and HR_{\max} parameters were calculated from the average values of three maximal incremental exercises. The duration of the incremental exercise was approximately 17.04 ± 1.65 minutes.

Arterial blood oxygen saturation

The results indicated that arterial blood oxygen saturation was significantly higher in the HO group than in the LO group at post-10 minutes and at post-30 minutes (post-10 minutes, HO vs. LO, $99.5\% \pm 0.5\%$ vs. $84.1\% \pm 6.7\%$, $p < 0.05$; post-30 minutes, HO vs. LO, $99.5\% \pm 0.8\%$ vs. $79.9\% \pm 7.6\%$, $p < 0.05$). The SpO_2 values in the LO group were also significantly lower than those in the NO group at post-10 minutes and post-30 minutes, respectively. However, there were no significant differences in SpO_2 between the NO and HO groups (Figure 1).

Time domain indices of HRV

Figure 2 demonstrates the results of HR, RR mean, SDNN, and RMSSD at post-10 minutes and post-30 minutes among different interventions. The HR, RR interval, SDNN, and RMSSD at post-10 minutes had

Table. Physical characteristics of subjects ($n = 8$)*

Age (yr)	19.9 ± 1.5
Height (cm)	177.8 ± 6.3
Weight (kg)	76.2 ± 12.7
HR_{rest} (beats min^{-1})	76.0 ± 11.3
$\dot{V}O_{2\max}$ ($\text{mL kg}^{-1} \text{min}^{-1}$)	58.4 ± 4.2
HR_{\max} (beats min^{-1})	185.0 ± 5.71

*Values are presented as mean \pm standard deviation. $\dot{V}O_{2\max}$ = maximal oxygen uptake; HR_{rest} = resting heart rate; HR_{\max} = maximal heart rate.

no significant differences among the NO, LO and HO groups. Compared with the LO group, RR mean was markedly higher and HR was significantly lower at post-30 minutes in the HO group. Nevertheless, there were no significant differences in heart rates and time domain indices between the NO and HO groups at post-30 minutes.

Frequency domain indices of HRV

There were also no significant differences in lnLF or lnHF powers among the three treatment groups at post-10 minutes. However, lnLF in the LO group was significantly lower than in the NO and HO groups (Figure 3). Furthermore, lnHF in the HO group was significantly higher than in the LO group. At post-30 minutes after maximal exercise, neither lnLF nor lnHF had significant differences between the NO and HO groups.

The normalized units of LF and HF powers, at post-10 minutes and at post-30 minutes, did not have any significant differences among the NO, LO and HO groups (Figure 4). There were no significant differences in lnLF:lnHF ratios at post-10 minutes and post-30 minutes among the three treatment groups (post-10 minutes, NO vs. LO vs. HO, 3.29 ± 2.36 vs. 19.41 ± 35.25 vs. 0.62 ± 4.44 , $p > 0.05$; post-30 minutes, NO vs. LO vs. HO, 2.94 ± 2.63 vs. 2.71 ± 1.37 vs. 1.95 ± 1.32 , $p > 0.05$).

There were no significant differences in CCV of LF or HF powers among the three treatment groups at post-10 minutes. There were also no significant differences

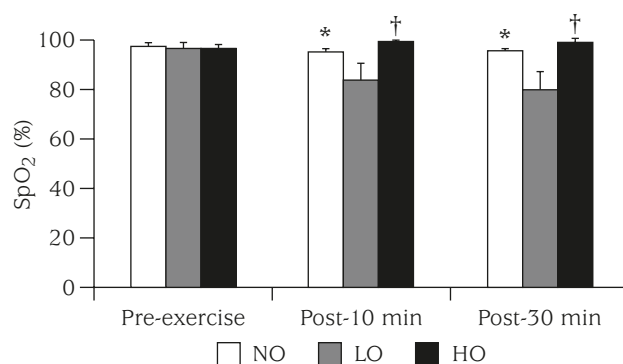


Fig. 1 Arterial blood oxygen saturation (SpO_2) at different time points during the experiments. *Significant difference between the NO and LO trials ($p < 0.05$); †significant difference between the HO and LO trials ($p < 0.05$). NO = normobaric normoxia; LO = normobaric hypoxia; HO = normobaric hyperoxia.

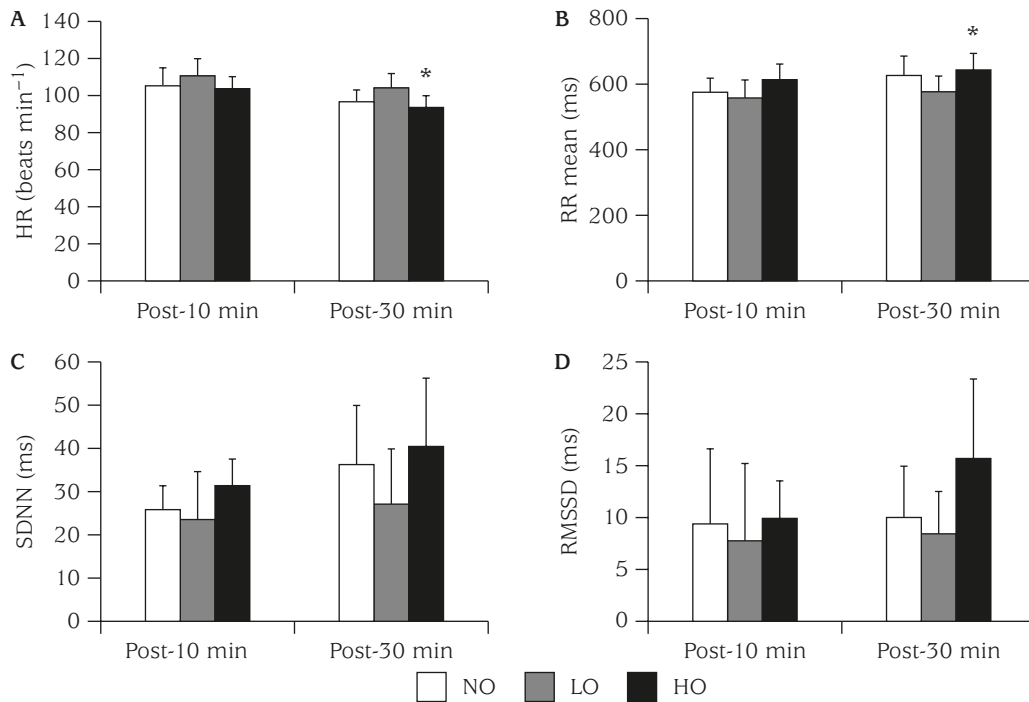


Fig. 2 Changes in heart rate and time domain indices of heart rate variability (HRV) after maximal exercise. (A) Heart rate (HR); (B) RR-interval variability; (C) standard deviation of all normal RR intervals (SDNN); (D) root of the mean squared successive differences between adjacent RR intervals (RMSSD). *Significant difference between the HO and LO trials ($p < 0.05$). NO = normobaric normoxia; LO = normobaric hypoxia; HO = normobaric hyperoxia.

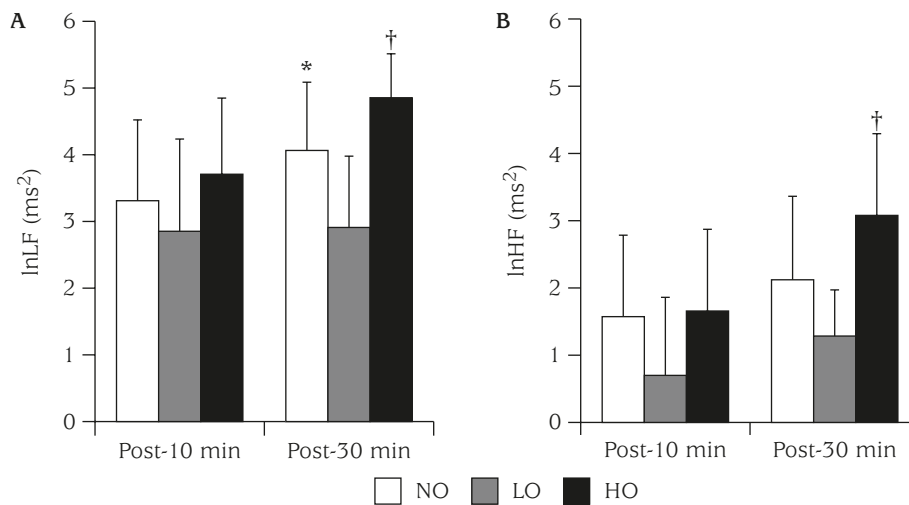


Fig. 3 (A) Low-frequency (LF) and (B) high-frequency (HF) after maximal exercise. *Significant difference between the NO and LO trials ($p < 0.05$); †significant difference between the HO and LO trials ($p < 0.05$). NO = normobaric normoxia; LO = normobaric hypoxia; HO = normobaric hyperoxia.

between the NO and HO groups at post-30 minutes. The CCVs of LF and HF in the HO group at post-30 minutes, however, were significantly higher than in the LO group (Figure 5).

Discussion

The present study was the first to investigate the effects of normobaric hyperoxia and hypoxia applied during

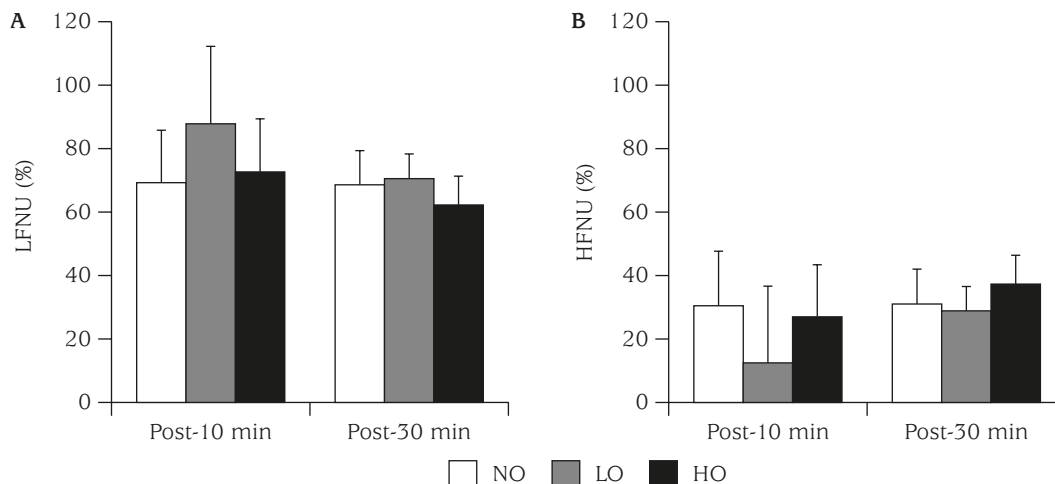


Fig. 4 Normalized units (NU) of (A) low-frequency (LF) and (B) high-frequency (HF) after maximal exercise. NO = normobaric normoxia; LO = normobaric hypoxia; HO = normobaric hyperoxia.

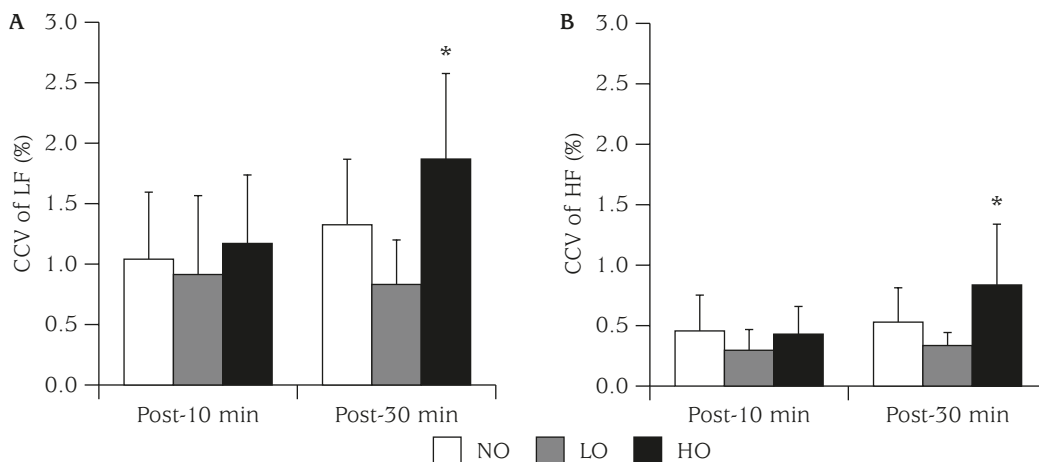


Fig. 5 Coefficient of component variance (CCV) of (A) low-frequency (LF) and (B) high-frequency (HF) after maximal exercise. *Significant difference between the HO and LO trials ($p < 0.05$). NO = normobaric normoxia; LO = normobaric hypoxia; HO = normobaric hyperoxia.

the recovery phase after acute maximal exercise on cardiac autonomic modulation. The main finding of this study indicated that the hyperoxic environment (60% O_2), compared with the hypoxic environment (12% O_2), significantly increased PNS activities and facilitated heart rate recovery after maximal exercise. However, there were no significant differences in cardiovascular adjustment between the normoxic and hyperoxic stimulus during the recovery phase.

Lodato (1989) suggested that normobaric hyperoxia decreased the resting heart rate in conscious dogs. Lund et al. (1999) found that the resting heart rate tended to decrease during normobaric hyperoxia (100% O_2) when

compared to normobaric normoxia, although there were no statistically significant differences among their treatments. Although SpO_2 during hypoxia was significantly lower than normoxia and hyperoxia, this present study only found that normobaric hyperoxia significantly decreased heart rate at 30 minutes after maximal exercise when compared to hypoxic treatment. Furthermore, there were no significant differences in heart rate during the recovery phase between normoxia and hyperoxia. Parekh & Lee (2005) suggested that exercise at 80% $\dot{V}O_{2R}$ ($\dot{V}O_2$ reserve) results in a greater postexercise shift in sympathovagal balance with a delayed vagal reactivation, compared to exercise at

50% $\dot{V}O_2R$. Thus, these discrepancies might be ascribed to factors such as the different percentages of oxygen, the implementation duration of oxygen treatment and the effect of maximal exercise.

Buchheit et al. (2004) reported that resting heart rate in hypoxia (11.5% O_2) was significantly higher than in normoxia. Our previous study also found that resting heart rate when in an upright sitting position was significantly higher during acute exposure to a moderate altitude (~2200–2600 m) than at sea level (Cheng et al. 2005). However, the present study found that there were no significant differences in recovery heart rate between normoxia and hypoxia. Still, the indicators of ANS regulation, i.e. lnLF and lnHF powers, decreased significantly more during hypoxia than normoxia and hyperoxia, but this was not reflected in the actual heart rate. Thus, it seems that heart rate as a sole variable is insensitive in predicting autonomic regulation of the heart after maximal exercise.

Although many studies have indicated that the time domain indices of HRV, such as RR mean, SDNN and RMSSD, could reflect the effects of exercise stimulation (Parekh & Lee 2005; Javorka et al. 2002), this study found that there was only a tendency to decrease at hypoxia and increase at hyperoxia on the time domain indices; in addition, the RR mean at post-30 minutes was significantly higher during hyperoxia than the other treatments. Buchheit et al. (2004) found that hypoxia induced a significant decrease in RMSSD at rest, whereas SDNN was unchanged. The possible explanation for the differences in these results could be mathematical methods and experimental designs. In the study of Buchheit et al. (2004), the time domain indices at hypoxia were calculated in relative values and they did not measure the effects of hypoxia after exercise. It seems that the time domain indices could not clearly reflect the effects of different percentages of oxygen during the recovery phase. Nevertheless, our previous study (Cheng et al. 2005) indicated that time domain analysis of HRV could validly reflect the effects of real moderate altitude environment on the modulation of the ANS. Therefore, we need further studies to examine the validity of using time domain analysis of HRV on the effects of different percentages of oxygen during the recovery phase.

The results of this study indicated that although there were no differences on the normalized units of LF and

HF power, i.e. LFNU and HFNU, among the three treatment groups, the lnHF and CCV of HF in hyperoxia were significantly higher than in hypoxia. However, the lnHF and CCV of HF in hyperoxia were only slightly higher than in normoxia. Lund et al. (1999) reported that the resting lnHF and CCV of HF in normobaric hyperoxia were significantly higher than in normoxia. The possible explanation for the discrepancies might be the different treatments. The concentration of oxygen and the duration of treatment in the study of Lund et al. (1999) were higher and longer than ours. Therefore, further studies need to investigate the effects of much higher concentrations of oxygen and longer treatment duration during the recovery phase on the modulation of cardiac autonomic function. However, the present study demonstrated that the application of hyperoxia (30 minutes, 60% O_2) during the recovery phase would increase PNS activities compared to the use of 12% O_2 .

Previous studies reported that the power spectral analysis of HRV showed that hypoxia, compared with normoxia, increased SNS and reduced PNS indices in sitting or supine positions (Buchheit et al. 2004; Sevre et al. 2001; Bernardi et al. 1998; Perini et al. 1996). The present study found that the lnHF and CCV of HF decreased during hypoxia, but there were no statistically significant differences between hypoxia and normoxia. Furthermore, there were no significant differences in recovery heart rate between hypoxia and normoxia. Possible explanations for the different results could be that the 30 minutes of hypoxia treatment would not observably affect PNS activities and/or that intense exercise stimulates hormonal secretion, such as epinephrine and norepinephrine (Buchheit et al. 2004; Perini & Veicsteinas 2003).

More controversial is the interpretation of the LF component, which is considered by some authors to be a marker of sympathetic modulation and by others as a parameter that includes sympathetic, vagal, and baroreflex influences (Aubert et al. 2003; Task Force of European Society of Cardiology and North American Society of Pacing and Electrophysiology 1996; Arai et al. 1989; Akselrod et al. 1985). In a meta-analysis of HRV studies, Eckberg (1997) showed that vagal contributions to LF RR-interval fluctuations are great, and that there is no convincing evidence that baseline LF

RR-interval spectral power is related quantitatively to SNS traffic. We found that the lnLF and CCV of LF during hyperoxia as well as the lnLF during normoxia were all significantly higher than during hypoxia. Casadei et al. (1995) also indicated that HRV is generated partly by non-neural mechanisms during strenuous exercise. Considering these data as a whole, we suggest that during recovery, LF is predominantly influenced by changes in PNS directly (through alterations in vagal-cardiac activity causing fluctuations in LF band) and/or indirectly (through changes in baroreflex sensitivity).

In conclusion, the present study demonstrated that the application of 30 minutes of 60% oxygen during the recovery phase would increase vagal modulation of heart rate and benefit physiologic restoration from intense exercise when compared to the utilization of 12% oxygen. Although there were no significant differences in the HRV indices between hyperoxia and normoxia, hyperoxia still had a tendency to having a lower heart rate than normoxia. Therefore, future studies should use > 60% oxygen to examine the effects of hyperoxia on physiologic recovery after heavy exercise.

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