Effects of short hypoxic pre-exposure on physiological responses to subsequent hypoxic exercise

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Abstract In mountain climbing, short pre-exposure to hypoxia at the midway point of a high mountain is often carried out before heading to a higher altitude. However, the effects of such exposure have not been examined experimentally. This study aimed at investigating the effects of short pre-exposure to hypoxia on physiological responses to subsequent hypoxic exercise. Thirteen male sea-level residents participated in 2 tests. Both tests consisted of 60-min normobaric exposure followed by 15-min stepwise incremental ergocycle exercise (five workloads) under hypoxic conditions (fractional inspired oxygen concentration [FiO₂] = 0.167). Conditions during normobaric exposure were hypoxic (FiO₂ = 0.167) or normoxic (FiO₂ = 0.209). Results of the two-way analysis of variance (oxygen concentration × exercise intensity) showed significant oxygen concentration effects on heart rate (HR), carbon dioxide production (VCO₂), and rating of perceived exertion during hypoxic exercise. Significant interaction effects were found in minute ventilation and VCO₂. Post hoc tests compared these parameters after hypoxic exposure with those after normoxic exposure at each workload, and only showed a significant difference in HR at workload 2. A significant negative correlation was observed between peak oxygen uptake (VO₂) measured in normoxia and ratio of arterial oxygen saturation (SpO₂) after hypoxic exposure to that after normoxic exposure at workload 5. The present study could not clearly show through post hoc tests the significant effects of short hypoxic pre-exposure on physiological responses to subsequent hypoxic exercise, while it indicated that those with relatively higher peak VO₂ showed a greater decrease in SpO₂ during hypoxic exercise after hypoxic exposure than after normoxic exposure.

Keywords: hypoxia, pre-exposure, individual difference, peak oxygen uptake

Introduction

Before climbing very high- and extreme-altitude mountains, climbers often acclimatize themselves to hypoxic environments by using a chamber or undertaking a sojourn at high altitudes. This acclimatization can delay the onset of acute mountain sickness and allow climbers to maintain their exercise capacity at high altitudes. Studies that reviewed the acclimatization to hypoxia recommended a ≥1 h of daily exposure to a simulated hypoxic environment at approximately 4,000 m for ≥1 week, or a sojourn at an altitude ≥2,200 m for ≥1 day in order to benefit from acclimatization. However, climbers seldom attempt hypoxic acclimatization in a chamber, or by taking a sojourn at altitude, in advance, when they ascend to the summit of mountains around 4,000 m high within 1 day by rapid passive transport, such as by car or train, or by starting a climb from the midway point. In most of these cases, climbers often stop at the midway point for several minutes to hours before heading to the summit.

To our knowledge, few studies have investigated the benefits of such a brief stop when ascending to a higher altitude. Considering that a brief stop at the midway point has often been conducted empirically, it may attenuate the decrease in exercise capacity under hypoxic conditions and/or delay the onset of acute mountain sickness. However, few experimental studies have reported the effects. Meanwhile, there is a possibility that even a short period of hypoxic exposure has the potential to affect the subsequent physiological responses to hypoxia. Hypoxic stimulation to peripheral chemoreceptors is known to increase ventilation. Easton et al. examined the ven...
tulatory responses to 25 min of sustained hypoxia. They found a rapid increase in ventilation immediately after starting hypoxic exposure, which peaked within 15 min and then declined to a plateau between the peak and sea-level values. The decline is termed hypoxic ventilatory decline (HVD), and the peripheral chemoreceptor desensitization is thought to be a causative factor of HVD. Peripheral chemoreceptors are also related to an increase in heart rate (HR) during hypoxic exercise. Therefore, we hypothesized that a short period of hypoxic exposure would attenuate the increase in ventilation and HR during subsequent hypoxic exercise through blunted chemoreflex sensitivity.

The present study aimed to investigate the effects of short pre-exposure to hypoxia on the physiological responses to subsequent hypoxic exercise. The hypoxic condition was set to simulate an altitude of 1,800 m, at which climbers actually make a short stop before heading to the summit of a high mountain. Furthermore, an altitude of 1,800 m is able to induce specific cardiorespiratory responses to hypoxic stimulation during exercise and is likely to prevent the effects of symptoms of acute mountain sickness on these responses. In addition, previous studies have demonstrated individual differences in physiological responses during exercise under acute hypoxic conditions. For example, the decreases in arterial oxygen saturation and maximal oxygen uptake during hypoxic exercise are greater in subjects with higher VO₂max. The greater decrease in arterial oxygen saturation in subjects with higher VO₂max was found even during submaximal exercise in hypoxia. HR and oxygen uptake responses to hypoxic exercise also show large individual variations even at submaximal intensity. Therefore, we added the investigation of individual differences in the effects of short pre-exposure to hypoxia on hypoxic exercise.

Materials and Methods

Subjects. Thirteen young male sea-level residents participated in the present study. None of the participants was a smoker, or had a history of cardiorespiratory disease. The mean age, height, and weight were 23.1 ± 0.9 years (mean ± standard deviation), 171.9 ± 9.3 cm, and 59.9 ± 6.5 kg, respectively. This study was designed and conducted in accordance with the Helsinki Declaration and approved by the Research Ethics Committee of The University of Tokyo. Each participant provided written informed consent prior to the commencement of the study.

Experimental protocol. All of the subjects performed 2 tests (Fig. 1). Both tests were composed of a 60-min stay in a normobaric chamber followed by an incremental ergocycle exercise in hypoxia. The fractional inspired oxygen concentration (FiO₂) in the normobaric chamber was either 0.167 (corresponding to an altitude of 1,800 m; hypoxic test) or 0.209 (corresponding to sea level; control test). The ergocycle exercise was performed outside the chamber while the subjects were breathing a hypoxic gas mixture (FiO₂ = 0.167) from a 200-L Douglas bag. The 2 tests were conducted with an interval of approximately 1 week. Although ventilation has been shown to differ between normobaric and hypobaric hypoxia, it is suggested that the barometric pressure difference probably does not affect hypoxic chemosensitivity. Thus, we used normobaric hypoxia instead of hypobaric hypoxia, and compared the effects of exposure to normobaric hypoxia with those to normobaric normoxia.

Prior to the experimental tests, the subjects performed a preliminary test in normoxic conditions to familiarize themselves with the experimental protocol and equipment. On a different day, the physical characteristics of the subjects, including height, weight, percentage of body fat (%fat), and peak VO₂ in normoxia, were measured. Preliminary testing and physical characteristic measure-

![Fig. 1 Experimental protocol.](image-url)

HR, heart rate; SpO₂, arterial oxygen saturation; VE, minute ventilation; VO₂, oxygen uptake; ÊCO₂, carbon dioxide production; Lac, blood lactate concentration; RPE, rating of perceived exertion. During the 60-min normobaric exposure and 15-min hypoxic exercise, hypoxic (16.7% O₂) or normoxic condition (20.9% O₂) was artificially produced.
ments were completed at least 1 week prior to initiation of the experiments. Measurement of %fat was performed by using bioelectrical impedance analysis (Body Composition Analyzer; Tanita Corporation, Tokyo, Japan). Lean body mass (LBM) was calculated by multiplying (1-%fat/100) by body weight. For the estimation of peak $\dot{V}O_2$, an incremental exercise test was conducted with a cycle ergometer. After 3 min of ergocycle exercise at 30 W, the workload was increased in a ramp fashion (25 W/min) until exhaustion. The subjects were verbally encouraged to continue exercising. Peak $\dot{V}O_2$ was calculated as the mean of 30 s of data that met all of the following 3 criteria: (1) $\dot{V}O_2$ reached a plateau (no further increase in $\dot{V}O_2$ with an increase in workload), (2) respiratory exchange ratio (RER) ≥1.1, and (3) HR ≥90% of age-predicted maximum HR. A previous study$^{15}$ reported that $\dot{V}O_2$max and LBM correlated with exercise capacity in acute hypoxia. Therefore, we investigated the involvement of peak $\dot{V}O_2$ and LBM in the effects of hypoxic pre-exposure on subsequent hypoxic exercise.

On the hypoxic and control test days, the subjects had breakfast by 7:30 AM and reported to the laboratory at around 10:00 AM. Ingestion of beverages containing caffeine was prohibited on the test days, and exercise and consumption of alcohol were also prohibited for 24 h before the tests. After the subjects had rested in a sitting position for 10 min, a 5-min measurement of resting cardiorespiratory conditions in normal air, such as HR, arterial oxygen saturation (SpO2), and minute ventilation ($\dot{V}E$), was started at around 10:30 AM (pre-test measurement). The subjects then moved into the normobaric chamber (232 cm W × 240 cm H × 228 cm D) and remained in a calm sitting position for 60 min. The subjects were blinded to the oxygen concentration of the chamber (FiO2 = 0.209 or 0.167), and the order of the hypoxic and control tests was randomly assigned. HR and SpO2 values were measured during the 60-min hypoxic or normoxic exposure.

After the 60-min exposure, the subjects then exited the chamber and put on a gas-analyzer facemask while sitting on the saddle of a cycle ergometer. Inhalation of a hypoxic gas mixture (FiO2 = 0.167) from a 200-L Douglas bag was started 7 min after the subjects exited the chamber. Hypoxic gas (FiO2 = 0.167) was continuously injected to the Douglas bag from a gas mixer of O2 and nitrogen (GB-2CS-SS; Kojima Instruments Inc., Kyoto, Japan). After 3-min inhalation of the hypoxic gas, the subjects started a 15-min incremental exercise test while continuing to inhale the hypoxic gas. The incremental exercise test was used in the present study because we were not sure whether the effects of short hypoxic pre-exposure on subsequent hypoxic exercise depended on exercise intensity. The workload was increased by (0.5 × body weight [kg]) W every 3 min (workloads 1-5). The absolute and relative values of the workloads were as follows: 29.9 ± 3.2 W and 24.6 ± 5.1% peak $\dot{V}O_2$ at workload 1, 59.9 ± 6.5 W and 35.8 ± 5.4% peak $\dot{V}O_2$ at workload 2, 89.8 ± 9.7 W and 47.1 ± 5.8% peak $\dot{V}O_2$ at workload 3, 120 ± 13 W and 58.3 ± 6.5% peak $\dot{V}O_2$ at workload 4, and 150 ± 16 W and 69.5 ± 7.4% peak $\dot{V}O_2$ at workload 5. The revolving speed of the cycle ergometer was kept at 60 rpm. HR, SpO2, $\dot{V}E$, $\dot{V}O_2$, and carbon dioxide production ($\dot{V}CO_2$) were measured continuously during exercise and blood lactate concentration (Lac) and rating of perceived exertion (RPE) were measured at the end of each workload. The laboratory and normobaric chamber were air-conditioned at a temperature of 24°C.

Physiological measurements. The analog signal of standard bipolar lead electrocardiography (ECG, Life Scope I; Nihon Koden Corporation, Tokyo, Japan) was processed with a data-acquisition system via an analog to digital converter (PowerLab; AD Instruments, Castle Hill, Australia) at a sampling rate of 1,000 Hz. From the digital ECG recordings, the R wave was detected and an instantaneous HR was calculated from the RR intervals. SpO2 was measured with a pulse oximeter (DDG-3100; Nihon Koden Corporation, Tokyo, Japan), the probe of which was attached to the middle finger of the right hand. SpO2 values were also processed with the data acquisition system (PowerLab, AD Instruments). The instantaneous HR and SpO2 values were averaged for every 10 min during the 60-min exposure in the chamber, for the last 1 min of the pre-test measurement, and for the last 30 s of each workload in the hypoxic incremental exercise and of the 3-min inhalation of hypoxic gas before starting exercise.

During the pre-test measurement and hypoxic exercise, respiration was analyzed using a gas analyzer (Aeromonitor AE-300S; Minato Medical Science, Osaka, Japan) with a breath-by-breath method. A two-way non-breathing valve was connected to the gas analyzer sensor attached to a facemask. During the hypoxic exercise, one end of a tube was connected to the intake side of the valve and the other end was connected to a Douglas bag containing a hypoxic gas mixture. $\dot{V}E$, $\dot{V}O_2$, and $\dot{V}CO_2$ were measured continuously and averaged for the last 1 min of the pre-test measurement, and for the last 30 s of each workload in the hypoxic incremental exercise and of the 3-min inhalation of hypoxic gas before starting exercise. To estimate the efficiency of ventilation, $\dot{V}E/\dot{V}O_2$ and $\dot{V}E/\dot{V}CO_2$ were calculated at each workload.

To measure Lac, approximately 5 μL of blood was obtained from the earlobe and analyzed with a portable blood lactate analyzer (Lactate Pro LT-1710; ARKRAY Inc., Kyoto, Japan) before the initiation of exercise and at the end of each workload during exercise. RPE at the end of each workload during exercise was measured using the Borg scale$^{29}$.

Statistical analysis. A paired t-test was performed to compare each of the cardiorespiratory indices assessed during the pre-test measurement between the hypoxic and control test days. Two-way analysis of variance (ANOVA;
Results

Resting cardiorespiratory conditions during pre-test measurement. All of the cardiorespiratory conditions assessed during the pre-test measurement were compared between the hypoxic and control test days. No significant differences were observed between the test days in HR (hypoxic test, 70.7 ± 10.5 bpm; control test, 71.1 ± 10.7 bpm), SpO₂ (hypoxic test, 97.5 ± 1.1%; control test, 97.2 ± 1.3%), and VE (hypoxic test, 8.66 ± 3.23 L·min⁻¹; control test, 8.59 ± 3.24 L·min⁻¹).

HR and SpO₂ during 60-min exposure. Table 1 shows the change in HR and SpO₂ during 60-min hypoxic and normoxic exposure. A two-way ANOVA test revealed no significant oxygen concentration, time, or interaction effects in HR, while it showed significant oxygen concentration (P < 0.001) and time (P < 0.001) effects in SpO₂. Post hoc tests showed significant differences (P < 0.001) between SpO₂ during hypoxic exposure and normoxic exposure for all 6 time ranges (1-10, 11-20, 21-30, 31-40, 41-50, and 51-60 min).

Physiological responses to hypoxic exercise. Fig. 2 and Table 2 demonstrate the physiological indices during incremental hypoxic exercise after exposure. Significant oxygen concentration effects were found in HR (P = 0.016), VE (P = 0.041), and RPE (P = 0.042). Significant interaction effects were found in VE (P = 0.020) and VCO₂ (P = 0.010). Post hoc tests showed a significant difference between HR after hypoxic exposure and normoxic exposure at workload 2 (P = 0.034). Significant intensity effects were found in all of the indices (HR, P < 0.001; SpO₂, P < 0.001; VE, P < 0.001; VO₂, P < 0.001; VCO₂, P < 0.001; VE/VO₂, P = 0.002; VE/VCO₂, P = 0.003; Lac, P = 0.001; RPE, P < 0.001).

Individual differences in hypoxic exposure effects. The peak VO₂ measured under normoxic conditions and LBM of our subjects were 40.1 ± 6.5 mL·kg⁻¹·min⁻¹ and 51.5 ± 5.6 kg, respectively. Peak VO₂ was significantly correlated with SpO₂ (r = -0.695, P = 0.008; Fig. 3), whereas no significant correlations were found between peak VO₂ and HR, VE, VO₂, VCO₂, VE/VO₂, VE/VCO₂, Lac, or RPE. A significant difference was found between the SpO₂ value at workload 5 in the three subjects with the highest peak VO₂ and that of the three subjects with the lowest peak VO₂.

Table 1. Heart rate and arterial oxygen saturation during 60 min of hypoxic and normoxic exposure.

<table>
<thead>
<tr>
<th></th>
<th>1-10 min</th>
<th>11-20 min</th>
<th>21-30 min</th>
<th>31-40 min</th>
<th>41-50 min</th>
<th>51-60 min</th>
<th>ANOVA</th>
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<tr>
<td>HR (bpm)</td>
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<tr>
<td>HE</td>
<td>70.4 ± 10.3</td>
<td>69.9 ± 8.5</td>
<td>70.9 ± 8.7</td>
<td>69.5 ± 8.4</td>
<td>70.8 ± 8.0</td>
<td>69.0 ± 7.2</td>
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<tr>
<td>NE</td>
<td>72.1 ± 10.3</td>
<td>70.9 ± 9.8</td>
<td>71.7 ± 9.1</td>
<td>71.0 ± 10.0</td>
<td>69.9 ± 10.7</td>
<td>71.8 ± 9.1</td>
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<tr>
<td>SpO₂ (%)</td>
<td>93.3 ± 1.2</td>
<td>93.3 ± 1.5</td>
<td>93.4 ± 1.3</td>
<td>93.9 ± 0.8</td>
<td>93.9 ± 0.9</td>
<td>94.1 ± 0.8</td>
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<tr>
<td>HE</td>
<td>97.1 ± 0.9</td>
<td>97.2 ± 0.8</td>
<td>97.5 ± 0.9</td>
<td>97.6 ± 1.0</td>
<td>97.7 ± 0.9</td>
<td>97.7 ± 0.9</td>
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<td>NE</td>
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The data are expressed as mean ± standard deviation. HR, heart rate; SpO₂, arterial oxygen saturation; HE, hypoxic exposure; NE, normoxic exposure; ANOVA, analysis of variance. * significant oxygen concentration effect; † significant time effect; ! significant difference between HE and NE judged by post hoc test. Statistical significance was judged as P < 0.05.
Discussion

In the present study, we investigated the effects of short pre-exposure to hypoxia on the physiological responses to subsequent hypoxic exercise and considered individual differences in the responses. Significant oxygen concentration effects were found in HR, $\dot{V}CO_2$, and RPE, and significant interaction effects were found in $\dot{V}E$ and $\dot{V}CO_2$. Meanwhile, the post hoc tests only showed a significant difference between HR after hypoxic exposure and normoxic exposure at workload 2. Thus, we could not clearly show the significant effects of hypoxic pre-exposure on physiological responses during hypoxic exercise.

Based on the data, significant oxygen concentration effects seem to be caused by lower HR, lower $\dot{V}CO_2$, and lower RPE during hypoxic exercise after hypoxic exposure. If these trends are confirmed to be significant by performing post hoc tests, short hypoxic pre-exposure will be shown to be advantageous for exercise under hypoxic conditions. In the present study, we used the absolute workloads for stepwise incremental exercise, which, as a result, produced a large variation in exercise intensity when they were expressed as a relative workload. For example, the range of relative workload at workload 5 was 57-81% peak $\dot{V}O_2$ measured in normoxia. If the relative workloads to the peak $\dot{V}O_2$, especially measured under hypoxic conditions, were used instead of absolute workloads, the large variation in the data might become smaller and the effects of hypoxic pre-exposure might be detected more clearly, especially in HR, $\dot{V}CO_2$, and RPE. To test this presumption, further studies should be undertaken using the relative workloads.

The present study showed a negative correlation between peak $\dot{V}O_2$ and SpO$_2$$_{HE/NE}$, indicating that those with a higher peak $\dot{V}O_2$ showed a greater decrease in SpO$_2$ during hypoxic exercise at workload 5 after hypoxic exposure than after normoxic exposure in our study population. The SpO$_2$ value per se at workload 5 after normoxic exposure tended to be smaller in subjects with a higher peak $\dot{V}O_2$ than those with a lower peak $\dot{V}O_2$. This trend is consistent with the fact that individuals with a high $\dot{V}O_2$max, such as endurance-trained athletes, have greater arterial desaturation during submaximal17,18) or maximal exercise16,17) under acute hypoxic conditions. Although the study population in the present study was not comprised of endurance-trained athletes but of individuals who had very low levels of aerobic fitness, the present study demonstrated for the first time that the greater arterial desaturation in individuals with relatively higher peak $\dot{V}O_2$ is accelerated after short hypoxic exposure. Studies have suggested that a decrease in SpO$_2$ during submaximal exercise can be induced by inadequate hyperventilation24,25) and/or ventilation-perfusion mismatches26,27), and that endurance-trained athletes have greater inadequate hyperventilation during submaximal hypoxic exercise than untrained subjects18. In the present study, $\dot{V}E/\dot{V}O_2$$_{HE/NE}$,
VE/VCO
2
HE/NE, and VE
2
HE/NE had no correlation with peak 
VO
2, indicating that the magnitude of changes in the efficiency and volume of ventilation due to short hypoxic exposure does not depend on the aerobic fitness level nor explain the greater decrease in SpO2 after hypoxic exposure in comparison with normoxic exposure. Moreover, the oxyhemoglobin dissociation curve could also have affected our study results. Studies29,30 have shown that individuals with a higher 
VO
2max because of endurance training have a right-shift in their oxyhemoglobin dissociation curves, indicating that oxygen dissociation from hemoglobin proceeds at a higher partial pressure of oxygen. Woorons et al.18 showed a small difference in SpO2 during submaximal exercise between trained and untrained subjects at an oxygen concentration of 17.3%, while the difference increased at an oxygen concentration of ≤15.4%. Involvement of the oxyhemoglobin dissociation curve was a suggested cause of this difference.

![Fig. 3 Correlation between peak 
VO
2 and effect of the hypoxic pre-exposure on SpO2 during subsequent hypoxic exercise.](image)

**Table 2. Hypoxic exercise after short exposure to hypoxia and normoxia.**

<table>
<thead>
<tr>
<th></th>
<th>rest</th>
<th>workload 1</th>
<th>workload 2</th>
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VO
2 (L·min⁻¹) | HE         | 0.366 ± 0.125 | 0.676 ± 0.093 | 1.00 ± 0.14 | 1.37 ± 0.20 | 1.71 ± 0.25 | 2.01 ± 0.34 | †    |
|               | NE         | 0.349 ± 0.124 | 0.676 ± 0.114 | 1.06 ± 0.17 | 1.38 ± 0.23 | 1.75 ± 0.29 | 2.12 ± 0.35 |       |
| 
VCO
2 (L·min⁻¹) | HE         | 0.305 ± 0.109 | 0.626 ± 0.123 | 0.959 ± 0.182 | 1.39 ± 0.25 | 1.81 ± 0.34 | 2.20 ± 0.42 | $, †, ‡ |
|               | NE         | 0.298 ± 0.096 | 0.610 ± 0.093 | 1.02 ± 0.13 | 1.43 ± 0.25 | 1.89 ± 0.31 | 2.35 ± 0.35 |       |
| VE/VCO
2 (L·L⁻¹) | HE         | 38.0 ± 9.3 | 30.3 ± 4.9 | 28.6 ± 3.7 | 29.4 ± 2.7 | 30.3 ± 3.1 | 32.7 ± 5.5 | †    |
|               | NE         | 39.1 ± 5.0 | 30.1 ± 3.7 | 29.4 ± 3.5 | 29.8 ± 3.7 | 31.3 ± 4.4 | 32.7 ± 4.9 |       |
| Lac (mmol·L⁻¹) | HE         | 1.03 ± 0.24 | 1.18 ± 0.42 | 1.33 ± 0.34 | 2.14 ± 0.80 | 3.56 ± 1.48 | 5.71 ± 2.00 | †    |
|               | NE         | 1.16 ± 0.36 | 1.21 ± 0.22 | 1.67 ± 0.37 | 2.52 ± 0.76 | 3.56 ± 1.28 | 5.91 ± 2.11 |       |
| RPE | HE         | 7.08 ± 1.68 | 8.58 ± 2.27 | 10.6 ± 2.6 | 12.4 ± 2.4 | 14.3 ± 2.1 | $, †       |
|               | NE         | 7.42 ± 1.78 | 9.17 ± 2.12 | 11.7 ± 1.7 | 13.5 ± 1.9 | 15.6 ± 2.0 |       |

The data are expressed as mean ± standard deviation. 
VO
2, oxygen uptake; 
VCO
2, carbon dioxide production; Lac, blood lactate concentration; RPE, rating of perceived exertion; HE, hypoxic exposure; NE, normoxic exposure; ANOVA, analysis of variance. $ significant oxygen concentration effect; † significant intensity effect; ‡ significant interaction effect. Statistical significance was judged as 
P < 0.05.
The oxygen concentration for the present study was set to 16.7%, which was between two oxygen concentration levels in Wooron’s study (15.4% and 17.3%). Therefore, a right-shift of the oxyhemoglobin dissociation curve may have affected the SpO2 levels in our study.

Although we did not have endurance-trained athletes among our study subjects, our results point to the involvement of peak VO2 in SpO2 during hypoxic exercise after hypoxic exposure. The decrease in SpO2 during hypoxic exercise could be accelerated in endurance-trained athletes after hypoxic exposure, which means that hypoxic pre-exposure could have a negative effect in endurance-trained athletes with regard to SpO2 values during hypoxic exercise. Further studies are needed to investigate the effects of hypoxic pre-exposure in endurance-trained athletes.

In conclusion, the present study examined the effects of short pre-exposure to hypoxia on the physiological responses to subsequent exercise in hypoxia. We could not clearly demonstrate the significant effects of short pre-exposure to hypoxia, but showed a correlation between peak VO2 and SpO2 response to hypoxic exercise after hypoxic exposure; those with relatively higher peak VO2 in our study population showed that the decrease in SpO2 was greater during hypoxic exercise after hypoxic exposure than after normoxic exposure. The experimental protocol used in the present study, including oxygen concentration, exposure duration, and exercise patterns, is one option. Because of the significant oxygen concentration effects in HR, V̇CO2, and RPE, as well as the significant interaction effects in V̇E and V̇CO2, in the present study, it is worthwhile to perform further studies using various oxygen concentrations and/or exposure durations and varying exercise intensities and/or durations to examine the effects of short hypoxic pre-exposure on subsequent hypoxic exercise.

**Conflict of Interests**

The authors declare that there is no conflict of interests regarding the publication of this article.

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