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## ORIGINAL RESEARCH

# Effect of hypobaria on maximal ventilation, oxygen uptake, and exercise performance during running under hypobaric normoxic conditions

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<https://doi.org/10.14814/phy2.14002>**Abstract**

During exposure to high altitude, hypoxia develops because of reductions in barometric pressure and partial pressure of O<sub>2</sub>. Although several studies have examined the effects of hypoxia on exercise performance and physiological responses, such as maximal minute ventilation ( $\dot{V}_{E\max}$ ) and maximal oxygen uptake ( $\dot{V}O_{2\max}$ ), how barometric pressure reduction (hypobaria) modulates them remains largely unknown. In this study, 11 young men performed incremental treadmill running tests to exhaustion under three conditions chosen at random: normobaric normoxia (NN; 763 ± 5 mmHg of barometric pressure, equivalent to sea level), hypobaric hypoxia (HH; 492 ± 1 mmHg of barometric pressure, equivalent to 3500 m above sea level (m a.s.l.)), and hypobaric normoxia (HN; 492 ± 1 mmHg of barometric pressure while breathing 32.2 ± 0.1% O<sub>2</sub> to match the inspiratory O<sub>2</sub> content under NN).  $\dot{V}_{E\max}$  was higher in HN than in NN (160.9 ± 10.7 vs. 150.7 ± 10.0 L min<sup>-1</sup>, *P* < 0.05). However, no differences in  $\dot{V}O_{2\max}$  and arterial oxyhemoglobin saturation were observed between NN and HN (all *P* > 0.05). Time to exhaustion was longer in HN than in NN (932 ± 83 vs. 910 ± 79 s, *P* < 0.05). These results suggest that reduced air density during exposure to an altitude of 3500 m a.s.l. increases maximal ventilation and extends time to exhaustion without affecting oxygen consumption or arterial oxygen saturation.

**Introduction**

Maximal oxygen uptake ( $\dot{V}O_{2\max}$ ) and endurance exercise performance decline with elevations in altitude because of reduced ambient partial O<sub>2</sub> pressure (Fulco et al. 1998; Derchak et al. 2000). Pulmonary ventilation increases exponentially with decreases in ambient partial O<sub>2</sub> pressure. This response partly counteracts reduced alveolar partial pressures of oxygen (P<sub>A</sub>O<sub>2</sub>) and thus, arterial oxyhemoglobin saturation (SaO<sub>2</sub>) (Calbet et al. 2003; Ogawa et al. 2007). Previous studies have demonstrated that individuals with greater increases in maximal minute

ventilation ( $\dot{V}_{E\max}$ ) under acute hypobaric hypoxia (HH) relative to normobaric normoxia (NN) showed smaller reductions in  $\dot{V}O_{2\max}$  (Marconi et al. 2004; Ogawa et al. 2007). Therefore, greater increases in ventilation during hypoxic exercise appear to be beneficial for minimizing reductions in  $\dot{V}O_{2\max}$ .

In most acute hypoxia studies, normobaric hypoxia (NH) condition is employed to investigate the influences of exposure to high altitude on physiological responses and exercise performance. However, whether HH and NH are physiologically equivalent remains debatable (Millet et al. 2012). For example, resting  $\dot{V}_E$  and SaO<sub>2</sub> tend to be

lower under HH conditions than under NH conditions (Coppel et al. 2015). Furthermore, Saugy et al. (2016) showed that the magnitude of the reduction in cycling performance was greater during exposures to HH compared to that with NH exposure (Coppel et al. 2015), which implied that the HH condition might be more detrimental to exercise performance and physiological responses.

Under HH condition (e.g., high-altitude exposure), air density, and therefore, air resistance, are lower than they are at sea level (Gautier et al. 1997). Thus, reductions in barometric pressure that are associated with acute high-altitude exposures could affect the physiological responses. Studies have demonstrated that breathing a helium–oxygen (He–O<sub>2</sub>) gas mixture, which could greatly reduce airflow resistance (Mink and Wood 1980; Papamoschou 1995), increases  $\dot{V}_{E_{\max}}$  during maximal exercise under hypoxic conditions relative to breathing non-He–O<sub>2</sub> under controlled conditions. Moreover, increases in  $\dot{V}O_{2\max}$  and  $\dot{V}_{E_{\max}}$  were observed by breathing He–O<sub>2</sub> compared to that with non-He–O<sub>2</sub> (Esposito and Ferretti 1997; Ogawa et al. 2010), even under the NN condition (Powers et al. 1986). Furthermore, the effect of hypobaric normoxia (HN) was explored in early studies (Cerretelli 1976; Marconi et al. 2004) of chronic high-altitude conditions with pure enriched O<sub>2</sub> gas mixture breathing. Those studies showed that  $\dot{V}O_{2\max}$  was higher in HN than in NN. Whether reduced air density in acute hypobaric conditions increases  $\dot{V}_{E_{\max}}$  and  $\dot{V}O_{2\max}$  in a similar manner to that observed with He–O<sub>2</sub> breathing and chronic HN remains to be determined.

Therefore, this study tested the hypothesis that acute hypobaria associated with exposure to the HH condition increases  $\dot{V}_E$  and  $\dot{V}O_{2\max}$ , thereby improving endurance exercise performance. Further, as a secondary purpose, we estimated whether hypobaria would lower the oxygen consumption of respiratory muscles. If reduced air density under hypobaric conditions could lower  $\dot{V}O_2$  in the respiratory muscles due to the decreased work of breathing, this might improve exercise performance. Similarly, Harms et al. (1997, 1998, 2000) reported that unloading the respiratory muscles' work during intensive exercise resulted in a greater distribution of the available cardiac output to the active locomotor muscles, thereby improving exercise tolerance with no change in  $\dot{V}O_2$ .

## Materials and Methods

### Ethical approval

This study was approved by the Human Subjects Committees of the University of Tsukuba in accordance with the guidelines set forth in the Declaration of Helsinki. All

participants provided verbal and written informed consent before participating in this study.

### Participants

Eleven healthy young men (age,  $24 \pm 4$  years; height,  $1.73 \pm 0.07$  m; body mass,  $63.3 \pm 4.8$  kg) including three physically active students and eight long- or middle-distance runners on the university track and field team participated in this study. All participants lived at low altitudes and had not been exposed to altitudes  $>1000$  m within the 6 months prior to the study.

### Incremental running test

Each participant performed an incremental running test to exhaustion in an environmental chamber (Shimazu Co. Ltd., Kyoto, Japan) under three conditions (performed randomly and on separate days): NN ( $20.9 \pm 0.1\%$  O<sub>2</sub> at  $763 \pm 5$  mmHg of barometric pressure, equivalent to sea level), HH ( $20.9 \pm 0.1\%$  O<sub>2</sub> at  $492 \pm 1$  mmHg of barometric pressure, equivalent to 3500 meters above sea level (m a.s.l.)), and hypobaric normoxia (HN;  $32.2 \pm 0.1\%$  O<sub>2</sub> at  $492 \pm 1$  mmHg of barometric pressure). The partial pressure of O<sub>2</sub> in NN and HN were matched (159 mmHg in both conditions), which enabled an assessment of the effects of reducing the barometric pressure without stimulating a hypoxic effect. The study room temperature was maintained at  $20.2 \pm 0.4^\circ\text{C}$  and was continuously ventilated to minimize increases in the CO<sub>2</sub> concentration in the air. Each participant performed self-selected warm-up exercises (stretching and jogging) outside the laboratory. The structure of the warm-up was similar in all three conditions. Thereafter, participants entered the environmental chamber. For the hypobaric conditions (i.e., HH and HN), the chamber was gradually decompressed to achieve a barometric pressure equivalent to that at 3500 m a.s.l. in 20 min. For safety reasons, we avoided rapid decompression of the chamber. Each running test began within 20 min after completing the decompression. Under all conditions, the participants breathed through a face mask that covered the nose and mouth. The mask was connected via low-resistance silicon pipes to a large reservoir bag. The incremental running test was performed on a treadmill at an inclination of  $0^\circ$ , which was maintained throughout the experiment. The initial running speed was set at 160 to 220 m/min, depending on the participant's running ability and was subsequently increased by 20 m/min every 2 min, such that 240 or 280 m/min was achieved within 15 min. Thereafter, the running speed was increased by 10 m/min every 1 min until exhaustion (Ogawa et al. 2007, 2010). When nearing  $\dot{V}O_{2\max}$ , the expired gas was collected in Douglas reservoir bags every 1 min.

## Mimic ventilation trial

As a secondary test, 10 of the 11 participants who completed the incremental running test subsequently participated in a mimic ventilation trial performed under NN and HH conditions (in random order) to determine the oxygen consumption of the respiratory muscles during the incremental running test. After obtaining 5-min baseline resting measurements in either NN or HH, the participants started a voluntary hyperventilation process while in the standing position. Since SaO<sub>2</sub> was 100% under HH conditions during the voluntary hyperventilation process, HH under the mimic ventilation trial was assumed to be the same as HN. The participants were instructed to reproduce the tidal volume (VT) and respiratory frequency (*f*<sub>R</sub>) observed at  $\dot{V}O_{2\max}$  under each condition for 7 min. VT and *f*<sub>R</sub> were adjusted to the target level using a computer that showed breath-by-breath measurements of VT and *f*<sub>R</sub>. During the mimic ventilation, 100% CO<sub>2</sub> was added to the inspiratory gas to maintain the end tidal pressure of CO<sub>2</sub> (P<sub>ET</sub>CO<sub>2</sub>) at normocapnic levels.

## Measurements

### Incremental running test

$\dot{V}O_2$ ,  $\dot{V}CO_2$ , and  $\dot{V}_E$  were calculated using the Douglas bag method. O<sub>2</sub> and CO<sub>2</sub> concentrations were measured using a mass spectrometer (ARCO1000; ARCO; Chiba, Japan), which was calibrated with a standardized gas of known composition (O<sub>2</sub>, 15.00%; CO<sub>2</sub>, 5.00%; and N<sub>2</sub>, balanced). The volume inside the bag was determined using a dry gas meter (DC-5A; Shinagawa; Tokyo, Japan), which was carefully calibrated with a 2-L syringe before the experiment. All participants accomplished two of the following three criteria for  $\dot{V}O_{2\max}$ : constant  $\dot{V}O_2$  despite increases in running speed (increase in <2.0 mL kg<sup>-1</sup> min<sup>-1</sup>); the respiratory quotient >1.1; maximal heart rate (HR<sub>max</sub>) achieved was >90% of the age-predicted value. Moreover, all participants reported a Borg scale of 20 and were not able to maintain the last-stage running speed despite strong verbal encouragement. We also measured expiratory O<sub>2</sub> and CO<sub>2</sub> fractions (F<sub>E</sub>O<sub>2</sub> and F<sub>E</sub>CO<sub>2</sub>) breath-by-breath using a mass spectrometer (ARCO1000). We estimated P<sub>A</sub>O<sub>2</sub> as:

$$PAO_2 = PIO_2 - (P_{ET}O_2/R),$$

where P<sub>I</sub>O<sub>2</sub> is the partial pressure of inspiratory O<sub>2</sub>, P<sub>ET</sub>O<sub>2</sub> is the end tidal O<sub>2</sub> pressure, and R is the respiratory quotient.

Alveolar ventilation ( $\dot{V}_A$ ) was calculated as:

$$\dot{V}_A = (\dot{V}O_2 \times R \times 0.863)/P_{ET}CO_2,$$

where P<sub>ET</sub>CO<sub>2</sub> is the end tidal CO<sub>2</sub> pressure. SaO<sub>2</sub> and heart rate (HR) were measured using a forehead pulse oximeter (N-595; Nellcor, Hayward, CA) and an HR monitor (Vantage NV; POLAR, Finland), respectively. In this study, time to exhaustion during incremental testing was used as an index of exercise performance.

### Mimic ventilatory test

Breath-by-breath F<sub>E</sub>O<sub>2</sub> and F<sub>E</sub>CO<sub>2</sub> and flow volume were determined using a mass spectrometer (ARCO1000) and a spirometer (MINATO AS300i; Minato Medical; Osaka, Japan), respectively. During voluntary hyperventilation,  $\dot{V}O_2$ ,  $\dot{V}_E$ , VT, and *f*<sub>R</sub> were calculated. The  $\dot{V}O_2$  of respiratory muscles ( $\dot{V}O_{2rm}$ ) was calculated by subtracting resting  $\dot{V}O_2$  from  $\dot{V}O_2$  recorded during the last 30 s of voluntary hyperventilation ( $\dot{V}O_{2vent}$ ). The mouth pressure was measured using a pressure transducer probe inserted into a mouthpiece and was reported at a sampling rate of 200 Hz. The peak inspiratory and expiratory mouth pressures (P<sub>I</sub>max and P<sub>E</sub>max) were determined during each respiratory cycle.

### Statistical analysis

Data are expressed as means ± standard deviations (SD). Variables obtained during the incremental exercise tests were analyzed using one-way repeated-measures analyses of variance with an experimental condition factor (NN, HH, and HN). After detecting the main effects, Fisher's least significant difference tests were performed as post hoc tests. Variables obtained during the mimic ventilatory test were analyzed using paired t-tests (NN vs. HN). *P* values < 0.05 were considered statistically significant. SPSS 24 (IBM Corp., Armonk, NY) was used for all statistical analyses.

## Results

### Incremental running test

Resting SaO<sub>2</sub> was similar for HN versus NN (98 ± 2% vs. 98 ± 2%).  $\dot{V}_{E\max}$  was 6.8% higher in HN than in NN (Table 1). As hypothesized,  $\dot{V}_{E\max}$  was higher (4.3%) in HN than in HH (Table 1). Similarly, *f*<sub>R</sub> was higher in HN than in HH (Table 1). Greater ventilation was not paralleled by greater  $\dot{V}O_{2\max}$  such that  $\dot{V}O_{2\max}$  was similar between HN and NN (Table 1). However, the time to exhaustion was longer in HN than in NN (Table 1). No difference in  $\dot{V}CO_{2\max}$  between NN and HN was noted.

**Table 1.** Variables measured at  $\dot{V}O_{2max}$ .

	NN	HH	HN
$\dot{V}O_{2max}$ [mL min <sup>-1</sup> ]	3974 ± 338	2860 ± 241*	4011 ± 327 <sup>†</sup>
$\dot{V}O_{2max}$ [mL kg <sup>-1</sup> min <sup>-1</sup> ]	63.0 ± 4.7	46.0 ± 5.6*	63.6 ± 5.6 <sup>†</sup>
$\dot{V}CO_{2max}$ [mL min <sup>-1</sup> ]	4580 ± 282	3506 ± 215*	4531 ± 327 <sup>†</sup>
$\dot{V}_{Emax}$ [L min <sup>-1</sup> ]	150.7 ± 10.0	154.2 ± 11.8	160.9 ± 10.6* <sup>†</sup>
$f_R$ [breaths min <sup>-1</sup> ]	68 ± 10	70 ± 10	73 ± 10* <sup>†</sup>
VT [L]	2.2 ± 1.03	2.25 ± 0.36	2.25 ± 0.3
$\dot{V}_E \dot{V}O_2^{-1}$ [ml ml <sup>-1</sup> ]	38.1 ± 3.6	54.3 ± 6.6*	40.4 ± 4.9* <sup>†</sup>
$\dot{V}_E \dot{V}CO_2^{-1}$ [ml ml <sup>-1</sup> ]	33.0 ± 3.1	44.0 ± 3.1*	35.6 ± 3.5* <sup>†</sup>
$\dot{V}_A$ [L min <sup>-1</sup> ]	101.8 ± 6.6	95.3 ± 10.0*	106.8 ± 8.6 <sup>†</sup>
$P_{ETCO_2}$ [mmHg]	39.2 ± 3.3	31.6 ± 3.9*	36.8 ± 3.5 <sup>†</sup>
$P_{AO_2}$ [mmHg]	128.5 ± 10.6	76.9 ± 3.5*	126.2 ± 4.2 <sup>†</sup>
SaO <sub>2</sub> [%]	91 ± 3	69 ± 4*	90 ± 5 <sup>†</sup>
HR <sub>max</sub> [beats min <sup>-1</sup> ]	195 ± 3	181 ± 8*	192 ± 8 <sup>†</sup>
Time to exhaustion [s]	910 ± 79	614 ± 73*	932 ± 83* <sup>†</sup>

Values are mean ± standard deviation ( $n = 11$ ).

NN: normobaric normoxia; HH: hypobaric hypoxia; HN: hypobaric normoxia;  $\dot{V}O_{2max}$ : maximal oxygen uptake;  $\dot{V}CO_{2max}$ : maximal carbon dioxide output;  $f_R$ : respiratory frequency; VT: tidal volume;  $\dot{V}_A$ : alveolar ventilation;  $P_{ETCO_2}$ : end tidal CO<sub>2</sub> pressure;  $P_{AO_2}$ : partial pressure of alveolar O<sub>2</sub>; SaO<sub>2</sub>: arterial oxyhemoglobin saturation; HR<sub>max</sub>: maximal heart rate.

\* $P < 0.05$  versus NN.

<sup>†</sup> $P < 0.05$  versus HH.

SaO<sub>2</sub> at the point of exhaustion did not differ between HH and HN and no difference in maximal HR<sub>max</sub> between NN and HN was observed (Table 1).

### Mimic ventilation trial

Table 2 and Figure 1 show the results of the mimic ventilation trials. The participants controlled their VT and  $f_R$  to achieve the level of  $\dot{V}_{Emax}$  in NN and HN. SaO<sub>2</sub> was 100 ± 0% in both HN and NN conditions.  $\dot{V}O_{2vent}$  was lower in HN than in NN.  $\dot{V}O_{2rm}$  was 23.1% lower in HN than in NN (5.7 ± 1.8 vs. 7.7 ± 2.0 mL kg<sup>-1</sup> min<sup>-1</sup>, respectively;  $P < 0.05$ ). Thus, the calculated percentage of  $\dot{V}O_{2rm}$  against whole-body  $\dot{V}O_{2max}$  was lower in HN than in NN (9.1 ± 3.4 vs. 12.4 ± 3.6%,  $P < 0.05$ ).  $P_{I_{max}}$  was 27.6% lower in HN than in NN.  $P_{E_{max}}$  was 23.2% lower in HN than in NN (Table 2).

### Discussion

To the best of our knowledge, this is the first study to assess the effects of reduced barometric pressure during acute hypobaric conditions on ventilatory and metabolic responses, as well as the effects on endurance exercise performance during maximal running exercise. The incremental running exercise was performed on separate days under NN (20.9 ± 0.1% O<sub>2</sub> at 763 ± 5 mmHg), HH (20.9 ± 0.1% O<sub>2</sub> at 492 ± 1.1 mmHg), and HN (32.2 ± 0.1% O<sub>2</sub> at 492 ± 1 mmHg) conditions.  $\dot{V}_{Emax}$  was higher in HN than in NN, although  $\dot{V}O_{2max}$  did not differ between HN

**Table 2.** Variables analyzed during the last 30 s of voluntary hyperventilation at rest.

	NN	HN	% change
$\dot{V}_E$ [L min <sup>-1</sup> ]	147.9 ± 11.9	158.1 ± 12.7*	6.9
$f_R$ [breaths min <sup>-1</sup> ]	68 ± 10	73 ± 11*	7.4
VT [L]	2.23 ± 0.28	2.24 ± 0.3	-0.2
$\dot{V}O_{2mimc}$ [mL kg <sup>-1</sup> min <sup>-1</sup> ]	12.19 ± 2.11	10.15 ± 1.66*	-15.5
$\dot{V}O_{2rest}$ [mL kg <sup>-1</sup> min <sup>-1</sup> ]	4.46 ± 0.84	4.48 ± 1.02	1.11
$\dot{V}O_{2vent}$ [mL kg <sup>-1</sup> min <sup>-1</sup> ]	7.73 ± 2.04	5.67 ± 1.80*	-23.1
% $\dot{V}O_{2max}$	12.4 ± 3.6	9.1 ± 3.4*	-23.4
SaO <sub>2</sub> [%]	100 ± 0	100 ± 0	0
$P_{I_{max}}$ [cmH <sub>2</sub> O]	8.98 ± 2.80	6.20 ± 2.00*	-27.6
$P_{E_{max}}$ [cmH <sub>2</sub> O]	-9.15 ± 2.11	-6.87 ± 1.59*	-23.2

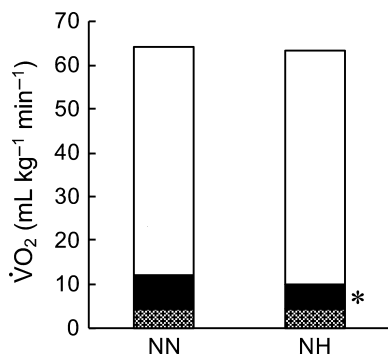
Values are mean ± standard deviation ( $n = 10$ ).

NN: normobaric normoxia; HN: hypobaric normoxia;  $\dot{V}_E$ : minute ventilation;  $f_R$ : respiratory frequency; VT: tidal volume;  $\dot{V}O_{2mimc}$ : oxygen uptake during mimic ventilation;  $\dot{V}O_{2rest}$ : oxygen uptake at rest;  $\dot{V}O_{2vent}$ : calculated  $\dot{V}O_2$  at respiratory muscles; % $\dot{V}O_{2max}$ : percentage occupation of  $\dot{V}O_{2vent}$  to  $\dot{V}O_{2max}$ ;  $P_{I_{max}}$ : peak inspiratory mouth pressure;  $P_{E_{max}}$ : peak expiratory mouth pressure.

\* $P < 0.05$  versus NN.

and NN. However, time to exhaustion was longer in HN than in NN. These results suggest that reduced air density associated with acute exposure to 3500 m a.s.l. increases ventilation and improves exercise performance without affecting whole-body aerobic metabolism.





**Figure 1.** Estimated oxygen consumption at  $\dot{V}O_{2max}$ . Grey area shows  $\dot{V}O_2$  at rest, the black area shows the  $\dot{V}O_2$  of the respiratory muscles, and the white area shows other tissues. NN, normobaric normoxia; HN, hypobaric normoxia. \* $P < 0.05$  versus NN.

Our results demonstrate that  $\dot{V}_{E_{max}}$  during maximal running is higher in HN than that in NN (Table 1), which could be attributed to reduced air resistance. Higher flow rates through the airways and alveolar branches occurring during maximal exercise often induce turbulent airflow, which is a factor that contributes to increased flow resistance (West 2005). Theoretically, air density would be  $0.83 \text{ kg m}^{-3}$  at 3500 m a.s.l. and  $1.20 \text{ kg m}^{-3}$  at sea level, indicating that flow resistance in the airways would be lower in HN than in NN. This ultimately may represent the underlying reason for the higher  $\dot{V}_{E_{max}}$  in HN. Our results also demonstrated that  $\dot{V}_E/\dot{V}O_2$  and  $\dot{V}_E/\dot{V}CO_2$  under HN were greater in comparison to those under NN, implying that air-flow resistance was altered by hypobaria.

Pulmonary ventilation exponentially increases with decreases in ambient partial pressures of  $O_2$ . As previously discussed, our results suggest that air decompression associated with exposure to HH could increase ventilation during exercise. The  $\dot{V}_{E_{max}}$  in HH was expected to be higher than that in the other two conditions as a consequence of hypoxia and air decompression. However, we observed that  $\dot{V}_{E_{max}}$  in HH was not different from that in NN and HN. The precise reason for this finding remains to be established. However, it may be attributable to the reduced absolute exercise intensity (running speed) at  $\dot{V}O_{2max}$  in HH relative to the other two conditions. Hence, greater ventilatory drive associated with the combination of hypoxia and air decompression is offset by a lower ventilatory drive associated with lower exercise intensity.

$SaO_2$  at maximal running in NN was 91% (Table 1), indicating that our participants developed exercise-induced arterial hypoxemia. Under the NN condition, any increase in oxygen supply due to increased ventilation appears to have increased  $SaO_2$  and  $\dot{V}O_{2max}$ . Although  $\dot{V}_{E_{max}}$  during maximal running was higher in HN than in

NN, neither  $SaO_2$  nor  $\dot{V}O_{2max}$  increased (Table 1). In contrast, Powers et al. (1986) reported that among individuals with exercise-induced arterial hypoxemia under NN, breathing He- $O_2$  resulted in increased  $\dot{V}O_{2max}$  and a 29% increase in  $\dot{V}_{E_{max}}$  during intense exercise. We also previously reported that in HH at 2500 m a.s.l., breathing He- $O_2$  increased  $\dot{V}O_{2max}$  and resulted in a 15.1% increase in  $\dot{V}_{E_{max}}$  (Ogawa et al. 2010). In the present study, the lack of effect from increased  $\dot{V}_E$  on  $SaO_2$  and  $\dot{V}O_{2max}$  under the HN condition could be due to a relatively smaller increase in  $\dot{V}_{E_{max}}$  (6.8%) relative to that experienced under the NN condition (previous studies utilizing He- $O_2$  gas showed a greater increase in  $\dot{V}_E$  of 15–29%). Moreover, this study demonstrated that the increase in  $\dot{V}_{E_{max}}$  was mainly caused by an increase in  $f_R$  without a measurable increase in VT. This result implies that a large portion of the increase in  $\dot{V}_{E_{max}}$  in HN relative to that in NN may have resulted from increased dead space with a minimal increase in alveolar ventilation. In fact,  $\dot{V}_A$  and  $P_{AO_2}$  were not different between HN and NN (Table 1). One might think that the reduced airway resistance associated with hypobaria would reduce turbulent airflow, thereby minimizing physiological dead space; however, this effect, if present, may have been overpowered by the rapid shallow breathing that occurred in HN.

The lack of effect of increased ventilation on  $\dot{V}O_{2max}$  in HN is in line with the estimations reported in previous studies. Regarding reduced air density, Esposito and Ferretti (1997) demonstrated that when  $\dot{V}_E$  increased with He- $O_2$  breathing,  $\dot{V}O_{2max}$  increased during He- $O_2$  breathing under hypoxic conditions, while  $\dot{V}O_{2max}$  did not increase under normoxic conditions. Although the air density in He- $O_2$  is greatly reduced compared to that in 3500 m a.s.l. hypobaria, our results under HN were consistent with the results of their normoxic He- $O_2$  breathing results. Further, as a limitation of  $\dot{V}O_{2max}$ , the ventilatory resistance that limits the flow of  $O_2$  from the atmosphere to the alveolar sacs could be analyzed using the multifactorial model proposed by di Prampero (2003). According to this model, the resistance imposed on  $O_2$  flow because of ventilatory resistance decreased by 13% under HN compared to that under NN (data not shown). If the resistance to  $O_2$  flow is altered, thereby changing  $\dot{V}O_{2max}$ , the fractional limitation to  $\dot{V}O_{2max}$  imposed by ventilatory resistance to  $O_2$  flow ( $F_v$ ) can be calculated. Ferretti and di Prampero (1995) reported that  $F_v$  was 5% under NN. The calculated  $F_v$  in the present study was 4%, which agrees closely with the estimations made by Ferretti and di Prampero (1995), implying that the contribution of  $\dot{V}_E$  was not a limiting factor for  $\dot{V}O_{2max}$  in NN among the participants in the current study.

Exercise performance based on the time to exhaustion was extended in HN compared with that in NN (Table 1).

This implies that reduced airway resistance associated with hypobaric exposure could improve endurance exercise performance. This may be counterintuitive, as  $\dot{V}O_{2\max}$  (aerobic energy supply) did not differ between HN and NN conditions in this study (Table 1). However, similar results were also reported by Marconi *et al.* (2004) with chronic hypobaric hypoxic exposure (5050 m a.s.l.). We do not know the exact mechanism by which reduced airway resistance under HH conditions improves endurance exercise performance without affecting  $\dot{V}O_2$ , but some insights could be gleaned from a previous work. Diaphragmatic fatigue during strenuous ventilation has been shown to increase the activity of sympathetic nerves that innervate muscles (Derchak *et al.* 2000). This results in reduced active muscle blood flow (Sheel *et al.* 2001).  $\dot{V}O_{2\text{rm}}$  comprises a significant portion of whole-body  $\dot{V}O_2$  because of hyperventilation that occurs during intense exercise (Aaron *et al.* 1992; Vella *et al.* 2006). Along these lines, Harms *et al.* reported that unloading the work of respiratory muscles because of inspiratory assistance during intensive exercise results in improved exercise tolerance with a greater distribution of the available cardiac output to active locomotor muscles with no increase in whole-body  $\dot{V}O_2$  (Harms *et al.* 1997, 1998, 2000). In our study,  $P_{\text{Imax}}$  and  $P_{\text{Emax}}$  were lower and  $\dot{V}_E$  was higher in HN compared with that in NN during the mimic ventilatory tests (Table 2). This suggests that air flow resistance during maximal exercise may be reduced because of reductions in air density associated with hypobaric exposure (3500 m a.s.l.). Further, decreased work during respiration was indirectly supported by our results. We demonstrated that the estimated  $\dot{V}O_{2\text{rm}}$  was lower under HN than under NN and that the estimated distribution of  $\dot{V}O_{2\text{rm}}$  was lower under HN than under NN (Table 2 and Fig. 1). These results suggest that the oxygen supply to active muscles was increased in exchange for reducing the oxygen consumption of the respiratory muscles. Therefore, this may improve exercise performance in HN compared with that in NN.

### Limitations

A limitation of this study was that participants knew the conditions under which they were exercising. We do not know if this might have affected our results and if so, to what extent. We assessed the influence of hypobaria by comparing responses between NN and HN conditions in the absence of hypoxia. Additional studies are required to elucidate whether hypobaria can modulate responses under hypoxic conditions. Our results also may have been different if a different exercise protocol had been employed. Finally, we did not directly assess airway

resistance. However, in the present study, we observed lower oral pressure and respiratory muscle  $\dot{V}O_2$  despite the fact that a higher  $\dot{V}_{E\max}$  was observed under HN compared with NN. Therefore, we believe that airway resistance was substantially reduced with exposure to HH. Moreover, had we employed a cycling model, we might have been able to assess the relationships between  $\dot{V}_E$  and  $\dot{V}O_2$  at a given work rate. This information would be helpful to evaluate whether respiratory efficiency would be altered under hypobaric conditions.

### Conclusion

We found that  $\dot{V}_{E\max}$  was higher and the time to exhaustion during incremental running was extended under HN compared with that in NN and there was no difference in  $\dot{V}O_{2\max}$ . This suggests that reduced air density under the hypobaric condition of 3500 m a.s.l. improved exercise performance without increasing aerobic energy supply, possibly because of a reduced oxygen supply to respiratory muscles and a concomitant increase in oxygen supply to active muscles.

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### Conflict of Interest

None.

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