Intermittent hypoxia increases ventilation and \( \text{SaO}_2 \) during hypoxic exercise and hypoxic chemosensitivity

KEISHO KATAYAMA,1 YASUTAKE SATO,1 YOSHIUMI MOROTOME,1 NORIHIRO SHIMA,1 KOJI ISHIDA,1 SHIGEO MORI,1 AND MIHARU MIYAMURA1

1Research Center of Health, Physical Fitness and Sports, and 2Space Medicine Research Center, Research Institute of Environmental Medicine, Nagoya University, Nagoya 464-8601, Japan

Received 5 October 2000; accepted in final form 2 November 2000

Katayama, Keisho, Yasutake Sato, Yoshifumi Morotome, Norihiro Shima, Koji Ishida, Shigeo Mori, and Miharu Miyamura. Intermittent hypoxia increases ventilation and \( \text{SaO}_2 \) during hypoxic exercise and hypoxic chemosensitivity. J Appl Physiol 90: 1431–1440, 2001.—The purpose of this study was 1) to test the hypothesis that ventilation and arterial oxygen saturation (\( \text{SaO}_2 \)) during acute hypoxia may increase during intermittent hypoxia and remain elevated for a week without hypoxic exposure and 2) to clarify whether the changes in ventilation and \( \text{SaO}_2 \) during hypoxic exercise are correlated with the change in hypoxic chemosensitivity. Six subjects were exposed to a simulated altitude of 4,500 m altitude for 7 days (1 h/day). Oxygen uptake (\( \text{Vo}_2 \)), expired minute ventilation (\( \text{Ve} \)), and \( \text{SaO}_2 \) were measured during maximal and submaximal exercise at 432 Torr before (Pre), after intermittent hypoxia (Post), and again after a week at sea level (De). Hypoxic ventilatory response (HVR) was also determined. At both Post and De, significant increases from Pre were found in HVR at rest and in ventilatory equivalent for \( \text{O}_2 \) (\( \text{Ve}/\text{Vo}_2 \)) and \( \text{SaO}_2 \) during submaximal exercise. There were significant correlations among the changes in HVR at rest and in \( \text{Ve}/\text{Vo}_2 \) and \( \text{SaO}_2 \) during hypoxic exercise during intermittent hypoxia. We conclude that 1 wk of daily exposure to 1 h of hypoxia significantly improved oxygenation in exercising during subsequent acute hypoxic exposures up to 1 wk after the conditioning, presumably caused by the enhanced hypoxic ventilatory chemosensitivity.

hypoxic ventilatory response; hypercapnic ventilatory response; altitude; arterial oxygen saturation

SEVERAL STUDIES HAVE INDICATED that hypoxic and hypercapnic ventilatory responses (HVR and HCVR, respectively), as indexes of ventilatory chemosensitivity to hypoxia and hypercapnia, correlate with ventilatory response to exercise in normoxia (16, 29, 39, 45) and that HVR correlates with ventilation and arterial oxygen saturation (\( \text{SaO}_2 \)) during hypoxic exercise (8, 45). Also, it has been reported that chronic exposure to hypoxia and sojourns at high altitude lead to increases in resting HVR accompanied by increases in pulmonary ventilation and \( \text{SaO}_2 \) at rest and during exercise in hypoxia (5, 18, 32, 46, 51, 56).

Similar to chronic exposure to hypoxia or a sojourn at high altitude, intermittent exposure to hypoxia with or without endurance exercise training using a hypobaric chamber has been utilized for preacclimatization before climbing to high altitude (9, 43, 44). When combining intermittent exposure to hypoxia with endurance exercise training, increases in HVR have been demonstrated in some (9, 21, 27) but not other (19) studies. However, there are few reports that have shown the changes in cardiorespiratory acclimatization during intermittent hypoxic exposure without endurance training. We previously found that resting HVR increased after short-term intermittent hypoxic exposure without endurance training (19). However, in that study, because we were unable to measure ventilation and \( \text{SaO}_2 \) during hypoxic exercise after intermittent hypoxia, it is unclear whether alterations of ventilation and \( \text{SaO}_2 \) during hypoxic exercise accompany the change in HVR.

Although the cardiorespiratory adaptations for altitude acclimatization have been reported by many investigators as mentioned above, physiological responses during deacclimatization have received little attention. Moreover, the measurements during deacclimatization have generally been performed only at low altitude. To elucidate the changes in cardiorespiratory response to hypoxic exercise during deacclimatization, Beidleman et al. (5) measured cardiorespiratory parameters during hypoxic exercise before and after deacclimatization to high altitude for 18 days (chronic hypoxic exposure) and 8 days after returning to sea level. They observed that a large degree of exercise responses associated with acclimatization was retained with reintroduction to altitude after 8 days at sea level [i.e., increases in ventilation and \( \text{SaO}_2 \) and a decrease in heart rate (HR)]. However, there are no available data concerning the influence of deacclimatization after intermittent hypoxic exposure on physiological responses in humans, except our previous study that indicated that increased HVR after 6 days of intermittent hypoxia was retained for 1 wk (19). If HVR is related to exercise ventilation and \( \text{SaO}_2 \) in...
hypoxia as proposed by previous studies (8, 45, 46), it is possible to hypothesize that increases in ventilation and SaO$_2$ during hypoxic exercise occur during short-term intermittent hypoxia and that increased ventilation and SaO$_2$ during hypoxic exercise after intermittent hypoxic exposure may also be retained for at least 1 wk.

The primary purpose of this study, therefore, was to test the hypothesis that ventilation and SaO$_2$ during hypoxic exercise may increase after short-term intermittent hypoxia and that these increases may remain for a week without hypoxic exposure. The secondary purpose was to clarify whether the changes in ventilation and SaO$_2$ during hypoxic exercise are correlated with the change in resting ventilatory chemosensitivity. For this purpose, we determined cardiorespiratory parameters during hypoxic exercise and resting ventilatory response to hypoxia and hypercapnia at sea level before and after intermittent hypoxic exposure.

**METHODS**

**Subjects.** Six healthy men with no history of cardiorespiratory diseases volunteered to participate in this study. Their physical characteristics are shown in Table 1. The subjects were informed of the experimental procedures and possible risks involved in the present study, and their informed consent was obtained. This study was approved by the Human Research Committee of the Research Center of Health, Physical Fitness and Sports of Nagoya University.

**Experimental procedures.** The time course of experimental procedures in the present study is presented in Fig. 1. Subjects were familiarized with the equipment used in this experiment at sea level and the hypobaric chamber. Before the intermittent exposure to altitude (Pre), the maximal exercise test was conducted at sea level (Fig. 1). The measurements of resting ventilatory chemosensitivity at sea level and maximal and submaximal exercise tests at 432 Torr in the hypobaric chamber (simulating an altitude of 4,500 m) were performed at P1 and P2 (Fig. 1), respectively (resting ventilatory chemosensitivity tests were always made before the exercise test). The same hypobaric chamber used in our previous studies (19–21) was utilized for the exercise test and for intermittent hypoxic exposure. The barometric pressure in the chamber was lowered to 432 Torr over a 30-min period and then held at that level for the next hour. For the maximal and submaximal exercise tests, the testing began within the first 0.5 h at 432 Torr. The subjects completed the self-assessment portion of the Lake Louise Consensus Questionnaire (15) each day doing the 7-day intermittent hypoxic exposure (D1 to D7, Fig. 1). The measurements of resting ventilatory chemosensitivity at sea level and the maximal and submaximal exercise tests at 432 Torr were performed after the intermittent hypoxic exposure (Post; D8 and D9). These measurements were taken again after the subjects had been away from hypoxic exposure for 1 wk (D15 and D16) as shown in Fig. 1.

**Maximal exercise test.** Maximum oxygen uptake (V$\dot{O}_2$ max) at sea level in each subject was determined only at Pre. The V$\dot{O}_2$ max at 432 Torr in a hypobaric chamber was measured at Pre (P1), Post (D8), and again at De (D15) as shown in Fig. 1. The measurement of V$\dot{O}_2$ max was conducted the same way as in our previous study (20). To measure V$\dot{O}_2$ max, an incremental protocol on an electromechanically braked bicycle ergometer was used at sea level and a mechanically braked bicycle ergometer (Monark) was used in the chamber. The maximal exercise test began at an initial power output of 60 W, and the workload was increased 30 W every 2 min until exhaustion. The pedaling rate was kept constant at 60 rpm with the aid of a metronome. During the test, expired gases were collected into a Douglas bag during the last 30 s of each intensity level until exhaustion.Expired minute ventilation (V$\dot{E}$, BTPS) was measured with a wet-gas meter (model 10

**Table 1. Physical characteristics and cardiorespiratory parameters of subjects at exhaustion at sea level**

<table>
<thead>
<tr>
<th>Age, yr</th>
<th>Height, cm</th>
<th>Weight, kg</th>
<th>V$\dot{O}_2$ max, l/min</th>
<th>V$\dot{O}_2$ max/BW, ml·kg$^{-1}$·min$^{-1}$</th>
<th>V$\dot{E}$ max, l/min</th>
<th>HR$\text{max}$, beats/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>21.5 ± 3.6</td>
<td>169.2 ± 3.6</td>
<td>63.4 ± 3.7</td>
<td>3.59 ± 0.34</td>
<td>56.6 ± 5.7</td>
<td>156.6 ± 23.9</td>
<td>190.7 ± 7.2</td>
</tr>
</tbody>
</table>

Values are means ± SD. V$\dot{O}_2$ max, maximal oxygen uptake; V$\dot{O}_2$ max/BW, V$\dot{O}_2$ max per kilogram of body weight; V$\dot{E}$ max, maximal expired minute ventilation; HR$\text{max}$, maximal heart rate.

![Fig. 1. Time course of the experiment. The measurements were performed before (Pre; P1 and P2) and after (Post; D8 and D9) intermittent hypoxia and again after 1 wk without hypoxic exposure (De; D15 and D16). HVR, hypoxic ventilatory response; HCVR, hypercapnic ventilatory response using the CO$_2$- rebreathing method; HCVRSB, hypercapnic ventilatory response using the single-breath CO$_2$- rebreathing method.](http://jap.physiology.org/)
liter, Shinagawa). Gas analysis was performed by means of an O₂ and CO₂ analyzer (model MG-360, Minato Ikagaku). HR was continuously recorded by a three-lead electrocardiogram (model OEC-6401, Nihon Koden) throughout the test. SaO₂ was measured by a finger pulse oximeter (model OLV-1200, Nihon Koden) throughout the test in the depressurized chamber. The accuracy of SaO₂ estimated by this oximeter has been proven by a previous study that compared SaO₂ assessed by the OLV-1200 with that determined directly from arterial blood (2). The maximal minute ventilation (Ve max) and the maximal HR value (HR max) were also measured. Oxygen uptake (Vo₂) derived during maximal exhaustive exercise was considered to be Vo₂ max when two of the following three criteria were satisfied: identification of a plateau in Vo₂ with an increase in power output (<150 ml Vo₂ increase), HR ± 10% of age-predicted maximum (220 – age), and respiratory exchange ratio (RER) ≥ 1.0 (7, 20).

Submaximal exercise test. Vo₂ in each subject during the submaximal exercise test was determined at Pre (P1), Post (P2), and De (P3) at 432 Torr in a hypobaric chamber as shown in Fig. 1. Before the submaximal exercise test, Vo₂ and carbon dioxide output (VCO₂), Ve, HR, and SaO₂ at rest were measured at 432 Torr in the chamber. Then, each subject exercised using the bicycle ergometer at 40% of his Vo₂ max at altitude for the first 10 min and 70% of his Vo₂ max at altitude from the 10th to the 20th min at 432 Torr (each intensity was calculated by Vo₂ max at 432 Torr on each preceding day). HR and SaO₂ were measured throughout the submaximal exercise test, and the mean value was obtained during the last minute of each exercise level. Expired gases were collected in a Douglas bag during the last minute of each exercise intensity, and Vo₂, VCO₂, RER, and Ve were determined using the same system as in the maximal exercise test mentioned above.

HVR. HVR measurements were performed at P1, D8, and D15 at sea level (Fig. 1). Resting HVR was determined by using a progressive isocapnic hypoxic test (54). A rebreathing system similar to that in our previous studies (19–21) was used. Tidal volume (VT), inspired minute ventilation (V˙I), end-tidal CO₂ and O₂ fraction (PETCO₂ and PETO₂, respectively), and SaO₂ were measured continuously during rebreathing. The subjects breathed through a mouthpiece attached to a hot-wire flowmeter (model RF-H, Minato Ikagaku). Sample gas was drawn through a sampling tube connected to the mouthpiece to measure PETCO₂ and PETO₂ by using gas analyzer (model MG-360, Minato Ikagaku), and end-tidal partial pressure of CO₂ and O₂ (PETCO₂ and PETO₂, respectively) were calculated from FETCO₂ and FETO₂. PETCO₂ was maintained within ±2 Torr of the resting level during measurement. SaO₂ was measured by means of a finger pulse oximeter (model OLV-1200, Nihon Koden). The signals from the flowmeter, gas analyzer, and pulse oximeter were sampled at a frequency of 100 Hz through an analog-to-digital converter (model ADX-98H, Canopus) and stored in a computer (model PC-9821XA, NEC). HVR was estimated as the slope of the line calculated by the linear regression relating Vt to SaO₂ (ΔVt/ΔSaO₂, where Δ is change; in l·min⁻¹·Torr⁻¹), and the slope was presented as positive numbers by convention.

HCVR. To assess central and peripheral chemosensitivities to hypercapnia, resting HCVR was determined by two methods: the CO₂-rebreathing (HCVR) and the single-breath CO₂ (HCVR sb) methods. The measurements of HCVR and HCVR sb were also similar to that of our previous study (20). HCVR measurements were determined at P1, D8, and D15 at sea level, whereas HCVR sb measurements were performed at P2, D9, and D16 (Fig. 1). In the rebreathing method, subjects rebreathed a gas mixture of 7% CO₂ in O₂ from a bag (5–6 liters) in a plastic box for 3–4 min (38). Vt and PETCO₂ were recorded in the same computer used in the HVR test. HCVR was assessed as the slope of the line determined by the linear regression relating PETCO₂ to Vt (ΔVt/ΔPETCO₂; in l·min⁻¹·Torr⁻¹). On the other hand, the single-breath CO₂ test was used for the evaluation of peripheral chemoreceptor response to CO₂ (HCVR sb) according to the protocol described by McClean et al. (31); i.e., application of a single CO₂ mixture composed of 13% CO₂-21% O₂-66% N₂ was repeated six to eight times with 2-3 min intervals for each subject. The apparatus consisted of a bag-in-box circuit similar to that used for the CO₂-rebreathing test. The subjects were seated comfortably in a chair and began breathing room air through a mouthpiece with a nose clip. The T valve was attached between the bag and the mouthpiece, and the port was connected to either room air or a bag containing the test gas. To avoid the possibility that the maneuver for administering the different gases was noticed by the subjects, a screen was placed between the subject and the T valve. During testing, Vt, VT, FETCO₂, and inspired time (t) were recorded continuously. When stable levels of PETCO₂ and Vt were achieved, the inspiratory gas was switched from room air to the bag for a single tidal breath by turning the T valve during the expiratory phase of the previous breath. During the expiratory phase of the test breath, the T valve was turned back again to the first air position. Data for analyzing HCVR sb were limited to breaths within the first 20 s, after transients of hypercapnia, to exclude contribution of the central CO₂ chemoreceptors to the response. HCVR sb was quantitated in a manner similar to that suggested by Khoo (22) (and expressed in units of ml·s⁻¹·Torr⁻¹): first, the changes in Vt/ΔVt (ΔVt/ΔTorr) and PETCO₂ (ΔPETCO₂) for a given breath after individual transients was computed; second, ΔPETCO₂ was corrected by means of correction formula by Khoo; then the six to eight measurements of ΔVt/ΔTorr and ΔPETCO₂ were averaged, respectively; and finally, the averaged ΔVt/ΔTorr was divided by the averaged ΔPETCO₂ to assess the ΔVt/ΔPETCO₂ for each subject.

Statistical analysis. Values are expressed as means ± SD. The changes in all parameters during the experimental periods were analyzed using one-way ANOVA with repeated measurements. Differences in the parameters at each session (Pre, Post, and De) were determined by using the Tukey’s honestly significant difference test. The relationships among the parameters were determined by simple linear regression analysis. The SPSS statistical package was used for these analyses. The level of significance was set at 0.05.

RESULTS

Baseline descriptive data. Table 1 indicates Vo₂ max, Ve max, and HR max at exhaustion during the maximal exercise test at sea level before intermittent hypoxic exposure. At D1 and D2 of intermittent hypoxic exposure, two of the subjects had slight headaches, fatigue, and/or weakness at 432 Torr, but thereafter there was a score of zero for the Lake Louise Consensus Questionnaire for intermittent hypoxic exposure.

Maximal exercise test. Table 2 and Fig. 2A demonstrate that there were no changes in Vo₂ max, VCO₂ max, Ve max, ventilatory equivalent for O₂ (Ve/VO₂), RER, and HR max determined at 432 Torr throughout the
shown in Fig. 2 at Post (D8) and remained at that level at De (D15) as (SaO₂; Fig. 2. Ventilatory equivalents for O₂ [expired minute ventilation experimental periods. On the other hand, SaO₂ at exhaustion at 432 Torr increased significantly (P < 0.05) at Post (D8) and remained at that level at De (D15) as shown in Fig. 2B.

Submaximal exercise test. Cardiorespiratory parameters obtained at rest and during the submaximal exercise test in the hypobaric chamber are presented in Table 2 and Fig. 2.

At rest in the chamber at 432 Torr, VO₂, VCO₂, RER, and HR did not show any changes at Pre (P2), Post (P9), and De (P13). Resting Ve and Ve/VO₂ at 432 Torr significantly (P < 0.05) at Post, and they remained at that level at De. Similarly, resting SaO₂ at 432 Torr showed a significant (P < 0.05) increase at Post compared with that at Pre, and it remained at that level at De as shown in Fig. 2B.

VO₂ and workload did not show significant changes at Pre, Post, and De at both 40 and 70% of VO₂ max exercise levels (Table 2). Ve and Ve/VO₂ at Post increased significantly (P < 0.05) at 40 and 70% of VO₂ max levels compared with those at Pre, and these variables remained at those levels at De (Table 2, Fig. 2A). As shown in Fig. 2B, SaO₂ at 40 and 70% of VO₂ max also showed significant (P < 0.05) increases at Post, and these increased levels of SaO₂ were retained at De. VO₂, RER, and HR did not change at 40 and 70% of VO₂ max throughout the experimental period (Table 2).

HVR. Tested at sea level, resting Vi, respiratory frequency (f), PetO₂, and PetCO₂ did not show any changes throughout the experimental period as shown in Table 3. Figure 3A indicates the changes in the ∆Vi/∆SaO₂. A significant (P < 0.05) increase in the ∆Vi/∆SaO₂ (l·min⁻¹·%⁻¹) was found at Post, and the increased ∆Vi/∆SaO₂ remained at De. A of the Vi-PetO₂ curve also increased at Post and De compared with that at Pre [113.9 ± 50.6 (Pre), 195.7 ± 83.9 (Post), and 191.5 ± 88.3 (De) l·min⁻¹·Torr⁻¹].

HCVRSB. As shown in Fig. 3C, HCVRSB increased significantly (P < 0.05) after intermittent hypoxic ex-

Table 2. Cardiorespiratory responses at rest, at 40 and 70% of VO₂ max, and at exhaustion at 432 Torr in a hypobaric chamber before, after, and 1 wk after intermittent hypoxic exposure

<table>
<thead>
<tr>
<th>Workload, W</th>
<th>VO₂, l/min</th>
<th>VCO₂, l/min</th>
<th>Ve, l/min</th>
<th>RER</th>
<th>HR, beats/min</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>De</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest</td>
<td>54.0 ± 7.6</td>
<td>53.0 ± 8.0</td>
<td>54.5 ± 6.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40</td>
<td>0.28 ± 0.04</td>
<td>0.27 ± 0.03</td>
<td>0.26 ± 0.03</td>
<td></td>
<td></td>
</tr>
<tr>
<td>70</td>
<td>1.68 ± 0.20</td>
<td>1.70 ± 0.17</td>
<td>1.67 ± 0.16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max</td>
<td>2.37 ± 0.24</td>
<td>2.38 ± 0.22</td>
<td>2.34 ± 0.51</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10.4 ± 2.1</td>
<td>12.8 ± 2.0*</td>
<td>13.2 ± 2.1*</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.80 ± 0.05</td>
<td>0.83 ± 0.04</td>
<td>0.81 ± 0.05</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>150.6 ± 9.9</td>
<td>153.6 ± 9.6</td>
<td>153.4 ± 12.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.20 ± 0.06</td>
<td>1.22 ± 0.06</td>
<td>1.20 ± 0.11</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post</td>
<td>0.24 ± 0.08</td>
<td>0.22 ± 0.04</td>
<td>0.22 ± 0.03</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40</td>
<td>0.81 ± 0.19</td>
<td>0.83 ± 0.09</td>
<td>0.79 ± 0.10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>70</td>
<td>1.79 ± 0.30</td>
<td>1.72 ± 0.21</td>
<td>1.74 ± 0.18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max</td>
<td>2.85 ± 0.28</td>
<td>2.89 ± 0.29</td>
<td>2.80 ± 0.44</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>37.2 ± 6.6</td>
<td>43.7 ± 8.6*</td>
<td>42.0 ± 8.2*</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.91 ± 0.05</td>
<td>0.91 ± 0.02</td>
<td>0.88 ± 0.03</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>155.8 ± 2.9</td>
<td>154.1 ± 5.8</td>
<td>157.9 ± 7.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>175.8 ± 7.7</td>
<td>177.7 ± 8.8</td>
<td>177.7 ± 8.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>De</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest</td>
<td>54.0 ± 7.6</td>
<td>54.5 ± 6.1</td>
<td>54.5 ± 6.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40</td>
<td>0.28 ± 0.04</td>
<td>0.26 ± 0.03</td>
<td>0.26 ± 0.03</td>
<td></td>
<td></td>
</tr>
<tr>
<td>70</td>
<td>1.68 ± 0.20</td>
<td>1.67 ± 0.16</td>
<td>1.67 ± 0.16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max</td>
<td>2.37 ± 0.24</td>
<td>2.34 ± 0.51</td>
<td>2.34 ± 0.51</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10.4 ± 2.1</td>
<td>13.2 ± 2.1*</td>
<td>12.2 ± 2.1*</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.80 ± 0.05</td>
<td>0.81 ± 0.05</td>
<td>0.81 ± 0.05</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>150.6 ± 9.9</td>
<td>153.6 ± 9.6</td>
<td>153.4 ± 12.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.20 ± 0.06</td>
<td>1.22 ± 0.06</td>
<td>1.20 ± 0.11</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Values are means ± SD. VO₂, oxygen uptake; VCO₂, carbon dioxide output; Ve, expired minute ventilation; RER, respiratory exchange ratio; HR, heart rate; Pre, before intermittent hypoxic exposure; Post, after intermittent hypoxic exposure; De, after 1 wk at sea level; 40, 40% of VO₂ max; 70, 70% of VO₂ max; max, at exhaustion. *Significantly different from Pre, P < 0.05.

Fig. 2. Ventilatory equivalents for O₂ [expired minute ventilation (Ve)/oxygen uptake (VO₂); A] and arterial oxygen saturation (SaO₂; B) at rest, at 40 and 70% of VO₂ max, and at exhaustion (max) at 432 Torr measured at Pre, Post, and De. Values are means ± SE. *Significantly different from Pre, P < 0.05.
Significant correlations were observed among $\dot{V}E/\dot{V}O_2$, and $d$ inspired minute ventilation; $f$, respiratory frequency; $PETCO_2$, end-tidal partial pressure of $O_2$; $PETO_2$, end-tidal partial pressure of $CO_2$.

There were significant correlations among absolute values of $V\dot{E}/V\dot{O}_2$ and $SaO_2$ at 40 and 70% of exposure; and $5^d$ not; $4^d$ increased level for 1 wk after cessation of hypoxic exposure for 7 consecutive days (Post). However, a significant loss of HCVR$_{SB}$ occurred 1 wk later (De).

Relationships among parameters during intermittent hypoxic exposure. Table 4 presents the correlation matrix among absolute values of resting HVR at sea level and $V\dot{E}/V\dot{O}_2$ and $SaO_2$ at rest and during exercise at 432 Torr at Pre and Post. There were significant correlations among HVR at rest, $V\dot{E}/V\dot{O}_2$ and $SaO_2$ at rest and during submaximal exercise at 432 Torr, but not among HVR at rest, $V\dot{E}/V\dot{O}_2$ and $SaO_2$ during maximal exercise. There were no significant relationships between HCVR or HCVR$_{SB}$ at rest for either $V\dot{E}/V\dot{O}_2$ or $SaO_2$ at rest or during exercise in hypoxia.

To compare among parameters during intermittent hypoxia in detail, the magnitude of changes in $V\dot{E}/V\dot{O}_2$ and $SaO_2$ at rest and during exercise ($dV\dot{E}/dV\dot{O}_2$ and $dSaO_2$) at 432 Torr and resting ventilatory responses to hypoxia ($dHVR$) and hypercapnia ($dHCVR$ and $dHCVR_{SB}$) at sea level were calculated individually as the difference between those obtained before and after intermittent exposure to altitude ($d = Post - Pre$). Significant correlations were observed among $dHVR$, $dV\dot{E}/dV\dot{O}_2$, and $dSaO_2$ at rest and at 40 and 70% of $V\dot{O}_2$ max exercise as shown in Table 5. However, no significant correlations among $dHVR$, $dV\dot{E}/dV\dot{O}_2$, and $dSaO_2$ at exhaustion were found. There were no significant relationships between $dHCVR$ or $dHCVR_{SB}$ for either $dV\dot{E}/dV\dot{O}_2$ or $dSaO_2$ at rest or during exercise in the hypobaric chamber during intermittent hypoxic exposure.

**DISCUSSION**

In the present study, we found that 1) ventilation and $SaO_2$ at rest and during exercise at light and moderate levels at 432 Torr in the hypobaric chamber (equivalent to 4,500 m altitude) increased significantly after 1 wk of intermittent hypoxic exposure; 2) increased ventilation and $SaO_2$ at rest and during submaximal exercise in hypoxia remained stable at this increased level for 1 wk after cessation of hypoxic exposure; 3) HVR and HCVR$_{SB}$ also showed significant increases after intermittent hypoxic exposure and increased HVR remained for 1 wk, whereas HCVR$_{SB}$ did not; 4) HCVR did not change after intermittent hypoxic exposure; and 5) significant correlations exist among absolute values of $V\dot{E}/V\dot{O}_2$ and $SaO_2$ at 40 and 70% of $V\dot{O}_2$ max exercise at 432 Torr and HVR at sea level and among $dV\dot{E}/dV\dot{O}_2$ and $dSaO_2$ during submaximal exercise at 432 Torr and $dHVR$ during intermittent hypoxic exposure, respectively.

**Acclimatization to intermittent hypoxia.** The earliest and most obvious response and adaptation of the sojourner to high altitude is an increase in ventilation (4, 7, 32, 35, 51), accompanied by hypocapnia and elevating alveolar and arterial oxygenation. This increasing ventilation in hypoxia may be advantageous for performance at altitude and prevents acute mountain sickness and high-altitude pulmonary edema (23, 33, 46). It is also well known that HVR, as an index of ventilatory chemosensitivity to hypoxia, increases during varying durations of continuous stays at altitude (11, 42, 47, 55) and that HVR at sea level is closely related to ventilation and $SaO_2$ during hypoxic exercise and performance at high altitude (8, 30, 45, 46). As described previously, Schoene et al. (46) studied the relationships among HVR at sea level, exercise ventilation, and $O_2$ saturation during acclimatization to high altitude. They indicated that HVR at sea level positively correlated with ventilation during exercise at altitude after acclimatization and suggested that a high HVR is one of the factors that minimizes $O_2$ desaturation at high altitude during acclimatization. Although there are many studies that have reported respiratory and cardiovascular responses during chronic hypoxic exposure or sojourns at altitude, the
effects of intermittent exposure to altitude on cardio-
respiratory parameters at rest and during exercise
have had little attention. In our previous study (19), it
was revealed that intermittent hypoxic exposure for 6
consecutive days elicited an increase in HVR at sea
level. Thus we hypothesized that intermittent expo-
sure to hypoxia for a short period also leads to in-
creases in ventilation and SaO2
during hypoxic exercise
as well as chronic hypoxic exposure as demonstrated
by Schoene et al (46). One of the purposes of the
present study was to test this hypothesis.

After intermittent hypoxic exposure for 1 wk, V˙O2 max
at 432 Torr did not change throughout the experiment (Table 2). This result concurs with the data showing
that either chronic (5, 32, 51, 56, 57) or intermittent
(40) exposure to altitude showed no effect on V˙O2 max
in hypoxia. Because V˙O2 at 40 and 70% of V˙O2 max at 432
Torr also did not change at Pre, Post, and De as shown
in Table 2, it is possible to compare cardiorespiratory
responses during hypoxic exercise throughout the ex-
perimental period.

During acclimatization to high altitude, an increase
in ventilation at rest has been well reported by numer-
ous studies that used chronic (4, 7, 18, 35) or intermit-
tent hypoxic exposure (36, 43). In the present study,
our data agree with these prior reports in which inter-
mittent hypoxic exposure led to an increase in V˙E/V˙O2
at rest at 432 Torr as shown in Fig. 2A. V˙E/V˙O2 at 40
and 70% of V˙O2 max exercise workloads also increased
significantly (P < 0.05) after 7 days of intermittent
hypoxic exposure (Post) as we had expected. V˙E/V˙O2 at
exhaustion in a hypobaric chamber tended to increase,
but not significantly, after intermittent hypoxic expo-
sure (Post) (Fig. 2A). Savourey et al. (43) reported that
exercise ventilation at light or moderate levels at 4,500
m increased significantly after intermittent exposure
to altitude. In addition, other studies have shown that
exercise ventilation at a modest level of exercise and at
exhaustion was elevated after chronic exposure to high
altitude (4, 5, 7, 32, 57). These observations are in
agreement with those of the present study. Overall,
these results suggest that short-term intermittent hy-
poxic exposure also leads to increases in ventilation at
light and moderate exercise levels in hypoxia as well as
chronic hypoxic exposure.

Resting ventilation at 432 Torr increased significantly
after intermittent hypoxia, whereas resting V˙i, f, PetO2,
and PetCO2 at sea level did not change as shown in Table
3. It has been demonstrated that an increase in V˙e and
a decrease in PetCO2 persist on return to sea level after an
altitude sojourn (4, 35). In contrast, several studies have
indicated that resting V˙e, PetO2, PetCO2, and pH did

### Table 4. Correlation matrix among absolute values of resting HVR at sea level and the V˙E/V˙O2
and SaO2 at rest and during exercise at 432 Torr at Pre and Post

<table>
<thead>
<tr>
<th></th>
<th>HVR</th>
<th>V˙E/V˙O2</th>
<th>SaO2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rest</td>
<td>40%</td>
<td>70%</td>
</tr>
<tr>
<td>HVR</td>
<td>1.00</td>
<td>0.75*</td>
<td>0.79*</td>
</tr>
<tr>
<td>V˙E/V˙O2</td>
<td>Rest</td>
<td>1.00</td>
<td>0.70*</td>
</tr>
<tr>
<td></td>
<td>40%</td>
<td>1.00</td>
<td>0.75*</td>
</tr>
<tr>
<td></td>
<td>70%</td>
<td>1.00</td>
<td>0.49</td>
</tr>
<tr>
<td></td>
<td>Max</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>SaO2</td>
<td>Rest</td>
<td>1.00</td>
<td>0.85*</td>
</tr>
<tr>
<td></td>
<td>40%</td>
<td>1.00</td>
<td>0.88*</td>
</tr>
<tr>
<td></td>
<td>70%</td>
<td>1.00</td>
<td>0.34</td>
</tr>
<tr>
<td></td>
<td>Max</td>
<td>1.00</td>
<td></td>
</tr>
</tbody>
</table>

SaO2, arterial oxygen saturation; V˙E/V˙O2, ventilatory equivalent for O2. *Significant relationship, P < 0.05.

### Table 5. Correlation matrix among the change in resting HVR at sea level, the changes in V˙E/V˙O2,
and SaO2 at rest and during exercise at 432 Torr

<table>
<thead>
<tr>
<th></th>
<th>ΔHVR</th>
<th>ΔV˙E/V˙O2</th>
<th>ΔSaO2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rest</td>
<td>40%</td>
<td>70%</td>
</tr>
<tr>
<td>ΔHVR</td>
<td>1.00</td>
<td>0.87*</td>
<td>0.81*</td>
</tr>
<tr>
<td>ΔV˙E/V˙O2</td>
<td>Rest</td>
<td>1.00</td>
<td>0.74</td>
</tr>
<tr>
<td></td>
<td>40%</td>
<td>1.00</td>
<td>0.72</td>
</tr>
<tr>
<td></td>
<td>70%</td>
<td>1.00</td>
<td>0.34</td>
</tr>
<tr>
<td></td>
<td>Max</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>ΔSaO2</td>
<td>Rest</td>
<td>1.00</td>
<td>0.88*</td>
</tr>
<tr>
<td></td>
<td>40%</td>
<td>1.00</td>
<td>0.76</td>
</tr>
<tr>
<td></td>
<td>70%</td>
<td>1.00</td>
<td>0.69</td>
</tr>
<tr>
<td></td>
<td>Max</td>
<td>1.00</td>
<td></td>
</tr>
</tbody>
</table>

ΔHVR, change in HVR; ΔV˙E/V˙O2, change in V˙E/V˙O2; ΔSaO2, change in SaO2. *Significant relationship, P < 0.05.
not show any changes after intermittent hypoxic exposure (20, 27, 48). These results are in agreement with those of the present study. Therefore, we suggest that short-term intermittent hypoxic exposure does not change oxygenation and acid-base balance at sea level. Thus it is likely that chemoreceptors were at comparable levels for each chemosensitive test at sea level throughout the experimental period.

It has hitherto been reported that resting HVR increases during chronic exposure to hypoxia (11, 35, 41, 42). When combining intermittent hypoxia with endurance exercise training, some studies have indicated increases in HVR (9, 21, 27), whereas others have not (19, 20). However, without endurance training, there are only a few reports that have demonstrated the changes in ventilatory chemosensitivity during intermittent hypoxia in humans: both our previous study (19) and Serebrovskaya et al. (48) reported that resting HVR at sea level increased significantly after short-term intermittent hypoxic exposure. A significant increase in HVR was also found in the present study (Fig. 3A), suggesting that short-term intermittent exposure to high altitude, without exercise training, certainly induces an increase in ventilatory sensitivity to hypoxia. In the present study, we used the resting PET\textsubscript{CO2} level for isocapnic HVR testing at sea level. If resting ventilation and PET\textsubscript{CO2} at sea level had changed after intermittent hypoxia, the resting PET\textsubscript{CO2} would not have been proper for isocapnic HVR testing at sea level. However, as mentioned above, resting V\textsuperscript{E} and PET\textsubscript{CO2} at sea level did not change subsequently throughout the experiment. Thus it does seem reasonable to suppose that resting the PET\textsubscript{CO2} level for isocapnic HVR testing at sea level in this study was appropriate and that the changes in HVR reflect the changes in the actual ventilatory sensitivity to hypoxia.

In addition to HVR, it has been shown that HCVR increases during sojourns at altitude or chronic exposure to hypoxia (10, 35, 42, 47, 55). To our knowledge, the effect of intermittent exposure to hypoxia on HCVR has not been demonstrated in the literature, except for our previous study, which reported no increase in HCVR (19). In the present study, there was also no change in the slope of HCVR after intermittent hypoxic exposure (Fig. 3B). Separation of peripheral and central contributions to the ventilatory response to hypercapnia is arduous (14). Although the ventilatory response to hypercapnia by means of the hyperoxic CO\textsubscript{2} rebreathing method includes a contribution from peripheral chemoreceptors, it is considered to be a response mediated primarily through the central chemoreceptors. Thus it may be that short-term intermittent exposure to high altitude does not elicit an increase in central hypercapnic chemosensitivity.

On the other hand, several investigators have proposed that a single breath of hypercapnic gas mixture is a useful method for evaluating sensitivities of peripheral chemosensitivity to hypercapnia, and, by using this method, ventilatory response mediated through the peripheral chemoreceptors can be studied independently of actions of the stimuli on the central chemoreceptors (13, 14, 31). However, a few investigators have indicated that peripheral hypercapnic chemosensitivity increases during sojourns at high altitude (25, 37). Thus we hypothesized that intermittent exposure to altitude may also lead to an increase in peripheral chemoreceptor responsiveness to hypercapnia. It is of interest that HCVR\textsubscript{SB} increased significantly after intermittent exposure to altitude as shown in Fig. 3C. Although the reasons for the discrepancies between HCVR and HCVR\textsubscript{SB} after intermittent hypoxia are unclear, these results suggest that hypercapnic chemosensitivity may be changeable more in the peripheral than in the central during intermittent hypoxic exposure for short periods.

Indeed, centrally mediated influences are included in the HVR determined by the progressive isocapnic hypoxic test, but hypoxic stimuli undoubtedly have a predominant peripheral chemoreceptor component (14). Some studies have demonstrated that the results of a single-breath CO\textsubscript{2} test do not correlate with those of the hypoxic test (10, 20, 24). These results suggest that it is possible to distinguish between the peripheral chemoreceptor responses to hypoxia and hypercapnia (34). Moreover, McClean et al. (31) have proposed that the presence of a peripheral CO\textsubscript{2} response does not necessarily prove the presence of a hypoxic response in the same subject, given that the two mechanisms are interdependent. In the present study, both HVR and HCVR\textsubscript{SB} increased significantly at Post, but there was no statistically significant correlation between absolute values of HVR and HCVR\textsubscript{SB} at Pre or Post, or between the individual changes in HVR and HCVR\textsubscript{SB} during intermittent hypoxia. Therefore, these results suggest that there may be at least partially separate pathways of increased peripheral chemoreception for O\textsubscript{2} and CO\textsubscript{2} stimuli during intermittent hypoxic exposure.

A number of studies have indicated that there is a significant relationship between resting ventilatory chemosensitivity and the ventilatory response to exercise in normoxia or hypoxia (8, 28, 29, 39, 45). However, as far as we know, only one study performed simultaneous measurements of HVR and exercise ventilation in hypoxia during acclimatization; i.e., Schoene et al. (46) reported that at light and moderate levels of exercise, exercise ventilation during hypoxia after chronic exposure to high altitude was correlated to resting HVR. In the present study, there were significant ($P < 0.05$) positive correlations between absolute values of HVR at sea level and $V\text{e}/V\text{O}_{2}$ at both 40 and 70% of $V\text{O}_{2\text{max}}$ at 432 Torr (Table 4) and between $\delta$HVR at sea level and $\delta V\text{e}/V\text{O}_{2}$ during submaximal exercise at 432 Torr during intermittent hypoxia (Table 5). These results indicate that the increased exercise ventilation at light and moderate levels at 432 Torr after intermittent hypoxic exposure could be primarily the result of an increase in ventilatory chemosensitivity to hypoxia. On the other hand, a significant relationship both between HVR and $V\text{e}/V\text{O}_{2}$ at exhaustion in hypoxia (Table 4) and between $\delta$HVR and $\delta V\text{e}/V\text{O}_{2}$ at exhaustion was not found during intermittent hypoxia (Table 5). Schoene (45) also observed that ventilation at high-
intensity exercise at altitude did not correlate to HVR at sea level and suggested that possibly other factors, e.g., potassium and lactic acid, influence exercise ventilation at a high level of exercise in hypoxia. Thus it is possible to assume that these factors, rather than hypoxic chemosensitivity, may strongly affect ventilation at exhaustion in hypoxia. Because these parameters were not measured during exercise in the present study, however, it is necessary to confirm this assumption by further study.

Resting SaO₂ at 432 Torr after intermittent hypoxic exposure increased significantly (P < 0.05) as shown in Fig. 2B. This result is in agreement with those of previous studies (4, 6, 19, 35, 43). Similarly, at all exercise levels (at 40 and 70% of VO₂ max, and at exhaustion) at 432 Torr, SaO₂ did show significant (P < 0.05) increases after intermittent hypoxia (Fig. 2B), and these data also coincide with those of studies that measured SaO₂ during exercise in continuous altitude hypoxic exposure (5–7, 32, 46, 51). From these data, we can be fairly certain that SaO₂ both at rest and during hypoxic exercise, increases after intermittent exposure to altitude, as well as after chronic exposure to altitude.

One methodological concern is the use of the pulse oximeter to measure SaO₂ because resting SaO₂ at 432 Torr (66.8 ± 6.4 Torr at Pre shown in Fig. 2B) obtained here is lower than those in some studies (43, 53). Although another study (26) indicated ~68% SaO₂ at 4,509 m and this does not differ from the present study, we need to consider whether SaO₂ values in this study are accurate. The accuracy of the OLV-1200 has been proven by Aoyagi (2), who described a high correlation between the calculated SaO₂ from arterial blood samples and SaO₂ estimated by the OLV-1200 (r = 0.99; P < 0.0001, n = 52) with a SE of estimate of 1.63% in SaO₂ values from 47 to 99% for the OLV-1200. Judging from these data, we conclude that the validity of the OLV-1200 pulse oximeter is sufficient to accurately measure SaO₂ and that the data collected using this pulse oximeter are reliable.

As shown in Tables 4 and 5, there were statistically significant (P < 0.05) relationships between absolute values of VE/VO₂ and SaO₂ at rest and at 40 and 70% of VO₂ max at 432 Torr and between dVE/VO₂ and dSaO₂ at rest and during submaximal exercise at 432 Torr during intermittent hypoxia. These results indicate that increased SaO₂ at rest and at 40 and 70% of VO₂ max at 432 Torr could be caused primarily by increased pulmonary ventilation. On the other hand, no significant relationship between VE/VO₂ and SaO₂ at exhaustion in hypoxia (Table 4) or between dVE/VO₂ and dSaO₂ at exhaustion was observed during intermittent exposure to hypoxia (Table 5). Thus the increase in SaO₂ at exhaustion in hypoxia might not be explained by the change in exercise ventilation. However, it has been demonstrated that after acclimatization to altitude, cardiac output falls at either maximal or submaximal exercise (1, 4, 17, 49–51, 56), and the lower blood flow can result in increased transit time of the erythrocyte in the pulmonary capillary (7). Prolongation of capillary transit time is likely to allow a saturation increase (3, 52). Therefore, one of the ways to explain increased SaO₂ during hypoxic exercise, either at maximal or submaximal levels, may be that falling cardiac output after intermittent exposure to hypoxia induces longer capillary transit time, although we did not measure this in the present study. Also, it is likely that hyperventilation during hypoxic exercise led to respiratory alkalosis, resulting in the leftward shift of the oxygen dissociation curve. This may explain the increased SaO₂ after intermittent exposure to altitude (7, 46).

Schoene et al. (46) demonstrated that HVR correlates positively with not only exercise ventilation but also SaO₂ during hypoxic exercise after acclimatization to high altitude. They also concluded that resting HVR at sea level is an important predictor of the degree of decrease in SaO₂ at altitude. We also found positive significant (P < 0.05) relationships between absolute values of HVR at sea level and SaO₂ at 40 and 70% of VO₂ max at 432 Torr (Table 4) and between dHVR at sea level and dSaO₂ during submaximal exercise at 432 Torr during intermittent hypoxia (Table 5). These results suggest that the change in SaO₂ during submaximal exercise in hypoxia can be estimated by the change in hypoxic ventilatory chemosensitivity measured at sea level during intermittent hypoxic exposure as well as during chronic exposure.

Deacclimatization to intermittent hypoxia. To our knowledge, cardiorespiratory responses at rest and to exercise during deacclimatization have received little attention. In our previous study, it was found that increased HVR at sea level after intermittent exposure to hypoxia without exercise training for short periods was retained for 1 wk (19). In the present study, retention of HVR was also found at De (D15) as shown in Fig. 3A, and this result confirms previous studies that indicated that elevated HVR after intermittent or chronic exposure to altitude for short periods was maintained 1 wk later (12, 19). In contrast, several investigators demonstrated that a significant loss of HVR occurred within 1 wk after a return to sea level (35, 41, 42). One concern may be the validity of the HVR test, because it may be that the increased HVR is not a result of the intermittent hypoxia but of the repeated HVR testing. To verify the reliability of the HVR test in the present study, we performed the test three times at 1-wk intervals in a different group of six male volunteers without intermittent hypoxic exposure (average values for age, height, body mass, and VO₂ max were 23.8 ± 3.1 yr, 171.0 ± 5.3 cm, 64.0 ± 5.4 kg, and 55 ± 6.5 ml·kg⁻¹·min⁻¹, respectively, and these values were not significantly different from those of the experimental group). The result was that there were no changes in HVR during the three tests (0.68 ± 0.24, 0.67 ± 0.23, and 0.70 ± 0.21 l·min⁻¹·%, respectively). Thus it seems reasonable to suppose that the values of HVR in the present study are valid and that the elevated HVR after intermittent hypoxia obtained here was not a result of the repeated testing. However, we are not certain of the reasons, and these discrepancies between other studies and the present one may be related to various factors such as the differences in altitude, the
procedure of hypoxic exposure, whether it was chronic or intermittent, and the characteristics of the subjects. Further research is required to elucidate this assumption.

Interestingly, increased ventilation at rest and during submaximal exercise at 432 Torr remained at De as shown in Table 2 and Fig. 2A, and increased SaO2 at rest and at all exercise levels at 432 Torr also remained at De (Fig. 2B), as we had expected. As far as we know, this is the first observation on the effects of deacclimatization on ventilatory and SaO2 responses to hypoxic exercise after utilization of intermittent hypoxia for short periods. These results concur with those of Beidleman et al. (5), who reported that cardiorespiratory responses to hypoxic exercise after a sojourn at altitude for 16 days were retained after 8 days at sea level. On the basis of these results, it seems reasonable to suppose that increased ventilatory and SaO2 responses to hypoxic exercise after short-term intermittent hypoxic exposure will be retained for at least 1 wk.

In contrast to increased HVR at De, a significant loss of HCVRSB, as an index of peripheral chemosensitivity to hypercapnia, occurred at De as shown in Fig. 3C. Pande et al. (37) demonstrated that chronic altitude exposure for 1 wk elicited an increase in peripheral hypercapnic chemosensitivity. However, elevated peripheral hypercapnic chemosensitivity tended to decrease to preexposure levels during the next week at altitude. Therefore, peripheral hypercapnic chemosensitivity may be more changeable than hypoxic chemosensitivity.

Numerous studies have found that arterial oxygenation and/or exercise performance at moderate and high altitudes are related to HVR. Thus an evaluation of HVR at sea level can be used as an indicator of a climber’s capability at high altitude (30, 46). A more vigorous ventilatory response to hypoxia is beneficial for the sojourner to avoid acute mountain sickness and may help performance at moderate and extremely high altitude (23, 33, 45, 46). We found in the present study that resting HVR at sea level and SaO2 and ventilation during hypoxic exercise increased at Post, and these variables were retained at those levels at De. Therefore, it is conceivable that increased SaO2 and ventilation during submaximal exercise in hypoxia may improve performance at both Post and De, although we did not evaluate endurance performance, such as submaximal exercise endurance in hypoxia. Thus further investigation is needed to clarify whether beneficial exercise response after intermittent hypoxic exposure is related to improvement of physical performance in hypoxia and to what extent it remains after returning to sea level.

In conclusion, after an intermittent exposure to 432 Torr (equivalent to 4,500 m altitude) in a hypobaric chamber for 1 wk, ventilation and SaO2 during submaximal exercise in hypoxia increased significantly, and the changes in these variables during submaximal exercise were related to the changes in the resting HVR but not HCVR and HCVRSB. Also, increased ventilatory and SaO2 responses to hypoxic exercise and elevated HVR after intermittent hypoxic exposure were retained after 1 wk without hypoxic exposure. The results from this study suggest that an increase in ventilation during submaximal exercise in hypoxia, which is accompanied by increases in SaO2, can be obtained by using short-term intermittent hypoxic exposure and that the increased ventilation and SaO2 during submaximal exercise in hypoxia are presumably caused by the enhanced hypoxic ventilatory chemosensitivity.

We appreciate the cooperation of the subjects in the present study. We also thank Dr. Y. Yasuda, M. Muramoto, and N. Katayama for assistance during the experiment and J. Fox for reviewing the English in the manuscript.

This research was supported in part by the Ono Sports Science Foundation and by a Grant-in-Aid for Science Research from the Japanese Ministry of Education, Science and Culture (Grant no. 12480009).

REFERENCES


