Ventilatory chemosensitive adaptations to intermittent hypoxic exposure with endurance training and detraining

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Ventilatory chemosensitive adaptations to intermittent hypoxic exposure with endurance training and detraining. J. Appl. Physiol. 86(6): 1805–1811, 1999.—The present study was performed to clarify the effects of intermittent exposure to an altitude of 4,500 m with endurance training and detraining on ventilatory chemosensitivity. Seven subjects (sea-level group) trained at sea level at 70% maximal oxygen uptake ($V_{\text{O2max}}$) for 30 min/day, 5 days/wk for 2 wk, whereas the other seven subjects (altitude group) trained at the same relative intensity (70% altitude $V_{\text{O2max}}$) in a hypobaric chamber. $V_{\text{O2max}}$, hypoxic ventilatory response (HVR), and hypercapnic ventilatory response, as an index of central hypercapnic chemosensitivity (HCVR) and as an index of peripheral chemosensitivities (HCVRSB), were measured. In both groups $V_{\text{O2max}}$ increased significantly after training, and a significant loss of $V_{\text{O2max}}$ occurred during 2 wk of detraining. HVR tended to increase in the altitude group but not significantly, whereas it decreased significantly in the sea-level group after training. HCVR and HCVRSB did not change in each group. After detraining, HVR returned to the pretraining level in both groups. These results suggest that ventilatory chemosensitivity to hypoxia is more variable by endurance training and detraining than that to hypercapnia.

hypoxic ventilatory chemosensitivity; hypercapnic ventilatory chemosensitivity; altitude training

It has been observed that humans have several physiological adaptations to extended exposure to altitude (15, 37, 38). Some of these physiological responses include an increase in ventilatory responses to hypoxia and hypercapnia (12, 34, 35, 38, 43). There are a few studies that investigated the effects of intermittent hypoxic exposure combined with exercise training on ventilatory chemosensitivities in humans at sea level, for example studies by Levine et al. (19) and Benoit et al. (3), which indicated that intermittent exposure to altitude combined with endurance training for several weeks induced an increase in hypoxic ventilatory response (HVR). Recently, we found that, for 6 consecutive days, intermittent exposure to high altitude with exercise training did not significantly increase the HVR and hypercapnic ventilatory response (HCVR), whereas without exercise training the HVR did increase (16). The discrepancy in observations between those of Levine et al. (19) and Benoit et al. (3) and our study (16) may be attributable to the duration of exposure to hypoxia with endurance training and/or the level of altitude. In other words, it is possible to hypothesize that HVR may increase after intermittent exposure to high altitude with exercise training as training periods are prolonged.

On the other hand, the HCVR is generally assessed by using rebreathing and steady-state methods (7, 31, 32). However, estimated HCVR by using these two methods may result in central or combined central and peripheral chemosensitive effects. McClean et al. (23) proposed the use of the single-breath carbon dioxide response test as a method of assessing peripheral chemosensitiveness to hypercapnia (HCVRSB), and they reported that there was no correlation between the results of HCVRSB and HCVR by using a rebreathing method that is considered to be a response mediated primarily through the central chemoreceptors. To our knowledge, because the effect of hypoxic exposure on ventilatory sensitivity to hypercapnia has been studied by the rebreathing test but not the single-breath test, we hypothesize that hypercapnic ventilatory adaptations determined by means of the rebreathing test and the single-breath test may obtain different results after hypoxic exposure combined with endurance training.

It is well known that, in sedentary individuals, endurance training results in marked improvements in exercise performance. Recent evidence has also demonstrated the influence of detraining on physiological adaptations such as maximum oxygen uptake ($V_{\text{O2max}}$), cardiovascular function, and skeletal muscle (29). However, there are no available data concerning the influence of detraining after intermittent hypoxic exercise training on ventilatory chemosensitivity except our previous study (16).

The primary purpose of this study, therefore, was to clarify the hypoxic and hypercapnic ventilatory adaptations to intermittent exposure to an altitude of 4,500 m with endurance training for 2 wk. A secondary purpose was to estimate the effects of detraining on ventilatory chemosensitivity. For this, resting HVR, HCVR, and HCVRSB were determined before and after endurance training.

METHODS

Subjects. Fourteen healthy male volunteers, who were not taking any kind of medication, volunteered to participate in this study. Each subject was assigned at random to an altitude training group (n = 7) or a sea-level training group (n = 7). Average values for age, height, and body mass were...
21.0 ± 3.1 (SD) yr, 174.6 ± 7.1 cm, and 65.5 ± 3.8 kg for the altitude training group and 21.7 ± 3.9 yr, 171.8 ± 3.4 cm, and 62.7 ± 4.6 kg for the sea-level training group, respectively. There were no significant differences in age and physical characteristics between both groups before the training. For obtaining informed consent, the subjects were advised of the experimental protocol and possible risk involved in this study. This study was approved by the Human Research Committee of the Research Center of Health, Physical Fitness and Sports at Nagoya University.

Experimental procedures. Subjects were first familiarized with the equipment used in the experiments at sea level and in the hypobaric chamber. Before the endurance exercise training, \( V_{O_{2\max}} \) at sea level was determined in each subject. To determine a training intensity, \( V_{O_{2\max}} \) in the subjects in the altitude training group were also measured in a hypobaric chamber, which simulated altitude of 4,500 m (432 Torr), by using the same maneuver performed at sea level. On another day three tests were conducted in each subject for determining HVR, HCVR, and HCVRSB, respectively. After the subjects were seated comfortably in a chair for 30 min, each test was conducted with subjects in a sitting position. These measurements were performed at sea level for both the pre- (Pre) and post-endurance exercise training. The posttraining test was performed twice, i.e., on the first day after 2 wk of exercise training (Post) and after 2 wk of detraining (2wk).

The sea-level training group trained at sea level for an intensity corresponding to 70% of \( V_{O_{2\max}} \) measured at sea level. The hypobaric chamber was used for exercise training in the altitude group. The pressure of the hypobaric chamber was maintained at 432 Torr, corresponding to an altitude of 4,500 m. The altitude training group performed endurance training at the same relative exercise intensity as the group at sea level (70% of altitude \( V_{O_{2\max}} \)). The subjects in the altitude group completed the self-assessment portion of the Lake Louise Consensus Questionnaire (14) before and after each training session in the hypobaric chamber. The subjects in both groups trained on a mechanically braked bicycle ergometer (Monark) with a frequency of 60 rpm. Both groups trained for 30 min/day, 5 days/wk for 2 wk. The subjects in the altitude group completed the self-assessment portion of the Lake Louise Consensus Questionnaire (14) before and after each training session in the hypobaric chamber. The subjects in both groups trained on a mechanically braked bicycle ergometer (Monark) with a frequency of 60 rpm. Both groups trained for 30 min/day, 5 days/wk for 2 wk. The subjects in the altitude group completed the self-assessment portion of the Lake Louise Consensus Questionnaire (14) before and after each training session in the hypobaric chamber.

VO_{2max} was measured at sea level before and after training by using a bicycle ergometer with incremental loading. In addition, VO_{2max} in the altitude training group was also measured in a hypobaric chamber, which was simulated at 4,500 m (432 Torr), by using the same maneuver used before training to determine their training intensity. To measure VO_{2max}, an incremental protocol on an electromechanically braked bicycle ergometer was used. The 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 maximum bicycle exercise, expired gases were collected into a Douglas bag during the last 30 s of each intensity level until exhaustion. Expired gas volume was measured with a dry-gas meter (type DC-2, Shinagawa) in a hypobaric chamber and with a wet-gas meter (type WE, Shinagawa) at sea level. Gas analysis was performed by means of an O2 and CO2 analyzer (type MG-360, Minato Ikagaku). Heart rate (HR) was continuously recorded by a three-lead electrocardiogram (type OEC-6401, NIHON Koden) throughout the maximal cycle ergometer test. The peak HR value was expressed as HR_{max} and the peak pulmonary ventilation (VE, BTS) value was estimated as VE_{max} \( V_{O_{2}\text{uptake}} \) derived during maximal exhaustive exercise was considered to be VO_{2max}, when two of the following three criteria were satisfied: identification of a plateau in \( V_{O_{2}} \) with an increase in power output (<150 ml \( V_{O_{2}} \) increase), HR ± 10% of age-predicted maximum (220 – age), and respiratory exchange ratio ≥1.0 (1).

HVR. Resting HVR at sea level was measured by using a progressive isocapnic hypoxic test proposed by Weil et al. (41). A rebreathing system similar to that in the previous study (16) was used. During rebreathing, tidal volume (VT), minute inspiratory flow volume (Vt), end-tidal CO2 and O2 fraction (\( F_{ETCO_{2}} \) and \( F_{ETO_{2}} \), respectively), and arterial oxygen saturation (\( Sa_{O_{2}} \)) were continuously determined. The subjects breathed through a mouthpiece attached to a hot-wire flowmeter (type RF-H, Minato Ikagaku). \( F_{ETCO_{2}} \) and \( F_{ETO_{2}} \) were analyzed by using a gas analyzer (type MG-360, Minato Ikagaku). To calculate end-tidal partial pressure of CO2 and O2 (\( P_{ETCO_{2}} \) and \( P_{ETO_{2}} \), respectively), sample gas was drawn through a sampling tube connected to the mouthpiece. \( Sa_{O_{2}} \) was measured on the tip of the left forefinger during rebreathing by a pulse oximeter (OLV-1200, NIHON Koden). The signals from the flowmeter, gas analyzer, and pulse oximeter, sampled at a frequency of 300 Hz through analog-digital conversion (AXD-98H, Canopus), were stored in the mass memory of a computer (PC-9821X, NEC). HVR was estimated as the slope of the line calculated by the linear regression relating \( V_{I} \) to oxyhemoglobin saturation (\( \Delta V_{I}/\Delta Sa_{O_{2}} \), 1·min\(^{-1} \cdot %^{-1} \)) and the slope was presented as positive numbers by convention.

HCVR. Resting HCVR values were measured by two methods, i.e., CO2 rebreathing (HCVR) and single-breath CO2 (HCVRSB). In the rebreathing method, subjects rebreathed a gas mixture of 7% CO2 in O2 from a bag (5–6 liters) in a box for 3–4 min (31). The recording of \( V_{I} \) and \( P_{ETCO_{2}} \) were made in a manner similar to the computing system used in the HVR test. HCVR was assessed as the slope of the line (S) determined by the linear regression relating \( P_{ETCO_{2}} \) to \( V_{I} \) (\( \Delta V_{I}/\Delta P_{ETCO_{2}} \), 1·min\(^{-1} \cdot \text{Torr}^{-1} \)). On the other hand, a single-breath CO2 test was used for the determination of peripheral chemoreceptor response to CO2 according to the protocol described by McClean et al. (23), i.e., application of a single CO2 mixture composed of 13% CO2-21% O2-66% N2 was repeated several times with 2- to 3-min intervals for each subject. The apparatus consisted of a bag-in-box circuit similar to that used for the HCVR test. The subjects were seated comfortably in a chair and began breathing room air through a mouthpiece with a nosedip. The T valve was attached between the bag and the mouthpiece, and the port was connected to either room air or a bag that contained 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, \( V_{T} \), \( V_{I} \), \( P_{ETCO_{2}} \), and inspiratory time (TI) were recorded continuously. When stable levels of \( P_{ETCO_{2}} \) and \( V_{I} \) had been achieved, the subjects switched 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 to the room air position. Baseline \( V_{I} \) and \( V_{I}/TI \) were determined from the five breaths preceding each transient, when \( P_{ETCO_{2}} \) and \( P_{ETO_{2}} \) remained relatively constant. All transients were given six to eight times (27). Analysis was limited to breaths from the five breaths preceding each transient. When \( P_{ETCO_{2}} \) and \( V_{I} \) had been achieved, the subjects switched 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 to the room air position. Baseline \( V_{I} \) and \( V_{I}/TI \) were determined from the five breaths preceding each transient, when \( P_{ETCO_{2}} \) and \( P_{ETO_{2}} \) remained relatively constant. All transients were given six to eight times (27). Analysis was limited to breaths from the five breaths preceding each transient.
change in corrected changes in $P_{\text{ETCO}_2}$ by using a correction formula that resulted from the transients.

Statistical analysis. The values were expressed as means $\pm$ SD. The differential changes in the parameters during the experimental periods between altitude and sea-level training groups were compared by using two-way repeated-measures ANOVA. Differences in the parameters at each session (Pre, Post, and 2wk) within each group were determined by using the Wilcoxon test, and the comparison of parameters between groups at each session was done by using the Mann-Whitney test. The level of significance was set at 0.05.

RESULTS

Baseline descriptive data. Resting $P_{\text{ETO}_2}$ and $P_{\text{ETCO}_2}$ did not change in both groups throughout the experimental period, as shown in Table 1. There was a score of zero for the Lake Louise Consensus Questionnaire after each 2-wk training session in the altitude training group.

HVR. Figure 1 indicates the HVR at Pre, Post, and 2wk in the two groups, and Fig. 2 shows an example of HVR (typical subjects in each group) under the three different conditions. There was no significant difference in the HVR between the altitude training group and the sea-level training group before training. In the altitude training group, the HVR tended to increase after intermittent exposure to altitude combined with 2 wk of training [0.49 $\pm$ 0.22 (Pre) to 0.67 $\pm$ 0.22 (SD) l·min$^{-1}$·%$^{-1}$ (Post)], but it was not statistically significant. After endurance exercise training at sea level, a significant ($P < 0.05$) decrease in the HVR was found in the sea-level training group, from 0.43 $\pm$ 0.22 (Pre) to 0.25 $\pm$ 0.19 l·min$^{-1}$·%$^{-1}$ (Post). There was a significant difference ($P < 0.05$) in HVR measured after training (Post) between the altitude training group and the sea-level training group. However, the changed HVR in both groups was restored at 2wk (0.42 $\pm$ 0.23 and 0.37 $\pm$ 0.23 l·min$^{-1}$·%$^{-1}$ in the altitude training group and the sea-level training group, respectively). There was a significant difference in the HVR between the altitude training group and the sea-level training group during the experimental period ($F = 5.71, P < 0.05$).

HCVR. Mean HCVR values measured at Pre, Post, and 2wk were 1.24 $\pm$ 0.55, 1.29 $\pm$ 0.34, and 1.30 $\pm$ 0.68 and 1.30 $\pm$ 0.77, 1.36 $\pm$ 0.85, and 1.20 $\pm$ 0.60 l·min$^{-1}$·%$^{-1}$ in the altitude training group and the sea-level training group, respectively. As shown in Fig. 3, there were no significant changes in the HCVR in either the altitude training group or the sea-level training group throughout the experimental period. Figure 4 indicates the HCVRSB obtained at Pre, Post, and 2wk in both groups. Mean values of HCVRSB determined at Pre, Post, and 2wk were 11.71 $\pm$ 6.20, 12.77 $\pm$ 7.17, and 11.54 $\pm$ 6.36 ml·s$^{-1}$·Torr$^{-1}$ in the

### Table 1. $P_{\text{ETO}_2}$ and $P_{\text{ETCO}_2}$ in both groups breathing room air before the HVR tests

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Values are means $\pm$ SD. Pre, before training; Post, the day after training; 2wk, 2-wk detraining; A, altitude training group; S, sea-level training group. $P_{\text{ETO}_2}$, end-tidal partial pressure of O$_2$; $P_{\text{ETCO}_2}$, end-tidal partial pressure of CO$_2$. 

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Fig. 1. Comparison of hypoxic ventilatory response (HVR) determined before (Pre) and on 1st day after (Post) exercise training and during detraining (2wk) for both groups. Values are means $\pm$ SD. *Significantly different from Pre, $P < 0.05$. 

Fig. 2. Example of HVR (typical subject in each group) pre- and postendurance training and during detraining for 2 wk in both groups. A: subject in altitude training group. B: subject in sea-level training group. $V_i$, minute inspiratory flow volume; $S_aO_2$, arterial O$_2$ saturation.
altitude training group and 11.47 ± 5.14, 11.33 ± 6.29, and 11.00 ± 6.75 ml·s⁻¹·Torr⁻¹ in the sea-level training group, respectively. Similar to HCVR, there were no significant changes in the HCVRSB after intermittent hypoxic exposure with training or endurance training at sea-level and detraining for 2 wk.

\( V_{O2\max} \) Table 2 indicates \( V_{O2\max} \), \( V_{E\max} \), and ventilatory equivalent for \( O_2 \) (\( V_{E/O_2} \)) and \( CO_2 \) (\( V_{E/CO_2} \)) obtained at exhaustion during the maximal bicycle ergometer test at sea level at Pre, Post, and 2wk in both groups. \( V_{O2\max} \) in the altitude training group was significantly (\( P < 0.05 \)) increased after combined hypoxia and exercise training [56.1 ± 5.3 (Pre) to 60.1 ± 5.7 ml·kg⁻¹·min⁻¹ (Post)], and a significant loss of \( V_{O2\max} \) occurred after 2 wk of detraining [56.9 ± 5.6 ml·kg⁻¹·min⁻¹ (2 wk)]. Similarly, in the sea-level training group \( V_{O2\max} \) was significantly (\( P < 0.05 \)) increased after sea-level exercise training over 2 wk [57.8 ± 4.4 (Pre) to 60.7 ± 3.9 ml·kg⁻¹·min⁻¹ (Post)], but it showed a loss after detraining [59.2 ± 3.5 ml·kg⁻¹·min⁻¹ (2 wk)] compared with the Pre value. There was no statistical difference in \( V_{O2\max} \) between both groups throughout the experimental period. After training and detraining for 2 wk, \( V_{E\max} \) was not significantly changed in both groups. \( V_{E/O_2} \) and \( V_{E/CO_2} \) obtained at exhaustion during the maximal bicycle ergometer test were not changed after intermittent hypoxic exposure with exercise training and detraining [\( V_{E/O_2} \): 41.5 ± 4.5 (Pre), 39.8 ± 4.6 (Post); \( V_{E/CO_2} \): 37.3 ± 2.6 (Pre), 37.6 ± 2.7 (Post), and 36.4 ± 3.4 (2wk)], whereas \( V_{E/O_2} \) and \( V_{E/CO_2} \) decreased significantly (\( P < 0.05 \)) after endurance training at sea level and detraining compared with before training [\( V_{E/O_2} \): 43.9 ± 5.4 (Pre), 40.7 ± 2.7 (Post), and 40.0 ± 3.7 (2wk); \( V_{E/CO_2} \): 39.3 ± 3.3 (Pre), 37.4 ± 3.1 (Post), and 36.9 ± 3.1 (2wk), respectively].

**DISCUSSION**

In the present study, we found that 1) HVR tended to increase after intermittent exposure to altitude of 4,500 m with endurance training for 2 wk, whereas it decreased significantly after endurance training at sea level; 2) HCVR and HCVRSB did not change in both groups after training; and 3) changed HVR after training was restored after 2 wk of detraining.

Most studies have shown that HVR, as an index of peripheral chemoreceptor sensitivity to hypoxia, increases during varying durations of continuous stay at altitude (12, 34, 35, 38, 43), whereas some studies demonstrated no increase in HVR after exposure to hypoxia (13, 22). A limited number of studies have shown the effect of intermittent exposure to hypoxia with endurance training on HVR; i.e., Levine et al. (19) and Benoit et al. (3) reported the resting HVR at sea level increased after intermittent hypoxic exposure with endurance training for several weeks, whereas we recently demonstrated no increase in resting HVR after endurance training during intermittent hypoxic exposure over 6 consecutive days and suggested that endurance training during intermittent exposure to hypoxia depresses the enhancement of hypoxic chemosensitiv-
In the present study, we found that HVR tended to increase after intermittent hypoxic exposure combined with 2 wk of endurance training but that this increase was not statistically significant, as shown in Fig. 1. Thus, as for intermittent hypoxic exposure combined with endurance exercise training, it is likely that the duration of hypoxic exposure with exercise training may be an important factor in the enhancement of resting HVR and that for several preceding weeks the enhancing effect on HVR during exposure to hypoxia may overcome the depressing effect on HVR by endurance exercise training.

It has hitherto been reported that resting HVR in endurance athletes is lower than that in untrained subjects (5, 36). Because no data are available concerning the effect of endurance training on HVR on normal subjects, this blunted HVR in endurance athletes is considered to be a hereditary factor (39). However, over 2 wk of endurance training at sea level led to a significant decrease (P < 0.05) in HVR, as shown in Fig. 1. This is the first study in humans to provide evidence of the declining effect of endurance training on resting HVR. In this study, the resting PETO2 and PETCO2 showed no changes in both groups during the three experimental periods (Pre, Post, and 2wk) (Table 1). These data are in agreement with the results in a study by Levine et al. (19). Thus it is likely that peripheral chemoreceptors were at comparable levels for each test in this study, and it does seem reasonable to suppose that the changes in HVR indicate the changes in the actual sensitivity. In contrast to results in this study, previous studies demonstrated that there was no change in HVR after endurance training at sea level for several weeks (3, 19). The discrepancy between those studies and the present one may be related to several factors, e.g., the characteristics of the subjects. For one, the aerobic work capacity of subjects, the subjects in the sea-level training group in this study showed VO2max of 57.8 ± 4.4 ml·kg⁻¹·min⁻¹ before training, whereas in studies by Benoit et al. (3) and Levine et al. (19) the subjects had VO2max levels below 50 ml·kg⁻¹·min⁻¹. Also, in contrast to the present study, the subjects in those studies included both genders. Although further investigation is needed to clarify these contradictory results, the results in the present study suggest that the blunted HVR in endurance athletes may result from not only a hereditary factor but also endurance exercise training.

It is well known that resting HCVR, as well as HVR, increases during sojourns at high altitudes or chronic exposure to hypoxia (38, 43). In the previous study, however, we obtained no change in resting HCVR during consecutive days in both control and endurance training groups after intermittent hypoxic exposure simulated at 4,500 m (16). In this study, there was also no change in HCVR by either endurance training with intermittent exposure to hypoxia or training at sea level (Fig. 3). This indicated that HCVR does not change readily by combined intermittent exposure to hypoxia and endurance training for 2 wk, as applied here. A few authors have investigated the effects of endurance training at sea level on HCVR and have reported different results. Although Bradley et al. (4) reported that HCVR did not change after endurance training at sea level over a period of 6–8 wk, Miyamura and Ishida (27) demonstrated that exercise training for several years induced a decrease in HCVR. These results suggest that one of the reasons for unchanged HCVR after training in this study may be related to the duration of the endurance exercise training. In addition, we tested peripheral chemoreceptor responsiveness to hypercapnia (i.e., HCVRSB) before and after exercise training by using the single-breath CO2 test proposed by McClean et al. (23) because endurance training is considered to affect not only central but also peripheral chemoreceptor sensitivity to hypercapnia. As shown in Fig. 4, however, no significant changes were found in HCVRSB after endurance training in both groups. To our knowledge, this is the first report on the effects of endurance training during intermittent hypoxic exposure and training at sea level on peripheral chemosensitivity to hypercapnia. These results suggest that central and peripheral hypercapnic chemosensitivity do not change after intermittent exposure to hypoxia combined with endurance training or endurance training at sea level for 2 wk.

HVR assessed by using the isocapnic progressive hypoxia test and HCVRSB, assessed by using single-breath CO2, are tests of peripheral chemosensitivity. As reported previously, some studies demonstrated that the results of a single-breath CO2 test do not correlate with those of the hypoxic tests (6, 18). These results suggest that it is possible to separate the carotid chemoreceptor responses to O2 and CO2 (28). In this study, there was also no statistically significant correlation between HVR and HCVRSB before training. The differences in the responses to O2 and CO2 after exercise training indicate that there may be at least partially separate pathways of chemoreception for these two stimuli (28). In a comparison between high-altitude natives and sea-level natives, however, each ventilatory response to single-breath O2 and CO2 was lower in high-altitude natives than in sea-level natives (40). Therefore, although there was no change in HCVRSB in this study, further research is required to examine longitudinal changes in peripheral chemosensitivity to hypoxia and hypercapnia during several situations, i.e., prolonged hypoxic exposure and physical training for long periods.

Little is known about the influence of detraining on the ventilatory response to hypoxia. In the present study it was found that, after 2 wk of detraining, HVR in both groups was restored to a level similar to that before training, as shown in Fig. 1. The lack of other studies on the effect of detraining on a HVR changed by intermittent hypoxic exposure with endurance training allows a comparison only with data obtained during deacclimatization (12, 34, 35). Forster et al. (12) reported that staying at an altitude of 3,100 m over 45 days led to an increase in HVR and that, after the subjects returned to sea level, this HVR remained higher than the prehypoxic level for 45 days. Moreover,
Sato et al. (35) showed that HVR was elevated after chronic exposure to an altitude of 3,810 m for 5 days and remained so for 4–7 days later at sea level. They also reported that increased HVR during 12 days at an altitude of 3,810 m was returned to the preacclimatization value during deacclimatization for 6 days (34). Their latter observation is very similar to our present result. By contrast, during detraining for 2 wk, HCVR and HCVRSB did not show any changes. Miyamura and Ishida (27) indicated that HCVR values decreased in healthy male subjects by endurance training for 4 yr are reversed during detraining for 2 yr. These results suggest that ventilatory hypoxic chemosensitivity is more changeable than hypercapnic chemosensitivity, not only during endurance training but also during detraining.

In recent years, altitude training has been adopted frequently in competitive athletes to improve sea-level performance. However, scientific evidence to support the potentiating effects of altitude training for performance at sea level is controversial. We measured VO_{2max} in both groups, but there was no apparent advantage of intermittent hypoxic training, even in a simulated altitude at 4,500 m (432 Torr), over training at sea level (Table 2). These results further confirm the data that have been reported that intermittent hypoxic exposure with endurance training showed no additional effect on VO_{2max} at sea level in untrained subjects (3, 8, 10, 11, 19, 26). The lack of additional improvement in VO_{2max} in the altitude training group suggests that intermittent hypoxic exposure with endurance training does not contribute significantly to the mechanism responsible for the improvement in VO_{2max} at sea level. Some investigators have demonstrated the influence of detraining on increased VO_{2max} after sea-level training (29, 33), but to our knowledge there has been no report of the detraining effect after intermittent exposure to hypoxia with endurance training. We found that, during 2 wk of detraining, increased VO_{2max} in both groups decreased to pretaining levels and was not significantly different between the groups. These results also suggest that there is no additional adaptation in the performance during detraining after endurance training with intermittent hypoxic exposure and at sea level, as applied here.

Cross-sectional studies have indicated that there is a significant relationship between resting HVR or HCVR and the ventilatory response to exercise (2, 20, 21, 30). If HVR is an important determinant of exercise ventilation, ventilatory equivalent after endurance training is considered to be increased during maximal exercise in the altitude training group and decreased in the sea-level training group. We observed that changes in HVR after endurance training and detraining in both groups were not associated with corresponding changes in exercise ventilation. Thus resting HVR may play little role in exercise ventilation at sea level as described by Levine et al. (19). In longitudinal studies, on the other hand, several authors have shown conflicting data, in that VE/VO_{2} levels during maximal exercise after endurance training at sea level are reported to be unchanged (19, 33) or decreased (9) and that the changes in the resting HVR or HCVR were not in agreement with the changes in the ventilatory equivalent during maximal exercise after endurance training or detraining (16, 19). It has been described that hypoxic and/or hypercapnic chemosensitivity, either central or peripheral chemoreceptors, is altered during exercise (21, 24, 25, 30, 42). One of these reports showed that exercise stimulated variable changes in sedentary subjects, and exercise induced different changes in chemosensitivity in endurance-trained subjects compared with that in control subjects (24). Also, some studies have reported a significant correlation between exercise ventilation and ventilatory chemosensitivity during exercise rather than at rest (21, 25). Therefore, it can be speculated that the subjects in both groups after endurance training and detraining may have a different change in ventilatory chemosensitivity during submaximal exercise compared with that at rest. Because we have no information on ventilatory chemosensitivity during submaximal exercise, further research is required to confirm this speculation.

In conclusion, HVR tended to increase after intermittent hypoxic exposure combined with endurance training for 2 wk, whereas it decreased significantly after endurance training at sea level. The changed HVR after endurance training in both groups returned to the initial level after detraining for 2 wk. Neither HCVR nor HCVRSB changed after endurance training, either in hypoxia or at sea level and detraining. These results suggest that hypoxic chemosensitivity is more variable than ventilatory training and detraining than hypercapnic chemosensitivity.

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