Living and training in moderate hypoxia does not improve $V_o_2 max$ more than living and training in normoxia

Kyle K. Henderson, Richard L. Clancy and Norberto C. Gonzalez


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Living and training in moderate hypoxia does not improve $\dot{V}O_2\text{max}$ more than living and training in normoxia

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Received 22 September 2000; accepted in final form 11 January 2001

Henderson, Kyle K., Richard L. Clancy, and Norberto C. Gonzalez. Living and training in moderate hypoxia does not improve $\dot{V}O_2\text{max}$ more than living and training in normoxia. J Appl Physiol 90: 2057–2062, 2001.—The objective of these experiments was to determine whether living and training in moderate hypoxia (MHx) confers an advantage on maximal normoxic exercise capacity compared with living and training in normoxia. Rats were acclimatized to and trained in MHx (inspired $P_O_2$ ($P_{O_2}$) = 110 Torr) for 10 wk (HTH). Rats living in normoxia trained under normoxic conditions (NTN) at the same absolute work rate: 20 ml/min on a 10° incline, 1 h/day, 5 days/wk. At the end of training, rats exercised maximally in normoxia. Training increased maximal $O_2$ consumption ($\dot{V}O_2\text{max}$) in NTN and HTH above normoxic (NS) and hypoxic (HS) sedentary controls. However, $\dot{V}O_2\text{max}$ and $O_2$ transport variables were not significantly different between NTN and HTH: $\dot{V}O_2\text{max}$ 86.6 ± 1.5 vs. 86.8 ± 1.1 ml·min$^{-1}$·kg$^{-1}$; maximal cardiac output 456 ± 7 vs. 443 ± 12 ml·min$^{-1}$·kg$^{-1}$; tissue blood $O_2$ delivery (cardiac output × arterial $O_2$ content) 95 ± 2 vs. 96 ± 2 ml·min$^{-1}$·kg$^{-1}$; and $O_2$ extraction ratio (arteriovenous $O_2$ content difference/arterial $O_2$ content) 0.91 ± 0.01 vs. 0.90 ± 0.01. Mean pulmonary arterial pressure ($P_{pa}$, mmHg) was significantly higher in HS vs. NS ($P < 0.05$) at rest (24.5 ± 0.8 vs. 18.1 ± 0.8) and during maximal exercise (32.0 ± 0.9 vs. 23.8 ± 0.6). Training in MHx significantly attenuated the degree of pulmonary hypertension, with $P_{pa}$ being significantly lower at rest (19.3 ± 0.8) and during maximal exercise (29.2 ± 0.5) in HTH vs. HS. These data indicate that, despite maintaining equal absolute training intensity levels, acclimatization to and training in MHx does not confer significant advantages over normoxic training. On the other hand, the pulmonary hypertension associated with acclimatization to hypoxia is reduced with hypoxic exercise training.

maximal $O_2$ uptake; maximal exercise capacity; exercise training; hypoxic exercise; systemic $O_2$ transport; tissue $O_2$ delivery; tissue $O_2$ extraction; hypoxic pulmonary vasoconstriction; hypoxic pulmonary hypertension

THE EFFECT OF HYPOXIC VS. NORMOXIC training on maximal exercise capacity has received considerable attention in sports circles; however, there have been relatively few well-controlled studies on the subject. Aerobic exercise training increases maximal $O_2$ consumption ($\dot{V}O_2\text{max}$) by increasing the rate at which $O_2$ is supplied to the exercising muscles, largely through an increase in cardiac output secondary to the increase in stroke volume (4, 27), and by improving the extraction of $O_2$ by the contracting muscles (25). Because artificially increasing hematocrit increases $\dot{V}O_2\text{max}$ (2, 5), it is possible that polycythemia induced by acclimatization to hypoxia could also lead to improved maximal exercise performance. However, acclimatization to hypoxia results in other cardiovascular and respiratory changes that also influence the $O_2$ transport system. These include pulmonary hypertension and right ventricular hypertrophy (21, 23), decreased chronotropic response to catecholamines in the presence of an elevated sympathetic drive (24), as well as a decrease in maximal heart rate (22) and cardiac output (7), all of which may offset the positive effects of polycythemia on exercise performance. Because the extent to which these changes occur depends on the severity and duration of hypoxia, it is difficult to predict whether the positive features of acclimatization will outweigh the negative ones in a given set of conditions and therefore whether hypoxic training will confer an advantage over normoxic training. In addition, the hypoxia-induced decrease in exercise capacity may make it difficult, depending on the severity of hypoxia, to maintain the same absolute training intensity as in normoxia, which further complicates the interpretation of the results.

The objective of these experiments was to determine the effect of living and training in hypoxia on maximal exercise capacity, using a design that would allow an assessment of the effects of acclimatization, training, and training plus acclimatization while maintaining the same absolute training intensity as normoxic trained controls. We selected a moderate level of hypoxia at which absolute training intensity could be maintained in normoxic and hypoxic conditions and which would adequately stimulate polycythemia (19). We hypothesized that, if absolute training intensity was the same, living and training in moderate hypoxia (MHx) would result in a larger increase in $\dot{V}O_2\text{max}$ than living and training in normoxia.

The studies were carried out in rats, an animal frequently employed in exercise and altitude studies.
that shares with humans several features of acclima-
tization to hypoxia (6–8). The preparation allowed for
characterization of the effects of hypoxia and training
on the various steps of the O₂ cascade from the atmo-
sphere to the tissues. Both normoxic and hypoxic
groups were trained at equal absolute work rates such
that the increase in O₂ requirements associated with
exercise training would be comparable in both groups,
independent of the prevailing P/O₂.

METHODS

Animal model and training protocol. Seven-week-old male
Sprague Dawley rats were randomly assigned to live in
normoxia [inspired P/O₂ (P吸入) = 147 Torr] or in MHx (P吸入 =
110 Torr). Each group was then subdivided into sedentary
and trained subgroups. This division resulted in four exper-
imental groups with 16 animals in each group: normoxic
and trained subgroups. This division resulted in four exper-
imental groups with 16 animals in each group: normoxic
and trained subgroups. This division resulted in four exper-
iments and outflowing O₂ concentrations and outflowing CO₂ concentration (inflowing gas was
CO₂ free) were measured continuously and simultaneously
by use of an Applied Electrochemistry O₂ analyzer and a
Columbus Instruments CO₂ analyzer, respectively. The O₂
and CO₂ analyzers were calibrated with gas mixtures mea-
sured with a precision of ±0.005%. The output of the O₂ and
CO₂ sensors was fed into a computer to provide determination
of VO₂, VCO₂, and respiratory exchange ratio (R) every 5 s.
VO₂ and VCO₂ (expressed in ml STPD·min⁻¹·kg⁻¹) were calcu-
lated from the inflowing and outflowing O₂ concentration
difference, the outflowing CO₂ concentration and the outflow-
ing gas flow.

Arterial and mixed-venous blood samples were analyzed for
pH, PO₂, and PCO₂ using appropriate electrodes at 38°C,
and for Hb concentration and O₂ saturation of Hb and was
corrected for the rectal temperature by using temperature
correction factors for rat blood (8). Whole blood lactate con-
tent was measured by use of a quantitative enzymatic
assay at 340 nm (Sigma Diagnostics).

Systemic and pulmonary arterial (Ppa) pressures were
recorded continuously, with mean pressures obtained by elec-
ronic integration. Heart rate (HR) was obtained directly
from the systemic arterial blood pressure tracing.

O₂ contents (ml/dl) of arterial (CaO₂) and of mixed venous
blood (CvO₂) were calculated from Hb concentration, P/O₂,
and the O₂ saturation of Hb by using a Hb-O₂ binding factor
of 1.34 ml STPD/g, and an O₂ solubility coefficient of 0.003
ml·Torr⁻¹·dl⁻¹. Cardiac output (Q, ml·min⁻¹·kg⁻¹) was calcu-
lated as the ratio of VO₂ to arteriovenous O₂ concentration
difference [VO₂/(CaO₂ – CvO₂)]. Stroke volume (ml/kg) was
calculated as Q/HR. The rate of convective blood O₂ transport
(ml·min⁻¹·kg⁻¹) was calculated as the product of Q times
CvO₂. The O₂ extraction ratio (O₂ ER) was calculated as
(CaO₂ – CvO₂)/CaO₂.

The data are expressed as means ± SE. Statistical analy-
sis was carried out using a one-way analysis of variance.
The effect of acclimatization was evaluated by comparing NS vs.
HS. The effect of training in normoxia and in hypoxia was
evaluated by comparing NS vs. NTN and NS vs. HTH,
respectively. Finally, comparison of NTN vs. HTH provided an
estimate of the effects of living and training in normoxia vs.
living and training in MHx. Significance was established
with the t-test using the Bonferroni correction for multiple
comparisons. A P value <0.05 was considered to indicate a
significant difference.

RESULTS

Each group was composed of 16 animals. Only the
data from the animals that achieved VO₂ max as defined
above are presented. The number of animals in each
group is listed in Table 1. Acclimatization to hypoxia in
the sedentary rats did not result in a significant in-
crease in VO₂ max (Table 1, NS vs. HS). This occurred in
Table 1. Oxygen transport variables in maximal exercise

<table>
<thead>
<tr>
<th>Variable</th>
<th>NS</th>
<th>HS</th>
<th>NTN</th>
<th>HTH</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO_{2max}, ml-min^{-1}-kg^{-1}</td>
<td>76.9 ± 0.9</td>
<td>77.0 ± 1.3</td>
<td>86.6 ± 1.5†</td>
<td>86.8 ± 1.1†</td>
</tr>
<tr>
<td>CaO_2, ml/dl</td>
<td>20.6 ± 0.2</td>
<td>21.7 ± 0.2*</td>
<td>20.7 ± 0.3</td>
<td>21.9 ± 0.3‡</td>
</tr>
<tr>
<td>CO_2, ml/dl</td>
<td>2.4 ± 0.2</td>
<td>3.3 ± 0.3*</td>
<td>1.9 ± 0.3</td>
<td>2.2 ± 0.3†</td>
</tr>
<tr>
<td>VO_{2max}/CaO_2, ml/dl</td>
<td>18.1 ± 0.2</td>
<td>18.4 ± 0.4</td>
<td>18.9 ± 0.2</td>
<td>19.6 ± 0.4‡</td>
</tr>
<tr>
<td>O_2 ER</td>
<td>0.88 ± 0.01</td>
<td>0.85 ± 0.02</td>
<td>0.91 ± 0.01</td>
<td>0.90 ± 0.01‡</td>
</tr>
<tr>
<td>PaO_2, Torr</td>
<td>62.0 ± 3.2</td>
<td>105.5 ± 1.9</td>
<td>103.4 ± 1.4</td>
<td>105.1 ± 1.0</td>
</tr>
<tr>
<td>VO_{2max}/PV O_2, ml-min^{-1}-kg^{-1}-Torr^{-1}</td>
<td>3.1 ± 0.1</td>
<td>2.8 ± 0.1</td>
<td>3.7 ± 0.1†</td>
<td>3.6 ± 0.2†</td>
</tr>
<tr>
<td>Hb, g/dl</td>
<td>16.1 ± 0.1</td>
<td>17.0 ± 0.1*</td>
<td>16.7 ± 0.2†</td>
<td>17.2 ± 0.2</td>
</tr>
<tr>
<td>Lactate, mM</td>
<td>18.8 ± 0.7</td>
<td>16.1 ± 0.8*</td>
<td>18.9 ± 0.8</td>
<td>16.1 ± 0.6‡</td>
</tr>
<tr>
<td>n</td>
<td>15</td>
<td>14</td>
<td>11</td>
<td>12</td>
</tr>
<tr>
<td>Body weight, g</td>
<td>379.2 ± 5.8</td>
<td>380.7 ± 7.5</td>
<td>336.5 ± 5.4</td>
<td>334.0 ± 10.2</td>
</tr>
</tbody>
</table>

Values are means ± SE; n = no. of animals in each group that reached VO_{2max}. NS and HS, normoxic and hypoxic sedentary control groups, respectively; NTN, normoxic group trained in normoxia; HTH, hypoxic group trained in moderate hypoxia; VO_{2max}, maximal O_2 consumption; CaO_2 and CO_2, arterial and mixed venous blood O_2 content, respectively; VO_{2max}/CaO_2, arterial minus mixed venous blood O_2 content; O_2 ER, O_2 extraction ratio [= (CaO_2 - CO_2)/CaO_2]; PaO_2 and PV O_2, arterial and mixed venous PO_2, respectively; VO_{2max}/PV O_2, tissue O_2 transfer capacity; Hb, arterial hemoglobin concentration; lactate, arterial blood lactate. Significant difference between NS and HS (P < 0.05). †Significant difference between NTN and HS or HTH and HS (P < 0.05). ‡Significant difference between NTN and HTH (P < 0.05).

spite of significant increases in Hb concentration and CaO_2 of ~5% in HS over NS (Table 1). Training, on the other hand, resulted in the expected increase in VO_{2max} in both the normoxic (Table 1, NS vs. NTN) and the hypoxic groups (Table 1, HS vs. HTH). The increase in VO_{2max} in both groups was mediated in part though an increase in the rate of O_2 delivery to the tissues (T0_{2max}, Table 2, NS vs. NTN and HS vs. HTH). The improvement in T0_{2max} resulted from an increase in Q_{max}, due exclusively to increases in maximal stroke volume (SV_{max}, Table 2). Training also increased the rate of tissue O_2 extraction. Both O_2 ER and VO_{2max}/PV O_2, a composite parameter that reflects the diffusional O_2 conductance at the tissue level (10, 26), were significantly higher in HTH than in HS (Table 1). In the normoxic group, training resulted in a significant increase in VO_{2max}/PV O_2 only (Table 1, NS vs. NTN). Blood lactate levels during maximal exercise were lower in HS and HTH than in NS and NTN, respectively (Table 1). This is in agreement with previous observations on the effect of acclimatization lowering blood lactate levels during maximal exercise (1). Exercise training resulted in similar maximal exercise blood lactate levels as those in sedentary rats (Table 1, NS vs. NTN and HS vs. HTH). This is also in agreement with previous observations of higher work output for similar blood lactate concentrations in trained vs. untrained subjects (11). Although training effectively enhanced maximal exercise capacity, the effect was the same for both normoxic trained and hypoxic trained animals, i.e., VO_{2max} increased to the same extent in NTN and in HTH (Table 1). As it occurred in the hypoxic sedentary animals, HTH had a small (~5%) but significant increase in CaO_2 (Table 1, NTN vs. HTH); however, this was not effectively translated into a higher VO_{2max}. Other than the effects on CaO_2 and blood lactate, there were no other significant differences in the O_2 transport system between NTN and HTH.

As expected, rats acclimatized to hypoxia developed pulmonary hypertension (Fig. 1, NS vs. HS and NTN vs. HTH); however, the degree of hypertension was significantly attenuated with hypoxic training (Fig. 1, HS vs. HTH). Because the Ppa-to-Q ratios (Ppa/Q; Table 2) parallel the changes in Ppa from rest to maximal exercise in all four groups, the pulmonary hypertension present in the acclimatized groups is not due to a higher blood flow. Therefore, it can be concluded that the increase in Ppa is due to an increase in pulmonary vascular resistance. Acclimatization to

Table 2. Hemodynamic variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>NS</th>
<th>HS</th>
<th>NTN</th>
<th>HTH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q_{max}, ml-min^{-1}-kg^{-1}</td>
<td>425.7 ± 7.8</td>
<td>417.1 ± 7.9</td>
<td>456.3 ± 6.5†</td>
<td>443.2 ± 11.8‡</td>
</tr>
<tr>
<td>SV_{max}, (ml/kg)</td>
<td>0.79 ± 0.01</td>
<td>0.79 ± 0.02</td>
<td>0.85 ± 0.02†</td>
<td>0.84 ± 0.02†</td>
</tr>
<tr>
<td>HR_{max}, b/min</td>
<td>536 ± 5</td>
<td>530 ± 2</td>
<td>535 ± 9</td>
<td>534 ± 9</td>
</tr>
<tr>
<td>T0_{2max}, ml-min^{-1}-kg^{-1}</td>
<td>87.3 ± 1.6</td>
<td>90.2 ± 1.7</td>
<td>94.7 ± 1.7†</td>
<td>96.4 ± 2.0*</td>
</tr>
<tr>
<td>Psa, mmHg</td>
<td>146 ± 3</td>
<td>152 ± 2</td>
<td>148 ± 2</td>
<td>147 ± 5</td>
</tr>
<tr>
<td>Ppa (rest), mmHg</td>
<td>18.1 ± 0.8</td>
<td>24.5 ± 0.8*</td>
<td>16.6 ± 0.7</td>
<td>19.3 ± 0.8‡</td>
</tr>
<tr>
<td>Ppa (exercise), mmHg</td>
<td>23.8 ± 0.6</td>
<td>32.0 ± 0.9*</td>
<td>23.3 ± 0.4</td>
<td>29.2 ± 0.5‡</td>
</tr>
<tr>
<td>Ppa/Q (rest), mmHg-mg·kg^{-1}</td>
<td>61.4 ± 2.8</td>
<td>83.0 ± 4.1*</td>
<td>51.8 ± 2.9</td>
<td>64.3 ± 3.8‡</td>
</tr>
<tr>
<td>Ppa/Q (exercise), mmHg·kg^{-1}</td>
<td>56.6 ± 1.9</td>
<td>77.1 ± 2.7*</td>
<td>50.4 ± 1.4</td>
<td>66.3 ± 1.8‡</td>
</tr>
</tbody>
</table>

Values are means ± SE. Q_{max}, SV_{max}, HR_{max}, maximal cardiac output, maximal stroke volume and maximal heart rate respectively; T0_{2max}, maximal rate of convective blood O_2 delivery [= CaO_2 · Q_{max}]; Psa and Ppa, systemic and pulmonary mean arterial pressures, respectively. *Significant difference between NS and HS (P < 0.05). †Significant difference between NTN and NS or HTH and HS (P < 0.05). ‡Significant difference between NTN and HTH (P < 0.05).
MHx significantly increased Ppa/Q by 35%, both at rest and during maximal exercise (Table 2, NS vs. HS), whereas acclimatization to and training in MHx resulted in a 5% increase in Ppa/Q at rest and a 17% increase during maximal exercise (Table 2, NS vs. HTH).

DISCUSSION

The main findings of this study are: 1) acclimatization to and training at equal absolute work rates at the level of hypoxia used in the present experiments do not improve maximal aerobic capacity above that obtained with normoxic training and 2) training in hypoxia moderates hypoxic pulmonary hypertension. Acclimatization to MHx in sedentary rats did not result in significant changes in Vo2max. This result is similar to those obtained after acclimatization to more severe levels of hypoxia, which have shown that Vo2max in rats (7) and humans (3) changes little, if at all, after acclimatization. One major factor for the modest effect of acclimatization to severe hypoxia on Vo2max is the reduction in Qmax, which offsets the increase in CaO2 and prevents substantial increases in the rate of O2 delivery to contracting muscles. The decrease in Qmax is in part due to a reduction in maximal heart rate (HRmax). Refs. 6, 7, 22). This results from a diminished chronotropic response to catecholamines as a consequence of the downregulation of myocardial β-adrenoceptors (14). The role of reduced Qmax in limiting Vo2max after acclimatization was demonstrated by the observation in acclimatized rats that an increase in Qmax produced by increasing HRmax by atrial pacing, was translated into a proportionate increase in Vo2max (6). The present study shows that, in contrast to more severe hypoxia, acclimatization to MHx does not lead to significant changes in Qmax, HRmax, or SVmax. Nevertheless, the fact remains that the increase in CaO2 of HS was not translated into an increase in V02max. Other things being equal, the increase in CaO2 should have been translated into a proportionate increase in V02max, as is seen, for example, when hematocrit is artificially increased by red blood cell infusion (2). It is possible that the effect of increased blood O2 content was offset by an aggregate of small decreases in O2 conductances caused by acclimatization: average Qmax was 2% lower (Table 2), O2 ER 3% lower (Table 1), and V02max/PvO2 10% lower (Table 1) in HS than in NS. Although the individual differences in these variables were not statistically significant, their combined effect may have offset the effect of the increase in CaO2 on V02max. The lower O2 ER and V02max/PvO2 values of HS suggest a negative effect of chronic hypoxia on the efficacy of capillary-to-tissue O2 transfer, a possibility that has been raised before (9, 18).

The PtO2 selected for these experiments represents a level of hypoxia sufficient to elicit a polycythemic response (Table 1) while also allowing hypoxic trained rats to maintain the same absolute training intensity as normoxic trained animals. In preliminary experiments, we determined that exercise at this PtO2 resulted in a reduction of V02max of ~10% below the normoxic value of sedentary rats. This relatively small effect allowed us to maintain the absolute training intensity in both groups at ~80% of the V02max of sedentary normoxic rats. Equal absolute training intensities have the same O2 requirements independent of the environmental PO2 and eliminate training intensity and O2 flux levels as confounding factors.

The exercise training protocol was effective in increasing maximal exercise capacity: V02max increased by ~13% in both HTH and NTN above their respective sedentary controls. However, there was no significant difference in V02max between NTN and HTH. The increase in V02max in the trained groups was mediated in part by an increase in the rate of O2 delivery to the tissues, as indicated by a 7–9% increase in TO2max in both NTN and HTH above their corresponding sedentary controls (Table 2). In each case, the factor responsible for the training-induced increase in TO2max was an increase in SVmax (Table 2), indicating that the mechanisms by which exercise training increases the maximal rate of blood O2 convection are similar in both the hypoxic and normoxic trained groups.

Exercise training also influenced O2 extraction by the tissues, although the evidence for this was more clear in HTH than in NTN. The efficacy of O2 extraction by the tissues was evaluated by the changes in CaO2 – CvO2, O2 ER, and the ratio V02max/PvO2. Training in hypoxia significantly increased all three indexes above the levels observed in the sedentary rats (Table 1, HS vs. HTH). On the other hand, V02max/PvO2 was the only variable of tissue O2 extraction that was significantly increased by normoxic training (Table 1, NS vs. NTN). The apparently larger effect of hypoxic training on O2 extraction may be due to the relatively
smaller values of the O$_2$ extraction indexes in HS mentioned above. The data suggest that acclimatization to hypoxia lowers O$_2$ ER in sedentary rats and that training in hypoxia increases O$_2$ ER more than normoxic training. Although the absolute training intensity was the same, training intensity relative to V$_{O_2 \text{max}}$ was higher in HTH, because hypoxia of this magnitude lowers V$_{O_2 \text{max}}$ by $\sim$10%. It is possible that the higher relative training intensity created a more severe hypoxic condition in the exercising muscles of HTH and thus produced a stronger stimulus for the mechanisms responsible for changes in tissue O$_2$ extraction.

The practice of “living high and training low” has been shown to improve running performance over living and training in normoxia because it elicits polycythemia while maintaining normoxic training levels (17, 19). The present studies show that if normoxic training intensity is maintained in hypoxia, there is no improvement on maximal exercise capacity above that achieved by living and training in normoxia. The apparently larger effect of hypoxic training on O$_2$ ER does not lead to an improvement of this parameter over NTN but simply offsets the negative effect of acclimatization on O$_2$ ER. The lack of improvement in V$_{O_2 \text{max}}$ of HTH over NTN implies that hypoxic training may oppose other possible beneficial aspects associated with acclimatization.

Both HS and HTH rats developed pulmonary hypertension; however, Ppa was significantly lower in the trained than in the sedentary rats both at rest and during maximal exercise (Table 2). Because Ppa was measured in normoxia, it is clear that the Ppa values observed under these conditions do not include a component of hypoxic pulmonary vasoconstriction (HPV). Accordingly, the most likely sources for the differences in Ppa between HS and HTH are due to an effect of exercise training on the extent of pulmonary vascular remodeling and/or in the balance of pulmonary vasodilators and vasoconstrictors. Chronic exercise training in normoxic conditions moderates HPV (15) and the response to vasoconstrictors in rats (16). A less intense HPV could result in a lower stimulus for pulmonary vascular remodeling and could therefore be responsible for the moderation of pulmonary hypertension in HTH during normoxic conditions. Additionally, it is possible that exercise training modifies the pulmonary vascular response to vasodilators or vasoconstrictors. Studies in pulmonary arterial rings suggest that chronic exercise training leads to increased endothelium-dependent vasodilation and reduced production of prostanoid vasoconstrictors (13). However, this appears to be restricted only to coronary artery-ligated animals (12). It was suggested that the different effects of exercise training on pulmonary vasoreactivity between coronary artery-ligated and normal animals could result from larger increases in vascular shear stress secondary to abnormal cardiac function in the coronary artery-ligated animals, thus leading to upregulation of endothelial NOS gene expression (12, 20). Whether a similar mechanism operates during hypoxic exercise training in the rat is not clear from the present studies and should be the subject of further research.

In summary, acclimatization to and training in MHx increase maximal exercise capacity to the same level observed after a training protocol of equal absolute intensity under normoxic conditions. The potential advantage conferred by the increase in CaO$_2$ was not translated into a significant increase in V$_{O_2 \text{max}}$ because of the aggregate effect of small offsetting factors. Training in hypoxia, on the other hand, resulted in a moderation of the hypoxic pulmonary hypertension, suggesting that chronic exercise training may assist in the acclimatization process by reducing pulmonary hypertension.

The skillful technical assistance of Julie Allen is gratefully acknowledged.

This study was supported by National Heart, Lung, and Blood Institute Grant HL-39443.

REFERENCES


