Acceleration of $\dot{V}O_2$ kinetics in heavy submaximal exercise by hyperoxia and prior high-intensity exercise

MAUREEN MACDONALD,1 PREBEN K. PEDERSEN,2 AND RICHARD L. HUGHSON1

1Department of Kinesiology, University of Waterloo, Waterloo, Ontario, Canada N2L 3G1; and 2Department of Physical Education, Odense University, Odense DK-5230, Denmark

MacDonald, Maureen, Preben K. Pedersen, and Richard L. Hughson. Acceleration of $\dot{V}O_2$ kinetics in heavy submaximal exercise by hyperoxia and prior high-intensity exercise. J. Appl. Physiol. 83(4): 1318–1325, 1997.—We examined the hypothesis that $O_2$ uptake ($\dot{V}O_2$) would change more rapidly at the onset of step work rate transitions in exercise with hyperoxic gas breathing and after prior high-intensity exercise. The kinetics of $\dot{V}O_2$ were determined from the mean response time (MRT; time to 63% of total change in $\dot{V}O_2$) and calculations of $O_2$ deficit and slow component during normoxic and hyperoxic gas breathing in one group of seven subjects during exercise below and above ventilatory threshold (VT) and in another group of seven subjects during exercise above VT with and without prior high-intensity exercise. In exercise transitions below VT, hyperoxic gas breathing did not affect the kinetic response of $\dot{V}O_2$ at the onset or end of exercise. At work rates above VT, hyperoxic gas breathing accelerated both the on- and off-transient MRT, reduced the $O_2$ deficit, and decreased the $\dot{V}O_2$ slow component from minute 3 to minute 6 of exercise, compared with normoxia. Prior exercise above VT accelerated the on-transient MRT and reduced the $\dot{V}O_2$ slow component from minute 3 to minute 6 of exercise in a second bout of exercise with both normoxic and hyperoxic gas breathing. However, the summated $O_2$ deficit in the second normoxic and hyperoxic steps was not different from that of the first steps in the same gas condition. Faster on-transient responses in exercise above, but not below, VT with hyperoxia and, to a lesser degree, after prior high-intensity exercise above VT support the theory of an $O_2$ transport limitation at the onset of exercise for workloads >VT. 

ventilatory threshold; oxygen transport; oxygen utilization; oxygen deficit; oxygen debt

A REDUCTION IN THE MAGNITUDE of the $O_2$ deficit at the onset of exercise during hyperoxic, compared with normoxic, breathing (19, 23) suggested that if one supplied more $O_2$ to working muscle during this transient, it could be used. These data were obtained with Douglas bag collections of mixed expired air during tests requiring ~70–80% of maximal $O_2$ uptake ($\dot{V}O_2$). To date, the only studies to follow the $\dot{V}O_2$ responses at the onset of exercise during hyperoxia with breath-by-breath techniques found that there was no difference from control (11, 18). It is possible that hyperoxia failed to accelerate $\dot{V}O_2$ kinetics because the fractional concentration of $O_2$ was relatively low (inspiratory $O_2$ fraction ($F_{iO_2}$) = 0.30) (18) or that the work rates studied were of a relatively lower intensity, at which increasing arterial $P_O_2$ has not been shown to increase $\dot{V}O_2$ kinetics (11, 18), than in those studies in which $\dot{V}O_2$ kinetics were accelerated (19, 23). In the face of conflicting evidence for accelerated or unaltered $\dot{V}O_2$ kinetics with hyperoxic gas breathing, it is appropriate to set out the potential explanations. It is possible that, at least over a range of work rates, adequate $O_2$ is delivered at the onset of exercise, and $O_2$ utilization establishes the rate at which $\dot{V}O_2$ increases (8). Alternatively, hyperoxia might not supply more $O_2$ over this same range of work rates because of reduced blood flow as noted by some (26), but not all (16), previous investigators.

For work rates above VT, making more $O_2$ available might accelerate $\dot{V}O_2$ kinetics. Breathing a 70% inspired $O_2$-gas mixture could increase dissolved $O_2$ by up to 10 ml $O_2$/l of blood. The examples of smaller $O_2$ deficits with hyperoxia were probably for work rates above VT (19, 23). Two reports (6, 7) have suggested that $\dot{V}O_2$ increased more rapidly in the second of two step transitions to work rates above VT and maximum $\dot{V}O_2$ and no effect of prior high-intensity exercise for a subsequent subthreshold exercise bout. They attributed this to the existing changes in local muscle environment that promoted both more rapid increases in blood flow and a rightward shift of the $O_2$-hemoglobin dissociation curve that facilitated $O_2$ release at the working muscle.

The purposes of this study were threefold. First, we wanted to obtain data from breath-by-breath analysis of $\dot{V}O_2$ with hyperoxic gas breathing during the challenge of exercise to work rates both below and above
VT. Second, we wanted to examine the relationships between the magnitude of the O₂ deficit and the slow component of the O₂ increase in normoxia and hyperoxia. Third, we wanted to determine whether the second of two step increases in work rate to intensities above VT might be further accelerated by a subject completing this exercise while breathing a hyperoxic gas mixture. These experiments allowed the testing of the hypothesis that, at least for work rates above VT, O₂ transport to the exercising muscle acts as the rate-limiting step for the increase in VO₂ at the onset of exercise.

METHODS

The present study was conducted in two parts. The first part examined the effect of hyperoxia on VO₂ kinetics in response to step changes in work rate to below and above VT. The second investigated the effect of hyperoxia and prior high-intensity exercise on VO₂ kinetics after step changes to above VT.

Subjects

Seven subjects participated in each part of the study, with one subject participating in both parts. In the first part, five men and two women volunteered, and in the second part four men and three women volunteered. Each subject signed a consent form approved by the Office of Human Research of the University of Waterloo after reading a description of the methods and possible risks. Preliminary testing of all subjects consisted of an incremental exercise test to exhaustion in normoxia by using a ramp work rate protocol (15 W/min per increment) to establish a baseline, before the following work rate changes: a step increase in work rate to a level halfway between VT and peak VO₂ for 10 min, this was followed by hyperoxic breathing in the first and second step transitions (NH), hypoxic breathing in the first and second step transitions (HH), and hyperoxic breathing in the first followed by normoxic breathing in the second step transition (HN).

Breath-by-Breath Data

Breath-by-breath ventilation and gas exchange were measured on a computerized system (First Breath, St. Agatha, ON), which sampled inspired and expired volumes with a volume turbine (VMM-110, Alpha Technologies, Laguna Beach, CA) and fractional concentrations of O₂, CO₂, and N₂ by mass spectrometry (Marquette MGA-1100A, Milwaukee, WI) at a frequency of 200 Hz. VO₂ and VCO₂ were calculated as alveolar values with compensation for lung-gas stores and with computation of the effective lung volume (15).

For the hyperoxic testing, a large Tissot tank was filled with inspiratory gases from cylinders containing 70% O₂-30% N₂. The gas was not humidified. The Tissot tank was connected to a Y valve (model 2730, Hans Rudolph, St. Louis, MO) to permit inspiration from the tank. The Y valve was open to room air during the normoxic transitions. The volume turbine was calibrated with a manually pumped syringe and with the equipment configured as it was during testing, including hyperoxic gas, for these tests. The mass spectrometer was calibrated for normoxia and hyperoxia by using two precision gas mixtures that spanned the anticipated fractional gas concentrations in both normoxia and hyperoxia. A calibration procedure was performed to determine the time required for gas transport and mass spectrometric response (lag time) (14). Separate lag times were determined for normoxia and hyperoxia because of the effect of gas density. The lag time for the hyperoxic mixture was ~30 ms slower than for the normoxic mixture (11). Heart rate was measured with an electrocardiograph (7803A, Hewlett-Packard) by using standard bipolar electrode placement. Mean heart rate over each breath was recorded.

Data Analysis

Breath-by-breath data for VO₂ from at least three repetitions of an identical test condition for each subject were linearly interpolated between breaths to give values at 1-s intervals. The identical tests were then time aligned, superimposed, and ensemble averaged to give a single data set per subject. The average individual response was fit to a curve by using an exponential model. The curve-fitting procedure involved the calculation of a modeled exponential output for test values of the various parameters by using the least-squares error approach (13). These modeled outputs were compared with the actual individual averaged data set for that variable. The curve-fitting procedure was iterated until any further changes in the parameters for the model did not result in a reduction in the mean squared error between the curve drawn from the model and the averaged data set.

Each step transition was fit to a two-component model for the high-step tests, to work rates above VT, and fit to a three-component model for the low-step tests, to work rates above VT, and fit to a three-component model. Steps from the baseline work rate to a higher work rate were referred to as “on-transients,” whereas steps from a higher work rate to the baseline work rate were referred to as “off-transients.” Work rate transitions to and from a work rate below VT were referred to as “low steps,” and transitions to and from a work rate above VT were referred to as “high steps.”
The two-component model used to fit the responses to the low-step tests had a baseline ($G_0$) and two amplitude terms ($G_1$ and $G_2$), two time constants ($\tau_1$ and $\tau_2$), and two time delays ($TD_1$ and $TD_2$) as previously described (13):

$$\dot{V}O_2(t) = G_0 + G_1[1 - e^{-t/TD_1}] \cdot u_1 + G_2[1 - e^{-t/TD_2}] \cdot u_2$$

where

- $u_1 = 0$ for $t < TD_1$ and $u_1 = 1$ for $t \geq TD_1$
- $u_2 = 0$ for $t < TD_2$ and $u_2 = 1$ for $t \geq TD_2$

$\dot{V}O_2(t)$ is the time-dependent variation in $\dot{V}O_2$.

The data from the high-step tests were fitted to a three-component model. The three-component model contained an extra amplitude term ($G_3$) and time constant ($\tau_3$) to fit the slower adaptive phase in these tests. In the absence of a rationale for letting the third component begin at some time after the second, we used a model equivalent to that of Linnarsson (18) and had the second and third components start together. This issue is considered further in DISCUSSION.

$$\dot{V}O_2(t) = G_0 + G_1[1 - e^{-t/TD_1}] \cdot u_1 + G_2[1 - e^{-t/TD_2}] \cdot u_2 + G_3[1 - e^{-t/TD_3}] \cdot u_3$$

where $u_1$ and $u_2$ were defined above and

- $TD_3 = TD_2$
- $u_3 = 0$ for $t < TD_2$ and $u_3 = 1$ for $t \geq TD_2$
- $u_2 = 0$ for $t < TD_2$ and $u_2 = 1$ for $t \geq TD_2$

The overall time course of the response was determined from mean response time (MRT). The MRT is the time it takes to reach ~63% of the total amplitude of the response from the baseline to the final plateau value. It was calculated as a weighted sum of the time delay and time constant for each component:

$$MRT = \sum \frac{[G_1/G_1 + G_2 + G_3] \cdot (TD_1 + \tau_1)}{TD_1} + \frac{[G_2/G_1 + G_2 + G_3] \cdot (TD_2 + \tau_2)}{TD_2} + \frac{[G_3/G_1 + G_2 + G_3] \cdot (TD_3 + \tau_3)}{TD_3}$$

In addition to the curve-fitting procedure, the $\dot{V}O_2$ responses were also analyzed by calculating the $O_2$ deficit and by determining the slow component response of the $\dot{V}O_2$ response from 3 to 6 min and from 6 to 10 min after the step change in work rate. The $O_2$ deficit was taken as the difference between the measured $\dot{V}O_2$ at any time after the start of the higher-work-rate exercise and the average $\dot{V}O_2$ measured during the last minute of exercise.

Statistics

Statistical analysis was performed by using two-way repeated measures analysis of variance of the main effects. In part 1 the main effects, i.e., inspired gas concentration and work rate, and in part 2 the main effects, i.e., prior exercise and inspired gas concentration, were examined across various parameter estimates for $\dot{V}O_2$. The parameters examined were those generated from the curve-fitting procedure when applied to the average individual data set for each subject. Significant differences in MRT because of main effects were interpreted as reflecting differences in kinetics, while differences in other parameters were also noted. In part 2, when no significant difference in MRT was observed within step 2 because of the effect of previous gas condition, tests with the same gas condition for step 2 and with different previous gas conditions in step 1 were treated as identical and averaged before further statistical analysis. When significant main effects were observed, post hoc testing included comparisons by the Student-Newman-Keuls test. A significance level of $P < 0.05$ was maintained for all comparisons.

RESULTS

The mean peak $\dot{V}O_2$ values of the subjects during testing in normoxia were 45.3 ± 1.6 (SE) ml·kg$^{-1}$·min$^{-1}$ in part 1 and 44.4 ± 2.4 ml·kg$^{-1}$·min$^{-1}$ in part 2. The mean $\dot{V}O_2$ values achieved during the below-VT (low-step) and above-VT (high-step) tests in part 1 were 50.4 ± 0.9 and 78.6 ± 1.0% of peak $\dot{V}O_2$ at average work rates of 125 and 215 W, respectively. In part 2, the mean $\dot{V}O_2$ achieved during the high-step tests was 82.0 ± 0.8% of peak $\dot{V}O_2$ at an average work rate of 195 W.

$\dot{V}O_2$ Response Fitting

Part 1. The effect of hyperoxic gas breathing on $\dot{V}O_2$ kinetics was examined for work rate transitions to and from below and above VT (Fig. 1, Table 1). The on-transient kinetics of $\dot{V}O_2$ represented by the MRT were not accelerated for low steps with exercise in hyperoxia compared with exercise in normoxia. In contrast, hyperoxic gas breathing resulted in a faster adjustment to steady-state $\dot{V}O_2$ for high steps. No effect of hyperoxic gas breathing on the kinetics of the off-transient responses was observed for either low- or high-step transitions. For both on- and off-transients, the MRT was significantly less for low steps compared with high steps regardless of gas-breathing condition. The high-step off-transient responses were faster than the corresponding on-transient responses, for both normoxic and hyperoxic gas-breathing conditions. The low-step off-transient responses were slower than the on-transient responses for hyperoxic gas breathing, and there was no difference between the on- and off-transients during normoxic gas-breathing tests.

![Fig. 1. Oxygen uptake ($\dot{V}O_2$) at baseline and during transitions in exercise to low and high work rates for 1 subject breathing normoxic gas (dotted line) and hyperoxic gas (solid line). Lines represent average response for 4 identical transitions.](http://jap.physiology.org/DownloadedFrom/https://doi.org/10.1373/ajp2017mtз94617)
effects of hyperoxia on off-transient \( VO_2 \) kinetics after step 1 was different from the on-transient for same work rate and same gas-breathing condition, both in hyperoxia than in normoxia, and this was true for the second of two exercise transitions (step 1 and step 2 transitions, it was found that there was no effect of prior gas breathing on the MRT of the second of two exercise transitions (P > 0.05). Consequently, results were pooled and analyzed according to the gas condition within the exercise transition being examined (Fig. 2, Table 2). As in part 1, during high-step exercise transitions the \( VO_2 \) on-response was faster in hyperoxia than in normoxia, and this was true for both steps 1 and 2 (Table 2). Similarly, there were no effects of hyperoxia on off-transient \( VO_2 \) kinetics after the step 1 or step 2 test. The \( VO_2 \) on-transient kinetics were significantly accelerated as a result of prior exercise in both the normoxic and hyperoxic gas-breathing tests. Prior high-intensity exercise had no effect on any of the off-transient MRT. In step 1, during normoxic gas breathing the off-transient responses were faster than the corresponding on-transient responses, and no difference was observed between the on- and off-transients during hyperoxic gas breathing. During the step 2 transition, slower \( VO_2 \) kinetics were observed during the off-transient in hyperoxia than during the corresponding on-transient, whereas there were no differences between the on- and off-transient responses in normoxic gas breathing.

Table 1. Parameter estimates from fitting \( VO_2 \) responses for step transitions below and above VT in normoxia and hyperoxia

<table>
<thead>
<tr>
<th></th>
<th>( G_0 )</th>
<th>( G_1 )</th>
<th>TD_1</th>
<th>( \tau_1 )</th>
<th>( G_2 )</th>
<th>TD_2</th>
<th>( \tau_2 )</th>
<th>( G_3 )</th>
<th>TD_3</th>
<th>( \tau_3 )</th>
<th>MRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>On-transient</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;VT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normoxia</td>
<td>734 ± 22</td>
<td>387 ± 42</td>
<td>3.4 ± 0.6</td>
<td>11.2 ± 1.1</td>
<td>561 ± 64</td>
<td>23.5 ± 1.2</td>
<td>19.8 ± 2.6</td>
<td>31.3 ± 1.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperoxia</td>
<td>742 ± 21</td>
<td>402 ± 52</td>
<td>3.6 ± 0.6</td>
<td>12.7 ± 1.7</td>
<td>578 ± 66</td>
<td>23.6 ± 1.3</td>
<td>18.0 ± 2.6*</td>
<td>31.4 ± 1.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;VT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normoxia</td>
<td>739 ± 24</td>
<td>614 ± 94t</td>
<td>3.4 ± 0.8</td>
<td>10.8 ± 2.3</td>
<td>779 ± 60t</td>
<td>17.8 ± 0.6t</td>
<td>17.6 ± 1.0t</td>
<td>516 ± 32</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperoxia</td>
<td>723 ± 20</td>
<td>539 ± 92t</td>
<td>3.6 ± 0.3</td>
<td>8.2 ± 1.6</td>
<td>1,180 ± 129t</td>
<td>16.6 ± 0.8t</td>
<td>23.6 ± 2.0t</td>
<td>239 ± 112*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Off-transient</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;VT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normoxia</td>
<td>1,682 ± 116‡</td>
<td>-324 ± 79t</td>
<td>1.7 ± 0.4</td>
<td>10.9 ± 3.5</td>
<td>-620 ± 92‡</td>
<td>16.6 ± 1.7‡</td>
<td>28.5 ± 0.6‡</td>
<td>34.6 ± 0.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperoxia</td>
<td>1,715 ± 125‡</td>
<td>-388 ± 113‡</td>
<td>2.4 ± 0.6</td>
<td>12.2 ± 3.4</td>
<td>-599 ± 120‡</td>
<td>14.9 ± 1.5‡</td>
<td>33.3 ± 2.4‡</td>
<td>35.4 ± 1.2‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;VT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normoxia</td>
<td>2,641 ± 173‡</td>
<td>-503 ± 95t‡</td>
<td>1.6 ± 0.2</td>
<td>14.7 ± 8.2</td>
<td>-1,084 ± 132‡</td>
<td>18.9 ± 0.4</td>
<td>21.9 ± 1.3‡</td>
<td>-265 ± 62‡</td>
<td>82.7 ± 8.8‡</td>
<td>43.5 ± 1.1‡</td>
<td></td>
</tr>
<tr>
<td>Hyperoxia</td>
<td>2,676 ± 195‡</td>
<td>-435 ± 63t‡</td>
<td>2.2 ± 0.4</td>
<td>11.2 ± 7.4</td>
<td>-1,218 ± 131‡</td>
<td>16.8 ± 0.9*</td>
<td>21.7 ± 0.6‡</td>
<td>-260 ± 34‡</td>
<td>78.1 ± 6.7‡</td>
<td>40.9 ± 1.4‡</td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± SE for at least 4 repetitions by 7 subjects. VT, ventilatory threshold; \( G_0 \), 2-component model baseline; \( G_1 \) and \( G_2 \), 2-component 2 amplitude terms; \( G_3 \), 3-component model amplitude term; TD_1 and TD_2, 2-component model time delays; \( \tau_1 \) and \( \tau_2 \), 2-component model time constants; \( \tau_3 \), 3-component model time constant; MRT, mean response time. *Significantly different from normoxia for same step change in work rate, P < 0.05. †Significantly different from <VT step in same gas-breathing condition, P < 0.05. ‡Significantly different from the on-transient for same work rate and same gas-breathing condition, P < 0.05.

Part 2. In this part of the study, when normoxic and hyperoxic gas breathing were balanced between the step 1 and step 2 transitions, it was found that there was no effect of prior gas breathing on the MRT of the second of two exercise transitions (P > 0.05). Consequently, results were pooled and analyzed according to the gas condition within the exercise transition being examined (Fig. 2, Table 2). As in part 1, during high-step exercise transitions the \( VO_2 \) on-response was faster in hyperoxia than in normoxia, and this was true for both steps 1 and 2 (Table 2). Similarly, there were no effects of hyperoxia on off-transient \( VO_2 \) kinetics after the step 1 or step 2 test. The \( VO_2 \) on-transient kinetics were significantly accelerated as a result of prior exercise in both the normoxic and hyperoxic gas-breathing tests. Prior high-intensity exercise had no effect on any of the off-transient MRT. In step 1, during normoxic gas breathing the off-transient responses were faster than the corresponding on-transient responses, and no difference was observed between the on- and off-transients during hyperoxic gas breathing. During the step 2 transition, slower \( VO_2 \) kinetics were observed during the off-transient in hyperoxia than during the corresponding on-transient, whereas there were no differences between the on- and off-transient responses in normoxic gas breathing.

O\(_2\) Deficit and \( VO_2 \) Slow Component

Low steps. There was no difference in the O\(_2\) deficit calculated for hyperoxic and normoxic tests to below VT. There was not a significant slow component of \( VO_2 \) in either hyperoxic or normoxic low-step transitions (Table 3). These results were consistent with those obtained by curve fitting (Table 1).

High steps. Also consistent with the curve-fitting results presented above were the observations of a significantly smaller O\(_2\) deficit in high-step transitions with hyperoxia compared with normoxia in both parts 1 and 2 (Table 3). However, calculated O\(_2\) deficit in the second normoxic and hyperoxic steps was not different from step 1 in the same gas conditions.

The indication of \( VO_2 \) kinetics, from the \( VO_2 \) slow component between minutes 3 and 6 of the high-step tests, was consistent with the curve-fitting results (Tables 1 and 2). There was significantly less slow component in hyperoxia compared with normoxia, and the step 1 transition had a greater \( VO_2 \) slow component than that in step 2 (Table 3). Only for step 2 in normoxia was there a significant further slow component in \( VO_2 \) between minutes 6 and 10 of the step tests. These results indicate that most effects of the experimental

Fig. 2. \( VO_2 \) at baseline and during transitions in exercise to high work rates for 1 subject breathing normoxic gas (dotted line) and hyperoxic gas (solid line). Lines represent average response for 4 identical transitions.
for parts 1 and 2
rate of increase in $V\dot{O}_2$ at the onset of exercise came
O2 deficit and $V\dot{O}_2$ slow component
Table 3. prior exercise at a similar high intensity might have
mixture (19, 23) and in which incomplete recovery after
deficit was reduced at the onset of moderately heavy
exercise. 
manipulations were complete within the first 6 min of
exercise.

**DISCUSSION**

Previous evidence that O2 transport might limit the rate of increase in $V\dot{O}_2$ at the onset of exercise came from experiments in which the magnitude of the O2 deficit was reduced at the onset of moderately heavy exercise while a subject breathed a hyperoxic gas mixture (19, 23) and in which incomplete recovery after prior exercise at a similar high intensity might have facilitated blood flow and O2 release from hemoglobin in a second bout of exercise (6, 7). This study has combined these methodologies in an attempt to examine the hypothesis that O2 transport, acts as the rate-limiting step for the increase in $V\dot{O}_2$ at the onset of exercise above VT. Both hyperoxia and prior exercise caused an acceleration of $V\dot{O}_2$ kinetics (i.e., faster MRT, smaller O2 deficit, and reduced $V\dot{O}_2$ slow component from 3 to 6 min of exercise) for work rates above VT. When the two manipulations were combined, there was further speeding of the $V\dot{O}_2$ response, indicating that the two stimuli may work independently to increase O2 transport at the onset of exercise. For work rates below VT, there was no significant effect of hyperoxia on the time course of increase in $V\dot{O}_2$ at the onset of exercise. The postexercise rate of decrease in $V\dot{O}_2$ was faster after the below-VT exercise than after the above-VT exercise, yet there was no difference between normoxia and hyperoxia.

**Methodological Considerations**

There are two components of the design of this study that merit further consideration before physiological interpretation of the data can be discussed. The first is the selection of the work rates for the study, and the second is the model used to fit the experimental data. We selected work rates that were constant across the normoxia or hyperoxia treatments even though the peak work rate and $V\dot{O}_2$ are often found to be increased by up to 10% by hyperoxia (25). It was felt that this would not affect the kinetics responses because in each of the below- and above-VT cases, the work rates were clearly within the domains required. Furthermore, it has been observed that kinetics of $V\dot{O}_2$ are altered across a range of work rates, being slower for above-VT work rates, as we found; except for minor differences in percentage of peak work rate, there is little effect on the time course of $V\dot{O}_2$ at the onset of exercise (4, 28). In this study, our focus was on the effects of hyperoxia and/or prior exercise on the $V\dot{O}_2$ response to a fixed work rate.

Fitting of the $V\dot{O}_2$ response at the onset and end of exercise has been done by a variety of methods, primarily on the basis of the observation of an exponential, or near-exponential, change (18). At the below-VT work rate, we used a two-component exponential, in which the first component accounted for the rapid increase in

Table 2. Parameter estimates for $V\dot{O}_2$ kinetics for step transitions above VT in normoxia and hyperoxia without and with prior exercise

<table>
<thead>
<tr>
<th>Parameter</th>
<th>On-transient</th>
<th>Off-transient</th>
</tr>
</thead>
<tbody>
<tr>
<td>$G_0$, ml/min</td>
<td>$670 \pm 41$</td>
<td>$680 \pm 42$</td>
</tr>
<tr>
<td>$G_1$, ml/min</td>
<td>$1,050 \pm 64$</td>
<td>$2,000 \pm 66$</td>
</tr>
<tr>
<td>TD, s</td>
<td>$6.7 \pm 0.3$</td>
<td>$6.2 \pm 0.3$</td>
</tr>
<tr>
<td>$\tau_r$, s</td>
<td>$1.5 \pm 0.1$</td>
<td>$1.5 \pm 0.1$</td>
</tr>
<tr>
<td>$G_2$, ml/min</td>
<td>$3,000 \pm 150$</td>
<td>$3,500 \pm 150$</td>
</tr>
<tr>
<td>TD, s</td>
<td>$6.7 \pm 0.3$</td>
<td>$6.2 \pm 0.3$</td>
</tr>
<tr>
<td>$\tau_r$, s</td>
<td>$1.5 \pm 0.1$</td>
<td>$1.5 \pm 0.1$</td>
</tr>
<tr>
<td>MRT, s</td>
<td>$6.7 \pm 0.3$</td>
<td>$6.2 \pm 0.3$</td>
</tr>
</tbody>
</table>

Values are means ± SE; n = 6 or 7 subjects. *Significantly different from normoxia for same step change in work rate, P < 0.05. †Significantly different from step 1 in the same gas-breathing condition, P < 0.05. ‡Significantly different from on-transient for same step change in work rate and same gas-breathing condition, P < 0.05.
\( \dot{V}O_2 \) at the onset or decrease in \( \dot{V}O_2 \) at the end of exercise, because the return of venous blood is altered with the change in work rate. The second component represents the major change to the new steady-state value and is described by a single time constant with time delay (15). The major difference between studies has been in the description of the \( \dot{V}O_2 \) response to work rates above VT. We used a three-component exponential model.

The first component of the above-VT model was identical to that in the below-VT exercise. The second and third components represent a relatively rapid and a more slowly developing component, respectively. This interpretation is consistent with other research (28) and with our observations from the \( \dot{V}O_2 \) slow-component analysis (Table 3). In accord with Linnarsson (18), we had both phases 2 and 3 start at the same time point. In contrast, some researchers have allowed the time delay of the third phase to vary, demonstrating that this component of the response started 90–120 s after the onset of the exercise (2, 22). Curve fitting of physiological responses can incorporate physiological correlates, or it can simply attempt to minimize the error of the distribution of the data points about the line of best fit. In this case, it is not possible to identify specifically the physiological mechanism responsible for the slow component of the \( \dot{V}O_2 \) response (28). Therefore, we justify our selection of the model with a common time delay for phases 2 and 3 by the absence of a statistically significant improvement in fit between our model and that with an extra parameter for a third time delay. Whichever model is selected, the physiological interpretation as presented below is not altered.

Effect of Hyperoxia

In the steady-state phases of the present experiments, there were only minor differences in measured \( \dot{V}O_2 \) between normoxia and hyperoxia. In the baseline period before step 1 of part 2 of the study (Table 2), there was a small but significantly greater \( \dot{V}O_2 \) with hyperoxia compared with normoxia. Later within this same protocol, during the baseline period before step 2, \( \dot{V}O_2 \) was also higher with hyperoxia. Some previous research (25) has found an increase in fat utilization with hyperoxic breathing, although this was not suggested in the present study because the respiratory exchange ratio was unaltered. The elevated \( \dot{V}O_2 \) could have also been a consequence of inadequate time for equilibration to hyperoxia. Careful calibration of the equipment in this study was performed. We cannot, however, totally disregard the possibility that small errors in our measurements might have caused this statistical finding.

The faster \( \dot{V}O_2 \) on-transient MRT and the smaller \( O_2 \) deficit and \( \dot{V}O_2 \) slow component observed for the above-VT steps in hyperoxia, compared with normoxia, are in agreement with previous studies using Douglas bags and measurements of \( O_2 \) deficit to estimate \( \dot{V}O_2 \) kinetics (19, 23). The faster \( \dot{V}O_2 \) responses at the same absolute work rate are consistent with the pattern to be expected when the relative work rate is reduced by hyperoxia. Closer examination of the parameter estimates for the exponential curve fitting (Tables 1 and 2) shows that the increase during phase 3 was less in the hyperoxia tests than in normoxia. Therefore, to attain similar \( \dot{V}O_2 \) values at the end of exercise, a greater slow increase (see \( G_3 \) and \( \tau_3 \) in Tables 1 and 2) occurred in normoxia. This observation is also supported by a greater slow component between minutes 3 and 6 during normoxia compared with hyperoxia (Table 3). This observation supports the findings of Paterson and Whipp (22).

Hyperoxic gas breathing was used in this study in an attempt to increase the transport of \( O_2 \) to working muscle and therefore to determine whether \( O_2 \) transport is a limiting factor in the transient \( \dot{V}O_2 \) response after a step increase in work rate above and below VT. Others have shown that hyperoxia does not accelerate the kinetics of \( \dot{V}O_2 \) for step transients below VT (11, 18). The mechanism responsible for this could be that adequate \( O_2 \) is already being delivered at the onset of this light exercise, and hence \( O_2 \) delivery would not be limiting, or that hyperoxia does not, in fact, provide more \( O_2 \) at the onset of exercise. During steady-state exercise, blood flow to working muscles is reduced (26) or unaltered (16) with hyperoxic gas breathing. It is not known whether hyperoxic breathing resulted in decreased blood flow to the exercising muscle in this study. A reduction in blood flow, to counter the increase in blood \( O_2 \) content, would serve to maintain the \( O_2 \) delivery to the working muscle at approximately the same level as in normoxia. Another unknown is the mean capillary \( P_O_2 \). Knight et al. (16) identified an apparent nonlinear relationship between their estimated value for mean capillary \( P_O_2 \) and peak leg muscle \( \dot{V}O_2 \) with hyperoxia. Among other mechanisms that might account for this, Knight et al. included heterogeneity of flow distribution to the exercising muscle because of hyperoxia-induced vasoconstriction. The observation that on-transient \( \dot{V}O_2 \) kinetics were accelerated with hyperoxic gas breathing for step transitions to levels above VT indicates that the rate of \( O_2 \) transport was probably accelerated by hyperoxia during these step transitions.

Effect of Prior Exercise

Prior high-intensity exercise was also used in this study as a means of attempting to increase the \( O_2 \) transport to the working muscle. A prior bout of high-intensity exercise (> VT) accelerated the \( \dot{V}O_2 \) on-transient kinetics in normoxia and in hyperoxia, as evidenced by a smaller MRT. These findings are in agreement with previous research using a similar work rate protocol (6, 7), which found that, for exercise in normoxia at work rates above VT, prior exercise accelerated the \( \dot{V}O_2 \) kinetics of a subsequent exercise bout.

Metabolic acidosis as a result of the prior exercise bout has been suggested as a possible explanation for the faster \( \dot{V}O_2 \) kinetics of the second exercise bout (6, 7). These previous reports postulated that the prior exercise elevated the concentration of blood lactate and decreased the pH in the working muscle, thereby
promoting changes in osmolality and acidity that result in vasodilation in the working muscles. Other vasoactive substances might also still be elevated after 6 min of recovery. An additional factor that could promote O₂ delivery to the working muscle would be a rightward shift of the O₂-hemoglobin dissociation curve resulting from the accumulation of H⁺ and increased CO₂ (5). These results support the theory that O₂ transport is a limiting factor to high-intensity-exercise VO₂ on-transient kinetics, although changes in the intracellular metabolic environment that might promote a more rapid increase in oxidative metabolism have not been investigated.

The time course of increase in oxidative phosphorylation at the onset of exercise has been estimated by a range of techniques, yet it is uncertain over what range of work rates the time course of the adaptive process remains constant (14, 20, 28). With cycling exercise, there are definitely slower kinetics for VO₂ measured at the mouth at high work rates (28). Results from recent studies with nuclear magnetic resonance spectroscopy indicate both slower changes (20) and no differences in the rates of change in phosphocreatine (30) at higher work rates. Measurement of muscle VO₂ as the product of blood flow and arteriovenous O₂ content difference also showed a slower response at higher work rates (14). None of the experimental conditions resulted in high-step kinetics that were as fast as the low-step kinetics (Tables 1 and 2). This indicates either that O₂ transport was not the only limiting factor for the high steps or that the experimental conditions did not completely alleviate the O₂ transport deficit.

O₂ Deficit and O₂ Debt

The literature contains reports of the magnitude of O₂ debt exceeding, equaling, or being less than the magnitude of the O₂ deficit. Part of this discrepancy arises from the differences in exercise work rates studied, and part arises from differences in baseline state after the exercise. In an earlier study (1) in which debt exceeded deficit, the intensity of exercise studied was high, and the baseline after exercise was considered to be basal rest. In many studies in which lighter intensities of exercise (<VT) were studied with either rest or light exercise baselines, O₂ deficit and O₂ debt were normally about equal (9, 27, 31). The present results for below VT in both normoxia and hyperoxia, in which the time course of recovery (MRT) and the magnitude of change are almost the same as those at the onset of exercise, are in agreement with this. When the O₂ deficit is increased, by β-adrenergic-receptor blockade (9) or by higher intensity exercise, as shown in the present study by the slower MRT, the O₂ debt can be found to be smaller than O₂ deficit when the recovery baseline is mild exercise. The most probable explanation for this is that lactate produced during the on-transient to compensate for the inadequate O₂ delivery is metabolized as a substrate during exercise and in the mild exercise recovery (3). That is, it is not necessary to repay this component of the debt (11).

Wilson et al. (29) have shown that the ATP-to-ADP ratio can be altered at a given steady-state VO₂ as a function of intracellular PO₂. This could account for the different concentrations of lactate observed in hypoxia vs. normoxia or hyperoxia (19). Recently, Hughson et al. (14) speculated that altered intracellular PO₂ at the onset of exercise might modify the VO₂ response during the non-steady-state transition. The intracellular PO₂ at this time would be a function of O₂ delivery (arterial PO₂ and blood flow) and O₂ utilization. The present results are consistent with this hypothesis for work rates >VT.

The O₂ deficit and VO₂ slow-component values were smaller than the corresponding measurements of Gerbino et al. (7). These differences are likely to be because of the higher work rates used in the high-step transitions of the previous study. Although in both studies subjects were assigned a high work rate that was approximately halfway between VT and peak VO₂, the measured values in the previous study (92% peak VO₂) were considerably higher than in the present study (79 and 82% of peak VO₂). These differences in protocol may also explain the observation that prior high-intensity exercise did not influence the magnitude of the O₂ deficit in the present study, in contrast to the findings of Gerbino et al. (7). The major contribution to O₂ deficit occurs before 3min. However, we measured O₂ deficit over the full 10 min of exercise. The lack of effect of prior exercise could have resulted from small differences in the early response or in the apparent plateau value with the longer exercise duration in this study.

Conclusions

The faster VO₂ kinetics observed for the on-transient during step changes above VT with hyperoxia, and to a lesser degree with prior exercise, provide evidence that the supply of O₂ contributes to the control of tissue VO₂ for this relatively high, exercise intensity. The observation of no change in VO₂ kinetics for steps below VT may indicate that O₂ transport is not a limiting factor in this light-exercise-intensity condition. However, in the absence of definitive data concerning O₂ transport in the critical adaptive phase, it is not possible to rule out the alternative hypothesis. Off-transient kinetics above VT did not change significantly because of prior exercise or hyperoxic gas breathing, indicating that regulatory mechanisms for O₂ supply and utilization may be different in on- and off-transients above VT.

This research was supported by the Natural Sciences and Engineering Research Council (NSERC) of Canada. M. MacDonald is an NSERC Graduate Scholarship recipient. Address for reprint requests: R. L. Hughson, Dept. of Kinesiology, Univ. of Waterloo, Waterloo, Ontario, Canada N2L 3G1 (E-mail: hughson@cgsa.uwaterloo.ca).

Received 24 September 1996; accepted in final form 11 June 1997.

REFERENCES


