Effects of respiratory muscle work on exercise performance

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Received 9 September 1999; accepted in final form 25 February 2000

Harms, Craig A., Thomas J. Wetter, Claudette M. St. Croix, David F. Pugeleow, and Jerome A. Dempsey. Effects of respiratory muscle work on exercise performance. J Appl Physiol 89: 131–138, 2000.—The normal respiratory muscle effort at maximal exercise requires a significant fraction of cardiac output and causes leg blood flow to fall. We questioned whether the high levels of respiratory muscle work experienced in heavy exercise would affect performance. Seven male cyclists [maximal O2 consumption (VO2) 63 ± 5 ml·kg⁻¹·min⁻¹] each completed 11 randomized trials on a cycle ergometer at a workload requiring 90% maximal VO2. Respiratory muscle work was either decreased (unloading), increased (loading), or unchanged (control). Time to exhaustion was increased with unloading in 76% of the trials by an average of 1.3 ± 0.4 min or 14 ± 5% and decreased with loading in 83% of the trials by an average of 1.0 ± 0.6 min or 15 ± 3% compared with control (P < 0.05). Respiratory muscle unloading during exercise reduced VO2, caused hyperventilation, and reduced the rate of change in perceptions of respiratory and limb discomfort throughout the duration of exercise. These findings demonstrate that the work of breathing normally incurred during sustained, heavy-intensity exercise (90% VO2) has a significant influence on exercise performance. We speculate that this effect of the normal respiratory muscle load on performance in trained male cyclists is due to the associated reduction in leg blood flow, which enhances both the onset of leg fatigue and the intensity with which both leg and respiratory muscle efforts are perceived.

METHODS

Subjects

Seven male cyclists (nonsmoking; competitive) with resting pulmonary function within normal limits were recruited to participate in this study. None of our subjects experienced significant reductions in arterial PO2 at maximal exercise (10, 11). Informed consent was obtained in writing from each subject, and all procedures were approved by the Institutional Review Board of the University of Wisconsin-Madison. The physical characteristics of the subjects were as follows: age 27.3 ± 3.1 (SD) yr, height 177.9 ± 2.4 cm, and weight 71.3 ± 4.3 kg.

Pressure and Gas Measurements

During all tests, the raw data were recorded for subsequent analysis on an eight-channel Hewlett-Packard tape recorder, Gould chart recorder, and computer. Flow rates, flow-volume, and total body VO2 and CO2 production were measured by using equipment and techniques previously reported (1, 15). Apparatus resistance was 0.80–1.49 cmH2O · l⁻¹ · s at flow rates from 0.5 to 9.0 l/s.

Inspiratory Unloading and Loading

A feedback-controlled proportional-assist ventilator (PAV) was used to reduce the work of the inspiratory muscles during exercise (7, 10, 11, 22). During practice and testing sessions, subjects were verbally coached to relax, reduce their inspiratory effort, and permit the PAV to assist each inspiratory effort.

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mourn pressure at the onset of each inspiration (7). To in-
crease inspiratory work during exercise, we added ventili-
tory loads that consisted of mesh screens in the inspiratory
line with resistances of 3–7 cmH2O · l−1 · s−1. The ventilation
settings and added resistances were chosen to cause in-
creases and decreases in inspiratory muscle work similar to
our previous studies (Refs. 10, 11; also see DISCUSSION for
values). Subjects participated in practice sessions to fami-
larize themselves with the inspiratory loading and unload-
ing.

**Experimental Protocols**

Subjects initially completed a progressive, incremental
 maximal VO2 (VO2 max) exercise test on an electromagneti-
cally braked cycle ergometer (Elema, Solna, Sweden), begin-
nating at 150 W (~30–40% VO2 max), followed by an increase in
work rate of 50 W every 2.5 min until exhaustion. Subjects
selected their preferred pedaling frequency during the test,
and this cadence was maintained constant throughout all
subsequent testing through visual inspection of a digital
cadence output. After 20 min of recovery, subjects cycled to
exhaustion at 5–10% above their peak workload (as deter-
mined by the prior progressive test) to verify VO2 max. A
plateau (<150 ml/min) or decrease in VO2 was observed for
each subject between the final two workloads of the incre-
mental VO2 max test and/or between the final workload of the
incremental test and the workload of the repeat test. The
mean VO2 max averaged 363 ± 48 W (range 300–425 W). Subjects were free to
choose their cadence (between 80 and 100 rpm), and
termination of the test was determined when a cadence of
≥50 rpm could not be maintained. Verbal encouragement
and cadence feedback was provided.

**Statistical Analysis**

Paired t-tests were used to determine treatment differ-
ences between group mean values between control and respi-
atory muscle load or unload. Relationships were determined
from simple regression and forward stepwise multiple re-
gression. The intraclass correlation coefficient of reliability
(\(R\)) was used to evaluate the repeatability of our measures
over three trials. As \(R\) approaches 1.0, greater repeatability
is implied; \(R < 0.4\) indicates poor reliability, \(0.4 < R < 0.75\)
fair to good repeatability, and \(R > 0.75\) excellent repeatability.
Significance was set at \(P \leq 0.05\).

**RESULTS**

Table 1 shows the reproducibility of time to exhaus-
tion (Tlim), VO2, dyspnea, and leg rating of perceived exertion (RPE) during repeat testing under control conditions (control/unload and control/load). Note that the mean values for Tlim during control conditions were significantly longer during the control sessions associ-
ated with the unloaded trials than with the loaded trials, the latter having been conducted later in the year. No systematic changes were found in any of the variables across three repeat trials at isotime (minute 5) or end exercise (\(P > 0.10\)). The \(R\) value indicated a

<table>
<thead>
<tr>
<th>Time, min</th>
<th>Control/unload</th>
<th>Control/load</th>
<th>Control/unload</th>
<th>Control/load</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO2, l/min</td>
<td>9.1 ± 3.3</td>
<td>6.8 ± 1.7</td>
<td>4.45 ± 0.45</td>
<td>4.48 ± 0.39</td>
</tr>
<tr>
<td>dyspnea, Borg</td>
<td>9.8 ± 0.7</td>
<td>9.9 ± 0.5</td>
<td>10.0 ± 0.0</td>
<td>10.0 ± 0.0</td>
</tr>
<tr>
<td>Leg RPE, Borg</td>
<td>10.0 ± 0.5</td>
<td>10.0 ± 0.0</td>
<td>10.0 ± 0.0</td>
<td>10.0 ± 0.0</td>
</tr>
</tbody>
</table>

Values are means ± SD. Control/unload or control/load refers to the exercise trials conducted under control conditions that were associated with either the unloaded or loaded experimental trials. VO2, O2 uptake; RPE, rating of perceived exertion; \(R\), coefficient of reliability.
high level of reliability in dyspnea and leg RPE ratings across trials, with poor to good reliability in $T_{\text{lim}}$ and $V\dot{O}_2$ (see METHODS for rating scale).

**Effect of Respiratory Muscle Loading and Unloading on $T_{\text{lim}}$**

Table 2 shows mean values in $T_{\text{lim}}$ between experimental conditions. With respiratory muscle unloading, subjects were able to exercise $1.3 \pm 2.0$ min longer (range $-1.2$–$5.3$ min; $+14.4 \pm 4.9\%$) than during control conditions ($P < 0.05$), whereas, with loading, $T_{\text{lim}}$ was significantly reduced by $1.0 \pm 0.8$ min (range $0.4$–$4.7$ min; $-15.1 \pm 3.3\%$; $P < 0.05$). Individual data for $T_{\text{lim}}$ changes with respiratory muscle unloading and loading are shown in Fig. 1. Subjects exercised longer with respiratory muscle unloading in 16 of 21 trials (76%) and shorter with loading in 15 of 18 trials (83%). The regression line of control vs. unloaded $T_{\text{lim}}$ was parallel to the line of identity (not shown), indicating that the effect of unloading on absolute $T_{\text{lim}}$ was similar across all performance times, whereas, with loading, the reduction in $T_{\text{lim}}$ tended to be greater the longer the control performance time.

**Effect of Respiratory Muscle Unloading and Loading on $V\dot{O}_2$ and $V\dot{E}$**

Figure 2 shows $V\dot{O}_2$ and minute ventilation ($V\dot{E}$)/$V\dot{O}_2$ plotted against time from the first minute of exercise to exhaustion. All subjects exercised at least 5 min under all conditions, and, as a result, continuous data are provided for the initial 5 min of exercise and for end exercise. Table 3 summarizes group mean values for all measured variables.

Figure 2B shows that, under control conditions, $V\dot{O}_2$ averaged $92 \pm 1\%$ (range 91–94%) at the beginning of the prescribed workload and then rose gradually with exercise duration to achieve 100% of $V\dot{O}_2\max$ at end exercise. With loading, $V\dot{O}_2$ averaged $6.3 \pm 0.2\%$ greater than control ($P < 0.05$) for minutes 3–5 but was equal to control at end exercise. With unloading, $V\dot{O}_2$ averaged $6.9 \pm 0.2\%$ lower than control at all time points throughout exercise, including end exercise ($P < 0.05$). Loading resulted in a significantly steeper slope of $V\dot{O}_2$ vs. exercise time compared with unloading (0.17 vs 0.13; $P < 0.05$), but neither of these slopes was different from its respective control. Table 3 and Figure 2C show that $V\dot{E}/V\dot{O}_2$ was significantly greater than control with unloading and less than control with loading, primarily due to changes in tidal volume.

**Effect of Respiratory Muscle Unloading and Loading on Leg RPE and Dyspnea Ratings**

Figure 3 shows the time course for leg RPE and dyspnea during exercise, and mean changes are shown in Table 3. Leg RPE (Fig. 3A) and dyspneic ratings (Fig. 3B) with respiratory muscle loading were both significantly higher than control for minutes 1–4 but not at end exercise. With unloading, leg RPE and dyspneic ratings were lower during minutes 3–5 but not at end exercise.
breathing frequency; VT, tidal volume; TI/TT, ratio of inspiratory and expiratory volumes; V˙O2, l/min for ventilation time to exhaustion in healthy, physically trained humans. We observed that decreasing the work of breathing consistently led to significantly longer exercise tolerance, whereas increasing the work of breathing curtailed performance. Respiratory muscle unloading during exercise was also associated with reduced V˙O2, hyperventilation, and reduced perceptions of respiratory and limb discomfort. These findings demonstrate that the work of breathing normally encountered during sustained heavy exercise has a significant influence on exercise performance. We believe the reason for this effect is multifactorial and may include the direct effects of high levels of respiratory muscle work on respiratory muscle fatigue and/or its “indirect” effects on limiting blood flow distribution to limb locomotor muscles.

Table 3. Group mean values at isotime (minute 5) and end exercise

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Unload</th>
<th>Control</th>
<th>Load</th>
</tr>
</thead>
<tbody>
<tr>
<td>V˙O2, l/min</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minute 5</td>
<td>4.23 ± 0.14</td>
<td>4.09 ± 0.12*</td>
<td>4.30 ± 0.14</td>
<td>4.49 ± 0.16†</td>
</tr>
<tr>
<td>End exercise</td>
<td>4.48 ± 0.11</td>
<td>4.23 ± 0.10*</td>
<td>4.46 ± 0.13</td>
<td>4.51 ± 0.14*</td>
</tr>
<tr>
<td>V˙E, l/min</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minute 5</td>
<td>166.4 ± 6.0</td>
<td>175.9 ± 6.0*</td>
<td>173.7 ± 4.5</td>
<td>155.0 ± 6.0†</td>
</tr>
<tr>
<td>End exercise</td>
<td>181.6 ± 4.7</td>
<td>199.6 ± 5.0*</td>
<td>191.7 ± 5.0</td>
<td>164.0 ± 6.5†</td>
</tr>
<tr>
<td>V˙V˙O2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minute 5</td>
<td>39.4 ± 1.0</td>
<td>43.0 ± 0.9*</td>
<td>40.4 ± 1.1</td>
<td>34.5 ± 1.3†</td>
</tr>
<tr>
<td>End exercise</td>
<td>40.5 ± 0.9</td>
<td>47.1 ± 1.4*</td>
<td>43.0 ± 1.0</td>
<td>36.4 ± 1.1†</td>
</tr>
<tr>
<td>f, breaths/min</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minute 5</td>
<td>51 ± 2</td>
<td>47 ± 2*</td>
<td>55 ± 2</td>
<td>53 ± 2†</td>
</tr>
<tr>
<td>End exercise</td>
<td>53 ± 1</td>
<td>52 ± 2</td>
<td>57 ± 2</td>
<td>53 ± 3</td>
</tr>
<tr>
<td>Vr, liters</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minute 5</td>
<td>2.84 ± 0.11</td>
<td>3.74 ± 0.14*</td>
<td>3.16 ± 0.14</td>
<td>2.92 ± 0.12†</td>
</tr>
<tr>
<td>End exercise</td>
<td>3.42 ± 0.13</td>
<td>3.85 ± 0.15*</td>
<td>3.36 ± 0.12</td>
<td>3.12 ± 0.12†</td>
</tr>
</tbody>
</table>
| T/T, ratio of inspiratory time to total time. Note that End-exercise time averaged 9.1 ± 2.6 min for control and 10.4 ± 2.9 min for unload, and 7.1 ± 1.7 min for control and 6.1 ± 1.2 min for load (see Table 2). *Significantly different from control, P < 0.05. †Significantly different from unload, P < 0.05.

Correlations Among Variables With a Changing Work of Breathing

Interindividual differences with loading and unloading for most variables as measured at isotime (minute 5) or in the slopes of the time-dependent effects were significantly interrelated (see Tables 4 and 5). Of particular relevance were the findings from the multiple-regression analysis that the total variation of changes in Tlim with unloading and loading were best accounted for by 1) the independent effects of changes at isotime in dyspnea perception ($r^2 = 0.29$) and 2) the combination of changes in slope for dyspnea perception plus those in $V_r$ vs. exercise time ($r^2 = 0.35$). Changes in both respiratory and limb discomfort with respiratory muscle loading and unloading were closely related to each other, especially at the isotime of exercise, and, in turn, changes in either of these perceptions with loading and unloading were most closely related to changes in V˙O2.

DISCUSSION

Major Findings

Our findings demonstrate a significant effect of the work of breathing during strenuous exercise on performance time to exhaustion in healthy, physically trained humans. We observed that decreasing the work of breathing consistently led to significantly longer exercise tolerance, whereas increasing the work of breathing curtailed performance. Respiratory muscle unloading during exercise was also associated with reduced V˙O2, hyperventilation, and reduced perceptions of respiratory and limb discomfort. These findings demonstrate that the work of breathing normally encountered during sustained heavy exercise has a significant influence on exercise performance. We believe the reason for this effect is multifactorial and may include the direct effects of high levels of respiratory muscle work on respiratory muscle fatigue and/or its “indirect” effects on limiting blood flow distribution to limb locomotor muscles.

Table 4. Correlation matrix of the changes from control with respiratory muscle loading and unloading at isotime (minute 5)

<table>
<thead>
<tr>
<th></th>
<th>Δ V˙O2</th>
<th>Δ Vr</th>
<th>Δ Leg RPE</th>
<th>Δ Dyspnea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Δ Tlim</td>
<td>-0.39*</td>
<td>0.29</td>
<td>-0.42*</td>
<td>-0.54*</td>
</tr>
<tr>
<td>Δ V˙O2</td>
<td>-0.37*</td>
<td>0.45*</td>
<td>0.51*</td>
<td></td>
</tr>
<tr>
<td>Δ Vr</td>
<td>-0.43*</td>
<td></td>
<td>-0.53*</td>
<td></td>
</tr>
<tr>
<td>Δ Leg RPE</td>
<td>0.78*</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Tlim, time to exhaustion; Δ, change. On the basis of stepwise multiple-regression analysis, changes in dyspnea perception accounted for 29% of the variance in ΔTlim: $ΔTlim = -0.027(Δ dyspnea) - 0.28 (P < 0.001). *P ≤ 0.05.
in very heavy exercise and on the intensity with which both respiratory and locomotor muscular efforts are perceived.

Limitations

Loading and unloading effects. We did not directly measure esophageal pressure (Pes) in our study, to avoid invasive instrumentation that might detract from performance time. In two previous studies from our laboratory (10, 11), measurements of Pes and Pes-volume loops during exercise at $V_{O2\text{max}}$ showed that, under control conditions, the work of breathing averaged 520–548 J/min and Pes averaged 28 cmH$_2$O at peak inspiration and 23 cmH$_2$O at peak expiration. Unloading caused the work of breathing to be reduced, on average, to 37–45% of control and Pes to be 6–8 cmH$_2$O more negative than control with inspiratory resistive loading throughout exercise. Accordingly, we avoided systematic changes within and between trials by randomly assigning experimental (unloading/loading) and control conditions while exposing each subject to several practice trials in addition to multiple trials per condition. Although we did observe random, intrasubject variability in $T_{lim}$ on repeat testing, no significant systematic learning effects occurred with repeat trials (see Table 2). We attribute the absence of any apparent learning effect to our use of highly trained competitive cyclists who had considerable experience with exhaustive exercise, together with the use of very high-intensity, fairly short-duration exercise trials that did not cause boredom or monotony.

Finally, we note that a time trial in which total power output and/or mileage completed in a fixed time is used to measure performance has been shown to be more reproducible than a fixed-work-rate test, at least when the latter requires only 75% of $V_{O2\text{max}}$ and lasts a 1 h or more (12). Unfortunately, time-trial tests were not feasible in our study because we found that application of the mechanical ventilator in the presence of a changing work rate was highly disruptive to breathing and often inconsistent in unloading the respiratory muscles.

Although use of the PAV caused subjects to express substantial relief in their perception of the difficulty of working at high intensities, it is also important to stress that the use of positive-pressure ventilation to reduce the work of breathing was not without significant side effects. Despite several practice sessions, the ventilator was occasionally disruptive to the subjects who had to concentrate on relaxing their chest wall while tolerating the foreign sensation of air being “pushed” into their lungs and the rare asynchrony between the ventilator breath and the subject’s respiratory effort. Clearly, these procedures often distracted the subject from concentrating on the main task of completing a maximal cycling performance to exhaustion. Accordingly, we suspect that the actual effect of the normally occurring amount of respiratory muscle work, per se, on high-intensity endurance exercise performance is probably even greater and more consistent than the 14 ± 5% improvement presently observed.

Comparison With Other Respiratory Muscle Unloading Studies

Contrary to our findings, several reports have shown no benefits of respiratory muscle unloading on exercise performance. Performance studies are typically prone to much variability in $T_{lim}$ because of day-to-day variations in subject motivation, effort perceptions, learning effects, normal biological variability, and so forth. Furthermore, in our study, we also introduced variable amounts of respiratory muscle work with unloading from trial to trial because the resultant amount of work was determined by the combined effects of the set amount of the ventilator’s pressure assist plus the subject’s ability to “relax” and to reduce the respiratory motor output (or effort) to breathe. Accordingly, we avoided systematic changes within and between trials by randomly assigning experimental (unloading/loading) and control conditions while exposing each subject to several practice trials in addition to multiple trials per condition. Although we did observe random, intrasubject variability in $T_{lim}$ on repeat testing, no significant systematic learning effects occurred with repeat trials (see Table 2). We attribute the absence of any apparent learning effect to our use of highly trained competitive cyclists who had considerable experience with exhaustive exercise, together with the use of very high-intensity, fairly short-duration exercise trials that did not cause boredom or monotony.

Table 5. Correlation matrix of the percent change from control in the slopes of exercise time vs. each variable with respiratory muscle loading and unloading

<table>
<thead>
<tr>
<th>%Δ $T_{lim}$</th>
<th>%Δ $V_{O2}$/time</th>
<th>%Δ $V_{E}$/time</th>
<th>%Δ RPE/time</th>
</tr>
</thead>
<tbody>
<tr>
<td>%Δ $V_{O2}$/time</td>
<td>0.38*</td>
<td>0.44*</td>
<td>0.24</td>
</tr>
<tr>
<td>%Δ $V_{E}$/time</td>
<td>0.05</td>
<td>0.05</td>
<td>0.42*</td>
</tr>
<tr>
<td>%Δ RPE/time</td>
<td>0.05</td>
<td>0.05</td>
<td>0.42*</td>
</tr>
</tbody>
</table>

On the basis of stepwise multiple regression analysis, changes in dyspnea ($P = 0.019$) and $V_{E}$ ($P = 0.042$) accounted for 32% of the variance in Δ$T_{lim}$: Δ$T_{lim} = −0.021 (Δ$ dyspnea/time$) − 0.129 (Δ$ V_{E}$/time$) + 18.9. *$P ≤ 0.05.
Subjects, whose \( \dot{V}O_2 \) max was 168 ± 3% of predicted. The work of breathing during near-maximal exercise has been shown to require ∼10% of total \( V_O_2 \), on average, for the moderately fit subjects, whereas, in the highly fit subjects at higher peak work rates and \( V_E \), the \( O_2 \) cost of breathing approaches 15% of \( V_O_2 \) max (1). Therefore, the effect of reducing the work of breathing during high-intensity exercise would be most noticeable in the highly fit subject. Second, the exercise intensity used in previous reports was ∼70–80% of \( V_O_2 \) max whereas our subjects began exercising at ∼90% \( V_O_2 \) max and reached \( V_O_2 \) max at end exercise. Our laboratory has reported that blood flow redistribution between the respiratory muscles and the legs occurred with loading and unloading at maximal exercise (10) but not during exercise at 50 or 75% \( V_O_2 \) max (20). Therefore, considering both previous and present studies, we would predict that endurance performance would not be increased with respiratory muscle unloading during more moderate-intensity exercise. Third, our experimental design included several practice trials on the ventilator and included trained cyclists to eliminate systematic learning effects on performance. Most importantly, we used multiple, randomized performance trials in an attempt to reduce the effect of random variability in performance time (see Limitations). Previous reports have used fewer trials, which raises the question of repeatability and their ability to detect significant systematic changes in performance beyond the “noise” of random variation.

Other attempts to unload the respiratory muscles have used helium-oxygen gas mixture (13, 21). In these studies, heliox acts to expand the maximal flow-volume loop and eliminate expiratory flow limitations that occur in many highly fit individuals. It was found that heliox did not affect exercise time and whole body \( V_O_2 \) at moderate work intensities; however, with exercise of >85–90% \( V_O_2 \) max breathing heliox significantly increased exercise time and reduced \( V_O_2 \) (near the end of exercise).

Previous studies of unloading reported either no change in \( V_E \) or increases that occurred only at lower exercise intensities or at early stages of prolonged, constant-load exercise (7, 16). In the present study, however, we found a significant hyperventilatory response to unloading that persisted throughout the prolonged heavy exercise (see Fig. 2). We are not sure why these findings differ. One interpretation of the increased \( V_E/V_O_2 \) with unloading is that the high level of normal respiratory muscle force exerted in heavy exercise caused reflex inhibition of central respiratory motor output and that this inhibition was relieved with unloading. On the other hand, we cannot rule out behavioral effects on respiratory motor output and ventilation secondary to application of PAV.

Why Did Unloading/Loading of The Respiratory Muscles Change Exercise Performance?

Our findings speak to three types of influences that have a potential bearing on why changes in respiratory muscle loading may have affected exercise performance. These include influences on \( O_2 \) transport to (and \( CO_2 \) transport from) locomotor muscles, on respiratory muscle fatigue, and on the perception of respiratory and/or locomotor muscle effort.

Effects of respiratory muscle loading on \( O_2 \) transport to locomotor muscles. In view of previous findings (see Comparison With Other Respiratory Muscle Unloading Studies; Refs. 10, 11) we would expect that, under the near-maximal and maximal conditions of exhaustive exercise encountered in the present study, the appropriate increases and decreases in limb vascular conductance, blood flow, and \( O_2 \) transport occurred with respiratory muscle unloading and loading, respectively. However, we emphasize that, with respiratory muscle unloading and less negative intrathoracic pressure, the stroke volume and cardiac output 

(10) and \( V_O_2 \) are also reduced, and, therefore, the effects on local limb blood flow, although consistent and significant, are relatively small (in the range of 5–7% increase from control). Nevertheless, limb muscle force output and fatigue have been shown to be highly responsive to even small changes in limb muscle blood flow under conditions of high intensities of muscle contraction (5). In contrast to these relatively small effects on limb blood flow with unloading of respiratory muscles, the effects are substantially greater with loading because the cardiac output remains unchanged from control and also because slightly greater changes are elicited in limb vasoconstriction. Consistent with these findings, we also found in the present study that unloading reduced total body \( V_O_2 \) throughout our prolonged exercise at >90% \( V_O_2 \) max whereas loading increased the \( V_O_2 \) up to end exercise, at which point \( V_O_2 \) in control and loaded conditions was equal and equivalent to \( V_O_2 \) max. The absence of an effect of added respiratory muscle load on \( V_O_2 \) at end exercise was because cardiac output had also achieved maximal levels (10). Presumably then, with loading, the observed reduction in limb blood flow was closely matched by an increase in blood flow to the respiratory muscles.

To summarize, we think it very likely that local changes in locomotor muscle blood flow did occur when we superimposed respiratory muscle loading and unloading during exhaustive endurance exercise and that these changes would have important effects on \( O_2 \) transport to and \( CO_2 \) removal from the working locomotor muscles and, therefore, on their fatigability.
Was respiratory muscle fatigue affected by loading and unloading and what were the consequences? Diaphragm fatigue is consistently caused by heavy sustained exercise when exercise intensity exceeds 85% of maximum (14). Furthermore, diaphragm fatigue is prevented when PAV is used to reduce diaphragmatic work during heavy, exhaustive exercise (3). On the basis of these findings, we presume that, in our study, diaphragm fatigue did occur during prolonged heavy exercise and that it was likely worsened by inspiratory resistive loading and relieved and delayed by unloading.

We must also ask how or even whether diaphragm or respiratory muscle fatigue actually influences endurance exercise performance. Theoretically, respiratory muscle fatigue could lead to alveolar hypoventilation (and reduced systemic O₂ transport and CO₂ elimination) if either “pump failure” occurred or a tachypneic breathing pattern caused high dead space and, therefore, reduced alveolar ventilation. However, cases of arterial hypoxemia are rare during prolonged submaximal exercise (9). Apparently, even though maximal force output of the diaphragm is reduced (in response to supramaximal phrenic nerve stimulation), and the relative contribution of the diaphragm to total inspiratory pleural pressure is reduced over the duration of heavy exercise (14), this is not sufficient to cause “task failure” or hypoventilation. In fact, hyperventilation commonly occurs over time during prolonged heavy exercise because of the extensive array of “accessory” respiratory muscles that are progressively recruited (Refs. 4, 14; see Fig. 2). Therefore, by itself, exercise-induced diaphragm fatigue probably did not influence the adequacy of alveolar ventilation or systemic O₂ transport.

Indirectly, diaphragm fatigue may have influenced performance by reducing the relative contribution of the diaphragm and promoting greater use of accessory respiratory muscles (14). This change in muscle recruitment patterns may have led to chest wall distortion, mechanical inefficiency of breathing, and, therefore, a greater work of breathing and increased metabolic and blood flow demand by the respiratory muscles (see above). This fatigue-induced increase in respiratory muscle work would also be expected to increase sensory input to the central nervous system, and, therefore, heighten awareness and perception of respiratory muscle effort (also see Role of changing perception of effort with respiratory muscle loading/unloading).

Role of changing perception of effort with respiratory muscle loading/unloading. Loading and unloading of the respiratory muscles during heavy exercise had substantial effects on the perception of both respiratory and limb effort; in turn, changes in Tlim correlated significantly with changes in both types of effort perception. The changes in these perceptions with changing loads on the respiratory muscles were usually similar for both respiratory and limb discomfort, both in time and amplitude, especially during unloading (see Fig. 3 and Table 5). Perhaps the influence of reducing respiratory muscle work on the perception of dyspnea is especially significant in our well-trained subjects, because, under near-maximal exercise conditions, their high ventilatory demand requires that inspiratory muscle force output commonly reach 90% of the capacity available for pressure generation (15).

The sources of both respiratory and limb discomfort perceptions have much in common because force output of respiratory and limb muscles increases with time, especially with the onset and development of muscle fatigue. For example, increased central motor command to the locomotor and to the respiratory muscles may be directly perceived via central corollary discharge as an increased sense of muscle effort (8). Furthermore, discomfort of limb and respiratory muscles may also arise from the periphery via activation of muscle type IV afferents as muscle metabolites accumulate with the onset of fatigue. Accordingly, we observed significant correlations between the change in perception of either limb or respiratory discomfort and changes in VO₂ vs. exercise time with unloading and loading. Therefore, these findings would predict that, during heavy, fatiguing exercise, subjects cannot discriminate with much sensitivity between the two different noxious sensations because both are expressions of similar internal perceptions.

O’Donnell et al. (19) have also reported a significant effect of respiratory muscle unloading on reducing limb discomfort perceptions and prolonging exercise in heart failure patients, even in the absence of measurable effects on dyspnea. These authors suggested that respiratory muscle work, per se, was not a major determinant of dyspnea in these patients, but, rather, their respiratory discomfort may originate in the expiratory flow limitation and hyperinflation they experience during even moderate-intensity exercise (19). This apparently specific effect of changes in the work of breathing, via pressure assist, on the perception of limb discomfort may have a physiological basis in the redistribution of cardiac output away from or to the exercising limb vasculature (10). This was apparently not the case in our study of prolonged heavy exhaustive exercise in healthy trained subjects, in whom reductions in respiratory muscle work and their associated energy expenditure had major effects on the perception of dyspnea throughout the exercise.

Summary and Relevance

In summary, we believe our findings, obtained during respiratory muscle unloading, have demonstrated a consistent, significant effect of the work of breathing that is normally achieved during very heavy exercise in trained subjects on endurance exercise performance. We speculate that the major links between respiratory muscle work and endurance exercise performance lie in a combination of the reflex sympathetic vasoconstrictor influences exerted by respiratory muscle work on limb vasoconstriction and blood flow, and, therefore, on limb muscle fatigability, together with its feedback effects on the intensity of effort perception. Further-
more, the influence of ventilatory work on dyspneic perceptions was also substantial and likely added significantly to the total perception of discomfort, which caused the performers to slow their pace. Finally, the diaphragm fatigue that accompanies heavy endurance exercise does not compromise an adequate alveolar ventilation but may indirectly curtail exercise performance if the excessive use of accessory respiratory muscles causes a mechanically inefficient ventilation.

Under what conditions is respiratory muscle work likely to influence exercise performance? Given our stated reasons for the link between respiratory muscle work and performance (see above), we propose that the exercise conditions must be sufficient to elicit a significant vasoconstrictor effect from the diaphragm to the limb muscle vasculature. This would occur in healthy subjects but only during very heavy exercise (i.e., >80–85% of VO2max) in which the work of breathing is sufficiently high and the cardiac output limited in its ability to distribute flow adequately to both respiratory and locomotor muscles (10). The appropriate conditions might also occur even at more moderate intensities of submaximal exercise when cardiac output is abnormally low and ventilatory work is high. This is likely to occur in exercising heart failure patients (17, 19) or during exercise in healthy subjects after acclimatization to the hypoxia of high altitudes (2).

We are indebted to Dr. Magdy Younes, who invented the proportional-assist ventilator and loaned us one of his prototypes to conduct this study. We also acknowledge our subjects for their willing participation in these studies.

This research was supported by National Heart, Lung, and Blood Institute (NHLBI) Grant RO1 HL-15469. C. A. Harms and T. J. Wetter were supported by a NHLBI training grant. C. A. Harms was additionally supported by a Parker B. Francis Foundation Fellowship.

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