Addition of inspiratory resistance increases the amplitude of the slow component of O₂ uptake kinetics

J. Carra, R. Candau, S. Keslacy, F. Giolbas, F. Borrani, G. P. Millet, A. Varray, and M. Ramonatxo. Addition of inspiratory resistance increases the amplitude of the slow component of O₂ uptake kinetics. J Appl Physiol 94: 2448–2455, 2003. First published February 21, 2003; 10.1152/japplphysiol.00493.2002. —The contribution of respiratory muscle work to the development of the O₂ consumption (V˙O₂) slow component is a point of controversy because it has been shown that the increased ventilation in hypoxia is not associated with a concomitant increase in V˙O₂ slow component. The first purpose of this study was thus to test the hypothesis of a direct relationship between respiratory muscle work and V˙O₂ slow component by manipulating inspiratory resistance. Because the conditions for a V˙O₂ slow component specific to respiratory muscle can be reached during intense exercise, the second purpose was to determine whether respiratory muscles behave like limb muscles during heavy exercise. Ten trained subjects performed two 8-min constant-load heavy cycling exercises with and without a threshold valve in random order. V˙O₂ was measured breath by breath using a fast gas exchange analyzer, and the V˙O₂ response was modeled after removal of the cardiodynamic phase by using two monoexponential functions. As anticipated, when total work was slightly increased with loaded inspiratory resistance, slight increases in base V˙O₂, the primary phase amplitude, and peak V˙O₂ were noted (14.2%, P < 0.01; 3.5%, P > 0.05; and 8.3%, P < 0.01, respectively). The bootstrap method revealed small coefficients of variation for the model parameter, including the slow-component amplitude and delay (15 and 19%, respectively), indicating an accurate determination for this critical parameter. The amplitude of the V˙O₂ slow component displayed a 27% increase from 8.1 ± 3.6 to 10.3 ± 3.4 mL/min · kg⁻¹ (P < 0.01) with the addition of inspiratory resistance. Taken together, this increase and the lack of any differences in minute volume and ventilatory parameters between the two experimental conditions suggest the occurrence of a V˙O₂ slow component specific to the respiratory muscles in loaded condition.

The characteristics of oxygen uptake (V˙O₂) kinetics in constant-load exercise have been well documented (3, 4, 7, 8, 14, 15, 21, 38, 39, 45). During the transition from rest or unloaded cycling to constant-load exercise of moderate intensity (i.e., below the ventilatory threshold), V˙O₂ rises after the cardiodynamic phase (phase I) in an approximately monoexponential fashion (phase II) to attain steady state (phase III) within 2–3 min. However, the V˙O₂ response to constant-load exercise of heavy intensity (i.e., above the ventilatory threshold) is more complex. The fundamental exponential response of pulmonary V˙O₂ is supplemented by the development of a slow-component phase (phase III) (4, 21).

Although the existence of the slow component has been demonstrated, the putative mechanisms have not been clearly established. Several hypotheses, including peripheral and central factors, have been proposed to explain the excess of V˙O₂. Of the peripheral factors, the recruitment of type II muscle fibers seems the most plausible explanation (6, 8, 12, 42, 43). Type II muscle fibers are currently reported to be less efficient than type I because the ADP/O ratio is 18% lower, partly because of the greater reliance on the α-glycerophosphate shuttle over the malate-aspartate shuttle (17, 44). Simultaneous measurement of pulmonary and leg V˙O₂ suggested that ~86% of the excess V˙O₂ observed with high-intensity exercise originates in the exercising limbs (39). This result further suggests that the coupling between chemical and mechanical energy is altered during the slow-component phase.

Central factors such as the O₂ cost of ventilatory muscles and/or cardiac muscle may also explain a part of the V˙O₂ slow component. Gaesser and Poole (21) noted that ventilation increased to a great extent during the slow component of V˙O₂. Because increases in ventilation are closely associated with increases in both mechanical work and the specific V˙O₂ of the respiratory muscles, these authors naturally suggested that ventilation contributes to the development of the V˙O₂ slow component. In a preliminary study (13), our laboratory assessed the role of increased ventilation during phase III. On the basis of the equations proposed by Coast et al. (16), the rise in ventilatory flow explained ~24% of the slow-component amplitude for an exercise...
intensity corresponding to 95% of maximum aerobic power (MAP). We further suggested that the part explained by respiratory \( \dot{V}O_2 \) varies with exercise intensity. The results of Engelen et al. (20), however, introduced controversy regarding the direct relationship between respiratory muscle work and the development of the \( \dot{V}O_2 \) slow component. These authors showed that ventilation increased by a greater proportion during phase III in hypoxia than in normoxia, although the slow-component amplitude was not significantly different. To our knowledge, no study has shown the effects of systematic modification of respiratory muscle work on the \( \dot{V}O_2 \) slow component. The first aim of the present study was thus to test whether increased respiratory muscle work induced by the addition of inspiratory resistance leads to a concomitant increase in \( \dot{V}O_2 \) throughout the exercise.

The main mechanism currently advanced to explain the contribution of peripheral factors to the \( \dot{V}O_2 \) slow component, i.e., a progressive recruitment of fast-twitch fibers, cannot be ruled out for the respiratory muscles since the conditions for the occurrence of a such phenomenon could be reached: 1) the respiratory muscles sustain a severe work rate during heavy constant-load exercise, associated with high ventilation levels (23–25), and during such intense exercise 14–16% of cardiac output is directed toward these muscles (24); and 2) the composition in myosin heavy chain isoforms is mixed in respiratory muscle, as it is in lower limb muscles (34, 41). The diaphragm and abdominal muscles include 50% slow-twitch fibers. The intercostals and the scalene muscle display a similar proportion, with 60% slow-twitch fibers. The respiratory muscles have a similar composition in IIa and IIb myosin heavy chain isoforms, except for the intercostals, which present the smallest proportion of the IIb type. The second purpose was thus to determine whether the respiratory muscles behave like the limb muscles during heavy exercise. We anticipated an increase in the amplitude of the \( \dot{V}O_2 \) slow component with the addition of inspiratory loading.

**METHODS**

**Subjects.** Ten trained young men participated in the study after being informed of its purpose and requirements, as well as their rights as subjects. The Local Review Board for Research on Human Subjects approved the protocol. All subjects were free of cardiac and pulmonary disease and fully familiar with laboratory exercise testing procedures. The criteria of study inclusion were the following: age between 20 and 30 yr, nonsmokers, and training volume between 7 and 10 h/wk, mainly in aerobic sports. Plethysmography was performed for each subject to assess respiratory function. The subject characteristics including age, weight, and maximal \( \dot{V}O_2 \) (\( \dot{V}O_2 \) max) are given in Table 1, and the plethysmographic results are shown in Table 2.

**Preliminary test.** Each subject performed an incremental cycling exercise to volitional exhaustion to determine ventilatory threshold and \( \dot{V}O_2 \) max, which was defined as the highest 30-s averaged \( \dot{V}O_2 \) attained. Pedaling frequency was fixed at 70 rpm. The incremental exercise test began with a 5-min warm-up at 60 W. The work rate then increased by 30 W every minute until the subjects reached volitional exhaustion. MAP was determined as the minimal power eliciting \( \dot{V}O_2 \) max.

A friction-loaded cycle ergometer (Monark 818 E, Stockholm, Sweden) fitted with a strain gauge and an incremental encoder ensured accurate measurement of power output. The ergometer was calibrated immediately before the start of the test with a known mass hung on the friction belt, and in an unloaded condition to give a 0 value (2). The saddle height and position of the hands on the handlebar were fixed for each subject. In addition, subjects were required to maintain the position of their shoulder and elbow joints steady. Experimenters checked these points and gave verbal feedback.

**Constant-load exercise.** Subjects performed two cycling exercises with and without an added inspiratory load in a balanced random order. The constant power output exercises consisted of 4 min of unloaded cycling, 8 min at 80% MAP, and then 10 min of recovery with unloaded cycling. The 4 min of unloaded cycling allowed subjects to begin the test with stable ventilatory parameters and respiratory exchange ratio (CO2 consumption/\( \dot{V}O_2 \)). The power output was adjusted over a period of <=2 s. A metronome and visual feedback from a speed transducer linked to a computer were used to maintain constant pedaling frequency at 70 rpm. The delay between the two tests ranged from 48 h to 6 days.

**\( \dot{V}O_2 \) measurement.** Breath-by-breath \( \dot{V}O_2 \) measurement was performed by using an automatic gas exchange system (CPX Medical Graphics, St. Paul, MN), including a cell of zirconium for \( \dot{O}_2 \) analysis, an infrared cell for CO2 analysis, and a heated pneumotachograph, type Fleisch (no. 3, Godart Statham, Holland). The \( \dot{CO}_2 \) and \( \dot{O}_2 \) analyzers were calibrated before each test with two gases of known composition (12% \( \dot{O}_2 \)-5% CO2). The calibration of the pneumotachograph was carried out by using a 3-liter syringe. For the constant-load exercise with added inspiratory load, a system of threshold valves (threshold IMT 730 EU-respironics, health scan asthma allergy producer) was inserted on the inspiratory circuit of the valve. This type of threshold valve maintains a constant resistance whatever the ventilation level (18); in other words, the increase in the work rate of breathing due to the addition of inspiratory resistance is independent of ventilation. The level of resistance can be adjusted with a screw pitch operating as a spring. After several tests with different resistances (10, 15, 20, 25 cmH2O) to ensure that the added loads were compatible with high-intensity exercise, the inspiratory resistance was fixed at 15 cmH2O. The two-way

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### Table 1. Anthropometric characteristics of subjects and results of incremental tests

<table>
<thead>
<tr>
<th>Subjects (n = 10)</th>
<th>Age, yr</th>
<th>Height, cm</th>
<th>Weight, kg</th>
<th>( \dot{V}O_2 ) max, ml·min⁻¹·kg⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>22.2</td>
<td>181.5</td>
<td>76.2</td>
<td>53.8</td>
</tr>
<tr>
<td>SD</td>
<td>1.8</td>
<td>3.6</td>
<td>4.9</td>
<td>6.6</td>
</tr>
</tbody>
</table>

\( \dot{V}O_2 \) max, maximal oxygen consumption; SD, standard deviation.

### Table 2. Characteristics of respiratory function

<table>
<thead>
<tr>
<th>Subjects (n = 10)</th>
<th>( P_{max} ), cmH2O</th>
<th>VC, liters</th>
<th>VC, %</th>
<th>FEV1, liters</th>
<th>Tiffenau Ratio (FEV1/FVC), %</th>
<th>TLC, liters</th>
<th>TLC, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>132</td>
<td>5.9</td>
<td>104</td>
<td>4.8</td>
<td>81</td>
<td>8.3</td>
<td>112</td>
</tr>
<tr>
<td>SD</td>
<td>23</td>
<td>0.6</td>
<td>10</td>
<td>0.5</td>
<td>5</td>
<td>0.9</td>
<td>15</td>
</tr>
</tbody>
</table>
valve of the open circuit specific to gas exchange was reinforced by a mica part to prevent gas from escaping during inspiratory loading. The total dead space was 100 ml. Breath-by-breath data for $\dot{V}O_2$ (in ml·min$^{-1}$·kg$^{-1}$), minute ventilation ($\dot{V}E$; in l/min), tidal volume ($\dot{V}T$; in liters), respiratory frequency (in breaths/min), $\dot{V}E$/inspiratory time (Ti; in l/s), total time (Ttot; in seconds), and heart rate (in beats/min) were collected continuously throughout testing. Heart rate was measured with an electrocardiogram, including standard bipolar electrode placement.

**Data analysis.** Nonlinear regression techniques were used to fit $\dot{V}O_2$ data after exercise onset by using a two monoexponential functions to describe the two main characteristics of the $\dot{V}O_2$ response: primary phase (phase II) and slow-component phase (phase III). The two monoexponential functions started after independent time delays ($\Delta t$). Because the primary phase was not distorted by any early cardiodynamic influence (36, 46), the cardiodynamic phase was not modeled (12)

$$\dot{V}O_2(t) = \dot{V}O_2_{base} + A_1 [1 - e^{(t - t_d1)/t_1}] + A_2 [1 - e^{(t - t_d2)/t_2}]$$

where $t$ is the time; $\dot{V}O_2_{base}$ is the unloaded cycling baseline value; $A_1$ and $A_2$ are the asymptotic values for the two exponential terms; $t_1$ and $t_2$ are the time constants; $t_d1$ and $t_d2$ are the delays for phase II and phase III, respectively; and $A_1 = 0$ for $t < t_d1$ or $A_2 = 0$ for $t < t_d2$. The phase II term was terminated at the start of phase III (i.e., at $t_d2$). The slow-component amplitude was assigned the value $A_2'$

$$A_2' = A_2 [1 - e^{(t - t_d2)/t_2}]$$

where $t_s$ is the time at the end of exercise. $\dot{V}O_2_{peak}$ corresponds to the $\dot{V}O_2$ achieved at the end of the submaximal constant-load exercise. The slow component began only when the preceding function reached its asymptote. A constraint was thus imposed in the model, ensuring that at least 98% of the amplitude of phase II was reached before the beginning of the slow component. The values of measured $\dot{V}O_2$ that were greater than three standard deviations from modeled $\dot{V}O_2$ were considered outliers and removed. These outlier values were assumed to be due to abnormal breaths during exercise such as shallow breathing or breath-holding. These values represented <1% of the total data collected.

Model parameters were determined with an iterative process by minimizing the sum of the squared errors between modeled $\dot{V}O_2$ and actual $\dot{V}O_2$. Iterations continued until successive repetitions reduced both the sum of the residuals by $<10^{-6}$ and the correlation coefficient of the relationship between residuals and time by $<10^{-4}$. To assess the validity of the model parameters, coefficients of variation were computed by using the bootstrap method (12, 19). Briefly, this consisted of resampling the original data set with replacements to create a number of “bootstrap replicate” data sets of the same size as the original data set. For each replicate set, model parameters were estimated following the same procedures as for original data. This operation was repeated 1,000 times, and the estimated parameters were retained. The coefficient of variation was computed to normalize the range of the confidence interval.

**Contribution of ventilation to the development of the $\dot{V}O_2$ slow component.** On the basis of the equations proposed by Coast et al. (16), the additional $\dot{V}O_2$ due to increased ventilation during the slow-component phase was estimated in the unloaded condition. Briefly, the procedure consisted of computing the work of breathing (Wb; in kg·m·min$^{-1}$) from

$$Wb = -0.251 + 0.0382 \dot{V}E + 0.00176 \dot{V}E^2$$

The $\dot{V}O_2$ used by the respiratory muscles ($\dot{V}RMO_{2b}$; in ml/min) was then inferred by

$$\dot{V}RMO_{2b} = 34.9 + 7.45 Wb$$

Finally, the additional $\dot{V}O_2$ of respiratory muscles ($\Delta \dot{V}RMO_{2b}$) due to increased ventilation during the slow component was calculated as

$$\Delta \dot{V}RMO_{2b} = \dot{V}RMO_{2b} - \dot{V}RMO_{2a}$$

where $\dot{V}RMO_{2a}$ and $\dot{V}RMO_{2b}$ were the $\dot{V}RMO_{2}$ at the beginning and end of the slow component, respectively. Because Wb was altered by the added inspiratory resistance, Coast et al.’s equations could not be used in this condition.

**Statistical analysis.** Fisher’s test was used to determine the model’s degree of significance. The quality of the adjusted model was assessed by the coefficient of determination ($r^2$) obtained between modeled $\dot{V}O_2$ and actual $\dot{V}O_2$. The random distribution of model residuals according to time was checked with linear and nonlinear regressions. The conditions of application for the parametric tests were checked by using the Shapiro-Wilk test for normality of distributions and the Fisher’s test for equality of variance. Paired t-tests compared the model parameters between the two experimental conditions. The relationship between slow-component amplitude and ventilation was assessed by Pearson’s correlation coefficients in the two experimental conditions. A two-way analysis of variance with repeated measures was used to identify any differences in ventilatory flow parameters (averaged over 20 s) at the beginning and end of phase III under the two experimental conditions. Differences were declared to be significant for $P < 0.05$.

**RESULTS**

No significant relationships were identified between residuals and time in either experimental condition, suggesting random distribution and an appropriate model to describe the $\dot{V}O_2$ kinetics in both conditions. Model adjustment to the $\dot{V}O_2$ kinetics led to coefficients of determination ranging between 0.83 and 0.96 (mean value of 0.92 ± 0.04). The Fisher’s test indicated a high degree of significance of the model for all subjects and conditions ($P < 0.001$). The mean $\dot{V}O_2$ response pattern for all subjects with and without inspiratory resistance and the associated fit curves obtained with the two monoexponential functions are presented in Fig. 1A. The distribution of residual errors as a function of time is shown in Fig. 1B for the condition without added inspiratory load. It is of interest to note that the same pattern of distribution was found for the condition with added inspiratory load.

An increase in $\dot{V}O_2$ was noted throughout the constant power output exercise. $\dot{V}O_2_{base}$ increased significantly (14.2%) with the added inspiratory load (9.1 ± 1.1 vs. 10.4 ± 1.6 ml·min$^{-1}$·kg$^{-1}$; $P < 0.01$), as did $\dot{V}O_2_{peak}$, i.e., 8.3% (49.1 ± 7.2 vs. 53.2 ± 7.2 ml·min$^{-1}$·kg$^{-1}$; $P < 0.01$) (Fig. 2). A slight (3.5%) but nonsignificant increase in the amplitude of the primary phase ($A_1'$) was noted. The values for the model pa-
rameters and for $V_\text{O}_2\text{base}$ and $V_\text{O}_2\text{peak}$ in the two conditions are listed in Table 3. The coefficients of variation are also presented in Table 3; it should be noted that the critical parameters in the present study, $t_{d2}$ and $A_2$, were 19 and 15%, respectively. The time delay ($t_{d1}$) and time constant of phase II ($\tau_1$) were not significantly different between the two experimental conditions. The added inspiratory load also did not modify $t_{d2}$ or $\tau_2$.

The most important result was the significant increase in slow-component amplitude ($P < 0.01$) when inspiratory resistance was added (Fig. 3). $A_2$ increased by 27% from $8.1 \pm 3.6\text{ml\cdot min}^{-1}\cdot\text{kg}^{-1}$ without inspiratory resistance to $10.3 \pm 3.4\text{ml\cdot min}^{-1}\cdot\text{kg}^{-1}$ with resistance. $V_\text{E}$ increased significantly from beginning to end of phase III ($\Delta V_\text{E}$) in each condition ($P < 0.01$), and $V_\text{E}$ was not significantly different between the two conditions (Fig. 4). The correlation between $\Delta V_\text{E}$ and $A_2$ reached significance in neither condition. The ventilatory parameters during phase III in the two conditions are shown on Table 4.

In control condition, estimated Wb was $17.2 \pm 5.4\text{kg}\cdot\text{m}^{-1}\cdot\text{min}^{-1}$ and $31.5 \pm 9.1\text{ml\cdot min}^{-1}\cdot\text{kg}^{-1}$ at the beginning and end of phase III, respectively. Hence, VRMO$_{2\text{b}}$ was $163.4 \pm 40.5\text{ml/min}$ and VRMO$_{2\text{e}}$ was $269.7 \pm 67.2\text{ml/min}$. $\Delta$VRMO$_2$ was $106.3 \pm 61.4\text{ml/min}$. The $V_\text{O}_2$ of the respiratory muscles due to increased ventilation during the slow component was
Figure 3. Amplitude of the \( V_\text{O}_2 \) slow component in the 2 experimental conditions: without added inspiratory load and with added inspiratory load. **Significant difference between experimental conditions \((P < 0.01)\).

Table 3. Parameters estimated for model fitting of the \( V_\text{O}_2 \) response during heavy exercise and \( V_\text{O}_2 \) peak in the 2 experimental conditions

<table>
<thead>
<tr>
<th>Parameter</th>
<th>U</th>
<th>L</th>
<th>CV, %</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>( A_1 ) ml \cdot min^{-1} \cdot kg^{-1} )</td>
<td>31.2 ± 5.5</td>
<td>32.3 ± 5.5</td>
<td>9 NS</td>
<td></td>
</tr>
<tr>
<td>( t_{d1} ), s</td>
<td>11.1 ± 5.6</td>
<td>12.1 ± 4.1</td>
<td>45 NS</td>
<td></td>
</tr>
<tr>
<td>( \tau_1 ), s</td>
<td>36.3 ± 13.3</td>
<td>38.2 ± 9.1</td>
<td>19 NS</td>
<td></td>
</tr>
<tr>
<td>( A_3 ), ml \cdot min^{-1} \cdot kg^{-1} )</td>
<td>8.1 ± 3.6</td>
<td>10.3 ± 3.4</td>
<td>15 *</td>
<td></td>
</tr>
<tr>
<td>( t_{d3} ), s</td>
<td>174.9 ± 43.4</td>
<td>221.8 ± 156.5</td>
<td>19 NS</td>
<td></td>
</tr>
<tr>
<td>( V_\text{O}_2 \text{ base, } \text{ml} \cdot \text{min}^{-1} \cdot \text{kg}^{-1} )</td>
<td>9.1 ± 1.1</td>
<td>10.4 ± 1.5</td>
<td>18 *</td>
<td></td>
</tr>
<tr>
<td>( V_\text{O}_2 \text{ peak, } \text{ml} \cdot \text{min}^{-1} \cdot \text{kg}^{-1} )</td>
<td>49.1 ± 7.2</td>
<td>53.2 ± 7.2</td>
<td>18 *</td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± SD; \( n = 10 \) subjects. \( V_\text{O}_2 \text{ base, } \text{baseline } V_\text{O}_2; A_1 \) and \( A_3 \), amplitudes of response of phases II and III, respectively; \( \tau_1 \) and \( \tau_2 \), time constants of phases II and III, respectively; \( t_{d1}, t_{d3} \), time delays of phases II and III, respectively; U, without added inspiratory load; L, with added inspiratory load; CV, coefficient of variation; NS, not significant. *\( P < 0.01 \) for differences with the condition without inspiratory resistance.

thus estimated at 21 ± 17% of the total slow component (Fig. 5).

**DISCUSSION**

The most important findings of the present study were 1) the increased \( V_\text{O}_2 \) throughout the exercise with the addition of inspiratory resistance and 2) the marked increase in the amplitude of the \( V_\text{O}_2 \) slow component associated with a lack of any difference in \( V_\text{E} \) and ventilatory parameters between the two experimental conditions during phase III.

**Limitations.** Several authors (5, 28) have used a procedure consisting of two or three measurements of the individual \( V_\text{O}_2 \) kinetics to decrease the variability inherent to breath-by-breath measurement of gas exchange. In the present study, this method was not applied because it is not possible to exclude that cycle-to-cycle variability may have physiological meaning since it is the case for heart rate, a factor of the cardiac output, and thus of \( V_\text{O}_2 \) (37). Several elements support the notion that the fits were of sufficient quality to determine the model parameters with only one transition: 1) the high degree of significance \((P < 0.001,\) number of points > 400 during the slow-component phase), 2) the coefficients of determination \((\text{average } = 0.92 ± 0.04)\) between modeled \( V_\text{O}_2 \) and actual \( V_\text{O}_2\), 3) the random distribution of the residuals, and 4) the relatively small coefficients of variation \((~17\%)\) obtained on the model parameters with the bootstrap method. Other recent studies (9, 12, 32, 35, 40) also completed only one transition to describe the \( V_\text{O}_2 \) kinetics since enough measurements were obtained to fit two monoexponential functions.

The added respiratory load may have not only increased respiratory muscle work but also slightly modified cardiac work because this latter can be slightly altered by changes in intrathoracic pressure (33). High intrathoracic pressures (e.g., those developed during the Vasalva maneuver) decrease venous return (33) and increase heart work. In contrast, inspiratory loading is associated with a more negative esophageal pressure of −6 to −7 cmH₂O at peak inspiration compared with control, although it is unchanged at expiration (23, 24). This more negative esophageal pressure may facilitate venous return and slightly decreases cardiac work rate. Although cardiopulmonary interactions were not addressed in the present study, a slight underestimation of the increase in \( V_\text{O}_2 \) attributed to the respiratory muscle work with added inspiratory resistance may therefore have resulted, but not an overestimation.

**Comparison with the literature.** The amplitude of the \( V_\text{O}_2 \) slow component without inspiratory resistance agreed with that of previous studies. Barstow and Mole (8) observed amplitudes of 0.88 and 0.96 l/min at exercise intensities of 85 and 100% of \( V_\text{O}_2 \text{ max} \), respectively. Engelen et al. (20) found amplitudes of 0.22 l/min at an intensity of 75% of \( V_\text{O}_2 \text{ max} \). A\( \dot{z} \) obtained during the present cycling exercise at 80% of \( V_\text{O}_2 \text{ max} \) without added resistance was 0.67 l/min. This value is in line with the assumption that the amplitude variation in...
the slow component is strongly dependent on exercise intensity (11, 29, 47). \( \dot{V}O_2 \) base without added inspiratory load also agreed with the values of the literature (8, 20). In agreement with the present study, with the addition of inspiratory resistance, a higher level of \( \dot{V}O_2 \) throughout the exercise was found compared with control (25). The difference reached significance from minute 2 to minute 5 of exercise.

**Does \( \dot{V}E \) contribute to the development of the slow component?** As anticipated, when total work (total work = work performed by exercising limbs + work by muscles indirectly involved) was increased in the loaded condition, a concomitant \( \dot{V}O_2 \) increase was noted throughout the exercise compared with the unloaded condition. The slight and significant increase \( (P < 0.01) \) in \( \dot{V}O_2 \) base and \( \dot{V}O_2 \) peak with added inspiratory resistance supports this notion, and the lack of significant increase (3.5%) in the primary phase amplitude may have been due to the greater variability found in transient phases compared with more stationary phases (31). We now emphasize that the only difference between the two conditions lies in the inspiratory resistance and that the additional work of breathing provokes a rise in \( \dot{V}O_2 \) throughout the exercise.

The present study provides direct evidence of the contribution of ventilatory work to the development of the slow component and, at first glance, it appears to contradict the study of Engelen et al. (20) on the role of the respiratory muscles. During the slow-component phase, \( \dot{V}O_2 \) and \( \dot{V}E \), and thus the \( W_b \) and the \( \dot{V}O_2 \) of the respiratory muscles, increased significantly \( (P < 0.01) \) in both conditions. The subjects who presented the greatest increase in ventilation during phase III in the two conditions displayed the biggest change in \( \dot{V}O_2 \) slow-component amplitude and vice versa, but the correlation did not reach statistical significance. The lack of a significant relationship is probably due to the relatively small contribution of ventilatory work to the slow component and to the small amplitude of the interindividual variations in \( \dot{V}E \) and \( \dot{V}O_2 \).

Any increase in ventilation during the \( \dot{V}O_2 \) slow component necessarily corresponds to an increase in the mechanical work of the respiratory muscles and consequently leads to increased \( O_2 \) demand in these muscles (1, 16). These variations between \( \dot{V}E \) and \( \dot{V}O_2 \) must be regarded as causal relationships. Therefore, the apparent contradiction with the results of Engelen et al. is undoubtedly explained by two mechanisms that are mutually compensated in hypoxia: the increase in \( \dot{V}O_2 \) of the respiratory muscles linked to increased ventilation during phase III is counterbalanced by lower \( \dot{V}O_2 \) of the peripheral muscles in hypoxia compared with normoxia or by lower \( O_2 \) delivery in hypoxia due to hemoglobin desaturation in arterial blood (10).

On the basis of the equations of Coast et al. (16), respiratory muscle \( \dot{V}O_2 \) due to increased ventilation can be evaluated as 21 ± 17% of the total slow component under normal conditions (at 80% MAP), which is slightly lower than the 24% observed at an intensity of 95% \( \dot{V}O_2 \) max (13) and much higher than the 7% observed at an intensity of 70% \( \dot{V}O_2 \) max (22). The relative part explained by ventilation depends on the exercise intensity. It is interesting to note that the value of 21% also falls within the range that Poole et al. (39) could not account for by measuring lower limb \( \dot{V}O_2 \).

**Can respiratory muscle display a slow component?** From the unloaded cycling period to the end of the primary phase, the slight increase of \( \dot{V}O_2 \) in response to the added inspiratory resistance clearly reflects the

### Table 4. Ventilatory parameters during phase III in the 2 experimental conditions

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Beginning phase 3</th>
<th>End phase 3</th>
<th>Beginning phase 3</th>
<th>End phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \dot{V}E ), l/min</td>
<td>86.0 ± 15.4*</td>
<td>122.6 ± 18.0*</td>
<td>87.9 ± 16.8*</td>
<td>122.1 ± 17.1*</td>
</tr>
<tr>
<td>( \dot{V}F ), liters</td>
<td>3.5 ± 0.4*</td>
<td>3.5 ± 0.4*</td>
<td>3.3 ± 0.5*</td>
<td>3.2 ± 0.5*</td>
</tr>
<tr>
<td>( f ), breaths/min</td>
<td>25.1 ± 4.6*</td>
<td>36.8 ± 6.2*</td>
<td>26.6 ± 5.5*</td>
<td>37.4 ± 7.2*</td>
</tr>
<tr>
<td>( T_i ), s</td>
<td>1.2 ± 0.2*</td>
<td>0.7 ± 0.1*</td>
<td>1.2 ± 0.3*</td>
<td>0.9 ± 0.2*</td>
</tr>
<tr>
<td>( T_e ), s</td>
<td>1.3 ± 0.3*</td>
<td>0.9 ± 0.2*</td>
<td>1.2 ± 0.3*</td>
<td>0.8 ± 0.2*</td>
</tr>
<tr>
<td>( T_{tot} ), s</td>
<td>2.5 ± 0.5*</td>
<td>1.6 ± 0.3*</td>
<td>2.4 ± 0.5</td>
<td>1.7 ± 0.4*</td>
</tr>
</tbody>
</table>

Values are means ± SE. \( \dot{V}E \), minute ventilation; \( \dot{V}F \), tidal volume; \( f \), respiratory frequency; \( T_i \), inspiratory time; \( T_e \), expiratory time; \( T_{tot} \), total time. Significantly different: *\( P < 0.01 \) compared with beginning of phase III; there was no modification in these parameters when the experimental condition without added inspiratory load (U) was compared with the condition with inspiratory resistance (L) (\( P > 0.05 \)).

![Fig. 5. Mean lines of best fit of the dynamic response of \( \dot{V}O_2 \) and \( \dot{V}O_2 \) of respiratory muscles (VRMO2) in constant-load exercise obtained by plotting the response with mean parameter estimates during the condition without inspiratory resistance.](http://jap.physiology.org/)

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The direct relationship between the Wb and VO₂. The subsequent increase in VO₂ in the slow-component period, associated with a 27% increase in the slow-component amplitude (P < 0.01), is probably more interesting. The question that should be addressed is why this additional Wb provokes a progressive rise in VO₂. On the basis of the lack of difference in VE and its factors between the two experimental conditions, one could argue that the increase in A2 with inspiratory resistance reflects a VO₂ slow component specific to the respiratory muscles. The type of threshold valves used in the present study is associated with an additional work independent of the ventilation level (18). The observation of no significant difference in VE or the breathing pattern at the beginning and end of the VO₂ slow-component phase (Fig. 4) when compared with control suggests that the additional work imposed on the respiratory muscles by the load was constant with time and provoked a VO₂ slow component. This information cannot be drawn from control studies during heavy exercise because ventilation typically increases with time (and thus the Wb). On the basis of the comparison between the two experimental conditions, it seems that the respiratory muscles behave just as the muscles directly concerned by the exercise: During a constant high-intensity work rate applied to the respiratory muscles, there is also a progressive decrease in muscular efficiency.

In agreement with this hypothesis, we can note that the main conditions for the occurrence of the VO₂ slow component were reached for the respiratory muscles, at least in the loaded condition. First, there is little doubt that the subjects of the present study performed at a severe respiratory muscle work rate with the inspiratory resistance of 15 cmH₂O, since VE reached 120 l/min (Fig. 4). Although the esophageal pressure was not measured directly to avoid invasive instrumentation, in similar conditions of heavy exercise and with an inspiratory resistance of 6–7 cmH₂O, the Wb measured directly from the esophageal pressure-volume loop increased to 128–157% of the control at peak inspiration (23, 24).

Second, as for the lower limb muscles, the myosin heavy chain isofrom composition of the respiratory muscle is mixed (34, 41). The main mechanism currently advanced to explain the slow component of VO₂ (6, 7, 12), i.e., a progressive recruitment of fast-twitch fibers, cannot ruled out for the respiratory muscles. In agreement with the Henneman et al. (27) law of motor unit recruitment, the slow-twitch fibers of the respiratory muscles that are mainly engaged at the beginning of exercise are likely to progressively reach a fatigued state, and new motor units are recruited to maintain the constant power output. It is not necessary to assume that the newly recruited fibers, mainly in the fast-twitch fiber pool, are less economic because 1) the great number of required active fibers implies substan-
tial ATPase activity at least regarding the work of the Na⁺/K⁺ and Ca²⁺ pumps against concentration gradi-

ents and 2) fast-twitch fibers display a higher optimal shortening velocity than slow-twitch fibers. On isolated human skeletal muscle fibers containing different myosin isofroms, He et al. (26) showed that the maximum efficiency was reached at a higher speed of shortening for the faster fibers. It follows that the newly recruited fast fibers must work in unfavorable conditions.

In conclusion, as hypothesized, the addition of inspiratory resistance provoked a proportional increase in VO₂ throughout exercise, supporting the role of the increase in VE during phase III in the development of the VO₂ slow component. The original finding of the present study was the marked increase (27%; P < 0.01) of the VO₂ slow-component amplitude with the addition of inspiratory resistance, whereas no significant differences in VE and ventilatory parameters were found between the two experimental conditions during phase III. It seems that the respiratory muscles behave like the limb muscles; they are likely to display a VO₂ slow component.

REFERENCES


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