Ventilatory response to exercise in aged runners breathing He-O₂ or inspired CO₂

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Babb, T. G., Darren S. DeLorey, and Brenda L. Wyrick. Ventilatory response to exercise in aged runners breathing He-O₂ or inspired CO₂. J Appl Physiol 94: 685–693, 2003; 10.1152/japplphysiol.00214.2002.—The ventilatory response to exercise below ventilatory threshold (VTh) increases with aging, whereas above VTh the ventilatory response declines only slightly. We wondered whether this same ventilatory response would be observed in older runners. We also wondered whether their ventilatory response to exercise while breathing He-O₂ or inspired CO₂ would be different. To investigate, we studied 12 seniors (63 ± 4 yr; 10 men, 2 women) who exercised regularly (5 ± 1 days/wk, 29 ± 11 mi/wk, 16 ± 6 yr). Each subject performed graded cycle ergometry to exhaustion on 3 separate days, breathing either room air, 3% inspired CO₂, or a heliox mixture (79% He and 21% O₂). The ventilatory response to exercise below VTh was 0.35 ± 0.10 l·min⁻¹·W⁻¹ and above VTh was 0.66 ± 0.10 l·min⁻¹·W⁻¹. He-O₂ breathing increased (P < 0.05) the ventilatory response to exercise both below (0.40 ± 0.12 l·min⁻¹·W⁻¹) and above VTh (0.81 ± 0.10 l·min⁻¹·W⁻¹). Inspired CO₂ increased (P < 0.001) the ventilatory response to exercise only below VTh (0.44 ± 0.10 l·min⁻¹·W⁻¹). The ventilatory responses to exercise with room air, He-O₂, and CO₂ breathing of these fit runners were similar to those observed earlier in older sedentary individuals. These data suggest that the ventilatory response to exercise of these senior runners is adequate to support their greater exercise capacity and that exercise training does not alter the ventilatory response to exercise with He-O₂ or inspired CO₂ breathing.

control of breathing during exercise; ventilatory responses to loaded and unloaded breathing; work of breathing during exercise

IN SEDENTARY AND FIT OLDER adults, the mechanical ventilatory constraints imposed on ventilation (VE) at peak exercise have been well described (5, 23–25, 29). Rather than focusing on VE at peak exercise only, we recently described the effect of age on the overall ventilatory response to incremental exercise (12), that is, the ventilatory response during submaximal exercise as well as during heavy exercise. To this end, the ventilatory response to exercise was described in terms of the response of VE below ventilatory threshold (VTh) and the response of VE above VTh for healthy seden-
tary individuals ranging from 35 to 95 yr of age (12). We had proposed that the age-related changes in maximal expiratory flow and lung volume could affect the ventilatory response to exercise differently, depending on the intensity of exercise. It was observed that the ventilatory response to exercise below VTh increased with aging, whereas the ventilatory response to exercise above VTh declined only slightly (12). This small decline was surprising when the marked mechanical ventilatory constraints that were observed with normal aging were considered. However, the ventilatory response is dependent on the balance among many factors, including ventilatory constraints, ventilatory load, and ventilatory demand, which vary across populations, exercise protocol, and individual motivation levels (22).

Thus we wondered what the overall ventilatory response to exercise for older runners would be below and above VTh. The overall ventilatory response to exercise for older runners has not been addressed in previous work. We hypothesized that, because of their greater exercise capacity, strong motivation, and substantially higher ventilatory demand at peak exercise (25, 29), they could be predisposed to greater mechanical ventilatory constraints and that their slope of VE above VTh could be reduced. That is, VE could be attenuated before they reached their peak exercise capacity. It was proposed that, below VTh where ventilatory capacity is greater than ventilatory demands, their slope would be similar to that measured previously for sedentary older adults (5, 12). Also, to investigate the effects of mechanical ventilatory constraints on the overall ventilatory response to exercise in runners further, airway resistance was decreased by giving them He-O₂ to breathe, or ventilatory demand was increased by giving them 3% CO₂ to breathe.

In our studies in aged sedentary subjects, we previously found that the ventilatory response below VTh was not altered by He-O₂ breathing but increased above VTh (5), which is similar to the results of others (8, 21, 43, 46). However, it was also observed that the increase in ventilatory response to exercise with He-O₂ breathing was similar among younger subjects (4),
older subjects (5), and older men and women with mild chronic airflow limitation (6). This suggested that the ventilatory response to He-O\textsubscript{2} breathing is independent of the magnitude of ventilatory demand or the extent of mechanical ventilatory constraints, which indicates that the response in runners may be no different from that in sedentary older adults. This is in contrast to data reported for younger fit women (30, 31). The effect of He-O\textsubscript{2} breathing on the overall ventilatory response in older trained adults has not been tested. We hypothesized that V\textsubscript{E} would be increased just as previously observed for sedentary subjects, despite the runners’ high ventilatory demand and high potential for increased ventilatory constraints.

In older sedentary subjects breathing 3\% inspired CO\textsubscript{2} during exercise (5, 6), V\textsubscript{E} was increased only below V\textsubscript{TTh}. In contrast, the ventilatory response to exercise was increased in younger subjects breathing 3\% inspired CO\textsubscript{2} (4), both below and above V\textsubscript{TTh}. Thus it has been suggested that the ability to increase V\textsubscript{E} is limited in the aged only at peak exercise. Although others have shown that V\textsubscript{E} cannot be increased in fit younger (26) or fit older men (25) at peak exercise, the effect of CO\textsubscript{2} on the overall ventilatory response has not been studied in older runners. We wondered whether the overall ventilatory response to exercise for older runners might be altered with CO\textsubscript{2} breathing, because runners have such high ventilatory demands during exercise. It was hypothesized that the runners would not be able to increase their ventilatory response to exercise above V\textsubscript{TTh} with inspired CO\textsubscript{2} because of limited ventilatory reserves and that exercise capacity may actually be decreased because ventilatory reserves may be low in exercise-trained older adults.

To investigate the overall ventilatory response to exercise in trained aged adults, 12 seniors (10 men, 2 women) who exercised regularly (5 ± 1 days/wk) were studied.

METHODS

Subjects. Volunteers were recruited through local advertisements. None of the subjects had a history of asthma, cardiovascular disease, or diabetes. All of the subjects participated in regular vigorous exercise and had been competing in road races, which ranged in distance from 5 km to ultramarathons. In accordance with the Institutional Review Board, all details of the study were discussed with the volunteers, and informed consent was obtained. All qualified participants were familiarized with exercise on the cycle ergometer and instructed to avoid food and caffeine for at least 2 h before exercise testing. They were also instructed to limit their exercise to easy runs 24 h before testing. None of the subjects was a smoker, but eight subjects had a history of cigarette smoking (mean ± SD: 26 ± 31 pack-yr). As a group, it had been 27 ± 12 yr since they quit smoking. Volunteers were accepted for study if their pulmonary function was considered normal.

Pulmonary function. All subjects had standard spirometry, lung volume, and diffusing capacity determinations (model 6200 body plethysmograph, SensorMedics, Yorba Linda, CA). Pulmonary function was performed according to guidelines of the American Thoracic Society (3). Predicted values were based on norms by Knudson et al. (27), Enright et al. (13), Goldman and Becklake (16), and Burrows et al. (9).

Resting respiratory mechanics. Maximal flow-volume loops and pressure-volume loops were measured in a pressure-corrected volume-displacement body plethysmograph to eliminate the gas compression artifact (SensorMedics 6200). Transpulmonary pressure (Ptp) was estimated by using an esophageal balloon placed 45 cm from the nostril (33). Isovolume pressure-flow curves were constructed (37) and subsequently used to determine the minimum pressure necessary to obtain maximal flow (critical pressure (Pcrit)) as previously described (5). These Pcrit data were used solely to confirm expiratory flow limitation during exercise (see below).

Gas exchange measurements. Measurements of oxygen uptake (V\textsubscript{O\textsubscript{2}}) and carbon dioxide production (V\textsubscript{CO\textsubscript{2}}) were made with the use of a custom gas-exchange system that was computerized. It was not possible to use the gas-exchange system when the subjects were breathing He-O\textsubscript{2} because of the deleterious effects of helium on mass spectrometer operation. V\textsubscript{TTh} was determined from the comparison of gas exchange indexes (10) and the V-slope method (45, 47). V\textsubscript{TTh} was calculated as the work rate that was most congruent among the different threshold determination methods. End-tidal P\textsubscript{CO\textsubscript{2}} (Pet\textsubscript{CO\textsubscript{2}}) was measured when the subjects were breathing room air, as well as when they were breathing He-O\textsubscript{2} and CO\textsubscript{2}, with the use of the Poet TE CO\textsubscript{2} monitor (model 602/11, Criticare Systems, Waukesha, WI).

Breathing mechanics. Expiratory and inspiratory flow were measured continuously during the exercise tests, as described previously (5). An esophageal balloon was placed as described above for continuous measurements of Ptp during the second through fourth maximal exercise tests (5). Maximal flow-volume and pressure-volume loops were determined at rest, while the subjects were seated on the cycle ergometer just before the baseline measurements, and within 2 min after exercise was terminated, to determine whether exercise had induced bronchodilation or bronchoconstriction, which none of the subjects experienced.

Inspiratory capacity (IC) was measured at rest and during exercise to determine placement of tidal flow-volume loops within the maximal flow-volume loop, as described previously (5). End-expiratory lung volume (EELV) was estimated from measurement of IC (EELV = TLC − IC, where TLC is total lung capacity) and reported as a percentage of TLC. End-inspiratory lung volume (EILV) was calculated (EILV = EELV + V\textsubscript{r}, where V\textsubscript{r} is tidal volume) and expressed as a percentage of TLC. IC was measured during the last 20 s of each exercise increment, and tidal flow-volume and pressure-volume loops were measured continuously.

Inspired gas mixtures. During rest and exercise, inspired gas was provided from a large inspiratory reservoir, as described previously (4, 5). The bag was filled with either room air, 3\% CO\textsubscript{2} in 21\% O\textsubscript{2} and 76\% N\textsubscript{2}, or 21\% O\textsubscript{2} and balance He (He-O\textsubscript{2}), which was humidified similar to that of room air as in prior studies (4, 5). External resistance (i.e., valve, tubing, and pneumotachographs) was matched between the room air and He-O\textsubscript{2} conditions. By matching external apparatus resistance, the He-O\textsubscript{2} effect was restricted to the respiratory airways. The subjects were blinded in each case to the content of the gas mixture.

Study protocol. After screening, all subjects performed four maximal exercise tests. The first test was a preliminary exercise test to clear subjects for further participation in the study. The next three tests were performed breathing either room air, CO\textsubscript{2}, or He-O\textsubscript{2}. The order was randomized. Subsequent randomized repeat testing demonstrated no effect of test order (data not shown).
Exercise protocol. All of the exercise tests followed the same sequence of procedures. Testing began with the subjects seated on the cycle ergometer while baseline measurements were obtained. After 3 min of baseline measurements, the subjects performed graded cycle ergometry on an electronically braked cycle ergometer (model CPE 2000, MedGraphics, St. Paul, MN). Exercise began at 15 W for the women, or 30 W for the men, and was incremented by 15 or 30 W, respectively, every minute. The test continued until the subjects stopped because of exhaustion, or the test was stopped because they could not keep the pedal rate at a frequency $>50$ rpm. Heart rate was monitored continuously through the use of a 12-lead electrocardiogram (model CS-100, Schiller, Baar, Switzerland), and blood pressure was monitored with the use of an automated system (model 4240, Suntech, Raleigh, NC). Arterial saturation was monitored at rest and continuously throughout the first exercise test by pulse oximetry (model 3700, Ohmeda, Louisville, CO). Ratings of perceived exertion (RPE) (Borg 20-point scale) and perceived breathlessness (RBP) (Borg 10-point scale) were recorded with the use of the procedures outlined by the American College of Sports Medicine (3) and were recorded at each work rate during the exercise test.

We tested these runners on the cycle ergometer instead of the treadmill because all of our previous data were collected during cycling. Thus, to compare results between this study and our earlier studies, we used the cycle (4–6, 12). Also, it is much easier to make our mechanics measurements while subjects are cycling than running. Nevertheless, we do not believe this negated the effects of training in this group; however, their measured peak $V_{\text{O2}}$ would have probably been higher during running.

Data analysis. An interactive computer program developed in this laboratory, as previously described (4, 5), was used to determine $V_T$, breathing frequency, $V_{\text{E}}$, and exercise tidal flow-volume and pressure-volume loops. Pulmonary resistance was computed on a breath-by-breath basis with multiple linear regression by the method of least squares for the whole breath, as described in method one by Officer and colleagues (36). Resistance was estimated from Ptp and flow on 5–10 breaths preceding the measurement of IC and then averaged. The mechanical work of breathing against the lung was estimated per breath from the area enclosed by the dynamic tidal pressure-volume loop (i.e., using Ptp), with the addition of that portion of a triangle describing work that fell outside the tidal pressure-volume loop (i.e., part of inspiratory elastic work) (32), and then averaged. Expiratory flow limitation was defined as the percentage of $V_T$ in which tidal expiratory flow impinged on maximal expiratory flow and in which Ptp simultaneously exceeded Pcrit, as described previously (4, 5). Briefly, the beginning and end of expiratory flow limitation were confirmed by determining where Ptp met or exceeded Pcrit rather than by the use of expiratory flow curves. Data were analyzed at rest, at VTh, and during peak exercise.

The relationship between $V_{\text{E}}$ and work rate was used to describe the overall ventilatory response to exercise. This method has been described previously (4–6). Briefly, $V_{\text{E}}$ was plotted against work rate, and slopes were calculated for each individual by using all of the points between rest and VTh or all of the points between VTh and peak exercise. Thus the overall ventilatory response was described as the ventilatory response below and above VTh. If an individual’s $R^2$ for $V_{\text{E}}$ vs. work rate was not $>0.85$ (i.e., indicating a poor fit of the data by linear least squares regression), then that particular slope was not included in the group analysis of ventilatory response. However, in almost all of these individuals as well as in other studies, linear analysis has been able to describe the ventilatory response accurately, both below and above VTh (4–6). We maintained this method because we wanted to be able to compare these results with our previous studies in the aged (4–6, 12). Also, this method was not dependent on attaining the same peak exercise work rate in all conditions, because we were determining the slope of the response, not the peak end point. Work rate was used in the determination of ventilatory response instead of $V_{\text{O2}}$ or $V_{\text{CO2}}$ so that comparisons could be made with the He–$V_{\text{O2}}$ tests, where it was not possible to make gas-exchange measurements. Also, $V_{\text{E}}$ was not compared with $P_{\text{ETCO2}}$, because $P_{\text{ETCO2}}$ does not rise during heavy exercise with room air or He–$V_{\text{O2}}$ breathing as in tests with inspired $V_{\text{CO2}}$.

The difference between means across all conditions was tested with the use of a one-way ANOVA for repeated measures at rest, VTh, and peak exercise. In some cases, the difference between means was tested with the use of paired t-tests. Relationships among physiological variables were analyzed by Pearson correlation coefficients.

RESULTS

Subjects. Ten men and two women participated in the study. Their characteristics are presented in Table 1. As expected, peak exercise capacity was above normal, on the basis of $V_{\text{O2}}$ as a percentage of age- and gender-corrected norms. As a result, their $V_{\text{E}}$ at peak exercise was much higher than observed previously in older (70 ± 3 yr) sedentary men and women (12). $V_{\text{E}}$ as a percentage of maximal voluntary ventilation was 74 ± 14%. Pulmonary function data are presented in Table 2 and are consistent with normal lung function. Only diffusing capacity appeared to be higher than expected compared with that in sedentary aged men and women (12).

Table 1. Subject characteristics

<table>
<thead>
<tr>
<th>Age, yr</th>
<th>Height, cm</th>
<th>Weight, kg</th>
<th>Smoking History, % pk-yr</th>
<th>Peak $V_{\text{O2}}$, %predicted Exercise, yr</th>
<th>Compete, yr</th>
<th>Training Summer, miles/wk</th>
<th>Training Winter, miles/wk</th>
<th>Peak $V_{\text{O2}}$, m/l/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>63 ± 4</td>
<td>175 ± 10</td>
<td>72 ± 10</td>
<td>26 ± 31</td>
<td>146 ± 27</td>
<td>20 ± 8</td>
<td>16 ± 6</td>
<td>30 ± 11</td>
<td>32 ± 14</td>
</tr>
</tbody>
</table>

Values are means ± SD; *n = 8. $V_{\text{O2}}$, oxygen uptake; Compete, no. of years participating in running races; Training Summer, average no. of training miles per week in the summer months; Training Winter, average no. of training miles per week in the winter months.
in $\dot{V}_E$ with CO2 and He-O2 breathing was due mainly to an increase in $V_t$ (Tables 3 and 4). In association with the increase in $\dot{V}_E$ with He-O2 breathing, there was a significant ($P < 0.001$) decrease in $P_{ETCO2}$ at rest, VTh, and peak exercise (Table 3). In contrast, there was an increase in $P_{ETCO2}$ with CO2 breathing (Table 4). The decrease in $P_{ETCO2}$ with He-O2 breathing supports the tendency for hyperventilation when breathing He-O2, even during peak exercise.

Ventilatory response to exercise. The ventilatory response to exercise below VTh increased from 0.35 ± 0.06 l·min⁻¹·W⁻¹ (n = 10) when breathing room air to 0.44 ± 0.11 l·min⁻¹·W⁻¹ when breathing CO2 ($P < 0.001$; Fig. 2). In contrast, the ventilatory response to exercise above VTh was lower with CO2 breathing (0.59 ± 0.12 l·min⁻¹·W⁻¹) compared with room air breathing (0.66 ± 0.10 l·min⁻¹·W⁻¹), but the difference failed to reach significance. With He-O2 breathing, the ventilatory response to exercise below VTh (0.40 ± 0.12 l·min⁻¹·W⁻¹) and above VTh (0.81 ± 0.10 l·min⁻¹·W⁻¹) was significantly greater ($P < 0.05$) compared with room air breathing.

Two subjects had an $R^2 < 0.85$ for $\dot{V}_E$ vs. work rate below VTh when breathing room air, which indicates that linear regression did not adequately describe their data. Thus only 10 subjects were used in the analysis for room air below VTh. Above VTh, despite a lower peak work rate when breathing CO2, an average of 4.00 ± 1.13 points was used in the linear regression vs. 4.58 ± 1.31 points when breathing room air. However, the fit of the data by linear regression was very good, as indicated by high $R^2$ values during all three exercise tests.

Other variables. Selected variables are presented in Tables 3 and 4 for room air, He-O2, and CO2 breathing at rest, VTh, and peak exercise. Peak exercise time and work rate were not different with He-O2 breathing (Table 3). In contrast, exercise time, work rate, and heart rate were slightly, but significantly, decreased at peak exercise with CO2 breathing (Table 4). RPE and RPB at peak exercise were not different with CO2 or He-O2 breathing. Pulmonary resistance (cmH2O·1⁻¹·s) and EELV were significantly reduced, whereas the total mechanical work of breathing against the lung was unchanged from that of room air when breathing He-O2, despite a significantly greater $\dot{V}_E$ at VTh and peak exercise (Table 3). Expiratory airflow limitation was decreased ($P < 0.05$) with He-O2 breathing (Table 3) but increased ($P < 0.05$) at peak exercise with CO2 breathing (Table 4). The mechanical work of breathing is plotted against work rate in Fig. 3 and shown in Tables 3 and 4. Only at rest and VTh with CO2 breathing was the work of breathing significantly increased ($P < 0.001$). There was no difference at peak exercise with any gas mixture.

DISCUSSION

The major finding of this study was that aged runners have a ventilatory response to exercise, both above and below VTh, that is similar to that previously observed for sedentary senior men and women (12). Furthermore, they increased their ventilatory response when breathing He-O2 during exercise, which was also similar to that observed previously for sedentary older men and women (5). The aged runners, however, were unable to significantly increase their ventilatory response to exercise above VTh with CO2 breathing, which was also similar to that observed previously for older sedentary men and women (5). Thus older runners respond to exercise, He-O2 breathing, and CO2 breathing in a manner that is similar to that of older sedentary men and women, despite the runners’ higher exercise capacity and increased ventilatory requirement at peak exercise. These data also suggest that the ventilatory response to exercise of these aged runners is adequate to support their greater exercise capacity and that the larger ventilatory demand does not result in limiting mechanical ventilatory constraints (25). Furthermore, these findings suggest that exercise training does not alter the ventilatory response to exercise with He-O2 or inspired CO2 breathing in aged runners.

Population studied. The subjects for this study were recruited on the basis of their reported exercise train-
Table 3. Selected variables for room air and He-O₂ tests

<table>
<thead>
<tr>
<th>Variable</th>
<th>Room Air</th>
<th>He-O₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest</td>
<td>VTh</td>
<td>Peak</td>
</tr>
<tr>
<td>Workload, W</td>
<td>0</td>
<td>106±38</td>
</tr>
<tr>
<td>Time, min</td>
<td>0</td>
<td>3.9±1.2</td>
</tr>
<tr>
<td>HR, %predicted</td>
<td>39±6</td>
<td>68±10</td>
</tr>
<tr>
<td>Vt, liters</td>
<td>0.93±0.21</td>
<td>1.9±0.49</td>
</tr>
<tr>
<td>f₂, breaths/min</td>
<td>14±4</td>
<td>25±3</td>
</tr>
<tr>
<td>PetCO₂, Torr</td>
<td>37±5</td>
<td>42±4</td>
</tr>
<tr>
<td>EFL, %VT</td>
<td>0</td>
<td>0.4±1.2*</td>
</tr>
<tr>
<td>EELV, %TLC</td>
<td>56±4</td>
<td>54±3</td>
</tr>
<tr>
<td>EILV, %TLC</td>
<td>70±6</td>
<td>83±6</td>
</tr>
<tr>
<td>Rl, cmH₂O·1⁻¹·s</td>
<td>1.90±0.84*</td>
<td>1.80±0.78*</td>
</tr>
<tr>
<td>WOB, J/min</td>
<td>4±1</td>
<td>40±28*</td>
</tr>
<tr>
<td>RPE (6–20 scale)</td>
<td>0</td>
<td>12±3</td>
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<tr>
<td>RPB (0–10 scale)</td>
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<td>4±3</td>
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<tr>
<td>Vt/Te, l/s</td>
<td>0.34±0.09</td>
<td>1.53±0.33</td>
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Values are mean ± SD (*n = 11, †n = 10, ‡n = 9, and ‡‡n = 8 subjects). VTh, ventilatory threshold; HR, heart rate; Vt, tidal volume; f₂, breathing frequency; PetCO₂, end-tidal PCO₂; EFL, expiratory flow limitation; EELV, end-expiratory lung volume; EILV, end-inspiratory lung volume; Rl, pulmonary resistance; WOB, mechanical work of breathing against the lung; RPE, rating of perceived exertion; RPB, rating of perceived breathlessness; Vt/Te, mean expiratory flow rate. *P < 0.05, †P < 0.01, and ‡P < 0.001.

Table 4. Selected variables for room air and CO₂ tests

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aging, whereas the ventilatory response above VTh changes little (12). These runners, although slightly younger, had comparable pulmonary function, a slightly lower aerobic capacity, a similar $V_{\dot{E}}$ at peak exercise, and a similar EILV ($\%TLC$), but a lower degree of expiratory flow limitation (9/1106 vs. 27% of $VT$) than the runners (all men) studied by Johnson et al. (25).

**Ventilatory response to exercise with He-O$_2$ breathing.** The increase in $V_{\dot{E}}$ with He-O$_2$ breathing was similar to that reported in the literature (8, 14, 21, 43, 46, 48). We also found the runners’ ventilatory response to exercise while breathing He-O$_2$ to be the same as observed earlier for younger subjects (4), older subjects (5), and older men and women with mild chronic airflow limitation (6). Thus, older runners, despite their higher exercise capacity and ventilatory demand, do not respond any differently to He-O$_2$ breathing than do sedentary older men and women.

Despite the runners’ increase in $V_{\dot{E}}$ with He-O$_2$ breathing, their exercise capacity was not increased, just as observed in previous studies (4–6). This finding agrees with the findings of others (14, 21, 43) and contrasts with the findings of some (7, 48). These differences among studies are most likely due to differences in subject ages, the variables used to measure exercise capacity (i.e., work rate and exercise time vs. $V_{O_2}$), and the exercise protocols used to determine exercise capacity. However, it was possible, given the runners’ greater exercise capacity and substantially higher ventilatory demand at peak exercise, that they could have been predisposed to greater mechanical ventilatory constraints, and their exercise tolerance might have been improved by a lower respiratory impedance. This was not the case, nor does it seem to be the case in lung patients who have marked ventilatory limitations to exercise (6, 35, 41). At this point, the importance of the increase in $V_{\dot{E}}$ with He-O$_2$ breathing must be more carefully evaluated, as others have suggested previously (28, 46).

Finally, breathing He-O$_2$ in the aged runners did not alter the relationship between the mechanical work of breathing and work rate. Whereas pulmonary resistance and respiratory impedance may be lower, the work of breathing of the lung is not lower for a given exercise work rate, even in these aged runners. Nor
was this relationship different from that observed in previous work in sedentary older men and women (5, 6). These findings support the contention that the ventilatory response to exercise can be altered by resistive unloading without affecting the relationship between the work of breathing and exercise capacity. This relationship appears to be more finely controlled during exercise than $V_E$ or gas-exchange indicators such as $P_{ETCO_2}$.

These findings with He-O$_2$ breathing also help to explain some of the differences observed between He-O$_2$ breathing and respiratory unloading with inspiratory assist (i.e., positive-pressure breathing). In He-O$_2$ breathing, $V_E$ is increased during exercise, but, with inspiratory pressure assist, $V_E$ is not increased (15, 28, 40). Our findings suggest that this difference is due to the fact that the mechanical work of breathing is not altered with He-O$_2$ breathing, whereas with inspiratory assist, the mechanical work of breathing is actually decreased for a given work rate. This may be why investigators have found exercise tolerance to be increased with inspiratory assist (20) and why we have found no change in exercise capacity with He-O$_2$ breathing.

**Ventilatory response to exercise with CO$_2$ breathing.** We found the runners’ ventilatory response to exercise while breathing inspired CO$_2$ to be the same as observed in earlier work in sedentary older men and women (5, 6). The runners, just like older sedentary subjects, were unable to increase their ventilatory response above $V_{Th}$ with CO$_2$ breathing (5, 6). This is similar to the findings of others who reported that older fit men could not significantly increase $V_E$ at peak exercise with CO$_2$ breathing (25). These are the first data in older runners to assess the ventilatory response to CO$_2$ breathing on all work rates above $V_{Th}$.

In contrast to these data and prior published results, a relatively small group of older sedentary subjects have been shown to have a parallel shift in $V_E$ throughout all phases of exercise with inspired CO$_2$ (22). These results differ not only from the results in fit older subjects in this study and others (25) but also from prior data observed in sedentary men and women (5, 6). This dissimilarity could reflect differences in factors such as exercise protocol (e.g., incremental vs. steady state), exercise mode (e.g., cycling vs. treadmill), and even subject motivation (see below for other alternatives), to mention a few possibilities, but ventilatory constraints were not markedly different. On the basis of our prior results and the results of this study, the ventilatory response to inspired CO$_2$ is not notably different between older fit and sedentary men and women during graded cycle ergometry to exhaustion.

The majority of findings in older adults are in contrast to those in younger adults, who could increase their ventilatory response to CO$_2$ above $V_{Th}$ (4, 11), but similar to those in younger endurance athletes, who could not increase $V_E$ at peak exercise with CO$_2$ breathing (26). It has been assumed that failure to increase $V_E$ with CO$_2$ breathing is an indicator of the limitations imposed by mechanical ventilatory constraints (i.e., expiratory flow limitation and lung volume). It may not be that simple. Even in young subjects, $V_E$ cannot be increased as much when the inspired CO$_2$ concentration goes >6% (11). In these circumstances, it is difficult to determine whether $V_E$ is limited because of decreased CO$_2$ responsiveness, mechanical ventilatory limitations, or an interaction between respiratory impedance and CO$_2$ responsiveness (11, 17). It has been shown that the ventilatory response to exercise with CO$_2$ breathing is incompletely defended when breathing impedance is imposed; however, the ventilatory response to exercise with increased breathing impedance alone is usually not affected (17, 39). Thus it is difficult to explain a lack of response based on just mechanical limitations alone.

It could be proposed that, with inspired CO$_2$, the ventilatory response to exercise might be determined by the respiratory controller’s balance between CO$_2$ drive and the propensity of the controller to minimize respiratory effort (34, 38). Recent data on the importance of respiratory work and diaphragm fatigue in the control of vascular blood flow or cardiac output during exercise certainly support this concept (18–20, 42, 44). Also, it is possible that sedentary or trained older adults are less responsive to ventilatory input (1), especially input that might increase the work of breathing during exercise. The relationship between the work of breathing and exercise intensity appears to be defended strongly, even at the cost of attenuating $V_E$ or exercise capacity in sedentary elderly (5, 6) and now the elderly runner.

In further support, CO$_2$ breathing in the runners resulted in a slight, but significant decrease in exercise capacity, which is in contrast to that observed in sedentary younger and older men and women (4, 5). This may be due to the fact that the runners, because of their higher exercise capacity and greater ventilatory demand, have a lower ventilatory reserve. However, $V_E$ was the same as when room air was breathed, as were mechanical ventilatory constraints. Also, RPE and RPB were also similar to room air breathing, although the mechanical work of breathing was increased with CO$_2$ breathing. This increase in the mechanical work of breathing was similar to that observed previously in older and younger sedentary men and women (4, 5). As proposed above, it may be that CO$_2$ breathing cannot alter the ventilatory response during heavy exercise in the elderly because of the increase in the mechanical work of breathing, which appears to affect exercise capacity.

**Conclusion.** In conclusion, the ventilatory responses to exercise with room air, He-O$_2$, and CO$_2$ breathing of these fit runners were similar to those observed earlier in older sedentary individuals. These data also suggest that the ventilatory response to exercise of these senior runners is adequate to support their greater exercise capacity and that exercise training does not alter the ventilatory response to exercise with He-O$_2$ or inspired CO$_2$ breathing. Furthermore, these findings on exercise capacity with CO$_2$ and He-O$_2$ breathing suggest that $V_E$ plays a less important role in exercise capacity than conventionally thought. This appears true despite
modest changes in $\text{PETO}_2$ and mechanical ventilatory constraints, which can also be modulated without affecting exercise capacity. The work of breathing, however, seems to be rather important to exercise capacity, as it does to the responsiveness of the elderly to ventilatory input during exercise.

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