Adaptation of pulmonary O2 uptake kinetics and muscle deoxygenation at the onset of heavy-intensity exercise in young and older adults

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DeLorey, Darren S., John M. Kowalchuk, and Donald H. Paterson. Adaptation of pulmonary O2 uptake kinetics and muscle deoxygenation at the onset of heavy-intensity exercise in young and older adults. J Appl Physiol 98: 1697–1704, 2005. First published January 7, 2005; doi:10.1152/japplphysiol.00607.2004.—The purpose was to examine the adaptation of pulmonary O2 uptake (V˙O2p) and deoxygenation of the vastus lateralis muscle at the onset of heavy-intensity, constant-load cycling exercise in young (Y; 24 ± 4 yr; mean ± SD; n = 5) and older (O; 68 ± 3 yr; n = 6) adults. Subjects performed repeated transitions on 4 separate days from 20 W to a work rate corresponding to heavy-intensity exercise. V˙O2p was measured breath by breath. The concentration changes in oxyhemoglobin, deoxyhemoglobin (HHb), and total hemoglobin/myoglobin were determined by near-infrared spectroscopy (Hamamatsu NIRS-300). V˙O2p data were filtered, interpolated to 1 s, and averaged to 5-s bins. HHb-near-infrared spectroscopy data were filtered and averaged to 5-s bins. A monoexponential model was used to fit V˙O2p [phase 2, time constant (τ) of V˙O2p] and HHb [following the time delay (TD) from exercise onset to the start of an increase in HHb] data. The τV˙O2p was slower (P < 0.001) in O (49 ± 8 s) than Y (29 ± 4 s). The HHb TD was similar in O (8 ± 3 s) and Y (7 ± 1 s); however, the τ HHb following TD was faster (P < 0.05) in O (8 ± 2 s) than Y (14 ± 2 s). The slower V˙O2p kinetics and faster muscle deoxygenation in O compared with Y during heavy-intensity exercise imply that the kinetics of muscle perfusion are slowed relatively more than those of V˙O2p in O. This suggests that the slowed V˙O2p kinetics in O may be a consequence of a slower adaptation of local muscle blood flow relative to that in Y.

CONSIDERABLE EVIDENCE EXISTS that suggests that the rate at which pulmonary O2 uptake (V˙O2; V˙O2p) adapts at the onset of moderate-intensity exercise in healthy, young adults is fundamentally limited by factors other than muscle O2 delivery (2, 25–27, 33). In contrast, the adequacy of muscle blood flow and O2 delivery at the onset of exercise in the older adult has been questioned, and several investigations (6, 9, 16, 18, 48) have reported that V˙O2p kinetics may be slowed at the onset of moderate-intensity exercise in older adults due to a slower adaptation of muscle blood flow. Specifically, slower heart rate (HR) kinetics at the onset of exercise in older adults (6, 9, 16, 18, 48) and age-associated changes in the cardiovascular system (29, 37, 38, 50) suggest that the ability of the older adult to increase muscle blood flow at the onset of exercise may be diminished and provides support for the assertion that V˙O2p kinetics may be limited by the convective delivery of O2 in older adults. We (16) recently studied the adaptation of V˙O2p and near-infrared (NIR) spectroscopy (NIRS) measurement of muscle deoxygenation simultaneously at the onset of moderate-intensity cycling exercise in older and younger adults. In that study, although V˙O2p kinetics were slower in older compared with younger adults, muscle deoxygenation adapted at a similar rate, suggesting that muscle microvascular blood flow and O2 delivery adapted at a slower rate at the onset of moderate-intensity exercise in older compared with younger adults and that V˙O2p kinetics may be limited by the convective delivery of O2 in older adults.

Relative to the moderate-intensity domain, muscle metabolic and O2 demand is elevated during heavy-intensity exercise, and previous reports (23, 39) have suggested that the adaptation of V˙O2p may be more complex during the on-transient of heavy- compared with moderate-intensity exercise. Furthermore, Grassi et al. (23) reported that the convective delivery of O2 may limit the rate of increase in V˙O2p at the onset of exercise at or near peak V˙O2 (V˙O2peak). Therefore, if the ability of the older adult to increase muscle blood flow and O2 delivery is diminished in the moderate-intensity domain, we reasoned that the increased muscle O2 demand during heavy-intensity exercise would result in a greater mismatch between local muscle O2 delivery and muscle O2 utilization in older adults. A mismatch between V˙O2p and blood flow would be seen as a faster rate of muscle deoxygenation in older compared with younger adults.

Additionally, during heavy-intensity exercise, an additional component of V˙O2p is superimposed on the fundamental response (39). This additional component is of delayed onset and results in a change in (Δ) V˙O2p/Δwork rate (WR) relationship above that determined during moderate-intensity exercise and has been termed the V˙O2p slow component. The underlying mechanisms responsible for the slow component of V˙O2p have not been identified; however, Poole et al. (40) reported that ~86% of the slow component can be accounted for by the exercising limbs. This increase in muscle O2 consumption could potentially impact upon the control of local muscle O2 delivery and metabolism/perfusion matching. However, to our knowledge, the balance between local muscle O2 delivery and utilization during the slow component of V˙O2p and the effect of age on the V˙O2p slow component have not been studied.

Therefore, the purpose of present study was to examine 1) the effect of age on the adaptation of V˙O2p, HR, and muscle deoxygenation during the on-transient of heavy-intensity cycling exercise; and 2) the relationship between the V˙O2p slow component and age.

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component and local muscle deoxygenation of the vastus lateralis during high-intensity, constant-load leg cycling exercise in older and younger adults. We hypothesized, at the onset of heavy-intensity exercise, the following. 1) VO_{2p} kinetics would be slower in older compared with younger adults, and there would be a faster adaptation and greater increase (i.e., Δ from pretransition baseline) of muscle deoxygenation in older compared with younger adults, reflecting a lower or more slowly adapting regional muscle blood flow in the older adult during the on-transient of exercise. 2) The magnitude of the VO_{2p} slow component would be smaller in older compared with younger adults, consistent with the previous findings of Bell et al. (5), whereas the magnitude of the change in deoxyhemoglobin/myoglobin (HHb) during the slow component would be greater in older adults, reflecting a lower muscle blood flow in older compared with younger adults during heavy-intensity, constant-load leg cycling exercise.

METHODS

Subjects. Five young (Y) (26 ± 3 yr, mean ± SD) and six older men (O) (68 ± 3 yr) volunteered and gave written, informed consent to participate in the study. All procedures were approved by The University of Western Ontario Ethics Committee for Research on Human Subjects. All subjects were healthy and physically active.

Protocol. Subjects reported to the laboratory on five separate occasions. A maximal cycle ergometer ramp test (25 W/min) was performed on the first day of testing for determination of the lactate threshold (θ_L and VO_{2 peak}). The θ_L was determined by visual inspection and defined as the VO_{2p} at which CO_2 production began to increase out of proportion in relation to VO_{2p}, with a systematic rise in minute ventilation/VO_{2p} and end-tidal P_{O_2} while minute ventilation/CO_2 production and end-tidal P_{CO_2} were stable. Following this test, subjects returned to the laboratory on four separate occasions to perform square-wave transitions in WR from 20 W to a heavy WR selected to elicit a VO_{2p} corresponding to θ_L plus 50% of the difference between θ_L and VO_{2 peak} (ΔΣ0). Each WR transition was 6 min in duration and was preceded and followed by 6 min of cycling at 20 W.

Measurements. Gas-exchange measurements were similar to those described previously (1). Briefly, inspired and expired flow rates were measured using a low dead space (90 ml) bidirectional turbine (Alpha Technologies VMM 110), which was calibrated before each test using a syringe of known volume. Inspired and expired gases were sampled continuously at the mouth and analyzed for concentrations of O_2, CO_2, and N_2 by mass spectrometry (Morgan Medical) after calibration with precision-analyzed gas mixtures. Changes in gas concentration were aligned with gas volumes by measuring the time delay (TD) for a square-wave bolus of gas passing the turbine to the resulting changes in fractional gas concentrations, as measured by the mass spectrometer. Data collected every 20 ms were transferred to a computer, which aligned concentrations with volume data to build a profile of each breath. Breath-by-breath alveolar gas exchange was calculated using algorithms of Beaver et al. (3). HR was continuously monitored by electrocardiogram.

Local muscle oxygenation profiles of the quadriceps vastus lateralis muscle were made with NIRS (Hamamatsu NIRO 300, Hamamatsu Photonics KK, Japan). Optodes were placed on the belly of the muscle midway between the lateral epicondyle and greater trochanter of the femur. The optodes were housed in an optically dense plastic holder, thus ensuring that the position of the optodes, relative to each other, was fixed and invariant. The optode assembly was secured on the skin surface with tape and then covered with an optically dense, black vinyl sheet, thus minimizing the intrusion of extraneous light and loss of NIR-transmitted light from the field of interrogation. The thigh, with attached optodes and covering, was wrapped with an elastic bandage, to minimize movement of the optodes while still permitting freedom of movement for cycling. This preparation essentially prevented any optode movement relative to the skin surface.

The theory of NIRS and operating characteristics of the NIRO 300 spectrometer have been described previously (20). At present, NIRS instrumentation is unable to accurately determine the relative contribution of myoglobin (Mb) to the total NIRS signal, because the Mb absorption spectrum overlaps that of hemoglobin (Hb) (14). However, Mb levels are small relative to those of Hb, and several studies (7, 8, 32, 49) have suggested that intracellular Mb contributes <10% to the total NIRS signal. Thus the preponderance of evidence in the literature would suggest that NIRS primarily monitors changes in vascular Hb oxygenation and deoxygenation, although Tran et al. (52) have reported that NIRS deoxygenation kinetics closely matched those of ^1^H-magnetic resonance spectroscopy-determined Mb desaturation, but not Hb desaturation, during plantar flexion exercise with pressure cuffing of the leg.

The interoptode spacing was 5 cm in the present study. Although values exist for differential pathlength factors in muscle for calf and forearm (19), there are presently no published values for the quadriceps muscle. In the present study, we used a value for the differential pathlength factor of 3.83; thus values for oxyhemoglobin (HbO_2), HHb, and total hemoglobin/myoglobin (Hb tot) are reported as a change from baseline in micromolar units.

The HHb signal can be regarded as being essentially blood-volume insensitive during exercise (12, 21); thus it was assumed to be a reliable estimator of changes in intramuscular oxygenation status and O_2 extraction in the field of interrogation (13, 21).

Analysis. Breath-by-breath gas-exchange data were interpolated to 1-s intervals, filtered for aberrant data points, and then ensemble averaged in 5-s time bins to yield a single response for each subject. Phase 2 VO_{2p} kinetics were determined from the phase 1-phase 2 interface, to the time point at which the model fit departed from monoexponentiality and the sum of least squares residuals increased (defined as the phase 2-phase 3 interface) by the use of a monoexponential model of the form:

\[
Y(t) = Y_0 + A \cdot \left[1 - e^{-\left(\frac{t - \theta}{\tau}\right)}\right]
\]

where \(Y\) represents VO_{2p} at any time (t), \(Y_0\) is the baseline value of \(Y\) at the point in time from which the data were fitted, \(A\) is the amplitude of the increase in \(Y\) above the baseline value, and \(\tau\) is the time constant defined as the duration of time through which \(Y\) increases to a value equivalent to 63% of \(A\). The phase 1–2 and phase 2–3 interfaces were determined according to the method of Rossiter et al. (45). The amplitude of the slow component of VO_{2p} (phase 3) was calculated as the difference between end-exercise VO_{2p} and the phase 2 VO_{2p} amplitude, with the phase 2 VO_{2p} being the projected asymptote, estimated to occur following four \(\tau\) values in each individual.

Beat-by-beat HR data were filtered for aberrant beats, time aligned, and averaged to 5-s time bins. HR data were then fit with a monoexponential model of the form in Eq. 1 from exercise onset to the time point representing the phase 2-phase 3 interface for VO_{2p}, to determine the rate of adaptation of HR during the primary adaptive phase of VO_{2p}. The amplitude of the increase in HR from the end of model fitting to end-exercise was also calculated.

The NIRS-derived HbO_2, HHb, and Hb tot data were time aligned and ensemble averaged to 5-s time bins to yield a single response for each subject. The time to the onset of an increase in HHb was determined as the first point greater than 1 SD above the mean of the baseline. This analysis was performed on each individual trial before averaging, and the TD for all four trials were averaged. Subsequently, HHb data were fit with a monoexponential model of the form in Eq. 1 from the time of initial increase in HHb to the time point representing the phase 2-phase 3 interface for VO_{2p}, to determine the rate of adaptation of muscle deoxygenation during the primary adaptive phase of VO_{2p}. Although we are not certain that the underlying
Table 1. Subject characteristics

<table>
<thead>
<tr>
<th></th>
<th>Age, yr</th>
<th>Height, cm</th>
<th>Body mass, kg</th>
<th>Peak WR, W</th>
<th>( \dot{V}_O^2) peak, l/min</th>
<th>( \dot{V}_O^2) peak, ml/kg⋅min⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young</td>
<td>5</td>
<td>26±3</td>
<td>181±3</td>
<td>78±4</td>
<td>366±30</td>
<td>3.8±0.4</td>
</tr>
<tr>
<td>Older</td>
<td>6</td>
<td>68±5*</td>
<td>178±3</td>
<td>84±10</td>
<td>218±27*</td>
<td>2.3±0.3*</td>
</tr>
</tbody>
</table>

Values are means ± SD; n, no. of subjects. WR, work rate; \( \dot{V}_O^2\) peak, peak oxygen uptake. *P < 0.001.

processes determining muscle deoxygenation are exponential in nature, visual inspection of the NIRS-derived HHb signal and analysis of least squares residuals suggested that fitting with a monoexponential model would yield a reasonable estimate of the time course of muscle deoxygenation (i.e., an effective \( \tau \)). The amplitude of the increase in HHb from the end of model fitting to end-exercise was also calculated. The \( \dot{O}_2\) and \( \dot{Hb}_o\) signals did not approximate an exponential response; thus these data were not modeled. However, the response of these signals was qualitatively compared with the HHb data at corresponding time intervals.

Statistical analysis. Comparisons between groups and between \( \dot{V}_O^2\)p, HHb, and HR kinetics within each group were made by independent \( t \)-tests and ANOVA. Relationships among key variables were determined by Pearson product correlation. All data are presented as means ± SD. A \( P \) value of <0.05 was considered statistically significant.

RESULTS

Subject characteristics and peak exercise values are presented in Table 1. Older subjects had a lower peak HR (\( P < 0.001 \)), peak WR (\( P < 0.01 \)), and absolute (l/min) and relative (ml·kg⁻¹·min⁻¹) \( \dot{V}_O^2\) peak (\( P < 0.01 \)). The absolute \( \dot{V}_O^2\)p attained during phase 2 of the heavy-intensity exercise was a similar percentage of \( \dot{V}_O^2\) peak in O (80 ± 5%) and Y (75 ± 3%) and represented a \( \Delta \dot{V}_O^2\)p of \( \Delta 46 \pm 8 \) in O and \( \Delta 43 \pm 5 \) in Y, demonstrating that both groups exercised at the prescribed intensity and at similar relative exercise intensities.

\( \dot{V}_O^2\)p kinetics. Phase 2 \( \tau \dot{V}_O^2\)p was greater (\( P = 0.001 \)) in O (49 ± 8 s) compared with Y (29 ± 4 s) during the on-transient of heavy-intensity exercise (Figs. 1 and 2, Table 2). Pretransition baseline \( \dot{V}_O^2\)p was lower (\( P < 0.01 \)) in O (0.79 ± 0.06 l/min) compared with Y (0.94 ± 0.07 l/min), and the amplitude of the increase in phase 2 \( \dot{V}_O^2\)p was lower in O (1.05 ± 0.10 l/min) compared with Y (1.92 ± 0.37 l/min; \( P < 0.001 \)). Thus the absolute \( \dot{V}_O^2\)p attained during phase 2 was lower (\( P < 0.001 \)) in O (1.85 ± 0.14 l/min) compared with Y (2.86 ± 0.36 l/min; \( P < 0.001 \)), reflecting the lower (\( P < 0.001 \)) WR in O (129 ± 10 W) compared with Y (228 ± 23 W). The gain (\( \Delta \dot{V}_O^2\)/\( \Delta \dot{W} \)) of the phase 2 \( \dot{V}_O^2\)p response was similar in O (9.7 ± 0.4 ml·min⁻¹·W⁻¹) and Y (9.2 ± 0.7 ml·min⁻¹·W⁻¹).

A \( \dot{V}_O^2\)p slow component (phase 3) was observed in both O and Y. The onset of the slow component was similar in O (146 ± 6 s) and Y (146 ± 5 s). The slow-component amplitude was smaller in O (0.13 ± 0.06 l/min) compared with Y (0.32 ± 0.11 l/min; \( P = 0.007 \)). The slow component represented a similar percentage of the total increase in \( \dot{V}_O^2\)p in O (11 ± 6%) and Y (14 ± 5%; \( P = 0.263 \)). End-exercise \( \dot{V}_O^2\)p was lower in O (1.98 ± 0.14 l/min) compared with Y (3.18 ± 0.30 l/min; \( P < 0.001 \)); however, relative to peak \( \dot{V}_O^2\)p, end-exercise \( \dot{V}_O^2\)p was similar in O (87 ± 6%) and Y (83 ± 3%).

HR. The phase 2 \( \tau \) HR was greater (\( P < 0.05 \)) in O (71 ± 31 s) compared with Y (36 ± 8 s; Fig. 3, Table 2). Baseline HR during the 20-W pretransition baseline was similar in O (86 ± 9 beats/min) and Y (85 ± 6 beats/min). The amplitude of the increase in HR during phase 2 was lower (\( P < 0.05 \)) in O (39 ± 6 beats/min) compared with Y (54 ± 13 beats/min), and, as a result, the HR attained during phase 2 was also lower (\( P = 0.048 \)) in O (125 ± 12 beats/min) compared with Y (139 ± 9 beats/min). Expressed as a percentage of peak HR, a similar HR response was observed in O (78 ± 5%) and Y (75 ± 5%) during phase 2. Additionally, the increase in HR for a given increase in \( \dot{V}_O^2\)p during phase 2 of the on-transient (\( \Delta \dot{Hr}/\Delta \dot{V}_O^2\)p) was greater (\( P < 0.05 \)) in O (40 ± 7 beats/l) compared with Y (28 ± 6 beats/l).

Following phase 2, HR continued to increase throughout the remainder of the exercise bout, with the amplitude of the increase being similar in O (10 ± 7 beats/min) and Y (9 ± 5 beats/min). End-exercise HR was similar in O and Y in absolute terms (O: 135 ± 17 beats/min; Y: 148 ± 9 beats/min) and relative to peak HR (O: 84 ± 8%; Y: 80 ± 5%).

NIRS. Following the step increase in WR, a similar TD HHb before an increase in NIRS-derived HHb was observed in O (8 ± 3 s) and Y (7 ± 1 s; Table 2). Following the TD, HHb increased rapidly in O and Y with the effective \( \tau \) (O: 8 ± 2 s; Y: 14 ± 2 s) and the HHb-mean response time (MRT) (O: 16 ± 1 s; Y: 22 ± 1 s) both being faster (\( P = 0.001 \)) in O compared with Y (Fig. 4, Table 2). The amplitude of the
V˙O₂p, with the magnitude of the increase being greater (\( O(3 \) M) throughout the V˙O₂p slow component in O compared with Y, suggesting that muscle blood flow increased at a slower rate throughout the exercise transient in O compared with Y. The slower V˙O₂p kinetics and apparently slower adaptation of muscle blood flow in O compared with Y suggest that V˙O₂p kinetics may be limited by local muscle O₂ delivery in older adults. However, the “steady-state” ∆HHb/∆V˙O₂p (calculated from values at the end of phase 2 of the V˙O₂p response) was similar in O and Y, showing that, after a slow increase in O₂ delivery during the on-transient of heavy-intensity exercise, muscle perfusion to metabolism matching was similar in Y and O.

V˙O₂p kinetics. Consistent with several previous studies in the moderate-intensity domain (6, 9, 16, 18, 48), phase 2 V˙O₂p kinetics at the onset of heavy-intensity exercise in the present study were slower in O compared with Y. Aging is associated with a reduced maximal HR (22), reduced left ventricular function (30, 51), increased total peripheral resistance (29), reduced capillary density (11), endothelial dysfunction (50), and altered capillary hemodynamics (46), which suggest that increase in HHb was lower (\( P < 0.05 \)) in O (12 ± 4 \( \mu \)M) compared with Y (21 ± 8 \( \mu \)M), whereas the increase in HHb (\( \Delta \)HHb) for a given increase in V˙O₂p (\( \Delta \)V˙O₂p) was similar in O (11 ± 4 \( \mu \)M·l⁻¹·min⁻¹) and Y (11 ± 5 \( \mu \)M·l⁻¹·min⁻¹).

Following phase 2, HHb continued to increase throughout the remainder of the exercise bout, with the amplitude of the increase being smaller (\( P < 0.05 \)) in O (2.5 ± 1.2 \( \mu \)M) compared with Y (5.2 ± 2.0 \( \mu \)M). However, when expressed as a percentage of the total HHb amplitude, the \( \Delta \)HHb was similar in O (18 ± 5 \%) and Y (20 ± 4 \%). During the period associated with the V˙O₂p slow component, the \( \Delta \)HHb-to-\( \Delta \)V˙O₂p ratio (\( \Delta \)HHb/\( \Delta \)V˙O₂p) was also similar in O (18 ± 4 \( \mu \)M·l⁻¹·min⁻¹) and Y (17 ± 6 \( \mu \)M·l⁻¹·min⁻¹).

The adaptation of HHb (MRT-HHb) during phase 2 of the exercise on-transient was faster than the adaptation of phase 2 V˙O₂p in both O and Y subjects (Table 2), and \( \tau \) V˙O₂p was negatively correlated (\( r = −0.644; P = 0.032 \)) with MRT-HHb when the O and Y data were collapsed into a single data set.

A similar decrease in HbO₂ was observed in O (12 ± 3 \( \mu \)M) and Y (9 ± 8 \( \mu \)M), immediately following the onset of exercise, which reached a nadir at 26 ± 3 s in O and 23 ± 13 s in Y. HbO₂ then increased throughout the phase 2 period of V˙O₂p, with the magnitude of the increase being greater (\( P < 0.05 \)) in O (7 ± 3 \( \mu \)M) compared with Y (3 ± 2 \( \mu \)M). HbO₂ continued to increase throughout the V˙O₂p slow component in O (3 ± 3 \( \mu \)M) and Y (2 ± 2 \( \mu \)M). Hb∕O₂ also decreased by a similar magnitude in O (5 ± 2 \( \mu \)M) and Y (4 ± 3 \( \mu \)M) at the onset of exercise, reaching a nadir in 7 ± 2 and 5 ± 2 s in O and Y, respectively. Thereafter, Hb∕O₂ increased by a similar magnitude in O (11 ± 4 \( \mu \)M) and Y (15 ± 5 \( \mu \)M) throughout the phase 2 component of V˙O₂p. Hb∕O₂ then increased by a similar magnitude throughout the V˙O₂p slow component in O (5 ± 2 \( \mu \)M) and Y (7 ± 2 \( \mu \)M). The adaptation of HHb, HbO₂, and Hb∕O₂ throughout the exercise transient for a representative O and Y is illustrated in Fig. 5.  

### Table 2. Kinetics parameters for V˙O₂p, HR, and HHb

<table>
<thead>
<tr>
<th></th>
<th>( \tau ) V˙O₂p, s</th>
<th>( \tau ) HR, s</th>
<th>( \tau ) HHb, s</th>
<th>HHb-TD, s</th>
<th>HHb-MRT, s</th>
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<tr>
<td>Young</td>
<td>29±4</td>
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<td>22±1‡</td>
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<td>Older</td>
<td>49±8</td>
<td>71±3†</td>
<td>8±2*</td>
<td>8±3</td>
<td>16±1§</td>
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</table>

Values are means ± SD. \( \tau \), Time constant; V˙O₂p, pulmonary oxygen uptake; HR, heart rate; HHb, deoxygenated hemoglobin/myoglobin; TD, time delay; MRT, mean response time; HHb-MRT, sum of HHb effective \( \tau \) and HHb-TD. Significant difference between young and older: *\( P = 0.001 \), †\( P < 0.05 \). Significantly different from \( \tau \) O₂, \( \tau > 0.05 \), \( \tau < 0.0001 \).
the convective delivery of O\textsubscript{2} to working muscle during exercise may be reduced in O compared with Y. These age-associated decrements in cardiovascular function, combined with the observation of slow V\textsubscript{O\textsubscript{2p}} and HR kinetics in older compared with young adults in previous studies (6, 9, 16, 18, 48), has led to the conclusion that muscle O\textsubscript{2} delivery may limit V\textsubscript{O\textsubscript{2p}} kinetics in older adults. However, reductions in mitochondrial quality and content have been associated with aging (10), which implies that skeletal muscle oxidative capacity could also limit V\textsubscript{O\textsubscript{2p}} kinetics in older adults.

Compared with the moderate-intensity domain, heavy-intensity exercise has a greater muscle O\textsubscript{2} demand and requires a greater fraction of maximal cardiac output (Q). If muscle O\textsubscript{2} delivery was slow to adapt at the onset of moderate-intensity exercise in O, it was expected that, during heavy-intensity exercise, there would be a greater mismatch between muscle O\textsubscript{2} delivery and muscle O\textsubscript{2} demand in O compared with Y. We reasoned that, if V\textsubscript{O\textsubscript{2p}} kinetics in older adults were limited by the adaptation of muscle blood flow, phase 2 V\textsubscript{O\textsubscript{2p}} kinetics would be slowed during heavy- compared with moderate-intensity exercise as the greater O\textsubscript{2} demand of heavy-intensity exercise would further exacerbate any existing O\textsubscript{2} delivery limitation. The subjects in the present study also participated in a previous study (16), which examined the adaptation of V\textsubscript{O\textsubscript{2p}} in the moderate-intensity domain. Two-way ANOVA revealed that phase 2 \( \tau \) V\textsubscript{O\textsubscript{2p}} was greater (\( P = 0.01 \)) during heavy- compared with moderate-intensity exercise in O (heavy: 49 \( \pm \) 8 s; moderate: 42 \( \pm \) 9 s), whereas phase 2 \( \tau \) V\textsubscript{O\textsubscript{2p}} was similar in Y (heavy: 29 \( \pm \) 4 s; moderate: 25 \( \pm \) 8 s; \( P = 0.13 \)). The significant slowing of phase 2 V\textsubscript{O\textsubscript{2p}} kinetics during heavy- compared with moderate-intensity exercise in O, but not Y, suggests that the process(es) limiting muscle O\textsubscript{2} consumption in O was exacerbated by the greater metabolic demand of heavy-intensity exercise. This slowing of V\textsubscript{O\textsubscript{2p}} kinetics in heavy exercise may indicate an O\textsubscript{2} delivery limitation. However, from moderate- to heavy-intensity exercise, there were similar relative increases in \( \tau \) V\textsubscript{O\textsubscript{2p}} (17\%) in both Y and O. Slower V\textsubscript{O\textsubscript{2p}} kinetics in heavy vs. moderate exercise may also relate to the recruitment of higher threshold motor units, and this may differ in the O and Y in this study, depending on such factors as the intensity of the exercise and the relative training status and fiber-type profile of the subject groups.

HR kinetics. Limited information is available on the blood flow response to heavy-intensity exercise in O. Poole et al. (41) reported attenuated leg blood flow responses during incremental cycling in older adults and attributed the decline in leg blood flow to a maldistribution of Q. Subsequently, this group reported that lower limb Q persists in older adults during incremental small muscle mass (knee extension) exercise, which is presumably not limited by maximal Q (31).

In the present study, HR kinetics were used as an indicator of the rate of adaptation of Q and presumably muscle O\textsubscript{2} delivery. HR kinetics were slower (\( P < 0.01 \)) in O compared

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**Fig. 4.** Adaptation of muscle deoxygenation Hb\textsubscript{b} during a step change in work rate for a representative young (top) and older subject (bottom). Monoeponential fit of data is also illustrated. Solid vertical line represents exercise onset.

**Fig. 5.** Adaptation of Hb\textsubscript{b} (circles), oxyhemoglobin (Hb\textsubscript{O\textsubscript{2}}; triangles) and total hemoglobin/myoglobin (Hb\textsubscript{tot}; squares) during a step change in work rate for a representative young (top) and older (bottom) subject. Solid vertical line represents exercise onset. Arrow indicates onset of V\textsubscript{O\textsubscript{2p}} slow component. \( \Delta \). Change.
with Y, suggesting that, at the onset of heavy-intensity exercise, Q and muscle O2 delivery adapted at a slower rate in O compared with Y. An inherent limitation to the use of HR kinetics is that it provides an indirect estimate of the adaptation of local muscle blood flow. However, the adaptation of HR is commonly used to examine the adaptation of Q, as stroke volume probably changes little after the initial adaptation from rest to the initial WR (20 W in the present study), and further increases in stroke volume during the exercise transient likely occur over the first heartbeats of the transient secondary to the muscle pump effect on end-diastolic volume. Therefore, HR kinetics provide a reasonable approximation of Q kinetics, as suggested by the data of De Cort et al. (15) and Yoshida and Whipp (54).

**Muscle deoxygenation kinetics.** If muscle microvascular blood flow and O2 delivery were slower to adapt in O compared with Y in the present study, a faster increase of muscle deoxygenation would be expected in O compared with Y. Following a TD, muscle deoxygenation (HHb) did increase toward a “steady-state” level at a faster rate in O (effective τ = 8 ± 2 s) compared with Y (effective τ = 14 ± 2 s). The markedly faster muscle deoxygenation in O (>40%) suggests that there was a greater mismatch between muscle O2 delivery and muscle O2 utilization during the exercise on-transient of heavy-intensity exercise in O compared with Y. The faster adaptation of muscle deoxygenation in O compared with Y, despite slower VO2p kinetics in O, suggests that muscle blood flow and O2 delivery adapted at a slower rate in O compared with Y.

Studies that have reported a lower limb blood flow during steady-state exercise in older compared with younger adults have also reported that an increased limb arteriovenous O2 difference (a-vO2diff) in older compared with younger adults compensated for the reduced O2 delivery to maintain steady-state VO2p at similar levels in the old and young (41, 42, 53).

However, little information is available about the O2 extraction during constant-load, heavy-intensity exercise in older adults. During incremental exercise to maximum, Poole et al. (41) and Lawrenson et al. (31) both reported that limb a-vO2diff was elevated in older compared with younger adults at moderate intensities of cycling and knee-extension exercise, respectively. Additionally, limb a-vO2diff was not increased above moderate-intensity exercise levels throughout incremental exercise to maximum in these studies (31, 41). In contrast, Proctor et al. (42) have reported an elevated a-vO2diff in older compared with younger adults during moderate-intensity exercise, followed by a progressive increase in a-vO2diff in both older and younger adults throughout incremental exercise. We previously reported (16) a similar ΔHHb in older and young adults during constant-load, moderate-intensity exercise, despite absolute VO2p being significantly lower in older compared with young adults. This suggested that, at the same VO2p, muscle deoxygenation and presumably O2 extraction were elevated in O compared with Y, which was supported by an elevated ΔHHb/ΔVO2p during moderate-intensity exercise in O compared with Y. A greater O2 extraction during moderate-intensity exercise also suggests that there may be a limited scope to further increase O2 extraction at higher exercise intensities. Furthermore, a decline in maximal skeletal muscle oxidative capacity with aging has been reported, suggesting that maximal O2 extraction may be lower in older compared with young adults (10, 11, 34–36). In the present study, the increase in HHb (ΔHHb) from the pretransition baseline to the end of phase 2 component of the VO2p response was significantly lower in O compared with Y; however, ΔHHb was greater than that previously observed during moderate-intensity exercise in both O and Y, demonstrating that both groups were able to further increase O2 extraction with an increase in exercise intensity. Additionally, the ΔHHb/ΔVO2p ratio was similar in O and Y during “steady-state” exercise, suggesting similar muscle perfusion to metabolism matching in O and Y. Therefore, the data from the present study suggest that muscle blood flow may increase at a slower rate at the onset of exercise in O compared with Y and may limit VO2p kinetics. However, these data also suggest that, if constant-load, heavy-intensity exercise is continued, a similar level of metabolism/perfusion matching and O2 extraction will be attained in O and Y.

Following the onset of constant-load, heavy-intensity cycling exercise, a TD of ~8 s was observed before an increase in the NIRS-derived HHb signal above preexercise baseline levels in both O and Y. We (17) and others (24) have previously documented a delay before an increase in HHb in O and Y at the onset of moderate-intensity cycling exercise, and Behnke et al. (4) have reported a similar delay in isolated animal muscle. The potential explanations for this delay have been discussed in detail previously (17). We believe that the HHb delay reflects a complex balance between Hb/Mb deoxygenation, O2 delivery, and the effect of muscle contraction on microvascular volume, such that muscle O2 consumption is actually increasing during the delay and an increase in HHb is “masked” by other factors that impact on the volume of Hb in the field of NIRS interrogation (17). The delay in the present study was shorter (P < 0.05) than the delay that we previously reported during moderate-intensity exercise in O and Y and suggests that the mismatch between muscle O2 delivery and O2 consumption occurs earlier in the exercise transient, with muscle O2 consumption increasing at a faster rate than muscle blood flow. It is possible, therefore, that the factors that enable local oxygenation status to be maintained during the early increase in muscle O2 consumption (potentially muscle pump and vasodilatory mediated increases in muscle blood flow and O2 delivery) may not be as effective at matching O2 delivery to O2 utilization at the onset of heavy- compared with moderate-intensity exercise in both O and Y.

**Slow component.** An additional goal of the present study was to determine whether the VO2p slow component was affected by advancing age and whether the relationship between local muscle O2 delivery and O2 utilization was altered during the VO2p slow component. A VO2p slow component, which evolved at a similar time, was evident in both O and Y. The absolute increase in VO2p during the slow component was smaller in O compared with Y, whereas the slow component represented a similar percentage of the total VO2p response in both O and Y. The mechanism(s) responsible for the VO2p slow component has not been established; however, others (40, 45) have reported that the exercising muscle accounts for as much as ~90% of the VO2p slow component. Recent studies (28, 44) have argued that the progressive recruitment of less efficient type II muscle fibers may be responsible for the increased O2 consumption during the VO2p slow component. Aging is associated with a loss of type II muscle fibers, and, therefore, a
smaller recruitment of type II fibers may explain the smaller absolute slow-component amplitude in the present study. However, Sabapathy et al. (47) reported a smaller absolute slow-component amplitude in older compared with young adults, whereas muscle fiber recruitment patterns were similar in both groups. Alternatively, the smaller absolute slow-component amplitude in older adults may be related to the lower absolute WR in O compared with Y, as others (5, 47) have suggested. The slow component being a similar percentage of the total $\dot{V}O_2p$ response in O and Y is consistent with the absolute slow-component amplitude being a function of the WR and suggests that the determinants of the $\dot{V}O_2p$ slow component are similar in O and Y.

An increase in HHb was also observed during the time period corresponding to the $\dot{V}O_2p$ slow component in both O and Y in the present study. The increase in HHb suggests that the local balance between muscle $O_2$ delivery and utilization was altered during the slow component and is consistent with the origin of the $\dot{V}O_2p$ slow component being predominantly in the exercising muscle. A slow increase in local muscle $O_2$ delivery compared with muscle $O_2$ utilization during the $\dot{V}O_2p$ slow component may explain a slow component-like increase in HHb in the present study. However, HbO2 and Hbtot increased throughout the time period corresponding to the $\dot{V}O_2p$ slow component in O and Y, suggesting that muscle $O_2$ delivery was also increasing. Although a direct relationship between muscle blood flow and local muscle Hb volume has not been established, a higher HbO2 and Hbtot concentration within the field of interrogation is consistent with a greater perfusion and thus $O_2$ availability. The increase in HHb during the $\dot{V}O_2p$ slow component was smaller in O compared with Y, whereas the $\Delta$HHb/$\Delta$VO2p was similar in O and Y during the $\dot{V}O_2p$ slow component, suggesting that muscle deoxygenation made a similar contribution to the increase in $\dot{V}O_2p$ during the slow component in O and Y. Collectively, these results suggest that muscle $O_2$ consumption, muscle blood flow, and muscle oxygen all increase throughout the slow component in both O and Y.

In conclusion, this study demonstrated slower phase 2 $\dot{V}O_2p$ and HR kinetics and a faster adaptation of muscle deoxygenation (HHb) in O compared with Y during a heavy-intensity WR transition. These results suggest local muscle perfusion may adapt at a slower rate in O compared with Y during the on-transient of heavy-intensity exercise. A $\dot{V}O_2p$ slow component was evident in O and Y and was accompanied by evidence of increases in both $O_2$ delivery and muscle deoxygenation.

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