Kinetics of estimated human muscle capillary blood flow during recovery from exercise

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The kinetic characteristics of muscle capillary blood flow ($Q_{\text{cap}}$) during recovery from exercise are controversial (e.g. one versus two phases). Furthermore, it is not clear how the overall $Q_{\text{cap}}$ kinetics are temporally associated with muscle oxygen uptake ($V_{O_2m}$) kinetics. To address these issues, we examined the kinetics of $Q_{\text{cap}}$ estimated from the rearrangement of the Fick equation ($Q_{\text{cap}} = V_{O_2m}/C_{(a-v)O_2}$) using the kinetics of pulmonary $V_{O_2}$ ($V_{O_2p}$, primary component) and deoxy-haemoglobin concentration ([HHb]) as indices of $V_{O_2m}$ and $C_{(a-v)O_2}$ (arterio-venous oxygen difference) kinetics, respectively. $V_{O_2p}$ (1 min⁻¹) was measured breath by breath and [HHb] (µM) was measured by near infrared spectroscopy during moderate (M; below lactate threshold, LT) and heavy exercise (H, above LT) in nine subjects. The kinetics of $Q_{\text{cap}}$ were biphasic, with an initial fast phase ($\tau_1$; $M = 9.3 \pm 4.9$ s and $H = 6.0 \pm 3.8$ s) followed by a slower phase 2 ($\tau_2$; $M = 29.9 \pm 8.6$ s and $H = 47.7 \pm 26.0$ s). For moderate exercise, the overall kinetics of $Q_{\text{cap}}$ (mean response time [MRT], $36.1 \pm 8.6$ s) were significantly slower than the kinetics of $V_{O_2p}$ ($\tau_2$; $27.8 \pm 5.3$ s) and [HHb] (MRT for [HHb]; $16.2 \pm 6.3$ s). However, for heavy exercise, there was no significant difference between MRT-[HHb] ($34.7 \pm 10.4$ s and $\tau_p$ for $V_{O_2p}$ ($32.3 \pm 6.7$ s), while MRT for $Q_{\text{cap}}$ ($48.7 \pm 21.8$ s) was significantly slower than MRT for [HHb] and $\tau_p$ for $V_{O_2p}$. In conclusion, during recovery from exercise the estimated $Q_{\text{cap}}$ kinetics were biphasic, showing an early rapid decrease in blood flow. In addition, the overall kinetics of $Q_{\text{cap}}$ were slower than the estimated $V_{O_2m}$ kinetics.

Muscle blood flow ($Q_m$), coupled with arterial O₂ content, will dictate the dynamics of O₂ delivery during the recovery period following cessation of exercise. Hence, the kinetics of $Q_m$ can have profound effects on the recuperation of muscle metabolism to pre-exercise levels depending on the population studied (trained subjects, Haseler et al. 1999; heart failure patients, Hanada et al. 2000). However, the temporal (kinetic) characteristics of $Q_m$ during recovery from exercise remain unclear.

It has been reported that the recovery of $Q_m$ was not exponential in human larger vessels (moderate and heavy exercise, Van Leeuwen et al. 1992) and in rat muscle feed arteries (high-intensity muscle contractions, Lash, 1994). In contrast, other investigators have used exponential equations to describe the $Q_m$ response during recovery from exercise (Shoemaker et al. 1994, 1997; Whipp et al. 1995). However, these studies either did not attempt to distinguish (Shoemaker et al. 1994; Whipp et al. 1995), or did not report (Shoemaker et al. 1997) whether the best description of the data was obtained by mono- or two-exponential functions. On the other hand, Leyk et al. (1999) contended that the recovery of blood flow did not have a fast component such as observed following the onset of exercise. Conversely, Van Leeuwen et al. (1992) reported an initial rapid decrease in $Q_m$, followed by a slower response after cessation of exercise, suggesting that the $Q_m$ response had at least two distinct phases. Thus, the question of whether $Q_m$ during recovery has one or two phases remains unresolved. This is an important issue because distinct mechanisms regulating muscle blood flow may operate in different phases of the response. For instance, following the onset of exercise $Q_m$ is biphasic and the initial phase (first 15–20 s) appears to be determined by a complex interaction between the muscle pump and vasodilation (Tschakovsky & Sheriff, 2004) while the subsequent increase in $Q_m$ is determined by neural, muscular and humoral factors.
vascular and metabolic factors (Laughlin & Korzick, 2001). Furthermore, computer simulations of $Q_m$ and muscle oxygen uptake ($V_{O_2,m}$) responses following the onset of exercise suggest that, since $Q_m$ on-kinetcs are biphasic, blood flow in the initial 10–30 s of exercise is critical in determining the adequacy of $O_2$ delivery to the contracting muscle (Ferreira et al. 2005a). Since a mechanical factor, such as the muscle pump, is involved in the early phase of $Q_m$ response following the onset of exercise (e.g. Sheriff & Hakeman, 2001), a qualitative symmetry of onset and recovery kinetics (i.e. biphasic recovery of $Q_m$) might be expected.

The muscle microcirculation is the primary site of $O_2$ exchange. Thus, muscle capillary blood flow ($Q_{cap}$) and $V_{O_2,m}$ kinetics will determine the dynamics of capillary $O_2$ extraction ($C_{a\rightarrow v}O_2 = V_{O_2,m}/Q_{cap}$). In humans, the dynamics of $O_2$ extraction in the microcirculation have been estimated non-invasively by the deoxy-haemoglobin concentration ([HHb]) signal from near infrared spectroscopy (NIRS; DeLorey et al. 2003; Grassi et al. 2003). Although the kinetics of [HHb] following the onset of exercise have been previously described (DeLorey et al. 2003; Grassi et al. 2003; Ferreira et al. 2005b), the time course of [HHb] during recovery from exercise is presently unknown. The study of microvascular $O_2$ pressure ($P_{mv,O_2}$) recovery kinetics (approximately equivalent to the time course of $O_2$ extraction) in the rat muscle microcirculation has revealed extremely different responses following the onset and cessation of muscle contraction (McDonough et al. 2001), indicating asymmetry of the temporal association between $V_{O_2,m}$ and $Q_m$ for the onset and recovery phases. In humans, following the transition from unloaded exercise to exercise the kinetics of $Q_m$ were similar to the $V_{O_2,m}$ kinetics (Grassi et al. 1996; Koga et al. 2004; Ferreira et al. 2005b). However, it is unclear whether blood flow and $O_2$ utilization remain coupled after cessation of exercise. Shoemaker et al. (1994) found similar $Q_m$ (femoral arterial) and estimated $V_{O_2,m}$ kinetics (but see Discussion), while data from other studies indicate that $Q_m$ recovered at a slower rate than $V_{O_2,m}$ after moderate (Leyk et al. 1999; Van Beekvelt et al. 2001) and heavy exercise (Bangsbo et al. 1994; Radegran & Saltin, 1999), although the kinetic parameters were not determined. Importantly, if the recovery kinetics of $Q_m$ were faster than the $V_{O_2,m}$ kinetics, such as following rest-to-exercise transitions (MacDonald et al. 1998; Behnke et al. 2002), there would be an $O_2$ delivery limitation to the restoration of muscle metabolism (Barstow et al. 1990). Therefore, it could be expected that the recovery of $Q_m$ would be slower than that of $V_{O_2,m}$ in normal healthy individuals, suggesting that $O_2$ delivery would not be a limiting factor to the recovery of muscle metabolism, as recently shown in sedentary individuals (Haseler et al. 2004).

Mechanistically, it is important to distinguish whether the kinetics of $Q_m$ are a first-order (i.e. one phase) or higher-order response. If the $Q_m$ kinetics are first order it implies, but does not prove, that a single mechanism is controlling $Q_m$ during recovery from exercise. Likewise, higher-order responses suggest that multiple mechanisms operate to maintain $Q_m$ elevated during recovery, and these vary as a function of time. Insights gained from this analysis would also be useful to understand the dynamics of muscle oxygenation ($\propto V_{O_2,m}/Q_m$) reported in physiological (Chance et al. 1992; McCully et al. 1994) and pathological conditions (Belardinelli et al. 1997; Hanada et al. 2000).

The purpose of the present study was to examine the estimated kinetics of $Q_{cap}$ to determine whether during recovery from exercise blood flow in the microcirculation has one or two phases. We hypothesized that the putative muscle pump effect observed following the onset of exercise would also be evident after cessation of exercise, leading to a biphasic recovery of $Q_{cap}$ similar to, but a mirror image of, the onset kinetics (Ferreira et al. 2005b). We also tested the hypothesis that the overall recovery kinetics of $Q_{cap}$ would be slower than the $V_{O_2,m}$ kinetics, which would indicate that different mechanisms are involved in the regulation of blood flow kinetics during recovery from cycling exercise compared to the onset, when the overall kinetics of $Q_m$ were similar to those of $V_{O_2,m}$ (transition from unloaded exercise to exercise, Grassi et al. 1996; Ferreira et al. 2005b; Koga et al. 2005).

**Methods**

Nine healthy subjects (7 men and 2 women) with mean ($\pm$ s.d.) age 24.7 $\pm$ 6.3 years, body weight 67.9 $\pm$ 12.2 kg and height 175.4 $\pm$ 13.1 cm participated in this study. All procedures were explained to each subject, who provided signed written informed consent before enrolment in the study. The protocol was approved by the Institutional Review Board for Research Involving Human Subjects at Kansas State University and followed the principles outlined in the Declaration of Helsinki.

The exercise protocol was performed on three separate days. All exercise tests were performed on an electronically braked cycle ergometer (Corival 400, Lode, The Netherlands). On the first test day, the subjects performed an incremental (ramp) exercise test for determination of peak oxygen uptake ($V_{O_2,peak}$) and the estimated lactate threshold (LT). From these, the work rates calculated to elicit 90% of the LT $V_{O_2}$ (90% LT) and a $V_{O_2}$ half-way between the LT and $V_{O_2,peak}$ (50% $\Delta = V_{O_2}$ LT + 0.5[$V_{O_2,peak} − V_{O_2}$ LT]) were determined. On each of the two consecutive visits to the laboratory, subjects performed four bouts of constant work rate exercise, the first three bouts at 90% LT (6 min each) interspersed by 6 min at 20 W and the last bout at 50% $\Delta$ (8 min duration).
The first bout was preceded by 4 min of baseline pedaling at 20 W. Therefore, a total of six transitions to the 90% LT and two transitions to the 50% Δ work rates were performed. Three subjects performed four transitions at the 90% LT work rate due to schedule conflicts. Pulmonary $V_{O_2}$ and muscle oxygenation by NIRS were measured in all subjects and transitions.

Pulmonary gas exchange ($V_{O_2}$ and $V_{CO_2}$) and minute expired ventilation ($V_E$) were measured breath-by-breath (CardiO2, MedGraphics, St Paul, MN, USA). Before each exercise test the volume signal was calibrated using a 31 syringe, while the $O_2$ and CO2 analysers were calibrated with gases of known concentration. Heart rate was recorded from the electrocardiogram using a modified lead I configuration and stored in the breath-by-breath file.

Muscle oxygenation was evaluated by a frequency-domain multidistance (FDMD) near-infrared spectrophotometer (OxiplexTS, ISS, Champaign, IL, USA) operating at two wavelengths (690 and 830 nm). The light-emitting diodes and light detector were connected to a plastic probe by optical fibres. The probe consisted of light source-detector separations of 2.0, 2.5, 3.0 and 3.5 cm for both wavelengths. The frequency modulation of laser intensity was 110 MHz and the heterodyne detection was performed at a 5 kHz frequency modulation of laser intensity was 110 MHz and the heterodyne detection was performed at a 5 kHz cross-correlation frequency. The output frequency for data storage was selected as 31.25 Hz. After the site had been carefully shaved and dried, the probe was positioned longitudinally over the belly of the vastus lateralis muscle ~15 cm above the patella, bound to the skin with a skin cement (Skin-Bond, Smith & Nephew, Largo, FL, USA) and secured with Velostraps around the thigh. The probe position was marked to check for any sliding and for accurate repositioning on subsequent test days. No movement (sliding) was observed in any exercise test. The near-infrared spectrometer was calibrated on each test day according to the manufacturer’s recommendations. To estimate the actual values of [HHb], [HbO2] and total haemoglobin concentration ([THb] = [HHb] + [HbO2]) dynamic measurements of the reduced scattering coefficient were performed continuously throughout the exercise and recovery periods and automatically incorporated into the algorithms utilized by the manufacturer’s software.

**Kinetics analysis**

The breath-by-breath $O_2$ and 31.25 Hz NIRS-oxygenation data were converted to second-by-second values, time aligned to the end of exercise and ensemble averaged for each subject, to generate a single data set for each variable, at each exercise intensity. The kinetics of $V_{O_2,p}$, [HHb] and $\dot{Q}_{cap}$ (see below) were determined by non-linear regression using a least squares technique (Marquadt-Levenberg, SigmaPlot 2001, Systat Software, Point Richmond, CA). The model used for fitting the [HHb] response was:

$$[\text{HHb}]_{(t)} = [\text{HHb}]_{(EE)} - A_p(1 - e^{-(t-TD_p)/\tau_p})$$

(1 component)

$$+ A_s(1 - e^{-(t-TD_s)/\tau_s})$$

(slow component)

(see definitions below). For responses without ‘undershoots’ or slow decreases in [HHb] after the fast component (e.g. Fig. 1) the parameter $A_s$ converged to zero, which is consistent with a monoexponential model. Whenever an undershoot was seen the slow component refers to the increase in [HHb] above the nadir achieved during the recovery period.

The $V_{O_2,p}$ response during recovery from exercise was fitted with the following model:

$$V_{O_2}(t) = V_{O_2,EE} - A_I(1 - e^{-(t-TD_I)/\tau_I})$$

(phase 1, initial component)

$$- A_p(1 - e^{-(t-TD_p)/\tau_p})$$

(phase 2, primary component)

$$- A_s(1 - e^{-(t-TD_s)/\tau_s})$$

(phase 3, slow component)

where, in eqns (1) and (2), EE refers to end of exercise; $A$, amplitude; TD, time delay; and $\tau$, the time constant of each phase of the response (subscripts I, P and S). For recovery from exercise below the LT only the initial and primary component were included in the non-linear regression function, whereas for recovery from exercise above the LT two different models were used. In model I, TDs was substituted for TDp (i.e. primary and slow components of recovery began together at the end of phase 1), whereas for model II, TDs $\neq$ TDp (i.e. the slow component emerged after an independent time delay). The two models were then compared by a $F$ test to determine whether model II described the data significantly better than model I (Motulsky & Ransnas, 1987). If so, model II was used in the procedures to estimate $Q_{cap}$ kinetics during recovery from heavy exercise, otherwise model I was employed. The time constant of the primary (fast) component, and the physiological interpretation, are different when the data are fitted by models I or II (Barstow & Mole, 1991). However, we utilized this approach for analysing the $V_{O_2,p}$ kinetics to estimate the temporal profile of $\dot{Q}_{cap}$ during recovery (see below). In this circumstance, the model that better described the $V_{O_2,p}$ data appeared to be the appropriate choice.

The initial (cardiodynamic) component of $V_{O_2,p}$ was described up to TDp and the amplitude of the response...
at TD_P (\(A'_1\)) was calculated as \(A'_1 = A_1 (1 - e^{-(T_D p/\tau_I)}\)). The relevant amplitude of the primary component was calculated as \(A_P = A'_1 + A_p\).

**Muscle capillary blood flow**

The \(\dot{Q}_{\text{cap}}\) response to exercise was derived from the kinetics of \(\dot{V}_{O_2,p}\) (time constants and amplitude of response) and raw [HHb] data. The methods employed to derive \(\dot{Q}_{\text{cap}}\) have been described in detail elsewhere (Ferreira et al. 2005b). Briefly, the kinetics of \(\dot{V}_{O_2,p}\) (primary component) during recovery from constant work rate exercise closely represents the muscle phosphocreatine and, presumably, \(\dot{V}_{O_2,m}\) kinetics (Rossiter et al. 2002), whereas [HHb] measured by NIRS is thought to reflect the muscle capillary fractional \(O_2\) extraction (DeLorey et al. 2003; Grassi et al. 2003). Therefore, by rearranging the Fick equation, the temporal characteristics of \(\dot{Q}_{\text{cap}}\) can be estimated from the ratio of \(\dot{V}_{O_2,m}\) to [HHb], specifically:

\[
\dot{Q}_{\text{cap}} = \frac{\dot{V}_{O_2,m}}{C(a - v)O_2} \frac{\dot{V}_{O_2,p}(\text{primary component})}{[\text{HHb}]} \tag{3}
\]

Under these circumstances, absolute values of \(\dot{Q}_{\text{cap}}\) are uncertain but its temporal (kinetic) characteristics are preserved (Ferreira et al. 2005b). The muscle \(O_2\) response was estimated using the kinetic parameters obtained from the curve fitting of \(\dot{V}_{O_2,p}\), i.e. by assuming that the recovery of \(\dot{V}_{O_2,m}\) was exponential, starting at the end of exercise with the time constant determined for \(\dot{V}_{O_2,p}\) (primary component) and amplitude equal to \(A'_p\) (Ferreira et al. 2005b). The resulting \(\dot{V}_{O_2,m}\) was used in the estimation of \(\dot{Q}_{\text{cap}}\) kinetics (e.g. Figs 3 and 4). The time course of \(\dot{Q}_{\text{cap}}\) was analysed by exponential equations as described above in eqn (2) (model II), where \(\dot{Q}_{\text{cap}}\) is substituted for \(\dot{V}_{O_2}\). This method is consistent with previous studies (Shoemaker et al. 1994, 1997). It is not known, at present, whether the \(\dot{Q}_{\text{cap}}\) profile during recovery has an initial fast component as seen following the onset of exercise (Kindig et al. 2002; see Discussion). Therefore, a model not including the initial (fast) phase 1 (monoexponential, moderate exercise and two-exponential, heavy exercise) was also employed for non-linear regression analysis and an \(F\) test was used to determine the better description of the data. The mean response time (MRT) for \(\dot{Q}_{\text{cap}}\), which approximates the time to reach 63% of the response, was calculated as:

\[
\text{MRT} = \frac{A'_1}{A'_P} \cdot (T_{D_P} + \tau_I) + \frac{A_P}{A_P} \cdot (T_{D_P} + \tau_P) \tag{4}
\]

where the parameters used in the equation are defined above.

**Data analysis for comparison of overall kinetics during recovery from heavy exercise**

To compare the overall kinetics of the estimated \(\dot{V}_{O_2,m}\) and \(\dot{Q}_{\text{cap}}\), we reanalysed the pulmonary \(\dot{V}_{O_2}\) response of each subject with a two-exponential model (phases 1–2 of eqn (2)) over the same region of data for the initial and primary components of \(\dot{Q}_{\text{cap}}\), i.e. the \(\dot{V}_{O_2,p}\) data corresponding in time to the slow component for \(\dot{Q}_{\text{cap}}\) (from \(t \approx T_{D_{\text{P}}}\) of \(\dot{Q}_{\text{cap}}\) to 480 s) were ignored in the non-linear regression. The resulting recovery kinetics of estimated \(\dot{V}_{O_2,m}\) (\(\tau_{pb}\)) were then compared to the MRT for both [HHb] and \(\dot{Q}_{\text{cap}}\).

**Statistical analysis**

To determine significant differences between two means, Student’s two-tailed paired \(t\) test, or Wilcoxon’s \(t\) test when appropriate, was performed. A repeated-measures analysis of variance was conducted to compare more than two means and the Tukey–Kramer’s \(post \text{ hoc}\) test was used for pairwise comparisons. The relationship between two variables was analysed by the Pearson product–moment correlation. Significance was accepted when \(P \leq 0.05\). All tests were conducted using a commercial statistical software package (NCCS 2000, NCSS Statistical Software, Kaysville, UT). Values were reported as means \pm s.d.

**Results**

\(\dot{V}_{O_2,p}\) was 48.8 \pm 7.0 ml kg\(^{-1}\) min\(^{-1}\) and the estimated LT occurred at 56.3 \pm 8.5% \(\dot{V}_{O_2,p}\). The work rates for the constant work rate tests were 115 \pm 36 W (90% LT) and 206 \pm 56 W (50% \(\Delta\)). In five subjects the \(\dot{V}_{O_2,p}\) response during recovery from heavy exercise was significantly better described by the model with the slow component emerging after an independent time delay (model II). The overall [HHb] profile beyond 60 s of recovery was variable among subjects and between exercise intensities (e.g. Fig. 1). However, in all subjects we observed a time delay before the decrease in [HHb]. The changes in total haemoglobin ([THb]) and oxyhaemoglobin concentration ([HbO\(_2\)]) are shown in Fig. 2. The [THb] responses suggest that there were changes in blood volume under the NIRS probe during the recovery period. However, these are expected to have minor effects on the [HHb] signal (Ferrari et al. 1997; Grassi et al. 2003).

Regarding the temporal profile of \(\dot{Q}_{\text{cap}}\), all recovery responses (for moderate and heavy exercise) were better described by the model which included an initial component, indicating that the primary response of the kinetics of muscle capillary blood flow during recovery was biphasic. The recovery responses of estimated \(\dot{V}_{O_2,m}\), \(\dot{Q}_{\text{cap}}\) and [HHb] of a representative subject are shown in Figs 3 (90% LT) and 4 (50% \(\Delta\)). The kinetic parameters
of [HHb] and $\dot{Q}_{cap}$ are shown in Table 1. The TD of [HHb] was shorter and $\tau$[HHb] was longer for recovery from moderate compared to heavy exercise ($P < 0.05$), while the MRT of [HHb] (TD + $\tau$) was significantly faster during recovery from moderate exercise ($P < 0.01$). The results for the overall kinetics of $\dot{V}_{O_2p}$ [HHb] and $\dot{Q}_{cap}$ are shown in Fig. 5. For moderate exercise, the overall kinetics of $\dot{Q}_{cap}$ (MRT) were significantly slower than the kinetics of $\dot{V}_{O_2p}$ (as $\tau_p$) and [HHb] (as MRT). In addition, [HHb] kinetics were faster than the $\dot{V}_{O_2p}$ kinetics. During recovery from heavy exercise, MRT-$\dot{Q}_{cap}$ was significantly slower than the ‘lumped’ time constant of $\dot{V}_{O_2p}$ ($\tau_p$), while $\tau_p$ of $\dot{V}_{O_2p}$ did not differ significantly from the MRT of [HHb]. There was a significant correlation between MRT-$\dot{Q}_{cap}$ and $\tau_p$ of $\dot{V}_{O_2p}$ ($r = 0.79$, $P < 0.01$; Fig. 6). However, the data points were widely scattered, indicating a dissociation between the overall recovery kinetics of $\dot{Q}_{cap}$ and muscle $\dot{V}_{O_2}$.

**Comparison with onset of exercise**

The results of selected parameters of $\dot{Q}_{cap}$ kinetics following the onset of exercise obtained from a previous study with the same subjects (Ferreira et al. 2005b) are shown in Table 2. For moderate exercise, the contribution of phase 1 to the overall response ($A'_I/A'_P$) was smaller during recovery, but the remaining kinetic parameters were not significantly different from the onset kinetics. The overall effect was a slower MRT-$\dot{Q}_{cap}$ during recovery. For heavy exercise, the $A'_I/A'_P$ was similar for the onset and recovery from exercise. However, the $\tau$ of the initial (phase 1) component ($\tau_I$) of $\dot{Q}_{cap}$ was longer during recovery, while both the duration of phase 1 (TDp) and $\tau_p$ were greater for recovery, resulting in a slower MRT-$\dot{Q}_{cap}$ during recovery compared to the onset of exercise. (N.B. This comparison should be made with caution because the temporal characteristics of $\dot{Q}_{cap}$ were estimated and not directly measured for both onset and recovery. However, the $\dot{Q}_{cap}$ kinetics were estimated for the same subjects and exercise bouts for both onset and recovery kinetics, which justifies comparison of the kinetic parameters.)

**Figure 1. Dynamics of deoxyhaemoglobin concentration ([HHb]) from three representative subjects**

Note that the responses are qualitatively similar during the initial 60 s, showing a short time delay and ‘rapid’ decrease (steep slope) thereafter. In general, these responses qualitatively resemble the dynamics of $C_{O_2-VO_2}$ shown by Van Beekvelt et al. (2001). The source of variability between subjects is unclear, but this is also seen for total haemoglobin concentration (Fig. 2) and probably involves differences in adipose tissue thickness, muscle capillarization (≈ capillary blood volume) and tissue scattering properties. Similarly, changes in [HHb] from moderate to heavy exercise within subjects can be misleading since $\Delta$[HHb] from unloaded cycling to peak work rate can range from 2.4 to 19.5 $\mu$M (Barstow et al. 2004).

**Figure 2. Representative responses of total haemoglobin concentration (●, [THb]) and oxyhemoglobin concentration (○, [HbO2])**

The data shown for top, middle and bottom panels are, respectively, from subjects depicted in Fig. 1. Although there are substantial changes in [THb], these are expected to have less effect on the [HHb] response, as previously shown (Grassi et al. 2003). Accordingly, in general the temporal profile of [HbO2] resembles that of [THb], further suggesting that changes in blood volume affect primarily the [HbO2] signal.
Discussion

This investigation is the first, to our knowledge, specifically to address the temporal kinetic characteristics of \([\text{HHb}]\) and muscle capillary blood flow (estimated) during recovery from exercise. In addition, we examined the association between the recovery kinetics of estimated \(\dot{Q}_{\text{cap}}\) and \(V_{\text{O}_2m}\). There are two principal new findings in the present study. First, the kinetics of \(\dot{Q}_{\text{cap}}\) were biphasic during recovery (similar to the characteristics following exercise onset), with an initial fast phase followed by a second slower response emerging \(\sim 15–30\) s after the end of exercise. Second, the overall kinetics of \(\dot{Q}_{\text{cap}}\) were slower than those of \(V_{\text{O}_2m}\), indicating a temporal dissociation between the recovery of \(O_2\) delivery and utilization. It is important to emphasize that \(\dot{Q}_{\text{cap}}\) kinetics were estimated by making two basic assumptions: (a) \(\tau_P \dot{V}_{\text{O}_2p} \approx \tau \dot{V}_{\text{O}_2m}\); and (b) \([\text{HHb}] (t) \propto C_{(a-v)}O_2 (t)\) (see Study limitations below). Therefore, some error will probably exist in the estimated \(\dot{Q}_{\text{cap}}\) kinetics when compared with the ‘true’

\[\dot{Q}_{\text{cap}}\]

response, as discussed in detail elsewhere (Ferreira et al. 2005b).

Recovery kinetics of muscle blood flow

The temporal profile of \(\dot{Q}_m\) during recovery from exercise has been investigated in several studies (Van Leeuwen et al. 1992; Lash, 1994; Leyk et al. 1999; Van Beekvelt et al. 2001), but the kinetic characteristics of \(\dot{Q}_m\) remain equivocal. Although the recovery of blood flow has been described by exponential equations (similar to eqn (2); Shoemaker et al. 1994, 1997; Whipp et al. 1995), these studies did not distinguish (or report) whether the response was better described by mono- or two-exponential models. Leyk et al. (1999) observed that leg blood flow (measured using Doppler ultrasound) during recovery from calf exercise did not show an initial fast response (i.e. the decline in \(\dot{Q}_m\) was monoexponential). In contrast, in a similar exercise model the recovery of \(\dot{Q}_m\) demonstrated an early rapid decrease after cessation of exercise (Van Leeuwen et al. 1992). However, the authors (Van Leeuwen et al. 1992) contended that the response was not universally exponential because in 50% of the subjects blood flow increased again for a very short period after the initial rapid decrease. In the present investigation, the estimated \(\dot{Q}_{\text{cap}}\) response was better described, in all subjects, by

\[\dot{Q}_{\text{cap}}\]

response, as discussed in detail elsewhere (Ferreira et al. 2005b).
the recovery period. The initial decrease in \( \dot{O}_2 \) of single or higher-order models because this implies the existence of multiple controlling mechanism(s), indicating that in the microcirculation the recovery of muscle blood flow was biphasic (Figs 3 and 4).

As stated in the Introduction, it is relevant to determine whether the recovery of \( \dot{Q}_{\text{cap}} \) is better described by first- or higher-order models because this implies the existence of single versus multiple controlling mechanism(s), respectively, for the variable studied. Therefore, this is an important step to clarify the mechanisms operating to sustain an elevated blood flow (and \( O_2 \) delivery) during the recovery period. The initial decrease in \( \dot{Q}_{\text{cap}} \) (phase 1) observed in our study \( (\tau_1 \approx 6–9\,\text{s}) \) was substantially faster than the estimated \( \tau V_{\dot{O}_2m} \) \( (\approx 30\,\text{s}) \) or the subsequent phase 2 of the \( \dot{Q}_{\text{cap}} \) response \( (\approx 29\,\text{s} \text{ for moderate exercise and } \approx 48\,\text{s} \text{ for heavy exercise}) \). It has been suggested that the skeletal muscle vasculature is able to respond (dilate or constrict) very rapidly during the transitional phase \( (\text{Hamann et al. 2004; Tschakovsky et al. 2004}) \). However, these suggestions are based on investigations of on-responses to a stimulus, while few studies have focused on the time course of response to the removal of a stimulus. In this context, direct recordings of arteriolar diameter after muscle contraction have shown a \( \approx 10\,\text{s} \) delay to the onset of arteriolar constriction \( (\text{i.e. arteriolar diameter temporarily remained similar to the exercise level; Gorczynski & Duling, 1978; VanTeeffelen & Segal, 2000}) \). These observations suggest that the initial

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<th>Moderate</th>
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<td>( A' )</td>
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<td>( \tau_1 )</td>
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<tr>
<td>( A'/A' )</td>
<td>( 0.31 \pm 0.11 )</td>
<td>( 0.39 \pm 0.13 )</td>
</tr>
</tbody>
</table>

Values are means \( \pm \) s.d. \( A' \), amplitude. \( T\tau \), time delay and \( \tau \), time constant of each component. \( l \), initial component; \( P \), primary component. \( A'/A' \), total amplitude of primary component of response \( (A' + A' \) for \( \dot{Q}_{\text{cap}} \). The units for amplitudes of \( \dot{Q}_{\text{cap}} \) and \([\text{HHb}]\) are in \( \text{ml min}^{-1}\mu\text{M} \) and \( \mu\text{M} \), respectively. \(* \) Significantly different from moderate exercise \( P < 0.05 \).

Figure 5. Overall kinetics of deoxyhaemoglobin concentration ([HHb]), pulmonary oxygen uptake (\( \dot{V}_{O_2} \)) and muscle capillary blood flow (\( \dot{Q}_{\text{cap}} \))

MRT, mean response time. The data for pulmonary \( \dot{V}_{O_2} \) represent the time constant of the primary component \( (\tau_\text{P}) \) of the response \( (\text{eqn (2)}) \). For heavy exercise, \( \tau_\text{P} \) was obtained by fitting the \( \dot{V}_{O_2} \) response over the time window corresponding to the initial and primary components of \( \dot{Q}_{\text{cap}} \) during recovery \( (\text{i.e. from end of exercise to TDS of } \dot{Q}_{\text{cap}}) \). The values shown are the means \( \pm \) s.d. \(* \) Significantly different from MRT-\( \dot{Q}_{\text{cap}} \) at the same exercise intensity \( (P < 0.05) \); \( \dagger \) significantly different from \( \tau V_{O_2} \) at the same exercise intensity \( (P < 0.05) \); \( \ddagger \) significantly different from heavy exercise value \( (P < 0.05) \); \( \S \) \( P = 0.068 \) compared with heavy exercise value.

Table 1. Kinetic parameters of \( \dot{Q}_{\text{cap}} \) and \([\text{HHb}]\) for recovery from moderate and heavy exercise

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Moderate</th>
<th>Heavy</th>
</tr>
</thead>
<tbody>
<tr>
<td>End exercise</td>
<td>( 63.4 \pm 21.2 )</td>
<td>( 96.3 \pm 33.0 )</td>
</tr>
<tr>
<td>( A' )</td>
<td>( 9.8 \pm 7.1 )</td>
<td>( 20.7 \pm 14.2 )</td>
</tr>
<tr>
<td>( \tau_1 )</td>
<td>( 9.3 \pm 4.9 )</td>
<td>( 6.0 \pm 3.8 )</td>
</tr>
<tr>
<td>( A' )</td>
<td>( 28.7 \pm 12.5 )</td>
<td>( 48.5 \pm 19.7 )</td>
</tr>
<tr>
<td>( T\tau )</td>
<td>( 18.7 \pm 6.7 )</td>
<td>( 30.0 \pm 16.4 )</td>
</tr>
<tr>
<td>( \tau_\text{P} )</td>
<td>( 29.9 \pm 8.6 )</td>
<td>( 47.7 \pm 26.0 )</td>
</tr>
<tr>
<td>( A'/A' )</td>
<td>( 0.31 \pm 0.11 )</td>
<td>( 0.39 \pm 0.13 )</td>
</tr>
</tbody>
</table>

Values are means \( \pm \) s.d. \( A' \), amplitude. \( T\tau \), time delay and \( \tau \), time constant of each component. \( l \), initial component; \( P \), primary component. \( A'/A' \), total amplitude of primary component of response \( (A' + A' \) for \( \dot{Q}_{\text{cap}} \). The units for amplitudes of \( \dot{Q}_{\text{cap}} \) and \([\text{HHb}]\) are in \( \text{ml min}^{-1}\mu\text{M} \) and \( \mu\text{M} \), respectively. \(* \) Significantly different from moderate exercise \( P < 0.05 \).

Figure 6. Relationship between the mean response time of estimated muscle capillary blood flow (MRT-\( \dot{Q}_{\text{cap}} \)) and time constant of pulmonary \( V_{O_2} \) (\( \tau V_{O_2P} \); primary component) for moderate and heavy exercise

Dashed line, regression line; continuous line, line of identity. It is reasonable to interpret this relationship as muscle metabolism \( (\dot{V}_{O_2m}) \) driving \( \dot{Q}_{\text{cap}} \). However, the overall recovery kinetics of \( \dot{Q}_{\text{cap}} \) (MRT) appear to become progressively greater (slower) than the kinetics of \( \dot{V}_{O_2} \) for individuals with slower \( \tau V_{O_2} \). See text and Fig. 4 for further details.
component of recovery of $Q_{cap}$ observed in the present study was determined primarily by a mechanical factor. Consistent with this, after cessation of calf exercise, the recovery of $Q_m$ (half-time) became progressively faster when contractions were performed in the supine, sitting and standing positions (Van Leeuwen et al. 1992). This speeding of the decline of $Q_m$ under conditions of augmented venous hydrostatic pressure was attributed to removal of the muscle pump (Van Leeuwen et al. 1992). In the present study we examined transitions from loaded to ‘unloaded’ cycling, which could have diminished the effect of the muscle pump when going from exercise to recovery (Sheriff & Hakeman, 2001; Shiotani et al. 2002). However, venous pressure in superficial veins (Shiotani et al. 2002) may not reflect the profile of intramuscular vessels that are subjected to contraction-induced pressure swings that will have substantial effects on the muscle pump-generated blood flow (Laughlin, 1987). Therefore, based on the $\sim 10$ s delay to the onset of arteriolar constriction observed in microcirculatory preparations, we speculate that the initial decrease in $Q_{cap}$ during recovery observed herein was largely caused by the removal of the muscle pump effect in the transition to unloaded pedalling. However, this hypothesis must await confirmation with kinetic analysis under experimental conditions that can modify the potential contribution of the muscle pump (e.g. body position).

As mentioned above, the second phase of $Q_{cap}$ was appreciably slower than the initial response. Considering that the putative mechanical factor is mostly evident during phase 1, phase 2 of $Q_{cap}$ would probably be determined by the interaction among vasoactive substances of neural (e.g. noradrenaline), muscular (metabolic byproducts) and vascular (endothelium) origin. For instance, pharmacologic intervention studies have shown that blockade of adenosine (Kille & Klabunde, 1984), prostaglandins (Kilbom & Wennmalm, 1976) and nitric oxide (Radegran & Saltin, 1999) decreased the muscle blood flow during recovery from exercise. Clearly, the mechanisms operating to keep blood flow elevated during recovery remain to be further investigated, and our results emphasize the importance of distinguishing the effects of each putative mechanism on each phase of the $Q_m$ response. The available evidence, however, suggests that the interaction among these factors (neural, muscular and vascular) will probably depend on the type (e.g. isometric or dynamic), intensity (moderate or heavy) and body position (supine versus upright) of exercise (reviewed by Bangsbo & Hellsten, 1998).

### Temporal relationship between $Q_m$ and $V_{O_2,m}$ during recovery

$Q_m$ and $V_{O_2,m}$ achieve their baseline (pre-exercise) levels within 3–4 min after the end of moderate exercise (Shoemaker et al. 1994; Radegran & Saltin, 1999; van Beekvelt et al. 2001). After heavy exercise $Q_m$ and $V_{O_2,m}$ remain elevated for a longer period of time (> 10–15 min; Bangsbo et al. 1991; Van Beekvelt et al. 2001). Accumulation of metabolites during the heavy exercise period has been considered as a possible mechanism for the elevated postexercise $Q_m$ (Bangsbo & Hellsten, 1998), whereas the cause of elevated $V_{O_2,m}$ is more controversial (for reviews see Gaesser & Brooks, 1984; Bangsbo & Hellsten, 1998). Although several studies have investigated the dynamics of both $V_{O_2,m}$ and $Q_m$ during recovery from exercise (e.g. Bangsbo et al. 1994; Radegran & Saltin, 1999; Van Beekvelt et al. 2001), the kinetic parameters of these variables have been determined in only a few studies (Shoemaker et al. 1994; Whipp et al. 1995). In the study of Shoemaker et al. (1994) the femoral artery blood flow kinetics were similar to the kinetics of $V_{O_2,p}$ (primary component) after moderate exercise. In the present study, the overall kinetics of $Q_{cap}$ were associated with (Fig. 4), but slower ($\sim 8$ and 16 s for moderate and heavy exercise, respectively) than the estimated $V_{O_2,m}$ kinetics. The cause of the discrepancy between our results and those of Shoemaker et al. (1994) is not clear. However, the monoeXponential model used by Shoemaker et al. (1994) for analysis of $Q_m$ included a time delay, but only the time constant was reported. Thus, it is possible that the reported $\tau$ reflected primarily the kinetics of $Q_m$ during phase 2. If true, their results would then be in agreement with the present results, where the kinetics of $\tau V_{O_2,p}$ (primary component) and $\tau_p$ for $Q_{cap}$ were not significantly different. Therefore, in agreement with results from other studies (van Beekvelt et al. 2001) our data indicate that after moderate exercise the overall kinetics of muscle blood flow were slower than the kinetics of $V_{O_2,m}$.

Although not the main focus of our study, the implications of the relationship between $V_{O_2,m}$ and $Q_{cap}$ kinetics need to be considered. Previous studies have shown that the recovery of muscle metabolism was limited by $O_2$ delivery in exercise-trained subjects (Haseler et al. 1999), possibly by a faster recovery of $Q_m$ compared to the $V_{O_2,m}$ kinetics (Barstow et al. 1990). In contrast, in

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Moderate exercise</th>
<th>Heavy exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>$A_i/A_p$</td>
<td>0.55 ± 0.17*</td>
<td>0.40 ± 0.11</td>
</tr>
<tr>
<td>$\tau_1$ (s)</td>
<td>6.7 ± 2.7</td>
<td>3.3 ± 1.6†</td>
</tr>
<tr>
<td>$T_{Dp}$ (s)</td>
<td>18.9 ± 4.6</td>
<td>13.6 ± 4.8*</td>
</tr>
<tr>
<td>$\tau_p$ (s)</td>
<td>28.3 ± 5.8</td>
<td>25.7 ± 5.0*</td>
</tr>
<tr>
<td>MRT (s)</td>
<td>25.4 ± 9.1*</td>
<td>25.7 ± 7.7*</td>
</tr>
</tbody>
</table>

$P < 0.05$ versus recovery (Table 1 and Fig. 4). † $P = 0.053$ versus recovery. See Table 1 for abbreviations and text for further details. Data from a previous study with the same subjects (Ferreira et al. 2005b).

### Table 2. Selected kinetic parameters of $Q_{cap}$ following the onset of moderate and heavy exercise

$Q_m$ and $V_{O_2,m}$ achieve their baseline (pre-exercise) levels within 3–4 min after the end of moderate exercise (Shoemaker et al. 1994; Radegran & Saltin, 1999; van Beekvelt et al. 2001). After heavy exercise $Q_m$ and $V_{O_2,m}$ remain elevated for a longer period of time (> 10–15 min; Bangsbo et al. 1991; Van Beekvelt et al. 2001). Accumulation of metabolites during the heavy exercise period has been considered as a possible mechanism for the elevated postexercise $Q_m$ (Bangsbo & Hellsten, 1998), whereas the cause of elevated $V_{O_2,m}$ is more controversial (for reviews see Gaesser & Brooks, 1984; Bangsbo & Hellsten, 1998). Although several studies have investigated the dynamics of both $V_{O_2,m}$ and $Q_m$ during recovery from exercise (e.g. Bangsbo et al. 1994; Radegran & Saltin, 1999; Van Beekvelt et al. 2001), the kinetic parameters of these variables have been determined in only a few studies (Shoemaker et al. 1994; Whipp et al. 1995). In the study of Shoemaker et al. (1994) the femoral artery blood flow kinetics were similar to the kinetics of $V_{O_2,p}$ (primary component) after moderate exercise. In the present study, the overall kinetics of $Q_{cap}$ were associated with (Fig. 4), but slower ($\sim 8$ and 16 s for moderate and heavy exercise, respectively) than the estimated $V_{O_2,m}$ kinetics. The cause of the discrepancy between our results and those of Shoemaker et al. (1994) is not clear. However, the monoeXponential model used by Shoemaker et al. (1994) for analysis of $Q_m$ included a time delay, but only the time constant was reported. Thus, it is possible that the reported $\tau$ reflected primarily the kinetics of $Q_m$ during phase 2. If true, their results would then be in agreement with the present results, where the kinetics of $\tau V_{O_2,p}$ (primary component) and $\tau_p$ for $Q_{cap}$ were not significantly different. Therefore, in agreement with results from other studies (van Beekvelt et al. 2001) our data indicate that after moderate exercise the overall kinetics of muscle blood flow were slower than the kinetics of $V_{O_2,m}$.

Although not the main focus of our study, the implications of the relationship between $V_{O_2,m}$ and $Q_{cap}$ kinetics need to be considered. Previous studies have shown that the recovery of muscle metabolism was limited by $O_2$ delivery in exercise-trained subjects (Haseler et al. 1999), possibly by a faster recovery of $Q_m$ compared to the $V_{O_2,m}$ kinetics (Barstow et al. 1990). In contrast, in...
sedentary individuals O2 delivery was not the limiting factor to the recovery kinetics of muscle phosphocreatine (∼V_{O2,m}(t)), suggesting that the recovery of Q_{m} was not faster than the kinetics of V_{O2,m}. Importantly, the slower recovery dynamics of Q_{cap} compared to V_{O2,m} can be considered indirect evidence that, in the population presently studied (healthy, physically active subjects), the recovery kinetics of V_{O2,m} were not limited by O2 availability. However, this hypothesis remains to be tested directly with interventions that would increase convective and/or diffusive O2 delivery during recovery from exercise.

It has been shown that after heavy exercise the recovery of Q_{m} was appreciably slower than that of V_{O2,m} (Bangsbo et al. 1994; Van Beekvelt et al. 2001). The difference between the MRT of the primary component of Q_{cap} estimated herein and τ_{P}V_{O2,p} for heavy exercise (∼16 s) was twice that for moderate exercise (∼8 s). This greater temporal dissociation of the restoration of O2 delivery and utilization, compared to moderate exercise, suggests that there is further alteration in the balance between sympathetic vasoconstriction and locally released vasodilators after heavy exercise. This is consistent with the progressively greater ‘functional sympatholysis’ observed at higher exercise intensities (Ruble et al. 2002).

Recovery of muscle oxygenation
in the microcirculation

The recovery kinetics of muscle oxygenation have been investigated in studies examining the dynamics of tissue O2 saturation (S_{O2}) in humans by NIRS (Chance et al. 1992; McCully et al. 1994; Belardinelli et al. 1997; Hanada et al. 2000) and microvascular O2 pressure (P_{mv,O2}) in rat muscle by phosphorescence quenching (McDonough et al. 2001). The overall kinetics of S_{O2}, after moderate cycling exercise (τ of 20–25 s; Chance et al. 1992) were, on average, slower than the [HHb] kinetics found in the present study (∼17 s). However, changes in vascular volume (i.e. total haemoglobin concentration; [THb] = [HHb] + [HbO2]) under the NIRS probe can distort the kinetics of S_{O2}, (S_{O2} = [HbO2]/[THb]) compared to the O2 extraction kinetics (MacDonald et al. 1999; for discussion see DeLorey et al. 2003; Grassi et al. 2003; Ferreira et al. 2005b). In contrast, [HHb] is less sensitive to changes in local vascular volume and will probably better reflect the dynamics of O2 extraction (Ferrari et al. 1997; Grassi et al. 2003), although the kinetics of [HHb] and O2 extraction have not been directly compared.

The analysis of individual parameters describing the kinetics of [HHb] showed that the TD of [HHb] was ∼5 s for moderate exercise and 11 s for heavy exercise (Table 1). After cessation of muscle contractions that did not elicit an increase in blood lactate concentration (relatively light–moderate intensity), a time delay to the onset of recovery of P_{mv,O2} (∼5 s) has also been observed (McDonough et al. 2001), which is very similar to the TD of [HHb] observed in our study. The overall P_{mv,O2} kinetics consisted of two phases, with an initial faster phase lasting ∼55 s followed by a sluggish P_{mv,O2} response (McDonough et al. 2001). The [HHb] response could also be considered to have at least two phases: an initial steep decrease in [HHb] (after the delay-like phase) followed by minor, slower changes thereafter (Figs 1, 3, 4). This [HHb] profile is probably a consequence of the concurrent monoexponential decrease in V_{O2,m} and a biphasic recovery of Q_{cap}, which is qualitatively similar to that observed following the onset of exercise (DeLorey et al. 2003; Grassi et al. 2003; Ferreira et al. 2005b).

One important aspect to consider is the effect of fibre type on the dynamics of skeletal muscle oxygenation. McDonough et al. (2004) demonstrated that P_{mv,O2} recovery kinetics of a slow-twitch (ST) muscle (rat soleus muscle) were faster than those of the fast-twitch (FT) counterpart (peroneal muscle). This suggests that the recovery of Q_{m} versus that of V_{O2,m} were slower for ST compared to FT muscles, which is consistent with the greater endothelium-dependent vasodilatation of ST muscles (Woodman et al. 2001). This aspect cannot be addressed with the present data because of the mixed composition of human muscles and lack of biopsy information from our subjects. However, we acknowledge that the slight predominance of FT fibres in superficial areas of vastus lateralis muscle (Lexell et al. 1983) sampled by the NIRS will probably lead to a slower mean response time of [HHb] than deeper muscle areas with a greater percentage of ST fibres.

Asymmetry of Q_{cap} kinetics during exercise onset
and recovery

Symmetry of on–off responses is a characteristic of linear control systems (Lamarra, 1990). In this context, the adjustment of cardiovascular variables (e.g. cardiac output and Q_{m}) in the transitional phases of exercise appear to be characteristically non-linear. The recovery kinetics of cardiac output (Yoshida & Whipp, 1994), forearm- (Van Beekvelt et al. 2001) and thigh-muscle blood flow (Whipp et al. 1995) were slower than their respective kinetics following the onset of exercise. Similarly, in the present study the estimated overall kinetics of Q_{cap} were slower during recovery compared to the onset of moderate and heavy exercise.

Assuming that a mechanical factor (muscle pump) is the primary mediator of phase 1 of Q_{cap} following the onset and recovery from exercise, one might expect that phase 1 characteristics would differ between these conditions. Following the onset of exercise the muscle pump is imposed on a ‘non-dilated’ vascular bed, whereas during recovery the removal of the muscle pump takes place under vasodilated conditions. In addition, arterial and venous...
pressures may be different at the end of exercise compared to unloaded exercise; prior to exercise. Therefore, potential differences in the physical properties of the muscle vascular system could account, at least in part, for the non-linearities of on–off kinetics. Moreover, phase 2 kinetics of \( \dot{Q}_{\text{cap}} \) during recovery from heavy exercise were slower than the on-kinetics, suggesting that different mechanisms (possibly metabolites; see above) are involved in the regulation of blood flow following the onset and recovery from exercise. Collectively, it seems reasonable to consider that the haemodynamic adjustments following the onset and recovery from exercise are asymmetrical, from central (cardiac output; Yoshida & Whipp, 1994) to peripheral circulation (larger vessels; Whipp et al. 1995; Van Beekvelt et al. 2001) and the microcirculation (present study).

**Study limitations**

The limitations of the methods used in our study, including the controversy regarding any potential myoglobin influence on the NIRS signal (Tran et al. 1999), and the assumptions made to estimate \( \dot{Q}_{\text{cap}} \) were addressed in detail previously (Ferreira et al. 2005b). Briefly, we assumed that the kinetics of the primary component of pulmonary \( \dot{V}_O_2 \), reflect the kinetics of muscle \( \dot{V}_O_2 \). Based on results from computer models (Barstow et al. 1990) and the close agreement between phosphocreatine (\( \approx \dot{V}_{O_2,m} \)) and the primary component of \( \dot{V}_{O_2,p} \) kinetics during recovery from exercise (Rossiter et al. 2002), this assumption appears to be valid. Moreover, we used the kinetics of [HHb] as a proxy of \( O_2 \) extraction. The [HHb] kinetics following the onset of exercise in humans (Grassi et al. 2003; Ferreira et al. 2005b) are similar to those of \( C_{(a-v)O_2} \) measured in different studies (Grassi et al. 1996, 2002). Although these observations were made for responses following the onset of exercise, there is no evidence to suggest that the relationship between [HHb] and \( C_{(a-v)O_2} \) during recovery would be disrupted. However, the kinetics of [HHb] and \( C_{(a-v)O_2} \) have not been directly compared. Van Beekvelt et al. (2001) reported that after moderate exercise forearm \( C_{(a-v)O_2} \) returned to baseline levels within 90 s, which is similar to the [HHb] response observed herein. In some subjects we observed undershoots in [HHb] during recovery that were qualitatively similar to the \( C_{(a-v)O_2} \) measurements of Van Beekvelt et al. (2001) for recovery from moderate and heavy exercise. Therefore, it is reasonable to assume that during recovery from exercise, as for the onset, changes in [HHb] reflect the dynamics of \( O_2 \) extraction in the microcirculation.

**Conclusions**

In summary, we have demonstrated that during recovery from exercise the estimated \( \dot{Q}_{\text{cap}} \) kinetics were biphasic, with an early rapid decrease followed by a slower phase that emerged after a time delay (\( \approx 15–30 \) s). We have suggested that, as for the onset of exercise (Sheriff & Hakeman, 2001), this early rapid phase of \( \dot{Q}_{\text{cap}} \) during recovery may be largely determined by a muscle pump effect, but this hypothesis needs to be tested. After cessation of exercise the overall kinetics of \( \dot{Q}_{\text{cap}} \) were slower than after the onset of exercise, suggesting an asymmetry of the mechanisms determining the on- versus off-kinetics of blood flow. In this context, following the onset of exercise the estimated \( \dot{Q}_{\text{cap}} \) kinetics were similar to the \( \dot{V}_{O_2,m} \) kinetics (Ferreira et al. 2005b), while the overall recovery kinetics of \( \dot{Q}_{\text{cap}} \) were slower than the \( \dot{V}_O_2 \) recovery kinetics, indicating that the mechanisms controlling \( \dot{Q}_{m} \) kinetics during recovery from exercise are not temporally associated to \( O_2 \) uptake.

**References**


**Acknowledgements**

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