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Effect of moderate-intensity work rate increment on phase II τVO_2, functional gain and Δ[HHb]

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Abstract This study systematically examined the role of work rate (WR) increment on the kinetics of pulmonary oxygen uptake (VO_{2p}) and near-infrared spectroscopy (NIRS)-derived muscle deoxygenation (Δ[HHb]) during moderate-intensity (Mod) cycling. Fourteen males (24 ± 5 years) each completed four to eight repetitions of Mod transitions from 20 to 50, 70, 90, 110 and 130 W. VO_{2p} and Δ[HHb] responses were modelled as a mono-exponential; responses were then scaled to a relative % of the respective response (0–100 %). The Δ[HHb]/VO_2 ratio was calculated as the average Δ[HHb]/VO_2 during the 20–120 s period of the on-transient. When considered as a single group, neither the phase II VO_{2p} time constant (τVO_{2p}; 27 ± 9, 26 ± 11, 25 ± 10, 27 ± 14, 29 ± 13 s for 50–130 W transitions, respectively) nor the Δ[HHb]/VO_2 ratio (1.04 ± 0.13, 1.10 ± 0.13, 1.08 ± 0.07, 1.09 ± 0.11, 1.09 ± 0.09, respectively) was affected by WR ($p > 0.05$); yet, the VO_2 functional gain (G; $\Delta VO_2/\Delta WR$) increased with increasing WR transitions (8.6 ± 1.3, 9.1 ± 1.2, 9.5 ± 1.0, 9.5 ± 1.0, 9.9 ± 1.0 mL min^{-1} W^{-1}; $p < 0.05$). When subjects were stratified into two groups [Fast ($n = 6$), $\tau VO_{2p130W} < 25$ s $< \tau VO_{2p130W}$, Slower ($n = 8$)], a group by WR interaction was observed for τVO_{2p}. The increasing functional G persisted ($p < 0.05$) and did not differ between groups ($p > 0.05$). The Δ[HHb]/VO_2 ratio was smaller ($p < 0.05$) in the Fast than Slower group, but was unaffected by WR. In conclusion, the present study demonstrated (1) a non-uniform effect of Mod WR increment on τVO_{2p}; (2) that τVO_{2p} in the Slower group is likely determined by an O_2 delivery limitation; and (3) that increasing Mod WR increments elicits an increased functional G, regardless of the τVO_{2p} response.

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Introduction

An abrupt increase in work rate (WR) produces an instantaneous increase in adenosine triphosphate (ATP) hydrolysis and thus the requirement for ATP re-synthesis; however, the adjustment of muscle oxidative phosphorylation (i.e., muscle VO_2 kinetics) towards the new steady-state requirement is exponential, rather than immediate (Linnarsson 1974; Whipp and Wasserman 1972). The profile of this exponential adjustment at the muscle can be reliably characterized (to within ~ 10 %) by pulmonary gas-exchange measures (Grassi et al. 1996) and is generally characterized by both its rate (quantified as the phase II pulmonary VO_2 time constant; τVO_{2p}) and the VO_{2p} amplitude (i.e., ΔVO_{2p} from baseline to steady-state VO_{2p}) or VO_{2p} functional gain ($G = \Delta VO_{2p}/\Delta WR$). Based on early observations of similar τVO_{2p} values (Whipp 1971) in response to different WR transitions within the

moderate-intensity domain (i.e., below the estimated lactate threshold; θ_L) as well as on-/off-transient symmetry (Griffiths et al. 1986; Paterson and Whipp 1991) in response to a single moderate-intensity exercise transition, it was believed that the characteristics of the VO_{2p} kinetic response were independent of WR within the moderate-intensity domain (Grassi et al. 1996; Linnarsson 1974; Whipp and Wasserman 1972).

The notion that the parameters describing VO_{2p} kinetics within the moderate-intensity domain are "WR independent" has not been thoroughly assessed. The WR independence of the VO_{2p} kinetics parameters has been challenged by the findings of several studies that have used a "double step" protocol in both young (Brittain et al. 2001; Hughson and Morrissey 1982; MacPhee et al. 2005) and older (Spencer et al. 2011a) adults; this "double step" protocol implies arrival at the final WR following two "step" transitions of equal magnitude, rather than a single "step" transition spanning the entire WR change. A feature shared amongst these studies is the observation of a greater τVO_{2p} values (i.e., slower adjustments) and greater functional G when exercise is initiated from an elevated WR, even within the moderate-intensity domain. As such, the primary focus of these studies (as well as that of Bowen et al. (2011)) was to elucidate the underlying cause of this slowing. Importantly, however, a consistent finding that has received somewhat less attention in the aforementioned studies was the principal cause of the trend (though not always significant) for smaller τVO_{2p} values (i.e., faster adjustments) and smaller functional G when the WR increment is smaller (where the pre-transition WR was constant and relatively low (i.e., rest or 20 W)). That is, in each of these studies, a "lower step" (i.e., generally to a WR corresponding to ~ 45 % of θ_L) was compared with a "full step" (i.e., generally with a WR corresponding to ~ 90 % of θ_L) where transitions were initiated from identical (low) baseline WRs. A concern with these results is the particularly small WR increment of the "lower step" and whether the lower step VO_{2p} kinetics parameters are accurate given the low signal-to-noise of the data. For example, both MacPhee et al. (2005) and Spencer et al. (2011a) reported 95 % confidence intervals for estimates of τVO_{2p} (CI_{95} τVO_{2p}) that were significantly greater for "lower" and "upper" (i.e., small WR increment) steps, compared with a "full step" (i.e., larger WR increment).

In addition to measures of VO_{2p} throughout exercise transitions, near-infrared spectroscopy (NIRS) has been used extensively of late to monitor changes in muscle deoxygenation ($\Delta[HHb]$), which reflects the balance between O_2 delivery and O_2 utilization (Ferrari et al. 2011). By pairing these respective signals (i.e., $\Delta[HHb]$ and VO_{2p}) and considering the rate of their adjustment relative to one another, our laboratory has recently identified an "overshoot" in the

$\Delta[HHb]/VO_2$ ratio, likely reflecting a transient local muscle O_2 delivery to O_2 utilization mismatch (Murias et al. 2011d). This $\Delta[HHb]/VO_2$ overshoot has been shown to be attenuated or abolished with training (Murias et al. 2010, 2011a) and heavy-intensity 'priming' exercise (Murias et al. 2011b; Spencer et al. 2012) and is exacerbated by exposure to acute hypoxia (Spencer et al. 2012).

Whereas Wilkerson et al. (2004) have described the effects of WR on phase II τVO_{2p} and functional G across a broad range of exercise intensity domains (i.e., from 60 % θ_L to 120 % of peak VO_2), and Scheuermann and Barstow (2003) described the VO_2 kinetic response to exercise at (i.e., 100 %) or near (i.e., 90 and 110 %) VO_{2max}, the effects of WR on VO_2 kinetic parameters within the moderate-intensity domain have not yet been thoroughly described. Furthermore, it remains unclear whether WR increment might affect the $\Delta[HHb]/VO_2$ ratio, which could provide important insights into mechanisms underlying possible differences in the phase II τVO_{2p} and functional G. Thus, the purpose of the present study was to systematically examine the role of WR increment (when initiated from a constant low WR of 20 W to five different moderate-intensity WRs between 50 and 130 W) on both τVO_{2p} and functional G in a group of healthy, young adults. Further, with the hypothesis of both smaller τVO_{2p} and functional G during transitions to lower WRs, we sought to investigate the potential mechanism(s) using measures of local muscle deoxygenation (to assess the balance between O_2 delivery and O_2 utilization) and to determine whether this mechanism differed between those individuals who presented with fast compared with slower VO_{2p} kinetics.

Methods

Subjects

Fourteen young men (24 ± 5 years; 80 ± 12 kg; 180 ± 6 cm; mean $\pm$ SD) volunteered and gave written informed consent to participate in the study. All procedures were approved by The University of Western Ontario Research Ethics Board for Health Sciences Research Involving Human Subjects. All subjects were non-smokers and were physically active. Additionally, no subjects were taking medications that are known to affect the cardiorespiratory, metabolic or haemodynamic responses to exercise.

Protocol

Initially, subjects reported to the laboratory to perform a ramp incremental test (25 W/min) to the limit of tolerance on a cycle ergometer (model: H-300-R Lode; Lode B.V.,

Groningen, Holland) for determination of peak VO_2 (VO_{2peak}) and θ_L. θ_L was defined as the VO_2 at which CO_2 output (VCO_2) began to increase out of proportion to VO_2 with a systematic rise in minute ventilation-to-VO_2 ratio and end-tidal PO_2, whereas minute ventilation-to-VCO_2 ratio and end-tidal PCO_2 were stable (Beaver et al. 1986; Whipp et al. 1986). Subsequent to the incremental test, subjects returned to the laboratory on six occasions during which a total of four repetitions of "step" changes in WR were completed per visit. During each visit, subjects completed a pair of successive moderate-intensity leg cycling transitions from a 6-min baseline WR of 20 W to 6 min at a WR corresponding to one of 50, 70, 90, 110 or 130 W separated by 6 min of 20 W cycling; following 20 min of seated recovery, subjects continued on to complete a second pair of identical transitions. Subjects were instructed to maintain a pedal cadence between 60 and 70 revolutions per minute (rpm) throughout 20 W baseline cycling and during each of the moderate-intensity cycling WRs. Cycle cadence was displayed continuously and the investigator ensured pedal cadence was in the 60–70 rpm range. The decision to test subjects at the same absolute WRs, rather than similar relative (i.e., % of θ_L) WRs, was made to avoid perpetuating potential errors in the original estimation of θ_L (which is likely to have a small, inherent error when estimated from gas-exchange data); that is, if θ_L was under- or over-estimated for a given subject, this error would be repeated five times when prescribing individual WRs. For each individual, the step transitions from 20 to 130 W were performed first to verify that this WR was within the moderate-intensity domain (with the absence of a VO_{2p} slow component); after this visit, the order of the WR transitions was randomized. For the 20- to 50-W transitions, a total of eight repetitions (i.e., 2 visits) were performed, as smaller WR transitions have been associated with reduced signal-to-noise ratios and thus (perhaps) less confidence in parameter estimates; for all other WRs, four transitions (i.e., 1 visit) were performed. We have previously shown that the effect of previous moderate-intensity transitions on the VO_{2p} kinetics response of subsequent moderate-intensity transitions is negligible (Spencer et al. 2011b). Each visit to the laboratory was separated by at least 24 h.

Measurements

Gas-exchange measurements were similar to those previously described (Babcock et al. 1994). 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 continuously sampled (50 Hz) at the mouth and analyzed for concentrations of O_2, CO_2 and N_2 by mass spectrometry

(Innovision, AMIS 2000, Lindvedvej, Denmark) after calibration with precision-analyzed gas mixtures. Changes in gas concentrations were aligned with gas volumes by measuring the time delay 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 were transferred to a computer, which aligned concentrations with volume information to build a profile of each breath. Breath-by-breath alveolar gas exchange was calculated using algorithms of Beaver et al. (1981).

Local muscle deoxygenation profiles of the quadriceps vastus lateralis muscle were made with continuous-wave NIRS (Hamamatsu NIRO 300, Hamamatsu Photonics, Hamamatsu, Japan). The physical principles of tissue spectroscopy and the manner in which these are applied have been explained by DeLorey et al. (2003). Briefly, optodes were placed on the belly of the muscle midway between the lateral epicondyle and greater trochanter of the right femur. The system consisted of both an emission probe that carries NIR light from the laser diodes and detector probe (interoptode spacing 5 cm); optodes were housed in an optically dense plastic holder and secured on the skin surface with tape and then covered with an optically dense, black vinyl sheet, thus minimizing the intrusion of extraneous light. The thigh was wrapped with an elastic bandage to minimize movement of the optodes. Four laser diodes ($\lambda = 775$, 810, 850, and 910 nm) were pulsed in a rapid succession and the light returning from the tissue was detected by the photodiode for online estimation and display of the concentration changes from the resting baseline for oxyhaemoglobin ($\Delta[HbO_2]$), deoxyhaemoglobin ($\Delta[HHb]$) and total haemoglobin ($\Delta[Hb_{tot}]$). One limitation of the NIRS technique is the overlapping absorption spectra of muscle myoglobin (Mb) and Hb (Bowen 1949); this makes separation of these absorbers difficult. However, the contribution of Mb to light absorption changes is estimated to be ~ 10 %, which lends to the interpretation that light absorption changes with NIRS are attributable mainly to the oxygenation status of Hb (Kalliokoski et al. 2006). Changes in light intensities were recorded continuously at 2 Hz and transferred to a computer for later analysis. The NIRS-derived signal was zero set with the subject sitting in a resting steady-state on the cycle ergometer prior to the onset of baseline exercise and changes in the concentration are reported as a delta (Δ) in arbitrary units (a.u.).

Data analysis

VO_{2p} data were filtered by removing aberrant data points that lay outside 4 SD of the local mean; the justification for this filtering process was provided by Lamarra et al. (1987), who demonstrated that "noise" observed within the

VO_{2p} signal conformed to a predictable Gaussian distribution, independent of WR. The data for each transition were linearly interpolated to 1 s intervals and time-aligned such that time zero represented the onset of exercise. Data from all same-WR transitions were ensemble-averaged to yield five averaged responses for each subject (i.e., one for each WR). These transitions were further time-averaged into 5 s bins to provide five time-averaged responses for each subject. (Ensemble- and time-averaged responses for 20 to 50 W transitions using only 4 and only 6 transitions were also generated in addition to that generated using all 8 transitions.) Baseline VO_{2p} (VO_{2pBSLN}) was calculated as the average VO_{2p} collected in the 2 min before an increase in WR. The on-transient responses for VO_{2p} were modelled using the following equation:

$$Y_{(t)} = Y_B + A\left(1 - e^{-(t-TD)/\tau}\right) \tag{1}$$

where $Y_{(t)}$ represents the VO_{2p} for any given time; Y_B is the VO_{2p} at baseline; A is the amplitude of the VO_{2p} response; t is a given amount of time; τ represents the time required to attain 63 % of the steady-state amplitude; and TD represents the time delay.

After excluding the initial 20 s of data (which, while not necessarily reflecting the exact duration of the 'cardiodynamic phase' in each individual, is most likely to avoid inclusion of data points from phase I VO_{2p} in the fitting of phase II VO_{2p} (Murias et al. 2011c), while still allowing TD to vary freely (in order to optimize accuracy of parameter estimates), VO_{2p} data were modelled from 20 s to 4 min (240 s) of the step-transition; this ensured that each subject had attained a VO_{2p} steady-state (VO_{2pSS}), yet did not bias the model fit during the on-transient (Bell et al. 2001; Murias et al. 2011c). The model parameters were estimated by least-squares nonlinear regression (Origin, OriginLab Corp., Northampton, MA, USA) in which the best fit was defined by minimization of the residual sum of squares and minimal variation of residuals around the Y-axis ($Y = 0$). The 95 % confidence interval for the estimated time constant (CI$_{95}$ τVO_{2p}) was determined after preliminary fit of the data with Y_B, A and TD constrained to the best-fit values and the τ allowed to vary.

In order to investigate whether the changes in τVO_{2p} and functional G differed between those individuals who presented with fast compared with slower VO_{2p} kinetics, the sample was sub-divided into two groups. A "cut-off" of $\tau VO_{2p} = 25$ s (during transitions to 130 W) was selected to separate the two groups. This value was selected in an effort to differentiate those individuals in whom an O_2 delivery-dependent limitation of τVO_{2p} was likely compared with those individuals in whom an O_2 delivery-dependant limitation of τVO_{2p} was less likely based on recent findings from our laboratory (Murias et al. 2010, 2011b, d; Spencer et al.

2012). While this value is not completely congruent with our findings of an "O_2 delivery independent" limitation of τVO_{2p} when $\tau VO_{2p} \leq 21$ s (Murias et al. 2011d), strict adherence to this 21 s value would have created a Fast group with only four subjects (and 10 in the Slower); this jeopardized the statistical power of the present study. Further, a strong linear relationship ($r = 0.91$) was established between the normalized $\Delta[HHb]/VO_2$ ratio and τVO_{2p} (Murias et al. 2011d), suggesting that in those individuals with τVO_{2p} values between 21 and 25 s, any O_2 delivery to O_2 utilization mismatch during the exercise on-transient would be modest.

Five NIRS-derived $\Delta[HHb]$ responses (i.e., one for each WR) were generated for each subject. The $\Delta[HHb]$ profile has been described to consist of a time delay at the onset of exercise, followed by an increase in the signal with an "exponential-like" time-course (DeLorey et al. 2003). The time delay for the $\Delta[HHb]$ response (TD $\Delta[HHb]$) was determined using second-by-second data and corresponded to the time, after the onset of exercise, at which the $\Delta[HHb]$ signal began a systematic increase from its nadir value. Determination of the TD $\Delta[HHb]$ was made on individual trials and averaged to yield a value for each individual in each of the five "conditions." The $\Delta[HHb]$ data were modelled from the end of the TD $\Delta[HHb]$ to 90 s of the transition using an exponential model as described in Eq. (1). As previously described by duManoir et al. (2010), different fitting strategies (i.e., 90–180 s) resulted in minimal differences (<2 s) in estimates of the $\Delta[HHb]$ time constant ($\tau\Delta[HHb]$) and the early exponential increase in $\Delta[HHb]$ was well characterized in the 90 s following exercise onset. The $\tau\Delta[HHb]$ described the time course for the increase in $\Delta[HHb]$, while the overall change of the effective $\Delta[HHb]$ ($\tau'\Delta[HHb] = $ TD $\Delta[HHb] + \tau\Delta[HHb]$) described the overall time course of the $\Delta[HHb]$ from the onset of exercise.

Additionally, the second-by-second $\Delta[HHb]$ and VO_{2p} data were normalized for each subject (0 %, representing the 20-W baseline value, and 100 %, representing the post-transition steady-state of the response). The normalized VO_{2p} was left-shifted by 20 s to account for the approximate phase I–phase II transition so that the onset of exercise coincided with the beginning of phase II VO_{2p} (Murias et al. 2011d), which has been previously described to coincide with muscle VO_2 within 10 % (Grassi et al. 1996). Following normalization and time-alignment, data were further averaged into 5 s bins for statistical comparison of the rate of adjustment for $\Delta[HHb]$ and VO_{2p}. Additionally, an overall $\Delta[HHb]/VO_2$ ratio for the adjustment during the exercise on-transient was derived for each individual as the average value from 20 to 120 s into the transition. The start point was selected to be 20 s to begin the analysis at the time region when the $\Delta[HHb]$ and VO_{2p} signals meet, reflecting the TD $\Delta[HHb]$ and early adjustment of $\Delta[HHb]$. An end

point of 120 s was selected as the time point at which the $\Delta[HHb]/VO_2$ ratio had reached a steady-state value of 1.0.

Statistics

Data are presented as mean $\pm$ SD. Independent samples t tests were used to detect between group differences in subject characteristics. Two-way (WR and group) repeated measures analyses of variance (ANOVA) were used to determine statistical significance for the dependent variables (i.e., VO_{2p} and $\Delta[HHb]$ kinetic parameter estimates). Tukey's post hoc analysis was used when significant differences were detected for the main effects of each dependent variable. Determination of whether a $\Delta[HHb]/VO_2$ ratio overshoot was significant was based upon a comparison (t test) of the WR- or WR by group-specific mean with a value of 1.0 (with no associated error). Pearson's product–moment correlation coefficients were used to quantify the strength of relationships between variables. All statistical analyses were performed using SPSS Version 19.0, (SPSS Inc., Chicago, IL, USA). Statistical significance was declared when $p < 0.05$.

Results

Subject characteristics are presented in Table 1. Peak WR was 361 ± 37 W, which yielded a VO_{2peak} of 4.13 ± 0.40 L min^{-1} (or 52.3 ± 6.8 mL kg^{-1} min^{-1}). When the sample ($n = 14$) was sub-divided into those with Fast (τVO_{2p} at 130 W <25 s; $n = 6$; $VO_{2peak} = 56.7 \pm 4.8$ mL kg^{-1} min^{-1}) and Slower (τVO_{2p} at 130 W >25 s; $n = 8$; $VO_{2peak} = 49.1 \pm 6.4$ mL kg^{-1} min^{-1}) VO_{2p} kinetics, a between-group difference ($p < 0.05$) was observed for 'relative' VO_{2peak}, but no other characteristics. The VO_{2p} responses elicited by transitions to 50, 70, 90, 110 and 130 W corresponded to 49 ± 6, 57 ± 7, 66 ± 7, 75 ± 7 and

Table 1 Subject characteristics

	All ($n = 14$)	Fast ($n = 6$)	Slower ($n = 8$)
Age (years)	24 ± 5	27 ± 7	22 ± 2
Mass (kg)	80 ± 12	76 ± 6	83 ± 14
Height (m)	1.80 ± 0.06	1.81 ± 0.07	1.80 ± 0.05
VO_{2peak} (mL kg^{-1} min^{-1})	52.3 ± 6.8	56.7 ± 4.8	49.1 ± 6.4*
Peak WR (W)	361 ± 37	374 ± 17	352 ± 46
θ_L (L min^{-1})	2.41 ± 0.20	2.43 ± 0.05	2.39 ± 0.27
WR at θ_L (W)	159 ± 18	162 ± 5	158 ± 24

Values are mean $\pm$ SD

* $p < 0.05$ from Fast

85 ± 8 % of θ_L. Importantly, no between-group differences were observed when WR was expressed as a relative % of θ_L ($p = 0.43$), rather than in absolute terms (i.e., W).

Figure 1 displays the profiles of VO_{2p} (5 s averaged, group mean data) for the Fast and Slower groups for exercise transitions from 20 to 50, 70, 90, 110 and 130 W. Group mean ($\pm$SD) VO_{2p} kinetic parameter estimates (i.e., derived from the mono-exponential non-linear regressions) for each of the five constant load WRs are illustrated in Fig. 2. VO_{2pBSLN} was consistent both amongst WRs and between groups ($p > 0.05$). Whereas no between-group differences were observed in the VO_{2p} amplitude (VO_{2pAMP}) response, there was a significant main effect of WR ($p < 0.05$) such that each progressive increase in WR yielded a greater VO_{2pAMP} response. A consequence of invariant VO_{2pBSLN} values, along with progressively increasing VO_{2pAMP} values with increasing WRs, was a progressively increasing VO_{2pSS} response ($p < 0.05$; not depicted in Fig. 2) which was observed in both the Fast and Slower groups. Transitions to greater WRs were associated with decreased CI$_{95}$ τVO_{2p} ($p < 0.05$). There was a significant increase ($p < 0.05$) in functional G during transitions to increasing WRs within the moderate-intensity domain; this finding was not associated with any between-group differences ($p > 0.05$). When considered as a single group, there was no main effect of WR on τVO_{2p}; however, both a main effect for group (i.e., Fast vs. Slower, $p < 0.05$) and a WR by group interaction ($p < 0.05$) were observed. Post hoc comparisons revealed significantly greater τVO_{2p} during transitions to 110 and 130 W (by design) in the Slower group, but not for transitions to 50, 70 and 90 W; these findings suggest a trend for increasing τVO_{2p} values during transitions to a higher WR in the Slower group which was absent in the Fast group (or decreasing τVO_{2p} values during transitions to a higher WR in the Fast group which was absent in the Slower group).

The effects of transition WR magnitude on $\Delta[HHb]$ kinetic parameter estimates are displayed in Fig. 3. The baseline $\Delta[HHb]$ ($\Delta[HHb]_{BSLN}$) was not different for any WR, but when the two groups were considered separately, the $\Delta[HHb]_{BSLN}$ was lower ($p < 0.05$) in the Fast compared with the Slower group; the between group difference observed ($p < 0.05$) is of little consequence, since the (Δ) units are arbitrary. Greater WR transitions were associated with lower 95 % confidence intervals (reflecting greater confidence in parameter estimation) for the $\tau \Delta[HHb]$ (CI$_{95}$ $\tau \Delta[HHb]$; $p < 0.05$), as well as greater ($p < 0.05$) $\Delta[HHb]$ amplitudes ($\Delta[HHb]_{AMP}$) and steady-state $\Delta[HHb]$ ($\Delta[HHb]_{SS}$) responses; again, the between-group differences ($\Delta[HHb]_{AMP}$ and $\Delta[HHb]_{SS}$; $p < 0.05$) and WR*group interaction ($\Delta[HHb]_{AMP}$; $p < 0.05$) are inconsequential. Modest but significant reductions in both $\tau \Delta[HHb]$ and TD $\Delta[HHb]$ were observed with increasing WR transitions
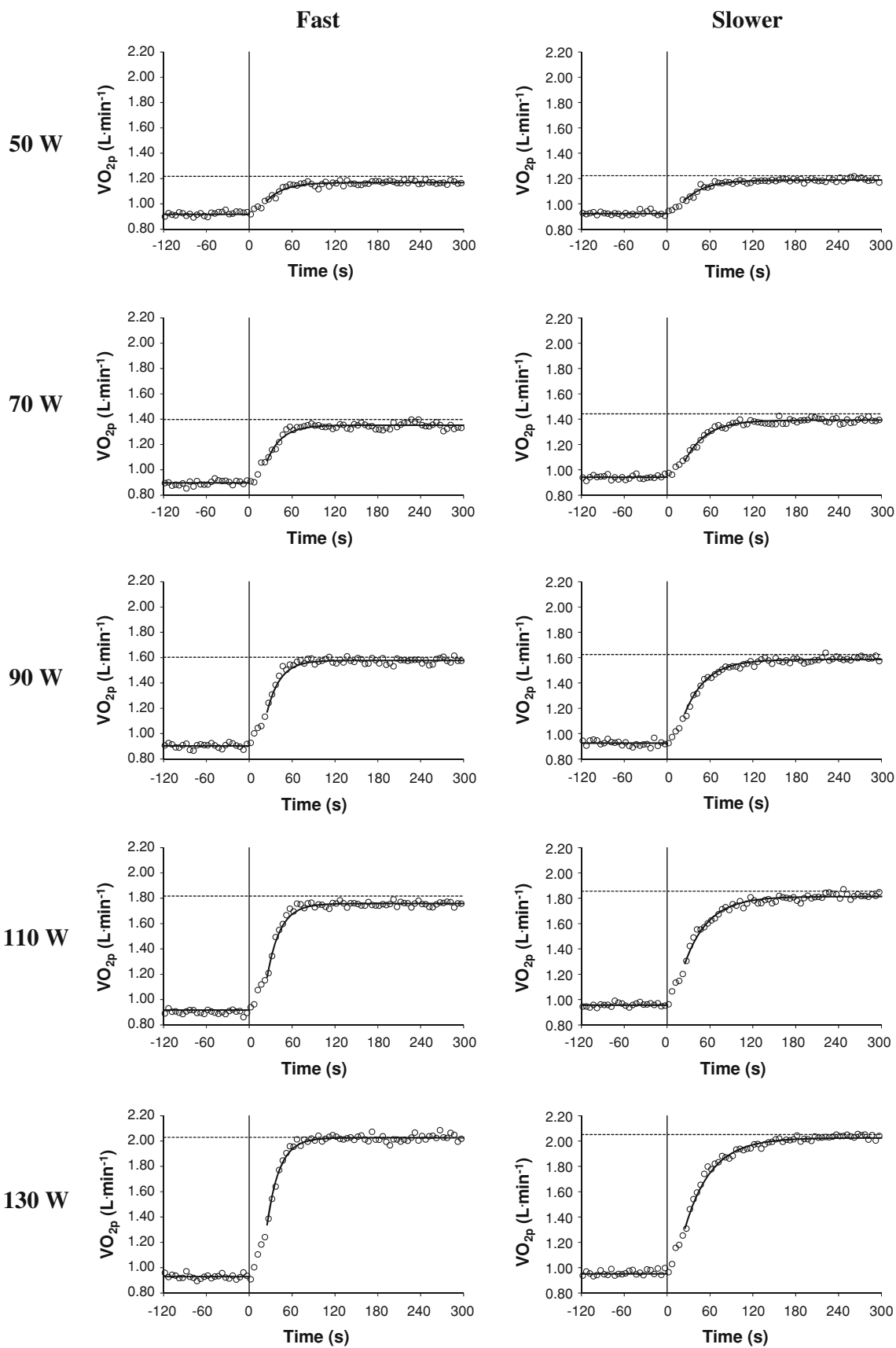
◀ **Fig. 1** Group mean (5 s averaged data) VO_{2p} profiles for transitions from 20 to 50 W (*top*), 70, 90, 110 and 130 W (*bottom*) in Fast (*left*) and Slower (*right*) groups. Mono-exponential models from group mean data superimposed. Exercise onset denoted by *solid vertical line*. *Dashed horizontal line* indicates predicted VO_{2p} assuming functional G of 10 mL min^{-1} W^{-1}

($p < 0.05$), and as a result, $\tau'\Delta[HHb]$ decreased with increasing WR transitions ($p < 0.05$). Whereas a main effect of group was observed for $\tau\Delta[HHb]$ (with Slower having a greater $\tau\Delta[HHb]$ response), this between-group difference was absent in both the TD $\Delta[HHb]$ and $\tau'\Delta[HHb]$ responses.

No effect of WR was observed with respect to the $\Delta[HHb]/VO_2$ ratio ($p > 0.05$); a main effect of group was identified ($p < 0.05$) such that the Slower group had a greater $\Delta[HHb]/VO_2$ ratio than the Fast group (Fig. 4). Furthermore, the $\Delta[HHb]/VO_2$ ratio observed in the Fast group did not

differ ($p > 0.05$) from 1.0 during transitions to any WR. Similar to previous studies from our laboratory (Murias et al. 2011b, d), the $\Delta[HHb]/VO_2$ ratio was associated with τVO_{2p} in the present study ($r = 0.71$; $p < 0.05$; Fig. 5).

Table 2 illustrates the effects of performing "additional" repetitions of small WR transitions (e.g., 20 to 50 W) on VO_{2p} kinetic parameter estimates. Briefly, no differences ($p > 0.05$) in any of VO_{2pBSLN}, VO_{2pAMP}, VO_{2pSS}, functional G and τVO_{2p} were observed when parameters were derived from the average of four, six or eight repetitions. Performing either six or eight repetitions yielded significant reductions in the CI$_{95}$ τVO_{2p} compared with performing only four ($p < 0.05$; $p = 0.13$ between 6 and 8 repetitions). Indeed, as shown in Fig. 1, even with eight repetitions the confidence in the τVO_{2p}, (and $\tau\Delta[HHb]$ as shown in Fig. 2) is two- to threefold less for the 50 W WR versus WRs above 100 W.
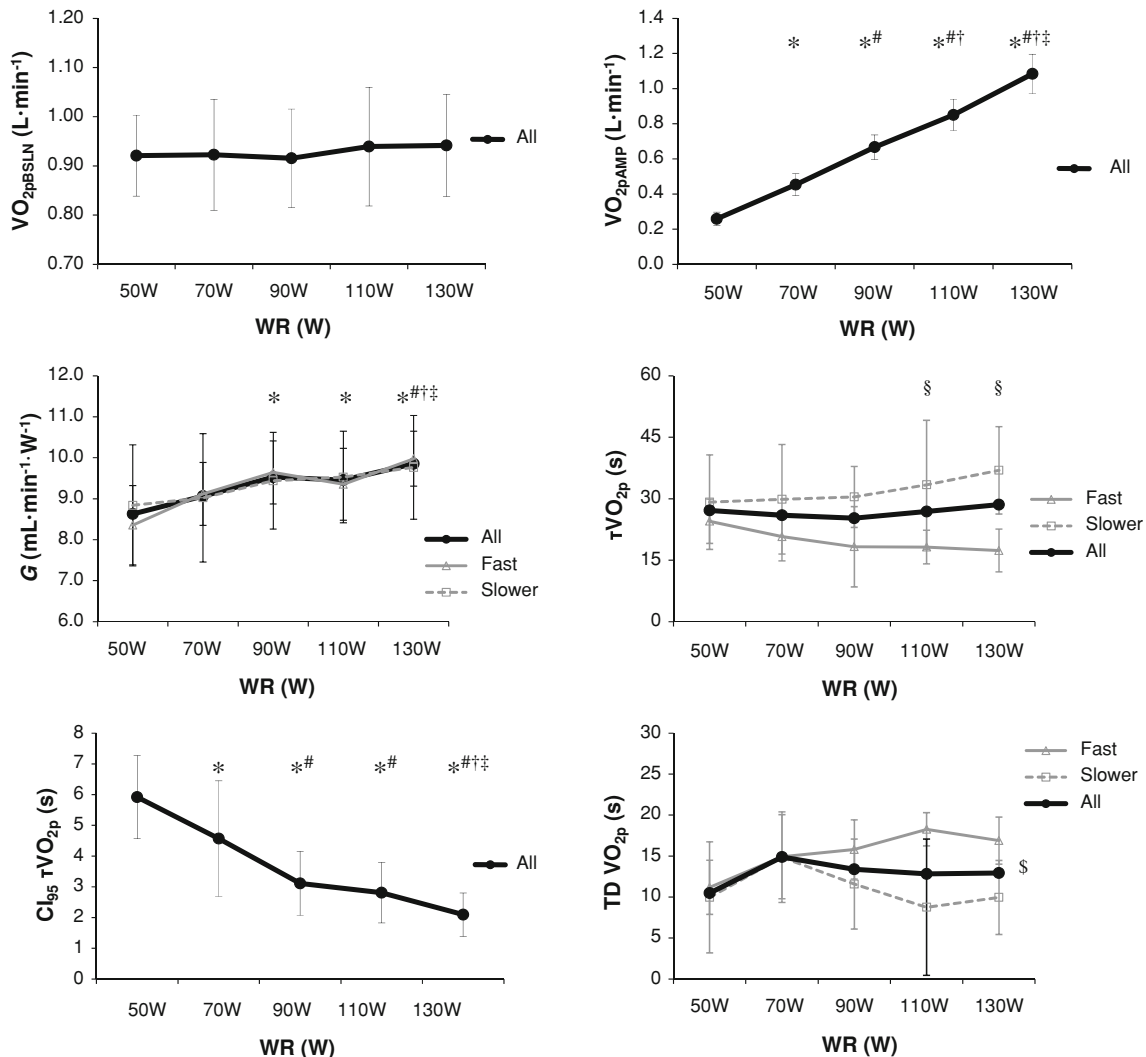

Fig. 2 Mean ($\pm$SD) VO_{2p} kinetic parameter estimates for transitions from 20 to 50, 70, 90, 110 and 130 W in All subjects (*filled circle*). $*p < 0.05$ from 50 W; $^\#p < 0.05$ from 70 W; $^\dagger p < 0.05$ from 90 W;

$^\ddagger p < 0.05$ from 110 W. Fast (*open triangle*) and Slower (*open square*) groups are depicted when main effect of GROUP ($^\$p < 0.05$) or WR*GROUP interaction ($^\$p < 0.05$) were detected
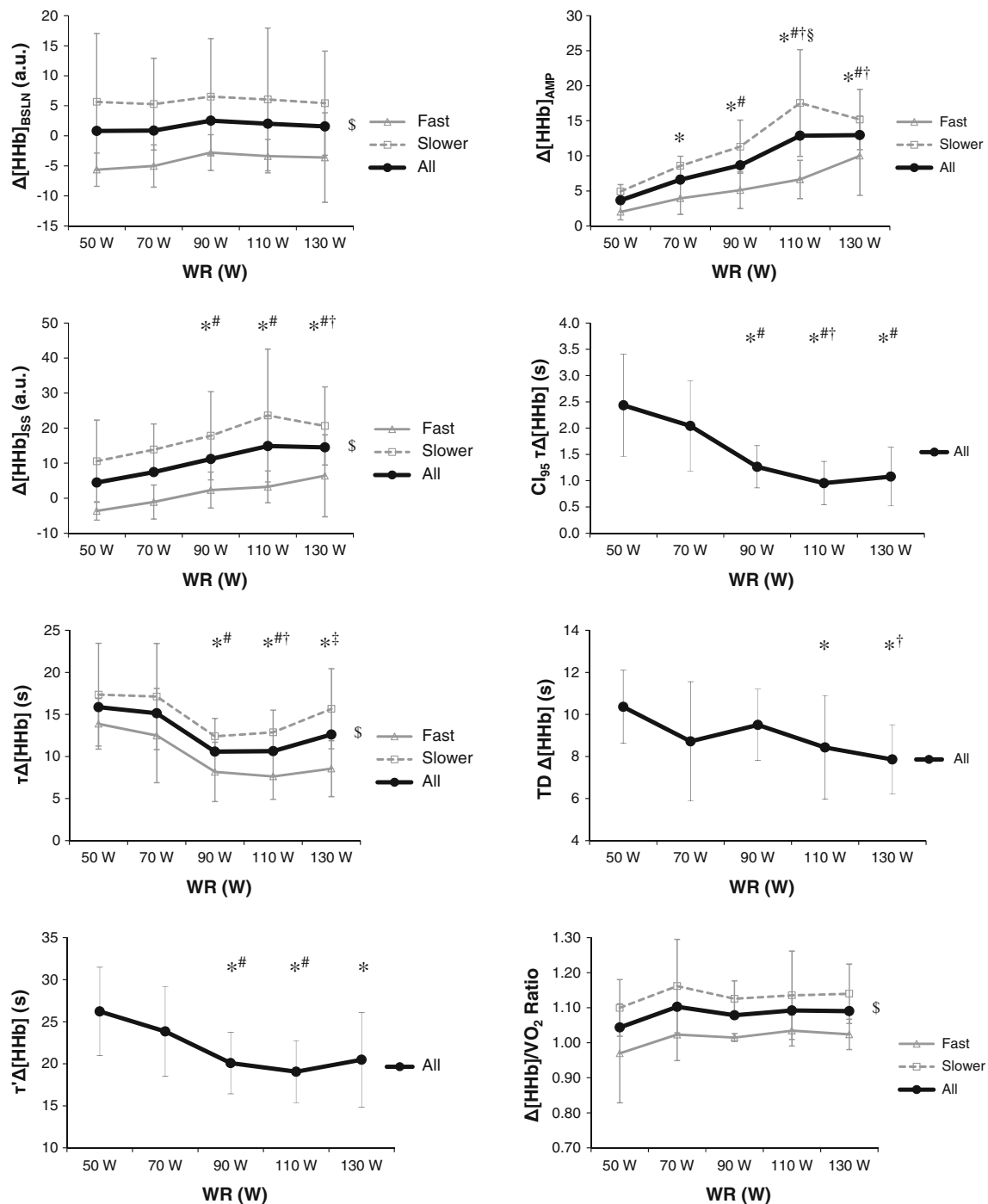
Fig. 3 Mean (±SD) Δ[HHb] kinetic parameter estimates for transitions from 20 to 50, 70, 90, 110 and 130 W in All subjects (*filled circle*). $*p < 0.05$ from 50 W; $^{\#}p < 0.05$ from 70 W; $^{\dagger}p < 0.05$ from 90 W; $^{\ddagger}p < 0.05$ from 110 W. Fast (*open triangle*) and Slower (*open square*) groups are depicted when main effect of GROUP ($^{\$}p < 0.05$) or WR*GROUP interaction ($^{\S}p < 0.05$) were detected

Discussion

The present study sought to systematically examine the role of WR increment (when initiated from a constant low WR of 20 W to WRs in the moderate-intensity exercise domain) on both τVO_{2p} and functional G in a group of healthy, young adults. Further, with the hypothesis of both

smaller τVO_{2p} and functional G during transitions to lower WRs, we sought to investigate the potential mechanism and to determine whether this mechanism differed between those individuals who presented with fast compared with slower VO_{2p} kinetics. The main findings of the study were that (1) during transitions to different WRs within the moderate-intensity domain, no differences in τVO_{2p} were

Fig. 4 Group mean (5 s averaged data) $\Delta[HHb]/VO_2$ profiles for transitions from 20 to 50 W (*top*), 70, 90, 110 and 130 W (*bottom*) in Fast (*left*) and Slower (*right*) groups. *Dashed horizontal line* indicates $\Delta[HHb]/VO_2 = 1.0$
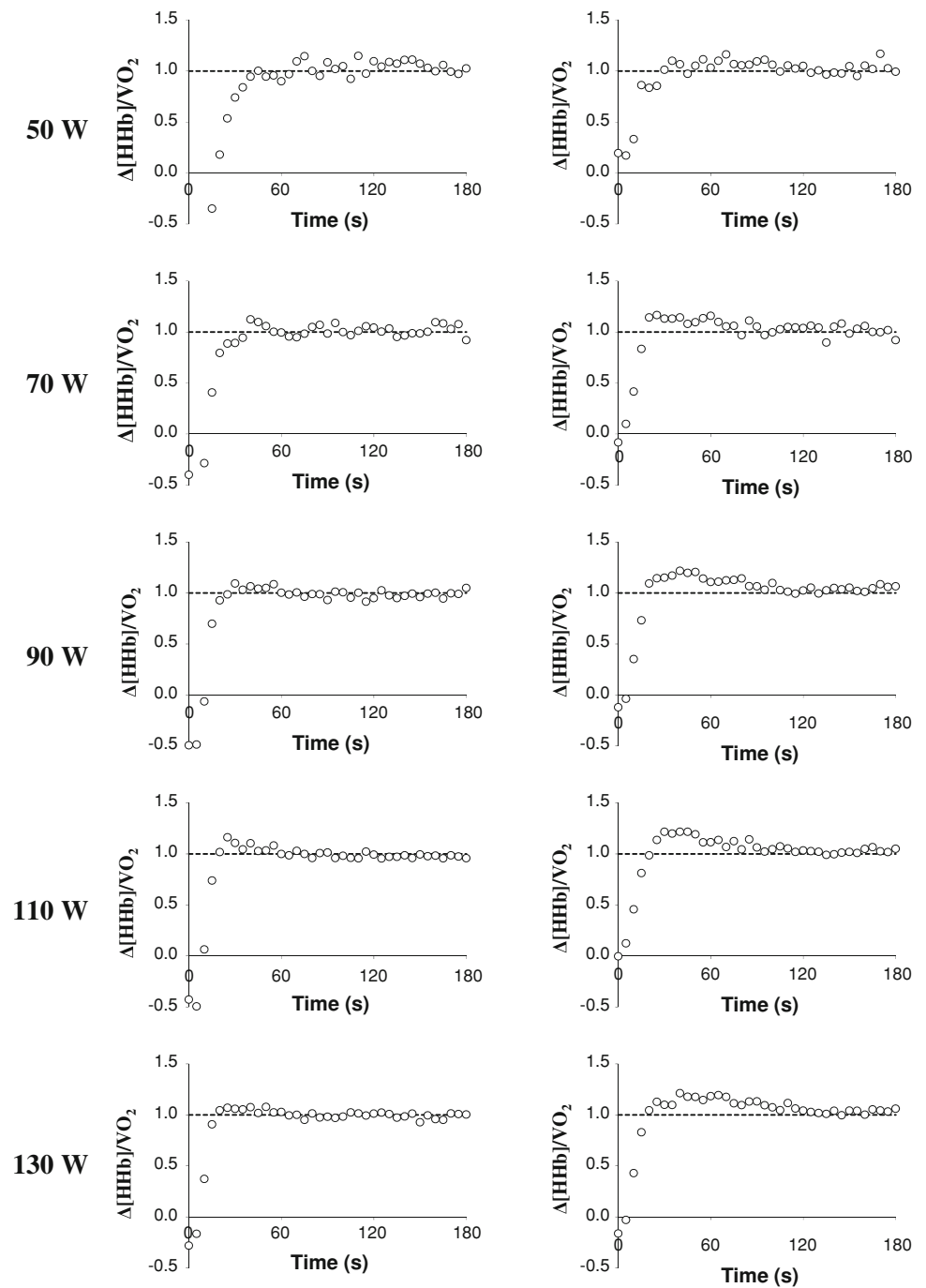
observed in this group of subjects ($\tau VO_{2p} \approx 27$ s); (2) when the sample was sub-divided into two groups (i.e., those with fast and slower VO_2 kinetics), there was an interaction between WR increment and group such that the τVO_{2p} responses appeared divergent between the Fast and Slower groups, with only the Slower group showing evidence of conformity to WR-dependent alterations in τVO_{2p} previously reported in the literature (i.e., in studies comparing a "lower step" to a "full step"); (3) the $\Delta[HHb]/VO_2$ ratio was smaller in the Fast compared with Slower

group (suggesting that the primary determinant of τVO_{2p} differs between groups), but was not affected by WR (suggesting that the divergent τVO_{2p} responses between Fast and Slower groups may not have been the result of O_2 availability during the exercise on-transient); (4) functional G was progressively greater during transitions of increasing WR increment; this was true for (and similar between) both the Fast and Slower groups, possibly suggesting that the mechanism(s) controlling the magnitude and the rate of the VO_{2p} response to a given WR transition may be
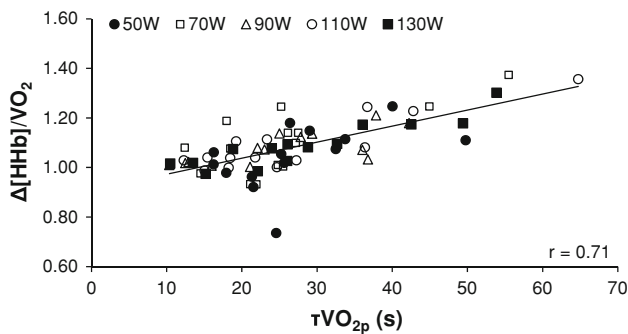
Fig. 5 Relationship ($r = 0.71$) between the $\Delta[HHb]/VO_2$ ratio and τVO_{2p} for all 14 subjects during transitions from 20 to 50, 70, 90, 110 and 130 W. $\Delta[HHb]/VO_2$ ratio was derived for each individual as the average of the 21 5 s ratio values from 20 to 120 s

Table 2 VO_{2p} kinetic parameter estimates for 20 to 50 W transitions when four, six or eight transitions were ensemble-averaged

	Number of repetitions		
	Four	Six	Eight
VO_{2pBSLN} (L min^{-1})	0.92 ± 0.08	0.92 ± 0.09	0.92 ± 0.09
VO_{2pAMP} (L min^{-1})	0.26 ± 0.04	0.26 ± 0.04	0.26 ± 0.04
VO_{2pSS} (L min^{-1})	1.19 ± 0.09	1.18 ± 0.09	1.18 ± 0.08
G (mL min^{-1} W^{-1})	8.7 ± 1.3	8.5 ± 1.3	8.6 ± 1.4
τVO_{2p} (s)	31.3 ± 14.1	27.2 ± 10.6	28.1 ± 9.3
CI τVO_{2p} (s)	8.3 ± 2.4	$6.6 \pm 1.4*$	$6.1 \pm 1.4*,†$
TD VO_{2p} (s)	5.3 ± 10.2	$10.4 \pm 6.2*$	$10.2 \pm 5.9*$

Values are mean $\pm$ SD

* $p < 0.05$ from four repetitions

† $p = 0.13$ from six repetitions

dissociated; and (5) performing either six or eight compared with four repetitions of small (i.e., 20 to 50 W) WR transitions improved the confidence in the estimation of τVO_{2p}, yet, there were no changes in other key VO_{2p} kinetic parameter estimates.

The present study was designed to elicit like VO_{2pBSLN} values amongst the different (WR) conditions, as well as progressively greater VO_{2pAMP} and VO_{2pSS} values during transitions to greater WRs; as such, these findings reported in Fig. 1 were to be expected. Thus, this discussion attempts to sort out the interrelations among three important findings of the present study, namely (1) divergent τVO_{2p} responses between Fast and Slower groups with respect to WR; (2) increasing functional G with increasing WR increments (irrespective of group); and (3) group differences in the $\Delta[HHb]/VO_2$ ratio, but with no influence of WR. As mentioned, previous studies examining the effects of either WR increment or pre-transition WR have focused much of their attention on discussing the slower adjustment and greater functional G observed when work is initiated from either an elevated WR (Brittain et al. 2001;

Hughson and Morrissey 1982; MacPhee et al. 2005; Spencer et al. 2011a) or an elevated metabolic rate (Bowen et al. 2011); nevertheless, these discussions have identified three potential causes for these trends which will form the basis for the present discussion:

1. an insufficient O_2 delivery, leading to a slowing of the VO_2 response during the exercise on-transient, was favoured by Hughson and Morrissey (1982) and later supported by MacPhee et al. (2005), but was largely refuted by the findings of Spencer et al. (2011a);

2. a hierarchical recruitment pattern favouring recruitment of the fastest kinetic, most efficient fibres to perform small WR transitions, leaving only those inherently slower kinetic, less efficient fibres to address the demands of a subsequent increase in WR was proposed by Brittain et al. (2001); such a system would allow for an 'intermediate' rate of adjustment of VO_2 and O_2 cost (per unit increase in WR) during larger WR transitions;

3. the influence of a potentially less favourable energetic status (i.e., less negative changes in Gibb's free energy; ΔG_{ATP}) resulting from either an elevated metabolic rate per se (i.e., irrespective of initial WR) (Glancy et al. 2008; Kemp 2008) or the fact that ΔG_{ATP} becomes progressively less negative throughout the transient (as [ADP] and [Pi] rise and [PCr] fall dynamically) and therefore demands an ATP turnover that continues to rise until the steady state is reached was favoured by Bowen et al. (2011).

Considering that smaller τVO_{2p} values often are reported during "half-steps" compared with "full-step" WR transitions within the moderate-intensity domain (when performed from a constant, low baseline WR) (Bowen et al. 2011; Brittain et al. 2001; Hughson and Morrissey 1982; MacPhee et al. 2005; Spencer et al. 2011a), the finding of invariant τVO_{2p} values in response to different moderate-intensity WRs in the present study was somewhat unexpected. However, when the present sample was sub-divided to create Fast and Slower VO_2 kinetics groups, their respective responses (with respect to increasing WR increment) were divergent, where the Slower, but not the Fast group tended to conform to the trend observed by previous studies (i.e., with between-group differences noted only at the higher WRs; see Fig. 1). Indeed, in the studies of Brittain et al. (2001) and Spencer et al. (2011a), where 'slow' VO_2 kinetics ($\tau VO_{2p} > 30$ s) were reported during large WR transitions within the moderate-intensity domain (90 % of θ_L), significant reductions of τVO_{2p} were reported during smaller WR transitions. In the study of MacPhee et al. (2005), in which the group mean τVO_{2p} in response to a large moderate-intensity WR increment was 28 ± 2 s (i.e., somewhat fast relative to those mentioned

immediately above), a trend for faster adjustment (to $\tau VO_{2p} = 24 \pm 3$ s) during smaller WR increment transitions may be inferred, but this trend did not reach the level of statistical significance. In contrast, in a group with relatively fast VO_2 kinetics, Wilkerson et al. (2004) reported no differences in τVO_{2p} values derived from transitions to 60 % θ_L (23.2 $\pm$ 2.1 s) compared with 90 % θ_L (21.8 $\pm$ 2.3 s). Thus, in agreement with previous findings (albeit from different studies), the divergent responses between Fast and Slower groups suggest that if or when the adjustment of VO_{2p} is already somewhat fast, there may be a reduced potential for further speeding (with smaller WR increments). The subject group of Bowen et al. (2011) might be characterized as "intermediate", neither fast nor slow ($\tau VO_{2p} = 26$ s), but did show a significantly reduced τVO_{2p} (to 20 s) when the WR increment was small compared with large.

Dynamic changes in near-infrared spectroscopy (NIRS)-derived muscle deoxygenation (Δ[HHb]) have been used extensively to provide insights into the balance between local muscle O_2 availability and O_2 utilization during exercise (Ferrari et al. 2011). During WR transitions in which Δ[HHb] adjusts more rapidly than VO_2, what results is a transient period characterized by an increased (relative) reliance on O_2 extraction to support a given metabolic rate; this temporary dissociation between the adjustments of Δ[HHb] and VO_2 suggests a transient O_2 delivery insufficiency. Thus, recent studies from our laboratory (Murias et al. 2010, 2011b, d; Spencer et al. 2012) have used the normalized Δ[HHb]/VO_2 ratio as an index of the matching (and mismatching) of O_2 delivery to O_2 utilization during the exercise on-transient. Cumulatively, these studies suggest that when $\tau VO_{2p} < \sim 20$ s, increases in τVO_{2p} are the result of progressively more severe O_2 delivery limitations. In this light, it is not surprising that the Δ[HHb]/VO_2 ratio was significantly different between the Fast and Slower groups. The present data do not support a role for an O_2 delivery-dependence limitation of τVO_{2p} in the Fast group (where the Δ[HHb]/VO_2 ratio is not significantly different from 1.0, implying no "mismatch" of O_2 delivery to O_2 utilization), but do support such a role in the Slower group (where the Δ[HHb]/VO_2 ratio is significantly greater than 1.0, implying an appreciable "mismatch" between O_2 delivery to O_2 utilization); these findings are in agreement with our previous studies on the topic.

In the present study, the adjustment of Δ[HHb] (i.e., a reduction of both $\tau\Delta$[HHb] and $\tau'\Delta$[HHb]) became progressively faster with increasing WR increments, and importantly, became faster than τVO_{2p} for a given WR. As a result, we expected to observe a significantly greater mismatch between O_2 delivery and O_2 utilization (as reflected with a greater Δ[HHb]/VO_2 ratio) as WR increment increased. The small changes in τVO_{2p} and "noise" in the Δ[HHb]/VO_2 ratio may make the index too

insensitive to detect differences. Indeed, across all WRs, the "overall" relationship between the Δ[HHb]/VO_2 ratio and τVO_{2p} was robust ($r = 0.71$) and even stronger at the higher WRs (110 W, $r = 0.88$; 130 W, $r = 0.91$). Nevertheless, the present data cannot be taken as supporting a role for O_2 delivery as an explanation for the divergent τVO_{2p} responses observed in the Fast and Slower groups; that is, implied increases in τVO_{2p} with increasing WR increment (in the Slower group) are likely not related to increasingly insufficient O_2 delivery. The present data do not allow us to speculate on the possible roles of fibre recruitment pattern or a lower free energy release with ATP hydrolysis (i.e., less negative ΔG_{ATP}) with increasing WR.

In the present study, increasing WR increments were associated with increasing functional G; interestingly, whereas the τVO_{2p} responses in the Fast and Slower groups were different (i.e., greater for the Slower group) and increasingly divergent at higher WRs (i.e., WR by group interaction observed), the functional G showed no such influence of group. When considered in light of the group—but not WR-mediated differences in the Δ[HHb]/VO_2 ratio, it seems clear that local muscle O_2 delivery to O_2 utilization dynamics do not explain the altered functional G in response to differing WRs. Again, this leaves either an orderly, hierarchical recruitment pattern or the fact that ΔG_{ATP} becomes progressively less negative throughout the transient as possible explanations for the WR-mediated differences in functional G. Taken alone, it is difficult to discern which of one or both of these hypotheses is likely to underlie the WR-mediated differences in functional G; however, neither hypothesis can presently accommodate both invariant τVO_{2p} and simultaneous changes in functional G during transitions to different moderate-intensity WRs as observed when the present sample was considered as a whole. The present data suggest, perhaps for the first time, that factors which determine τVO_{2p} may be independent from factors which determine the functional G during moderate-intensity WR transitions of different magnitudes.

One potential problem in evaluating the role of WR transitions on the kinetics parameters is that smaller WR transitions are likely to have reduced signal-to-noise ratios, and thus, potentially reduced confidence in parameter estimates. Indeed, the present study confirmed the idea that transitions to progressively greater WRs (i.e., those with a greater signal-to-noise ratio (Lamarra et al. 1987) were associated with improved confidence in estimates of τVO_{2p} (and $\tau\Delta$[HHb], as reflected by the reduced CI_{95} (i.e., greater confidence in the estimation of the time constant) for both τVO_{2p} and $\tau\Delta$[HHb]). To this end, Lamarra et al. (1987) established that the effect of interbreath fluctuations (i.e., "noise") could be dampened by averaging multiple transitions together when characterizing a signal with an

inherently low sampling frequency (i.e., breath-by-breath gas exchange). Given that during small WR transitions, the VO_{2p} "signal" is essentially fixed, the only available strategy for improving confidence in kinetic parameter estimates is to have subjects perform multiple repetitions to reduce the "noise"; however, to date, the precise number of transitions required for accurate characterization of small WR transitions has not been described. This information is potentially important when studying individuals in whom small amplitudes are particularly likely, such as heart failure patients (Bowen et al. 2012; Kemps et al. 2010) or those with COPD (Puente-Maestu et al. 2001). The present data illustrate that the inclusion of either two or four "additional" repetitions of 20 to 50 W transitions does not significantly affect any of the key VO_{2p} kinetic parameters; yet, the inclusion of two "additional" (to a total of 6) repetitions significantly reduced the CI_{95} τVO_{2p}, with no further reduction ($p = 0.13$) by ensemble-averaging eight transitions. These findings add to those previously reported by our laboratory, showing that during transitions of ~ 100 W (i.e., 20 to 120 W), the day-to-day reproducibility of τVO_{2p} was not improved by averaging more than three repetitions (Spencer et al. 2011b).

In conclusion, this study presented novel data demonstrating a non-uniform effect of moderate-intensity WR increment on τVO_{2p}, depending upon whether the entire group response was considered or if the divergent responses for individuals with Fast (τVO_2 <25 s) and Slower (τVO_2 >25 s) VO_2 kinetics were considered. Furthermore, this study demonstrated that increasing moderate-intensity WR increments elicits an increased functional G, regardless of the τVO_{2p} response. Neither the divergent τVO_{2p} responses nor the functional G appear to be related to the dynamic matching of O_2 delivery to O_2 utilization during the exercise on-transient; yet, the observation of invariant τVO_{2p} values with simultaneously increasing functional G in the overall (i.e., not group specific) response suggests that these features of the VO_2 response during moderate-intensity exercise may be controlled by separate mechanisms.

References

Babcock MA, Paterson DH, Cunningham DA, Dickinson JR (1994) Exercise on-transient gas exchange kinetics are slowed as a function of age. Med Sci Sports Exerc 26:440–446

Beaver WL, Lamarra N, Wasserman K (1981) Breath-by-breath measurement of true alveolar gas exchange. J Appl Physiol 51:1662–1675

Beaver WL, Wasserman K, Whipp BJ (1986) A new method for detecting anaerobic threshold by gas exchange. J Appl Physiol 60:2020–2027

Bell C, Paterson DH, Kowalchuk JM, Padilla J, Cunningham DA (2001) A comparison of modelling techniques used to characterise oxygen uptake kinetics during the on-transient of exercise. Exp Physiol 86:667–676

Bowen WJ (1949) The absorption spectra and extinction coefficients of myoglobin. J Biol Chem 179:235–245

Bowen TS, Murgatroyd SR, Cannon DT, Cuff TJ, Lainey AF, Marjerrison AD, Spencer MD, Benson AP, Paterson DH, Kowalchuk JM, Rossiter HB (2011) A raised metabolic rate slows pulmonary O_2 uptake kinetics on transition to moderate-intensity exercise in humans independently of work rate. Exp Physiol 96:1049–1061

Bowen TS, Cannon DT, Murgatroyd SR, Birch KM, Witte KK, Rossiter HB (2012) The intramuscular contribution to the slow oxygen uptake kinetics during exercise in chronic heart failure is related to the severity of the condition. J Appl Physiol 112:378–387

Brittain CJ, Rossiter HB, Kowalchuk JM, Whipp BJ (2001) Effect of prior metabolic rate on the kinetics of oxygen uptake during moderate-intensity exercise. Eur J Appl Physiol 86:125–134

DeLorey DS, Kowalchuk JM, Paterson DH (2003) Relationship between pulmonary O_2 uptake kinetics and muscle deoxygenation during moderate-intensity exercise. J Appl Physiol 95:113–120

duManoir GR, DeLorey DS, Kowalchuk JM, Paterson DH (2010) Kinetics of VO_2 limb blood flow and regional muscle deoxygenation in young adults during moderate intensity, knee-extension exercise. Eur J Appl Physiol 108:607–617

Ferrari M, Muthalib M, Quaresima V (2011) The use of near-infrared spectroscopy in understanding skeletal muscle physiology: recent developments. Philos Transact A Math Phys Eng Sci 369:4577–4590

Glancy B, Barstow T, Willis WT (2008) Linear relation between time constant of oxygen uptake kinetics, total creatine, and mitochondrial content in vitro. Am J Physiol Cell Physiol 294:C79–C87

Grassi B, Poole DC, Richardson RS, Knight DR, Erickson BK, Wagner PD (1996) Muscle O_2 uptake kinetics in humans: implications for metabolic control. J Appl Physiol 80:988–998

Griffiths TL, Henson LC, Whipp BJ (1986) Influence of inspired oxygen concentration on the dynamics of the exercise hyperpnoea in man. J Physiol 380:387–403

Hughson RL, Morrissey M (1982) Delayed kinetics of respiratory gas exchange in the transition from prior exercise. J Appl Physiol 52:921–929

Kalliokoski KK, Scheede-Bergdahl C, Kjaer M, Boushel R (2006) Muscle perfusion and metabolic heterogeneity: insights from noninvasive imaging techniques. Exerc Sport Sci Rev 34:164–170

Kemp G (2008) Physiological implications of linear kinetics of mitochondrial respiration in vitro. Am J Physiol Cell Physiol 295:C844–C846 (author reply C847–C848)

Kemps HM, Schep G, Zonderland ML, Thijssen EJ, De Vries WR, Wessels B, Doevendans PA, Wijn PF (2010) Are oxygen uptake kinetics in chronic heart failure limited by oxygen delivery or oxygen utilization? Int J Cardiol 142:138–144

Lamarra N, Whipp BJ, Ward SA, Wasserman K (1987) Effect of interbreath fluctuations on characterizing exercise gas exchange kinetics. J Appl Physiol 62:2003–2012

Linnarsson D (1974) Dynamics of pulmonary gas exchange and heart rate changes at start and end of exercise. Acta Physiol Scand Suppl 415:1–68

MacPhee SL, Shoemaker JK, Paterson DH, Kowalchuk JM (2005) Kinetics of O₂ uptake, leg blood flow, and muscle deoxygenation are slowed in the upper compared with lower region of the moderate-intensity exercise domain. J Appl Physiol 99: 1822–1834

Murias JM, Kowalchuk JM, Paterson DH (2010) Speeding of VO₂ kinetics with endurance training in old and young men is associated with improved matching of local O₂ delivery to muscle O₂ utilization. J Appl Physiol 108:913–922

Murias JM, Kowalchuk JM, Paterson DH (2011a) Speeding of VO₂ kinetics in response to endurance-training in older and young women. Eur J Appl Physiol 111:235–243

Murias JM, Spencer MD, Delorey DS, Gurd BJ, Kowalchuk JM, Paterson DH (2011b) Speeding of VO₂ kinetics during moderate-intensity exercise subsequent to heavy-intensity exercise is associated with improved local O₂ distribution. J Appl Physiol 111:1410–1415

Murias JM, Spencer MD, Kowalchuk JM, Paterson DH (2011c) Influence of phase I duration on phase II VO₂ kinetics parameter estimates in older and young adults. Am J Physiol Regul Integr Comp Physiol 301:R218–R224

Murias JM, Spencer MD, Kowalchuk JM, Paterson DH (2011d) Muscle deoxygenation to VO₂ relationship differs in young subjects with varying τVO₂. Eur J Appl Physiol 111:3107–3118

Paterson DH, Whipp BJ (1991) Asymmetries of oxygen uptake transients at the on- and offset of heavy exercise in humans. J Physiol 443:575–586

Puente-Maestu L, Sanz ML, Sanz P, Nunez A, Gonzalez F, Whipp BJ (2001) Reproducibility of the parameters of the on-transient cardiopulmonary responses during moderate exercise in patients with chronic obstructive pulmonary disease. Eur J Appl Physiol 85:434–441

Scheuermann BW, Barstow TJ (2003) O₂ uptake kinetics during exercise at peak O₂ uptake. J Appl Physiol 95:2014–2022

Spencer MD, Murias JM, Kowalchuk JM, Paterson DH (2011a) Pulmonary O₂ uptake and muscle deoxygenation kinetics are slowed in the upper compared with lower region of the moderate-intensity exercise domain in older men. Eur J Appl Physiol 111:2139–2148

Spencer MD, Murias JM, Lamb HP, Kowalchuk JM, Paterson DH (2011b) Are the parameters of VO₂, heart rate and muscle deoxygenation kinetics affected by serial moderate-intensity exercise transitions in a single day? Eur J Appl Physiol 111: 591–600

Spencer MD, Murias JM, Grey TM, Paterson DH (2012) Regulation of VO₂ kinetics by O₂ delivery: insights from acute hypoxia and heavy-intensity priming exercise in young men. J Appl Physiol 112:1023–1032

Whipp BJ (1971) Rate constant for the kinetics of oxygen uptake during light exercise. J Appl Physiol 30:261–263

Whipp BJ, Wasserman K (1972) Oxygen uptake kinetics for various intensities of constant-load work. J Appl Physiol 33:351–356

Whipp BJ, Ward SA, Wasserman K (1986) Respiratory markers of the anaerobic threshold. Adv Cardiol 35:47–64

Wilkerson DP, Koppo K, Barstow TJ, Jones AM (2004) Effect of work rate on the functional 'gain' of phase II pulmonary O₂ uptake response to exercise. Respir Physiol Neurobiol 142: 211–223