Research Quarterly for Exercise and Sport

Moderate-intensity oxygen uptake kinetics: is a mono-exponential function always appropriate to model the response?

Journal:	*Research Quarterly for Exercise and Sport*
Manuscript ID	17-05-PHY-04.R2
Manuscript Type:	Original Article
Manuscript Category:	Physiology
Keyword:	Phase II, Pulmonary VO2, Tau, VO2 kinetics

Moderate-intensity oxygen uptake kinetics: is a mono-exponential function always appropriate to model the response?

JULIAN DALE AND MARK GLAISTER.

School of Sport, Health, and Applied Sciences, St Mary's University, Strawberry Hill, Twickenham TW1 4SX, UK.

Contact information

M. Glaister, School of Sport, Health, and Applied Sciences, St Mary's University, Waldegrave Road, Strawberry Hill, Twickenham TW1 4SX, UK

Tel: 0208 240 4012

Fax: 0208 240 4212

E-mail: mark.glaister@stmarys.ac.uk

Running head: Moderate-intensity exercise oxygen uptake kinetics

ABSTRACT

Purpose: This study investigated the existence of the oxygen uptake ($\dot{V}O_2$) overshoot, and the effects of exercise intensity and fitness status on the $\dot{V}O_2$ response during moderate-intensity exercise. **Methods:** Twelve 'high-fitness' (age: 26 ± 5 years; height: 184.1 ± 5.4 cm; body-mass: 76.6 ± 8.9 kg; $\dot{V}O_{2peak}$: 59.0 ± 3.3 $mL \cdot kg^{-1} \cdot min^{-1}$) and eleven 'moderate-fitness' (age: 29 ± 5 years; height: 178.7 ± 7.5 cm; body-mass: 81.7 ± 10.9 kg; $\dot{V}O_{2peak}$: 45.2 ± 3.1 $mL \cdot kg^{-1} \cdot min^{-1}$) participants performed square-wave transitions from unloaded cycling to three different intensities (70%, 82.5%, and 95% of gas exchange threshold). The data were modelled using both a mono-exponential function (Model 1), and a function that included a switch-on component (Model 2). The overshoot was computed by subtracting the steady-state from the peak of the modelled response and by calculating the area of the curve that was above steady-state. **Results:** The goodness of fit was affected by model type (p = .002) and exercise intensity ($p < .001$). High-fitness participants displayed a smaller τ ($p < .05$), a larger amplitude ($p < .05$), and were more likely to overshoot the steady-state (p = .035). However, whilst exercise intensity did affect the amplitude ($p < .001$), it did not affect τ ($p \geq .05$) or the likelihood of an overshoot occurring (p = .389). **Conclusion:** Whilst exercise intensity did not alter the $\dot{V}O_2$ response, fitness status affected τ and the likelihood of an overshoot occurring. The overshoot questions the traditional approach to modelling moderate-intensity $\dot{V}O_2$ data.

Key Words: Phase II; Pulmonary $\dot{V}O_2$; Tau; $\dot{V}O_2$ kinetics

Following a sudden step change in exercise intensity the new energetic requirement cannot be met instantaneously by the aerobic energy-system. However, stored adenosine triphosphate (ATP) and ATP that is re-synthesized by the anaerobic energy pathways allows this intensity of exercise to be performed, with the difference between the desired and the actual oxygen uptake ($\dot{V}O_2$) forming the oxygen (O_2) deficit (Timmons, Gustafsson, Sundberg, Jansson, & Greenhaff, 1998). The mathematical function used to model the $\dot{V}O_2$ response varies depending on the intensity of exercise performed. Following the cardio-dynamic phase, during both moderate- and severe-intensity exercise, the $\dot{V}O_2$ on-response is well described by a mono-exponential function, whereas during both heavy- and very-heavy-intensity exercise, the presence of the $\dot{V}O_2$ slow component dictates that the addition of a second, delayed, exponential component provides a preferred function for modelling the response (Özyener, Rossiter, Ward, & Whipp, 2001).

The 'moderate-intensity' domain represents all exercise intensities beneath the lactate threshold (Rossiter, 2011). During moderate-intensity exercise, it was traditionally believed that the response adhered to the principles of first-order linear kinetics (McNarry, Kingsley, & Lewis, 2012), implying that the time constant (τ) was unaffected by exercise intensity (DiMenna & Jones, 2009). Whilst a substantial volume of research has found τ to be invariant within this domain (Barstow, Casaburi, & Wasserman, 1993; Barstow & Mole, 1991; Hughson & Morrissey, 1982; Macphee, Shoemaker, Paterson, & Kowalchuk, 2005; Wilkerson, Koppo, Barstow, & Jones, 2004), in a review of the literature, Robergs (2014) presented evidence from several studies to suggest that τ actually increases with intensity (Bowen et al., 2011; Brittain, Rossiter, Kowalchuk, & Whipp, 2001; Carter, Pringle, Jones, & Doust, 2002; Casaburi, Barstow, Robinson, & Wasserman, 1989; Hughson & Morrisey, 1983; Koppo, Bouckaert, & Jones, 2004a). Moreover, Robergs (2014) proposed that, based on data from Hickson, Bomze, and Hollozy (1978), endurance training could dampen the increase in τ with intensity, creating an interaction effect.

One issue that needs to be addressed, however, before revisiting the idea of differential effects of fitness status on τ within the moderate-intensity domain, is the possibility that well-trained individuals display a transient overshoot in $\dot{V}O_2$ before a steady-state is achieved. Whilst a $\dot{V}O_2$

Email: RQESjournal@illinois.edu Address: Dept. of Kinesiology & Community Health, University of Illinois, Urbana, IL 61801

overshoot has not frequently been reported in the literature, the available evidence suggests that this response may occur in well-trained cyclists (Hoogeveen & Keizer, 2003; Kilding & Jones, 2008; Koppo, Whipp, Jones, Aeyels, & Bouckaert, 2004b) and may be more commonly found when low-intensity exercise transitions are performed (Koppo et al., 2004b). Having averaged the response from six identical transitions, both Kilding and Jones (2008) and Koppo et al. (2004b) quantified an overshoot by subtracting the steady-state $\dot{V}O_2$ (the average $\dot{V}O_2$ during the last 30 s of exercise) from the peak of the response and by also calculating the area of overshoot that was greater than the steady-state using integration. Although the use of repeated transitions reduces the level of noise associated with $\dot{V}O_2$ data, it may be more appropriate to use a mathematical model to fit the data before determining the $\dot{V}O_2$ overshoot. Indeed, Hoogeveen and Keizer (2003) proposed a function that utilises the traditional mono-exponential equation with the addition of a 'switch-on' component to account for the $\dot{V}O_2$ overshoot. However, to-date, no study has attempted to fit $\dot{V}O_2$ data using this function or to quantify the overshoot using a mathematical model. The purpose of the current study was, therefore, to investigate the existence of the $\dot{V}O_2$ overshoot, and to examine the effects of fitness status and exercise intensity on the pattern of the $\dot{V}O_2$ response.

Methods

Participants

Twelve endurance-trained ('high-fitness') cyclists ($\dot{V}O_{2peak}$ > 55 mL·kg^{-1}·min^{-1}) and eleven active ('moderate-fitness') individuals ($\dot{V}O_{2peak}$ < 50 mL·kg^{-1}·min^{-1}), who participated in a variety of sports (five cyclists, three racket-sport players, two weight-trainers, and one runner), volunteered to participate in this study. Participant characteristics for the high- and moderate-fitness groups are displayed in Table 1. Prior to commencing the study, all participants completed a physical activity readiness questionnaire and provided written informed consent. Participants were required to be at least three hours post-prandial, to avoid strenuous exercise and alcohol for 24 hours, and caffeine for

Email: RQESjournal@illinois.edu Address: Dept. of Kinesiology & Community Health, University of Illinois, Urbana, IL 61801

12 hours, prior to testing. The study was performed under the guidelines of the Declaration of Helsinki and was granted ethical approval by St. Mary's University Ethics Committee.

Experimental Overview

All participants were initially required to complete two incremental cycling tests to evaluate the $\dot{V}O_2$-power output relationship, the gas exchange threshold (GET), and $\dot{V}O_{2peak}$. During each of the subsequent trials, the participants performed three 10-minute cycling bouts at different exercise intensities. The exercise intensities were selected following pilot testing, with the aim of spanning the moderate-intensity spectrum. The order of the exercise bouts was randomised and 10 minutes separated each transition to allow $\dot{V}O_2$ to return to its baseline level. Participants were required to maintain a cadence of 80 rpm during all trials. To minimise diurnal variances, trials for each participant were conducted at approximately the same time of day.

Equipment

All exercise was performed on an electromagnetically-braked cycle ergometer (Excalibur Sport, Lode, Groningen, The Netherlands). During all trials, participants wore a facemask and head-cap assembly (7600 Series V2 Mask, Hans Rudolph, Shawnee, United States of America). A computerised metabolic measurement system (Oxycon Pro, Erich Jaeger GmbH, Hoechberg, Germany) was used to measure gas-exchange variables on a breath-by-breath basis. Prior to each trial, the flow sensor was calibrated using a multi-flow 3 L syringe and the gas-analyser was calibrated using gases of a known concentration (16% O_2; 5% CO_2) and the ambient conditions (temperature, pressure, and relative humidity) at the time of testing. In Trial 1, capillary blood samples were analysed for lactate concentration using an automated analyser (Biosen C-line Analyser, EFK Diagnostics, Barleben, Germany), which was calibrated prior to each trial in accordance with the manufacturer's guidelines.

Email: RQESjournal@illinois.edu Address: Dept. of Kinesiology & Community Health, University of Illinois, Urbana, IL 61801

Procedures

During the first visit to the laboratory measurements of height, body-mass, and body-fat (determined from a four-site skinfold protocol [Durnin & Womersley, 1974]) were taken. The cycle ergometer was then adjusted for the participant with the seat height and the handlebar positions recorded to facilitate replication in the subsequent trials. The participants then performed a step-incremental exercise test which started at an intensity of 75 W for the moderate-fitness group and at 100 W for the high-fitness group. Intensity increased for both groups by 20 W per stage. Stages lasted three minutes and at the end of each stage the participants stopped pedalling for 30 s to allow for a 20 µL capillary blood sample to be taken from the earlobe, which was subsequently analysed for lactate concentration. Exercise continued until a blood lactate concentration greater than 4 $mmol \cdot L^{-1}$ was recorded. The mean value of the $\dot{V}O_2$ data from the last 30 s of each stage was used to determine the $\dot{V}O_2$-power output relationship for each participant via linear regression. After five minutes of passive rest, participants performed a ramp test to exhaustion. The moderate-fitness group began at an intensity of 75 W with a ramp-rate of 5 W every 12 s and the high-fitness group began at 100 W with a ramp-rate of 5 W every 10 s. $\dot{V}O_{2peak}$ was calculated as the highest 30 s rolling average. The GET was determined from visual inspection of a plot of the rate of carbon dioxide produced ($\dot{V}CO_2$) versus $\dot{V}O_2$ from the ramp test using the V-slope method (Beaver, Wasserman, & Whipp, 1986). The GET was independently determined by two researchers, with the mean used as the confirmed value. Cycling intensities designed to elicit $\dot{V}O_2$ values of 70%, 82.5%, and 95% of the GET were then calculated using the $\dot{V}O_2$-power output relationship of each participant.

The remaining trials began with participants sitting passively on the ergometer for five minutes before a resting $\dot{V}O_2$ measurement (120 s average) was recorded. The participants then performed three 10-minute cycling bouts consisting of four minutes of unloaded pedalling, followed by six minutes at the desired intensity. As endurance-trained individuals have a higher $\dot{V}O_{2peak}$ and GET than their untrained counterparts (Koga, Shiojiri, & Kondo, 2005), it was expected that the

Email: RQESjournal@illinois.edu Address: Dept. of Kinesiology & Community Health, University of Illinois, Urbana, IL 61801

amplitude (signal) would be greater in the high-fitness participants for each of the intensity transitions. A greater signal results in an improved signal-to-noise ratio, meaning that those participants would be required to perform fewer repetitions of the transitions (Koga et al., 2005). Therefore, the high-fitness participants performed three repetitions, whilst the moderate-fitness participants performed four repetitions of each intensity transition.

Data Analysis

Analysis of the $\dot{V}O_2$ data began by removing any errant breaths that may have been caused by coughing, swallowing or sighing. A breath was considered to be errant if the value was outside four standard deviations of the local mean (the two breaths preceding and following the breath of interest). The data were then linearly interpolated to give second-by-second values, which were time aligned, and averaged to reduce the breath-by-breath noise. The onset of exercise was defined as time zero and the first 20 s of data (the cardio-dynamic phase) were excluded from the fitting field (Koppo et al., 2004a). The data were then modelled using a mono-exponential function (Equation 1); after which, the data were re-modelled with the inclusion of an additional ‘switch on’ component (Equation 2 [Hoogeveen & Keizer, 2003]). The parameters of both models were determined using non-linear least-squares regression techniques (XLfit, IDBS Ltd, Guildford, UK), where $\dot{V}O_2(t)$ is the absolute $\dot{V}O_2$ at any given time greater than TD_0 and $\dot{V}O_{2baseline}$ is the average $\dot{V}O_2$ during the last 60 s of unloaded pedalling; A is the amplitude, τ is the time constant, and TD_0 the time delay for the classic exponential equation; B represents a constant, TD_1 an independent time delay and c a rate constant for the switch-on element, whereby the amplitude of the switch-on component (A_1) equates to $B \cdot (e \cdot c)^{-1}$ (Hoogeveen & Keizer, 2003).

$$\dot{V}O_2(t) = \dot{V}O_{2baseline} + A * \left[1 - e^{-\frac{t - TD_0}{\tau}}\right] \quad (1)$$

$$\dot{V}O_2(t) = \dot{V}O_{2baseline} + A * \left[1 - e^{-\frac{t - TD_0}{\tau}}\right] + B * (t - TD_1) * \left[e^{-((t - TD_1) * c)}\right] \quad (2)$$

Email: RQESjournal@illinois.edu Address: Dept. of Kinesiology & Community Health, University of Illinois, Urbana, IL 61801

To deal with the possibility that Model 2, if unconstrained, might fail to achieve a steady-state and instead decrease progressively over time (Figure 1A), the parameters of the mono-exponential component were first derived with the possible overshoot data removed (Figure 1B). In the study by Kilding and Jones (2008), the authors reported that the overshoot lasted 51 ± 15 s. Therefore, in the current study, it was decided that 90 s of data (> mean + 2 × SD, reported by Kilding and Jones [2008]) would provide a sufficient duration of data removal to capture the overshoot. To select the start-point for data removal, the time-point equating to TD_0 plus 2 × τ from Model 1 was chosen. This was selected as the starting point as it kept a large percentage of the data during the initial growth-phase of the response prior to any possible overshoot, and also provided an individualised approach to the modelling process. The parameters of the switch-on component were then calculated by applying Model 2 to the full data set with A, τ, and TD_0 fixed (Figure 1C). The goodness of model fit (r^2) for Model 1 and Model 2 was computed by software (XLfit, IDBS Ltd, Guildford, UK).

Overshoot Quantification

The overshoot was quantified using the steady-state of Model 2 (defined as the average of the last 60 s of the modelled data). If the modelled response displayed a continuous growth to the steady-state, no further action was taken. However, if the peak of the modelled response occurred prior to the steady-state being achieved the overshoot was computed by subtracting the steady-state from the peak of the response and then by determining (via integration) the area of the curve that was greater than the steady-state (Figure 2).

Statistical Analyses

All statistical analyses were conducted using the Statistical Package for the Social Sciences software (SPSS Version 22, IBM, Armonk, United States of America). Independent *t*-tests were used to assess differences between group characteristics (Table 1). Dependent *t*-tests were used to establish whether the participants' steady-state $\dot{V}O_2$ in the experimental trials (average $\dot{V}O_2$ during the last 60 s of exercise) matched the predicted values. The inter-rater reliability of the GET estimates was evaluated using the intraclass correlation coefficient (ICC). X^2 tests of independence were used to assess the effects of both fitness status and exercise intensity on the likelihood of an overshoot occurring. In individuals where a positive integral was computed, Pearson's correlation coefficient was calculated to evaluate the relationship between $\dot{V}O_{2peak}$ and the magnitude of the overshoot. A 2 × 3 mixed ANOVA was used to assess the effects of fitness status and exercise intensity on $\dot{V}O_{2baseline}$, the parameters of the mono-exponential component, and the amplitude and the time delay of the switch-on component. (If the assumption of homogeneity of variance was not satisfied, appropriate transformations were made. If the data were not normally distributed, a Mann Whitney U test was used to examine the effect of fitness status and a Friedman's ANOVA was used to examine the effect of exercise intensity). Finally, a 2 × 2 × 3 (model × fitness status × exercise intensity) mixed ANOVA was used to evaluate the goodness of model fit. If the assumption of sphericity was violated, the Greenhouse-Geisser correction was applied. *Post hoc* tests were performed using a Bonferroni correction. Statistical significance was set *a priori* at $p < .05$.

Results

Model parameters

The average time course of $\dot{V}O_2$ over the 10-minute cycling period for the two groups at the three intensities is displayed in Figure 3. The goodness of fit, for the two models, for the two groups, over the three exercise intensities, is displayed in Table 2. A significant main effect was found for model type ($F_{(1,21)} = 11.900$, $p = .002$, $\eta^2_{partial} = .362$) and exercise intensity ($F_{(2,42)} = 55.434$, $p < .001$, $\eta^2_{partial} = .725$), with the goodness of fit increasing significantly with intensity. However, fitness status did not significantly ($F_{(1,21)} = .739$, $p = .400$, $\eta^2_{partial} = .034$) affect the goodness of fit. $\dot{V}O_{2baseline}$ and the parameters of the classic mono-exponential component of both Model 1 and Model 2, as well as the amplitude of the switch-on component and TD_1 are displayed in Table 3. $\dot{V}O_{2baseline}$, the amplitude

Email: RQESjournal@illinois.edu Address: Dept. of Kinesiology & Community Health, University of Illinois, Urbana, IL 61801

of the switch-on component, TD_0 (irrespective of model), and TD_1 were not significantly affected ($p \geq .05$) by fitness status or exercise intensity. There was also no significant effect of exercise intensity on τ (Model 1: $F_{(2,42)} = 1.002$, $p = .376$, $\eta^2_{partial} = .046$; Model 2: $F_{(2,42)} = 2.092$, $p = .136$, $\eta^2_{partial} = .091$). However, there was a significant effect of exercise intensity on amplitude (Model 1: $F_{(1.308,27.471)} = 318.594$, $p < .001$, $\eta^2_{partial} = .938$; Model 2: $F_{(1.352,28.394)} = 290.752$, $p < .001$, $\eta^2_{partial} = .933$), with values increasing progressively, and significantly, with increases in intensity. Fitness status had a significant effect on amplitude (Model 1: $F_{(1.,21)} = 5.992$, $p = .023$, $\eta^2_{partial} = .222$; Model 2: $F_{(1,21)} = 5.899$, $p = .024$, $\eta^2_{partial} = .219$) and τ (Model 1: $F_{(1,21)} = 6.148$, $p = .022$, $\eta^2_{partial} = .226$; Model 2: $F_{(1,21)} = 11.274$, $p = .003$, $\eta^2_{partial} = .349$), with the high-fitness group displaying a greater amplitude and a smaller τ. A significant fitness status × exercise intensity interaction was observed for amplitude (Model 1: $F_{(1.308,27.471)} = 5.995$, $p = .015$, $\eta^2_{partial} = .222$; Model 2: $F_{(1.352,28.394)} = 5.099$, $p = .023$, $\eta^2_{partial} = .195$), with the magnitude of the effect of fitness status increasing with increases in exercise intensity. In contrast, there was no fitness status × exercise intensity interaction on τ (Model 1: $F_{(2,42)} = .345$, $p = .710$, $\eta^2_{partial} = .016$; Model 2: $F_{(2,42)} = .219$, $p = .804$, $\eta^2_{partial} = .010$).

$\dot{V}O_2$ overshoot

Example transitions where a noticeable overshoot, a small overshoot, and no overshoot were found are displayed in Figure 4. In 61% of the transitions performed by the moderate-fitness group and in 83% of the transitions performed by the high-fitness group, the peak of the modelled response was greater than the steady-state (Table 4). The results of the X^2 tests of independence revealed a significant relationship between fitness status [X^2 (1, n = 69) = 4.457, $p = .035$] and the occurrence of an overshoot, but not exercise intensity [X^2 (2, n = 69) = 1.888, $p = .389$]. The integral volume and the difference between the peak and steady-state values for the participants that displayed an overshoot are shown in Table 5. Whilst weak to moderate correlations were found between $\dot{V}O_{2peak}$ and the magnitude of the overshoot (see Figure 5), in all cases, the relationship was found to be non-significant ($p \geq .05$).

Validity and Reliability

The inter-rater level of agreement for the assessment of the GET was high (ICC = .972). In both the high- and moderate-fitness groups all steady-state values of $\dot{V}O_2$ were below the GET. However, the actual $\dot{V}O_2$ steady-state was lower than the predicted value (see Table 6) for both the high- (mean difference = 95 $mL \cdot min^{-1}$; 95% likely range 43 to 147 $mL \cdot min^{-1}$) and moderate-fitness (mean difference = 53 $mL \cdot min^{-1}$; 95% likely range 5 to 101 $mL \cdot min^{-1}$) groups during the 95% GET transition; as well as for the high-fitness group (mean difference = 96 $mL \cdot min^{-1}$; 95% likely range 49 to 144 $mL \cdot min^{-1}$) during the 82.5% GET transition.

Discussion

The aim of this study was to investigate the existence of the $\dot{V}O_2$ overshoot, as well as the effects of fitness status and exercise intensity on the $\dot{V}O_2$ response during moderate-intensity exercise. The current study was the first to model $\dot{V}O_2$ data using a function that included a switch-on component. The goodness of model fit was affected by both model type and exercise intensity. The $\dot{V}O_2$ overshoot was more likely to occur in individuals with a high level of aerobic fitness. However, the relationship between the size of the overshoot and the individual's $\dot{V}O_{2peak}$ ranged from weak to moderate and was not statistically significant. Individuals with a high aerobic fitness-status were also found to have a significantly smaller τ. However, exercise intensity did not affect τ or the likelihood of an overshoot occurring. There was also no evidence of an exercise intensity by fitness status interaction on τ. However, an interaction effect was noted for the amplitude of the traditional exponential equation.

The present study modelled data using the mathematical function that was proposed by Hoogeveen and Keizer (2003). The analysis revealed that model type and exercise intensity affected the goodness of model fit. An enhancement in the goodness of model fit alongside an increase in exercise intensity was expected and was most likely explained by an improvement in the signal to noise ratio (Koga et al., 2005). With regards to model type, it was not surprising that the goodness of fit improved by applying a more complex function to the data set; especially when considering the complex function included the components of the more basic model. However, in cases where a large overshoot was computed (see Figure 4A), there was a clear discrepancy between the fit of the two models. This finding not only raises questions about the suitability of applying a mono-exponential growth function to all moderate-intensity data sets, but also raises concerns about the procedure used to calculate the O_2 deficit (Hoogeveen & Keizer, 2003; Kilding & Jones, 2008). However, in cases where a small overshoot was computed (see Figure 4B), the difference between the models becomes less clear. Considering the mean overshoot values found, and the large levels of inter- and intra-participant variability, as well as the possibility that Model 2 may be biased towards suggesting that an overshoot occurred, it would be advisable for criteria to be developed to determine the magnitude of the change that depicts a meaningful overshoot.

The suggestion that the $\dot{V}O_2$ response does not always rise to the new steady-state following a mono-exponential time course has been made previously (Hoogeveen & Keizer, 2003; Kilding & Jones, 2008; Koppo et al., 2004b). However, the current findings were not in absolute agreement with those of Koppo et al. (2004b). Koppo et al. (2004b) examined the effects fitness status (well-trained and untrained) and exercise intensity (60% GET, 80% GET, and 50% of the difference between GET and $\dot{V}O_{2max}$) on the $\dot{V}O_2$ overshoot. From their findings, the authors suggested that an overshoot may only occur during moderate-intensity exercise transitions, that it may be more prevalent at lower work-rates, and that it may only occur in highly trained individuals. Whilst the current findings indicated that an overshoot was more likely to occur in individuals with a high aerobic capacity, there was no apparent relationship between $\dot{V}O_{2peak}$ and the magnitude of the overshoot (both integral volume and peak minus steady state), and a substantial percentage of the moderate-fitness group also displayed this response. In addition, exercise intensity did not affect the likelihood of an overshoot occurring. Overall, despite differences in the methods used to quantify the overshoot it is difficult to explain between-study discrepancies in the prevalence of the response; particularly since the 'moderately-trained' participants of the current study were similar to the 'untrained' participants of Koppo et al. (2004b) ($\dot{V}O_{2max}$: 42.9 ± 5.1 mL·kg^{-1}·min^{-1}).

From a physiological perspective, the mechanisms that could account for the $\dot{V}O_2$ overshoot remain a topic for debate. Both Koppo et al. (2004b) and Kilding and Jones (2008) noted a heart-rate overshoot in several of their data sets. However, both authors reported that the overshoot in heart-rate was not consistently found in participants that demonstrated a $\dot{V}O_2$ overshoot. Furthermore, Hoogeveen and Keizer (2003) did not see an overshoot in heart-rate in any of their participants; although, the authors did suggest that alterations in stroke volume remain a possible explanatory factor (Hoogeveen & Keizer, 2003). However, as heart-rate was not monitored during the constant load trials in the current study, it is not possible to support or refute these suggestions. A transient hyper-ventilatory response, which would result in an increase in diaphragmatic work and thus a subsequent increase in whole-body $\dot{V}O_2$, was also discounted by both Kilding and Jones (2008) and Koppo et al. (2004b), as the responses in tidal volume, breathing frequency, end-tidal gas tensions, $\dot{V}CO_2$, and respiratory exchange ratio were as expected. Kilding and Jones (2008) did, however, speculate that the $\dot{V}O_2$ overshoot was most likely to have been caused by either a non-constant ATP requirement, with the demand being greater at exercise onset, or by a transient over recruitment of muscle fibres.

With regards to the kinetics of the response, irrespective of the model selected, the amplitude increased with intensity and was greater in the high-fitness group, whereas τ was unaffected by exercise intensity and was smaller in the high-fitness group. The amplitude response was in-line with previous research (Koppo et al., 2004a) and was, therefore, as expected. A reduction in τ as a result of endurance training is also in agreement with previous findings, having been demonstrated when transitions are performed at the same absolute (Norris & Petersen, 1998) and the same relative exercise-intensities (Cleuziou et al., 2005; Dogra, Spencer, Murias, & Paterson, 2013; Grey et al., 2015), and during both cross-sectional (Koppo et al., 2004a; Marwood, Roche, Rowland, Garrard, & Unnithan, 2010) and longitudinal research (Norris & Petersen, 1998). With regards to exercise intensity, when transitions have been performed from rest or a low baseline, several studies have found τ to be unaffected by exercise intensity in the moderate domain (Barstow et al., 1993; Barstow & Mole, 1991; Hughson & Morrissey, 1982; Macphee et al., 2005; Wilkerson et al., 2004). However, this was contrary to the suggestion by Robergs (2014) that τ increases with intensity within this domain. The current data also provided no evidence to suggest that endurance training dampens the increase in τ with intensity.

From a methodological perspective, additional considerations include: the procedure that was used to quantify the $\dot{V}O_2$-power output relationship, as well as modifications that were made to the modelling process. Initially, on a number of occasions, when Model 2 was applied to the data set, the derived model parameters suggested that if the exercise bout was extended, then the $\dot{V}O_2$ requirement would continue to decrease for some time. To overcome this issue, modifications were made to the modelling procedure to ensure that a steady-state would be achieved. This restriction may not, however, have been necessary if the constant load trials had been conducted over a greater duration, as the impact of fluctuations in $\dot{V}O_2$ would have been reduced. With regards to the $\dot{V}O_2$-power output relationship, within $\dot{V}O_2$ kinetics research, this relationship has frequently been established using a ramp exercise-test. However, the increase in $\dot{V}O_2$ lags behind the increase in work-rate during a ramp test (Faude, Meyer, & Kindermann, 2006) and if this lag is not accounted for then the derived power outputs could be overestimated in the subsequent constant-load trials. Consequently, the participants may not actually perform moderate-intensity exercise. Therefore, in the current study, the $\dot{V}O_2$-power output relationship was calculated by averaging the last 30 s of $\dot{V}O_2$ data gathered during each three-minute stage of a step incremental exercise-test. During the subsequent constant-load trials, when comparing the actual steady-state $\dot{V}O_2$ with the desired levels, this method appeared to be appropriate for the lowest exercise intensity selected. However, the power outputs for both the 82.5% GET and 95% GET transitions in the high-fitness group and the 95% GET transition in the moderate-fitness group appear to have been underestimated.

The deviations found in the $\dot{V}O_2$-power output relationship could be explained by the $\dot{V}O_2$ slow component. During exercise transitions at the same absolute intensity, endurance training has been shown to dampen the magnitude of the $\dot{V}O_2$ slow component (Womack et al., 1995). However, when transitions were performed at the same relative intensity, Koppo et al. (2004a) found that the onset of the slow component was earlier and the time constant smaller in trained individuals. This could explain why the distortion of the relationship was relatively greater in the high-fitness group. Then again, using an incremental exercise test similar to the protocol used in the current study, Muniz-Pumares, Pedlar, Godfrey, and Glaister (2017) found that the $\dot{V}O_2$-power output relationship remained linear even when exercise intensity increased above the lactate threshold. Therefore, as it is not currently possible to confidently account for the pattern of this response, to quantify the $\dot{V}O_2$-power output relationship for exercise transitions in the moderate-intensity domain, it is suggested that a series of constant load trials, at intensities beneath the GET, are performed.

In conclusion, the current investigation found that an overshoot was not exclusively found in individuals with a high aerobic capacity, but it was more likely to occur in these individuals. Irrespective of the model selected, the amplitude was found to be higher and τ smaller in the high-fitness group. Whilst exercise intensity affected the amplitude, it did not affect τ or the likelihood of an overshoot occurring. Finally, deriving the $\dot{V}O_2$-power output relationship from a three-minute stage-duration incremental test may underestimate the subsequent power outputs for exercise transitions in the upper regions of the moderate-intensity domain.

What does this article add?

The use of a mono-exponential function to model data within the moderate intensity-domain has been a central component of $\dot{V}O_2$ kinetics research, providing information on the magnitude and the rate of the response. However, if, as observed in the present study and several others (Hoogeveen & Keizer, 2003; Kilding & Jones, 2008; Koppo et al., 2004b), a $\dot{V}O_2$ overshoot occurs, the approach may not provide the best representation of the data. Modelling overshoot data using a mono-exponential function may result in a smaller τ and an amplitude that exceeds the eventual steady-state (Kilding & Jones, 2008). However, the severity of the consequences of using a mono-exponential function on the resultant amplitude, τ, and O_2 deficit requires further investigation. Additionally, given the possibility that the procedure used in the present study to identify the presence of an overshoot may be biased towards detecting this phenomenon, it is recommended that minimum thresholds are defined to identify when an elevation in $\dot{V}O_2$ above the steady-state depicts a meaningful overshoot.

Acknowledgements

The authors would like to express their gratitude to all the participants for their enthusiasm and commitment to the project.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

Barstow, T. J., Casaburi, R., & Wasserman, K. (1993). O_2 uptake kinetics and the O_2 deficit as related to exercise intensity and blood lactate. *Journal of Applied Physiology, 75,* 755-762.

Barstow, T. J., & Molé, P. A. (1991). Linear and nonlinear characteristics of oxygen uptake kinetics during heavy exercise. *Journal of Applied Physiology, 71,* 2099-2106.

Beaver, W. L., Wasserman, K., & Whipp, B. J. (1986). A new method for detecting anaerobic threshold by gas exchange. *Journal of Applied Physiology, 60,* 2020-2027.

Bowen, T. S, Murgatroyd, S. R., Cannon, D. T., Cuff, T. J., Lainey, A. E., Marjerrison, A. D., . . . Rossiter, H. B. (2011). A raised metabolic rate slows pulmonary O_2 uptake kinetics on transition to moderate-intensity exercise in humans independently of work rate. *Experimental Physiology, 96,* 1049-1061.

Brittain, C. J., Rossiter, H. B., Kowalchuk, J. M., & Whipp, B. J. (2001). Effect of prior metabolic rate on the kinetics of oxygen uptake during moderate-intensity exercise. *European Journal of Applied Physiology, 86,* 125-134.

Carter, H., Pringle, J. S., Jones, A. M., & Doust, J. H. (2002). Oxygen uptake kinetics during treadmill running across exercise intensity domains. *European Journal of Applied Physiology, 86,* 347-354.

Casaburi, R., Barstow, T. J., Robinson, T., & Wasserman, K. (1989). Influence of work rate on ventilatory and gas exchange kinetics. *Journal of Applied Physiology, 67,* 547-555.

Cleuziou, C., Perrey, S., Lecoq, Candau, R., Courteix, & Obert, P. (2005). Oxygen uptake kinetics during moderate and heavy intensity exercise in humans: the influence of hypoxia and training status. *International Journal of Sports Medicine, 26,* 356-362.

DiMenna, F. J. & Jones A. M. (2009). "Linear" versus "nonlinear" $\dot{V}O_2$ responses to exercise: reshaping traditional beliefs. *Journal of Exercise Science & Fitness, 7,* 67-84.

Email: RQESjournal@illinois.edu Address: Dept. of Kinesiology & Community Health, University of Illinois, Urbana, IL 61801

Dogra, S., Spencer, M. D., Murias, J. M., & Paterson, D. H. (2013). Oxygen uptake kinetics in endurance trained and untrained post-menopausal women. *Applied Physiology, Nutrition, and Metabolism 38,* 154-160.

Durnin, J. V. G. A, & Womersley, J. (1974). Body fat assessed from total body density and its estimation from skinfold thickness: measurements on 481 men and women aged from 16 to 72 years. *The British Journal of Nutrition, 32,* 77-97.

Faude, O., Meyer, T., & Kindermann, W. (2006). The work rate corresponding to ventilator threshold during steady-state and ramp exercise. *International Journal of Sports Physiology and Performance, 1,* 222-232.

Grey, T. M., Spencer, M. D., Belfry, G. R., Kowalchuk, J. M., Paterson, D. H., & Muris, J. M. (2015). Effects of age and long-term endurance training on $\dot{V}O_2$ kinetics. *Medicine & Science in Sports & Exercise, 47,* 289-298.

Hickson, R. C., Bomze, H. A., & Hollozy, J. O. (1978). Faster adjustment of O_2 uptake to the energy requirement of exercise in the trained state. *Journal of Applied Physiology: Respiratory, Environmental and Exercise Physiology, 44,* 877-881.

Hoogeveen, A. R., & Keizer, H. A. (2003). The $\dot{V}O_2$ overshoot at the onset of constant-load exercise in elite cyclists: an undescribed phenomenon. *Journal of Exercise Physiology Online, 6, 34-41.*

Hughson, R. L., & Morrissey, M. (1982). Delayed kinetics of respiratory gas exchange in the transition from prior exercise. *Journal of Applied Physiology: Respiratory, Environmental and Exercise Physiology, 52,* 921-929.

Kilding, A. E., & Jones, A. M. (2008). $\dot{V}O_2$ 'overshoot' during moderate-intensity exercise in endurance-trained athletes: The influence of exercise modality. *Respiratory Physiology & Neurobiology, 160,* 139-146.

Email: RQESjournal@illinois.edu Address: Dept. of Kinesiology & Community Health, University of Illinois, Urbana, IL 61801

Koga, S., Shiojiri, T., & Kondo, N. (2005). Measuring $\dot{V}O_2$ kinetics: the practicalities. In A. M. Jones, & D.C. Poole (Eds.), *Oxygen uptake kinetics in sport, exercise and medicine* (pp 39-61). London: Routledge

Koppo, K., Bouckaert, J., & Jones, A. M. (2004a). Effects of training status and exercise intensity on phase II $\dot{V}O_2$ kinetics. *Medicine & Science in Sports & Exercise, 36,* 225-232.

Koppo, K., Whipp, B. J., Jones, A. M., Aeyels, D., & Bouckaert, J. (2004b). Overshoot in $\dot{V}O_2$ following the onset of moderate-intensity cycle exercise in trained cyclists. *European Journal of Applied Physiology, 93,* 366-373.

MacPhee, S. L., Shoemaker, J. K., Paterson, D. H., & Kowalchuk, J. M. (2005). Kinetics of O_2 uptake, leg blood flow, and muscle deoxygenation are slowed in the upper compared with the lower region of the moderate-intensity exercise domain. *Journal of Applied Physiology, 99,* 1822-1834.

Marwood, S., Roche, D., Rowland, T., Garrard, M., & Unnithan, V. B. (2010). Faster pulmonary oxygen uptake kinetics in trained versus untrained male adolescents. *Medicine & Science in Sports & Exercise, 42,* 127-134.

McNarry, M. A., Kingsley, M. I., Lewis, M. J. (2012). Influence of exercise intensity on pulmonary oxygen uptake kinetics in young and late middle-aged adults. *American Journal of Physiology. Regulatory, Integrative and Comparative Physiology, 303,* 791-798.

Muniz-Pumares, D., Pedlar, C., Godfrey, R., & Glaister, M. (2017). The effect of the oxygen uptake-power output relationship on the prediction of supramximal oxygen demands. *Journal of Sports Medicine and Physical Fitness, 57,* 1-7.

Norris, S. R., & Petersen, S. R. (1998). Effects of endurance training on transient oxygen uptake responses in cyclists. *Journal of Sports Sciences, 16,* 733-738.

Özyener, F., Rossiter, H. B., Ward, S. A., & Whipp, B. J. (2001). Influence of exercise intensity on the on- and off-transient kinetics of pulmonary oxygen uptake in humans. *The Journal of Physiology, 533,* 891-902.

Robergs, R. A., (2014). A critical review of the history of low- to moderate-intensity steady-state VO_2 kinetics. *Sports Medicine, 44,* 641-653.

Rossiter, H. B. (2011). Exercise: kinetic considerations for gas exchange. *Comprehensive Physiology, 1,* 203-244.

Timmons, J. A., Gustafsson, T., Sundberg, C. J., Jansson, E., & Greenhaff, P. L. (1998). Muscle acetyl group availability is a major determinant of oxygen deficit in humans during submaximal exercise. *The American Journal of Physiology, 274,* 377-380.

Wilkerson, D. P., Koppo, K., Barstow, T. J., & Jones A. M. (2004). Effect of work rate on the functional 'gain' of phase II pulmonary O_2 uptake response to exercise. *Respiratory Physiology & Neurobiology, 142,* 211-223.

Womack, C. J., Davis, S. E., Blumer, J. L., Barrett, E., Weltman, A. L., & Gaesser, G. A. (1995). Slow component of O_2 uptake during heavy exercise: adaptation to endurance training. *Journal of Applied Physiology, 79,* 838-845.

Email: RQESjournal@illinois.edu Address: Dept. of Kinesiology & Community Health, University of Illinois, Urbana, IL 61801

Table 1. Participant characteristics for the two fitness groups. Data are displayed as mean ± standard deviation.

Fitness Status	Age (years)	Height (cm)	Body-mass (kg)	Body-fat (%)	Training volume (hours·week^{-1})	Relative $\dot{V}O_{2peak}$ (mL·kg^{-1}·min^{-1})	Power at GET (W)
High	26 ± 5	184.1 ± 5.4	76.6 ± 8.9	14.7 ± 3.5*	8.0 ± 2.7	59.0 ± 3.3*	155 ± 30*
Moderate	29 ± 5	178.7 ± 7.5	81.7 ± 10.9	18.5 ± 4.9	7.8 ± 3.0	45.2 ± 3.1	127 ± 33

Note: GET = Gas Exchange Threshold; * denotes a significant difference ($p < 0.05$) from the moderate-fitness group.

Table 2. The goodness of model fit for the two model types over the three exercise intensities for the two groups. Significant main effects were found for both model type and exercise intensity.

Model Type	Model 1			Model 2		
Exercise Intensity	70% GET	82.5% GET	95% GET	70% GET	82.5% GET	95% GET
Moderate Fitness	0.42 ± 0.21	0.56 ± 0.17	0.69 ± 0.11	0.45 ± 0.21	0.58 ± 0.17	0.70 ± 0.11
High Fitness	0.39 ± 0.13	0.53 ± 0.09	0.61 ± 0.14	0.41 ± 0.13	0.54 ± 0.09	0.63 ± 0.14

Note: GET denotes the gas exchange threshold.

Table 3. The kinetic parameters of the two models for the two groups (high- versus moderate-fitness) over the three exercise intensities (70%, 82.5%, and 95% of the gas exchange threshold).

		70% GET		82.5% GET		95% GET		Significance
		High	Moderate	High	Moderate	High	Moderate	
	$\dot{V}O_{2baseline}$ (mL·min^{-1})	969 ± 106	994 ± 101	951 ± 106	993 ± 118	948 ± 93	994 ± 95	
Model 1	A_0 (mL·min^{-1})	697 ± 208	511 ± 242	988 ± 253*	722 ± 227	1296 ± 321*	967 ± 300	†, ‡, §
	τ (s)	16.3 ± 4.9	21.7 ± 8.7	14.6 ± 3.2	22.6 ± 11.3	14.4 ± 4.7	21.2 ± 8.3	‡
	TD_0 (s)	18.4 ± 4.7	19.2 ± 4.7	19.0 ± 1.8	17.6 ± 3.5	18.8 ± 3.2	17.0 ± 3.9	
Model 2	A_0 (mL·min^{-1})	692 ± 205	507 ± 243	981 ± 251*	719 ± 225	1285 ± 321*	962 ± 296	†, ‡, §
	τ (s)	18.6 ± 6.3	25.4 ± 9.3	18.2 ± 5.2	27.6 ± 10.6	16.5 ± 5.3	21.6 ± 6.5	‡
	TD_0 (s)	16.9 ± 6.7	17.8 ± 5.4	17.2 ± 2.9	14.8 ± 5.2	17.8 ± 3.2	16.9 ± 3.3	
	A_1 (mL·min^{-1})	47.6 ± 34.8	27.8 ± 68.2	70.1 ± 33.2	43.7 ± 55.5	74.0 ± 65.2	31.7 ± 44.4	
	TD_1 (s)	8.8 ± 71.8	27.2 ± 10.0	30.2 ± 4.1	29.7 ± 4.5	30.7 ± 6.8	26.9 ± 9.1	

Note: $\dot{V}O_{2baseline}$ denotes the average oxygen uptake recorded during the last 60 s of unloaded pedalling; A_0 is the amplitude, τ is the time constant and TD_0 is the time delay for the mono-exponential growth component for both Model 1 and Model 2; A_1 denotes the amplitude and TD_1 the time delay for the switch-on component for Model 2. GET denotes the gas exchange threshold. * denotes a significant difference ($p < 0.05$) between the high- and moderate-fitness groups at the same exercise intensity, † denotes a significant ($p < 0.05$) effect of exercise intensity, ‡ denotes a significant ($p < 0.05$) effect of fitness status, and § denotes a significant ($p < 0.05$) exercise intensity × fitness status interaction. The data are displayed as mean ± standard deviation.

Table 4. The number and percentage of participants where an overshoot was computed.

Fitness Status	70% GET	82.5% GET	95% GET	Overall
High	9/12 (75%)	12/12 (100%)	9/12 (75%)	30/36 (83%)
Moderate	7/11 (64%)	7/11 (64%)	6/11 (55%)	20/33 (61%)
Overall	16/23 (70%)	19/23 (83%)	15/23 (65%)	

Note: GET denotes the gas exchange threshold.

Table 5. The mean ± standard deviation of the peak minus the steady-state and the integral volume for high- and moderate-fitness participants where a positive integral ($\dot{V}O_2$ overshoot) was computed.

	High			Moderate		
	70% GET (n = 9)	82.5% GET (n = 12)	95% GET (n = 9)	70% GET (n = 7)	82.5% GET (n = 7)	95% GET (n = 6)
Peak minus steady-state ($mL \cdot min^{-1}$)	33.2 ± 23.9	34.7 ± 15.4	62.7 ± 32.6	34.8 ± 20.6	33.3 ± 30.8	31.3 ± 41.5
Integral volume (mL)	42.9 ± 30.7	47.3 ± 22.3	85.1 ± 44.1	54.6 ± 37.2	45.2 ± 43.5	44.8 ± 55.6

Note: GET denotes the gas exchange threshold.

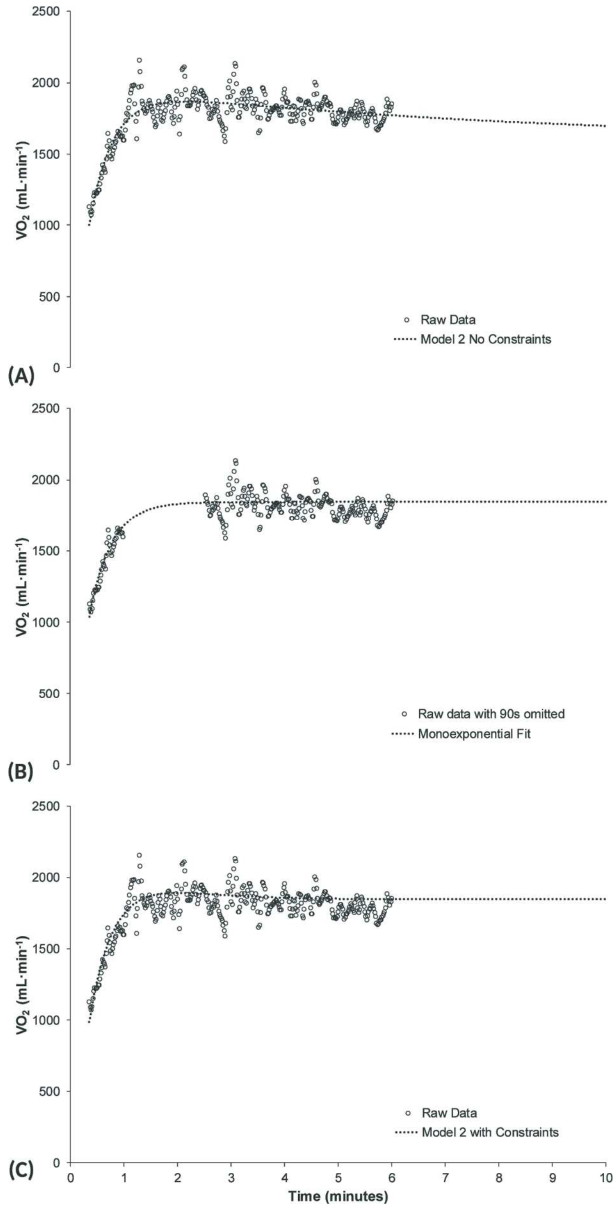

Figure 1. Application of Model 2 extrapolated for a further four minutes to an example data set with: (A) no constraints; (B) only the mono-exponential component applied to the data set with 90 s of data removed; and (C) with the mono-exponential parameters constrained.

113x224mm (300 x 300 DPI)

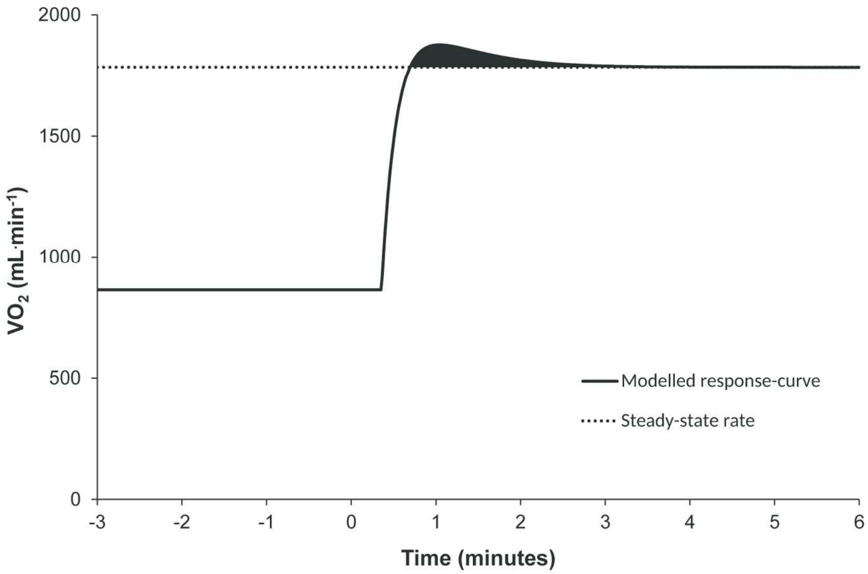

Figure 2. Quantification procedure for the $\dot{V}O_2$ overshoot. The shaded area beneath the modelled response-curve that is greater than the steady-state rate depicts the overshoot.

168x110mm (300 x 300 DPI)

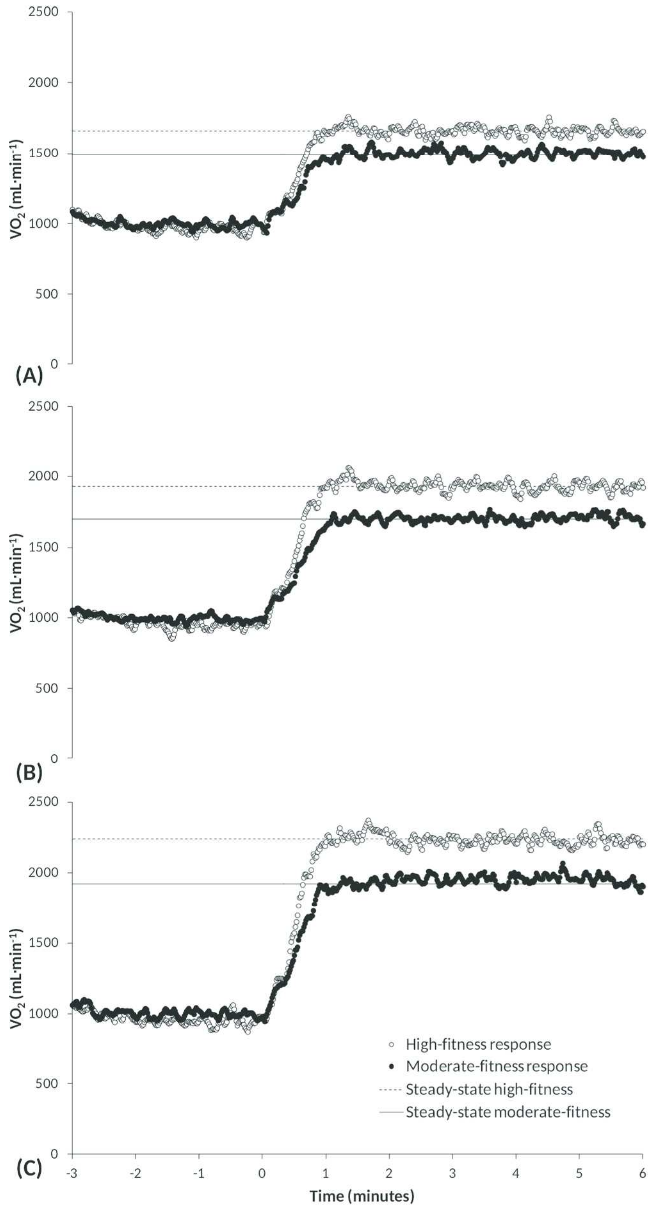

Figure 3. The mean VO_2 response for the high- and moderate-fitness groups during 10 minutes of cycling, transitioning from unloaded pedalling to (A) 70%, (B) 82.5%, and (C) 95% of the gas exchange threshold.

114x215mm (300 x 300 DPI)

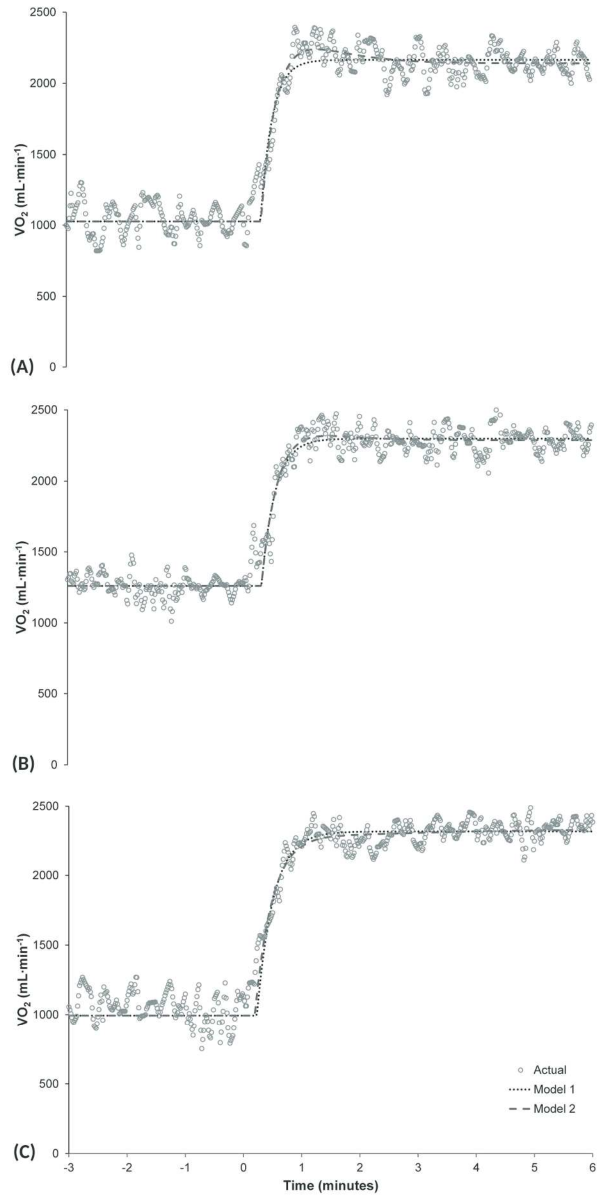

Figure 4. The actual oxygen uptake (VO_2) response, as well as the two model fits, over the 10 minute cycling period, for representative participants

122x236mm (300 x 300 DPI)

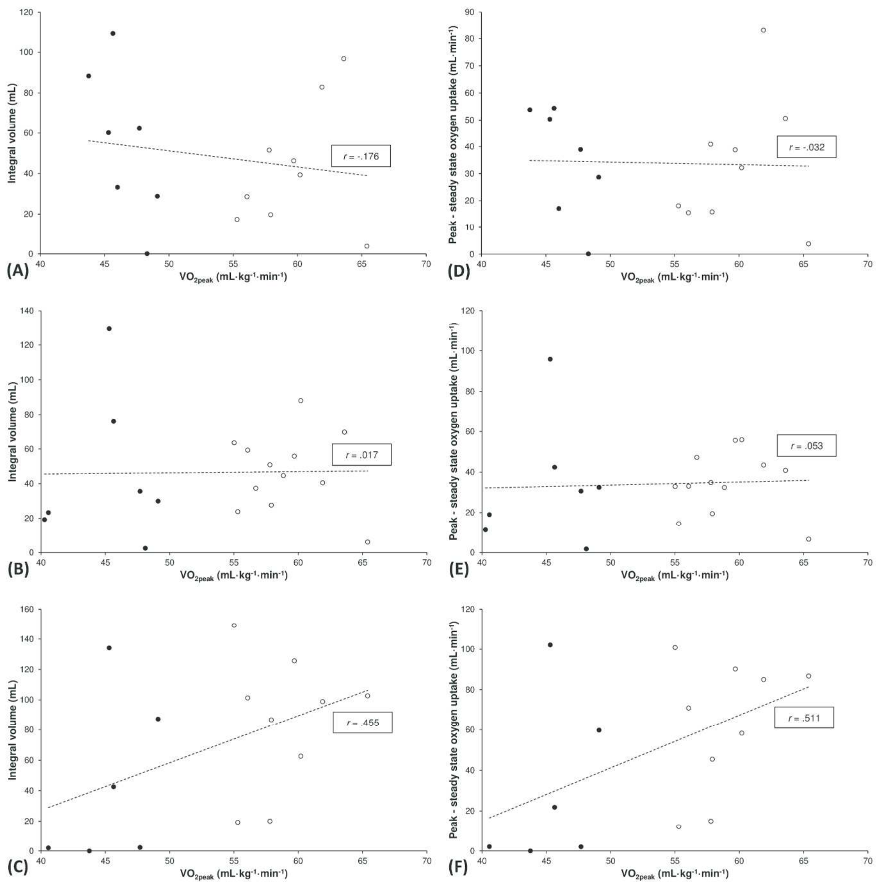

Figure 5. The relationship between the peak rate of oxygen uptake and the size of the $\dot{V}O_2$ overshoot during bouts of submaximal exercise performed at three different intensities (70% [A & D], 82.5% [B & E] and 95% [C & F] of the gas exchange threshold). The size of the overshoot was quantified by two different methods (the integral volume [A, B, & C], and the difference between the peak and steady-state $\dot{V}O_2$ responses [D, E, & F]). Dashed lines represent lines of best fit. Filled circles (●) represent moderate-fitness individuals ($\dot{V}O_{2peak}$ < 50 mL·kg^{-1}·min^{-1}); open circles (○) represent high-fitness cyclists ($\dot{V}O_{2peak}$ > 55 mL·kg^{-1}·min^{-1}).

210x210mm (300 x 300 DPI)