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The on- and off-transient phase two $\dot{V}O_2$ kinetics during submaximal exercise in young men

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RESUMEN

Material y métodos: En jóvenes voluntarios sanos se evaluó si la respuesta fundamental de $\dot{V}O_2$ ($\Phi_2\dot{V}O_2$) al ejercicio submáximo (on-transitoria) y su recuperación (off-transitoria) muestran una cinética de la $\Phi2$ $\dot{V}O_2$ ($\tau2$, constante dos de tiempo) (Φ_2 $\dot{V}O_2$: $\tau2_{on}$ similar a $\tau2_{off}$) caracterizada mediante modelos exponenciales de mejor ajuste. Los voluntarios (n = 8; media ± SE: 25.2 ± 3.0 años) hicieron una prueba inicial de rampa (25 W•min^{-1}) hasta el agotamiento, de la que fueron identificados el umbral ventilatorio (θ) y las intensidades de trabajo al 80% q (ModRel) y 120% q (HvyRel), además se seleccionó una intensidad absoluta de 50 W (ModAbs) (ejercicio submáximo). On y off fueron desde una línea de base sin previo aviso al voluntario. Cada una duró 6 min y se repitió entre 4-6 veces para cada intensidad. La $\dot{V}O_2$ fue mediada de respiración a respiración en una línea de base y en cada transición. Los datos fueron filtrados, interpolados y sobrepuestos a intervalos de 1 s para obtener un perfil de respuesta individual para cada sujeto e intensidad. Esta respuesta de cada voluntario fue ajustada con modelos exponenciales de dos- (2C), y tres-componentes (3C) usando diferentes ventanas de ajuste, y los parámetros (P) estimados (v.gr., $\tau2$) fueron determinados para cada componente. **Resultados.** Los mejores modelos de ajuste estadístico y/o fisiológico mostraron valores transitorios simétricos de $\tau2$ para Mod con $2C7P_{\dot{V}O2\ on}$ (Abs = 23.21 ± 12.1 s, Rel = 28.30 ± 9.1 s) y off (Abs = 25.08 ± 8.4 s); para Rel (Mod = 22.50 ± 4.2 s, Hvy = 22.8 ± 6.0 s) con $2C{,}7P_{\text{Omitiendo la fase 1}\dot{V}O2\ off}$, y para HvyRel (25.30 ± 7.0 s) con $3C10P_{\dot{V}O2\ on}$ (gran media $\tau2$: on = 25.36 ± 9.5 s, off = 23.44 ± 6.2 s). **Conclusión.** La simetría entre las cinéticas on y off de la respuesta transitoria de la ϕ_2 $\dot{V}O_2$ está notablemente influenciada por la dinámica de la $\dot{V}O_2$ durante el ejercicio muscular submáximo en hombres adultos jóvenes.

Palabras clave: *Cinética de la fase dos de* O_2, *transiciones de respuesta y de recuperación de* O_2, *constante de tiempo, hombres jóvenes.*

ABSTRACT

Material and methods. We assessed in young healthy male volunteers if the fundamental $\dot{V}O_2$ response (Φ_2 $\dot{V}O_2$) to submaximal exercise (on-transient response) and its recovery (off-transient response) show in the ϕ_2 $\dot{V}O_2$ kinetics (τ, time constant two) on-off symmetry (Φ_2 $\dot{V}O_2$: τ_{on} similar τ_{off}) characterised from best exponential fitting models. Subjects (n = 8; mean ± SD: 25.2 ± 3.0 yrs) completed an initial incremental ramp test (25 W•min$_{-1}$) to volitional fatigue from which the ventilatory threshold (θ) and work rates corresponding to 80% θ (ModRel) and 120% q (HvyRel) were identified, plus a selected "absolute" work rate of 50 W (ModAbs) (submaximal exercise). On and off step-transitions in work rate were initiated from a baseline without warning to the subject. Each transition (on, off) lasted 6 min and 4-6 transitions were performed at each intensity. The $\dot{V}O_2$ response was measured breath-by-breath at baseline and throughout each transition. Data were filtered, interpolated to 1-s intervals and ensemble-averaged to yield a single response profile for each subject and intensity. The averaged response for each subject was fit with a two- (2C), and three-component (3C) exponential model by using different fitting windows, and parameter (P) estimates (i.e., $\tau2$) were determined for each component. **Results.** Our best statistically and/or physiologically fitting models showed symmetry $\tau2$ values for Mod with $2C7P_{\text{Entire }\dot{V}O2}$ on (Abs = 23.21 ± 12.1 s, Rel = 28.30 ± 9.1 s)-, and off (Abs = 25.08 ± 8.4 s)-transient responses; for Rel (Mod = 22.50 ± 4.2 s, Hvy = 22.8 ± 6.0 s) with $2C{,}7P_{\text{Omitting phase 1}\dot{V}O2\text{ off-transient response}}$, and for HvyRel (25.30 ± 7.0 s) with $3C10P_{\text{Entire }\dot{V}O2\text{ on-transient response}}$ (great mean $\tau2$: on = 25.36 ± 9.5 s, off = 23.44 ± 6.2 s). **Conclusion.** The symmetry between the on- and off-transient Φ_2 $\dot{V}O_2$ kinetics is strikingly influenced by the dynamics of the $\dot{V}O_2$ during muscular submaximal exercise in young adult men.

Key words: O_2 *uptake kinetics, on- and off-phase two* O_2, *time constant, young adults.*

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INTRODUCTION

The ability to sustain a broad spectrum of intensity exercise depends for example on the pulmonary maximum oxygen uptake ($\dot{V}O_{2max}$), the ventilatory threshold ($\dot{V}O_2$ θ) above ($> \theta$) which there is a sustained increase in blood lactate, and the time constant for oxygen uptake ($\tau\dot{V}O_2$).[1,2] During $< \theta$ the rate of increase in and demand is an approximately linear function of exercise intensity, whilst $< \theta$ the function is nonlinear. With an increase in activity or exercise, there is a transient non-steady-state period (transient response) during which physiological adaptations adjust to meet the increased mass muscle metabolic demand, named fundamental component ($\Phi_2\dot{V}O_2$, phase two $\dot{V}O_2$) which rate of change in $\dot{V}O_2$ becomes proportionally smaller as the subject approaches ($< \theta$) or not ($> \theta$) a new steady state (end exercise on-transient $\dot{V}O_2$, end off-transient $\dot{V}O_2$) in a first order kinetics fashion.[3]

The τ of the $\Phi_2\dot{V}O_2$ mathematically describes the profile of this adaptive phase and is a reflection of the response of the hemato-cardiovascular system and muscles to a step up in external work rate. A wash-in exponential function (single mono exponential function) including one time delay (δ, one component = 1C)[4] describes this relation in terms of the 1C mono-exponential function (1CModel) and therefore calculates instantaneous $\dot{V}O_{2(t)}$ at time t. Thus, the τ of the $\Phi_2\dot{V}O_2$ is a useful measure in the assessment of cardiovascular and pulmonary fitness, the effects of exercise training[5] and in recovery compared end exercise from different intensities of exercise.[3 6 7] However, on modelling the on- and off-transient $\dot{V}O_2$ response for a broad spectrum of intensity exercise, different ways of modelling have been used in the search of the influence of exercise intensity on the on- and off-transient $\dot{V}O_2$ kinetics of response, besides the influence of individual biological variability. The $\dot{V}O_2$, data prepared according to Rossiter, *et al.*,[7] kinetics for moderate exercise ($< \theta$) has been described by a mono-exponential function, omitting (first 20s) the cardiodynamic phase ($\Phi_1\dot{V}O_2$) with similar on- and off-$\dot{V}O_2$ time constants (omitting $\Phi_1\dot{V}O_2$, $\tau\Phi_2\dot{V}O_2$)[6] to conform to both mono-exponentiality and 'on-off' symmetry, consistent with a system manifesting linear control dynamics. Even a mono-exponential modelling of the fundamental response following the phase one region (omitting $\Phi_1\dot{V}O_2$) for $\dot{V}O_2$ provided an adequate characterisation of the responses in moderate intensity-exercise, however, it has been reported on-off asymmetry in the $\dot{V}O_2$ response kinetics for moderate intensity exercise, with the off-transient being longer than the on-transient.[7] For heavy exercise ($> \theta$) Özyener, *et al.*[6] included a second slow and delayed exponential component ($\Phi_3\dot{V}O_2$) for and adequate description of this on-transient $\dot{V}O_2$ response (omitting $\Phi_1\dot{V}O_2$, $\tau\Phi_2\dot{V}O_2$, $\tau\Phi_3\dot{V}O_2$) and the off-transient $\dot{V}O_2$ kinetics remained mono-exponential (omitting $\Phi_1\dot{V}O_2$, $\tau\Phi_2\dot{V}O_2$). During high intensity exercise neither mono-exponentiality nor on-off symmetry have been shown to appropriately characterise the $\dot{V}O_2$ slow component response reflected within the exercising muscle by its [PCr] response.[6 7] Özyener, *et al.*,[6] also observed, that for very heavy- and highest intensity (severe)-exercise the on- and off-$\dot{V}O_2$ kinetics became more complex, both with respect to model order and the dynamic asymmetries between the on- and off-transient responses, concluding that these kinetics of the $\dot{V}O_2$ during skeletal muscle mass exercise were influenced by the intensity of exercise.[6] Evermore, it has been observed that responses to the heaviest work rate were mono-exponential in some subjects but bi-exponential responses in others.[8]

Taking in consideration that during the $\Phi_2\dot{V}O_2$ the external respiration (pulmonary) is exponentially trying to match the internal respiration (exercise energy metabolism), we have already assessed the best statistically and/or physiologically exponential mathematical fitting models from models previously published in the literature, as another approach, for the $\Phi 2$ $\dot{V}O_2$ on- and off-transient kinetic (Φ_2 $\dot{V}O_2$ τ) response to submaximal exercise intensity ($< \theta$ and $> \theta$) in young adult men.[4,9] In consequence, in this study we compared on-transient *vs.* off-transient responses to submaximal exercise in terms of the Φ_2 $\dot{V}O_2$ τ characterised by those best fitting models[4 9] in the search of the mechanisms underlaying for the on-off symmetry for exercise $< \theta$ and the asymmetry for exercise $> \theta$.

Hypothesis

If the fundamental $\dot{V}O_2$ response (Φ_2 $\dot{V}O_2$) is consistent with a system manifesting linear control dynamics for moderate- and heavy-intensity exercise and its recovery, then the Φ_2 $\dot{V}O_2$ kinetics should result in an on-off symmetry (Φ_2 $\dot{V}O_2$: τ_{on} similar τ_{off}) characterised from best fitting models.

MATERIAL AND METHODS

Subjects

The subjects in this study were 8 healthy males aged 23-30 years. Data were obtained from the studies carried out under control conditions in our laboratory over several years. Subjects performed cycle ergometer exercise in both the moderate-intensity exercise and the heavy intensity exercise. The Review Board for Research Using Human Subjects provided ethical approval and each subject gave their

Table 1. Subject characteristics.

Age (years)	Height (cm)	Mass (kg)	$\dot{V}O_2$ peak (l•min^{-1})	$\dot{V}O_2$ peak (mL•kg^{-1}•min^{-1})	θ (mL•kg^{-1}•min^{-1})
25.2 ± 3.0	179.1 ± 5.1	80.3 ± 9.0	3.75 ± 0.62	46.69 ± 6.40	24.27 ± 3.2

All data are mean ± SD from 8 male young sample size. θ: ventilatory threshold. $\dot{V}O_2$ peak: maximal aerobic power.

informed consent. Subjects were of similar physical characteristics and cardio-respiratory fitness (Table 1).

Testing procedures

The determination of maximal oxygen uptake ($\dot{V}O_2$ max) and the $\dot{V}O_2$ at ventilatory threshold (θ) was carried out on an electrically braked cycle ergometer (Lode H-300-R Roxon Medi-Tech). The test was performed as a ramp function with work rate increasing at a rate of 25 W min^{-1}. The θ was determined by visual inspection of data using the criteria outlined previously[10] of a systematic increase in $\dot{V}_E/\dot{V}O_2$ ($\dot{V}_E$, expired gas volume) and in end-tidal O_2 pressure ($P_{ET}O_2$) with no concomitant rise in $\dot{V}_E/\dot{V}CO_2$ ($\dot{V}/CO_2$, CO_2 uptake) or a decrease in end-tidal CO_2 pressure ($P_{ET-}CO_2$). Constant-load exercise tests were performed on subsequent visits to the laboratory. Exercise began with 6 min of loadless (~15 W) cycling. The work rate was then increased as a step function to an intensity corresponding to a $\dot{V}O_2$ of approximately 80% of the $\dot{V}O_2$ at θ (ModRel, relative moderate-intensity) or the $\dot{V}O_2$ of approximately 120% of the $\dot{V}O_2$ at θ (HvyRel, relative heavy-intensity). Also, it was selected an absolute work rate of 50 W (ModAbs, absolute moderate-intensity) corresponding of approximately 62% of the $\dot{V}O_2$ at θ. The subjects exercised at the appropriate work rate for 6 min (on-transient $\dot{V}O_2$ response), after which the work rate was abruptly decreased and the subjects continued loadless cycling for 6 min (off-transient $\dot{V}O_2$ response).

Data collection and analysis

Gas exchange was determined using previously reported methods.[9] Throughout exercise, inspired and expired gas volumes ($\dot{V}_I$ and $\dot{V}_E$) were measured using a low dead space (90 mL) bidirectional turbine (VMM110, Alpha technologies), which was calibrated prior to each test using a syringe of known volume (3.01 l). Respired gases were sampled continuously (1 mL s^{-1}) at the mouth and analysed for concentrations of O_2, CO_2 and N_2 by mass spectrometry (MGR 9N, Airspec 2000) after calibration with precision-analysed gas.

Mixtures

Changes in gas concentration were aligned with gas volumes by measuring the time delay for a bolus of gas to pass the turbine to the resulting changes in fractional gas concentrations as measured by the mass spectrometer. Breath-by-breath alveolar gas exchange was calculated using previously described algorithms.[11] The breath-by-breath data were interpolated to 1 s intervals. In order to improve the signal-noise ratio each subject performed a number of repetitions of the exercise protocol. For Mod were performed 6-8 constant-load exercise tests for each condition (2-4 transitions visit^{-1}) and for HvyRel were performed 2-3 constant-load exercise tests (1 transition visit^{-1}). The interpolated data were then averaged for each individual to yield a single response. The single response (50 W, 80% θ, 120% θ overlayed data) was used for determining the kinetics of the $\dot{V}O_2$ on- and off-transient responses to submaximal exercise.

Models

In these analyses only the data for $\dot{V}O_2$ on- and off-transients were modelled with our best fitting models previously assessed.[9,12] For moderate-intensity exercise, exponential models with one or two components were fitted to the data. For heavy-intensity exercise exponential models with one, two and three components were fitted to the data.[9,12] The models were of the form:

- $\dot{V}O_2(t) = A_0 + A_1\{1 - \exp[-(t\text{-}\delta1)/\tau1]\}$
  [i.e. 1 component model (1C), 4 fitting parameters (4P: A_0, A_1, δ_1, τ_1)].
- $\dot{V}O_2(t) = A_0 + A_1\{1 - \exp[-(t\text{-}\delta1)/\tau1]\} + A_2\{1 - \exp[-(t\text{-}\delta_2)/\tau_2]\}$
  [i.e. 2 components model (2C), 7 fitting parameters (7P)].
- $\dot{V}O_2(t) = A_0 + A_1\{1 - \exp[-(\tau\text{-}\delta1)/\tau1]\} + A_2\{1 - \exp[-(t\text{-}\delta_2)/\tau_2]\} + A_3\{1 - \exp[-(t\text{-}\delta_3)/\tau_3]\}$
  [i.e. 3 components model (3C), 10 fitting parameters (10P)].

Where:

- t is time.
- A_0 is the baseline $\dot{V}O_2$.
- A_1, A_2 and A_3 are the increases in the amplitude of $\dot{V}O_2$ for each component.
- τ_1, τ_2 and τ_3 are time constants for each component (the time taken to reach 63% of the amplitude of the corresponding phase).
- δ_1, δ_2 and δ_3 are time delays for each component, with δ_1 not set to time 0, but allowed to vary in order to optimise the fit of all parameters (thus, δ_1 has no physiological interpretation).

Additionally, to describe $\dot{V}O_2$ kinetics of the overall response total amplitude ($ATot = A_1 + A_2 + A_3$) was calculated.

Data were modelled using the single or multi-component models described above using non-linear leastsquares regression techniques, and the best fit defined by the minimisation of the residual sum of squares.[9,12] We used initial estimates of: δ_1, 0 s; δ_2, 20 s; δ_3, 180 s; τ_1, 5 s; τ_2, 30 s; τ_3,180 s. Usually 100 iterations were run and the parameter estimates examined to allow further iterations with the estimates obtained. The models were run with phase 2 τ underestimated (e.g. 15 s) or overestimated (e.g. 70 s) to assure that the minimised residuals were not due to a localised minimised least squares residuals.[13] For the models starting at 20 s, the 20 s $\dot{V}O_2$ was used as the A_0 (a virtual A_0) and thus the amplitude terms are calculated relative to this starting point, the use of the virtual A_0 allows accurate parameter estimation.

Specific details of each best model with reference to start and end-point of each fit is shown in table 2. Model 1 for the moderate-intensity exercise off-transient $\dot{V}O_2$ was the 20 s to 6 min (1C,4P0.3333 min-6 min): a mono-exponential (one-component model) fitted to phase 2, omitting phase 1 data (i.e. first 20 s), to end-exercise.[12] Model 2 for the submaximal exercise (Mod and Hvy) on-transient $\dot{V}O_2$ 20 s to 3 min (1C,4P0.3333 min-3 min): a mono-exponential fit to phase 2, omitting phase 1 data, to a presumed steady-state by 3 min.[9] Model 3 for moderate-intensity exercise either 2 min BaSeLine-6 min (on- transient $\dot{V}O_2$ Mod)[9] or 1 min BSL-6 min (off- transient $\dot{V}O_2$ ModAbs only)[12] (2C,7PBSL-6 min): a two-component exponential fitted from BSL-start to end-exercise with two exponential equations differentiating phase 1 and phase 2. Model 4 for heavy-intensity exercise either 20 s to 6 min (off-transient $\dot{V}O_2$ ModRel and HvyRel only)[12] (2C,7P0.3333 min-6 min): a two-component exponential fit to phase 2, omitting phase 1 data, to end-exercise or Model 5 with a fitting window

Table 2. Five best different exponential mathematical fitting models used to assess the $\dot{V}O_2$ on- and off-transient responses during submaximal exercise in eight young adult men.

Model number Transition	Fitting model	Temporal parameter									
		1 $A_{mplitud}0$	2 A1	3 A2 (mLO$_2$ • min^{-1})	4 A3	5 $T_{ime}D_{elay}1$	6 TD2	7 TD3 (s)	8 τ1	9 τ2	10 τ3
1 Off-Mod	1C,4Parameters^S 0.3333 min to 6 min	[Virtual BSL]	-	✓	-	-	✓	-	-	✓	-
2 On-Mod&Hvy	1C,4P^S 0.3333 min to 3 min	[Virtual BSL]	-	✓	-	-	✓	-	-	✓	-
3 Off-ModAbs On-Mod	2C,7P^C BSL to 6 min	✓	✓	✓	-	✓	✓	-	✓	✓	-
4 Off-Rel	2C,7P$^{S/C}$ 0.3333 min to 6 min	[Virtual BSL]	-	✓	✓	-	✓	✓	-	✓	✓
5 On-Hvy	3C,10P^C BSL1 min to 6 min	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

–: no estimated temporal parameter. Mod: moderate (Abs and Rel) intensity exercise. θ: ventilatory threshold. Abs: absolute work rate exercise (on-transient = 50 W, off-transient = recovery 50 W). Rel: relative work rate exercise equivalent to 80% θ (on-transient = 85 ± 12 W, off-transient = recovery 85 ± 12 W). Hvy: heavy work rate exercise equivalent to 120% θ (on-transient = 158 ± 18 W, off-transient = recovery 158 ± 18 W). S: simple model. C: complex model.

from 2 min BaSeLine-6 min (on- transient $\dot{V}O_2$ HvyRel) (3C,10PBSL-6 min): a three-component exponential fitted from BSL-start to end-exercise[9] (Table 2).

Statistical analyses

Estimated values of the phase 2 τ from the different models used were compared, on *vs.* off exercise intensity group, using two-way analysis of variance all pairwise multiple comparison procedures (Holm-Sidak method) with repeated measures14. The Student's t-test was used to determine if the mean values of two conditions were significantly different.[14] The probability level of 0.05 was chosen as the criterion for acceptance of statistical significance.

RESULTS

The on- and off-transient pulmonary oxygen uptake response profiles to ModAbs (on = 50 W, off = recovery 50W), ModRel (80% θ: on = 85 ± 12 W, off = recovery 85 ± 12 W), and HvyRel (120% θ: on = 158 ± 18 W, off = recovery 158 ± 18 W) square wave exercise is shown in figure 1. Steady states of $\dot{V}O_2$ on and off transients were attained at moderate (Mod) but not at heavy (Hvy) intensities (Figure 1).

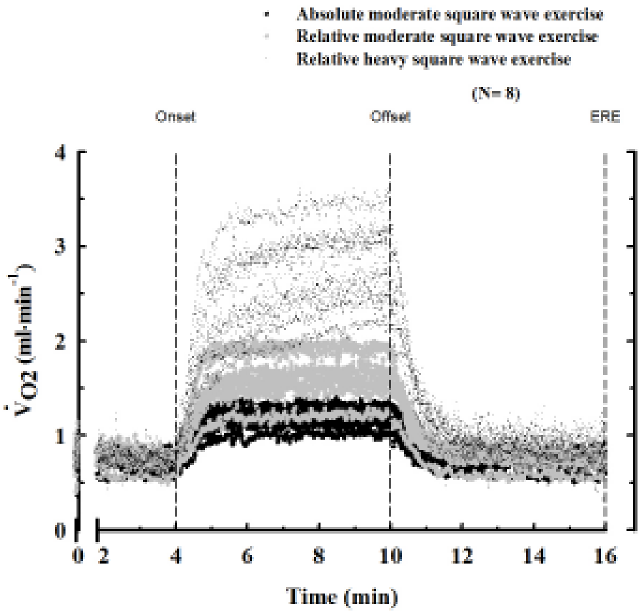

Figure 1. *Groups on- and off-transient pulmonary oxygen uptake (*$\dot{V}O_2$*) response profiles to absolute moderate (50 W), relative moderate (80% θ), and relative heavy (120% θ) square wave exercise. Exercise onset (start) is at four min and offset (end) is at ten min. Data points (symbols) are the breath-by-breath interpolated to second-by-second pulmonary* $\dot{V}O_2$ *(experimental data) from either two min baseline (2 min to 4 min) to the entire on-transient response (Onset to Offset) or one min baseline (9 to 10 min) to the entire off-transient response (Offset to* $E_{nd}R_{ecovery}E_{xercise}$*). The eight subjects submaximal exercise at each intensity (n = 8) are displayed. θ: ventilatory threshold.*

The fundamental temporal parameter for the on-transient $\dot{V}O_2$ *vs.* off-transient $\dot{V}O_2$ submaximal exercise comparisons from best fitting models are shown in table 3. Either the amplitude Φ_2 $\dot{V}O_2$ or the time constant Φ_2 $\dot{V}O_2$ resulted similar between on and off transitions for each submaximal exercise intensity (Table 3). Generally speaking, the time delay Φ_2 $\dot{V}O_2$ off-transient showed a tendency to be fast (small θ numeric value) compared the time delay Φ_2 $\dot{V}O_2$ on-transient, being significantly ($P < 0.05$) fast θ_{off} for Mod exercise modelled with complex models: Abs with $2C7P_{\text{Entire off-transient response}}$ and Rel with 2C,7P omitting Φ1 $\dot{V}O_2$ off-transient response (Table 3). In contrast, significantly slow ($P < 0.05$) θ_{off} for HvyRel exercise modelled with the simple model 2C,7P omitting Φ_1 $\dot{V}O_2$ compared its θ_{on} negative numeric value (Table 3). Nevertheless, when the on- and off-transient $\dot{V}O_2$ for HvyRel exercise was modelled with the complex model $3C{,}10P_{\text{Entire response}}$, the on-$\theta_2$ resulted similar to off-θ_2 being positives these numeric time delay values (Table 3).

Monoexponential modelling Rel submaximal exercise $\dot{V}O_2$ omitting phase one to either 3 min on-transient (Rel, Hvy) response or to 6 min off-transient (ModRel) response gave a no physiological sense negative θ numeric value (Table 3). However, complex models showed fast θ_{off} for Mod (Abs, Rel) exercise only (Table 3). Evermore, tripleexponential (3C10PEntire off-transient response) modelling HvyRel exercise give no physiological sense negative θ_1 numeric value (-0.58 ± 2.9 s).

Double exponential modelling provided an adequate characterisation of the on-, and off-transient Φ_2 $\dot{V}O_2$ kinetics (τ2) for both moderate and heavy (except the on-transient response) exercise intensities (Table 2 and 3): mod exercise modelled with $2C7P_{\text{Entire }\dot{V}O2\text{ on(Abs,Rel)- and off (Abs)-transient responses}}$, physiologically isolated Φ_2 O_2; Rel exercise (Mod, Hvy) modelled with $2C{,}7P_{\text{Omitting }\Phi 1\ \dot{V}O2\text{ off-transient response}}$, physiologically semi-isolated Φ_2 $\dot{V}O_2$; and, HvyRel exercise modelled with $3C10P_{\text{Entire }\dot{V}O2\text{ on-transient response}}$ physiologically isolated Φ_2 $\dot{V}O_2$ (Tables 2 and 3). These final best fitting models ($2C7P_{\text{Entire }\dot{V}O2\text{ transient responses}}$, $2C{,}7P_{\text{Omitting }\Phi 1\ \dot{V}O2\text{ transient response}}$, $3C10P_{\text{Entire }\dot{V}O2\text{ transient response}}$). Tabla 2 showed only significantly ($t = 6.7$, $P < 0.0012$) fast θ_{off} compared θ_{on} for each of the three exercise intensities (Table 3).

Table 3. Fundamental temporal parameter for the on-transient vs. off-transient $\dot{V}O_2$ submaximal exercise comparisons from best fitting models.

Exercise Intensity	Parameter	Phase II $\dot{V}O2$ from Simplest models[A] On	Off	Complex models[B] On	Off	Final best fitting models[C] On	Off
Mod:	Amplitude, mL•min^{-1}	315.6 ± 72.1	245.8 ± 48.8	291.6 ± 64.1	244.1 ± 110	245.8 ± 48.8	244.1 ± 110
Abs	Time delayed, s	2.60 ± 3.2	0.10 ± 2.8	25.5 ± 5.6^b	17.01 ± 5.1^b	25.50 ± 5.6^d	17.01 ± 5.1^d
	Time constant, s	23.39 ± 8.9	28.00 ± 4.0	23.21 ± 12	25.10 ± 8.4	23.21 ± 12.1	25.08 ± 8.4
Mod	Amplitude, mL•min^{-1}	645.0 ± 191	505.4 ± 164	631.7 ± 125	441.8 ± 96.0	491.0 ± 160	441.8 ± 96.01
Rel	Time delayed, s	-1.30 ± 2.1	-3.9 ± 6.3	20.00 ± 1.1^c	6.50 ± 3.4^c	20.00 ± 2.0^e	7.00 ± 3.4^e
	Time constant, s	25.70 ± 8.5	31.20 ± 5.3	27.58 ± 9.4	22.50 ± 4.1	28.30 ± 9.1	22.50 ± 4.2
Hvy	Amplitude, ml•min^{-1}	1287.9 ± 327	1058.6 ± 370	1140.40 ± 531	1269.3 ± 353	1140.4 ± 531	1152.1 ± 175
Rel	Time delayed, s	-0.26 ± 6.1^a	5.94 ± 4.6^a	19.00 ± 4.8	21.8 ± 5.8	19.00 ± 5.0^f	6.00 ± 4.6^f
	Time constant, s	30.93 ± 7.1	22.80 ± 6.0	25.30 ± 7.0	28.25 ± 4.8	25.30 ± 7.0	22.8 ± 6.0

All data are mean ± SD from 8 male young sample size. -: no data. $\dot{V}O_2$: pulmonary oxygen uptake. A: The 1C,4P with a transient fitting window either from 0.3333 to 3 min (theoretically start and end Phase II $\dot{V}O_2$) or from 0.3333 to 6 min (semi-isolated Phase II $\dot{V}O_2$) and the 2C,7P0.333 to 6 min (semi-isolated Phase II $\dot{V}O_2$). B: The 2C,7P (except moderate- and heavy- relative intensity exercise) and the 3C,10P both with an entire transient fitting window from BSL to 6 min (Isolated Phase II $\dot{V}O_2$). C: Mod with 2C7PEntire $\dot{V}O_2$ on(Abs,Rel)-, and off(Abs)-transient responses, Rel Mod, Hvy) with 2C,7P$_{\text{Omitting phase 1 }\dot{V}\text{O2 off-transient response}}$, and HvyRel with 3C10P$_{\text{Entire }\dot{V}\text{O2 on-transient response}}$. BSL: baseline. ModAbs: absolute moderate exercise (50 W). ModRel: relative moderate exercise (80% θ). HvyRel: relative heavy exercise (120% θ). Ventilatory threshold: θ. SubMaxExerc: Mod + Hvy. The differences in the mean values among the treatment conditions are a statistically significant difference for the same pears of lowercase letters (on *vs.* off) allocated by Two Way ANOVA all pairwise multiple comparison procedures (Holm-Sidak method): $^{a-c}$Fvalue: 40, P < 0.005. $^{d\,f}$Fvalue = 25.5, P < 0.001.

DISCUSSION

The on-transient (exercise $\dot{V}O_2$) *vs.* the off-transient (post-exercise $\dot{V}O_2$ recovery) responses to the exercise tests for 50 W, absolute moderate (ModAbs) exercise; for 80% θ, relative moderate (ModRel) exercise and; for relative heavy (HvyRel, 120% θ) exercise (submaximal exercise) cycling (on-transient) and constant off-loadless (off-transient) cycling were analysed with best statistically and/or physiologically exponential mathematical fitting models[9,12] that characterised the on Φ_2 $\dot{V}O_2$ kinetics (on $\tau\Phi_2$ $\dot{V}O_2$) and the off Φ_2 $\dot{V}O_2$ kinetics (off $\tau\Phi_2$ $\dot{V}O_2$) for this submaximal exercise in young healthy adult men.

On- vs. *off-transient Φ_2 $\dot{V}O_2$ time delay*

The time delay (δ_2) can be explained by feedforward activation of ventilation and the time needed for blood to flow from working muscles to lungs related with temporal physiological considerations modulating muscle efficiency.[15] The off time delay Φ_2 $\dot{V}O_2$ transient was fast (9.82 ± 6.7, s) that at the on-transient (21.42 ± 5.1, s) submaximal exercise response. We explain this $\delta_{2on} > \delta_{2off}$ because on the rate at which pulmonary oxygen uptake increases during exercise; for the muscle is already flow limited while the lung venous blood inflow has a diminished O_2 content; this is raised to arterial level during the pulmonary-capillary transit, necessitating a blow-dependent $\dot{V}O_2$ increase even if venous blood O_2 remains constant.[16] This is a more slow time delay process (up-hill) during the ontransient of a step-increase in work rate compared that at the off transient (down-hill) $\dot{V}O_2$ profile. Besides, according to Barstow, *et al.*,[17] the best model is one that simulates the known responses well, has parameters with direct physiological correlates, and provides testable hypotheses regarding the underlying physiology and control features. Our best statistically and/or physiologically fitting models, Mod with 2C7PEntire $\dot{V}O_2$ on(Abs andRel)-, and off(Abs)-transient responses, Rel (Mod, Hvy) with 2C,7P$_{\text{Omitting phase 1 }\dot{V}\text{O2 off-transient response}}$, and HvyRel with 3C10P$_{\text{Entire }\dot{V}\text{O2 on-transient response}}$, predict a time delay and meets all three of these conditions. Evermore, the calculated mean transit time from the muscle capillary to the lung is 17 s and decreased to 10-12 s after 5 s and 6-9 s after several minutes during passive knee- extensor exercise[17] indicate that it is necessary to take account of this transit delay from muscle to mouth if pulmonary $\dot{V}O_2$ kinetics are to be used to estimate the kinetics of muscle $\dot{V}O_2$ consumption. In consequence, the removal of the first 20 s of pulmonary data from consideration effectively time aligns the muscle and pulmonary signals results in close agreement between the responses[15] when omitting phase one models are used to determine the $\dot{V}O_2$ transient response.

On- vs. *off-transient Φ_2 $\dot{V}O_2$ kinetics ($\tau 2$)*

The Φ_2 $\dot{V}O_2$ on-transient response to submaximal exercise profile is based on the fact that as muscle oxygen consumption is under the dominant feedback control of enzymatic processes linked to high-energy phosphate use in terms on an intramuscular phosphocreatine profile inference and from direct determination of muscle blood flow and its arteriovenous $\dot{V}O_2$ content difference. However, the rate at which pulmonary oxygen uptake (i.e, Φ_2 $\dot{V}O_2$) increases during exercise is another expectation; for example, the Φ_2 $\dot{V}O_2$ on-transient response exponentiality inheres in its response to a change in work rate, most either simply for moderate-intensity exercise or complex kinetics for heavy exercise.[18] During the transition from exercise to recovery (off-transient response) the muscles' energy demands drop towards the resting levels but pulmonary oxygen uptake recovery (i.e., Φ_2 $\dot{V}O_2$ off-transient response) which suggests that Φ_2 $\dot{V}O_2$ off-transient response is also both multi-factorially regulated and with similar kinetics ($\tau 2$ numeric value) that at the Φ_2 $\dot{V}O_2$ on-transient response for moderate- and heavy-exercise.[6] As expected, in this study the $\tau\Phi_2\dot{V}O_2$ off-transient was not discernible different from that at the on-transient submaximal exercise response. It is noteworthy, that this Φ_2 $\dot{V}O_2$ symmetry from our on and off kinetics transients ($\tau 2$: on and off averaged 24.40 ± 8.0) resulted in agreement with those observed from Özyener, *et al.*,[6] even in despite that they modelled for both the moderate exercise, the $\dot{V}O_2$ kinetics by a simple mono-exponential function, following a short cardiodynamic phase, with the on- and off-transients having similar time constants ($\tau 2$ averaged: on = 33 ± 16 s, off = 29 ± 6 s) and the heavy exercise by either the inclusion of a second slow and delayed exponential component for the τ_2 averaged on (32 ± 17 s) or by a mono-exponential for the τ_2 averaged off (42 ± 11 s).[6] We therefore confirm that the kinetics of the Φ_2 $\dot{V}O_2$ during dynamic muscular exercise is strikingly influenced with respect to dynamic symmetries between the on- and off-transient responses.

Isolated- vs. *semiisolated-Φ_2 $\dot{V}O_2$*

The difference between the semiisolated-Φ_2 $\dot{V}O_2$ and the isolated-Φ_2 $\dot{V}O_2$ is that while the former is obtained trying to improve the phase II fit by arbitrary constraining the fitting window to start some time after the exercise onset (i.e, 20 s) perhaps violating the high degree of interdependency in the parameters and possibly affecting the remained parameter values.[19] The isolated-Φ_2 $\dot{V}O_2$ makes more physiological sense because it is obtained by fitting the entire response with and exponential mathematical model identifying the three theoretical phases named the cardiodynamic phase (Φ_1 $\dot{V}O_2$), the fundamental exponential phase (Φ_2 $\dot{V}O_2$) and the subsequent (Φ_3 $\dot{V}O_2$) either steady-state for moderate exercise or the phase of delayed onset for exercise above lactate threshold that yields a slowly developing supplemental rise in $\dot{V}O_2$ resulting in what has been termed excess $\dot{V}O_2$ specially for supra lactate threshold exercise.[20] Whether or not these phases Φ_1 $\dot{V}O_2$ and Φ_3 $\dot{V}O_2$ are exponentials or not is matter of debate. However, in this study the isolated and semiisolated Φ_2 $\dot{V}O_2$ phases for submaximal exercise from the on- and off- transients showed symmetry to each other; confirming that our best statistically and physiologica[12,19] fitting model constituents reflected the system's physiological features, with implications for its control mechanisms which may ultimately lead to deeper insights for their confirmation or not. Certainly, when it is possible we prefer those best fitting models that isolate the Φ_2 $\dot{V}O_2$ from the remain transient phases Φ_1 $\dot{V}O_2$ and Φ_3 $\dot{V}O_2$, specially when the mathematical models make strict and accurate physiological sense.

CONCLUSION

The symmetry between the on- and off-transient phase two $\dot{V}O_2$ kinetics ($\tau 2$) is strikingly influenced by the dynamics of the $\dot{V}O_2$ during muscular submaximal exercise in young adult men.

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REFERENCES

1. Margaria R, Edwards HT, Dill DB. The possible mechanism of contracting and paying the oxygen debt and the role of lactic acid in muscular contraction. Am J Physiol 1933; 106: 689-715.

2. Whipp BJ, Davis JA, Torres F, Wasserman K. Atest to determine parameters of aerobic function during exercise. J App Physiol 1981; 50: 217-21.
3. Paterson DH, Whipp BJ. Aysmmetries of oxygen uptake transients at the on and offset of heavy exercise in humans. J Physiol (Lond) 1991; 443: 575-86.
4. Padilla JP. La respuesta exponencial y su modelado matemático. En: Esfuerzo Físico-deportivo. 2a Ed. México, D.F.: SEP, IPN; 2011, p. 152-85.
5. Markovitz GH, Sayre JW, Storer TW, Cooper CB. On issues of confidence in determining the time constant for oxygen uptake kinetics. Br J Sports Med 2004; 38: 553-60.
6. Özyener F, Rossiter HB, Ward SA, Whipp BJ. Influence of exercise intensity on the on- and offtransient kinetics of pulmonary oxygen uptake in humans. J Physiol 2001; 533.3: 891-902.
7. Rossiter HB, Ward SA, Kowalchuk JM, Howe FA, Griffiths JR, Whipp BJ. Dynamic asymmetry of phosphocreatine concentration and O2 uptake between the on- and off-transients of moderate and high-intensity exercise in humans. J Physiol 2002; 541(3): 991-1002.
8. Barstow TJ, Molé PA. Linear and nonlinear characteristics of oxygen uptake kinetics during heavy exercise. J Appl Physiol 1991; 71: 2099-106.
9. Padilla JP, Kowalchuk JM, Taylor AW, Paterson DH. Determinación de la cinética de la fase dos transitoria de la $\dot{V}O_2$ durante ejercicio de carga constante de intensidades moderada e intensa en hombres jóvenes. Rev Hosp Juárez Mex 2007; 74(4): 231-44.
10. Davis JA, Frank MH, Whipp BJ, Wasserman K. Anaerobic threshold alterations caused by endurance training in middle-aged men. J App Physiol 1979; 46: 1039-46.
11. Beaver WL, Lamarra N, Wasserman K. Breath-by-breath measurements of true alveolar gas exchange. J Appl Physiol 1981; 51: 1662-75.
12. Padilla JP. Comparison of modelling techniques used to characterize moderate and heavy phase two recovery O2 kinetics in young men. Rev Hosp Jua Méx 2012; 79(3): 159-73.
13. Motulsky HJ, Ransnas LA. Fitting curves to data using nonlinear regression: a practical and nonmathematical review. FASEB J 1987; 1: 365-74
14. Zar JH. Biostatistical analysis. 3rd Ed. New Jersey, USA: Englewood Cliffs: Prentice-Hall; 1996, p. 162-473.
15. Perrey S, Burnley M, Millet GP, Jones AM, Poole DC, Hamard L, et al. Comments on Point: Counterpoint: The kinetics of oxygen uptake during muscular exercise do/do not manifest time-delayed phases. J Appl Physiol 2009; 107: 1669-75.
16. Krogh A, Lindhard J. The regulation of respiration and circulation during the initial stages of muscular work. J Physiol 1913; 47: 112-36.
17. Barstow TJ, Lamarra N, Whipp BJ. Modulation of muscle and pulmonary O2 uptakes by circulatory dynamics during exercise. J Appl Physiol 1990; 68: 979-89.
18. Whipp BJ. The kinetics of oxygen uptake during muscular exercise do manifest time-delayed phases. J Appl Physiol 2009; 107: 1663-8.
19. Perrey S, Betik A, Candau R, Rouillon JD, Hughson RL. Comparison of oxygen uptake kinetics during concentric and eccentric cycle exercise. J Appl Physiol 2001; 91: 2135-42.
20. Whipp BJ. Dynamics of pulmonary gas exchange. Circulation 1987; 76(Suppl. VI): 18-28.

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