The on- and off-transient phases two \( \Phi_{2} VO_2 \) kinetics during submaximal exercise in old men

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RESUMEN

Se evaluó en adultos maduros voluntarios sanos si la respuesta fundamental de \( \Phi_{2} VO_2 \) al ejercicio submáximo (ontransitoria) y su recuperación (offtransitoria) muestran una cinética similar \((\tau_{2On} vs. \tau_{2Off})\) de la \( \Phi_{2} VO_2 \) (\( \tau_{2} \), constante fundamental de tiempo) de modelos exponenciales de mejor ajuste ya evaluados. Los voluntarios \((n = 9; \text{media } \pm \text{SD}: 72 \pm 4 \text{ años})\) hicieron una prueba inicial de rampa \((15 \text{ W.min}^{-1})\) hasta el agotamiento, de la que fueron identificados el umbral ventilatorio \((\theta)\) y las intensidades de trabajo submáximo para 80\% \(\theta\) (ModRel) y 120\% \(\theta\) (HvyRel); además se seleccionó una intensidad absoluta de 50 W (ModAbs). On y off transitorias fueron desde una línea de base \((\text{LB})\) sin previo aviso al voluntario. Cada una duró 6 min y se repitió entre 4-6 veces para cada intensidad. \( \Phi_{2} VO_2 \) fue mediada de respiración a respiración en una LB 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 fue ajustada con modelos exponenciales de dos \((2C)\) y tres componentes \((3C)\), usando diferentes ventanas de ajuste, y los parámetros \((P)\) estimados \((v.gr., \tau_{2})\) fueron determinados para cada componente. Nuestros mejores modelos de ajuste estadístico y/o fisiológico mostraron valores transitorios simétricos \((\text{on similar off})\) de \( \tau_{2} \Phi_{2} VO_2 \) \((s)\) con 2C, 7P \((\text{ModAbs and Rel: on } = 57 \pm 15 \text{ y off } = 56 \pm 14);\) y para HvyRel \((\text{on } = 40 \pm 9 \text{ y off } = 39 \pm 7)\) con 3C, 10P. La LB \((\text{mL.min}^{-1})\) de Hvyon \((744 \pm 115)\) fue menor que Hvyoff \((982 \pm 288).\) Tiempo medio de la respuesta cinética global \((s)\) Hvyon \((82 \pm 18)\) fue menor que Hvyoff \((55 \pm 8).\) Las cinéticas on y off de la respuesta transitoria de la \( \Phi_{2} VO_2 \) están notablemente influenciadas por la dinámica de la \( \Phi_{2} VO_2 \) durante el ejercicio muscular submáximo en hombres adultos mayores.

Palabras clave: Cinética de la fase dos de \( O_2 \) transiciones de respuesta y de recuperación de \( O_2 \) constante de tiempo, hombres adultos mayores.

ABSTRACT

We assessed in old healthy male volunteers if the fundamental \( \Phi_{2} VO_2 \) \((\Phi_{2} \Phi_2 VO_2)\) to submaximal exercise \((\text{ontransient response})\) and its recovery \((\text{offtransient response})\) show in the VO\(_2\) kinetics \((\tau_{2}, \text{time constant two})\) on-off symmetry \((\tau_{2On} vs. \tau_{2Off})\) characterised from best exponential fitting models previously assessed. Volunteers \((n = 9; \text{mean } \pm \text{SD: } 72 \pm 4 \text{ yrs})\) completed an initial incremental ramp test \((\text{W.min}^{-1})\) to volitional fatigue from which the ventilatory threshold \((\theta)\) and work rates corresponding to 80\% \(\theta\) (ModRel) and 120\% \(\theta\) (HvyRel) were identified, plus a selected “absolute” work rate of 50 W (ModAbs) \((\text{submaximal exercise})\). On and off step-transitions in work rate were initiated from a baseline \((\text{BL})\) without warning to the subject. Each transition \((\text{On, Off})\) lasted 6 min and 4-6 transitions were performed at each intensity. The \( \Phi_{2} VO_2 \) response was measured breath-by-breath at BL and throughout each transition. On and off 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 using different fitting windows, and parameter \((P)\) estimates \((v.gr., \tau_{2})\) were determined for each component. Our best statistically and/or physiologically fitting models showed symmetry \( \tau_{2} \) values for Mod with 2C, 7P \((\text{ModAbs and Rel: on } = 57 \pm 15 \text{ and off } = 56 \pm 14);\) and for HvyRel \((\text{on } = 40 \pm 9 \text{ y off } = 39 \pm 7)\) with 3C, 10P. BL \((\text{mL.min}^{-1})\) Hvyon \((744 \pm 115)\) was low compared Hvyoff \((982 \pm 288).\) Overall
mean response time (s) Hvyon $(82 \pm 18)$ resulted low compared Hvyoff $(55 \pm 8)$. The on and off kinetics of the transient responses of the $\phi_1 V_{O2}$ are strongly influenced by the dynamics of $V_{O2}$ during muscular submaximal exercise in older men.

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

## INTRODUCTION

Greater understanding of oxygen ($O_2$) kinetics control and, in particular, its relation to the plasticity of the $O_2$ transport/utilization system is important for improving the human condition, crucially for patients suffering from pathologically slowed $O_2$ kinetics and the elderly population. A slowing of pulmonary oxygen uptake ($V_{O2}$) kinetics during the on-transition to a step increase in work rate (WR) of moderate intensity require to be characterized by an exponential model with two components and seven parameters $(2C,7P)$, below what has been termed the anaerobic threshold. For heavy exercise (above anaerobic threshold), the physiological basis for phases 1 ($\theta_1$) and 2 ($\theta_2$) transitions in $V_{O2}$ kinetics is evident while $\theta_2$ to $\theta_1$ (phase three) transitions in heavy exercise are complex, with asymmetries of $V_{O2}$ transients at the onset and offset, and require complex model like an exponential model with three components and 10 parameters $(3C,10P)$, for appropriate characterisation as a result of a slow kinetic component which is of delayed onset of approximately $\geq 2$ min, supporting the possibility of a more complex link between muscle force production and the metabolic mechanisms of energy transfer at a work rate, specially above anaerobic threshold, both during the ontransient and offtransient (recovery) responses to submaximal exercise. The end of exercise does not indicate the cessation of functional and metabolic activities in the body systems, it is necessary for the body to normalize its function and settle the active metabolism during this post-exercise recovery period (i.e., $V_{O2}$ off transient response). The slower $V_{O2}$ off transient component had a small amplitude and long time constant, but did not differ significantly among the various tests and also the off transient kinetics for $V_{O2}$ has been reported it was independent of the magnitude of the contribution to the slow phase from the ontransient kinetics. Even more, following muscular contractions the rate of recovery is strongly dependent upon muscle fibre oxidative capacity since it has been observed that following submaximal intensity muscle contractions, the speed of recovery of microvascular $O_2$ pressures recovers much faster in the more oxidative mixed gastrocnemius than in the less oxidative white gastrocnemius. It has been also observed, that both the kinetic responses of femoral artery blood flow and the muscle capillary blood flow appear to be coupled with muscle oxygen uptake during recovery from moderate knee-extension exercise, such that extraction falls, because the cellular energetic state is not further compromised, throughout recovery. However on one hand, it is important to mention that dependent upon the relative speed of $V_{O2}$ and blood flow kinetics, the exercise offtransient may represent a condition of sub- or supra-optimal perfusion. On the other hand, $V_{O2}$ and phosphocreatine kinetics during exercise of a muscle group accustomed to daily activity are not compromised in physically active older humans, and phosphocreatine kinetics reflect the kinetics of muscle $O_2$ consumption, and are expressed at the pulmonary $V_{O2}$ kinetics after a transit delay. It has been observed also that the $V_{O2}$ kinetics remained slow when contractions were initiated from an elevated baseline despite experimentally increased blood flow and uniform fibre activation, adding evidence that muscle $V_{O2}$ control is more complex than previously suggested. In consequence our current understanding of the control of muscle $V_{O2}$ in correspondence to the fundamental pulmonary $V_{O2}$ kinetics demand consideration of new alternative mediators for $V_{O2}$ control.

The ontransient and offtransient (recovery) responses to submaximal exercise have been modelled based on the fact that the mean transit time from the muscle capillary to the lung is approximately 15-20 s, clearly indicate that it is necessary to take account of this transit delay “from muscle to mouth” if pulmonary $V_{O2}$ kinetics are to be used to estimate the kinetics of muscle $O_2$ consumption and even the removal of the first 20 s of pulmonary data from consideration effectively “time aligns” the muscle and pulmonary signals and results in close agreement between the responses, however the ontransient vs. offtransient responses to submaximal exercise have not been assessed physiological/statistically isolating their $\theta_2 V_{O2}$ dynamics.

Taking in consideration that “the issue is not simply a mathematical quibble over fitting strategies but one with significant physiological implications” (Whipp) the purpose in this study was to assess with exponential mathematical models the isolated $\phi_1$ from both the ontransient (exercise $\phi_1 V_{O2}$) and the offtransient (post-exercise $\phi_2 V_{O2}$ recovery) responses to submaximal exercise in old men,
using the 2C,7P for moderate intensity exercise (Mod) and the 3C,10P model for heavy intensity exercise (Hvy).

**Hypothesis**

If the isolated exponential $\phi_2 \gamma \text{VO}_2$ ontransient- and offtransient responses to forcing functions of submaximal exercise are kinetically symmetrical to each other then the time constant duration ($\tau_2$, $\gamma \text{VO}_2$) from the two component and three component models should not be significantly different to each other ($\tau_{2\text{on}}$, similar to $\tau_{2\text{off}}$) in old men.

**MATERIAL AND METHODS**

**Subjects**

The subjects in this study were 9 healthy males aged ranged from 66 to 79 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 informed consent.

**Testing procedures**

The determination of maximal oxygen uptake $(\gamma \text{VO}_2, \text{max})$ and the $\gamma \text{VO}_2$ at ventilatory threshold ($\theta$) 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 15 W·min⁻¹. The $\theta$ was determined by visual inspection of data using the criteria outlined previously³ of a systematic increase in $\gamma \text{VO}_2 (\gamma \text{VO}_2, \text{expired gas volume})$ and in end-tidal $\text{O}_2$ pressure $(p_{\text{ET}2\text{O}_2})$ with no concomitant rise in $\gamma /\gamma \text{CO}_2 (\gamma \text{CO}_2, \text{CO}_2$ uptake) or a decrease in end-tidal $\text{CO}_2$ pressure $(p_{\text{ET}2\text{CO}_2})$.

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 $\gamma \text{VO}_2$ of approximately 80% of the $\gamma \text{VO}_2$ at $\theta$ (ModRel, relative moderate-intensity) or the $\gamma \text{VO}_2$ of approximately 120% of the $\gamma \text{VO}_2$ at $\theta$ (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 $\gamma \text{VO}_2$ at $\theta$. The subjects exercised at the appropriate work rate for 6 min (ontransient $\gamma \text{VO}_2$ response), after which the work rate was abruptly decreased and the subjects continued loadless cycling for 6 min (offtransient $\gamma \text{VO}_2$ response).

**Data collection and analysis**

Gas exchange was determined using previously reported methods.⁹ Throughout exercise, inspired and expired gas volumes ($\gamma_i$ and $\gamma_e$) 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 (9%$O_2$, 7%$CO_2$). 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.¹⁶ 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% $\theta$, 120% $\theta$ overlayed data) was used for determining the kinetics of the $\gamma \text{VO}_2$ on- and offtransient responses to submaximal exercise.

**Models**

In these analyses only the ontransient and offtransient data for $\gamma \text{VO}_2$ were modelled with our best fitting models previously assessed.³,⁹ For moderate-intensity exercise, exponential model with two components and seven parameters (2C,7P) were fitted to the data (Table 1). For heavy-intensity exercise exponential model with three components and 10 parameters (3C,10P) were fitted to the data (Table 1). Additionally, to describe $\gamma \text{VO}_2$ kinetics of the overall response both the total amplitude (ATot = $A_1 + A_2 + A_3$) and the overall $\gamma \text{VO}_2$ kinetics named mean response time (MRT) for MRT Mod (Figure 1) and for MRT HvyRel (Figure 2) were calculated; where TD is time delayed, $\tau$ is the time constant, and subscripts 1, 2, and 3 refers to the phases $\phi_1$, $\phi_2$, and $\phi_3$ of the entire $\gamma \text{VO}_2$ response, respectively. Data were modelled using these 2C,7P and 3C,10P models described above using non-linear leastsquares regression techniques, and the best fit defined by the minimisation of the residual sum of squares.¹⁷ We used initial estimates of: TD1, 0 s; TD2, 20 s; TD3, 180 s; $\tau_1$, 5 s; $\tau_2$, 30 s; $\tau_3$, 180 s.
Table 1. The best physiological and statistical fitting models and their exponential mathematical models, applied to characterized the (τ 2) phase two both ontransient and offtransient VO 2 during submaximal (moderate and heavy) exercise in nine old men.

<table>
<thead>
<tr>
<th>Exponential Mathematical Model</th>
<th>Fitting Model</th>
<th>( t \phi, \tau ) VO 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate intensity (50 Watts, 80% ( \theta )) exercise</td>
<td>( VO_2(t) = A_0 + A_1 \cdot [1 - e^{-(t - TD1)/\tau 1}] + A_2 \cdot [1 - e^{-(t - TD2)/\tau 2}] )</td>
<td>( 2C, 7P ) baseline to 6 min entire transient response</td>
</tr>
<tr>
<td>Relative (120 %( \theta )) Heavy intensity exercise</td>
<td>( VO_2(t) = A_0 + A_1 \cdot [1 - e^{-(t - TD1)/\tau 1}] + A_2 \cdot [1 - e^{-(t - TD2)/\tau 2}] + A_3 \cdot [1 - e^{-(t - TD3)/\tau 3}] )</td>
<td>( 3C, 10P ) baseline to 6 min entire transient response</td>
</tr>
</tbody>
</table>

Exercise transient \( VO_2 \): Pulmonary \( O_2 \) uptake \( (VO_2) \) corporal response from the start (onset) to end (offset) of the exercise of an application of an ergometric forced function lasting 6 min (ontransient \( VO_2 \)) to the 6 min end exercise recovery (offtransient \( VO_2 \)). \( \theta \), ventilatory threshold. Stat, statistically significant based on Fisher’s test. Phys, physiological sense based on the differentiation of the phases and the numeric values of the estimated temporal parameters, of the transient \( VO_2 \) response, according to the intensity of the exercise modelled. \( VO_2(t) \), mass rate of change per unit of time \( (dVO_2 \cdot dt^{-1}) \), mL • min^{-1}. \( TD \), time delay, s; \( A_0 \), baseline \( (VO_2) \) at the start of the model. \( A \), the \( VO_2 \) distance value from \( A_0 \) to the \( VO_2 \) required for phase one \( (A_1) \), phase two \( (A_2) \) and phase three \( (A_3) \) amplitudes, mL. \( 1-e^{-t/\tau} \), the negative exponential distribution (Evans, Hasting and Peacock, 1993); \( e^{-t/\tau} \), the die-away factor with the time constant \( t \) (s), for an exponential increase (offtransient \( VO_2 \) response); \( t \), the time in which the transient \( VO_2 \) response is gradually (exponentially) dying away, when \( t = \tau \) means the time required for the transient \( VO_2 \) response to die away to \( e^{-1} \) part \( (e^{-1} = 1/2.71828 = 0.3678) \) of its original value, thus, \( \tau = 1 - 0.3678 = 0.63 \), and \( e = 2.718281 \) = \( (1 + n^{-1})^n \), \( n \geq 10 \) and \( 'e' \) is incommensurable with one. Two components \( (2C) \), TD1 and TD2. Three components \( (3C) \), 2C and TD3. 7P: seven parameters \( (A_0, A_1, A_2, TD_1, TD_2, \tau_1, \tau_2) \). 10P: ten parameters \( (7P, A_3, TD_3, \tau_3) \). The \( \theta \) means that even the mathematical exponential model fit the entire experimental data, phase one \( (\phi_1) \) did not behave in an exponential way and probably phase three will not \( (\phi_3) \).

Table 2. Subject characteristics and data for maximal and submaximal exercise in nine old men.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Height (cm)</th>
<th>Mass (kg)</th>
<th>Work Rate Max (Watts)</th>
<th>( VO_2 ) peak (mL•kg^{-1}•min^{-1})</th>
<th>( \theta ) (mL•min^{-1})</th>
<th>( \theta ) (mL•kg^{-1}•min^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>72.4 ± 4.4</td>
<td>173.8 ± 5.5</td>
<td>79.8 ± 9.9</td>
<td>127.8 ± 20.7</td>
<td>2.2 ± 0.4</td>
<td>27.8 ± 6.8</td>
<td>1,333.2 ± 138.6</td>
</tr>
</tbody>
</table>

Submaximal exercise

<table>
<thead>
<tr>
<th>( 50 ) W( ^{\circ} ) ( VO_2 ) (mL•min^{-1})</th>
<th>( 50 ) W( ^{\circ} ) ( VO_2 ) (mL•kg^{-1}•min^{-1})</th>
<th>( PO ) (W)</th>
<th>( \theta ) (mL•min^{-1})</th>
<th>( \theta ) (mL•kg^{-1}•min^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,180.3 ± 1( ^{a} )</td>
<td>14.9 ± 1.4( ^{c} )</td>
<td>35.7 ± 11.1( ^{a} )</td>
<td>1,049.6 ± 198( ^{c} )</td>
<td>13.2 ± 2.2( ^{d} )</td>
</tr>
</tbody>
</table>

All data are mean ± SD. \( ^{a} \)Absolute \( PO \); \( \theta \), ventilatory threshold. \( PO \), power output. \( VO_2 \), pulmonary oxygen uptake. mL • kg^{-1} • min^{-1}, \( VO_2 \) relative to total body mass. Significant differences between means with different letter, allocated by Two way ANOVA procedure, post-hoc Holm-Sidak (P < 0.001): \( ^{a} {F}_{\text{ratio}} = 24 \), \( ^{c} {F}_{\text{ratio}} = 20 \), \( ^{d} {F}_{\text{ratio}} = 52 \).
The ontransient and offtransient pulmonary oxygen uptake response profiles to absolute moderate intensity (ModAbs = 50 ± 0 W), relative moderate-intensity (ModRel100%θ = 36 ± 11 W), and relative heavy-intensity (HvyRel120%θ = 89 ± 17 W) square wave exercise is shown in figure 3. Steady states of VO2 ontransient and offtransient were attained at moderate (Mod) but not at heavy (Hvy) intensities (Figure 3).

The VO2 baseline On and Off comparisons from our three different submaximal exercise intensities are shown in figure 4. Analysis showed high On VO2 baseline compa-
The submaximal ontransient and offtransient \( \text{VO}_2 \) kinetics in old men.

The \( \text{VO}_2 \) ontransient and offtransient MRT comparisons from three different submaximal exercise intensities in this study are shown in figure 5. Analysis showed that only the HvyRel \( \text{VO}_2 \) ontransient MRT (not the moderate-intensities: ModAbs and ModRel) resulted significantly high (t = 5, P < 0.001) compared \( \text{VO}_2 \) offtransient MRT (Figure 4).

The fundamental temporal parameters (A, TD, \( \tau \)) for the ontransient \( \text{VO}_2 \) vs. offtransient (P > 0.05) \( \text{VO}_2 \) submaximal exercise comparisons from our best fitting models (Table 1) are shown in table 3. Either the amplitude \( \phi \) \( \text{VO}_2 \) or the time constant \( \phi \) \( \text{VO}_2 \) resulted similar between on and off transitions for each submaximal exercise intensity (Table 3).

### Table 3. Fundamental temporal parameter for the ontransient vs. offtransient \( \text{VO}_2 \) submaximal exercise comparisons from best fitting models.

<table>
<thead>
<tr>
<th>Exercise intensity</th>
<th>Best fitting model</th>
<th>Parameter</th>
<th>Isolated phase II ( \text{VO}_2 ) transient response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolute moderate (50 W)(^{f,s})</td>
<td>2C,7P</td>
<td>Amplitude, mL ( \cdot ) min(^{-1})</td>
<td>245 \pm 52, 262 \pm 109</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Time delayed, s</td>
<td>27.2 \pm 4.3, 26.3 \pm 4.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Time constant, s</td>
<td>51.9 \pm 12.9, 51.0 \pm 12.7</td>
</tr>
<tr>
<td>Relative moderate (80% ( \theta ))</td>
<td>2C,7P</td>
<td>Amplitude, mL ( \cdot ) min(^{-1})</td>
<td>143 \pm 94, 121 \pm 69</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Time delayed, s</td>
<td>26.1 \pm 7.4, 24.3 \pm 7.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Time constant, s</td>
<td>61.6 \pm 16.0, 60.9 \pm 14.0</td>
</tr>
<tr>
<td>Relative heavy (120% ( \theta ))</td>
<td>3C,10P</td>
<td>Amplitude, mL ( \cdot ) min(^{-1})</td>
<td>607 \pm 208, 613 \pm 250</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Time delayed, s</td>
<td>22.0 \pm 3.8, 27.0 \pm 5.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Time constant, s</td>
<td>40.2 \pm 8.4, 38.7 \pm 6.6</td>
</tr>
</tbody>
</table>

All data are mean \( \pm \) SD from 9 male old sample size. \( \text{VO}_2 \) pulmonary oxygen uptake, \( \theta \): ventilatory threshold. The 2C\(^{temporal}\), 7P\(^{pontential}\), and the 3C\(^{temporal}\), 10P\(^{potential}\) both with an entire transient fitting window from baseline to 6 min, isolated phase II \( \text{VO}_2 \) ontransient and offtransient responses (P > 0.05) to submaximal (moderate and heavy) exercise.

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**Figure 4.** Pulmonary oxygen uptake (\( \text{VO}_2 \)) baseline On (pO) and Off (ERE) comparisons from three different submaximal exercise intensities. Absolute moderate (ModAbs = 50 W), relative moderate (ModRel = 80% \( \theta \)), and relative heavy (HvyRel = 120% \( \theta \)) square wave exercise. * P < 0.001.

**Figure 5.** Pulmonary oxygen uptake (\( \text{VO}_2 \)) Ontransient and Offtransient overall mean response time (MRT) comparisons from three different submaximal exercise intensities. MRT, the time required to achieve the 63.22% of the entire \( \text{VO}_2 \) transient of response. Absolute moderate (ModAbs = 50 W), relative moderate (ModRel = 80% \( \theta \)), and relative heavy (HvyRel = 120% \( \theta \)) square wave exercise. * P < 0.001.
**DISCUSSION**

The $\vartheta O_2$ kinetic analysis used in the present study isolates the fundamental phases of $\varphi$, $\vartheta O_2$ dynamics, which in normal conditions in healthy participants closely reflects the skeletal muscle $\varphi$, $\vartheta O_2$ dynamics.\textsuperscript{6,6} The ontransient (exercise $\varphi$, $\vartheta O_2$) vs. the offtransient (post-exercise $\varphi$, $\vartheta O_2$ recovery) responses to the exercise tests for absolute moderate exercise; for relative moderate exercise and; for relative heavy exercise (submaximal exercise) cycling (ontransient) and constant off-loadless (offtransient) cycling were analysed with best statistically and/or physiologically exponential mathematical fitting models\textsuperscript{3,9} that characterised the on $\varphi$, $\vartheta O_2$ kinetics (on $\tau_0$, $\vartheta O_2$) and the off $\varphi$, $\vartheta O_2$ kinetics (off $\tau_0$, $\vartheta O_2$) for this submaximal exercise in older men. The on isolated- and off isolated-$\varphi$, $\vartheta O_2$ makes a physiological sense because it is obtained by fitting the entire (on, off) response with and exponential mathematical model identifying the three theoretical phases named the cardiodynamic phase ($\varphi$, $\vartheta O_2$), the fundamental exponential phase ($\varphi$, $\vartheta O_2$) and the subsequent ($\varphi$, $\vartheta O_2$) 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 $\vartheta O_2$ resulting in what has been termed ‘excess’ $\vartheta O_2$ specially for supra lactate threshold exercise.\textsuperscript{20} Whether or not these phases $\varphi$, $\vartheta O_2$ and $\varphi$, $\vartheta O_2$ are exponentials or not is matter of debate. However, in this study the isolated $\varphi$, $\vartheta O_2$ exponential phase for submaximal exercise from the ontransient and offtransient showed symmetry to each other; confirming that our best statistically and physiologically\textsuperscript{11,19} fitting model constituents reflected the system’s physiological features, with implications for its control mechanisms due to the fact that the pulmonary $\vartheta O_2$ kinetics usefully reflect the entire response of the muscle fibers that are contributing to force production. Besides, physiological systems analysis constitutes a tested and valuable tool that enhances understanding of the physiology of gas exchange kinetics and muscle energetics.\textsuperscript{21}

Steady states of $\vartheta O_2$ ontransient and offtransient observed at moderate (Mod) but not at heavy (Hvy) intensities in this study agreed with previous observations from other researchers\textsuperscript{5,15,20} confirming that for exercise above anaerobic threshold, the $\vartheta O_2$ dynamics are more complex.

The fundamental temporal parameters ($\Delta t'$, $TD_{2'}$, $\tau_2$) for the ontransient $\vartheta O_2$ vs. offtransient $\vartheta O_2$ submaximal exercise comparisons from our best fitting models resulted similar between on and off transitions for each submaximal exercise intensity. Thus characterizing the fundamental $\vartheta O_2$ kinetics should take into account these temporal physiological considerations modulating muscle efficiency since this $\vartheta O_2$ clearly reflects the fundamental kinetics of the muscle energy metabolism during/recovery of this exercise intensity.\textsuperscript{8} Thus an association between muscle phosphocreatine decrease, determined by magnetic resonance spectroscopy, and pulmonary oxygen kinetics exists. However, on considering the entire temporal kinetic parameters, it has been observed dynamic asymmetry of phosphocreatine concentration and $\vartheta O_2$ between the ontransient and offtransient of moderateand high-intensity exercise in humans.\textsuperscript{22,23} This is on the other hand, in partial agreement with our observation that the $\vartheta O_2$ ontransient and offtransient MRT comparisons from the three different submaximal exercise intensities in this study resulted similar for the moderate-intensities (ModAbs and ModRel) but the HvyRel $\vartheta O_2$ ontransient MRT resulted significantly high compared $\vartheta O_2$ ontransient MRT. Again, a more complex kinetics exists in this HvyRel exercise.\textsuperscript{5,22} suggesting that overall mean response time up-hill (Hvyon MRT) is harder than its Hvyoff MRT (down-hill); this observation also agrees with the fact, that in this study the $\vartheta O_2$ OffBaseline was low compared $\vartheta O_2$ OnBaseline in each of the three different submaximal exercise intensities and also it is explained because in the onset of exercise there is a rapid adjustment of blood flow required to facilitate adequate O$_2$ delivery as metabolic rate increases; in contrast, a slower adjustment of flow following cessation of exercise would speed recovery as the metabolic rate returns to its resting level.\textsuperscript{32} Besides, it has been observed that slowed oxidative energy provision at the onset of exercise was correlated with the transient skeletal muscle deoxygenation peak and the reduced spatial distribution but it was not correlated with a microvascular O$_2$, probably due to an absolute, rather than kinetic, mismatch of microvascular O$_2$ delivery and consumption affecting the kinetics of muscular oxidative energy provision when muscle deoxygenation reaches some ‘critical’ level.\textsuperscript{24}

**CONCLUSIONS**

The on and off fundamental kinetics of the transient responses of the $\varphi$, $\vartheta O_2$ are strongly influenced by the dynamics of the $\vartheta O_2$ during muscular submaximal exercise in older men.

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