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

Javier Padilla-Pérez*

RESUMEN

Se evaluó en adultos maduros voluntarios sanos si la respuesta fundamental de $\dot{V}O_2$ (Φ_2 $\dot{V}O_2$) al ejercicio submáximo (ontransitoria) y su recuperación (offtransitoria) muestran una cinética similar (τ_{2On} *vs.* τ_{2Off}) de la ϕ_2 $\dot{V}O_2$ (τ_2, constante fundamental de tiempo) de modelos exponenciales de mejor ajuste ya evaluados. Los voluntarios (n = 9; media ± SD: 72 ± 4 años) hicieron una prueba inicial de rampa (15 W·min^{-1}) hasta el agotamiento, de la que fueron identificados el umbral ventilatorio (θ) y las intensidades de trabajo submáximo para 80%θ (ModRel) y 120%θ (HvyRel); además se seleccionó una intensidad absoluta de 50 W (ModAbs). On y off transitorias fueron desde una línea de base (LB) sin previo aviso al voluntario. Cada una duró 6 min y se repitió entre 4-6 veces para cada intensidad. $\dot{V}O_2$ 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., τ_2) fueron determinados para cada componente. Nuestros mejores modelos de ajuste estadístico y/o fisiológico mostraron valores transitorios simétricos (on similar off) de $\tau_2\dot{V}O_2$ (s) con 2C, 7P (Mod_Abs and Rel: on = 57 ± 15 y off = 56 ± 14); y para HvyRel (on = 40 ± 9 y off = 39 ± 7) con 3C, 10P. La LB (mL · min^{-1}) de Hvyon (744 ± 115) fue menor que Hvyoff (982 ± 288). Tiempo medio de la respuesta cinética global (s) Hvyon (82 ± 18) fue menor que Hvyoff (55 ± 8). Las cinéticas on y off de la respuesta transitoria de la Φ_2 $\dot{V}O_2$ están notablemente influenciadas por la dinámica de la $\dot{V}O_2$ 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 $\dot{V}O_2$ (Φ_2 $\dot{V}O_2$) to submaximal exercise (ontransient response) and its recovery (offtransient response) show in the $\dot{V}O_2$ kinetics (τ_2, time constant two) on-off symmetry (τ_{2On} *vs.* τ_{2Off}) characterised from best exponential fitting models previously assessed. Volunteers (n = 9; mean ± SD: 72 ± 4 yrs) completed an initial incremental ramp test (W·min^{-1}) to volitional fatigue from which the ventilatory threshold (θ) and work rates corresponding to 80%θ (ModRel) and 120%θ (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 (BL) 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 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 by using different fitting windows, and parameter (P) estimates (i.e., τ_2) were determined for each component. Our best statistically and/or physiologically fitting models showed symmetry τ_2 values for Mod with 2C, 7P (Mod_Abs and Rel: on = 57 ± 15 and off = 56±14); and for HvyRel (on = 40 ± 9 y off = 39 ± 7) with 3C, 10P. BL (mL·min^{-1}) Hvyon (744 ± 115) was low compared Hvyoff (982 ± 288). Overall

* Escuela Superior de Medicina, IPN. Canadian Centre for Activity and Ageing, School of Kinesiology, The University of Western Ontario 6501811FTGAF), London, Ontario, Canada N6A 3K7.

mean response time (s) Hvyon (82 ± 18) resulted low compared Hvyoff (55 ± 8). The on and off kinetics of the transient responses of the ϕ_2 $\dot{V}O_2$ are strongly influenced by the dynamics of $\dot{V}O_2$ 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.[1] A slowing of pulmonary oxygen uptake ($\dot{V}O_2$) kinetics during the on-transition to a step increase in work rate (WR) of moderate intensity[2] require to be characterized by an exponential model with twocomponents and seven parameters (2C,7P),[3] below what has been termed the anaerobic threshold. For heavy exercise (above anaerobic threshold), the physiological basis for phases 1 (θ_1) and 2 (θ_2) transitions in $\dot{V}O_2$ kinetics is evident while θ_2 to θ_3 (phase three) transitions in heavy exercise are complex,[4] with asymmetries of $\dot{V}O_2$ transients at the onset and offset, and require complex model[5] like an exponential model with three components and 10 parameters (3C,10P),[3] for appropriate characterisation as a result of a slow kinetic component which is of delayed onset of approximately ≥ 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,[6-8] specially above anaerobic threshold, both during the ontransient and offtransient (recovery) responses to submaximal exercise.[9] 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., $\dot{V}O_2$ offtransient response). The slower $\dot{V}O_2$ 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 $\dot{V}O_2$ has been reported it was independent of the magnitude of the contribution to the slow phase from the ontransient kinetics.[10] 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.[11] 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.[12] However on one hand, it is important to mention that dependent upon the relative speed of $\dot{V}O_2$ and blood flow kinetics, the exercise offtransient may represent a condition of sub- or supra-optimal perfusion.[11] On the other hand, $\dot{V}O_2$ 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 $\dot{V}O_2$ kinetics after a transit delay.[13] It has been observed also that the $\dot{V}O_2$ kinetics remained slow when contractions were initiated from an elevated baseline despite experimentally increased blood flow and uniform fibre activation, adding evidence that muscle $\dot{V}O_2$ control is more complex than previously suggested. In consequence our current understanding of the control of muscle $\dot{V}O_2$ in correspondence to the fundamental pulmonary $\dot{V}O_2$ kinetics demand consideration of new alternative mediators for $\dot{V}O_2$ control.[14]

The ontransient and offtransient (recovery) responses to submaximal exercise has 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 $\dot{V}O_2$ 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,[8] however the ontransient *vs.* offtransient responses to submaximal exercise have not been assessed physiological/statistically isolating their θ_2 $\dot{V}O_2$ dynamics.

Taking in consideration that "the issue is not simply a mathematical quibble over fitting strategies but one with significant physiological implications" (Whipp)[15] the purpose in this study was to assess with exponential mathematical models the isolated ϕ_2 from both the ontransient (exercise ϕ_2 $\dot{V}O_2$) and the offtransient (post-exercise ϕ_2 $\dot{V}O_2$ 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 $\phi_2\dot{V}O_2$ ontransient- and offtransient responses to forcing functions of submaximal exercise are kinetically symmetrical to each other then the time constant duration ($\tau\phi_2$ $\dot{V}O_2$) from the two component and three component models should not be significantly different to each other (τ_{2on} similar to τ_{2off}) 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 ($\dot{V}O_2$ 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 15 $W\cdot min^{-1}$. The θ was determined by visual inspection of data using the criteria outlined previously[3] 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 (ontransient $\dot{V}O_2$ response), after which the work rate was abruptly decreased and the subjects continued loadless cycling for 6 min (offtransient $\dot{V}O_2$ 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 $mL\cdot s^{-1}$) 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 $transitions\cdot visit^{-1}$) and for HvyRel were performed 2-3 constant-load exercise tests (1 $transition\cdot visit^{-1}$). 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 offtransient responses to submaximal exercise.

Models

In these analyses only the ontransient and offtransient data for $\dot{V}O_2$ were modelled with our best fitting models previously assessed.[3,9] For moderate-intensity exercise, exponential model with twocomponents 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[3,9] (Table 1). Additionally, to describe $\dot{V}O_2$ kinetics of the overall response both the total amplitude ($ATot = A_1 + A_2 + A_3$) and the overall $\dot{V}O_2$ kinetics named mean response time (MRT) for MRT_{Mod} (Figure 1) and for MRT_{HvyRel} (Figure 2) were calculated; where TD is time delayed, τ is the time constant, and subscripts 1, 2, and 3 refers to the phases $\phi1$, $\phi2$, and $\phi3$ of the entire $\dot{V}O_2$ 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; τ1, 5 s; τ2, 30 s; τ3,180 s.

Table 1. The best physiological and statistical fitting models and their exponential mathematical models, applied to characterized the ($\tau 2$) phase two both ontransient and offtransient $\dot{V}O_2$ during submaximal (moderate and heavy) exercise in nine old men.

ExponentialMathematicalModel	FittingModel	$\tau \phi_2 \dot{V}O_2$
Moderate intensity (50 Watts, 80% θ) exercise $\dot{V}O_2(t) = A_0 + A_1 \bullet [1-e^{-[(t - TD1) / \tau 2]}] + A_2 \bullet [1-e^{-[(t-TD2)/\tau 2]}]$	$2C,7P_{\text{Baseline to 6 min Entire transient response}}$ $\therefore \phi_{2\text{Isolated\_Stat \& Phys}}\ \dot{V}O_2(t) = A_0 + A_2 \bullet [1-e^{-[(t-TD2)/\tau 2]}]$	τ "ϕ_1", $\tau\phi_{2\text{Isolated\_Stat \& Phys}}$
Relative (120 %θ) Heavy intensity exercise $\dot{V}O_2(t) = A_0 + A_1 \bullet [1-e^{-[(t-TD1)/\tau 1]}] + A_2 \bullet [1-e^{-[(t-TD2)/\tau 2]}] + A_3 \bullet [1-e^{-[(t-TD3)/\tau 3]}]$	$3C,10P_{\text{Baseline to 6 min Entire transient response}}$ $\therefore \phi_{2\text{Isolated\_Phys \& Stat}}\ VO_2(t) = A_0 + A_2 \bullet [1-e^{-[(t-TD2)/\tau 2]}]$	τ "ϕ_1", $\tau\phi_{2\text{Isolated\_Stat \& Physs,}}$ "ϕ_3"

Exercise transient $\dot{V}O_2$: Pulmonary O_2 uptake ($\dot{V}O_2$) corporal response from the start (onset) to end (offset) of the exercise of an application of an ergometric forced function lasting 6 min (ontransient $\dot{V}O_2$) to the 6 min end exercise recovery (offtransient $\dot{V}O_2$). θ, 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 $\dot{V}O_2$ response, according to the intensity of the exercise modelled. $\dot{V}O_2(t)$, mass rate of change per unit of time ($d\dot{V}O_2 \bullet dt^{-1}$), mL • min^{-1}. TD: time dalay, s; A_0: baseline (the $\dot{V}O_2$ at the start of the model). A, the $\dot{V}O_2$ distance value from A_0 to the $\dot{V}O_2$ 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 $\dot{V}O_2$ response); t, the time in which the transient $\dot{V}O_2$ response is gradually (exponentially) dying away, when $t = \tau$ means the time required for the transient $\dot{V}O_2$ 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, TD1, TD2, $\tau 1$, $\tau 2$). 10P: ten parameters (7P, a_3, TD3, $\tau 3$). The θ means that even the mathematical exponential model fit the entire experimental data, phase one ("ϕ_1") did not behave in an exponential way and probably phase three will not ("ϕ_3").

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

Age (years)	Height (cm)	Mass (kg)	Work Rate Max (Watts)	$\dot{V}O_2$ peak ($l \cdot min^{-1}$)	$\dot{V}O_2$ peak ($mL \cdot kg^{-1} \cdot min^{-1}$)	θ ($mL \cdot min^{-1}$)	θ ($mL \cdot kg^{-1} \cdot min^{-1}$)
72.4 ± 4.4	173.8 ± 5.5	79.8 ± 9.9	127.8 ± 20.7	2.2 ± 0.4	27.8 ± 6.8	1,333.2 ± 138.6	17.0 ± 2.7

Submaximal exercise

50 W[§ e] $\dot{V}O_2$ ($mL \cdot min^{-1}$)	50 W[§ e] ($mL \cdot kg^{-1} \cdot min^{-1}$)	Moderate intensity exercise PO (W)	Moderate intensity exercise $\dot{V}O_2$ ($mL \cdot min^{-1}$)	Moderate intensity exercise ($mL \cdot kg^{-1} \cdot min^{-1}$)	Heavy intensity exercise PO (W)	Heavy intensity exercise $\dot{V}O_2$ ($mL \cdot min^{-1}$)	Heavy intensity exercise ($mL \cdot kg^{-1} \cdot min^{-1}$)
1,180.3 ± 1[a]	14.9 ± 1.4[c]	35.7 ± 11.1[e]	1,049.6 ± 198[b]	13.2 ± 2.2[d]	89.1 ± 16.6[f]	1,782.6 ± 332.6[b]	22.6 ± 5.3[d]

All data are mean ± SD. [§]Absolute PO. q: ventilatory threshold. PO: power output. $\dot{V}O_2$: pulmonary oxygen uptake. mL • kg^{-1} • min^{-1}, $\dot{V}O_2$ relative to total body mass. Significant differences between means with different letter, allocated by Two way ANOVA procedure, *post-hoc* Holm-Sidak ($P < 0.001$): $^{a \neq b}F_{ratio} = 24$, $^{c \neq d}F_{ratio} = 20$, $^{e \neq f}F_{ratio} = 52$.

$$MRT_{Mod} = [A_1/(A_1 + A_2)] \bullet (TD_1 + \tau_1) + [A_2/(A_1 + A_2)] \bullet (TD_2 + \tau_2)$$

Figure 1. *MRT_{Mod}.*

$$MRT_{HvyRel} = [A_1/(A_1 + A_2 + A_3)] \bullet (TD_1 + \tau_1) + [A_2/(A_1 + A_2 + A_3)] \bullet (TD_2 + \tau_2) + [A_3/(A_1 + A_2 + A_3)] \bullet (TD_3 + \tau_3)$$

Figure 2. *MRT_{HvyRel}.*

Usually 100 iterations were run and the parameter estimates examined to allow further iterations with the estimates obtained. The models were run with $\phi 2\ \tau$ 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.[18] Specific details of each best model with reference to start and end-point of each fit has been published some where else.[3 9] However in brief in this study the 2C,7P modelled for moderate intensity exercise only either from 2 min $B_aS_eL_{ine}$ to 6 min ontransient $\dot{V}O_2$ Mod[3] or from 1 min BSL to 6 min offtransient $\dot{V}O_2$ ModAbs.[9] This $2C,7P_{BSL\ to\ 6\ min}$ was a twocomponent exponential fitted from BSL-start to end-exercise with two exponential equations differentiating θ_1 and θ_2. The 3C10P modelled for heavy-intensity exercise with a fitting window either from 2 min BSL to 6 min ontransient $\dot{V}O_2$ HvyRel or from 1 min BSL to 6 min offtransient $\dot{V}O_2$ HvyRel. This $3C,10P_{BSL\ to\ 6\ min}$ was a three component exponential fitted from BSL_start to either end-, or recovery-exercise[3,9] with three exponential equations differentiating ϕ_1, ϕ_2 and ϕ_3 (Table 1).

Statistical analyses

Estimated values of the $\theta_2\ \tau$ and estimated parameters of interest from the different models used were compared, on *vs.* off exercise intensity group, using two-way analysis of variance all pairwise multiple comparison procedures *(post-hoc* Holm-Sidak) with repeated measures.[19] The Student's *t*-test was used to determine if the mean values of two conditions were significantly different.[19] The probability level of 0.05 was chosen as the criterion for acceptance of statistical significance.

RESULTS

Subjects were of similar physical characteristics and cardiorespiratory fitness (Table 2). As expected, analysis showed that the power output and the pulmonary oxygen uptake both absolute and relative to total body mass, from the three different exercise intensities were significantly different ($P < 0.05$) to each other (Table 2).

The ontransient and offtransient pulmonary oxygen uptake response profiles to absolute moderate intensity (ModAbs = 50 ± 0 W), relative moderate-intensity ($ModRel_{80\%\theta}$ = 36 ± 11 W), and relative heavy-intensity ($HvyRel_{120\%\theta}$ = 89 ± 17 W) square wave exercise is shown in figure 3. Steady states of $\dot{V}O_2$ ontransient and offtransient were attained at moderate (Mod) but not at heavy (Hvy) intensities (Figure 3).

The $\dot{V}O_2$ baseline On and Off comparisons from our three different submaximal exercise intensities are shown in figure 4. Analysis showed high On $\dot{V}O_2$ baseline compa-

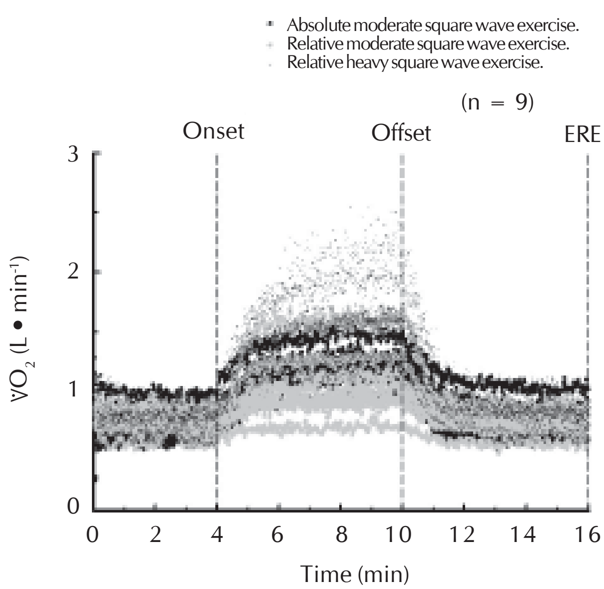

Figure 3. *Groups ontransient and offtransient pulmonary oxygen uptake ($\dot{V}O_2$) response profiles to absolute moderate (50 W), relative moderate (80% θ), and relative heavy (120% θ) square wave exercise. Exercise onset (start) is at four min and offset (end) is at ten min. Data points (symbols) are the breath-by-breath interpolated to second-by-second pulmonary $\dot{V}O_2$ (experimental data) from either two min baseline (On_baseline: 2 min to 4 min) to the entire ontransient response (Onset to Offset) or one min baseline (Off_baseline: 9 min to 10 min) to the entire offtransient response (Offset to "$E_{nd}R_{ecovery}E_{xercise}$" baseline). The nine subjects submaximal exercise at each intensity (n = 9) are displayed. θ: ventilatory threshold.*

red Off $\dot{V}O_2$ baseline for absolute moderate-intensity (ModAbs: t = 4.4, P < 0.001), relative moderate-intensity (Mod Rel: t = 6.5, P < 0.001) and relative heavy-intensity (HvyRel: t = 3.2, P = 0.002) (Figure 4).

The fundamental temporal parameters (A_2, TD_2, τ_2) for the ontransient $\dot{V}O_2$ *vs.* offtransient (P > 0.05) $\dot{V}O_2$ submaximal exercise comparisons from our best fitting models (Table 1) 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).

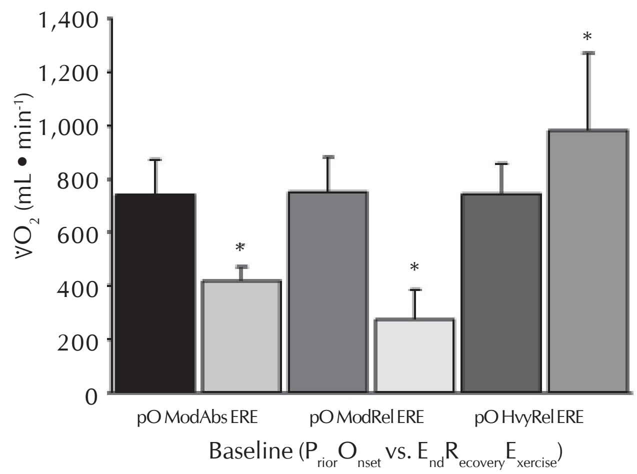

Figure 4. *Pulmonary oxygen uptake ($\dot{V}O_2$) baseline On (pO) and Off (ERE) comparisons from three different submaximal exercise intensities. Absolute moderate (ModAbs = 50 W), relative moderate (ModRel = 80% θ), and relative heavy (HvyRel = 120% θ) square wave exercise. * P < 0.001.*

The $\dot{V}O_2$ 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 $\dot{V}O_2$ ontransient MRT (not the moderate-intensities: ModAbs and ModRel) resulted significantly high (t = 5, P < 0.001) compared $\dot{V}O_2$ offtransient MRT (Figure 4).

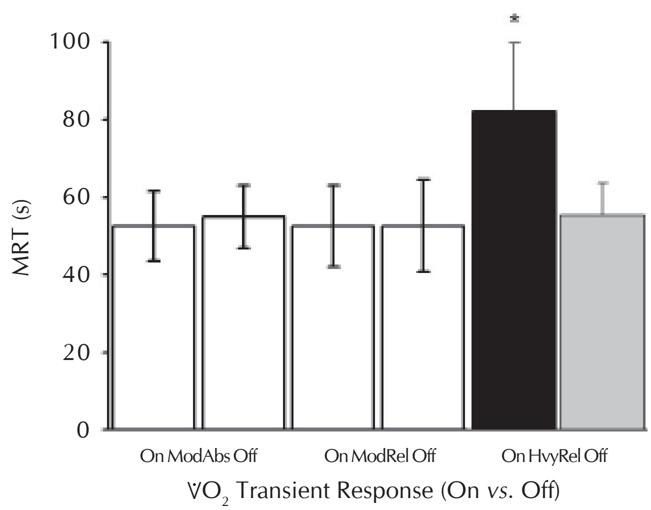

Figure 5. *Pulmonary oxygen uptake ($\dot{V}O_2$) Ontransient and Offtransient overall mean response time (MRT) comparisons from three different submaximal exercise intensities. MRT, the time required to achieve the 63.22% of the entire $\dot{V}O_2$ transient of response. Absolute moderate (ModAbs = 50 W), relative moderate (ModRel = 80% θ), and relative heavy (HvyRel = 120% θ) square wave exercise.* P < 0.001.*

Table 3. Fundamental temporal parameter for the ontransient *vs.* offtransient $\dot{V}O_2$ submaximal exercise comparisons from best fitting models.

Exercise intensity	Best fitting model$_{On-, Off-window}$	Parameter	Isolated phase II $\dot{V}O_2$ transient response On¶	Isolated phase II $\dot{V}O_2$ transient response Off§
Absolute moderate (50 W)¶ §	2C,7P On_baseline 2 min to 6 min end exercise Off_baseline 1 min to 6 min exercise recovery	Amplitude, mL • min^{-1}	245 ± 52	262 ± 109
		Time delayed, s	27.2 ± 4.3	26.3 ± 4.0
		Time constant, s	51.9 ± 12.9	51.0 ± 12.7
Relative moderate (80% θ)¶ §	2C,7P On_baseline 2 min to 6 min end exercise Off_baseline 1 min to 6 min exercise recovery	Amplitude, mL • min^{-1}	143 ± 94	121 ± 69
		Time delayed, s	26.1 ± 7.4	24.3 ± 7.0
		Time constant, s	61.6 ± 16.0	60.9 ± 14.0
Relative heavy (120% θ)	3C,10P On_baseline 2 min to 6 min end exercise Off_baseline 1 min to 6 min exercise recovery	Amplitude, mL • min^{-1}	607 ± 208	613 ± 250
		Time delayed, s	22.0 ± 3.8	27.0 ± 5.5
		Time constant, s	40.2 ± 8.4	38.7 ± 6.6

All data are mean ± SD from 9 male old sample size. $\dot{V}O_2$: pulmonary oxygen uptake. θ: ventilatory threshold. The $2C_{omponents}$, $7P_{arameters}$ and the $3C_{omponents}$, $10P_{arameters}$ both with an entire transient fitting window from baseline to 6 min, isolated phase II $\dot{V}O_2$ ontransient and offtransient responses (P > 0.05) to submaximal (moderate and heavy) exercise.

DISCUSSION

The $\dot{V}O_2$ kinetic analysis used in the present study isolates the fundamental phase 2 ($\phi_2\dot{V}O_2$) component of the response to submaximal exercise, which in normal conditions in healthy participants closely reflects the skeletal muscle $\phi_2\dot{V}O_2$ dynamics.[6-8] The ontransient (exercise $\phi_2\dot{V}O_2$) *vs.* the offtransient (post-exercise ϕ_2 $\dot{V}O_2$ 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[3,9] 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 old healthy adult men. The on isolated- and off isolated-ϕ_2 $\dot{V}O_2$ 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 (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 ϕ_2 $\dot{V}O_2$ exponential phase for submaximal exercise from the ontransient and offtransient showed symmetry to each other; confirming that our best statistically and physiological[3 9] fitting model constituents reflected the system's physiological features, with implications for its control mechanisms due to the fact that the pulmonary $\dot{V}O_2$ 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.[21]

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

The fundamental temporal parameters (A_2, TD_2, τ_2) for the ontransient $\dot{V}O_2$ *vs.* offtransient $\dot{V}O_2$ submaximal exercise comparisons from our best fitting models resulted similar between on and off transitions for each submaximal exercise intensity. Thus characterizing the fundamental $\dot{V}O_2$ kinetics should take into account these temporal physiological considerations modulating muscle efficiency since this $\theta_2\dot{V}O_2$ clearly reflects the fundamental kinetics of the muscle energy metabolism during/recovery of this exercise intensity.[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 $\dot{V}O_2$ between the ontransient and offtransient of moderate- and high-intensity exercise in humans.[22,23] This is on the other hand, in partial agreement with our observation that the $\dot{V}O_2$ 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 $\dot{V}O_2$ ontransient MRT resulted significantly high compared $\dot{V}O_2$ offtransient MRT. Again, a more complex kinetics exists in this HvyRel exercise,[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 $\dot{V}O_2$ $Off_{Baseline}$ was low compared $\dot{V}O_2$ $On_{Baseline}$ 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.[12] 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.[24]

CONCLUSIONS

The on and off fundamental kinetics of the transient responses of the ϕ_2 $\dot{V}O_2$ are strongly influenced by the dynamics of the $\dot{V}O_2$ during muscular submaximal exercise in older men.

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Solicitud de sobretiros:

Javier Padilla P.MD, MSc, PhD (Candidate)
Fisiología del Ejercicio
Escuela Superior de Medicina
Instituto Politécnico Nacional
Casco de Santo Tomás, DMH
C.P.11340, México, D.F.
Tel.: (55) 5729-6300, Ext. 62733
Fax (ext.): 62801
Correo electrónico: japadillap@ipn.mx