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Phase two on-transient $\dot{V}O_2$ kinetics is slow age-related during submaximal exercise in adult men

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RESUMEN

Introducción. La cantidad y curso temporal del consumo muscular de oxígeno ($\dot{V}O_{2M}$) se refleja en su captación pulmonar ($\dot{V}O_2$, mL•min-1), en términos de tres fases de una respuesta transitoria al ejercicio; la cardio dinámica (Φ_1 $\dot{V}O_2$), el estado estable del ejercicio o el componente lento (Φ_3 $\dot{V}O_2$) y la que refleja (Φ_2 $\dot{V}O_2$) la $\dot{V}O_{2M}$. La respuesta cinética transitoria de la Φ_2 $\dot{V}O_2$ (τ, constante de tiempo, s) sigue siendo importantísima en la investigación detallada de la $\dot{V}O_{2M}$ y del grado de entropía de la Φ_2 $\dot{V}O_2$ τ de un sistema vivo (S Φ_2 $\dot{V}O_2$ τ, cal•°C-1•s). **Material y métodos.** Ocho jóvenes (YG = 25 ± 3 años; media ± DE) y nueve adultos mayores (OG = 71 ± 5) masculinos, hicieron una prueba rampa de ejercicio de ciclismo de piernas (YG: 25W•min-1; OG: 15W•min-1). Cada uno completó de 4 8 repeticiones de ejercicio de ciclismo de piernas a base de uno de intensidad moderada absoluta (50W) y dos relativos al umbral láctico estimado ($\hat{\theta}_L$; moderado: 80% $\hat{\theta}_L$, intenso: 120% $\hat{\theta}_L$) (submáximo = moderado + intenso) con duración de 6 min cada uno. Comparamos Φ_2 $\dot{V}O_2$ τ de YG y OG, del modelado con regresión no lineal de datos de $\dot{V}O_{2\ \text{respiración por respiración}}$, mediante aislamiento fisiológico previo de la Φ_2 $\dot{V}O_2$ ajustada (v_{entana} $m_{odelada}$: desde una Línea Basal_Inicio al Final ejercicio) con modelos exponenciales de dos y tres componentes para el moderado y intenso respectivamente. El relativo fue determinado de la prueba rampa para poner al mismo nivel energético de ejercicio a las personas. **Resultados.** Observamos la respuesta característica de cinética lenta de la Φ_2 $\dot{V}O_2$ del ejercicio de adultos mayores comparados con jóvenes (τ2: OG > YG), no sólo para el relativo (moderado: 62 ± 16 > 28 ± 10 e intenso: 40 ± 7 > 26 ± 10), sino también para el absoluto (52 ± 13 > 23 ± 12) (submáximo: 51.3 ± 15.1 > 25.7 ± 10.3), así como para la S Φ_2 $\dot{V}O_2$ τ (x10-3) de cada uno de ellos ($S\tau 2_{absoluto}$: 14 ± 1 > 11 ± 2; $S\tau 2_{moderado\ relativo}$: 15 ± 1 > 12 ± 1, $S\tau 2_{intenso}$: 13 ± 1 > 12 ± 2 y $S\tau 2_{submaximo}$: 14 ± 1 > 12 ± 2). **Conclusión.** La cinética lenta de la Φ_2 $\dot{V}O_2$ y su entropía aumentada se relacionaron con la edad, tanto para las pruebas de carga constante del mismo nivel energético (relativo: moderado e intenso) como absoluta moderada.

Palabras clave: *Envejecimiento, oxígeno, cinética, constante de tiempo, entropía.*

ABSTRACT

Introduction. The magnitude and time course of muscle oxygen ($\dot{V}O_2$) consumption ($\dot{V}O_{2M}$) is reflected in that of pulmonary $\dot{V}O_2$ uptake ($\dot{V}O_2$, mL•min-1) in terms of three on transient phases of response; the cardio dynamic one (Φ_1 $\dot{V}O_2$), the exercise steady state or slow component (Φ_3 $\dot{V}O_2$) and that one (Φ_2 $\dot{V}O_2$) reflecting the $\dot{V}O_{2M}$. The Φ_2 $\dot{V}O_2$ on transient response kinetics (τ, time constant, s) remains important in gaining insights into $\dot{V}O_{2M}$ and the degree of a living system Φ_2 VO_2 τ entropy (S Φ_2 $\dot{V}O_2$ τ, cal•°C-1•s). **Material and methods.** Eight young (YG = 25 ± 3 yrs; mean ± sd) and nine (OG = 71 ± 5) male subjects performed a one legs cycling exercise ramp test (YG: 25W•min-1; OG: 15W•min-1). Each subject completed 4 8 repetitions under each of one moderate (absolute: 50W) and two relative to the estimated ventilatory threshold ($\hat{\theta}_L$; moderate: 80% $\hat{\theta}_L$, heavy: 120% $\hat{\theta}_L$) intensity legs cycling exercise (submaximal = moderate + heavy) lasting 6 min. We compared the Φ_2 $\dot{V}O_2$ τ of YG and OG, provided by the breath by breath $\dot{V}O_2$ data modelled by non linear regression with the best physiologically isolated Φ_2 $\dot{V}O_2$ fit (f_{itting} w_{indow}: from BaseLine_Start to End) previously tested with two and three component exponential model for moderate and heavy, respectivelly. The relative was determined from a ramp test to put at the same energy exercise level our subjects. **Results.** We observed the slow Φ_2 $\dot{V}O_2$ kinetics characteristic of the exercise response of old men compared young men (τ2: OG > YG), not only for relative (moderate: 62 ± 16 > 28 ± 10, heavy: 40 ± 7 > 26 ± 10) but also for absolute (52 ± 13 > 23 ± 12) (submaximal: 51.3 ± 15.1 > 25.7 ± 10.3), and for the S Φ_2 $\dot{V}O_2$ τ (x10-3) for moderate ($S\tau 2_{absolute}$: 14 ± 1 > 11 ± 2, $S\tau 2_{relative}$: 15 ± 1 > 12 ± 1), heavy Sτ2 (13 ± 1 > 12 ± 2) and submaximal Sτ2: 14 ± 1 > 12 ± 2 as well. **Conclusion.** The slow Φ_2 $\dot{V}O_2$ kinetics and its increased entropy were age related for both the same energy exercise level (relative) and absolute work rate constant load exercise tests.

Key words: *Ageing, oxygen, kinetics, time constant, entropy.*

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INTRODUCTION

The living system characteristics are negentropy (-S), self-freproducibly (reproduction), the exchange of matter energy and information with its environment, its order is based on still other unknown laws of physics (statistical laws). The -S of a physical system decays when its entropy (S) increases by the amount of the heat of fusion divided by the temperature of a melting point; thus, the unit in which S is measured is cal•°C^{-1}. For example, the S of any substance is zero at roughly -273 °C. The S is calculated in terms of the Boltzmann's constant (k) and the quantitative measure of the atomistic disorder of a living system (D) (S k•logD).[1] A living system evades the decay to equilibrium or maximum S by eating, breathing and in the case of plants assimilating.[1] In consequence, entropy is a statistical thermodynamical estimation of the order (-S) or disorder (S) based on the statistical physics (concerned microscopic properties) investigation of Boltzmann and Gibbs (free energy), that could be empirically applied to the study of oxygen (O_2) kinetics in living systems and this is the first study that did it. The O_2 mass rate of chance per unit of time is named O_2 kinetics. Since O_2 kinetics change with age[2] and the level of fitness[3,4] or disease,[5] then it is possible to estimate the degree of S by an empirical substitution of D by one of the O_2 kinetic parameters (τ, time constant, MRT_{exp}, exponential mean response time). Upon a step increase in power output, the on-transient pulmonary O_2 uptake ($\dot{V}O_2$) increase ($\dot{V}O_2$ kinetics) is slower than the step increase in ATP utilization.[6,7] Muscle O_2 consumption ($\dot{V}O_{2M}$) occurs during the finite rate of adjustment of muscle oxidative phosphorylation to create a sudden increases in energy demand ($\dot{V}O_{2M}$ kinetics).[6] The pulmonary-blood-cardiovascular functions make a complex coupling system between $\dot{V}O_2$ kinetics and $\dot{V}O_{2M}$ kinetics. Upon a step increase in workload, variables related to O_2 delivery like heart rate, cardiac output, and muscle blood flow adjust to the new requirements according to finite kinetics, slower than the increase in metabolic demand, and could therefore represent (O_2 delivery limitation hypothesis)[6] a determinant of the relatively slow rate of increase of oxidative phosphorylation at exercise start (onset).[6] Conversely, the finite kinetics of $\dot{V}O_2$ adjustment to workload increases is attributable to delayed metabolic activation, of intracellular oxidative metabolism to adjust to the new metabolic requirement (metabolic limitation hypothesis).[6,8] The regulating factors of these O_2 kinetics has been a matter of debate and controversy for many years.[6]

For a given O_2 delivery the amount of O_2 that can be extracted and used by the working muscle is determined by the O_2 conductance and the O_2 partial pressure gradient from the red cell to the mitochondria.[9] The magnitude and time course of $\dot{V}O_{2M}$ is reflected in that of $\dot{V}O_2$; and in consequence, we need information regarding the characteristics and control of muscles' aerobic energy transfer indirectly determined from $\dot{V}O_2$ kinetics.[10] Upon a step increase in workload, there is a period of time for a cardiodynamic gas exchange (phase 1, Φ_1)[11] that consists in an increased pulmonary blood flow itself, during the phase in which alterations of muscle venous composition do not yet influence gas exchange at the lung;[10] however, the Φ_1 change in $\dot{V}O_2$ during constant-load exercise has been used as an index of the adequacy of cardiac function, because the magnitude and time course of $\dot{V}O_2$ during this phase is proportionally coupled to the change in pulmonary blood flow.[12,13] The subsequent increasing in O_2 extraction in the contracting muscles, causes diminution of the mixed venous O_2 content supplementing the continuing cardiodynamic component to yield the exponential phase 2 (Φ_2) response.[10] The start of Φ_2 is delayed as a result of the vascular transit delay between the exercising muscles and the pulmonary capillaries (≈15 to 20 s).[10] The time taken for the O_2 content in the venous effluent from the exercising musculature to influence the blood mixed venous $\dot{V}O_2$ content entering the pulmonary capillary bed is named time delay (TD).[10] The Φ_3 response gives either the steady-state $\dot{V}O_2$ during moderate-intensity exercise (Mod) or none steady state $\dot{V}O_2$ during heavy- intensity exercise (Hvy).[10]

Diverse model-fitting strategies for the $\dot{V}O_2$ response to either a Mod or a Hvy square-wave increase of work have been designed.[10] Among these model-fitting strategies, there are those exponential mathematical models: the onecomponent (1C, one exponential term and one TD included) and twocomponent (2C, two exponential term and two TD included) for the fitting of Mod intensity domain, and also the threecomponent model (3C, three exponential term and three TD included) for the fitting of Hvy intensity domain.[10] By using these model-fitting strategies for the $\dot{V}O_2$ response to submaximal exercise (Sub Mod + Hvy), we assessed the best (physiological and or statistical) fitting models, holding different number of parameters (P), to fit the $\dot{V}O_2$ on-transient response (particularly the Φ_2 $\dot{V}O_2$ τ) from Sub in young[14] and old adult men.[15] These exponential mathematical models were the 1C,4P ("a_0", "baseline"; a, amplitude of the response; TD, time delay; τ, time constant) for Sub and the 2C,7P (a_0, a1, a2; TD1, TD2; τ1, τ2) for Mod, and also the 3C,10P (a_0, a1, a2, a3; TD1, TD2, TD3; τ1, τ2, τ3) for Hvy; where 1, 2, and 3 stands for Φ_1 $\dot{V}O_2$, Φ_2 $\dot{V}O_2$ and Φ_3 $\dot{V}O_2$ respectively, and τ is the time required to reach 63% of a final amplitude, describing the rate at which $\dot{V}O_2$ rises towards its Φ_3 $\dot{V}O_2$.[10]

We isolated Φ_2 $\dot{V}O_2$ either from Φ_1 $\dot{V}O_2$ and steady-state (Mod Φ_3 $\dot{V}O_2$) with 2C,7P or from ${}_1\dot{V}O_2$ and non steady-state (Hvy Φ_2 $\dot{V}O_2$) with 3C,10P.[15,16]

In the search of the mechanisms that causes the O_2 kinetics pattern, new technological approaches are emerging, like the phosphorescence quenching techniques to estimate intracellular O_2 tension in isolated single myocytes across the transition from rest to contractions[17] or the study of O_2 dynamics in the microvasculature of muscle following the start of contractions[18] and also the isolated *in situ* muscle preparation and the direct Fick technique to examine O_2 kinetics across the contracting muscle,[6] as well as the simultaneous measurement use of pulmonary gas exchange and muscle high-energy phosphates (derived from magnetic resonance spectroscopy) to explore the characteristics and control of $\dot{V}O_{2M}$ kinetics during exercise in humans.[19] However, the measurement of $\dot{V}O_2$ kinetics is still a good non-invasive estimation of those occurring across the lungs and this technique remains important both in describing the response of the whole organism and in gaining insight into $\dot{V}O_{2M}$ kinetics.[20]

The Φ_2 $\tau\dot{V}O_2$ is important because during this phase both $\dot{V}O_{2M}$ and $\dot{V}O_2$ rise in a near- exponential fashion towards the anticipated (Mod) steady-state O_2 demand.[20] During Mod work rates (below the estimated lactate threshold, $< \hat{\theta}_L$), the $\dot{V}O_{2M}$ and $\dot{V}O_2$ responses at which a steady state in O_2 is attained rather rapidly, provides a close match to the muscle ATP turnover.[21] Heavy work rates (above $\hat{\theta}_L$, $> \hat{\theta}_L$) that elicit a lactic acidosis, shows additional complexities in the $\dot{V}O_{2M}$ and $\dot{V}O_2$ kinetic response to exercise, particularly is continued increase in $\dot{V}O_2$ observed beyond 2 to 3 min of Hvy exercise ($\dot{V}O_2$ slow component, Hvy Φ_3 $\dot{V}O_2$) that leads, eventually, to $\dot{V}O_2$ at higher values than would have been predicted for the external work rate.[22] This $\dot{V}O_2$ slow component represents an increasing inefficiency, reflected in an increased muscle energy turnover[22] and continued reduction in muscle phosphocreatine concentration ([Pcr]).[23] In consequence, delta efficiency has been proposed as the best estimate of the efficiency of the working muscle for Mod.[24] Maximal exercise capacity is related with $\dot{V}O_2$ kinetics during exercise and $\dot{V}O_2$ response kinetics also impact the O_2 deficit for Sub.[10]

Slow $\dot{V}O_2$ on-transient kinetics are characteristic of the Mod relative (ModRel: $< \hat{\theta}_L$) and Hvy relative (HvyRel: $> \hat{\theta}_L$) exercise responses of older men compared to young men,[9,25,26] but it has not been explored neither for an absolute work rate constant load exercise test (Abs) nor to study the entropy of the Φ_2 $\dot{V}O_2$ kinetics (S Φ_2 $\dot{V}O_2$ τ) from both the same energy exercise level ($< \hat{\theta}_L$ and $> \hat{\theta}_L$) and Abs work rate constant load exercise tests.

The purpose of the present work was to assess for differences of the phase two $\dot{V}O_2$ on-transient kinetics and its degree of entropy, between young and old adult men during both the same energy exercise level (Rel: 80% $\hat{\theta}_L$ and 120% $\hat{\theta}_L$) and absolute (Abs: 50 Watts) work rate constant load exercise tests, in the search for determinant mechanisms or factors possibly involved in the $\dot{V}O_2$ kinetics of adult men.

Hypothesis

If the exponential Φ_2 $\dot{V}O_2$ on-transient response to forcing functions of relative and absolute work rate constant load exercise tests is slow-age related in terms of $\tau 2$ duration, thus Φ_2 $\dot{V}O_2$ τ and their S Φ_2 $\dot{V}O_2$ τ estimated values from Rel and Abs, should be significantly higher in old compared to young men.

MATERIAL AND METHODS

The detailed methodology used in this study has been already described somewhere else.[15,16] However, in brief as follows.

Subjects

The subjects in this study were 17 healthy males divided in eight younger adults (YG, aged 23 to 30 years,) and nine older adults (OG, aged 64 to 78 years). These experiments included moderate and heavy domains. Their normal levels of physical activity ranged from to light to high.[15,16]

Testing procedures

The determination of maximal oxygen uptake ($\dot{V}O_{2max}$) and the $\dot{V}O_2$ at $\hat{\theta}_L$ was carried out on a cycle ergometer (Lode H-300-R Roxon Medi-Tech, electrically braked).The test was performed as a ramp function with work rate increasing at 25 W•min^{-1} for YG and at 15 W•min^{-1} for OG. The $\dot{V}O_2$ averaged over the final 15 s of the incremental test prior to fatigue was taken as $\dot{V}O_{2peak}$. The $\hat{\theta}_L$ was determined using the criteria outlined by Davis, et al.[27] Constant-load exercise tests were performed on subsequent visits to the laboratory. The work rate was then increased as a step function to an intensity corresponding to a $\dot{V}O_2$ of both at 80% of the $\dot{V}O_2$ at $\hat{\theta}_L$ (ModRel) or the at 120% of the $\dot{V}O_2$ at $\hat{\theta}_L$ (HvyRel) (Rel ModRel + HvyRel). Constant-load cycle exercise was also performed at 50 W or absolute power output (ModAbs). Preceded by 6 min cycling at a baseline of 20 W, the subjects exercised at this work rate for 6 min, after which the work rate was abruptly decreased and the subjects continued loadless cycling for 6 min.[15,16]

Data Collection and Analysis

Gas exchange and heart rate data were determined using the methods as described by Scheuermann, et al.[28] Throughout exercise, inspired and expired gas volumes were measured using a low dead space (90 mL) bidirectional turbine (Alpha technologies VMM110), 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 (Airspec 2000 MGR 9N) after calibration with precision analysed gas mixtures (i.e., 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 data were calculated using previously described algorithms.[29] The breath-by-breath data were interpolated to 1 s intervals. The Mod performed was 6 to 8 constant-load exercise tests for each condition (2 to 4 transitions per visit) and the HvyRel was performed 2 to 4 constant-load exercise tests per condition (1 transition per visit). The interpolated data were then ensemble averaged for each individual to yield a single response.

Arterialized-venous blood was drawn into syringes containing lithium heparin, mixed, and placed in an ice water slurry and analysed after a short delay. Whole blood samples (200 μL) were analysed (at 37 °C) for plasma concentrations of lactate ([La$^-$]p) using selective electrode (StatProfile 9 Plus Blood Gas-Electrolyte Analyser, Nova Biomedical Canada Ltd.); the electrode was calibrated prior to each test and at regular intervals during the analysis. The variability of measurement of this variable was assessed previously in our laboratory.[30]

Models

In these analyses only $\dot{V}O_2$ data were modelled to assess Φ_2 $\dot{V}O_2$ on-transient kinetics (Φ_2 $\dot{V}O_2\tau$). For Mod, exponential mathematical model with two component were fit to data.[15,16] This Mod $\dot{V}O_2$ mass rate of change per unit of time (d$\dot{V}O_2$•dt^{-1}), assuming $T_{ime}D_{elay}$ equals zero, was the $\dot{V}O_2(\tau)$ modelled with $2C_{omponent}$, $7P_{arameter}$ model (Figure 1) of the form: $\dot{V}O_2(t)$ $\dot{V}O_{2Baseline} + \dot{V}O_{2\ amplitude1} \bullet [1-e^{-[(time-TimeDelay1)/\tau ime\ constant1]}] + \dot{V}O_{2\ amplitude2} \bullet [1-e^{-[(time-TimeDelay2)/\tau ime\ constant2]}]$. This $2C_{omponent}$, $7P_{arameters}$ model has an exponential mean response time (MRTexp) of the form: MRT_{exp} *(s)* $(_{amplitude1} \bullet A_{mplitudeTOTAL}{}^{-1})(\tau_{ime}C_{onstatnt1} + T_{ime}D_{elay1}) + (_{amplitude2} \bullet A_{mplitudeTOTAL}{}^{-1})(\tau_{ime}C_{onstatnt2} + T_{ime}D_{elay2})$. For example, MRT_{exp} *(s)* *(175, mL/527.50, mL) (12.80,s + 1.20, s) + (351.90, mL/527.50, mL)(38.60, s + 27.20, s)* *48.54, s.*

For heavy intensity, exponential mathematical model with three component were fit to the data.[15,16] This heavy intensity d$\dot{V}O_2$•dt^{-1}, assuming $T_{ime}D_{elay}$ equals zero, was the $\dot{V}O_2$(t) modelled with $3C_{omponent}$, $10P_{arameter}$ model (Figure 2) of the form: $\dot{V}O_2(t)$ $\dot{V}O_{2\ Baseline} + \dot{V}O_{2\ amplitude1} \bullet [1-e^{-[(\tau ime-TimeDelay1)/\tau imeconstant1]}] + \dot{V}O_{2\ amplitude2} \bullet [1-e^{-[(time-TimeDelay2)/\tau ime\ constant2]}] + \dot{V}O_{2\ amplitude3} \bullet [1-e^{-[(time-TimeDelay3)/\tau ime\ constant3]}]$. This $3C_{omponent}$, $10P_{arameter}$ model has MRTexp of the form: MRT_{exp} *(s)* $(_{amplitude1} \bullet A_{mplitudeTOTAL}{}^{-1})(\tau_{ime}C_{onstatnt1} + T_{ime}D_{elay1}) + (_{amplitude2} \bullet A_{mplitudeTOTAL}{}^{-1})(\tau_{ime}C_{onstatnt2} + T_{ime}D_{elay2}) + (_{amplitude3} \bullet A_{mplitudeTOTAL}{}^{-1})(\tau_{ime}C_{onstatnt3} + T_{ime}D_{elay3})$. For example, MRT_{exp} *(s)* *(703.56, mL/1996.98, mL)(27.00, s + 6.24, s) + (522.90, mL/1996.98, mL) (28.34, s + 23.26, s) + (770.52, mL/1996.98, mL)(256.14, s + 89.88, s)* *158.73, s.*

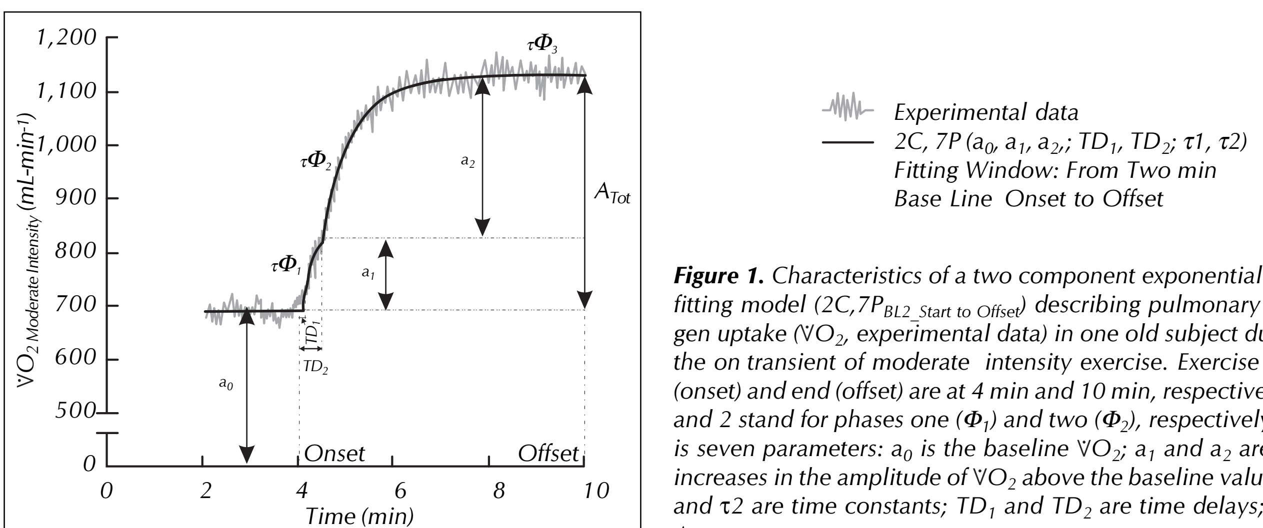
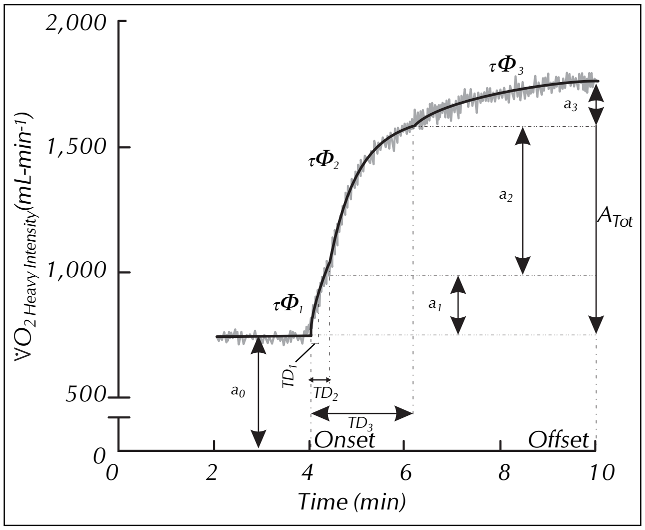


Figure 1. *Characteristics of a two component exponential (2C) fitting model (2C,7P$_{BL2_Start\ to\ Offset}$) describing pulmonary oxy gen uptake ($\dot{V}O_2$, experimental data) in one old subject during the on transient of moderate intensity exercise. Exercise start (onset) and end (offset) are at 4 min and 10 min, respectively; 1 and 2 stand for phases one (Φ_1) and two (Φ_2), respectively; 7P is seven parameters: a_0 is the baseline $\dot{V}O_2$; a_1 and a_2 are the increases in the amplitude of $\dot{V}O_2$ above the baseline value; τ1 and τ2 are time constants; TD_1 and TD_2 are time delays; and $A_{Tot} = a_1 + a_2$.*



Experimental data
3C, 10P, (a_0, a_1, a_2, a_3; TD_1, TD_2, TD_3; τ1, τ2, τ3)
Fitting Window: From Two min BaseLine Onset to Offset

Figure 2. *Characteristics of a three component exponential (3C) fitting model ($3C,10P_{BL2\_Start\ to\ End}$) describing pulmonary oxygen uptake ($\dot{V}O_2$, experimental data) in one old subject during the on transient of heavy intensity exercise (120% $\hat{\theta}_L$). Exercise start (onset) and end (offset) are at 4 min and 10 min, respectively; 1,2, and 3 stand for phases one (Φ_1), two (Φ_2) and three (Φ_3), respectively; 10P is seven parameters: a_0 is the base line $\dot{V}O_2$; a_1, a_2 and a_3 are the increases in the amplitude of $\dot{V}O_2$ above the baseline value; τ1, τ2 and τ3 are time constants; TD_1, TD_2 and TD_3 are time delays; and A_{Tot} = a_1 + a_2 + a_3.*

Responses were modelled by means of nonlinear regression techniques[31] with $2C_{omponent}$ model[32] and $3C_{omponent}$ model[33] with a fitting window from two min baseline_start-exercise to end-exercise for Mod ($2C,7P_{BL2\ to\ 6\ min}$) and HvyRel ($3C,10P_{BL2\ to\ 6\ min}$), respectively. We also assessed from the best statistically and/or physiologically fitting models, $2C,7P_{BaseLine\_Start\ to\ Offset}$ for Mod exercise and $3C,10P_{BaseLine\_Start\ to\ Offset}$ for Hvy exercise, the Φ_2 $\dot{V}O_2$ kinetics from fitting with either a unrestricting TD1 < > zero value or restricting TD1 < > zero value. The kinetic analysis of Φ_2 $\dot{V}O_2$ was assessed in terms of the τ Φ_2 (τ2, time constant two). These multi-component fitting models resulted physiologically and statically best for the assessment of the isolated Φ_2 from fitting the $\dot{V}O_2$ on-transient response to Sub.[15,16] The goodness of fit for each fitting model was assessed using the lowest residual sum of squares (RSS values) from a computerized nonlinear regression technique.[34] The kinetic analysis of Φ_2 $\dot{V}O_2$ was assessed in terms of the τ Φ_2 (τ2).

The magnitude and slope of the $\dot{V}O_2$ slow component were determined as the difference between the $\dot{V}O_2$ at the end of exercise and the $\dot{V}O_2$ at 3 min of exercise ($\Delta\dot{V}O_{2(6\text{-}3min)}$); $\dot{V}O_2$ at 3 min was taken as the mean $\dot{V}O_2$ between 2.75 and 3.15 min, and the end-exercise $\dot{V}O_2$ was taken as the mean $\dot{V}O_2$ during the last 0.25 min of exercise. The magnitude and kinetics of the slow component were also described by the parameter estimates derived from the 3-component exponential model fit.

Oxygen deficit

Oxygen deficit was calculated from the increase in $\dot{V}O_2$ (total gain or amplitude, A_{total}) for a given increase in each of our submaximal work rate loads as followed: *O_2 Deficit (mL)   (A_{total}, mL/60,s) • MRT_{exp},s* ; where parameters (A_{total} and MRTexp) came from either $2C,7P_{BaseLine\ to\ End\ Moderate\ Exercise}$ (A_{total} amplitude1 + amplitude2) or $3C,10P_{BaseLine\ to\ End\ Heavy\ Exercise}$ (A_{total} amplitude1 + amplitude2 + amplitude3).[35] For example: *O_2 Deficit (mL)   (1067.78,mL/60,s) • 81.64,s   1453, mL.*

Slope subthreshold N $\dot{V}O_2$ - power relationship

We calculated also the slope subthreshold $\dot{V}O_2$ - power relationship and the $\dot{V}O_2$ during loadless pedalling cycling.[36-38]

Δ[La⁻]p

We determined the change in plasma [La⁻]p ($\Delta[La^-]p_{(6\text{-}3min)}$) as well.[30]

Exercise capacity

Exercise capacity was evaluated as well as in terms of significant relationships for both the $\dot{V}O_{2peak}$ and τ2 and the $\dot{V}O_2\,\hat{\theta}_L$ and τ2, and also work rate max and τ2 in young and old adult men.[2,5]

Delta efficiency

Delta efficiency of each of our submaximal work rate loads, was calculated as the mathematical ratio of the increase in $\dot{V}O_2$ ($\Delta\dot{V}O_2$) for a given increase in work rate (ΔWR) or gain ($\Delta\dot{V}O_2$/ΔWR) according to Pool, et al.:[39]

Delta Efficiency (%) $\{(\Delta WR, W\bullet 0.01434, kcal\bullet min^{-1}) / [\Delta\dot{V}O2, mL\bullet (5, kcal/1000, mL)]\}\bullet 100$; where $\Delta\dot{V}O_2$ $\dot{V}O_{2\,steady\text{-}state\,exercise}$ - $\dot{V}O_{2baseline}$ and ΔWR $Watts_{exercise}$ - $Watts_{baseline}$. For example, *Delta Efficiency (%)* $\{((100W_{Exercise} - 20\,W_{BaseLine})\bullet 0.01434, kcal\bullet min^{-1}\bullet W^{-1}) / [(1700\,mL\bullet min^{-1}Exercise - 700\,mL\bullet min^{-1}{}_{BaseLine})\bullet (5, kcal/1000, mL)]\}\bullet 100$ *22.94%*.

Phase 2 $\dot{V}O_2$ Kinetics Entropy

The entropy[1] of the submaximal $\Phi_2\ \dot{V}O_2\ \tau$ (S $\Phi_2\ \dot{V}O_2\ \tau$) was calculated in terms of the Boltzmann's constant (k 3.2983•10-4, cal•ºC-1) by empirically substituting the quantitative measure of the atomistic disorder of a living system (D) in the formula of entropy (S k • logD) by τ2: S $\Phi_2\ \dot{V}O_2\ \tau$ *(cal• ºC-1•s-1)* *k • log(*$\Phi_2\ \dot{V}O_2\ \tau$*)*. For example, S $\Phi_2\ \dot{V}O_2\ \tau$ *(cal• ºC-1•s-1)* *3.2983•10-4, cal• ºC-1 • log(28.34, s)* *0.010, cal• ºC-1•s-1* *0, kcal• ºC-1•s-1*.

Statistical Analyses

Kinetic parameter estimates (amplitude, time delay, time constant, MRTexp) were analyzed using either a one way or a two way measures analysis of variance (ANOVA) for young *versus* old transitions as the main effects. Data treatment consisted of group analyses performed using either a with parametric *post-hoc* analyses or when variances of the dependent variable were unequal or the distribution of the dependent variable was not normal we used non parametric *post-hoc* analyses, to compare kinetic temporal parameters from the exercise square waves between groups.[40] Estimated values of the $\Phi_2\ \dot{V}O_2\ \tau$ from the two complex models used here were compared between groups, within each submaximal exercise intensity. The best statistical (Fish, based on either Fisher's test)[34] and/or on the physiological (Phys) meaning of the understanding of the existence of the different on-transient $\dot{V}O_2$ phases[10] fitting models assessed, showing negative TD1 values were refitted forcing TD1 ≥ 0 in either YG or OG, to compare these two group in terms of those parameters of interest, particularly those from the on-transient $\Phi_2\ \dot{V}O_2$ data. We also assessed the parameters (τ, TD, and amplitude) effect of omitting $\Phi_1\dot{V}O_2$ on $\Phi_2\dot{V}O_2$ kinetics for comparisons between YG and OG, from $2C,7P_{BaseLine\_Start\ to\ End}$ for moderate intensity exercise and $3C,10P_{BaseLine\_Start\ to\ End}$ for heavy intensity exercise, models that resulted best fit the on-transient $\dot{V}O_2$ entire data set ($\Phi_{2\_Isolated}\dot{V}O_2$),[15a,15b] and from that one that fit $\Phi_2\dot{V}O_2$ only ($\Phi_{2postulated}\dot{V}O_2$) like $1C,4P_{0.3333\ to\ 3\ min\ exercise}$ for submaximal exercise, omitting $\Phi_1\dot{V}O_2$ and $\Phi_3\dot{V}O_2$ in young and old adult men. Student t-test was used to assess for significant differences between variable means between.[40] We used the Pearson's correlation coefficient and linear regression to assess relationships between variables of interest.[40] The probability level denoted significance at $p \leq 0.05$. Except where otherwise stated, data are presented as mean ± $s_{TANDARD}d_{EVIATION}$.

RESULTS

The physiological characteristics of the subjects are displayed in table 1. The end-exercise $\dot{V}O_2$ ($\dot{V}O_{2\,EE}$), and the exercise intensity expressed as both the absolute (50 W) power output and the relative to the ventilatory threshold (80% $\hat{\theta}_L$ and 120% $\hat{\theta}_L$), and also the %$\dot{V}O_{2peak}$ and delta $\dot{V}O_2$ (%Δ) as well, are presented in table 2. The summary data for heavy exercise above the ventilatory lactate threshold are presented in tables 3 to 5. The Mod exercise $\dot{V}O_2$ on-transient parameter estimated with $2C,7P_{BL2\_Onset\ to\ Offset}$ and also, those parameter estimated for Hvy exercise with $3C,10P_{BL2\_Onset\ to\ Offset}$, are presented in table 6. Examples of the both the two- and three- component exponential fitting models describing $\dot{V}O_2$ during the on-transient of Mod- and Hvy-exercise, in one old subject, are shown in figures 1 and 2 respectively. The HvyRel exercise 6 min minus 3 min on-transient $\dot{V}O_2$ associations with plasma lactate concentration, in young adult men, are shown in figure 3. The Mod-, and HvyRel- exercise on-transient phase two $\dot{V}O_2$ time constant and its entropy associations with $\dot{V}O_{2peak}$ relative to total body weight, in young adult men, are shown in figures 4 and 5, respectively. The phase two parameters (time delay,

Table 1. Subject characteristics from eight young and nine old adult men.

Group	Age (yrs)	Mass (kg)	Height (cm)	$\dot{V}O_{2peak}$ (L•min-1)	$\dot{V}O_{2peak}$ (mL•kg-1•min-1)	$\hat{\theta}_L$ (mL•min-1)	$\hat{\theta}_L$ (%$\dot{V}O_{2peak}$)
Young	25*	79	180	3.7*	47.4*	1,919*	52*
	± 3	± 9	± 5	± 0.6	± 6.0	± 189	± 4
Old	71*	80	174	2.2*	28.3*	1,333*	62*
	± 5	± 10	± 6	± 0.4	± 7.2	± 139	± 8

Values are mean ± sd. * Denotes significant difference ($p < 0.05$) between young and old adults. $\hat{\theta}_L$ Estimated lactate threshold.

Table 2. Summary data for exercise at the same absolute (50 W) power output (PO), and during relative intensity exercise below (Moderate) and above (Heavy) the estimated lactate threshold ($\hat{\theta}_L$) in eight young and nine old adult men.

	Absolute PO			Moderate Intensity				Heavy Intensity				
	$\dot{V}O_{2EE}$ (mL/min)	% $\hat{\theta}_L$	% $\dot{V}O_{2peak}$	PO (W)	$\dot{V}O_{2EE}$ (mL/min)	% $\hat{\theta}_L$	% $\dot{V}O_{2peak}$	PO (W)	$\dot{V}O_{2EE}$ (mL/min)	% $\hat{\theta}_L$	% $\dot{V}O_{2peak}$	%Δ+
Young	1,182	62*	32*	84*	1,632*	85	44	160*	2,716*	143	75	47
	± 87	± 7	± 4	± 14	± 213	± 5	± 4	± 24	± 380	± 11	± 10	± 13
Old	1,180	89*	56*	37*	1,050*	79	49	90*	1,770*	121	81	58
	± 145	± 15	± 16	± 11	± 198	± 12	±11	± 17	± 333	± 17	± 14	± 37

Values are mean ± sd. * Denotes significant difference ($p < 0.05$) between young and old adults. + %Δ calculated as {[($\dot{V}O_{2\ EE}$ $\dot{V}O_2\hat{\theta}_L$)/($\dot{V}O_{2\ peak}$ $\dot{V}O_2\hat{\theta}_L$)]•100}, where EE = end exercise.

Table 3. Summary data for heavy exercise above the estimated lactate threshold ($\hat{\theta}_L$) in eight young and nine old adult men.

	Age (yrs)	$\dot{V}O_{2peak}$ (mL•kg^{-1}•min)	$W_{ork}R_{ate}$ (W)	% $\hat{\theta}_L$	120% $\hat{\theta}_L$ % $\dot{V}O_{2peak}$	$\dot{V}O_{2(EE)}$ (mL•min^{-1})	[La$^-$]$p_{(EE)}$ (mmol•l^{-1})
Young	25*	47*	160*	143	75	2,716*	8.5*
	± 3	± 6	± 24	± 11	± 10	± 380	± 1.7
Old	71*	28*	90*	121	81	1,770*	5.1*
	± 5	± 7	± 17	± 17	± 14	± 333	± 0.6

Values are mean ± sd. * Denotes significant difference ($p < 0.05$) between young and old adults. [La]$p_{(EE)}$: Plasma lactate concentration; where EE = end exercise.

Table 4. Summary of $\dot{V}O_2$ kinetics for heavy exercise above the estimated lactate threshold ($\hat{\theta}_L$) in eight young and nine old adult men.

	a_0 (mL•min^{-1})	a_1 (mL•min^{-1})	a_2 (mL•min^{-1})	A_{total} (mL•min^{-1})	TD1 (s)	TD2 (s)	τ1 (s)	τ2 (s)	MRT_{exp} (s)
120% $\hat{\theta}_L$									
Young	741	686*	1,059*	2,182*	0.5	19.3	20.1	26.2*	92.3
	± 77	± 453	± 370	± 382	± 5.0	±4.1	± 11	± 10	± 41.0
Old	744	300*	593*	1,068*	0.8	23.4	14.6	40.2*	81.6
	± 116	± 104	± 209	± 326	± 7.3	± 4.8	± 9.9	± 7.4	± 17.5

Values are mean ± sd. * Denotes significant difference ($p < 0.05$) between young and old adults.

Table 5. Summary of $\dot{V}O_2$ slow component kinetics during heavy exercise above the estimated lactate threshold ($\hat{\theta}_L$) in eight young and nine old adult men.

	TD3 (s)	a_3 (mL•min^{-1})	τ3 (s)	$\Delta\dot{V}O_{2(6\text{-}3min)}$ (mL•min^{-1})	Δ[La$^-$]$p_{(6\text{-}3min)}$ (mmol•l^{-1})
120% $\hat{\theta}_L$					
Young	105	437*	183	173	3.1*
	± 59	± 256	± 82	± 72	± 1.1
Old	152	176*	111	99	1.8*
	± 41	± 140	± 38	± 44	± 0.3

Values are mean ± sd. * Denotes significant difference ($p < 0.05$) between young and old adults.

Table 6. Summary of parameter estimates during the $\dot{V}O_2$ on transient for exercise at the same absolute (50W) power output (PO), and during relative intensity exercise below (Moderate) and above (Heavy) the estimated lactate threshold ($\hat{\theta}_L$) in young and old adult men.

	a_0 (mL•min^{-1})	a_1 (mL•min^{-1})	a_2 (mL•min^{-1})	a_3 (mL•min^{-1})	A_{total} (mL•min^{-1})	TD1 (s)	TD2 (s)	TD3 (s)	τ1 (s)	τ2 (s)	τ3 (s)	MRT_{exp} (s)
Absolute PO												
Young	739	193†,‡	246‡		439†,‡	1	26		16	23*		35‡
	± 79	± 64	± 49		± 59	± 4	± 6		± 6	± 12		± 6
Old	742	193	245		439‡	0.1	27		18	52*		53‡
	± 130	± 55	± 52		± 62	± 4	± 4		± 7	± 13		± 9
Moderate Intensity												
Young	738	384*,†	505§		890*,†,§	1.29	20		16	28*		34§
	± 80	± 129	± 164		± 209	± 3	± 2		± 4	± 10		± 7
Old	751	138*,§	143§		282*,§	1.1	26		21	62*		53§
	± 131	± 64	± 94		± 150	± 12	± 7		± 9	± 16		± 11
Heavy Intensity												
Young	741	686*,‡	1,059*,‡,§	437*	2,182*,‡,§	0.53	19	105	20	26*	183	92‡,§
	± 77	± 453	± 370	± 256	± 382	± 5	± 4	± 59	± 11	± 10	± 82	± 41
Old	744	300*,§	593*,§	176*	1,068*,‡,§	0.8	23	152	15	40*	111	82‡,§
	± 116	± 104	± 209	± 140	± 326	± 7	± 5	± 41	± 10	± 7	± 38	± 18

Values are mean ± sd Young = 8 Old = 9

***:** Denotes significant difference ($p < 0.05$) between young and old adults within an exercise condition.

†: Denotes significant difference ($p < 0.05$) between absolute and moderate intensity (80% $\hat{\theta}_L$) condition within an age group.

‡: Denotes significant difference ($p < 0.05$) between absolute and heavy intensity (1,290% $\hat{\theta}_L$) condition within an age group.

§: Denotes significant difference ($p < 0.05$) between moderate and heavy intensity condition within an age group.

TD: Time dalay of phase (Φ) one (TD1), Φ two (TD2) and Φ three (TD3).

τ: Time constant of Φ one (τ1), Φ two (τ2) and Φ three (τ3).

a: Amplitude; 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 Φ one (a_1), Φ two (a_2) and Φ three (a_3) amplitudes; A_{total}, Total amplitude. MRT_{exp}: Exponential mean response time.

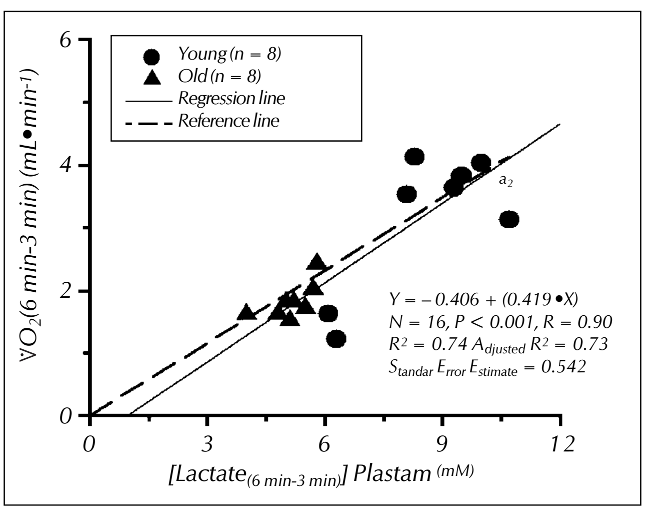


Figure 3. Heavy intensity exercise. *Heavy relative (120% $\hat{\theta}_L$) intensity exercise 6 min minus 3 min on transient pulmonary oxygen uptake ($\dot{V}O_2$) associations (linear regression) with plas ma lactate concentration in young and old adult men; (n) is sample size. $\hat{\theta}_L$, estimated lactate threshold.*

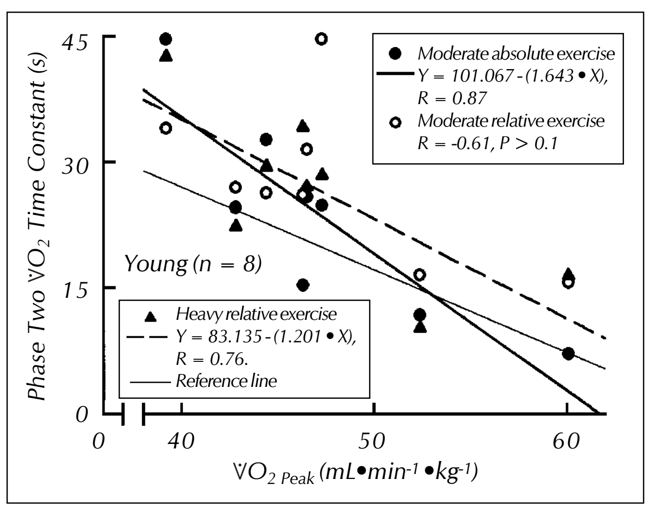


Figure 4. *Moderate absolute (50 W) intensity , and heavy relati ve (120% $\hat{\theta}_L$) intensity exercise on transient phase two pulmona ry oxygen uptake ($\dot{V}O_2$) time constant associations (linear regres sion) with $\dot{V}O_{2peak}$ relative to total body weight in young adult men; (n) is sample size. $\hat{\theta}_L$, estimated lactate threshold.*

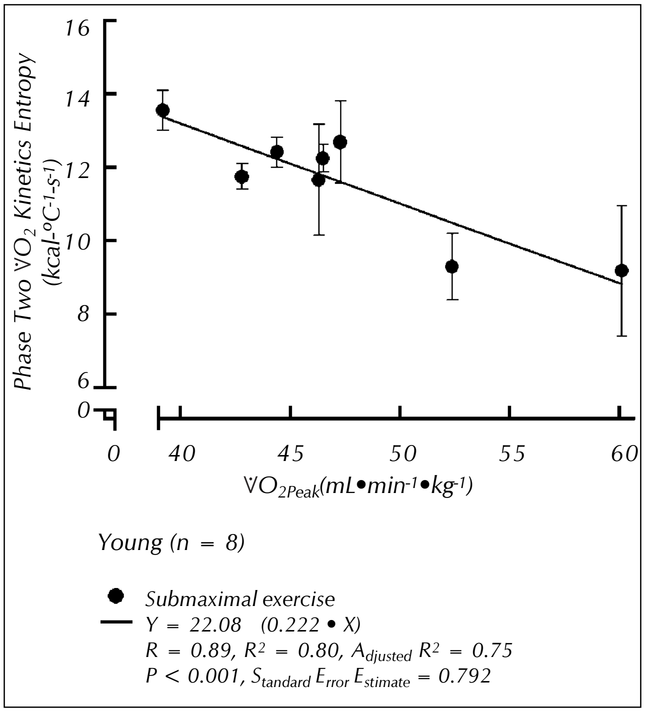


Figure 5. *Mean (± sd) submaximal (moderate + heavy) exercise intensity on transient phase two pulmonary oxygen uptake ($\dot{V}O_2$) kinetic entropy associations (linear regression) with $\dot{V}O_{2peak}$ relative to total body weight in young adult men; (n) is sample size; mod, abs (50W) and rel (80% $\hat{\theta}_L$); heavy, 120% $\hat{\theta}_L$. $\hat{\theta}_L$, estimated lactate threshold.*

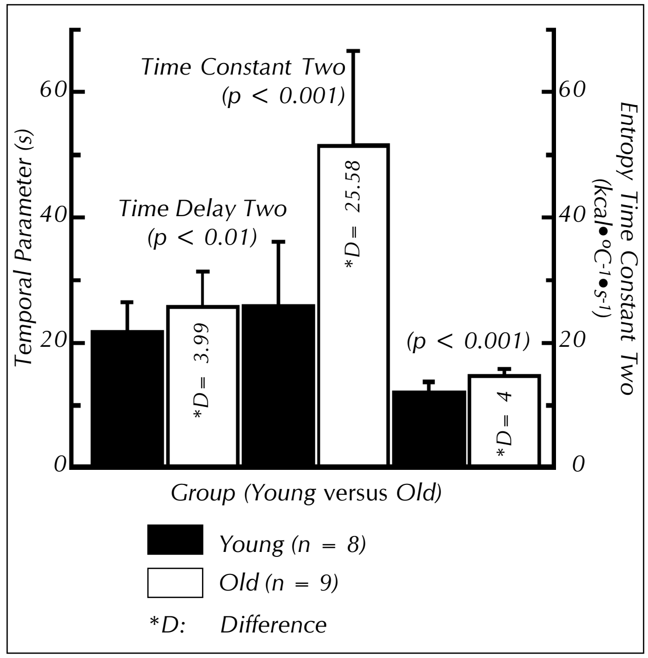


Figure 6. Submaximal exercise. *Mean (± sd) phase two parameters (time delay, time constant and entropy's time constant) quantifying the dynamic response of pulmonary oxygen uptake ($\dot{V}O_2$) in young versus old adult men during the on transient of submaximal (moderate + heavy) exercise intensity; (n) is sample size group; mod, abs (50W) and rel (80% $\hat{\theta}_L$); heavy, 120% $\hat{\theta}_L$; and (p < 0.05) is a statistically significant difference between groups. $\hat{\theta}_L$, estimated lactate threshold.*

time constant and its entropy) quantifying the dynamic response of $\dot{V}O_2$ in young *vs.* old adult men, during the on-transient of Sub are shown in figure 6.

Exercise Intensity, Aerobic Parameters and Power Output

Age, $\hat{\theta}_L$%$\dot{V}O_{2peak}$ (Table 1) and ModAbs %$\hat{\theta}_L$ $\dot{V}O_2$ and %$\dot{V}O_{2peak}$ (Table 2), as expected, resulted lower in the YG compared to OG (t 3, $p < 0.05$). On the contrary, $\dot{V}O_{2peak}$, $\hat{\theta}_L$ $\dot{V}O_2$ (Table 1), and relative- intensity power output, and $\dot{V}O_{2\,EE}$ (Table 2) were higher in the YG compared to OG (t 3, $p < 0.05$). The HvyRelexercise (120% $\hat{\theta}_L$) represented end-exercise $[La^-]p$ (Table 3), $\Delta\dot{V}O_{2(6\text{-}3min)}$ and $\Delta[La^-]p_{(6\text{-}3min)}$ (Table 5) higher in the YG compared to OG (t 3, $p < 0.05$). Furthermore, there were positive relationships between $\Delta\dot{V}O_{2(6\text{-}3min)}$ and $\Delta[La^-]p_{(6\text{-}3min)}$ for Mod exercise (Y 3.386 + (22.717 • X), n 32, r 0.53, $p < 0.002$, R^2 0.28, $A_{djusted}R^2$ 0.26, $S_{tandard}\,E_{rror}E_{stimate}$ 19.7) and HvyRel exercise, and also we distinguished the OG and YG (except two subjects) from these relationships for this exercise intensity domain (Figure 3).

As expected too, the slope of the subthreshold $\dot{V}O_2$ -power output relationship ($\Delta\dot{V}_2/\Delta PO$, mL•min^{-1}•W^{-1}: YG, 12.5 ± 1.4 and OG 12.0 ± 1.2) and the $\dot{V}O_2$ during loadless cycling ($\dot{V}O_{2\_loadless}$, mL•min^{-1}: YG,745 ± 86 and OG, 758 ± 78) were similar in the two age groups. Evermore, it was not a surprise that the O_2 deficit (mL) was smaller in the YG (255 ± 48) compared to OG (380 ± 45) for Mod exercise but higher for relative- intensity exercise in the YG (ModRel 485 ± 103, HvyRel 3234 ± 1224) compared to OG (ModRel253 ± 156, HvyRel 1496 ± 698) (t 3.8, $p < 0.05$). However, only ModRel exercise delta efficiency (%) resulted higher in the YG (21 ± 1.4) compared OG (15 ± 6) (t 2.5, $p < 0.05$). ModAbs exercise delta efficiency resulted similar between YG (20 ± 2.4) and OG (20 ± 3).

$\dot{V}O_2$ Kinetics

- ***Phase Two $\dot{V}O_2$ Kinetics Exercise Capacity, Entropy, and $\dot{V}O_{2peak}$ Relationships:*** The estimated exercise capacity (Φ_2 $\dot{V}O_2$ τ, s) for ModAbs exercise, resulted significantly ($p < 0.003$) negatively correlated with either $\dot{V}O_{2peak}$ relative to total body mass (r -0.87) (Figure 4) or $\dot{V}O_2$ $\hat{\theta}_L$ (r -0.88) in the YG only. The Φ_2 $\dot{V}O_2$ τ for HvyRel exercise was significantly ($p < 0.03$) negatively correlated (r -0.76) with $\dot{V}O_{2peak}$ (Figure 4). Evermore, it was notably that these relationships (linear regression, Y) resulted more closely between the phase two $\dot{V}O_2$ kinetics entropy (S Φ_2 $\dot{V}O_2$ τ, cal• ºC^{-1}• s) and $\dot{V}O_{2peak}$ relative to total body mass for Sub (Figure 5) as follows:

i) for ModAbs exercise (Y 0.0264 - 0.000326 * X, SEE 0.001, r -0.94, $p < 0.001$, n 8);
ii) for ModRel exercise (Y 0.0191 - 0.000150 * X, SEE 0.001, r -0.73, $p < 0.040$, n 8); and
iii) for HvyRel exercise (Y 0.0207 - 0.000191 * X, SEE 0.001, r -0.73, $p < 0.04$, n 8) in the YG only.

- ***Phase Two $\dot{V}O_2$ Kinetics Entropy (S Φ_2 $\dot{V}O_2$ τ) (Young* vs. *Old):*** The S Φ_2 $\dot{V}O_2$ τ (kcal• ºC^{-1}• s^{-1}) resulted lower ($p < 0.01$) in the YG compared OG for Sub exercise (Figure 6) within an exercise condition as follows:

i) for ModAbs exercise ($11 \pm 2 < 14 \pm 1$, t 4.2);
ii) for ModRel exercise ($12 \pm 1 < 15 \pm 1$, t 5.4); and
iii) for HvyRel exercise ($12 \pm 2 < 13 \pm 1$, t 3).

- ***Moderate (Absolute and Relative)* vs. *Heavy Relative Conditions Within an Age Group:*** Generally speaking the a_1 (Kruskal-Wallis ANOVA, H 32, $p < 0.001$, *post hoc* Dunn's method), a_2 (Kruskal-Wallis ANOVA, H 42, $p < 0.001$, *post hoc* Dunn's method), and A_{total} (Kruskal-Wallis ANOVA, H 43, $p < 0.001$, *post hoc* Dunn's method) resulted lower in Mod exercise conditions compared to HvyRel exercise condition in the YG and in the OG (Table 6). The MRT_{exp} resulted faster (Kruskal-Wallis ANOVA, H 38, $p < 0.001$, *post hoc* Dunn's method) in Mod exercise conditions compared to HvyRel exercise condition in the YG and in the OG.

Parameters within an Exercise Condition (Young vs. *Old)*

- ***Amplitude:*** Analyses showed a statistically significant difference between constant work rate intensities, for amplitude two (a_2, mL•min^{-1}) for $\Phi_{2\_Isolated}\dot{V}O_2$ values ($\Phi_{2\_Isolated}\dot{V}O_2$ a_2: ModAbs < ModRel < HvyRel, Table 6) and for $\Phi_{2postulated}\dot{V}O_2$ values from the exercise conditions in both the YG ($\Phi_{2postulated}\dot{V}O_2$ a_2: ModAbs_310.0 ± 58.1 < ModRel_650.6 ± 58.1 < HvyRel_1243.0 ± 58.1) and the OG ($\Phi_{2\_Isolated}\dot{V}O_2$ a_2: Mod < Hvy, Table 6; $\Phi_{2postulated}\dot{V}O_2$ a_2: ModAbs_306.569 ± 54.767 similar to ModRel_209.893 ± 54.767 < HvyRel_670.236 ± 54.767). The a_2 from all of the relative conditions resulted, a statistically significant higher in the YG compared to OG for both, the $\Phi_{2\_Isolated}\dot{V}O_2$ a_2 (two way ANOVA: Φ_{value} 26.7, $p < 0.001$, *post hoc* Holm-Sidak method at $p < 0.05$: t_{ModRel} 3.7 and t_{HvyRel} 5,) and the $\Phi_{2postulated}\dot{V}O_2$ a_2 (two way ANOVA: Φ_{value} 54.1, $p < 0.001$, *post hoc* Holm-Sidak method, at $p < 0.05$: t_{ModRel} 5.5 and t_{HvyRel} 7.2). In addition, the relative conditions resulted in lower phase one amplitude (Kruskal-Wallis ANOVA, H 32, $p < 0.001$, *post hoc* Dunn's method) and in lower total amplitude of the response (Kruskal-Wallis ANOVA, H 43, $p < 0.001$, *post hoc* Dunn's method) in the OG compared to YG (Table 6). The HvyRel phase two and three amplitudes were lower (Kruskal-Wallis ANOVA, H 42, $p < 0.001$, *post hoc* Dunn's method; t 3, $p < 0.02$) in the OG compared to YG (Table 6).
- ***Time Delay:*** Analyses showed a statistically significant ($p < 0.001$) difference between $\Phi_{2\_Isolated}\dot{V}O_2$ time delay (TD2, s) (Table 6) and $\Phi_{2postulated}\dot{V}O_2$ TD duration in the YG (21.9 ± 5.2 > 1.4 ± 5.4, t 13.4, n 24) and the OG (25.6 ± 8.1 > 2.6 ± 8.4, t 10.2, n 27) for Sub. In addition, the phase one $\dot{V}O_2$ TD difference from YG minus OG was -0.5 ± 6.9 s for Sub; however, TD2 resulted in the YG (21.6 ± 4.9) lower (t 3, $p < 0.05$) than OG (25.6 ± 5.7) for Sub (Fig. 6).
- ***Time Constant:*** Analyses showed slow age-related $\Phi_2\dot{V}O_2$ kinetics (τ2, s) for Sub (Φ_2 $\dot{V}O_2$ τ values: OG > YG). This slow age-related Φ_2 $\dot{V}O_2$ kinetics resulted either for the $\Phi_{2\_Isolated}\dot{V}O_2$ τ obtained with the two component model ($2C,7P_{BaseLine\_Start\ to\ End}$) for Mod exercise and three component model ($3C,10P_{BaseLine\_Start\ to\ End}$) for Hvy exercise (Table 6), or for $\Phi_{2postulated}\dot{V}O_2$ τ obtained with the one component model ($1C,4P_{0.3333\ to\ 3\ min\ exercise}$) for ModAbs condition (OG > YG: 41.6 ± 3.4 > 22.9 ± 3.6), ModRel condition (50.0 ± 3.4 > 26.5 ± 3.6), and HvyRel condition (40.9 ± 3.4 > 29.4 ± 3.6) exercise; in other words, the two way ANOVA (Φ_{value} 60.2, $p < 0.001$) *post hoc* Holm-Sidak method (t 6.24, $p < 0.05$) showed slow-age related $\Phi_{2\_Isolated}\dot{V}O_2$ τ for Sub (OG > YG: 49.2 ± 14.8 > 24.1 ± 8.5); and two way ANOVA (Φ_{value} 39, $p < 0.001$) *post hoc* Holm-Sidak method (t 6.24, $p < 0.05$) showed slow- age related $\Phi_{2postulated}\dot{V}O_2$ τ for Sub (OG > YG: 44.2 ± 12.2 > 26.2 ± 8.1). In addition, the phase one $\dot{V}O_2$ τ difference from YG minus OG was 17.6 ± 8.2 for Sub. The phase two $\dot{V}O_2$ τ resulted in the YG (25.7 ± 10.3) faster (t 7, $P < 0.001$) than OG (51.3 ± 15.1) for Sub (Figure 6). Evermore, we also observed

from the best statistically and/or physiologically fitting models, $2C,7P_{BaseLine\_Start\ to\ Offset}$ for Mod exercise and $3C,10P_{BaseLine\_Start\ to\ Offset}$ for Hvy exercise, a slow age-related Φ_2 $\dot{V}O_2$ kinetics from fitting with either a unrestricted TD1 < > zero value (Φ_2 $\dot{V}O_2$ τ: OG_49.2 ± 15 > 25 ± 9.3_YG, t 7, $p < 0.001$) or a restricted TD1 zero value (Φ_2 $\dot{V}O_2$ τ: OG_49 ± 15 > 24 ± 9_YG, t 7, $p < 0.001$) for Sub.

- ***Exponential Mean Response Time:*** There were a slow age-related $\dot{V}O_2$ exponential mean response time (MRT_{exp}, s) (OG_52.6 ± 9.5 > 34.2 ± 6.1_YG) for Mod exercise condition (t 6.7, $p < 0.001$) but not for HvyRel exercise (Table 6).

DISCUSSION

Exercise Intensity, Aerobic Parameters and Power Output

The low age-related Sub exercise capacity in terms of $\dot{V}O_{2peak}$ (an independent predictor of functional capacity), $\dot{V}O_2\hat{\theta}_L$ and $\hat{\theta}_L\%\dot{V}O_{2peak}$,[41] proved the well known biological deterioration with aging in the absence of clinical disease in our experimental group[42,43] due to a progressively mainly reduction in maximal cardiac output that in turns is mediated in part by diminished maximal left ventricular contractility and heart rate as a partial consequence of decreased - adrenergic-receptor responsiveness.[44] The rate of decline in $\dot{V}O_{2peak}$, in men,[41] is -0.034 L•min^{-1}•yr^{-1} or 0.31 mL•kg^{-1}•min^{-1}•yr^{-1}.

- ***Moderate exercise conditions:*** In spite of these low age-related effects in Sub exercise capacity the slope of the subthreshold $\dot{V}O_2$- power output relationship ($\Delta\dot{V}O_2/\Delta PO$) during Mod exercise ($< \hat{\theta}_L$) legs cycling resulted similar in young and adult men observed in this study, meaning that $\Delta\dot{V}O_2/\Delta PO$ is not age-related and that $\dot{V}O_2$ rises in nature exponentially to its new steady state for work rate increments $< \hat{\theta}_L$.[45] In consequence, the steady state in either $\dot{V}O_2$ or $\Delta[La^-]_{plasma}$ was proven by the observation that there was no difference between the 3- and 6-min values for moderate- intensity exercise,[35] and also the increase in $\dot{V}O_2$ in response to simultaneous increase in work rate (or $P_{ower}O_{utput}$, W) under steady-state aerobic work ($\Delta\dot{V}O_2/\Delta PO$) may be used to estimate the efficiency for muscular work.[46] Evermore, in this study, $\dot{V}O_{2\ EndExercise}$ (mL•min^{-1}) for ModAbs exercise was similar in the two age groups; however, this exercise condition resulted in a high age-related relative intensity (%$\hat{\theta}_L$: OG > YG ; %$\dot{V}O_{2peak}$: OG > YG). In addition, while both the PO and $\dot{V}O_{2EE}$ were low age-related for ModRel exercise; nevertheless, this exercise condition resulted in a similar relative intensity (%$\hat{\theta}_L$ and %$\dot{V}O_{2peak}$) in the two age groups. These age-related relative intensity observations for the Mod exercise conditions, suggested to us a mitigating deleterious effects of ageing in the endurance- related parameters.[2,47,48]
- ***Heavy exercise condition:*** The non steady-state in both the $\dot{V}O_2$ and the $\Delta[La^-]p_{(6\text{-}3min)}$, was proven by the observation that there were difference between the 3- and 6-min values for Hvy exercise.[35] Again, in spite of the low age-related effects in Sub exercise capacity, this exercise condition $> \hat{\theta}_L$ was probed to be similar in terms of relative intensity in the two age groups (%$\hat{\theta}_L$, %$\dot{V}O_{2peak}$ and %Δ) but low age-related effects in terms of PO, $\dot{V}O_{2\ EE}$, $\dot{V}O_{2(6\text{-}3min)}$ (mL•min^{-1}) , end-exercise plasma $[La^-]$ (mmol•l^{-1}) and, $\Delta[La^-]p_{(6\text{-}3min)}$ (mmol•l^{-1}). These similar relative intensity values observed between OG and YG, are also explained in terms of a mitigating deleterious effects of senescence in the functional capacity,[47,48] like the low amplitudes and long $\tau 2$ age-related parameters observed in this study. Besides, during this exercise condition there is some additional energy requirements supplied by an increased rate of anaerobic glycolysis, causing an increasing in the production of lactate,[35] as it was observed in this study where plasma $[La^-]$ and $\Delta[La^-]_{(6\text{-}3min)}$ resulted low age-related. Evermore, it is known also that loss of type II fibres with aging might also cause a change in the lactate accumulation, causing in the older men to attain a similar blood lactate concentration but at a higher percentage of $\hat{\theta}_L$ than the younger men.[49] This[49] could explain an age-related effect observation of the positive relationships between $\Delta\dot{V}O_{2(6\text{-}3min)}$ and and $\Delta[La^-]p_{(6\text{-}3min)}$ for heavy exercise condition. In addition, there is a sustained increase in arterial La^- and a sustained decrease in pH that characterize this exercise condition, but with time these responses either stabilize or even decline back towards baseline.[50] However, for practical reasons, La^- production occurs when O_2 is not used in the reactions rather than implying that O_2 was not available to be used[51] and whether or not the limitation of O_2 availability, enzymatic rate limitations and fiber- type composition of muscle are the causes of $\hat{\theta}_L$, is matter of debate.
- ***O_2 Deficit:*** The O_2 deficit is defined as the integral with respect to time of the difference between the O_2 demand for that particular exercise intensity and the O_2 uptake during the whole exercise bout. The magnitude of the O_2 deficit is linked to both the O_2 equivalent of the total energy demands of the task and the kinetics of $\dot{V}O_2$.[10] It is used to quantify the anaerobic energy contribution to the work performed. We analy-

sed the O_2 deficit to determine the efficiency of non steady-state exercise, and our observation that it was high age-related for ModAbs exercise, suggested its link to a slow $\dot{V}O_2$ kinetics; however, since the O_2 deficit resulted as low age-related for the relative exercise conditions, then it is probable that the magnitude of O_2 deficit was caused by work rate intensity too.[50] These observations are explained as well as, because studies on the efficiency of the cycle ergometer exercise of muscular work before $\dot{V}O_2$ reaches a steady state, showed that the O_2 deficit reached a plateau value at approximately 4 min,[35] and in this study the Sub lasted 6 min. In consequence, the O_2 deficit is provided if the duration of exercise is sufficiently long (i.e., 4 to 6 min) for $\dot{V}O_2$ to reach a steady state.[35] Thus, for Mod exercise condition the O_2 deficit, represents the energy equivalent to the depletion of high-energy phosphate (Creatine Phosphate and ATP) stores and O_2 stored in the body at the start of the exercise.[46] For Hvy exercise condition the O_2 deficit, includes, in addition, the energy equivalent of the anaerobic;[46] therefore, the estimation of O_2 deficit during heavy exercise transitions, can be also consider the slow component of $\dot{V}O_2$ as an additional deficit component with delayed start.[45] Nevertheless, we considered that this did not affect the differences in O_2 deficit observed between YG and OG for Hvy exercise condition in this study. The high O_2 age-related deficit observed in this study for ModAbs exercise, is explained mainly, because ageing is associated with poor muscle function[52] that yielded slow $\dot{V}O_2$ kinetics and a large O_2 deficit.

- ***Delta Efficiency:*** Efficiency in general was restricted to Mod exercise conditions, because $\dot{V}O_2$ during Hvy exercise condition or a higher intensity work rate resulted high.[51] However, in this study we observed a low age-related delta efficiency for ModRel exercise only. In consequence, in spite of the low age-related exercise capacity, there was not delta efficiency age-related effect even though the delta efficiency is not affected by body mass or change in body weight.[53]
- ***Moderate (Absolute and Relative) vs Heavy Relative Conditions Within an Age Group:*** Both, the low exercise intensity domain- related a_1, a_2, and A_{total} and the fast exercise intensity domain- related MRT_{exp} in the YG and in the OG, observed in this study for ModAbs exercise, agreed with previous comunications.[32,46,54]

$\dot{V}O_2$ kinetics

- ***Phase Two $\dot{V}O_2$ Kinetics Exercise Capacity. Moderate Exercise Condition:*** In this study the on-transient Φ_2 $\dot{V}O_2$ kinetics (Φ_2 $\dot{V}O_2$ τ) was age-related for Mod exercise conditions. The importance of the on-transient Φ_2 $\dot{V}O_2$ kinetics resides in the fact that, this Φ_2 $\dot{V}O_2$ τ may be used as a proxy function (≈ 10% degree of uncertainty) for $\dot{V}O_{2M}$ kinetics.[10] The Φ_2 $\dot{V}O_2$ τ normally ranges between 30 to 40 s in healthy young individuals, tending to be smaller in endurance-trained individuals[55] and to be appreciably larger in elderly sedentary individuals[25] and in patients with pulmonary and cardiovascular disease.[10] This slow $\dot{V}O_2$ kinetics in older adults may be limited by a slow adaptation of muscle blood flow and $\dot{V}O_2$ delivery;[56] however, when muscle blood flow and O_2 delivery are adequate, $\dot{V}O_{2M}$ in both old and young adults is limited by intracellular processes within the exercising muscle.[57] Evermore, It has been showed that elderly subjects (mean age 68.8 years) had nearly 50% lower oxidative capacity per volume of muscle than adult subjects and that the cellular basis of this drop was a reduction in mitochondrial content, as well as a lower oxidative capacity of the mitochondria with age.[58] Nevertheless, the precise control mechanisms of Φ_2 $\dot{V}O_2$ τ remain to be elucidated.[10]
- ***Heavy Exercise Condition:*** In this study the on-transient Φ_2 $\dot{V}O_2$ kinetics (Φ_2 $\dot{V}O_2$ τ) was age-related for HvyRel exercise ($> \hat{\theta}_L$) as well, where $\dot{V}O_2$ kinetics become more complex.[10] For example, the difference between the expected steady-state $\dot{V}O_2$ value and the actual $\dot{V}O_2$ achieved in the quasisteady state (delayed by as much as 10 to 15 min) is positive, as it was observed in this study (positive $\Delta\dot{V}O_{2(6\text{-}3min)}$ and positive $\Delta[La^-]p_{(6\text{-}3min)}$) in the two age groups, for this exercise condition. As a result of that, the overall gain results markedly increased from the normal or Mod exercise condition.[10] These excess increment in Φ_3 $\dot{V}O_2$ is the result of a slow component, which appears to be of delayed origin and which is superimposed on that of the Φ_2 $\dot{V}O_2$ kinetics;[10] however, there is doubt about when the slow component is manifest.[10] Besides, on one hand, there is no convincing mechanistic evidence that slow component is intrinsically monoexponential; in consequence, both the TD and the τ of the slow component $\dot{V}O_2$ should, at present, therefore be considered parameters of convenience, rather than control parameters having physiological equivalents.[10] On the other hand, the $\Phi_2\dot{V}O_2$ τ may increase at intensity domains above $\hat{\theta}_L$[33] but this is not consistently the case.[54] These discrepancies may reflect interindividual differences in factors such as the involved muscle fibre types (i.e., slower kinetics of fast-twitch muscle fibers), muscle recruitment patterns, kinetic profiles of the recruited musculature, and the degree to which portions of

muscle with slow kinetics can attenuate the predominant signal coming from recruited slow-twitch fibres.[10] Interestingly, the Φ_2 $\dot{V}O_2$ τ for Hvy exercise remains similar to that of below $\hat{\theta}_L$ exercise (i.e., Mod condition) or perhaps slightly slower;[51] in this study, the Hvy Φ_2 $\dot{V}O_2$ τ and Mod Φ_2 $\dot{V}O_2$ τ were similar within an age groups, confirming that the Φ_2 $\dot{V}O_2$ kinetics remains exponentially independently of the range of work rate intensities of Sub, from either Abs or Rel exercise conditions.

- ***Slow Age-Related Φ_2 $\dot{V}O_2$ Kinetics: Metabolic Consequences:*** One of the metabolic consequences of this slow age-related Φ_2 $\dot{V}O_2$ τ, was the observation of two different groups (OG from YG) from the positive relationships between $\Delta\dot{V}O_{2(6\text{-}3min)}$ and $\Delta[La^-]p_{(6\text{-}3min)}$. We explain this because based on our observations that both the $\Delta\dot{V}O_{2(6\text{-}3min)}$ and the $[La^-]p$ resulted low age-related, are in agreement with the theoretical concept that the greatest the difference in $\Delta\dot{V}O_{2(6\text{-}3min)}$ the more the delay to reach the steady-state $\dot{V}O_2$ and that the degree of delay to reach the steady-state is related to anaerobic metabolism (i.e., lactate energy system).[10] Nevertheless, in this study occurred low age-related $\dot{V}O_{2\,EE}$ for relative conditions and $\Delta[La^-]p_{(6\text{-}3min)}$ for Hvy exercise condition, but not for ModAbs exercise. In consequence, there was a slow age-related effect on either the time to reach the steady-state $\dot{V}O_2$ for relative exercise conditions, or the lactate energy metabolism in terms of plasma lactate for HvyRel exercise.
- ***Φ_2 $\dot{V}O_2$ Kinetics Exercise Capacity and Φ_2 $\dot{V}O_2$ Kinetics Entropy:*** As an open system in a thermodynamic sense; the human body lives on negentropy absorbed from his environment but the arrow of time points to his ever- increasing maximum entropy (death).[59] In consequence, the decreased exercise capacity age-related, observed in this study, make sense in that the OG showed certain degree of increased Φ_2 $\dot{V}O_2$ τ entropy. Our observations that the $\dot{V}O_2$ on-transient kinetics (Φ_2 $\dot{V}O_2$ τ, s) for exercise either ModAbs- or HvyhRel-exercise, resulted negatively correlated with $\dot{V}O_{2peak}$ (mL•min^{-1}•kg^{-1}) in the YG only, is explained because this fitter YG showed faster kinetics (short τ2 value)[51] than those from the less fit OG (τ2 value 26 s higher). This better Φ_2 $\dot{V}O_2$ kinetics exercise capacity in the YG, is explained because this $\dot{V}O_{2peak}$ has shown strong relationship with both the number of capillaries per fibre in the skeletal muscle that maintain or elongate blood flow mean transit time, that in turn enhances O_2 delivery by maintaining oxygen extraction (aO_2 - $\bar{v}O_2$ difference)[60] and the increased oxidative enzyme activities even at high rates of skeletal muscle blood flow.[60] The rate of ATP generation is dependent on the $\dot{V}O_2$ relative to total body mass that can be maintained during Sub, which is determined by the subject's $\dot{V}O_{2peak}$ relative to total body mass and the percent of this $\dot{V}O_{2peak}$ at which the subject can perform.[60] In consequence and for the first time, we observed on one hand, high age-related Φ_2 $\dot{V}O_2$ τ entropy (S Φ_2 $\dot{V}O_2$ τ, cal• °C^{-1}• s) for Sub and, on the other hand, S Φ_2 $\dot{V}O_2$ τ (cal• °C^{-1}• s) and $\dot{V}O_{2peak}$Rel (mL•min^{-1}•kg^{-1}) resulted close negatively correlated for Sub in the YG only. These observations are also explained because, in the YG exist a wide range of homeostasis, particularly in aerobic power and, on the contrariwise, in the OG, the aerobic power decline converges in narrowed range of homeostasis.[41] Thus, an age-related narrow range of aerobic power (low negentropy) did not show relationship between Φ_2 $\dot{V}O_2$ kinetics entropy and the fitness measure of cardiorespiratory adaptation to endurance training ($\dot{V}O_{2peak}$). This communication opens for the first time the potential application of the S Φ_2 $\dot{V}O_2$ τ to discriminate demarcations between the fitness measure of cardiorespiratory adaptation to endurance training and the Φ_2 $\dot{V}O_2$ kinetics entropy in their degree of relationships with $\dot{V}O_{2\,M}$ kinetics in studies on physical activity and ageing process. For example, this increased age-related S Φ_2 $\dot{V}O_2$ kinetics, suggests a substantial O_2- related on transient slow muscle energy metabolic limitation, because S is a result of an energy rate of change between to states. In contras to the high age-related O_2 deficit observed only for moderate absolute- intensity exercise; this high age-related Φ_2 $\dot{V}O_2$ kinetics entropy, was very consistently across the work rate power outputs of the Sub and, we intuitively explain them because the Boltzmann's k related thermodynamically, at molecular level,[1] the Φ_2 $\dot{V}O_2$ kinetics. We brought about the empirical substitution of the quantitative measure of the atomistic disorder of a living system (D) by the Φ_2 $\dot{V}O_2$ kinetic parameter (τ2) into the equation of entropy; in other words, we estimated S k • log Φ_2 $\dot{V}O_2$ t instead of S k • logD, because:

i) one way of the human being to either evade the decay to equilibrium (maximum S) or increase his order (negentropy, -S k • log 1/D) is by breathing (-S k • log Φ_2 $\dot{V}O_2$ τ), and
ii) an estimation of this degree of -S and disorder (S) by the statistical physics investigation of Boltzmann and Gibbs showed an exact quantitative connection that is expressed by the equation of entropy.[1]

Boltzmann concept deals with the problem of distribution of molecules among a set of energy states of any kind;[59] D is the total number or choices towards equilibrium and D is a very large number for a real system, thus it is more convenient to apply the quantitative lnD (or logD) rather than D.[59] Both S and D are extensive properties that depend on the size of the system and the amount substance present (i.e., volume, mass, and energy). Like D, S increases in a spontaneous process, and any spontaneous process in an open system (i.e., human being) must lead too an increase in S (second law of thermodynamics).[59] Finally, since the second law of thermodynamics only tells us which processes (thermodynamically controlled or not spontaneous) can occur but not the rate at which they occur (i.e., kinetically controlled metabolic reactions),[59] then the S Φ_2 $\dot{V}O_2$ τ seems to be another fundamental parameter to study the transient response of gas exchange kinetics. Further research is guaranteed on S Φ_2 $\dot{V}O_2$ τ and $\dot{V}O_{2peak}$ relative to total body mass to determine if their close negatively relationships are coincidental or are related in a cause- effect mode for the degree of fitness measure of cardiorespiratory adaptation to endurance training and ageing.

- ***Parameters Within an Exercise Condition (Young* vs. *Old):*** We observed slow age-related Φ_2 $\dot{V}O_2$ kinetics (τ2, s) for all of the conditions of , from either isolated or postulated phase two $\dot{V}O_2$, in each of the constant load exercise tests is in agreement with previous studies already done for relative exercise conditions[9,20,21] and for the first time for ModAbs exercise in this study. Evermore, our observations of a slow age-related $\Phi_{2\ Isolated}$ $\dot{V}O_2$ kinetics from fitting with time delay either equals to zero or unrestricted for Sub and that the phase one $\dot{V}O_2$ τ was delayed age-related (≈ 18 s) for Sub, and that it was observed a slow time delay in $\Phi_{2postulated}\dot{V}O_2$ compared $\Phi_{2\_Isolated}\dot{V}O_2$; allowed us to say, that the fitting models a 2C,7P$_{Baseline_Start\ to\ End}$ for Mod exercise condition and a 3C,10P$_{Baseline_Start\ to\ End}$ for Hvy exercise condition, are the best preferred rather than those avoiding phase one (i.e., 1C,4P$_{0.3333\ to\ 3\ min\ exercise}$), for both physiologically isolating $\Phi_2\dot{V}O_2$ and kinetically characterizing it from entire submaximal $\dot{V}O_2$ on-transient response data, in young and old men for $\Phi_2\dot{V}O_2$ kinetic comparisons.
- ***Amplitude:*** As expected, we observed differences in $\Phi_2\dot{V}O_2$ amplitudes from all of the exercise conditions ($\Phi_2\dot{V}O_2$ a_2: ModAbs < ModRel < HvyRel)[21] and we explain the low age-related amplitude two from all of the relative conditions, because of the different power output between our constant load exercise tests.[21] In spite of these differences in amplitude two between constant load exercise tests; we explain the lack of an age-related effect in the $\dot{V}O_2$ magnitude of the response (amplitude) for absolute power output was both, the lowest power output of this ModAbs exercise condition and mainly; because Φ_2 $\dot{V}O_2$ on-transient kinetics, appears to be preserved in the legs for leg cycling- pedalling but, according to literature data regarding the Φ_1 and Φ_2 exercise on-set kinetics, both phases are slow with age in the arms.[9] However, the $\dot{V}O_2$ amplitudes for the relative exercise conditions, resulted low age-related and these agreed with the slow Φ_2 $\dot{V}O_2$ kinetics age-related[25,61] observed in this study as well and that we explain because of the low age-related exercise capacity.[14,43]
- ***Time Delay:*** In this study, the lack of age-related effects in both TD1 for Sub and TD3 for HvyRel exercise values, agreed

  i) for TD1, with the $\Phi_1\dot{V}O_2$ mechanism contributions to exercise hyperaemia that appear to be preserved in the legs of the OG,[9] and also
  ii) for TD3, with $\Phi_3\dot{V}O_2$ mechanism contributions in terms of the $\dot{V}O_2$ slow component values that were not age-related too. Besides, there is a significant between- limb vascular heterogeneity in humans that is influenced by age and exercise training[9] where the limb vascular and, likely, metabolic differences, complicated by both age- and activity- induced modulation that make more complex for both the designing and interpreting research and clinical testing of limb vascular conductance- O_2 delivery function.[9,62] In contrast, the slow age-related TD2 for s Sub and since TD2 reflects a temporal (dynamic) characteristic of the $\Phi_2\dot{V}O_2$ response, thus a slow age-related time delay indicates the sluggishness of start of control mechanisms in old adult men in this study.[63]

- ***Time Constant:*** The time constant describes the rate at which $\dot{V}O_2$ rises towards the steady-state (≈ four τ or 98% of its final amplitude). In this study, the lack of age-related $\Phi_1\dot{V}O_2$ τ for s Sub is explained also because $\Phi_1\dot{V}O_2$ mechanism contributions to exercise hyperaemia appear to be age-preserved in the legs.[63] However, the slow age-related Φ_2 $\dot{V}O_2$ kinetics resulted ≈ 26 s high, meaning that the OG steady-state $\dot{V}O_2$ was attained ≈ 144 s (4 • 26 s) later compared to YG.[19] The Φ_2 $\dot{V}O_2$ represents the fundamental (predominant) exponential rise in $\dot{V}O_2$ toward the expected steady- state.[20] Thus, we observed slow Φ_2 $\dot{V}O_2$ kinetics age-related across not only for two relative- intensity exercise condition (80% $\hat{\theta}_L$ power output and 120% $\hat{\theta}_L$ power output) but also for an absolute power output; that agreed with a slow Φ_2 $\dot{V}O_2$ kinetics age-related for relative power output of energy levels of 80% $\hat{\theta}_L$ and 120% $\hat{\theta}_L$ previously observed.[14,25] In this study, for the first time were compared Φ_2 $\dot{V}O_2$ kinetics toward the expected steady-state, between young and old adult men in terms of 50W or absolute power output. In consequence, there should be a linking ATP consumption with mitochondrial ATP production and $\dot{V}O_{2M}$.[6] Evermore, if the rate with which $\dot{V}O_2$ rises in Φ_2 faithfully reflects the for $\dot{V}O_{2M}$ in the exercising muscles to within 10%[19,64] then slow $\dot{V}O_{2M}$ kinetics should be age-related as well.

- ***MRT_{exp}*:** The MRT_{exp} is a parameter of the overall $\dot{V}O_2$ on-transient kinetics and, it is a measure of time required for the entire $\dot{V}O_2$ to reach 63% of its final amplitude. We observed in this study a slow age-related MRT_{exp} (except for Hvy exercise condition) that agreed to a slow Φ_2 $\dot{V}O_2$ kinetics age-related observed in this study for Mod exercise conditions. However, the lack of a slow age-related MRT_{exp} for hvy exercise is explained because of the effect of the $\dot{V}O_2$ slow component of the more complex kinetics for this exercise condition.[10]

CONCLUSIONS

The submaximal exercise on-transient $\Phi_2\dot{V}O_2$ kinetics ($\tau 2$), time delayed (TD2), the slow component (a_3) and the overall $\dot{V}O_2$ on-transient kinetics (MRT_{exp}) resulted slow age-related in spite of similar $\Phi_2\dot{V}O_2$ τ across the submaximal (80% $\hat{\theta}_L$ and 120% $\hat{\theta}_L$ power outputs) work rate intensities, included by first time a moderate absolute-intensity exercise (50W $P_{ower}O_{utput}$) within an age groups. Particularly, there were an age-related mitigating effects in terms of $\hat{\theta}_L$ %$\dot{V}O_{2peak}$ and deleterious effects in $\dot{V}O_{2peak}$, $\dot{V}O_2\,\hat{\theta}_L$, and O_2 deficit for moderate absolute- intensity exercise. On-transient $\Phi_2\dot{V}O_2$ kinetics for moderate absolute-, moderate relative-, and heavy relative- intensity exercise, were also age related. Next, increased age-related on-transient $\Phi_2\dot{V}O_2$ entropy for moderate absolute-, moderate relative-, and heavy relative- intensity exercise (submaximal $S\tau 2$). Thus, a slow on-transient phase two pulmonary O_2 uptake kinetics and its increased entropy were age-related, and that they remain exponentially independently of the range of work rate intensities of submaximal exercise (included an absolute exercise condition) in both young and old adult men.

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