Effect of work: rest cycle duration on VO2 fluctuations during intermittent exercise

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Running Head: Oxygen uptake and intermittent exercise

Abstract

The succession of on-transient phases that induce a repetition of metabolic changes is a possible mechanism responsible for the greater response to IT. The objective of this study was to quantify metabolic fluctuations during intermittent exercise characterized by the same work:rest ratio, but different durations and identify which duration leads to the greatest fluctuations. Ten participants (24±5 years; $\dot{V}O_{2max}$: 42±7 mL·min^{-1}·kg^{-1}) performed: 1) an incremental test to exhaustion to determine peak work rate (WR_{peak}) and oxygen uptake ($\dot{V}O_{2max}$), 2), and three 1-hour intermittent exercises alternating work period at 70% WR_{peak} with passive recovery period of different 1:1 work:recovery duty-cycles (30s:30s, 60s:60s, 120s:120s). $\dot{V}O_2$ response analysis revealed differences in the fluctuations across the intermittent conditions despite an identical total energy expenditure. The sum of the cycle's nadir-to-peak $\dot{V}O_2$ differences ($\Sigma\Delta\dot{V}O_2$) and the oxygen fluctuation index (OFI) were both greater in the 60s:60s condition ($\Sigma\Delta\dot{V}O_2$: +38±13%and +19±18% vs. 120s:120s and 30s:30s, $p<0.05$; OFI: +41±29% and +67±62% vs. 120s:120s and 30:30s, $p<0.05$). $\dot{V}O_2$fluctuations analysis was successful in identifying the intermittent condition associated with the greatest disturbances: the 60s:60s duty-cycle induces more $\dot{V}O_2$ fluctuations. The present findings also demonstrate that the selection of the duty-cycle duration for submaximal intermittent exercise prescription is of interest to produce high $\dot{V}O_2$fluctuations.

Key Words: VO_2, intermittent exercise, work:rest cycle duration, training prescription, VO_2 fluctuations,

Introduction

Regular physical activity and exercise are associated with numerous physical health benefits. Successful endurance training interventions require a thoughtful manipulation of training intensity, duration and frequency, with the implicit goal of enhancing exercise tolerance and associated physiological characteristics (Gorostiaga, Walter, Foster, & Hickson, 1991; Seiler, Jøranson, Olesen, & Hetlelid, 2013). Maximal oxygen uptake ($\dot{V}O_{2max}$), a measure of aerobic power and a major predictor of all-cause mortality in normal subjects and cardiovascular disease, can be enhanced following endurance training (Myers et al., 2002). Different exercise modalities such as continuous or intermittent exercise may be used to improve aerobic capacity (Gorostiaga et al., 1991; MacDougall et al., 1998).

Three mechanisms can be put forward to explain the improvements of $\dot{V}O_{2max}$ following intermittent training (IT). First, the exercise intensity is an important determinant of the physiological responses to exercise training. Greater improvements in $\dot{V}O_{2max}$ were reported with vigorous intensity exercise training (60-84% $\dot{V}O_{2max}$) compared with moderate exercise (40-59% $\dot{V}O_{2max}$)(Swain, 2005). Second, the intermittent exercise allows more time to be spent at a high level of $\dot{V}O_2$, which is considered very effective when aiming at maximizing a training stimulus (Billat, 2001; Seiler et al., 2013). The third possible mechanism responsible for the greater response to IT would relate to the succession of on-transient phases that induce a repetition of metabolic changes, defined in the present paper as $\dot{V}O_2$ fluctuations. Our group recently observed that greater $\dot{V}O_2$ fluctuations, observed during an intermittent exercise modality, induces a greater activation of signaling pathways involved in oxidative metabolism when compared to a single bout of continuous exercise of matched work and intensity (Combes et al., 2015).

Because $\dot{V}O_2$ fluctuations are argued to be one of the most important mechanisms underpinning chronic adaptations following intermittent training (Cochran et al., 2014; Edge et al., 2013; Tucker, Sawyer, Jarrett, Bhammar, & Gaesser, 2015), the present study will quantify the

$\dot{V}O_2$ fluctuations during three intermittent exercises characterized by the same work:rest ratio, but different durations. Identification of a protocol inducing the greatest fluctuations would be very informative to maximize rehabilitation program effects. We compared three different intermittent exercises interval exercise allows performed at 70% of peak work rate (WR_{peak}) which is an intensity currently recommended and used in rehabilitation programs (Garber et al., 2011). We hypothesized that the work:rest cycle duration will influence the $\dot{V}O_2$ fluctuations during intermittent exercised realized at a same intensity.

Materials and Methods

Subjects

Ten healthy active men participated in this study (mean±SD: 24±5 years; 74±11kg; 1.79±0.06m; 13.9±3.1% of Body Fat; $\dot{V}O_{2max}$,: 42±7mL·min^{-1}·kg^{-1}). All the subjects provided signed informed consent prior to their participation. The protocol was approved by the University of Brighton Ethics Committee and the study was conducted according to the Declaration of Helsinki.

Experimental Design

Participants performed the following cycling trials: 1) an incremental test, 2) three 1-hour intermittent exercises separated by a minimum of 48-hours.

Assessment of $\dot{V}O_{2peak}$ and WRpeak

The test was performed on an electrically-braked cycle (SRM, Germany) and began with a 3-min stage at 75W followed by increments of 25W every 2-min until volitional exhaustion. Each subject carried out a maximal effort according to Howley et al. (1995).

Ventilatory parameters ($\dot{V}_E$, $\dot{V}O_2$, $\dot{V}CO_2$) were measured breath by breath and $\dot{V}O_{2max}$ was defined as the highest 30s average $\dot{V}O_2$. Peak work rate correspond to the power associated to the last increment completed. Heart rate was monitored continuously (RS 800, Polar, Kempele, Finland).

Exercise protocols

The intermittent exercises were performed on a customized cycle ergometer (620 Ergomedic; Monark, Varberg, Sweden) fitted with power measuring cranks (Pro Track, 8; SRM). After a standardized 10-min warm-up performed at 40%WRpeak, subjects performed the intermittent tests at 70%WR_{peak} interrupted by passive recovery period, each with a different 1:1 work:recovery duty-cycle (30s:30s, 60s:60s, 120s:120s).

Apparatus and analysis

Pulmonary gas exchange were recorded breath-by-breath using an on-line gas analysis system (MediSoft, Germany). Average oxygen uptake values over 5-s periods were used to calculate the mean $\dot{V}O_2$ (L·min^{-1}) over the exercise period. The $\dot{V}O_2$ fluctuations were quantified using three distinct variables: 1) A sum of $\dot{V}O_2$ peak-to-nadir amplitudes (L·min^{-1}) were computed for each exercise transition and subsequently summed for the entire exercise period ($\Sigma\Delta\dot{V}O_2$, Fig. 1A), this quantitative parameter represent the volume of the $\dot{V}O_2$ fluctuations; 2) for every second of exercise, the rate of change in the $\dot{V}O_2$ response was computed (+d$\dot{V}O_2$·dt^{-1}) and the time spent at a rate of rise higher than 20mL·s^{-1} was determined ($T\dot{V}O_{2RR}$ in s, Fig. 1B), this qualitative parameter reflect the duration where high velocity of $\dot{V}O_2$ fluctuations occurred; the choice of a threshold of 20mL·s^{-1} was arbitrary but with similar results obtained over a wider range of limits (5 to 60mL·s^{-1}; unpublished data); and 3) A $\dot{V}O_2$ Fluctuations Index (OFI) was finally computed (Equation 1) from the average of the $\dot{V}O_2$ peak-to-nadir amplitude (A, in mL·s^{-1}) and the rate of rise ($RR_{mean,}$ in mL·s^{-1}) for the exercise and its cycle duration (T, in seconds), this parameter combine qualitative and quantitative aspects of $\dot{V}O_2$fluctuations.

Equation 1: $\dot{V}O_2$ Fluctuations Index (OFI in mL^2·s^{-3}) = $\frac{A \cdot RR_{mean}}{T}$

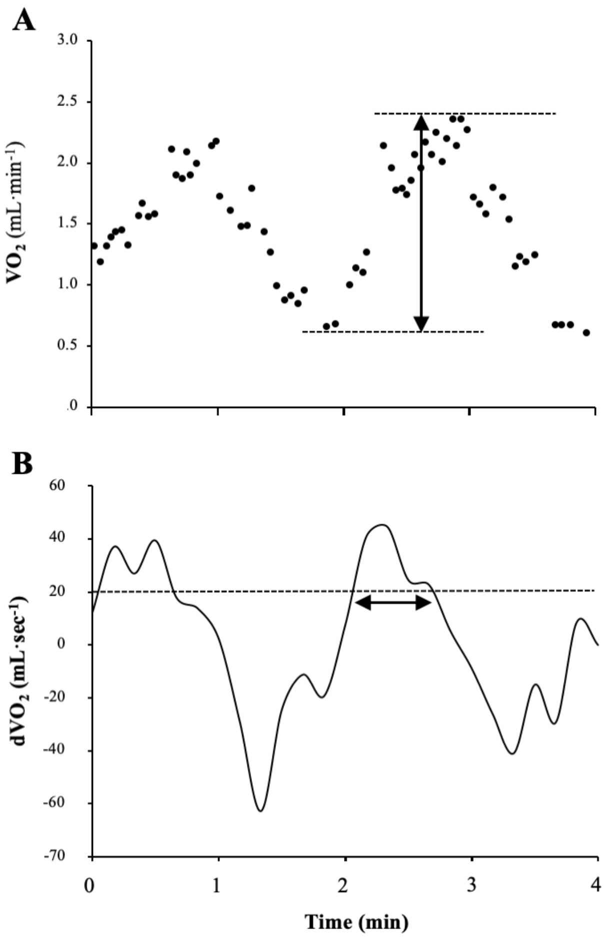

Figure 1. Fluctuations analysis. Representative calculation of (A) sum of the peak-to-nadir amplitude (L) for the calculation of P Δ and (B) rate of rise (+d dt–1) higher than 20 mL· s–1 for the calculation of TRR.

Capillary blood lactate concentrations

During the assessment of $\dot{V}O_{2max}$, capillary blood samples were taken at rest, immediately at the end of exercise and 3-min after the end of exercise. For the intermittent exercises, capillary blood samples were taken at rest, after the warm-up, at 30-min and immediately at the end of exercise. Blood lactate concentration ($[La]_b$) was determined using a Yellow Springs Instrument (YSI 2300 Stat Plus; Analox, Sheffield, UK).

Perception of exertion

The rate of perceived exertion (RPE) was measured using a Borg's category scale 20 (Borg, 1982) at the end of each stage during the incremental exercise, and at the end of both warm-up and intermittent exercise.

Statistical analysis

Data are presented as means±SD. Statistical analyses were performed using Sigma Stat for Windows (version 3.0, SPSS Inc., Chicago, IL). A two-way ANOVA with repeated measures, and a post-hoc Tukey test, were performed to examine the influence of time and duty-cycle on the four samples of $[La]_b$. To compare the total work done and all variables associated with the $\dot{V}O_2$ measurements between the three intermittent exercises, a one-way ANOVA was used and followed with a post-hoc Tukey test. The significance level was set at $p < 0.05$.

Results

No significant difference was found for the mean $\dot{V}O_2$ between the three exercises (in $L \cdot min^{-1}$: 1.51±0.19, 1.45±0.25 and 1.51±0.17 for 30s:30s, 60s:60s and 120s:120s, respectively). The total amount of work accumulated was also not different between all three conditions (in kJ: 344±33, 345±34 and 343±35, for 30s:30s, 60s:60s and 120s:120s, respectively).

The analysis of the $\dot{V}O_2$ oscillations revealed that the duty-cycle duration influences the peak to nadir amplitude (p<0.05, figure 2, table 1). Both peaks and nadirs of the $\dot{V}O_2$ oscillations increased slightly over the first cycles until the values remained unchanged. The mean peak to nadir amplitude increased with the cycle duration (table 1, p<0.05) and remained constant from the second repetition of the 60s:60s and 30s:30s exercises and from the first repetition of the 120s:120s modality (p<0.05, table 2). The peak of the $\dot{V}O_2$ oscillation was also influenced by the duty-cycle duration (p<0.05). Mean $\dot{V}O_2$ values reached 60±8, 72±9 and 84±11 % of $\dot{V}O_{2max}$ respectively during the 30s:30s, 60s:60s and 120s:120s modality (p<0.05).

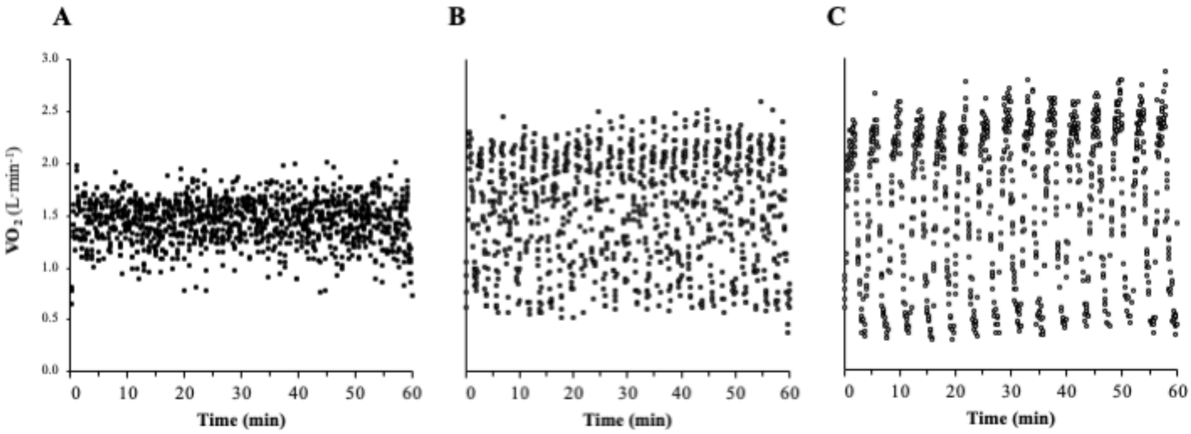

Figure 2. Representative responses. Representative response (subject 10) of breath-by-breath oxygen uptake () for 30 s:30 s exercise (A), 60 s:60 s exercise (B) and 120 s:120 s exercise (C).

Table 1: Mean responses to three different intermittent exercises (70% of maximal work rate; 3 durations of 1:1 work to rest ratio).

		30s:30s	60s:60s	120s:120s
$\dot{V}O_2$peak	Absolute (L·min-1)	1.825±0.227	2.204±0.348*	2.589±0.242*#
	Relative (%$\dot{V}O_{2max}$)	60±8	72±9*	86±11*#
$\dot{V}O_2$nadir	Absolute (L·min-1)	1.211±0.182	0.727±0.157*	0.453±0.093*#
	Relative (%$\dot{V}O_{2peak}$)	40±5	24±5*	15±3*#
$\dot{V}O_2$oscillation amplitude (L·min-1)		0.629±0.100	1.477±0.242*	2.133±0.186*#
Mean $\dot{V}O_2$ (L·min-1)		1.511±0.190	1.449±0.251	1.511±0.173

Values are expressed as mean±SD. *Significantly different from 30s:30s ($p<0.05$), #significantly different from 60s:60s ($p<0.05$); n=10 for each group.

With a higher amplitude and percentage of $\dot{V}O_{2max}$ recorded in the 120s:120s exercise but a lower number of work to rest transitions performed in the hour of exercise (15 repetitions *vs.* 30 and 60, respectively for 60s:60s and 30s:30s), $\Sigma\Delta\dot{V}O_2$ was actually found to be greater in the 60s:60s exercise (+38±13 % and +19±18 % when compared to 120s:120s and. 30s:30s, respectively; $p<0.05$, Fig. 3A). $T\dot{V}O_{2RR}$ was also greater in the 60s:60s exercise compared to the 30s:30s exercise (+58±42 %, $p<0.05$, Fig. 3B) and the difference was close to significance when compared to the 120s:120s exercise (+13±16 %, p=0.08, Fig. 3B). OFI was higher in the 60s:60s (+41±29% and +67±62% when compared to 120s:120s and 30s:30s respectively; p<0.05, Fig. 3C).

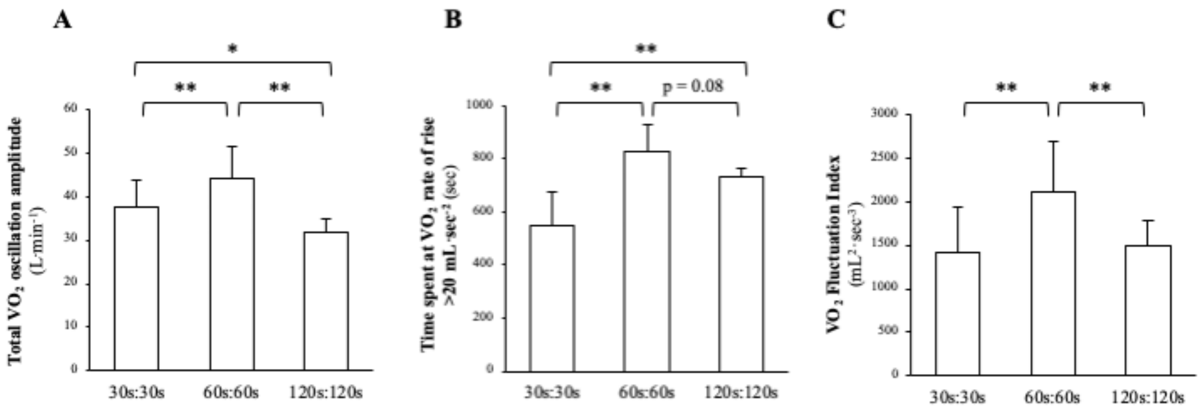

Figure 3. Quantification of fluctuations. Effects of duty cycle duration (30 s:30 s, 60 s:60 s and 120 s:120 s) on total oscillation amplitude (A), time spent at rate of rise above 20 mL·s–1 (B) and oxygen fluctuations index (OFI, C). Values are expressed as mean±SD. *P < 0.05; **P < 0.01; n = 10 for each group.

$[La]_b$ at 30 minutes and at the end of exercise were higher during the 120s:120s compared to the 30s:30s and 60s:60s (p<0.05, table 3). For the three exercises, no difference was observed between 30-min and the end of exercise. The rate of perceived exertion was also higher for the 120s:120s compared to the 30s:30s and 60s:60s (p<0.05, table 3).

Table 3: Blood lactate concentration and Borg Rating Scale of Perceived Exertion during three intermittent exercises (70% WRpeak; 3 durations of 1:1 work to rest ratio).

Condition	**30s:30s**	**60s:60s**	**120s:120s**
Blood Lactate concentration (mM)			
Rest	1.73±0.47	1.14±0.33	1.34±0.49
30-min	1.80±0.76	2.28±0.98	3.54±1.79*#
End	1.73±0.63	1.97±0.82	3.72±1.65*#
Borg Rating Scale of Perceived Exertion			
Warm-up	9±2	9±2	9±2
End	12±2*	13±1*	14±1*#

Values are expressed as mean±SD. RPE= Rate of Perceived Exertion. *Significantly different from rest (blood lactate concentration) or warm-up (RPE) ($p<0.05$), #significantly different from 30s:30s and 60s:60s ($p<0.05$); n=10 for each group.

Discussion

The present study aimed to compare the $\dot{V}O_2$ fluctuations of intermittent exercises of same work rate but different duty-cycle duration in order to identify which duty-cycle duration induces the highest $\dot{V}O_2$fluctuations. The 60s:60s condition is shown to produce greater fluctuations, as illustrated by greater sum of the $\dot{V}O_2$ peak-to-nadir amplitude over the exercise, $\dot{V}O_2$ rate of rise during the oscillations and OFI.

$\dot{V}O_2$ oscillations

We selected a submaximal exercise intensity (70%WRpeak) to determine the effect of the work:rest cycle duration on $\dot{V}O_2$ oscillations. This intensity avoid a $\dot{V}O_2$ slow component to occur as it has been observed in a previous study using higher exercise intensity and similar work:rest cycle duration (Turner et al., 2006). Moreover, this submaximal intensity was also selected in order to not accumulate blood lactate that has been shown to increase for long work:rest cycle duration and induce a $\dot{V}O_2$ slow component (Margaria, Oliva, Di Prampero, & Cerretelli, 1969; Turner et al., 2006).

In the present study, $\dot{V}O_2$ nadir and $\dot{V}O_2$ peak, and consequently the amplitude of the on-transient $\dot{V}O_2$ responses did not change significantly after the first cycles of exercise. Concomitantly, we did not observe any difference in the blood lactate concentration between the 30rd min and the end of the exercise. In a previous study, Turner *et al.* (2006) observed a slow component using 60s:120s and 90s:120s modalities whereas the responses remained stable during the 10s:20s and 30s:60s modalities. But these authors used an intensity of 120%WR_{peak} which is much greater than the intensity in the present study (70%WR_{peak}), the latter being considered as an heavy intensity which is associated with a $\dot{V}O_2$ slow component with a time delay of 90-180s (Rossiter, 2011). Probably because of the lower intensity we chose, and the short work:rest cycle durations of the three intermittent exercises, the amplitude of the $\dot{V}O_2$ oscillations did not increase over time with no slow component observed as previously described at higher work rates (Hughson & Kowalchuk, 1995).

Analysis of the $\dot{V}O_2$ responses revealed that the amount of $\dot{V}O_2$ fluctuations is specific to each condition. The 30s:30s exercise condition was characterized by a smaller amplitude both during the work and recovery periods compared to the other two modalities. A duration of 30-s is not long enough for the $\dot{V}O_2$ response to reach a steady state during the work period performed at 70%WR_{peak} and during the subsequent recovery period. The 30-s duration of this rest period does not allow for the $\dot{V}O_2$ to return to resting values. Furthermore, examination of the 60s:60s exercise condition revealed that this duty-cycle duration produces the highest $\dot{V}O_2$ fluctuations. These results confirm that the amplitude of $\dot{V}O_2$ oscillations during intermittent exercise is directly related to work:rest cycle duration and work:rest ratio (Skiba, Jackman, Clarke, Vanhatalo, & Jones, 2014; Turner et al., 2006). Increased work:rest cycle duration as well as work:rest ratio induce an increase of $\dot{V}O_2$ oscillation amplitude.

A work and rest period of 60-s allows for the $\dot{V}O_2$ on- and off-transient to approach a steady state during both periods. The 120s:120s exercise condition produced the largest $\dot{V}O_2$

amplitude. However, a steady state in the response during the work exercise period could also be seen. This is illustrated by the lower amount of time associated with a rate of rise in the $\dot{V}O_2$ by more than 20ml.min^{-1}. Because fewer repetitions are being performed in this condition, the overall (accumulated) amplitude of the $\dot{V}O_2$ fluctuations was lower. Concomitantly, the time spent at high $\dot{V}O_2$ rate of rise was also lower in 120:s:120s condition. Therefore, the OFI, used to quantify the $\dot{V}O_2$ fluctuations, was also lower than during the 60-s condition.

Control of $\dot{V}O_2$

During exercise, mitochondrial ATP production is stimulated to match a demand. The kinetic control of $\dot{V}O_2$ is proposed to occurs in response to an increase not only in [ADP] and [P_i] but is also associated with a fall in Gibbs free energy of ATP splitting (ΔG_{ATP}) (Glancy, Barstow, & Willis, 2008). Bowen et *al.* (2011) proposed that reduced cellular energetic state (i.e. reduced [PCr] and increased [ADP] and [Pi]) resulting in a less negative ΔG_{ADP} (Jones, Fulford, & Wilkerson, 2008) would slow "mitochondrial power" delivery to ATP consuming process (where "mitochondrial power" is the product of ATP production rate and ΔG_{ADP}) linked to $\dot{V}O_2$ by P/O ratio (Glancy et al., 2008). Therefore, a higher $\dot{V}O_2$ at the beginning of the working period would be associated with a less negative ΔG_{ATP} and induced a greater ATP production rate by muscle mitochondria to sustain a constant mitochondrial power delivery. Our findings are in line with previous studies that observed slower $\dot{V}O_2$ kinetics when exercise is initiated from a higher $\dot{V}O_2$ (Bowen et al., 2011; Brittain, Rossiter, Kowalchuk, & Whipp, 2001; Wust et al., 2014). These results support the hypothesis that the rate of $\dot{V}O_2$ rise was directly influenced by the $\dot{V}O_2$ at the beginning of exercise. However, the comparison of $\dot{V}O_2$ kinetics from different metabolic rate shows conflicting results: a reduced intracellular energetic state *per se* may (Bowen et al., 2011) or may not (DiMenna, Bailey, Vanhatalo, Chidnok, & Jones, 2010) coincide with a slower $\dot{V}O_2$ kinetics during exercise starting at higher metabolic rates.

Practical considerations

It is established that the fitness level may influence the constant time (tau) that determines the speed of $\dot{V}O_2$ kinetics, endurance-trained subjects and elite athletes have fast (<30s) $\dot{V}O_2$ kinetics, in contrast with slow (>40s) values observed in elderly and patients (Rossiter, 2011). Therefore the duration of the work period during intermittent exercise need to be adapted if the objective of the exercise is to maximize the $\dot{V}O_2$ fluctuations over the exercise period. One may speculate that longer duty-cycle durations should be adopted for patients than the present duration (60-s) identified as most suitable for our sedentary participants.

The accumulation of time at high percentage of $\dot{V}O_{2\,max}$ and the repetition of metabolic disturbances during exercise are the two mechanisms often put forward to explain the higher benefits of IT. In line with these approaches, it has been shown that increasing in exercise intensity during IT induced higher metabolic disturbances that led to greater aerobic performance improvements (Mohr et al., 2007; Weston et al., 1997). An alternative approach to augment the metabolic and acid-base disturbances is to play with the characteristics of intermittent exercise. This study focused on the quantification of $\dot{V}O_2$ fluctuations, surrogate of metabolic disturbances, to assess their changes with manipulation of the duration of the exercise work:rest cycle. Our results are in line with previous studies (Skiba et al., 2014; Turner et al., 2006) as they demonstrate the influence of the duty-cycle duration on $\dot{V}O_2$ fluctuations. It is clear from the present findings that the duty-cycle duration should be chosen wisely in practical settings when the aim is to maximize these $\dot{V}O_2$ fluctuations. However, the intracellular adaptations induced by these exercises are unknown.

In summary, the present study offers an innovative method for the quantification of $\dot{V}O_2$ fluctuations during intermittent exercise of different work:rest cycle durations. Comparison of three different durations for the same work rate (70% of WR_{peak}) revealed different levels of $\dot{V}O_2$ fluctuations. In active participants, the 120s:120s condition demonstrates greater changes in the $\dot{V}O_2$ response during both work and recovery periods. However, due to the greater number of repetitions in the 60s:60s modality, the latter induces a greater overall $\dot{V}O_2$ fluctuations despite a similar total work done, when compared to the 30s:30s and 120s:120s modalities.

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Table 2: Characterization of $\dot{V}O_2$ fluctuations to three different intermittent exercises (70% of maximal work rate; 3 durations of 1:1 work to rest).

		Work:rest cycle number							
		1	2	3	4	5	15	30	60
30s:30s	Peaks	1.55±0.25	1.86±0.27	1.66±0.32	1.76±0.34	1.74±0.24	1.70±0.20	1.76±0.18	1.87±0.29
	Nadirs	0.24±0.07	1.15±0.17	1.01±0.20	1.14±0.17	1.22±0.24	1.18±0,09	1.19±0.21	1.12±0.15
	Amplitude	1.31±0.23*	0.54±0.18	0.56±0.15	0.61±0.23	0.52±0.18	0.52±0.18	0.57±0.24	0.61±0.11
60s:60s	Peaks	2.06±0.37	2.05±0.30	2.20±0.27	2.12±0.29	2.17±0.34	2.26±0.30	2.27±0.44	
	Nadirs	0.22±0.09	0.81±0.19	0.73±0.19	0.69±0.13	0.70±0.21	0.80±0.14	0.73±0.19	
	Amplitude	1.84±0.32*	1.24±0.25	1.46±0.18	1.43±0.29	1.47±0.28	1.46±0.26	1.53±0.30	
120s:120s	Peaks	2.49±0.24	2.52±0.24	2.64±0.32	2.56±0.32	2.60±0.30	2.67±0.27		
	Nadirs	0.24±0.07	0.44±0.09	0.43±0.12	0.44±0.13	0.47±0.15	0.44±0.10		
	Amplitude	2.26±0.20	2.08±0.18	2.20±0.29	2.13±0.28	2.13±0.24	2.23±0.21		

$\dot{V}O_2$ is expressed in L·min^{-1}. Data are expressed as mean±SD. *Significantly different from the other cycle ($p<0.05$)