

INTERVAL EXERCISE INDUCES MILDER RESPIRATORY RESPONSES COMPARED TO
CONTINUOUS EXERCISE ¹

ABSTRACT

The purpose of this study was to explore the respiratory response of acute interval and continuous exercise of low and high intensity. Fourteen recreational athletes (7 men and 7 women; $\text{VO}_{2\text{max}} = 35.7 \pm 6.1$ ml/kg/min) performed a bout of continuous and a bout of interval exercise both consisted of 5 min cycling at low intensity [80% of the power output (W) of the predetermined gas exchange threshold (GET) ($80\%W_{\text{GET}}$)] and 5 min cycling at high intensity $\{W_{\text{GET}}$ plus the work rate corresponding to 50% of the difference between peak power output (PPO) at oxygen uptake ($\text{VO}_{2\text{max}}$) test and the W_{GET} [$W_{\text{GET}} + 0.50 \Delta(\text{PPO} - W_{\text{GET}})$]\}. Continuous exercise compared to interval exercise induced significant higher heart rate and ventilation as well as significant higher levels of mouth occlusion pressure for 0.1 sec ($P_{0.1}$) ($P < 0.05$) during low and high intensities. Our results indicate that continuous exercise stimulates respiration more than interval exercise when the exercise is performed at the same relative intensity.

KEYWORDS: Intermittent exercise, ventilation, mouth occlusion pressure

INTRODUCTION

Growing evidence in literature supports the positive effects of regular exercise on fitness, health, performance and overall quality of life (Ross, Freeman, & Janssen, 2000; Thompson et al., 2001). Regarding the mode of exercise, the guidelines highlight continuous exercise (CE) of moderate intensity as the type of training that promotes health and quality of life (Garber et al., 2011). Indeed, it is well documented that even a single bout of CE may cause favorable cardiovascular and metabolic effects (e.g., blood pressure and glucose levels, respectively) (Thompson et al., 2001). However, in recent investigations, it was demonstrated that high intensity interval exercise (IE), performed by healthy young individuals, may cause similar or even greater improvements in aerobic capacity as well as in cardiovascular and metabolic parameters compared to CE (Babraj et al., 2009; Burgomaster, Heigenhauser, & Gibala, 2006; Dorneles, da Silva, Peres, & Romao, 2019; Gibala & McGee, 2008; Malik, Williams, Weston, & Barker, 2019; Oliveira, Barker, Debras, Kranen, & Williams, 2019). Moreover, in both healthy and diseased populations, IE found to cause beneficial changes in insulin sensitivity, blood glucose levels, blood pressure, ventricular function and arrhythmias, brachial artery endothelial-dependent function and limb arterial stiffness (Ciolac et al., 2009; Currie, Dubberley, McKelvie, & MacDonald, 2013; Guiraud et al., 2013; Guiraud et al., 2011; Meyer et al., 2012; Tomczak et al., 2011; Tordi, Mourot, Colin, & Regnard, 2010; Whyte, Ferguson, Wilson, Scott, & Gill, 2013).

In chronic diseases (i.e., in heart failure patients), a single bout of IE seems to cause greater exercise adherence and efficiency causing greater exercise tolerance compared to CE despite the similar cardiopulmonary and hemodynamic responses (da Silva et al., 2019; Gayda et al., 2012; Normandin et al., 2013). It was proposed that despite the greater peripheral muscle loading, IE induced milder physiological responses compared to CE (i.e., ventilation, oxygen consumption, dyspnea and perceived effort) (Gayda et al., 2012; Gibala, Little, Macdonald, & Hawley, 2012; MacInnis et al., 2017; Vogiatzis et al., 2004; Vogiatzis, Nanas, & Roussos, 2002). The differences in ventilation and dyspnea observed between CE and IE could be attributed to the different neuromuscular activation of the respiratory system. Indeed, in chronic obstructive pulmonary disease patients, it was proposed that the dyspnea is not related only to the respiratory muscle load but also to the central motoneural output (Marin, Montes de Oca, Rassulo, & Celli, 1999).

Despite the recent growing evidence on the effects of IE training on health and performance, there is lack of data regarding the acute effects of IE on physiological parameters related to respiratory system in

healthy individuals. So, the purpose of the present investigation was to examine the effects of acute CE and IE of low and high intensity on neuromuscular activation of respiratory muscles via mouth occlusion pressure 0.1 sec ($P_{0.1}$) and on ventilatory parameters during exercise. We hypothesized that CE would produce higher central motoneural output to the respiratory muscles and thus higher respiratory stress compared to IE.

MATERIALS AND METHODS

Subjects

Fourteen young healthy recreational athletes (7 males and 7 females) volunteered to participate in the study (Table 1). Body mass (kg) was measured without shoes on a standing scale that was calibrated to 0.1 kg. Body height was measured without shoes on a wall-mounted stadiometer. Subjects were instructed to abstain from food and alcohol for 4 hours prior exercise and heavy physical activity during the last 24 hours before measurements. A written consent was obtained from all participants, after they were informed for the procedures and the risks of the study. The procedures were in accordance with the Helsinki declaration of 1975, as revised in 2000.

Experimental Testing and Procedures

Subjects visited the experimental laboratory at three separate occasions. During visit 1, baseline anthropometric measurements (i.e., body weight and height) and VO_{2max} was assessed using an incremental cycling test to exhaustion. Briefly, after a 3-min warm-up at 30 W, workload increased by 20 W every minute until exhaustion. The test was terminated when fulfilled the pre-requisite criteria: i) maximal respiratory quotient, ii) age specific maximal heart rate, and iii) maintenance of constant pedal rate at 60 reps/min. The ventilatory threshold during the cycling incremental test was determined according to Beaver et al. (1986).

During visits 2 and 3 (Figure 1), subjects performed the CE and the IE tests, respectively, while the two tests were separated by 14 days. Both bouts were performed in the morning (i.e., 9:00 – 11:00) and the environmental conditions were kept constant (i.e., 22°C temperature and 50% relative humidity). After a warm up (i.e., 2 min cycling at 30 W), subjects performed 2 bouts (i.e., low and high intensity exercise) of 5 min each, during both CE and IE (Fig. 1). The low intensity exercise bout was performed at 80% power output (W) of the predetermined gas exchange threshold (GET) ($80\%W_{GET}$). The high intensity exercise bout

was performed at W_{GET} plus the work rate corresponding to 50% of the difference between peak power output (PPO) at VO_{2max} test and the W_{GET} [$W_{GET} + 0.50 \Delta(PPO - W_{GET})$]. Between the two low and high intensity exercise was adopted a 5 min active recovery (i.e., cycling at 30 W). Continuous exercise was performed with non-stop cycling for 5 min at the predefined low and high intensities, while interval exercise was consisted of 5 experimental interventions lasted 1 min each followed by very low intensity intermission of equal duration (i.e., 1:1 ratio) during both low and high intensities. The CE and IE lasted 21 and 29 minutes, respectively.

Instrumentation

All exercise tests were performed on an electric cycle ergometer (Jaeger 800, Germany). Respiratory gas variables were measured using a metabolic cart (Jaeger Oxycon Alpha, Germany), which was calibrated before each test using standard gases of known concentration. The respiratory variables included minute ventilation (VE), tidal volume (V_T), respiratory frequency and respiratory ratio (RR). Continuous measurement of heart rate was also performed during both CE and IE using heart rate monitors (Polar, Finland) and 4 ECG electrodes (Jaeger-ECG Scope, QRS card/232 ECG System).

Mouth occlusion pressure was tested at rest and during exercise using a spirometer via a plethysmographer (Jaeger, Muster screen Body, Germany). The mouth occlusion pressure was set at 0.1 s after the initiation of inspiration ($P_{0.1}$) and was measured with a respiratory pressure module system (Medgraphics RPM system, St. Paul, MN, USA) which was calibrated against an independent pressure system. The inspiratory line was occluded without the subjects' knowledge, in intervals of about 15 second, for less than 0.5 second using a pneumatic inflatable balloon (Series 9300; Hans-Rudolph, Kansas City, Missouri, USA) while the mean of at least five measurements was used for the statistical analysis. The plethysmographer was connected to a computer and were measured the non-invasive tension-time index of the inspiratory muscles (T_{TMUS}), the mouth occlusion pressure for 0.1 sec ($P_{0.1}$), the tidal volume (V_T), the inspiration time (T_i), the total time of respiratory cycle (T_{TOT}) and the duty cycle given by the ratio T_i/T_{TOT} .

Statistical Analysis

Statistical analysis was performed by STATISTICA Statistical Software (Version 6, USA). All data are presented as mean and standard error of the mean (mean \pm SEM). A three-way ANOVA [mode of exercise (CE

and IE) x intensity (low and high) x time (min of exercise)] with repeated measures on time and subjects was used to examine the effects of the mode and the intensity of exercise on respiratory system. If a significant interaction was obtained, a one-way ANOVA was performed and a Newman-Keuls t-test analysis was used. The level of significance was set at $p < 0.05$.

RESULTS

The effect of exercise mode

At rest, no significant differences were found in any of the dependent variables between the CE and the IE ($P > 0.05$). Contrary, during exercise, $P_{0.1}$ was significantly higher in CE compared to the IE test in both low and high intensities ($P < 0.01$) (Figure 2A). $P_{0.1}/T_v/T_i$ was significantly higher at the CE compared to the IE test, only during the high intensity ($P < 0.01$) (Figure 2B). Regarding VE, the CE caused significantly higher values compared to IE in both low and high intensities ($P < 0.01$) (Figure 3A). Significantly higher values in VT/Ti ratio and VT was also observed in CE compared to the IE in both low and high intensities ($P < 0.01$) (Figure 3B).

T_i , T_{TOT} and T_i/T_{TOT} were found to be significantly higher during the CE compared to the IE only during the high intensity condition ($P < 0.01$) (Table 2 and Table 3). Continuous exercise also lead to significantly higher T_{TMUS} compared to IE in both the low and high intensities ($P < 0.01$) (Table 2 and Table 3). Finally, HR was significantly higher during the CE compared to the IE test for both low and high intensities ($P < 0.01$) (Figure 4).

The effect of exercise intensity

Significant differences were found in the dependent variables between the low and the high intensities in both CE and IE. Specifically, the low intensity caused significantly lower $P_{0.1}$ compared to the high intensity in both CE and IE ($P < 0.05$) (Figure 2). $P_{0.1}/VT/T_i$ was significantly lower during the low compared to high intensity only in the CE ($P < 0.05$). VE, VT, VT/Ti, T_{TOT} , T_i/T_{TOT} and T_{TMUS} were found to be lower in low compared to high intensity in both CE and IE ($P < 0.05$), while T_i was significantly higher in the low compared to high intensity in both CE and IE ($P < 0.05$) (Table 2 and Table 3). Finally, HR was found to be significantly lower in the low compared to high intensity in both CE and IE ($P < 0.05$).

DISCUSSION

Continuous moderate intensity exercise has been recognized as an effective mode of exercise and was prescribed in both healthy and diseased populations (Ross et al., 2000; Thompson et al., 2001). However, new research evidence have revealed that IE is also as effective or even more beneficial than continuous exercise in sports, health and illness (Dorneles et al., 2019; Hwang, Wu, & Chou, 2011; Malik et al., 2019; Oliveira et al., 2019; Tjonna et al., 2009; Weston, Wisloff, & Coombes, 2014; Wisloff et al., 2007). The exact physiological mechanism that leads to similar or even greater improvements in performance and health with intermittent exercise is still not clear. It is known, however, that IE causes greater loading of the peripheral muscles without overloading the central circulatory system (Gibala et al. 2012), while it has been shown that IE may lead to lower ventilation, lower degree of dyspnea and lower perception of breathlessness compared to CE (Gibala et al., 2012; Vogiatzis et al., 2004; Vogiatzis et al., 2002), possibly improving exercise tolerance.

This is the first study that has investigated differences in parameters that are associated with neuromuscular activation of the respiratory muscles during acute CE and IE. It was found that the CE causes greater respiratory responses (i.e., higher ventilation) in both low intensity (i.e., below the anaerobic threshold) and high intensity (i.e., above the anaerobic threshold) compared to IE. During low intensity, the higher ventilation in CE compared to IE test appears to be exclusively attributed to neural factors and not factors related to lung function. This could be attributed to the higher $P_{0.1}$ values [an established index of neuromuscular activation of the respiratory system (Whitelaw et al. 1975)] found in CE compared to IE. However, during high intensity exercise, the higher ventilation found in CE compared to IE, appears to be partially explained by neural factors based on the parameters $P_{0.1}$ and $P_{0.1}/(V_T/T_i)$ [an index of inspiratory impedance (Hussain, Pardy, & Dempsey, 1985)]. Hence, it is possible that during high intensity exercise, the differences observed in ventilation between CE and IE could be caused not only to neuromuscular activation of the respiratory muscles, but also due to other factors related to lung function and breathing mechanics.

The possible mechanisms through which the rest periods in the IE could have affected the metabolic byproducts were not studied in the present investigation. However, it is known that active recovery stimulates the wash-off of metabolic byproducts possibly affecting in our case the neural drive to ventilation (Belcastro & Bonen, 1975). Indeed, previous research has shown that muscular accumulation of metabolic byproducts increases the neurogenic input to ventilation via intramuscular ergoreceptors (Edgell & Stickland,

2014; Piepoli, Clark, & Coats, 1995), while, in healthy individuals, lactate concentration and metabolic acidosis has been shown to be a key trigger for hyperventilation (Chang, Ortega, Riegler, Madison, & Krasnow, 2015; Sostaric et al., 2006). Another possible physiological mechanism is that the rest periods in IE may have caused active hyperemia, a parameter that could also contribute to the lower neural drive (Crececius, Kirby, Luckasen, Larson, & Dinunno, 2013). More research is certainly needed to examine the physiological mechanisms responsible for the lower neuromuscular activation of the respiratory muscles during IE.

In consistency with the parameters of respiratory system, heart rate was also found to be higher in CE compared to IE. The longer duration of the exercise phases during CE, could be attributed to the significant higher response of heart rate compared to IE. Additionally, the intervals that were adopted during IE test might have allowed subjects to partly recover and experience a decline in heart rate towards resting values that, in turn, led to lower overall heart rate. Indeed, previous research has shown that IE might activate less the muscle ergo reflex system due to its intermittent mode of exercise, thus leading to lower autonomic and heart rate responses (Edgell & Stickland, 2014; Piepoli et al., 1995).

A limitation of the present study design could be the consistency of the performed modes of exercise, that is the CE was always completed first and the IE was followed. However, despite the fact that the two tests were separated by 14 days, performing the two modes of exercise in random order would be a more accurate study design.

CONCLUSIONS

It was found that CE results in higher ventilatory responses compared to IE performed on a cycle ergometer while this phenomenon is independent of exercise intensity. The findings of the present investigation could be attributed to the higher neuromuscular activation of the respiratory muscles during CE compared to IE, possibly explaining and better exercise tolerance and the subjects' compliance during IE. More research is needed in order to establish the neuromuscular activation of the respiratory muscles and to explore possible physiological mechanisms.

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DECLARATION OF INTEREST

The authors report no conflict of interest.

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FIGURE LEGENDS

Figure 1. Study design. The low and the high intensity interventions during the continuous (A) and the interval exercise (B) test. W_{GET} : Watts at gas exchange threshold; PPO: peak power output at VO_2 max test

Figure 2. Mouth occlusion pressure for 0.1 sec ($P_{0.1}$; A) and mouth occlusion pressure in relation to tidal volume and inspiration time [$P_{0.1}/(V_T/T_i)$; B] in continue (black markers, continuous line) and interval exercise (white markers, dashed line). *statistical significant difference between continuous and interval exercise $p<0.05$; † statistical significant difference between low and high intensity in continuous exercise; ‡ statistical significant difference between low and high intensity in interval exercise.

Figure 3. Minute ventilation (V_E ; A) and tidal volume in relation to inspiration time (V_T/T_i ; B) in continue (black markers, continuous line) and interval exercise (white markers, dashed line). *statistical significant difference between continuous and interval exercise $p<0.05$; † statistical significant difference between low and high intensity in continuous exercise; ‡ statistical significant difference between low and high intensity in interval exercise.

Figure 4. Heart rate (HR) in continue (black markers, continuous line) and interval exercise (white markers, dashed line). *statistical significant difference between continuous and interval exercise $p<0.05$; † statistical significant difference between low and high intensity in continuous exercise; ‡ statistical significant difference between low and high intensity in interval exercise.

INTERVAL EXERCISE INDUCES Milder RESPIRATORY RESPONSES COMPARED TO
CONTINUOUS EXERCISE

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ABSTRACT

1 The purpose of this study was to explore the respiratory response of acute interval and continuous exercise of
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3 low and high intensity. Fourteen recreational athletes (7 men and 7 women; $VO_{2max} = 35.7 \pm 6.1$ ml/kg/min)
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5 performed a bout of continuous and a bout of interval exercise both consisted of 5 min cycling at low
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7 intensity [80% of the power output (W) of the predetermined gas exchange threshold (GET) ($80\%W_{GET}$)]
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9 and 5 min cycling at high intensity $\{W_{GET}$ plus the work rate corresponding to 50% of the difference between
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11 peak power output (PPO) at oxygen uptake (VO_{2max}) test and the W_{GET} [$W_{GET} + 0.50 \Delta(PPO - W_{GET})$].
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13 Continuous exercise compared to interval exercise induced significant higher heart rate and ventilation as
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15 well as significant higher levels of mouth occlusion pressure for 0.1 sec ($P_{0.1}$) ($P < 0.05$) during low and high
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17 intensities. Our results indicate that continuous exercise stimulates respiration more than interval exercise
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19 when the exercise is performed at the same relative intensity.
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26 **KEYWORDS:** Intermittent exercise, ventilation, mouth occlusion pressure
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INTRODUCTION

1 Growing evidence in literature supports the positive effects of regular exercise on fitness, health,
2 performance and overall quality of life (Ross, Freeman, & Janssen, 2000; Thompson et al., 2001). Regarding
3 the mode of exercise, the guidelines highlight continuous exercise (CE) of moderate intensity as the type of
4 training that promotes health and quality of life (Garber et al., 2011). Indeed, it is well documented that even
5 a single bout of CE may cause favorable cardiovascular and metabolic effects (e.g., blood pressure and
6 glucose levels, respectively) (Thompson et al., 2001). However, in recent investigations, it was demonstrated
7 that high intensity interval exercise (IE), performed by healthy young individuals, may cause similar or even
8 greater improvements in aerobic capacity as well as in cardiovascular and metabolic parameters compared to
9 CE (Babraj et al., 2009; Burgomaster, Heigenhauser, & Gibala, 2006; Dorneles, da Silva, Peres, & Romao,
10 2019; Gibala & McGee, 2008; Malik, Williams, Weston, & Barker, 2019; Oliveira, Barker, Debras, Kranen,
11 & Williams, 2019). Moreover, in both healthy and diseased populations, IE found to cause beneficial
12 changes in insulin sensitivity, blood glucose levels, blood pressure, ventricular function and arrhythmias,
13 brachial artery endothelial-dependent function and limb arterial stiffness (Ciolac et al., 2009; Currie,
14 Dubberley, McKelvie, & MacDonald, 2013; Guiraud et al., 2013; Guiraud et al., 2011; Meyer et al., 2012;
15 Tomczak et al., 2011; Tordi, Mourot, Colin, & Regnard, 2010; Whyte, Ferguson, Wilson, Scott, & Gill,
16 2013).

17 In chronic diseases (i.e., in heart failure patients), a single bout of IE seems to cause greater exercise
18 adherence and efficiency causing greater exercise tolerance compared to CE despite the similar
19 cardiopulmonary and hemodynamic responses (da Silva et al., 2019; Gayda et al., 2012; Normandin et al.,
20 2013). It was proposed that despite the greater peripheral muscle loading, IE induced milder physiological
21 responses compared to CE (i.e., ventilation, oxygen consumption, dyspnea and perceived effort) (Gayda et
22 al., 2012; Gibala, Little, Macdonald, & Hawley, 2012; MacInnis et al., 2017; Vogiatzis et al., 2004; Vogiatzis,
23 Nanas, & Roussos, 2002). The differences in ventilation and dyspnea observed between CE and IE could be
24 attributed to the different neuromuscular activation of the respiratory system. Indeed, in chronic obstructive
25 pulmonary disease patients, it was proposed that the dyspnea is not related only to the respiratory muscle
26 load but also to the central motoneural output (Marin, Montes de Oca, Rassulo, & Celli, 1999).

27 Despite the recent growing evidence on the effects of IE training on health and performance, there is
28 lack of data regarding the acute effects of IE on physiological parameters related to respiratory system in
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healthy individuals. So, the purpose of the present investigation was to examine the effects of acute CE and IE of low and high intensity on neuromuscular activation of respiratory muscles via mouth occlusion pressure 0.1 sec ($P_{0.1}$) and on ventilatory parameters during exercise. We hypothesized that CE would produce higher central motoneural output to the respiratory muscles and thus higher respiratory stress compared to IE.

MATERIALS AND METHODS

Subjects

Fourteen young healthy recreational athletes (7 males and 7 females) volunteered to participate in the study (Table 1). Body mass (kg) was measured without shoes on a standing scale that was calibrated to 0.1 kg.

Body height was measured without shoes on a wall-mounted stadiometer. Subjects were instructed to abstain from food and alcohol for 4 hours prior exercise and heavy physical activity during the last 24 hours before measurements. A written consent was obtained from all participants, after they were informed for the procedures and the risks of the study. The procedures were in accordance with the Helsinki declaration of 1975, as revised in 2000.

Experimental Testing and Procedures

Subjects visited the experimental laboratory at three separate occasions. During visit 1, baseline anthropometric measurements (i.e., body weight and height) and VO_2 max was assessed using an incremental cycling test to exhaustion. Briefly, after a 3-min warm-up at 30 W, workload increased by 20 W every minute until exhaustion. The test was terminated when fulfilled the pre-requisite criteria: i) maximal respiratory quotient, ii) age specific maximal heart rate, and iii) maintenance of constant pedal rate at 60 reps/min. The ventilatory threshold during the cycling incremental test was determined according to Beaver et al. (1986).

During visits 2 and 3 (Figure 1), subjects performed the CE and the IE tests, respectively, while the two tests were separated by 14 days. Both bouts were performed in the morning (i.e., 9:00 – 11:00) and the environmental conditions were kept constant (i.e., 22°C temperature and 50% relative humidity). After a warm up (i.e., 2 min cycling at 30 W), subjects performed 2 bouts (i.e., low and high intensity exercise) of 5 min each, during both CE and IE (Fig. 1). The low intensity exercise bout was performed at 80% power output (W) of the predetermined gas exchange threshold (GET) ($80\%W_{GET}$). The high intensity exercise bout

was performed at W_{GET} plus the work rate corresponding to 50% of the difference between peak power output (PPO) at VO_{2max} test and the W_{GET} [$W_{GET} + 0.50 \Delta(PPO - W_{GET})$]. Between the two low and high intensity exercise was adopted a 5 min active recovery (i.e., cycling at 30 W). Continuous exercise was performed with non-stop cycling for 5 min at the predefined low and high intensities, while interval exercise was consisted of 5 experimental interventions lasted 1 min each followed by very low intensity intermission of equal duration (i.e., 1:1 ratio) during both low and high intensities. The CE and IE lasted 21 and 29 minutes, respectively.

Instrumentation

All exercise tests were performed on an electric cycle ergometer (Jaeger 800, Germany). Respiratory gas variables were measured using a metabolic cart (Jaeger Oxycon Alpha, Germany), which was calibrated before each test using standard gases of known concentration. The respiratory variables included minute ventilation (VE), tidal volume (V_T), respiratory frequency and respiratory ratio (RR). Continuous measurement of heart rate was also performed during both CE and IE using heart rate monitors (Polar, Finland) and 4 ECG electrodes (Jaeger-ECG Scope, QRS card/232 ECG System).

Mouth occlusion pressure was tested at rest and during exercise using a spirometer via a plethysmographer (Jaeger, Muster screen Body, Germany). The mouth occlusion pressure was set at 0.1 s after the initiation of inspiration ($P_{0.1}$) and was measured with a respiratory pressure module system (Medgraphics RPM system, St. Paul, MN, USA) which was calibrated against an independent pressure system. The inspiratory line was occluded without the subjects' knowledge, in intervals of about 15 second, for less than 0.5 second using a pneumatic inflatable balloon (Series 9300; Hans-Rudolph, Kansas City, Missouri, USA) while the mean of at least five measurements was used for the statistical analysis. The plethysmographer was connected to a computer and were measured the non-invasive tension-time index of the inspiratory muscles (T_{TMUS}), the mouth occlusion pressure for 0.1 sec ($P_{0.1}$), the tidal volume (V_T), the inspiration time (T_i), the total time of respiratory cycle (T_{TOT}) and the duty cycle given by the ratio T_i/T_{TOT} .

Statistical Analysis

Statistical analysis was performed by STATISTICA Statistical Software (Version 6, USA). All data are presented as mean and standard error of the mean (mean \pm SEM). A three-way ANOVA [mode of exercise (CE

and IE) x intensity (low and high) x time (min of exercise)] with repeated measures on time and subjects was used to examine the effects of the mode and the intensity of exercise on respiratory system. If a significant interaction was obtained, a one-way ANOVA was performed and a Newman-Keuls t-test analysis was used. The level of significance was set at $p < 0.05$.

RESULTS

The effect of exercise mode

At rest, no significant differences were found in any of the dependent variables between the CE and the IE ($P > 0.05$). Contrary, during exercise, $P_{0.1}$ was significantly higher in CE compared to the IE test in both low and high intensities ($P < 0.01$) (Figure 2A). $P_{0.1}/T_v/T_i$ was significantly higher at the CE compared to the IE test, only during the high intensity ($P < 0.01$) (Figure 2B). Regarding VE, the CE caused significantly higher values compared to IE in both low and high intensities ($P < 0.01$) (Figure 3A). Significantly higher values in VT/Ti ratio and VT was also observed in CE compared to the IE in both low and high intensities ($P < 0.01$) (Figure 3B).

T_i , T_{TOT} and T_i/T_{TOT} were found to be significantly higher during the CE compared to the IE only during the high intensity condition ($P < 0.01$) (Table 2 and Table 3). Continuous exercise also lead to significantly higher T_{TMUS} compared to IE in both the low and high intensities ($P < 0.01$) (Table 2 and Table 3). Finally, HR was significantly higher during the CE compared to the IE test for both low and high intensities ($P < 0.01$) (Figure 4).

The effect of exercise intensity

Significant differences were found in the dependent variables between the low and the high intensities in both CE and IE. Specifically, the low intensity caused significantly lower $P_{0.1}$ compared to the high intensity in both CE and IE ($P < 0.05$) (Figure 2). $P_{0.1}/VT/T_i$ was significantly lower during the low compared to high intensity only in the CE ($P < 0.05$). VE, VT, VT/Ti, T_{TOT} , T_i/T_{TOT} and T_{TMUS} were found to be lower in low compared to high intensity in both CE and IE ($P < 0.05$), while T_i was significantly higher in the low compared to high intensity in both CE and IE ($P < 0.05$) (Table 2 and Table 3). Finally, HR was found to be significantly lower in the low compared to high intensity in both CE and IE ($P < 0.05$).

DISCUSSION

Continuous moderate intensity exercise has been recognized as an effective mode of exercise and was prescribed in both healthy and diseased populations (Ross et al., 2000; Thompson et al., 2001). However, new research evidence have revealed that IE is also as effective or even more beneficial than continuous exercise in sports, health and illness (Dorneles et al., 2019; Hwang, Wu, & Chou, 2011; Malik et al., 2019; Oliveira et al., 2019; Tjonna et al., 2009; Weston, Wisloff, & Coombes, 2014; Wisloff et al., 2007). The exact physiological mechanism that leads to similar or even greater improvements in performance and health with intermittent exercise is still not clear. It is known, however, that IE causes greater loading of the peripheral muscles without overloading the central circulatory system (Gibala et al. 2012), while it has been shown that IE may lead to lower ventilation, lower degree of dyspnea and lower perception of breathlessness compared to CE (Gibala et al., 2012; Vogiatzis et al., 2004; Vogiatzis et al., 2002), possibly improving exercise tolerance.

This is the first study that has investigated differences in parameters that are associated with neuromuscular activation of the respiratory muscles during acute CE and IE. It was found that the CE causes greater respiratory responses (i.e., higher ventilation) in both low intensity (i.e., below the anaerobic threshold) and high intensity (i.e., above the anaerobic threshold) compared to IE. During low intensity, the higher ventilation in CE compared to IE test appears to be exclusively attributed to neural factors and not factors related to lung function. This could be attributed to the higher $P_{0.1}$ values [an established index of neuromuscular activation of the respiratory system (Whitelaw et al. 1975)] found in CE compared to IE. However, during high intensity exercise, the higher ventilation found in CE compared to IE, appears to be partially explained by neural factors based on the parameters $P_{0.1}$ and $P_{0.1}/(V_T/T_i)$ [an index of inspiratory impedance (Hussain, Pardy, & Dempsey, 1985)]. Hence, it is possible that during high intensity exercise, the differences observed in ventilation between CE and IE could be caused not only to neuromuscular activation of the respiratory muscles, but also due to other factors related to lung function and breathing mechanics.

The possible mechanisms through which the rest periods in the IE could have affected the metabolic byproducts were not studied in the present investigation. However, it is known that active recovery stimulates the wash-off of metabolic byproducts possibly affecting in our case the neural drive to ventilation (Belcastro & Bonen, 1975). Indeed, previous research has shown that muscular accumulation of metabolic byproducts increases the neurogenic input to ventilation via intramuscular ergoreceptors (Edgell & Stickland,

2014; Piepoli, Clark, & Coats, 1995), while, in healthy individuals, lactate concentration and metabolic acidosis has been shown to be a key trigger for hyperventilation (Chang, Ortega, Riegler, Madison, & Krasnow, 2015; Sostaric et al., 2006). Another possible physiological mechanism is that the rest periods in IE may have caused active hyperemia, a parameter that could also contribute to the lower neural drive (Crececius, Kirby, Luckasen, Larson, & Dinunno, 2013). More research is certainly needed to examine the physiological mechanisms responsible for the lower neuromuscular activation of the respiratory muscles during IE.

In consistency with the parameters of respiratory system, heart rate was also found to be higher in CE compared to IE. The longer duration of the exercise phases during CE, could be attributed to the significant higher response of heart rate compared to IE. Additionally, the intervals that were adopted during IE test might have allowed subjects to partly recover and experience a decline in heart rate towards resting values that, in turn, led to lower overall heart rate. Indeed, previous research has shown that IE might activate less the muscle ergo reflex system due to its intermittent mode of exercise, thus leading to lower autonomic and heart rate responses (Edgell & Stickland, 2014; Piepoli et al., 1995).

A limitation of the present study design could be the consistency of the performed modes of exercise, that is the CE was always completed first and the IE was followed. However, despite the fact that the two tests were separated by 14 days, performing the two modes of exercise in random order would be a more accurate study design.

CONCLUSIONS

It was found that CE results in higher ventilatory responses compared to IE performed on a cycle ergometer while this phenomenon is independent of exercise intensity. The findings of the present investigation could be attributed to the higher neuromuscular activation of the respiratory muscles during CE compared to IE, possibly explaining and better exercise tolerance and the subjects' compliance during IE. More research is needed in order to establish the neuromuscular activation of the respiratory muscles and to explore possible physiological mechanisms.

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DECLARATION OF INTEREST

The authors report no conflict of interest.

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FIGURE LEGENDS

Figure 1. Study design. The low and the high intensity interventions during the continuous (A) and the interval exercise (B) test. W_{GET} : Watts at gas exchange threshold; PPO: peak power output at VO_2 max test

Figure 2. Mouth occlusion pressure for 0.1 sec ($P_{0.1}$; A) and mouth occlusion pressure in relation to tidal volume and inspiration time [$P_{0.1}/(V_T/T_i)$; B] in continue (black markers, continuous line) and interval exercise (white markers, dashed line). *statistical significant difference between continuous and interval exercise $p<0.05$; † statistical significant difference between low and high intensity in continuous exercise; ‡ statistical significant difference between low and high intensity in interval exercise.

Figure 3. Minute ventilation (V_E ; A) and tidal volume in relation to inspiration time (V_T/T_i ; B) in continue (black markers, continuous line) and interval exercise (white markers, dashed line). *statistical significant difference between continuous and interval exercise $p<0.05$; † statistical significant difference between low and high intensity in continuous exercise; ‡ statistical significant difference between low and high intensity in interval exercise.

Figure 4. Heart rate (HR) in continue (black markers, continuous line) and interval exercise (white markers, dashed line). *statistical significant difference between continuous and interval exercise $p<0.05$; † statistical significant difference between low and high intensity in continuous exercise; ‡ statistical significant difference between low and high intensity in interval exercise.

Table 1. Subject characteristics (N=14; mean \pm SEM)

Variable	
Age (<i>yr</i>)	22 \pm 6
Height (<i>cm</i>)	171 \pm 9
Weight (<i>kg</i>)	65.4 \pm 12
$\dot{V}O_2$ max (<i>ml</i> · <i>kg</i> ⁻¹ · <i>min</i> ⁻¹)	35.3 \pm 6
GET (<i>W</i>)	150 \pm 48
PPO (<i>W</i>)	211 \pm 59

GET: gas exchange threshold; PPO: Peak power output

Table 2. Mean (\pm SEM) respiratory response during continuous (CE) and interval exercise (IE) of low and high intensity in 14 subjects.

	min	Ti		T _{TOT}		Ti/T _{TOT}		VT		T _{TMUS}	
		CE	IE	CE	IE	CE	IE	CE	IE	CE	IE
Low intensity	0	1.46 (\pm 0.34) [†]	1.52 (\pm 0.36) ^{*†}	3.42 (\pm 0.71) [†]	3.54 (\pm 0.85) [†]	0.43 (\pm 0.04)	0.43 (\pm 0.04)	0.75 (\pm 0.16) [†]	0.76 (\pm 0.11) [†]	0.08 (\pm 0.04) [†]	0.08 (\pm 0.05) [†]
	1	1.17 (\pm 0.27) [†]	1.10 (\pm 0.24) ^{*†}	2.48 (\pm 0.59) [†]	2.31 (\pm 0.49) ^{*†}	0.44 (\pm 0.04)	0.48 (\pm 0.02)	1.51 (\pm 0.38) [†]	1.47 (\pm 0.30) [†]	0.19 (\pm 0.07) [†]	0.19 (\pm 0.08)
	2	1.07 (\pm 0.27) [†]	1.03 (\pm 0.23) [†]	2.25 (\pm 0.60) [†]	2.15 (\pm 0.49) [†]	0.45 (\pm 0.03) [†]	0.48 (\pm 0.03) [†]	1.71 (\pm 0.42) [†]	1.57 (\pm 0.27) ^{*†}	0.23 (\pm 0.08) [†]	0.20 (\pm 0.08) ^{*†}
	3	1.01 (\pm 0.22) [†]	1.01 (\pm 0.23) [†]	2.13 (\pm 0.48) [†]	2.15 (\pm 0.52) [†]	0.44 (\pm 0.03) [†]	0.47 (\pm 0.03) [†]	1.81 (\pm 0.40) [†]	1.59 (\pm 0.30) ^{*†}	0.24 (\pm 0.07) [†]	0.20 (\pm 0.08) ^{*†}
	4	0.97 (\pm 0.19) [†]	0.99 (\pm 0.21) [†]	2.01 (\pm 0.43) [†]	2.09 (\pm 0.43) [†]	0.45 (\pm 0.02) [†]	0.48 (\pm 0.03) [†]	1.84 (\pm 0.45) [†]	1.59 (\pm 0.28) ^{*†}	0.26 (\pm 0.08) [†]	0.21 (\pm 0.09) ^{*†}
	5	0.94 (\pm 0.18) [†]	0.97 (\pm 0.17) [†]	1.94 (\pm 0.41) [†]	2.03 (\pm 0.41) [†]	0.45 (\pm 0.03) [†]	0.48 (\pm 0.03) [†]	1.86 (\pm 0.50) [†]	1.63 (\pm 0.28) ^{*†}	0.27 (\pm 0.09) [†]	0.23 (\pm 0.09) ^{*†}
High intensity	0	1.07 (\pm 0.19)	1.07 (\pm 0.15)	2.44 (\pm 0.42)	2.42 (\pm 0.46)	0.41 (\pm 0.02)	0.45 (\pm 0.04)	1.29 (\pm 0.19)	1.23 (\pm 0.22)	0.13 (\pm 0.05)	0.13 (\pm 0.05)
	1	0.93 (\pm 0.16)	0.96 (\pm 0.13)	1.95 (\pm 0.41)	2.01 (\pm 0.34)	0.45 (\pm 0.03)	0.48 (\pm 0.04)	1.69 (\pm 0.40)	1.64 (\pm 0.33)	0.21 (\pm 0.09)	0.22 (\pm 0.10)
	2	0.83 (\pm 0.19)	0.89 (\pm 0.14)	1.68 (\pm 0.40)	1.80 (\pm 0.26)	0.46 (\pm 0.02)	0.49 (\pm 0.02)	2.06 (\pm 0.46)	1.68 (\pm 0.39) [*]	0.27 (\pm 0.07)	0.22 (\pm 0.08) [*]
	3	0.80 (\pm 0.13)	0.88 (\pm 0.15) [*]	1.61 (\pm 0.28)	1.82 (\pm 0.28) [*]	0.47 (\pm 0.02)	0.49 (\pm 0.03) [*]	2.20 (\pm 0.52)	1.73 (\pm 0.41) [*]	0.31 (\pm 0.08)	0.23 (\pm 0.08) [*]
	4	0.78 (\pm 0.14)	0.90 (\pm 0.19) [*]	1.54 (\pm 0.31)	1.81 (\pm 0.38) [*]	0.48 (\pm 0.02)	0.50 (\pm 0.03) [*]	2.27 (\pm 0.51)	1.78 (\pm 0.40) [*]	0.35 (\pm 0.10)	0.25 (\pm 0.08) [*]
	5	0.73 (\pm 0.14)	0.88 (\pm 0.23) [*]	1.44 (\pm 0.32)	1.77 (\pm 0.46) [*]	0.48 (\pm 0.02)	0.50 (\pm 0.03) [*]	2.30 (\pm 0.56)	1.82 (\pm 0.45) [*]	0.38 (\pm 0.10)	0.26 (\pm 0.08) [*]

Ti: inspiratory time, T_{TOT}: total time of respiratory cycle, Ti/T_{TOT}: duty cycle, VT: Tidal Volume, T_{TMUS}: Tension – Time muscles index, 0: pre exercise values

* p<0.05 between CE and IE, † p<0.05 between Low and High intensity

Figure 1

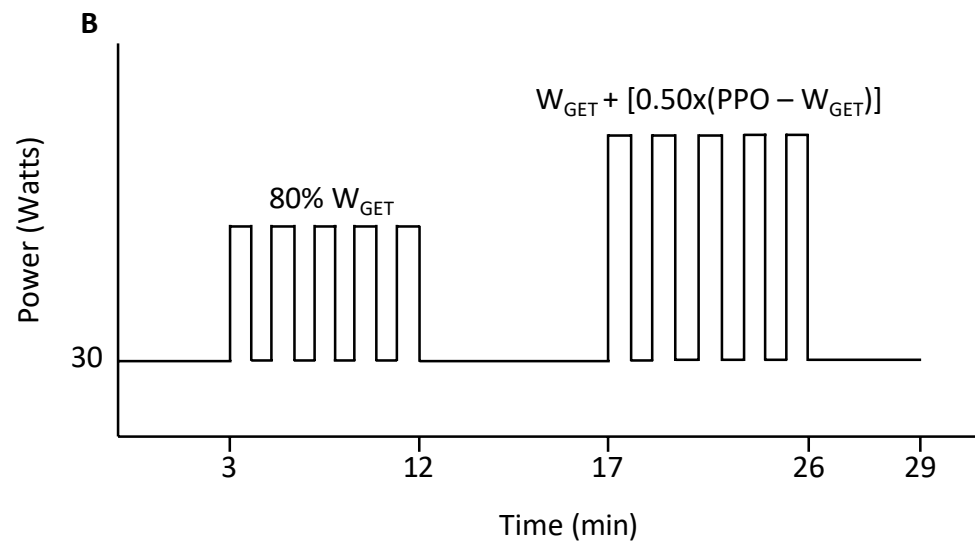
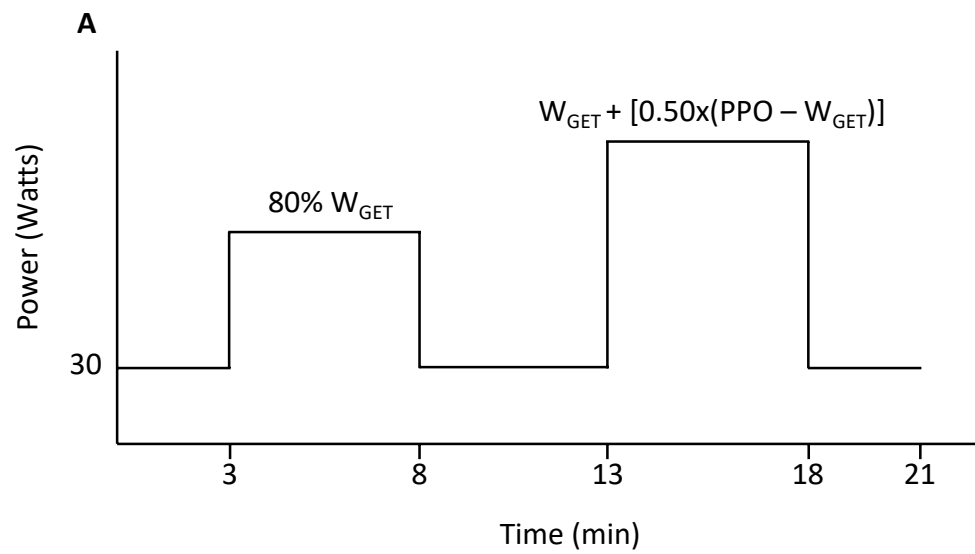
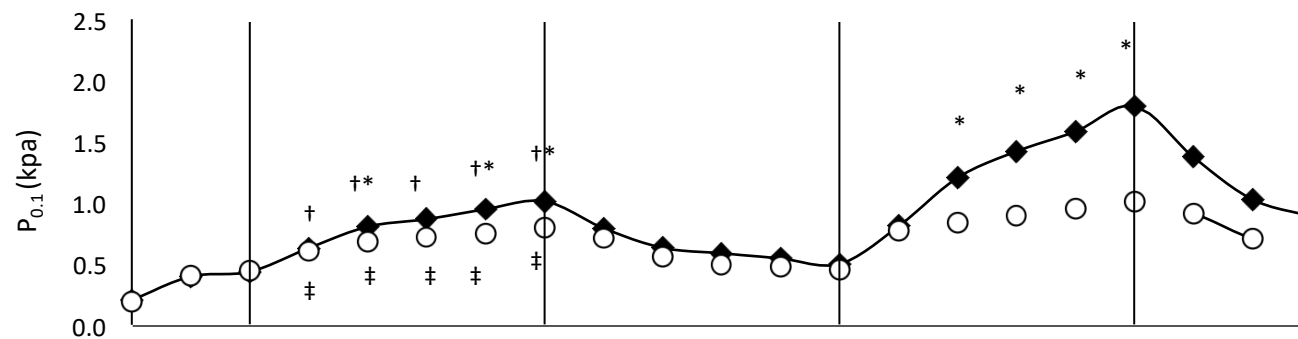


Figure 2

A



B

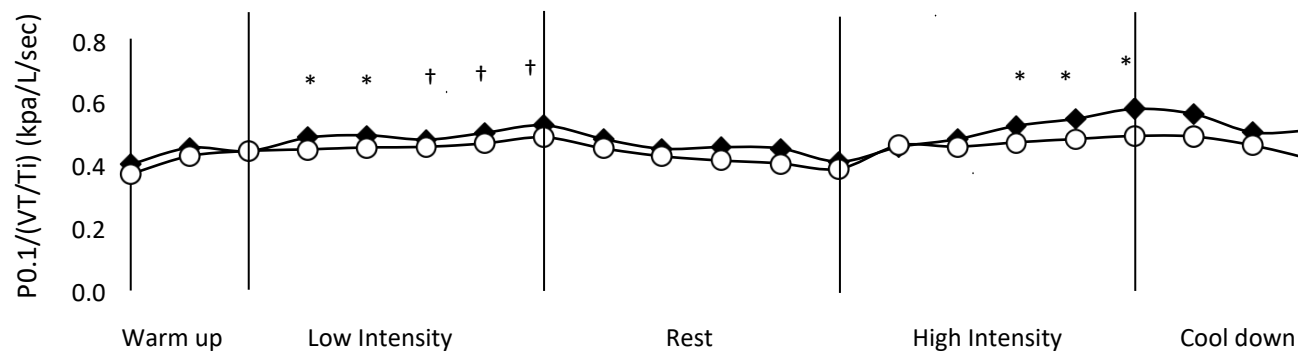
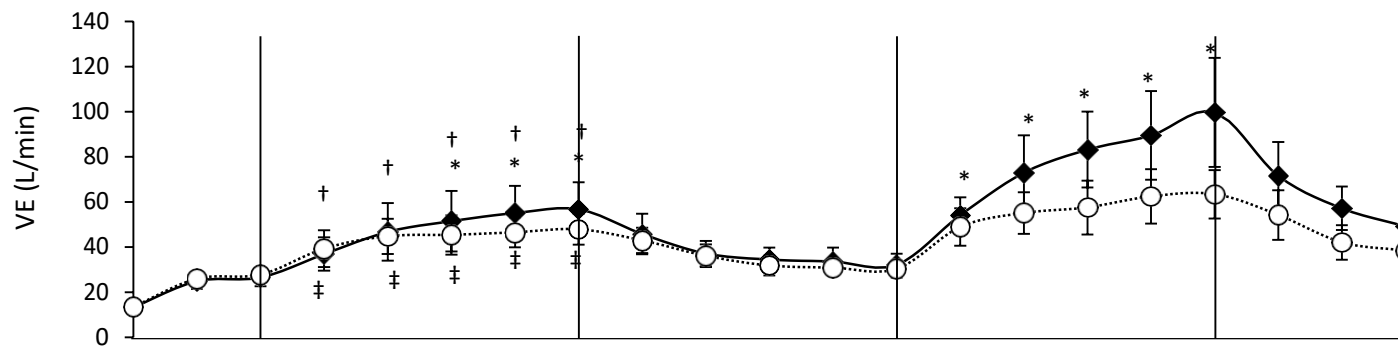


Figure 3

A



B

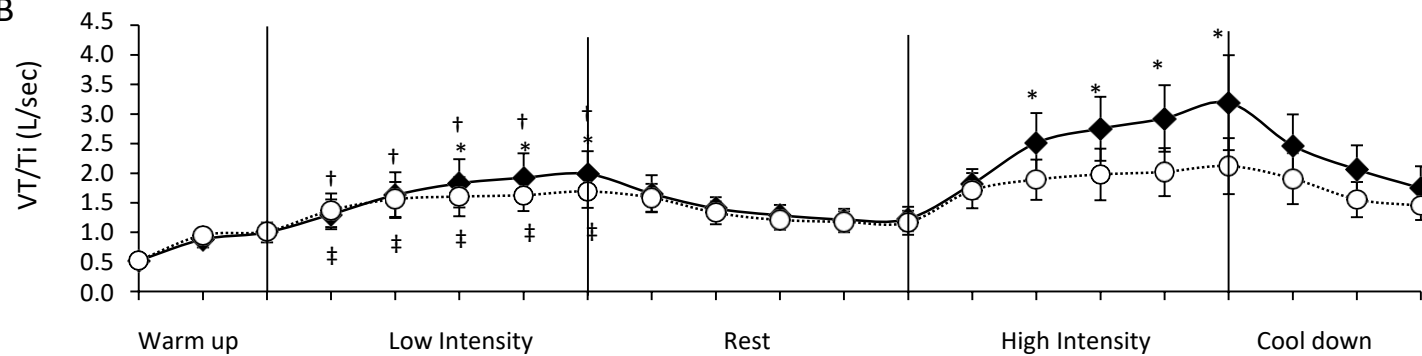


Figure 4

