©Journal of Sports Science and Medicine (2015) **14,** 849-856
http://www.jssm.org

Research article

Similar Anti-Inflammatory Acute Responses from Moderate-Intensity Continuous and High-Intensity Intermittent Exercise

Carolina Cabral-Santos [1], José Gerosa-Neto [1], Daniela Sayuri Inoue [1], Valéria Leme Gonçalves Panissa [2], Luís Alberto Gobbo [1], Alessandro Moura Zagatto [3], Eduardo Zapaterra Campos [1] and Fábio Santos Lira [1]✉

[1]Exercise and Immunometabolism Research Group, Department of Physical Education, Universidade Estadual Paulista, Presidente Prudente, São Paulo, Brazil. [2] Department of Sports, School of Physical Education and Sports, University of São Paulo, São Paulo, Brazil. [3] Department of Physical Education, Universidade Estadual Paulista, Bauru, São Paulo, Brazil

Abstract

The purpose of this study was to compare the effect of high-intensity intermittent exercise (HIIE) versus volume matched steady state exercise (SSE) on inflammatory and metabolic responses. Eight physically active male subjects completed two experimental sessions, a 5-km run on a treadmill either continuously (70% vVO_2max) or intermittently (1:1 min at vVO_2max). Blood samples were collected at rest, immediately, 30 and 60 minutes after the exercise session. Blood was analyzed for glucose, non-ester fatty acid (NEFA), uric acid, lactate, cortisol, and cytokines (IL-6, IL-10 and TNF-α) levels. The lactate levels exhibited higher values immediately post-exercise than at rest (HIIE 1.34 ± 0.24 to 7.11 ± 2.85, and SSE 1.35 ± 0.14 to 4.06±1.60 $mmol \cdot L^{-1}$, $p < 0.05$), but HIIE promoted higher values than SSE ($p < 0.05$); the NEFA levels were higher immediately post-exercise than at rest only in the SSE condition (0.71 ± 0.04 to 0.82±0.09 mEq/L, respectively, $p < 0.05$), yet, SSE promoted higher values than HIIE immediately after exercise (HIIE 0.72±0.03 vs SSE 0.82±0.09 $mEq \cdot L^{-1}$, $p < 0.05$). Glucose and uric acid levels did not show changes under the different conditions ($p > 0.05$). Cortisol, IL-6, IL-10 and TNF-α levels showed time-dependent changes under the different conditions ($p < 0.05$), however, the area under the curve of TNF-α in the SSE were higher than HIIE ($p < 0.05$), and the area under the curve of IL-6 in the HIIE showed higher values than SSE ($p < 0.05$). In addition, both exercise conditions promote increased IL-10 levels and IL-10/TNF-α ratio ($p < 0.05$). In conclusion, our results demonstrated that both exercise protocols, when volume is matched, promote similar inflammatory responses, leading to an anti-inflammatory status; however, the metabolic responses are different.

Key words: High intensity intermittent exercise, steady state exercise, metabolism, inflammation, energy expenditure, cytokines.

Introduction

Metabolic diseases are frequently observed in modern society, primarily as persistent, chronic low-grade inflammation conditions. These disorders are caused predominantly by physical inactivity and food intake imbalance (Pedersen, 2009). There is evidence that a single session of exercise promotes a lower risk of chronic disease, which is associated with morbidity, compared to sedentary individuals, and contributes to improvements in health (Bassuk and Manson, 2005).

It is well established that, in long-term training, physical exercise mediates and promotes improved metabolic processes (such as reduced total cholesterol, triglycerides and low density lipoprotein, and enhances high density lipoprotein) and may act as a trigger for reduction in body fat, principally through increased energy expenditure and adaptations of oxidative metabolism, especially in skeletal muscle (Gillen et al., 2013). In addition, this training protocol is powerful in inducing the inflammatory response (hence skeletal muscle is the major source of the increase in the release of interleukin-6 (IL-6), interleukin-10 (IL-10), it is an interleukin 1 receptor antagonist (IL-1ra), and it reduces tumor necrosis factor alpha (TNF-α) and interleukins (1β, IL-2) (Neto et al., 2011; Pedersen and Fabbraio, 2009).

The metabolic and inflammatory changes from regular exercise training are dependent on duration, intensity and session volume, and these are crucial aspects of training (Lira et al., 2012; Neto et al., 2011). However, recently, studies have suggested that aerobic exercise performed at a high intensity (typically ~90% VO_2max) and separated by recovery periods of lower intensity or complete rest, is a time-efficient strategy with a small total volume work and has the potential to promote similar health benefits compared to traditional aerobic exercises programs – such as improved maximal aerobic capacity functions, promotion of the reduction in body fat and serving to control body weight (Gibala 2012).

Study have indicate that high-intensity intermittent training (HIIT) (performed 8-12 HIIT sessions, with 60 x 75 second active rest, at 100% VO_2peak) increase the plasma concentrations levels of IL-10 during a following prolonged exercise in recreationally active males (Zwetsloot et al., 2014). In addition, the increase of IL-10 levels in athletes after HIIE (4 HIIT sessions of Wingate tests at 100% VO_2peak), implying that approaches designed to promote anti-inflammatory effects should be useful in attenuating the inflammatory milieu (Lira et al., 2015).

Especially worthy of note, the factor that probably has the greatest impact on inflammatory responses promoted by exercise session is workload, which is orchestrated by the duration and intensity (Pedersen, 2009). Most studies (Leggate et al., 2010; Skelly et al., 2014)

Received: 04 August 2015 / Accepted: 23 October 2015 / Published (online): 24 November 2015

have used protocols emphasing exercise intensity, but these protocols have no equality of duration and volume of exercise session, which is a relevant aspect that must be considered in studies with the purpose of investigating the metabolic/immune responses during different exercise modes. The volume performed may not have been properly controlled and this is an important methodological issue that causes leads to mistakes in the interpretation of studies that compared the effects of steady state and intermittent exercise on the magnitude of responses. Therefore, the aim of present study was to compare the effect of HIIE versus volume matched SSE on inflammatory and metabolic responses in young males.

Methods

Subjects

Eight physically active male subjects volunteered to participate in this study. Participants were free of health problems and/or neuromuscular disorders that could affect their ability to complete the study protocol. All procedures performed in studies involving human participants were in accordance with the ethical standards of the Research Ethics Committee of UNESP – Presidente Prudente/SP and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Written informed consent was obtained from all subjects after participants volunteered to participate in the study, after being informed about the purpose and risks of the study. Before conducting the study we checked the sample size needed (n = 6) using the G*Power 3.1 software (Düsseldorf, Germany) to guarantee an 80% power and a 5% significance level based on IL-10 using studies that measured differences between both protocols (Wadley et al., 2015) and using studies that measured the IL-6 pre and immediately post exercise as referenced by similar protocol (high intensity intermittent exercise) (Meckel et al., 2009; 2011; Legatte et al., 2010; Lira et al., 2015).

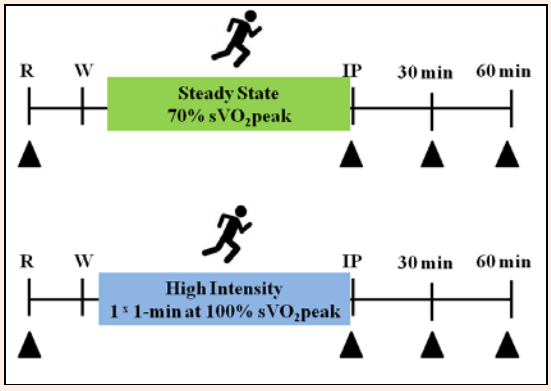


Figure 1. Schematic representation of the study protocol. ▲ Blood samples (rest, immediately, and 30 and 60 minutes after exercise). IP = immediately post-exercise; R= rest; W= warm up (n = 8).* = different from rest ($p < 0.05$)

Procedures

Subjects completed three experimental sessions separated by at least 72 hours. During the first session, anthropometric, peak oxygen uptake (VO_2peak) and speed associated with VO_2peak (sVO_2peak) measurements on a treadmill were performed. Two more experimental sessions were applied in randomized cross-over order: HIIE – a session in which participants performed a high-intensity intermittent aerobic exercise, and a steady state exercise (SSE) – a session in which participants performed a moderate continuous exercise. All tests took place at the same time of the day for each subject. The subjects were instructed to abstain from any strenuous exercise for at least 24 hours before each testing session and were encouraged to maintain their nutritional and hydration routines (Figure 1).

Bioelectrical impedance

Bioelectrical impendence in individuals was measured using the octopolar InBody 720 Composition Analyzer (Copyright®, 1996-2006, by Biospace Corporation, USA). The participant's age, gender and height were entered into the machine. The participants stood barefoot on the metal footplate and held the handles with their arms relaxed by their sides. Once impedance was measured, the results of Fat Mass (FM), Fat Free Mass (FFM) and %BF for five different body locations, each arm, each leg, and the trunk and one general overall set was printed. All anthropometric measurements were checked by the same person throughout the study to minimize interpersonal variations. Participants were asked to abstain from eating or drinking for two hours as well as to refrain from moderate or vigorous exercise for 24 hours before all testing. They were told to obtain a restful night's sleep, remain well hydrated, refrain from alcohol, and eat a regular meal in the morning before testing.

Maximal endurance running test

The subjects performed an incremental test to volitional exhaustion (Panissa et al., 2013). The initial treadmill (Inbramed, modelo MASTER CI, Brazil) speed was set at 8.0 $km \cdot h^{-1}$ and it was increased by 1 $km \cdot h^{-1}$ per 2-min stage until the participant could no longer continue. Strong verbal encouragement was given during the test. The oxygen uptake was measured (Quark PFT, Cosmed, Rome, Italy) throughout the test and the average of the last 30 s was defined as peak oxygen uptake (VO2peak). When the subject was not able to finish the 2-min stage, the speed was expressed according to the permanence time in the last stage, determined as the following: sVO_2peak = speed of last stage complete + [(time, in seconds, remained at the last stage incomplete / by 120s) * 1 $km.h^{-1}$] (Kuipers et al., 1985). Heart rate was also continuously recorded throughout the tests (Polar Vantage NV, Electro Oy, Finlândia). The 6–20 Borg scale (Borg, 1982) was used to measure the rating of perceived exertion during the test.

In order to establish whether subjects had given all-out effort, the verification procedure used for determination was three or more of the following criteria: (i) VO2 plateau ($\leq$ 150 $mL \cdot min^{-1}$), (ii) attainment of the percentage of the age-predicted maximal heart rate (HRmax) within ± 5 beats/min; (iii) the rating of perceived exertion (RPE) $\geq$ 18; and (iv) respiratory exchange ratio (RER) $\geq$ 1.10 (Howley 1995).

High-intensity intermittent exercise

Participants performed a warm-up at 50% at sVO2peak for five minutes, and after a 1-min interval the exercise session was started. The exercise consisted of a 5-km run on treadmill performed in intermittently at 1-min at the sVO_2peak followed by 1-min of passive recovery. The subjects remained standing or sitting after each exercise bout (Table 2).

Steady state exercise

Participants performed a warm-up at 50% at sVO2peak for five minutes, and after a 1-min interval the exercise was started. The endurance exercise consisted of a continuous 5-km run on a treadmill at 70% of sVO2peak (Table 2).

Exercise energy expenditure

To estimate the energy expenditure of all exercises, the sum of the contribution of the three energy systems (aerobic, anaerobic lactic and alactic) was used. Aerobic metabolism was estimated using the oxygen uptake during the exercise, anaerobic alactic using the fast phase of excess of oxygen uptake and the lactic using delta of blood lactate (Bertuzzi et al., 2007; Di Prampero and Ferretti, 1999; Zagatto et al., 2011).

Oxygen uptake was measured continuously and at 60 min after all the exercise sessions. At 1, 3, 5 and 7 min after the end of each test, blood was collected to measure lactate concentration.

The highest value measured was considered the peak lactate concentration ([La-1]peak). The difference between the [La-]peak and pre exercise lactate concentration ([La-]rest) was expressed as a delta value ([La-]delta). A value of 1 mmol·L-1 [La-] delta was considered to be the equivalent to 3 $mLO2 \cdot kg^{-1}$ body mass (Di Prampero and Ferretti, 1999). The fast component of excess post-exercise oxygen consumption was determined using a modified bi-exponential decay equation and the anaerobic alactic metabolism corresponded to the product of amplitude and tau (Bertuzzi et al., 2007; Zagatto et al., 2011). The aerobic metabolism was estimated by subtracting rest oxygen consumption from exercise oxygen consumption. To estimate the total energy expenditure and oxygen consumption during each protocol, the energy expenditure were summed and converted to kcal (Skelly et al., 2014)

Blood sampling and analyses

The blood samples were collected at rest, and immediately, 30, and 60 minutes after acute exercise sessions during HIIE and SSE. The blood samples (15 ml) were immediately allocated into two 5 mL vacutainer tubes (Becton Dickinson, BD, Juiz de Fora, MG, Brazil) containing EDTA for plasma separation and into one 5 mL dry vacutainer tube for serum separation. The tubes were centrifuged at 3.500 g for 15 minutes at 4ºC, and plasma and serum samples were stored at -20ºC until analysis. Cytokines IL6, IL-10 and TNF-α were assessed using ELISA commercial kits (R&D Systems, 614 McKinley Place NE, Minneapolis, MN 55413, USA). Glucose, uric acid, and lactate were assessed using commercial kits (Labtest®, São Paulo, Brazil). Non-ester fatty acid (NEFA) was assessed by a colorimetric method with a commercial kit (Wako, 1-2, doshomachi 3-Chome, Chuo-Ku, Osaka 540-8605, Japan). Serum cortisol was assessed using commercial kits (Cayman Chemical, Michigan, USA). Cortisol and glucose levels were assessed using serum, and NEFA levels were assessed using plasma.

Statistical analyses

The data normality was verified using the Shapiro-Wilk test. For each variable, mean and standard deviations were calculated, and they were analyzed using the SAS statistical package (SAS version 9.3). Mixed models for repeated measures were used to examine differences in blood variables according to condition, time and interactions. The Tukey test was used post hoc when differences were found. The unpaired t test was used to examine differences in energy expenditure. The significance level was set at 5%.

Results

The subjects' characteristics, anthropometry measures and summary of incremental test are show in Table 1.

Table 1. Subject characteristics. Values are mean (± standard deviation).

Variable	Subjects (n = 8)
Age (years)	24.56 (6.02)
Body Mass (kg)	74.69 (7.48)
Height (m)	1.75 (0.06)
BMI ($kg \cdot m^{-2}$)	24.28 (1.74)
Fat Mass (kg)	12.71 (4.18)
%BF	16.85 (4.81)
FFM (kg)	35.38 (3.38)
VO_2peak ($ml \cdot kg \cdot min^{-1}$)	59.93 (6.77)

BMI= Body Mass Index; %BF= % Body Fat; FFM= Fat Free Mass; VO_2peak= peak oxygen uptake; sVO_2peak= Speed correspondent vVO_2peak.

A summary of both exercise protocols are shown in Table 2. For energy expenditure, heart rate, and time commitment during exercises there was a greater effect for condition ($p < 0.01$) in HIIE than in SSE exercises.

Table 2. Summary of exercise descriptors for high-intensity exercise (HIIE) and steady state exercise (SSE) protocols (n = 8). Values are mean (± standard deviation).

Variable	SSE	HIIE
Protocol	run at 70% of sVO_{2peak}	60 x 60-second rest of 100% sVO_{2peak}
Duration (min)	30.78 (2.09)	42.09 (2.93) *
Speed ($km \cdot h^{-1}$)	9.65 (0.69)	13.79 (0.98)
EExp (kcal)	454.4 (56.7)	523.0 (40.1) *
HR_{max} ($beats \cdot min^{-1}$)	171 (8)	182 (11) *
$[La^-]$rest ($mmol \cdot L^{-1}$)	1.35 (.14)	1.34 (.24)
$[La^-]$peak ($mmol \cdot L^{-1}$)	4.06 (1.60)	7.11 (2.85) *
RPE_{final}	15.0 (2.8)	20.0 (3.7)

EExp = Energy Expenditure HR_{max}= Maximal Heart Rate in exercise; $[La^-]$= lactate concentration, RPE= Rate of perceived exertion. * = different from SSE ($p < 0.05$).

For [La-] there was a main effect of condition ($p < 0.001$), with higher values in HIIE than SSE ($p < 0.001$),

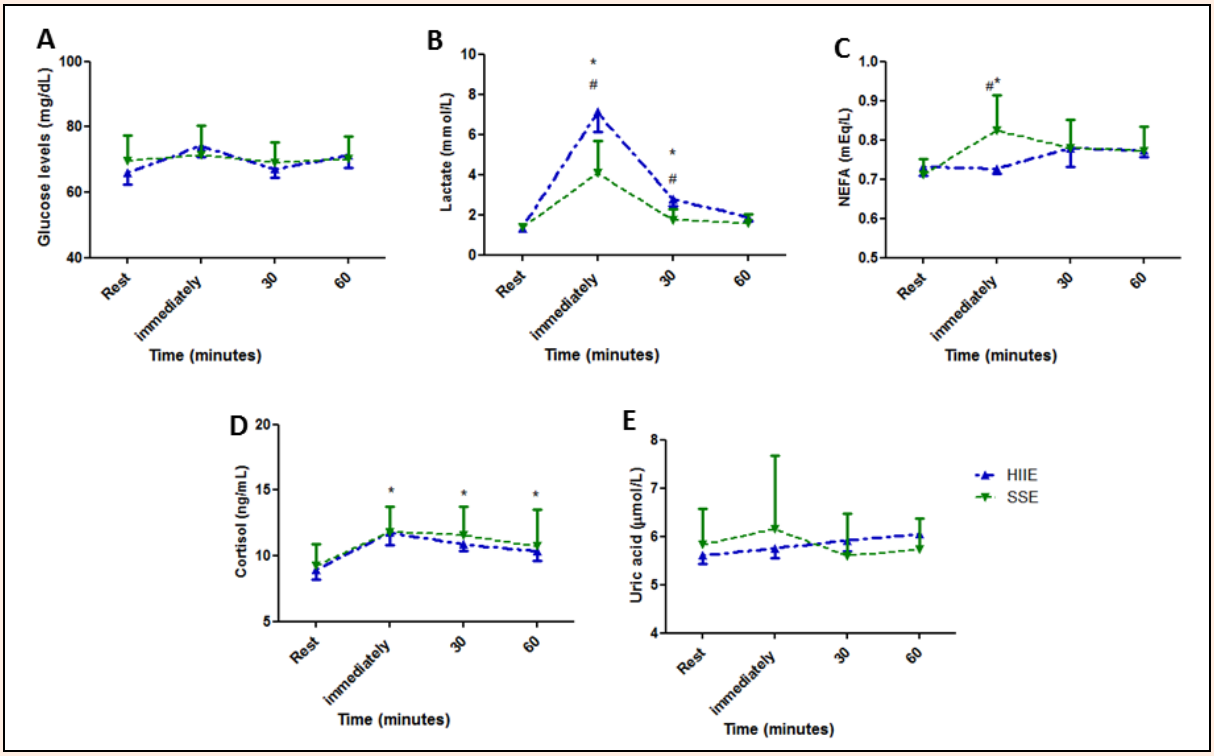


Figure 2. Metabolic parameters before and after a single bout of SSE and HIIE exercise in males (n = 8; values are mean ± standard deviation). Figures: 2A (Glucose), 2B (Lactato), 2C (NEFA), 2D (Cortisol) and 2E (Acid Uric). * = different from rest ($p < 0.05$); ** = different SSE ($p < 0.05$); # = different from 30 minutes; $ = different from 60 minutes.

and in moment ($p<0.001$), with higher values immediately post exercise than at rest, 30 and 60 min-post exercise ($p < 0.001$ for all comparisons, Figure 2B). Moreover, there was a condition of interaction and moment ($p < 0.001$) in HIIE where the values immediately post exercise were higher than at rest, 30 and 60 min-post exercise in the same condition ($p < 0.001$ for all comparisons); in SSE the values immediately post exercise were higher than at rest ($p < 0.001$), 30 ($p = 0.003$) and 60-min post exercise ($p = 0.001$) in the same condition.

For NEFA there was an interaction effect ($p = 0.044$), with higher values in SSE immediately post exercise than in HIIE at the same moment ($p < 0.050$); higher values in SSE immediately post exercise than at rest to the same condition ($p = 0.030$, Figure 2C). For glucose and uric acid there was no effect (Figure 2A and 2E).

For cortisol there was a main effect of moment ($p < 0.001$) with values at rest lower than immediately ($p < 0.001$), post-30 ($p = 0.003$), and post 60-min of exercise ($p = 0.024$, Figure 2D).

As regards the cytokine levels (Figure 3), for TNF-α there was a main effect of condition ($p = 0.012$) with HIIE lower than SSE ($p = 0.012$), and for moment ($p = 0.050$) with values immediately post exercise higher than at rest ($p = 0.037$, Figure 3B). For IL-6 there was a main effect of condition ($p = 0.012$) with HIIE higher than SSE ($p = 0.012$), and moment ($p < 0.001$), with values at rest lower than immediately post-exercise ($p = 0.009$) and 30min-post exercise ($p = 0.039$); at 60min-post exercise lower than at immediately post-exercise ($p = 0.001$) and 30min-post exercise ($p = 0.007$, Figure 3A). For IL-10 there was a main effect of moment ($p = 0.002$), with values at rest lower than immediately ($p = 0.007$), 30min ($p = 0.047$) and 60 min-post exercise ($p = 0.001$, Figure 3C).

For IL10/TNF-α ratio there was a main effect of moment ($p = 0.015$), with higher values immediately post exercise than at rest ($p = 0.019$). There was also an interaction of condition and moment ($p = 0.002$), where, in the HIIE condition, the values 30min-post exercise were higher than at rest ($p = 0.011$), immediately ($p = 0.006$) and 60min-post exercise ($p = 0.042$) in the same condition; and in the SSE condition 30min-post exercise the values were higher than at rest ($p = 0.005$) immediately ($p=0.004$) and 60min-post exercise ($p = 0.020$, Figure 3D).

Discussion

The main finding of the present study was that HIIE elicited different total energy expenditure during exercise from SSE, despite matched volume. By design, energy expenditure was ~13% higher in the HIIE group (523 ± 40.06 *versus* 453 ± 56.72 kcal for SSE, $p < 0.02$) and session exercise time was 39% higher than the SSE group (30.78 ± 2.09 min *versus* 42.09 ± 2.93 min), whereas the session exercise time in the HIIE group that was spent in recovery between intense pause/session of run, thus actual exercise time was ~21 minutes compared to SSE. Recently, study have related similar energy expenditure (EE) in response to HIIE (10×60s at a workload that elicited 90% maximal heart rate with 60-s of active recovery at 50 W) and SSE (cycling at a workload that elicited 70% of

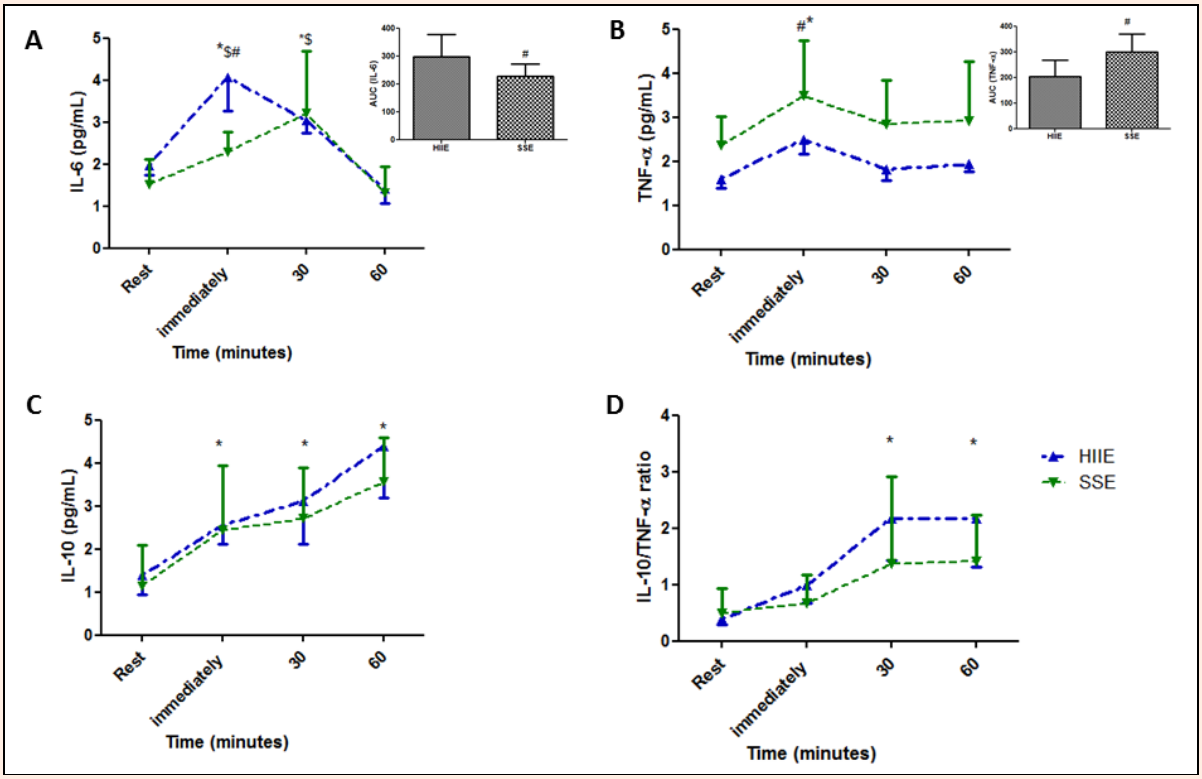


Figure 3. Cytokine levels before and after a single session of SSE and HIIE exercise in males (n = 8; values are mean ± standard deviation). Figures: 3A (IL-6), 3B (TNF-α), 3C (IL-10), 3D (IL-10/ TNF-α). * = different from rest ($p < 0.05$); ** = different SSE ($p < 0.05$); # = different from 30 minutes; $ = different from 60 minutes.

maximal heart rate for 50 min) after 24h (Skelly et al., 2014), even despite the fact that the total energy expenditure during the exercise session was superior in SSE than HIIE (352 ± 34 *versus* 547 ± 65kcal, respectively; $p < 0.001$). This suggests that a session of HIIE may promote greater physiological stress than a bout of SSE, principally due to an increased hormonal response. Although our data has not exhibited significant differences between both protocol sessions, the energy expenditure following exercise (1h recovery) was 14% higher in HIIE than SSE. The difference in EE during exercise bouts (SSE vs HIIE) found in present study may be due to exercise protocols utilized, and here, we demonstrated that when the volume was equal between SSE and HIIE sessions, HIIE leads to more EE.

In addition, the alterations found in our data after both exercise sessions are due to, at least in part, of hormonal changes, given that acute exercise promotes the enhancement of several hormones, principally the ones related to lipolysis in adipose tissue and glycogenolysis in skeletal muscle and the liver, promoting the availability of energetic substrates mainly by NEFA and glucose for muscle workload. Concomitant with the increased cortisol levels, our data demonstrate that HIIE promotes greater demands on the anaerobic metabolism (seen by peak lactate, Figure 2B) compared to SSE, while SSE promotes great demands on the aerobic metabolism (seen by peak NEFA, Figure 2C) compared with HIIE.

In our data, the HIIE did not promote accumulated NEFA levels immediately after exercise, while SSE did. During the steady state exercise, higher utilization of lipids in comparison with intermittent exercise is observed. Moreover, Jeppense and Kiens (2012) have reported that this response depends on acetyl CoA and CoA concentration ratios, carnitine availability, and hydrogen ion concentration. This last is likely higher during HIIE, due to anaerobic metabolism. More studies are needed to better understand the mechanisms involved in this response.

The lack of accumulated NEFA levels immediately after HIIE can be, at least in part, a result of the higher fatty acid uptake by skeletal muscle during the repeated metabolic perturbations in the transitions from rest to exercise (pause/session cycles). We suggest that HIIE may be important in stimulate the lipolysis process, however an efficient clearance during pause favored by fatty acid uptake by skeletal muscle occurs, indicating that a supply for energy demand by aerobic metabolism also occurs. Studies have related that physiological adaptations resulting from brief sessions in Wingate-based HIIT over two weeks is a potential stimulus to enhance skeletal muscle oxidative capacity and induce adaptations that are apparent after several weeks, such as reduced rate of glycogen utilization and lactate production during exercise, and an increased capacity for whole-body and skeletal muscle lipid oxidation (Gibala et al., 2009; Burgomaster et al., 2008). Recently, our group has demonstrated that low-volume HIIE performance (4 sessions of Wingate-based HIIT, 30s x 3 minutes rest, ~2 minutes of exercise) promotes accumulated serum NEFA levels after

the last session followed by rest (Lira et al., 2015). The higher serum NEFA levels can be a result of the lipolysis process; the need for an available substrate for maintenance of muscle contraction during exercise, but, as the exercise performed was short-duration, free fatty acid uptake by the skeletal muscle can be reduced, exposing the blood circulation to high concentrations of NEFA. Our data suggest that, HIIE performed in high-volume (5km) provides increased fatty acid uptake, principally by skeletal muscle.

On the other hand, a robust inflammatory response during the exercise session is observed. Skeletal muscle is a major source of some cytokines and the response is dependent on duration, intensity and session volume of exercise (Pedersen and Febbraio, 2009; Neto et al., 2011). The cytokines exert several functions, and have a crucial role in energy metabolism, such as IL-6 and TNF-α, that are important in the anti-inflammatory response and exert effects on glucose and lipid metabolism, stimulating increases in the lipolysis and glycogenolysis process in order to provide an energy supply for the skeletal muscle and other tissue after exercise.

In the present study, we observed that together with high cortisol levels in the SSE session, higher TNF-α levels, and the immune-endocrine profile can exert a potential effect on the lipolysis process, leading to accumulated NEFA levels after exercise. Rosa et al. (2009) have related that acute exhaustive exercise induces a pro-inflammatory response in the adipose tissue (observed by elevated IL-6 and TNF-α levels in adipose tissue) and this increase can contribute to lipolysis and the release of fatty acids as an energy supply for muscle and other tissues immediately after exercise. On the other hand, in the HIIE session higher IL-6 values were observed. Particularly, this immune-endocrine profile can favor the glucogenolysis process and the available glucose for skeletal muscle work. The results suggest that the alterations regarding cytokine kinetics during exercise are dependent on the exercise mode. However, more studies are needed for a better understanding of the mechanism involved.

In addition, increased IL-10 levels and IL-10/TNF-α ratio were observed in both exercise protocols, showing the anti-inflammatory role promoted by exercise sessions. Classically, exercise leads to an anti-inflammatory status, and its condition is induced by an increase in IL-6 production in the skeletal muscle and, after exercise, higher IL-1ra and IL-10 levels are observed. The increased IL-10 levels can be related to higher IL-6 and TNF-α levels, and the principal role of these is to prevent the exacerbation of the pro-inflammatory status, blocking a possible persistent inflammatory status. Both HIIE and SSE were able to promote an anti-inflammatory status, as seen in an increased IL-10/TNF-α ratio. This suggests that both can be utilized as strategies for different populations, such as obesity, diabetes, dyslipidemia. More studies are necessary to better understand the mechanisms involved in HIIT in anti-inflammatory responses.

This study is limited mainly by the difference in total work performed. Even though the exercise volume was the same, HIIE likely induced higher internal loads. Future studies may want to verify whether work-matched HIIE and SSE exhibit different inflammatory and metabolic responses.

Conclusion

In conclusion, our results demonstrated that in both exercise protocols, when total volume is matched, the inflammatory response did not differ between group exercise modalities, leading to an anti-inflammatory status; however the metabolic response is different.

To the best of our knowledge, this is the first study comparing the metabolic and inflammatory responses to volume matched HIIE and SSE. Our initial hypothesis was that a more pronounced response would be found in the HIIE, and would result in an increase in energetic substrates and cytokine levels. However this hypothesis was not confirmed.

Acknowledgements

Fabio Santos Lira thanks Fapesp for their support (2013/25310-2).The authors declare that they have no conflict of interest.

References

Bassuk, S.S. and Manson, J.E. (2005) Epidemiological evidence for the role of physical activity in reducing risk of type 2 diabetes and cardiovascular disease. *Journal of Applied Physiology* **99(3),** 1193-1204.

Bertuzzi, R.C., Franchini, E., Kokubun, E. and Kiss, M.A. (2007) Energy system contributions in indoor rock climbing. *European Journal of Applied Physiology* **101(3),** 293-300.

Borg, G.A. (1982) Psychophysical bases of perceived exertion. *Medicine and Science in Sports and Exercise* **14(5),** 877.

Burgomaster, K.A.1., Howarth, K.R., Phillips, S.M., Rakobowchuk, M., Macdonald, M.J., McGee, S.L. and Gibala, M.J. (2008) Similar metabolic adaptations during exercise after low volume sprint interval and traditional endurance training in humans. *Jounal of Physiology* **586(1),** 151-160.

di Prampero, P.E. and Ferretti, G. (1999) The energetics of anaerobic muscle metabolism: a reappraisal of older and recent concepts. *Respiration Physiology* **118(2-3),** 103-115.

Gibala, M.J., Little, J.P., Macdonald, M.J. and Hawley, J.A. (2012) Physiological adaptations to low-volume, high-intensity interval training in health and disease. *Journal of Physiology* **590(5),** 1077-1084.

Gibala, M.J., McGee, S.L., Garnham, A.P., Howlett, K.F., Snow, R.J. and Hargreave, M. (2009) Brief intense interval exercise activates AMPK and p38 MAPK signaling and increases the expression of PGC-1alpha in human skeletal muscle. *Journal of Applied Physiology* **106(3),** 929-934.

Gillen, J.B., Percival, M.E., Ludzki, A., Tarnopolsky, M.A. and Gibala, M.J. (2013) Interval training in the fed or fasted state improves body composition and muscle oxidative capacity in overweight women. *Obesity* **21(11),** 2249-2255.

Howley, E.T., Bassett, D.R.Jr. and Welch, H.G. (1995) Criteria for maximal oxygen uptake: review and commentary. . *Medicine and Science in Sports and Exercise* **27(9),** 1292-1301.

Jeppesen, J. and Kiens, B. (2012) Regulation and limitations to fatty acid oxidation during exercise. *Journal of Physiology* **590(5),** 1059-1068.

Kuipers, H., Verstappen, F.T., Keizer, H.A., Geurten, P. and Van Kranenburg, G. (1985) Variability of Aerobic Performance in the Laboratory and Its Physiologic Correlates. *International Journal of Sports Medicine* **6(4),** 197-201.

Leggate, M., Nowell, M.A., Jones, S.A. and Nimmo, M.A. (2010) The response of interleukin-6 and soluble interleukin-6 receptor isoforms following intermittent high intensity and continuous moderate intensity cycling. *Cell Stress and Chaperones* **15(6),** 827-833.

Lira, F.S., Panissa, V.L., Julio, U.F. and Franchini, E. (2015) Differences in metabolic and inflammatory responses in lower and

upper body high-intensity intermittent exercise. *European Journal of Applied Physiology* **115(7),** 1467-1474.

Lira, F.S., Yamashita, A.S., Rosa, J.C., Koyama, C.H., Caperuto, E.C. and Batista ML Jr, Seelaender MC. (2012) Exercise training decreases adipose tissue inflammation in cachectic rats. *Hormone and Metabolic Research* **44(2),** 91-98.

Meckel, Y., Eliakim, A., Seraev, M., Zaldivar, F., Cooper, D.M., Sagiv, M. and Nemet D. (2009) The effect of a brief sprint interval exercise on growth factors and inflammatory mediators. *Journal of Strength and Conditioning Research* **23(1),** 225-230.

Meckel, Y., Nemet, D., Bar-Sela, S., Radom-Aizik, S., Cooper, D.M., Sagiv, M. and Eliakim, A. (2011) Hormonal and inflammatory responses to different types of sprint interval training. *Journal of Strength and Conditioning Research* **25(8),** 2161-2169.

Neto, J.C., Lira, F.S., de Mello, M.T. and Santos, R.V. (2011) Importance of exercise immunology in health promotion. *Amino Acids* **41(5),** 1165-1172.

Panissa, V.L.G., Azevedo, N.R., Julio, U.F. Andreato, L.V., Pinto e Silva, C.M., Hardt, F. and Franchini, E. (2013) Maximum number of repetitions, total weight lifted and neuromuscular fatigue in individuals with different training backgrounds. *Biology of Sport* **30,** 131-136.

Pedersen, B.K. and Febbraio, M.A. (2008) Muscle as an endocrine organ: focus on muscle-derived interleukin-6. *Physiological Reviews* **88(4),** 1379-1406.

Pedersen, B.K. (2012) Muscular interleukin-6 and its role as an energy sensor. *Medicine and Science in Sports and Exercise* **44(3),** 392-396.

Pedersen, B.K. (2009) The diseasome of physical inactivity--and the role of myokines in muscle--fat cross talk. *Journal of Physiology* **587(23),** 5559-5568.

Rosa, J.C., Lira, F.S., Eguchi, R., Pimentel, G.D., Venâncio, D.P., Cunha, C.A., Oyama, L.M., De Mello, M.T., Seelaender, M. and do Nascimento, C.M. (2011) Exhaustive exercise increases inflammatory response via Toll like receptor-4 and NF-κBp65 pathway in rat adipose tissue. *Journal of Cellular Physiology* **226(6),** 1604-1607.

Skelly, L.E., Andrews, P.C., Gillen, J.B., Martin, B.J., Percival, M.E. and Gibala, M.J. (2014) High-intensity interval exercise induces 24-h energy expenditure similar to traditional endurance exercise despite reduced time commitment. *Applied Physiology, Nutrition, and Metabolism* **39(7),** 845-848.

Zagatto, A., Redkva, P., Loures, J., Kalva Filho, C., Franco, V., Kaminagakura, E. and Papoti, M. (2011) Anaerobic contribution during maximal anaerobic running test: correlation with maximal accumulated oxygen deficit. *Scandinavian Journal of Medicine & Science in Sports* **21(6),** 222-230.

Zwetsloot, K.A., John, C.S., Lawrence, M.M., Battista, R.A. and Shanely, R.A. (2014) High-intensity interval training induces a modest systemic inflammatory response in active, young men. *Journal of Inflammation Research* **9(7),** 9-17.

Key points

- Metabolic contribution of both exercise, HIIE and SSE, was different.
- Both protocols leading to an anti-inflammatory status.
- HIIE induce a higher energy expenditure take into account total session duration.

AUTHOR BIOGRAPHY

Carolina CABRAL-SANTOS
Employment
Member of Exercise and Immunometabolism Research Group, (UNESP) – Presidente Prudente, Brazil
Degree
MSc
Research interest
Exercise physiology, Immunometabolism, High Intensity Intermittent Exercise
E-mail:carolina-cabralsantos@hotmail.com

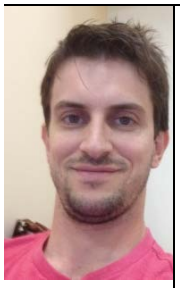
José GEROSA-NETO
Employment
Prof., Depart. of Physical Education, Universidade Estadual Paulista (UNESP) – Presidente Prudente, Brazil
Degree
Master
Research interest
Exercise physiology, Immunometabolism
E-mail: netoef@yahoo.com.br

Daniela Sayuri INOUE
Employment
Member of Exercise and Immunometabolism Research Group, (UNESP) – Presidente Prudente, Brazil
Degree
M.S.
Research interest
Exercise physiology, Immunometabolism
E-mail: dsinoue@gmail.com

Valéria Leme Gonçalves PANISSA
Employment
Researcher, School of Physical Education and Sport, University of São Paulo (USP), Brazil
Degree
PhD
Research interest
Sport and Exercise Physiology, Appetite and Exercise, High Intensity Intermittent Exercise
E-mail: valeriapanissa@gmail.com

Luís Alberto GOBBO
Employment
Assistant Professor, Departament of Physical Education, Universidade Estadual Paulista (UNESP) – Presidente Prudente, Brazil
Degree
PhD
Research interest
Epidemiology, Aging, Physical Activity, Exercise
E-mail: luisgobbo@fct.unesp.br

Alessandro Moura ZAGATTO
Employment
Professor, Universidade Estadual Paulista (UNESP) – Bauru, Brazil
Degree
PhD
Research interest
Sport and Exercise Physiology, Sport Performance
E-mail: azagatto@yahoo.com.br



Eduardo Zapaterra CAMPOS
Employment
Professor, Departament of Physical Education, Universidade Estadual Paulista (UNESP) – Presidente Prudente, Brazil
Degree
Doctor
Research interest
Exercise Physiology, Immunometabolism, Sport Performance
E-mail: zacampos@yahoo.com.br

Fábio Santos Lira
Employment
Professor, Departament of Physical Education, Universidade Estadual Paulista (UNESP) – Presidente Prudente, Brazil
Degree
PhD
Research interest
Sport and Exercise Physiology, Metabolism, Inflammation, Nutrition
E-mail: fabiolira@fct.unesp.br

✉ **Fábio Santos Lira**
Exercise and Immunometabolism Research Group, Department of Physical Education, Universidade Estadual Paulista, UNESP, Rua Roberto Simonsen, 305, 19060-900 Presidente Prudente, SP, Brazil