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ORIGINAL ARTICLE

Capsaicin supplementation increases time to exhaustion in high-intensity intermittent exercise without modifying metabolic responses in physically active men

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Abstract

Purpose The purpose of this study was to investigate the acute effect of capsaicin supplementation on performance and physiological responses during high-intensity intermittent exercise (HIIE).

Method Thirteen physically active men (age = 24.4 ± 4.0 years; height = 176.4 ± 6.9 cm; body mass = 78.7 ± 13.8 kg; running training per week = 3.9 ± 0.9 h) performed an incremental running test to determine peak oxygen uptake ($\dot{V}O_{2Peak}$) and the speed associated with $\dot{V}O_{2Peak}$ ($s\dot{V}O_{2Peak}$). Thereafter, subjects completed two randomized, double-blind HIIE (15s:15 s at 120% $s\dot{V}O_{2Peak}$) trials 45-min after consuming capsaicin (12 mg) or an isocaloric placebo. Time to exhaustion, blood lactate concentration, oxygen consumption during and 20 min post-exercise, energy expenditure, time spent above 90% of $\dot{V}O_{2Peak}$, and the rate of perceived exertion were evaluated.

Results There was no difference between capsaicin and placebo for any variable except time to exhaustion [capsaicin: 1530 ± 515 s (102 efforts) vs placebo: 1342 ± 446 s (89 efforts); $p < 0.001$].

Conclusion In conclusion, capsaicin supplementation increased time to exhaustion in high-intensity intermittent exercise without modifying the metabolic response of exercise or the rate of perceived exertion in physically active men. Capsaicin could be used to increase the training load during specific exercise training sessions.

Keywords Excess post-oxygen consumption · Lactate · Energy system contribution

Abbreviations

CAP	Capsaicin
EPOC	Excess of post-exercise oxygen consumption
HIIE	High-intensity intermittent exercise
RPE	Rate of perceived exertion
$s\dot{V}O_{2Peak}$	Speed associated with $\dot{V}O_{2Peak}$
TRPV1	Transient receptor potential vanilloid-1
$\dot{V}O_{2Peak}$	Peak oxygen uptake

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Introduction

High-intensity intermittent exercise (HIIE) is an effective training modality to improve body composition (Keating et al. 2017), health outcomes, and cardiorespiratory fitness (Helgerud et al. 2007; Milanovic et al. 2015). Although there are different HIIE protocols at the literature, one of them known as short-duration HIIE is characterized by short efforts (less than 1 min) interspersed by the same effort duration, with intensities ranging from 100 to 120% of maximal aerobic power. Short-duration HIIE has been widely utilized to improve aerobic power (Billat et al. 2001; Buchheit and Laursen 2013a). Enhancement of aerobic fitness with HIIE may occur as a result of the extended time spent at or over 90% of maximum oxygen uptake (Buchheit and Laursen 2013b). In this perspective, one may suggest that enhancing time to exhaustion during HIIE (i.e., the number of bouts performed) could lead to greater fitness gains. Nutritional ergogenic aids are often used to achieve this goal.

Capsaicin (CAP), 8-methyl-*N*-vanillyl-trans-6-nonenamide, is a natural substance and bioactive phytochemical found primarily in chili peppers and others spicy food, which gives the characteristic of pungent flavor (Ludy et al. 2012). The multiple metabolic effects of CAP have received much attention from researchers. For example, CAP agonizes transient receptor potential vanilloid-1 (TRPV1) in many organs (Szallasi and Blumberg 1999), leading to the sensation of heat, activation of the sympathetic nervous system (Shin and Moritani 2007), with increased catecholamine secretion, fat oxidation, and energy expenditure (Kawada et al. 1986; Josse et al. 2010; Ludy et al. 2012). CAP has, therefore, been studied as a potential anti-obesity agent in humans and animals (Leung 2014; Tremblay et al. 2016), demonstrating the effectiveness of CAP supplementation on abdominal fat loss in overweight men and women (Snitker et al. 2009).

In addition, CAP has been investigated to improve endurance exercise performance. Animal studies have demonstrated that CAP supplementation increases swimming time to exhaustion, and performance gains were explained in part by an increase in plasma free fatty acids as a result of higher epinephrine release, leading a glycogen sparing effect (Kim et al. 1997, 1998; Oh and Ohta 2003). In humans, our group found that 12 mg of CAP supplementation improved 1500-m running performance and reduced the rate of perceived exertion (RPE) in physically active adults (De Freitas et al. 2018). On the other hand, Opheim and Rankin (2012) did not report any significant time reduction in repeated-sprint exercise (15 × 30-m *all-out* sprints with 35-s rest intervals) in healthy athletes following the ingestion of 28.5 mg of CAP ingested via 3 g of powdered Capsicum frutescent (cayenne pepper) capsules for 7 days.

Regarding the other potential mechanisms to explain effects of CAP on performance previous studies showed that CAP activates the TRVP1 receptor in skeletal muscle, and increases the release of calcium by the sarcoplasmic reticulum (Lotteau et al. 2013), resulting in an enhanced interaction between actin-myosin filaments and greater force output (Homsher et al. 1996; Linari et al. 2015).

While CAP supplementation influences performance in animals and humans (De Freitas et al. 2018; Kim et al. 1997) and metabolic responses in animals (Kim et al. 1997, 1998; Oh and Ohta 2003), investigations of metabolic responses in humans concomitantly with performance are very scarce. Moreover, the scientific literature has demonstrated that the intensity of exercise affects metabolic responses (Franchini et al. 2016; Gaitanos et al. 1993; Panissa et al. 2018) and the effect of CAP ingestion on the performance achieved during the HIIE protocols is currently unknown.

Thus, the purpose of this study was to investigate the acute effect of CAP supplementation (12 mg) on time to exhaustion and physiological responses related to energy metabolism such as oxygen consumption during exercise, post-exercise oxygen consumption (fast phase and after 20 min), lactate levels, and, consequently, energy expenditure as well as time spent above 90% of $\dot{V}O_{2Peak}$ during HIIE (15 s of effort at 120% performance interspersed 15 s of passive recovery) in physically active men. We hypothesized that capsaicin consumption would increase time to exhaustion during HIIE, the time spent at or over 90% of maximum oxygen uptake, and excess post-exercise oxygen consumption magnitude.

Methods

Experimental design

This study utilized a randomized, double-blind, crossover design as demonstrated in Fig. 1. Subjects completed three experimental trials, performed at the same time of day (7–9 AM), and separated by 1 week. During the first visit, anthropometric measurements were taken and an incremental test was performed to determine peak oxygen uptake ($\dot{V}O_{2Peak}$) and the speed associated with $\dot{V}O_{2Peak}$ ($s\dot{V}O_{2Peak}$). On the following two visits, each participant randomly consumed either the placebo or capsaicin and then completed a bout of HIIE (see below for exercise procedures). Blood lactate and oxygen consumption were analyzed during and after the exercise protocol to determine metabolic cost, and RPE was collected after exercise.

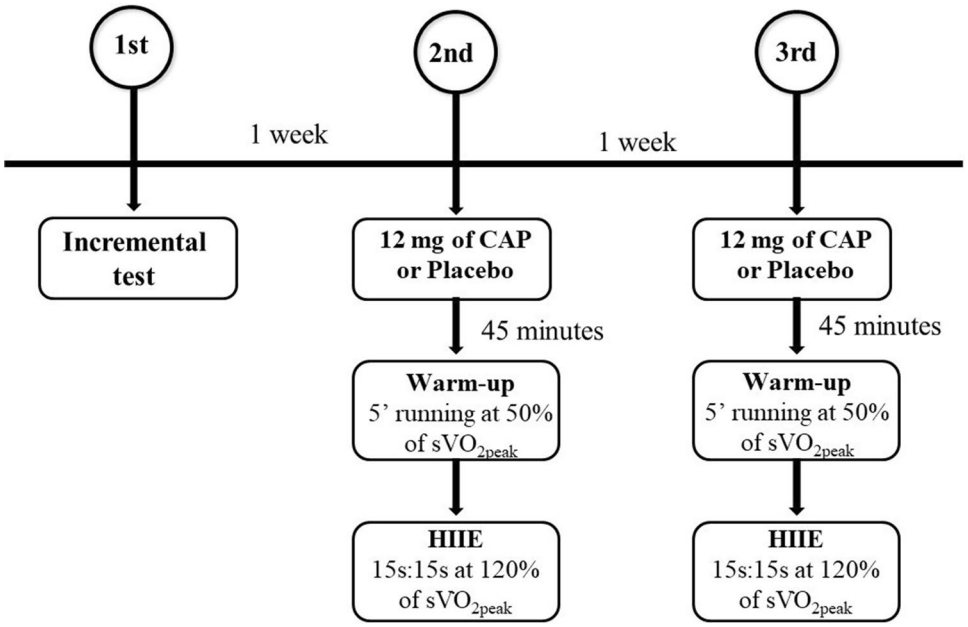

Fig. 1 Experimental Design

Subjects

Thirteen physically active men were recruited for this study (age = 24.4 ± 4.0 years; height = 176.4 ± 6.9 cm; weight = 78.7 ± 13.8 kg; VO_{2Peak} = 52.0 ± 8.0 mL/kg/min; running experience = 3.5 ± 2.9 years). Inclusion criteria were as follows: participating in regimented running training during the previous 6 months with a minimum weekly frequency of twice a week; between 20 and 35 years age; no medical contraindications that might interfere with the exercise protocol; and, not taking any ergogenic substance during the previous 12 months and not smoking. The study was approved by the Ethics Research Group of the University of Sao Judas, Sao Paulo-SP, Brazil (Protocol number: 66523717.2.0000.0089), and the research was conducted according to the 2008 Revision of the Declaration of Helsinki and all participants signed a consent form and were informed about the purpose of the study and the possible risks.

Procedure

Anthropometric measurements, dietary intake assessment, and supplementation protocol

A fixed stadiometer was used to measure height with an accuracy of 0.1 cm. Body mass was measured using an electronic scale (Filizola PL50, Filizola Ltda., Brazil). Food questionnaires were distributed to all the participants to record food and fluid intake for pre-exercise meal (breakfast) and for 24 h prior to each trial. Participants were instructed to consume breakfast at home 1 h and a half before each experimental trial, and to replicate the dietary intake during all the experimental trials. All food intakes were analyzed for total kilocalorie and macronutrient intakes (Software—Dietpro version 5.8) to ensure that dietary intake was similar between experimental trials. The software utilized the database of Brazilian food composition table (TACO) to calculate dietary intake. The participants were instructed not to consume chili peppers or other spicy foods as well as coffee, tea, alcohol, and/or stimulant drinks during the study period as well as were instructed not to use any other supplement or ergogenic substance, and make changes to their regular diet.

On the experimental trials, each participant randomly consumed either the placebo (12 mg of starch; energy: 0.46 kcal) or 12 mg of purified capsaicin (Pharma Nostra—Campinas, Brazil). Identical capsules without flavor were used and a person who does not belong to the research team was assigned to deliver the supplements to every subject to ensure a double-blind design. Placebo or CAP were taken in the lab and ingested 45 min prior to the experimental (Conrado De Freitas et al. 2017). This dosage was selected, because the other studies have reported that supplementation of more than 33 mg per day of capsaicinoids increases gastric motility (Whiting et al. 2014).

Incremental test

Participants were submitted to an incremental test on a treadmill (Inbramed MASTER CI, Inbrasport®, Porto Alegre, Brazil). The initial speed was at 8 km/h, increasing by 1 km/h every 2 min until volitional exhaustion. Verbal encouragement was given throughout the incremental test. The oxygen uptake was measured (Quark PFT, Cosmed®,

Rome, Italy) during the test and the average of the last 30 s defined as $\dot{V}O_{2Peak}$. The sVO_{2Peak} was assumed as the final incremental test speed. When the participants were unable to complete a stage, the speed was selected according to the time in the final stage, as demonstrated following: $s\dot{V}O_{2Peak}$ = speed of final complete stage + [(time, in seconds, remaining at the final incomplete stage/120 s) × 1 km h] (Kuipers et al. 1985).

High-intensity intermittent exercise (HIIE) protocol

For each exercise trials, the subjects performed a warm-up consisting of running at 50% of $s\dot{V}O_{2Peak}$ for 5 min at 1% incline. The HIIIE was performed intermittently with subjects running on a treadmill for 15 s at 120% of $s\dot{V}O_{2Peak}$, interspersed by 15 s of passive recovery. Both experimental trials were conducted until voluntary exhaustion, which was determined when the subjects were not capable of maintaining the pace anymore. The performance was determined by time until exhaustion (in seconds).

Blood lactate and the rate of perceived exertion

Blood samples collected from the ear lobe were used to analyze the lactate concentration. Measurements were obtained at rest and 3, 5, and 7 min after exercise. The delta lactate (highest value minus rest values − [ΔLa^-]) was utilized to compared conditions. The analyses were performed using the lactate analyzer Yellow Spring 1500 Sport (Yellow Springs, USA). The rate of perceived exertion (RPE) was measured after exercise session using the 6–20 point Borg scale (Borg et al. 1987).

Oxygen uptake

Oxygen uptake ($\dot{V}O_2$) was measured during exercise and 20-min post to examine excess of post-exercise oxygen consumption (EPOC). Analysis of $\dot{V}O_2$ during exercise was performed considering total workout, only during effort, only during the pause, and the difference between effort and pause were conducted considering the $\dot{V}O_2$ means in each period. These variables were also calculated relatively to $\dot{V}O_{2Peak}$. Time spent at or above 90% of $\dot{V}O_{2Peak}$ was determined from $\dot{V}O_2$ values relative to respective percentages of $\dot{V}O_{2Peak}$. The calculation of this time was conducted observing the average 5-s periods. The time above 90% was determined from the average values obtained. EPOC was calculated by subtracting resting $\dot{V}O_2$ from average of $\dot{V}O_2$ during 20-min recovery (Townsend et al. 2013).

Energy expenditure

To have a better understanding of energy system contribution in different conditions (capsaicin or placebo during HIIE), energy expenditure was estimated from oxidative, glycolytic, and phosphagen energy systems (Margaria et al. 1933; Di Prampero and Ferretti 1999). Albeit there are limitations using this method in intermittent activities, the method employed could provide further understanding about the impact of capsaicin supplementation on the energy system contribution.

The contribution of the oxidative energy system was estimated by subtracting resting $\dot{V}O_2$ from the $\dot{V}O_2$ average during overall exercise. The glycolytic energy system contribution was calculated using [ΔLa^-], which was converted to oxygen equivalents, assuming that the accumulation of 1 mmol/L [La^-] is equivalent to 3 mL O_2/kg of body mass (Di Prampero and Ferretti 1999). The phosphagen energy system contribution was assumed as the sum of $\dot{V}O_2$-time average during the HIIE recovery periods (ΣEPOC) (Zagatto et al. 2011; Milioni et al. 2017; Panissa et al. 2018). The $\dot{V}O_2$ -time average during the HIIE recovery periods was used due to the inability to identify the fast component of EPOC as originally proposed (Margaria et al. 1933) and considering that 15-s recovery between efforts is likely predominantly devoted to the reestablishment of creatine phosphate stores (Bogdanis et al. 1995). In addition, the fast component of EPOC (i.e., estimated using $\dot{V}O_2$ kinetics as the product of $\dot{V}O_2$ amplitude and time constant using a bi-exponential fit) was calculated for the last effort utilizing the software Origin version 2019 (OriginLab Corporation, Microcal, Massachusetts, USA). All oxygen equivalents were converted to energy equivalents assuming 20.92 kJ for each 1 L of O_2 utilized (Gastin 2001) prior to energy expenditure evaluation. The overall energy expenditure was estimated during HIIE and corresponded to the sum of the contributions of the oxidative and anaerobic energy systems.

Statistical analysis

Data were reported as means and standard deviation (SD). Data normality was verified using the Shapiro–Wilk test. $\dot{V}O_2$ during effort and pause was analyzed by a mixed model [Condition (placebo and CAP) vs Time (effort and pause)] followed by the Tukey's post hoc test. Energy expenditure from different energy system was analyzed by a mixed model [Condition (placebo and CAP) vs energy system contribution (oxidative, glycolytic, and phosphagen)] followed by the Tukey's post hoc test. Time to exhaustion, [ΔLa^-], RPE, EPOC, $EPOC_{fast}$, average of $\dot{V}O_2$, and energy expenditure were analyzed by a paired *t* test. Statistical significance was set at $p < 0.05$. The data were analyzed using SAS (version 9.3). Standardized effect sizes were also calculated from

Table 1 Dietary intake and macronutrient distribution 24 h before each trial

Dietary intake	Placebo	Capsaicin	*p*
Carbohydrate (g)	302 ± 146	271 ± 137	0.409
Protein (g)	104 ± 42	103 ± 14	0.947
Lipid (g)	68 ± 23	74 ± 35	0.309
Total intake (kcal)	2231 ± 612	2172 ± 576	0.595

Data are mean ± standard deviation

Table 2 Physiological responses for each condition

	Capsaicin	Placebo
Rating of perceived exertion (a.u.)	18 ± 1	18 ± 1
Δ[La$^-$] (mmol/L)	5.9 ± 2.3	5.5 ± 2.6
$EPOC_{20min}$ (L/min)	0.60 ± 0.15	0.58 ± 0.14
T90% $\dot{V}O_{2Peak}$ (s)	308 ± 241	331 ± 249
T90% $\dot{V}O_{2Peak}$ % to Tlim (%)	20 ± 15	25 ± 17
$\dot{V}O_2$ average (mL/kg/min)	38.1 ± 6.9	39.4 ± 7.7
$\dot{V}O_2$ average relative to $\dot{V}O_{2Peak}$ (%)	73.2 ± 8.2	75.8 ± 7.3
$\dot{V}O_2$ difference between effort and pause (mL/kg/min)	2.8 ± 2.4	3.7 ± 1.4
$\dot{V}O_2$ difference between effort and pause relative to $\dot{V}O_{2Peak}$ (%)	5.4 ± 3.4	7.0 ± 1.9
Time to reach 90% of $\dot{V}O_{2Peak}$	266 ± 204	165 ± 138
Number of efforts performed	102 ± 34[a]	89 ± 30

Data are mean ± standard deviation

[a]Higher than placebo

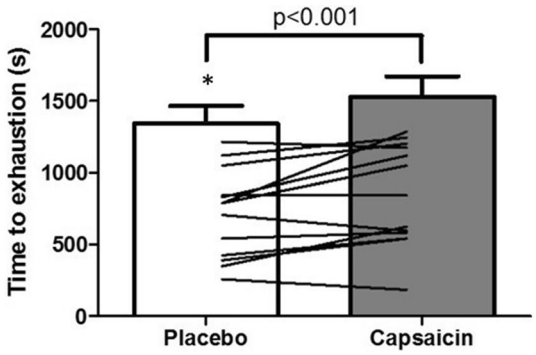

Fig. 2 The comparison of time to exhaustion for each condition. Data are mean ± standard deviation. Lines represent individual time to exhaustion for each condition. Asterisk: lower than capsaicin condition

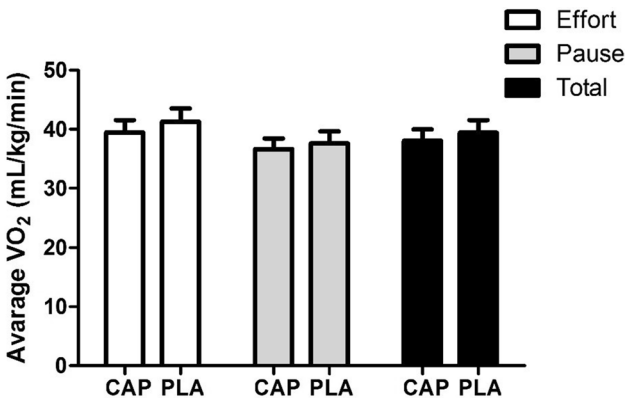

Fig. 3 The comparison of VO_2 average between effort, pause, and total. Data are mean ± standard deviation

the Cohen's equations (1969) with the following threshold values: < 0.2—trivial; > 0.2 and < 0.6—small; > 0.6 and < 1.2—moderate; > 1.2 and < 2.0—large; > 2.00 and < 4.0—very large; < 4.0—nearly perfect (Hopkins 2015). The chances of a possible substantial benefit or harm were calculated [assuming the value of 0.2 multiplied by the between-subject deviation as the smallest worthwhile change (SWC)].

Results

Table 1 shows the mean and standard deviation for dietary intake and macronutrient intakes averaged of each experimental trial. There were no statistically significant differences between conditions.

Table 2 shows physiological response for each condition. Paired *t* test did not reveal difference between conditions for RPE [$p = 0.165$; $d = 0.00$ (trivial)], $EPOC_{fast}$ [$p = 0.662$; $d = 0.00$ (trivial)], $EPOC_{20min}$ [$p = 0.551$; $d = 0.138$ (trivial)], time above 90% $\dot{V}O_{2Peak}$ [$p = 0.692$; $d = 0.094$ (trivial)], time above 90% $\dot{V}O_{2Peak}$ relative to time to exhaustion ($p = 0.149$; $d = 0.312$ (small)], $\dot{V}O_2$ average [$p = 0.389$; $d = 0.178$ (trivial)], relative $\dot{V}O_2$ average [$p = 0.339$; $d = 0.335$ (small)], and time to reach 90% of $\dot{V}O_{2Peak}$ [$p = 0.123$; $d = 0.580$ (small)]. However, there was a significant difference in time to exhaustion [$p < 0.001$; $d = 0.390$ (small)], and 9 out of 13 subjects with performance higher than SWC boundary [$p = 0.018$ $d = 0.405$ (small)] (Fig. 2).

Figure 3 shows the comparison of VO_2 average between effort, pause and total vs condition. There was no main effect of time ($F = 0.80$; $p = 0.389$) and condition ($F = 0.49$; $p = 0.479$) not any interaction ($F = 0.03$; $p = 0.865$). The $\dot{V}O_2$ relative to $\dot{V}O_{2Peak}$ displayed a main effect of time ($F = 34.11$; $p < 0.001$), with greater values in effort than pause ($p < 0.001$), while no effect was found for condition ($F = 0.84$; $p = 0.377$) or interaction ($F = 0.48$; $p = 0.502$).

For energy system contribution (Table 3), there was only main effect for type of energy system ($F = 183.4$;

Table 3 Energy system contribution and energy expenditure for each condition

	Oxidative	Glycolytic	ATP-CP	Total
CAP (kcal)	344.0 ± 132.4[a]	6.7 ± 2.2	175.2 ± 63.1[b]	525.9 ± 195.4
Placebo (kcal)	315.3 ± 128.3[a]	6.4 ± 2.7	161.1 ± 63.0[b]	482.8 ± 190.8

Data are mean ± standard deviation

[a]Higher than glycolytic and ATP-CP ($p < 0.05$)

[b]Higher than glycolytic ($p < 0.05$)

$p < 0.001$) with oxidative greater than glycolytic and ATP-CP ($p < 0.001$ for both), and ATP-CP greater than glycolytic ($p < 0.001$). There was no effect for condition ($F = 1.09$; $p = 0.301$) or interaction ($F = 0.35$; $p = 0.703$). There was no difference between total energy expenditure between conditions ($p = 0.115$).

Discussion

To our knowledge, this was the first study to investigate the effect of CAP supplementation on performance and physiological responses during an HIIE protocol in physical active men. This particular exercise protocol was chosen to mimic a typical training session aimed at improving aerobic fitness in healthy eutrophic (Little et al. 2010; Lira et al. 2017) and overweight/obese populations (Gillen et al. 2013; Smith-Ryan et al. 2015; Sawyer et al. 2016). The current results can, therefore, be easily applied to field practice. The main finding of this study was that CAP supplementation increased time to exhaustion during HIIE by 188 s (13 efforts more than in placebo which represents a 13% improvement in performance), and that 9 out of 13 subjects displayed a performance change higher than the SWC boundary. However, this ergogenic effect was not associated with changes in oxygen consumption during and after exercise, time to reach 90% of $\dot{V}O_{2Peak}$, time above 90% of VO_{2max} energy expenditure, lactate levels nor RPE.

In terms of physiological responses arising from our HIIE protocol, the comparison with the other studies is limited, since there are many variables, such as the duration and intensity of the effort and recovery (Dupont et al. 2002; Zaferiridis et al. 2010) can directly affect the outcomes. Considering these variations in protocols, we reported that the time to exhaustion (PLA: ~ 22 min; CAP: ~ 25 min), and time spent above 90% of $\dot{V}O_{2Peak}$ (PLA: ~ 20% of Tlim; CAP: ~ 25% of Tlim) are similar to the values reported in the previous studies that analyzed these responses in similar protocols (Zaferiridis et al. 2010; Thevenet et al. 2007).

Total energy expenditure from aerobic:anaerobic energy system contribution was ~ 65%:~ 35% in PLA and ~ 60%:~ 40% in CAP. These values are also well in line with a previous study (aerobic ~ 68%, anaerobic ~ 32%) that analyzed 10 efforts of 1 min at s$\dot{V}O_{2max}$ interspersed by 1 min of passive recovery (Panissa et al. 2018), demonstrating that our protocol had a demand coming from both aerobic and anaerobic metabolism with greater participation from aerobic metabolism. This metabolic repartition is typical of protocols aiming at improving aerobic fitness (Buccheit and Laursen 2013a, b).

The previous studies demonstrated that acute CAP supplementation may be used as ergogenic aid for endurance exercise. In rodents, studies observed that CAP supplementation induced an increase in time until exhaustion during swimming with a concomitant sparing of tissue glycogen (Kim et al. 1997, 1998; Oh et al. 2003). De Freitas et al. (2018) investigated the effect of CAP supplementation on performance, RPE, and blood lactate concentrations during middle distance running in physically active adults. The results showed that CAP improved middle distance running (1500-m) performance and reduced RPE. In contrast, Opheim and Rankin (2012) demonstrated that CAP supplementation (25.8 mg/d) for 7 days did not increase repeated-sprint performance (15 × 30-m sprints with 35-s intervals) in experienced athletes.

The present results are in accord with rodent's studies (Kim et al. 1997, 1998; Oh et al. 2003) and Freitas et al. (2018), and demonstrate the ergogenic effects of CAP supplementation on time to exhaustion during HIIE in physically active men. However, the divergent results between Opheim and Rankin's study and the present investigation are likely associated with the CAP supplement type and dosage. Our study used 12 mg of capsaicin, whereas Opheim and Rankin used a larger dosage (25.8 mg) in the form of cayenne pepper. Importantly, Opheim and Rankin (2012) reported that such a high dose of cayenne pepper supplementation induced gastrointestinal discomfort in 25% of participants. It is, therefore, likely that such level of physical discomfort affected the physical capacity of the participants and limited the interpretations derived from Opheim and Rankin's study about the true effects of CAP. We observed that dose and form of CAP used in the present study were well tolerated by every participant.

Peripheral fatigue is the most likely limiting factor that affects exercise performance, resulting in lower calcium release by the sarcoplasmic reticulum induced by accumulation hydrogen ions and inorganic phosphate (Rockwell et al. 2003; Leppik et al. 2004; Allen et al. 2008), which leads impairment on contraction efficiency and myofiber force production (Homsher et al. 1996; Linari et al. 2015). Thus, the potential mechanisms by which CAP may improve performance are likely a result of TRPV1 activation in skeletal

muscle. The activation of this receptor increases calcium release by sarcoplasmic reticulum (Luo et al. 2012; Lotteau et al. 2013), leading to higher interaction of actin–myosin filaments and potentially resulting in attenuated force production. In accordance, the other studies have demonstrated that CAP may increase muscle strength. Hsu et al. (2016) showed that 6 weeks of CAP supplementation increased relative forelimb grip strength in a dose-dependent manner, with the greatest values observed in the group receiving 1025 mg/kg/day CAP (approximately fivefold the human equivalent dose). Recently, our group demonstrated that acute supplementation of 12 mg of CAP improved squat exercise performance (four sets until movement failure at 70% of one repetition maximum with 90 s of rest interval between sets) by increasing the total volume performed in trained young men (Conrado De Freitas et al. 2017).

Interestingly, while our data showed an enhanced time to exhaustion during HIIE after CAP supplementation, we did not observe any significant changes in variables related to oxygen consumption during exercise, EPOC, energy expenditure from different energy system contribution, lactate, and RPE. These results refute our initial hypothesis that capsaicin consumption would increase the time spent at or over 90% of maximum oxygen uptake, and excess post-exercise oxygen consumption magnitude. While we expected to observe a greater EPOC after CAP supplementation due to a longer performance, this did not occur, probably because the additional sprints did not enhance the energy expenditure sufficiently.

It is possible that the intake of CAP enhanced running economy, as a result of greater myofiber force generation by the TRPV1 activation and more calcium release from sarcoplasmic reticulum (Luo et al. 2012; Lotteau et al. 2013). Supporting this hypothesis, Kazuya et al. (2014) analyzed the effects of a single intake of a low (10 mg/kg body wt) and a high (100 mg/kg) dose of CAP on gastrocnemius muscle function and energetics in mice. The results showed that CAP reduced the ATP cost during 6 min of repeated fatiguing isometric contractions with the higher dose also increasing force-generating capabilities in skeletal muscle. In accordance, Yashiro et al. (2015) found that CAP supplementation (10- or 100-mg/kg body weight) for 2 weeks also reduced the ATP cost for muscle contraction during 6 min of electrostimulation in mice. Therefore, these findings support the hypothesis that less energy is needed for a similar and/or greater amount of force production during exercise.

Thus, it is interesting that despite a greater volume (188 s; 13 efforts more) was observed in the CAP condition in the present study, there were no significant differences for energy expenditure and oxygen consumption compared to placebo. Based on these findings, acute CAP supplementation increased time until exhaustion in HIIE by generating running economy. However, more accurate measurement of running economy at with sub-maximal constant load is needed to substantiate this hypothesis (Saunders et al. 2004). In addition, if capsaicin was a mediator of running economy improvement and, consequently, postpone time to exhaustion, higher training loads may be investigated.

Form and dose of capsaicin in this study and in our previous studies (Conrado de Freitas et al. 2017; De Freitas et al. 2018) were well tolerated, and none of the subjects reported any "hot" sensations or gastrointestinal distress. However, some limitations need to be mentioned, such as a lack of neuromuscular analysis and measurement of the variables related to energy system in a steady-state exercise to assess the running economy. The current estimation of energy system contribution also has limitations, since it is an indirect method, and estimations from the similar protocols are scarce in the literature. Finally, the present study used a convenience sample of physically active men and other populations should be investigated. Thus, we suggest future researchers to investigate the effect of CAP supplementation on neuromuscular capacity and during running, and to verify the chronic effect of CAP supplementation on adaptive responses induced by HIIE in different populations.

In conclusion, CAP supplementation increased time until exhaustion in high-intensity intermittent exercise without modify energy cost, oxygen consumption, lactate, and the rate of perceived exertion physically active men. This nutritional supplement could, therefore, be used to enhance training load during high-intensity training.

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Author contributions Study design and organization of the manuscript were performed by MCF, FB, VLGP, FER, CF, EC, and FSL. Data analysis, statistical analysis, and the first draft of the manuscript were performed by MCF, VLGP, FER, FB, and FSL. The manuscript review was performed by MCF, FB, VLGP, FER, CF, EC, and FSL. The final approval for publication was performed by FSL.

References

Allen DG, Lamb GD, Westerblad H (2008) Impaired calcium release during fatigue. J Appl Physiol 104(1):296–305. https://doi.org/10.1152/japplphysiol.00908.2007

Billat VL, Slawinksi J, Bocquet V, Chassaing P, Demarle A, Koralsztein JP (2001) Very short (15 s–15 s) interval-training around the critical velocity allows middle-aged runners to maintain VO_{2max} for 14 minutes. Int J Sports Med 22(3):201–208. https://doi.org/10.1055/s-2001-16389

Bogdanis GC, Nevill ME, Boobis LH, Lakomy HK, Nevill AM (1995) Recovery of power output and muscle metabolites following 30 s of maximal sprint cycling in man. J Physiol 80:876–884

Borg G, Hassmen P, Lagerstrom M (1987) Perceived exertion related to heart rate and blood lactate during arm and leg exercise. Eur J Appl Physiol Occup Physiol 56(6):679–685

Buchheit M, Laursen PB (2013a) High-intensity interval training, solutions to the programming puzzle. Part II: anaerobic energy, neuromuscular load and practical applications. Sports Med 43(10):927–954. https://doi.org/10.1007/s40279-013-0066-5

Buchheit M, Laursen PB (2013b) High-intensity interval training, solutions to the programming puzzle: Part I: cardiopulmonary emphasis. Sports Med 43(5):313–338. https://doi.org/10.1007/s40279-013-0029-x

Conrado de Freitas, M, Cholewa JM, Freire RV, Carmo BA, Bottan J, Bratfich M et al (2017) Acute capsaicin supplementation improves resistance training performance in trained men. J Strength Cond Res. https://doi.org/10.1519/JSC.0000000000002109

De Freitas MC, Cholewa JM, Gobbo LA, de Oliveira JVNS, Lira FS, Rossi FE (2018) Acute capsaicin supplementation improves 1,500-m running time-trial performance and rate of perceived exertion in physically active adults. J Strength Cond Res 32(2):572–577

Di Prampero PE, Ferretti G (1999) The energetics of anaerobic muscle metabolism: a reappraisal of older and recent concepts. Respir Physiol 118(2–3):103–115

Dupont G, Blondel N, Lensel G, Berthoin S (2002) Critical velocity and time spent at a high level of VO_2 for short intermittent runs at supramaximal velocities. Can J Appl Physiol 27(2):103–115

Franchini E, Takito MY, Dal'Molin Kiss MA (2016) Performance and energy systems contributions during upper-body sprint interval exercise. J Exerc Rehabil 31(6):535–541. https://doi.org/10.12965/jer.1632786.393

Gaitanos GC, Williams C, Boobis LH, Brooksm S (1993) Human muscle metabolism during intermittent maximal exercise. J Appl Physiol 75(2):712–719. https://doi.org/10.1152/jappl.1993.75.2.712

Gastin PB (2001) Energy system interaction and relative contribution during maximal exercise. Sports Med 31(10):725–741

Gillen JB, Percival ME, Ludzki A, Tarnopolsky MA, Gibala M (2013) Interval training in the fed or fasted state improves body composition and muscle oxidative capacity in overweight women. Obesity 21:2249–2255

Helgerud J, Høydal K, Wang E, Karlsen T, Berg P, Bjerkaas M et al (2007) Aerobic high-intensity intervals improve VO_{2max} more than moderate training. Med Sci Sports Exerc 39(4):665–671. https://doi.org/10.1249/mss.0b013e3180304570

Homsher E, Kim B, Bobkova A, Tobacman LS (1996) Calcium regulation of thin filament movement in an in vitro motility assay. Biophys J 70(4):1881–1892. https://doi.org/10.1016/S0006-3495(96)79753-9

Hopkins WG (2015) Individual responses made easy. J Appl Physiol 118(12):1444–1446. https://doi.org/10.1152/japplphysiol.00098.2015

Hsu YJ, Huang WC, Chiu CC, Liu YL, Chiu WC, Chiu CH et al (2016) Capsaicin supplementation reduces physical fatigue and improves exercise performance in mice. Nutrients 8(10):E648. https://doi.org/10.3390/nu8100648

Josse AR,. Sherriffs SS, Holwerda AM, Andrews R, Staples AW, Phillips SM (2010) Effects of capsinoid ingestion on energy expenditure and lipid oxidation at rest and during exercise. Nutr Metab 7:65. https://doi.org/10.1186/1743-7075-7-65

Kawada T, Hagihara K, Iwai K (1986) Effects of capsaicin on lipid metabolism in rats fed a high fat diet. J Nutr 116(7):1272–1278. https://doi.org/10.1093/jn/116.7.1272

Kazuya Y, Tonson A, Pecchi E, Dalmasso C, Vilmen C, Fur YL et al (2014) A single intake of capsiate improves mechanical performance and bioenergetics efficiency in contracting mouse skeletal muscle. Am J Physiol Endocrinol Metab 306(10):E1110–E1119. https://doi.org/10.1152/ajpendo.00520.2013

Keating SE, Johnson NA, Mielke GI, Coombes JS (2017) A systematic review and meta-analysis of interval training versus moderate-intensity continuous training on body adiposity. Obes Rev 18(8):943–964. https://doi.org/10.1111/obr.12536

Kim KM, Kawada T, Ishihara K, Inoue K, Fushiki T (1997) Increase in swimming endurance capacity of mice by capsaicin-induced adrenal catecholamine secretion. Biosci Biotechnol Biochem 61(10):1718–1723. https://doi.org/10.1271/bbb.61.1718

Kim KM, Kawada T, Ishihara K, Inoue K, Fushiki T (1998) Inhibition by a capsaicin antagonist (capsazepine) of capsaicin-induced swimming capacity increase in mice. Biosci Biotechnol Biochem 62(12):2444–2445

Kuipers H, Verstappen FT, Keizer HA, Geurten P, Van Kranenburg G (1985) Variability of aerobic performance in the laboratory and its physiologic correlates. Int J Sports Med. 6(4):197–201. https://doi.org/10.1055/s-2008-1025839

Leppik JA, Aughey RJ, Medved I, Fairweather I, Carey MF, McKenna MJ (2004) Prolonged exercise to fatigue in humans impairs skeletal muscle Na^+-K^+-ATPase activity, sarcoplasmic reticulum Ca^{2+} release, and Ca^{2+} uptake. J Appl Physiol 97(4):1414–1423. https://doi.org/10.1152/japplphysiol.00964.2003

Leung FW (2014) Capsaicin as an anti-obesity drug. Prog Drug Res 68:171–179

Linari M, Brunello E, Reconditi M, Fusi L, Caremani M, Narayanan T et al (2015) Force generation by skeletal muscle is controlled by mechanosensing in myosin filaments. Nature 528(7581):276–279. https://doi.org/10.1038/nature15727

Lira FS, dos Santos T, Caldeira RS, Inoue DY, Panissa VLG, Cabral-Santos C, Campos EZ, Rodrigues B, Monteiro P (2017) Short-term high- and moderate-intensity training modifies inflammatory and metabolic factors in response to acute exercise. Frontiers Physiol 8:856

Little JP, Safdar A, Wilkin GP, Tarnopolsky MA, Gibala MJ (2010) A practical model of low-volume high-intensity interval training induces mitochondrial biogenesis in human skeletal muscle: potential mechanisms. J Physiol 588:1011–1022

Lotteau. S, Ducreux S, Romestaing C, Legrand C, Van Coppenolle F (2013) Characterization of functional TRPV1 channels in the sarcoplasmic reticulum of mouse skeletal muscle. PLoS One 8(3):e58673. https://doi.org/10.1371/journal.pone.0058673

Ludy MJ, Moore GE, Mattes RD (2012) The effects of capsaicin and capsiate on energy balance: critical review and meta-analyses of studies in humans. Chem Sens 37(2):103–121. https://doi.org/10.1093/chemse/bjr100

Luo Z, Ma L, Zhao Z, He H, Yang D, Feng X et al (2012) TRPV1 activation improves exercise endurance and energy metabolism through PGC-1alpha upregulation in mice. Cell Res 22(3):551–564. https://doi.org/10.1038/cr.2011.205

Margaria R, Edwards HT, Dill DB (1933) The possible mechanisms of contracting and paying the oxygen debt and the rôle of lactic acid in muscular contraction. Am J Physiol Leg Content 106(3):689–715. https://doi.org/10.1152/ajplegacy.1933.106.3.689%3E

Milanovic Z, Sporis G, Weston M (2015) Effectiveness of high-intensity interval training (HIT) and continuous endurance training for VO_{2max} improvements: a systematic review and meta-analysis of controlled trials. Sports Med 45(10):1469–1481. https://doi.org/10.1007/s40279-015-0365-0

Milioni F, Zagatto AM, Barbieri RA, Andrade VL, Dos Santos JW, Gobatto CA et al (2017) Energy systems contribution in running-based anaerobic sprint test. Int J Sports Med 38(3):226–232. https://doi.org/10.1055/s-0042-117722

Oh TW, Ohta F (2003) Capsaicin increases endurance capacity and spares tissue glycogen through lipolytic function in swimming rats. J Nutr Sci Vitaminol 49(2):107–111

Oh TW, Oh TW, Ohta F (2003) Dose-dependent effect of capsaicin on endurance capacity in rats. Br J Nutr 90(3):515–520

Opheim MN, Rankin JW (2012) Effect of capsaicin supplementation on repeated sprinting performance. J Strength Cond Res 26(2):319–326. https://doi.org/10.1519/JSC.0b013e3182429ae5

Panissa VL, Fukuda DH, Caldeira RS, Gerosa-Neto J, Lira FS, Zagatto A et al (2018) Is oxygen uptake measurement enough to estimate energy expenditure during high-intensity intermittent exercise? Quantification of anaerobic contribution by different methods. Front Physiol 9:868. https://doi.org/10.3389/fphys.2018.00868

Rockwell MS, Rankin JW, Dixon H (2003) Effects of muscle glycogen on performance of repeated sprints and mechanisms of fatigue. Int J Sport Nutr Exerc Metab 13(1):1–14

Saunders PU, Pyne DB, Telford RD, Hawley JA (2004) Factors affecting running economy in trained distance runners. Sports Med 34(7):465–485. https://doi.org/10.2165/00007256-200434070-00005

Sawyer BJ, Tucker WJ, Bhammar DM, Ryder JR, Sweazea KL, Gaesser GA (2016) Effects of high-intensity interval training and moderate-intensity continuous training on endothelial function and cardiometabolic risk markers in obese adults. J App Physiol 121:279–288

Shin KO, Moritani T (2007) Alterations of autonomic nervous activity and energy metabolism by capsaicin ingestion during aerobic exercise in healthy men. J Nutr Sci Vitaminol 53(2):124–132

Smith-Ryan AE, Melvin MN, Wingfield HL (2015) High-intensity interval training: Modulating interval duration in overweight/obese men. Phys Sportsmed 43:107–113

Snitker S, Fujishima Y, Shen H, Ott S, Pi-Sunyer X, Furuhata Y et al (2009) Effects of novel capsinoid treatment on fatness and energy metabolism in humans: possible pharmacogenetic implications. Am J Clin Nutr 89(1):45–50. https://doi.org/10.3945/ajcn.2008.26561

Szallasi A, Blumberg PM (1999) Vanilloid (Capsaicin) receptors and mechanisms. Pharmacol Rev 51(2):159–212

Thevenet D, Tardieu M, Zouhal H, Jacob C, Abderrahman BA, Prioux J (2007) Influence of exercise intensity on time spent at high percentage of maximal oxygen uptake during an intermittent session in young endurancetrained athletes. Eur J Appl Physiol 102(1):19–26. https://doi.org/10.1007/s00421-007-0540-6

Townsend J, Stout J, Morton AB, Jajtner AR, González AM, Wells AJ, Mangine., et al (2013) Excess post-exercise oxygen consumption (EPOC) following multiple effort sprint and moderate aerobic exercise. Kinesiology 45(1):16–21

Tremblay A, Arguin H, Panahi S (2016) Capsaicinoids: a spicy solution to the management of obesity? Int J Obes 40(8):1198–1204. https://doi.org/10.1038/ijo.2015.253

Whiting S, Derbyshire EJ, Tiwari B (2014) Could capsaicinoids help to support weight management? A systematic review and meta-analysis of energy intake data. Appetite 73:183–188. https://doi.org/10.1016/j.appet.2013.11.005

Yashiro K, Tonson A, Pecchi É, Vilmen C, Le Fur Y, Bernard M et al (2015) Capsiate supplementation reduces oxidative cost of contraction in exercising mouse skeletal muscle in vivo. PLoS One 10(6):e0128016. https://doi.org/10.1371/journal.pone.0128016

Zafeiridis A, Sarivasiliou H, Dipla K, Vrabas IS (2010) The effects of heavy continuous versus long and short intermittent aerobic exercise protocols on oxygen consumption, heart rate, and lactate responses in adolescents. Eur J Appl Physiol 110(1):17–26. https://doi.org/10.1007/s00421-010-1467-x

Zagatto A, Redkva P, Loures J, Kalva Filho C, Franco V, Kaminagakura E et al (2011) Anaerobic contribution during maximal anaerobic running test: correlation with maximal accumulated oxygen deficit. Scand J Med Sci Sports 21(6):e222–e230. https://doi.org/10.1111/j.1600-0838.2010.01258.x