Capsaicin Supplementation during High-intensity Continuous Exercise: A Double-blind Study

Authors

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ABSTRACT

To investigate the effect of acute capsaicin (CAP) supplementation on time to exhaustion, physiological responses and energy systems contribution during continuous high-intensity exercise session in runners. Fifteen recreationally-trained runners completed two randomized, double-blind continuous high-intensity exercises at the speed eliciting 90 % $\dot{V}O_{2peak}$ (90 % s $\dot{V}O_{2peak}$), 45 minutes after consuming capsaicin or an isocaloric placebo. Time to exhaustion, blood lactate concentration, oxygen consumption during and 20-min post-exercise, energy systems contribution, time to reach $\dot{V}O_{2peak}$, heart rate and the rate of perceived exertion (RPE) were evaluated. There was no significant difference between conditions for time to reach $\dot{V}O_{2peak}$ (CAP:391.71 ± 221.8 vs. PLA:298.20 ± 174.5 sec, ES:0.58, p = 0.872), peak lactate (CAP:7.98 ± 2.11 vs. PLA:8.58 ± 2.15 µmol, ES: − 0.28, p = 0.257), time to exhaustion (CAP:654.28 ± 195.44 vs. PLA:709.20 ± 208.44 sec, ES: − 0.28, p = 0.462, end-of-exercise heart rate (CAP:177.6 ± 14.9 vs. PLA:177.5 ± 17.9 bpm, ES: − 0.10, p = 0.979) and end-of-exercise RPE (CAP: 19 ± 0.8 vs. PLA: 18 ± 2.4, ES: 0.89, p = 0.623). In conclusion, acute CAP supplementation did not increase time to exhaustion during high-intensity continuous exercise nor alter physiological responses in runners.

Introduction

Several sports require performing high-intensity exercise (HIE) over a sustained period, such as in middle distance running and cycling, or short repeated bursts of HIE interspersed with periods of rest or low-intensity exercise, such as in team and racket sports [1]. Energy production necessary for muscle contractions during HIE is derived from anaerobic sources, such as phosphocreatine (PCr) and carbohydrates, and from an important contribution to aerobic sources, via glucose and fatty acid [2]. The reliance on anaerobic energy is determined by the rate and amount of adenosine triphosphate (ATP) necessary for skeletal muscle work [1]. Importantly, such processes can be optimized by the consumption of some ergogenic aids, particularly supplementation with capsaicin (CAP) [3].

CAP, 8-methyl-N-vanillyl-trans-6-nonenamide, is a natural photochemical agent found mostly in red pepper, as well as other foods [4]. Previous studies have shown that the action of CAP is mediated by the transient receptor potential vanilloid-1 (TRPV1), found

in several tissues [5]. After activation of TRPV1, CAP stimulates the increase of sympathetic modulation and thermogenesis [6], and these processes potentiate lipolysis, lipid oxidation, and energy expenditure [7]. CAP also exerts peripheral effects on muscle cells by increasing the release of calcium by the endoplasmic reticulum, allowing a greater sensitization of this ion in the contractile machinery and subsequent greater force production [8, 9]. Therefore, the effects of CAP on physical performance have been investigated in studies with humans and rodents in order to explore possible strategies to optimize physical performance [10, 11].

Our group recently showed that supplementation of 12 mg of CAP increased time to exhaustion in high-intensity intermittent exercise (running 15 s at the speed corresponding to 120 % of $\dot{V}O_{2max}$ interspersed by 15 s of passive recovery), a typical protocol to improve aerobic power, but this performance improvement was not associated with changes in energy system contribution and variables related to oxygen uptake (time above 90 % of $\dot{V}O_{2max}$ and time to reach $\dot{V}O_{2max}$) [10]. However, the examination of energy system contribution during intermittent exercise is limited because the glycolytic contribution is mostly based on assumptions derived from lactate accumulation during overall exercise, with no access to the rate of accumulation and clearance. Furthermore, the phosphagen system contribution is also only estimated from oxygen uptake measured during the recovery periods between efforts [12]. A more objective way to identify energy system contribution is using a unique high-intensity effort, which has been widely used to identify energy system contribution among different conditions [13–15].

Therefore, the purpose of this study was to investigate the effects of CAP supplementation on time to exhaustion, physiological responses, and energy system contribution during continuous high-intensity exercise in recreationally rained runners. Based on previous work pointing to improved metabolic efficiency, we hypothesized that CAP supplementation would increase the time to exhaustion with the same oxidative system contribution.

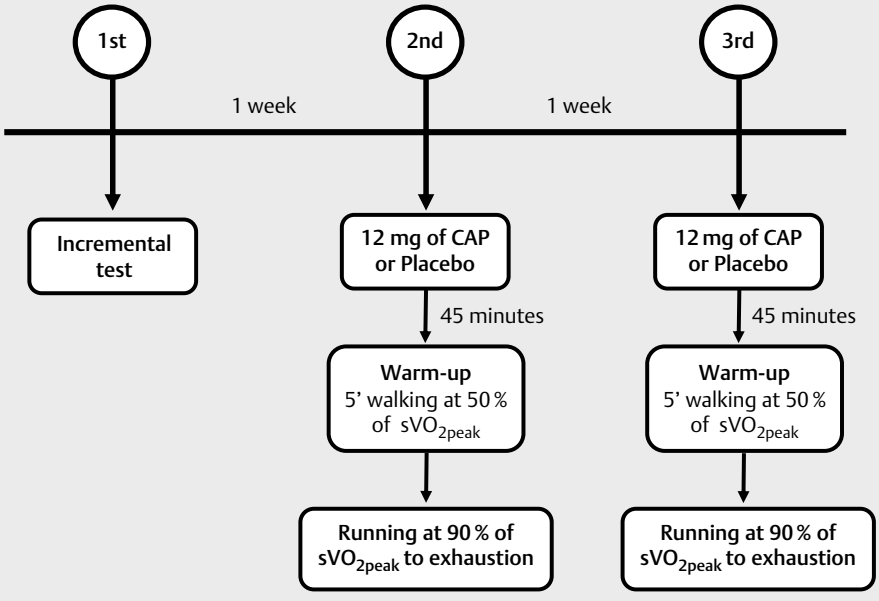
Materials and Methods

Experimental approach to the problem

This study was conducted in accordance with a double-blind and placebo-controlled design (▶ **Fig. 1**). The subjects completed three experimental trials at the same time of day (7–9 AM) separated by 72 h. At the first visit, anthropometric measurements were evaluated and the incremental test was performed to determine peak oxygen uptake ($\dot{V}O_{2peak}$) and the speed associated with $\dot{V}O_{2peak}$ (s $\dot{V}O_{2peak}$). At the next two visits, the participants randomly consumed either the placebo or capsaicin and then completed a running-time-to-exhaustion test at 90 % s $\dot{V}O_{2peak}$. The lactate from blood sample concentration was analyzed at baseline, immediately after, and 3, 5 and 7 minutes after the test. The oxygen uptake was measured during rest, warm-up, exercise, and up to 20 min after the end of the tests to determine metabolic cost. Rate of perceived exertion (RPE) and heart rate (HR) were analyzed at rest, during warm-up and the test, immediately after the test, and then every 5 min for up to 20 min.

Subjects

Fifteen young adult men who were recreationally trained runners were recruited to participate in this study (22.1 ± 3.07 y; 179.4 ± 0.6 cm; 74.3 ± 10.2 kg; $\dot{V}O_{2Peak}$ = 53.6 ± 5.7 mL/kg/min). The inclusion criteria adopted were as follows: participating in regimented running training during the previous 6 months with a minimum weekly frequency of twice a week; between 18 to 35 years old; no musculoskeletal and cardiovascular contraindications that would interfere with the exercise protocol; and last but not least,



▶ **Fig. 1** Experimental study design.

not having ingested any ergogenic substance and not smoking in the last 12 months. After approval by the Ethics Research Group, this study was conducted according to the 2013 revision of the Declaration of Helsinki [16] and meets the ethical standards of the International Journal of Sports Medicine [17]. The participants signed a consent form and were informed about the purpose of the study and the possible risks.

Anthropometric measurements and supplementation protocol

Height was measured using a fixed stadiometer with an accuracy of 0.1 cm and the participant's body weight was measured using an electronic scale (Filizola PL50, Filizola Ltda., Brazil). Body composition components (free fat mass and fat mass) were estimated by bioelectrical impedance (Bia Analyzer; Nutritional Solutions Corp., Harrisville, MI, USA). Participants were instructed to arrive fed at the laboratory at least one hour and a half before each experimental trial and were instructed not to consume any spicy foods or any stimulant drinks (e.g., coffee, tea or alcohol) during the study period.

At 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). The capsules were identical and contained no flavor, and a person who was not part of the research team was assigned to deliver the supplements to every subject. Placebo or CAP was taken in the laboratory 45 min prior to the experimental trial [3]. The capsules were standardized to contain 40 % capsaicinoids (capsiate) and the final product contained a 50 % extract from capsicum (Purifarma-Gemini Pharmaceutical Industry Ltda, Anapolis, GO, Brazil). The correction factor in assay calculation was used to guarantee 100 % capsaicinoids. This dosage was selected because other studies have reported that supplementation of more than 33 mg per day of capsaicinoids increases gastric motility [18].

Incremental test

The incremental test was conducted on a treadmill (Inbramed MASTER CI, Inbrasport®, Porto Alegre, Brazil). Participants started the test at an initial speed of 6 km.h^{-1} and then increased by 1 km.h^{-1} every 2 min. The test was interrupted when the participants reached their volitional exhaustion. The oxygen uptake ($\dot{V}O_2$) was measured using Quark PFT (Cosmed®, Rome, Italy) during the test and the average of the last 30 s defined as $\dot{V}O_{2Peak}$. The s $\dot{V}O_{2Peak}$ was assumed based on the time in the final stage, as demonstrated in the 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] [19].

Continuous high-intensity exercise protocol

The participants engaged in a running training routine of short and middle distances at least twice a week. They were all familiar with this type of effort. At each experimental trial, the participants performed a warm-up at 50 % of s $\dot{V}O_{2peak}$ for 5 min at 1 % treadmill incline. The participants performed the continuous exercise protocol session until exhaustion at 90 % of s $\dot{V}O_{2peak}$. Both experimental trials were conducted until voluntary exhaustion, which was determined when the participants were no longer capable of maintaining the pace. Performance was determined by time to exhaustion (in seconds).

Blood lactate and rate of perceived exertion

The lactate concentration was analyzed in blood samples collected from the ear lobe at rest, immediately after, and 3, 5, and 7 minutes after the exercise protocol. To compare both exercise sessions, the delta lactate (highest value minus rest values - [ΔLa^-]) was utilized. The analyses were performed using a lactate analyzer (YSI 1500 Sport; Yellow Spring Instruments, Yellow Springs, OH, USA). RPE was measured at rest, after warm-up, immediately after, and five, ten, fifteen, and twenty minutes after the exercise session using the 6–20 point Borg scale [20].

Oxygen uptake

$\dot{V}O_2$ was measured during rest, warm-up, exercise, and 20 min post-exercise to examine the excess of post-exercise oxygen consumption (EPOC). Time spent to reach 100 % of $\dot{V}O_{2peak}$ was determined from VO_2 values relative to the respective percentages of $\dot{V}O_{2peak}$. The calculation of this time was conducted observing the average 5-s periods. EPOC was calculated by subtracting resting $\dot{V}O_2$ from average of $\dot{V}O_2$ during 20-min recovery [21].

Energy expenditure

Energy expenditure was estimated from oxidative, glycolytic, and phosphagen energy systems [22, 23]. The contribution of the oxidative energy system was assumed as an integral $\dot{V}O_2$ area during effort. 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 [22]. The phosphagen energy system contribution was assumed by adjustment of the relative values of $\dot{V}O_2$ 20 min post-exercise. All oxygen equivalents were converted to energy equivalents assuming 20.92 kJ for each 1L of O_2 utilized prior to exergy expenditure evaluation. The overall energy expenditure was estimated by the sum of the contributions of the oxidative and anaerobic energy systems [24].

Statistical analysis

Data are reported as means and standard deviation (SD). Data normality was verified using the Shapiro-Wilk test. A paired *t*-test was used to compare conditions (placebo and capsaicin). Statistical significance was set at $p < 0.05$. 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)). The data were analyzed using GraphPad Prism 7.

Results

▶ **Table 1** presents the mean and SD of participants' general characteristics. ▶ **Table 2** presents the means and SD, and lower and upper values of physiological responses in the placebo and capsaicin conditions. There was no significant difference between conditions for time to reach $\dot{V}O_{2peak}$ (CAP: 391.71 ± 221.8 vs. PLA: 298.20 ± 174.5 sec, ES: 0.58, $p = 0.872$, t: 0.163); peak [La^-] (CAP: 7.98 ± 2.11 vs. PLA: 8.58 ± 2.15 µmol, ES: –0.28, $p = 0.257$, t: 1.18);

final session HR (CAP: 177.6 ± 14.9 vs. PLA: 177.5 ± 17.9 bpm, ES: −0.10, $p = 0.979$, t: 0.02); and final session RPE (CAP: 19 ± 0.8 vs. PLA: 18 ± 2.4, ES: 0.89, $p = 0.623$, t: 1.90). Besides, there was no significant difference for time to exhaustion between conditions (CAP: 654.28 ± 195.44 vs. PLA: 709.20 ± 208.44 sec, ES: − 0.28, $p = 0.462$, t: 0.74). Importantly however, 4 out of 15 subjects presented performance higher than the determined SWC boundary (▶ **Fig. 2**).

▶ **Table 3** presents the means and SD, lower 95 % CI, and upper 95 % CI values of the relative and absolute energy system contribution for each condition (placebo and capsaicin). There was no significant difference for absolute values of oxidative system contribution (ES: − 0.17, p = 0.583, t: 0.22), glycolytic system contribution (ES: − 0.24, p = 0.828, t: 0.81), and energy expenditure in $EPOC_{20min}$ (ES: 0.21, p = 0.490, t: 0.75).

▶ **Table 1** General characteristics of participants.

Variables	Mean ± SD
Age (years)	22.1 ± 3.0
Height (cm)	179.0 ± 0.6
Weight (kg)	74.3 ± 10.1
Fat mass (kg)	12.6 ± 6.7
Fat-free mass (kg)	63.6 ± 6.4
VO_2 peak ($L \cdot min^{-1}$)	3.89 ± 0.5
VO_2 peak ($mL \cdot min^{-1} \cdot Kg^{-1}$)	53.6 ± 5.7
Maximal aerobic speed (km/hr^{-1})	14.1 ± 2.0
Resting HR (bpm)	74.9 ± 12
Maximal HR (bpm)	177.5 ± 17.9

Data are presented as mean ± standard deviation (SD). VO_2 peak, peak oxygen uptake; HR, heart rate.

Discussion

To the best of our knowledge, this study is the first to investigate the effects of CAP supplementation on performance and physiological responses during a continuous high-intensity exercise to exhaustion in recreationally trained adult male runners.

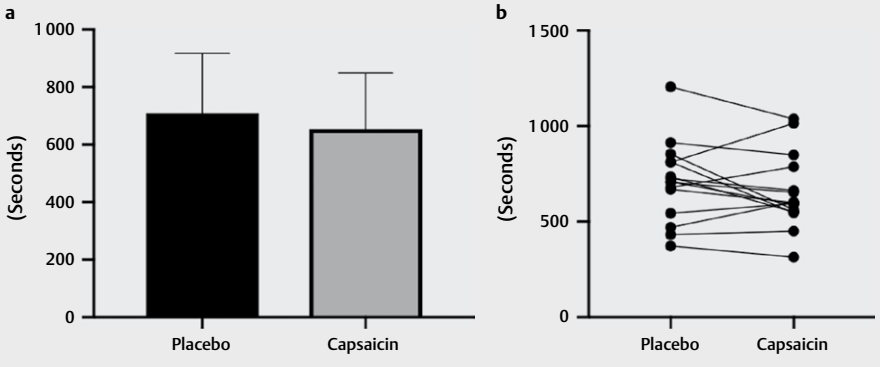
The main findings of this present study were that CAP supplementation did not improve performance or physiological responses during this type of exercise. Thus, our results refute our initial hypothesis that CAP supplementation would be an ergogenic aid by increasing the time to exhaustion with the same energy expenditure during effort. Our results are in agreement with the study by Opheim and Rankin (2012) [25]. On the other hand, previous studies from our research group reported the ergogenic effects of CAP in different exercise protocols. Recently, De Freitas and colleagues (2019) investigated the effect of CAP supplementation on time to exhaustion in high-intensity intermittent exercise (120 % $\dot{V}O_{2max}$) in physically active men. The authors demonstrated an increase in time to exhaustion of 188 s (13 % increase of performance) during high-intensity interval exercise (HIIE), which corresponded to 13 more efforts performed in CAP than in the placebo condition but without modified oxygen consumption during and post-exercise, time spent above 90 % of $\dot{V}O_{2Peak}$, and RPE in physically active men [10], corroborating our current study. Therefore, it seems that CAP supplementation may improve performance, but the effects depend on the protocol used, such as HIIE and moderate continuous aerobic exercise (i.e., 1500 m), but not in continuous high-intensity exercise to exhaustion. That said, physiological outcomes were not affected by CAP in either HIIE or continuous high-intensity [26].

Currently, there is insufficient research regarding the effects of CAP supplementation on performance and physiological respons-

▶ **Table 2** Physiological responses for capsaicin and placebo condition (n = 15).

	Placebo			Capsaicin		
	Lower 95 % CI	Mean ± SD	Upper 95 % CI	Lower 95 % CI	Mean ± SD	Upper 95 % CI
Time to reach $\dot{V}O_2$peak (s)	240.9	325.3 ± 154.2	450.5	210.1	391.7 ± 221.8	509.7
Peak [La^-] (mmol/L)	7.38	8.58 ± 2.15	9.76	6.81	7.98 ± 2.11	9.15
Final session HR (bpm)	167	177 ± 17	187	168	177 ± 14	186
Final session RPE (a.u.)	16.7	18.1 ± 2.4	19.4	18	19.3 ± 0.8	19.59

Data are presented in lower 95 % CI, mean ± SD, and upper 95 % CI of placebo and capsaicin condition.



▶ **Fig. 2** Time to exhaustion in CAP and placebo condition. Mean and SD values **a** and individual response values **b**.

▶ **Table 3** Energy system contribution for each condition.

	Placebo			Capsaicin		
	Lower 95 % CI	**Mean ± SD**	**Upper 95 % CI**	**Lower 95 % CI**	**Mean ± SD**	**Upper 95 % CI**
Relative						
Oxidative (%)	83.5	92.3 ± 3.0	96.0	84.5	91.4 ± 3.2	96.3
Glycolytic (%)	2.3	4.1 ± 1.9	8.4	2.3	4.3 ± 1.6	7.2
Phosphagen (%)	1.6	3.6 ± 1.6	8.2	1.4	4.3 ± 1.9	8.5
Absolute						
Oxidative (Kcal)	78.9	193.3 ± 71.2	350.1	70.2	180.3 ± 71.8	347.8
Glycolytic (Kcal)	3.3	8.1 ± 3.1	16.2	0.6	7.5 ± 2.6	14.4
Phosphagen (kcal)	3.6	7.3 ± 2.3	10.5	3.5	7.1 ± 1.9	10.2
VO_2 (L)	15.8	38.6 ± 14.2	56.0	21.4	36.0 ± 14.4	69.6
$EPOC_{5min}$ (L)	0.7	1.5 ± 0.4	2.1	0.7	1.4 ± 0.3	2.0
$EPOC_{20min}$ (L/min)	1.7	2.6 ± 0.7	4.3	1.4	2.3 ± 0.8	3.6
Delta lactate (mmol/l)	3.2	7.2 ± 2.4	11.9	3.7	6.6 ± 2.6	11.9

Data are presented in lower 95 % CI, mean ± SD, and upper 95 % CI in placebo and capsaicin condition.

es in humans. One may speculate that differences in exercise protocol duration and participant training status could contribute to the discrepancies reported in the above-mentioned studies. In fact, a pioneer study published by Hermansen and colleagues (1967) investigated the pattern of glycogen depletion during prolonged exercise. The results showed that the pattern of glycogen decrease over time was the same during both continuous exercise and intermittent work [27]. Thus it is now well-known that the improvement in endurance performance is partially attributed to the sparing of muscle glycogen as a result of higher lipolysis via a greater release of epinephrine, norepinephrine, and free fatty acids during exercise induced by CAP supplementation [28].

Peripheral fatigue is the most likely limiting factor during exercise performance, resulting in part from the lower calcium release by the sarcoplasmic reticulum caused by the accumulation of hydrogen ions and inorganic phosphates [29], which in turn leads to impairment in contraction efficiency and myofibril force production [8]. In this scenario, CAP may improve physical performance owing to its different impact on the transient receptor potential TRPV1 activation within the skeletal muscle [11]. The activation of this receptor increases calcium release by the sarcoplasmic reticulum, which results in a higher interaction of actin-myosin filaments and increases the force production [9]. Despite the lack of difference between CAP and PLA in the present study for lactate concentration and energy system contribution during continuous high-intensity exercise, we still believe that less energy may be needed for a similar and/or greater amount of force production during exercise [30–32]. Overall, we suggest CAP could be a potent ergogenic aid for intermittent, but not continuous, exercise. Our data indicate that CAP could enhance the training load (and thereby adaptations) during high-intensity interval training, but appears of limited help for other types of training. Furthermore, additional mechanistic and applied studies are warranted with other populations (e.g., overweight/obese, deconditioned, women) to confirm or refute these findings and better comprehend the impact of the characteristics of the exercise.

In conclusion, CAP supplementation did not increase time to exhaustion during high-intensity continuous exercise at 90 % of the speed eliciting $\dot{V}O_{2peak}$ or alter positively the physiological responses in recreationally trained runners.

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Conflict of Interest

The authors declare they have no conflict of interest.

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