

The use of energy drinks in sport: perceived ergogenicity and side effects in male and female athletes

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Abstract

The use of caffeine containing energy drinks has dramatically increased in the last few years, especially in the sport context because of its reported ergogenic effect. The ingestion of low to moderate doses of caffeinated energy drinks has been associated with adverse side effects such as insomnia or increased nervousness. The aim of the present study was to assess psycho-physiological changes and the prevalence of side effects resulting from the ingestion of 3 mg caffeine/kg body mass in the form of an energy drink. In a double-blind and placebo controlled experimental design, ninety experienced and low-caffeine-consuming athletes (fifty-three male and thirty-seven female) in two different sessions were provided with an energy drink that contained 3 mg/kg of caffeine or the same decaffeinated energy drink (placebo; 0 mg/kg). At 60 min after the ingestion of the energy drink, participants completed a training session. The effects of ingestion of these beverages on psycho-physiological variables during exercise and the rate of adverse side effects were measured using questionnaires. The caffeinated energy drink increased self-perceived muscle power during exercise compared with the placebo beverage (6.41 (SD 1.7) *v.* 5.66 (SD 1.51); $P=0.001$). Moreover, the energy drink produced a higher prevalence of side effects such as insomnia (31.2 *v.* 10.4%; $P<0.001$), nervousness (13.2 *v.* 0%; $P=0.002$) and activeness (16.9 *v.* 3.9%; $P=0.007$) than the placebo energy drink. There were no sex differences in the incidence of side effects ($P>0.05$). The ingestion of an energy drink with 3 mg/kg of caffeine increased the prevalence of side effects. The presence of these side effects was similar between male and female participants.

Key words: Energy drinks: Side effects: Ergogenic effects: Sport: Sex differences

Caffeine (1,3,7-trimethylxanthine) is a natural alkaloid present in varying quantities in the leaves, fruits and seeds of various plants (coffee, kola, tea, maté, etc.). Furthermore, caffeine can be artificially synthesised in the laboratory and is frequently included in over-the-counter medications, nutritional supplements and commercially available beverages⁽¹⁾. Caffeine is the most frequently consumed psychoactive drug in the current society, despite this substance having no nutritional value and not being essential for any physiological process⁽²⁾. However, caffeine is a potent stimulant of the central nervous system and is primarily used for increasing vigour and activeness, warding off drowsiness and restoring alertness. In the sport setting, caffeine is also the most consumed substance⁽³⁾ because of its effectiveness to increase performance in a wide variety of sport disciplines⁽⁴⁾. The amount of caffeine consumed per d depends on many factors, such as the source of intake, age, sex, nutritional status, fitness level, peer behaviour and habituation⁽⁵⁾.

Caffeine metabolism is quite different between habitual caffeine consumers and non-consumers⁽⁶⁾. The sensitivity of

caffeine consumers to the mood- and performance-enhancing effects of caffeine is related to their levels of habitual intake⁽⁷⁾. A greater and longer-lasting ergogenic effect has been found for non-consumers than for caffeine consumers after a dose of 5 mg caffeine/kg⁽⁸⁾. Furthermore, genetic diversity can influence the response to caffeine, especially by genetic variations in cytochrome P-450 enzymes, responsible for caffeine metabolism, and by variations in A_{2A} receptors, which play a role in the effects of caffeine on arousal⁽⁹⁾.

The main sources of caffeine in nutritional products are brewed coffee, tea, cocoa products and cola beverages. Moreover, the ingestion of caffeine-containing energy drinks has dramatically increased in the last few years, especially in the sport context⁽¹⁰⁾. Nowadays, energy drinks have become the most widely used means of caffeine intake in the sports population^(10–12). Energy drinks contain carbohydrate, caffeine and/or other nutrients that may affect mental focus and concentration, and have the potential to affect exercise capacity and perceptions of energy and/or fatigue⁽¹³⁾. Current evidence,

Abbreviation: RPE, rate of perceived exertion.

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although scarce, suggests that consumption of energy drinks is safe in a healthy population and similar to ingesting other foods and beverages containing caffeine⁽¹³⁾. For adults consuming moderate amounts of coffee (3–4 cups/d, providing 300–400 mg caffeine/d), there is little evidence of health risks and some evidence of health benefits^(14,15). However, some groups, including individuals with hypertension, children, adolescents and the elderly, may be more vulnerable to the adverse effects of caffeine intake⁽¹⁴⁾.

The ingestion of caffeine or caffeinated products is typically accompanied by several side effects including insomnia, nervousness, restlessness, gastric irritation, nausea, vomiting, tachycardia, tremors and anxiety^(13,16). In a survey about energy drink consumption patterns among college students, Malinauskas *et al.*⁽¹⁷⁾ found that, in energy drink users who consumed greater than one energy drink per month, the most frequent side effects were jolt (increased alertness and energy) and crash (sudden drop in energy) episodes (29% of users), headaches (22% of users) and heart palpitations (19% of users). Moreover, there was a significant dose–effect relationship between the volume of energy drink consumed and the frequency of jolt and crash episodes.

Different national and international poison centres have reported several adverse events associated with consumption of energy drinks including liver damage, kidney failure, agitation, seizures, tachycardia, cardiac dysrhythmias, hypertension and sudden death. The minimum and maximum symptomatic caffeine levels have been reported to be 4 mg/kg in a 13-year-old patient and 36 mg/kg in a 14-year-old patient, respectively⁽¹⁸⁾.

During exercise, the acute ingestion of caffeine at a dose of 9 mg/kg body mass has been found to drastically increase the frequency of adverse side effects compared with caffeine ingestion at a dose of 3 or 6 mg/kg⁽¹⁹⁾. Especially, insomnia (54%), increased urine production (54%) and gastrointestinal problems (38%) augmented at a dose of 9 mg/kg⁽¹⁹⁾. Lower doses (e.g. 3 mg/kg body mass) increased the feeling of vigour and activeness in comparison to a placebo without caffeine content, but did not increase other side effects such as gastrointestinal problems or insomnia⁽²⁰⁾.

In contrast, ingestion of energy drink can improve psychophysiological factors related to exertion in exercise⁽²¹⁾. Caffeine ingestion has been demonstrated to change the mood state response to exercise, with a greater vigour score and a lower fatigue score compared with placebo ingestion^(22,23). Ingestion of caffeine has been shown to induce a reduction in the rate of perceived exertion (RPE) in exercise^(21,24–27), decreasing muscular pain perception^(26,27) and increasing the readiness to invest effort^(21,27). Moreover, caffeine has been reported to enhance executive control and working memory, and to reduce reaction times in simple and choice reaction time tasks^(23,28).

Sex interaction in terms of the effects of caffeine is still not clear. In a randomised double-blind placebo study on 688 young adults (238 men and 450 women), caffeine administration induced a greater decrease in somnolence in men than in women. Moreover, the increase in subjective activation after the administration of a caffeinated beverage was greater in men than in women⁽²⁹⁾. Similarly, Temple *et al.*⁽³⁰⁾ found in

young individuals that males may be more susceptible to the reinforcing effects of caffeine. In the prevalence of different adverse effects after ingestion of energy drinks, Malinauskas *et al.*⁽¹⁷⁾ did not find differences between male and female participants in a survey-based study. In the use of energy drinks with exercise, no sex interactions were found in relation to the effects of caffeine on RPE, mood state and readiness to invest physical effort in endurance activities⁽²⁷⁾.

The aim of the present study was to assess psycho-physiological changes and the prevalence of side effects resulting from the ingestion of 3 mg caffeine/kg body mass in the form of an energy drink, and to determine the differences between males and females in these potential effects.

Experimental methods

Participants

A total of ninety-eight athletes from seven different sport disciplines (rugby, volleyball, tennis, badminton, swimming, soccer and hockey) volunteered to participate in the study (Table 1). All of them competed at the national or regional level with more than 8 years of training experience in their disciplines and over 5 h of weekly training. Thus, the study sample can be categorised as experienced and trained athletes. All the participants were especially recruited because they were light caffeine consumers (<60 mg/d, approximately 1 cup of coffee). Participants were non-smokers and were not under medical treatment during the study period. Of these participants, eight did not complete all the required experimental protocols and their results were excluded from the statistical analysis. Thus, the study sample was composed of ninety participants (fifty-three male, thirty-seven female). We performed *a priori* statistical power analysis based on a previous study with the same caffeinated energy drink⁽²⁰⁾. To obtain significant differences between the ingestion of a caffeinated energy drink *v.* a placebo drink with an 80% of statistical power and with an α value of 1.96 (95% of confidence), we required a sample size of seventy-four participants to detect changes in nervousness or gastrointestinal side effects.

The present study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving human subjects were approved by the Camilo José Cela University Ethics Committee. Written informed consent was obtained from all subjects. All this individual information was obtained by pre-recruiting questionnaires. Once participants fulfilled the inclusion criteria, they were fully informed

Table 1. Age and anthropometric characteristics of the study sample (Mean values and standard deviations, *n* 90)

	<i>n</i>	Age (years)		Body weight (kg)		Height (cm)	
		Mean	SD	Mean	SD	Mean	SD
Total	90	23.9	5.7	70.4	11.2	173.7	10.1
Male	53	25.0	6.2	75.9	9.3	178.9	7.1
Female	37	23.2	4.5	63.2	8.1	167.1	9.5

of any risks and discomforts associated with the experiments and gave their informed written consent to participate. The study was approved by a local Research Ethics Committee in accordance with the latest version of the Declaration of Helsinki.

Experimental design

A double-blind and placebo-controlled experimental design was used for the present study. Each participant took part in two different experimental trials under the same experimental conditions and standardisations. The order of the experimental trials (e.g. caffeinated energy drink or placebo beverage) was randomised for each participant. To control for the order effects, the order of the experimental trials was counterbalanced and forty-five participants performed caffeinated energy drink and placebo beverage order while the remaining forty-five participants performed the placebo beverage and caffeinated energy drink order. To comply with these two criteria, each participant was assigned with a number by an experimenter who did not take part in the experiment. Odd numbers received the caffeinated energy drink and placebo beverage order while even numbers received the placebo beverage and caffeinated energy drink order. The experimental trials were separated by 1 week to allow complete caffeine washout. On one occasion, participants ingested 3 mg caffeine/kg body mass (3 mg/kg) by means of a powdered caffeine-containing energy drink (Fure®; Pro-Energetics) dissolved in 250 ml of tap water. On another occasion, participants ingested the same amount of energy drink but with no caffeine content (placebo; 0 mg/kg). The two experimental drinks had a similar taste and appearance and they only differed in the amount of caffeine they contained. The energy drinks also contained taurine (18.7 mg/kg), sodium bicarbonate (4.7 mg/kg), L-carnitine (1.9 mg/kg) and maltodextrin (6.6 mg/kg); however, these substances were ingested in identical proportions in the two experimental trials. Both experimental trials were performed at the same time of the day to avoid the effects of circadian rhythms in the studied variables⁽³¹⁾.

The experimental beverages were ingested 60 min before the onset of the experimental trials to allow for complete caffeine absorption⁽³²⁾, and they were provided in opaque plastic bottles to avoid identification. An alphanumeric code was assigned to each trial to blind participants and investigators to the beverage tested.

Standardisation

The day before each experimental trial, participants were nude weighed (± 50 g; Radwag) to calculate the amount of caffeine required for each individual caffeinated energy drink. The amount of the energy drinks was individually calculated to avoid the effects of body mass on the variables under investigation. On that day, participants refrained from strenuous exercise and adopted a similar diet and fluid intake regimen. Participants were encouraged to withdraw from all dietary sources of caffeine (coffee, cola drinks, chocolate, etc.) and alcohol 48 h before testing. In addition, participants were instructed to have a light meal at least 2 h before the onset of the experimental trials. These standardisations were reported

to the technical staff of the teams and food and fluid diaries were obtained to ensure compliance.

Experimental protocol

On the day of testing, participants ingested the corresponding beverage (caffeine-containing energy drink or placebo energy drink) and completed a specific sport session, including a standardised warm-up and a simulated competition. Thereafter, participants were required to fill out a questionnaire about their sensations of muscle power, endurance and perceived exertion (RPE) during the test. This questionnaire included a 1- to 10-point scale to assess each item, and participants were previously informed that 1 point meant minimal amount of that item and 10 points meant maximal amount of the item. Moreover, participants were asked to indicate on a yes/no scale whether they had had any perceptible effect. In addition, participants were provided with a survey to be filled out before going to sleep about nervousness, gastrointestinal problems, muscular pain, headache and activeness they had perceived in the hours after the drink ingestion. In the following morning after the ingestion of the energy drinks, participants were asked about sleep quality (e.g. insomnia) on a yes/no scale and about perceived fatigue on a 1- to 10-point scale. This survey has been previously used to assess side effects resulting from energy drink ingestion⁽²⁰⁾. Participants who did not complete these questionnaires on time were eliminated from the analysis. Thus, eight participants were excluded from the statistical analysis based on this criterion, as indicated in the 'Participants' section.

Statistical analysis

Results of quantitative data are presented as means and standard deviations. Differences in the 1- to 10-point scale were analysed using the Wilcoxon signed-rank test. Effect size was calculated (Cohen's *d*) for each item. Results of qualitative data (e.g. side effects) are presented as percentages. Differences in side effects after beverage intake were analysed using the McNemar test. Sex influences on the tested variables were verified by using a general linear model and a two-way repeated-measures ANOVA (beverage \times sex). The criterion for statistical significance in all these tests was set at $P < 0.05$. The SPSS for Windows 19.0 statistical package (SPSS, Inc.) was used to analyse the data.

Results

Table 2 outlines the perception of muscle power, endurance and exertion of athletes during their sport practice after the ingestion of the caffeine-containing energy drink or the placebo energy drink. In comparison to the placebo energy drink, the pre-exercise ingestion of the caffeine-containing energy drink significantly increased muscle power perception during exercise ($P = 0.001$), although the effect size was low ($d = 0.13$). The increased muscle power perception was present in both male ($d = 0.10$; $P = 0.019$) and female participants ($d = 0.18$; $P < 0.05$). On the contrary, there were no differences in perceived endurance and exertion ($P > 0.05$).

Table 2. Subjective perception of power, endurance and exertion of athletes during exercise after ingestion of a caffeine (CAFF)-containing energy drink or a placebo (PLA) energy drink

 (Mean values and standard deviations; mean differences and 95 % confidence intervals, n 90)

		CAFF		PLA		Mean difference	95 % CI	<i>P</i>	<i>P</i> (two-way ANOVA; sex×PLA/CAFF)
		Mean	SD	Mean	SD				
Power	Total	6.41	1.7	5.66	1.51	0.75	0.33, 1.18	0.001*	0.288
	Male	6.23	1.61	5.66	1.52	0.57	0.08, 1.06	0.019*	
	Female	6.68	1.75	5.65	1.51	1.03	0.26, 1.80	0.014*	
Endurance	Total	6.10	1.79	5.83	1.69	0.27	-0.21, 0.74	0.255	0.339
	Male	6.02	1.89	5.94	1.61	0.08	-0.46, 0.61	0.832	
	Female	6.22	1.67	5.68	1.81	0.54	-0.35, 1.43	0.197	
Exertion	Total	5.70	1.68	5.40	2.06	0.30	-0.15, 0.77	0.130	0.941
	Male	6.00	1.48	5.68	1.94	0.32	-0.16, 0.81	0.130	
	Female	5.26	1.88	4.97	2.19	0.29	-0.64, 1.21	0.514	

 * $P < 0.05$.

The caffeinated energy drink was equally ineffective with regard to the subjective feelings of endurance and exertion in male and female athletes. Overall, caffeine effects on perceived power, endurance and exertion were of the same magnitude in male and female athletes (interaction sex × drink condition; $P > 0.05$).

In the morning after the intake of the experimental beverage, females showed higher perceived fatigue after the intake of the placebo beverage ($d = 0.17$; $P = 0.035$), while males showed no effect ($d = 0.08$; $P = 0.109$; Table 3). There was a statistically significant effect observed for sex interaction ($P = 0.008$).

The ingestion of the caffeinated energy drink produced a higher prevalence of side effects such as insomnia (31.2% caffeine *v.* 10.4% placebo; $P < 0.001$), nervousness (13.2% caffeine *v.* 0% placebo; $P = 0.002$) and activeness (16.9% caffeine *v.* 3.9% placebo; $P = 0.007$) than the ingestion of the placebo energy drink (Table 4). In these three variables, there were significant differences in the female subpopulation, while in the male subpopulation there were only significant differences between caffeine and placebo in the prevalence of insomnia. There were no sex differences in the incidence of side effects (sex × beverage interaction; $P > 0.05$).

As shown in Fig. 1, the ingestion of 3 mg caffeine/kg in the form of an energy drink produced an appreciable effect in 37% of the participants, while ingestion of the placebo energy drink also produced appreciable effects only in 12.3% of the participants ($P = 0.001$). In males, 36.2% of participants reported appreciable effects after the ingestion of the caffeinated energy drink while 10.6% reported these effects with the placebo

($P = 0.012$). In females, similar results were obtained (38.2 *v.* 14.7%; $P = 0.057$). There was no effect observed for the sex × beverage interaction ($P = 0.556$).

Discussion

The aim of the present study was to assess psycho-physiological changes and side effects resulting from the ingestion of a caffeinated energy drink in a group of trained individuals. For this purpose, we provided a caffeinated energy drink (3 mg caffeine/kg body mass) or a placebo energy drink 60 min before a regular training session, and measured subjective feelings of performance and side effects for 24 h after the ingestion of these beverages. In comparison to the placebo beverage, ingestion of the caffeinated energy drink enhanced the subjective perception of muscle power during exercise and reduced overall fatigue the following morning after the intake of the beverage. Moreover, the caffeinated energy drink increased the prevalence of side effects such as insomnia, activeness and nervousness. Interestingly, the caffeinated energy drink affected both male and female participants in a similar manner.

In comparison to the placebo energy drink, the pre-exercise ingestion of the caffeinated energy drink increased power perception during exercise ($P = 0.001$). In contrast to endurance activities, where the ergogenic benefits of caffeine ingestion have been repeatedly evidenced⁽³³⁾, in activities with a clear reliance on anaerobic pathways controversial results have been obtained. While several studies have failed to find improvements^(34–36), more recent studies^(19,20,37) have reported enhanced muscle power output with an identical

Table 3. Subjective perception of fatigue of athletes after ingestion of a caffeine (CAFF)-containing energy drink or a placebo (PLA) energy drink

 (Mean values and standard deviations; mean differences and 95 % confidence intervals, n 90)

		CAFF		PLA		Mean difference	95 % CI	<i>P</i>	<i>P</i> (two-way ANOVA; sex×PLA/CAFF)
		Mean	SD	Mean	SD				
Perceived fatigue	Total	5.25	2.11	5.40	2.19	-0.15	-0.66, 0.34	0.540	0.008
	Male	5.69	1.77	5.29	1.93	0.40	-0.16, 0.97	0.109	
	Female	4.62	2.41	5.57	2.52	-0.95	-10.82, -0.07	0.035*	

 * $P < 0.05$.

Table 4. Prevalence of side effects after ingestion of a caffeine (CAFF)-containing energy drink or a placebo (PLA) energy drink†

Item		% CAFF (all)	% PLA (all)	<i>P</i>	<i>P</i> (by sex)
Nervousness	Total	13.2	0	0.002*	0.291
	Male	3.6	0	0.125	
	Female	24	0	0.031*	
Insomnia	Total	31.2	10.4	<0.001*	0.705
	Male	25	7.5	0.002*	
	Female	37.8	13.5	0.022*	
Gastrointestinal problems	Total	10.5	5.3	0.508	0.592
	Male	10	2.5	0.625	
	Female	11.1	8.3	1.000	
Activeness	Total	16.9	3.9	0.007*	0.580
	Male	12.5	5.0	0.146	
	Female	21.6	2.7	0.039*	
Irritable	Total	3.9	3.9	0.688	0.689
	Male	2.5	2.5	0.625	
	Female	5.6	5.6	1.000	
Muscular pain	Total	28.6	35.1	0.556	0.730
	Male	27.5	27.5	1.000	
	Female	29.7	43.2	0.267	
Headache	Total	7.8	11.7	1.000	0.150
	Male	10	2.5	0.109	
	Female	5.4	21.6	0.109	

* $P < 0.05$.

† Data are percentage affirmative responses obtained from ninety trained athletes.

dose (e.g. 3 mg/kg) to that used in the present study. Therefore, subjective perception of participants about muscle power coincides with empirical data obtained in experimental conditions.

In contrast, the administration of the caffeine-containing energy drink did not produce any differences in the subjective feelings of endurance and exertion during the practice of a high-intensity exercise bout with respect to the placebo drink ($P > 0.05$). Curiously, endurance athletes such as cyclists, rowers or triathletes are among the athletes with the highest caffeine intake before or during sport competition⁽³⁾, probably because of its reported ergogenic properties in these sport disciplines^(38–40). Furthermore, the intake of caffeine has demonstrated ergogenic effects on other endurance activities^(4,13,38,41), and has reduced the RPE during prolonged exercise^(21,24–27). This effect of caffeine on reducing self-perceived fatigue could partly explain the ergogenic effects of caffeine on performance⁽²⁵⁾. In the present study, participants competed in a sport-simulated competition and, thus, exercise intensity was not standardised between the experimental trials. It is likely that our participants exercised at a higher intensity in the caffeinated energy drink condition than in the placebo condition, and this could be the reason for comparable exertion scores between the conditions.

Insomnia was the principal side effect resulting from the ingestion of the caffeinated-energy drink, with 31% of the participants reporting sleep disorders during the night after ingestion of this beverage. The prevalence of insomnia in female athletes reached 37.8%, although this value was not statistically different from male participants (Table 4). Previous research^(19,20) did not find significant differences for insomnia with the same dose of 3 mg caffeine/kg as that used in the present study, while caffeine ingestion at a dose of 9 mg/kg increased the frequency of sleep disturbances⁽¹⁹⁾. It has

been reported that caffeine ingestion time could affect the incidence of insomnia especially when caffeine or caffeine-containing products are administered in the afternoon⁽⁴²⁾. Pallares *et al.*⁽¹⁹⁾ administered the caffeinated (e.g. 3, 6 or 9 mg/kg) or placebo beverages at 07.00 hours, so the influence of these caffeine dosages on sleep quality could have decreased. Because altered sleep–wake cycles could negatively affect sport performance⁽⁴³⁾, the use of caffeinated energy drinks in sport must be controlled, especially in the afternoon.

Caffeine ingestion has been associated with a moderate hypoalgesic effect during high-intensity exercise^(24,44), mainly by reducing muscular pain perception during exercise. Nevertheless, other studies have not found this effect of caffeine ingestion on pain perception^(45,46), as reported in the present study. All of these cited studies employed doses

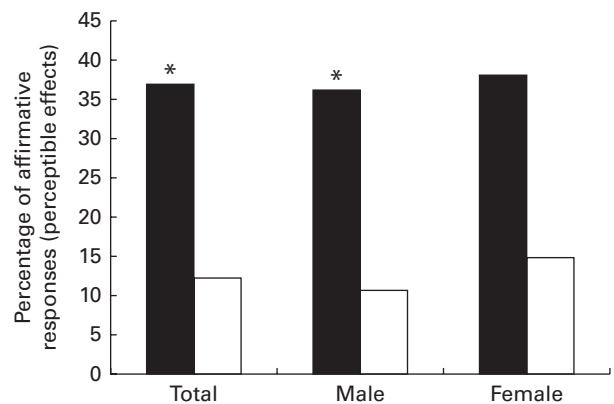


Fig. 1. Self-reported appreciable effects with the ingestion of a caffeinated energy drink (■) or a placebo energy drink (□). Data are percentages of affirmative responses obtained from ninety trained athletes. * Percentage value was significantly different from that of the placebo energy drink ($P < 0.05$).

of 5 mg/kg, so this analgesic effect is controversial. One explanation for these contradictory outcomes could be the different intensities involved in each experimental condition, because in the trials with caffeine, participants were able to perform at a higher intensity which could mask the effects of caffeine on the perceived level of pain^(45,46). When the intensity was the same, the pain was reduced⁽⁴⁴⁾. For this reason, it is important to standardise exercise intensity when studying the effect of caffeine on muscle pain. Further research is warranted in this area.

Increased activeness and alertness could be a psycho-physiological advantage for sport performance⁽⁴⁷⁾. Most studies investigating the effects of energy drink ingestion before exercise have reported improvements in mood, reaction time and markers of alertness^(13,48,49). In the present study participants, there was an increased frequency for enhanced activeness after energy drink ingestion (16.9 *v.* 3.9%), although this effect was more frequent in female participants. However, nervousness was also increased and this side effect could be a negative outcome of caffeinated energy drink ingestion because anxiety decreases motor performance^(50,51). More information is necessary to elucidate whether increased activeness and nervousness affect sport performance.

Another objective of the present study was to analyse sex differences in the outcomes resulting from the ingestion of a caffeine-containing energy drink. In the variables analysed in the present investigation, we did not find differences between the responses of male and female athletes except for perceived fatigue the following morning after the intake of the energy drinks (Table 3). Only the female participants reported reduced fatigue after ingestion of the caffeinated energy drink in comparison to that of the placebo energy drink. The absence of sex differences in most effects resulting from energy drink intake is supported by previous investigations with similar objectives^(17,27). A recent study has described cytochrome P-450 as the primary group of liver enzymes for caffeine metabolism. Thus, cytochrome P-450 has been suggested as a key for the effects obtained with caffeine ingestion on human performance and its adverse effects⁽⁹⁾. A higher activity of cytochrome P-450 has been shown in men than in women⁽⁵²⁾, although it seems that sex is not the primary variable to explain inter-individual differences in the activity of the cytochrome P-450 enzyme⁽⁵³⁾. It appears that male and female athletes have similar caffeine pharmacokinetics⁽⁵⁴⁾, and no differences were found in various psycho-physiological measures (e.g. mood state, readiness to invest physical effort, RPE and muscular pain) after the intake of energy drinks⁽²⁷⁾. Thus, the perceived ergogenicity and the prevalence of side effects after the ingestion of a caffeinated energy drink are similar between males and females.

Several investigations have described that the perception of consuming a substance that purportedly enhances performance is sufficient to improve sport performance (e.g. 'placebo effect')^(55,56). This placebo effect has been specifically reported in studies with simulated caffeine ingestion^(55,57). In these studies, physical performance was significantly improved when participants were informed that they had been supplemented with caffeine despite them having

ingested a placebo. In the present study, only 37% of the participants reported identifiable effects with the caffeinated energy drink, while 12.3% of the participants reported that the placebo drink produced perceptible effects. These data indicate that most participants were not aware of the beverages tested in each experimental trial. Moreover, these results confirm the blinding of the participants to the treatments and the absence of the 'placebo effect' in the outcomes of this investigation.

A limitation of the present study is that the energy drinks (both the caffeinated one and the placebo) contained not only caffeine but also carbohydrates, and other compounds. To set the ecological validity of the experimental design, we selected a commercially available energy drink that contained caffeine, taurine, sodium bicarbonate, L-carnitine and maltodextrin, although these components were included in the same proportion in the placebo drink. Interestingly, with the exception of carbohydrates, there is a lack of evidence to substantiate claims that components of energy drinks, other than caffeine, contribute to the enhancement of physical^(58,59) or cognitive performance^(58,60). Furthermore, the amount of carbohydrate provided with the beverages in the experimental trials (2 g) was not enough to produce the purported benefits obtained with carbohydrate ingestion during exercise. So, we speculate that caffeine is the only substance responsible for the effects obtained with the caffeinated energy drink.

Although the study of the effects of caffeine ingestion on human performance started one century ago⁽⁶¹⁾, the varied and complex properties of caffeine to modify human physiology and its exact mechanisms of action are not yet completely understood⁽³³⁾. Acute caffeine ingestion elicits a number of hormonal, metabolic and physiological effects, both at rest and during exercise⁽¹⁾, while multiple mechanisms have been proposed to explain the effects of caffeine ingestion on human performance⁽⁴¹⁾. In addition to positive effects, numerous investigations have determined several adverse effects after the intake of caffeine or caffeinated products in low to moderate doses. Most studies investigating the side effects associated with caffeine ingestion have been carried out with acute caffeine intake and small subject samples^(19,20), or survey-based studies conducted with larger subject samples but without the control of real caffeine intake (e.g. dose according to body mass) and established by energy drink consumers⁽¹⁷⁾. The present study is a first step to understanding the side effects resulting from the ingestion of a caffeine-containing energy drink in the sport context. Further research is needed to unveil health-related outcomes after acute energy drink ingestion. Well-controlled laboratory studies including direct (e.g. heart rate, blood pressure, urine production, etc.) and indirect (questionnaire about sleep quality or other health disorders) variables, standardised caffeine dosage and covariates such as ingestion time, user's habituation or genetic factors must be developed after energy drink ingestion to ensure the safety of these beverages.

The effects of long-term consumption of caffeine or caffeinated products (mainly coffee) are numerous, and they affect the functioning of different physiological systems.

Long-term consumption of this substance has been associated with several pathological conditions, such as CVD, reproductive disorders, Ca loss, osteoporosis and psychiatric disturbances. However, the chronic ingestion of caffeine has also been associated with a protective effect on neurodegenerative disorders and Parkinson's disease⁽¹⁹⁾. Specifically, there are only a few well-controlled experimental studies that have investigated the side effects resulting from the acute ingestion of energy drinks^(20,62). These investigations have reported increased resting blood pressure but with minimal effects in the prevalence of typical side effects produced after caffeine ingestion. To our knowledge, only one study has investigated the effects of prolonged ingestion of caffeinated energy drinks⁽⁶³⁾. These authors found that blood markers for hepatic, renal, cardiovascular and immune function revealed no adverse effects in response to 10 weeks of daily energy drink intake. In contrast, several case studies have reported serious adverse side effects (for a review, see Seifert *et al.*⁽¹⁸⁾). However, case studies about the side effects resulting from the ingestion of energy drinks are typically related to the ingestion of unbearable amounts of energy drinks or to subjects with previous conditions that exacerbated the adverse effects of the caffeinated beverages⁽⁶⁴⁾. So, more research is warranted to determine the long-term effects of habitual energy drink intake.

Several previous investigations have focused on the effects of caffeinated energy drinks on physical performance of athletes, and the ergogenicity of these beverages has been well documented⁽¹³⁾. In addition, recent data reveal the positive effects of energy drink ingestion on perception of exertion, perception of leg muscle pain and readiness to invest effort^(26,27). All of this information might indicate that energy drinks are an effective nutritional aid to improve the performance of athletes by increasing both the physical functioning and the volitional capacity of the athlete. In contrast, we obtained a greater prevalence of side effects such as nervousness and insomnia after the ingestion of the caffeinated beverage. Thus, the recommendation of caffeinated energy drinks should take into consideration these negative side effects, and the athletes and coaches should consider the potential adverse outcomes of energy drink ingestion, especially in competitive situations. Since large differences in individual responses have been found after the intake of caffeine⁽⁹⁾, athletes must experiment with these beverages in training sessions and consider its use afterwards.

In conclusion, the ingestion of a caffeinated energy drink (3mg caffeine/kg body mass) improved perceived muscle power during intense exercise, although it did not affect subjective feelings of endurance or exhaustion. Following the exercise bout, the ingestion of the caffeine-containing energy drink significantly increased the prevalence of side effects, such as insomnia, activeness and nervousness. The presence of these side effects was similar between male and female participants. These data indicate that energy drinks produce minor side effects, and special attention should be paid to these beverages when they are ingested in the afternoon.

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References

- Magkos F & Kavouras SA (2005) Caffeine use in sports, pharmacokinetics in man, and cellular mechanisms of action. *Crit Rev Food Sci Nutr* **45**, 535–562.
- Heckman MA, Weil J & Gonzalez de Mejia E (2010) Caffeine (1, 3, 7-trimethylxanthine) in foods: a comprehensive review on consumption, functionality, safety, and regulatory matters. *J Food Sci* **75**, R77–R87.
- Del Coso J, Muñoz G & Muñoz-Guerra J (2011) Prevalence of caffeine use in elite athletes following its removal from the World Anti-Doping Agency list of banned substances. *Appl Physiol Nutr Metab* **36**, 555–561.
- Burke LM (2008) Caffeine and sports performance. *Appl Physiol Nutr Metab* **33**, 1319–1334.
- Brice CF & Smith AP (2002) Factors associated with caffeine consumption. *Int J Food Sci Nutr* **53**, 55–64.
- Van Soeren MH, Sathasivam P, Spriet LL, *et al.* (1993) Caffeine metabolism and epinephrine responses during exercise in users and nonusers. *J Appl Physiol* (1985) **75**, 805–812.
- Attwood AS, Higgs S & Terry P (2007) Differential responsiveness to caffeine and perceived effects of caffeine in moderate and high regular caffeine consumers. *Psychopharmacology (Berl)* **190**, 469–477.
- Bell DG & McLellan TM (2002) Exercise endurance 1, 3, and 6 h after caffeine ingestion in caffeine users and nonusers. *J Appl Physiol* (1985) **93**, 1227–1234.
- Yang A, Palmer AA & de Wit H (2010) Genetics of caffeine consumption and responses to caffeine. *Psychopharmacology* **211**, 245–257.
- Hoffman JR (2010) Caffeine and energy drinks. *Strength Cond J* **32**, 15–20.
- Froiland K, Koszewski W, Hingst J, *et al.* (2004) Nutritional supplement use among college athletes and their sources of information. *Int J Sport Nutr Exerc Metab* **14**, 104–120.
- Kristiansen M, Levy-Milne R, Barr S, *et al.* (2005) Dietary supplement use by varsity athletes at a Canadian university. *Int J Sport Nutr Exerc Metab* **15**, 195–210.
- Campbell B, Wilborn C, La Bounty P, *et al.* (2013) International Society of Sports Nutrition position stand: energy drinks. *J Int Soc Sports Nutr* **10**, 1.
- Higdon JV & Frei B (2006) Coffee and health: a review of recent human research. *Crit Rev Food Sci Nutr* **46**, 101–123.
- Nawrot P, Jordan S, Eastwood J, *et al.* (2003) Effects of caffeine on human health. *Food Addit Contam* **20**, 1–30.
- Clauson KA, Shields KM, McQueen CE, *et al.* (2008) Safety issues associated with commercially available energy drinks. *J Am Pharm Assoc* (2003) **48**, e55–e63, quiz e4–e7.
- Malinauskas BM, Aeby VG, Overton RF, *et al.* (2007) A survey of energy drink consumption patterns among college students. *Nutr J* **6**, 35.
- Seifert SM, Schaechter JL, Hershorin ER, *et al.* (2011) Health effects of energy drinks on children, adolescents, and young adults. *Pediatrics* **127**, 511–528.

19. Pallares JG, Fernandez-Elias VE, Ortega JF, *et al.* (2013) Neuromuscular responses to incremental caffeine doses: performance and side effects. *Med Sci Sports Exerc* **45**, 2184–2192.
20. Del Coso J, Salinero JJ, Gonzalez-Millan C, *et al.* (2012) Dose response effects of a caffeine-containing energy drink on muscle performance: a repeated measures design. *J Int Soc Sports Nutr* **9**, 21.
21. Duncan MJ, Smith M, Cook K, *et al.* (2012) The acute effect of a caffeine-containing energy drink on mood state, readiness to invest effort, and resistance exercise to failure. *J Strength Cond Res* **26**, 2858–2865.
22. Duncan MJ & Oxford SW (2011) The effect of caffeine ingestion on mood state and bench press performance to failure. *J Strength Cond Res* **25**, 178–185.
23. Giles GE, Mahoney CR, Brunye TT, *et al.* (2012) Differential cognitive effects of energy drink ingredients: caffeine, taurine, and glucose. *Pharmacol Biochem Behav* **102**, 569–577.
24. Duncan MJ & Oxford SW (2012) Acute caffeine ingestion enhances performance and dampens muscle pain following resistance exercise to failure. *J Sports Med Phys Fitness* **52**, 280–285.
25. Doherty M & Smith PM (2005) Effects of caffeine ingestion on rating of perceived exertion during and after exercise: a meta-analysis. *Scand J Med Sci Sports* **15**, 69–78.
26. Duncan MJ, Stanley M, Parkhouse N, *et al.* (2013) Acute caffeine ingestion enhances strength performance and reduces perceived exertion and muscle pain perception during resistance exercise. *Eur J Sport Sci* **13**, 392–399.
27. Duncan MJ & Hankey J (2013) The effect of a caffeinated energy drink on various psychological measures during submaximal cycling. *Physiol Behav* **116–117**, 60–65.
28. Haskell CF, Kennedy DO, Wesnes KA, *et al.* (2005) Cognitive and mood improvements of caffeine in habitual consumers and habitual non-consumers of caffeine. *Psychopharmacology (Berl)* **179**, 813–825.
29. Adan A, Prat G, Fabbri M, *et al.* (2008) Early effects of caffeinated and decaffeinated coffee on subjective state and gender differences. *Prog Neuropsychopharmacol Biol Psychiatry* **32**, 1698–1703.
30. Temple JL, Bulkley AM, Briatico L, *et al.* (2009) Sex differences in reinforcing value of caffeinated beverages in adolescents. *Behav Pharmacol* **20**, 731–741.
31. Mora-Rodriguez R, Garcia Pallares J, Lopez-Samanes A, *et al.* (2012) Caffeine ingestion reverses the circadian rhythm effects on neuromuscular performance in highly resistance-trained men. *PLOS ONE* **7**, e33807.
32. Armstrong LE (2002) Caffeine, body fluid-electrolyte balance, and exercise performance. *Int J Sport Nutr Exerc Metab* **189**–206.
33. Davis JK & Green JM (2009) Caffeine and anaerobic performance: ergogenic value and mechanisms of action. *Sports Med* **39**, 813–832.
34. Collomp K, Ahmaidi S, Audran M, *et al.* (1991) Effects of caffeine ingestion on performance and anaerobic metabolism during the Wingate Test. *Int J Sports Med* **12**, 439–443.
35. Forbes SC, Candow DG, Little JP, *et al.* (2007) Effect of Red Bull energy drink on repeated Wingate cycle performance and bench-press muscle endurance. *Int J Sport Nutr Exerc Metab* **17**, 433–444.
36. Hoffman JR, Kang J, Ratamess NA, *et al.* (2009) Examination of a pre-exercise, high energy supplement on exercise performance. *J Int Soc Sports Nutr* **6**, 2.
37. Lane SC, Areta JL, Bird SR, *et al.* (2013) Caffeine ingestion and cycling power output in a low or normal muscle glycogen state. *Med Sci Sports Exerc* **45**, 1577–1584.
38. Ganio MS, Klau JF, Casa DJ, *et al.* (2009) Effect of caffeine on sport-specific endurance performance: a systematic review. *J Strength Cond Res* **23**, 315–324.
39. Hodgson AB, Randell RK & Jeukendrup AE (2013) The metabolic and performance effects of caffeine compared to coffee during endurance exercise. *PLOS ONE* **8**, e59561.
40. Carr AJ, Gore CJ & Dawson B (2011) Induced alkalosis and caffeine supplementation: effects on 2,000-m rowing performance. *Int J Sport Nutr Exerc Metab* **21**, 357–364.
41. Goldstein ER, Ziegenfuss T, Kalman D, *et al.* (2010) International Society of Sports Nutrition position stand: caffeine and performance. *J Int Soc Sports Nutr* **7**, 5.
42. Drake C, Roehrs T, Shambroom J, *et al.* (2013) Caffeine effects on sleep taken 0, 3, or 6 hours before going to bed. *J Clin Sleep Med* **9**, 1195–1200.
43. Reilly T & Edwards B (2007) Altered sleep-wake cycles and physical performance in athletes. *Physiol Behav* **90**, 274–284.
44. Gliottoni RC, Meyers JR, Arngrimsson SA, *et al.* (2009) Effect of caffeine on quadriceps muscle pain during acute cycling exercise in low versus high caffeine consumers. *Int J Sport Nutr Exerc Metab* **19**, 150–161.
45. Astorino TA, Terzi MN, Roberson DW, *et al.* (2011) Effect of caffeine intake on pain perception during high-intensity exercise. *Int J Sport Nutr Exerc Metab* **21**, 27–32.
46. Astorino TA, Cottrell T, Talhami Lozano A, *et al.* (2012) Effect of caffeine on RPE and perceptions of pain, arousal, and pleasure/displeasure during a cycling time trial in endurance trained and active men. *Physiol Behav* **106**, 211–217.
47. Hull JT, Wright KP Jr & Czeisler CA (2003) The influence of subjective alertness and motivation on human performance independent of circadian and homeostatic regulation. *J Biol Rhythms* **18**, 329–338.
48. Alford C, Cox H & Wescott R (2001) The effects of red bull energy drink on human performance and mood. *Amino Acids* **21**, 139–150.
49. Seidl R, Peyrl A, Nicham R, *et al.* (2000) A taurine and caffeine-containing drink stimulates cognitive performance and well-being. *Amino Acids* **19**, 635–642.
50. McCarthy PJ, Allen MS & Jones MV (2013) Emotions, cognitive interference, and concentration disruption in youth sport. *J Sports Sci* **31**, 505–515.
51. Rathsclag M & Memmert D (2013) The influence of self-generated emotions on physical performance: an investigation of happiness, anger, anxiety, and sadness. *J Sport Exerc Psychol* **35**, 197–210.
52. Landi MT, Sinha R, Lang NP, *et al.* (1999) Human cytochrome P4501A2. *IARC Sci Publ* **173**–195.
53. Bebia Z, Buch SC, Wilson JW, *et al.* (2004) Bioequivalence revisited: influence of age and sex on CYP enzymes. *Clin Pharmacol Therap* **76**, 618–627.
54. Graham TE (2001) Caffeine and exercise: metabolism, endurance and performance. *Sports Med* **31**, 785–807.
55. Duncan MJ, Lyons M & Hankey J (2009) Placebo effects of caffeine on short-term resistance exercise to failure. *Int J Sports Physiol Perform* **4**, 244–253.
56. Beedie CJ & Foad AJ (2009) The placebo effect in sports performance: a brief review. *Sports Med* **39**, 313–329.
57. Beedie CJ, Stuart EM, Coleman DA, *et al.* (2006) Placebo effects of caffeine on cycling performance. *Med Sci Sports Exerc* **38**, 2159–2164.
58. McLellan TM & Lieberman HR (2012) Do energy drinks contain active components other than caffeine? *Nutr Rev* **70**, 730–744.

59. Tallis J, Higgins MF, Cox VM, *et al.* (2014) Does a physiological concentration of taurine increase acute muscle power output, time to fatigue, and recovery in isolated mouse soleus (slow) muscle with or without the presence of caffeine? *Can J Physiol Pharmacol* **92**, 42–49.
60. van den Eynde F, van Baelen PC, Portzky M, *et al.* (2008) De effecten van energiedranken op de cognitieve prestaties (The effects of energy drinks on cognitive performance). *Tijdschr Psychiatr* **50**, 273–281.
61. Rivers WH & Webber HN (1907) The action of caffeine on the capacity for muscular work. *J Physiol* **36**, 33–47.
62. Kurtz AM, Leong J, Anand M, *et al.* (2013) Effects of caffeinated versus decaffeinated energy shots on blood pressure and heart rate in healthy young volunteers. *Pharmacotherapy* **33**, 779–786.
63. Lockwood CM, Moon JR, Smith AE, *et al.* (2010) Low-calorie energy drink improves physiological response to exercise in previously sedentary men: a placebo-controlled efficacy and safety study. *J Strength Cond Res* **24**, 2227–2238.
64. Burrows T, Pursey K, Neve M, *et al.* (2013) What are the health implications associated with the consumption of energy drinks? A systematic review. *Nutr Rev* **71**, 135–148.