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ORIGINAL ARTICLE

Comparative effects of caffeine, beta-alanine, and their combination on mechanical, physiological, and perceptual responses to upper-body superset resistance training

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Abstract

Caffeine and beta-alanine are widely used in multi-ingredient pre-workout supplements believed to enhance resistance training, but their specific role in driving this effect remains unclear. The current study employed a randomized, triple-blinded, placebo-controlled and crossover experimental design to explore the acute effects of caffeine (200 mg), beta-alanine (3 g), or their combination (200 mg caffeine and 3 g beta-alanine; C+B-A) administered 30 min prior to resistance training (RT) on mechanical, physiological, and perceptual variables. Twenty-one young resistance-trained males (age = 23.5 ± 4.5 years, body mass = 82.1 ± 10.2 kg) visited the laboratory on six occasions: one familiarization session, one preliminary testing session for load determination, and four experimental sessions which differed only in supplementation condition and involved four supersets of bench press and bench pull exercises. The supplement condition did not significantly affect any mechanical variables ($p \geq 0.335$), except for the velocity of the last repetition of the set, where beta-alanine produced lower values (0.383 m/s) compared to placebo (0.407 m/s; $p < 0.05$), with no differences observed for C+B-A (0.397 m/s) and caffeine (0.392 m/s). Heart rate was consistent across the different supplement conditions with the exception of the higher values observed immediately before the start of the RT session for placebo compared to caffeine ($p = 0.010$) and C+B-A ($p = 0.019$). Post-RT blood lactate concentration ($p = 0.384$), general and local ratings of perceived exertion ($p = 0.177$ and 0.160, respectively), and readiness ($p = 0.281$–0.925), did not differ significantly between supplement conditions. Selected supplements have minimal effects on performance and physiological responses in agonist–antagonist upper-body superset RT not leading to failure.

Keywords Ergogenic aids · Fatigue · Performance · Strength training

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Abbreviations

ANOVA	Analysis of variance
C+B-A	Caffeine and beta-alanine
HR	Heart rate
MIPS	Multi-ingredient pre-workout supplements
$MV_{average}$	Average mean velocity of a set
$MV_{fastest}$	Fastest mean velocity of a set
MV_{last}	Mean velocity of the last repetition of a set
N_{rep}	Number of repetitions completed in a set
OMNI-RES	OMNI-Resistance Exercise Scale of perceived exertion
RM	Repetition maximum
RPE	Rating of perceived exertion
RT	Resistance training

Introduction

The type and magnitude of the adaptations induced by resistance training (RT) significantly rely on the mechanical and metabolic demands of the training stimulus (Egan and Sharples 2023). The simplest and most effective way of modulating such demands consists of selectively manipulating training variables such as the load lifted, proximity to failure, or lifting tempo (Suchomel et al. 2018). For instance, the mechanical performance is maximized when individuals are instructed to lift the loads at the maximum intended velocity (Weakley et al. 2021), whereas different markers of fatigue (neural, mechanical, metabolic, and perceptual) are attenuated when sets are terminated far from failure (Jukic et al. 2023). One advanced strategy, extensively explored in scientific research and increasingly used in practice, with potential to further modulate RT responses beyond the basic manipulation of training variables is the use of nutritional supplements such as multi-ingredient pre-workout supplements (MIPS) (Harty et al. 2018).

A remarkable gap in scientific research is that the effects of MIPS have been predominantly examined during RT sessions leading to failure (Bergstrom et al. 2018; Beyer et al. 2024; Collins et al. 2017; Jagim et al. 2016; Jung et al. 2017; Nicoll et al. 2023; Schwarz and McKinley-Barnard 2020), or with individuals who were not instructed to lift at maximal intended velocity (Bergstrom et al. 2018; Collins et al. 2017; Jung et al. 2017; Kaczka et al. 2020; Schwarz and McKinley-Barnard 2020; Stratton et al. 2022). Recent evidence suggests that training to muscular failure does not induce superior gains in muscle strength and hypertrophy compared to non-failure training. Additionally, improvements in tasks where maximal power and rate of force development (RFD) are crucial, such as vertical jumps, sprints, and changes of direction, seem to favor non-failure training (Grgic et al. 2022). Furthermore, training to failure may be less efficient as it significantly increases fatigue extending the time required for recovery both between sets (Vieira et al. 2022) and between sessions (Morán-Navarro et al. 2017). There is also considerable evidence that training adaptations are superior when mechanical performance during RT is maximized either by instructing individuals to lift at maximal intended velocity (González-Badillo et al. 2014), or by increasing their motivation and competitiveness through the provision of real-time velocity feedback (Weakley et al. 2023). Therefore, we consider that it is significant to evaluate the acute effects of MIPS on mechanical performance and metabolic responses to RT during non-failure training protocols performed at maximal intended velocity.

Caffeine is one of the most common ingredients contained in MIPS, with a prevalence of 86% in the bestselling MIPS (Jagim et al. 2019). Its ingestion has been progressively increasing within the context of athletic performance, especially since 2004 when it was removed from the list of banned substances of the World Anti-Doping Agency (Del Coso et al. 2011). Acute ingestion of caffeine seems to evoke effects on increased wakefulness, diuresis, heart rate and metabolic function, and decreased sleepiness, fatigue, rating of perceived exertion (RPE) and pain perception (Grgic et al. 2019). Moderate-to-high quality systematic reviews provide moderate-quality evidence supporting the ergogenic benefits of caffeine on muscle endurance, muscle strength, anaerobic power, and aerobic endurance (Grgic et al. 2020). Additionally, acute caffeine supplementation seems to be highly ergogenic for movement velocity in RT, enhancing both mean and peak velocity under different loads and for both upper- and lower-body exercises (Raya-González et al. 2020). Therefore, caffeine is well-supported for its ergogenic effects on mechanical performance in RT (Grgic et al. 2019, 2020; Raya-González et al. 2020). To our knowledge, only one study has examined the acute effects of caffeine on supersets, although this study combined upper-body with lower-body exercises (Jacobs et al. 2003).

Another substance that can be found in many MIPS is beta-alanine, a non-essential amino acid synthesized in the liver (Matthews and Traut 1987). The ingestion of beta-alanine increases muscle carnosine concentration (Saunders et al. 2017), a dipeptide which acts as an intramuscular buffer of the hydrogen ions caused by exercise, helping the muscles to maintain a stable environment and delaying muscle fatigue (Harty et al. 2018; Saunders et al. 2017). The only known adverse effect of beta-alanine is paresthesia, which manifests as various types of itching sensations in different parts of the body, such as the ears, scalp, hands, and torso (Décombaz et al. 2012; Smith-Ryan et al. 2012). Some studies have revealed that the ingestion of beta-alanine increases training volume (Trexler et al. 2015). Greater ergogenic effects are observed in exercises lasting from 30 s to 10 min and in untrained versus trained individuals (Saunders et al. 2017). The chronic effects of beta-alanine supplementation on RT adaptations are varied. Some studies reported positive results on the endurance capacity of the knee extensors at 45% maximal voluntary isometric contraction (Sale et al. 2012), and an increase in the back squat 1RM (Maté-Muñoz et al. 2018). Other studies observed no effect on 1RM and 60% 1RM performance in bench press and back squat (de Camargo et al. 2023), and neither on the 1RM performance in box squat, bench press and deadlift, isokinetic force production of the knee extensors, and on the muscular endurance of the flexor muscles of the arms (Kendrick et al. 2008). These two last studies also did not report any effects on body composition (de Camargo et al. 2023; Kendrick et al. 2008). Only one study examined the acute effects of beta-alanine showing a positive effect on knee extensors maximum isometric force and counter-movement jump (CMJ) performance (Invernizzi et al. 2016). However, the acute effect of beta-alanine intake on mechanical performance during upper-body supersets RT remains unknown.

A recent narrative review highlights the effectiveness of caffeine and beta-alanine as standalone supplements and recognizes them as key dietary aids widely accepted by the sport and exercise science community as evidence-based ergogenic enhancers (Murphy et al. 2022). These two ingredients are also among the primary components in many commercially available MIPS (Jagim et al. 2019). However, although MIPS contain additional ingredients beyond caffeine and beta-alanine, the interactions between these compounds make it difficult to determine which are the primary active ergogenic ingredients and which may be unnecessary. Therefore, the present study aims to explore the acute effects of caffeine alone (200 mg), beta-alanine alone (3 g), or their combination (200 mg caffeine and 3 g beta-alanine) administered 30 min prior to RT (four supersets of bench press and bench pull) on mechanical, metabolic, cardiovascular, and perceptual variables. We hypothesized that the supplement combining caffeine with beta-alanine will produce more beneficial effects on the mentioned variables compared to placebo, caffeine alone, and beta-alanine alone.

Methods

Participants

An a priori analysis was performed using G*Power (version 3.1.9.4.), determining that 19 participants were necessary to achieve a power of 0.85 with an effect size of 0.3 and an alpha level of 0.05. To ensure robustness, we recruited 21 participants, all of whom completed the study (age = 23.5 ± 4.5 years, body mass = 82.1 ± 10.2 kg, height = 179.4 ± 6.7 cm, bench press one-repetition maximum [1RM] = 95.2 ± 13.4 kg, and bench pull 1RM = 89.8 ± 12.5 kg). The inclusion criteria to participate in this study were: (1) being 18–40 years old; (2) body mass index (BMI): 18–30 kg/m^2; (3) being able to comprehend technical executions and accustomed to exercises performed during the study (bench press and bench pull). The exclusion criteria were: (1) history of a major adverse cardiovascular event, renal failure, cirrhosis, eating disorder, weight control surgical intervention, type 2 diabetes mellitus, or HIV/AIDS; (2) any chronic condition in which high-intensity strength exercises are not recommended; (3) any condition that, in the investigator's judgment, impairs the ability to participate in the study or poses a personal risk to the participant, (4) use of medications that may affect study outcomes; (5) unstable body weight for 3 months prior to the start of the study (>4 kg weight loss or gain); (6) active tobacco abuse or illicit drug use or history of alcohol abuse treatment; (7) being on a special or prescribed diet related to a medical condition, such as a gluten-free, ketogenic, or low-sodium diet, and (8) taking any form of nutritional supplementation. Participants enrolled in the study through a poster that was shared via social media. The study protocol and design were approved by the Research Ethics Committee (SICEIA) of the Andalusian Regional Government (SICEIA-2024-000283). All participants provided informed consent and had the freedom to withdraw from the study at any time. The study protocol adhered to the latest revised edition of the Declaration of Helsinki (2013).

Experimental design

The current study was a randomized, triple-blinded, placebo-controlled and crossover experimental trial designed to explore the acute effects of caffeine alone (200 mg), beta-alanine alone (3 g), or their combination (200 mg caffeine and 3 g beta-alanine) administered 30 min prior to RT (four supersets of bench press and bench pull) on mechanical, metabolic, cardiovascular, and perceptual variables. The supplements were administered 30 min before the workout because oral ingestion of caffeine, the primary ingredient in many MIPS, typically reaches peak concentration around that time (Cox et al. 2002). The implementation of stringent methodological tools, including the use of randomization software for participant allocation, the application of blinding procedures for both participants and researchers during data collection, and the meticulous adherence to these protocols, minimized potential sources of bias. Consequently, these measures enhanced the validity and reliability of the data. (Lang and Stroup 2020). By keeping the participants, researchers, and data analysts unaware of the supplementation allocation, we aimed to reduce potential biases.

Participants visited the laboratory on six occasions: one familiarization session, one preliminary testing session, and four experimental sessions. In the first session, participants underwent assessments of anthropometric variables, were familiarized with the bench press and bench pull exercises performed with maximum intent, and were asked about years of RT experience. In the preliminary testing session, the 1RM and 20RM loads were determined. The four experimental sessions had the same protocol, only differing in the supplement condition. All sessions were conducted with a minimum of 48-h separation in between to guarantee full recovery from central and peripheral fatigue (Carroll et al. 2017). Each participant completed all sessions at consistent times of the day, ensuring a maximum range of ±2 h difference between sessions. For all sessions, participants were instructed to avoid consuming stimulants on the testing day, and refrain from engaging in resistance exercise training

24 h before the visit. Participants completed each session in a well-hydrated state and were instructed to refrain from eating for at least 3 h prior to testing. Although all participants dined in the faculty canteen, it is important to note that their specific meals varied from day to day, which may have introduced some nutritional variability. However, no strict control over diet or specific nutritional guidelines was imposed beyond these recommendations.

Supplementation procedures

The four supplement conditions comprised of caffeine (200 mg), beta-alanine (3 g), a combination of caffeine (200 mg) and beta-alanine (3 g), and placebo. The supplement dosage conditions for caffeine and beta-alanine were matched to the typical concentrations found in a single dose of pre-workout supplements (Jagim et al. 2019). The supplements and placebo were prepared and packaged by a researcher not involved in the study at a separate facility (Life Pro Nutrition Industries, Madrid, Spain). The supplements were in powder form, each contained in numbered packages from 1 to 4 to ensure blinding. A previous study demonstrated that the combination of caffeine (300 mg) and beta-alanine (4 g) for 28 days was safe and could provide benefits in athletic performance (Kendall et al. 2014). To reduce possible bias, the Research Randomizer online software (www.randomizer.org) was used to assign participants to each supplement condition. The content of each supplement package remained unknown until a third-party researcher performed all statistical analyses. The placebo contained 5 g of maltodextrin, along with silicon dioxide (E-551) as an anti-caking agent, citric acid (E-330) as an acidity regulator and flavoring, beet red (E-162) as a coloring, and sucralose (E-955) as a sweetener. Citric acid (E-330) was used as both an acidity regulator and flavoring agent, while sucralose (E-955) served as a sweetener to mask the taste of caffeine and beta-alanine. All supplements were identical in appearance, taste, and color. In each supplement condition, 5 g of powdered supplement was dissolved in 250 ml of water and then offered to the participants in a transparent glass 30 min prior to the beginning of the RT session.

Preliminary testing session

The aim of this session was to determine the corresponding load for 1RM and 20RM for the bench press and bench pull exercises. The order was as follows: (1) submaximal incremental load test in bench press; (2) sets until failure at 60% and 80% of 1RM in bench press; (3) submaximal incremental load test in bench pull; (4) sets until failure at 60% and 80% of 1RM in bench pull. Both exercises were performed using free weights. A linear position transducer was used to measure bar velocities (GymAware; Kinetic Performance Technologies, Canberra, Australia).

1RM load assessment

For both exercises, the incremental load test began with the unloaded bar (20 kg), and the load was progressively increased from 5 to 20 kg until the mean velocity of the barbell was less than 0.3 m/s for bench press and less than 0.6 m/s for bench pull (García-Ramos et al. 2018a; Pérez-Castilla et al. 2023). Three repetitions were performed for light loads (≥0.80 m/s for bench press and ≥1.00 m/s for bench pull), two for medium loads (0.80–0.60 m/s for bench press and 1.00–0.80 m/s for bench pull) and one for heavy loads (≤0.60 m/s for bench press and ≤0.80 m/s for bench pull). Recovery intervals between sets were established at 3 min for light and medium loads, and 5 min for heavy loads. The participants were instructed to lift the bar at maximal voluntary velocity for each repetition. The fastest mean velocity of each load was used to determine the individualized load–velocity relationship through a linear regression model. The load associated with a mean velocity of 0.17 m/s for the bench press and 0.45 m/s for the bench pull was used to estimate the 1RM (García-Ramos et al. 2018a, 2019).

20RM load assessment

The mean velocity of the fastest repetition of the set and the total number of repetitions completed were obtained with the two loads lifted (60% 1RM and 80% 1RM). These variables were modeled through a linear regression equation to determine the mean velocity corresponding to the 20RM load. The absolute load corresponding to the velocity of the 20RM load, determined in the first experimental session through sets of approximation, was used in the four experimental sessions. Previous studies have shown that the fastest repetition in a set accurately predicts the number of repetitions that can be performed until reaching muscular failure in the bench press (García-Ramos et al. 2018b) and bench pull exercises (Miras-Moreno et al. 2023).

Experimental sessions

The four experimental sessions were divided into four stages: PRE1, PRE2, Training, and POST. The PRE1 stage began when the participant arrived at the laboratory. They were requested to sit in a chair for approximately 2 min to relax. Subsequently, their heart rate (HR) was measured for 2 min, questionnaires regarding itching and readiness were administered, and finally, the supplement was ingested. A 30-min period was allowed for the supplement to take effect during which the participant did not engage in any activity. After the 30 min elapsed, the PRE2 stage began, and the same tests as in PRE1 (HR and questionnaires) were repeated. Then, participants were instructed to perform a general and specific warm-up before performing the training which comprised four supersets of bench press and bench pull with a 2-min rest between exercises. HR was measured throughout the whole training. Upon completing the last set of the intervention, participants transitioned to the POST stage, where blood lactate levels were measured, and HR was monitored. Finally, they were asked to report their local and general rating of perceived exertion (RPE) in a scale from 1 to 10 and the questionnaire about itching was administered.

Regarding the training stage, each participant had 5 min to perform a general warm-up consisting of light intensity activities (running, cycling or rowing) and upper-body joint mobility exercises. Participants were free to perform the general warm-up of their choice, but with the condition of repeating the same warm-up routine in all experimental sessions. The specific warm-up consisted of three incremental sets in both exercises: five repetitions with light loads, three repetitions with medium loads, and two repetitions with the load at which the velocity corresponding to the 20RM was achieved. The rest between sets during the specific warm-up was 90 s. Three minutes after the last set of the specific warm-up, participants began the RT protocol, consisting of four supersets composed of bench press initially, followed by bench pull with a 2-min rest time between exercises. The set ended when the mean velocity of two consecutive repetitions fell below 0.35 m/s for bench press and 0.60 m/s for bench pull, or when the participant could not perform any more repetitions before falling below those velocities. The same absolute load, equivalent to the 20RM determined in the first experimental session, was used in all four experimental sessions. Participants were always asked to lift the bar as fast as possible.

Measurement equipment and data analysis

Mechanical variables

A GymAware linear position transducer was used to measure the mean velocity of all repetitions. The number of repetitions completed in each set (N_{rep}), the fastest velocity of the set ($MV_{fastest}$), the average velocity of the set ($MV_{average}$), and the velocity of the last repetition of the set (MV_{last}) were recorded for subsequent analyses.

Physiological variables

The average HR, monitored using the Polar H10 HR monitor (Polar Electro, Kempele, Finland), was utilized to quantify the cardiovascular impact of the intervention. During the PRE1, PRE2 and POST stages, participants sat in a chair for 2 min without engaging in any activity. In the training stage, average HR was continuously measured from the start of the first superset to the completion of the last repetition of the session. Data were directly obtained from the Polar Flow app.

The metabolic impact of the intervention was quantified by measuring the blood lactate concentration from the right earlobe was 90 s after finishing the training protocol with the Lactate Pro 2 device (Arkray, Kyoto, Japan).

Perceptual variables

The readiness questionnaire employed a 1–5 scale, with 1 indicating the lowest and 5 indicating the highest score, assessing overall energy level, pain, stress, nutrition, hydration, and sleep quality from the preceding night. Additionally, the number of hours slept the previous night was recorded.

The itching questionnaire gathered data on participants' experience of itching, including its type (tingling, stabbing, burning, uncomfortable, unbearable, and worrisome) and intensity (none, a little, moderately, and a lot). The participants were also provided with illustrations of the front and back of a human body, with body parts numbered from 1 to 23, enabling them to indicate where they experienced itching.

The OMNI-Resistance Exercise Scale (OMNI-RES) of perceived exertion was used as a measure of perceptual fatigue (Robertson et al. 2003). Three minutes after finishing the last set, the participants gave their RPE using the OMNI-RES scale (0–10) where 0 is extremely easy and 10 represents extremely hard. An image of the OMNI-RES scale was shown to the participants.

Statistical analyses

The descriptive values of the dependent variables are presented as means and standard deviations. The normal distribution of the variables was explored by the Shapiro–Wilk test. The mechanical and physiological variables were normally distributed ($p > 0.05$), but the normal distribution assumption was violated for perceptual variables ($p < 0.05$). A three-way repeated measures analysis of variance (ANOVA; supplement [caffeine vs. beta-alanine vs. combination of caffeine and beta-alanine [C+B-A] vs. placebo] × exercise [bench press vs. bench pull] × set number [set 1 vs. set 2 vs. set 3 vs. set 4]) was applied to each mechanical variable (N_{rep}, $MV_{fastest}$, $MV_{average}$, and MV_{last}). One-way repeated measures ANOVA were used to compare HR values between the supplement conditions separately for each stage (PRE1, PRE2, Training, and POST). The effect of the supplement condition on blood lactate values were compared through a one-way repeated measures ANOVA. The non-parametric Friedman test was used to compare the perceptual variables separately for each stage (PRE1, PRE2, and POST) between the supplement conditions. Cohen's *d* effect size (ES) = ([placebo − supplement condition]/pooled SD) and their 95% confidence intervals were calculated to compare the magnitude of the difference between sessions with placebo and those with caffeine, beta-alanine, or C+B-A supplementation. The magnitude of the ES was interpreted as follows: trivial (<0.20), small (0.20–0.59), moderate (0.60–1.19), large (1.20–2.00), or very large (>2.00) (Hopkins et al. 2009). When the assumption of sphericity was violated according to Mauchly's test ($p < 0.05$), the Greenhouse–Geisser correction was applied. Post hoc comparisons were performed using the least significant differences method. Statistical analyses were performed using the software package SPSS (IBM SPSS version 25.0, Chicago, IL, USA). Statistical significance was set at $p < 0.05$.

Results

Mechanical variables

The training protocol successfully induced mechanical fatigue, as evidenced by the significant decreases observed across sets in N_{rep} (from 17.8 to 10.7; $p < 0.001$), $MV_{fastest}$ (from 0.78 to 0.69 m/s; $p < 0.001$), and $MV_{average}$ (from 0.62 to 0.56 m/s; $p < 0.001$) (Table 1). The main effect of supplement was only significant for MV_{last} due to lower values for beta-alanine (0.383 m/s) compared to placebo (0.407 m/s; $p < 0.05$) with no significant differences with respect to C+B-A (0.397 m/s) and caffeine (0.392 m/s). The only significant interaction observed for the supplement condition was with the factor exercise for N_{rep} ($p = 0.027$). This significant interaction was caused because during the bench pull participants completed more repetitions using the caffeine (14.5 repetitions) and placebo (14.6 repetitions) compared to using the beta-alanine (13.8 repetitions) and C+B-A (13.8 repetitions), whereas during the bench press N_{rep} remained constant across the supplement conditions (13.4, 13.4, 13.3, and 13.0 repetitions for caffeine, beta-alanine, C+B-A, and placebo, respectively).

Physiological variables

The ANOVAs applied to HR values was only significant at PRE2 ($p = 0.028$) due to the greater values observed using placebo (69.5 ± 9.8 bpm) compared to caffeine (64.2 ± 8.2 bpm; $p = 0.010$) and C+B-A (64.9 ± 6.9 bpm; $p = 0.019$) (Fig. 1). The ANOVA applied to blood lactate values did not reach statistical significance ($p = 0.384$) (Fig. 2).

Perceptual variables

No significant differences between the supplement conditions were observed for any variable related to the readiness questionnaire at PRE1 (*p* ranged from 0.281 to 0.925) or PRE2 (*p* ranged from 0.304 to 0.896). The beta-alanine and C+B-A supplements, but not caffeine nor placebo, elicited mild itching in approximately half of the participants at PRE2, with virtually no itching reported post-training for any supplement condition (Table 2). No significant differences between the supplement conditions were observed for general RPE ($p = 0.177$) or local RPE ($p = 0.160$) (Fig. 3).

Discussion

This study investigated the immediate effects of caffeine, beta-alanine, and their combination (C+B-A) when ingested prior to a non-failure agonist–antagonist upper-body superset RT session, examining various mechanical, physiological, and perceptual responses. Beta-alanine and C+B-A, but not caffeine nor placebo, induced mild itching in approximately half of the participants just before the commencement of the RT session. However, none of the supplements demonstrated efficacy in enhancing mechanical performance during RT compared to placebo. Metabolic (blood lactate concentration) and perceptual (local and general RPE) responses to RT were also similar across all supplement conditions. Heart rate tended to be consistent across the different supplement conditions, except for slightly higher values observed immediately before the start of the RT session for placebo compared to caffeine and C+B-A supplements. These findings suggest that the supplements examined in this study have minimal effects on both performance and physiological responses in recreationally trained males who engage in non-failure agonist–antagonist upper-body superset RT.

The results indicate that while caffeine and beta-alanine are the primary ingredients in many MIPS (Beyer et al. 2024; Jagim et al. 2016), their individual and combined effects are insufficient to produce positive impact on RT variables in the current dosages as some MIPS may provide (Beyer et al. 2024; Jagim et al. 2016). For example, a single dose of the SHIFTED Maximum pre-workout supplement, containing 2.5 g of beta-alanine and 300 mg of caffeine among the other substances, enabled participants to perform more repetitions and experience lower RPE during upper-body training compared to placebo condition (Beyer et al. 2024). Similarly, another MIPS containing 2 g of beta-alanine, 300 mg of caffeine, and additional ingredients improved upper-body power endurance, allowing for greater total training volume compared to a placebo (Jagim et al. 2016). However, other studies have shown that supplementation with MIPS containing

Table 1 Three-way analysis of variance (ANOVA) comparing the mechanical variables between exercises, sets and supplement conditions

Variable	Exercise	Set	Supplement				ANOVA
			Caffeine	Beta-alanine	C+B-A	Placebo	
N_{rep}	Bench press	1	18.0 ± 2.9	18.0 ± 2.0	18.5 ± 2.9	17.1 ± 2.5	E: $F = 1.1$, $p = 0.298$
		2	14.5 ± 2.5	14.3 ± 1.7	14.2 ± 1.5	13.9 ± 1.4	**S: $F = 192.6$, $p < 0.001$**
		3	11.3 ± 2.1	11.2 ± 1.9	10.9 ± 2.2	11.2 ± 1.8	Sup: $F = 1.2$, $p = 0.335$
		4	9.7 ± 2.1	10.0 ± 1.6	9.6 ± 1.8	9.9 ± 1.9	**E × S: $F = 4.8$, $p = 0.029$**
	Bench pull	1	17.8 ± 5.7	17.0 ± 6.0	17.5 ± 6.1	18.7 ± 6.6	**E × Sup: $F = 3.3$, $p = 0.027$**
		2	15.2 ± 4.1	14.3 ± 4.0	14.0 ± 4.3	14.5 ± 4.0	S × Sup: $F = 1.2$, $p = 0.304$
		3	13.3 ± 3.5	12.1 ± 3.8	12.6 ± 3.7	13.1 ± 3.3	E × S × Sup: $F = 1.2$, $p = 0.273$
		4	11.5 ± 3.6	11.7 ± 3.9	11.2 ± 3.6	12.1 ± 3.9	
$MV_{fastest}$	Bench press	1	0.72 ± 0.09	0.72 ± 0.08	0.72 ± 0.10	0.71 ± 0.09	**E: $F = 55.6$, $p < 0.001$**
		2	0.67 ± 0.08	0.67 ± 0.09	0.67 ± 0.11	0.67 ± 0.09	**S: $F = 112.1$, $p < 0.001$**
		3	0.62 ± 0.09	0.61 ± 0.11	0.62 ± 0.11	0.62 ± 0.10	Sup: $F = 1.0$, $p = 0.379$
		4	0.58 ± 0.09	0.59 ± 0.10	0.59 ± 0.10	0.60 ± 0.10	**E × S: $F = 21.6$, $p < 0.001$**
	Bench pull	1	0.87 ± 0.08	0.83 ± 0.09	0.84 ± 0.09	0.85 ± 0.10	E × Sup: $F = 1.9$, $p = 0.145$
		2	0.83 ± 0.09	0.83 ± 0.09	0.82 ± 0.09	0.85 ± 0.11	S × Sup: $F = 1.0$, $p = 0.418$
		3	0.81 ± 0.09	0.79 ± 0.08	0.79 ± 0.08	0.81 ± 0.09	E × S × Sup: $F = 0.8$, $p = 0.564$
		4	0.78 ± 0.09	0.78 ± 0.08	0.78 ± 0.08	0.79 ± 0.09	
$MV_{average}$	Bench press	1	0.53 ± 0.06	0.54 ± 0.05	0.54 ± 0.06	0.53 ± 0.06	**E: $F = 185.4$, $p < 0.001$**
		2	0.50 ± 0.06	0.50 ± 0.05	0.50 ± 0.07	0.50 ± 0.05	**S: $F = 112.2$, $p < 0.001$**
		3	0.47 ± 0.06	0.47 ± 0.07	0.47 ± 0.07	0.47 ± 0.06	Sup: $F = 1.1$, $p = 0.371$
		4	0.45 ± 0.06	0.46 ± 0.06	0.46 ± 0.06	0.46 ± 0.07	**E × S: $F = 18.5$, $p < 0.001$**
	Bench pull	1	0.72 ± 0.05	0.70 ± 0.05	0.70 ± 0.06	0.71 ± 0.06	E × Sup: $F = 2.6$, $p = 0.074$
		2	0.70 ± 0.06	0.69 ± 0.05	0.69 ± 0.05	0.70 ± 0.06	S × Sup: $F = 0.7$, $p = 0.703$
		3	0.68 ± 0.05	0.67 ± 0.04	0.67 ± 0.04	0.68 ± 0.06	E × S × Sup: $F = 1.2$, $p = 0.319$
		4	0.67 ± 0.05	0.66 ± 0.05	0.67 ± 0.04	0.68 ± 0.06	
MV_{last}	Bench press	1	0.24 ± 0.06	0.25 ± 0.05	0.27 ± 0.04	0.28 ± 0.04	**E: $F = 930.2$, $p < 0.001$**
		2	0.25 ± 0.05	0.23 ± 0.05	0.24 ± 0.05	0.25 ± 0.04	S: $F = 0.9$, $p = 0.440$
		3	0.25 ± 0.05	0.25 ± 0.05	0.26 ± 0.06	0.26 ± 0.06	**Sup: $F = 2.8$, $p = 0.048$**
		4	0.25 ± 0.05	0.25 ± 0.06	0.26 ± 0.05	0.26 ± 0.05	E × S: $F = 1.6$, $p = 0.191$
	Bench pull	1	0.55 ± 0.04	0.51 ± 0.09	0.52 ± 0.09	0.55 ± 0.05	E × Sup: $F = 0.7$, $p = 0.539$
		2	0.54 ± 0.06	0.53 ± 0.09	0.54 ± 0.04	0.54 ± 0.06	S × Sup: $F = 0.4$, $p = 0.947$
		3	0.53 ± 0.07	0.52 ± 0.08	0.53 ± 0.07	0.56 ± 0.04	E × S × Sup: $F = 1.3$, $p = 0.251$
		4	0.53 ± 0.06	0.52 ± 0.09	0.55 ± 0.05	0.56 ± 0.05	

Bold numbers indicate p values below 0.05

C+B-A combination of caffeine and beta-alanine, N_{rep} number of repetitions completed, $MV_{fastest}$ fastest mean velocity of the set, $MV_{average}$ average velocity of the set, MV_{last} mean velocity of the last repetition of the set, *E* exercise, *S* set, *Sup* supplement condition

similar amounts of caffeine and beta-alanine did not enhance or only selectively affected specific mechanical, perceptual, or metabolic variables during RT (Snyder et al. 2024; Stratton et al. 2022). A possible explanation for these mixed results is the complex interaction of different compounds within MIPS, making it difficult to determine which ingredients are responsible for the observed performance enhancements and which may be unnecessary. Taken together, neither caffeine nor beta-alanine, whether individually or in combination at typical MIPS dosages, appears solely responsible for producing ergogenic effects on RT performance.

The number of repetitions performed was consistent across supplement conditions, diverging from existing research that highlights enhanced muscular endurance following caffeine ingestion (Ferreira et al. 2021; Grgic 2021; Grgic et al. 2020). However, most existing studies utilized training protocols where participants reached muscular failure (Ferreira et al. 2021; Grgic 2021; Grgic et al. 2020). It is well established that reaching muscular failure does not result in more beneficial adaptations compared to stopping short of failure (Grgic et al. 2022). Therefore, further research is needed on the effect of caffeine on muscular endurance in non-failure RT. The caffeine dosage in our

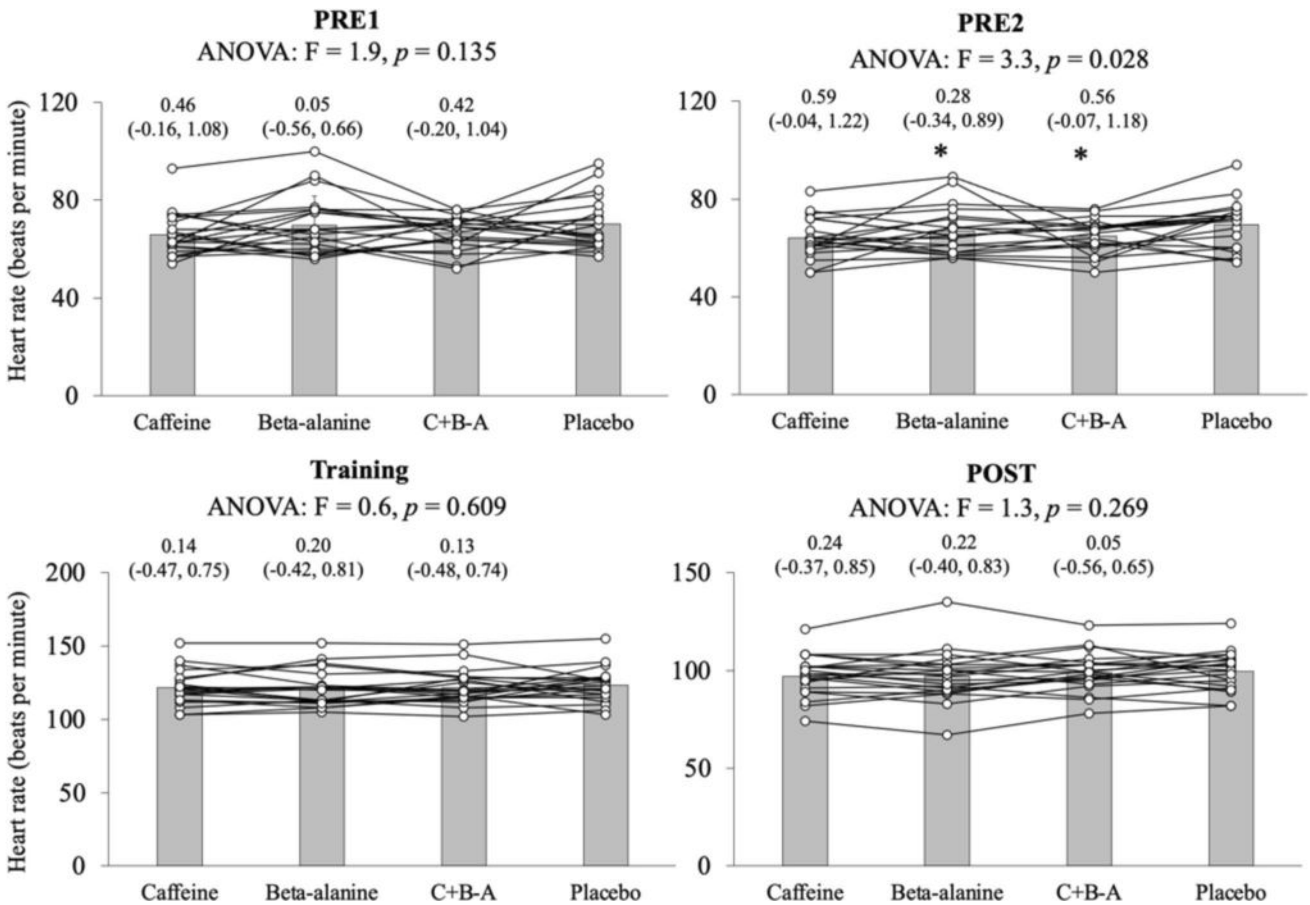

Fig. 1 Comparison of heart rate values between the supplement conditions prior to the supplement administration (PRE1; upper-left panel), 30 min after supplement administration (PRE2; upper-right panel), during the training intervention (Training; lower-left panel) and 5 min after finishing the training intervention (POST; lower-right panel). * Significantly lower than placebo. C+B-A, combination of caffeine and beta-alanine. ES = Cohen's *d* effect size ([post − pre/]/SD both)

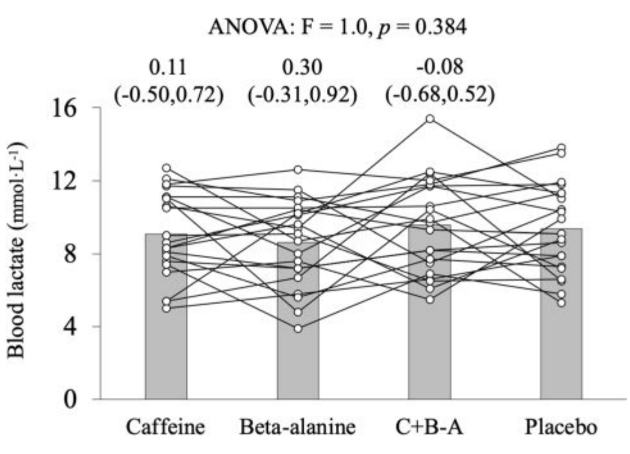

Fig. 2 Comparison of blood lactate concentration between the supplement conditions. C+B-A, combination of caffeine and beta-alanine

study was 200 mg (approximately 2.44 mg/kg), lower than the commonly reported doses of at least 300 mg or 3 mg/kg (Da Silva et al. 2015; Diaz-Lara et al. 2016; Richardson and Clarke 2016; Salatto et al. 2020; Souza et al. 2019; Trexler et al. 2016; Wilk et al. 2019a, b), potentially explaining the observed lack of significant effects. Nevertheless, there are studies using caffeine doses of 200 mg or lower that have found positive effects on exercise performance (Collins et al. 2017; Forbes et al. 2007; Goldstein et al. 2010; Spriet 2014).

Although caffeine and beta-alanine are commonly combined in many MIPS, their synergistic impact on RT performance has not been previously investigated. This gap in research is partly attributed to the personalized nature of athletes' supplementation routines, which are often difficult to standardize or modify for the purposes of a controlled study. This is particularly significant as athletes typically consume multiple supplements simultaneously, often without accounting for the total dosage, the variety of ingredients, or the potential interactions (Burke 2017). This is a significant issue, given that the prevalence of supplement use among athletes ranges from 40 to 100%, depending on the sport and level of competition (Garthe and Maughan 2018). The requirement to discontinue supplementation

Table 2 Type and intensity of itching reported for the different supplement conditions prior to the supplement administration (PRE1), 30 min after supplement administration (PRE2), and 5 min after finishing the training intervention (POST)

Stage	Supplement	Itching (type and intensity)					
		Tingling	Stabbing	Burning	Uncomfortable	Unbearable	Worrisome
PRE1	Caffeine	0 (20), 1 (1)	0 (21)	0 (21)	0 (21)	0 (21)	0 (21)
	Beta-alanine	0 (21)	0 (21)	0 (21)	0 (21)	0 (21)	0 (21)
	C+B-A	0 (20), 1 (1)	0 (21)	0 (21)	0 (21)	0 (21)	0 (21)
	Placebo	0 (21)	0 (21)	0 (21)	0 (21)	0 (21)	0 (21)
PRE2	Caffeine	0 (20), 1 (1)	0 (21)	0 (21)	0 (21)	0 (21)	0 (21)
	Beta-alanine	0 (11), 1 (5), 2 (4), 3 (1)	0 (17), 1 (4)	0 (20), 3 (1)	0 (19), 1 (1), 2 (1)	0 (21)	0 (21)
	C+B-A	0 (14), 1 (4), 2 (3)	0 (18), 1 (2), 2 (1)	0 (19), 2 (1), 3 (1)	0 (20), 2 (1)	0 (20), 2 (1)	0 (20), 1 (1)
	Placebo	0 (21)	0 (21)	0 (21)	0 (21)	0 (21)	0 (21)
POST	Caffeine	0 (20), 1 (1)	0 (21)	0 (21)	0 (20), 3 (1)	0 (21)	0 (21)
	Beta-alanine	0 (20), 1 (1)	0 (21)	0 (21)	0 (20), 1 (1)	0 (21)	0 (21)
	C+B-A	0 (21)	0 (21)	0 (21)	0 (21)	0 (21)	0 (21)
	Placebo	0 (20), 1 (1)	0 (21)	0 (21)	0 (21)	0 (21)	0 (21)

The first number represents the intensity of itching, with 0 indicating no itching, 1 indicating a little, 2 indicating moderate itching, and 3 indicating severe itching. The number in brackets represents the count of participants experiencing each intensity level. C+B-A, combination of caffeine and beta-alanine

weeks before experimental sessions for an adequate washout period further complicates participant recruitment and hampers the ability to conduct methodologically rigorous studies that accurately assess the effectiveness of individual and combined supplements.

We chose to explore the sole effect of caffeine because it is considered one of the most critical components in many pre-workout MIPS. For example, Jagim et al. (2016) found that MIPS containing caffeine can enhance the sensation of energy during exercise compared to those without caffeine. In this study, neither the caffeine-only session nor its combination with beta-alanine significantly improved upper-body endurance. This suggests that higher doses of caffeine than those typically found in MIPS might be necessary to achieve noticeable enhancements in resistance training performance. However, as Spriet (2014) observed, caffeine can enhance performance even at lower doses, suggesting that the effectiveness of caffeine may vary from individual to individual. Similarly, the acute effect of beta-alanine alone did not enhance upper-body performance. While beta-alanine is believed to promote increased training volume (Trexler et al. 2015), its positive effects tend to be long-term, requiring daily intake for at least 2–4 weeks and potentially higher doses than those used in our study or found in commercially available MIPS, which typically range from 3.2 to 6.4 g/day (Saunders et al. 2017).

There were no significant differences in velocity performance ($MV_{fastest}$ and $MV_{average}$) between the different supplement conditions. The primary ingredient in MIPS that can enhance bar movement velocity is caffeine (Lane and Byrd 2018; Raya-González et al. 2020). A meta-analysis on the effect of caffeine on velocity in RT indicated that caffeine has a pronounced effect on movement velocity in upper-body exercises (Raya-González et al. 2020). However, most studies included in the meta-analysis measured velocity using different protocols, such as incremental load tests (Del Coso et al. 2012; Diaz-Lara et al. 2016), a single set to muscular failure (Diaz-Lara et al. 2016), a single set with the load corresponding to a mean velocity of 1 m/s (Mora-Rodríguez et al. 2012), or sets of 3 repetitions at 25% 1RM (Pallarés et al. 2013) or 30% 1RM (Wise et al. 2014), two repetitions at 50% 1RM (Pallarés et al. 2013; Venier et al. 2019), and one repetition at 75% 1RM (Mora-Rodríguez et al. 2012; Pallarés et al. 2013; Venier et al. 2019) or 90% 1RM (Pallarés et al. 2013; Venier et al. 2019). Therefore, positive effects of caffeine on performance are observed, possibly because these are shorter protocols in which the participant can consciously exert maximum effort. In contrast, in a protocol of four supersets, it may be more challenging to maintain maximum focus on performing all repetitions at maximum velocity due to the high volume of work and accumulated fatigue. Only one study measured bar velocity in a more extended training protocol with 10 sets of 3 repetitions at 80% 1RM after caffeine ingestion showing positive effects in performance in bench press peak velocity and mean velocity (Lane and Byrd 2018). Although both the protocol implemented by Lane and Byrd (2018) and our study induced some level of fatigue, differences in set configuration (10 sets of 3 repetitions vs. 4 supersets performed until the velocity dropped below 0.35 m/s for the bench press and 0.60 m/s for the bench pull), intensity (80% of 1RM vs.

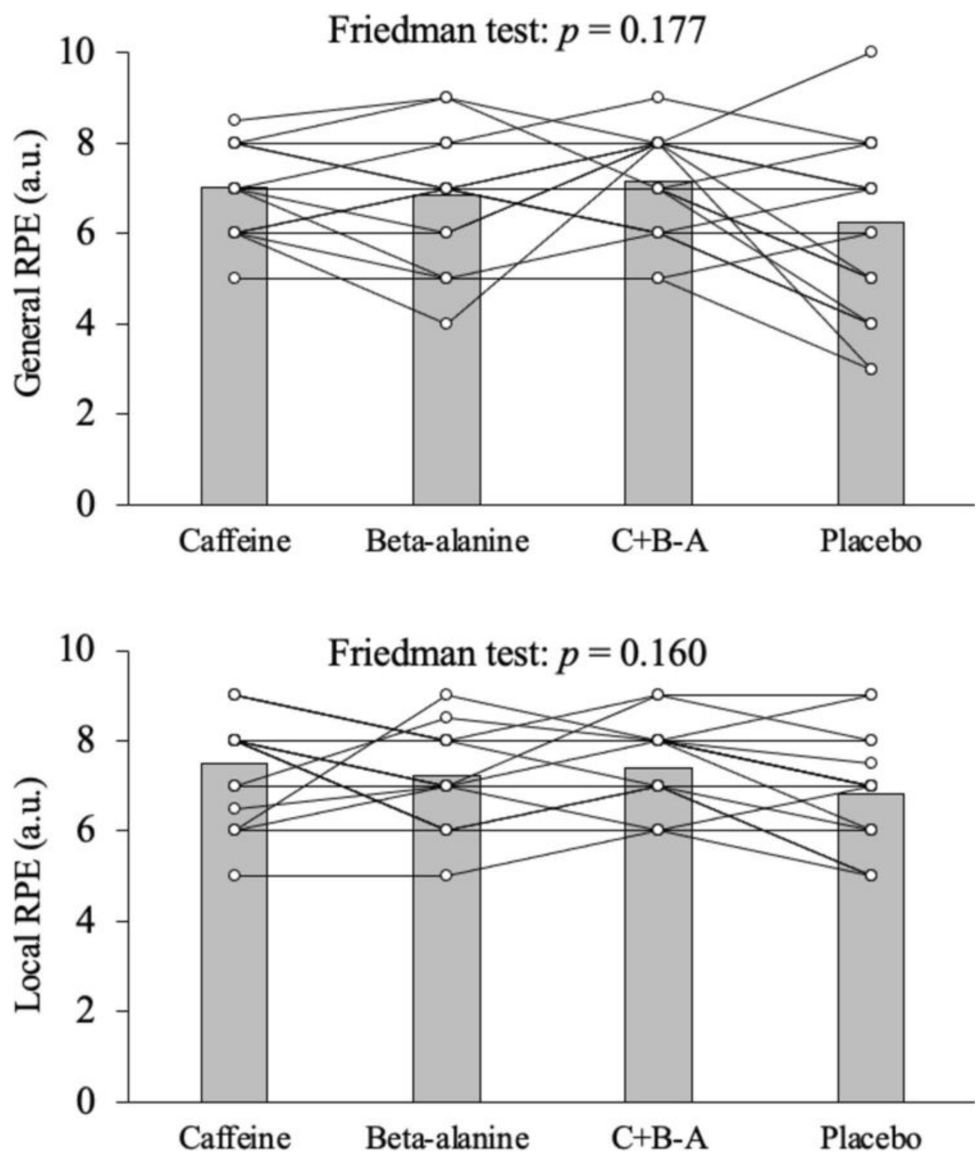

Fig. 3 Comparison of general (upper panel) and local (lower panel) ratings of perceived exertion (RPE) between the supplement conditions. C+B-A, combination of caffeine and beta-alanine

a 20RM load), and the total number of repetitions in a single session (30 vs. approximately 100) may explain the observed variations in caffeine's effectiveness.

No significant differences were observed in any of the readiness questionnaire variables between the supplement conditions at PRE1 or PRE2. These results are consistent with other studies that also found no differences in perceptual variables between different supplements in RT protocols (Kruszewski et al. 2022; Tinsley et al. 2017). Similarly, no significant differences in RPE were observed between the supplement conditions. These results align with other findings (Duncan et al. 2013; Green et al. 2007; Kruszewski et al. 2022; Nicoll et al. 2023; Tinsley et al. 2017). Thus, in accordance with a previous meta-analysis (Doherty and Smith 2005), the perceived effort and fatigue after a demanding RT session may be similar regardless of supplement intake.

In line with previous studies examining the acute effect of MIPS on blood lactate levels following RT (Blake et al. 2020; Jagim et al. 2016; Lane and Byrd 2018; Negro et al. 2022; Venier et al. 2019), no significant differences in lactate levels were observed between the different supplement conditions in the present study. These results are expected, given that the total number of repetitions and their execution velocity were comparable across the experimental conditions. No remarkable findings were observed regarding heart rate among the different supplement conditions. Therefore, in accordance with previous research (Blake et al. 2020; Curtis et al. 2022; Jung et al. 2017; William Kedia et al. 2014), it can be concluded that acute ingestion of the studied supplements in RT is safe. However, it is noteworthy that the supplement conditions containing beta-alanine elicited mild itching in approximately half of the participants at PRE2. This phenomenon is a common occurrence known as paresthesia that occurs after beta-alanine ingestion (Décombaz et al. 2012; Smith-Ryan et al. 2012). This may not be considered a serious adverse effect, as it does not impact performance and the sensation disappears after the RT session.

A strength of our study is that we used a crossover experimental design with a triple-blinded design, considered the gold standard to minimize bias and ensure the validity of the findings (Lang and Stroup 2020). Additionally, performing a training protocol of four supersets allowed us to assess the ability to maintain performance in a practical training setting, rather than in a laboratory-like test environment. However, the present investigation is not without limitations. A potential limitation is the use of absolute doses of the different supplements. More consistent results might have been obtained by administering doses tailored specifically to each participant's body mass. However, absolute doses were chosen as this is the recommended form of ingestion in commercially available products. The current study was conducted in an acute setting. As such, we do not have information on how these supplements would affect performance following chronic ingestion. Additionally, the participants were recreationally trained individuals with at least 1 year of RT experience, making it unclear how this supplementation might impact other populations.

Conclusions

The ingestion of caffeine alone, beta-alanine alone, or their combination has minimal effects on exercise performance, as well as physiological and perceptual responses during a non-failure upper-body superset RT session. The only adverse effect was mild paresthesia in those taking supplements containing beta-alanine; however, the acute ingestion of these supplements can be considered safe, as the itching subsided after completing the RT session. Future research should explore the effects of these supplements over long-term ingestion, varying doses, diverse RT stimuli, and across different populations.

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Author contributions AM, PJ, CA and AG conceived and designed research. AM, SM and DM conducted experiments. AM and AG analyzed data. AM, ZL and AG wrote the manuscript. All authors read and approved the manuscript.

Data availability The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Conflict of interest PJ-M, CA-F, and DJ serve as scientific advisors for the sports supplement brand Life Pro Nutrition. The other authors affirm that their research was conducted impartially, without any commercial or financial affiliations that might be perceived as a conflict of interest.

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