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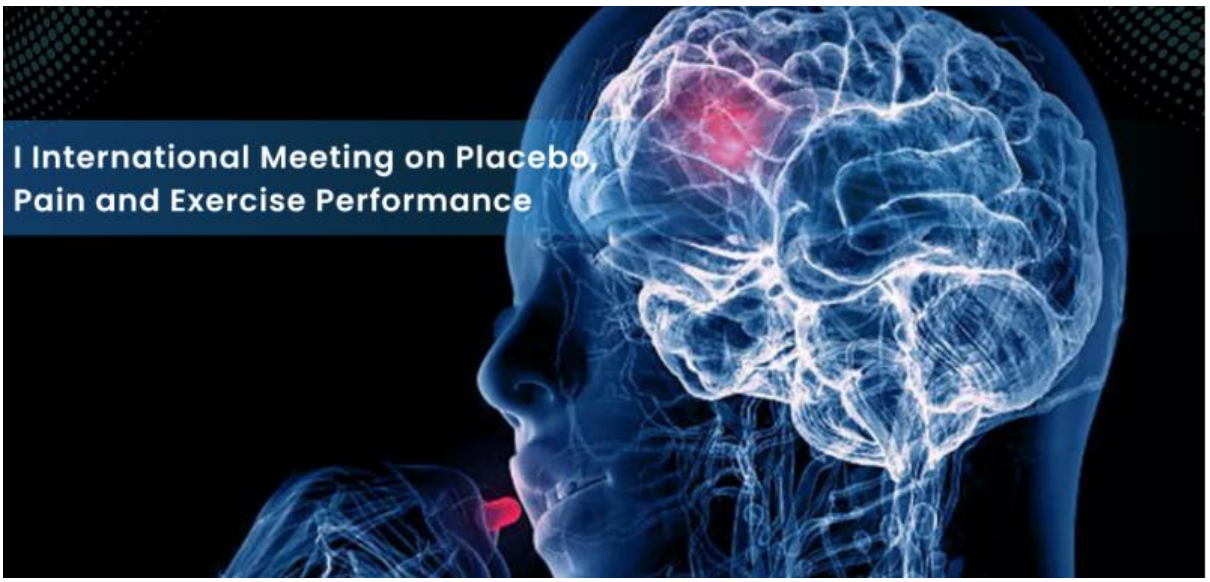

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Calcium Lactate Supplementation Neither Mitigates the Mental Fatigue Nor Improves Endurance Performance

Fernanda da Silva Valim Belozo[1], Miller Pereira Guimarães[1,2,3,4], Camila Vilas Boas Teixeira[4], Gilmar de Jesus Esteves[1,2,5,6], Paulo Eduardo Pereira[1,2,7], Paulo Henrique Silva Marques de Azevedo[1,2]

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Introduction: Mental fatigue has been shown to impair physical performance by increasing the rating of perceived effort. Lactate serves as a preferred energy substrate for neurons during periods of high metabolic demand. Given this, we aimed to determine whether calcium lactate supplementation can attenuate mental fatigue and enhance endurance performance during a 5-km running time trial performed under mental fatigue. **Methods:** This double-blind, placebo-controlled study included ten recreational runners (6 women, 4 men; 18–40 years old) with at least one year of training experience and ≥3 weekly sessions. Participants attended five sessions, spaced 5–7 days apart. Session 1 involved anthropometric assessment and familiarization. In session 2, the control condition (CTRL), runners completed a 5-km treadmill in their best time. In session 3, the mental fatigue (MF) situation, participants performed a Stroop task (a mentally fatiguing test) before the 5 km run. In Sessions 4 and 5, participants ingested either calcium lactate (150 mg·kg^{-1}; LAC) or a placebo (PLA) before the Stroop task, followed by the 5 km time trial. Outcomes included running time, heart rate, Rating of Perceived Effort (RPE), subjective mental fatigue (Visual Analogue Scale), and Stroop performance. For all variables, descriptive analyses were performed using mean and standard deviation values, a repeated-measures ANOVA, and Bayesian factor analysis. **Results:** The Stroop test indicated that mental fatigue was induced. The supplementation conditions (lactate and placebo) improved running performance compared with the mental fatigue condition. The control condition showed performance similar to that in the mental fatigue condition. Heart rate and Rating of Perceived Effort were influenced only by the moment (kilometer covered). **Conclusion:** Neither calcium lactate nor placebo supplementation mitigates the effects of mental fatigue over endurance performance during a 5 – Km running time trial in mentally fatigued runners.

Keywords: Perceived Effort, Sports Performance, Endurance Exercise, Cognitive Task.

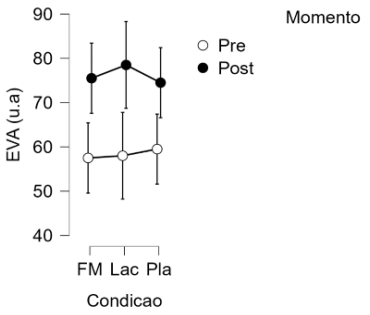

Figure 1. Descriptive analysis of the visual analogue scale.

Table 1: Descriptive analysis of the number of errors on the Stroop Test.

	MF	LAC	PLA
B1	12.7±15.00	12.7±16.9	12.6±15.04
B2	17.2±17.13	17.00±18.10	13.8±13.17
B3	16.5±16.19	16.5±18.99	21.7±22.65
B4	23.00±23.22	23.00±23.22	19.7±18.57
B5	15.6±8.99	21.40±17.36	20.00±19.74

Table 2: Descriptive analysis of the number of correct answers on the Stroop Test.

	MF	LAC	PLA
B1	406.30±46.37	387.30±16.90	387.40±15.04
B2	393.10±37.64	383.00±18.10	386.20±13.17
B3	393.50±38.09	383.50±18.99	378.30±22.65
B4	398.20±51.83	377.00±23.22	380.30±18.57
B5	377.40±19.76	378.60±17.36	380.00±19.74

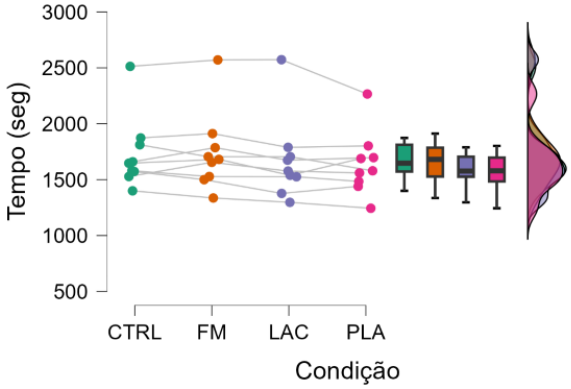

Figure 2. Performance time in seconds of participants according to the conditions.

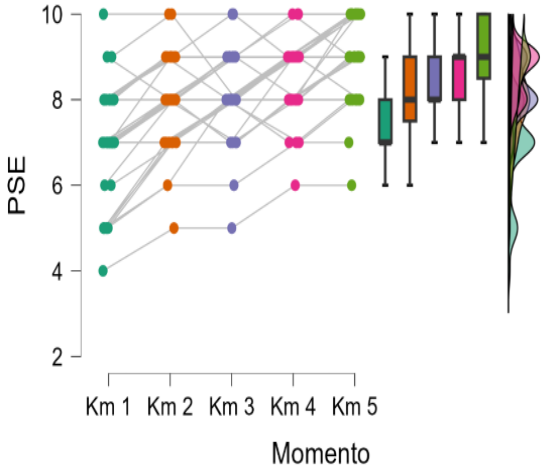

Figure 3. Rating of Perceived Effort (RPE) of the participants according to the moment (distance covered in km).

Transcultural adaptation and validation of the Stanford Expectations of Treatment Scale (SETS) for assessing the expectations of participants in clinical trials.

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Introduction: Participant's expectations about a given treatment can shape its outcome assessment in a scientific context. The Stanford Expectations of Treatment Scale is a questionnaire to assess participants' expectation in an experiment but there is not yet a validated Brazilian-portuguese version. Therefore, the aim of this study was to conduct a cross-cultural adaptation of the scale to Brazilian individuals. **Method:** 66 participants took part of this study (28 men and 38 women) over 18 years old and undergraduate students. 38 were enrolled in an experiment about the effects of caffeine on physical performance, and 28 in an experiment about the effects of binaural stimulation on physical performance. The adaptation protocol consisted of six stages: I) translation; II) translation synthesis; III) back-translation; IV) documental analysis by an expert committee; V) questionnaire testing and VI) publication of the results. A confirmatory factorial analysis and invariance analysis were used to test fitness of the adapted model. **Results:** The factorial analysis showed a good model fit the data, with minimal discrepancy value (0.878) between the original translated version. The adequacy level (0.998) indicated a good fit of the model adjusted by the covariance among the observed data. The Tucker-Lewis Index (1.028) and the Comparative Fit Index (1.000) indicated a good fit of the proposed model to the data, and the Root Mean Square Error of Approximation indicated an excellent fit between the conceptual and structural models. The internal consistency analysis was satisfactory for both positive and negative expectancy (α = 0.66; 95% CI = 0.49–0.77 and α = 0.64; 95% CI = 0.46–0.77, respectively). The invariance analysis showed that regardless of the expected manipulation, the adaptation revealed a good fitness (ΔX^2=7.987, df=16, p=0.241). **Conclusion:** The translated version maintained the original semantic and conceptual structure, without the need for major adjustments, regardless of the expected intervention, allowing reliable use in research on treatment expectations. Since this scale measures the individual's expectation, it may impact how research participants interpret the placebo effect.

Placebo perceived as paracetamol rather than open-label placebo, improves cycling performance for individuals with muscle pain

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Introduction: The placebo effect arises from the expectancy of an individual in a determined intervention, such as analgesics, and that improves an outcome. One of the most studied interventions to elicit the placebo effects are the analgesics that are also investigated by their ergogenic effects in cycling performance. In this study we aimed to investigate if the placebo perceived as paracetamol could improve cycling performance when compared to open-label placebos. We hypothesized that the placebo, perceived as paracetamol, would improve cycling time-to-exhaustion performance. **Methods:** Twelve male participants 22.0 ± 3.5 years old, with body mass of 73.4 ± 6.7 kg, height of 176 ± 0.05 cm, and body fat of 10.9 ± 3.6 % . Attended six visits to the laboratory. I) anthropometric assessments, familiarization with procedures and a maximal incremental test to define the 80% of WPEAK as the workload of time-to-exhaustion tests (TTE); II) TTE without intervention; III and IV) TTE after either hypertonic saline, or isotonic saline injection; V and VI) experimental sessions with hypertonic saline injection and either placebo perceived as paracetamol or open label placebo. The interventions with placebo perceived as paracetamol or open-label placebo were given 50 minutes before the beginning of TTE. All the experimental sessions were performed in randomized and counterbalanced order. **Results:** Placebo perceived as paracetamol improved TTE performance when compared to open label placebo (415.3 ± 150.1 s vs 358.0 ± 175.2 s, p= 0.022; d = 0.95; ES = extremely large), representing an increase of approximately 15%. **Conclusion:** The placebo effect derived from the expectancy to get paracetamol improved cycling performance by around 15%, probably due changes involved the affective-emotional and cognitive-evaluative dimensions, leading participants not to give up on the exercise and to believe they were gaining a greater benefit by continuing.

Keywords: Placebo effect, Expectation, Cycling performance, Open-label placebo, Paracetamol

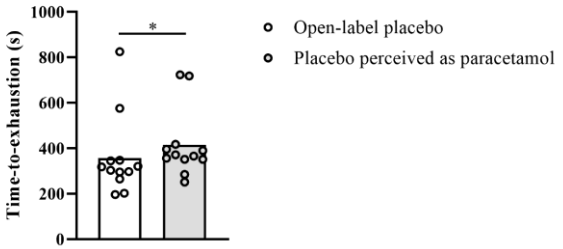

Figure 1. Time-to-exhaustion in open-label placebo (white circle) and placebo perceived as paracetamol. * Denotes significant differences between conditions (p= 0.022; ES = extremely large).

Placebo perceived as caffeine does not influence cortical asymmetry index or physical performance

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Introduction: The placebo effect has been described as a phenomenon capable of altering neurophysiological responses through expectations generated by an inert substance. Thus, substances known for their ergogenic effects could also carry an expectancy component and contribute to changes in cortical activity, particularly frontal cortex asymmetry, a marker associated with motivational states that may influence physical performance. The present study investigated whether the expectation of being supplemented with caffeine could influence frontal cortex asymmetry and physical performance. **Methods:** 30 healthy participants (attended six laboratory sessions, with the first 3 dedicated to familiarization and control, and the final three for experimental procedures, as follows: 1 and 2) presentation of the study and

familiarization with the experimental procedures; 3) baseline measurements; 4 and 5) placebo design perceived as caffeine or placebo; 6) positive control with caffeine. Responses for the integral of the force-time curve at 80% of isometric maximal voluntary contraction and frontal asymmetry index were compared using one-way ANOVA analyzed following the manipulation of expectation in time to exhaustion test during plantar flexion. **Results:** When compared to baseline (pre-ingestion) measures, the condition ($p = 0.98$), time ($p = 0.64$), and their interaction ($p= 0.95$) did not alter the pattern of frontal asymmetry. For the integral of the force–time curve corresponding to 80% of MVC, no effect of asymmetry predominance was observed, either for the left ($p = 0.48$) or for the right hemisphere ($p = 0.94$). In fact, the performance of both cortical predominance groups showed comparable time to exhaustion across the conditions: placebo perceived as placebo, placebo perceived as caffeine, and caffeine. **Conclusion:** The findings indicate that the expectation of caffeine supplementation did not modify frontal asymmetry nor significantly affect physical performance, suggesting that the caffeine placebo effect, under the tested conditions, did not influence these outcomes. These results reinforce the view that cortical asymmetry represents a neurophysiological trait linked to cognitive and emotional processes that influence physical exercise, rather than a variable easily modulated by expectancy or practice.

Keywords: Placebo effect, Frontal Asymmetry, EEG, Physical Performance, Caffeine.

Personality Traits Do Not Moderate the Placebo Effect on Strength Performance

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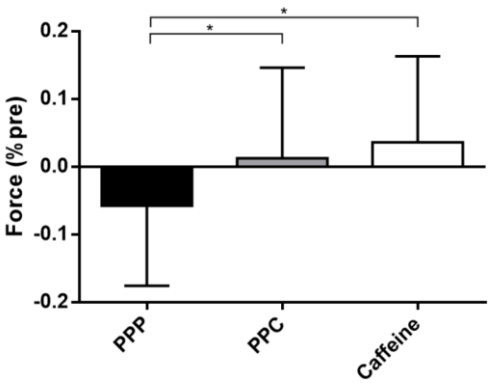
The placebo effect is a phenomenon in sports science and can influence physical performance through psychobiological mechanisms mediated by expectations and individual differences. Among these, personality traits have been suggested as potential moderators of susceptibility to placebo responses; however, current evidence remains inconclusive. To examine whether personality traits moderate the effects of placebo on physical performance under different experimental conditions. Methods: After familiarization and control sessions, thirty participants (15 men, 15 women) took part in the study (24.43 ± 4.90 years; 1.69 ± 0.09 m; 70.67 ± 13.46 kg; 20.87 ± 11.55%). Each participant completed three experimental conditions (placebo perceived as placebo, placebo perceived as caffeine, and caffeine). Physical performance was assessed using a maximal voluntary contraction (MVC). Personality traits were evaluated with the Big Five inventory. Data were analyzed with a linear mixed model (random intercepts for participants) including condition, personality trait, and their interaction as fixed effects. A significant main effect of condition was found on performance ($F(2,50) = 6.91$, $p = 0.002$). Neither sex ($F(1,25) = 0.12$, $p = 0.728$) nor personality traits ($F(1,25) = 0.50$, $p = 0.485$) showed significant main effects, and no significant Condition × Personality trait interaction was observed ($F(2,50) = 1.68$, $p = 0.197$). Performance was influenced by the experimental condition, but the assessed personality traits did not moderate the placebo effect. In conclusion, placebo improves strength performance, but personality traits do not moderate this effect. Other individual characteristics may play a more prominent role in placebo responsiveness in sports contexts.

Keywords: Placebo effect, Personality traits, and Physical performance



Expectations Matter: Expectation Manipulation Is Crucial for Placebo Effects

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Introduction: Placebos are considered as the gold-standard method to control potential expectancy bias in randomized controlled trials. However, studies have been shown that even in a randomized controlled trial, individuals can experience expectancies effect and produce similar responses to the real treatment. Especially in the context of exercise, the placebo effect is widely studied, and numerous studies reported its effect. Therefore, the aim of this study was to investigate the potential placebo effect in a simulated randomized controlled trial. **Methods:** Thirty participants (15 male and 15 female) were enrolled in this study. This study is a simulated randomized controlled clinical trial but using placebos in both sessions. Participants were informed that each experimental session would have a 50% chance of containing caffeine or placebo; however, they received placebo in both. After the randomized controlled clinical trial, participants received caffeine and were correctly informed about this allocation as a positive control. The study consisted of 5 visits: Visits 1 and 2: Familiarization; visits 3 and 4: simulated randomized clinical trial; visit 5: open-label caffeine. After a warm-up, physical performance was assessed by means of maximal voluntary contraction (MVC), rate of force development (RFD), and time-to-failure task at 80% of MVC force. **Results:** Participants who ingested open-label caffeine but not any placebo sessions improved motor performance. There was a main effect of caffeine on MVC ($p = 0.009$; $d = 4.2$), and time-to-failure task ($p < 0.001$; $d > 4.0$). However, the rate of force development remained unchanged ($p = 0.78$, $d = 0.09$). **Conclusion:** These results suggest that placebo effects could not be evoked when participants don't have expectations manipulation.

Keywords: Placebo, Physical Performance, Expectation.

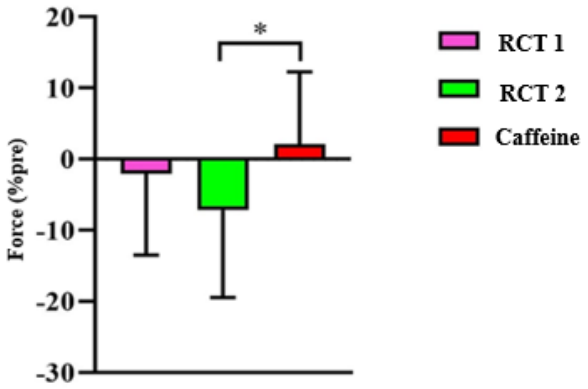

Figure 1: Force during maximal voluntary contraction (MVC) in placebo sessions in a randomized clinical trial (RCT) design. Values are expressed as percentage change (%) from baseline (mean ± SD).

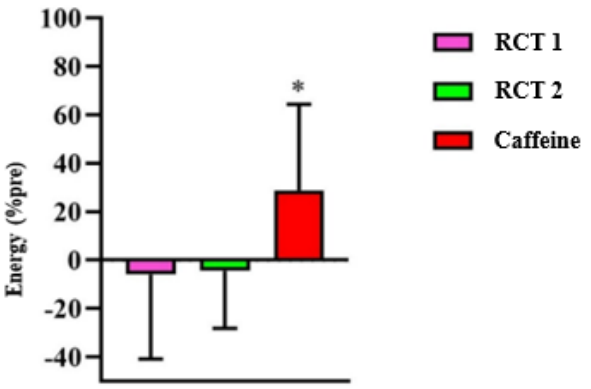

Figure 2: Energy during the 80% time-to-failure task in placebo sessions in a randomized controlled trial (RCT) design. Values are expressed as percentage change (%) from baseline (mean ± SD).

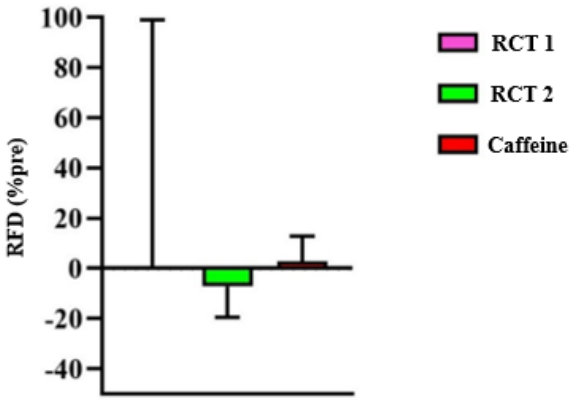

Figure 3. Rate of force development (RFD) during maximal voluntary contraction (MVC) in placebo sessions in a randomized controlled trial (RCT) design. Values are expressed as percentage change (%) from baseline (mean ± SD).

Reported Side-Effects of Consuming Caffeine and a Placebo Perceived as Caffeine in Healthy Men

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Introduction/Objectives: Placebo perceived as caffeine can enhance exercise performance, with reports that it may also elicit caffeine-like side-effects, such as tachycardia, alertness and tremors. However, no study has directly examined these effects. This study investigated the prevalence and intensity of side-effects following ingestion of a placebo perceived as caffeine. **Methods:** Twenty-two healthy men (22 ± 6 years) completed three randomized and counterbalanced sessions: caffeine perceived as caffeine (3 mg/kg), placebo perceived as caffeine and placebo perceived as placebo. Participants abstained from caffeine for 24 h before each trial. In each session, they rated 18 caffeine-related symptoms (0–4) at two time points (pre- and ~50 min post-supplementation). Symptoms were classified as psychological or physical. Intensity was analyzed using linear mixed-effects models, and prevalence using binomial mixed models. Effect sizes (partial eta squared, η^2p) were calculated for all models. Analyses were conducted in RStudio ($\alpha = 0.05$). **Results:** Psychological symptoms increased slightly from pre- to post-supplementation in all conditions (Table 1). A significant main effect of condition was found for the intensity of all symptoms ($p < 0.001$, $\eta^2p = 0.008$), but not for time ($p = 0.28$) or the interaction between condition and time ($p = 0.82$). Psychological symptoms showed significant effects for condition ($p < 0.001$, $\eta^2p = 0.03$) and time ($p = 0.046$, $\eta^2p = 0.006$). Prevalence of psychological symptoms also differed between conditions ($p < 0.05$), with higher values for caffeine-caffeine and placebo-caffeine compared to placebo-placebo (Figure 1). Physical symptoms showed a small effect of condition ($p = 0.025$, $\eta^2p = 0.0045$), but no differences after correction and no effect of time or interaction. Contrast analyses indicated significant differences only between caffeine-caffeine and placebo-placebo for psychological symptoms pre- and post-supplementation (Figure 2). All effect sizes were small. **Conclusion:** There were no effects of caffeine or placebo-caffeine on the change in incidence or intensity of caffeine-associated side-effects. Prevalence of psychological symptoms was higher for all conditions compared to physical symptoms. Significant main effects of condition were observed, but they were attributed to the differences at baseline.

Keywords: Placebo effect. Psychological symptoms.

Table 1. Estimated marginal means (EMMs) of psychological symptoms (0–4) pre and post-supplementation and effect size.

Condition	Pre-supplementation	Post-supplementation
Caffeine	0.95	1.04
Placebo-caffeine	0.78	0.89
Placebo	0.64	0.78

Overall effect of condition: $\eta^2p = 0.03$

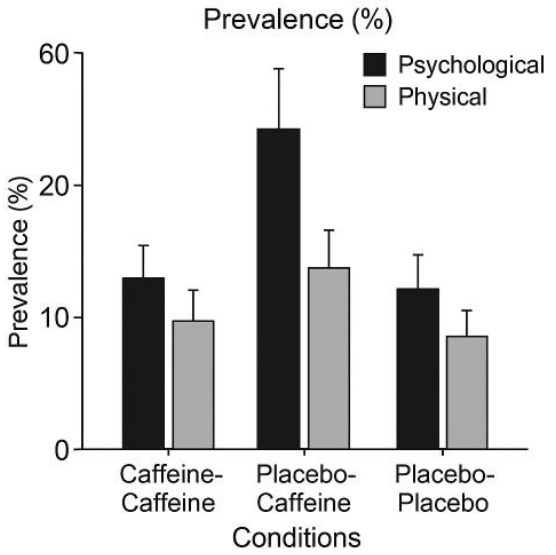

Figure 1. Prevalence of psychological and physical symptoms post-supplementation across conditions. Caffeine shows the highest prevalence, followed by placebo-caffeine and placebo.

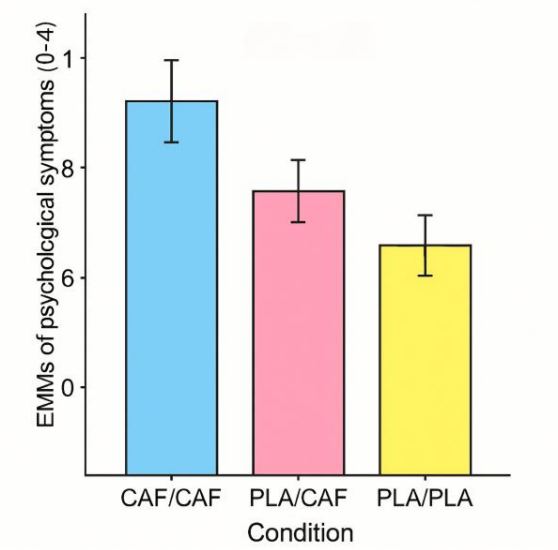

Figure 2. Estimated marginal means of psychological symptoms post-supplementation.

Effect of Open-Label Placebo on Performance in CrossFit® Practitioners during the Cindy Benchmark

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Introduction: Athletes frequently use ergogenic aids to enhance exercise performance, yet, a substantial proportion of these performance improvements can be attributed to placebo effects. Open-label placebo (OLP) interventions, where participants knowingly receive an inert substance, have recently emerged as a promising and ethically acceptable strategy to harness these effects. Evidence suggests that OLP can enhance performance in certain exercise modalities through expectation-driven and neurobiological mechanisms influencing perception, motivation, and effort. However, findings remain inconsistent and further research is needed to determine its effectiveness across different exercise types. To date, no study has examined OLP effects on high-intensity, intermittent exercise such as CrossFit®. Investigating OLP effects on CrossFit® performance is essential to establish its potential as a performance-enhancing strategy for this activity.

Objectives: This study aims to evaluate the effect of an acute OLP intervention on performance, and physiological and psychological responses during the Cindy benchmark in trained CrossFit® practitioners. We hypothesize that OLP administration will improve performance outcomes.

Planned Methods: This study will use a randomized, counterbalanced, crossover design. CrossFit® practitioners aged 18–45 years, with at least one year of training experience, will participate in four sessions: two for familiarization with the experimental procedures, one for the OLP intervention, and one control session. The OLP intervention will include a standardized presentation explaining placebo mechanisms and the concept of OLP, emphasizing that placebo effects are powerful, may occur automatically, and that taking the capsules is essential. This will be followed by ingestion of two inert red-and-white capsules (each containing 100 mg of flour) 15 minutes before the benchmark *Cindy*. The control session will not include any specific information or capsule ingestion. The total number of repetitions completed during the 20-minute *Cindy* protocol (5 pull-ups, 10 push-ups, and 15 air squats) will be used as the performance outcome. Heart rate and ratings of perceived exertion will be measured throughout exercise.

Keywords: Athletic performance, Weightlifting, Nutritional Supplements, Placebo Effect, Fatigue.

Superstitious Behaviors in Trained Brazilian Athletes: Preliminary Findings on the Acceptance of Placebo Administration by Athletes and Professionals

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Introduction: Superstitious behaviors occur when an incorrect assumption of a cause–effect relationship leads to repeated behavior. In athletes, these practices may modulate internal states by reducing anxiety and enhancing self-confidence, with benefits suggested to arise through placebo effects. Although superstitions may influence sport performance and involve placebo effects, no study has evaluated superstitious behaviors in trained Brazilian athletes. This study reports the prevalence and forms of superstitions among athletes, using data from an ongoing questionnaire on acceptance of placebo administration by athletes and professionals. **Methods:** An anonymous online survey was conducted using a convenience sample. Participants reported their superstitious behaviors, perceived influence on performance, and related details. Data on superstitious behavior were content-analyzed, coded, and validated by triangulation. **Preliminary Results:** From 118 athletes, 30 (25.4%) reported engaging in rituals or superstitions before training, 76 (64.4%) did not, and 12 (10.2%) were unsure; among those engaging or unsure, 73% believed these practices improved or greatly improved performance. Content analysis identified five categories (Figure 1). The two largest were *Practices before and during competition* (49%) and *Omens, premonitions, and beliefs about the result of a contest* (35%), while the remaining three account for 16% combined (Figure 1). These two main categories were further subcategorized (Figure 2): Practices before and during competition—Entry/Initiation (29%), Order/Control (24%), Food (19%), Music/Focus (19%); Omens, premonitions, and beliefs—Spiritual/Religious (60%) and Future Self-Projection (40%). **Future Directions:** Among 118 respondents, only 30 reported superstitions, which may relate to prior evidence that athletes frequently regard them negatively. However, among those who reported superstitions, most believed they improved performance. Our next step is to assess how these practices relate to athletes' acceptance of placebo use and to identify which athlete characteristics are associated with superstitious behaviors.

Funding

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Keywords: Superstitions; Rituals; Placebo Effects; Sports Performance.

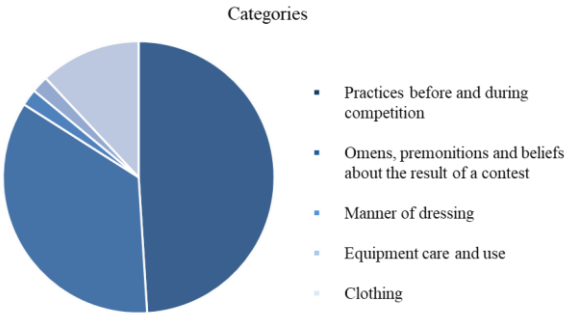

Figure 1. Categories.

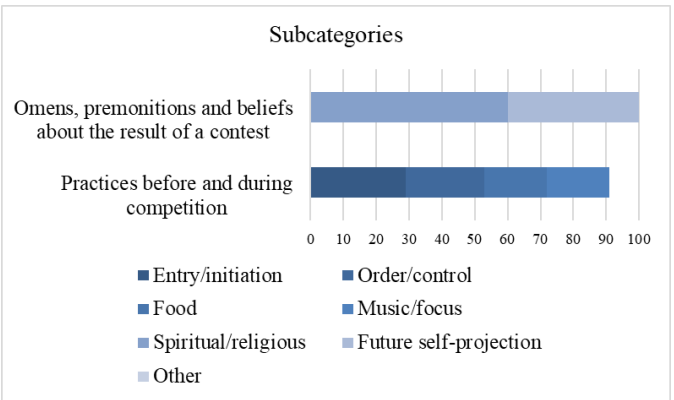

Figure 2. Subcategories

Deceived vs. open-label placebo: Effect of Placebo Perceived as Caffeine in Human Performance

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Introduction: Placebo effect is characterized by a change in a specific outcome, caused by the expected benefit from the use of a substance or active treatment. In exercise studies, the placebo perceived as caffeine is commonly used to investigate its effect on motor performance. Recently, open-label placebos have risen as a non-deceptive form of placebo to improve exercise. Therefore, our aim was to investigate the potential ergogenic effect of placebo perceived as caffeine and open-label placebo in motor performance outcomes. Furthermore, we analyzed whether the intervention has a different effect on men and women. **Methods:** Thirty volunteers (15 women and 15 men) were underwent to 8 experimental visits. In this study we addressed 2 of them that are related to our aim. Participants received either a placebo perceived as caffeine (told caffeine, received placebo) and an open-label placebo (told placebo, received placebo) 50 minutes before the motor performance assessment. A maximal voluntary contraction of 5 seconds and a time-to-failure (80% maximal voluntary contraction) test were performed to assess the motor performance in a plantar flexion test. All outcomes were assessed as percentage of pre-intervention. **Results:** The maximal voluntary contraction force was improved in the placebo perceived as caffeine condition, compared to open-label placebo (- 1% vs – 3%, p=0.04). An interaction between condition and sex showed that male participants exhibited greater force than female in OLP condition (p=0.01), not in PPC (p=0.02). PPC also improved the time-to-failure task (29% vs 4%, p=0.02), but there were no sex differences. **Conclusion:** PPC improves physical performance disregarding the sex and this effect is more pronounced in time to failure task.

Keywords: Placebo effect, Placebo Perceived as Caffeine, Physical Performance, Open-label Placebo.

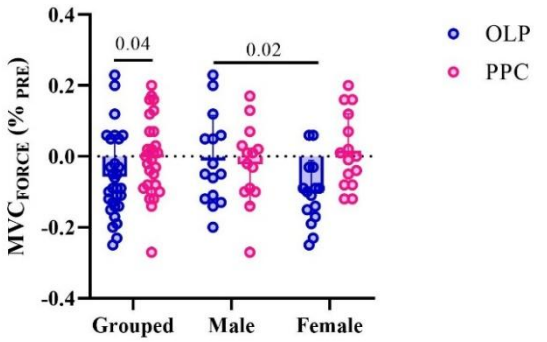

Figure 1. Comparison between sexes in maximal voluntary contraction (MVC) in open-label placebo (OLP) and placebo perceived as caffeine (PPC). Values expressed as mean and standard deviation.

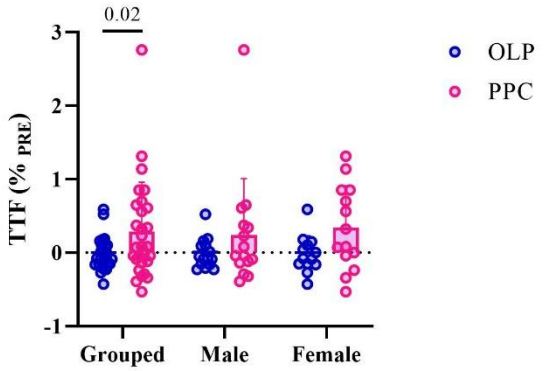

Figure 2. Comparison between sexes in test to failure (TTF) in open-label placebo (OLP) and placebo perceived as caffeine (PPC). Values expressed as mean and standard deviation.

Efficacy of a placebo perceived as paracetamol on exercise performance in individuals with prior muscle pain

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Introduction: To isolate the effects of pain without the confounding influence of fatigue,

hypertonic saline injections have been used in previous studies to experimentally induce muscle pain. The painful experience preceding the task may modulate exercise-related sensations (i.e., effort, pain, and affect), thereby impairing performance. In this context, substances with analgesic properties have been tested as strategies to attenuate the negative effects of pain on exercise performance. **Objective:** To investigate whether a placebo perceived as paracetamol can improve physical performance during exercise performed under prior pain induction and to examine its effects on perceptual responses of effort, pain, and affect throughout the task. **Methods:** Twelve healthy men (age: 22.0 ± 3.5 years; body mass: 73.4 ± 6.7 kg; height: 176 ± 0.05 cm) completed two experimental sessions in a crossover and counterbalanced design. In each session, participants performed a cycling time-to-exhaustion test (TTE) following the injection of hypertonic saline solution to induce muscle pain, after ingesting either a placebo perceived as paracetamol (PCT) or a placebo openly described as inert (PLA). Perceptual responses of effort, pain, and affect were assessed at rest and during exercise. Differences in performance among PCT and PL with pain conditions were tested using a T-students test. Perceptual responses (RPE, pain, and affect) were compared between PCT and PLA using a mixed model with condition (PCT vs. PLA) and time (25%, 50%, 75%, and 100% of the TTE) as fixed factors. **Results:** Analysis revealed that participants increased their time to exhaustion when they perceived the placebo as PCT compared with PLA (PCT = 415.3 ± 150.1 s vs. PLA = 358.0 ± 175.2 s; $p = 0.022$; $d = 0.95$; ES = extremely large; Figure 1). The longer TTE under PCT was accompanied by greater perceived exertion ($p = 0.04$; $d = 0.87$; ES = very large), whereas no significant differences were observed for pain ($p = 0.76$; $d = 0.12$; ES = small) or affect ($p = 0.85$; $d = 0.07$; ES = trivial) during exercise (Figure 2). **Conclusion:** A placebo perceived as paracetamol enhanced cycling performance in participants experiencing prior muscle pain.

Keywords: Placebo; Muscle Pain; Hypertonic Saline; Exercise Performance; Fatigue.

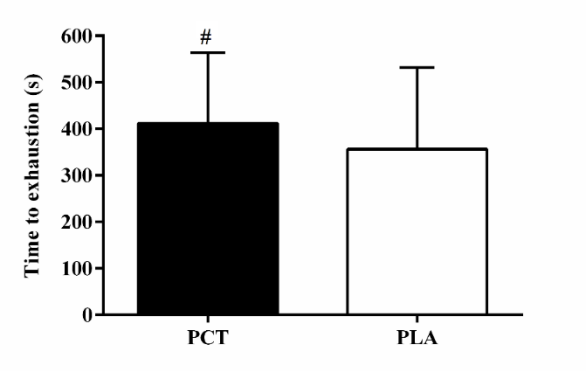

Figure 1.

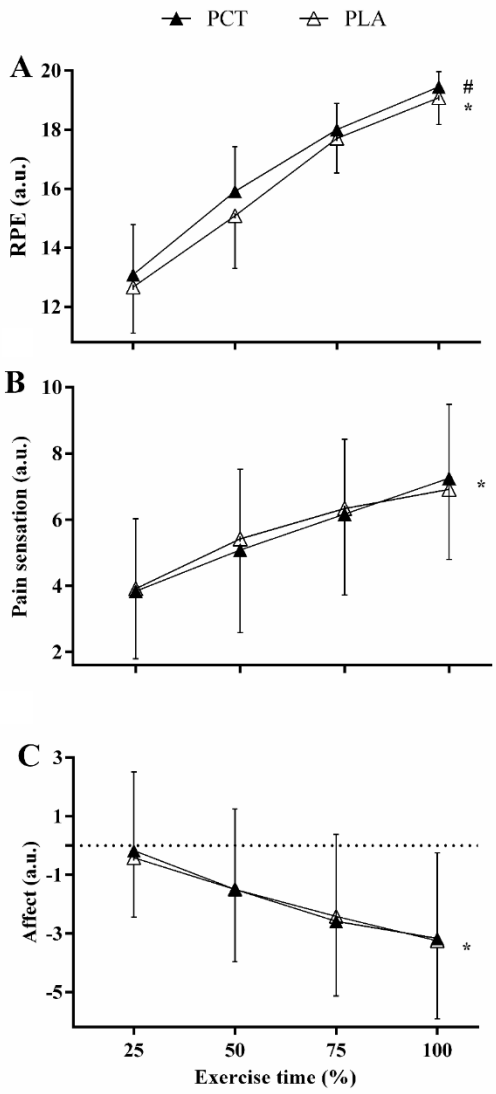

Figure 2.

The impact of altitude expectation on running performance: protocol of a balanced placebo design study

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In the past 20-years, a body of evidence demonstrates that placebo and nocebo effects can significantly influence exercise performance. However, no study has examined these phenomena during exercise in relation to both hypoxic and normoxic conditions. This abstract outline a novel protocol for a study that aims to (1) investigate how altitude expectation influences 5-km running performance in hypoxia (simulating 1,800 m; FiO_2 = 16.8%) and normoxia (0 m; FiO_2 = 21.0%), and (2) determine whether physiological responses are also affected by altitude expectation. This randomized, within-participant, balanced placebo trial will recruit 20 trained runners (≥18 y, any gender), who will complete six 5-km time-trials on a treadmill: two familiarization sessions followed by four experimental sessions. During the experimental trials, participants will perform under four randomized conditions: (1) told hypoxia/given hypoxia, (2) told hypoxia/given normoxia, (3) told normoxia/given hypoxia, and (4) told normoxia/given normoxia. All trials will take place inside a normobaric hypoxic chamber. The researcher will be unblinded, while participants will be blinded in the deceptive conditions. Expectation will be manipulated using standardized verbal instructions delivered by the same researcher and reinforced with fake environmental screens displayed inside the chamber. Expectation will be assessed before each session, while perceptions and side-effects will be recorded immediately after completion. Oxygen saturation, blood lactate, and ratings of perceived exertion will be assessed before and after exercise, and heart rate will be continuously monitored. To control for prior exercise and diet, participants will record training and food intake before each trial. Following completion of all experimental sessions, participants will undertake an incremental test to determine maximal oxygen uptake. Data will be analysed using linear mixed models, including a random intercept for participants and a fixed effect of condition, with planned contrasts between each experimental condition. This study has received ethical approval from the Research Ethics Panel at Canterbury Christ Church University (ETH2425-0201), and recruitment and data collection are currently underway. The full protocol has been registered on the OSF but will remain private until the end of data collection, as it contains sensitive information that could compromise the study.

Keywords: Hypoxia, Running, Outcome expectations.

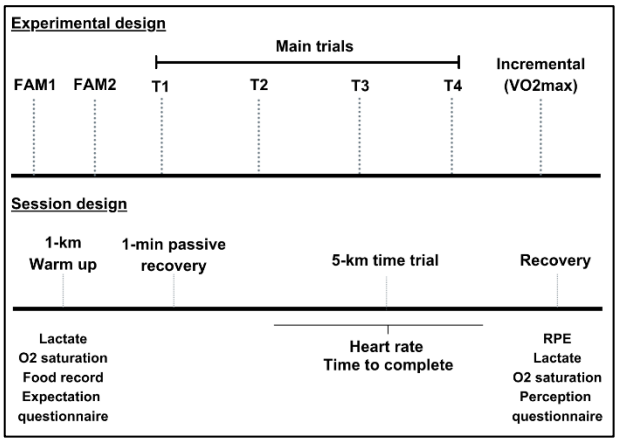

Figure 1. Experimental timeline and within-session structure.

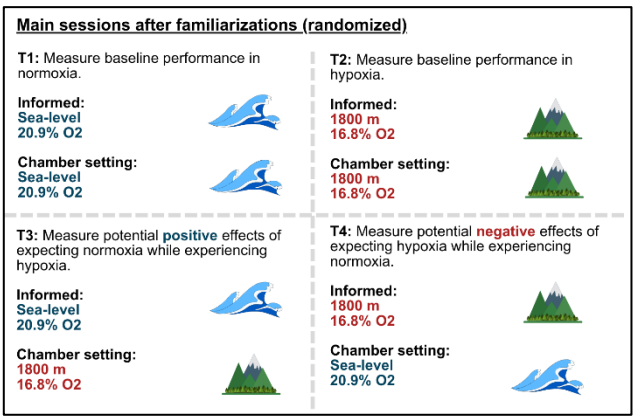

Figure 2. Balanced placebo design and main experimental conditions.

Effect of Expectancy on Physical Performance: Comparison Between Randomized Clinical Trial and Perceived Placebo Designs

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Introduction: The placebo effect can significantly modulate physical performance depending on participants' expectations, influencing the interpretation of ergogenic interventions. Although placebo control is considered the gold-standard method to minimize expectancy bias, some studies suggest that even within a randomized controlled trial (RCT), participants' expectations can still influence performance outcomes. Therefore, this study aimed to compare a simulated RCT design with a perceived-placebo design to examine how expectancy manipulation affects motor performance. **Methods:** Thirty healthy adults (15 men, 15 women; 18–40 years) participated in a crossover study. Each participant completed 8 visits over 21–35 days. Visits 1 and 2) familiarization with instruments and procedures; visit 3) baseline assessment; visit 4 and 5) an simulated RCT; visits 6 and 7) placebo perceived-as-caffeine design; visit 8) true caffeine In the RCT design, participants were informed that each session had a 50% chance of containing caffeine or placebo, but all capsules contained placebo. In the perceived-placebo design, participants were explicitly told whether they were ingesting caffeine or placebo, although all capsules also contained placebo. Both designs were conducted sequentially, with intra-design counterbalancing. Performance outcomes included maximal voluntary contraction (MVC), time to failure task and rate of force development. **Results:** A main effect of design was found for time to failure task ($F = 3.57$; $p = 0.02$; $d = 0.50$), but not for MVC ($F = 2.45$; $p = 0.07$; $d = 0.40$) or rate of force development ($F = 0.22$; $p = 0.88$; $d = 0.12$). The placebo perceived as caffeine produced greater energy output than placebo in one RCT session ($p = 0.04$), with borderline effects in the other sessions. **Conclusion:** Expectancy manipulation significantly influenced physical performance, particularly in muscle endurance outcomes. Belief in caffeine intake enhanced performance even without an active substance, emphasizing the need to control expectancy effects when interpreting ergogenic interventions.

Keywords: Placebo effect, Placebo Perceived as Caffeine, Physical Performance, Open-label Placebo.

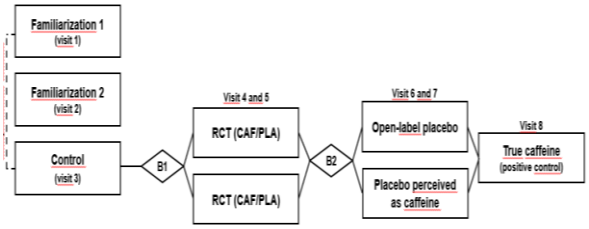

Figure 1: Study Design

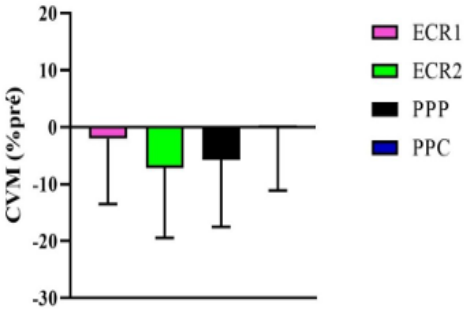

Figure 2. Maximal voluntary contraction (MVC) during placebo sessions in the randomized clinical trial (RCT), placebo perceived as caffeine (PPC), and placebo perceived as placebo (PPP) designs. Values are expressed as percentage change (%) relative to baseline measurements (mean ± SD).

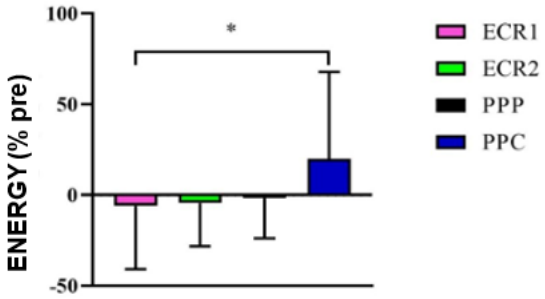

Figure 3. Energy output during placebo sessions in the randomized clinical trial (RCT), placebo perceived as caffeine (PPC), and placebo perceived as placebo (PPP) designs. Values are expressed as percentage change (%) relative to baseline measurements (mean ± SD).

Effect of Caffeine and Placebo Perceived as Caffeine on Performance in a 4-km Time Trial Test

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Introduction: It is suggested in the literature that the use of caffeine (CAF) as an ergogenic supplement may improve performance in endurance exercises, since from a psychological standpoint, CAF is associated with a reduction in the perception of fatigue. Although the mechanisms underlying the placebo effect are not fully elucidated, its influence on performance is well documented, as the expectation of receiving a beneficial supplement can activate neural tissue involved in brain reward pathways. The present study aimed to investigate the effect of caffeine (CAF) and a placebo perceived as caffeine (PPC) on performance in a 4-km time trial (TT4km). The hypothesis was that both CAF and PPC would enhance cyclists' performance. **Methods:** Eleven male volunteers participated in the study (age: 32.0 ± 7.5 years; body mass: 74.9 ± 8.6 kg; height: 175.5 ± 5.5 cm). Three pre-test interventions for the TT4km were used: a control (CON), caffeine (CAF), and a placebo perceived as caffeine (PPC). The participants completed four visits: one for familiarization with the procedures and preliminary TT4km testing, and three for the experimental interventions (CON, CAF, and PPC). In each visit, only one intervention was administered, in a randomized and counterbalanced order. The interval between sessions was 3–7 days to avoid fatigue and residual effects of the ingested substance. Both caffeine and placebo doses were standardized at 6 mg/kg of body mass. The dependent variable, maximal power output (Wmax), was used as the primary outcome to assess performance differences among interventions. **Results:** A main effect of intervention on performance was observed (P = 0.02), with a significant improvement in CAF compared to PPC (CAF: 331.45 ± 13.19 vs. PPC: 306.25 ± 12.76), but not when compared to CON (CAF: 331.45 ± 13.19 vs. CON: 312.86 ± 13.86). In addition, the main effect of time was observed (P = 0.002), but no time × intervention interaction effect (P = 0.18). **Conclusion:** The findings for CAF are consistent with the literature, suggesting that caffeine supplementation can induce performance improvements. However, no improvement was observed in the PPC intervention when compared with the CON group.

Keywords: Caffeine; Placebo; Performance; Power; Fatigue.

Brain responses to Caffeine and Placebo perceived as Caffeine during visual checkerboard stimulation in healthy men: preliminary data from an fMRI study

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Introduction/Objective: The placebo effect is a neurobiological response to placebo treatment associated with positive outcomes. Caffeine is one of the most investigated substances in placebo research on sports performance, with strong evidence showing performance benefits after ingestion of placebo perceived as caffeine. Neuroscience findings indicate that placebo effects are mediated by neural mechanisms similar to those they mimic. However, it remains unclear whether brain activity changes following a placebo perceived as caffeine mimic those shown with caffeine. This study aimed to assess how caffeine and a placebo perceived as caffeine influence brain activity, as

measured by functional magnetic resonance imaging (fMRI). **Methods:** Twenty-two healthy men (22 ± 6 years) completed a modified balanced placebo design with three randomized and counterbalanced conditions: caffeine (3 mg/kg) perceived as caffeine (CAF/CAF), placebo perceived as caffeine (PLA/CAF), and placebo perceived as placebo (PLA/PLA). In each condition, participants underwent fMRI scans before and 60 min after supplementation. During scans, they completed a passive visual stimulation task with a flickering checkerboard presented in a standard sequence: fixation cross (25 s) + checkerboard (5 s) x 8 repetitions (Figure 1). Higher-level analyses were conducted in FSL (v6.0.7.8) using FEAT/GLM with a two-paired group difference design under a Fixed Effects model, comparing post- vs. pre-supplementation across participants to evaluate consistent activation patterns in the sample. **Partial results:** Several significant clusters were observed after CAF/CAF supplementation (up to 1,828 voxels; $p < 0.001$; Z_max = 10.2), predominantly located in the occipital cortex (Figure 2). This pattern suggests greater activation in visual areas following CAF/CAF intake. After PLA/CAF supplementation, a small but significant cluster was detected (47 voxels; $p = 0.008$; Z_max = 5.03), also located in the occipital cortex (Figure 3). In contrast, no significant clusters were found after PLA/PLA supplementation, indicating an absence of increased activation when the treatment was presented as a placebo (Figure 4). **Perspectives:** Supplementation of both caffeine and placebo perceived as caffeine activated visual areas, with caffeine producing much larger effects, while open supplementation of placebo did not alter brain activity. The next step is to refine data processing and continue with confirmatory analyses.

This study was financed by the São Paulo Research Foundation (FAPESP), Brazil. Process numbers: 2021/06836-0; 2025/04119-0; 2024/16981-5. The first author receives a PhD scholarship from CAPES: 88887.895557/2023-00.

Keywords: Placebo effect. Expectancy. BOLD signal. Visual cortex. Brain activation.

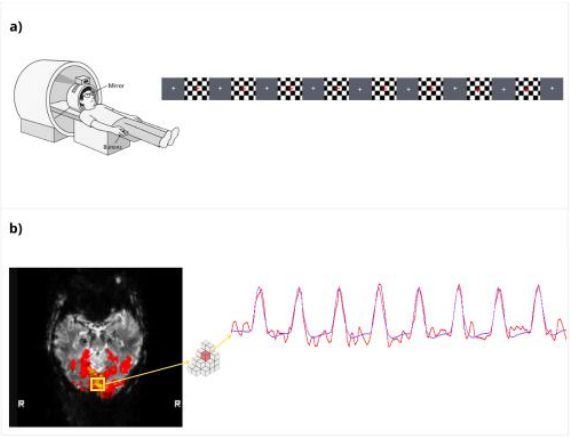

Figure 1. Experimental set-up and task-fMRI design. a) Set-up: participant inside scanner fixate on a mirror for viewing the visual-task (25 s fixation + 5 s stimulation x 8). b) Example of occipital activation from one participant and the BOLD response at one voxel.

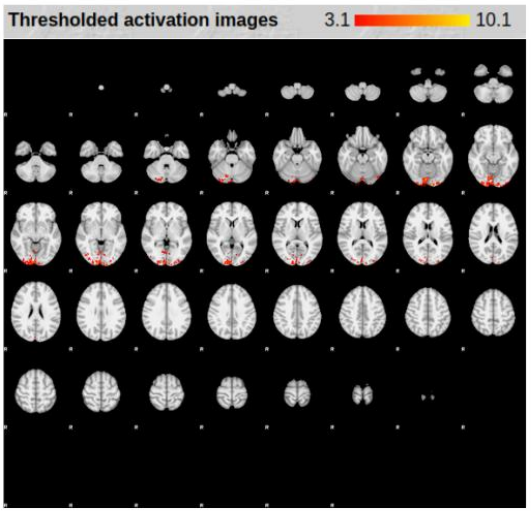

Figure 2. Group-level statistical activation map (Fixed Effects analysis). Z-statistical map (Z = 3.1–10.1) showing significant clusters of BOLD activation for the contrast condition post > pre (post > pre supplementation after caffeine perceived as caffeine intake).

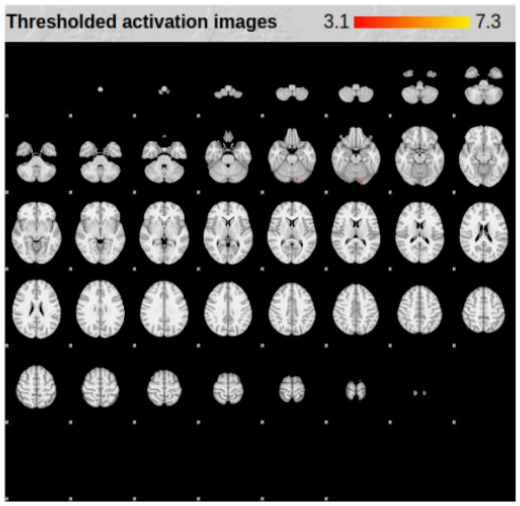

Figure 3. Group-level statistical activation map (Fixed Effects analysis). Z-statistical map (Z = 3.1–7.3) showing significant clusters of BOLD activation for the contrast condition post > pre (post > pre supplementation after placebo perceived as caffeine intake).

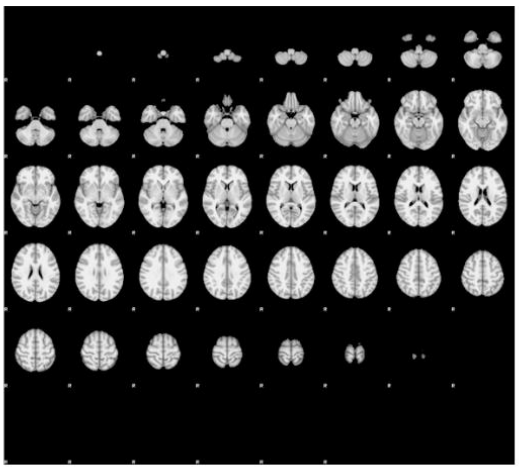

Figure 4. Group-level statistical activation map (Fixed Effects analysis). Z-statistical map showing absence of significant clusters of BOLD activation for the contrast condition post > pre (post > pre supplementation after placebo perceived as placebo intake).

Effect of different doses of theacrine supplementation on endurance performance

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Theacrine (1,3,7,9-tetramethyluric acid) is a purine alkaloid that is naturally found in tea plants (Camellia assamica var kucha), in the Brazilian fruit Cupuaçu (Theobroma grandiflorum) and many species of coffee. Their potential benefits may improve endurance performance through related effects acting as a non-selective antagonist of adenosine receptors without side effects and habituation. However, experimental evidence supporting this assumption is still lacking. The aim of the present study was to test the effects of different doses of anhydrous theacrine (3 and 6 mg·kg^{-1} of body mass) on 4 km cycling time trial performance. Using a double-blind, randomized and counterbalanced study design, nineteen (11 men and 8 women) cyclists (30.8 ± 10.0 years, 71.7 ± 11.8 kg, 170.1 ± 9.0 cm, 17.0 ± 6.2% of body fat) completed three 4 km cycling time trials after ingesting either placebo (control condition), or 3 or 6 mg·kg^{-1} of body mass of theacrine. No significant differences ($p > 0.05$) were observed in time to cover the 4 km cycling time trial between the placebo, 3 mg·kg−1 of theacrine, and 6 mg·kg^{-1} of theacrine conditions. However, the intake of theacrine at the dose of 6 mg·kg^{-1} increased resting systolic (SBP, $p = 0.03$) and diastolic blood pressure (DBP, $p < 0.04$). Some side effects, such as gastrointestinal discomfort, perception of tachycardia, dizziness, headache, head pressure, hand tremor, and lack of disposition were reported after the ingestion of either 3 or 6 mg·kg^{-1} of body mass of theacrine. In conclusion, different doses of theacrine supplementation does not improve endurance

performance compared with placebo condition, while provoking side effects that might restrict its use as a supplement.

Keywords: Endurance performance, Ergogenic aid, Nutritional supplementation.

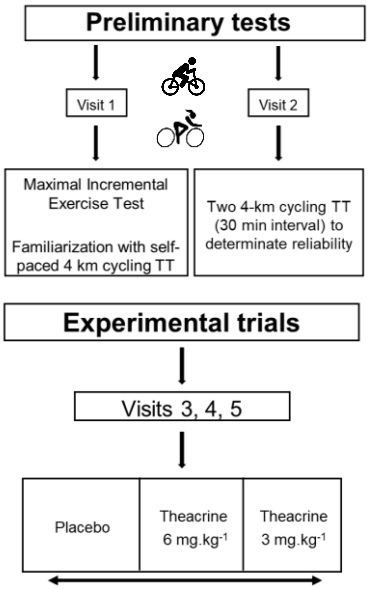

Figure 1: Experimental design. Bidirectional arrows indicated double-blind, randomized and counterbalanced.

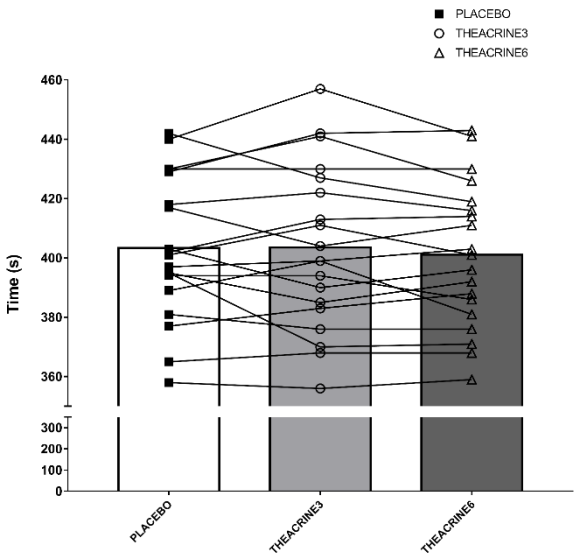

Figure 2: Performance time during a 4 km cycling time trial after ingestion of placebo, 3 mg·kg−1 of body mass of theacrine (THEACRINE3), and 6 mg·kg−1 of body mass of theacrine (THEACRINE6).

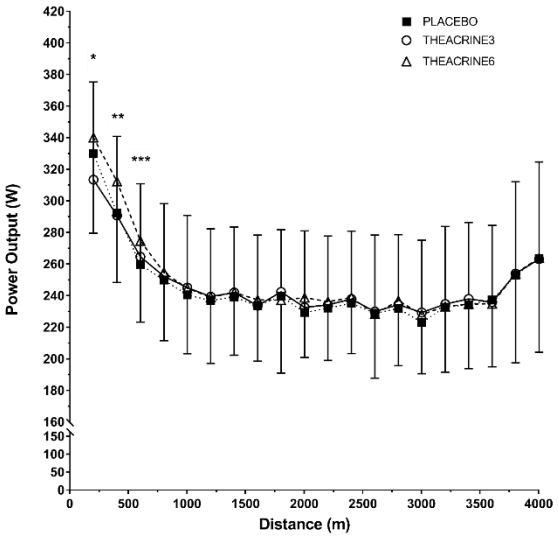

Figure 3: Power output during 4 km cycling TT after ingestion of placebo, 3 mg·kg−1 of body mass of theacrine (THEACRINE3), and 6 mg·kg−1 of body mass of theacrine (THEACRINE6). ∗Higher than all other distance points, except 400 and 4000 m, regardless of the condition. ∗∗Higher than all other distance points, except 3800 and 4000 m, regardless of the condition. ∗∗∗Higher than 1000–3600 m, regardless of the condition.

Table 1. Pre-trial perceived motivation, perception of fatigue, heart rate, and systolic and diastolic blood pressure after ingestion of placebo, 3 mg.kg^{-1} of body mass of theacrine (THEACRINE3), and 6 mg.kg^{-1} of body mass of theacrine (THEACRINE6)

	Placebo	Theacrine3	Theacrine6
Perceived motivation (mm)	70 ± 16	70 ± 16	65 ± 21
Perception of fatigue (mm)	41 ± 21	55 ± 26	40 ± 23#
Resting heart rate (bpm)	70 ± 14	67 ± 13	66 ± 12
Resting systolic blood pressure (mmHg)	114 ± 12	115 ± 14	118 ± 18*
Resting diastolic blood Pressure (mmHg)	63 ± 21	70 ± 17	73 ± 18*

#THEACRINE6 lower than THEACRINE3 ($p < 0.05$).
*THEACRINE6 higher than PLACEBO ($p < 0.05$).

Table 2. Self-reported side effects 120 minutes after the ingestion of placebo, 3 mg.kg^{-1} of body mass of Theacrine (THEACRINE3), and 6 mg.kg^{-1} of body mass of theacrine.

	Placebo	Theacrine3	Theacrine6
Gastrointestinal discomfort	1 (5.2%)	---	1 (5.2%)
Perception of tachycardia	---	1 (5.2%)	1 (5.2%)
Dizziness	---	1 (5.2%)	1 (5.2%)
Headache	---	1 (5.2%)	---
Head pressure	---	---	1 (5.2%)
Hand tremor	---	1 (5.2%)	---
Lack of disposition	---	2 (10.5%)	1 (5.2%)

Data are number of participants, with percentage in relation to total participants reported in the parentheses.

The Epigenetic Potential of the Placebo Effect: The Role of Environment, Expectation, and Nutrition in Gene Modulation Associated with Physical Exercise

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Objective: To explore the potential epigenetic mechanisms underlying the placebo effect in the context of physical exercise and nutritional interventions, emphasizing how environmental, psychological, and dietary factors may modulate gene expression and physiological responses. **Search Methods:** A narrative review was performed between 2020 and 2025 using multiple databases, including PubMed, Scopus, ScienceDirect, SpringerLink, Nature Portfolio, and Frontiers. The search employed the keywords *placebo effect*, *epigenetics*, *exercise*, *nutrition*, *gene expression*, and *neuroendocrine modulation*. Peer-reviewed articles, systematic reviews, and experimental studies describing molecular, neuroendocrine, and behavioral mechanisms linking expectation, physical activity, and dietary factors to epigenetic modulation were selected. Additional references were identified through cross-searching relevant reviews and journals such as Sports Medicine, Free Radical Biology & Medicine, Frontiers in Psychology, Frontiers in Sports and Active Living, Epigenetics & Chromatin, *and* Nature Reviews Neuroscience. Studies in humans and animal models were included when they addressed DNA methylation, histone acetylation, or microRNA changes induced by exercise, nutritional interventions, or placebo-related mechanisms. **Synthesis of Findings:** Recent evidence indicates that psychological expectations can trigger measurable biological responses through neuroendocrine and immune pathways, influencing DNA methylation and histone acetylation patterns in genes associated with stress regulation (NR3C1), inflammation (IL6, TNF), and neuroplasticity (BDNF). Physical exercise and diet act as co-regulators of these pathways, potentially amplifying or mitigating placebo-induced effects. Nutritional compounds such as polyphenols, omega-3 fatty acids, and vitamins B6/B9/B12 have been linked to improved epigenetic resilience, contributing to favorable placebo responses and enhanced exercise adaptation. **Final Considerations:** Understanding the epigenetic foundations of the placebo effect may redefine how we interpret subjective and physiological responses to exercise and nutrition. Integrating genetic and lifestyle data can support more personalized, mind–body–environment approaches in clinical and sports settings. Future studies should clarify dose–response relationships and identify biomarkers predicting individual susceptibility to placebo-driven adaptations.

Keywords: Placebo effect; Epigenetics; Exercise and nutrition

Mind over Menstruation: Do menstrual cycle expectations influence exercise performance? Insights from a scoping review of comparative studies

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Introduction: The menstrual cycle may influence exercise performance through a range of parameters, including hormonal

fluctuations, menstrual symptoms and potentially expectancy. Currently, most sport and exercise research focuses on hormonal fluctuations and menstrual symptoms, however expectancy may also meaningfully influence women's experience of their cycle. This is particularly relevant in modern societies, considering the volume of often-conflicting information available via social media, tracking applications and informal advice, which may exert placebo or nocebo effects on exercise performance. Comparative studies based on non-human models offer a potential means to isolate biological effects from sociocultural influences, but this approach is rarely used in sport and exercise research. Therefore, the aim of this scoping review was to map available evidence related to reproductive cycle influence on performance related outcomes in non-human models. **Methods:** Pubmed was systematically searching using search terms, based on the concept of interest (e.g., reproductive cycle, estrous etc), models (e.g., animals, rodents, primates, equine etc) and the outcomes (e.g., exercise, performance etc). Studies that compared physiological, cognitive, behavioral or exercise performance related outcomes at distinct moments of the reproductive cycle in any animal model were selected. Information regarding the model, study design, phases studied, outcomes evaluated and primary results were extracted. **Results:** Twenty-six articles were identified, with 4 investigating performance animals (racehorses or greyhounds; 15%); 19 were conducted under controlled laboratory conditions using murine or primate models (74%) and 3 were based on observations of primate species in their natural environment (11%). A median of 3 reproductive cycle phases, representing distinct hormonal profiles were assessed (range 1 – 5). Outcomes were grouped as physiological (39%); behavioral or social (26%); cognitive (29%) or performance (6%). Results varied across models and outcomes, but several studies reported physiological, cognitive or behavioral differences between phases. Direct exercise performance outcomes were the least studied, although assumed performance effects were often inferred from changes in other parameters, suggesting that expectation may influence interpretation even in comparative models. **Conclusion:** Comparative research provides a valuable opportunity to isolate biological and performance variation across reproductive cycle phases, but care must be taken to avoid expectancy-driven assumptions when examining cycle-related variation.

Keywords: Reproductive Cycles; Estrous; Menstruation; Performance; Behavior; Expectancy.

The influence of an injected placebo perceived to be an anabolic steroid on the nutritional habits of resistance-trained men

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Introduction: Athletes' beliefs and expectations about a treatment can shape both their psychological and behavioural responses. Larger placebo effects have been reported when participants believe they are receiving banned performance-enhancing substances. Receiving a placebo perceived to be an anabolic steroid has been shown to improve exercise performance acutely; however, whether such expectations also influence long-term lifestyle behaviours remains unknown. These preliminary dietary findings derive from a study investigating whether a placebo perceived to be an anabolic steroid influences lifestyle behaviours in resistance-trained men. **Methods:** Forty resistance-trained individuals with habitual protein intake >0.8 g/kg/day were recruited and monitored for four weeks using dietary records. Participants were randomized into Control (CON; N=20) or Placebo (EAP; N=20) groups. The CON group continued remote monitoring, while the EAP group received weekly placebo injections for 10 weeks. Both groups maintained dietary and training records throughout the intervention; complete data for 15 participants were analysed (CON, N=5; EAP, N=10). Food intake was assessed using three non-

consecutive dietary diaries per week and analyzed in Dietbox. Additionally, participants joined brief focus groups to report experiences related to lifestyle and dietary changes. Mixed-effects models evaluated dietary changes across conditions (CON, EAP) and time (PRE and POST). **Preliminary results:** There were no differences in energy or lipid intake (all $p>0.05$). There was a significant condition*time interaction for protein ($p=0.012$), driven by a reduction from PRE to POST in EAP (−24.5 g/day, $p=0.0065$), while CON showed no change (+7.8 g/day, $p=0.393$). Carbohydrate intake also showed a significant interaction ($p=0.002$), increasing from PRE to POST in CON (+37.2 g/day, $p=0.034$) and decreasing in EAP (-37.8 g/day, $p=0.028$). Qualitative reports aligned with these patterns; for example, an EAP participant noted increasing overall food quantity ("I started eating ten more bread rolls a day"), whereas one CON participant described improved dietary control due to regular dietary logging and not wanting to make a bad impression. **Perspectives:** Preliminary data suggest that injections of a placebo perceived to be an anabolic steroid may modify dietary choices and that participation in an experimental study may influence dietary behaviours, highlighting the impact of psychological factors on nutritional choices.

Keywords: Expectancy; Nutritional Self-Regulation; Diet Adaptations; Deceptive Placebo.

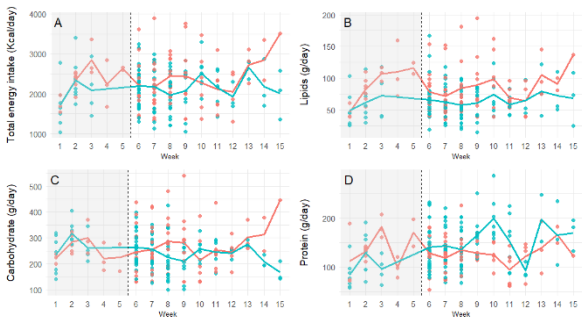

Figure 1. Changes in nutrient intake over time. Blue = placebo injections perceived as anabolic steroid; Pink = Control.

Actual and perceived caffeine effects on working memory performance: a modified balanced placebo design study

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Introduction/Objectives: Caffeine, an adenosine antagonist, can influence cognitive and physical performance, and expectancy alone may also alter behavior. Despite evidence that caffeine improves alertness, attention, and working memory, it remains unclear whether a placebo perceived as caffeine can produce measurable cognitive changes. This study examined the effects of caffeine and expectancy on working-memory performance using a modified balanced-placebo design. **Methods:** Twenty-two healthy men (22 ± 6 y) completed three counterbalanced conditions: caffeine perceived as caffeine (CAFCAF; 3 mg/kg), placebo perceived as caffeine (PLACAF), and placebo perceived as placebo (PLAPLA). Each session included a six-block N-Back task (alternating 0-back and 3-back). Accuracy (%) was computed for each block (Figure 1). Analyses included repeated-measures ANOVA (3×2; Condition × Time), change-score analysis (Δ = post – pre), and linear mixed-effects models. **Results:** Across all conditions, mean accuracy remained low (~25–40%), consistent with the high cognitive load of mixed 0/3-back blocks (Figure 1). The repeated-measures ANOVA showed no significant effects of condition ($p = .789$) or time ($p = .672$), and the Condition × Time interaction only approached significance ($p = .054$; Table 1). Descriptively, CAFCAF showed a slight decrease from pre- to post-test,

PLACAF remained stable, and PLAPLA showed a small increase, though none reached statistical significance (Figure 2). Change-score analysis (Δ accuracy) also revealed no significant effect of condition ($p = .070$; Table 2). Individual trajectories emphasized large within-condition variability and the absence of systematic pharmacological or expectancy-driven improvement (Figure 3). **Conclusion:** Across all analytical approaches, neither caffeine nor expectancy produced meaningful changes in N-Back accuracy. The uniformly low accuracy suggests that the mixed 0/3-back task may have been too demanding to detect subtle cognitive effects. Future studies using larger samples, reaction-time outcomes, and N-Back versions with more stable accuracy ranges may better clarify the contributions of caffeine and expectancy to working-memory performance.

Keywords: Caffeine; Expectancy; Working memory.

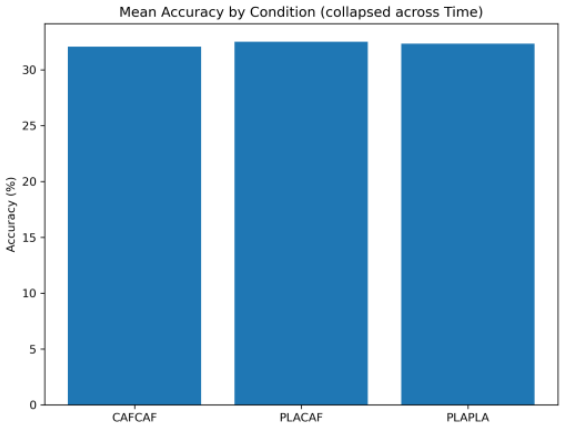

Figure 1. Mean accuracy by condition (all blocks combined).

Table 1. Descriptive accuracy means (Condition × Time)

Effect	F	df (Num, Den)	p
Condition	0.239	2, 34	0.789
Time	0.186	1, 17	0.672
Condition × Time	3.181	2, 34	0.054

Note. Values represent raw (unadjusted) mean accuracy (%) for each condition at pre- and post-test. These descriptive statistics summarize the data but do not reflect model-adjusted effects.

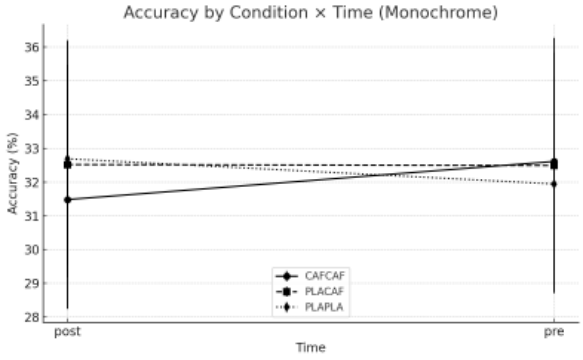

Figure 2. Mean Accuracy (%) During the N-Back Task by Condition and Time (pre vs post). Error bars represent mean ± standard deviation (SD). Values correspond to raw, non-model-adjusted means for each condition (CAFCAF, PLACAF, PLAPLA) at pre- and post-supplementation. Distinct line and marker styles distinguish conditions in this monochrome rendering.

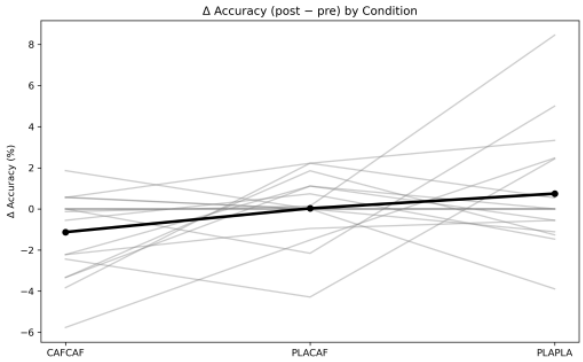

Figure 3. Individual Δ accuracy trajectories (post–pre) across conditions. Note: Each line represents one participant. Values show substantial within-condition variability, with no consistent pattern supporting pharmacological or expectancy effects.

Bias Verification Procedures Regarding Physical and Motor Performance Studies Using Placebos: A Narrative Review

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Introduction: The placebo effect is a response raised from an inert treatment which evokes similar effects to a treatment. Studies using physical and motor performance tasks should take precautions to ensure placebo effects do not alter the main intervention's magnitude, as

differing expectations of receiving an active treatment in the control condition can summarize or minimize the actual effect. **Methods:** The current study carried out a review of the scientific literature in the placebo effect in order to: (I) investigate aspects with potential to influence the placebo effect, (II) indicate what level of influence can be expected in which of them and (III) summarize recommendations to deal with their influence in clinical investigations. All the studies included in this review are from sports science and exercise area. **Results:** The placebo effect is a phenomenon mainly triggered by expectation, influencing perceptual and motor responses through endogenous mediated reward circuits, acting as a key source of bias. The experimental design plays a significant role on placebo effect studies: randomized, double- blinded controlled trials tend to minimize but do not eliminate expectancy variability, while manipulated-expectancy designs provide greater control and effectively direct participant's expectancy towards the active treatment. The type of treatment and personality traits exert a moderate level of influence in the magnitude of placebo effect. Socially accepted treatments enhance placebo responses over alternative treatments, and optimist individuals respond more favorably to placebo interventions in comparison to neurotic individuals, although associated with stronger responses to placebo, representing a specific interest. Factors such as gender and type of outcome assessed can affect placebo magnitude, but its level of influence remains uncertain. **Conclusion:** Factors with a high level of influence on the magnitude of the placebo effect include the type of experimental design, the nature of treatment and the personality traits of the volunteers. Gender and type of outcome assessed, on the other hand, remain uncertain in their influence. Future studies should be aware of other potential sources of bias not addressed here.

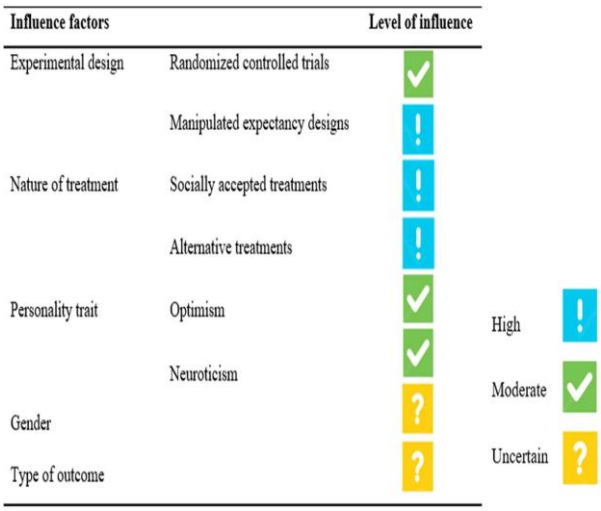

Figure 1. Influence factors of placebo effect in motor outcomes, ranked as high, moderate and uncertain level of influence.

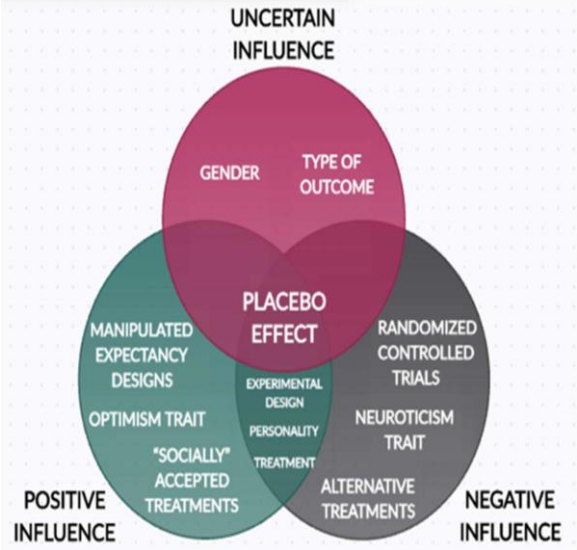

Figure 2. Interaction between factors with potential to influence the placebo effect in motor outcome studies.