Can 3 mg·kg\textsuperscript{−1} of Caffeine Be Used as An Effective Nutritional Supplement to Enhance the Effects of Resistance Training in Rugby Union Players?

This is the Published version of the following publication

Tamilio, Ryan A, Clarke, Neil D, Duncan, Michael J, Morris, Rhys, Grgic, Jozo and Tallis, Jason (2021) Can 3 mg·kg\textsuperscript{−1} of Caffeine Be Used as An Effective Nutritional Supplement to Enhance the Effects of Resistance Training in Rugby Union Players? Nutrients, 13 (10). ISSN 2072-6643

The publisher’s official version can be found at https://www.mdpi.com/2072-6643/13/10/3367/htm
Note that access to this version may require subscription.

Downloaded from VU Research Repository https://vuir.vu.edu.au/42721/
Can 3 mg·kg$^{-1}$ of Caffeine Be Used as An Effective Nutritional Supplement to Enhance the Effects of Resistance Training in Rugby Union Players?

Ryan A. Tamilio 1, Neil D. Clarke 1*, Michael J. Duncan 1, Rhys Morris 1, Jozo Grgic 2 and Jason Tallis 1,2*

Abstract: The present study uniquely examined the effect of 3 mg·kg$^{-1}$ chronic caffeine consumption on training adaptations induced by 7-weeks resistance training and assessed the potential for habituation to caffeine’s ergogenicity. Thirty non-specifically resistance-trained university standard male rugby union players (age (years): 20 ± 2; height (cm): 181 ± 7; body mass (kg): 92 ± 17) completed the study), who were moderate habitual caffeine consumers (118 ± 110 mg), completed the study. Using a within-subject double-blind, placebo-controlled experimental design, the acute effects of caffeine intake on upper and lower limb maximal voluntary concentric and eccentric torque were measured using isokinetic dynamometry (IKD) prior to and immediately following a resistance training intervention. Participants were split into strength-matched groups and completed a resistance-training program for seven weeks, consuming either caffeine or a placebo before each session. Irrespective of group, acute caffeine consumption improved peak eccentric torque of the elbow extensors ($p < 0.013$), peak concentric torque of the elbow flexors ($p < 0.005$), total eccentric work of the elbow flexors ($p < 0.003$), total concentric work of the knee extensors ($p < 0.001$), and total concentric and eccentric work of the knee flexors ($p < 0.046$) following repeated maximal voluntary contractions. Many of these acute caffeine effects were still prevalent following chronic exposure to caffeine throughout the intervention. The training intervention resulted in significant improvements in upper and lower body one-repetition maximum strength ($p < 0.001$). For the most part, the effect of the training intervention was equivalent in both the caffeine and placebo groups, despite a small but significant increase ($p < 0.037$) in the total work performed in the participants that consumed caffeine across the course of the intervention. These results infer that caffeine may be beneficial to evoke acute improvements in muscular strength, with acute effects prevalent following chronic exposure to the experimental dose. However, individuals that consumed caffeine during the intervention did not elicit superior post-intervention training-induced adaptations in muscular strength.

Keywords: resistance exercise; strength; power; ergogenic aids; performance

1. Introduction

A wealth of scientific evidence, summarised in a recent umbrella review [1], documents small but significant improvements in aerobic endurance [2], anaerobic power [2,3], muscular endurance and strength [4,5], and sport-specific skills [6] following acute caffeine ingestion. Given caffeine’s widespread performance-enhancing benefits, it is a popular ingredient in many commercially available products targeted to augment adaptions evoked by exercise training. Most previous research has focused on acute caffeine effects on a single exercise bout [2,7,8]. However, there is a dearth of evidence examining if such acute benefits applied over the long-term can manifest in enhanced, chronic adaptations to exercise training.
Several meta-analyses have reported an ergogenic effect of acute caffeine ingestion for muscular strength [1,3,5]. Due to these acute effects, it would seem intuitive that improved performance in a bout of resistance exercise multiplied over the duration of a resistance training regime may evoke an elevated training response [9]. However, this assumption has not been thoroughly explored and the potential beneficial response of caffeine during chronic exposure may be offset by habituation to its effects. Although a point of contention [10–12] there is evidence to suggest that chronic consumption of 3 mg·kg⁻¹ of caffeine in low habitual caffeine users (<75 mg/day⁻¹) results in intolerance after 4 weeks [13]. Furthermore, in some cases, acute effects of caffeine on exercise performance are not demonstrated in high habitual users (426 mg/day) [14]. Direct comparisons are challenging given the lack of standardised thresholds for determining high and low habitual caffeine use [15]. However, confounding ideas surrounding the chronic use of caffeine for exercise performance would appear to work in paradox, inciting a need for further investigation.

Only two studies examined if chronic caffeine ingestion can augment resistance training adaptations. In resistance-trained males, Kemp et al. [9] demonstrated that 3 mg·kg⁻¹ of caffeine consumed before every exercise session resulted in superior improvements in the bench press and squat one repetition maximum (1RM) compared to the placebo group following 6 weeks of resistance training. Using the same dose and a similar population, recent work by Giráldez-Costas et al. [16] indicated no significant difference in training-induced adaptions in bench press 1RM between groups ingesting either caffeine or placebo during a 4-week resistance training intervention. However, the group ingesting caffeine had a more pronounced improvement in movement velocity when assessed across the force-velocity spectrum.

The disparity in caffeine-induced improvements in maximal strength may be related to the difference in the training regimes and duration of the program. Furthermore, previous studies did not account for baseline strength when assigning participants to training groups, which may have influenced the results. Given the limited research in the area and the inconclusive findings, further investigation is required. Whilst these initial studies offer important insight, work is now needed to understand if chronic caffeine consumption during resistance training induces regional and contractile mode-specific changes given that caffeine’s effect on strength may differ between concentric and eccentric models of activity, contractile velocity, and specific muscle groups [17–20]. Furthermore, previous work fails to consider intersessional performance between caffeine and placebo groups across the course of the training intervention, which is an important driver to enhance resistance-training adaptation. Moreover, previous studies also fail to consider the potential impact of habituation, which may limit the proposed benefits of chronic caffeine supplementation. For this to be achieved, a more complex within and between subject’s experimental design is needed.

Given the outlined important gaps in the literature, the aims of the present study were threefold: (1) using a within-subjects experimental design the present work sought to assess the acute effect of 3 mg·kg⁻¹ of caffeine consumption on the maximal voluntary concentric and eccentric strength of the knee and elbow flexors and extensors in a population of male rugby union players; (2) using a between-subjects experimental design to assess the effects of 3 mg·kg⁻¹ of caffeine consumption on adaptations to a 7-week resistance training program in participants matched for baseline strength; (3) using a within-subjects experimental design to reassess the acute effect of 3 mg·kg⁻¹ of caffeine consumption on the maximal voluntary concentric and eccentric strength of the knee and elbow flexors and extensors post completion of the training regime. As such, the present work provides the most detailed examination of the effects of chronic caffeine consumption on regional and contractile mode-specific adaptations to resistance training and uniquely considers the impact of caffeine habituation in inhibiting augmentation of the training response. It was hypothesised that (1) acute caffeine consumption would evoke improved muscular strength, which would manifest in a small but significant superior training adap-
tations; (2) that the group that consumed caffeine during the training intervention would demonstrate a reduced acute effect of caffeine on measures of muscular strength following the intervention.

2. Materials and Methods

2.1. Participants

Following ethics approval from Coventry University (reference code; P76381; approved on 3/12/2018) and informed consent, 40 apparently healthy participants from the Coventry University Men’s rugby union team agreed to participate in the study. The current study was also in compliance with the declaration of Helsinki [21]. Participants trained with the team twice per week and played competitively once per week. This continued throughout the duration of the study. Potential participants were excluded if they were: suffering from a musculoskeletal injury that prevented safe completion of the exercise trials; were consuming psychoactive medication; had any other underlying contradictions to exercise; or habitually consumed high levels of caffeine (i.e., >6.00 mg/kg/day) [15]. Participants completed a health screen questionnaire prior to each visit. Over the course of the investigation, 10 participants dropped out due to injury (n = 3) (not related to the experimental protocol), illness (n = 2), or for reasons not stated (n = 5) leaving a total sample of 30 (mean ± standard deviation (SD); Age (years): 20 ± 2; height (cm): 181 ± 7; body mass (kg): 92 ± 17).

2.2. Experimental Design

Following baseline assessments of maximal strength and a familiarisation trial, the acute effects of caffeine on maximal strength were assessed, which was immediately followed by chronic caffeine consumption through a resistance training program (Figure 1). Finally, the acute effects of caffeine on muscular strength were reassessed following completion of the training program.

Prior to the assessment of the acute effects of caffeine, participants were asked to abstain from caffeine at least 12 h before testing and intense physical activity at least 48 h prior. As outlined below, when prescribed participants consumed caffeine (3 mg·kg−1; Myprotein, UK) or a placebo (3 mg·kg−1; maltodextrin; Myprotein, UK) issued in a transparent capsule (BulkTM, UK). The ergogenic effect of caffeine supplementation at this dose is well established [3,22,23], and also closely represents a dose achievable without the need for caffeine anhydrous.
2.3. Acute Effect of Caffeine on Upper and Lower Body Strength

The acute effects of caffeine on muscular strength were assessed using a double-blind, randomised, and counterbalanced within-subject experimental design. For this part of the study, the participants were asked to visit the human performance laboratory at Coventry University for one familiarisation and two experimental trials (i.e., caffeine and placebo ingestion).

2.4. Familiarisation

The first visit was to familiarise participants with the experimental procedures to be used for the assessment of the acute caffeine effect. Initially, assessments were made barefoot in shorts and a t-shirt, and measures of height (cm) and body mass (kg) were taken using a SECA 213 portable stadiometer (SECA 213, Hamburg, Germany) and electronic weighing scales (SECA 803, Hamburg, Germany), respectively. Participants were then asked to complete a caffeine consumption questionnaire [24] to determine typical caffeine consumption habits and a caffeine expectancy questionnaire [25] to determine their perception of caffeine as a performance enhancer. The caffeine expectancy questionnaire consisted of 47 questions, which were categorised into the following: withdrawal/dependence (12 questions), energy/work enhancement (8 questions), appetite suppression (5 questions), social mood enhancement (6 questions), physical performance enhancement (3 questions), anxiety/negative physical effect (9 questions), and sleep disturbance (4 questions). Participants were asked to respond to statements using the following cues: “very unlikely”, “unlikely”, “a little unlikely”, “a little likely”, “likely”, and very likely”. These answers were then transformed into a number with 1 being “very unlikely” and 6 being “very likely” [25]. Scores from each subsection were averaged for each individual.

2.5. Warm-Up

Prior to completion of the physical assessments, participants were asked to complete a standardised warm-up of the upper and lower body. The upper body warm-up consisted of 5 min of arm crank ergometry (Lode, Angio) with an unloaded cradle fixed at 70 revs·min⁻¹, followed by static and dynamic stretching of the elbow flexors (biceps brachii and brachialis). Then, the participants completed a lower-body warm-up that consisted of 5 min of cycling on an exercise ergometer (Monark 824E Ergomedic) with an unloaded cradle fixed at 70 revs·min⁻¹ immediately followed by static and dynamic stretching, focusing on the knee extensors (vastus intermedius, vastus medialis, vastus lateralis, and rectus femoris).

2.6. Isokinetic Strength Assessment

After completing the warm-up procedure, participants completed the strength assessment. Skeletal muscle contractile performance was assessed using isokinetic dynamometry in accordance with previously published protocols [18,20,22]. Isokinetic dynamometry is commonly used to evaluate muscular strength [26] and has shown good test-retest reliability in similar populations [27,28]. Furthermore, evidence suggests that a single familiarisation session in athletes adequately addresses potential learning effects for measures of peak torque [29].

Maximal voluntary isokinetic torque (Nm) of the elbow flexors and extensors for the dominant side was measured using an isokinetic dynamometer (Humac Norm, CSMi, model 502140, Stoughton, MA, USA) set up following the manufacturer’s instructions. The rotational axis of the dynamometer head was aligned with the lateral epicondyle of the humerus on the dominant side, with an elbow rest positioned relative to this. A handgrip bar at the opposing end of the lever arm was adjusted relative to the length of the hand and forearm to allow the participant a comfortable grip. During concentric measures, participants were instructed to pull upwards on the bar as hard as possible through a fixed range of motion (80°–120° relative to anatomic zero). During eccentric measures, participants were asked to resist the movement of the lever arm moving through
the same range of motion. Average and maximal concentric and eccentric forces were measured at fixed angular velocities of 60, 120, and 180 deg/s. Participants warmed up with 3 submaximal attempts at each speed to become familiarised with the movements and test speeds. During the assessment of maximal voluntary torque, participants performed 3 attempts separated by 60-s rest. The best attempt of the three was used for the analysis. Each speed was separated by a two-minute rest period. Following the measure of maximal concentric and eccentric force, the participants performed 3 sets of 10 maximal repetitions at 60 deg/s with individual repetitions being summed across the 30 repetitions. Each set was separated by 10 s. All torque values collected were corrected for gravity effects by estimation of limb weight prior to the assessment of maximal voluntary torque. Following each set, Rate of Perceived Exertion (RPE) was measured [30].

Participants then completed an assessment of the maximal voluntary isokinetic torque (Nm) of the knee flexors and extensors. Each participant was strapped to the dynamometer chair in a seated position, and the lever arm axis of rotation was aligned with the lateral femoral epicondyle of the dominant limb. The distal end of the lever arm was fitted with a shin pad which was aligned with the lateral malleolus. A strap was placed across the midpoint of the upper limb of the participant’s dominant leg. Throughout the testing, participants were instructed to keep their arms fixed across the chest. The range of motion was fixed at 10°–80° relative to anatomic zero. The testing protocol was then carried out in the way that described for the assessment of maximal voluntary torque of the elbow flexors and extensors.

2.7. Experimental Trials

The experimental protocol followed the procedure outlined above but was proceeded by a treatment ingestion period (Figure 2). Participants consumed either 3 mg·kg⁻¹ caffeine or a placebo 45 min prior to completion of the warm-up. Treatments were issued 45 min prior to the warm-up so that the experimental trial commenced 60 min post-ingestion. Previous work indicates that maximal blood plasma concentration of caffeine occurs 60 min post-consumption [23]. Readiness to Invest Effort (RTE) [31] and Felt Arousal Scale (FAS) [32] were measured pre-consumption, 15, 30, and 45 min after consumption. An analogue scale was used to measure RTE with a scale from “not ready at all” to “totally ready”. A scale of 1–6 was used for FAS with 1 being “low arousal” and 6 being “high arousal”.

![Figure 2. Schematic of the experimental trial.](image-url)
2.8. Chronic Effects of Caffeine Ingestion during a 7-Week Resistance Training Program

To assess if chronic caffeine ingestion can augment adaptations to resistance training, a between subject’s experimental design was conducted. Participants were randomly split into a control (n = 15) or caffeine (n = 15) group. Groups were matched based on habitual caffeine use, using the data obtained from the caffeine consumption questionnaire, and for baseline strength, using the procedures outlined in the statistical method. Following the assessment of 1RM, all participants then completed the same training regime as indicated below (Figure 3).

![Figure 3. Schematic of Resistance training sessions.](image)

2.9. Assessment of 1 Repetition Maximum

1RM values in the six exercises were assessed over two visits to program the training regime and as an additional baseline marker of muscular strength. On the initial visit, the researcher provided a demonstration of the correct lifting techniques for all used exercises. For all exercises, participants then completed 8–10 unweighted repetitions to ensure the correct lifting technique was achieved. Participants completed assessments of 1RM for squats (SQ), deadlifts (DL), chest press (CP), seated shoulder press (SSP), power clean (PC), and hang clean (HC). All exercises were completed using a 20 kg Eleiko barbell and in accordance with published protocols [33–35]. Prior to 1RM attempts participants started at 50% of estimated 1RM for 3–5 repetitions, progressing to 70% for 1–3 repetitions, and 90% for 1 repetition. All 1RM values were determined by progressively increasing the weight (e.g., 5 kg per attempt) lifted until the participant failed to lift the set weight through a full range of motion and using the correct form [36,37]. A trained researcher/spotter was present during all testing sessions to ensure a proper range of motion. Any lift that deviated from proper technique was not counted. This included a lack of full range of motion exhibited during the lift or technique that did not conform to guidelines for the execution of the exercise in question as defined by Baechle and Earle [38]. This procedure was then repeated on the second visit, which occurred at least 2 days later. A minimum of 1 min of rest was permitted between attempts and a minimum of 5 min rest between lifts. Lifts were altered between the upper and lower body to reduce fatigue and their order was consistent in each testing session.

2.10. Resistance Training Intervention (7-Weeks)

The effect of caffeine on resistance training was assessed using a double-blind, between-subject experimental design. Participants were asked to abstain from caffeine 12 h prior to the commencement of each training session. Forty-five minutes before the commencement of each training session participants in the caffeine group consumed 3 mg·kg⁻¹
caffeine and those in the placebo group an equivalent dose of maltodextrin in the same manner as previously outlined. The intention of the resistance training intervention was to develop upper and lower body maximal strength and strength endurance. Following a standardised warm-up consisting of static and dynamic stretches focusing on the upper and lower body muscles participant completed a circuit training program consisting of 8 exercises. The exercises were CP, SSP, SQ, DL, PC, HC, sit up, and press-ups. The load for CP, SSP, SQ, DL, PC, HC was set at 70% of 1RM; sit-ups and press-ups were performed without any external load. Throughout the course of the intervention, all exercises were performed with “repetitions until failure” (RTF), meaning that the participants lifted 70% of 1RM until exhaustion. Previous resistance training interventions commonly used loads of 60–80% of 1RM [39–42] given that such loads have been shown to increase muscular strength [38,43]. Previous work has demonstrated that resistance training intervention implementing repetitions until failure protocols are effective for improving muscular strength and strength endurance [44–46]. Repetitions until failure was favoured over protocols using a fixed training load given that the open-ended nature of repetitions until failure protocol allowed for a more robust assessment of the effect of acute caffeine consumption across the course of the training intervention. All participants completed two circuits of all 8 exercises, alternating between upper and lower body exercises. A minimum of 2 min rest was provided between exercises and 10 min rest between circuits. The number of successful repetitions and RPE were collected after each exercise. Circuit training sessions took place Tuesday morning and Thursday evening for 7-weeks. Previous work has shown that resistance-training interventions of similar duration are effective in increasing muscular strength [9,41,47]. Upon completion of the 7-week intervention training programme, all participants completed reassessments 1RM.

2.11. Statistical Analysis

Data analysis was performed using Statistical Package for the Social Sciences (IBM SPSS Statistics Version 25) and Excel (Microsoft Windows Version 16.41 2020). Initially, appropriate tests of normality and homogeneity were performed. To match groups for baseline strength prior to completion of the resistance training program, a Pearson’s or Spearman’s correlation was performed between all measures of 1RM. All measures, other than DL and PC (R = 0.364 p = 0.048) and DL and HC (R = 0.239, p = 0.203), were significantly correlated (R = 0.463–0.820, p < 0.05 in all cases). Given that 28 of 30 1RM comparisons demonstrated a significant correlation, all the data were transformed to a Z-score using the formula \((x-\mu)/\sigma\), summed and compared using an independent sample t-test. The acute effects of caffeine on measures of peak torque (PT), total work (TW), and RPE, were assessed using a 4-factor mixed-model ANOVA. The between factor being Group (caffeine and placebo) and within factors being Time (pre-and post-intervention), Treatment (caffeine or placebo), and Speed/Set (60, 120, and 180/ Set 1, Set 2, and Set 3). Furthermore, RTE and FAS were assessed using a 4-factor mixed-model ANOVA. The between factor being Group (caffeine and placebo) and within factors being Time (pre-and post-intervention), Treatment (caffeine or placebo), and Minutes (pre, 15, 30, and 45-min post-ingestion). Maximal strength (i.e., 1RM) measures were assessed using a single factor ANOVA with the fixed factor of Time (pre-and post-intervention). All intervention data (RTF and RPE) were analysed using an imputation method [48,49] followed by a 3-factor mixed model ANOVA with a between factor of Group (caffeine or placebo) and within factors of Session (1–14) and Set (Set1 and Set2). All violations of sphericity were adjusted using Greenhouse–Geisser where appropriate. Relevant main effects and significant interactions were further analysed in a Bonferroni adjusted pairwise comparison. Cases of violated normality were present; however, ANOVA was still considered a robust method of statistical analysis in such cases [50]. Partial eta squared \((\eta^2)\) was reported with significant ANOVA main effects as a measure of effect size [51]. Additionally, effect size \((d)\) from the pairwise comparison (bias-corrected (Hedges) was calculated using the difference in means divided by the SD of the compared variables. Effect size was reported using the following categories:
trivial < 0.20, small 0.20–0.49, medium 0.50–0.79, and large > 0.80 [52]. Data were presented as Mean ± SD with statistical significance set at a level of $p < 0.05$.

3. Results

3.1. Participation Characteristics

Age (caffeine group: 20 ± 2 years; placebo group: 19 ± 2 years; $p = 0.66$), height (caffeine group: 181 ± 8 cm; placebo group: 181 ± 5 cm; $p = 0.78$), or body mass (caffeine group: 89 ± 10 kg; placebo group: 95 ± 22 kg; $p = 0.30$) did not differ between individuals assigned to the caffeine or placebo groups. Average caffeine consumption was 133 ± 123 mg per day and 121 ± 95 mg per day for the caffeine and placebo groups, respectively, with four participants reporting no caffeine use (caffeine group $n = 2$; placebo group $n = 2$). Average caffeine consumption did not differ between groups ($p = 0.888, d = 0.11$). The perceived effect of caffeine in energy/work enhancement and sleep disturbance were significantly higher in the placebo group (Table 1: $p < 0.045, d = 0.97$); however, there were no other significant differences for any other caffeine expectancy subscale (Table 1: $p < 0.744, d < 0.97$). Baseline strength was comparable between the groups prior to completing the resistance training program ($p = 0.40, d > 0.31$).

Table 1. Caffeine expectancy between caffeine and placebo groups.

| Caffeine Intervention Group | Placebo Intervention Group |
|----------------------------|---------------------------|
| Withdrawal / Dependence ($n = 12$) | 2 ± 1 | 2 ± 1 |
| Energy / Work Enhancement ($n = 8$) | 4 ± 1 | 5 ± 1 |
| Appetite Suppression ($n = 5$) | 2 ± 1 | 3 ± 1 |
| Social mood Enhancement ($n = 6$) | 3 ± 1 | 3 ± 1 |
| Physical Performance Enhancement ($n = 3$) | 3 ± 1 | 4 ± 1 |
| Anxiety / Negative Physical Effect ($n = 9$) | 2 ± 1 | 2 ± 1 |
| Sleep Disturbance ($n = 4$) | 3 ± 1 | 4 ± 1 |

Total Questions ($n = 47$)

Note: Values are represented as means ± SD, $n = number of questions.$

3.2. Peak Torque

3.2.1. Elbow Extension Peak Torque

For eccentric PT of the elbow extensors, there was a significant Treatment*Speed interaction (Table 2: $p = 0.001, \eta_p^2 = 0.336$). Pairwise comparison indicated that eccentric PT at 120 and 180°/s was higher following caffeine supplementation compared to placebo (Table 2: $p < 0.013, d > 0.24$). Furthermore, eccentric PT was greater at 180°/s compared to that at 60 and 120°/s, but only in the caffeine trial (Table 2: $p < 0.005, d > 0.17$). For both concentric and eccentric PT there were no other significant interactions (Table 2: $p > 0.055, \eta_p^2 < 0.098$). Concentric PT was significantly affected by Speed (Table 2: $p = 0.001, \eta_p^2 = 0.708$) with PT at 180°/s being lower than that at 60 and 120°/s (Table 2: $p < 0.001$ in both cases). There were no other significant main effects (Table 2: $p > 0.208, \eta_p^2 < 0.088$).
Table 2. Acute effect of caffeine treatment (3 mg·kg⁻¹) pre and post-7-week of resistance training on concentric and eccentric PT (Nm) of the elbow and knee flexors and extensors.

| Angular Velocity (Deg/s) | Caffeine Intervention Group | Placebo Intervention Group |
|--------------------------|----------------------------|----------------------------|
|                          | Acute Placebo  | Acute Caffeine  | Acute Placebo  | Acute Caffeine  |
| Pre-Int                  | Post-Int       | Pre-Int          | Post-Int       | Pre-Int          | Post-Int       |
| Elbow Extension          |               |                 |                |                 |
| Con 60                   | 38 ± 8        | 42 ± 8          | 41 ± 12        | 40 ± 7          | 36 ± 10        | 41 ± 11        | 42 ± 14        | 42 ± 10        |
| Con 120                  | 32 ± 8        | 38 ± 9          | 38 ± 14        | 35 ± 6          | 30 ± 9         | 25 ± 11        | 36 ± 14        | 38 ± 8         |
| Con 180                  | 30 ± 6        | 32 ± 7          | 33 ± 15        | 32 ± 6          | 30 ± 9         | 32 ± 8         | 32 ± 8         | 36 ± 8         |
| Ecc 60                   | 44 ± 11       | 48 ± 9          | 50 ± 16        | 46 ± 10         | 46 ± 18        | 48 ± 15        | 51 ± 17        | 49 ± 17        |
| Ecc 120                  | 40 ± 10 *     | 46 ± 8 *        | 56 ± 19 *      | 48 ± 8 *        | 41 ± 22 *      | 49 ± 13 *      | 52 ± 13 *      | 54 ± 25 *      |
| Ecc 180                  | 40 ± 10 *     | 49 ± 10 *       | 59 ± 20 *      | 50 ± 11 *       | 44 ± 28 *      | 51 ± 14 *      | 55 ± 16 *      | 62 ± 27 *      |
| Knee Extension           |               |                 |                |                 |
| Con 60                   | 51 ± 7 *#     | 56 ± 10 *#      | 58 ± 16 *#     | 56 ± 9 *#       | 51 ± 10        | 56 ± 15        | 60 ± 16 *#     | 61 ± 18 *#     |
| Con 120                  | 50 ± 10 *#    | 51 ± 9 *#       | 52 ± 15 *#     | 53 ± 10 *#      | 45 ± 11        | 54 ± 16        | 55 ± 15 *#     | 58 ± 11 *#     |
| Con 180                  | 45 ± 8 *#     | 48 ± 7 *#       | 48 ± 15 *#     | 49 ± 9 *#       | 50 ± 12        | 49 ± 14        | 41 ± 11 *#     | 50 ± 10 *#     |
| Ecc 60                   | 54 ± 15       | 59 ± 12         | 61 ± 15        | 63 ± 21         | 62 ± 17        | 68 ± 22        | 64 ± 16        | 67 ± 21        |
| Ecc 120                  | 61 ± 17       | 59 ± 12         | 61 ± 15        | 63 ± 16         | 59 ± 13        | 68 ± 20        | 68 ± 19        | 70 ± 19        |
| Ecc 180                  | 61 ± 14       | 63 ± 10         | 61 ± 14        | 66 ± 14         | 65 ± 11        | 70 ± 17        | 62 ± 20        | 72 ± 19        |

Note: Values are represented as means ± SD, PT = Peak Torque, Con = Concentric, Ecc = Eccentric, Pre-Int= Pre-training intervention, and Post-Int= Post-training intervention, matching * represents a significant effect of caffeine prior to the intervention, matching # represents a significant effect of caffeine post-intervention, matching * represents a significant difference on peak torque post the intervention.

3.2.2. Elbow Flexion Peak Torque

For concentric PT of the elbow flexors, there was a significant Group*Time*Treatment interaction (Table 2: p = 0.024 ηp² = 0.168) and for both concentric and eccentric PT a significant Time*Treatment*Speed interaction (Table 2: p < 0.034 ηp² > 0.112). Pairwise comparisons indicated that for the caffeine group, concentric PT was higher post intervention and increased in the placebo group but only when the pre to post caffeine trial was compared (Table 2: p < 0.008, d > 0.17). Eccentric PT was not significantly increased post-intervention (Table 2: p > 0.094, d < 0.53) and was not affected by acute caffeine treatment either pre- or post-the intervention (Table 2: p > 0.209, d < 0.35). However, acute caffeine treatment increased concentric PT measured at 60 and 120°/s both pre and post the training intervention (Table 2: p < 0.005, d > 0.19). In some cases, PT was affected by speed. Following the intervention concentric PT at 180°/s was higher than that at 60 and 120°/s (Table 2: p < 0.003 in both cases) and following the placebo treatment PT at 60°/s was higher than 120 and 180°/s (Table 2: p < 0.030, d > 0.09).
3.2.3. Knee Extension Peak Torque

For eccentric PT of the knee extensors, there was a significant Group*Time*Treatment*Speed interaction (Table 2: \( p = 0.016 \eta_p^2 = 0.138 \)). Pairwise comparison indicated that the caffeine group had an increase in PT at 60°/s post the exercise intervention at a level that was approaching significant (Table 2: \( p = 0.053, d > 0.22 \)), whereas the placebo group had no significant training effect (Table 2: \( p = 0.083, d > 0.09 \)). There was no effect of acute caffeine supplementation or speed (Table 2: \( p > 0.166 \eta_p^2 < 0.001 \)). For concentric PT, there was a significant Group*Time interaction (Table 2: \( p = 0.010 \eta_p^2 = 0.212 \)). Pairwise comparison indicated PT was improved following the intervention in the caffeine group (Table 2: \( p = 0.010, d > 0.27 \)) but unchanged in the placebo group (Table 2: \( p = 0.275, d < 0.47 \)). For concentric PT, there were no other significant interactions (Table 2: \( p > 0.097 \eta_p^2 < 0.114 \)) or a main effect of acute caffeine treatment (Table 2: \( p = 0.344 \eta_p^2 = 0.114 \)). However, PT was significantly affected by speed (Table 2: \( p < 0.001 \eta_p^2 = 0.665 \)) with PT at 180°/s being lower than that at 60 and 120°/s (Table 2: \( p < 0.001 \) in both cases \( d > 0.27 \)).

3.2.4. Knee Flexion Peak Torque

For concentric and eccentric PT of the knee flexors there were no significant interactions (Table 2: \( p > 0.094 \eta_p^2 > 0.002 \)) and no main effect of Group (Table 2: \( p > 0.417 \eta_p^2 > 0.004 \)). For concentric PT, there was no main effect of Treatment (Table 2: \( p = 0.075 \eta_p^2 = 0.109 \)), but there was a main effect of Time (Table 2: \( p = 0.007 \eta_p^2 = 0.230 \)) with PT post the exercise intervention being significantly higher than pre-intervention exercise. There was also a main effect of speed (Table 2: \( p = 0.001 \eta_p^2 = 0.418 \)) with performance at 180°/s being lower than that at 60 and 120°/s (Table 2: \( p < 0.003 \) in both cases \( d > 0.16 \)). For eccentric PT, there was no main effect of speed (Table 2: \( p = 0.316 \eta_p^2 = 0.040 \)). However, there was a main effect with treatment (Table 2: \( p = 0.007 \eta_p^2 = 0.223 \)) where acute caffeine increased eccentric PT compared to the placebo trial.

3.3. Total Work

3.3.1. Elbow Extension Total Work

For concentric and eccentric TW of the elbow extensors there was no significant interactions (Table 3: \( p > 0.065 \eta_p^2 > 0.003 \)), no main effects of Group (Table 3: \( p > 0.762 \eta_p^2 > 0.003 \)), Treatment (Table 3: \( p = 0.151 \eta_p^2 > 0.072 \)), or Time (Table 3: \( p = 0.578 \eta_p^2 > 0.006 \)). However, there were significant main effects of Set (Table 3: \( p = 0.001 \eta_p^2 = 0.527 \)) with performance at Set1 being higher than that at Set2 and Set3 (Table 3: \( p < 0.001, d > 0.36 \)) and performance at Set2 being higher than that at Set3 (Table 3: \( p = 0.001, d > 0.33 \)).

3.3.2. Elbow Flexion Total Work

For concentric and eccentric TW of the elbow flexors, there was a significant interaction between Time*Set (Table 3: \( p < 0.047 \eta_p^2 > 0.113 \)). Pairwise comparison for concentric TW indicated that pre-exercise intervention, Set1 TW was higher than post-intervention (Table 3: \( p = 0.002, d > 0.30 \)). Furthermore, both pre- and post- the intervention performance in Set2 and Set3 was significantly lower than at Set1 (Table 3: \( p < 0.001 \) for both concentric and eccentric TW. No other significant interactions were identified (Table 3: \( p > 0.096 \eta_p^2 < 0.931 \)) and there was no main effect of Group (Table 3: \( p > 0.271 \eta_p^2 < 0.035 \)). Concentric TW was not affected by Treatment (Table 3: \( p = 0.231 \eta_p^2 = 0.051 \)); however, there was a main effect of Treatment for eccentric TW (Table 3: \( p = 0.003 \eta_p^2 = 0.272 \)), where TW following acute caffeine treatment was greater than the placebo treatment.
Table 3. Acute effect of caffeine treatment (3 mg kg⁻¹) pre and post-7-week resistance training on concentric and eccentric TW (Nm) of the elbow and knee flexors and extensors.

| Set  | Caffeine Intervention Group | Placebo Intervention Group |
|------|----------------------------|---------------------------|
|      | Acute Placebo Pre-Int     | Acute Placebo Post-Int    | Acute Caffeine Pre-Int | Acute Caffeine Post-Int | Acute Placebo Pre-Int | Acute Placebo Post-Int | Acute Caffeine Pre-Int | Acute Caffeine Post-Int |
|      |                            |                            |                        |                          |                            |                            |                        |                          |
| **Elbow Extension** |                            |                            |                        |                          |                            |                            |                        |                          |
| Con  | 393 ± 168                  | 370 ± 66                   | 348 ± 75               | 411 ± 228                | 344 ± 87                  | 349 ± 105                 | 369 ± 137               | 356 ± 66                  |
| Set 1| 298 ± 140                  | 281 ± 63                   | 266 ± 60               | 328 ± 230                | 277 ± 86                  | 278 ± 63                  | 311 ± 124               | 314 ± 85                  |
| Set 2| 232 ± 138                  | 216 ± 53                   | 216 ± 74               | 268 ± 213                | 213 ± 78                  | 220 ± 61                  | 246 ± 112               | 262 ± 98                  |
| Ecc  | 428 ± 309                  | 381 ± 91                   | 410 ± 118              | 421 ± 193                | 366 ± 202                 | 398 ± 132                 | 444 ± 167               | 425 ± 141                 |
| Set 1| 334 ± 253                  | 313 ± 72                   | 334 ± 94               | 339 ± 225                | 303 ± 161                 | 336 ± 108                 | 478 ± 533               | 346 ± 131                 |
| Set 2| 279 ± 266                  | 248 ± 52                   | 265 ± 67               | 295 ± 208                | 237 ± 127                 | 278 ± 104                 | 303 ± 130               | 280 ± 95                  |
| **Elbow Flexion** |                            |                            |                        |                          |                            |                            |                        |                          |
| Con  | 486 ± 116                  | 458 ± 91                   | 490 ± 102              | 463 ± 71                 | 500 ± 119                 | 463 ± 107                 | 523 ± 129               | 478 ± 92                  |
| Set 1| 377 ± 84                   | 361 ± 70                   | 369 ± 90               | 360 ± 82                 | 395 ± 77                  | 383 ± 104                 | 412 ± 68                | 403 ± 76                  |
| Set 2| 312 ± 69                   | 319 ± 78                   | 321 ± 87               | 315 ± 71                 | 341 ± 67                  | 325 ± 68                  | 362 ± 83                | 354 ± 80                  |
| Ecc  | 538 ± 166 *                | 465 ± 87 *                 | 551 ± 134 *            | 505 ± 131 *              | 493 ± 187 *               | 521 ± 205 *              | 587 ± 194 *             | 537 ± 156 *               |
| Set 2| 416 ± 149 *                | 376 ± 80 *                 | 431 ± 118 *            | 402 ± 126 *              | 408 ± 136 *               | 453 ± 149 *              | 472 ± 133 *             | 448 ± 97 *                |
| Set 3| 345 ± 116 *                | 352 ± 89 *                 | 373 ± 85 *             | 345 ± 95 *               | 372 ± 114 *               | 389 ± 104 *              | 425 ± 135 *             | 409 ± 122 *               |
| **Knee Extension** |                            |                            |                        |                          |                            |                            |                        |                          |
| Con  | 612 ± 359 *                                      | 1010 ± 361 *                               | 1080 ± 375 *                                      | 1045 ± 374                     | 648 ± 402 *                                      | 1036 ± 250 *                                      | 981 ± 304 *                               | 1120 ± 279                     |
| Set 2| 553 ± 342 *                                      | 980 ± 351 *                               | 989 ± 278 *                                      | 971 ± 296                     | 603 ± 403 *                                      | 1006 ± 237 *                                      | 1013 ± 164 *                               | 1003 ± 189                     |
| Set 3| 495 ± 325 *                                      | 856 ± 250 *                               | 911 ± 265 *                                      | 893 ± 252                     | 598 ± 454 *                                      | 903 ± 169 *                                      | 967 ± 206 *                               | 915 ± 124                     |
| Ecc  | 586 ± 267                                      | 1036 ± 383                               | 1179 ± 417                                      | 1144 ± 466                    | 738 ± 407                                      | 1251 ± 423                                      | 1223 ± 401                               | 1246 ± 275                     |
| Set 2| 503 ± 261                                      | 1011 ± 353                               | 1084 ± 351                                      | 1061 ± 453                    | 552 ± 345                                      | 1238 ± 415                                      | 1213 ± 320                               | 1176 ± 253                     |
| Set 3| 435 ± 216                                      | 918 ± 301                                | 990 ± 314                                      | 940 ± 368                     | 572 ± 334                                      | 1171 ± 375                                      | 1110 ± 370                               | 1164 ± 304                     |
| **Knee Flexion** |                            |                            |                        |                          |                            |                            |                        |                          |
| Con  | 524 ± 99                                       | 574 ± 179                                | 569 ± 179                                      | 644 ± 169                     | 547 ± 152                                      | 542 ± 127                                      | 563 ± 144                               | 542 ± 144                     |
| Set 2| 442 ± 114                                       | 521 ± 173                                | 485 ± 137                                      | 568 ± 104                     | 448 ± 115                                      | 449 ± 96                                       | 477 ± 132                               | 492 ± 150                     |
| Set 3| 404 ± 116                                       | 467 ± 140                                | 476 ± 125                                      | 503 ± 97                      | 379 ± 109                                      | 421 ± 110                                      | 450 ± 120                               | 441 ± 108                     |
| Ecc  | 505 ± 178 *                                    | 630 ± 241                                | 601 ± 235 *                                    | 699 ± 261                     | 610 ± 214 *                                    | 657 ± 210                                      | 668 ± 235                               | 630 ± 166                     |
| Set 2| 496 ± 268                                       | 537 ± 200                                | 528 ± 172                                      | 610 ± 220                     | 514 ± 166 *                                    | 542 ± 165                                      | 589 ± 213                               | 578 ± 173                     |
| Set 3| 422 ± 214                                       | 516 ± 193                                | 482 ± 163                                      | 561 ± 203                     | 430 ± 112 *                                    | 536 ± 182                                      | 551 ± 199                               | 545 ± 126                     |

Note: Values are represented as means ± SD, TW = Total Work, Con = Concentric, Ecc = Eccentric, Pre-Int= Pre-training intervention, and Post-Int= Post-training intervention, matching * represents a significant effect of caffeine prior to the intervention, matching # represents a significant effect of caffeine post-intervention, matching # represents a significant difference on total work post the intervention.

3.3.3. Knee Extension Total Work

For eccentric TW of the knee extensors there were no significant interactions (Table 3: p > 0.130). For concentric TW there was a significant Time*Treatment interaction (Table 3: p = 0.001). Pairwise comparison indicated an increase in TW post-intervention (Table 3: p = 0.001, d < 1.04). Furthermore, TW was significantly increased in the caffeine trial prior to the exercise intervention (Table 3: p = 0.001, d < 1.34), however, post-intervention there was no significant difference between the caffeine and placebo trial (Table 3: p = 0.599, d < 0.18). For concentric TW there were no other significant interactions (Table 3: p > 0.184). For both concentric and eccentric TW there was no effect of Group (Table 3: p > 0.494). Eccentric TW reported no other main effects (Table 3: p > 0.140). TW at Set1 was higher than Set2 and Set3 (Table 3: p < 0.010, d > 0.11) and performance at Set2 was higher than that at Set3 (Table 3: p = 0.001, d > 0.009).
3.3.4. Knee Flexion Total Work

For concentric TW of the knee flexors there were no significant interactions (Table 3: $p > 0.113 \eta^2_p < 0.075$), but for eccentric TW there was a Group*Treatment*Set interaction (Table 3: $p = 0.029 \eta^2_p = 0.119$). Pairwise comparison indicated that there was no effect of Group (Table 3: $p > 367, d = 0.12–2.00$). However, eccentric TW was greater in the placebo group during caffeine trials (Table 3: $p = 0.046, d > 0.13$). In the caffeine group Set1 TW was significantly higher during the caffeine trials (Table 3: $p = 0.029, d > 0.26$).

For eccentric TW there was no main effect of Time (Table 3: $p = 0.007 \eta^2_p = 0.235$) and for concentric TW there was no main effect of Group (Table 3: $p = 0.256 \eta^2_p = 0.046$) or Time (Table 3: $p = 0.148 \eta^2_p = 0.073$). However, concentric TW was significantly increased following caffeine treatment (Table 3: $p = 0.014 \eta^2_p = 0.198$). Concentric and eccentric TW was effected by Set (Table 3: $p = 0.001 \eta^2_p = 0.629$) with performance at Set1 being higher than that at Set2 and Set3 (Table 3: $p < 0.010, d > 0.61$) and performance at Set2 being higher than that at Set3 (Table 3: $p = 0.001, d > 0.014$).

3.4. Rate of Perceived Exertion

3.4.1. Elbow Extension Rate of Perceived Exertion

RPE following repeated MVC of the elbow extensors there were significant Group*Time (Table 4: $p = 0.025 \eta^2_p = 0.167$), Time*Treatment (Table 4: $p = 0.003 \eta^2_p = 0.267$), Time*Set (Table 4: $p = 0.011 p = 0.025 \eta^2_p = 0.186$), and Treatment*Set (Table 4: $p = 0.050 p = 0.025 \eta^2_p = 0.115$) interactions. Pairwise comparison indicated no group difference in RPE following MVC (Table 4: $p < 0.437, d < 0.62$). The caffeine group had increased RPE following MVC post-training intervention (Table 4: $p = 0.001 d > 0.097$). Furthermore, the placebo group had a treatment effect post-intervention, with RPE during the caffeine trial being higher than the placebo trial (Table 4: $p < 0.006$) at Set2 (Table 4: $d = 0.87$) and Set3 (Table 4: $d = 0.76$). Irrespective of treatment, RPE following Set3 was higher than that following completion of Set1 and Set2 (Table 4: $p = 0.001 d > 0.97$). There were no other significant interactions (Table 4: $p > 0.085 \eta^2_p < 0.936$).

Table 4. Acute effect of caffeine treatment (3 mg·kg$^{-1}$) pre and post-7-week resistance training on RPE following repeated MVC.

|                     | Caffeine Intervention Group |                      | Placebo Intervention Group |                      |
|---------------------|----------------------------|----------------------|---------------------------|----------------------|
|                     | Acute Placebo              | Acute Caffeine       | Acute Placebo             | Acute Caffeine       |
|                     | Pre-Int                    | Post-Int             | Pre-Int                   | Post-Int             |
| Elbow Extension     | Set1 14 ± 3                | 16 ± 2               | 13 ± 2                    | 16 ± 2               |
|                     | Set2 15 ± 2                | 17 ± 2               | 15 ± 2                    | 17 ± 2               |
|                     | Set3 17 ± 2                | 19 ± 2               | 16 ± 2                    | 19 ± 1               |
| Elbow Flexion       | Set1 14 ± 3                | 16 ± 2               | 14 ± 2                    | 14 ± 3               |
|                     | Set2 15 ± 2                | 18 ± 2               | 16 ± 2                    | 18 ± 1               |
|                     | Set3 17 ± 2                | 19 ± 2               | 17 ± 2                    | 19 ± 1               |
| Knee Extension      | Set1 13 ± 3                | 17 ± 2               | 13 ± 2                    | 16 ± 2               |
|                     | Set2 14 ± 3                | 18 ± 2               | 15 ± 2                    | 18 ± 1               |
|                     | Set3 15 ± 2                | 19 ± 2               | 17 ± 2                    | 19 ± 1               |
| Knee Flexion        | Set1 14 ± 2                | 16 ± 2               | 14 ± 2                    | 16 ± 2               |
|                     | Set2 15 ± 2                | 17 ± 2               | 15 ± 2                    | 17 ± 1               |
|                     | Set3 17 ± 2                | 19 ± 2               | 17 ± 2                    | 19 ± 1               |

Note: Values are represented as means ± SD. RPE = Rate of Perceived Exertion, MVC = Maximum voluntary contraction, Pre-Int = Pre-training intervention, and Post-Int = Post-training intervention, matching represents a significant effect of caffeine post-intervention.
3.4.2. Elbow Flexion Rate of Perceived Exertion

For RPE following repeated MVC of the elbow flexors, there was a significant Time*Set interaction (Table 4: \( p = 0.001 \eta_p^2 = 0.222 \)). Pairwise comparisons indicated an increase in RPE following MVC post-exercise intervention (Table 4: \( p = 0.001 \eta_p^2 > 0.48 \)). Both pre-and post-exercise intervention, RPE following Set 3 was higher than that following Set 1 and Set 2 (Table 4: \( p < 0.001 \eta_p^2 > 0.62 \)). There were no other significant interactions (Table 4: \( p > 0.072 \eta_p^2 < 0.064 \)) and no main effect of Group (Table 4: \( p = 0.771 \eta_p^2 < 0.014 \)) or Treatment (Table 4: \( p = 0.961 \eta_p^2 = 0.001 \)).

3.4.3. Knee Extension Rate of Perceived Exertion

For RPE following repeated MVC of the knee extensors, there was a significant Group*Time*Set interaction (Table 4: \( p = 0.017 \eta_p^2 = 0.135 \)). Pairwise comparison indicated no group effect pre-or post-exercise intervention (Table 4: \( p > 0.130 \eta_p^2 < 2.18 \)). However, both treatment groups indicated increased RPE post the exercise intervention across (Table 4: \( p < 0.001 \eta_p^2 > 0.40 \)). RPE following Set3 was significantly higher than Set1 and Set2 (Table 4: \( p < 0.001 \eta_p^2 < 2.18 \)). There was also a Time*Treatment interaction (Table 4: \( p = 0.001 \eta_p^2 = 0.396 \)), where RPE was higher post-intervention in both treatments (Table 4: \( p = 0.001 \eta_p^2 > 0.97 \)). Furthermore, prior to the exercise intervention, RPE was significantly higher following caffeine treatment (Table 4: \( p = 0.001 \eta_p^2 > 0.76 \)).

3.4.4. Knee Flexion Rate of Perceived Exertion

For RPE following repeated MVC of the knee flexors, there was no significant interaction (Table 4: \( p > 0.061 \eta_p^2 < 0.975 \)). However, there was a main effect with Time (Table 4: \( p = 0.001 \eta_p^2 = 0.748 \)) with post-training intervention RPE being increased. There was also a main effect with Set (Table 4: \( p = 0.001 \eta_p^2 = 0.898 \)) with RPE following Set3 being higher than Set1 and Set2. There were no main effects of Group (Table 4: \( p = 0.760 \eta_p^2 = 0.002 \)) or Treatment (Table 4: \( p = 0.666 \eta_p^2 = 0.006 \)).

3.5. Readiness to Invest Effort and Felt Arousal Scale

For RTE Physical, RTE Mental, and FAS there were no significant interactions (Table S1: \( p > 0.150 \eta_p^2 > 0.007 \)). RTE Physical, RTE Mental, and FAS were significantly affected by time post-ingestion (Table S1: \( p < 0.001 \eta_p^2 > 0.245 \)). Both RTE Physical and FAS reported 45 min post-treatment were significantly higher than pre, 15- and 30-min post-treatment (Table S1: \( p < 0.015 \eta_p^2 > 0.68 \)). However, RTE Mental 30 min post-treatment was higher than pre, 15-, and 45-min post-treatment (Table S1: \( p < 0.050 \eta_p^2 < 0.30 \)). There were no significant main effects of Group (Table S1: \( p > 0.415 \eta_p^2 > 0.003 \)), Time (Table S1: \( p > 0.057 \eta_p^2 > 0.124 \)) or Treatment (Table S1: \( p > 0.415 \eta_p^2 > 0.003 \)).

3.6. 1RM

For 1RM performance, there were no significant Group*Time interaction (Figure 4: \( p < 0.962 \eta_p^2 < 0.008 \)). Following the resistance training intervention, 1RM improved in all lifts (Figure 4: \( p < 0.001 \eta_p^2 > 0.633 \)). There was no significant effect of Group in all exercises (Figure 4: \( p > 0.850 \eta_p^2 < 0.071 \)) apart from DL (Figure 4: \( p = 0.001 \eta_p^2 = 0.493 \)) with the placebo group having a greater performance during 1RM assessment.
3.5. Readiness to Invest Effort and Felt Arousal Scale

For RTE Physical, RTE Mental, and FAS there were no significant interactions (Table S1: $p > 0.060 \eta^2 > 0.001$). RTE Physical, RTE Mental, and FAS were significantly affected by time post-ingestion (Table S1: $p < 0.001 \eta^2 > 0.245$). Both RTE Physical and FAS reported 45 min post-treatment were significantly higher than pre, 15- and 30-min post-treatment (Table S1: $p < 0.015$ in all cases $d < 0.68$). However, RTE Mental 30 min post-treatment was higher than pre, 15-, and 45-min post-treatment (Table S1: $p < 0.050$ in all cases $d < 0.30$).

There were no significant main effects of Group (Table S1: $p > 0.150 \eta^2 > 0.007$), Time (Table S1: $p > 0.057 \eta^2 > 0.124$) or Treatment (Table S1: $p > 0.415 \eta^2 > 0.003$).

3.6. 1RM

Figure 4. Effect of caffeine treatment (3 mg·kg$^{-1}$) pre and post-7-week resistance training program on pre-intervention 1RM and post-intervention 1RM, * represents a significant increase in performance post exercise intervention. The post intervention increase in 1RM was 16% and 16% CP; 19% and 22% SSP; 24% and 25% SQ; 24% and 24% DL; 42% and 40% HC; 30% and 27% PC for the placebo intervention group and caffeine intervention group, respectively. There was no main effect of intervention group for each exercise ($p > 0.850$) other than the DL ($p = 0.001$).

3.7. Intervention Repetitions until Failure

For all exercises, there were no significant interactions (Figure 5: $p = 0.998$). However, RTF across the training intervention was higher in the caffeine group for SSP, SQ, DL, and HC (Figure 5: $p < 0.037 d < 0.13$). The placebo group outperformed the caffeine group in PC (Figure 5: $p = 0.005 d < 0.18$), and there were no between-group differences for CP (Figure 5: $p = 0.618$). For all exercises, there was also a main effect of Session (Figure 5: $p < 0.005$). Whilst there were some differences between specific sessions, there were clearer trends for an increase in CP, SSP, DL, and PC RTF as the duration of the intervention increased. Furthermore, for all exercises, there was a main effect of Set with RTF being higher in Set1 compared to Set2 (Figure 5: $p < 0.001 d < 0.14$).

3.8. Intervention RPE

For both SQ and HC, sessional RPE of the caffeine group was lower than that of the placebo group (Table S2: $p < 0.035 d < 0.62$). For CP, SQ, and DL there was a main effect of Session (Table S2: $p < 0.034$). Pairwise comparisons show some session-specific differences for SQ and DL, but no clear trends. Furthermore, for all exercises, there was a main effect of Set, with RPE being higher in Set1 compared to Set2 (Table S2: $p < 0.044 d > 0.49$). There were no significant interactions (Table S2: $p > 0.072$).
Figure 5. Effect of caffeine treatment (3 mg·kg\(^{-1}\)) during the 7-week resistance training program on sessional RTF.
4. Discussion

Data from the present study indicate that prior to the training intervention the acute ingestion of 3 mg·kg\(^{-1}\) caffeine increased specific measures of muscular strength in a muscle- and contractile mode-specific manner. Twice weekly ingestion of caffeine during the 7-week resistance-training program had little effect on caffeine’s ability to evoke an acute benefit, with many of the reported caffeine-induced improvements in muscular strength still prevalent in both the caffeine and placebo groups when reassessed upon completion of the training intervention. Although the seven-week resistance training intervention significantly improved 1RM and specific measures of maximal isokinetic torque—other than the PT of the knee extensors, which was only improved in the caffeine treated group—benefits were not statistically different between the group that consumed caffeine prior to each session compared to those that consumed a placebo. This similar increase in performance upon completion of the exercise intervention was apparent despite the greater number of resistance exercise repetitions performed for numerous exercises in the caffeine group across the course of the intervention. As such, the results of this study demonstrate that: (1) 3 mg·kg\(^{-1}\) may be useful to evoke acute enhancements in muscular strength; (2) relatively short-term chronic ingestion of 3 mg·kg\(^{-1}\) of caffeine may not lead to habituation to its effects; (3) chronic caffeine supplementation for 7-week may not enhance resistance-training induced gains in strength.

4.1. Acute Effects of Caffeine on Muscular Strength

Recent meta-analyses indicate that acute caffeine consumption may enhance muscular strength, including strength assessed using isokinetic dynamometry [1,3,5]. In line with these findings, the results of the present study indicate that acute caffeine ingestion increased specific measures of PT and TW when compared to a placebo. More specifically, an acute ergogenic effect of caffeine was observed for: (a) eccentric PT of the elbow extensors at higher angular velocities and concentric PT of the elbow flexors; (b) elbow flexion TW; (c) eccentric PT of the knee flexors; and (d) knee extension TW (pre-intervention) and knee flexion TW (both pre-and post-intervention). Based on these data and in accordance with previous work [17–20], it can be concluded that caffeine has a muscle- and contractile mode-specific effect. Whilst our data indicate caffeine-induced benefits for both concentric and eccentric PT, there appears to be a greater number of benefits for upper body musculature. This contradicts previously published work indicating superior benefits for lower limb musculature, attributed to mechanisms of the central nervous system stemming a greater increase in muscular recruitment within larger muscle groups [7]. Conversely, a more recent meta-analysis by Grgic et al. [3] indicated that caffeine effects on strength and power were more evident in the upper body.

Mechanistically, the ability of caffeine to evoke improved exercise performance is primarily attributed to its effects as a central adenosine receptor antagonist [53–56]. Caffeine and adenosine share similar molecule structures. Because of their similar structure, they compete for adenosine binding sites resulting in a surge excitatory neurotransmitter causing reduced pain perception [22,57], a rise in motor unit recruitment, and improved excitation-contraction coupling [22,58,59]. Caffeine may act directly on skeletal muscle [60–63], increasing the release and myofibril sensitivity to Ca\(^{2+}\) [64–66], resulting in increased crossbridge formation. In support, the exposure of isolated skeletal muscle to physiological concentrations of caffeine has been shown to evoke increased muscular power [22].

Although it was not the purpose of the present study to determine the mechanisms underpinning the acute effects of caffeine on muscular strength, the influences of some of these mechanisms can be determined. When measured in the arm of the experiment examining the acute effects of caffeine, post-exercise RPE was in the most part unaffected by caffeine, and on some occasions was increased following acute caffeine ingestion. This coincides with previous work where caffeine ingestion had a limited effect on perceived effort or pain in scenarios where exercise performance was unchanged [39,67,68] or improved [69–71] following caffeine consumption. Intersessional RPE following CP and PC
exercise was not different between the groups. However, RPE following SSP, SQ, DL, and HC was reduced in the caffeine group. This may in part support the concept of caffeine as a pain suppressor in some circumstances, though this should be interpreted with caution given that this part of the protocol used a between subject’s design. Interestingly, caffeine did not have an effect on RTE physical and mental effort when measured in the arm of the experiment examining the acute effects of caffeine. This coincides with previous research [68,72]. Whilst these findings point to physiological mechanisms being the cause of the documented effects, the impact of caffeine on arousal during the exercise as a mechanism cannot be ruled out. To some extent, the results of perceptual measures needed to be interpreted with caution given their sensitivity to change following caffeine ingestion have not been robustly explored.

4.2. Habituation to Chronic Caffeine Consumption

There is a debate in the literature as to whether the acute benefits of caffeine on physical performance are reduced following chronic exposure, with some evidence indicating habituation to caffeine’s effect [12,13] and others suggesting no habituation effects [11,73–75]. In the present study, the acute effects of caffeine on PT and TW were reasonably uniform prior to and following the training intervention. For example, acute caffeine-induced increases in eccentric elbow extension PT, concentric elbow flexion PT, eccentric knee flexion PT, eccentric elbow flexion TW, and concentric knee flexion TW that was demonstrated prior to the intervention were still prevalent in the caffeine intervention group when acute caffeine responses were reassessed post-intervention.

These results suggested that consuming 3 mg·kg−1 of caffeine, twice per week for 7-weeks, in a population of 30 moderate habitual caffeine consumers, did not reduce the caffeine’s ergogenicity. Although there are varying methodological approaches to assess caffeine habituation, the findings of the present work agree with previous evidence that indicates that caffeine evokes equivalent performance-enhancing effects in low and high habitual caffeine users [1,8,11,74,76]. For example, Gonçalves et al. [11] demonstrated that 6 mg·kg−1 of caffeine improved cycling time trial performance in low (58 mg/day), moderate (143 mg/day), and high (351 mg/day) habitual caffeine users. Still, although models stratifying participants by typical caffeine consumption habits for examining the potential for habituation have value, the results from these studies may be limited by the reliance on subjective caffeine recall used to quantify caffeine use.

The disparity between the current data and studies that have directly measured and have indicated habituation to caffeine effects is likely due to differences in the population characteristics, the dose, and duration of caffeine administration, and the outcome variables assessed. For example, Beaumont et al. [13] included low habitual caffeine consumers (<75 mg/day) randomly assigned to consume placebo or caffeine (1.5–3 mg·kg−1) for 28 days. Results indicated that the acute effect of caffeine on cycling performance was evident pre-supplementation and was no longer apparent after 4 weeks of caffeine supplementation. Lara et al. [12] used a caffeine dose of 3 mg·kg−1 supplementation for 20 consecutive days, during which performance in a Wingate test was evaluated. While caffeine increased cycling power, the ergogenic effects attenuated over the course of the study, suggesting progressive tolerance. Indirect assessments of the impact of habituation have also be made by studies that stratify their participant groups by habitual caffeine use. Several studies demonstrate an ergogenic effect in high caffeine users across anaerobic and aerobic modes of exercise [1,11,73,74,76]. Studies examining caffeine habituation specifically for measures of muscular strength are limited, and as such, these findings make a novel contribution to the literature.

4.3. Effects of Chronic Caffeine Consumption on Resistance Training

Irrespective of the supplement provided, the training intervention resulted in a significant increase in all assessments of 1RM and specific measures of PT and TW. The more pronounced effects of the training intervention of 1RM were expected due to training
specificity [77]. Post-intervention concentric PT of the knee extensors at all angular velocities and eccentric PT at 60 deg/s was improved only in the caffeine group. Other improvements in PT, TW, and measures of 1RM were uniform across the caffeine and placebo-treated groups, indicating a limited effect of chronic caffeine ingestion to augment adaptations to resistance exercise. The chronic effect of caffeine as a nutritional strategy to support training has received little attention. Our findings differ from the findings presented by Kemp et al. [9] who demonstrated that strength-trained participants that consumed 3 mg·kg\(^{-1}\) caffeine before each session of a 6-week resistance training intervention had superior improvements in the bench press and squat 1RM compared to those that consumed a placebo for the duration of the intervention. However, our data support work by Giraldez-Costas et al. and Pakulak et al. [16,78] who indicated no significant differences in 1RM strength gains between caffeine and placebo groups following 4 or 6 weeks of resistance training intervention.

We progress previous findings by demonstrating this relationship following a longer intervention period and across a larger range of strength assessments considering not only 1RM in different exercises but also maximal voluntary concentric and eccentric muscle functions across a range of joint angular velocities. The disparity between the present findings and those of Kemp et al. [9] may be related to differences between populations. Kemp et al. [9] used specifically strength-trained participants, and it has been suggested that caffeine may have a greater effect on this population as compared to untrained individuals [3,79,80]. Whereas this may in part be related to improved repeatability of performance in specifically trained individuals [3,79,80], this suggestion has some mechanistic underpinning. Previous research suggests that trained individuals have a greater adenosine receptor density compared to those who are less trained or untrained [81]. Those with an increased adenosine receptor density may evoke amplified caffeine [82]. However, this is speculative and requires further investigation in light of evidence reporting similar caffeine-induced benefits in performance in both trained and untrained participants [80,83], and in some cases, increased responses in untrained individuals [80].

This study is the first to monitor the acute effect of caffeine during each session of a training intervention. Interestingly, across the training intervention, RTF was higher in SSP, SQ, DL, and HC for the caffeine group. While this may add further weight to the acute benefits of caffeine, it demonstrates the small but significant increase in the relative total weight lifted was not substantial enough in magnitude to evoke a superior training response. Furthermore, sessional RPE was either unchanged or in some cases decreased in the caffeine group, this again indicates that the ability of caffeine to suppress perception of pain/effort may be more prevalent during sustained contractions [40,67,68].

5. Limitations and Future Direction

The present study offers valuable insight with respect to the effects of chronic caffeine supplementation as a nutrition strategy to augment resistance training, though it is not without limitation. Firstly, a resistance-training program with a weekly training frequency greater than that adopted in the present study would likely evoke greater adaptations in the measured outcomes [84]. However, the training frequency used in the present study was designed to coincide with other commitments of the club. That said, the training regime adopted successfully improved measures of muscular strength and therefore was appropriate to address the experimental aims.

Our data indicate a small but significant increase in training volume across the course of the intervention, whilst this did not manifest in an enhanced training response in the measured outcomes there is the possibility that a sustained increase in training volume over a longer period may evoke enhanced adaptations. This is an avenue for future investigation.

We did not measure genetic influencers that potentially may influence the caffeine’s performance-enhancing effect [3,85,86]. A recent review has indicated that the CYP1A2 and the ADORA2A may be important influencers of the caffeine response [87]. Future
work should consider genetic influences that underpin caffeine’s effect when assessing the impact of chronic ingestion as a method to elicit superior training adaptations.

Furthermore, this study used individuals that were physically conditioned but not specifically resistance trained. Although the demonstrated effects may be relevant to a broad population that is relatively naive to resistance training, they may not be generalisable to individuals that are specifically resistance trained. Future work should look to directly compare trained against untrained participants using a similar approach to that adopted in the present study. Future work should also look to repeat this study using different doses of caffeine. We selected 3 mg·kg\(^{-1}\) for the present study as it typically considered the minimum dose needed to evoke an improved exercise performance \cite{88-90} and more closely represents caffeine consumed from commercially available products. Previous work exploring the acute effects of caffeine on physical performance is focused on males \cite{1-5,7} and there is recent growing interest in establishing the caffeine response in females \cite{91}. Whilst it seems that the effects of caffeine on resistance exercise performance are similar between males and females \cite{92}, future similar studies performed with females as study participants are nevertheless needed.

6. Conclusions

This study examined the acute effects of 3 mg·kg\(^{-1}\) caffeine consumption on muscular strength and explored if chronic use of caffeine could be used as an effective nutrition strategy to augment the response to resistance training. The data presented herein indicate a muscle and contractile mode-specific acute benefit of caffeine consumption, effects that were not dampened following twice-weekly consumption over the time course of a seven-week resistance training intervention. Whilst the training intervention resulted in significant improvements in 1RM performance and specific measures of isokinetic PT and TW of the upper and lower limb musculature, for the most part, the effects were equivalent in both the group ingesting caffeine and in the group ingesting a placebo. These effects were prevalent despite a small but significant increase in RTF across the training intervention in the caffeine group. In summary, our results infer that caffeine may be beneficial to evoke acute improvements in muscular strength but has limited benefits across the course of a resistance training intervention.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/nu13103367/s1, Table S1: Acute effect of caffeine treatment (3 mg·kg\(^{-1}\)) pre-and post-7-week resistance training programme on readiness to invest effort physically, readiness to invest effort mentally, and felt arousal scale; Table S2. Effect of caffeine treatment (3 mg·kg\(^{-1}\)) during the 7-week resistance training programme on sessional RPE.

Author Contributions: Conceptualization, J.T., R.A.T., N.D.C.; Methodology, J.T., R.A.T.; Formal Analysis, R.A.T.; Investigation, R.A.T.; Data Curation, R.A.T., J.T.; Writing—Original Draft Preparation, R.A.T., J.T. Writing—Review and Editing, J.T., R.A.T., N.D.C., M.J.D., R.M., J.G.; Visualization, R.A.T.; Supervision, J.T., N.D.C., M.J.D., R.M.; Project Administration, R.A.T. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Ethics Committee of Coventry University (reference code; P76381; approved on 3 December 2018).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest.
References

1. Grgic, J.; Grgic, I.; Pickering, C.; Schoenfeld, B.J.; Bishop, D.J.; Pedisic, Z. Wake up and smell the coffee: Caffeine supplementation and exercise performance—An umbrella review of 21 published meta-analyses. Br. J. Sports Med. 2020, 54, 681–688. [CrossRef]

2. Astorino, T.A.; Roberson, D.W. Efficacy of acute caffeine ingestion for short-term high-intensity exercise performance: A systematic review. J. Strength Cond. Res. 2010, 24, 257–265. [CrossRef] [PubMed]

3. Grgic, J.; Trexler, E.T.; Lazinica, B.; Pedisic, Z. Effects of caffeine intake on muscle strength and power: A systematic review and meta-analysis. J. Int. Soc. Sports Nutr. 2018, 15, 11. [CrossRef] [PubMed]

4. Polito, M.D.; Souza, D.B.; Casonatto, J.; Farinatti, P. Acute effect of caffeine consumption on isotonic muscular strength and endurance: A systematic review and meta-analysis. Sci. Sports 2016, 31, 119–128. [CrossRef]

5. Grgic, J.; Pickering, C. The effects of caffeine ingestion on isokinetic muscular strength: A meta-analysis. J. Sci. Med. Sport 2019, 22, 353–360. [CrossRef] [PubMed]

6. Salinero, J.J.; Lara, B.; Del Coso, J. Effects of acute ingestion of caffeine on team sports performance: A systematic review and meta-analysis. Res. Sports Med. 2019, 27, 238–256. [CrossRef] [PubMed]

7. Warren, G.L.; Park, N.D.; Maresca, R.D.; McKibans, K.L.; Millard-Stafford, M.L. Effect of caffeine ingestion on muscular strength and endurance: A meta-analysis. Med. Sci. Sports Exerc. 2010, 42, 1375–1387. [CrossRef]

8. Grgic, J.; Mikulic, P.; Schoenfeld, B.J.; Bishop, D.J.; Pedisic, Z. The influence of caffeine supplementation on resistance exercise: A review. Sports Med. 2019, 49, 17–30. [CrossRef]

9. Kemp, J.; Eaton, T.; Jarvis, S.; Meehan, D.; Whyte, D.G. Caffeine improves strength gains in response to 6 weeks of resistance training. J. Aust. Strength Cond. 2012, 20, 48–51.

10. Del Coso, J.; Lara, B.; Ruiz-Moreno, C.; Salinero, J.J. Challenging the myth of non-response to the ergogenic effects of caffeine ingestion on exercise performance. Nutrients 2019, 11, 732. [CrossRef]

11. Gonçalves, L.D.S.; Painelli, V.D.S.; Yamaguchi, G.; Oliveira, L.F.d.; Saunders, B.; da Silva, R.P.; Maciel, E.; Artioli, G.G.; Roschel, H.; Gualano, B. Dispelling the myth that habitual caffeine consumption influences the performance response to acute caffeine supplementation. J. Appl. Physiol. 2017, 123, 213–220. [CrossRef]

12. Lara, B.; Ruiz-Moreno, C.; Salinero, J.J.; Del Coso, J. Time course of tolerance to the performance benefits of caffeine. PLoS ONE 2019, 14, e0210275. [CrossRef]

13. Beaumont, R.; Cordery, P.; Funnell, M.; Mears, S.; James, L.; Watson, P. Chronic ingestion of a low dose of caffeine induces tolerance to the performance benefits of caffeine. J. Sports Sci. 2017, 35, 1920–1927. [CrossRef]

14. Wilk, M.; Filip, A.; Krzysztofik, M.; Maszczyk, A.; Zajac, A. The acute effect of various doses of caffeine on power output and velocity during the bench press exercise among athletes habitually using caffeine. Nutrients 2019, 11, 1465. [CrossRef]

15. Filip, A.; Wilk, M.; Krzysztofik, M.; Del Coso, J. Inconsistency in the ergogenic effect of caffeine in athletes who regularly consume caffeine: Is it due to the disparity in the criteria that defines habitual caffeine intake? Nutrients 2020, 12, 1087. [CrossRef]

16. Giráldez-Costas, V.; Ruiz Moreno, C.; González-García, J.; Lara, B.; Del Coso, J.; Salinero, J.J. Pre-exercise caffeine intake enhances bench press strength training adaptations. Front. Nutr. 2021, 8, 3. [CrossRef]

17. Tallis, J.; Yavuz, H.C. The effects of low and moderate doses of caffeine supplementation on upper and lower body maximal voluntary concentric and eccentric muscle force. Appl. Physiol. Nutr. Metab. 2018, 43, 274–281. [CrossRef] [PubMed]

18. Tallis, J.; Muhammad, B.; Islam, M.; Duncan, M.J. Placebo effects of caffeine on maximal voluntary concentric force of the knee flexors and extensors. Muscle Nerve 2016, 54, 479–486. [CrossRef]

19. Timmins, T.D.; Saunders, D.H. Effect of caffeine ingestion on maximal voluntary contraction strength in upper-and lower-body muscle groups. J. Strength Cond. Res. 2014, 28, 3239–3244. [CrossRef] [PubMed]

20. Tallis, J.; James, R.S.; Cox, V.M.; Duncan, M.J. Is the ergogenicity of caffeine affected by increasing age? The direct effect of a physiological concentration of caffeine on the power output of maximally stimulated EDL and diaphragm muscle isolated from the mouse. J. Nutr. Health Aging 2017, 21, 440–448. [CrossRef] [PubMed]

21. General Assembly of the World Medical Association World Medical Association Declaration of Helsinki: Ethical principles for medical research involving human subjects. J. Am. Coll. Dent. 2014, 81, 14–18.

22. Tallis, J.; Duncan, M.J.; James, R.S. What can isolated skeletal muscle experiments tell us about the effects of caffeine on exercise performance? Br. J. Pharmacol. 2015, 172, 3703–3713. [CrossRef]

23. Graham, T.E. Caffeine and exercise. Sports Med. 2001, 31, 785–807. [CrossRef] [PubMed]

24. Shohet, K.L.; Landrum, R.E. Caffeine consumption questionnaire: A standardized measure for caffeine consumption in undergraduate students. Psychol Rep 2001, 89, 521–526. [CrossRef] [PubMed]

25. Huntley, E.D.; Juliano, L.M. Caffeine Expectancy Questionnaire (CaffEQ): Construction, psychometric properties, and associations with caffeine use, caffeine dependence, and other related variables. Psychol. Assess. 2012, 24, 592. [CrossRef] [PubMed]

26. Stark, T.; Walker, B.; Phillips, J.K.; Fejer, R.; Beck, R. Hand-held dynamometry correlation with the gold standard isokinetic dynamometry: A systematic review. PMR 2011, 3, 472–479. [CrossRef] [PubMed]

27. Habets, B.; Staal, J.B.; Tijssen, M.; van Cingel, R. Intra-tester reliability of the Humac NORM isokinetic dynamometer for strength measurements of the knee and shoulder muscles. BMC Res. Notes 2018, 11, 1–5. [CrossRef] [PubMed]

28. Seven, B.; Cobanoglu, G.; Oskay, D.; Atalay-Guzel, N. Test–Retest Reliability of Isokinetic Wrist Strength and Proprioception Measurements. J. Sport Rehabil. 2019, 28. [CrossRef]
29. Eustace, S.J.; Page, R.M.; Greig, M. Angle-specific isokinetic metrics highlight strength training needs of elite youth soccer players. J. Strength Cond. Res. 2020, 34, 3258–3265. [CrossRef]
30. Borg, G.A. Psychophysical bases of perceived exertion. Med. Sci. Sports Exerc. 1982, 14, 377–381. [CrossRef]
31. Duncan, M.J.; Smith, M.; Cook, K.; James, R.S. The acute effect of a caffeine-containing energy drink on mood state, readiness to invest effort, and resistance exercise to failure. J. Strength Cond. Res. 2012, 26, 2858–2863. [CrossRef]
32. Raedeke, T.D.; Focht, B.C.; Scales, D. Mediators of affective responses to acute exercise among women with high social physique anxiety. Psychol. Sport Exerc. 2009, 10, 573–578. [CrossRef]
33. Suchomel, T.J.; Beckham, G.K.; Wright, G.A. The impact of load on lower body performance variables during the hang power clean. Sports Biomech. 2014, 13, 87–95. [CrossRef]
34. Kawamori, N.; Crum, A.J.; Blument, F.A.; Kulik, J.R. Influence of different relative intensities on power output during the hang power clean: Identification of the optimal load. J. Strength Cond. Res. 2005, 19, 698. [CrossRef]
35. MacKenzie, S.J.; Lavers, R.J.; Wallace, B.B. A biomechanical comparison of the vertical jump, power clean, and jump squat. J. Sports Sci. 2014, 32, 1576–1585. [CrossRef] [PubMed]
36. Kraemer, W.J.; Fry, A.C.; Ratamess, N.; French, D. Strength testing: Development and evaluation of methodology. Physiol. Assess. Hum. Fit. 1995, 2, 119–150.
37. Aragon-Vela, J.; Casuso, R.A.; Casals, C.; Plaza-Diaz, J.; Fontana, L.; Huertas, J.R. Differential IL 10 serum production between an arm-based and a leg-based maximal resistance test. Cytokine 2020, 126, 154915. [CrossRef] [PubMed]
38. Baechle, T.R.; Earle, R.W. Essentials of Strength Training and Conditioning; Human Kinetics: Champaign, IL, USA, 2008.
39. Duncan, M.J.; Oxford, S.W. Acute caffeine ingestion enhances performance and dampens muscle pain following resistance exercise to failure. J. Sports Med. Phys. Fit. 2012, 52, 280–285.
40. Duncan, M.J.; Oxford, S.W. The effect of caffeine ingestion on mood state and bench press performance to failure. J. Strength Cond. Res. 2011, 25, 178–185. [CrossRef] [PubMed]
41. Martorelli, S.; Cadore, E.L.; Izquierdo, M.; Celes, R.; Martorelli, A.; Cleto, V.A.; Alvarenga, J.G.; Bottaro, M. Strength training with repetitions to failure does not provide additional strength and muscle hypertrophy gains in young women. Eur. J. Transl. Myol. 2017, 27, 6339. [CrossRef] [PubMed]
42. Williams, A.D.; Cribb, P.J.; Cooke, M.B.; Hayes, A. The effect of ephedra and caffeine on maximal strength and power in resistance-trained athletes. J. Strength Cond. Res. 2008, 22, 464–470. [CrossRef]
43. Garber, C.E.; Blissmer, B.; Deschenes, M.R.; Franklin, B.A.; Lamonte, M.J.; Lee, I.; Nieman, D.C.; Swain, D.P. Quantity and Quality of Exercise for Developing and Maintaining Cardiorespiratory, Musculoskeletal, and Neuromotor Fitness in Apparently Healthy Adults: Guidance for Prescribing Exercise; Columbia University: Columbia, SC, USA, 2011.
44. Willardson, J.M. The application of training to failure in periodized multiple-set resistance exercise programs. J. Strength Cond. Res. 2007, 21, 628.
45. Rooney, K.J.; Herbert, R.D.; Bahnhave, R.J. Fatigue contributes to the strength training stimulus. Med. Sci. Sports Exerc. 1994, 26, 1160–1164. [PubMed]
46. Drinkwater, E.J.; Lawton, T.W.; Lindsell, R.P.; Pyne, D.B.; Hunt, P.H.; McKenna, M.J. Training leading to repetition failure enhances bench press strength gains in elite junior athletes. J. Strength Cond. Res. 2005, 19, 382–388. [PubMed]
47. Davies, T.; Orr, R.; Halaki, M.; Hackett, D. Effect of training leading to repetition failure on muscular strength: A systematic review and meta-analysis. Sports Med. 2016, 46, 487–502. [CrossRef]
48. van Ginkel, J.R. SPSS Syntax for Applying Rules for Combining Multivariate Estimates in Multiple Imputation. Cytokine 2020, 126, 154915. [CrossRef] [PubMed]
49. van Ginkel, J.R.; Kroonenberg, P.M. Analysis of variance of multiply imputed data. Multivar. Behav. Res. 2014, 49, 78–91. [CrossRef] [PubMed]
50. Blanca, M.J.; Alarcón, R.; Arnau, J.; Bono, R.; Bendayan, R. Non-normal data: Is ANOVA still a valid option? Psicothema 2017, 29, 552–557. [PubMed]
51. Tabachnick, B.G.; Fidell, L.S.; Ullman, J.B. Using Multivariate Statistics; Pearson: Boston, MA, USA, 2007.
52. Cohen, J. Statistical Power Analysis for the Behavioral Sciences; Academic Press: Cambridge, MA, USA, 2013.
53. Okada, M.; Kiryu, K.; Kawata, Y.; Mizuno, K.; Wada, K.; Tasaki, H.; Kaneko, S. Determination of the effects of caffeine and carbamazepine on striatal dopamine release by in vivo microdialysis. Eur. J. Pharmacol. 1997, 321, 181–188. [CrossRef]
54. Fredholm, B.B. Adenosine, adenosine receptors and the actions of caffeine. Pharmacol. Toxicol. 1995, 76, 93–101. [CrossRef]
55. Fredholm, B.B. On the mechanism of action of theophylline and caffeine. Acta Med. Scand. 1985, 217, 149–153. [CrossRef]
56. Vallar, T. Evolution of the mechanism of action of methylxanthines: From calcium mobilizers to antagonists of adenosine receptors. Pharmacologist 1982, 24, 277–287.
57. Davis, J.K.; Green, J.M. Caffeine and anaerobic performance. Sports Med. 2009, 39, 813–832. [CrossRef]
58. Dunford, M.; Doyle, J.A. Nutrition for Sport and Exercise; Cengage Learning: Boston, MA, USA, 2008.
59. Hodgson, A.B.; Randell, R.K.; Jeukendrup, A.E. The metabolic and performance effects of caffeine compared to cooffee during endurance exercise. PLoS ONE 2013, 8, e59561. [CrossRef]
60. Damiani, E.; Larsson, L.; Margreth, A. Age-related abnormalities in regulation of the ryanodine receptor in rat fast-twist muscle. Cell Calcium 1996, 19, 15–27. [CrossRef]
61. Bhat, M.B.; Zhao, J.; Zang, W.; Balke, C.W.; Takeshima, H.; Wier, W.G.; Ma, J. Caffeine-induced release of intracellular Ca2 from Chinese hamster ovary cells expressing skeletal muscle ryanodine receptor: Effects on full-length and carboxyl-terminal portion of Ca2 release channels. J. Gen. Physiol. 1997, 110, 749–762. [CrossRef] [PubMed]

62. Fredholm, B.B.; Bättig, K.; Holmén, J.; Nehlig, A.; Zvartau, E.E. Actions of caffeine in the brain with special reference to factors that contribute to its widespread use. Pharmacol. Rev. 1999, 51, 83–133. [PubMed]

63. Rossi, R.; Bottinelli, R.; Sorrentino, V.; Reggiani, C. Response to caffeine and ryanodine receptor isoforms in mouse skeletal muscles. Am. J. Physiol.-Cell Physiol. 2001, 281, C585–C594. [CrossRef]

64. Allen, D.G.; Lee, J.A.; Westerblad, H. Intracellular calcium and tension during fatigue in isolated single muscle fibres from Xenopus laevis. J. Physiol. 1989, 415, 433–458. [CrossRef]

65. Westerblad, H.; Allen, D.G. Changes of myoplasmic calcium concentration during fatigue in single mouse muscle fibers. J. Gen. Physiol. 1991, 98, 615–635. [CrossRef]

66. Allen, D.G.; Westerblad, H. The effects of caffeine on intracellular calcium, force and the rate of relaxation of mouse skeletal muscle. J. Physiol. 1995, 487, 331–342. [CrossRef]

67. Astorino, T.A.; Terzi, M.N.; Roberson, D.W.; Burnett, T.R. Effect of two doses of caffeine on muscular function during isokinetic exercise. Med. Sci. Sports Exerc. 2010, 42, 2205–2210. [CrossRef]

68. Da Silva, V.L.; Messias, F.R.; Zanchi, N.E.; Gerlinger-Romero, F.; Duncan, M.J.; Guimarães-Ferreira, L. Effects of acute caffeine ingestion on resistance training performance and perceptual responses during repeated sets to failure. J. Sports Med. Phys. Fit. 2015, 55, 383–389.

69. Duncan, M.J.; Stanley, M.; Parkhouse, N.; Cook, K.; Smith, M. Acute caffeine ingestion enhances strength performance and reduces perceived exertion and muscle pain perception during resistance exercise. Eur. J. Sport Sci. 2013, 13, 392–399. [CrossRef]

70. Arazì, H.; Sotoudeh, K.; Sadeghi, M.M.; Mohammadi, S.M.; Saeedi, T. Influence of Upper-Body Exercise Order on Repetition Performance and Ratings of Perceived Exertion during a Super-Set Resistance Training Session. J. Sport Sci. 2015, 8, 24–27.

71. Grgic, J.; Mikulic, P. Caffeine ingestion acutely enhances muscular strength and power but not muscular endurance in resistance-trained men. Eur. J. Sport Sci. 2017, 17, 1029–1036. [CrossRef]

72. de Azevedo, A.P.; Guerra, M.A.; Caldas, L.C.; Guimarães-Ferreira, L. Acute caffeine ingestion did not enhance punch performance in professional mixed-martial arts athletes. Nutrients 2019, 11, 1422. [CrossRef]

73. Bell, D.G.; McLellan, T.M. Exercise endurance 1, 3, and 6 h after caffeine ingestion in caffeine users and nonusers. J. Appl. Physiol. 2002, 93, 1227–1234. [CrossRef] [PubMed]

74. Wilk, M.; Filip, A.; Krzysztofik, M.; Gepfert, M.; Zajac, A.; Del Coso, J. Acute caffeine intake enhances mean power output and bar velocity during the bench press throw in athletes habituated to caffeine. Nutrients 2020, 12, 406. [CrossRef] [PubMed]

75. Grgic, J.; Mikulic, P. Acute effects of caffeine supplementation on resistance exercise, jumping, and Wingate performance: No influence of habitual caffeine intake. Eur. J. Sport Sci. 2020, 1–11. [CrossRef]

76. Wilk, M.; Krzysztofik, M.; Filip, A.; Zajac, A.; Del Coso, J. Correction: Wilk et al. “The Effects of High Doses of Caffeine on Maximal Strength and Muscular Endurance in Athletes Habituated to Caffeine” Nutrients 2019, 11(8), 1912. Nutrients 2019, 11, 2660. [CrossRef] [PubMed]

77. Williams, T.D.; Tolusso, D.V.; Fedewa, M.V.; Esco, M.R. Comparison of periodized and non-periodized resistance training on maximal strength: A meta-analysis. Sports 2017, 47, 2083–2100. [CrossRef]

78. Pakulak, A.; Candow, D.G.; Totosy de Zepetnek, J.; Forbes, S.C.; Basta, D. Effects of Creatine and Caffeine Supplementation During Resistance Training on Body Composition, Strength, Endurance, Rating of Perceived Exertion and Fatigue in Trained Young Adults. J. Diet. Suppl. 2021, 1–16. [CrossRef]

79. Astorino, T.A.; Cottrell, T.; Lozano, A.T.; Aburto-Pratt, K.; Duhon, J. Effect of caffeine on RPE and perceptions of pain, arousal, and pleasure/displeasure during a cycling time trial in endurance trained and active men. Physiol Behav 2012, 106, 211–217. [CrossRef] [PubMed]

80. Brooks, J.H.; Wydl, K.; Christmas, B.C. Acute Effects of Caffeine on Strength Performance in Trained and Untrained Individuals. J. Athl. Enhanc. 2015, 5, 31–33. [CrossRef]

81. Mizuno, M.; Kimura, Y.; Tokizawa, K.; Ishii, K.; Oda, K.; Sasaki, T.; Nakamura, Y.; Muraoka, I.; Ishiwata, K. Greater adenosine A2A receptor densities in cardiac and skeletal muscle in endurance-trained men: A [11C]TMSX PET study. Nucl. Med. Biol. 2005, 32, 831–836. [CrossRef] [PubMed]

82. Pickering, C.; Kiely, J. What should we do about habitual caffeine use in athletes? Sports Med. 2019, 49, 833–842. [CrossRef] [PubMed]

83. Porterfield, S.; Linderman, J.; Laubach, L.L.; Dapранo, C.M. Comparison of the effect of caffeine ingestion on time to exhaustion between endurance trained and untrained men. J. Exerc. Physiol.-Online 2013, 16, 90–99.

84. Grgic, J.; Schoenfeld, B.J.; Davies, T.B.; Lazinica, B.; Krieger, J.W.; Pedisic, Z. Effect of resistance training frequency on gains in muscular strength: A systematic review and meta-analysis. Sports Med. 2018, 48, 1207–1220. [CrossRef]

85. Fulton, J.L.; Dinsa, P.C.; Carrillo, A.E.; Edsall, J.R.; Ryan, E.J.; Ryan, E.J. Impact of genetic variability on physiological responses to caffeine in humans: A systematic review. Nutrients 2018, 10, 1373. [CrossRef]

86. Southward, K.; Rutherford-Markwick, K.; Badenhorst, C.; Ali, A. The role of genetics in moderating the inter-individual differences in the ergogenicity of caffeine. Nutrients 2018, 10, 1352. [CrossRef]
87. Tennent, R.; Ali, A.; Wham, C.; Rutherfurd-Markwick, K. Narrative Review: Impact of Genetic Variability of CYP1A2, ADORA2A, and AHR on Caffeine Consumption and Response. *J. Caffeine Adenosine Res.* 2020, 10, 125–134. [CrossRef]

88. Doherty, M.; Smith, P.M. Effects of caffeine ingestion on exercise testing: A meta-analysis. *Int. J. Sport Nutr. Exerc. Metab.* 2004, 14, 626–646. [CrossRef]

89. Ganio, M.S.; Klau, J.F.; Casa, D.J.; Armstrong, L.E.; Maresh, C.M. Effect of caffeine on sport-specific endurance performance: A systematic review. *J. Strength Cond. Res.* 2009, 23, 315–324. [CrossRef]

90. Pickering, C.; Kiely, J. Are low doses of caffeine as ergogenic as higher doses? A critical review highlighting the need for comparison with current best practice in caffeine research. *Nutrition* 2019, 67, 110535. [CrossRef] [PubMed]

91. Mielgo-Ayuso, J.; Marques-Jiménez, D.; Refoyo, I.; Del Coso, J.; León-Guereño, P.; Calleja-González, J. Effect of caffeine supplementation on sports performance based on differences between sexes: A systematic review. *Nutrients* 2019, 11, 2313. [CrossRef]

92. Grgic, J. Effects of Caffeine on Resistance Exercise: A Review of Recent Research. *Sports Med.* 2021, 1–18. [CrossRef]