Abstract

Objectives: The aims of this paper are threefold: (1) to summarize the research examining the effects of caffeine on isokinetic strength, (2) pool the effects using a meta-analysis, and (3) to explore if there is a muscle group or a velocity specific response to caffeine ingestion.

Design: Meta-analysis.

Methods: PubMed/MEDLINE, Scopus, and SPORTDiscus were searched using relevant terms. The PEDro checklist was used for the assessment of study quality. A random-effects meta-analysis of standardized mean differences (SMDs) was done.

Results: Ten studies of good and excellent methodological quality were included. The SMD for the effects of caffeine on strength was 0.16 (95% CI=0.06, 0.26; p=0.003; +5.3%). The subgroup analysis for knee extensor isokinetic strength showed a significant difference (p=0.004) between the caffeine and placebo conditions with SMD value of 0.19 (95% CI=0.06, 0.32; +6.1%). The subgroup analysis for the effects of caffeine on isokinetic strength of other, smaller muscle groups indicated no significant difference (p=0.092) between the caffeine and placebo conditions. The subgroup analysis for knee extensor isokinetic strength at angular velocities of $60°\cdot s^{-1}$ and $180°\cdot s^{-1}$ showed a significant difference between the caffeine and placebo conditions with SMD value of 0.21 (95% CI=0.07, 0.36; p=0.004; +6.0%) and 0.23 (95% CI=0.07, 0.38; p=0.005; +5.5%), respectively. No significant effect (p=0.193) was found at an angular velocity of $30°\cdot s^{-1}$.

Conclusions: This meta-analysis demonstrates that acute caffeine ingestion caffeine may significantly increase isokinetic strength. Additionally, this meta-analysis reports that the effects of caffeine on isokinetic muscular strength are predominantly manifested in knee extensor muscles and at greater angular velocities.

Keywords: caffeine; exercise; muscles; power; torque

1. Introduction

Caffeine, a trimethylxanthine, is one of the most commonly consumed drugs in the world.[1] The use of caffeine is high both in the general population and among athletes.[2,3] Van Thuyne and colleagues reported that athletes in strength-based sports such as weightlifting and powerlifting are among the highest users of caffeine.[4] However, the effects of caffeine on strength performance remain a matter of debate in the scientific literature. Several narrative reviews[5,6] have highlighted that the effects of caffeine ingestion on muscular strength remain unclear. Indeed, while some report an increase in strength following caffeine ingestion[7, 8] others do not.[9] Methodological differences between studies, such as caffeine dose and training status of the participants, have been suggested as reasons for the equivocal evidence on the topic[6] (albeit, there is a lack of direct evidence to support these claims).[10]

It needs to be acknowledged that small sample sizes are a mainstay in the research examining the effects of caffeine on exercise performance. Therefore, it is possible that some studies lack sufficient statistical power to observe significant effects. For instance, Astorino et al.[11] reported that the ingestion of caffeine (in a dose of 6 $mg \cdot kg^{-1}$) over placebo improved resistance exercise performance in nine out of the 14 resistance-trained men included as participants, yet, no statistically significant increases in weight lifted were found. Therefore, it is possible that the study was underpowered to find significant effects.

Meta-analyses have helped to elucidate equivocal topics within nutritional supplement research as they allow the pooling of outputs from many studies.[12] Such statistical procedures provide more conclusive statements than individual trials and are set at the top of the hierarchy of evidence in the recent International Olympic Committee consensus statement. [12] Two meta-analyses thus far have examined the effects of caffeine on strength. Warren et al.[13] found that caffeine ingestion can increase strength, with the effect being predominantly in the knee extensor muscles, but not in smaller muscle groups such as the elbow flexors. Of the 22 peer-reviewed studies included in the analysis by Warren et al.[13] 17 examined the effects of caffeine on isometric strength. Three included studies examined the effects of caffeine on isokinetic strength, and two examined the effects of caffeine ingestion on one-repetition maximum (1RM). Therefore, it can be argued that the results provided by Warren et al.[13] are specific to the effects of caffeine on isometric strength. A recent meta-analysis by Grgic et al.[14] focused on 1RM and found a significant ergogenic effect with caffeine ingestion. A subgroup analysis from their review showed that caffeine ingestion had a significant effect on upper-body, but not on lower-body strength; results which somewhat are in contrast to those presented for isometric strength by Warren et al.[13]

The assessment of strength forms an important component of monitoring the effects of various training interventions.[15] Additionally, assessment of strength is often used by researchers in order to understand the relative significance of strength to a specific trait, outcome (such as falls in older adults),[16] and/or sports performance. Furthermore, assessing strength levels of an individual may be utilized within talent identification,[15] and to identify injury risk.[17, 18] Strength can be assessed through a variety of techniques, including isometric, 1RM, and isokinetic methods. An important consideration is that the various types of strength assessment have different characteristics, and thus cannot be considered as interchangeable or equivalent measures of strength.[19] Moreover, they can even produce conflicting results.[20]

Given that during an isometric muscle action the muscle-tendon unit does not change its length, isometric strength only provides information regarding strength levels at a specific point of application within a joint's range of motion.[21] Also, isometric muscular actions might have less applicability to most sporting situations as these commonly include dynamic muscle actions.[10] While the 1RM test includes dynamic muscle actions, in this test, velocity cannot be controlled, and, additionally, the muscle can be overloaded only by the amount of weight that can be lifted through the weakest part of the exercised range of motion.[21] Furthermore, the complexity of some exercises (such as the free weight barbell squat) used for the 1RM test may require several familiarization sessions to obtain a reliable measurement given the considerable skill component of such movements.[22]

While isokinetic strength assessment is not without its limitations, it does provide certain advantages including: (1) maximal resistance throughout the exercised range of motion (i.e., no fixed resistance in the weakest point of the movement); (2) the use of accommodating resistance, which provides a safety mechanism given that the accommodating mechanism disengages when the participant senses pain; (3) the use and control of different velocities; and (4) isokinetic assessments allow the quantification of torque (the force measured about a joint's axis of rotation), work (force and distance of a given muscular action), and power (time required to produce work).[21] Furthermore, isokinetic assessment has been shown to be a highly reliable measure of strength.[21, 23]

Several studies have previously investigated the effects of caffeine ingestion on isokinetic strength, with equivocal findings. [24-33] Thus, the aims of this paper are to: (1) summarize the research examining the effects of caffeine on isokinetic strength, (2) pool the effects using a meta-analysis, and (3) to explore if there is a muscle group or a velocity specific response to caffeine ingestion.

2. Methods

For this paper, peer-reviewed literature was searched on the effects of caffeine ingestion on isokinetic strength, defined as the peak torque produced during an isokinetic maximal voluntary contraction. The literature search was done on May 26th, 2018. The primary search occurred via Scopus, PubMed/MEDLINE, and SPORTDiscus databases through titles, abstracts, and keywords. The search syntax included the following words coupled with Boolean operators: caffeine AND (strength OR force OR torque OR isokinetic). The secondary searchers consisted of: (1) examining the reference lists of the studies found meeting the inclusion criteria, (2) examining papers that cited the included studies through the Scopus database, and (3) scanning through the reference lists of relevant review papers.[1, 5, 6, 13, 14] In order to prevent any selection bias, the search was done independently by the two authors of the review.

Studies meeting the following criteria were included in the present review: (1) published in a peer-reviewed, English-language journal, (2) included humans as participants, (3) utilized a crossover design with at least one placebo and one caffeine trial, and (4) isokinetic muscular strength was assessed. Studies in which other potentially ergogenic compounds such as taurine were used were not considered for the present review. Additionally, studies with a between-group design were not included due to poor control of the inter-individual variability in response[34] to caffeine ingestion in such study designs.

The following data were extracted from the included studies: (1) authors and publication date, (2) participants characteristics, (3) the tested muscle group, and (4) means and standard deviations for isokinetic strength from the caffeine and placebo trials. If data were presented in figures, the Web Plot Digitizer software (V.3.11. Texas, USA: Ankit Rohatgi, 2017) was used for the extraction of raw values. Standard errors (SEs) were converted to standard deviations, using the following formula: $(SE \cdot \sqrt{n})$.

The Physiotherapy Evidence-Based Database Scale (PEDro) was used for the assessment of study quality. This scale has a total of 11 items. The maximum possible score on the scale is 10 points as the first item is not included in the total score. The full details regarding the PEDro scale can be found elsewhere.[35] The study quality was classified as in the review by McKendry and colleagues[36] and by others[14, 37] in which 9-10 points corresponds to excellent quality, 6-8 points correspond to good quality, 4-5 points corresponds to fair quality, and less than 3 points correspond to poor methodological quality.

2.1 Statistical analysis

The extracted isokinetic muscular strength data were converted to standardized mean differences (Hedge's g) and 95% confidence intervals (CIs). The following data were needed for the calculation of standardized mean differences: (1) mean ± standard deviation of the caffeine and placebo trials, (2) sample size (*n*), and (3) inter-trial correlation. None of the included studies presented inter-trial correlation. Therefore, as suggested in the Cochrane Handbook[38] the correlation was estimated using the following formula:

$$r = \frac{S^2_{placebo} + S^2_{caffeine} - S^2_D}{2 \cdot S_{placebo} \cdot S_{caffeine}}$$

S represents the standard deviation while S_D is the standard deviation of the difference score, which was calculated as:

$$S_D = \left(\frac{S^2_{placebo}}{n} + \frac{S^2_{caffeine}}{n}\right)^{1/2}$$

When a study measured strength under multiple conditions, such as multiple caffeine doses, standardized mean differences and variances were averaged across the different conditions and the average values were used for the analysis. The main analysis consisted of all isokinetic muscular strength data. A sensitivity analysis was performed by excluding the study with the lowest score on the PEDro checklist.[24] Two subgroup analyses that focused on the size of the assessed muscle group were performed, one in which only knee extensor data was analyzed, and one for all other muscle groups (such as knee flexors, elbow flexors, ankle plantar flexors, and wrist flexors). We analyzed knee extensor data in isolation to explore the impact of caffeine on individual muscle groups, with a previous meta-analysis[13] suggesting that caffeine's positive impact on strength occurs predominantly within the knee extensors. In order to explore the effects of caffeine on different angular velocities, subgroup analyses were done for angular velocities of 30, 60, and 180°·s^{-1}. A subgroup analysis for other angular velocities such as 250°·s^{-1} could not be explored due to the limited data.

Hedge's g values of ≤0.2, 0.2-0.5, 0.5-0.8, and >0.8 were considered to represent small, medium, large, and very large effects, respectively.[39] Heterogeneity was assessed using the I^2 statistic. The following classification was used for heterogeneity: low levels (≤50%), moderate levels (50-75%), and high levels (>75%) of heterogeneity. Funnel plots were used for detecting publication bias with the Duval and Tweedie's trim and fill method. Percent changes between the placebo and caffeine conditions were also calculated. The random-effects model was used for all analyses. The statistical significance threshold was set at $p < 0.05$. All analyses were performed using the Comprehensive Meta-analysis software, version 2 (Biostat Inc., Englewood, NJ, USA).

3. Results

The search through the three databases resulted in a total of 3283 relevant publications. Of the total number, 3238 items were excluded after reading the title or the abstract which left 45 full-text papers to be examined. Out of the 45 full-text papers, 35 were excluded as they did not meet the inclusion criteria, leaving a total of ten included studies.[24-33] The secondary searches did not result in any additional inclusion of studies.

A summary of all study details can be found in Table 1. In total, 133 participants were included across the studies (men = 120 *n*; women = 13 *n*). The median number of participants per study was 13. In five of the studies,[24, 25, 29-31] the participants were reported as athletes or resistance-trained while in the remaining five the participants were either recreationally trained or untrained individuals.[26-28, 32, 33] In nine of the ten studies, the participants were of young age, while one study included older adults.[28] Seven studies measured only lower-body strength,[24-26, 27, 29, 31, 32] two examined both lower and upper-body strength,[30, 33] while one study measured only upper-body strength.[27]

Table 1
Summary of the included studies.

Reference	Study design	Sample	Caffeine dose	Timing of caffeine ingestion	Muscle group tested	Percent changes (%)[a]
Ali et al.[31]	Randomized, double-blind crossover	10 young female team sport athletes	6 mg kg^{-1}	60 min pre-exercise	Eccentric and concentric knee extensor and knee flexor at 30° s^{-1} (tested on multiple occasions)	Eccentric knee extensors pre: ↑ 3.4 Eccentric knee extensors mid: ↑ 17.9 Eccentric knee extensors post: ↑ 7.0 Eccentric knee extensors 12 h post: ↑ 6.0 Concentric knee extensors pre: ↑ 8.7 Concentric knee extensors mid: ↑ 10.5 Concentric knee extensors post: ↑ 1.8 Concentric knee extensors 12 h post: ↑ 20.4 Eccentric knee flexors pre: ↑ 7.5 Eccentric knee flexors mid: ↑ 17.9 Eccentric knee flexors post: ↑ 10 Eccentric knee flexors 12 h post: ↑ 15.5 Concentric knee flexors pre: ↓ 5.0 Concentric knee flexors mid: ↑ 3.8 Concentric knee flexors post: ↑ 3.9 Concentric knee flexors 12 h post: ↑ 7.9
Astorino et al.[26]	Randomized, single-blind crossover	15 young recreationally active men	2 and 5 mg kg^{-1}	60 min pre-exercise	Knee extensor and knee flexor at 180° s^{-1} (2 bouts)	Knee extensor 2 mg kg^{-1} (bout 1): ↑ 0.7 Knee extensor 5 mg kg^{-1} (bout 1): ↑ 1.5 Knee extensor 2 mg kg^{-1} (bout 2): ↓ 1.7 Knee extensor 5 mg kg^{-1} (bout 2): ↔ 0.0 Knee flexor 2 mg kg^{-1} (bout 1): ↑ 4.5 Knee flexor 5 mg kg^{-1} (bout 1): ↑ 5.7 Knee flexor 2 mg kg^{-1} (bout 2): ↔ 0.0 Knee flexor 5 mg kg^{-1} (bout 2): ↑ 3.6
Bazzucchi et al.[27]	Randomized, double-blind crossover	14 young recreationally active men	6 mg kg^{-1}	60 min pre-exercise	Elbow flexor at 0° s^{-1}, 30° s^{-1}, 60° s^{-1}, 120° s^{-1}, 180° s^{-1}, 250° s^{-1}	Elbow flexor 0° s^{-1}: ↑ 6.7 Elbow flexor 30° s^{-1}: ↑ 15.4 Elbow flexor 60° s^{-1}: ↑ 6.3 Elbow flexor 120° s^{-1}: ↑ 5.1 Elbow flexor 180° s^{-1}: ↑ 7.3 Elbow flexor 250° s^{-1}: ↑ 10.0
Bond et al.[24]	Randomized, crossover	12 young male intercollegiate track sprinters	5 mg kg^{-1}	60 min pre-exercise	Knee extensor and knee flexor at 30° s^{-1}, 150° s^{-1}, 300° s^{-1}	Knee extensor 30° s^{-1}: ↓ 1.3 Knee extensor 150° s^{-1}: ↑ 0.6 Knee extensor 300° s^{-1}: ↓ 8.0 Knee flexor 30° s^{-1}: ↓ 9.6 Knee flexor 150° s^{-1}: ↓ 3.3 Knee flexor 300° s^{-1}: ↓ 2.3
Duncan et al.[29]	Randomized, double-blind crossover	10 young resistance-trained men	6 mg kg^{-1}	60 min pre-exercise	Knee extensor at 30° s^{-1}, 150° s^{-1}, 300° s^{-1}	Knee extensor at all velocities: ↑ 8.3
Jacobson et al.[25]	Randomized, double-blind crossover	20 young male college athletes	7 mg kg^{-1}	60 min pre-exercise	Knee extensor and flexor at 30° s^{-1}, 150° s^{-1}, 300° s^{-1}	Knee extensor 30° s^{-1}: ↑ 10.5 Knee extensor 150° s^{-1}: ↑ 5.9 Knee extensor 300° s^{-1}: ↑ 7.1 Knee flexor 30° s^{-1}: ↑ 2.0 Knee flexor 150° s^{-1}: ↑ 5.7 Knee flexor 300° s^{-1}: ↑ 4.1
Tallis et al.[28]	Randomized, double-blind crossover	12 (9 males and 3 females) untrained older adults	3 mg kg^{-1}	60 min pre-exercise	Knee extensor at 30° s^{-1}	Knee extensor 30° s^{-1}: ↓ 3.8
Tallis et al.[32]	Randomized, single-blind crossover	14 untrained young men	5 mg kg^{-1}	60 min pre-exercise	Knee extensor and flexor at 30° s^{-1} and 120° s^{-1} (with different caffeine and placebo trials)	Knee extensor 30° s^{-1} (told caffeine, given caffeine): ↑ 5.4 and 16.6 Knee extensor 30° s^{-1} (told placebo, given caffeine): ↑ 2.6 and 13.5 Knee extensor 120° s^{-1} (told caffeine, given caffeine): ↑ 6.8 and 12.5 Knee extensor 120° s^{-1} (told caffeine, given caffeine): ↑ 1.8 and 7.2 Knee flexor 30° s^{-1} (told caffeine, given caffeine): ↑ 6.3 and 12.3 Knee flexor 30° s^{-1} (told placebo, given caffeine): ↓ 0.6 and ↑ 5.0 Knee flexor 120° s^{-1} (told caffeine, given caffeine): ↓ 4.8 and 6.5 Knee flexor 120° s^{-1} (told caffeine, given caffeine): ↓ 1.5 and 3.3
Tallis and Yavuz[33]	Randomized, double-blind crossover	10 young recreationally active men	3 and 6 mg kg^{-1}	60 min pre-exercise	Eccentric and concentric knee extensor and elbow flexor at 60° s^{-1}, 180° s^{-1}	Eccentric knee extensors 60° s^{-1} (3 mg kg^{-1}): ↑ 14.5 Eccentric knee extensors 60° s^{-1} (6 mg kg^{-1}): ↑ 6.0 Eccentric knee extensors 180° s^{-1} (3 mg kg^{-1}): ↑ 13.8 Eccentric knee extensors 180° s^{-1} (6 mg kg^{-1}): ↑ 16.0 Concentric knee extensors 60° s^{-1} (3 mg kg^{-1}): ↑ 4.4 Concentric knee extensors 60° s^{-1} (6 mg kg^{-1}): ↑ 6.0 Concentric knee extensors 180° s^{-1} (3 mg kg^{-1}): ↑ 21.6 Concentric knee extensors 180° s^{-1} (6 mg kg^{-1}): ↑ 26.3 Eccentric elbow flexor 60° s^{-1} (3 mg kg^{-1}): ↓ 8.8 Eccentric elbow flexor 60° s^{-1} (6 mg kg^{-1}): ↓ 5.2 Eccentric elbow flexor 180° s^{-1} (3 mg kg^{-1}): ↓ 0.3 Eccentric elbow flexor 180° s^{-1} (6 mg kg^{-1}): ↓ 4.0 Concentric elbow flexor 60° s^{-1} (3 mg kg^{-1}): ↓ 6.1 Concentric elbow flexor 60° s^{-1} (6 mg kg^{-1}): ↓ 3.6 Concentric elbow flexor 180° s^{-1} (3 mg kg^{-1}): ↓ 2.4 Concentric elbow flexor 180° s^{-1} (6 mg kg^{-1}): ↑ 0.8
Timmins and Saunders[30]	Randomized, single-blind	16 young resistance-trained men	6 mg kg^{-1}	30 min pre-exercise	Knee extensor, ankle plantar flexors, elbow flexor and wrist flexor at 60° s^{-1}	Knee extensors 60° s^{-1}: ↑ 13.7 Ankle plantar flexors 60° s^{-1}: ↑ 11.2 Elbow flexors 60° s^{-1}: ↑ 9.1 Wrist flexors 60° s^{-1}: ↑ 6.3

↑ = increase; ↓ = decrease; ↔ = no change.
[a] Calculated as percent change with caffeine over placebo.

Based on the PEDro checklist, six studies[25, 27-29, 31, 33] were classified as excellent quality while four[24, 26, 30, 32] were classified as good quality. The mean ± standard deviation score was 9 ± 1 (range = 6 to 10 points). Individual scores for the quality assessment can be found in Table 2.

Table 2
Results from the PEDro checklist.

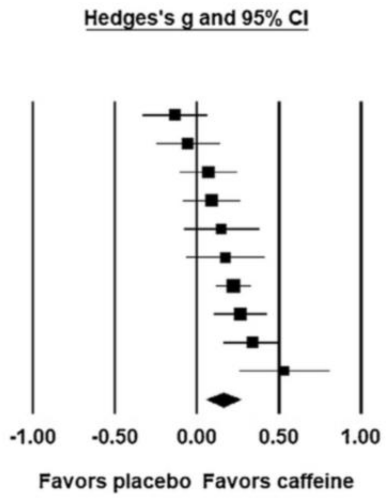
Study	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Total score
Ali et al.[31]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Astorino et al.[26]	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	8
Bazzucchi et al.[27]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Bond et al.[24]	No	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	6
Duncan et al.[29]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Jacobson et al.[25]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Tallis et al.[28]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Tallis et al.[32]	No	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	8
Tallis and Yavuz[33]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Timmins and Saunders[30]	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	8

Yes = criterion is satisfied; No = criterion is not satisfied.

The main meta-analysis results showed a significant difference (p = 0.003) between the caffeine and placebo conditions. The standardized mean difference for the effects of caffeine on strength was 0.16 (95% CI = 0.06, 0.26; +5.3%; I^2 = 15%). The sensitivity analysis in which the study with the lowest quality was excluded changed the standardized mean difference value to 0.19 (95% CI = 0.10, 0.28; p < 0.001). The forest plot of the analysis is presented in Figure 1. The subgroup analysis for knee extensor isokinetic strength showed a significant difference (p = 0.004) between the caffeine and placebo conditions. The standardized mean difference for the effects of caffeine on strength was 0.19 (95% CI = 0.06, 0.32; +6.1%; I^2 = 11%). The subgroup analysis for the isokinetic strength of other muscle groups indicated no significant difference (p = 0.092) between the caffeine and placebo conditions with the standardized mean difference value of 0.10 (95% CI = -0.02, 0.21; +3.9%; I^2 = 19%).

The subgroup analysis for isokinetic strength at 30°·s^{-1} indicated no significant difference (p = 0.193) between the caffeine and placebo conditions with the standardized mean difference value of 0.16 (95% CI = -0.08, 0.39; +6.2%; I^2 = 0%). The subgroup analysis for isokinetic strength at 60°·s^{-1} showed a significant difference (p = 0.004) between the caffeine and placebo conditions. The standardized mean difference for the effects of caffeine on strength was 0.21 (95% CI = 0.07, 0.36; +6.0%; I^2 = 7%). The subgroup analysis for isokinetic strength at 180°·s^{-1} showed a significant difference (p = 0.005) between the caffeine and placebo conditions. The standardized mean difference for the effects of caffeine on strength was 0.23 (95% CI = 0.07, 0.38; +5.5%; I^2 = 0%). No asymmetry was noted in the funnel plots in any of the analyses and the Duval and Tweedie's trim and fill correction did not have any effect.

Study name	Hedges's g	Lower limit	Upper limit	p-Value
Bond et al. (1986)	-0.13	-0.33	0.06	0.184
Tallis et al. (2013)	-0.05	-0.25	0.14	0.589
Tallis et al. (2016)	0.07	-0.11	0.25	0.434
Astorino et al. (2010)	0.09	-0.09	0.27	0.314
Ali et al. (2016)	0.15	-0.08	0.38	0.205
Tallis and Yavuz (2018)	0.17	-0.07	0.41	0.160
Jacobson et al. (1992)	0.22	0.12	0.33	0.000
Timmins and Saunders (2014)	0.27	0.10	0.43	0.002
Bazzucchi et al. (2011)	0.34	0.16	0.51	0.000
Duncan et al. (2014)	0.53	0.26	0.81	0.000
	0.16	0.06	0.26	0.003



4. Discussion

The main finding of the present meta-analysis suggests that acute caffeine ingestion may increase isokinetic strength when compared to placebo. Furthermore, it appears that caffeine improves strength predominantly in the knee extensors and at higher angular velocities. Given its performance-enhancing effect, caffeine may be used as an effective aid for an amplified acute training stimulus. Based on the good and excellent quality of the included studies it can be concluded that the results of the present analysis are not confounded by studies with poor methodological quality.

The results presented herein corroborate previous meta-analytic data by Warren et al.[13] and Grgic et al.[14] As previously discussed, Warren et al.[13] found that caffeine may have a greater effect on the knee extensor musculature than on smaller muscle groups such as elbow flexors. Knee extensor activation is usually around 85 to 95% of its maximal capacity during a maximal voluntary contraction.[40] In contrast to knee extensors, smaller muscle groups such as the plantar flexors are activated up to 99% of their maximum during a maximal voluntary contraction.[40] Thus, given the possible ceiling effect of activation in smaller muscle groups, Warren et al.'s suggestion was that the enhancement of central excitability[41,42] and increase in motor unit recruitment[41,42] with caffeine ingestion might predominately be manifested in the knee extensors.[13] Our results appear to confirm such an effect. The work by Black et al.[43] provided some further support for these results. The authors used the interpolated-twitch electrical stimulation protocol and examined the percentage of motor-unit recruitment of the knee extensors and the elbow flexors during a strength assessment. Before the ingestion of caffeine, the mean percentage of motor-unit recruitment of the elbow flexors during a maximal voluntary contraction was at 97%. However, for the knee extensors, the values were only 83%. Likely because of these differences at baseline, after the ingestion of caffeine, a significant increase ($p = 0.014$; +6.3%) in maximal voluntary contraction was seen in the knee extensors, but not in the elbow flexors. While the present meta-analysis does show that caffeine ingestion may have a significant effect on the strength of knee extensors, given the small number of studies (i.e., seven) that are directly comparing the effects of caffeine on smaller vs. larger muscle groups, future work is warranted.

Besides the increases in motor-unit recruitment, it has been suggested that a decrease in pain perception might contribute to the enhanced strength with caffeine ingestion.[41, 42] Caffeine is a competitive adenosine receptor antagonist, and thus, after ingestion, binds to A_1 and A_{2a} adenosine receptors.[44] Due to its analgesic properties (which are likely due to the modification of caffeine on nociceptive processing),[1] caffeine is used in a variety of pain medications.[41, 42] Motl and colleagues reported a reduction in pain perception after the ingestion of caffeine in prolonged, aerobic exercise.[45] Only one of the ten included studies in the present review examined the effects of caffeine on strength and the associated pain perception values. Tallis and Yavuz[33] reported no effect of caffeine on pain perception, even though significant increases in peak torque of the knee extensors was seen both with the 3 $mg \cdot kg^{-1}$ and 6 $mg \cdot kg^{-1}$ caffeine dose. These results would suggest that different mechanism(s) other than reductions in pain perception contributed to the enhanced performance. One often proposed mechanism is that caffeine increases intracellular calcium ion concentrations,[46] which in turn enhances cross-bridge attachment and hence force production (as reviewed by Sökmen and colleagues).[47] However, it is evident that future work is needed in this area before making any firm conclusions.

The effects of caffeine on isokinetic strength as assessed by different angular velocities may not be uniform.[33] To explore this matter, we conducted a subgroup analysis focusing on the effects of caffeine on strength at different angular velocities. The results of this analysis indicated that caffeine ingestion may have a more pronounced effect on strength when assessed at greater velocities (such as 60 and 180°·s^{-1}) as compared to a lower angular velocity of 30°·s^{-1}. These results provide some support for the findings by Tallis and Yavuz[33] who also observed that caffeine ingestion may have a greater effect at higher velocities. While this is indeed an exciting finding, given the small number of studies, these results should be interpreted with a degree of caution. Specifically, the analyses for angular velocities of 30, 60, and 180°·s^{-1} included only six, three, and three studies, respectively. Given this limitation, future work on this topic is needed.

Only two studies examined the effects of caffeine on both upper and lower-body strength in the same cohort, with equivocal findings.[30, 33] Due to the lack of such studies, it could not be explored whether there is a differential response to caffeine ingestion between upper and lower-body. Timmins and Saunders[30] investigated the effect of 6 mg·kg^{-1} of caffeine on isokinetic strength of knee extensors, ankle plantar flexors, elbow flexors, and wrist flexors. The authors reported that caffeine ingestion improved strength in all muscle groups, with the increases ranging from +6.3% to +13.7%. In contrast to these results, Tallis and Yavuz[33] reported that 3 mg·kg^{-1} and 6 mg·kg^{-1} of caffeine increased strength only in the knee extensors, but not in the upper-body musculature (i.e., elbow flexors). It might be that these differences in results are due to the training status of the participants as Timmins and Saunders[30] included resistance-trained men, while Tallis and Yavuz[33] included individuals without any previous resistance exercise experience. That said, this remains speculative at this point and thus, this area merits further research.

Besides the effects of caffeine on pain perception, the effects of caffeine on strength at different velocities, and the effects of caffeine on upper vs. lower-body strength, several interesting areas could be explored in future research. For instance, future studies are needed among women as, out of the 133 pooled participants across the studies, 120 of them were men. Also, none of the studies explored whether there is a sex-specific response to caffeine ingestion, which is something that might be of interest for future studies. Furthermore, most of the studies used only a single dose of caffeine, most commonly between 3-7 $mg \cdot kg^{-1}$. Of the two studies that did utilize multiple caffeine doses, Tallis and Yavuz[33] reported that both the lower (3 $mg \cdot kg^{-1}$) and the higher (6 $mg \cdot kg^{-1}$) caffeine doses enhanced strength in the lower-body musculature. Astorino and colleagues compared 2 and 5 $mg \cdot kg^{-1}$ caffeine doses, while finding that only the higher dose enhanced performance. As such, it is not clear what the optimal caffeine dose is for enhancing strength, and indeed this may even differ for both contraction type[33] and individuals.[34] Thus, future research may wish to explore the dose-response of caffeine ingestion of isokinetic performance. Also, given that only two studies compared the effects of caffeine on concentric vs. eccentric muscle actions,[31, 33] future studies addressing this subject are also needed.

It is well-established that there is a considerable inter-individual variation in the responses to caffeine ingestion.[34] Using a 10-km cycling time trial, Guest et al.[48] recently reported that the *CYP1A2* gene impacts the ergogenic effects of caffeine on performance. The results showed that the AA genotype increased performance following caffeine ingestion, while the C allele carries either showed no improvement (AC genotype) or even decreases in performance (CC genotype) with caffeine. Similar results have been reported in terms of the effect of acute caffeine ingestion on muscular endurance,[49] although the impact on maximum strength is currently unexplored, representing a future avenue for exploration.

Finally, only one of the studies in this meta-analysis examined the impact of caffeine in older adults, reporting no significant effects of caffeine on isokinetic strength in the knee extensors. Using a mice model, the same research group reported a reduction (but not an elimination) of the ergogenic effects of caffeine on strength performance in older muscles.[50] This results tentatively suggest the potential for a reduction in caffeine sensitivity, mediated by a reduction in excitation-contraction coupling, with age.[50] Again, future research in this area is required to confirm these initial findings.

From a practical standpoint, the main use of isokinetic tests is in assessing strength, as opposed to its use as a training aid. These results suggest that the outcomes of such an assessment could be modified by caffeine ingestion. As such, when utilizing isokinetic strength assessments, researchers and practitioners should attempt to control for caffeine intake, particularly when seeking to explore differences between individuals.

5. Conclusion

In conclusion, this meta-analysis demonstrates that acute caffeine ingestion may lead to significant increases in isokinetic strength performance. Additionally, this meta-analysis reports that the effects of caffeine on isokinetic muscular strength are predominantly manifested in knee extensor muscles and at higher angular velocities. Finally, these conclusions are based on studies with excellent to good methodological quality, and on analyses with low levels of heterogeneity.

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