Effect of Caffeine Ingestion on Muscular Strength and Endurance: A Meta-Analysis

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ABSTRACT

WARREN, G. L., N. D. PARK, R. D. MARESCA, K. I. MCKIBANS, and M. L. MILLARD-STAFFORD. Effect of Caffeine Ingestion on Muscular Strength and Endurance: A Meta-Analysis. *Med. Sci. Sports Exerc.*, Vol. 42, No. 7, pp. 1375–1387, 2010. **Purpose**: Our objective was to perform a systematic review and meta-analysis of the research literature assessing the effect of caffeine ingestion on maximal voluntary contraction (MVC) strength and muscular endurance. **Methods**: Thirty-four relevant studies between 1939 and 2008 were included in the meta-analyses of caffeine's effects on MVC strength (n = 27 studies) and muscular endurance (n = 23 studies). Effect sizes (ES) were calculated as the standardized mean difference and meta-analyses were completed using a random-effects model. **Results**: Overall, caffeine ingestion was found to result in a small beneficial effect on MVC strength (overall ES = 0.19, P = 0.0003). However, caffeine appears to improve MVC strength primarily in the knee extensors (i.e., by ~7%, ES = 0.37) and not in other muscle groups such as the forearm or the knee flexors. In an attempt to offer a physiological mechanism behind caffeine's ability to improve MVC strength, a meta-analysis was run on ES from nine studies that measured percent muscle activation during MVC in trials comparing caffeine versus placebo; the overall ES (0.67) was highly significant (P = 0.00008) and of moderate to large size, thus implicating an effect of caffeine on the CNS. Caffeine ingestion was also found to exert a small beneficial effect on muscular endurance (overall ES = 0.28, P = 0.00005). However, it appears caffeine improves muscular endurance only when it is assessed using open (i.e., by ~18%, ES = 0.37) and not fixed end point tests. **Conclusions**: Overall, caffeine ingestion improves MVC strength and muscular endurance. The effect on strength appears exclusively in the knee extensors, and the effect on muscular endurance appears only detectable with open end point tests. **Key Words:** SYSTEMATIC REVIEW, FORCE, TORQUE, MAXIMAL VOLUNTARY CONTRACTION, MUSCLE ACTIVATION

The evidence is quite strong that caffeine ingestion can enhance performance during both endurance and short-term, high-intensity exercise (see reviews by Burke (7), Doherty and Smith (10), and Ganio et al. (14)). The mechanism(s) for caffeine's ergogenic effect is (are) not clear. The originally proposed mechanism (i.e., an enhancement of fat oxidation with sparing of limited and critical muscle glycogen stores) has fallen out of favor over the last 20 yr (15,16). A decreased respiratory exchange ratio and an increased plasma free fatty acid level are most often absent during endurance exercise after caffeine ingestion (15). Furthermore, this hypothesis cannot explain improved performance in short-term, high-intensity exercise where carbohydrate stores are not a limiting factor.

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Alternative mechanisms for caffeine's ergogenic effect have been proposed but not comprehensively tested. Caffeine may permit one to exercise at higher intensities and/or for a longer time by reducing pain and/or sensation of force (37,43,45,48). Caffeine may also improve skeletal muscle function through increased force production (15). Improvements in maximal voluntary contraction (MVC) strength resulting from weight training have been associated with improvements in performance during both endurance and short-term, high-intensity exercise (19,20,36,41,46,53), and thus caffeine may have a similar mechanism of action. The means by which a strength increase might result from caffeine ingestion could be by a direct effect on muscle (e.g., maintaining electrolyte homeostasis or enhancing sarcoplasmic reticulum Ca^{2+} release) (15,57) or by an effect on the CNS (e.g., increasing motor unit recruitment) (27,29). However, the literature is unclear on the effect of caffeine ingestion on muscular strength, with some traditional narrative reviews stating that there is (27,29) or is not (38,57) a beneficial effect, whereas other content experts call for more research on the topic (15). Furthermore, unlike the case for caffeine's effect on endurance and short-term, high-intensity exercise, there have been no systematic reviews and/or meta-analyses evaluating caffeine's effect on muscular strength and endurance.

The objective of this study was to clarify caffeine's effect on skeletal muscle function using a rigorous systematic review and a meta-analytic approach. We sought to determine whether caffeine ingestion improves 1) MVC strength in the unfatigued state and 2) muscle endurance, that is, resistance to fatigue. Upon finding a significant overall beneficial effect of caffeine on MVC strength, we then sought to assess whether the effect was due to an effect on muscle tissue and/or the CNS. We also attempted to explain the disparate findings of previous research into caffeine's effect on muscle by examining the effects of various experimental factors (e.g., dosage, duration of withdrawal before testing, muscle group studied) that have varied among investigations.

METHODS

Systematic Review

We searched the research literature on the effects of caffeine ingestion on MVC strength or muscular endurance. MVC strength was operationally defined as 1) the peak force or torque produced during an isometric or an isokinetic MVC or 2) the maximum load that could be lifted during a single isotonic contraction (i.e., one-repetition maximum). Muscular endurance was operationally defined as 1) the maximum time that a prescribed submaximal isometric force could be maintained, 2) the maximum number of contractions or work done while ensuring that the peak force did not fall below a prescribed submaximal value while performing isokinetic contractions, 3) the maximum number of contractions or work done while performing isotonic contractions using a prescribed submaximal load, or 4) the maximum amount of work done while performing a set number of isokinetic or isotonic contractions. Our literature search began October 2007 and continued through May 2009. PubMed, SportDiscus, ISI Web of Knowledge, ProQuest Dissertation & Theses, and the American College of Sports Medicine database of annual meeting proceedings were searched. The search terms and strategy used were caffeine AND (strength OR force OR torque OR endurance). Where possible, the retrieved studies were delimited to those using human subjects. Reference lists from the 47 fully evaluated publications and those of relevant review articles (7,15,27,29) were also examined for studies not found with the online database searches.

Study inclusion and exclusion criteria. Studies meeting the following criteria were considered for review: 1) the study was conducted on humans, 2) the study contained at least two trials (or separate groups of subjects) in which the subjects consumed caffeine in one trial (or group) and placebo in the other, and 3) some form of MVC strength or muscular endurance (as defined above) was measured. In addition, studies were also included that measured electrically evoked strength under supramaximal stimulation conditions or percent muscle activation during an MVC; this latter measure was assessed with either the central activation ratio or the interpolated twitch procedure. Studies were excluded for the following reasons. First, the effect observed in a study could not be attributed specifically to caffeine (e.g., the two conditions differed by more than caffeine). Second, caffeine was coingested with other known or potentially ergogenic compounds (e.g., creatine, ginseng, and taurine). Caffeine added to decaffeinated coffee or to sweetened or sugar-free, citrus-flavored drink was, however, permitted. Third, the subjects had exercised or were fatigued before testing. Fourth, there were insufficient data reported in a study to calculate an effect size (ES) for MVC strength or muscular endurance. In such studies, we attempted to retrieve the necessary data by contacting the corresponding author by email, telephone, and/or letter; we were successful in only one of three attempts.

Selection of studies. A total of 1705 relevant publications were originally identified through the database searches and review of article reference lists. Of those, 1658 were initially excluded on the basis of the title and/or review of the abstract. At this point, 47 publications were fully evaluated via a careful review of the full text. On the basis of the inclusion and exclusion criteria, 13 articles were excluded, leaving a total of 34 articles to be included in the meta-analyses.

Data extraction and study quality assessment. For the meta-analyses, MVC strength and muscular endurance data were usually (i.e., 74%–78% of all studies) extracted in the form of means, SD, and sample sizes (n) for both the caffeine and the placebo conditions. These descriptors were ones reported for either posttreatment measurements only or for percent changes from pretreatment to posttreatment. In studies that did not report all three descriptors, the following were extracted: 1) means, sample sizes, and P value or; 2) effect direction, sample sizes, and P value. If available, individual subject data were also extracted so that intertrial correlations for the MVC strength and muscular endurance measures could be calculated. If a study tested conditions other than caffeine and placebo, the data for those conditions were not used in the meta-analysis. All 34 studies were assessed for quality on the basis of the Physiotherapy Evidence-Based Database Scale (PEDro) independently by at least two of the present study's authors. The scale yields a total possible score of 11 points, with more points corresponding to higher quality (42).

Meta-Analysis

The extracted muscular strength and endurance data were converted to a standard format by calculating the standardized mean difference, which will be called the ES in the Results and Discussion sections. For crossover studies in which means, SD, and sample sizes were reported (i.e., the most common scenario), the paired difference (i.e., caffeine mean − placebo mean) and the paired difference SD (i.e., (caffeine SD^2 + placebo SD^2 − 2 × intertrial correlation × caffeine SD × placebo SD)$^{1/2}$) were initially calculated. They were next used to calculate the standardized mean difference (i.e., paired difference × (2(1 − intertrial

TABLE 1. Characteristics of the 34 studies examining the effect of caffeine ingestion on MVC strength and/or muscular endurance.

Reference	Publication Type	Research Design	Subject Info	Caffeine Dosage ($mg \cdot kg^{-1}$)[a]	Muscle Group Tested	Type of Contraction	Strength Measure	Muscular Endurance Measure	PEDro Quality Score
Astorino et al. (1)	Published, peer reviewed	Double blind, crossover	22 trained males	6	Pectorals, anterior deltoid, and triceps; hip and knee extensors	Isotonic	1RM concentric	No. contractions at 60% 1RM load	11
Bailey (2)	Doctoral dissertation	Double blind, crossover	13 males	5	Forearm flexors, knee extensors	Isometric	MVC	Time to maintain 40% MVC	11
Bond et al. (3)	Published, peer reviewed	Crossover	12 trained males	5	Knee extensors, knee flexors	Isokinetic	Concentric strength at $30°\cdot s^{-1}$, $150°\cdot s^{-1}$, and $300°\cdot s^{-1}$	Work done during last 20 contractions	7
Bugyi (6)	Published, peer reviewed	Crossover	25 males	2.3, 4.5, 6.8	Forearm flexors	Isometric	MVC	Force–time integral over 13 contractions	8
Dierberger (9)	Master's thesis	Double blind, crossover	23 males, 14 females	7.5	Forearm flexors, knee extensors, wrist flexors	Isometric, isokinetic	MVC, concentric strength at $60°\cdot s^{-1}$		11
Doyle (11)	Master's thesis	Double blind, crossover	10 males	6	Knee extensors	Isometric	MVC		11
Farmer (13)	Master's thesis	Double blind, independent groups	12 males, 16 females	4.6	Knee extensors	Isokinetic		No. eccentric and concentric contractions performed at 20% max effort	11
Green et al. (17)	Published, peer reviewed	Double blind, crossover	13 trained males, 4 trained females	6	Pectorals, anterior deltoid, and triceps; hip and knee extensors	Isotonic		No. contractions done at 10RM load during three sets	11
Hudson et al. (23)	Published, peer reviewed	Double blind, crossover	15 trained males	6.2	Elbow flexors, knee extensors	Isotonic		No. contractions done at 12RM load during four sets	11
Jacobs et al. (24)	Published, peer reviewed	Double blind, crossover	13 trained males	4	Multiple	Isotonic		Work done during three sets	11
Jacobson and Edwards (25)	Published, peer reviewed	Double blind, independent groups	20 males, 16 females,	4.3, 8.6	Knee extensors, knee flexors	Isokinetic	Concentric strength at $75°\cdot s^{-1}$, $180°\cdot s^{-1}$, and $300°\cdot s^{-1}$	Total torque for 15 contractions	11
Jacobson et al. (26)	Published, peer reviewed	Double blind, crossover	20 trained males	7	Knee extensors, knee flexors	Isokinetic	Concentric strength at $30°\cdot s^{-1}$, $150°\cdot s^{-1}$, and $300°\cdot s^{-1}$		11
Kalmar and Cafarelli (28)	Published, peer reviewed	Double blind, crossover	11 males	6	Knee extensors	Isometric	MVC, % muscle activation	Time to maintain 50% MVC	11
Kalmar and Cafarelli (30)	Published, peer reviewed	Double blind, crossover	7 males	6	First dorsal interosseous	Isometric	MVC, % muscle activation, electrically evoked strength		11
Kalmar and Cafarelli (31)	Published, peer reviewed	Double blind, crossover	8 males	6	Knee extensors	Isometric	MVC, % muscle activation	No. sets completed while maintaining 50% MVC	11
Kalmar et al. (32)	Published, peer reviewed	Double blind, crossover	10 males	6	Ankle plantarflexors	Isometric	MVC, % muscle activation, electrically evoked strength	Time to maintain 50% MVC	11
Lanigan et al. (34)	Published, peer reviewed	Double blind, crossover	7 males, 4 females	8.7, 8.9	Knee extensors, respiratory muscles	Isometric	MVC, max static inspiratory mouth pressure, max static expiratory mouth pressure		8
Lopes et al. (35)	Published, peer reviewed	Double blind, crossover	5	7.5	Adductor pollicis	Isometric	Electrically evoked strength	Time to maintain 50% MVC	7

(continued on next page)

TABLE 1. *(Continued)*

Reference	Publication Type	Research Design	Subject Info	Caffeine Dosage ($mg \cdot kg^{-1}$)[a]	Muscle Group Tested	Type of Contraction	Strength Measure	Muscular Endurance Measure	PEDro Quality Score
Meyers and Cafarelli (39)	Published, peer reviewed	Double blind, crossover	10 males	6	Knee extensors	Isometric	MVC, % muscle activation, electrically evoked strength	Time to maintain 50% MVC	11
Miller et al. (40)	Published, peer reviewed	Independent groups	188 males	1, 3	Forearm flexors	Isometric	MVC		10
Norager et al. (44)	Published, peer reviewed	Double blind, crossover	15 males, 15 females	6	Elbow flexors	Isometric	MVC	Time to maintain 50% MVC	11
Park et al. (47)	Published, peer reviewed	Double blind, crossover	4 males, 9 females	6	Knee extensors	Isometric	MVC, % muscle activation, electrically evoked strength		11
Plaskett and Cafarelli (48)	Published, peer reviewed	Double blind, crossover	15 males	6	Knee extensors	Isometric	MVC, % muscle activation, electrically evoked strength	Time to maintain 50% MVC	11
Putnam (49)	Master's thesis	Double blind, crossover	10 males	5	Knee extensors	Isokinetic	Concentric strength at 60°/s		11
Schabel (51)	Master's thesis	Double blind, independent groups	31 males, 22 females	5	Knee extensors	Isokinetic		No. of eccentric and concentric contractions performed at >20% max effort	11
Supinski et al. (54)	Published, peer reviewed	Double blind, crossover	8 males, 4 females	8.7	Respiratory muscles	Isometric	Max static inspiratory mouth pressure	Time to maintain 79% or 90% max static inspiratory mouth pressure	10
Tarnopolsky and Cupido (56)	Published, peer reviewed	Double blind, crossover	12 males	6	Ankle dorsiflexors	Isometric	MVC, % muscle activation, electrically evoked strength		11
Tarnopolsky et al. (58)	Published, peer reviewed	Double blind, crossover	6 trained males	6	Knee extensors	Isometric	MVC, % muscle activation, electrically evoked strength		11
Thornton et al. (59)	Published, peer reviewed	Double blind, crossover	2 males, 1 female	4.3	Forearm flexors	Isometric	MVC	Time to maintain 67% MVC	8
van Duinen et al. (60)	Published, peer reviewed	Double blind, crossover	11 males, 13 females	3	First dorsal interosseous	Isometric	MVC		10
Williams et al. (61)	Published, peer reviewed	Double blind, crossover	9 trained males	3.6	Pectorals, anterior deltoid, and triceps; latissimus dorsi, trapezius, and biceps	Isotonic	1RM concentric	No. contractions at 80% 1RM × 80% 1RM load	11
Williams et al. (62)	Published, peer reviewed	Double blind, crossover	6 males	7	Forearm flexors	Isometric	MVC	Time to maintain 50% MVC	10
Williams (63)	Doctoral dissertation	Double blind, crossover	16 trained males	5	Knee extensors, knee flexors	Isokinetic	Concentric strength at $60° \cdot s^{-1}$ and $240° \cdot s^{-1}$	Work done during last 5 of 20 contractions	11
Woolf et al. (64)	Published, peer reviewed	Double blind, crossover	19 trained males	5	Pectorals, anterior deltoid, and triceps; hip and knee extensors	Quasi-isokinetic		Work done during one set	11

[a] For the nine studies that only reported caffeine dosage in milligrams, caffeine dosage normalized to BW ($mg \cdot kg^{-1}$) was calculated by dividing the dosage in milligrams by the subjects' mean BW. If mean BW was not reported for a study, it was estimated that the mean BW values for males and females were 74 and 60 kg, respectively.

correlation))$^{1/2}$/paired difference SD) and standardized mean difference SE (i.e., (1/n + standardized mean difference^2/(2n))$^{1/2}$(2(1 − intertrial correlation))$^{1/2}$). Because intertrial correlations could be calculated for only 8 of the 27 studies reporting MVC strength data and 6 of the 23 studies reporting muscular endurance data, the respective median intertrial correlation was substituted in the calculations for studies without correlations. Median intertrial correlations were 0.81 and 0.28 for absolute strength and percent changes in strength, respectively. For absolute endurance measures, the median intertrial correlation was 0.86. There were no percent changes in endurance reported. For the few crossover studies reporting data in other formats (e.g., with P values) and the four studies using a randomized controlled trial design with ≥2 independent groups, standardized mean differences were calculated as detailed by Borenstein (4). When a study measured MVC strength and/or muscular endurance under multiple conditions (e.g., used more than one caffeine dose, muscle group, or type of contraction), standardized mean differences and variances were averaged across the different condition levels.

Meta-analyses were run with a random-effects model that accounts for true interstudy variation in effects as well as for random error within each study (5). A random-effects model was chosen over a fixed-effect model because of the wide variation in experimental factor levels (e.g., caffeine dosage, muscle group tested, how strength and endurance were measured) used in the 34 studies. We also sought to determine the role of experimental factors in explaining the considerable interstudy variation observed in ES. These experimental factors can be treated as moderator variables in a meta-analysis. Meta-regressions (using a method-of-moments model) or subgroup meta-analyses (i.e., meta-analyses comparing subsets of studies using Q tests on the basis of ANOVA) were used to probe the following potential moderator variables: 1) the dosage, restriction duration, and type of caffeine ingested; 2) whether the study was published or not; 3) the research design (crossover vs independent groups); 4) the subject's gender and their state of training; 5) the contractile mode used for testing; 6) the muscle group examined as well as its size or location; and 7) the type of endurance test (open vs fixed end point) and its loading strategy (constant vs variable). In studies with more than one experimental factor level being evaluated (e.g., a study using both large and small muscle groups in the subgroup meta-analysis evaluating the effect of muscle group size), an ES was calculated for each level and was treated as if it originated from an independent study.

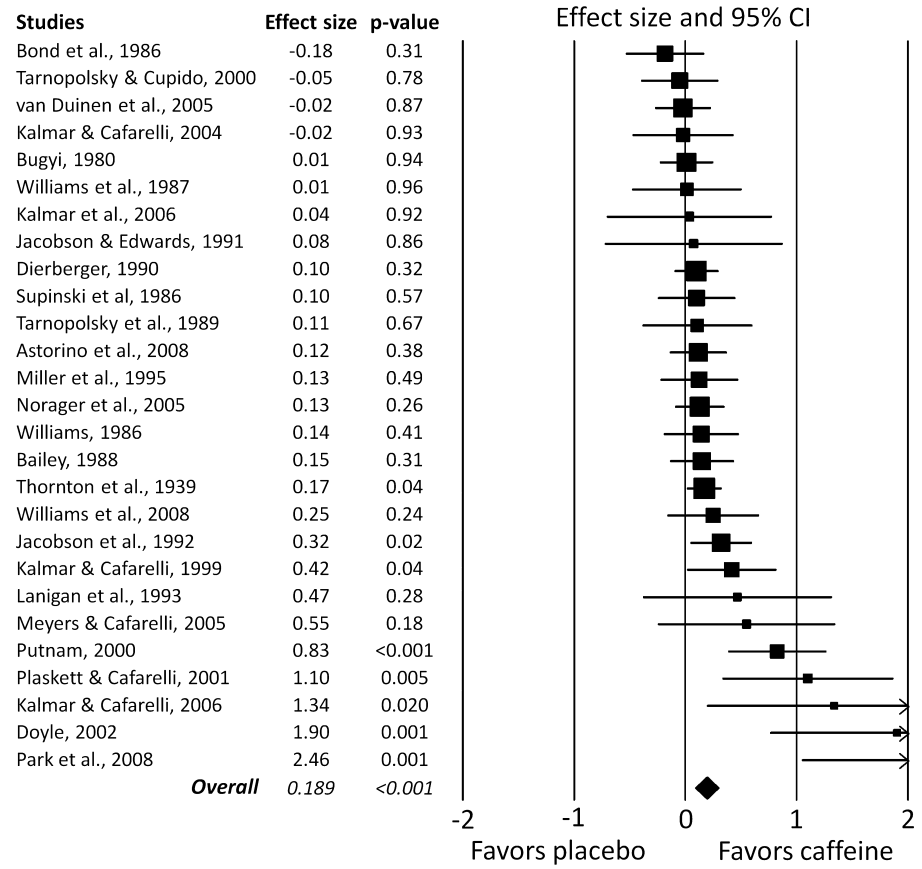

FIGURE 1—Forest plot of effect sizes from the 27 studies that assessed the effect of caffeine ingestion on MVC strength. A square represents the effect size for a given study with the size of the square being proportional to the weighting of that study in the meta-analysis. A horizontal line indicates the 95% confidence interval (CI) for an effect. Studies are arranged from the lowest to highest effect size. The diamond at the bottom represents the overall effect size calculated using a random-effects model. The width of the diamond represents the 95% CI for the overall effect size.

TABLE 2. Summary of subgroup meta-analyses examining potential moderator variables that might influence the effect of caffeine ingestion on MVC strength.

Moderator Variable	Comparison	*Q* Test *P* Value
Published	Yes (n = 22, ES = 0.16) vs no (n = 5, ES = 0.31)	0.26
Research design	Crossover (n = 25, ES = 0.20) vs independent (n = 2, ES = 0.11) groups	0.72
Subjects' gender	Males (n = 19, ES = 0.21) vs mixed (n = 8, ES = 0.15)	0.58
Subjects' state of training	Trained (n = 6, ES = 0.13) vs untrained (n = 21, ES = 0.21)	0.50
Form of caffeine ingested[a]	Solid (n = 18, ES = 0.25) vs liquid (n = 8, ES = 0.05)	0.07
Type of contraction[b]	Isokinetic (n = 6, ES = 0.21) vs isometric (n = 20, ES = 0.18)	0.84
Muscle group size	Large (n = 18, ES = 0.31) vs small (n = 12, ES = 0.05)	0.003
Muscle group location	Upper body (n = 13, ES = 0.07) vs lower body (n = 18, ES = 0.29)	0.01
Muscle group[c]	Knee extensors (n = 15, ES = 0.40) vs knee flexors (n = 4, ES = 0.04) vs forearm flexors (n = 6, ES = 0.07)	0.01 [KE > KF (P = 0.05); KE > FF (P = 0.03)]

[a] Sixty-three percent of the studies using a liquid form of caffeine also used small muscle groups, whereas only 33% of the studies using a solid form of caffeine also used small muscle groups.
[b] Only two studies measured strength using isotonic contractions, and thus this contraction type was not compared against the other two. All studies using isokinetic contractions measured strength concentrically; eccentric contractions were not used.
[c] Only the three muscle groups shown here were used by more than two studies.

Meta-analyses and meta-regressions were conducted with the Comprehensive Meta-analysis software (Version 2.2; Biostat Inc., Englewood, NJ). An exception was that TableCurve 2D software (Version 5.01; Systat Software Inc., Richmond, CA) was used to run meta-regressions using a quadratic function (i.e., to test for an inverted-U relationship between caffeine dosage and study ES). An α level of 0.05 was used in all analyses, except when a moderator variable with more than two levels was being probed in a meta-analysis. In this situation, a Benjamini and Hochberg false discovery rate adjustment was applied to the P value to correct for multiple *post hoc* comparisons. ES of 0.2, 0.5, and 0.8 were considered to be small, moderate, and large, respectively (8); we considered an ES of 0.1 as trivial. The effect of publication bias on the primary meta-analyses was addressed by combining a funnel plot assessment with the Duval and Tweedie's trim and fill correction (12). This is a preferred method for assessing the extent of publication bias as well as for making a correction to the overall ES.

RESULTS

Description of included studies. In total, 34 studies between 1939 and 2008 were included for meta-analyses of caffeine's effects on MVC strength (n = 27 studies) and muscular endurance (n = 23 studies); the characteristics of those investigations are summarized in Table 1. Twenty-seven studies were published in peer-reviewed journals, whereas there were five master's theses and two doctoral dissertations that did not appear to be published but were available electronically via the ProQuest Dissertation and Theses database. Only two studies reported being funded by a commercial interest (61,64). All but four studies used a crossover experimental research design, whereas the other four used a randomized controlled trial design with ≥2 independent groups. A total of 726 subjects were used in the 34 studies; 576 and 388 subjects were used in the studies investigating MVC strength and muscular endurance, respectively. The median subject number per study was 13. Subject gender was either exclusively male (n = 22 studies) or a mixture of males and females (n = 11 studies). No studies used only females. One study did not report subject gender (35). Ten studies reported their subjects as being endurance-, sprint-, and/or resistance-trained or familiar with resistance training. All subjects were of college

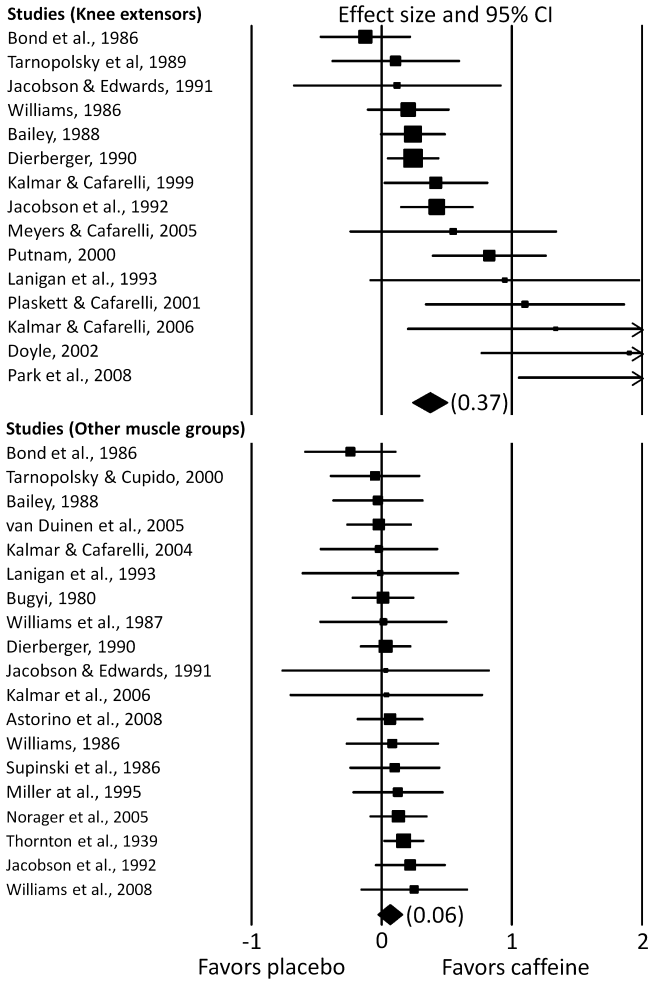

FIGURE 2—Forest plot of effect sizes from the subgroup meta-analysis comparing the effect of caffeine ingestion on MVC strength for the knee extensors compared with all other muscle groups. The top 15 studies are those that tested the knee extensors, whereas the bottom 20 studies are those that tested all other muscle groups. A diamond with an adjacent number in parentheses reflects the overall effect size for that muscle group.

age, except for those from one study (44). The caffeine dosage used in these studies ranged from 1 to approximately 9 $mg \cdot kg^{-1}$, with a median dose of 6 $mg \cdot kg^{-1}$. Fourteen different muscle groups were tested in the 34 studies, with the knee extensors being by far the most often tested, that is, in 18 studies, followed by the forearm flexors (n = 6 studies). The PEDro quality scores for the studies ranged from 7 to 11. There were only five studies with scores below 10, and those were older studies that often lacked detail in their methods section.

MVC strength meta-analysis. Considerable variation was observed among studies probing the effect of caffeine ingestion on MVC strength, with ES ranging from −0.18 to 2.46 (Fig. 1). Only the first four of the 27 studies illustrated in Figure 1 exhibited negative effects of caffeine on strength, that is, favoring placebo over caffeine. Conversely, 23 of the 27 studies exhibited positive, beneficial effects of caffeine compared with placebo. Overall, meta-analysis on the 27 studies yielded a statistically significant and small ES, indicating that caffeine ingestion can improve MVC strength (overall ES = 0.19, P = 0.0003; Fig. 1). This ES equates approximately to 4% greater strength after ingestion of caffeine compared with placebo. There was no single study that dominated the overall ES. The study of Putnam (49) had the most beneficial influence; if that study was removed from the meta-analysis, the overall ES would fall to 0.16, but it would still be highly significant (P = 0.001).

Publication bias was assessed by examining a funnel plot of standard error versus ES. Minor asymmetry was noted in the plot, and thus a Duval and Tweedie's trim and fill correction to the overall ES was calculated. This correction shifted the overall ES very slightly from 0.19 to 0.17, with no effect on the P value. Publication bias was also assessed by a subgroup meta-analysis comparing the overall ES of published studies versus that of the unpublished studies we were able to identify. On the assumption unpublished studies tend to be ones with nonsignificant and/or negative findings (i.e., the file-drawer phenomenon), one would predict the overall ES would be smaller for unpublished versus published studies. As shown in Table 2, this was

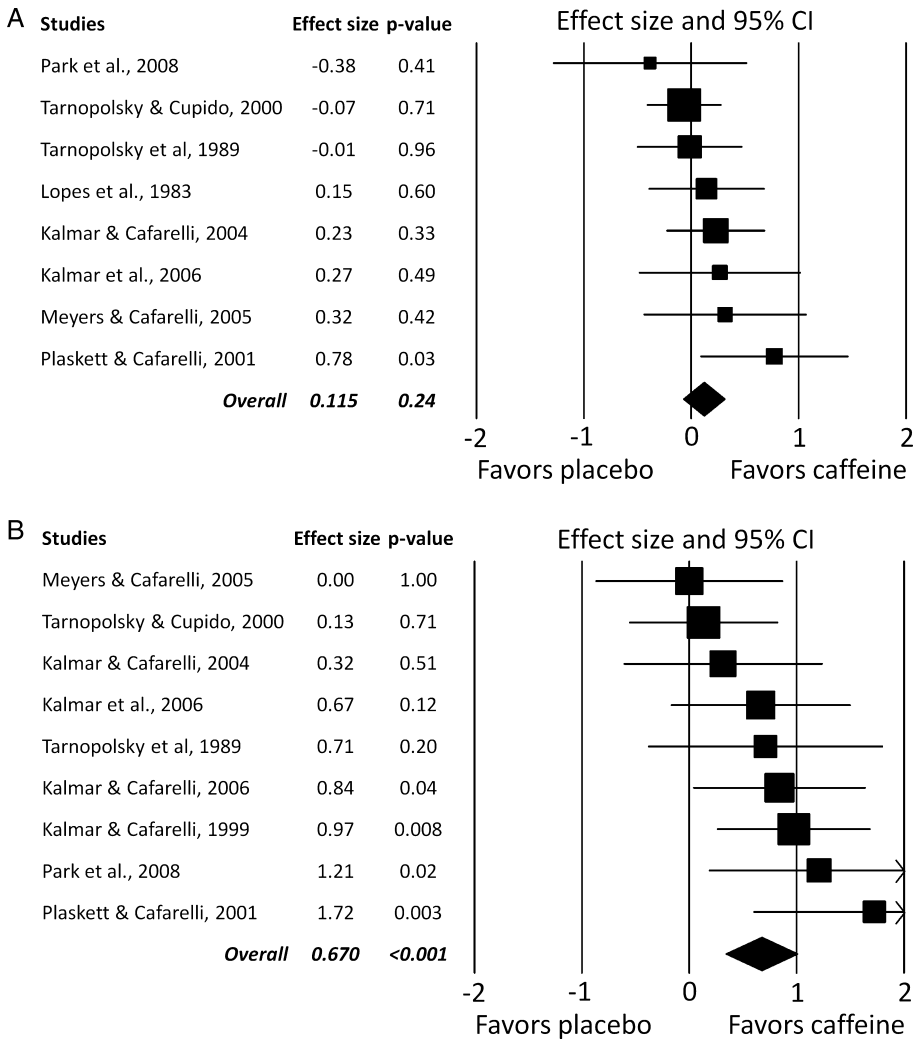

FIGURE 3—Forest plot of effect sizes from studies that assessed the effect of caffeine ingestion on electrically evoked strength under supramaximal stimulation conditions (A) or percent muscle activation during an MVC (B).

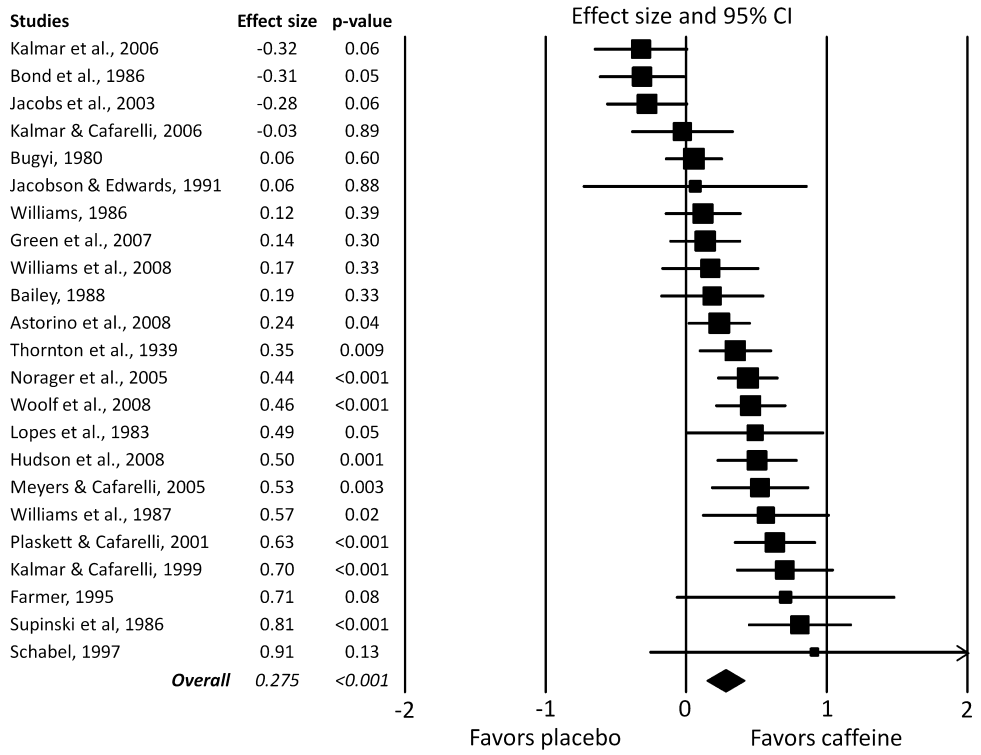

FIGURE 4—Forest plot of effect sizes from the 23 studies that assessed the effect of caffeine ingestion on muscular endurance.

not the case. There was no significant difference in overall ES between the published and the unpublished studies ($P = 0.26$).

Table 2 also summarizes the findings of the subgroup meta-analyses probing possible roles that eight experimental factors might have in explaining ES dispersion among the 27 studies. Muscle group size and location were significant factors ($P \leq 0.01$). Specifically, studies investigating large (i.e., greater than or equal to the size of the plantarflexors) or lower-body muscle groups had a four- to sixfold larger overall ES compared with studies investigating small or upper-body muscle groups. Follow-up subgroup meta-analyses were conducted to determine whether studies on a specific muscle group reported a higher ES. Knee extensor investigations were associated with a sixfold greater overall ES ($P = 0.0002$) compared with studies on all other muscle groups combined (Fig. 2). The 0.37 overall ES calculated for the knee extensor investigations equates approximately to a 7% improvement in MVC strength with caffeine compared with placebo. For the Figure 2 studies that investigated other muscle groups, the study ES are tightly clustered around zero which indicates a consistent lack of caffeine effect. There is, however, substantial ES dispersion among the knee extensor studies that we were unable to account for with any experimental factor.

Meta-regression analysis was used to assess the relationship between caffeine dosage (in milligrams per kilogram of body weight (BW)) and study ES. There was no significant linear or quadratic (e.g., inverted-U) relationship when analyzing all 27 studies ($P \geq 0.47$) or only the 15 studies testing the knee extensors ($P \geq 0.74$). Similarly, there was no linear relationship between the duration of caffeine

TABLE 3. Summary of subgroup meta-analyses examining potential moderator variables that might influence the effect of caffeine ingestion on muscular endurance.

Moderator Variable	Comparison	*Q* Test *P* Value
Published	Yes (n = 19, ES = 0.27) vs no (n = 4, ES = 0.31)	0.86
Research design	Crossover (n = 20, ES = 0.26) vs independent (n = 3, ES = 0.50) groups	0.44
Subjects' gender	Males (n = 15, ES = 0.21) vs mixed (n = 7, ES = 0.43)	0.15
Subjects' state of training[a]	Trained (n = 6, ES = 0.07) vs untrained (n = 15, ES = 0.37)	0.08
Form of caffeine ingested	Solid (n = 15, ES = 0.23) vs liquid (n = 8, ES = 0.39)	0.31
Type of contraction	Isokinetic (n = 6, ES = 0.20) vs isometric (n = 12, ES = 0.36) vs isotonic (n = 5, ES = 0.16)	0.41
Type of endurance test	Open end point (n = 18, ES = 0.37) vs fixed end point (n = 5, ES = −0.08)	0.001
Type of load	Constant (n = 18, ES = 0.33) vs variable (n = 5, ES = 0.09)	0.13
Muscle group size	Large (n = 17, ES = 0.23) vs small (n = 8, ES = 0.40)	0.20
Muscle group location	Upper body (n = 12, ES = 0.37) vs lower body (n = 15, ES = 0.25)	0.33
Muscle group[b]	Knee extensors (n = 11, ES = 0.33) vs knee flexors (n = 3, ES = −0.07) vs forearm flexors (n = 4, ES = 0.31) vs pectorals/ant shoulders/triceps (n = 4, ES = 0.31) vs hip and knee extensors (n = 3, ES = 0.21)	0.46

[a] Sixty-three percent of the studies using trained subjects were open end point studies, whereas 87% of the studies using untrained subjects were open end point studies.
[b] Only the five muscle groups shown here were used by more than two studies.

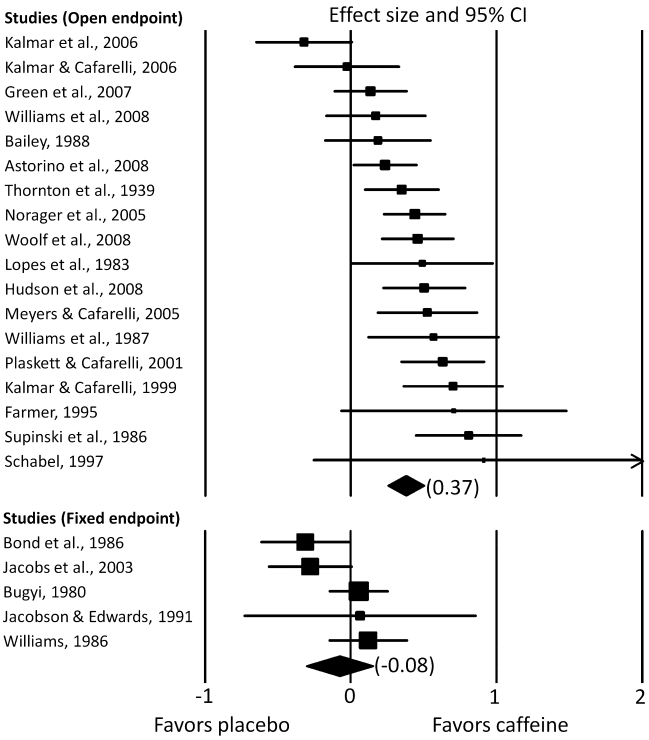

FIGURE 5—Forest plot of ES from the subgroup meta-analysis comparing the effect of caffeine ingestion on muscular endurance assessed using open end point tests compared with fixed end point tests. The top 18 studies are those that used open end point tests whereas the bottom five studies are those that used fixed end point tests.

restriction before testing (i.e., ranging from 0 to 168 h) and study ES when analyzing all studies combined ($P = 0.51$).

In an attempt to offer a physiological mechanism behind caffeine's ability to improve MVC strength, a meta-analysis was run on ES from eight studies that measured electrically evoked strength using supramaximal stimulation in trials that compared caffeine with a placebo. Study ES ranged from −0.38 to 0.78, with three being less than zero (Fig. 3A). The overall ES (0.12) was not statistically different from zero ($P = 0.24$). The statistical finding was unchanged even if the analysis was limited to the four knee extensor studies ($P = 0.40$). A meta-analysis was also run on ES from nine studies that measured percent muscle activation during MVC in trials that compared caffeine to a placebo. Study ES were only positive, ranging from 0.00 to 1.72 (Fig. 3B). The overall ES (0.67) was of moderate to large size and highly significant ($P = 0.00008$).

Muscular endurance meta-analysis. Less variation in ES was observed among studies that assessed the effect of caffeine ingestion on muscular endurance as compared with the MVC strength meta-analysis (compare Fig. 4 with Fig. 1). Figure 4 ES range from −0.32 to 0.91; only 4 of the 23 studies exhibited negative effects of caffeine on muscular endurance. Overall, meta-analysis on the 23 studies indicates a small beneficial effect of caffeine ingestion on muscular endurance that was statistically significant (overall ES = 0.28, $P = 0.00005$; Fig. 4). This ES equates approximately to a surprisingly large 14% improvement in muscular endurance after ingestion of caffeine compared with placebo. Analogous to the MVC strength meta-analysis, there was no single study that dominated the overall ES. The study by Supinski et al. (54) had the most beneficial influence and if that study was removed from the meta-analysis, the overall ES would be slightly lower at 0.25 but would remain highly significant ($P = 0.0002$).

In the assessment of publication bias, moderate asymmetry was noted in a funnel plot of the muscular endurance data. A Duval and Tweedie's trim and fill correction shifted the overall ES from 0.28 to 0.23, with no effect on the P value. As observed in the MVC strength meta-analysis, there was no significant difference in overall ES between published and unpublished studies ($P = 0.86$; Table 3).

Table 3 summarizes the results of the subgroup meta-analyses, probing the possible roles that 10 experimental factors might have on ES dispersion among the 23 muscular endurance studies. Only the type of endurance test used in a given study could explain a significant portion of the ES dispersion ($P = 0.001$; Fig. 5). Studies using open end point type of tests (e.g., the time a prescribed submaximal isometric force could be maintained) had a small- to moderate-sized overall ES (0.37), whereas studies that used fixed end point type of tests (e.g., the maximum amount of work done in a set number of isokinetic contractions) had a slightly negative overall ES (−0.08) that was not significantly different from zero. The 0.37 ES calculated for the studies with open end point tests equates approximately to an 18% improvement in muscular endurance with caffeine compared with placebo. In contrast to the situation for MVC strength, there was no effect of muscle group size or location on ES ($P \geq 0.20$). Similarly, there were no significant differences in overall ES among the various muscle groups tested ($P = 0.46$).

Meta-regression analysis was used to assess the relationship between caffeine dosage and muscular endurance study

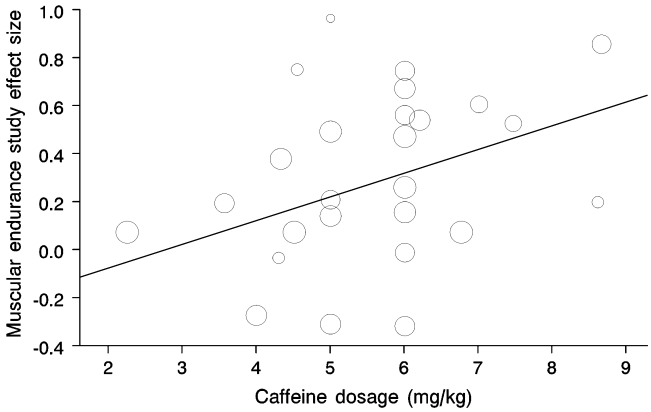

FIGURE 6—Meta-regression analysis of the relationship between caffeine dosage and muscular endurance study ES. Each effect is represented by a circle and the size of a circle reflects the degree of weighting for that data point. The line reflects the line of best fit, which was statistically significant ($P = 0.02$).

ES. Unlike the findings for the MVC strength analysis, there was a linear relationship (slope = 0.095 kg·mg^{-1}, P = 0.02; Fig. 6). Thus, for every 1 mg·kg^{-1} BW increase in caffeine dosage, study ES increased by 0.1. Although statistically significant, the caffeine dosage–study ES relationship was weak, with only 16% of the between-study variance being explained by the meta-regression model. Finally, as for the MVC strength analysis, there was no relationship found between the duration of caffeine restriction before testing and the muscular endurance study ES (P = 0.49).

DISCUSSION

The main finding of this study was that caffeine ingestion can improve both MVC strength and muscular endurance. However, caffeine appears to primarily improve knee extensor MVC strength (i.e., by ~7%, ES = 0.37) and not strength in other muscle groups such as the forearm or the knee flexors. It also appears that caffeine improves muscular endurance only when it is assessed with open end point tests (i.e., by ~18%, ES = 0.37). Because caffeine versus placebo comparisons in the meta-analyses were based on experimental, within-study research designs (i.e., each study in a meta-analysis had both caffeine and placebo conditions/groups that were randomly assigned), one can make cause-and-effect claims regarding the effect of caffeine. However, the situation differs for comparisons among various muscle groups on MVC strength and the comparison between open versus fixed end point muscular endurance tests. In those subgroup meta-analyses, comparisons were done primarily between studies and thus were not experimental in nature. Thus, cause-and-effect claims cannot be made with regard to these comparisons.

Potential limitations of our systematic review and meta-analyses include 1) inclusion of unpublished and/or low quality studies, 2) publication bias, and 3) failure to know the intertrial correlations in many of the crossover studies. These will be discussed in order. The inclusion of unpublished data might be questioned because these have not passed peer review. However, the peer-review filter may be imperfect. Inclusion of unpublished data can sometimes alter meta-analysis findings such that they lose their statistical significance, indicating that the published literature is affected by selective reporting biases (33). For this reason, it is recommended that the results of studies found in the gray literature (i.e., literature not controlled by commercial publishers) should be included in meta-analyses (21). Thus, we included in our meta-analyses the five master's theses and the two doctoral dissertations found in our systematic review. There are no apparent reasons why these seven studies were not published, at least concerning the quality of the studies gauged by the PEDro scoring system. PEDro quality scores for all seven were the highest possible. As mentioned in the Results section and as shown in Tables 2 and 3, the overall ES for the unpublished studies was not significantly different from that for published studies and therefore did not contribute to a bias in our meta-analyses.

There were only five studies in our systematic review with a PEDro quality score below 10, and those were the oldest studies reviewed. We do not believe these studies were inferior methodologically but rather the expectations for describing a study's methodology in a research article more than 20 yr ago were less rigorous (e.g., regarding description of the randomization and/or blinding). If the five studies were excluded, overall ES for the effect of caffeine on MVC strength and endurance would actually rise, that is, from 0.19 to 0.23 and from 0.28 to 0.31, respectively. Thus, inclusion of studies with lower PEDro quality scores did not bias us toward finding a benefit of caffeine ingestion on MVC strength and endurance. In fact, the effect was just the opposite.

Publication bias occurs when research that appears in the published literature is systematically unrepresentative of the population of completed studies (55). The tendency is for studies with nonsignificant and/or negative findings to not be published, that is, the file-drawer phenomenon (18,22). Meta-analyses will therefore tend to be based to a greater extent on published studies because of the difficulty of identifying unpublished research and obtaining from those studies the results necessary to calculate an ES. The net effect of not including all completed studies in a meta-analysis is that the overall ES tends to be inflated. In our assessment of the effect of publication bias on the primary meta-analyses, minor to moderate asymmetry was noted in the funnel plots, and the Duval and Tweedie's trim and fill correction shifted the overall ES lower by 0.02–0.05. However, these shifts did not affect the qualitative assessment of the overall ES. According to Cohen (8), both overall ESs would be considered small with or without the correction.

The remaining limitation to be discussed, that is, not knowing the intertrial correlations in many of the crossover studies, is a common problem when conducting a meta-analysis (5). Most primary research studies fail to report this correlation or to provide the data necessary to calculate the correlation. Borenstein et al. (5) recommend a sensitivity analysis be conducted by assessing the effect of varying the assumed intertrial correlation in the studies for which an intertrial correlation could not be calculated. For the meta-analysis that assessed the effect of caffeine on MVC strength, it was determined that the lowest overall ES occurred when the assumed intertrial correlation was increased from 0.81 to 0.9 for studies that reported absolute strength measures and reduced from 0.28 to 0 for studies that reported percent changes in strength measures. As a result, the overall ES was reduced slightly from 0.19 to 0.16 but remained highly significant (i.e., P = 0.0004). For the meta-analysis that assessed the effect of caffeine on muscular endurance, it was determined that the lowest overall ES occurred when the assumed intertrial correlation was increased from 0.86 to 0.9. Again, the overall ES was reduced slightly, that is, from 0.28 to 0.25, but remained highly significant (i.e., P = 0.0003).

Thus, the sensitivity analysis indicates that not knowing the intertrial correlations for many of the crossover studies probably had minimal effect on the overall ES as well as its qualitative assessment.

A unique aspect of this study was that it provides insight into caffeine's mechanism for improving MVC strength. The findings suggest that it is probably due to an effect on the CNS. The best evidence for this was the moderate-to-large beneficial effect of caffeine ingestion found in the meta-analysis of the nine studies that assessed percent muscle activation during an MVC (overall ES = 0.67; Fig. 3B). This indicates that caffeine ingestion can enhance motor unit recruitment during an MVC, which presumably contributes to a strength increase. Interestingly, six of the nine studies in this meta-analysis used the knee extensors in their assessment of muscle activation, and five of the six yielded the highest ES in the meta-analysis (i.e., the bottom five studies in Fig. 3B). We noted earlier that the knee extensors appear to be the most sensitive to caffeine ingestion. These observations suggest that caffeine can more easily enhance activation of the knee extensors compared with other muscle groups. It was previously noted the activation level during an MVC is normally lower for the knee extensors than for the other muscle groups (i.e., 85%–95% vs 90%–99%, respectively) (52). If caffeine does improve MVC strength by enhancing muscle activation, then there is a logical explanation why other muscle groups are relatively insensitive to caffeine. It is likely because their activation is already near 100%, and thus there is minimal room for improvement.

Additional evidence for caffeine acting on the CNS to improve MVC strength comes from a lack of a caffeine effect on electrically stimulated strength. No significant effect of caffeine ingestion was found in the meta-analysis of the eight studies that measured electrically evoked strength with supramaximal stimulation (Fig. 3A). It would take 18 additional studies, each with an ES equaling the current overall ES (i.e., 0.12), to obtain a statistically significant overall ES. An effect of this magnitude would still be considered trivial. The present study does not discount the possibility that caffeine may have a direct effect on muscle, for example, submaximal force production enhancement or fatigue attenuation (34,35,56). However, if caffeine ingestion does have a direct effect on muscle to improve MVC strength, it appears to be relatively small compared with the effect on the CNS.

Unfortunately, the mechanism by which caffeine ingestion improves muscular endurance is not as readily explained in the present study. There are no comparable measures to those of electrically evoked strength and percent muscle activation, which can be used to help explain a strength gain. Because the improvements in muscular endurance are most likely intertwined with those in MVC strength (e.g., an improvement in strength should result in greater endurance when a set absolute isotonic load is used for testing), one could speculate that the mechanism for muscular endurance increases might be the same as that for strength. However, it may not be. It is also possible that the effect of caffeine on endurance may be due to a direct effect on muscle because there were no significant effects found in the subgroup meta-analyses probing how the muscle group examined, as well as its size or location affect endurance ES. These observations suggest that caffeine ingestion works equally well on all muscle groups in improving endurance, which is in sharp contrast to its effect on MVC strength.

This study's findings provide justification for future research. First, experimental studies should be conducted to determine whether caffeine ingestion improves MVC strength more so in the knee extensors than that in other muscle groups. Similarly, experimental studies are needed to determine whether the type of test used affects the outcome caffeine has on muscular endurance. Second, studies are needed to test whether caffeine's ability to improve performance in both prolonged and short-term, high-intensity exercise is mediated by an improvement in MVC strength and/or muscular endurance. It is interesting that the muscle group most affected by caffeine (i.e., the knee extensors) plays an important role in the exercise modes most commonly tested (i.e., cycling and running). During cycling, the knee extensors provide by far the most (≥33%) mechanical energy generated by the body's musculature (50). Thus, it is plausible that small gains in knee extensor strength and endurance after caffeine ingestion could translate into performance improvements commonly observed in endurance and short-term, high-intensity exercise.

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The results of the present study do not constitute endorsement by the American College of Sports Medicine.

REFERENCES

1. Astorino TA, Rohmann RL, Firth K. Effect of caffeine ingestion on one-repetition maximum muscular strength. *Eur J Appl Physiol*. 2008;102(2):127–32.
2. Bailey ML. Caffeine: effects on blood pressure, heart rate and short term muscular endurance in static exercise of muscle groups of varying mass [dissertation]. Bloomington (IN): Indiana University; 1988. p. 137.
3. Bond V, Gresham K, McRae J, Tearney RJ. Caffeine ingestion and isokinetic strength. *Br J Sports Med*. 1986;20(3):135–7.
4. Borenstein M. *Meta-Analysis: Computing Treatment Effects and Effect Sizes*. West Sussex (UK): Wiley; 2009. p. 256.
5. Borenstein M, Hedges LV, Higgins J, Rothstein HR. *Introduction to Meta-Analysis*. West Sussex (UK): Wiley; 2009. p. 421.
6. Bugyi GJ. The effects of moderate doses of caffeine on fatigue parameters of the forearm flexor muscles. *Am Correct Ther J*. 1980;34(2):49–53.
7. Burke LM. Caffeine and sports performance. *Appl Physiol Nutr Metab*. 2008;33(6):1319–34.

8. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. Hillsdale (NJ): Lawrence Erlbaum Associates; 1988. p. 567.
9. Dierberger SL. The ergogenic effect of caffeine on voluntary force production in large and small muscle groups [master's thesis]. Fullerton (CA): California State University, Fullerton; 1990. p. 50.
10. Doherty M, Smith PM. Effects of caffeine ingestion on exercise testing: a meta-analysis. *Int J Sport Nutr Exerc Metab*. 2004; 14(6):626–46.
11. Doyle AG. Recruitment thresholds and firing rates of single motor units recruited during voluntary and reflex contractions: effect of caffeine [master's thesis]. Toronto (ON): York University; 2002. p. 93.
12. Duval S. The trim and fill method. In: Rothstein HR, Sutton AJ, Borenstein M, editors. *Publication Bias in Meta-Analysis*. West Sussex (UK): Wiley; 2005. p. 127–44.
13. Farmer KG. The effects of caffeine ingestion on isokinetic muscular endurance [master's thesis]. Buffalo (NY): D'Youville College; 1995. p. 45.
14. Ganio MS, Klau JF, Casa DJ, Armstrong LE, Maresh CM. Effect of caffeine on sport-specific endurance performance: a systematic review. *J Strength Cond Res*. 2009;23(1):315–24.
15. Graham TE. Caffeine and exercise: metabolism, endurance and performance. *Sports Med*. 2001;31(11):785–807.
16. Graham TE, Battram DS, Dela F, El-Sohemy A, Thong FS. Does caffeine alter muscle carbohydrate and fat metabolism during exercise? *Appl Physiol Nutr Metab*. 2008;33(6):1311–8.
17. Green JM, Wickwire PJ, McLester JR, et al. Effects of caffeine on repetitions to failure and ratings of perceived exertion during resistance training. *Int J Sports Physiol Perform*. 2007;2(3):250–9.
18. Hall R, de Antueno C, Webber A. Publication bias in the medical literature: a review by a Canadian research ethics board. *Can J Anaesth*. 2007;54(5):380–8.
19. Hickson RC, Dvorak BA, Gorostiaga EM, Kurowski TT, Foster C. Potential for strength and endurance training to amplify endurance performance. *J Appl Physiol*. 1988;65(5):2285–90.
20. Hickson RC, Rosenkoetter MA, Brown MM. Strength training effects on aerobic power and short-term endurance. *Med Sci Sports Exerc*. 1980;12(5):336–9.
21. Hopewell S, Clarke M, Mallett S. Grey literature and systematic reviews. In: Rothstein HR, Sutton AJ, Borenstein M, editors. *Publication Bias in Meta-Analysis*. West Sussex (UK): Wiley; 2005. p. 49–72.
22. Hopewell S, Loudon K, Clarke MJ, Oxman AD, Dickersin K. Publication bias in clinical trials due to statistical significance or direction of trial results. *Cochrane Database Syst Rev*. 2009;(1): MR000006.
23. Hudson GM, Green JM, Bishop PA, Richardson MT. Effects of caffeine and aspirin on light resistance training performance, perceived exertion, and pain perception. *J Strength Cond Res*. 2008; 22(6):1950–7.
24. Jacobs I, Pasternak H, Bell DG. Effects of ephedrine, caffeine, and their combination on muscular endurance. *Med Sci Sports Exerc*. 2003;35(6):987–94.
25. Jacobson BH, Edwards SW. Influence of two levels of caffeine on maximal torque at selected angular velocities. *J Sports Med Phys Fitness*. 1991;31(2):147–53.
26. Jacobson BH, Weber MD, Claypool L, Hunt LE. Effect of caffeine on maximal strength and power in elite male athletes. *Br J Sports Med*. 1992;26(4):276–80.
27. Kalmar JM. The influence of caffeine on voluntary muscle activation. *Med Sci Sports Exerc*. 2005;37(12):2113–9.
28. Kalmar JM, Cafarelli E. Effects of caffeine on neuromuscular function. *J Appl Physiol*. 1999;87(2):801–8.
29. Kalmar JM, Cafarelli E. Caffeine: a valuable tool to study central fatigue in humans? *Exerc Sport Sci Rev*. 2004;32(4):143–7.
30. Kalmar JM, Cafarelli E. Central fatigue and transcranial magnetic stimulation: effect of caffeine and the confound of peripheral transmission failure. *J Neurosci Methods*. 2004;138(1–2):15–26.
31. Kalmar JM, Cafarelli E. Central excitability does not limit post-fatigue voluntary activation of quadriceps femoris. *J Appl Physiol*. 2006;100(6):1757–64.
32. Kalmar JM, Del Balso C, Cafarelli E. Increased spinal excitability does not offset central activation failure. *Exp Brain Res*. 2006; 173(3):446–57.
33. Kyzas PA, Loizou KT, Ioannidis JP. Selective reporting biases in cancer prognostic factor studies. *J Natl Cancer Inst*. 2005;97(14): 1043–55.
34. Lanigan C, Howes TQ, Borzone G, Vianna LG, Moxham J. The effects of beta 2-agonists and caffeine on respiratory and limb muscle performance. *Eur Respir J*. 1993;6(8):1192–6.
35. Lopes JM, Aubier M, Jardim J, Aranda JV, Macklem PT. Effect of caffeine on skeletal muscle function before and after fatigue. *J Appl Physiol*. 1983;54(5):1303–5.
36. Marcinik EJ, Potts J, Schlabach G, Will S, Dawson P, Hurley BF. Effects of strength training on lactate threshold and endurance performance. *Med Sci Sports Exerc*. 1991;23(6):739–43.
37. Maridakis V, O'Connor PJ, Dudley GA, McCully KK. Caffeine attenuates delayed-onset muscle pain and force loss following eccentric exercise. *J Pain*. 2007;8(3):237–43.
38. Maughan RJ, King DS, Lea T. Dietary supplements. *J Sports Sci*. 2004;22(1):95–113.
39. Meyers BM, Cafarelli E. Caffeine increases time to fatigue by maintaining force and not by altering firing rates during submaximal isometric contractions. *J Appl Physiol*. 2005;99(3):1056–63.
40. Miller LS, Lombardo TW, Fowler SC. Caffeine and time of day effects on a force discrimination task in humans. *Physiol Behav*. 1995;57(6):1117–25.
41. Millet GP, Jaouen B, Borrani F, Candau R. Effects of concurrent endurance and strength training on running economy and $\dot{V}O_2$ kinetics. *Med Sci Sports Exerc*. 2002;34(8):1351–9.
41. Moseley AM, Herbert RD, Sherrington C, Maher CG. Evidence for physiotherapy practice: a survey of the physiotherapy evidence database (PEDro). *Aust J Physiother*. 2002;48(1):43–9.
43. Motl RW, O'Connor PJ, Dishman RK. Effect of caffeine on perceptions of leg muscle pain during moderate intensity cycling exercise. *J Pain*. 2003;4(6):316–21.
44. Norager CB, Jensen MB, Madsen MR, Laurberg S. Caffeine improves endurance in 75-yr-old citizens: a randomized, double-blind, placebo-controlled, crossover study. *J Appl Physiol*. 2005; 99(6):2302–6.
45. O'Connor PJ, Motl RW, Broglio SP, Ely MR. Dose-dependent effect of caffeine on reducing leg muscle pain during cycling exercise is unrelated to systolic blood pressure. *Pain*. 2004;109(3): 291–8.
46. Paavolainen L, Hakkinen K, Hamalainen I, Nummela A, Rusko H. Explosive-strength training improves 5-km running time by improving running economy and muscle power. *J Appl Physiol*. 1999;86(5):1527–33.
47. Park ND, Maresca RD, McKibans KI, Morgan DR, Allen TS, Warren GL. Caffeine's enhancement of maximal voluntary strength and activation in uninjured but not injured muscle. *Int J Sport Nutr Exerc Metab*. 2008;18(6):639–52.
48. Plaskett CJ, Cafarelli E. Caffeine increases endurance and attenuates force sensation during submaximal isometric contractions. *J Appl Physiol*. 2001;91(4):1535–44.
49. Putnam SR. The effect of caffeine and ephedrine on strength, power, and quickness [master's thesis]. Springfield (MA): Springfield College; 2000. p. 88.
50. Raasch CC, Zajac FE, Ma B, Levine WS. Muscle coordination of maximum-speed pedaling. *J Biomech*. 1997;30(6):595–602.
51. Schabel DM. The effects of caffeine ingestion on isokinetic endurance according to subjects self-reported habitual daily caffeine intake [master's thesis]. Buffalo (NY): D'Youville College; 1997. p. 58.

52. Shield A, Zhou S. Assessing voluntary muscle activation with the twitch interpolation technique. *Sports Med*. 2004;34(4):253–67.
53. Støren O, Helgerud J, Stoa EM, Hoff J. Maximal strength training improves running economy in distance runners. *Med Sci Sports Exerc*. 2008;40(6):1087–92.
54. Supinski GS, Levin S, Kelsen SG. Caffeine effect on respiratory muscle endurance and sense of effort during loaded breathing. *J Appl Physiol*. 1986;60(6):2040–7.
55. Sutton AJ. Publication bias. In: Cooper H, Hedges LV, Valentine JC, editors. *The Handbook of Research Synthesis and Meta-Analysis*. New York (NY): Russell Sage Foundation Publishers; 2009. p. 435–52.
56. Tarnopolsky M, Cupido C. Caffeine potentiates low frequency skeletal muscle force in habitual and nonhabitual caffeine consumers. *J Appl Physiol*. 2000;89(5):1719–24.
57. Tarnopolsky MA. Effect of caffeine on the neuromuscular system–potential as an ergogenic aid. *Appl Physiol Nutr Metab*. 2008;33(6):1284–9.
58. Tarnopolsky MA, Atkinson SA, MacDougall JD, Sale DG, Sutton JR. Physiological responses to caffeine during endurance running in habitual caffeine users. *Med Sci Sports Exerc*. 1989;21(4):418–24.
59. Thornton GR, Holck HGO, Smith EL. The effect of benzedrine and caffeine upon performance in certain psychomotor tasks. *J Abnorm Soc Psychol*. 1939;34(1):96–113.
60. van Duinen H, Lorist MM, Zijdewind I. The effect of caffeine on cognitive task performance and motor fatigue. *Psychopharmacology (Berl)*. 2005;180(3):539–47.
61. Williams AD, Cribb PJ, Cooke MB, Hayes A. The effect of ephedra and caffeine on maximal strength and power in resistance-trained athletes. *J Strength Cond Res*. 2008;22(2):464–70.
62. Williams JH, Barnes WS, Gadberry WL. Influence of caffeine on force and EMG in rested and fatigued muscle. *Am J Phys Med*. 1987;66(4):169–83.
63. Williams KW. The effects of caffeine on muscular strength, power, and power-endurance [dissertation]. Hattiesburg (MS): University of Southern Mississippi; 1986. p. 117.
64. Woolf K, Bidwell WK, Carlson AG. The effect of caffeine as an ergogenic aid in anaerobic exercise. *Int J Sport Nutr Exerc Metab*. 2008;18(4):412–29.