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THE EFFECTS OF LOW AND MODERATE DOSE CAFFEINE SUPPLEMENTATION ON UPPER AND LOWER BODY MAXIMAL VOLUNTARY CONCENTRIC AND ECCENTRIC MUSCLE FORCE

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ABSTRACT

Despite the growing quantity of literature exploring the effect of caffeine on muscular strength, there is a dearth of data that directly explores differences in ergogenicity between upper and lower body musculature and the dose response effect. The present study sought to investigate the effects of low and moderate dose caffeine on the maximal voluntary strength of the elbow flexors and knee extensors. Ten non-specifically strength trained, recreationally active participants (21 ± 0.3 yrs) completed the study. Using a randomised, counterbalanced and double blind approach, isokinetic concentric and eccentric strength was measured at 60 and 180 deg/s following administration of a placebo, 3 mg · kg⁻¹ body mass caffeine and 6 mg · kg⁻¹ body mass caffeine. There was no effect of caffeine on the maximal voluntary concentric and eccentric strength of the elbow flexors, or the eccentric strength of the knee extensors. Both 3 and 6 mg · kg⁻¹ body mass caffeine caused a significant increase in peak concentric force of the knee extensors at 180 deg/s. No difference was apparent between the two concentrations. Only 6 mg · kg⁻¹ body mass caused an increase in peak concentric force during repeated contractions. The results infer that the effective caffeine concentration to evoke improved muscle performance may be related to muscle mass and contraction type. The present work indicates that relatively low dose caffeine treatment may be effective for improving lower body muscular strength, but may have little benefit for the strength of major muscular groups of the upper body.

Key Words: Ergogenic Aids, Isokinetic Dynamometry, Skeletal Muscle, Strength, Maximal Voluntary Contraction, Repeated Contractions
INTRODUCTION

Caffeine (common name for 1,3,7-trimethlyxanthine) is one of the most commonly consumed drugs in the world (Nawrot et al. 2003), and the vast quantity of scientific literature documenting its ability to elicit improvements in both cognition (Nehlig 2010) and exercise performance (Graham 2001; Davis et al. 2009) have made it a popular nutritional supplement consumed by recreational and elite athletes as a method to evoke a legal, and sometimes substantial, improvement in performance. Generally, it is considered that caffeine has the potential to improve performance in endurance, power and strength based activities (Graham 2001), and there are a number of published literature reviews and meta-analyses (Graham 2001; Magkos et al. 2005; Burke 2008; Davis and Green 2009; Astorino et al. 2010a; Warren et al. 2010) that substantiate this.

Although generally there seems to be support for a caffeine induced improvement in strength performance (Astorino and Roberson 2010a; Warren, Park et al. 2010), findings from research exploring the caffeine effect using such exercise modalities appear to be more equivocal than studies examining the ergogenic properties of caffeine using endurance based exercise protocols. Despite the likely publication bias that exist within this field, where research studies showing effects are favoured, there are still many studies that fail to demonstrate an effect of caffeine on muscular strength (Bond et al. 1986; Jacobson et al. 1991; Jacobs et al. 2003; Astorino et al. 2008; Williams et al. 2008; Tallis et al. 2013). The degree of ambiguity can largely be attributed to differences in the caffeine dose and method of administration, the exercise protocol (i.e. 1 repetition maximum, repetitions until failure, maximal voluntary contractions), the muscle group tested, the possibility of habituation in high caffeine users, and differences that may be apparent between specifically trained...
and novice participants. Despite this, caffeine use amongst strength and power athletes is rife (Van Thuyne et al. 2005; Del Coso et al. 2011), and as such, further research is needed to more accurately quantify the caffeine effect.

A meta-analysis by Warren, Park et al. (2010), demonstrated that caffeine elicited a small ergogenic effect on measures of maximal voluntary force, with lower body or larger muscle groups demonstrating a greater benefit compared to upper body or small muscle groups. This phenomenon was attributed to a lower neural activation of larger muscle groups and the mechanistic action of caffeine to act via the central nervous system (CNS) to promote greater muscular recruitment. As such, these findings further rationalise the equivocal results demonstrated in studies evaluating the effect of caffeine on muscular strength. Interestingly, conclusions by Warren, Park et al. (2010) are based largely on indirect comparisons of studies that have assessed the effect of caffeine on one of either upper body or lower body strength.

Black et al. (2015) demonstrated that a 5 mg · kg⁻¹ caffeine treatment resulted in an increased maximal voluntary isometric force and motor unit activation of the knee extensors. However, this dose failed to elicit any effect on the muscular strength of the elbow flexors in the same set of participants. Beyond this work there is a distinct lack of research data that examines the effect of caffeine on maximal voluntary force using different muscle groups in the same participant. The present study builds on work by Black, Waddell et al. (2015) by examining the effect of caffeine dose on upper body and lower body maximal voluntary force during concentric and eccentric muscle activity.

Typically, researchers’ examining the ergogenic effect of caffeine on exercise performance have done so using moderate doses (5-6 mg · kg⁻¹ body mass) that
are dissolved in fluid and consumed orally (Plaskett et al. 2001; Green et al. 2007; Astorino et al. 2010b; Timmins et al. 2014; Tallis et al. 2016). Doses between 2.5 to 7 mg · kg⁻¹ body mass has been reported to improve high intensity exercise performance (Astorino and Roberson 2010a), however it is widely accepted that within and above this concentration range, caffeine fails to elicit a dose dependant effect irrespective of exercise modality. It is surprising however that based on an evaluation of the available literature, this conclusion has been derived from a relatively small number of studies, with a fewer number directly assessing dose response effects in measurements of muscular strength (Jacobson and Edwards 1991; Astorino, Terzi et al. 2010b; Del Coso et al. 2012). Of these studies, Jacobson and Edwards (1991) failed to demonstrate any performance enhancing benefit irrespective of treatment dose, while Del Coso, Salinero et al. (2012) demonstrated that 3 mg · kg⁻¹ body mass elicited an improvement in half-squat and bench-press performance that was not seen using a 1 mg · kg⁻¹ body mass treatment. Similarly, Astorino, Terzi et al. (2010b) demonstrated a positive effect of 5 mg · kg⁻¹ body mass caffeine on peak knee flexion torque, knee extension/flexion total work, and knee extension/flexion power, but no effect on the same measures when using a 2 mg · kg⁻¹ body mass concentration.

Given the ambiguity in research examining the effect of caffeine on muscle strength and the distinct lack of studies examining the dose response relationship, further research is warranted to evaluate the dose dependant effects of caffeine on maximal voluntary muscle force in both the upper and lower body using concentrations between 2.5 and 7 mg · kg⁻¹ body mass, which has previously been outlined as the dose needed to elicit a positive response (Astorino and Roberson 2010a).
addition, there needs to be further focus of the dose response effect of caffeine
treatment on eccentric measures of muscle contractility, given the importance of this
type of muscle activity for sports performance (i.e. change of direction, declaration,
movement control). Considering this, the present study aimed to assess the effects
of low and moderate dose caffeine supplementation on the maximal voluntary
concentric and eccentric force of the elbow flexors and knee extensors in the same
participant. As such, the study provides important insight as to whether caffeine
elicits a dose response effect on both concentric and eccentric measurements of
muscle strength, and further considers whether caffeine supplementation has a
greater performance enhancing benefit in upper or lower body regions. It is
hypothesised that only the moderate 5 mg \( \cdot \) kg\(^{-1} \) body mass caffeine treatment will
elicit improved muscular strength of the elbow flexors. However, the low 3 mg \( \cdot \) kg\(^{-1} \)
body mass dose will induce improved performance of the knee extensor
musculature, with a trend for a greater ergogenic benefit with the moderate dose.
MATERIALS & METHOD

Following ethical approval from the host institute and completion of informed consent, ten apparently healthy, recreationally active (participating in physical activity 2-3 times per week for longer than 6 months), but non-specifically strength trained males (Mean ± SE: Age: 21 ± 0.3 yrs; height: 176 ± 2.1; body mass: 73.9 ± 3.4) agreed to participate in the study. Participants were low habitual caffeine users (Mean ± SE: 122 ± 40.9 mg/day) as identified by the completion of a caffeine consumption questionnaire (Maughan 1999).

Participants were asked to attend the human performance laboratory at Coventry University on four occasions. As per the procedures of previous research investigating the performance enhancing effect of caffeine, participants were asked to abstain from caffeine consumption and physical activity 48 hours prior to each session (Astorino, Rohmann et al. 2008; Tallis, Muhammad et al. 2016). Each visit to the laboratory was separated by at least 48 hours, and participants were asked to attend at the same time of day to avoid circadian variation.

Familiarisation

The intention of the first visit was to familiarise participants to the experimental procedures to be used in the study. Initially, shoes and heavy clothing were removed and measures of height (cm) and body mass (kg) were taken using a stadiometer (SECA Instruments Ltd., Germany) and electronic weighing scales (SECA Instruments Ltd., Germany). Participants then completed a standardised upper body warm-up consisting of 5 minutes of arm crank ergometry (Monark 857E Ergomedic,
Monark, Varberg, Sweden) using an unloaded cradle and a fixed cadence of 70rpm, immediately followed by 5 minutes of static and dynamic stretches, focusing on the elbow flexors (biceps brachii and brachialis).

Average and maximal voluntary isokinetic force (N) of the elbow flexors for the dominant side was then measured using an isokinetic dynamometer (Kin-Com 125 AP, Chattanooga Tennessee USA), which was set up in accordance with the manufacturer's instructions. Each participant was strapped to the dynamometer chair in a seated position with the ipsilateral leg anchored behind the shin attachment. The rotational axis of the dynamometer head was aligned with the lateral epicondyle of the humorous on the dominant side, with an elbow rest positioned relative to this. A hand grip bar at the opposing end of the leaver arm was adjusted relative to the length of the hand and forearm to allow the participant a comfortable grip. During concentric measures, participants were instructed to pull upwards on the bar as hard a possible through a fixed range of 80° - 120° (relative to anatomical zero for the elbow). During eccentric measures, participants were asked to resist the movement of the leaver arm moving from 120° - 80°. Measures of average and maximal concentric and eccentric force were measured at fixed speeds of 60 deg/s and 180 deg/s. Participants used the inbuilt warm-up feature of the dynamometer to become familiarised with the movements and test speeds. During the assessment of maximal voluntary force, participants performed a series of tests at each speed until maximal force was determined (usually within 3 attempts). Attempts were separated by a 60 second rest period. On completion, participants performed 30 consecutive repetitions at 180 deg/s, and maximal concentric and eccentric force was recorded for each repetition. All force values collected were corrected for gravity effects by estimation.
of limb weight (elbow fixed at 90°) prior to the assessment of maximal voluntary force.

Participants then completed a standardised warm up of the lower body, consisting of 5 minutes of cycling (Monark 824E Ergomedic, Monark, Varberg, Sweden) using an unloaded cradle and a fixed cadence of 70rpm, immediately followed by 5 minutes of static and dynamic stretches, focusing on the knee extensors (vastus intermedius, vastus medialis, vastus lateralis and rectus femoris).

The isokinetic dynamometer was then set up for the assessment of the average and maximal voluntary isokinetic force (N) of knee extensors in accordance with published protocols (Tallis, Duncan et al. 2013; Tallis, Muhammad et al. 2016). Each participant was strapped to the dynamometer chair in a seated position, and the lever arm axis of rotation was aligned with the lateral femoral epicondyle of the dominant limb. The distal end of the lever arm was fitted with a shin pad which was aligned with the lateral malleolus. A strap was placed across the midpoint of the upper limb of the test leg. Throughout the duration of the test participants were instructed to keep their arms fixed across the chest. The range of motion was fixed 10°-80° (relative to anatomical zero for the knee). The testing protocol was then carried out in the way as that described for the assessment of maximal voluntary force of the elbow flexors. All force values collected were corrected for gravity effects by estimation of limb weight carried out according to the manufacturer’s instructions (knee fixed at anatomical zero). This was measured prior to the assessment of maximal voluntary force.

The dynamometer positions for upper and lower body assessments were stored and recalled during subsequent visits.
Experimental Procedures

Participants were asked to consume a similar diet for the 24h prior to each experimental trial. Compliance was verbally acknowledged on arrival to the laboratory at each visit. Upon arrival to the laboratory, participants were fitted with telemetric HR monitor (Polar FS1, Kempele, Finland), and then began 5 minutes of seated rest. Upon completion HR was measured. Participants then consumed one of the three experimental solutions; placebo, 3 mg · kg\(^{-1}\) body mass caffeine, 6 mg · kg\(^{-1}\) body mass caffeine.

Experimental solutions were administered in a double-blinded, counterbalanced and randomised fashion. Caffeine drinks contained either 3 or 6 mg · kg\(^{-1}\) body mass of caffeine (Myprotein, UK) diluted in 4 ml · kg\(^{-1}\) body mass water and 1 ml · kg\(^{-1}\) body mass double concentrate sugar free orange cordial (Sainsbury’s, UK), and were artificially sweetened with 3 mg · kg\(^{-1}\) body mass sucralose (Myprotein, UK). Placebo solutions were prepared in the same way with the absence of caffeine. 3 mg · kg\(^{-1}\) body mass caffeine has commonly been cited as the lowest concentration needed to elicit a performance enhancing effect (Graham 2001; Astorino and Roberson 2010a), whilst 6 mg · kg\(^{-1}\) body mass is used regularly to represent a moderate caffeine dose (Plaskett and Cafarelli 2001; Green, Wickwire et al. 2007; Astorino, Terzi et al. 2010b; Timmins and Saunders 2014; Tallis, Muhammad et al. 2016). Each solution was served in an identical opaque sports bottle and on no occasion did participants disclose to the research team they knew the content of the solution. Participants were asked to fully consume the contents within 5 minutes and then rested for 45 minutes, which was immediately followed by a measure of resting HR. Participants then completed the warm up procedure as previously described.
The strength assessments began 60 minutes post-ingestion in line with previous evidence that demonstrates maximal blood plasma concentration of caffeine occurs one hour post-consumption (Graham 2001). The strength assessments were carried out using the isokinetic dynamometer in the same manner as previously described. Prior to and immediately following the 30 repeated contractions, HR and Perception of pain using Cook’s Pain scale (Cook et al. 1998) were measured.

**Statistical Method**

Normality and homogeneity of variance were tested using Shapiro–Wilk and Mauchly tests respectively. Where data was non-normally distributed, log10 transformation was performed and normality re-assessed. Eight 3 (treatment) x 2 (speed) factor repeated measures ANOVA’s were performed on both biceps and quadriceps maximal and average eccentric and concentric force data. This was repeated in order to assess a potential order effect of treatment administration. In order to determine the effect of caffeine treatment on muscle performance during the repeated contractions protocol, four 3 (treatment) x 30 (rep) factor repeated measures ANOVA’s were performed for both the biceps and quadriceps concentric and eccentric data. Violations of sphericity were corrected using Greenhouse–Geisser where applicable.

HR was analysed using a 3 (treatment) x 6 (time) repeated measures ANOVA. Similarly, perception of pain was analysed using a 3 (treatment) x 2 (time) repeated measure ANOVA, using non-normally distributed data in order to avoid type one error when performing multiple non-parametric tests.

Where appropriate, pairwise comparisons with LSD corrections were performed to identify differences between each treatment. Partial eta squared ($\eta^2$) was used as a
measure of effect size and was reported for significant ANOVA main effects. Partial
\( \eta^2 \) is commonly used in analysis of variance and provides a measure of the variance
in the dependant variable attributable to the factor in question (Tabachnick et al. 2006). In other instances, effect size (\( d \)) was calculated using the differences in
means divided by the pooled SD of the compared trials (Nakagawa et al. 2007)

Data are presented as mean ± SE. Statistical analysis was performed using SPSS
22.0 (Chicago, IL, USA). Statistical significance was set at a level of \( P < 0.05 \).
RESULTS

The statistical results indicate that there was no order effect of treatment administration ($F_{(2, 18)}<2.79; P>0.07$). This therefore dictates that any treatment effect on the measured variables herein were due to an effect of caffeine.

Upper Body

Maximal concentric and eccentric force of the elbow flexors was not significantly affected by treatment ($F_{(2, 18)}=<0.53; P>0.72$). The maximal concentric force of the elbow flexors was significantly reduced at 180 deg/s compared to 60 deg/s ($F_{(1, 9)}=9.63; P=0.013; \eta^2=0.52$), however the maximal eccentric force was unaffected by speed ($F_{(1, 9)}=0.14; P=0.72$). There was no significant treatment*speed interaction in each case ($F_{(2, 18)}=0.759$ & $F_{(1, 9)}=0.607$ receptively; $P>0.48$). Similarly, the average concentric and eccentric work of the elbow flexors was unaffected by treatment ($F_{(2, 18)}<0.25; P>0.77$). The average concentric and eccentric force of the elbow flexors was significantly lower at the greater angular velocity ($F_{(1, 9)}=6.39; P<0.04; \eta^2>0.41$). There was no significant treatment*speed interaction in each case ($F_{(2, 18)}< 1.9; P>0.17$).

Lower Body

Two factor repeated measures ANOVA revealed a significant treatment*speed interaction for maximal concentric force of the knee extensors ($F_{(2, 18)}=4.64; P=0.024$), and subsequently the effect of treatment was analysed independently at
each speed using single factor ANOVA. There was no effect of caffeine treatment on maximal concentric force tested at 60 deg/s (Fig 2A. $F_{(2, 18)}=0.334; P=0.721$). The main effect for treatment was significant for tests at 180 deg/s (Fig 2A. $F_{(2, 18)}=4.16; P=0.033; \eta^2=0.316$). LSD Pairwise comparisons demonstrated that force was significantly greater following consumption of the moderate dose caffeine ($P=0.033; \eta^2=0.58$) and had a statistical tendency to be greater following consumption of the low dose of caffeine ($P=0.083; \eta^2=0.58$), when compared to the placebo control. There was however no difference in response between the low and moderate caffeine dose ($P=0.643$).

Average concentric and maximal and average eccentric force of the knee extensors was not affected by treatment (Fig 2B, C & D. $F_{(2, 18)}<2.60; P>0.104$). Average concentric and eccentric force was significantly lower at the higher test speeds (Fig 2C & D. $F_{(1, 9)}>26.04; P<0.001; \eta^2>0.74$), but maximal eccentric force was unaffected by speed (Fig 2B. $F_{(1, 9)}=0.595; P=0.460$). No significant treatment*speed interactions were found for these variables ($F_{(2, 18)}<2.31; P>0.128$ in each case).

**Maximal Repeated Contractions**

The main effect for treatment was approaching significance for the maximal concentric force of the knee extensors during the repeated contractions protocol (Fig 3C. $F_{(2, 18)}=3.04; P=0.073; \eta^2=0.253$), with pairwise comparisons demonstrating that this difference was apparent in the moderate caffeine dose ($P=0.059; \eta^2=0.47$), but not the low caffeine dose ($P=0.241$) when compared to the placebo trial.

The repeated maximal performance of the knee extensors activated eccentrically and the elbow flexors activated both concentrically and eccentrically were not significantly different between the treatments (Fig 3A, B & D. $F_{(2, 18)}<2.46; P>0.123$).
For all four of the dependant variables, force over the time course of the test was significantly affected by time (Fig 3. F\(_{(29, 261)}\) > 1.9; P < 0.005; \(\eta^2_p > 0.17\)), and there was no significant treatment*rep interaction (Fig 3. F\(_{(58, 522)}\) < 1.296; P > 0.081).

HR & Perception of Pain

Perception of pain for the arms and the legs was not significantly affected by treatment (Fig 4A. F\(_{(2, 18)}\) < 1.00 P > 0.386), although in both cases the perception of pain was significantly higher immediately following completion of the respective repeated contractions protocol (Fig 4A. F\(_{(1, 9)}\) > 11.00; P < 0.01 \(\eta^2_p > 0.54\)). There was no significant treatment*time interaction (Fig 4A. F\(_{(2, 18)}\) < 0.195; P > 0.825).

HR was not significantly affected by treatment (Fig 4B. ANOVA F\(_{(2, 18)}\) = 0.39; P = 0.704), but was significantly affected by time (Fig 4B. F\(_{(3, 22)}\) = 82.70; P < 0.001; \(\eta^2_p = 0.902\)). There was no significant treatment*time interaction (Fig 4B. F\(_{(12, 108)}\) = 0.97; P = 0.480).
DISCUSSION

Results from the present study indicate that caffeine may be an effective nutritional supplement to induce some improvements in the maximal voluntary strength of non-specifically trained individuals. It appears however that these benefits may be limited to the concentric activity of lower limb muscle working at a higher contraction velocity, as there were no measured effects of caffeine (irrespective of concentration) on the contractile measures of the elbow flexors or eccentric measures of the knee extensors. Although some aspects of contractility appeared to be improved using the low 3 mg · kg⁻¹ body mass caffeine dose, the 6 mg · kg⁻¹ body mass caffeine treatment appeared to be more effective in eliciting a performance enhancing response. Despite this, the results fail to demonstrate a clear dose response relationship, rather the effective caffeine concentration to evoke improved muscle performance may be related to muscle mass and contraction type.

The demonstrated increase in peak concentric strength of the knee extensors and performance during the repeated repetitions protocol, adds further weight to the growing body of evidence that demonstrates that caffeine may be effective in improving strength performance (Jacobson et al. 1992; Hoffman et al. 2008; Woolf et al. 2008; Astorino, Terzi et al. 2010b; Del Coso, Salinero et al. 2012; Tallis, Muhammad et al. 2016). The lack of response in all other measures however help to further rationalise the equivalent evidence in this area of research (Bond, Gresham
et al. 1986; Jacobson and Edwards 1991; Jacobs, Pasternak et al. 2003; Astorino, Rohmann et al. 2008; Williams, Cribb et al. 2008; Tallis, Duncan et al. 2013). The present findings infer that the caffeine response may be effected by treatment concentration, muscle group tested, and elicit diverse effects during different contractile activity within the same individual. As such these findings demonstrate a further complexity with respect to identifying the optimum conditions for a caffeine induced increase in muscle strength.

*Upper Body vs. Lower Body*

This data fills a gap in the literature whereby there is a distinct lack of studies that directly examine the effect of caffeine on upper body and lower body maximal voluntary force. Timmins and Saunders (2014) demonstrated that a 6 mg · kg⁻¹ body mass was effective at increasing the peak concentric torque of the knee, elbow and wrist flexors, and the ankle plantar flexors in resistance trained participants. However, the performance enhancing benefit was greatest in the knee extensors, and was reduced in the smaller elbow and wrist flexor muscle groups. The lack of response seen in the elbow flexors of the present study is in agreement with work conducted by Black, Waddell et al. (2015) and would appear to contradict this previous work. This may therefore indicate that the performance enhancing benefit of caffeine is not concurrent across all muscles. This discrepancy is likely to relate to differences between the trained and the untrained participants used in the present study compared to previous work. It is considered that the ergogenic benefit is greater in specifically trained participants, rationalised by a greater motivation to repeatedly produce maximal efforts (Astorino and Roberson 2010a). This could further relate to the ability of caffeine to act directly at the muscle (Tallis et al. 2015)
via increased Ca\textsuperscript{2+} release from the sarcoplasmic reticulum, the efficiency of which is likely to be improved in trained individuals (Munkvik et al. 2010).

In general, the current findings further support the conclusion of Warren, Park et al. (2010), who demonstrated using indirect comparisons, that caffeine would elicit a greater improvement in muscular strength of lower body or larger muscle groups compared to upper body or small muscle groups. The present findings also further previous work examining the effect of caffeine on upper and lower body maximal voluntary force (Timmins and Saunders 2014), by uniquely demonstrating that the discrepancies between the improvement in maximal force of lower body musculature and the lack of response seen in upper body musculature is concurrent across acute, one-off maximal contractile function and a protocol of sustained contractions.

**Dose Response Effect**

Given the ambiguity and the distinct lack of evidence, the present study sought to further examine the dose response effect of caffeine on muscular strength. The data indicates that where caffeine acted to elicit a performance enhancing response, there was no clear dose response effect. The lower dose of caffeine (3 mg \cdot kg\textsuperscript{-1} body mass) elected an increase in the peak concentric force of the knee extensors at 180 deg/s that was approaching significance and equal in magnitude to the increase seen using the moderate caffeine dose (6 mg \cdot kg\textsuperscript{-1} body mass), which did reach statistical significance when compared to the placebo condition. Given that there was no significant difference in the response between the low and moderate caffeine doses, these results indicate that lower doses of caffeine, which are closer in concentration to that of commercially available products, may be effective in increasing some aspects of muscular strength in an equal proportion to that
achieved using a much higher concentration. The present results infer that greater
doses fail to elicit a superior response, rather there is a threshold concentration
whereby caffeine either elicits a positive outcome, or fails to have an effect. A similar
conclusion has been demonstrated in a study examining the dose response effect of
physiological concentrations of caffeine on mammalian isolated skeletal muscle
contractility (Tallis et al. 2012).

Astorino, Terzi et al. (2010b) demonstrated a positive effect of 5 mg · kg⁻¹ body
mass caffeine on peak knee flexion torque, knee extension/flexion total work, and
knee extension/flexion power, but no effect of the same measures when using a 2
mg · kg⁻¹ body mass concentration. Our results in part support these findings
demonstrating that the higher 6 mg · kg⁻¹ body mass dose was effective in inducing
improvements in peak concentric force of the knee extensors at 180 deg/s and
sustained performance during repeated contractions. However, unlike the 2 mg ·
kg⁻¹ body mass concentration used by Astorino, Terzi et al. (2010b), 3 mg · kg⁻¹
body mass caffeine treatment in the present study was effective at eliciting an
improvement in peak muscular strength. This difference may be apparent as lower
dose of caffeine used in the current study falls within the 2.5 - 7 mg · kg⁻¹ body
mass that has been shown to be the effective range for inducing improved muscular
strength (Astorino and Roberson 2010a).

Interestingly, the present work is the first to show variation in contractile response
between different concentrations of caffeine. Whilst both the low and moderate
caffeine dose appeared to be effective in increasing peak concentric force of the
knee extensors at 180 deg/s, only the moderate dose induced an improvement in the
sustained contractile performance at this angular velocity. These results indicate that
the effectiveness of different caffeine doses may further depend on the measured contractile parameter, where some contractility types favour lower caffeine concentrations.

The present work is the first to examine the dose response effect of caffeine on maximal voluntary force of upper body musculature. The lack of any demonstrated effect contradicts work conducted by Del Coso, Salinero et al. (2012) who demonstrated that 3 mg · kg\(^{-1}\) body mass caffeine increased maximal power output in the bench press, although no effect was demonstrated using a 1 mg · kg\(^{-1}\) body mass treatment. As such, it is recommended that more work is conducted to evaluate the dose response effects of caffeine on fixed load strength measures, as these may offer different results to measures of maximal voluntary force.

Effect of Caffeine on Pain Perception

The present findings demonstrate that during the protocol of repeated contractions for both the elbow flexors and the knee extensors, there was no effect of either caffeine dose on pain perception. There is evidence to suggest that mechanistically caffeine can induce performance enhancing benefits by manipulating pain perception (Doherty et al. 2005). As there was no change in performance during the repeated contraction protocol of the elbow flexors, it was unsurprising that perception of pain was not affected by the caffeine treatment. The improved performance of the knee extensors during repeated contractions, coincides with the growing body of evidence that demonstrates a caffeine induced increase in performance without notable modulation of pain perception (Tallis, Duncan et al. 2013; Duncan et al. 2014; Tallis, Muhammad et al. 2016). As such, the given improvement in muscle performance demonstrated in the present study is likely to relate to the action of caffeine as a
CNS stimulant (Nehlig et al. 1992) and (or) its ability to act directly on skeletal muscle (Tallis, Duncan et al. 2015).

**Limitations & Future Direction**

A small number of research studies that have examined the effect of caffeine on exercise performance have used doses greater than the moderate 6 mg · kg⁻¹ body mass used in the present study (Perkins et al. 1975; Williams et al. 1987; Graham et al. 1991; Jacobson, Weber et al. 1992; Cohen et al. 1996; Glaister et al. 2012), with doses up to 13 mg · kg⁻¹ body mass being reported (Pasman et al. 1995). As such, there is the possibility that higher doses of caffeine may elicit a greater response with respect to measures of muscular strength. Currently this remains un-researched, as high doses of caffeine have been associated with adverse effects such as anxiety, gastrointestinal discomfort, and impairment of fine motor control (Smith 2002; Burke 2008). Such side effects may cause performance to be decreased. Furthermore, it would have been useful to measure salivary or plasma caffeine concentration following the administration of each dose. Previous work has indicated a genetic influence with respect to speed of caffeine metabolism (Yang et al. 2010), and as such, this may result in an individual dose response effect.

As a positive caffeine response in the concentric action of the knee extensors was seen at 180 deg/s and not 60 deg/s, future work should consider evaluating the dose response effect of caffeine using faster contraction speeds. Irrespective of the dose response relationship, there is a lack of studies that have examined the effect of caffeine using high speed isokinetic assessments. Furthermore, the present work and previous literature (Jacobson and Edwards 1991; Astorino, Terzi et al. 2010b; Del Coso, Salinero et al. 2012) has focused on evaluating the dose response effects
of caffeine in non-specifically trained athletes. Future work should adopt a similar
experimental approach to assess dose response effects of caffeine in resistance
trained participants, where it is proposed that caffeine elicits a greater benefit.

The present work examines the dose response effect of caffeine at a group level.
Previous literature has indicated that the rate of caffeine digestion and metabolism
may differ between individuals, which has mechanistically been accounted for by
differences in genotype (Astorino and Roberson 2010a). As such, future work should
consider a greater sample size to better understand the dose response effect on an
individual level.

Conclusion

The results of the present study demonstrate that both low and moderate dose
caffeine were effective in increasing peak concentric force of the knee extensors at
faster contraction velocities. There was no effect of either caffeine dose on the
concentric or eccentric action of the elbow flexors, or the eccentric action of the knee
extensors. As such, the findings demonstrate that relatively low doses of caffeine
may be effective to induce some improvements in muscular strength in non-
specifically trained individuals, but this is limited to larger muscle groups of the lower
limb. Where caffeine elicited a performance enhancing effect, there was no clear
dose response relationship with both the low and moderate doses eliciting similar
benefits. Only the moderate dose of caffeine caused an improvement in performance
during repeated concentric contractions of the knee extensors, indicating that the
effective caffeine concentration may be further related to contraction type. The
findings demonstrate a further level of complexity with respect to identifying the
optimum conditions for a caffeine induced increase in muscle strength.
CONFLICT OF INTEREST

The authors report no conflicts of interest associated with this manuscript.
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FIGURES

Figure 1. The effect of 3 mg · kg⁻¹ and 6 mg · kg⁻¹ body mass caffeine treatment on peak and average isokinetic concentric (A & C) and eccentric force (B & D) of the elbow flexor muscles at 60 and 180 deg/s [Data are represented as mean ± SE; n=10]

Figure 2. The effect of 3 mg · kg⁻¹ and 6 mg · kg⁻¹ body mass caffeine treatment on peak and average isokinetic concentric (A & C) and eccentric force (B & D) of the knee extensor muscles at 60 and 180 deg/s [Data are represented as mean ± SE; n=10; * represents statistically significant difference (P=0.033; d=0.68) between Placebo and 6 mg/kg caffeine; # represents statistical tendency (P=0.083; d=0.83) between Placebo and 3 mg/kg caffeine]

Figure 3. The effect of 3 mg · kg⁻¹ and 6 mg · kg⁻¹ body mass caffeine treatment on peak isokinetic concentric and eccentric force of the elbow flexors (A & B) and knee extensors (C & D) over 30 repeated maximal voluntary contractions at 180 deg/s [Data are represented as mean ± SE; n=10; # represents statistical tendency (P=0.059; d=0.47) between Placebo and 6 mg/kg caffeine]

Figure 4. The effect of 3 mg · kg⁻¹ and 6 mg · kg⁻¹ body mass caffeine treatment on perception of pain and HR during measures of isokinetic muscle force [Data are represented as mean ± SE; n=10; UReps indicates upper body repetitions, LReps indicates lower body repetitions]
Fig 1

131x91mm (300 x 300 DPI)
Fig 2

130x89mm (300 x 300 DPI)
Fig 3

135x95mm (300 x 300 DPI)
Fig 4

104x58mm (300 x 300 DPI)