

The Effects of Low and Moderate Dose Caffeine Supplementation on Upper and Lower Body Maximal Voluntary Concentric and Eccentric Muscle Force

Tallis, J & Yavuz, HCM

Author post-print (accepted) deposited by Coventry University's Repository

Original citation & hyperlink:

Tallis, J & Yavuz, HCM 2017, 'The Effects of Low and Moderate Dose Caffeine Supplementation on Upper and Lower Body Maximal Voluntary Concentric and Eccentric Muscle Force' *Applied Physiology, Nutrition, and Metabolism*, vol 43, pp. 274-281

<https://dx.doi.org/10.1139/apnm-2017-0370>

DOI 10.1139/apnm-2017-0370

ISSN 1715-5312

ESSN 1715-5320

Publisher: NRC Research Press

Copyright © and Moral Rights are retained by the author(s) and/ or other copyright owners. A copy can be downloaded for personal non-commercial research or study, without prior permission or charge. This item cannot be reproduced or quoted extensively from without first obtaining permission in writing from the copyright holder(s). The content must not be changed in any way or sold commercially in any format or medium without the formal permission of the copyright holders.

This document is the author's post-print version, incorporating any revisions agreed during the peer-review process. Some differences between the published version and this version may remain and you are advised to consult the published version if you wish to cite from it.

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

4 Jason Tallis (✉), Harley, C. M. Yavuz

5 School of Life Sciences, James Starley Building, Coventry University, Priory Street,
6 Coventry CV1 5FB, UK

7 Email: tallisj2@uni.coventry.ac.uk

8

9

10

11

12

13

14

15

16

17

18

19

20 **ABSTRACT**

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

41

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

44 INTRODUCTION

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

56 Although generally there seems to be support for a caffeine induced improvement in
57 strength performance (Astorino and Roberson 2010a; Warren, Park et al. 2010),
58 findings from research exploring the caffeine effect using such exercise modalities
59 appear to be more equivocal than studies examining the ergogenic properties of
60 caffeine using endurance based exercise protocols. Despite the likely publication bias
61 that exist within this field, where research studies showing effects are favoured, there
62 are still many studies that fail to demonstrate an effect of caffeine on muscular strength
63 (Bond et al. 1986; Jacobson et al. 1991; Jacobs et al. 2003; Astorino et al. 2008;
64 Williams et al. 2008; Tallis et al. 2013). The degree of ambiguity can largely be
65 attributed to differences in the caffeine dose and method of administration, the
66 exercise protocol (i.e. 1 repetition maximum, repetitions until failure, maximal voluntary
67 contractions), the muscle group tested, the possibility of habituation in high caffeine
68 users, and differences that may be apparent between specifically trained and novice

69 participants. Despite this, caffeine use amongst strength and power athletes is rife
70 (Van Thuyne et al. 2005; Del Coso et al. 2011), and as such, further research is
71 needed to more accurately quantify the caffeine effect.

72 A meta-analysis by Warren, Park et al. (2010), demonstrated that caffeine elicited a
73 small ergogenic effect on measures of maximal voluntary force, with lower body or
74 larger muscle groups demonstrating a greater benefit compared to upper body or small
75 muscle groups. This phenomenon was attributed to a lower neural activation of larger
76 muscle groups and the mechanistic action of caffeine to act via the central nervous
77 system (CNS) to promote greater muscular recruitment. As such, these findings further
78 rationalise the equivocal results demonstrated in studies evaluating the effect of
79 caffeine on muscular strength. Interestingly, conclusions by Warren, Park et al. (2010)
80 are based largely on indirect comparisons of studies that have assessed the effect of
81 caffeine on one of either upper body or lower body strength. Black et al. (2015)
82 demonstrated that a $5 \text{ mg} \cdot \text{kg}^{-1}$ caffeine treatment resulted in an increased maximal
83 voluntary isometric force and motor unit activation of the knee extensors. However,
84 this dose failed to elicit any effect on the muscular strength of the elbow flexors in the
85 same set of participants. Beyond this work there is a distinct lack of research data that
86 examines the effect of caffeine on maximal voluntary force using different muscle
87 groups in the same participant. The present study builds on work by Black, Waddell et
88 al. (2015) by examining the effect of caffeine dose on upper body and lower body
89 maximal voluntary force during concentric and eccentric muscle activity.

90 Typically, researchers' examining the ergogenic effect of caffeine on exercise
91 performance have done so using moderate doses ($5\text{-}6 \text{ mg} \cdot \text{kg}^{-1}$ body mass) that are
92 dissolved in fluid and consumed orally (Plaskett et al. 2001; Green et al. 2007; Astorino

93 et al. 2010b; Timmins et al. 2014; Tallis et al. 2016). Doses between 2.5 to 7 mg ·
94 kg⁻¹ body mass has been reported to improve high intensity exercise performance
95 (Astorino and Roberson 2010a), however it is widely accepted that within and above
96 this concentration range, caffeine fails to elicit a dose dependant effect irrespective of
97 exercise modality. It is surprising however that based on an evaluation of the available
98 literature, this conclusion has been derived from a relatively small number of studies,
99 with a fewer number directly assessing dose response effects in measurements of
100 muscular strength (Jacobson and Edwards 1991; Astorino, Terzi et al. 2010b; Del
101 Coso et al. 2012). Of these studies, Jacobson and Edwards (1991) failed to
102 demonstrate any performance enhancing benefit irrespective of treatment dose, while
103 Del Coso, Salinero et al. (2012) demonstrated that 3 mg · kg⁻¹ body mass elicited an
104 improvement in half-squat and bench-press performance that was not seen using a 1
105 mg · kg⁻¹ body mass treatment. Similarly, Astorino, Terzi et al. (2010b) demonstrated
106 a positive effect of 5 mg · kg⁻¹ body mass caffeine on peak knee flexion torque, knee
107 extension/flexion total work, and knee extension/flexion power, but no effect on the
108 same measures when using a 2 mg · kg⁻¹ body mass concentration.

109 Given the ambiguity in research examining the effect of caffeine on muscle strength
110 and the distinct lack of studies examining the dose response relationship, further
111 research is warranted to evaluate the dose dependant effects of caffeine on maximal
112 voluntary muscle force in both the upper and lower body using concentrations between
113 2.5 and 7 mg · kg⁻¹ body mass, which has previously been outlined as the dose
114 needed to elicit a positive response (Astorino and Roberson 2010a). In addition, there
115 needs to be further focus of the dose response effect of caffeine treatment on eccentric
116 measures of muscle contractility, given the importance of this type of muscle activity

117 for sports performance (i.e. change of direction, deceleration, movement control).
118 Considering this, the present study aimed to assess the effects of low and moderate
119 dose caffeine supplementation on the maximal voluntary concentric and eccentric
120 force of the elbow flexors and knee extensors in the same participant. As such, the
121 study provides important insight as to whether caffeine elicits a dose response effect
122 on both concentric and eccentric measurements of muscle strength, and further
123 considers whether caffeine supplementation has a greater performance enhancing
124 benefit in upper or lower body regions. It is hypothesised that only the moderate 5 mg
125 $\cdot \text{kg}^{-1}$ body mass caffeine treatment will elicit improved muscular strength of the
126 elbow flexors. However, the low 3 mg $\cdot \text{kg}^{-1}$ body mass dose will induce improved
127 performance of the knee extensor musculature, with a trend for a greater ergogenic
128 benefit with the moderate dose.

129

130

131

132

133

134

135

136

137

138 **MATERIALS & METHOD**

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

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

153 *Familiarisation*

154 The intention of the first visit was to familiarise participants to the experimental
155 procedures to be used in the study. Initially, shoes and heavy clothing were removed
156 and measures of height (cm) and body mass (kg) were taken using a stadiometer
157 (SECA Instruments Ltd., Germany) and electronic weighing scales (SECA Instruments
158 Ltd., Germany). Participants then completed a standardised upper body warm-up
159 consisting of 5 minutes of arm crank ergometry (Monark 857E Ergomedic, Monark,
160 Varberg, Sweden) using an unloaded cradle and a fixed cadence of 70rpm,

161 immediately followed by 5 minutes of static and dynamic stretches, focusing on the
162 elbow flexors (biceps brachii and brachialis).

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

185 Participants then completed a standardised warm up of the lower body, consisting of
186 5 minutes of cycling (Monark 824E Ergomedic, Monark, Varberg, Sweden) using an
187 unloaded cradle and a fixed cadence of 70rpm, immediately followed by 5 minutes of
188 static and dynamic stretches, focusing on the knee extensors (vastus intermedius,
189 vastus medialis, vastus lateralis and rectus femoris).

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

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

206 *Experimental Procedures*

207 Participants were asked to consume a similar diet for the 24h prior to each
208 experimental trial. Compliance was verbally acknowledged on arrival to the laboratory

209 at each visit. Upon arrival to the laboratory, participants were fitted with telemetric HR
210 monitor (Polar FS1, Kempele, Finland), and then began 5 minutes of seated rest. Upon
211 completion HR was measured. Participants then consumed one of the three
212 experimental solutions; placebo, 3 mg · kg⁻¹ body mass caffeine, 6 mg · kg⁻¹ body
213 mass caffeine.

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

233 dynamometer in the same manner as previously described. Prior to and immediately
234 following the 30 repeated contractions, HR and Perception of pain using Cook's Pain
235 scale (Cook et al. 1998) were measured.

236 *Statistical Method*

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

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

251 Where appropriate, pairwise comparisons with LSD corrections were performed to
252 identify differences between each treatment. Partial eta squared (η^2) was used as a
253 measure of effect size and was reported for significant ANOVA main effects. Partial η^2
254 is commonly used in analysis of variance and provides a measure of the variance in
255 the dependant variable attributable to the factor in question (Tabachnick et al. 2006).

256 In other instances, effect size (d) was calculated using the differences in means
257 divided by the pooled SD of the compared trials (Nakagawa et al. 2007)

258 Data are presented as mean \pm SE. Statistical analysis was performed using SPSS
259 22.0 (Chicago, IL, USA). Statistical significance was set at a level of $P < 0.05$.

260

261

262

263

264

265

266

267

268

269

270

271

272

273

274

275 RESULTS

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

279 *Upper Body*

280 Maximal concentric and eccentric force of the elbow flexors was not significantly
281 affected by treatment (Fig 1A & B. $F_{(2, 18)} < 0.53$; $P > 0.72$). The maximal concentric
282 force of the elbow flexors was significantly reduced at 180 deg/s compared to 60 deg/s
283 (Fig 1A. $F_{(1, 9)} = 9.63$; $P = 0.013$; $P\eta^2 = 0.52$), however the maximal eccentric force was
284 unaffected by speed (Fig 1B $F_{(1, 9)} = 0.14$; $P = 0.72$). There was no significant
285 treatment*speed interaction in each case (Fig 1A & B. $F_{(2, 18)} = 0.759$ & $F_{(1, 11)} = 0.607$
286 respectively; $P > 0.48$). Similarly, the average concentric and eccentric work of the elbow
287 flexors was unaffected by treatment (Fig 1C & D. $F_{(2, 18)} < 0.25$; $P > 0.77$). The average
288 concentric and eccentric force of the elbow flexors was significantly lower at the
289 greater angular velocity (Fig 1C & D. $F_{(1, 9)} > 6.39$; $P < 0.04$; $P\eta^2 > 0.41$). There was no
290 significant treatment*speed interaction in each case (Fig 1C & D. $F_{(2, 18)} < 1.9$; $P > 0.17$).

291 *Lower Body*

292 Two factor repeated measures ANOVA revealed a significant treatment*speed
293 interaction for maximal concentric force of the knee extensors ($F_{(2, 18)} = 4.64$; $P = 0.024$),
294 and subsequently the effect of treatment was analysed independently at each speed
295 using single factor ANOVA. There was no effect of caffeine treatment on maximal
296 concentric force tested at 60 deg/s (Fig 2A. $F_{(2, 18)} = 0.334$; $P = 0.721$). The main effect
297 for treatment was significant for tests at 180 deg/s (Fig 2A. $F_{(2, 18)} = 4.16$; $P = 0.033$;

298 $P\eta^2=0.316$). LSD Pairwise comparisons demonstrated that force was significantly
299 greater following consumption of the moderate dose caffeine ($P=0.033$; $d=0.68$) and
300 had a statistical tendency to be greater following consumption of the low dose of
301 caffeine ($P=0.083$; $d=0.83$), when compared to the placebo control. There was
302 however no difference in response between the low and moderate caffeine dose
303 ($P=0.643$).

304 Average concentric and maximal and average eccentric force of the knee extensors
305 was not affected by treatment (Fig 2B, C & D. $F_{(2, 18)}<2.60$; $P>0.104$). Average
306 concentric and eccentric force was significantly lower at the higher test speeds (Fig
307 2C & D. $F_{(1, 9)}>26.04$; $P<0.001$; $P\eta^2>0.74$), but maximal eccentric force was unaffected
308 by speed (Fig 2B. $F_{(1, 9)}=0.595$; $P=0.460$). No significant treatment*speed interactions
309 were found for these variables ($F_{(2, 18)}<2.31$; $P>0.128$ in each case).

310 *Maximal Repeated Contractions*

311 The main effect for treatment was approaching significance for the maximal concentric
312 force of the knee extensors during the repeated contractions protocol (Fig 3C. $F_{(2, 18)}=3.04$;
313 $P=0.073$; $P\eta^2=0.253$), with pairwise comparisons demonstrating that this
314 difference was apparent in the moderate caffeine dose ($P=0.059$; $d=0.47$), but not the
315 low caffeine dose ($P=0.241$) when compared to the placebo trial.

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

322 *HR & Perception of Pain*

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

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

331

332

333

334

335

336

337

338

339

340

341

342 **DISCUSSION**

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

355 The demonstrated increase in peak concentric strength of the knee extensors and
356 performance during the repeated repetitions protocol, adds further weight to the
357 growing body of evidence that demonstrates that caffeine may be effective in
358 improving strength performance (Jacobson et al. 1992; Hoffman et al. 2008; Woolf et
359 al. 2008; Astorino, Terzi et al. 2010b; Del Coso, Salinero et al. 2012; Tallis,
360 Muhammad et al. 2016). The lack of response in all other measures however help to
361 further rationalise the equivalent evidence in this area of research (Bond, Gresham et
362 al. 1986; Jacobson and Edwards 1991; Jacobs, Pasternak et al. 2003; Astorino,
363 Rohmann et al. 2008; Williams, Cribb et al. 2008; Tallis, Duncan et al. 2013). The
364 present findings infer that the caffeine response may be effected by treatment
365 concentration, muscle group tested, and elicit diverse effects during different

366 contractile activity within the same individual. As such these findings demonstrate a
367 further complexity with respect to identifying the optimum conditions for a caffeine
368 induced increase in muscle strength.

369 *Upper Body vs. Lower Body*

370 This data fills a gap in the literature whereby there is a distinct lack of studies that
371 directly examine the effect of caffeine on upper body and lower body maximal
372 voluntary force. Timmins and Saunders (2014) demonstrated that a 6 mg · kg⁻¹ body
373 mass was effective at increasing the peak concentric torque of the knee, elbow and
374 wrist flexors, and the ankle plantar flexors in resistance trained participants. However,
375 the performance enhancing benefit was greatest in the knee extensors, and was
376 reduced in the smaller elbow and wrist flexor muscle groups. The lack of response
377 seen in the elbow flexors of the present study is in agreement with work conducted by
378 Black, Waddell et al. (2015) and would appear to contradict this previous work. This
379 may therefore indicate that the performance enhancing benefit of caffeine is not
380 concurrent across all muscles. This discrepancy is likely to relate to differences
381 between the trained and the untrained participants used in the present study compared
382 to previous work. It is considered that the ergogenic benefit is greater in specifically
383 trained participants, rationalised by a greater motivation to repeatedly produce
384 maximal efforts (Astorino and Roberson 2010a). This could further relate to the ability
385 of caffeine to act directly at the muscle (Tallis et al. 2015) via increased Ca²⁺ release
386 from the sarcoplasmic reticulum, the efficiency of which is likely to be improved in
387 trained individuals (Munkvik et al. 2010).

388 In general, the current findings further support the conclusion of Warren, Park et al.
389 (2010), who demonstrated using indirect comparisons, that caffeine would elicit a

390 greater improvement in muscular strength of lower body or larger muscle groups
391 compared to upper body or small muscle groups. The present findings also further
392 previous work examining the effect of caffeine on upper and lower body maximal
393 voluntary force (Timmins and Saunders 2014), by uniquely demonstrating that the
394 discrepancies between the improvement in maximal force of lower body musculature
395 and the lack of response seen in upper body musculature is concurrent across acute,
396 one-off maximal contractile function and a protocol of sustained contractions.

397 *Dose Response Effect*

398 Given the ambiguity and the distinct lack of evidence, the present study sought to
399 further examine the dose response effect of caffeine on muscular strength. The data
400 indicates that where caffeine acted to elicit a performance enhancing response, there
401 was no clear dose response effect. The lower dose of caffeine ($3 \text{ mg} \cdot \text{kg}^{-1}$ body
402 mass) elicited an increase in the peak concentric force of the knee extensors at 180
403 deg/s that was approaching significance and equal in magnitude to the increase seen
404 using the moderate caffeine dose ($6 \text{ mg} \cdot \text{kg}^{-1}$ body mass), which did reach statistical
405 significance when compared to the placebo condition. Given that there was no
406 significant difference in the response between the low and moderate caffeine doses,
407 these results indicate that lower doses of caffeine, which are closer in concentration
408 to that of commercially available products, may be effective in increasing some
409 aspects of muscular strength in an equal proportion to that achieved using a much
410 higher concentration. The present results infer that greater doses fail to elicit a superior
411 response, rather there is a threshold concentration whereby caffeine either elicits a
412 positive outcome, or fails to have an effect. A similar conclusion has been
413 demonstrated in a study examining the dose response effect of physiological

414 concentrations of caffeine on mammalian isolated skeletal muscle contractility (Tallis
415 et al. 2012).

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

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

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

445 *Effect of Caffeine on Pain Perception*

446 The present findings demonstrate that during the protocol of repeated contractions for
447 both the elbow flexors and the knee extensors, there was no effect of either caffeine
448 dose on pain perception. There is evidence to suggest that mechanistically caffeine
449 can induce performance enhancing benefits by manipulating pain perception (Doherty
450 et al. 2005). As there was no change in performance during the repeated contraction
451 protocol of the elbow flexors, it was unsurprising that perception of pain was not
452 affected by the caffeine treatment. The improved performance of the knee extensors
453 during repeated contractions, coincides with the growing body of evidence that
454 demonstrates a caffeine induced increase in performance without notable modulation
455 of pain perception (Tallis, Duncan et al. 2013; Duncan et al. 2014; Tallis, Muhammad
456 et al. 2016). As such, the given improvement in muscle performance demonstrated in
457 the present study is likely to relate to the action of caffeine as a CNS stimulant (Nehlig
458 et al. 1992) and (or) its ability to act directly on skeletal muscle (Tallis, Duncan et al.
459 2015).

460 *Limitations & Future Direction*

461 A small number of research studies that have examined the effect of caffeine on
462 exercise performance have used doses greater than the moderate $6 \text{ mg} \cdot \text{kg}^{-1}$ body
463 mass used in the present study (Perkins et al. 1975; Williams et al. 1987; Graham et
464 al. 1991; Jacobson, Weber et al. 1992; Cohen et al. 1996; Glaister et al. 2012), with
465 doses up to $13 \text{ mg} \cdot \text{kg}^{-1}$ body mass being reported (Pasman et al. 1995). As such,
466 there is the possibility that higher doses of caffeine may elicit a greater response with
467 respect to measures of muscular strength. Currently this remains un-researched, as
468 high doses of caffeine have been associated with adverse effects such as anxiety,
469 gastrointestinal discomfort, and impairment of fine motor control (Smith 2002; Burke
470 2008). Such side effects may cause performance to be decreased. Furthermore, it
471 would have been useful to measure salivary or plasma caffeine concentration following
472 the administration of each dose. Previous work has indicated a genetic influence with
473 respect to speed of caffeine metabolism (Yang et al. 2010), and as such, this may
474 result in an individual dose response effect.

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

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

491 *Conclusion*

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

506

507

508 **CONFLICT OF INTEREST**

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

510

511

512

513

514

515

516

517

518

519

520

521

522

523

524

525

526

527 **ACKNOWLEDGEMENTS**

528 The authors would like to thank Roy Petticrew and Susie Wilson for technical support.

529

530

531

532

533

534

535

536

537

538

539

540

541

542

543

544

545

546 **REFERENCES**

547 Astorino, T.A. and Roberson, D.W. 2010a. Efficacy of acute caffeine ingestion for
548 short-term high-intensity exercise performance: a systematic review. **J. Strength**
549 **Cond. Res.** 24: 257-65.

550 Astorino, T.A., Rohmann, R.L., and Firth, K. 2008. Effect of caffeine ingestion on one-
551 repetition maximum muscular strength. **Eur. J. Appl. Physiol.** 102: 127-32.

552 Astorino, T.A., Terzi, M.N., Roberson, D.W., and Burnett, T.R. 2010b. Effect of two
553 doses of caffeine on muscular function during isokinetic exercise. **Med. Sci. Sports**
554 **Exerc.** 42: 2205-10.

555 Black, C.D., Waddell, D.E., and Gonglach, A.R. 2015. Caffeine's Ergogenic Effects on
556 Cycling: Neuromuscular and Perceptual Factors. **Med. Sci. Sports Exerc.** 47: 1145-
557 58.

558 Bond, V., Gresham, K., McRae, J., and Tearney, R.J. 1986. Caffeine ingestion and
559 isokinetic strength. **Br. J. Sports Med.** 20: 135-7.

560 Burke, L.M. 2008. Caffeine and sports performance. **Appl. Physiol. Nutr. Metab.** 33:
561 1319-34.

562 Cohen, B.S., Nelson, A.G., Prevost, M.C., Thompson, G.D., Marx, B.D., and Morris,
563 G.S. 1996. Effects of caffeine ingestion on endurance racing in heat and humidity.
564 **Eur. J. Appl. Physiol. Occup. Physiol.** 73: 358-63.

565 Cook, D.B., O'Connor, P.J., Oliver, S.E., and Lee, Y. 1998. Sex differences in naturally
566 occurring leg muscle pain and exertion during maximal cycle ergometry. **Int. J.**
567 **Neurosci.** 95: 183-202.

568 Davis, J.K. and Green, J.M. 2009. Caffeine and anaerobic performance: ergogenic
569 value and mechanisms of action. **Sports Med.** 39: 813-32.

570 Del Coso, J., Munoz, G., and Munoz-Guerra, J. 2011. Prevalence of caffeine use in
571 elite athletes following its removal from the World Anti-Doping Agency list of banned
572 substances. **Appl. Physiol. Nutr. Metab.** 36: 555-61.

573 Del Coso, J., Salinero, J.J., Gonzalez-Millan, C., Abian-Vicen, J., and Perez-Gonzalez,
574 B. 2012. Dose response effects of a caffeine-containing energy drink on muscle
575 performance: a repeated measures design. **J. Int. Soc. Sports Nutr.** 9: 21.

576 Doherty, M. and Smith, P.M. 2005. Effects of caffeine ingestion on rating of perceived
577 exertion during and after exercise: a meta-analysis. **Scand. J. Med. Sci. Sports,** 15:
578 69-78.

579 Duncan, M.J., Clarke, N.D., Tallis, J., Guimaraes-Ferreira, L., and Leddington Wright,
580 S. 2014. The effect of caffeine ingestion on functional performance in older adults. **J.**
581 **Nutr. Health Aging,** 18: 883-7.

582 Glaister, M., Patterson, S.D., Foley, P., Pedlar, C.R., Pattison, J.R., and McInnes, G.
583 2012. Caffeine and sprinting performance: dose responses and efficacy. **J. Strength**
584 **Cond. Res.** 26: 1001-5.

585 Graham, T.E. 2001. Caffeine and exercise: metabolism, endurance and performance.
586 **Sports Med.** 31: 785-807.

587 Graham, T.E. and Spriet, L.L. 1991. Performance and metabolic responses to a high
588 caffeine dose during prolonged exercise. **J. Appl. Physiol.** 71: 2292-8.

589 Green, J.M., Wickwire, P.J., McLester, J.R., Gendle, S., Hudson, G., Pritchett, R.C.,
590 and Laurent, C.M. 2007. Effects of caffeine on repetitions to failure and ratings of
591 perceived exertion during resistance training. **Int. J. Sports Physiol. Perform.** 2: 250-
592 9.

593 Hoffman, J.R., Ratamess, N.A., Ross, R., Shanklin, M., Kang, J., and Faigenbaum,
594 A.D. 2008. Effect of a pre-exercise energy supplement on the acute hormonal
595 response to resistance exercise. **J. Strength Cond. Res.** 22: 874-82.

596 Jacobs, I., Pasternak, H., and Bell, D.G. 2003. Effects of ephedrine, caffeine, and their
597 combination on muscular endurance. **Med. Sci. Sports Exerc.** 35: 987-94.

598 Jacobson, B.H. and Edwards, S.W. 1991. Influence of two levels of caffeine on
599 maximal torque at selected angular velocities. **J. Sports Med. Phys. Fitness**, 31: 147-
600 53.

601 Jacobson, B.H., Weber, M.D., Claypool, L., and Hunt, L.E. 1992. Effect of caffeine on
602 maximal strength and power in elite male athletes. **Br. J. Sports Med.** 26: 276-80.

603 Magkos, F. and Kavouras, S.A. 2005. Caffeine use in sports, pharmacokinetics in
604 man, and cellular mechanisms of action. **Crit. Rev. Food Sci. Nutr.** 45: 535-62.

605 Maughan, R.J. 1999. Nutritional ergogenic aids and exercise performance. **Nutr. Res.**
606 **Rev.** 12: 255-80.

607 Munkvik, M., Rehn, T.A., Slettalokken, G., Hasic, A., Hallen, J., Sjaastad, I., Sejersted,
608 O.M., and Lunde, P.K. 2010. Training effects on skeletal muscle calcium handling in
609 human chronic heart failure. **Med. Sci. Sports Exerc.** 42: 847-55.

610 Nakagawa, S. and Cuthill, I.C. 2007. Effect size, confidence interval and statistical
611 significance: a practical guide for biologists. **Biol. Rev. Camb. Philos. Soc.** 82: 591-
612 605.

613 Nawrot, P., Jordan, S., Eastwood, J., Rotstein, J., Hugenholtz, A., and Feeley, M. 2003.
614 Effects of caffeine on human health. **Food Addit. Contam.** 20: 1-30.

615 Nehlig, A. 2010. Is caffeine a cognitive enhancer? **J. Alzheimers Dis.** 20 Suppl 1:
616 S85-94.

617 Nehlig, A., Daval, J.L., and Debry, G. 1992. Caffeine and the central nervous system:
618 mechanisms of action, biochemical, metabolic and psychostimulant effects. **Brain**
619 **Res. Brain Res. Rev.** 17: 139-70.

620 Pasman, W.J., van Baak, M.A., Jeukendrup, A.E., and de Haan, A. 1995. The effect
621 of different dosages of caffeine on endurance performance time. **Int. J. Sports Med.**
622 16: 225-30.

623 Perkins, R. and Williams, M.H. 1975. Effect of caffeine upon maximal muscular
624 endurance of females. **Med. Sci. Sports**, 7: 221-4.

625 Plaskett, C.J. and Cafarelli, E. 2001. Caffeine increases endurance and attenuates
626 force sensation during submaximal isometric contractions. **J. Appl. Physiol.** 91: 1535-
627 44.

628 Smith, A. 2002. Effects of caffeine on human behavior. **Food Chem. Toxicol.** 40:
629 1243-55.

630 Tabachnick, B.G. and Fidell, L.S. 2006. **Using multivariate statistics**: Pearson
631 Education, London.

632 Tallis, J., Duncan, M.J., and James, R.S. 2015. What can isolated skeletal muscle
633 experiments tell us about the effects of caffeine on exercise performance? **Br. J.**
634 **Pharmacol.** 172: 3703-13.

635 Tallis, J., Duncan, M.J., Wright, S.L., Eyre, E.L., Bryant, E., Langdon, D., and James,
636 R.S. 2013. Assessment of the ergogenic effect of caffeine supplementation on mood,
637 anticipation timing, and muscular strength in older adults. **Physiol. Rep.** 1: e00072.

638 Tallis, J., James, R.S., Cox, V.M., and Duncan, M.J. 2012. The effect of physiological
639 concentrations of caffeine on the power output of maximally and submaximally
640 stimulated mouse EDL (fast) and soleus (slow) muscle. **J. Appl. Physiol.** 112: 64-71.

641 Tallis, J., Muhammad, B., Islam, M., and Duncan, M.J. 2016. Placebo effects of
642 caffeine on maximal voluntary concentric force of the knee flexors and extensors.
643 **Muscle Nerve**, 54: 479-86.

644 Timmins, T.D. and Saunders, D.H. 2014. Effect of caffeine ingestion on maximal
645 voluntary contraction strength in upper- and lower-body muscle groups. **J. Strength**
646 **Cond. Res.** 28: 3239-44.

647 Van Thuyne, W., Roels, K., and Delbeke, F.T. 2005. Distribution of caffeine levels in
648 urine in different sports in relation to doping control. **Int. J. Sports Med.** 26: 714-8.

649 Warren, G.L., Park, N.D., Maresca, R.D., McKibans, K.I., Millard-Stafford, M.L. 2010.
650 Effect of caffeine ingestion on muscular strength and endurance: a meta-analysis.
651 **Med. Sci. Sports Exerc.** 42: 1375-87.

652 Williams, A.D., Cribb, P.J., Cooke, M.B., and Hayes, A. 2008. The effect of ephedra
653 and caffeine on maximal strength and power in resistance-trained athletes. **J.**
654 **Strength Cond. Res.** 22: 464-70.

655 Williams, J.H., Barnes, W.S., and Gadberry, W.L. 1987. Influence of caffeine on force
656 and EMG in rested and fatigued muscle. **Am. J. Phys. Med.** 66: 169-83.

657 Woolf, K., Bidwell, W.K., and Carlson, A.G. 2008. The effect of caffeine as an
658 ergogenic aid in anaerobic exercise. **Int. J. Sport. Nutr. Exerc. Metab.** 18: 412-29.

659 Yang, A., Palmer, A.A., and de Wit, H. (2010). Genetics of caffeine consumption and
660 responses to caffeine. **Psychopharmacology**, 211: 245-57.

661

662

664 **FIGURES**

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

668 Figure 2. The effect of 3 mg · kg⁻¹ and 6 mg · kg⁻¹ body mass caffeine treatment on
669 peak and average isokinetic concentric (A & C) and eccentric force (B & D) of the knee
670 extensor muscles at 60 and 180 deg/s [Data are represented as mean ± SE; n=10; *
671 represents statistically significant difference (P=0.033; d=0.68) between Placebo and
672 6 mg/kg caffeine; # represents statistical tendency (P=0.083; d=0.83) between
673 Placebo and 3 mg/kg caffeine]

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

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