

Placebo effects of caffeine on maximal voluntary concentric force of the knee flexors & extensors

Tallis, J. , Muhammad, B. , Islam, M. and Duncan, M.J.

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

Original citation & hyperlink:

Tallis, J. , Muhammad, B. , Islam, M. and Duncan, M.J. (2016) Placebo effects of caffeine on maximal voluntary concentric force of the knee flexors & extensors. *Muscle & Nerve*, volume 54 (3): 479-486

<http://dx.doi.org/10.1002/mus.25060>

DOI 10.1002/mus.25060

ISSN 0148-639X

ESSN 1097-4598

Publisher: Wiley

This is the peer reviewed version of the following article: Tallis, J. , Muhammad, B. , Islam, M. and Duncan, M.J. (2016) Placebo effects of caffeine on maximal voluntary concentric force of the knee flexors & extensors. *Muscle & Nerve*, volume 54 (3): 479-486, which has been published in final form at

<http://dx.doi.org/10.1002/mus.25060>

This article may be used for non-commercial purposes in accordance with Wiley Terms and Conditions for Self-Archiving.

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 **PLACEBO EFFECTS OF CAFFEINE ON MAXIMAL VOLUNTARY CONCENTRIC FORCE**
2 **OF THE KNEE FLEXORS & EXTENSORS**

3

4 Jason Tallis PhD (✉), Bilal Muhammad BSc, Mohammed Islam BSc, Michael J Duncan PhD

5

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

7 5FB, UK

8

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

10

11 **RUNNING TITLE:** Performance Enhancing Effect of Placebo

12

13 **FINANCIAL DISCLOSURE:** The project was funded by Coventry University.

14

15 **CONFLICT OF INTEREST:** None.

16

17

18

19

20

21

22

23

24

25

26

27

28

29

30

31 **PLACEBO EFFECTS OF CAFFEINE ON MAXIMAL VOLUNTARY CONCENTRIC FORCE**
32 **OF THE KNEE FLEXORS & EXTENSORS**

33

34 **ABSTRACT**

35

36 *Introduction:* We examined the placebo effect of caffeine and the combined effect of caffeine and
37 caffeine expectancy on maximal voluntary strength. *Methods:* Fourteen men completed 4 randomized
38 single-blind experimental trials: 1) Told caffeine, given caffeine (5mg.kg) (CC); 2) Told caffeine,
39 given placebo (CP); 3) Told placebo, given placebo (PP); 4) Told placebo, given caffeine (PC).
40 Maximal voluntary concentric force and fatigue resistance of the knee flexors and extensors was
41 measured using isokinetic dynamometry. *Results:* A significant and equal improvement in peak
42 concentric force was found in the CC and PC trials. Despite participants believing caffeine would
43 evoke a performance benefit, there was no effect of CP. *Conclusion:* Caffeine caused an improvement
44 in some aspects of muscle strength, however there was no additional effect of expectancy. Performance
45 was poorer in participants who believed caffeine would have the largest benefit, which highlights a link
46 between expected ergogenicity, motivation, and personality characteristics.

47

48 **KEY WORDS:** Strength, Isokinetic Dynamometry, Ergogenic Aids, Deception, Caffeine, Placebo.

49

50

51

52

53

54

55

56

57

58

59

60

61 INTRODUCTION

62

63 The popularity of caffeine as an ergogenic aid is supported by a growing body of literature that
64 demonstrates its performance-enhancing effects across a range of sporting activities and exercise
65 intensities (See reviews ¹⁻⁴) Recently, a relatively small number of studies have shown that the
66 expectation of caffeine is sufficient to elicit a performance-enhancing response, when in fact a placebo
67 was consumed (⁵⁻⁹). Such findings highlight an important additional mechanism underpinning the
68 performance-enhancing effect of caffeine. To date, placebo effects of caffeine have only been
69 examined using a limited range of exercise modes and intensities. Consequently, there is a need for
70 additional studies on this topic to better elucidate the extent to which the expectancy of performance-
71 enhancement of caffeine or the actual effect of caffeine ingestion contribute to improved exercise
72 performance.

73

74 The placebo effect is a favorable outcome arising purely from the belief that one has received a
75 beneficial treatment (¹⁰). Although not a particularly new concept, the placebo effect has been
76 demonstrated to be a powerful tool for manipulating physiological, psychological, and behavioral
77 variables, (¹¹) and its positive effects in medicine are widely appreciated (¹²). A recent meta-analysis
78 considered that, although only a relatively small number of studies have examined the placebo effect
79 on sports performance, different forms of placebo may evoke substantial performance enhancement (¹³).

80

81 Likely due to its widespread use and well documented effects as an ergogenic aid (¹), a relatively small
82 number of research papers have examined the placebo effect on sports performance in relation to
83 caffeine (see review ¹⁴). Beedie *et al.* (⁵) reported that a caffeine placebo caused increased mean power
84 during 10km time trial performance in well trained cyclists, which was greatest when participants
85 believed they had ingested a higher concentration of caffeine. This was later supported by Foad,
86 Beedie, and Coleman (⁶), who demonstrated that caffeine, and the perception of consuming caffeine,
87 caused small improvements in 40km cycling performance. Work by Foad, Beedie, and Coleman (⁶) and
88 Duncan (⁹) represent only a small number of research papers that have used a double dissociation
89 protocol to assess the placebo effect of caffeine. This design allows the assessment of independent
90 effects of placebo, the pharmacological effects of the treatment, and their interaction, and is considered

91 to be a more robust measure of placebo effects ⁽¹²⁾. Duncan ⁽⁹⁾ demonstrated a significant increase in
92 mean and peak Wingate power when participants consumed placebo that they believed to be caffeine,
93 and a further improvement was seen when participants consumed caffeine that they perceived to be
94 caffeine. This indicates that the expectation of caffeine could be an ecologically valid mechanism for
95 the caffeine effect in sport and exercise, but this has still to be measured in relation to maximal muscle
96 strength.

97

98 Using a more traditional protocol of deception, Pollo *et al.* ⁽⁷⁾ demonstrated that when compared to a
99 non-ergogenic placebo, there was a significant increase in the mean work of the quadriceps muscle
100 during a 60% 1RM (Rep Max) protocol to voluntary exhaustion in participants who believed they had
101 consumed a high dose of caffeine. Interestingly, the placebo-induced increase in work was greater
102 when a conditioning procedure, consisting of a pre-test lifting protocol which was surreptitiously
103 lowered to 45% 1RM, was used to reinforce the placebo effect. This result was later confirmed by
104 Duncan *et al.* ⁽⁸⁾ who reported a significant increase in the number of knee extensions until failure,
105 using a similar 60% 1RM protocol, when participants perceived they had consumed caffeine. These
106 results further demonstrated that the increase in performance was associated with a reduction in Rating
107 of Perceived Exertion (RPE), indicating that a caffeine-induced reduction in the perception of effort
108 may mechanistically contribute to the demonstrated improvement in performance.

109

110 The majority of studies of the effect of caffeine on exercise performance have implemented a placebo
111 controlled double blind experimental protocol ⁽¹⁵⁻¹⁸⁾, and although this is considered the most robust
112 way of examining the effect of caffeine on performance, such products are purchased by consumers
113 with the expectancy of an improvement in performance which may pose additional benefits to the
114 typical cognitive and physiological changes evoked by caffeine consumption ^(19, 20). Beedie ⁽²¹⁾
115 considered that such placebo controlled trials may mask the true caffeine effect. The pharmacologically
116 and mechanistically inert placebo may evoke psychological responses, as participants expect to
117 consume caffeine at some point during the experiment.

118

119 The study we report here looks to build on previous work by investigating the placebo effect of
120 caffeine on maximal voluntary peak and average concentric force of the knee flexor and extensor

121 muscles at two different angular velocities. A double deception protocol, as in Beadie and Foad ⁽¹²⁾,
122 was implemented to assess the placebo effect of caffeine and the effect of caffeine expectancy on
123 maximal voluntary force production of skeletal muscle. Furthermore this study investigated the placebo
124 effect of caffeine and the effect of caffeine expectancy on the ability to produce maximal voluntary
125 concentric force over 40 repeated contractions. Gains in maximal muscle strength and the ability to
126 sustain this improvement over time would be desirable across a range of sport and exercise activities.
127 In addition, improved maximal voluntary force production may translate to improved performance
128 across a range of contractile intensities, as skeletal muscle will theoretically be able to produce the
129 desired force at lower intensities with a smaller number of recruited fibers.

130

131

132

133

134

135

136

137

138

139

140

141

142

143

144

145

146

147

148

149

150

151 **METHODS**

152

153 *Participants*

154

155 Following ethical approval from the host institute (Coventry University) and obtaining informed
156 consent, 14 apparently healthy men (mean \pm SE = age 21 ± 0.7 years; height 177 ± 1.3 cm; body mass
157 76 ± 2.2 kg) agreed to take part in the study. Participants were told that they would be taking part in a
158 study examining the repeatability of the effects of caffeine on maximal muscular strength and
159 fatigability of maximal voluntary force production. Over the duration of the experiment, 3 participants
160 had to withdraw from the study due to injuries that were not associated with the experimental
161 procedure. The participants who completed the tests were naive to strength training and habitually
162 consumed caffeine, but were not heavy caffeine users (91.8 ± 16.1 mg/day). Caffeine intake was
163 measured using a 24 hour recall questionnaire ⁽²²⁾.

164

165 All experiments took place at the same time of day to avoid circadian variation ⁽²³⁾, and participants
166 were asked to abstain from high intensity activity and caffeine 48 hours prior to each visit to the
167 laboratory. Participants visited the laboratory at Coventry University on 5 occasions, and each visit was
168 separated by at least 48 hours.

169

170 *Familiarization*

171

172 In the first visit heavy clothing and shoes were removed, and measures of height (cm) and mass (kg)
173 were taken to the nearest cm and 100g, using a stadiometer (SECA Instruments Ltd., Germany) and
174 electronic weighing scales (SECA Instruments Ltd., Germany). Participants were then familiarized
175 with isokinetic dynamometry (Kin-com 125 AP, Chattanooga, Tennessee, USA) and the experimental
176 procedure.

177

178 Similar to the study by Green *et al.* ⁽²⁴⁾, participants completed a 5 minute warm-up on a cycle
179 ergometer (Monark 857E, United States) at 70 rpm (unloaded cradle), followed by 5 minutes of static
180 and dynamic stretches of the muscle groups involved (gastrocnemius, soleus, hamstrings, and

181 quadriceps). Participants then used the warm-up feature on the isokinetic dynamometer and were
182 instructed to perform concentric extension and flexion of the knee at a moderate intensity. The
183 isokinetic dynamometer was set up in accordance with the manufacturer's instructions, and the lateral
184 femoral epicondyle and lateral malleolus were used as the anatomical reference points for the knee and
185 ankle ⁽²⁵⁾. Dynamometer head and seat position for each individual were stored and recalled for each
186 subsequent visit. Maximal voluntary peak and average concentric force during knee flexion and
187 extension of the dominant leg were reordered through a range of motion of 80⁰-10⁰, at velocities of 30⁰
188 and 120⁰/second. Each velocity was separated by 60 seconds recovery. Maximal voluntary force was
189 achieved with 2-3 attempts, which is common for this type of testing ⁽²⁵⁾. Following a 10 minute rest
190 period, participants then performed a bout of 40 repetitions of knee extension and flexion of the
191 dominant leg at a velocity of 120⁰/second in the same manner as previously described. Peak and
192 average force for knee extension and flexion were recorded for each repetition.

193

194 *Experimental Procedure*

195

196 Prior to participation, and before each trial where participants believed caffeine would be consumed, a
197 brief synopsis of the performance-enhancing effects of caffeine on measures of maximal strength was
198 provided verbally. Participants completed 4 experimental trials in a counterbalanced, randomized
199 format using a single blind, double-disassociation procedure. This has previously been used in studies
200 of the placebo effect on sports performance ⁽¹²⁾. The experimental conditions were as follows: 1) Told
201 caffeine, given caffeine (CC); 2) Told caffeine, given placebo (CP); 3) Told placebo, given placebo
202 (PP); 4) Told placebo, given caffeine (PC). Caffeine drinks contained 5 mg/kg body mass of caffeine
203 (Myprotein, UK) diluted in 4 ml/kg water and 1ml/kg double concentrate sugar free orange cordial
204 (Sainsbury's, UK), and were artificially sweetened with 3mg/kg sucralose (Myprotein, UK). Five
205 mg/kg represents a moderate caffeine dose and is regularly used in studies examining its ergogenic
206 effect on sports performance ^(15, 17, 18). Placebo drinks were prepared in the same way with the absence
207 of caffeine. Following a 10 minute rest period and resting measures of Heart Rate (HR; measured in
208 bpm) and Blood Lactate (BLa; measured in mmol/l), drinks were presented to participants in an opaque
209 sports bottle and were asked to consume the contents within 5 minutes. HR was assessed using heart
210 rate telemetry (Polar Electro, Finland), and BLa was measured from a finger prick sample using a

211 Lactate Pro (Akray, Japan). The participants then rested for 45 minutes, and resting HR and BLA
212 measures were taken. Following this, the participants completed the warm up procedure as previously
213 described. The strength assessments began 60 minutes post-ingestion in line with previous evidence
214 that demonstrates maximal blood plasma concentration of caffeine occurs 1 hour post-consumption
215 (Graham *et al.* 2001). The strength assessments were carried out using the isokinetic dynamometer in
216 the same manner as previously described. Further HR and BLA measures were taken prior to the 40
217 repeated contractions, on completion of the exercise protocol, and 5 minutes post-recovery. Pain
218 perception was recorded immediately after assessment of maximal voluntary force at both 30⁰ and
219 120⁰/second and again immediately after the 40 contractions using the pain perception scale ⁽²⁶⁾.

220

221 *Perception of Caffeine as a Performance Enhancer*

222

223 Prior to the experimental protocol, participants were asked to rate the extent to which they believed
224 caffeine would affect their performance on a scale from -5, a very negative effect, to +5, a very positive
225 effect. Following the experimental trials, but prior to debriefing, participants were asked to rate their
226 belief about caffeine for a second time to see if the experimental protocol affected the participants'
227 perception of caffeine as a performance enhancer. At no point during any of the experimental trials did
228 participants correctly identify the test substance consumed or the true nature of the study.

229

230 *Statistical Method*

231

232 Normality and homogeneity of variance were tested using Shapiro–Wilk and Mauchly tests
233 respectively. A series of Treatment (4) X Speed (2) repeated measures ANOVAs were used to examine
234 statistical differences in peak and average concentric force of the knee flexors and extensors, and the
235 perception of pain following the measurement of contractile force. Similarly, Treatment (4) x Rep (40)
236 repeated measures ANOVAs were used to assess potential treatment-induced changes in peak and
237 average force produced during the repeated 40 contraction protocol. A further series of Treatment (4) x
238 Time (4) repeated measures ANOVAs were used to assess changes in HR and BLA at rest and during
239 exercise. Finally, single factor repeated measures ANOVA was used to examine main effects for
240 perception of pain. Pairwise comparisons were used for treatment where appropriate. Partial eta

241 squared (η^2) was used as a measure of effect size. Partial η^2 is commonly used in analysis of variance
242 and provides a measure of the variance in the dependant variable attributable to the factor in question
243 ⁽²⁷⁾.

244

245 A paired *t*-test was used to examine if the perception of caffeine as a performance enhancer changed
246 significantly post-completion of the experimental trials. Following the debriefing session, no
247 participant confessed to have predicted the true nature of the experiment. Considering that the
248 perception of a performance-enhancing benefit underpins the nature of the placebo effect, it was
249 considered important to examine these results on an individual level. The percentage change in
250 maximal peak and average force from the PP trial to the CP trial was calculated and a series of Pearson
251 correlations were used to examine the relationship between maximal voluntary strength and the score
252 given on the post-experimental caffeine perception questionnaire.

253

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

256

257

258

259

260

261

262

263

264

265

266

267

268

269

270

271 **RESULTS**

272

273 *Maximal Peak & Average Force*

274

275 There was no significant treatment*speed interaction for peak and average knee flexor and extensor
276 force in any of the statistical tests (Fig 1; ANOVA $F < 1.4$; $P > 0.27$; $P\eta^2 < 0.12$ in each case). Peak and
277 average concentric force production of the knee flexors and extensors was significantly reduced at
278 $120^\circ/s$ compared to $30^\circ/s$ (Figure 1 A-D; ANOVA $F > 20$; $P < 0.001$; $P\eta^2 > 0.66$ in all cases).

279

280 Peak concentric force of the knee extensors was significantly affected by treatment (Figure 1 A;
281 ANOVA $F = 8.3$; $P < 0.01$; $P\eta^2 = 0.454$). Peak force produced during the PC and CC trial was
282 significantly greater than the PP trial (by 12.8% and 15.8% respectively at $30^\circ/\text{second}$ and 6.8% and
283 11.2% respectively at $120^\circ/\text{second}$; Figure 1 A, pairwise $P < 0.05$ in both cases), but the given increase
284 in force was not different between PC and CC trials (Figure 1 A, t -test $P > 0.6$ for both speeds). Average
285 force was also significantly affected by treatment (Figure 1 B, ANOVA $F = 5.8$; $P = 0.003$; $P\eta^2 = 0.37$),
286 with that produced in the CC trial being significantly greater than PP (by 18.0% and 14.4% at 30° and
287 $120^\circ/\text{second}$; Figure 1 B; pairwise $P = 0.02$). Peak and average force of the hamstrings was not
288 significantly affected by treatment (Figure 1 C,D; $F < 0.17$; $P > 0.74$; $P\eta^2 < 0.04$ in both cases).

289

290 There was no significant effect of treatment, speed, or interaction of these factors for measurements of
291 pain perception (Table 1; ANOVA $F < 2.4$; $P > 0.08$; $P\eta^2 < 0.2$ in each case).

292

293 *** Figure 1 and Table 1 around here ***

294

295 *Repeated Maximal Voluntary Contractions*

296

297 Both peak and average force of the knee extensors and flexors was significantly reduced over the
298 course of the 40 repeated contraction protocol (Figures 2&3; $F > 51.5$; $P < 0.001$; $P\eta^2 > 0.83$ in all cases),
299 however there was no significant effect of treatment (Figures 2&3; $F < 1.05$; $P > 0.38$; $P\eta^2 < 0.095$ in all

300 cases). Furthermore there was no significant treatment*rep interaction in all cases (Figures 2&3; $F < 1.3$;
301 $P > 0.06$; $P\eta^2 < 0.12$).

302 *** Figure 2 & 3 around here ***

303

304 Although HR and BLa were both significantly affected by time (Table 2; ANOVA $F > 36.7$; $p < 0.001$;
305 $P\eta^2 > 0.78$ in each case), no effects of treatment were found (Table 2: ANOVA $F < 0.3$; $p > 0.83$;
306 $P\eta^2 < 0.03$ in each case). There was no significant Treatment*Time interaction (Table 2; ANOVA
307 $F < 1.3$; $p > 0.27$; $P\eta^2 < 0.11$). Furthermore the perception of pain was not significantly affected by
308 treatment (Table 1; ANOVA $F = 1.01$; $p = 3.99$; $P\eta^2 = 0.092$).

309

310 *** Table 2 around here ***

311

312 *The Effect of Caffeine Perception on Performance.*

313

314 Prior to participating in the experimental protocol, all participants believed that the consumption of
315 caffeine would result in improved exercise performance (mean $+3.09 \pm 0.435$), which had not
316 significantly changed at the end of the protocol (mean $+3.18 \pm 0.423$, paired samples t -test $t = -1.00$
317 $P = 0.341$). Table 3 demonstrates that when participants considered caffeine to be more beneficial to
318 performance, there was a negative association with performance in the CP trial, although this was only
319 significant in peak force of the knee extensors measured at $120^\circ/\text{second}$.

320

321 *** Table 3 around here ***

322

323

324

325

326

327

328

329

330 **DISCUSSION**

331

332 Regardless of expectation, caffeine treatment caused a significant increase in peak concentric force of
333 the knee extensors. There were no caffeine or caffeine placebo effects on maximal peak and average
334 force of the knee flexors, or the ability of the knee flexors and extensors to maintain peak and average
335 force over 40 repeated contractions. These findings add further weight to the evidence which suggests
336 that caffeine may be used as an ergogenic aid in events requiring acute maximal strength, but they
337 demonstrate that the perception of caffeine is not sufficient to elicit a performance-enhancing effect in
338 this mode of exercise. As such these results provide an important insight into the relationship between
339 physiological and psychological effects of caffeine as a performance enhancer for skeletal muscle
340 contractility

341

342 *Placebo Effect of Caffeine*

343

344 The findings contradict the previous evidence that a caffeine placebo can cause a significant increase in
345 exercise performance ^(6-9, 21). More specifically, these results directly contradict the findings of Pollo *et*
346 *al.* ⁽⁷⁾ and Duncan ⁽⁸⁾, who reported a caffeine placebo caused significant improvements in measures of
347 muscle work and repetitions until failure using a 60% 1RM protocol. Initially this may indicate that the
348 mechanism by which a placebo elicits its effect is in some way limited during activities requiring
349 sustained maximal effort. Although few studies have examined a placebo effect on measures of
350 maximal strength, there is some evidence that a performance benefit can be elicited following acute
351 and chronic supplementation of different placebos, where an increased performance is expected ^(28, 29).

352

353 Beyond the work of Kalasountas *et al.* ⁽²⁹⁾ there is a distinct lack of evidence investigative the effect of
354 an acute placebo on maximal strength. Furthermore, a number of methodological discrepancies should
355 be considered when comparing the present findings to the positive effect demonstrated in previous
356 studies examining placebo effects on measures of muscular strength ^(7, 8, 28, 29). Most notably a number
357 of studies use submaximal measures of strength, and the use of free weights is mechanically different
358 for assessing strength at a fixed velocity. Additionally, differences occur in the nature and duration of
359 the placebo and the ability of the participants, cumulatively making comparisons between these studies

360 problematic. Furthermore an experimental effect is more likely in open-ended tests of muscle strength
361 (as in ^{7, 9}) compared to the fixed-end test we used⁽³⁰⁾.

362

363 The effectiveness of the placebo to elicit a performance-enhancing effect is attributed to the perception
364 that one believes that a performance-enhancing benefit will occur ⁽¹⁰⁾. Geers *et al.* ⁽³¹⁾ concluded that
365 personality and situational variables interact to determine the response to a placebo, and that perceived
366 optimism or pessimism will result in a positive or negative placebo response. When the results are
367 explored on an individual level, all participants believed that caffeine would cause a performance-
368 enhancing effect, however this did not result in a significant change in maximal voluntary strength
369 when the CP trial was compared to the PP trial. Interestingly, these results infer that when the benefit is
370 perceived to be small, the placebo effect is greater, and when the benefit is perceived to be large, the
371 placebo effect is smaller. This may appear to contradict the underpinning theory that supports the
372 placebo effect, and although the rationale for this is not clear, we speculate that this finding may relate
373 to individual motivation to complete the task. For example, the belief that the consumed substance will
374 cause a significant improvement in maximal voluntary strength may result in reduced effort, as a high
375 performance is expected. In light of these findings, more should be made of the reinforcement
376 approach introduced by Pollo *et al.* ⁽⁷⁾, as having a physical demonstration of the effectiveness of the
377 treatment, albeit false, may more strongly manipulate the power of perception.

378

379 Mechanistically, the placebo effect can in part be attributed to its effect on modulating pain perception
380 ^(5, 9). In support of this, some previous studies have demonstrated positive effects of a caffeine placebo
381 on RPE in relation to improvements in exercise performance that may underpin this as a mechanism for
382 the placebo effect in sporting activities. Contradictory findings in our study demonstrate that the
383 perception of pain is unchanged when a perceived performance-enhancing placebo is administered.
384 This may not be particularly surprising, since there was no effect of placebo on exercise performance,
385 but it may leave one to speculate that the lack of effect may be attributed to a lack of change in this
386 measure.

387

388 *The Effect of Caffeine on Maximal Strength*

389

390 The only significant effect of treatment found in this study was a caffeine-induced improvement in
391 peak and average concentric force of the knee flexors. Interestingly, even when the participants
392 believed they were completing a placebo trial, caffeine still caused a significant and equal increase in
393 maximal concentric force of the quadriceps. This result in particular supports the value of caffeine in
394 improving maximal voluntary force; however this effect cannot be maintained during repeated
395 contractions. Furthermore, the results demonstrate that this effect is not uniform across all skeletal
396 muscle.

397

398 Unlike the research investigating the performance enhancing effect of caffeine on endurance exercise,
399 the body of work exploring the ergogenic effect of caffeine on measures of muscle strength are much
400 more equivocal, with evidence of both substantial strength gains ⁽³²⁻³⁴⁾ and no effect ⁽³⁵⁻³⁷⁾. The nature of
401 these discrepancies has largely been attributed to methodological differences, including participant
402 training status, assessment methods, muscle groups tested, and concentration of caffeine. Although it is
403 generally considered that caffeine elicits greater effects in trained athletes ⁽⁴⁾, our study further
404 demonstrates the value for untrained participants.

405

406 Although not statistically significant, Timmins and Saunders ⁽³⁸⁾ suggested that the benefit of caffeine
407 on muscle strength may relate to muscle size. This may partially be why there was no effect of caffeine
408 on the knee flexors, although Timmins and Saunders ⁽³⁸⁾ demonstrated performance-enhancing benefits
409 in muscles much smaller than the hamstrings. Furthermore, studies using isolated muscle have
410 demonstrated fiber type specific effects on contractility following direct caffeine treatment ⁽³⁹⁾ which
411 may have also caused the varying effect. It may also be that the action of producing maximal voluntary
412 concentric force of the hamstrings is a more irregular muscle action, and hence the repeatability of
413 maximal force between trials may influence the results.

414 There is a distinct lack of studies of the effects of caffeine on the ability to sustain force over repeated
415 contractions. Although our findings infer that there is no additional caffeine benefit, caffeine-induced
416 increases in maximal voluntary force production may translate into improved resistance to fatigue at
417 submaximal exercise intensities, as theoretically the muscle will be able to produce greater work with a
418 smaller number of recruited fibers.

419

420 The hydrophobic nature of caffeine allows it to pass across all biological membranes ⁽¹⁹⁾, and as such,
421 caffeine may elicit a performance-enhancing effect by a number of mechanisms. Most commonly
422 reported, and aligned to the mode of exercise used in this study, is the action of caffeine as a central
423 nervous system stimulant. Caffeine has been demonstrated to act as a central adenosine receptor
424 antagonist, particularly on A1 and A2a receptors, promoting an elevated release of neurotransmitters
425 ⁽⁴⁰⁻⁴²⁾. The subsequent reduction in the adenosine-induced suppression of dopamine release ^(43, 44) is
426 believed to contribute to the commonly reported increased alertness and arousal ⁽²⁰⁾. In addition, a
427 recent review ⁽³⁹⁾ has indicated that caffeine may work directly to increase the force-producing capacity
428 of skeletal muscle. A reduction in pain perception has also been attributed to the performance gains
429 demonstrated in previous studies of caffeine-induced improvements in muscle strength ^(3, 45, 46).
430 However, our findings add to the growing body of evidence indicating that modulation of pain
431 perception is not a primary mechanism causing performance-enhancement in muscle strength ^(47, 48).

432

433 An additional aim of this work was to examine whether caffeine expectancy caused a further
434 enhancement in performance. This is considered a more ecologically valid method of testing the
435 caffeine effect on sports performance, as caffeine-containing products are purchased with the intention
436 of seeking an improvement in exercise performance. As no significant difference was found in the
437 improvement in the concentric action of knee flexors and extensors between the CC and PC trials, or in
438 any of the placebo trials, we believe that caffeine expectancy does not further augment the
439 physiological and psychological benefits provided by caffeine alone.

440

441 *Conclusion*

442

443 In contrast to previous studies using different modes of exercise, the present work demonstrates that a
444 caffeine placebo fails to elicit a performance enhancing effect on measures of maximal voluntary
445 strength. These findings are particularly interesting, since all participants believed that caffeine
446 treatment would lead to a substantial improvement in performance. Uniquely, we found that
447 participants who perceived the performance effect to be greater demonstrated the smallest change in
448 performance in the exercise trial, which potentially highlights a link between expected ergogenicity,
449 motivation to perform high intensity fatiguing exercise, and personality characteristics. These findings

450 further demonstrate that caffeine treatment caused significant improvement in some aspects of acute
451 maximal voluntary strength. When caffeine treatment and caffeine expectancy were combined, there
452 was no additional benefit. These findings highlight the importance of the mechanistic changes caused
453 by caffeine to evoke an improvement in performance, however when a perceived treatment-induced
454 enhancement of performance is expected, this does not necessarily translate to improved exercise
455 performance. Future research examining the placebo effect should look to further investigate the
456 relationship between the magnitude of the perceived benefit and exercise performance.

457

458

459

460

461

462

463

464

465

466

467

468

469

470

471

472

473

474

475

476

477

478

479

480 **ABBREVIATIONS**

481

η^2	Partial eta squared
$^{\circ}$	Degrees
ANOVA	Analysis of Variance
BLa	Blood Lactate
CC	Told Caffeine, Given Caffeine
Cm	Centimetres
CP	Told Caffeine, Given Placebo
Fig	Figure
HR	Heart Rate
Km	Kilometres
Mg	Milligrams
ml	Millilitre
mmol/l	millimole per litre
PC	Told Placebo, Given Caffeine
PP	Told Placebo, Given Placebo
RM	Rep Max
RPE	Rating of Perceived Exertion
SE	Standard Error of the Mean
SPSS	Statistical Package for the Social Science

482

483

484

485

486

487

488

489

490

491

492

493

494

495

496

497

498

499

500

501

502 **REFERENCES**

- 503 1. Graham TE. Caffeine and exercise. Metabolism, endurance and performance' J Sports Med
504 2001; 31:785-807.
- 505
- 506 2. Davis JK, Green JM. Caffeine and anaerobic performance: Ergogenic value and mechanisms
507 of action. J Sports Med 2009; 39:813-832.
- 508
- 509 3. Goldstein ER, Ziegenfuss T, Kalman D, Kreider R, Campbell B, Wilborn C, et al.
510 International society of sports nutrition position stand; caffeine and performance. J Int Soc
511 Sports Nutr, 2010; 7:1-15.
- 512
- 513 4. Astorino TA, Roberson DW. Efficacy of acute caffeine ingestion for short-term high-intensity
514 exercise performance: a systematic review. J Strength Cond Res 2010; 24:257-265.
- 515
- 516 5. Beedie CJ, Stuart EM, Coleman DA, Foad AJ. Placebo effect of caffeine in cycling
517 performance. Med Sci Sports Exerc 2006; 38:2159–2164.
- 518
- 519 6. Foad AJ, Beedie CJ, Coleman DA. Pharmacological and psychological effects of caffeine
520 ingestion in 40-km cycling performance. Med Sci Sports Exerc 2008; 40:158-165.
- 521
- 522 7. Pollo A, Carlino E, Benedetti F. The top-down influence of ergogenic placebos on muscle
523 work and fatigue. Eur J Neurosci 2008; 28:379-388.
- 524
- 525 8. Duncan M J, Lyons M, Hankey J. Placebo effects of caffeine on short-term resistance exercise
526 to failure. Int J Sports Physiol Perform 2009; 4:244-253.
- 527
- 528 9. Duncan MJ. Placebo effects of caffeine on anaerobic performance in moderately trained
529 adults. Serb J Sports Sci 2010; 4:99-106
- 530
- 531 10. Clark V, Hopkins W, Hawley J, Burke L. Placebo Effect of Carbohydrate Feedings during A
532 40-Km Cycling Time Trial. Med Sci Sports Exerc 2000; 1642-1647.
- 533
- 534 11. Evans D. Placebo: The Belief Effect. London: Harper Collins. 2003 p 25-43.
- 535
- 536 12. Beedie CJ, Foad AJ. The Placebo Effect in Sports Performance. J Sports Med 2009; 39: 313-
537 329.
- 538
- 539 13. Berdi M, Kotele F, Szabo A, Bardos G. Placebo effects in sport and exercise. Eur J Mental
540 Health, 2011; 6:196-212.
- 541
- 542 14. Beedie CJ. All in the mind? Pain, placebo effect, and ergogenic effect of caffeine in sports
543 performance. Sports Med 2010 (open access)
- 544
- 545 15. Collomp K, Ahmaidi S, Audran M, Chanal JL, Prefaut C. Effects of caffeine ingestion on
546 performance and anaerobic metabolism during the wingate test. Int J Sports Med 1991;
547 12:439-443.
- 548
- 549 16. Bruce CR, Anderson ME, Fraser SF, Stepto NK, Klein R, Hopkins WG, et al. Enhancement of
550 2000-m rowing performance after caffeine ingestion. Med Sci Sport Exerc 2000; 32:1958-
551 1963.
- 552
- 553 17. Bell DG, Mcllellan TM. Exercise endurance 1, 3, and 6 hours after caffeine ingestion in
554 caffeine users and non-users. J Appl Physiol 2002; 93:1227-1234.
- 555
- 556 18. O'Rourke MP, O'Brien BJ, Knez WL, Paton CD. Caffeine has a small effect on 5-km running
557 performance of well-trained and recreational runners. J Sci Med Sport 2006; 11:231-233.
- 558
- 559 19. Magkos F, Kavouras SA. Caffeine use in sports, pharmacokinetics in man, and cellular
560 mechanisms of action. Crit Rev Food Sci Nutr, 2005; 45:535-562.

- 561
562
563
564
565
566
567
568
569
570
571
572
573
574
575
576
577
578
579
580
581
582
583
584
585
586
587
588
589
590
591
592
593
594
595
596
597
598
599
600
601
602
603
604
605
606
607
608
609
610
611
612
613
614
615
616
617
618
619
620
20. Nehlig A. Is caffeine a cognitive enhancer? *J Alzheimer Dis* 2010; 20:85-94.
 21. Beedie CJ. Placebo effects in competitive sport: Qualitative data. *J Sports Sci Med* 2007; 6:21-28.
 22. Maughan RJ. Nutritional ergogenic aids and exercise performance. *Nutr Res Rev* 1999; 12:225-280.
 23. Atkinson G, Reilly T. Circadian Variation in Sports Performance' *Sports Med* 1996; 21:292-312.
 24. Green J, Wickwire P, McLester J, Gendle S, Hudson G, Pritchett R, et al. Effects of Caffeine on Repetitions to Failure and Ratings of Perceived Exertion During Resistance Training. *Int J Sports Physiol Perform* 2007; 2:250-259.
 25. Bond V, Gresham M, McRae M, Tearney R. Caffeine Ingestion and Isokinetic Strength. *Br J Sports Med* 1986; 20:135-137.
 26. Cook D, O'Connor P, Oliver S, Lee Y. Sex Differences in Naturally Occurring Leg Muscle Pain and Exertion during Maximal Cycle Ergometry. *Int J Neurosci* 1998; 95:183-202.
 27. Tabachnick BG, Fidell LS. Using multivariate statistics. Fifth Edition. Pearson Education, London. 2007.
 28. Maganaris CN, Collins D, Sharp M. Expectancy effects and strength training: do steroids make a difference? *Sport Psych* 2000; 14:272-278.
 29. Kalasountas V, Reed J, Fitzpatrick J. The effect of placebo-induced changes in expectancies on maximal force production in college students. *J Appl Psych* 2007; 19:116-124.
 30. Warren G, Park N, Maresca R, Mckibans K, Millard-Stafford M. Effect of Caffeine Ingestion on Muscular Strength and Endurance. *Med Sci Sports Exerc* 2010; 42:1375-1387.
 31. Geers A, Helfer S, Kosbab K, Weiland P, Landry S. Reconsidering the role of personality in placebo effects: Dispositional optimism, situational expectations, and the placebo response. *J Psychosom Res* 2005; 58:121-127.
 32. Forbes SC, Candow DG, Little JP, Magnus C, Chillibeck, PD. Effect of red bull energy drink on repeated wingate cycle performance and bench press muscle endurance. *Int J Sport Nutr Exerc Metab* 2007; 17:433-444.
 33. Beck TW, Housh TJ, Schmidt RJ, Johnson GO, Housh DJ, Coburn JW, et al. The acute effects of a caffeine-containing supplement on strength, muscular endurance, and anaerobic capabilities. *J Strength Cond Res* 2006; 20:506-510.
 34. Hoffman JR, Ratamess NA, Ross R, Shanklin M, Kang J, Faigenabum AD. Effect of pre-exercise energy supplement on the acute hormonal response to resistance exercise. *J Strength Cond Res* 2008; 22:874-822.
 35. 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; 99:2302-2306.
 36. Beck TW, Housh TJ, Malek M H, Mielke M, Hendrix R. The acute effects of a caffeine-containing supplement on bench press strength and time to exhaustion. *J Strength Cond Res* 2008; 22:1654-1658.
 37. Astorino TA, Rohmann RL, Firth K. Effect of caffeine ingestion on one repetition maximum muscular strength. *Eur J Appl Physiol* 2008; 102:127-132.

- 621
622 38. Timmins TD, Saunders DH. Effect of Caffeine Ingestion on Maximal Voluntary Contraction
623 Strength in Upper- and Lower-Body Muscle Groups. *J Strength Cond Res*, 2014; 11:3239-
624 3244.
625
626 39. Tallis J, Duncan M, James R. What Can Isolated Skeletal Muscle Experiments Tell Us About
627 The Effects Of Caffeine On Exercise Performance? *Br J Pharmacol*, 2015; 172 : 3703-3713
628
629 40. Fredholm BB, Battif K, Holmen J, Nehlig AN, Zvartau EE. Actions of caffeine in the brain
630 with special reference to factors that contribute to its widespread use. *Pharmacol Rev*, 1999;
631 51:83-133.
632
633 41. Garrett BE, Griffiths RR. The role of dopamine in the behavioural effects of caffeine in
634 animals and humans. *Pharmacol Biochem Be*, 1997; 57: 533-541.
635
636 42. Ribeiro JA, Sebastião AM. Caffeine and Adenosine. *J Alzheimers Dis*, 2010; 20: 3-15.
637
638 43. Okada M, Kiryu K, Kawata Y, Mizuno K, Wada K, Tasaki H, et al. Determination of the
639 effects of caffeine and carbamazepine on striatal dopamine release by in vivo microdialysis.
640 *Eur J Pharmacol*, 1997; 26: 181-188
641
642 44. Davis JM, Zhao Z, Stock HS, Mehl KA, Buggy J, Hand GA. Central nervous system effects
643 of caffeine and adenosine on fatigue. *Am J Physiol Regul Integr Comp Physiol*, 2003; 287:
644 399-404.
645
646 45. Doherty M, Smith P, Hughes MG, Davison RC. Caffeine lowers perceptual response and
647 increases power output during high intensity cycling. *J Sports Sci* 2004; 22: 637-643.
648
649 46. Doherty M, Smith P. Effects of caffeine ingestion on the rating of perceived exertion during
650 and after exercise: A Meta-analysis. *Scand J Sports Med Sci Sports* 2005; 15:69-78.
651
652 47. Jacobs I, Pastemak H, Bell DG. Effects of ephedrine, caffeine, and their combination on
653 muscular endurance. *Med Sci Sports Exerc* 2003; 35:987-994.
654
655 48. Duncan MJ, Oxford SO. The effect of caffeine ingestion on mood state and bench press
656 performance to failure *J Strength Cond Res* 2011; 25:178-185.
657
658
659
660
661
662
663
664
665
666
667
668

669 **FIGURES**

670 Figure 1. The placebo effect of caffeine on peak and average maximal voluntary concentric contractile
671 force of the knee extensor (A & B) and flexor muscles (C & D) at 30⁰ and 120⁰/s [Data are represented
672 as mean \pm SE; n=11 in each case; matching symbols indicate statistically significant differences]

673

674 Figure 2. The placebo effect of caffeine on peak (A) and average (B) concentric force of the knee
675 extensors over 40 repeated maximal voluntary contractions. [Data represented as mean \pm SE; n=11 in
676 each case]

677

678 Figure 3. The placebo effect of caffeine on peak (A) and average (B) concentric force of the knee
679 flexors over 40 repeated maximal voluntary contractions. [Data represented as mean \pm SE; n=11 in
680 each case]

681

682

683

684

685

686

687

688

689

690

691

692

693

694

695

696

697

698

699 TABLES

Table 1. The placebo effect of caffeine on pain perception following maximal voluntary isokinetic force of the knee flexors and extensors measured at 30, 120, and 40 repeated contractions

	30°/s	120°/s	Post 40
PP	2.5±0.6	2.1±0.6	6±0.6
CP	2.3±0.4	1.7±0.5	7±0.6
PC	2.1±0.5	2.5±0.6	6±0.6
CC	1.8±0.4	2.5±0.5	6±0.6

700 [Data represented as mean ± SE; n=11 in each case]

701

702

703

704

705

706

707

708

709

710

711

712

713

714

715

716

717

718

719

720

Table 2. The placebo effect of caffeine on resting and post exercise measures of HR and BLa

	Pre-Ing	Post-Ing	Pre 40 reps	Post 40 reps	5 min post
<i>HR (BPM)</i>					
PP	71±5	75±6	89±5	147±7	101±6
CP	69±4	73±4	85±5	151±7	105±6
PC	71±4	70±4	90±6	155±7	103±6
CC	69±4	73±5	83±5	156±7	105±4
<i>Bla (mmol/l)</i>					
PP	2.3±0.4	2.0±0.2	2.8±0.8	6.4±1.2	6.0±0.9
CP	2.9±0.5	1.8±0.1	2.5±0.4	5.5±0.8	5.7±0.8
PC	1.9±0.3	2.0±0.2	2.5±0.3	6.8±1.1	6.2±2.1
CC	1.9±0.2	3.1±0.8	2.8±0.4	5.6±0.5	7.3±1.2

721 [Data represented as mean ± SE; n=11 in each case]

722

723

724

725

726

727

728

729

730

731

732

733

734

735

736

737

Table 3. Individual percentage difference in maximal voluntary muscle strength between PP and CP trial correlated against the perceived benefit of caffeine

Test	R	P
KE Peak 30°/s	-0.03	0.93
KE Peak 120°/s	-0.62	0.04
KE Average 30°/s	-0.014	0.967
KE Average120°/s	-0.487	0.129
KF Peak 30°/s	-0.375	0.255
KF Peak 120°/s	-0.147	0.666
KF Average 30°/s	-0.438	0.666
KF Average120°/s	-0.44	0.899

738 [KE: Knee Extensor; KF: Knee Flexor; n=11 in each case]

739