

Acute caffeine intake improves lower body resistance exercise performance with blood flow restriction

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1 Original investigation

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3 Acute caffeine intake improves lower body resistance exercise performance with
4 blood flow restriction

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6 Running head: Exercise with blood flow restriction and caffeine

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8

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24 **ABSTRACT**

25 **Purpose:** The purpose of this study was to examine the effects of acute caffeine intake
26 on physical performance in three sets of unilateral knee extension with blood flow
27 restriction. **Methods:** In a double-blind crossover design, 22 trained men ingested 6
28 mg/kg of caffeine (CAF) or a placebo (PLA), 1 hour prior to performing unilateral knee
29 extension exercise with blood flow restriction until exhaustion (30% of 1RM). **Results:**
30 There was a significant difference in the number of repetitions between the CAF and
31 PLA conditions in the 1st set (28.3 ± 5.3 vs 23.7 ± 3.2 ; $P=0.005$), 2nd set (11.6 ± 3.1 vs
32 8.9 ± 2.9 ; $P=0.03$), and total repetitions performed across the three sets (44.5 ± 9.4 vs
33 35.0 ± 6.6 ; $P=0.001$). Blood lactate was also significantly different ($P=0.03$) after
34 exercise between the CAF (7.8 ± 1.1 mmol.L⁻¹) and PLA (6.0 ± 0.9 mmol.L⁻¹). In regard
35 to pain perception, there was a difference between the CAF and PLA in the 2nd ($6.9 \pm$
36 1.5 vs 8.4 ± 1.4 ; $P=0.04$) and 3rd sets (8.7 ± 0.4 vs 9.5 ± 0.6 ; $P=0.01$). No differences
37 were found for perceived effort. **Conclusion:** Acute caffeine intake increases
38 performance, blood lactate concentration and reduces perception of pain in unilateral
39 knee extension exercise with blood flow restriction.

40

41

42

43 INTRODUCTION

44 Resistance training of moderate/high load (> 60% of 1 maximal repetition -
45 RM) is considered an integral part of any physical conditioning program to increase
46 muscle strength or muscle mass for health in adults¹. However, in recent years
47 resistance training with low loads (<30% 1RM), performed with blood flow restriction
48 (BFR), has been suggested as being similarly effective as moderate/high-load
49 resistance training in increasing strength and muscle mass². Although the
50 physiological mechanisms regarding the improvement of strength and muscle mass
51 after a low-load resistance training program with BFR are still unclear^{3,4}, this training
52 model has application both for healthy, non-trained subjects at different ages^{5,6} and
53 athletes⁴. In this context, while resistance training with BFR is not significantly better
54 than traditional moderate/high-load resistance training to improve strength and/or
55 muscle mass, it can be added into the training routine as a variation of exercises and
56 may provide an alternative exercise mode that some individuals find more appealing
57 than traditional resistance training.

58 In the context of resistance training to increase physical performance, in
59 addition to training *per se*, it is common for athletes and recreational exercisers to use
60 ergogenic aids⁷ as a means to increase or accelerate changes in physical
61 performance. Caffeine, for example, is one of the most widely used ergogenic aids,
62 often employed to increase performance in exercises involving muscular strength⁸,
63 especially when performing several repetitions until exhaustion⁹. The mechanism of
64 action for caffeine has been explained by the high affinity of caffeine with adenosine
65 receptors, inhibiting the action of this substance¹⁰ and, consequently, reducing the
66 perception of effort and pain¹¹. Likewise, caffeine can promote greater performance in
67 the propagation of signals between the brain and neuromuscular junction¹², acting

68 peripherally on the ryanodine channels in the release of calcium, optimizing the
69 process of excitation-contraction of the skeletal musculature¹³. In the context of the
70 BFR-resistance exercise model, sustained blood flow reduction to the muscle during
71 exercise may reduce intramuscular calcium influx¹⁴, which could theoretically limit the
72 effect of caffeine on the excitation-contraction coupling process in skeletal muscles.
73 However, the possible ergogenic effects of caffeine have not yet been investigated in
74 low intensity resistance exercise with BFR. Given there is potential for both caffeine
75 ingestion and BFR to act independently and possibly synergistically, it is important to
76 examine if this is the case. No study to date has examined this issue.

77 In this sense, the purpose of this study was to examine the effects of acute
78 caffeine intake on physical performance in three sets of unilateral knee extension with
79 BFR to failure. Additionally, rating of perceived exertion, perceived pain and blood
80 lactate concentration were analyzed.

81

82 **MATERIALS AND METHODS**

83 **Subjects**

84 Sample size calculation was performed considering a difference between
85 two means of three repetitions, an expected standard deviation of 2, statistical power
86 of 80%, and level of significance lower than 0.05 in a pilot sample of this study. Thus,
87 the minimum sample required was 16 subjects. Consequently, the sample in the
88 current study included 22 trained men (Table 1) to account for potential drop out during
89 the experimental procedures. The inclusion criteria to take part were: non-smokers,
90 non-users of dietary supplements, non-users of anabolic steroids, the absence of
91 muscular or metabolic problems, body mass index below 30 kg.m², trained in
92 bodybuilding for at least 12 months (but without experience with BFR exercises), and

93 non-habitual caffeine users. Individuals were instructed not to engage in vigorous
94 exercise or consume alcoholic beverages for 72 h prior to each testing session until
95 the end of the experiment. All participants were informed about the study procedures
96 and possible effects of caffeine intake and provided informed consent to participate.
97 The study was approved by institutional ethics of the State University of Londrina
98 (application number 1.141.230/2015).

99

100 **Experimental design**

101 The study employed a repeated-measures, within-subjects design and was
102 conducted during four non-consecutive days with intervals of between 48-72 h.
103 Anthropometric measurements and 1RM testing was performed during the first visit.
104 This was followed by familiarization with the scales that were used for subjective
105 perception of effort (RPE)¹⁵ and pain (PP)¹⁶. On the second visit, the 1RM retest was
106 performed. The remaining two visits were assigned to the experimental sessions
107 administered using a randomized double-blind cross-over design. The subjects
108 ingested either one capsule of caffeine (CAF) or a placebo (PLA) and, after 60 min,
109 performed unilateral knee extension exercise with BFR (three sets to exhaustion, 1
110 min recovery interval between sets, at an intensity of 30% 1RM). The BFR was
111 maintained throughout the whole exercise bout (all sets and repetitions). Subjects were
112 instructed and verbally encouraged to perform the maximum number of repetitions
113 during each set. The repetitions were performed at a rate of 1.5 seconds (via digital
114 metronome) for both concentric and eccentric contractions. The RPE and PP were
115 applied after the end of each set. Blood lactate was collected after the end of the
116 exercise. At the end of the experiment, the subjects were questioned as to whether
117 they were able to distinguish between the two capsules to identify which was caffeine,

118 in order to determine efficacy of blinding and the individual perception of the effect of
119 this substance.

120

121 **Maximum strength test**

122 The 1RM test and retest were performed within a 48-h interval using a
123 unilateral extensor chair (the dominant leg) (TechnoGym®, Rome, Italy), was
124 determined according to methods accomplished by Seo et al.¹⁷. A warm-up was
125 performed with a set of 10 repetitions (~50% of predicted 1RM). Individuals were
126 allowed up to five attempts to determine 1RM, with a recovery interval of 3-5 min. All
127 subjects were instructed and verbally encouraged to perform one correct repetition.
128 The load was considered maximal when the subjects performed only one complete
129 repetition. The highest load obtained in either the test or retest 1RM trials was used in
130 subsequent experimental trials. Test/retest reliability for the 1RM was performed and
131 a high intraclass correlation coefficient (ICC) was found, $R = 0.80$.

132

133 **Caffeine or placebo intake**

134 For the experimental sessions, each subject ingested a capsule containing
135 6 mg of caffeine per kilogram of body weight and a placebo capsule (maltodextrin) with
136 200 ml of water administered in a randomized order. The habitual average caffeine
137 intake of the participants was assessed through a questionnaire¹⁸ translated to
138 Portuguese. All participants were considered low habitual caffeine users (80.1 ± 10.4
139 $\text{mg}\cdot\text{day}^{-1}$). The same list was used to instruct the individuals not to consume the same
140 substances for 48 h prior to testing.

141

142 **Blood flow restriction**

143 To elicit BFR, a cuff 18 cm wide and 90 cm long was positioned on the
144 proximal third of the thigh. A vascular Doppler (MARTEC DV600, São Paulo, Brazil)
145 positioned on the posterior tibial artery was used to identify the sound of the passage
146 of blood flow. From identification of the sound, the cuff was inflated until the sound was
147 interrupted and, at that moment, the restriction value was recorded. Cuff pressure
148 during the experimental session was maintained at 80% of the total blood flow
149 restriction value and was released only after the end of the final set.

150

151 **Blood lactate collection**

152 Blood lactate concentration was obtained at the moment of rest during the
153 first visit to the laboratory and at an interval of up to two minutes after the end of the
154 final set of each experimental session. Prior to the blood sample collection, asepsis
155 was performed with 70% alcohol on the digital pulp of the middle finger of the right
156 hand. The puncture was performed using disposable lancets, the drop of blood (5µl) in
157 suspension being applied to a specific area of the reactive strip and analyzed by means
158 of a portable lactometer (AccutrendPlus, USA).

159

160 **Rating of perceived exertion and perceived pain**

161 To measure perceived exertion and perceived muscle pain, the OMNI 0-10
162 rating of perceived exertion (RPE)¹⁵ and a perceived pain (PP) visual analog scales¹⁶
163 were used respectively. Familiarization with the scales was performed on the first day
164 of the individuals' visit to the laboratory. Subsequently, during experimental trials, at
165 the end of each set, the RPE and PP values were also collected.

166

167 **Statistical analyses**

168 The Shapiro-Wilk test was used to verify the distribution of the data and the
169 Levene's test to verify the homogeneity of the variances. Considering the normal
170 distribution of data, for the comparison of the number of repetitions, RPE, and PP a
171 two-way ANOVA with repeated measures was used (caffeine/placebo x number of
172 sets). The Student T-test for dependent samples was applied for the blood lactate
173 analysis. Two-way ANOVA was used to compare the performance in the total number
174 of repetitions, RPE, and PP, among those who identified correctly and those who made
175 a mistake about the intake of the caffeine capsule. In all cases, the Tukey *post-hoc*
176 test was used to identify significant results. Additionally, to determine the magnitude of
177 the findings, Cohen's d effect sizes (ES) were calculated for the differences between
178 PLA and CAF, following the classification: small ($0.20 < ES < 0.50$), medium
179 ($0.50 \leq ES < 0.80$) or large ($ES \geq 0.80$). The level of significance adopted was $P < 0.05$. The
180 data were analyzed in Statistica 12.0 software (Statsoft, Tulsa, OK, USA).

181

182 **RESULTS**

183 Values are expressed as mean and standard deviation.

184 Table 1 presents the general characteristics of the sample. Randomization
185 showed that 10 subjects started with the CAF session and 12 subjects started with the
186 PLA session.

187 Table 2 shows the number of repetitions performed, RPE, and PP in the
188 CAF and PLA conditions. For the number of repetitions performed, there was a
189 significant interaction between CAF and PLA ($F=18.45$; $P=0.02$) with the Tukey post-
190 hoc test identifying a significant difference between the 1st and 2nd sets. The RPE
191 analysis demonstrated no significant inter-group interaction. However, there was a

192 significant intra-group interaction in CAF ($F=14.37$; $P=0.04$) and PLA ($F=16.65$;
193 $P=0.03$) conditions. RPE scores was significantly lower after the 1st set of CAF and
194 PLA in relation to the other sets. For the PP analysis, there was significant interaction
195 between CAF and PLA ($F=23.78$; $P=0.01$). The PP results demonstrated a progressive
196 increase in the CAF condition from the 1st to 3rd sets. Conversely, in the PLA condition
197 PP was only significantly different in the 1st set compared to the 2nd and 3rd sets.
198 Furthermore, PP was significantly different between CAF and PLA in the 2nd and 3rd
199 sets.

200 The analysis of blood lactate, by Student's T-test, showed no significant
201 differences in resting values between the CAF (2.1 ± 0.3 mmol.L⁻¹) and PLA (2.2 ± 0.2
202 mmol.L⁻¹; Cohen's d ES = 0.39). After the end of the exercise, the values were
203 significantly higher ($P=0.002$) than those observed at rest, and a significant difference
204 ($P=0.03$) was observed between the CAF (7.8 ± 1.1 mmol.L⁻¹) and PLA (6.0 ± 0.9
205 mmol.L⁻¹; Cohen's d ES = 1.79) conditions.

206 Table 3 shows the two-way ANOVA results for the total number of
207 repetitions performed between subjects who correctly determined which condition was
208 the caffeine condition and which the placebo. Nine subjects correctly identified the
209 caffeine trial (true positive) and also performed more repetitions in this condition than
210 after placebo intake. Similarly, those failing to correctly identify the caffeine trial also
211 performed more repetitions than after taking the placebo. However, there was a
212 significant difference in the number of repetitions completed after caffeine intake
213 between those who identified and those who did not correctly identify caffeine (P
214 <0.05). No differences were observed for RPE, PP, or lactate.

215 Figure 1 presents the individual responses between CAF and PLA in terms
216 of the total number of repetitions performed.

217

218 INSERT TABLE 1

219 INSERT TABLE 2

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221 INSERT FIGURE 1

222

223 DISCUSSION

224 The main findings of the present study were: 1) caffeine intake increased
225 both the number of repetitions performed and capillary blood lactate whilst also
226 reducing pain sensation in knee extension exercise with BFR; 2) subjects who
227 accurately interpreted the caffeine trial as such performed more repetitions than those
228 who did not perceive it accurately. In both cases, the Cohen's d ES were large, ratifying
229 the significant level identified. No study to date has examined the concurrent effects of
230 caffeine ingestion and BFR on strength performance and few prior studies examining
231 caffeine ingestion have also examined whether the participant's perception of the
232 substance ingested influences the response to the subsequent exercise protocol. As
233 such the results of the present study are novel and extend the literature pertaining to
234 effects of caffeine ingestion on exercise performance.

235 One of the possible mechanisms of action of caffeine on physical
236 performance occurs through the increase in the release of calcium in the sarcoplasmic
237 reticulum, boosting the excitation-contraction process¹³. However, it is possible that
238 calcium availability may be impaired under hypoxia conditions¹⁴. Thus, one of the
239 potential explanations is that exercise with BFR reduced the availability of calcium and,
240 consequently, compromised performance. In the present study, as performance did
241 not decrease, on the contrary, it increased, we suggest two hypotheses to explain the

242 seemingly paradoxical findings we present. A BFR threshold of 80% BFR was
243 employed in the present study as this threshold is commonly used in the literature¹⁹.
244 As a consequence the experimental model did not apply vascular occlusion that
245 interrupted 100% of the blood flow. This means, in the current study, there was no total
246 hypoxia condition, despite less oxygen availability. Thus, even assuming a lower
247 availability of calcium, this may not have been sufficient to compromise performance.
248 Secondly, the release of calcium into the sarcoplasmic reticulum is not the only
249 mechanism of action by which caffeine influences performance²⁰. Given that there is
250 debate in regard to the mechanism by which caffeine is ergogenic, the results of the
251 current study would imply that increased caffeine availability in the sarcoplasmic
252 reticulum might not be the prime mechanism by which caffeine ingestion enhances
253 muscular performance.

254 It has previously been established that caffeine can also act in the central
255 nervous system by blocking adenosine receptors²¹, attenuating the action of adenosine
256 and increasing the release of adrenergic neurotransmitters to reduce PP²². In the
257 context of the current study, this may have helped individuals to continue performing
258 the exercise for a longer duration and, consequently, increasing the number of
259 repetitions performed with a concomitant increase in blood lactate values post
260 exercise. The observed increase in blood lactate might also be associated with
261 increased PP. However, in the present study, PP was lower in the caffeine condition
262 (with large Cohen's d ES) throughout the sets. In addition, lactate appears to influence
263 PP depending on the concentration of protons and ATP²⁴. Thus, high lactate values
264 may not increase PP. This finding aligns with other studies that have also reported
265 dampened PP during resistance exercise with caffeine ingestion¹¹. Conversely, no
266 significant differences in RPE were identified as a consequence of the substance

267 ingested. Such a finding is congruent with other resistance exercise data, where the
268 authors hypothesized that caffeine may be able to improve performance by maintaining
269 similar levels of perceived exertion to those who produced less work²³.

270 Concerning the number of repetitions during exercise with BFR, there was
271 a significant difference between CAF and PLA until the 2nd set ($P < 0.05$ and large
272 Cohen's d ES). The non-significant difference in the 3rd set may be associated with
273 fatigue in both groups. In this context, the ergogenic effect of caffeine may not be
274 realized when several sets are performed to exhaustion and could be indicative that
275 caffeine enhances peak strength performance. It is important to note that there was a
276 significant difference in repetitions between subjects who correctly identified caffeine
277 intake and those who did not identify the intake of caffeine. Some studies have carried
278 out an individual analysis on the effects of caffeine on performance and identified that
279 some subjects did not present an ergogenic effect²⁵. In other studies, the authors
280 analyzed the side effects of caffeine action to see if the sample could identify the
281 substance ingested²⁶. In the present study, we did not perform individual performance
282 analysis and also did not verify side effects - we only asked the subjects at the end of
283 the experiment if they thought that caffeine had been the first or second capsule
284 consumed. It is important to reinforce that, irrespective of whether subjects correctly
285 identified the caffeine ingestion trial or not, the participants performed more repetitions
286 when they ingested caffeine compared to when placebo was ingested. However,
287 subjects who correctly identified caffeine performed more repetitions than those who
288 did not. Our results agree with the study by Saunders et al.²⁷ The authors found that
289 cyclists who correctly identified caffeine improved cycling performance to a greater
290 extent than the overall effect of caffeine; and the performance also improved when
291 participants ingested caffeine while believed they were ingesting placebo. Therefore,

292 the results of this study reinforces the possibility that caffeine has an individualized
293 physiological and psychological action, allowing some subjects to have a superior
294 ergogenic effect to others as a consequence of their expectancy of the effect of the
295 substance they have ingested.

296 In regard to blood lactate responses to exercise, we observed an increase
297 in this variable after exercise in both the placebo and caffeine conditions. Studies have
298 shown that resistance exercise with BFR may result in blood lactate concentration
299 values similar⁵ or higher²⁸ when compared to high intensity exercise without BRF. It is
300 worth mentioning that this type of exercise has some peculiarities in relation to
301 conventional training of moderate-high intensity, among them is maintaining the blood
302 flow restriction even in the recovery periods, which can significantly decrease the
303 removal of blood lactate in the target muscles⁶.

304 However, in the current study, blood lactate was higher after the exercise
305 performed with caffeine intake. Such a finding is congruent with recent meta-analytical
306 data identifying that acute caffeine intake significantly increases plasma lactate²⁹. In
307 the present study, a possible explanation the greater number of repetitions performed
308 after caffeine ingestion, would have also been associated with a longer duration of
309 effort and a longer time in the BFR condition. As a consequence of this, blood lactate
310 may have been elevated simply because of the greater work performed in the caffeine
311 condition rather than because of the caffeine ingested. Despite this potential
312 explanation, some studies have shown that plasma lactate did not change after
313 caffeine intake even with increased performance³⁰. In this sense, the effect of caffeine
314 on plasma lactate is still inconclusive and requires further investigation.

315

316 **PRACTICAL APPLICATIONS**

317 The present study is the first to investigate the acute effects of caffeine on
318 an exercise performed with BFR. The positive effect of acute caffeine intake to increase
319 the number of repetitions during unilateral knee extension with BFR may help
320 practitioners, athletes and coaches to optimize the performance in this model of
321 resistance exercise. Notwithstanding, regardless of the results presented, there are
322 some limitations of the current study. We used a single unilateral lower limb exercise
323 as our outcome measure of resistance exercise performance. The results of the
324 present study are only reflective of this type of exercise and we cannot confirm that the
325 results presented herein would be reproducible in bilateral exercises and/or with
326 different muscle mass. Plasma caffeine concentration was not measured and thus we
327 cannot confirm the bioavailability of this substance in all study subjects. We did not test
328 the reliability of the measurements during the exercises protocols. Although our
329 subjects were familiar with resistance exercise protocols, they were not regular
330 practitioners of resistance exercise with BFR. Exercise with BFR may feel different to
331 exercise without BFR and as such some of the observed changes might be attributable
332 to the feeling of the exercise, the error of measurement or to learning effects. Finally,
333 as this is an acute study, we cannot verify whether the greater number of repetitions
334 performed after caffeine intake would be significant to promote a superior effect on
335 strength or muscle mass when analyzed in the long term. Future research would be
336 welcome examines these issues and also seeks to replicate the results of the current
337 study.

338

339 **CONCLUSION**

340 Acute caffeine supplementation increases physical performance and
341 decreases PP in an exercise session of unilateral knee extension with BFR.

342

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345 Research Development (CNPq).

346

347 **CONFLICT OF INTEREST**

348 The authors declare that they have no conflicts of interest.

349

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- 442

444 **Table 1.** General characteristics of the sample (n=22).

Age (years)	23.4 ± 4.1
Height (cm)	177.2 ± 3.9
Weight (kg)	76.7 ± 4.0
Time of training (years)	2.6 ± 1.1
Level of BFR during exercise (mmHg)	131.4 ± 14.6
Habitual caffeine consumption (mg.day⁻¹)	80.1 ± 10.4
1 RM (kg)	87.2 ± 61.1
30% of 1 RM (kg)	26.2 ± 2.5

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447 **Table 2.** Results of the two-way ANOVA with repeated measures to effect of caffeine supplementation on the number of repetitions,
 448 rating of perceived exertion and pain perceived.

	Caffeine	Placebo	Inter-group P value (caffeine vs placebo)	Cohen's d effect size	Cohen' d classification
Repetitions					
1st set	28.3 ± 5.3*	23.7 ± 3.2*	0.005	1.05	Large
2nd set	11.6 ± 3.1†	8.9 ± 2.9†	0.03	0.90	Large
3rd set	4.6 ± 3.6	2.4 ± 3.0	NS	0.66	Medium
Total	44.5 ± 9.4	35.0 ± 6.6	0.001	1.17	Large
Rating of perceived exertion					
1st set	6.3 ± 1.5*	6.1 ± 1.9*	NS	0.11	Small

2nd set	8.4 ± 1.1	8.5 ± 1.5	NS	0.07	Small
3rd set	9.4 ± 0.3	9.6 ± 0.8	NS	0.33	Small
<hr/> Pain perceived					
1st set	5.2 ± 1.0*	5.9 ± 2.2*	NS	0.40	Small
2nd set	6.9 ± 1.5†	8.4 ± 1.4	0.04	1.03	Large
3rd set	8.7 ± 0.4	9.5 ± 0.6	0.01	1.57	Large

449 * Intra-groups significant difference (P=0.02) from 1st and 2nd sets; † Intra-groups significant difference (P=0.04) from 3rd set; NS =
450 non-significant difference

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453 **Table 3.** Results of the two-way ANOVA to the total number of repetitions performed between subjects who scored correctly and
 454 those who made a mistake about caffeine intake.

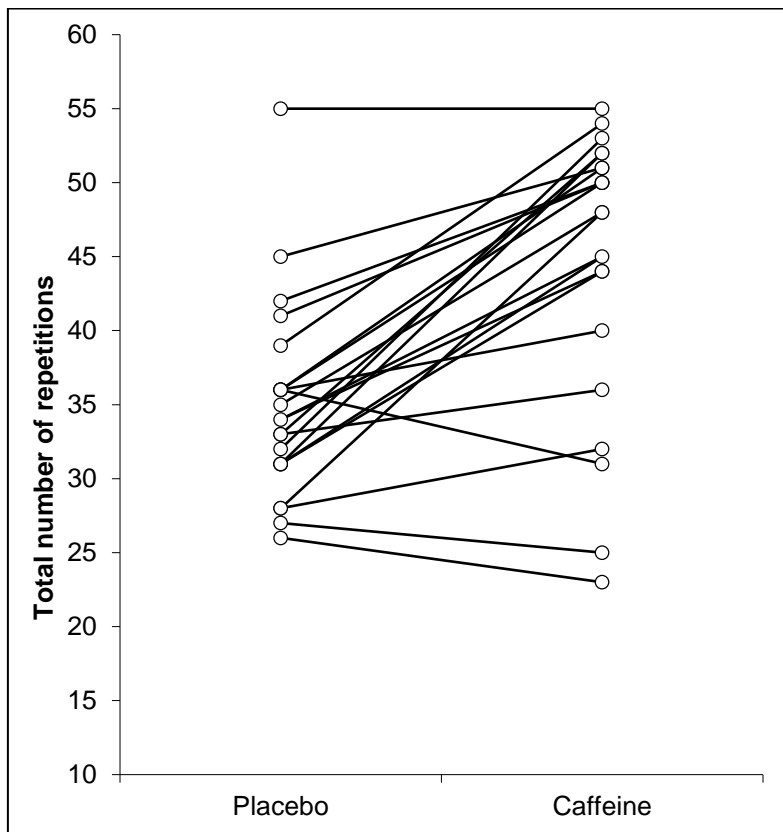
	Caffeine	Placebo	Inter-group P value (caffeine vs placebo)	Cohen's d effect size	Cohen's d classification
Correct identification of caffeine (n=9)	48.8±4.8	35.7±7.7	0.002	2.04	Large
Non-correct identification of caffeine (n=13)	41.5±7.1	34.5±6.0	0.001	1.06	Large
Intra-groups P value (correct vs non-correct)	0.04	NS	-	-	-

455 NS = non-significant difference

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460 Figure 1. Individual responses between caffeine and placebo sessions