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Resistance Exercise: A Review*

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1 **The influence of caffeine supplementation on resistance exercise: a review**

2 Jozo Grgic¹, Pavle Mikulic², Brad J. Schoenfeld³, David J. Bishop^{1, 4}, Zeljko Pedisic¹

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4 ¹Institute for Health and Sport (IHES), Victoria University, Melbourne, Australia

5 ²Faculty of Kinesiology, University of Zagreb, Zagreb, Croatia

6 ³Department of Health Sciences, Lehman College, Bronx, NY, USA

7 ⁴School of Medical and Health Sciences, Edith Cowan University, Joondalup, Australia

8

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11 **Corresponding author:**

12 Jozo Grgic

13 Institute for Health and Sport (IHES), Victoria University, Melbourne, Australia

14 Email: jozo.grgic@live.vu.edu.au

15

16 **Abstract**

17 This paper aims to critically evaluate and thoroughly discuss the evidence on the topic of
18 caffeine supplementation when performing resistance exercise, as well as provide practical
19 guidelines for the ingestion of caffeine prior to resistance exercise. Based on the current
20 evidence, it seems that caffeine increases both maximal strength and muscular endurance.
21 Furthermore, power appears to be enhanced with caffeine supplementation, although this
22 effect might, to a certain extent, be caffeine dose- and external load-dependent. A reduction in
23 rating of perceived exertion (RPE) might contribute to the performance-enhancing effects of
24 caffeine supplementation, as some studies have observed decreases in RPE coupled with
25 increases in performance following caffeine ingestion. However, the same does not seem to
26 be the case for pain perception, as there is evidence showing acute increases in resistance
27 exercise performance without any significant effects of caffeine ingestion on pain perception.
28 Some studies have reported that caffeine ingestion did not affect exercise-induced muscle
29 damage but that it might reduce perceived resistance exercise-induced delayed onset muscle
30 soreness; however, this needs to be explored further. There is some evidence that caffeine
31 ingestion, compared to a placebo, may lead to greater increases in the production of
32 testosterone and cortisol following resistance exercise. However, given that the acute changes
33 in hormone levels seem to be weakly correlated with hallmark adaptations to resistance
34 exercise, such as hypertrophy and increased muscular strength, these findings are likely of
35 questionable practical significance. Although not without contrasting findings, the available
36 evidence suggests that caffeine ingestion can lead to acute increases in blood pressure
37 (primarily systolic), and, thus, caution is needed regarding caffeine supplementation among
38 individuals with high blood pressure. In the vast majority of studies, caffeine was
39 administered in capsule or powder forms, and therefore, the effects of alternative forms of
40 caffeine such as chewing gums or mouth rinses on resistance exercise performance remain

41 unclear. The emerging evidence suggests that coffee might be at least equally ergogenic as
42 caffeine alone when the caffeine dose is matched. Doses in the range of 3 to 9 mg·kg⁻¹ seem
43 to be adequate for eliciting an ergogenic effect when administered 60 min pre-exercise. In
44 general, caffeine seems to be safe when taken in the recommended doses. However, at doses
45 as high as 9 mg·kg⁻¹ or higher, side-effects such as insomnia might be more pronounced. It
46 remains unclear whether habituation reduces the ergogenic benefits of caffeine on resistance
47 exercise, as no evidence exists for this type of exercise. Caution is needed when extrapolating
48 these conclusions to females as the vast majority of studies involved only male participants.

49

50 **Key points**

- 51 • Caffeine supplementation may acutely enhance muscular endurance, maximal
52 strength, and power in resistance exercise.
- 53 • Doses in the range 3 to 9 mg·kg⁻¹ seem to be adequate for eliciting ergogenic effects.
54 Caffeine seems to be generally safe when taken in these doses. However, at doses as
55 high as 9 mg·kg⁻¹ or higher, side effects might be more pronounced.
- 56 • Blood pressure may be increased following caffeine ingestion, and, therefore, caution
57 is needed regarding caffeine supplementation among individuals with high blood
58 pressure.
- 59 • The mechanism by which caffeine intake affects resistance exercise performance is
60 likely multifactorial.

61

62

63 **1 Introduction**

64 Caffeine is one of the most commonly consumed drugs in the world [1], and a national survey
65 indicated that 89% of American adults ingest caffeine with an average daily consumption
66 (mean \pm standard deviation) of 211 ± 472 mg [2]. This amount of caffeine is contained in
67 approximately two cups of brewed coffee. Because of the ergogenic effects of caffeine on
68 exercise performance, its use is also very prevalent among athletes [3]. Although several
69 previous reviews have focused on the ergogenic benefits of caffeine on exercise performance
70 [1, 4-11], none of them explicitly focused on resistance exercise. Therefore, there remains
71 ambiguity regarding the effects of caffeine supplementation on resistance exercise.

72

73 Several muscular qualities are important when discussing resistance exercise, including
74 muscular strength, muscular endurance, and muscular power. Muscular strength is ‘the
75 capacity to exert force under a particular set of biomechanical conditions’ [12]. The following
76 forms of muscular strength are usually assessed in research studies: dynamic strength
77 (concentric actions coupled with eccentric actions), isometric strength (a muscle action in
78 which the muscle-tendon complex does not change its length), and reactive strength (an
79 ability to change quickly from eccentric to concentric muscle actions) [13]. A commonly used
80 field-based test for assessing dynamic strength is the one-repetition maximum (1RM) test,
81 while in laboratory settings dynamic strength is commonly assessed using isokinetic
82 dynamometers [14]. Several neural factors such as motor unit recruitment, motor unit
83 synchronization, rate coding, and neuromuscular inhibition underpin strength (a more detailed
84 discussion of these factors can be found elsewhere [15]). Muscular endurance can be defined
85 as ‘the ability of a muscle or muscle group to perform repeated contractions against a load for
86 an extended period’ [16]. Muscular endurance is commonly assessed by performing
87 repetitions of a given task to momentary muscular failure with a load corresponding to, for

88 example, 50-60% of 1RM, or by measuring the time that a person is able to maintain force
89 production at a given percentage of the force that corresponds to their maximal voluntary
90 contraction (MVC). Muscular power denotes the rate of muscular work [17] and, in resistance
91 exercise, it is commonly assessed by using linear position transducer(s) or a force plate [17].

92

93 There is a growing number of studies investigating the effects of caffeine supplementation on
94 pain perception, ratings of perceived exertion (RPE), muscular qualities (e.g. maximal
95 strength, muscular endurance and power), muscle damage and cardiovascular and hormonal
96 responses to resistance exercise. However, given their mixed results, this paper aims to
97 critically evaluate and thoroughly discuss the evidence on the topic and to provide practical
98 guidelines for the application of caffeine supplementation when performing resistance
99 exercise.

100

101 **2 Possible mechanisms for the ergogenic effect of caffeine on exercise performance**

102 Some of the initially-proposed mechanisms for the ergogenic effect of caffeine on exercise
103 performance were enhanced fat oxidation and subsequent glycogen sparing [18]. However,
104 these proposed mechanisms received little support in the literature, given that caffeine
105 ingestion has been observed to be beneficial even in shorter duration exercise protocols (e.g.,
106 <30 minutes) in which glycogen levels do not appear to be a limiting factor [1]. These
107 mechanisms also could not explain the observed ergogenic effects of caffeine on high-
108 intensity, short-duration, anaerobic exercise performance [6]. Currently accepted
109 mechanism(s) relate to the antagonistic effect of caffeine on adenosine receptors [19]. The
110 binding of adenosine to A₁ and A_{2a} G protein-coupled receptors [19] inhibits the release of
111 various neurotransmitters (such as acetylcholine and dopamine). Caffeine is structurally

112 similar to adenosine, and, therefore, when ingested it blocks the binding of adenosine to the
113 A₁ and A_{2a} receptors and promotes the release of these neurotransmitters [19]. Thus, caffeine
114 exerts central nervous system effects and alters arousal, which may lead to improvements in
115 performance [6]. Caffeine also increases calcium release from the sarcoplasmic reticulum and
116 motor unit recruitment, which may result in a more forceful muscular contraction and help
117 explain some of the ergogenic effects of caffeine on resistance exercise performance [20, 21].
118 Furthermore, studies conducted in both animals and humans suggest that caffeine may have a
119 direct effect on the skeletal muscle tissue, which may, at least partially, explain the ergogenic
120 effect of caffeine [22-24].

121

122 **2.1 Effects of caffeine on ratings of perceived exertion**

123 RPE is commonly assessed using the Borg 0-10, or the 6-20 point scale [25]. Caffeine may
124 reduce RPE, which might allow an individual to perform more work with reduced subjective
125 strain [20]. When assessed in an aerobic exercise setting, the reductions in RPE explain up to
126 29% of the ergogenic effect of caffeine on submaximal aerobic exercise performance [26],
127 suggesting that a reduced RPE is a relevant factor in performance-increasing mechanisms.

128

129 Several studies observing a positive effect of caffeine on performance (e.g., acute increases in
130 strength and muscular endurance) have also reported a reduction in RPE. For instance, Grgic
131 and Mikulic [27] showed a 3% increase in 1RM barbell back squat performance and a
132 corresponding 7% reduction in RPE (using the 6-20 point scale) with caffeine ingestion in a
133 sample of resistance-trained individuals. Using a protocol that focused on muscular
134 endurance, Duncan and Oxford [28] also reported a 13% decrease in RPE (using the 0-10
135 point scale) and an ergogenic effect of caffeine on muscular endurance. A subsequent study

136 by Duncan et al. [29] confirmed these findings. However, the majority of the remaining
137 studies have observed no significant effect of caffeine ingestion on RPE. For instance,
138 Astorino et al. [30] did not find a reduction in RPE at doses of 2 and 5 mg·kg⁻¹ of caffeine
139 even though improvements in strength were evident with the 5 mg·kg⁻¹ dose. Similarly,
140 Duncan and Oxford [31] did not find a significant reduction in RPE ($p = 0.082$) when using a
141 dose of 5 mg·kg⁻¹ administered one hour before performing repetitions to momentary
142 muscular failure with 60% 1RM on the bench press. Similar results have also been observed
143 in other related studies [32-36]. While Arazi et al. [37] found that a dose of 2 mg·kg⁻¹ is
144 sufficient to achieve an RPE-reducing effect, this reduction in RPE was not accompanied by
145 any increases in muscular strength or muscular endurance.

146

147 It can be hypothesized that exercise selection may determine the RPE response, given that
148 complex, multi-joint exercises activate more muscle groups and, thus, require greater
149 exertion. Two studies that did not observe a reduction in RPE used single-joint exercises, such
150 as knee extensions and arm curls, which are less demanding than multi-joint exercises [34,
151 38]. While exercise selection might play a role in determining this effect, this hypothesis
152 remains speculative as some studies using single-joint exercises reported a reduction in RPE
153 following caffeine ingestion [38] and others using the bench press exercise (i.e., a multi-joint
154 upper-body exercise) did not show significant reductions in RPE following caffeine ingestion
155 [32, 35, 36]. Doherty and Smith [26] reported that RPE is lowered during prolonged aerobic
156 exercise, but that it remains unaltered when assessed at exercise termination. Due to the
157 nature of resistance exercise, RPE is evaluated almost exclusively at exercise termination,
158 which might be a reason why studies have often reported no differences in RPE following
159 caffeine ingestion. While a reduction in rating of perceived exertion might contribute to the

160 performance-enhancing effects of caffeine, a firm conclusion cannot be made on this topic
161 due to the inconsistent evidence presented in the literature.

162

163 **2.2 Effects of caffeine on pain perception**

164 Due to its blockade of adenosine receptors, caffeine is a common ingredient of over-the-
165 counter medications for pain relief [39]. Resistance exercise may lead to significant acute
166 increases in pain perception [40], which raises the possibility that a reduction in pain
167 perception might contribute to the ergogenic effects of caffeine. Some studies have reported
168 that caffeine ingestion decreases pain perception but without any significant effects on
169 performance [27, 37]. Tallis and Yavuz [41] and Sabblah et al. [42] did not observe any
170 significant reductions in pain perception, although caffeine ingestion increased muscular
171 strength, suggesting that factors other than the reduced perception of pain contributed to the
172 ergogenic effect. Although two studies reported that improvements in performance were
173 accompanied by a decrease in pain perception [28, 29], there was also a decrease in RPE that
174 made it difficult to determine exactly what contributed to the ergogenic effect. Based on the
175 current evidence, it seems that mechanism(s) other than reductions in pain perception
176 contribute to the enhanced resistance exercise performance with caffeine ingestion.

177

178 **3 Effects of caffeine on strength**

179 **3.1 1RM strength**

180 Some of the initial studies that investigated the effects of caffeine on 1RM dynamic strength
181 did not show a significant ergogenic effect. For instance, Astorino and colleagues [43] did not
182 find any performance-enhancing effects of caffeine ingestion on 1RM strength in the bench

183 press and leg press exercises among resistance-trained men. However, a study by Goldstein et
184 al. [44], involving resistance-trained women, showed that caffeine ingestion may significantly
185 improve upper-body 1RM as assessed by the bench press exercise.

186

187 A prevalent issue among individual studies examining the effects of caffeine supplementation
188 on resistance exercise performance is the use of small sample sizes [45], which may result in
189 low statistical power. To better understand the equivocal evidence reported in the literature,
190 Grgic et al. [46] recently conducted a meta-analysis of studies assessing the impact of caffeine
191 on 1RM muscular strength. The findings of this review suggested that caffeine ingestion
192 enhances 1RM muscular strength compared to placebo (Fig. 1). Subgroup analyses revealed
193 that caffeine ingestion increased upper- but not lower-body strength. The raw difference
194 between the mean effects of placebo and caffeine in the subgroup analysis equated to 3.5 kg
195 (95% confidence interval [CI]: 1.5, 4.8 kg) and 1.7 kg (95% CI: -1.7, 5.0 kg) of lifted weight
196 for the upper-body and the lower-body, respectively. From a physiological perspective, there
197 appears to be no rationale as to why caffeine would increase upper- but not lower-body
198 strength. In fact, as we discuss below (section 3.2), due to the differences between the upper-
199 and lower-body in the amount of muscle mass involved, the opposite results might be
200 expected. That said, the subgroup analyses for lower- and upper-body strength were limited as
201 they included only seven and eight studies, respectively. While the meta-analysis provided
202 some evidence that caffeine increases 1RM strength, given the relatively small number of
203 studies investigating this topic, future research is warranted.

204

205 *****Insert Fig. 1 about here*****

206

207 **3.2 Isometric and isokinetic strength**

208 Using a model focused on the dorsiflexor muscles, Tarnopolsky and Cupido [47] reported no
209 significant effect of caffeine ingestion on enhancing MVC. However, in an experiment
210 performed by Park et al. [48] that focused on the knee extensor muscles, caffeine led to
211 significant increases (+10%) in MVC compared to a placebo. Some of these findings can
212 possibly be attributed to differences in the activation of smaller versus larger muscle groups.
213 Indeed, a meta-analytic review by Warren et al. [49], which pooled MVC tests (with the
214 majority of studies using isometric tests of strength), reported that caffeine ingestion may
215 significantly increase MVC by ~4%. However, this effect seemed to be evident primarily in
216 the knee extensor muscles (+7%) and not in smaller muscle groups, such as the dorsiflexors.

217

218 During a MVC, the activation of the knee extensor muscles is usually lower when compared
219 with other muscle groups [49, 50]. For instance, smaller muscles such as the tibialis anterior
220 can be activated up to 99% of their maximum during a MVC and, hence, the activation of
221 these muscles is already at near-maximal level [51, 52]. However, knee extensor activation is
222 usually 85 to 95% of its maximal activation and, therefore, Warren et al.'s hypothesis was that
223 with caffeine ingestion, the muscle activation in this muscle group can be enhanced, which in
224 turn can augment the MVC [49]. Caffeine ingestion has been reported to increase cortical and
225 spinal neuron excitability [53], which might increase muscle activation through an increase in
226 motor unit recruitment. Indeed, Black et al. [54] demonstrated that caffeine ingestion
227 enhances MVC and motor unit recruitment in the knee extensors but not in the elbow flexors,
228 supporting the hypothesis by Warren et al. [49].

229

230 Recently, Tallis and Yavuz [41] reported that caffeine ingestion enhanced isokinetic strength
231 in the knee extensors but not in the elbow flexors, adding to the evidence showing that
232 benefits of supplementation might be related to the different activation of smaller versus
233 larger muscle groups. The results by Tallis and Yavuz [41] for isokinetic strength were
234 confirmed in a recent meta-analysis [55], whereby the pooled relative effect size from ten
235 included studies was 0.16 (+6%), suggesting that caffeine ingestion enhances isokinetic
236 strength. However, again, this effect was not observed in smaller muscle groups such as the
237 elbow flexors and was predominately manifested in the knee extensors.

238

239 In summary, the current evidence suggests that caffeine ingestion may have an ergogenic
240 effect on muscular strength across all muscle action types [56]. As such, these findings are
241 likely to have the highest application in sports such as powerlifting and weightlifting.
242 However, studies conducted specifically among competitive powerlifters and weightlifters are
243 needed, given that most of the previous studies included untrained or recreationally trained
244 individuals. More evidence is needed to examine the differences between small and large
245 muscle groups, as well as between the upper- and lower-body musculature. Although it seems
246 that caffeine enhances MVC, isometric actions and isokinetic apparatuses are used to a lesser
247 degree in traditional resistance exercise routines, which somewhat limits the practical
248 application of these findings.

249

250 **4 Effects of caffeine on muscular endurance**

251 Several individual studies [28, 29, 32] and meta-analytic reviews [49, 57] show that caffeine
252 (most commonly administered in a dose of 5 to 6 mg·kg⁻¹) can have an ergogenic effect on
253 muscular endurance, with improvements found for both the upper-body [28] and the lower-

254 body [29] musculature. Forest plots in the reviews conducted by Polito et al. [57] and Warren
255 et al. [49] indicate that studies almost never show that caffeine produces an ergolytic effect on
256 muscular endurance performance. Specifically, in the work by Warren et al. [49], out of the
257 23 studies included in the meta-analysis, sample effect sizes for only four studies [53, 58-60]
258 favored the placebo group. The effect sizes in these four studies ranged from -0.32 to -0.03,
259 but none were statistically significant. In the review by Polito et al. [57], none of the studies
260 favored placebo. The pooled effect sizes in these reviews ranged from 0.28 to 0.38, that is,
261 +6% to +7%. The raw difference between mean effects of placebo and caffeine for the
262 number of completed repetitions in the studies included in the Polito et al. [57] review ranged
263 from -0.3 to +6 repetitions. In the studies identified by Warren et al. [49], the time to maintain
264 an isometric contraction at a given percentage of MVC (a test used to assess muscular
265 endurance) with caffeine ingestion ranged from 8 to 32 s. Future long-term studies are needed
266 to explore if these small acute increases in performance also impact long-term adaptations to
267 resistance exercise.

268

269 Limited evidence also shows an ergogenic effect of caffeine on muscular endurance in a
270 sleep-deprived condition (6 hours of sleep or less) [61]. Several studies that carried out
271 muscular endurance assessments following maximum strength testing did not observe a
272 significant ergogenic effect of caffeine on muscular endurance [27, 43, 44], suggesting that
273 caffeine supplementation may not be as effective on muscular endurance as fatigue develops.
274 These results seem surprising given that caffeine ingestion has been shown to slow down the
275 fatigue-induced loss of force production [62]. Caffeine ingestion should, therefore,
276 theoretically be ergogenic even in the presence of fatigue and the exact reasons for the lack of
277 an ergogenic effect of caffeine in the referenced studies remain unclear. Studies that
278 investigated the effects of caffeine supplementation on muscular endurance among females

279 also did not show a significant performance-enhancing effect [37, 42, 44]; albeit, with sample
280 sizes of 15, 10, and eight participants, respectively. Phases of the menstrual cycle might play
281 an important role in studies involving women given that caffeine clearance is slower in the
282 luteal phase of the cycle [63]. Furthermore, the use of oral contraceptives may alter caffeine
283 metabolism [64], which also needs to be considered when conducting studies among women.
284 This topic seems to be under-investigated in this population and requires further attention. In
285 summary, it seems that caffeine can acutely enhance muscular endurance, but details such as
286 fatigue-related and sex-specific responses require future study to better determine its
287 effectiveness.

288

289 **5 Effects of caffeine on power**

290 Most of the studies on power outcomes focused on variations of jump performance [46],
291 power recorded during the Wingate 30-s test [65], or repeated and intermittent-sprints
292 performance [66, 67]. Caffeine may acutely enhance these components of power [46, 65-67],
293 but there is limited research on the effects of caffeine on power expression measured as
294 contraction velocity during traditional dynamic resistance exercises. In a study by Mora-
295 Rodríguez et al. [68], 12 trained men performed three exercise trials: (i) a morning training
296 session (10:00 a.m.) after the ingestion of 3 mg·kg⁻¹ of caffeine, (ii) a morning training session
297 after ingesting a placebo, and (iii) an afternoon session (18:00 p.m.) following the ingestion of
298 a placebo. Bar displacement velocity was measured during the squat and bench press
299 exercises with loads that elicited a bar velocity of 1 m·s⁻¹ and with a load corresponding to
300 75% of 1RM. Results showed that power increased with all loads with caffeine ingestion,
301 except for the bench press velocity at 1 m·s⁻¹ ($p = 0.06$, Cohen's $d = 0.68$). Using the same
302 dose of caffeine in a group of 14 Brazilian jiu-jitsu athletes, Diaz-Lara et al. [69] confirmed

303 that caffeine may be ergogenic for power, showing an increase in maximal power and mean
304 power in the bench press exercise.

305

306 Pallarés et al. [70] sought to investigate contraction velocity at three different doses of
307 caffeine (i.e., 3, 6, and 9 mg·kg⁻¹) and across four different loading schemes, namely, 25%,
308 50%, 75%, and 90% of 1RM performed using the bench press and barbell back squat
309 exercises. When measured at loads of 25% and 50% of 1RM, all doses of caffeine resulted in
310 increased power in both exercises. At higher loads, higher doses seem to be needed to
311 augment power, both in the bench press and in the squat exercises. These results suggest that
312 greater doses of caffeine might be warranted for a performance-enhancing effect when
313 exercising with higher loads. Such large doses of caffeine also seem to generate more side
314 effects [70], which also needs to be considered. In the same sample, caffeine has been shown
315 to have a more pronounced effect on power when administered in the morning versus in the
316 afternoon hours [71]. Such results could be due to the reduced capacity to activate/recruit the
317 musculature in the morning hours [71]. Therefore, when administered in the morning, caffeine
318 may augment the ability to activate/recruit the musculature [71]. Also, side effects such as
319 insomnia may be even more prevalent when supplementing with caffeine in the afternoon
320 hours [71], which does highlight that time-of-day is an important variable to consider when
321 prescribing caffeine supplementation.

322

323 It seems that caffeine may enhance contraction velocity, although this finding is based only on
324 the results from a few studies. Given some of the mixed evidence presented for maximal
325 strength, this might indicate that caffeine has a more pronounced effect on contraction
326 velocity than on maximal force production. Future studies should consider examining changes

327 in both 1RM strength and contraction velocity (with lower loads) in the same group of
328 participants to investigate if this is indeed the case. The limited research to date suggests that
329 caffeine ingestion may acutely increase muscle power in resistance exercise and, therefore,
330 athletes competing in events in which power is a significant performance-related variable
331 might consider using caffeine supplementation pre-exercise.

332

333 **6 Effects of caffeine on muscle damage and delayed onset muscle soreness**

334 **6.1 Delayed onset muscle soreness**

335 Resistance exercise may lead to exercise-induced muscle damage and delayed onset muscle
336 soreness (DOMS) [72]. Exercise-induced muscle damage commonly brings about DOMS,
337 which can be defined as the pain felt upon palpation or movement of the affected tissue [73].
338 DOMS appears within a few hours post workout, peaks 1 to 3 days following the exercise
339 session, and can last up to 10 days [74]. Because caffeine is an adenosine antagonist, its
340 consumption might increase the response of the sympathetic nervous system, and, thus,
341 decrease the perception of muscle soreness [75].

342

343 Two of the initial studies [38, 76] that investigated the effects of caffeine ingestion on DOMS
344 following resistance exercise observed that caffeine might indeed reduce DOMS. Hurley et al.
345 [38] employed a training protocol that consisted of five sets of biceps curls exercise
346 performed with a load corresponding to 75% of 1RM. On days 1 to 5, the participants were
347 required to assess their levels of soreness on three different scales: overall soreness, overall
348 fatigue, and soreness on a palpation scale. Administration of caffeine ($5 \text{ mg} \cdot \text{kg}^{-1}$) allowed the
349 participants to perform a significantly greater number of repetitions during the fifth set of
350 bicep curls. However, despite greater total work performed following caffeine ingestion, the

351 overall perception of soreness was significantly lower on day 2 and day 3 with caffeine
352 ingestion as compared to placebo. Because soreness peaks 1 to 3 days following exercise, the
353 results of this study indicate that caffeine can significantly reduce the perception of soreness
354 following resistance exercise. Hurley et al. [38] also assessed creatine kinase levels and,
355 consistent with the results of Machado et al. [77] (see section 6.2), they reported that caffeine
356 ingestion did not significantly affect creatine kinase levels.

357

358 In the Maridakis et al. [76] study, during the first visit (no supplement ingestion), the
359 participants underwent an electrically-stimulated eccentric exercise of the quadriceps that
360 consisted of 64 eccentric actions; a protocol known to bring about DOMS [78]. Twenty-four
361 and 48 hours following the protocol, the participants consumed either a placebo or caffeine (5
362 mg·kg⁻¹) in a counterbalanced fashion and expressed their perceived levels of soreness after
363 performing an MVC and a submaximal eccentric test. The results showed that with the
364 ingestion of caffeine there was a significant reduction in DOMS with a greater effect observed
365 during the MVC as compared to submaximal eccentric movements. In a recent study, Green
366 et al. [79] showed that caffeine increased peak torque but did not impact the perception of
367 soreness in a group of 16 participants using a caffeine dose of 6 mg·kg⁻¹. While Maridakis et
368 al. [76] used a protocol that involved maximal and submaximal eccentric movements, the
369 protocol in this study for assessing DOMS involved expressing subjective levels of soreness
370 after stepping down from a box [80], which might explain the differences in results between
371 the studies. The use of different methods for assessing DOMS somewhat limits the
372 comparison of results between the studies.

373

374 In summary, there is some preliminary evidence to suggest that caffeine ingestion may indeed
375 reduce DOMS, which is not surprising given that caffeine can have a hypoalgesic effect. That
376 said, given the small number of studies, further research exploring this topic is warranted. The
377 studies that have been conducted so far mostly administered caffeine only pre-exercise.
378 However, Caldwell et al. [81] recently explored the effects of ingesting caffeine on perceived
379 soreness in the days following exercise (i.e., a 164 km endurance cycling event). Given that
380 the authors reported positive effects of caffeine on relieving feelings of soreness during the
381 three days of recovery post-exercise, this is an area that could be further explored in resistance
382 exercise as well.

383

384 **6.2 Muscle damage**

385 Machado et al. [77] investigated the effects of caffeine ingestion on blood markers of muscle
386 damage, including creatine kinase, lactate dehydrogenase, alanine aminotransferase, and
387 aspartate aminotransferase. Fifteen participants took part in a resistance exercise protocol
388 consisting of six exercises performed in three sets of ten repetitions. The caffeine dose was
389 $4.5 \text{ mg}\cdot\text{kg}^{-1}$. All the abovementioned markers of muscle damage increased after the resistance
390 exercise session with no significant differences found between the caffeine and placebo
391 conditions. In this study, researchers equated the total work (calculated as load \times sets \times
392 repetitions) between the caffeine and placebo sessions. However, given that caffeine may
393 enhance acute exercise performance, this might consequently lead to greater increases in
394 markers of muscle damage. This hypothesis could be explored in future studies that do not
395 equate the total work between the caffeine and placebo trials.

396

397 **7 Effects of caffeine on hormonal responses**

398 Acute increases in hormones such as testosterone (a primary anabolic hormone), cortisol (a
399 systemic catabolic marker), and growth hormone (a hormone associated with reproduction
400 and stimulation of cellular growth) following resistance exercise have received considerable
401 attention in the literature [82]. It has been suggested that acute changes in these hormones
402 influence resistance training adaptations such as muscular hypertrophy and increases in
403 strength [82]. However, others recently found that the acute changes in hormones are weakly
404 correlated with long-term adaptations to resistance training [83]. Thus, although some studies
405 [35, 84-86] reported that caffeine ingestion, as compared to placebo, may lead to greater
406 increases in the production of testosterone and cortisol following resistance exercise (even
407 when the workload is matched between the conditions), the practical applicability of these
408 findings remains unclear.

409

410 **8 Effects of caffeine on muscle protein synthesis and anabolic signaling**

411 One of the hallmark adaptations to resistance exercise is muscular hypertrophy. In general, it
412 is accepted that the anabolic mammalian mechanistic target of rapamycin complex 1
413 (mTORC1) signaling cascade mediates muscular hypertrophy which is a cumulative result of
414 acute increases in protein synthesis above protein degradation (i.e., net protein accretion) [87,
415 88]. Some of the studies conducted in cultured cells have observed that caffeine inhibited
416 mTOR activity [89, 90], albeit, such effects were seen at supra-physiological concentrations
417 of caffeine. A recent study by Moore et al. [91] conducted in mice (with physiological
418 concentrations of caffeine that would be observed in humans following moderate caffeine
419 intake), showed that caffeine did not negatively affect mTOR activity or muscle protein
420 synthesis after a bout of electrically-stimulated contractions. Moreover, caffeine even
421 enhanced the phosphorylation of ribosomal protein S6 suggesting a positive effect of caffeine
422 on anabolic signaling. Furthermore, work on rats in the same study showed that caffeine did

423 not affect plantaris muscle hypertrophy [91]. While cell culture and animal models may
424 provide some interesting findings, they also may have limited relevance to humans. Currently,
425 there are no published studies examining the effects of caffeine on muscle protein synthesis
426 and anabolic signaling in response to resistance exercise in humans. While there are some
427 unpublished observations involving resistance-trained men in whom caffeine ingestion did not
428 negatively affect muscle protein synthesis responses following resistance exercise [92], these
429 results remain to be published. Therefore, this is an interesting area that could be explored in
430 future research.

431

432 **9 Effects of caffeine on cardiovascular responses**

433 **9.1 Blood pressure**

434 Even under resting conditions, caffeine ingestion of 250 mg has been shown to increase blood
435 pressure [93]. Also, resistance exercise may lead to significant acute increases in systolic and
436 diastolic blood pressure [94]. Therefore, it is possible that the combination of this type of
437 exercise with caffeine ingestion might augment acute blood pressure responses.

438

439 Only a few studies to date have focused on the effects of caffeine on the cardiovascular
440 system in resistance exercise. Jacobs and colleagues [59] initially reported that the ingestion
441 of caffeine did not increase systolic blood pressure more than the ingestion of placebo during
442 a resistance exercise session consisting of three supersets (leg press exercise followed by the
443 bench press exercise). Following caffeine ingestion, Astorino et al. [95] reported increases in
444 systolic but not diastolic blood pressure. In a study including normotensive and hypertensive
445 men, Astorino et al. [96] confirmed their initial findings by showing that caffeine ingestion
446 increases resting, exercise, and recovery systolic blood pressure. The same effect on blood

447 pressure was observed in a study by Goldstein et al. [44], in which the ingestion of caffeine
448 led to an increase in systolic blood pressure by 4 mmHg. Comparable results were observed
449 by others as well [35]. When ingested before physical activity, caffeine may reduce
450 myocardial blood flow during exercise [97]. This reduction in blood flow likely explains the
451 augmented increases in blood pressure that may occur with the ingestion of caffeine in
452 resistance exercise [97].

453

454 Passmore et al. [98] have reported that caffeine doses of 45, 90, 180, and 360 mg increase
455 blood pressure in a dose-response fashion (i.e., greater increases with higher doses).
456 Therefore, the discrepancy in findings between studies of subjects participating in resistance
457 exercise might be explained by the caffeine dose, as Jacobs et al. [59] used a dose of 4.5
458 $\text{mg}\cdot\text{kg}^{-1}$, while Astorino et al. [95] and, subsequently, Goldstein et al. [44], used a dose of 6
459 $\text{mg}\cdot\text{kg}^{-1}$. Although variations in dosage might help explain these findings, it is important to
460 highlight that a caffeine dose of 4 $\text{mg}\cdot\text{kg}^{-1}$ was reported to increase blood pressure [99].
461 Furthermore, in some studies, a dose of 5 $\text{mg}\cdot\text{kg}^{-1}$ did not result in greater increases in blood
462 pressure over placebo alone, highlighting the equivocal nature of research done in this area
463 [36]. Factors such as participants' posture, arm support, arm position, left or right-hand side,
464 cuff, and empty/full bladder are all known to influence blood pressure estimates [100].
465 However, most of the studies only reported the timing of measurement and posture, making
466 the between-study comparison of the results difficult. Due to the effects of caffeine on blood
467 pressure, this supplement might not be recommendable for individuals with high blood
468 pressure, as it may result in excessive cardiovascular demands [101]. Therefore, caution is
469 needed when considering caffeine supplementation in these populations.

470

471 **9.2 Heart rate**

472 Besides blood pressure, heart rate is another important cardiovascular variable that needs to
473 be considered. Astorino et al. [95] also evaluated heart rate responses in a cohort of
474 resistance-trained men performing 1RM and muscular endurance tests on both the bench press
475 and leg press exercises. They observed that heart rate before starting the exercise bout and
476 pre- bench-press increased by ten beats per min with the ingestion of caffeine. While some
477 studies observed similar effects of caffeine on this variable [33, 34, 102], others have reported
478 no differences in heart rate responses between the caffeine and placebo conditions [28, 32, 35,
479 36, 96, 99]. Some discrepancies between the studies might be related to the habitual caffeine
480 intake of participants. Specifically, there is evidence to suggest that increases in heart rate
481 with caffeine ingestion are exacerbated in individuals who habitually consume lower amounts
482 of caffeine as compared to high habitual users [103, 104]. However, while some studies did
483 not assess habitual caffeine intake [28, 33], the participants in others reported a wide range of
484 habitual caffeine intake varying from 30 to 600 mg [95]. Given these limitations, future
485 studies should consider exploring potential differences in the effects of caffeine ingestion on
486 heart rate responses in resistance exercise between low and high habitual caffeine users.
487 Future work is warranted on the effects of caffeine on heart rate variability (time differences
488 between consecutive heartbeats) in resistance exercise, as there is evidence (in other forms of
489 exercise) that caffeine ingestion may negatively impact this outcome [105].

490

491 **10 Caffeine form**

492 The most common forms of caffeine administration for supplementation purposes are
493 capsules and powder mixed with liquid. Currently, there is a growing interest in investigating
494 the effects of caffeine administered in alternative forms such as chewing gums, bars, gels,

495 mouth rinses, energy drinks, and aerosols [11]. Some of these forms of caffeine may have a
496 faster absorption rate, which might be of interest in many sporting situations [11]. For
497 instance, Kamimori et al. [106] observed that the time to reach maximal caffeine
498 concentration in the blood was 44 to 80 min with caffeine administered in chewing gum,
499 while in the capsule trials this time amounted to 84 to 120 min. Pharmacokinetics of different
500 forms of caffeine are discussed in more detail in a recent paper by Wickham and Spriet [11].
501 For resistance exercise protocols only three studies have been conducted with alternative
502 forms of caffeine. One study explored the effect of caffeine mouth rinse on muscular
503 endurance and reported no significant increases in volume load with caffeine ingestion [107].
504 This can probably be explained by the observation that caffeine administered in this form
505 does not increase blood caffeine concentration [108]. Another study investigated the effects of
506 a sugar-free drink containing a fixed dose of 160 mg of caffeine and a placebo beverage on
507 1RM bench press performance and upper-body muscular endurance [109]. No significant
508 increases in either strength or muscular endurance were found following caffeine ingestion.
509 Some unpublished observations suggest that consumption of caffeinated chewing gum (fixed
510 dose of 75 mg of caffeine) can increase 1RM squat performance [110]. However, the study
511 has yet to be published, which precludes its scrutinization. This area of research is currently in
512 its infancy and needs further exploration.

513

514 Researchers have only recently begun to compare the effects of caffeine alone and caffeinated
515 coffee using a resistance exercise protocol. The first study that examined this matter was
516 conducted by Trexler et al. [111]. The authors investigated the effects of: (i) caffeine
517 administered in an absolute dose of 300 mg, (ii) coffee with a dose of 303 mg of caffeine, and
518 (iii) a placebo. The effects of coffee on 1RM leg press exercise performance were greater than
519 the effects of caffeine ingestion. The second study that investigated this topic in relation to

520 resistance exercise is the work by Richardson and Clarke [102] who tested muscular
521 endurance in the squat exercise. Results showed that both caffeinated coffee and decaffeinated
522 coffee plus 5 mg·kg⁻¹ of anhydrous caffeine resulted in significantly better squat exercise
523 performance compared to other conditions. Therefore, notwithstanding the lack of studies
524 conducted in this area, based on the current evidence, it may be inferred that both coffee and
525 caffeine anhydrous are suitable pre-workout options, while the choice would be a matter of
526 personal preference.

527

528 **11 Caffeine dose, timing, and habitual intake**

529 The most commonly used dose of caffeine in studies examining the effects of caffeine on
530 exercise performance is 6 mg·kg⁻¹ [1]. This dose is relatively high, as, for an 85-kg individual,
531 it equates to the amount of caffeine in approximately four to five cups of coffee. As discussed
532 elsewhere [10], there is a growing interest in investigating the effects of lower doses of
533 caffeine (i.e., ≤3 mg·kg⁻¹) on exercise performance as these doses may still lead to
534 improvements in alertness and mood during exercise and are associated with few, if any, side
535 effects [10].

536

537 Astorino et al. [30] reported that performance of the knee extension and flexion exercises was
538 significantly improved with a 5 mg·kg⁻¹ dose of caffeine. However, no improvement in
539 performance was observed with a 2 mg·kg⁻¹ dose. Using the same doses, Arazi et al. [37]
540 observed that caffeine did not improve leg press strength and muscular endurance at either 2
541 or 5 mg·kg⁻¹ doses. Tallis and Yavuz [41] observed that both 3 and 6 mg·kg⁻¹ caffeine doses
542 were effective for increasing lower-body strength. Furthermore, as stated earlier when
543 discussing power outcomes (section 5), three studies [68-70] have investigated the effects of 3

544 mg·kg⁻¹ of caffeine on resistance exercise performance and power and suggested that this
545 dose can be ergogenic. However, at specific external loads, a higher dose was needed to
546 achieve an increase in performance. A meta-regression by Warren et al. [49] suggested that
547 there is a dose-response relationship between the doses of caffeine and the magnitude of the
548 effects on muscular endurance. Specifically, for an increase in caffeine dose of 1 mg·kg⁻¹
549 muscular endurance effect size increased by 0.10. However, optimal doses of caffeine still
550 need to be further explored in resistance exercise protocols and other sport and exercise
551 settings [22]. Starting with a lower dose (such as 3 mg·kg⁻¹) may be a good initial option; the
552 doses can be adjusted after that according to the individual responses.

553

554 As with the caffeine dose, the optimal timing of caffeine supplementation has been under-
555 investigated. Caffeine has a half-life of 4 to 6 hours, and its plasma concentration reaches
556 maximum approximately one hour after ingestion (although this can depend on the source of
557 caffeine and can vary considerably between individuals) [4, 112]. Therefore, in most studies,
558 the exercise session begins one hour after the supplement is ingested. Instead of the common
559 60-min waiting time, some studies have used a 45-min [45] or a 90-min [59] waiting time and
560 did not show performance-enhancing effects of caffeine. However, it remains unclear if the
561 waiting time was responsible for the lack of a significant effect. This might have been a
562 consequence of other factors, such as small sample sizes, as the studies included nine and 13
563 participants, respectively [45, 59]. Also, genetic differences in caffeine metabolism among the
564 participants (as discussed in section 12) may have contributed to the outcomes. Because of the
565 lack of studies, the optimal timing of caffeine intake for resistance exercise remains unclear.
566 Nevertheless, it is well-established that ergogenic effects can be seen one hour post ingestion
567 when using capsule or powder forms of caffeine [46, 49, 55, 57].

568

569 There is limited research regarding the influence of habitual caffeine intake and the acute
570 effects of caffeine supplementation on exercise performance. Based on the available evidence,
571 it does not seem that habitual caffeine ingestion reduces the ergogenic benefits of acute
572 caffeine supplementation [47, 103, 113-116]. However, there are some contrasting findings
573 [117, 118] suggesting that non-habitual caffeine users experience a greater magnitude of the
574 ergogenic effect with caffeine supplementation compared with caffeine habitual users. Some
575 limitations of these studies include that Bell and McLellan [117] did not report if the
576 questionnaire they used for assessing habitual caffeine intake had previously been validated
577 while Evans et al. [118] used a dose of caffeine that was relatively small (on average, 2.5
578 $\text{mg}\cdot\text{kg}^{-1}$; ~ 200 mg vs. 3 to 6 $\text{mg}\cdot\text{kg}^{-1}$ in most other studies). It might be that habitual
579 consumers need more caffeine to achieve the same ergogenic effect as low habitual users.

580

581 Gonçalves et al. [113] explored this topic in a large sample ($n = 40$) grouped into tertiles
582 representing low, moderate, and high habitual caffeine users, where the habitual caffeine
583 intake was assessed using a previously validated questionnaire. This study suggested that
584 habitual caffeine intake does not cancel out the performance benefits of the acute
585 supplementation with caffeine. However, this study used a 30-min cycling time trial test and
586 given that there is no research done in this area using resistance exercise protocols, this
587 remains an important avenue for future research.

588

589 Additional factors such as ingestion of caffeine in a fed vs. fasted state are important to
590 consider given that the absorption of caffeine is slower in a fed state [19]. Indeed, a dose of 3
591 $\text{mg}\cdot\text{kg}^{-1}$ of caffeine administered 60-90 min pre-exercise has been shown to be ergogenic in a
592 fasted [119] but not in a fed state [120]. Additionally, withdrawal is another variable to

593 consider given that habitual caffeine users may experience headache and increased irritability
594 after caffeine abstinence of 24 hours [121]. These symptoms may confound the study design,
595 because the performance under the placebo condition may be impaired due to the withdrawal
596 effects [19].

597

598 **12 Genetic differences in responses to caffeine ingestion**

599 There is a substantial inter-individual variability in responses to caffeine ingestion [122].
600 While some individuals experience enhanced performance, others show no improvement, and,
601 in some cases, even performance decrements [122]. Based on some recent evidence it seems
602 that genotype might play an important role in the inter-individual variability in responses. The
603 initial studies that explored the genetic differences in responses to caffeine ingestion while
604 using an exercise protocol report mixed findings [123-125]. For instance, Womack et al. [123]
605 reported a greater effect of caffeine on exercise performance in AA than in C allele carriers
606 while others found no significant effect of this polymorphism on caffeine's ergogenic effect
607 [125]. Most of these studies had small to moderate sized samples ($n = 16$ to 35). However, in
608 a large cohort of male athletes ($n = 101$), Guest et al. [126] showed that the individuals with
609 the AA genotype had a 5% and 7% improvement in time trial performance with the ingestion
610 of $2 \text{ mg}\cdot\text{kg}^{-1}$ and $4 \text{ mg}\cdot\text{kg}^{-1}$ of caffeine, respectively. Individuals with the AC genotype did not
611 improve performance following caffeine supplementation, and those with the CC genotype
612 experienced decreases in performance after the ingestion of caffeine. Recently, Rahimi [127]
613 assessed the effects of caffeine ingestion on muscular endurance using a resistance exercise
614 protocol. A significant difference was observed between the groups for the total number of
615 performed repetitions following caffeine ingestion (AA = +13% vs. AC/CC = +1%; $p =$
616 0.002). While this is the only study that examined this topic using a resistance exercise

617 protocol, it does provide compelling evidence in support of the importance of considering
618 genotype when assessing the response to caffeine ingestion.

619

620 **13 Placebo effects of caffeine supplementation**

621 Pollo et al. [128] investigated the placebo effect on leg extensions exercise performance and
622 reported that the administration of a placebo, alongside the suggestion that it was caffeine,
623 increased mean muscle work and decreased self-perceived muscle fatigue. Duncan et al. [129]
624 confirmed the findings by Pollo et al. [128] as their results showed that the participants were
625 able to perform two more repetitions under the perceived caffeine condition, and this was
626 accompanied by a reduced RPE, thereby highlighting the power of a placebo for driving
627 positive effects on exercise outcomes [130].

628

629 In their proof-of-principle study, Saunders et al. [131] reported that the participants who
630 correctly identified placebo experienced possible harmful effects on performance.
631 Furthermore, those who thought that they ingested caffeine while ingesting placebo also
632 appeared to improve their performance. Therefore, to investigate if any performance-
633 enhancing effects are undoubtedly related to caffeine ingestion or merely a placebo effect, it
634 would be of importance to ask the participants to indicate which trial they perceived to be the
635 caffeine trial. Unfortunately, this question was not asked in several studies examining the
636 effects of caffeine on resistance exercise [27, 32, 36, 44, 45] and the results of such studies
637 therefore need to be interpreted with caution. Although not in all cases, some studies that
638 investigated the effectiveness of the blinding indicated that blinding of the participants is
639 effective, as only 29% to 60% of the participants correctly identified the caffeine trials [29,
640 43, 132]. It is interesting that in the Bond et al. [58] study, there was no blinding of the

641 participants or the investigators, yet, no effect of caffeine on performance was seen (the
642 percent changes and effect sizes actually favored the placebo trial). Furthermore, in the work
643 by Tallis et al. [133] an equal improvement in peak concentric force was found in the trial in
644 which the participants were told that they were given caffeine and did indeed receive a
645 caffeine dose, and in the trial in which the participants were told that they were given placebo
646 even though they received caffeine. These results seem encouraging as they reflect the true
647 effect of caffeine supplementation on performance. Nonetheless, future research is necessary
648 to differentiate between the actual effects of caffeine and placebo effects.

649

650 **14 Conclusions**

651 Current evidence suggests that caffeine ingestion increases maximal strength, as assessed by
652 1RM and MVC tests, and muscular endurance. Furthermore, studies show that power is
653 enhanced by caffeine supplementation, although this effect might be caffeine dose- and
654 external load-dependent. While a reduction in RPE potentially contributes to the performance-
655 enhancing effects of caffeine supplementation, the same was not found for pain perception.
656 Some studies have reported that caffeine ingestion did not affect exercise-induced muscle
657 damage but that it might even reduce resistance exercise-induced DOMS. There is some
658 evidence that caffeine ingestion, as compared to placebo, leads to greater increases in the
659 production of testosterone and cortisol following resistance exercise. However, given that the
660 acute changes in hormone levels are weakly correlated with long-term adaptations to
661 resistance exercise, such as hypertrophy and increased muscular strength, these findings are
662 likely of questionable practical significance.

663

664 Although not without contrasting findings, the available evidence suggests that caffeine
665 ingestion can lead to acute increases in blood pressure (primarily systolic), and, thus, caution
666 is needed regarding caffeine supplementation among individuals with high blood pressure. In
667 the vast majority of studies, caffeine was administered in capsule or powder forms, and the
668 effects of alternative forms such as chewing gums or mouth rinses on resistance exercise
669 performance therefore remain unclear. The emerging evidence suggests that coffee is at least
670 equally ergogenic as caffeine alone when the caffeine dose is matched. Nevertheless, more
671 research is needed on this topic. Doses in the range 3-9 mg·kg⁻¹ seem to be adequate for
672 eliciting an ergogenic effect when administered 60 min pre-exercise. It remains unclear what
673 the minimal effective doses are for different types of resistance exercise.

674

675 In general, caffeine was found to be safe when taken in the recommended doses. However, at
676 doses as high as 9 mg·kg⁻¹ or higher, side-effects such as insomnia are more pronounced,
677 which needs to be considered when prescribing caffeine supplementation. It remains unclear
678 whether habituation cancels out the ergogenic benefits of caffeine on resistance exercise
679 performance, as no evidence exists for this type of exercise. In some cases, administering
680 placebo alone with the suggestion that it is caffeine has also been shown to enhance
681 performance and reduce RPE. Therefore, the effectiveness of the blinding needs to be
682 considered in future research. Caution is needed when extrapolating these conclusions to
683 females as the vast majority of studies involved only male participants. Finally, most of the
684 studies done in this area report small-to-moderate acute improvements in resistance exercise
685 performance with caffeine ingestion. Therefore, future long-term intervention studies are
686 needed to explore if such acute increases in performance with caffeine ingestion also impact
687 long-term adaptations to resistance exercise.

688 **Compliance with Ethical Standards**

689 **Conflict of interest**

690 Jozo Grgic, Pavle Mikulic, Brad J. Schoenfeld, David J. Bishop and Zeljko Pedisic declare
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