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1 **Athletes Intending to Use Sports Supplements Are More Likely to Respond to a Placebo**

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8 **Abstract**

9 **Purpose:** We investigated associations between athletes' use of sport supplements and their  
10 responsiveness to placebo and nocebo interventions. **Methods:** Participants (n=627) reported  
11 their intention to use, and actual use of, sport supplements. They then completed a 5x20m  
12 repeat sprint protocol in the baseline condition, prior to being randomized to one of three  
13 treatments. Participants in the positive-belief treatment were administered an inert capsule  
14 described as a potent supplement which would improve sprint performance. Participants in the  
15 negative-belief treatment were administered an inert capsule described as a potent supplement  
16 which would negatively affect sprint performance. Participants in the control treatment  
17 received neither instruction nor capsule. 20 minutes following baseline trials, all participants  
18 completed the same repeat sprint protocol in the experimental condition. **Results:** Compared  
19 to controls, no mean differences in performance were observed between baseline and  
20 experimental conditions for the positive-belief treatment ( $-0.07 \pm 0.27\%$ ,  $d=0.02$ ), but mean  
21 differences were observed for the negative-belief treatment ( $-0.92 \pm 0.31\%$ ,  $d=0.32$ ),  
22 suggesting a moderate nocebo effect. In the positive-belief treatment however, a relationship  
23 between intention to use supplements and performance was observed. Performance worsened  
24 by  $-1.10\% \pm 0.30\%$  compared to baseline for participants not intending to use supplements,  
25 worsened by  $-0.64 \pm 0.43\%$  among those undecided about supplement use, but improved by  
26  $0.19 \pm 0.24\%$  among those participants intending to use supplements. **Conclusion:** Information  
27 about a harmful supplement worsened repeat sprint performance (a mean nocebo effect),  
28 whereas information about a beneficial supplement did not improve performance (no mean  
29 placebo effect was observed). However, participants' intention to use sport supplements  
30 influenced the direction and magnitude of subsequent placebo responses, with participants  
31 intending to use supplements more likely to respond to the positive intervention.

32 **Key words:** Nocebo, responders, beliefs, ergogenic aids

### 33 **Introduction**

34 A placebo effect is a positive psychobiological response to a purported beneficial treatment  
35 (11). Placebo effects have been extensively studied in sport (3, 4, 7, 8, 12, 15, 21, 31, 32, 34,  
36 35, 39), with a systematic review (6) reporting that placebo treatments can exert a significant  
37 effect on sport performance. For example, Ross et al. (34) reported a 1.2% improvement in 3-  
38 km running time-trial performance when participants self-administered saline injections  
39 believing it to be a performance enhancing substance. Likewise, Saunders et al. (35) reported  
40 that mean power output improved by 3.7% among cyclists deceptively administered a placebo  
41 when they believed they had ingested caffeine.

42 While there is empirical support for the potential role of the placebo effect in sports  
43 performance, there is less evidence for the nocebo effect; that is, a negative psychobiological  
44 response to a purported harmful treatment. Arguably the first study of the nocebo effect in sport  
45 was conducted by Beedie et al. in 2007 (5). These authors reported that n=21 participants who  
46 believed they had ingested a placebo, that is a capsule described as a beneficial sport  
47 supplement, ran progressively faster compared to baseline. Likewise, n=21 participants who  
48 believed they had ingested a nocebo, that is a capsule described as a supplement likely to be  
49 detrimental to performance, ran progressively slower compared to baseline. Findings  
50 highlighted the potentially significant impact of positive and negative expectations on sports  
51 performance.

52 However, the study in question (5) lacked a no-treatment control. It is therefore problematic to  
53 estimate the true relative magnitude of the placebo and nocebo effects reported; changes in  
54 performance could be attributed to statistical or methodological artefacts such as regression to  
55 the mean or spontaneous improvements/decrements in performance (25). Further, it is  
56 problematic from this uncontrolled study to discern whether actual effects were all positive, all  
57 negative, or whether both placebo and nocebo effects occurred. As a result, the reported

58 magnitude of either the nocebo or placebo effect might have been overestimated. Further, while  
59 the n=42 reported was relatively large for an intervention study in sport, it was however too  
60 small to facilitate the reliable identification of any psychosocial variables that might have been  
61 associated with the placebo and nocebo responses observed.

62 In most studies of the placebo/nocebo effect in sport, the standard deviation of the dependent  
63 measure is greater in experimental conditions than at baseline (6). This suggests that, even if a  
64 mean placebo effect is observed, there is considerable inter-individual variability in response  
65 to the treatment. Few studies have attempted to identify the variables related to placebo  
66 responses, and those that have are perhaps methodologically unsatisfactory. For example,  
67 Beedie et al. (7) identified a possible link between placebo responding and personality factors,  
68 but the sample size was too small for their findings to be considered reliable. In fact, the small  
69 sample sizes of nearly all studies of the placebo effect in sport has precluded the reliable  
70 investigation of any factor that might be associated with placebo responding. If our knowledge  
71 and understanding of the placebo and nocebo effects is to progress beyond simple description,  
72 we need to better understand the relevant antecedents and mechanisms.

73 We aimed to extend Beedie et al.'s study (5) via two specific criteria, each allowing us to test  
74 two novel hypotheses. First, by using a no-treatment control we were able to estimate the  
75 relative magnitude of placebo and nocebo effects in response to treatments. In this context we  
76 hypothesised that compared to controls, positive effects on performance would be associated  
77 with a positive belief (placebo) treatment, while negative effects on performance would be  
78 associated with a negative belief (nocebo) treatment. Second, by using a sufficiently large  
79 sample, we were able to reliably identify factors that might be associated with observed placebo  
80 and/or nocebo responses. Given the range of such factors is potentially large, we were  
81 presented with a number of possible hypotheses. Recent data from both medicine and  
82 psychology suggest that prior use of a treatment can influence the response of a patient to a

83 subsequent placebo treatment (10). We hypothesised that athletes with prior experience of sport  
84 supplements would be more likely to respond to a placebo sport supplement than those who do  
85 not use sport supplements. Furthermore, prior use of a supplement is suggested to be influenced  
86 via a person's intention to use that substance (33). We therefore further hypothesised that those  
87 intending to use supplements would also be more likely to respond to a placebo intervention.

88 The idea that greater understanding of the placebo effect among athletes and coaches might  
89 reduce doping has been proposed (6, 26, 31, 32). Given the gateway hypothesis (26), which  
90 posits that supplement use can lead to doping, it is reasonable to suggest that, over and above  
91 enhancing our understanding of placebo and nocebo effects in sport, this study could also  
92 enhance our understanding of factors that underpin doping.

## 93 **Methods**

### 94 Design

95 The placebo and nocebo interventions used in this study required the deceptive administration  
96 of an inert capsule delivered to members of teams in their usual team environment. We  
97 therefore used a cluster randomized controlled trial design to minimize cross-contamination  
98 between experimental and control treatments. Participants completed a pre-experimental  
99 questionnaire relating to sport supplementation, before performing 5 × 20-m repeat sprint with  
100 30s recovery at baseline. Following Beedie et al.'s original design (5), participants in the  
101 positive-belief treatment (n = 288) were deceptively administered an inert capsule described as  
102 a potent supplement which would improve sprint performance. Also following the original  
103 design, participants in the negative-belief treatment (n = 232) were deceptively administered  
104 an inert capsule described as a potent supplement which would negatively affect sprint  
105 performance. However, extending the original study, no-treatment control participants (n =  
106 192) received neither instruction nor placebo. Twenty minutes following the administration of

107 the capsules, participants completed the experimental condition, which was a repeat of the 5 ×  
108 20-m sprints.

## 109 Participants

110 We used convenience sampling, and invited athletes from a range of sports to participate in the  
111 study. Seven hundred and twelve competitive athletes from 43 different teams (number of  
112 athletes in each team: median = 14; range = 8 to 40) were initially recruited to the study.  
113 Participant demographics are presented in Table 1. All participants were aware that their  
114 involvement in the study was voluntary and that all data collected would be treated as  
115 confidential. Ethical approval was granted by the Institutional Research Ethics Committee.  
116 Participants gave written informed consent once they had read the participant information  
117 sheet.

## 118 Measures

### 119 Pre-experimental questionnaire

120 All participants were asked to complete a pre-experimental questionnaire detailing sex, age,  
121 sport played and competitive level (club, county, regional or national). They were asked to  
122 indicate whether they used sports supplements (yes or no), the total number of supplements  
123 used, and the frequency of use (daily, weekly, monthly or never). They were also asked to  
124 indicate their agreement with a statement of their intention to use sport supplements in the next  
125 three months on a 6 point Likert-type scale anchored at strongly disagree (1), through to  
126 strongly agree (6). Those scoring 1 and 2 were grouped as ‘not intending’, 3 and 4 as  
127 ‘undecided’, 5 and 6 as ‘intending’.

### 128 Repeat sprint performance

129 Whereas Beedie et al. (5) used a 3 × 30-m repeat sprint protocol, Schimpchen, Skorski, Nopp  
130 and Meyer (36) reported that four or more sprints should be used to decrease the typical error

131 and improve the precision of estimating true changes in performance. Furthermore, the  
132 majority of sprinting in team sports events occurs over relatively short distances (i.e. <30-m;  
133 (14)) and short durations (i.e. <4 seconds; (37)). For these reasons, participants were asked to  
134 complete five 20-m maximal intensity repeat sprints with 30 seconds of recovery between each  
135 sprint. Sprint time was measured using an automated, single-beam photocell, light gate system  
136 (Smartspeed Pro<sup>TM</sup>, Fusion Sport Inc., Australia). Single-beam light gate systems are the most  
137 common method for measuring sprint performance and have been shown to have good  
138 reliability (20).

### 139 Belief Manipulation

140 During the 20-minute recovery period between baseline and experimental conditions,  
141 participants in the positive- and negative-belief treatments were given a capsule described as a  
142 potent sport supplement, 'inorganic nitrate.' Similar to Beedie et al. (5), the positive-belief  
143 treatment participants were given two red and white, size 1 (20-mm), gelatine capsules  
144 containing 200-mg of cornflour (Sainsbury's, London UK) and informed that inorganic nitrate  
145 would improve both endurance and repeat sprint performance. Negative-belief treatment  
146 participants were given two red and black, size 1 (20-mm), gelatine capsules containing 200-  
147 mg of cornflour and informed that inorganic nitrate would improve endurance but have a  
148 negative effect on sprint speed. The effectiveness of the belief manipulation was assessed  
149 during a debrief immediately following the experimental trials, at which point the true nature  
150 of the study was revealed. Participants were asked to respond on a 10 point Likert-type scale,  
151 how much they believed the treatment influenced their performance (1 = no influence to 10 =  
152 high influence).

### 153 Procedure



154 Testing was performed at the 43 different training facilities habitually used by the teams  
155 recruited to the study. All data per each participant were collected on one day to minimize  
156 meteorological and biological variation. Teams were randomised to the three treatments (i.e.  
157 positive, negative and control) using a computer generated cluster programme (allocation ratio  
158 1:1:1), which was performed by the lead author who was also involved in delivering the  
159 intervention. To reduce potential confounding, only one team per club were permitted to take  
160 part in the study. All treatments were conducted on separate days and at separate sites to  
161 maintain the experimental blind.

162 Participants completed the sprints in footwear and clothing suitable for high intensity exercise,  
163 and were encouraged to perform their standard warm-up. They began each sprint in a stationary  
164 position, ~50-cm behind the first light gate. They were instructed not to rock back and forth  
165 prior to the sprint, but were permitted to start the sprint in any position (e.g. split-stance or  
166 crouch start), which was replicated for each sprint. Each sprint was started by a green LED,  
167 which would flash up on the photocell. Participants were encouraged to sprint as fast as  
168 possible for the full 20-m, with times recorded to the nearest 1/100<sup>th</sup> of a second. Participants  
169 were given thirty seconds to jog back to the start position and begin the next sprint. This process  
170 was continued until each participant had completed five sprints.

171 After the baseline condition, participants in the positive- and negative-belief treatments  
172 received the capsules and the belief manipulation. All participants then completed a 20-minute  
173 recovery consisting of light exercise to minimize the search for physiological symptoms  
174 associated with the intervention (16), before commencing the experimental condition in the  
175 same manner as the first. The total duration of the repeat sprint protocol, including recovery,  
176 was less than 30-minutes per participant. On completion, participants were debriefed about the  
177 true nature of the study in line with American Psychological Association guidelines for  
178 deceptive research (1).

179 Statistical analysis

180 Data were inputted into SPSS version 23.0 (IBM, Armonk, NY, USA) and tested for  
181 homogeneity of variance, normal distribution and anomalies. Inspection of the data indicated  
182 that 55 participants (8%) did not complete the experimental condition (positive-belief treatment  
183 n = 20; negative-belief treatment n = 16; control n = 19). In addition, data values that exceeded  
184 2.5 times the standard deviation were identified as extreme outliers (30). Thirty participants  
185 (4%) were identified as extreme outliers (positive-belief treatment n = 7; negative-belief  
186 treatment n = 7; control n = 16) and were subsequently removed from further analysis (27).  
187 Data for the remaining sample of 627 participants (positive-belief treatment n = 261; negative-  
188 belief treatment n = 209; control n = 157) were entered into subsequent statistical analyses.

189 One-way Analysis of Variance (ANOVA) and chi-square ( $\chi^2$ ) tests were used to compare  
190 continuous (years training, hours per week training and number of supplement used) and  
191 categorical (sex, age, sport, ability, supplement use, frequency of supplement use and intention  
192 to use supplements) variables between treatments, respectively.

193 Sprint times for each condition (i.e. baseline and experimental) and treatment (i.e. positive,  
194 negative and control) were inputted into Hopkins' (22) reliability spreadsheet. Data were log  
195 transformed to reduce non-uniform errors and the intra-class correlation (ICC) provided  
196 estimates of reliability. The precision of ICC was interpreted as extremely high = 0.99; very  
197 high = 0.90; high = 0.75; moderate = 0.50; low = 0.20 (22).

198 Hopkins, Hawley and Burke (24) suggest that research investigating athletic performance  
199 should report outcome as a percentage change from baseline. Sprint times were therefore  
200 converted to the proportion of the first sprint speed, expressed as a percentage. Differences  
201 between participant's average performance for each condition (i.e. performance average for  
202 baseline [sprints 1 to 5] and experimental conditions [sprints 6 to 10]), and the difference in

203 the fastest sprint trial in each condition (i.e. fastest individual sprint at baseline minus fastest  
204 individual sprint at experimental) were calculated.

205 Repeated measures ANOVA identified differences in sprint performance between each  
206 condition, with treatment included as a between-subject factor. Greenhouse-Geisser epsilon  
207 was reported where sphericity was violated, and post-hoc LSD tests were conducted where a  
208 significant interaction was observed. Point-Biserial correlations ( $r_{pb}$ ) were used to assess the  
209 relationship between performance and categorical variables (i.e. sex, age, ability, sport  
210 supplement use, frequency of sport supplement use, intention to use sport supplements, belief  
211 manipulation scores). Data of the variables that correlated significantly with performances  
212 were further analysed using repeated measures ANOVA and Multivariate ANOVA  
213 (MANOVA). Given the possibility that differences between treatments may reflect the large  
214 sample size and sampling variability (38), Cohen's  $d$  ( $d$ ) effect sizes were calculated.  
215 Differences between 0.2 and  $<0.5$  were interpreted as a small effect, between 0.5 and  $<0.8$  as  
216 moderate, and  $\geq 0.8$  as large (13). Data are presented as mean  $\pm$  standard error of the mean  
217 (SEM), with statistical significance accepted at  $P \leq 0.05$ .

## 218 **Results**

### 219 Participant demographics

220 No significant differences were observed between treatments for number of years training  
221 ( $F_{(2,573)} = 2.072$ ,  $P = 0.127$ ), hours per week training ( $F_{(2,580)} = 0.403$ ,  $P = 0.669$ ), sex ( $\chi^2 = 5.28$ ,  
222  $P = 0.071$ ), supplement use ( $\chi^2 = 2.32$ ,  $P = 0.312$ ), frequency of supplement use ( $\chi^2 = 6.50$ ,  $P =$   
223  $0.370$ ) and intention to use supplements ( $\chi^2 = 4.65$ ,  $P = 0.098$ ). Differences between treatments  
224 were observed for age ( $\chi^2 = 21.99$ ,  $P = 0.001$ ), ability ( $\chi^2 = 21.69$ ,  $P = 0.001$ ) and sport played  
225 ( $\chi^2 = 225.76$ ,  $P < 0.001$ ). Covariate analysis, adjusting for the differences in categorical

226 variables, revealed no effect on the outcome of the performance sprint data ( $P > 0.05$ ). The  
227 results of the subsequent analyses are therefore reported with unadjusted covariate data.

#### 228 Reliability of sprint trials

229 Baseline sprints (i.e. trials 1 – 5) were associated with very high reliability in the positive-belief  
230 treatment (ICC = 0.94), negative-belief treatment (ICC = 0.96) and control treatment (ICC =  
231 0.90). Similar reliability coefficients were also observed for experimental sprints (i.e. trials 6 –  
232 10) in the positive-belief treatment (ICC = 0.94), negative-belief treatment (TE = 0.94) and  
233 control treatment (ICC = 0.94).

234 We also investigated the possibility that greater reliability was associated with fewer than 5  
235 sprint trials. If for example, reliability between sprint trials 1 – 4 or 1 – 3 are more reliable than  
236 1 – 5, this could reduce the error and improve the chances of finding a true effect of the  
237 intervention on sprint performance. ICC's were however, similar for trials 1 – 4 (ICC range =  
238 0.92 to 0.96) and 1 – 3 (ICC range = 0.93 to 0.96). Therefore, sprint trials 1 – 5 are reported in  
239 the subsequent analysis.

#### 240 Differences in baseline and experimental performance between treatments

241 No between-treatment differences were observed at baseline ( $F_{(2,624)} = 0.149$ ,  $P = 0.861$ ).  
242 However, between-treatment differences were observed in experimental trials ( $F_{(2,624)} = 5.879$ ,  
243  $P = 0.001$ ). In the negative-belief treatment, performance was worse than at baseline ( $-1.42 \pm$   
244  $0.15\%$ ,  $P < 0.001$ ,  $d = 0.56$ ), and also worse than performance in the positive-belief treatment  
245 ( $-1.04 \pm 0.28\%$ ,  $P < 0.001$ ,  $d = 0.34$ ) and in the control treatment ( $-0.92 \pm 0.31\%$ ,  $P < 0.001$ ,  $d$   
246  $= 0.32$ ). No differences were observed between the positive-belief and control treatments ( $-$   
247  $0.07 \pm 0.27\%$ ,  $P = 0.696$ ,  $d = 0.02$ ). Figure 1 illustrates the differences in performance for each  
248 condition between treatments.

#### 249 Correlations between performance and categorical variables

250 Point-Biserial correlations revealed a significant relationship between participant's intention to  
251 use supplements and performance (average performance in each condition:  $r_{pb} = 0.106$ ,  $P =$   
252  $0.012$ ; fastest performance difference between conditions:  $r_{pb} = 0.101$ ,  $P = 0.016$ ). No other  
253 significant relationships were observed between other categorical variables for average  
254 performance in each condition (sex  $r_{pb} = -0.009$ ,  $P = 0.819$ ; age  $r_{pb} = 0.006$ ,  $P = 0.891$ ; ability  
255  $r_{pb} = -0.039$ ,  $P = 0.353$ ; use of supplements  $r_{pb} = 0.071$ ,  $P = 0.078$ ; frequency of supplements  
256  $r_{pb} = 0.075$ ,  $P = 0.074$ ; belief manipulation scores  $r_{pb} = -0.035$ ,  $P = 0.563$ ) or fastest  
257 performance between conditions (sex  $r_{pb} = -0.014$ ,  $P = 0.723$ ; age  $r_{pb} = 0.005$ ,  $P = 0.906$ ; ability  
258  $r_{pb} = -0.042$ ,  $P = 0.318$ ; use of supplements  $r_{pb} = 0.075$ ,  $P = 0.071$ ; frequency of supplements  
259  $r_{pb} = -0.062$ ,  $P = 0.135$ ; belief manipulation scores:  $r_{pb} = 0.025$ ,  $P = 0.677$ ; fastest performance:  
260  $r_{pb} = 0.025$ ,  $P = 0.677$ ).

261 Differences in baseline and experimental performance between supplement intention

262 Further analysis using repeated measures ANOVA identified differences in participant's repeat  
263 sprint performance in each treatment by intention to use sport supplements (i.e. not intending;  
264  $n = 174$ ; undecided;  $n = 112$ ; and intending;  $n = 284$ ). No differences between baseline and  
265 experimental conditions were observed for participants in the positive-belief treatment  
266 intending to use supplements ( $0.28 \pm 0.14\%$ ,  $P = 0.886$ ,  $d = 0.01$ ). However, sprint performance  
267 worsened for participants in the positive-belief treatment who were undecided about  
268 supplement use ( $-0.67 \pm 0.36\%$ ,  $P = 0.039$ ;  $d = 0.22$ ), and not intending to use sport  
269 supplements ( $-0.64\% \pm 0.25$ ,  $P = 0.036$ ;  $d = 0.23$ ; figure 2A). No differences in sprint  
270 performance by intention to use supplements were observed in the negative-belief (figure 2B)  
271 and control (figure 2C) treatments ( $P > 0.05$ ).

272 Between-treatment differences in fastest performance by intention

273 Differences in fastest sprint performance and intention to use supplements were analysed using  
274 MANOVA. The performance of participants intending to use supplements in the positive-belief  
275 treatment was more positive compared to that of participants in the negative-belief treatment  
276 ( $1.29 \pm 0.37\%$ ,  $P = 0.001$ ,  $d = 0.51$ ) and control treatment ( $0.90 \pm 0.41\%$ ,  $P = 0.029$ ,  $d = 0.33$ ).  
277 Performance for participants not intending to use supplements in the negative-belief treatment  
278 was worse compared than controls (negative-belief vs. controls =  $-1.34 \pm 0.48\%$ ,  $P = 0.005$ ,  $d$   
279 =  $0.52$ ). This trend was similar between the positive-belief and control treatment ( $-0.91 \pm$   
280  $0.45\%$ ,  $P = 0.060$ ;  $d = 0.38$ ). No differences were observed for participant's undecided about  
281 supplement use between all three treatments ( $P > 0.05$ ; figure 3).

282 Within-treatment differences in fastest performance by intention

283 Differences in fastest sprint performance by intention to use supplements were observed in the  
284 positive-belief treatment ( $F_{(2,239)} = 4.952$ ,  $P = 0.008$ ) but not in negative-belief treatment  
285 ( $F_{(2,197)} = 1.247$ ,  $P = 0.290$ ) or control treatment ( $F_{(2,131)} = 0.637$ ,  $P = 0.530$ ). In the positive-  
286 belief treatment, fastest sprint performance in experimental compared to baseline for  
287 participants not intending to use supplements worsened by  $-1.10\% \pm 0.30\%$ , performance of  
288 those undecided about supplement use worsened by  $-0.64\% \pm 0.43\%$ , while performance of  
289 those intending to use supplements improved by  $0.19\% \pm 0.24\%$  (figure 3). In the positive-  
290 belief treatment, change in performance from baseline and experimental also differed  
291 significantly between those participants intending to use supplements and those not intending  
292 to use supplements ( $1.29\% \pm 0.38\%$ ,  $P = 0.003$ ,  $d = 0.49$ ). No other within-treatment  
293 differences in fastest sprint performance between baseline and experimental were observed  
294 when classified by intention to use supplements ( $P > 0.05$ ; figure 3).

295 **Discussion**

296 We aimed to replicate a previous study of placebo and nocebo effects in repeat sprint  
297 performance (5), albeit with the inclusion of a no-treatment control and a larger sample. We  
298 observed a mean nocebo effect in repeat sprint performance across the sample, but no mean  
299 placebo effect when compared to a no-treatment control. This suggests that, while receiving a  
300 purported harmful supplement significantly impaired performance, receiving a purported  
301 beneficial supplement did not enhance it. This finding differs to those of Beedie et al. (5) who  
302 reported significant placebo and nocebo effects in repeated sprinting.

303 Although no mean placebo effect was observed, data from the positive-belief treatment did  
304 suggest that the performance of participants intending to use supplements improved to a greater  
305 degree in the experimental conditions than the performance of participants not intending to use  
306 supplements ( $d = 0.49$ , figure 3). These improvements were also greater than those observed  
307 among participants of equivalent intention in the negative-belief treatment ( $d = 0.51$ ) and  
308 control treatment ( $d = 0.33$ ). Given that effect sizes  $>0.2$  are considered potentially beneficial  
309 for sport performance (23), these improvements in repeat sprint performance are likely  
310 meaningful for athletes. Furthermore, given that this relationship was observed only in the  
311 positive-belief treatment is of particular importance, as it supports our hypothesis that intention  
312 to use sports supplements might relate to placebo responding.

313 While intention to use supplements influenced the placebo response, this relationship was not  
314 shown for prior supplement use ( $r_{pb} = 0.071$ ,  $P = 0.078$ ). We did however examine the effect  
315 on performance of intention to use supplements and its interaction with prior supplement use.  
316 Intention to use supplements was strongly associated with prior supplement use ( $r_{pb} = 0.666$ ;  
317  $P < 0.001$ ). This suggests that intention to use supplements is associated with prior supplement  
318 use and may moderate an athlete's responsiveness to a placebo intervention. Although the  
319 design of this research precluded a robust test of this relationship, it is an intriguing research  
320 question that should be addressed in future research.

321 In consideration of the above, placebo responding is arguably a learned phenomenon. Research  
322 has shown that placebo effects can be initiated via verbal instructions (creating an expectation  
323 of a drug; (28)) and/or via repeat exposure to a drug with a subsequent placebo intervention  
324 mirroring the action of that drug (9). Previous experiences of a drug are therefore remembered,  
325 creating a memory of effective and ineffective treatments (29). This learning process is  
326 manifest in specific brain regions, with expectations and conditioning cues mediating and  
327 maintaining the turnover of, for example dopamine (19), and creating rewarding stimuli. On  
328 this basis, for a placebo responsive athlete, a placebo induced improvement in performance is  
329 the result of verbal information about the treatment (e.g. the suggestion that a supplement can  
330 improve performance) and/or cued or contextual conditioning (e.g. repeated exposure to a real  
331 treatment that results in treatment-like effects even when the treatment is replaced by a  
332 placebo). The athlete then recalls previous experiences and information about the effectiveness  
333 or ineffectiveness of the treatment, which shapes their subsequent intention to use it. This is  
334 perhaps a reason why athletes intending to use supplements are more likely to use these  
335 substances (17) and are arguably more likely to use other forms of performance enhancements  
336 (26).

337 The finding that intention may influence the placebo effect has particular relevance to sports  
338 practitioners aiming to improve an athlete's performance. Specifically, if improvements in  
339 performance following administration of a treatment (e.g. caffeine, sodium bicarbonate,  $\beta$ -  
340 alanine) are the result of both pharmacological and placebo effects (3), but the athlete does not  
341 have a prior intention to use that treatment, it may not elicit a placebo response and the athlete  
342 may not fully benefit from the treatment. Ultimately, a treatment may be more effective when  
343 an athlete intends to use it than when they do not. Sport practitioners should therefore be aware  
344 of an athlete's intentions towards a treatment prior to its administration, to ensure the



345 effectiveness of the treatment. This is also important in research, in which intentions towards  
346 a treatment could likewise influence outcomes.

347 Any reference to the results of our study should take into account potential limitations. First,  
348 we did not control for the presence of others or social support (e.g. cheering from teammates)  
349 during the sprint trials, and this may have affected performance. Second, while participants  
350 were asked to report on a Likert-type scale from 1 to 10 the degree to which they believed the  
351 treatment influenced their performance, they were not specifically asked if they believed the  
352 information they were given. We are therefore unable to assess the credibility of the belief-  
353 manipulation. Finally, the use of self-reported sport supplement use may not be reliable, as  
354 there may be differences between what athletes' report and what they actually think and/or do.

355 Given that previous studies have used expensive and complex techniques such as positron  
356 emission tomography (2) and genotyping (18) to identify placebo responders/non-responders,  
357 a self-report measure could provide a cost-effective and practical alternative. Future research  
358 should aim to further explore the impact of intention on the effects of legitimate sports  
359 supplements, and how this could influence an athlete's decision to use other forms of  
360 performance enhancements (e.g. doping). This understanding could enhance treatments, and  
361 inform athlete education and anti-doping strategy (26).

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367 of this study are presented clearly, honestly and without fabrication, falsification or  
368 inappropriate data manipulation

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- 459

**Table 1. Demographics of participants between treatments**

		<b>Positive</b>	<b>Negative</b>	<b>Control</b>	<b>Overall</b>
	<b>n =</b>	288	232	192	712
<b>Gender (%)</b>	Male	83.1	76.9	71.0	78.0
	Female	16.9	23.1	29.0	22.0
<b>Age (%)</b>	18 to 24	66.7	65.0	79.0	69.4
	25 to 34	29.6	30.0	18.8	26.8
	35 to 44	3.7	5.1	2.3	3.8
<b>Sport (%)</b>	Rugby Union	46.2	42.7	22.3	39.0
	Soccer	42.9	36.9	44.1	41.3
	Field Hockey	5.3	8.9	2.8	5.8
	Other	5.6	11.6	30.7	13.9
<b>Ability (%)</b>	Club	25.5	35.4	21.1	27.5
	County	39.9	38.8	30.4	37.0
	Regional	25.9	19.6	32.7	25.7
	National	8.7	6.2	15.8	9.8
<b>Intention to use sport supplements (%)</b>	Not intending	23.9	33.5	35.6	30.0
	Undecided	21.6	18.9	18.1	19.8
	Intending	54.5	47.6	46.3	50.2
<b>Use of Supplements (%)</b>	Yes	51.1	50.9	52.7	51.5
	No	48.9	49.1	47.4	48.5
<b>Frequency of supplement use (%)</b>	Daily	24.1	26.6	26.2	25.5
	Weekly	22.6	21.0	24.4	22.5
	Monthly	4.4	3.3	1.8	3.4
	Never	48.9	49.1	47.6	48.6
<b>Mean ± SEM</b>	Years training	10.77 ± 0.38	10.94 ± 0.59	9.68 ± 0.45	10.68 ± 0.24
	Hours per week training	6.13 ± 0.25	5.93 ± 0.25	5.84 ± 0.30	5.9 ± 0.15
	Amount of supplements used	1.14 ± 0.10	1.11 ± 0.10	1.20 ± 0.13	1.09 ± 0.06

SEM, standard error of the mean

461 **Figure captions**

462 **Figure 1.** Average performance in each condition between treatments. Note: \*baseline vs.  
463 experimental for negative-belief =  $P < 0.05$ ; \*\*positive-belief and control vs. negative-belief =  
464  $P < 0.05$ .

465

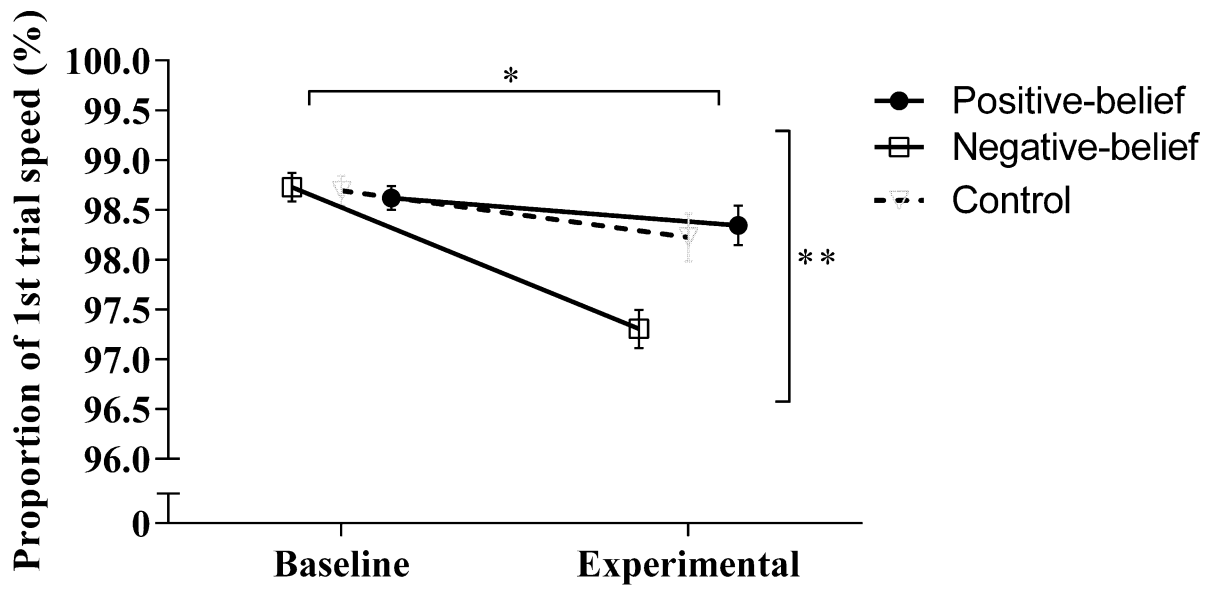
466 **Figure 2.** Average performance in condition by each treatment separated by participants'  
467 intention to use sport supplements in the next three months. **A.** Positive-belief treatment. Note:  
468 \*Baseline vs. Experimental for those not intending to use supplements =  $P < 0.05$ ; \*\*intending  
469 to use supplements vs. not intending to use supplements =  $P < 0.05$ . **B.** Negative-belief  
470 treatment. Note: \*baseline vs. experimental for those not intending, undecided and intending  
471 to use supplements =  $P < 0.05$ . **C.** No-treatment control.

472

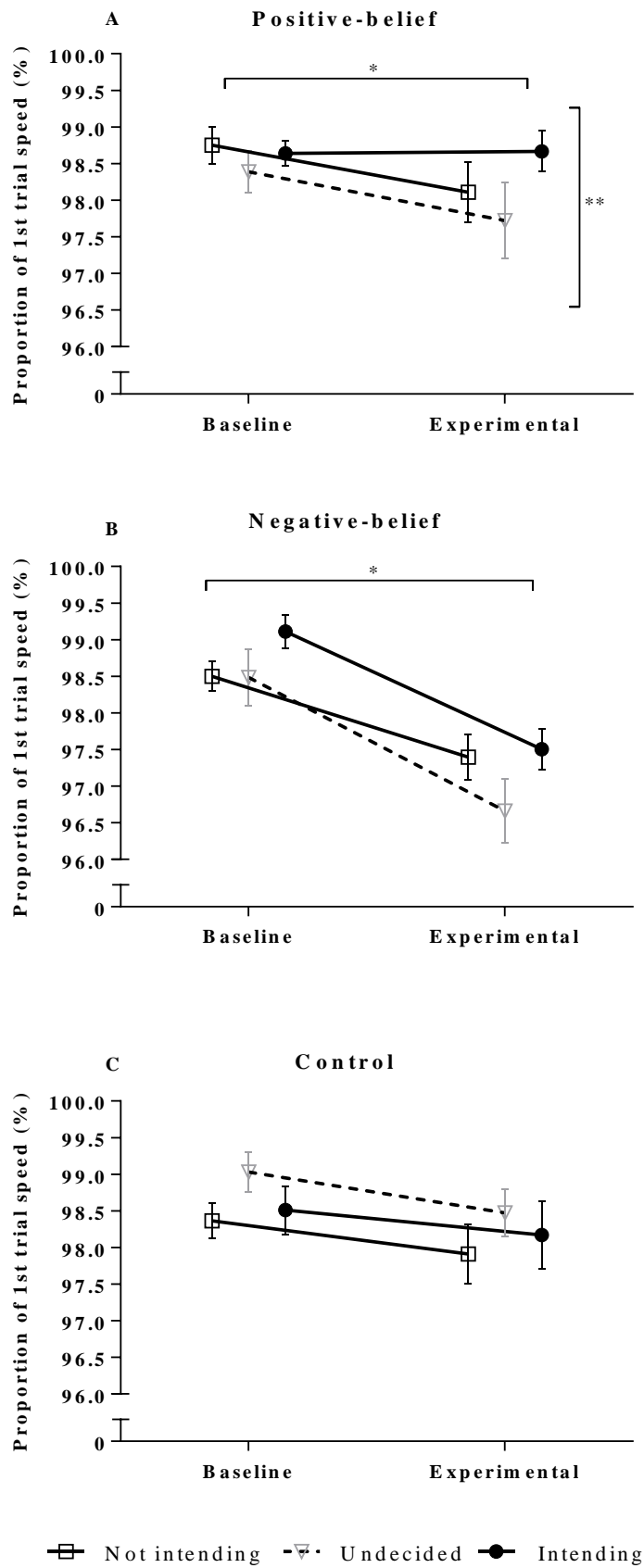
473 **Figure 3.** Differences in fastest performance between conditions, grouped by intention to use  
474 sport supplements. Note: \*control vs. positive-belief and negative-belief =  $P < 0.05$ , \*\*positive-  
475 belief vs. negative-belief =  $P < 0.05$ , †positive-belief intention vs. positive-belief no intention  
476 =  $P < 0.05$

477

478 **Figure 1**







480 **Figure 3.**

