

Research article

## Identification of placebo responsive participants in 40km laboratory cycling performance

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### Abstract

The placebo effect, a positive outcome resulting from the belief that a beneficial treatment has been received, is widely acknowledged but little understood. It has been suggested that placebo responsiveness, the degree to which an individual will respond to a placebo, might vary in the population. The study aimed to identify placebo-responsive participants from a previously published paper that examined the effects of caffeine and placebos on cycling performance. A quantitative model of placebo responsiveness was defined. 14 male participants were subsequently classified as either placebo responsive or non-responsive. Interviews were conducted to corroborate these classifications. Secondary quantitative analyses of performance data were conducted to identify further placebo responses. Finally, the five factor model of personality was used to explore relationships between personality and placebo responsiveness. Overall, 5 of 14 participants were classified as placebo responsive. Performance data suggested that 2 participants were placebo responsive whilst 12 were not. Interview data corroborated experimental data for these participants and for 9 of the remainder, however it suggested that the remaining 3 had experienced placebo effects. Secondary quantitative analysis revealed that performance for these 3 participants, whilst no better than for non-responsive participants, was associated with substantially increased oxygen uptake in the 2 conditions in which participants believed caffeine had been administered ( $7.0\% \pm 15.1$ ; 95% confidence intervals -2.6 to 16.7, and  $6.0\% \pm 15.4$ ; -3.9 to 15.9 respectively). Finally, data suggested that the personality factors of extroversion, agreeableness, openness and neuroticism may relate to placebo responding. Placebo effects such as pain tolerance and fatigue resistance might be experienced by a percentage of participants but might not always be manifest in objective measures of performance.

**Key words:** Caffeine; personality; placebo effect; nocebo effect; qualitative.

### Introduction

Despite widespread acknowledgement of the existence of placebo/nocebo effects, little is known about the nature of the effects *per se*, and questions remain as to their cause and prevalence. It was suggested over 50 years ago by Beecher (1955) that not all individuals will respond to the belief that an intervention has been received. Beecher's data suggested that the figure was approximately 35% of the population. Estimates of the rate of placebo responding in two recently published experimental studies in sport vary between 35% of 42 participants in a study of field repeat sprint trials (Beedie et al., 2007) to 72% of 7 participants in 10-km laboratory cycle time trials (Beedie

et al., 2006). Beedie (2007) also reported that 73% of 30 athletes canvassed reported experiencing a placebo effect or similar belief effect at some time during sports training or competition.

Variability in placebo responsiveness has implications for research and practice; if the number of placebo responsive participants in the experimental group in a placebo controlled study substantially exceeds the number of placebo responsive participants in the control group, all else being equal, an over-estimation of true effect will result (the opposite case, in which a bias towards placebo responsiveness in the control group might reduce the apparent magnitude of observed effects, also holds true, and explains why some drug manufacturers identify control participants who respond positively to a placebo in pilot studies and exclude them from subsequent clinical trials (Senn, 1997). In repeated measures designs, in which individual difference variables such as placebo responsiveness are expected to be balanced over conditions, variability in placebo response might still reduce the apparent reliability of the measure. In the applied setting, the degree to which an athlete is placebo responsive might have a substantial impact on their performance. It may also influence the approach that a practitioner adopts to working with them. Documented reports from elite sport as far back as the early 1960's suggest that practitioners have successfully used false beliefs about performance (e.g., Gallagher, 1970; Vogt, 1999). If such belief interventions are successful, the mechanisms underlying them warrant further investigation by sports scientists.

Although traditionally viewed as a positive phenomenon – the common sense model of the placebo effect is one in which an individual *benefits* from false information such as “the tablet I am about to give you will enhance your power output in the upcoming competition” – growing experimental support for the idea of the nocebo effect suggests that placebo/nocebo responsiveness might represent a disadvantage to an individual. In Beedie et al., (2006), one participant discontinued an experimental trial, later reporting in interview that he believed the placebo capsule he had ingested to be a large dose of caffeine, and furthermore, that the caffeine had caused severe nausea. Beedie et al., (2007) reported that participants ran significantly slower in conditions in which they believed that a placebo they had ingested was a drug likely to impair running performance. The understanding and prevention of such nocebo responses should be the concern of sports practitioners.

In the medical and psychological domains, placebo

responsive participants have been identified post-hoc; however, little progress has been made in identifying variables that might explain the phenomenon. Researchers have tended to focus on single-factor causal mechanisms such as conditioning (e.g., Ader, 1997; Siegel, 2002) or expectation (e.g., Bootzin and Caspi, 2002; Montgomery and Kirsch, 1997). Theoretically however, a variety of potentially interacting factors, ranging from the nature of the substance and the situation through to the personality, beliefs and expectations of the participants, might influence placebo responsiveness. A further limitation of much of the previous research was the fact that individual placebo responsive participants were identified in placebo controlled trials in which they were instructed that they had only a 50:50 chance of receiving a placebo or an active treatment. Such a conditional expectation does not represent the way in which beliefs operate in the real world.

The aim of the present study was to identify placebo responsive individuals from a sports performance study in which participants believed they had 100% or 0% chance of receiving an active substance (in this case caffeine). A secondary aim was to examine factors that might explain such responsiveness. To this end, secondary analyses of a previously published experimental dataset were conducted. Foad et al., (2008) used the balanced placebo design (Marlatt and Rohsenow, 1980) in an attempt to quantify the respective pharmacological and psychological contributions to the ergogenic effects of caffeine in 40-km cycling performance. Participants performed 14, weekly, 40-km time trials on the SRM cycle ergometer (Ingenieurburo Schoberer, Julich, Germany). Six baseline trials were interspersed between eight experimental trials over four experimental conditions; informed caffeine/received caffeine, informed caffeine/received placebo, informed no treatment/received caffeine, and informed no treatment/received no treatment. The authors reported that, although caffeine exerted an ergogenic effect irrespective of belief and an interaction between belief and pharmacology was observed, at a group level the hypothesised placebo effect of caffeine on performance in the informed caffeine/received placebo condition failed to materialise. These findings run counter to those of previous sport research of substantially improved performance in conditions in which participants believed they had ingested an ergogenic substance (Ariel and Saville, 1972; Beedie et al., 2006; Clark et al., 2000; Maganaris et al., 2000; McLung and Collins, 2007). The present study describes four brief analyses that were designed to explore the original findings of Foad et al., in greater depth. In stage 1, a within-participant analysis of Foad et al.'s data is reported. This stage aimed to identify any individual placebo responses on performance that might have been masked in the original between-participants analyses. In stage 2, data derived from semi-structured interviews are presented and the degree of corroboration between these qualitative data and previous experimental data is addressed. In stage 3, and based on the findings of stage 2, a secondary statistical analysis of physiological data from Foad et al., is reported. In phase 4, a psychometric measure of personality is used to explore differences between those participants classified as

placebo responders and those classified as non-responders.

## Methods

### Participants

14 competitive male cyclists who had previously participated in the experimental study volunteered to take part in this study (mean age  $\pm$  SD = 42.6  $\pm$  6.8 yrs.).

### Ethical considerations

Recorded interviews and psychometric tests were to comprise part of the study, therefore confidentiality of information and interpretation and explanation of test results were prime ethical concerns. The guidelines of the American Psychological Association (2002), specifically Guideline 4 'Privacy and Confidentiality', and Guideline 9 'Assessment' informed the research process throughout. All study procedures were explained verbally and in writing before informed consent was obtained from each participant. The study was approved by the faculty research ethics committee.

### Stage 1

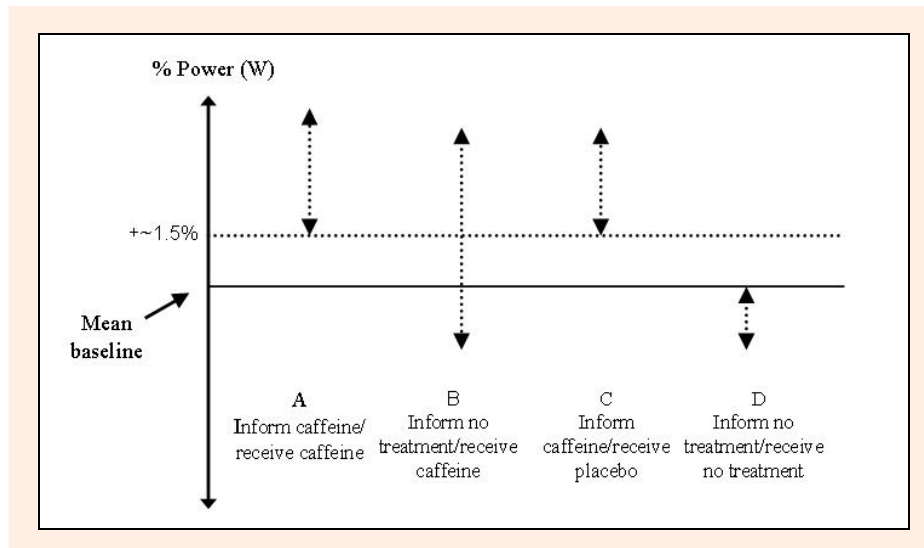
To enable identification of placebo responsive individuals, performance data from Foad et al., (2008), originally analysed on a group basis were reanalysed by individual participant. Data for the four experimental conditions for each participant were compared with a hypothesised quantitative model of placebo responsiveness (Figure 1).

In order to create this model, a number of assumptions regarding the nature of hypothesised placebo and pharmacological effects in 40-km cycling performance had to be made:

1. the direction of any placebo effects (positive or negative)
2. the pharmacological effects of caffeine (positive, negative, or neutral)
3. the relationship between placebo and pharmacological effects (additive or interactive)

With reference to point 1, the direction of any placebo effects was assumed to be positive. This assumption was based on the intuitive likelihood that participants would *want* to experience enhanced performance, and would *expect* to experience such enhancement on the basis of their general knowledge of the ergogenic effects of caffeine. Participants' beliefs and expectations were also reinforced via provision of literature attesting to the ergogenic efficacy of caffeine and discussion of anecdotal evidence of caffeine use amongst elite cyclists. Thus, given the purported linear relationship between desire, beliefs, and expectations, and a positive placebo response (Fillmore and Vogel-Sprott, 1995; Kirsch and Weixel, 1988; Marlatt and Rohsenow, 1980), the direction of any observed placebo effects was assumed to be positive.

With regards to point 2, it is important to determine the direction of any expected pharmacological effects because a negative effect on performance may mask any placebo effects, as illustrated in Figure 2. The extant research evidence (e.g., Graham, 2001), generally supports the hypothesis that administration of a moderate



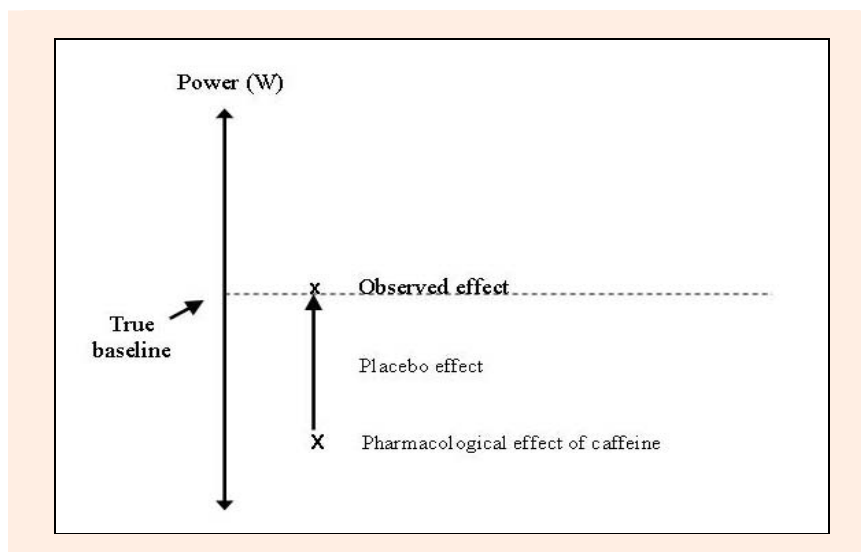
**Figure 1.** Hypothesised power output profile for a placebo responsive subject. Note: although vertical lines represent zones for each condition, to be classified as placebo responsive, subjects would be expected to produce greatest power output in condition A, less power in conditions B and C, and less power again in condition D.

( $\sim 5\text{mg}\cdot\text{kg}^{-1}$ ) dose of caffeine may exert a biologically active, beneficial effect, particularly on endurance performance. However, the large individual variability in the response to caffeine makes it impossible to predict whether the performance of a particular individual will improve. Thus the pharmacological effects of  $5\text{mg}\cdot\text{kg}^{-1}$  caffeine on performance were assumed to be either positive or neutral.

Finally, with reference to point 3, the relationship between placebo and pharmacological effects was generally assumed to be additive. Whilst several authors have questioned the appropriateness of assuming an additive model (e.g., de la Fuente Fernández and Stoessl, 2002; Kirsch and Rosadino, 1993), additivity is assumed in the assessment of drug effects by comparison with placebo responses in placebo-controlled trials. Experimental participants receive everything that placebo participants receive (e.g., pill or capsule, expectancy for improve-

ment), so that the *additional* benefit of *adding* a pharmacologically active agent can be assessed. However, evidence for the possibility of interactions between the effect of the active treatment and the placebo effect, for example Leuchter et al's (2002) finding that placebos and antidepressants, while exerting nearly equivalent benefits, exhibit different effects on the brain, suggest that this assumption be made with caution and that the profile of a placebo responsive individual be flexible enough to encompass the possibility of interactive effects.

Participants were therefore classified as placebo responsive if they exhibited quantifiably enhanced performance ( $\sim 1.5\%$  over baseline) in conditions in which caffeine was *believed* to have been received, that is, the inform caffeine/receive caffeine and inform caffeine/receive placebo conditions. A minimum increase in power of 1.5% was chosen because a change of this magnitude represents the smallest practical beneficial improvement



**Figure 2.** Hypothesised effects in the caffeine (inform caffeine/receive caffeine) condition when the pharmacological effect of caffeine is negative, but the placebo effect is positive.

in performance for a cyclist over 40-km (Paton and Hopkins, 2006). Performance in the inform no treatment/receive caffeine condition was hypothesised to be no greater than that in the inform caffeine/receive caffeine condition, whilst performance in the inform no treatment/receive no treatment condition was hypothesised to be no greater than at baseline. Participants whose data conformed to this model would be classified as placebo responsive and grouped as such for further analysis. Participants whose data did not conform to this model would be classified as non-responsive.

### Stage 2

Whilst placebo/nocebo effects might be *inferred* from observed performance, the possibility that such effects resulted from mechanisms other than belief, or that participants experienced placebo/nocebo effects not manifest in power output, remains. Semi-structured interviews were carried out with each participant to further explore the findings of the quantitative analysis in stage 1. These took place within a week of completion of all experimental trials to facilitate accurate recollection and report. An interview schedule, consisting of an integrated question and debrief protocol, was prepared in advance.

### Procedure

Interviews were conducted in an office at the University at which the experimental trials had taken place. Although informed consent had previously been obtained, permission was once again requested to audiotape the interview. Questions asked before the reveal of the experimental blind included 'can you describe any occasions where you might have used caffeine in the past'; 'what expectations did you have of caffeine'; 'did you want caffeine to improve your performance'; 'can you describe any subjective symptoms you noticed'; and 'how did you approach the trials after you'd been given caffeine'? Questions asked following the reveal of the blind included 'does this information change anything you said previously'; 'were you aware of any discrepancy between what you were informed you were receiving and how you felt'; and 'can you describe any incidences when you'd not received a capsule where you thought 'this feels like caffeine' or vice versa'? During the interviews prompts were used as little as possible, and the participants were allowed to answer questions or respond to ideas as fully as possible in their own time. Responses to main questions were followed up by corollary questions. Efforts were made to ensure that questions were neutral, rather than leading or value-laden and open-ended rather than closed. The interviews were stored as one taped copy and as verbatim transcriptions comprising over 15,000 words. Informal conversation extraneous to the investigation was not transcribed.

### Analysis

Data analysis was based on a generic approach apparent in much qualitative analysis but not labelled within one of the specific traditions of qualitative research. The approach stemmed from a critical realist position, the intention being to facilitate "naturalistic generalisation" by

presenting the participants' experiences as simply as possible (Eccles et al., 2002). As noted by Faulkner and Biddle (2004), simple presentation of interview data departs from traditional forms of representing results in psychological domains, however it allows a greater degree of trust to be shared with the reader in interpreting and evaluating the data from their own perspective.

### Stage 3

Interview data suggested that five participants had experienced placebo effects on subjective experience, manifest as increased motivation, pain tolerance and fatigue resistance. Experimental data suggested that these subjective placebo responses were associated with increased power output for two participants.

On the basis of Stages 1 and 2 of the present study, participants whose experimental and interview data suggested they had experienced placebo effects were defined as 'objective placebo responders'. Participants whose interview data alone suggested that they experienced placebo effects were defined as 'subjective placebo responders'.

### Analysis

Using independent t-tests, change scores relative to baseline for  $\text{VO}_2$ , HR and blood lactate for subjective placebo responders ( $n = 3$ ) were compared with change scores for placebo non-responders ( $n = 9$ ). It was hypothesised that performance of the subjective responders in the informed caffeine/received caffeine and informed caffeine/received placebo conditions would be associated with greater efficiency equating to lower percentage change scores than for non-responders. Objective placebo responders ( $n = 2$ ) were excluded from the analysis. Data are expressed as means  $\pm$  SD. Precision of estimates of outcome statistics are reported as 95% confidence limits of the difference between conditions, and as probabilities that the true effect is substantially positive/beneficial, negligible/trivial, or negative/harmful (Batterham and Hopkins, 2005).

### Stage 4

The aim of the final stage of the study was to use a quantitative psychometric measure to investigate any relationships between personality and placebo responsiveness. Although it was deemed unlikely that personality alone among psychological variables would predict placebo responsiveness, personality was selected on the basis that it is a relatively stable psychological construct with demonstrated relationships with less stable constructs such as anxiety and motivation. Furthermore, given the lack of any specific hypothesis relating factors such as anxiety or motivation to placebo responding in sports performance, and given the time required of participants to complete multiple psychometric inventories, use of a single measure of personality, with the possibility of subsequently inferring potential links with other psychological variables from personality scores, seemed the most parsimonious approach. Any relationships identified in the present study might allow future researchers to narrow their approach and target specific cognitive or emotional variables linked to placebo responsiveness.

## Measure

Personality was measured using the International Personality Item Pool (IPIP) representation of the revised NEO personality inventory (IPIP-NEO). The inventory is based on an IPIP inventory developed by Goldberg (1999) and consists of 120 items that assess the domain constructs of the Five-Factor Model of personality as expressed in Costa and McCrae's (1992) revised NEO personality inventory (NEO-PI-R), that is, openness to experience, conscientiousness, extraversion, agreeableness and neuroticism. The 120-item IPIP-NEO capitalises on the broad base of theoretical and empirical research supporting a five factor conception of personality. Although Eysenck (1992) and Kline (1998) have questioned the NEO-PI's empirical and theoretical underpinnings, particularly the provenance of the openness, conscientiousness, and agreeableness factors, the Five-Factor Model arguably represents the most commonly, although not universally accepted personality framework in the current psychological literature (Brand and Egan, 1989; Egan et al., 2000; Wiggins and Trapnell, 1997). The measure consists of a number of brief statements, for example "I try to lead others," "I worry about things," and "I carry out my plans". Responses are anchored along a 5- point scale (very inaccurate, moderately inaccurate, neither inaccurate nor accurate, moderately accurate, and very accurate). Values of 1, 2, 3, 4, and 5 are associated with these respective responses for positively keyed items, and 5, 4, 3, 2, and 1 for negatively keyed items. Evidence for the reliability and validity of the measure has been reported elsewhere (Buchanan et al., 2005).

## Procedure

A paper and pencil version of the IPIP-NEO was administered at the beginning of the debrief interviews described in stage 2 above. All instructions provided by the authors of the measure were adhered to. Personality scores were fed back to participants at the completion of the study via

a printed report outlining scores per factor in relation to population norms.

## Analyses

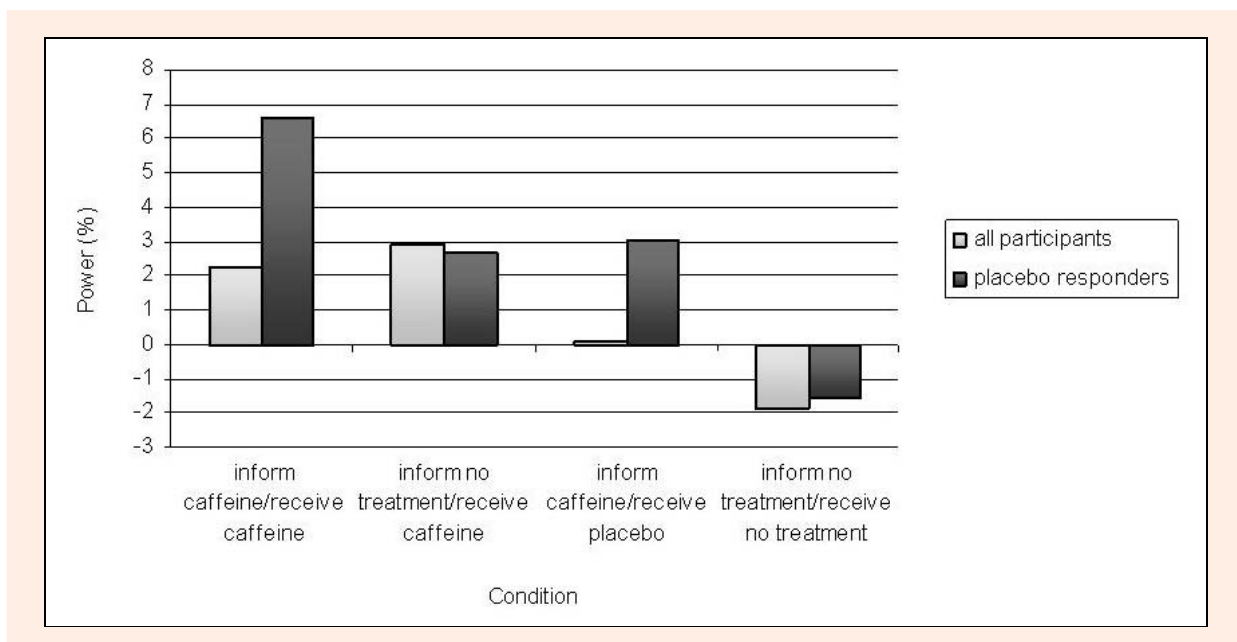
To identify any differences in personality scores between participants defined as placebo responders and those defined as non-responders, scores for each factor for both groups were analysed using independent t-tests. Personality scores were also combined with experimental data from the previous study in regression analyses. Data are expressed as means  $\pm$  SD. Precision of estimates of outcome statistics are shown as 95% confidence limits and as probabilities that the true effect is positive, trivial, or negative (Batterham and Hopkins, 2005).

## Results

### Stage 1

Analysis of data for each individual participant suggested that the performances of only two, participants 6 and 7, were consistent with the hypothesised quantitative model for placebo responsiveness. Although not a deviation from the hypothesised model, power for both participants was below baseline in the informed no treatment/received no treatment condition. Mean data for these participants is presented alongside the mean data for all participants in Figure 3.

Across the group as a whole, variability in the response to the informed caffeine/received placebo treatment was evident. Several participants, namely 1, 3, 6, 7, 9, 11, and 14, displayed enhanced performance but failed to exhibit the full trend in performance hypothesised to characterise a placebo responder. That is, with the exception of participants 6 and 7, these participants also performed better in the informed no treatment/received caffeine condition than in the informed caffeine/received caffeine condition. No participants were identified as nocebo responders.



**Figure 3.** Mean percent differences in power between experimental conditions in all participants ( $n = 14$ ) and in objective placebo responders ( $n = 2$ ).

## Stage 2

### Corroboratory evidence: Placebo responders

On the basis of their power data, in Stage 1 above participants 6 and 7 were classified as placebo responsive. Interview data for both participants corroborated this finding. Both participants reported unambiguous responses to the ingestion of the placebo capsule they were informed was caffeine. Participant 6, stated that “at about 15k I started to feel a bit of a kick... it felt like someone had taken the brakes off the bike.” Participant 7 stated “It seemed that my legs felt a little better, they were able to cope, maybe the term cope with a bit more pain might not be the totally accurate way, but that was almost the perception, that I was able to manage a bit more.”

When asked to describe the response to the knowledge that caffeine would be administered, Participant 6 remarked “...when I was told I was going to get caffeine I wasn't scared that I was going to blow up at 30k... I was thinking, “great, I'm on caffeine, that's going to get me through this”.” Conversely, of trials in which he did not believe caffeine had been administered he said “when I didn't think I was getting it I would probably ride more conservatively thinking... “I don't want to end up in a mess with 30k to go and not finish it or feel like crap”.” Participants 6 and 7 also alluded to perceived analgesic effects experienced during placebo trials.

### Corroboratory evidence: non placebo-responders

Interview data from nine participants, namely 1, 2, 3, 5, 8, 9, 11, 12 and 14, corroborated highly with findings from the experimental trials. That is, no placebo effects were experienced by these participants. Representative of responses was Participant 14's sentiment: “I arrived at that time and thought “it must be soon, must be soon, nothing's happening, nothing's happening”... in my mind I was waiting for something that physically felt better, easier, faster or something and it never happened.” Failure to perceive an ergogenic effect from trials in which participants believed they had received caffeine was often met with disappointment. Participant 2 remarked “I do remember thinking umm, “bloody hell if that was caffeine I still felt groggy and still felt crap so god knows what I'd have been like without it”.” However, as Participant 14 recalled, after initial expectations had diminished, disappointment soon faded to indifference: “I quickly got back to my “no, let's get on with it, do what you've got to do and get through it”.” Recollecting his first informed caffeine/received placebo trial, Participant 8 noted “I can remember the first time I thought, “oooh, I've got some caffeine, lets see what this is like”.” However, after failing to perceive any performance effects he remarked “...after that I can remember riding and I had trouble remembering if, had I taken anything or hadn't I?... Like I said, if I felt good I just rode well and if I didn't, I didn't.”

### Non-corroboratory evidence: Subjective placebo responders

Responses from three participants, namely 4, 10 and 13, did not corroborate experimental findings. These participants described an awareness of incongruence between

the ‘experience’ of the performance and the actual performance outcome during the informed caffeine/received placebo condition. For example, Participant 4 stated “...about 12k into it I definitely felt something different – something happened. It could have just been coincidence but something that day definitely happened... I started going up through the gears etc. and at about 12k I thought “right, keep going”, and I just kept going at quite a high rate...It felt as if the edge had been took off the pain... the pain don't go away but you're in a situation where ... you can actually feel, “yeh, I can sort this out”... something definitely was different on that occasion, definitely.

Similarly Participant 1 stated “I wasn't aware of going faster but felt [I] could tolerate the pain more.” Participant 10 remarked “what I found is that it made you feel better in yourself but the performance was no different. So you felt on top of the world doing it but you weren't going any faster.” Participant 13 noted “...there was a definite difference...well, perceived difference. Better...not faster particularly, but that I could endure the same level for longer without much drop-off.” In contrast to participants 6 and 7 for whom the subjective feelings resulted in markedly enhanced performance, the performance of these individuals was *quantifiably* unaffected by belief of receipt of caffeine, despite perceptions of enhanced experience of performance.

## Stage 3

Given the similarity in subjective reports for all five responsive individuals, but also given that different performance effects were observed among these, it is reasonable to hypothesise that either two different types of placebo response, one objective on performance and one subjective on experience, had been observed. Alternatively, it is possible that the same placebo effect on experience had resulted in increased power output for two participants whilst apparently not resulting in increased power output for the remaining three. Given that the subjective symptoms of placebo response reported might reasonably be expected to result in enhanced performance, it was hypothesised that the latter scenario was a more parsimonious explanation, and that a placebo effect, arguably mimicking the expected effects of caffeine, accounted for the improvement in performance for objective placebo responders (participants 6 and 7) whilst resulting in greater *efficiency* of performance for subjective placebo responders (participants 4, 10 and 13).

Results of independent t-tests of physiological variables for conditions in which participants believed caffeine to have been administered are presented in Tables 1, 2 and 3. Counter to the hypothesis above, data for oxygen uptake and blood lactate suggest that performance in these conditions for subjective placebo responders was associated with substantially *higher* physiological cost than for non-responsive participants. Data for heart rate were less easy to interpret, and although possibly suggestive of an increase associated with the ingestion of caffeine in the informed caffeine/received caffeine condition, were this the case it is perhaps surprising that this pattern was not also observed for blood lactate values.

**Table 1.** Mean oxygen uptake for subjective placebo responders (n = 3) and percentage difference from mean oxygen uptake for placebo non-responders (n = 9) in informed caffeine/received caffeine and informed caffeine/received placebo conditions.

Condition	Oxygen uptake	Difference (%) from placebo non-responders		Chances effect is clinically beneficial (trivial/harmful) <sup>+</sup>
	l min <sup>-1</sup>	Mean (SD)	95% CI*	
Informed caffeine/received caffeine	3.5 (0.4)	7.0 (10.9)	-2.6 to 16.7	4 (8/89)
Informed caffeine/received placebo	3.6 (0.1)	6.0 (11.6)	-3.9 to 15.9	6 (11/83)

\* 95% CI = 95% confidence interval. <sup>+</sup> smallest worthwhile effect of 1.5%.

#### Stage 4

Data from stages 1 and 2 of the present study allowed the researchers to classify participants as either objective placebo responders (n = 2), subjective placebo responders (n = 3) or placebo non-responders (n = 9). Irrespective of the different effects on performance observed between the two placebo responsive groups, sufficient similarities between the experience of placebo effects reported by both allow the researchers to conclude that all experienced a similar phenomenon. On this basis, for the final analysis all placebo responders are grouped as one (n = 5). Personality scores for placebo responders and non-responders are presented in Table 4. Data suggest that placebo responders scored substantially higher on the traits of extroversion, openness to experience and agreeableness. No substantial differences were observed between groups on conscientiousness and neuroticism.

Results of regression analyses of the personality scores for all participants and power output in the experimental placebo condition from the previous study are presented in Table 5. A substantial, positive correlation between performance in placebo trials and scores on the neuroticism trait was evident. High levels of conscientiousness and agreeableness were negatively correlated with performance in the placebo condition.

#### Discussion

Quantitative and qualitative data suggest that, in the experimental study conducted by Foad et al. (2008), five of fourteen participants experienced a placebo effect resulting from the belief that caffeine had been ingested. This rate of placebo responding is consistent with previous data from sport (Beedie et al., 2007) and elsewhere (Beecher, 1955). Data also suggest that what appears to be the same qualitative response experienced by all five placebo responders, that is, increased motivation, pain tolerance and fatigue resilience, resulted in substantially increased power output for two participants but decreased physiological efficiency for the remaining three, the latter producing similar power output to placebo non-responsive

participants but at a substantially greater physiological cost. It is in fact not unreasonable to suggest that the increased physiological cost observed in subjective placebo responders constitutes a negative placebo, or nocebo, effect (that is, a negative outcome driven by a false belief). However, an alternative interpretation might be that these participants, despite being able to use more oxygen in conditions in which they believed that they had ingested caffeine, simply reached a mechanical or physiological ceiling. A further possibility is that the increases in oxygen uptake and blood lactate observed were the result of placebo-induced increases in arousal, mimicking those which would be anticipated to result from the ingestion of caffeine. This arousal could have been independent of, and consequently in addition to, the physiological arousal associated with cycling performance.

A substantial quantitative nocebo effect on performance in the informed no treatment/received no treatment condition was observed by Foad et al. (2008) in their original study. Data from the present study provided no clear explanation for this finding. That a participant from the study has since suggested that arriving for a no treatment trial was like reaching into his pocket for an energy bar near the end of a long road race only to find he had none left, perhaps provides some clues however. It might be argued that two types of nocebo effect could operate; the effects of negative beliefs associated with participants not having received a desired intervention (e.g., "I wish I had been given caffeine"), and the effects of negative beliefs of participants about an intervention that has been received (e.g., "I have been given caffeine but I think it might cause nausea"). On the basis that interview data suggested that all participants in the present study had either positive or neutral expectations of caffeine, the most parsimonious explanation for the nocebo effect is the former.

It is noteworthy that whilst qualitative data in stage 2 corroborated performance data for the two objective placebo-responsive participants and the nine placebo non-responsive participants identified in stage 1, physiological data from stage 3 likewise corroborated the qualitative

**Table 2.** Mean blood lactate for subjective placebo responders (n = 3) and percentage difference from mean blood lactate for placebo non-responders (n = 9) in informed caffeine/received caffeine and informed caffeine/received placebo conditions.

Condition	Lactate	Difference (%) from placebo non-responders		Chances effect is clinically beneficial (trivial/harmful) <sup>+</sup>
	mmol/l	Mean (SD)	95% CI*	
Informed caffeine/received caffeine	7.4 (0.8)	19.3 (49.0)	-26.6 to 65.2	17 (4/80)
Informed caffeine/received placebo	7.2 (1.1)	16.7 (49.1)	-27.1 to 60.4	19 (4/77)

\* 95% CI = 95% confidence interval. <sup>+</sup> smallest worthwhile effect of 1.5%.

**Table 3.** Mean heart rate (HR) for subjective placebo responders (n = 3) and percentage difference from mean heart for placebo non-responders (n = 9) in informed caffeine/received caffeine and informed caffeine/received placebo conditions.

Condition	HR	Difference (%) from placebo non-responders		Chances effect is clinically beneficial (trivial/harmful) <sup>†</sup>
	beats·min <sup>-1</sup> Mean (SD)	Mean (SD)	95% CI <sup>*</sup>	
Informed caffeine/received caffeine	161 (3)	-2.3 (1.8)	-4.1 to -0.6	0 (16/84)
Informed caffeine/received placebo	159 (1)	-.3 (2.4)	-3.1 to 2.5	8 (74/18)

\* 95% CI = 95% confidence interval. † smallest worthwhile effect of 1.5%.

data for the three subjective placebo responders identified in stage 2 (perhaps more accurately, physiological data from these three participants suggested they differed substantially from the nine non-responsive participants in their physiological response to the two informed caffeine conditions). This suggests that both qualitative and quantitative methods might be required to fully elucidate placebo effects in performance research. Furthermore, it suggests that calculation of rates of placebo responding based on performance measures alone might be inadequate. Given that in stage 1, two responders were identified whilst in stage 2, all five were identified, it might be argued that qualitative methods are in fact more sensitive to the phenomenon. There are however issues inherent in self-report data that warrant consideration, for example, the degree to which participants might have intentionally or unconsciously responded in a manner thought to be desired by the interviewer. Indeed, the observation that placebo responders reported higher levels of agreeableness than non-responders suggests that social desirability in responding might have been a factor. Having said this, on the basis of the previous literature, we might have hypothesised that less than 50% of participants would be placebo responsive, that a greater number of participants would experience placebo effects on perception than on performance, and that extroversion and neuroticism might relate to placebo responding. The fact that present data are consistent with previous findings and support these tentative hypotheses suggests that the mixed measures used were useful. It is recognised that the personality data from study 4 are highly speculative, primary because of the limited sample size, and that on this basis no firm conclusions can be drawn. However, given the exploratory nature of the study as a whole, the authors considered these data worthy of inclusion.

## Conclusion

Placebo effects such as pain tolerance and fatigue

resistance might be experienced by a percentage of participants but might not always be manifest in objective measures of performance. Future research should aim to identify placebo responsive individuals in sports performance and, via mixed methods, seek to identify factors that might explain placebo responding.

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**Table 4.** Scores on five personality factors for all placebo responders (n = 5) and placebo non-responders (n = 9), and differences for placebo responders (n = 5) from scores for placebo non-responders (n = 9).

International Personality Item Pool Factor	Trait score	Trait score	Difference from placebo non-responders		Chances effect is clinically positive (neutral/negative) <sup>†</sup>
	Placebo responders Mean (SD)	Placebo non-responders Mean (SD)	Mean (SD)	95% CI <sup>†</sup>	
Extraversion	89.4 (10.8)	78.8 (8.7)	10.6 (9.8)	-.9 to 22.1	95 (3/2)
Agreeableness	95.4 (12.1)	88.4 (9.8)	7.0 (11.0)	-6.0 to 19.9	80 (12/8)
Conscientiousness	98.0 (13.3)	96.0 (12.3)	2.0 (12.8)	-13.3 to 17.3	48 (25/27)
Neuroticism	60.8 (11.1)	59.7 (10.2)	1.1 (10.7)	-11.7 to 13.9	50 (15/35)
Openness to experience	78.6 (7.7)	72.9 (7.0)	5.7 (7.4)	-3.1 to 14.5	86 (7/6)

\* 95% CI = 95% confidence interval. † smallest worthwhile effect of 0.2 of standard deviation of placebo non-responders for each factor.



**Table 5. Correlations between personality scores and power output in the experimental placebo condition (n = 14).**

Personality trait	Correlation with power output in placebo trials	95% CI*	Chances effect is clinically positive (trivial/negative) <sup>†</sup>
Extraversion	-.1	-.6 to .5	29 (25/46)
Agreeableness	-.5	-.8 to .0	1 (5/94)
Conscientiousness	-.7	-.9 to -.3	0 (1/99)
Neuroticism	.5	-.0 to .8	94 (5/1)
Openness to experience	-.3	-.7 to .3	10 (17/73)

\* 95% CI = 95% confidence interval. <sup>†</sup> smallest worthwhile correlation of 0.1.

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### Key points

- Beliefs can have both positive (placebo) and negative (nocebo) effects
- Placebo effects may be experienced both objectively and subjectively
- Certain personality traits may be related to placebo responding
- A multi-method approach may best elucidate placebo effects in sport

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