Title: The importance of context when making research recommendations: A response to Painelli et al.

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Dear Editor,

We thank Painelli and colleagues [1] for their comments on our recent article, "Caffeine and Exercise: What Next?" [2]. In their letter, Painelli et al. [1] highlight three major points for future studies exploring the effects of caffeine on exercise:

1. The role of expectancy;
2. The effectiveness of blinding;
3. The use of a control condition within performance trials.

The role of expectancy on the ergogenic effects experienced following caffeine ingestion is indeed very interesting, and highly relevant. Unfortunately, due to space considerations, we were unable to delve into great detail on this topic—and many others—within our review. We did, however, note that expectancy was a topic worth further exploration, and pointed interested readers towards a recent review article on the topic [3], which reads: "Additionally, a review by Shabir et al. [194] reported potential expectancy effects of caffeine in 13 out of 17 identified studies, suggesting that if an individual believes they have consumed caffeine, and believes that caffeine is ergogenic, they are likely to experience a performance benefit, even if caffeine has not been consumed." Therefore, whilst Painelli and colleagues [1] point out some interesting aspects, the role of expectancy has, as referenced in our review, been discussed in detail elsewhere [3].

The second major point raised relates to the effectiveness of the blinding. The authors reference studies that explored the effects of caffeine on muscle strength and time-trial performance, and detailed whether they assessed the effectiveness of the blinding to the caffeine and placebo conditions. This aspect of the study design has been linked to the findings by Saunders et al. [4] who reported that correct supplement identification may influence the outcome of an exercise task, and be a possible source of bias in studies exploring the effects of caffeine on exercise performance. Whilst we certainly agree that studies should explore the effectiveness of the blinding (as mentioned in our paper), it is important to note that there are studies in which there was no blinding of participants or investigators and yet caffeine was not found to be ergogenic for exercise performance [5,6]. Furthermore, in one study, blinding was not highly effective as 11 out of the 12 participants were able to identify the caffeine condition correctly [7]. However, despite the lack of effective blinding, caffeine was also not found to be ergogenic for isometric strength. Therefore, we would be cautious in discrediting the findings of studies only because they did not explore the effectiveness of the blinding. Painelli et al. [1] also suggest the use of specific statistical methods for evaluating the effectiveness of the blinding. These are already being utilized in research and, to the best of our knowledge, we were the first to use some of the methods, such as the Bang's Blinding Index in a set of recent studies from our research group [8-11].

Interestingly, even though a major focus by Painelli et al. [1] was given to the effects of placebo on exercise performance, data from one relevant study was not referenced. Tallis et al. [12] explored the effects of caffeine on voluntary strength under four conditions: (1) told caffeine, given caffeine; (2) told caffeine, given placebo; (3) told placebo, given placebo; and (4) told placebo, given caffeine. An equal improvement in concentric force was found in both of the trials when the participants ingested caffeine. Even though the participants believed that caffeine would evoke a performance benefit, muscle strength was not improved in the "told caffeine, given placebo" condition. These data indicate a true effect of caffeine on exercise performance.

The final major point by Painelli et al. [1] is the use of a control condition in studies exploring the effects of caffeine on exercise. We recently incorporated a control condition in a study in which we explored the effects of three doses of caffeine on upper and lower-body muscular strength and endurance [11]. Interestingly, in all of the four used tests, the performance in the control and placebo condition was almost identical, with no significant differences between the conditions. The blinding in this study was highly effective as only 1% and 14% of the participants were able to identify the placebo condition beyond random chance when assessed pre and post-exercise session, respectively. We are not the first to show very similar performance between control and placebo conditions; Gonçalves et al. [13] also reported that caffeine ingestion was ergogenic as compared to control and placebo, but there were no significant differences in performance between the placebo and control conditions. This was also demonstrated by McNaughton et al. [14] who used a one-hour cycling time trial test and reported performance data of 28.0 ± 1.3 km, 26.4 ± 1.5 km, and 26.3 ± 1.5 km for the caffeine, placebo, and control conditions, respectively. Therefore, while we do not necessarily object the use of a control condition in future studies, the data from the referenced studies suggest that a placebo condition is still a highly valid comparison to the caffeine condition. Finally, the authors should consider that adding more testing conditions exposes the participants to additional possible (perhaps even unnecessary) risks.

We thank Painelli and colleagues [1] for drawing attention to this important topic, as well as their provision of methodological suggestions for future studies. However, we also feel that additional context is required when discussing these recommendations in terms of the current and future body of research.

We would also like to add that, along with the factors identified by Painelli et al. [1] as modifying factors of expectancy and the placebo response, important further avenues for exploration in the caffeine-expectancy realm include:

- Does genotype modify the expectancy and/or placebo response to caffeine ingestion, as per the "placebome" suggested by Hall et al. [15]? This adds further complexity to the effects of genetic variation on both caffeine's ergogenic effects [16,17], ingestion parameters [18], and habituation [19].
- How does the magnitude of expectancy and/or placebo differ between sensory signals of caffeine presence, such as taste [20], smell [21], etc.?

Future work in this area will no doubt continue to drive the field of caffeine's effects on sporting and exercise performance forwards, adding further—and much needed—nuance.

Compliance with Ethical Standards

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Conflicts of Interest

Both authors declare they have no conflict of interest relevant to the content of this article.

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