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Are caffeine's performance-enhancing effects partially driven by its bitter taste?

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A B S T R A C T

Caffeine is a well-established ergogenic aid, with its performance-enhancing effects replicated across a variety of exercise types. Caffeine exerts its performance-benefits through many mechanisms, including acting as an adenosine receptor antagonist, and serving to reduce sensations of fatigue and pain. One potential mechanism that is currently underexplored is whether caffeine's bitter taste mediates some of its ergogenic effects, which is discussed in this article. Previous research has demonstrated that bitter tastants have the ability to enhance performance, and this effect is mediated by bitter taste receptors in the mouth and gastrointestinal tract. Additionally, the ability to detect bitter tastes is subject to individual variation, raising the potential that the demonstrated inter-individual response to a standardised caffeine dose is potentially driven by differences in taste response. Finally, it appears that some of caffeine's performance-enhancing effects are driven by expectancy. As bitter taste may serve as a signal that caffeine has been ingested, it is possible that some of the expectancy effects of caffeine ingestion are driven by its bitter taste. These aspects all have potentially important implications for future research, as well as for how athletes and coaches utilise caffeine around competition, both of which are explored in depth here.

Introduction

Caffeine is a well-established ergogenic aid, with its performance benefits established across a variety of meta-analyses [1]. Caffeine has a reliable and replicated ergogenic effect on endurance performance [2–7], muscular endurance [8], muscular strength and power [9–13], and sporting performance [14,15]. Whilst caffeine has the potential to exhibit ergogenic effects on sprint performance [16–20], the findings at meta-analysis level have so far been equivocal [21,22]. Recently, caffeine's performance benefits have been demonstrated across a range of specific sports [23], such as soccer [24], rugby [16,25], basketball [26], volleyball [27], and swimming [17,28]. Accordingly, there is a high frequency of caffeine use around sporting competition, with recent research suggesting around 75% of athletes do so [29]. Whilst doses of 3–6 mg/kg are found to elicit the optimal ergogenic effect [30], lower doses of caffeine also have the potential to be ergogenic [31], and there is considerable variation in the "optimal" caffeine dose for athletes [32,33].

Caffeine appears to exert its ergogenic effects via a variety of mechanisms. Caffeine acts as a competitive adenosine receptor antagonist [34], limiting the downregulation of arousal caused by adenosine [35]. When caffeine binds to adenosine receptors, there is an increase in both neurotransmitter release and muscle firing rates [36]. Caffeine also serves to stimulate adrenaline secretion [37], reduce perception of effort [38], increase sarcoplasmic calcium release [39], and decrease the perception of pain [40,41], all of which have performance-enhancing potential. Additionally, caffeine enhances mental alertness [42] and mood [43], as well as ameliorating the expected performance-decrements demonstrated following a lack of sleep [44–46] and mental fatigue [47,48]; these factors may also serve to enhance sporting performance.

Accordingly, much of caffeine's role in enhancing performance is well understood, although there are still some unanswered questions [49]. One potential area that is currently underexplored is the role of taste as a mechanism by which caffeine may exert its performance-benefit. Caffeine is a bitter tastant [50], and there are a number of bitter taste receptors located in the oral cavity [51], which have been shown to be activated when exposed to caffeine [52]. There is emerging evidence that bitter tastants may exert an ergogenic effect on exercise performance [53]. In this paper, I will explore whether caffeine's bitter taste is potentially responsible for its ergogenic effects. If it is, then inter-individual variation in the ability to taste bitter compounds [52] may be, at least partially, responsible for the observed individual variation in response to caffeine supplementation on performance [32,33]. Furthermore, there is evidence that caffeine's ergogenic effects are partially mediated via expectancy [54–56]. If the ability to detect caffeine's bitter taste affects performance, then there is the potential that this is further driven via expectancy, an aspect explored later in the paper.

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Are bitter tastants ergogenic?

Caffeine is a well-established bitter tasting compound, with oral caffeine intake shown to stimulate a number of bitter taste receptors [50]. Bitter tastants themselves have been shown to be ergogenic, with the leading review in this area authored by Gam and colleagues [53]. Here, the authors noted that the evidence suggests that carbohydrate mouth swilling enhances performance [57,58]; as the carbohydrate is not ingested, the demonstrated performance enhancement may be centrally mediated. In this case, carbohydrate receptors in the mouth, associated with sweet tastes, appear to activate particular regions in the brain, leading Gam and colleagues [53] to explore whether other tastes drive the same response. This is especially pertinent from the perspective of caffeine, as bitter solutions have been demonstrated to elicit large and long-lasting changes within the autonomic nervous system [59], potentially due to evolutionary protective mechanisms designed to prevent ingestion of toxic substances [60,61].

This hypothesis has been explored experimentally. Gam and colleagues [62] utilised quinine, a bitter agent found in tonic water, in a mouth wash immediately prior to a maximal 30-second cycle sprint in a group of male cyclists. Here, the quinine solution was rinsed for 10 s, and then ingested, with significant improvements in peak and mean power output compared to plain water, a sweet solution, or no solution. Subsequent research, utilising a mouth rinse only (i.e. no ingestion) [63], did not elicit a performance improvement, suggesting that ingestion is a potentially important aspect of the performance-enhancing component of the ergogenic effects of bitter tastants [64]. Ingestion may be important as the upper gastrointestinal tract, and not just the mouth, also contains bitter taste receptors [64], and so consumption of caffeine may further increase the magnitude of signals from these receptors. Outside of the work of Gam and colleagues [62–64], there is little research exploring the potentially ergogenic effects of bitter taste, but the tentative results to date suggest that a bitter taste may indeed be performance enhancing [53].

An important consideration, when interpreting these results within the context of caffeine, is the strength of the bitter tastant. In their studies, Gam and colleagues [62] utilised solutions of between 2 mmol/L quinine (for rinse and ingestion [62]) to 10 mmol/L (for rinse only [63]), which is significantly greater than the concentration of quinine found in commercial solutions such as tonic water. Whilst caffeine and quinine appear to be similarly bitter [65], the ingestion of highly concentrated liquid forms of caffeine may prove difficult from the perspective of palatability. Furthermore, the concentrations of caffeine in commercially available caffeinated sports drinks and coffee may not be sufficient to provoke an ergogenic bitter taste response. This is of further importance when exploring the effects of a caffeinated mouth rinse on exercise performance, a relatively new field of research [66], which requires consideration as the action of rinsing caffeine around the mouth should allow caffeine to interact with the bitter taste receptors located there, potentially driving performance improvements. A small number of studies have explored the use of caffeine mouth rinsing on performance [67–73], summarized in table 1 below.

These equivocal results suggest there is a general trend for no demonstrated performance improvements when caffeine is rinsed around the mouth, both for endurance and high-intensity exercise. This suggests that either caffeine's bitter taste does not drive its performance benefits, that the solutions of caffeine utilised were insufficient to provoke a substantial bitter taste response, or that ingestion of the caffeine solution following mouth rinsing, similar to that of the quinine solution [64], is important. Interestingly, a number of trials [68] reported no change in plasma caffeine concentrations following a mouth rinse; whilst not unexpected, this does provide support regarding the need for subsequent ingestion of the caffeine solution as a means of harnessing a performance benefit. Outside of physical performance improvement, Pomportes et al. [74] demonstrated improvements in cognitive function during prolonged aerobic exercise following a

Table 1
Studies exploring the use of caffeine mouth rinse on exercise performance.

Study	Subjects	Caffeine Procedure	Test	Outcome
Beaven et al. [67]	12 males	25 ml of placebo, 6% glucose, or 1.2% caffeine solution rinsed in mouth for 5 s prior to each sprint	5 × 6 s cycle ergometer sprints with 24 s active recovery	Caffeine enhanced initial sprint performance, but potentially harmed later sprint performance. Caffeine with carbohydrate improve performance to a greater extent than caffeine alone.
Clarke et al. [69]	15 recreationally trained males	25 ml of 6% carbohydrate, 1.2% caffeine, caffeine + carbohydrate, or water, rinsed for 10 s prior to exercise	1RM bench press, followed by 60% of 1RM to failure	Rinsing with caffeine and carbohydrate, either alone or in combination, had no meaningful effect on maximum strength or muscular endurance.
Doering et al. [68]	10 well trained male cyclists	25 ml mouth rinse with placebo or caffeine (35 mg), rinsed for 10 s, eight times throughout exercise trial.	Cycle time trial, equivalent to 75% peak aerobic power output for 60 min.	No improvement in performance, and no increase in plasma caffeine.
Kizzi et al. [70]	8 recreationally active males	2% caffeine solution compared to a placebo solution, rinsed for 10 s prior to each sprint.	5 × 6 s cycle ergometer sprints, with 24 s active recovery. The evening prior, subjects had undertaken a carbohydrate lowering exercise bout.	Following carbohydrate depletion, caffeine mouth rinse significantly improved peak and mean power compared to placebo.
Pataky et al. [71]	38 recreational cyclists	Ingestion of 6 mg/kg caffeine or placebo, along with 25 ml of 1.14% caffeine or placebo solution mouth rinse	3 km cycle time trial	Using the magnitude-based inferences method, the caffeine mouth rinse was determined to have a "possible" trivial effect.
Bottoms et al. [72]	12 active males	6.4% carbohydrate, caffeine (32 mg in 125 ml water), or water mouth rinse, rinsed for 5 s at 6 min intervals	30-minute self-paced cycle trial	Distance travelled during the caffeine trial was significantly greater compared to placebo, with no difference between caffeine and carbohydrate trials.
Dolan et al. [73]	10 collegiate male lacrosse players	6% carbohydrate, 1.2% caffeine, caffeine + carbohydrate, and placebo solutions.	Yo-Yo Level 1	No performance benefit from either caffeine or carbohydrate mouth rinses, either alone or in combination.

caffeinated mouth rinse, and De Pauw and colleagues [75] suggested that a caffeine mouth rinse may enhance reaction time. Furthermore, Van Cutsem et al. [76] demonstrated the effectiveness of a caffeine mouth rinse on reducing mental fatigue during a cognitively challenging task. These latter results suggest that, whilst a caffeine mouth rinse without subsequent ingestion may not directly enhance physical performance, it may have a role to play in the maintenance of cognitive function, which in turn could enhance sporting performance.

In summarizing this section, there is tentative evidence that bitter tastants may exhibit ergogenic effects, as exemplified by the research on quinine [53]. Additionally, these research findings suggest that the harnessing of these ergogenic effects requires stimulation of bitter taste receptors in both the mouth and gastrointestinal tract, in turn necessitating both a mouth rinse and ingestion of the bitter tastant [53]. Further support for this hypothesis is given by the generally negative results on caffeine mouth rinses (with non-ingestion), which suggests that caffeine ingestion is also required.

Inter-individual variation in bitter tasting ability

In recent years there has been an increased interest in the individual variation in response to caffeine supplementation, with a number of reviews published on the subject [32,33,77]. The drivers of this individual variation are wide and varied, but include genetic variation [78,79], habitual caffeine use [80], expectancy [54], and potentially epigenetic modifications [32].

Alongside individual variation in the ergogenic response to caffeine, the ability to detect a bitter taste is also subject to individual variation [52,81]. Bitter compounds are detected by taste receptor cells in the mouth, with these cells encoded by Taste 2 Receptor (*TAS2R*) genes [82,83]. Variation in a particular TAS2R gene, *TAS2R38*, is associated with an ability to detect the bitter compounds phenylthiocarbamide (PTC) and 6-n-propylthiouracil (PROP) [84], leading to some individuals, who are sensitive to these bitter tastes, to be labelled as "supertasters" [85]. This variation in taste sensitivity has been associated with variation in consumption of alcohol [84,86], coffee [86] and vegetables [87], and variation in other TAS2R genes is associated with the palatability of coffee [88,89]. Furthermore, a number of SNPs have been associated with bitter taste reception through genome-wide association studies [90,91], suggesting that the ability to taste bitter compounds, including caffeine, is partially heritable. Finally, the bitter taste response to caffeine appears to be somewhat modifiable. Repeated exposure to caffeine reduces the sensation of bitterness [92], as does smoking [93] and aging [94].

Accordingly, there is the possibility that, as caffeine is a bitter tastant, and bitter compounds have the potential to be ergogenic, the ability to detect caffeine's bitter taste, and the magnitude at which this occurs, may well explain some of the demonstrated individual variation in caffeine ergogenicity [32], although at present this is somewhat speculative and requires further exploration.

Bitter taste and expectancy

In their seminal study, Beedie and colleagues [54] demonstrated that, when informed that they had consumed a caffeine dose of 4.5 mg/kg and 9 mg/kg, subjects increased their power output in a cycle ergometer test in a dose-response manner, even though they had been deceptively administered placebo as opposed to caffeine. Similar findings (e.g. Saunders et al. [55]), suggest that, if an individual believes they have consumed caffeine, and they believe that caffeine is ergogenic, they will potentially experience a performance benefit, even if no physiologically active substance has been consumed. The expectancy-derived ergogenic effect of caffeine has been demonstrated across a variety of exercise types, including aerobic endurance [54,55,95] and muscular strength and endurance [96–98], along with improvements in cognitive function [99,100], reaction time [101], and mood [102,103].

Placebos have been extensively shown to be effective in the management of pain [104], and one of the methods through which this occurs is by providing an expectation of pain relief [105]. As one of the proposed mechanisms by which caffeine enhances performance is via a reduction in pain [106] and RPE [38], it's clear to see that belief of caffeine ingestion may directly influence this pathway. The bitter and recognizable taste of caffeine represents a clear signal that caffeine is being consumed, and, if the athlete believes that caffeine is ergogenic—either through information provided by a coach or nutritionist, or prior experience—then they may expect performance to improve. Furthermore, ritualistic behaviours also appear to enable placebo/expectancy effects within athletes [107]. In this case, the pre-competition consumption of a caffeine substance that stimulates bitter taste receptors may have the dual performance-benefit of the athlete recognizing the ritualistic behavior (i.e. consumption of a specific brand of sports drink) and bitter taste, remembering that these two signals are associated with enhanced performance, an effect potentially accentuated by previously enhanced performance following caffeine ingestion. Whilst taste represents just one way that caffeine intake may be signaled to the athlete, along with self-rated changes in mood [54], motivation [101], and an increased perception of physiological arousal [101], it represents an interesting avenue for future exploration. As such, there is the potential that caffeine's ergogenic effects, previously demonstrated to be partially placebo/expectancy based [54,56], may be modified by the bitter taste of caffeine driving these placebo/expectancy effects. Furthermore, inter-individual variation in the ability to detect caffeine's bitter taste may in turn affect the magnitude and occurrence of placebo/expectancy following caffeine ingestion, as may individual susceptibility to placebo [108]. Tentative evidence regarding the ergogenic effects of decaffeinated coffee [109,110] demonstrate the potential of expectancy and placebo—potentially mediated by bitter taste—to enhance performance within the context of caffeine. Additionally, recent research [111] suggests that cues related to coffee increase arousal without a need for coffee ingestion, further strengthening this hypothesis.

What is bitter taste?

As detailed in the Section "Are bitter tastants ergogenic?", caffeinated mouth rinses appear to have the potential to enhance exercise performance [62], but only when the caffeine is subsequently ingested [64]. One of the key potential explanations for this difference in effect between protocols is that stimulation of bitter receptors in the upper GI tract—and not just on the tongue—is an important driver of caffeine's ergogenic effects [64]. This raises the question of how we define "taste" within this context, as the bitter receptors in the upper GI tract are not necessarily linked to gustatory neurons [112]; this means that, whilst the activation of the bitter receptors in the upper GI may be important, we do not "taste" the bitterness in this scenario. In terms of caffeine use in sport, this could be important, given that caffeine is often consumed in energy and/or sports drink form; here, the addition of carbohydrates and other ingredients masks the bitter taste of caffeine, potentially modifying the perception of bitterness (i.e. the expectancy effect detailed in the Section "Bitter taste and expectancy"), but not the activation of bitter receptors contained within the mouth and upper GI tract. Accordingly, it is important to consider that "bitterness" can therefore be comprised of both taste (i.e. the stimulation of gustatory neurons) and the activation of bitter receptors – with the two not always occurring in conjunction.

Conclusion

In pulling the various threads discussed in this article together, we can tentatively conclude that:

1. Caffeine is a bitter tastant [50].

2. Bitter tastants have the potential to be ergogenic [53], although this ergogenic benefit may require ingestion [64], and not merely mouth rinsing [63], with the additional caveat that, at present, this research is primarily focused around quinine and not caffeine.
3. Non-ingestion of caffeine, in the form of a mouth rinse, appears to be insufficient to evoke an ergogenic response (Table 1). This is potentially surprising, given the fact that adenosine receptors are found in the mouth [113], and that caffeine can be absorbed by the buccal membrane [66]. However, the limited period of time that caffeine is present in the oral cavity during a mouth rinse (typically ~10 s) may explain this, given that caffeine absorption in the gut typically takes ~45 min [114]. As such, a caffeine mouth rinse likely does not provide sufficient time for the caffeine to be adequately absorbed via the buccal membrane, which is supported by the lack of a rise in plasma caffeine concentrations following a caffeine mouth rinse in some investigations [68].
4. However, evidence suggests that some of caffeine's ergogenic benefits are partially mediated via expectancy [54,56], and there is the potential that recognition of this bitter taste when consuming caffeine may support its performance enhancing effects.

Additionally, there is considerable variation in the ability to taste bitterness between humans [115], as well as considerable variation in the ergogenic response to a standardised caffeine dose [32]. Accordingly, in serving to enhance our knowledge of optimal caffeine strategies in sport [49], further research should seek to explore; a) whether bitter taste detection is responsible for some of caffeine's ergogenic effects, b) whether variation in the ability to detect bitter taste modifies caffeine's performance benefits, and c) what factors, such as genotype and dietary history, affect this bitter taste response. Furthermore, from the perspective of caffeine mouth rinse research, increasing the concentration of the caffeine within the solution (to potentially harness the bitter taste), and subsequent ingestion of the caffeine solution, should be explored to determine whether this caffeine use method holds utility. In terms of exploring the individual variation in caffeine's ergogenic effects, and whether these are driven by variation in bitter taste receptors (Section "Inter-individual variation in bitter tasting ability"), it would be useful to explore whether variation in TAS2R genes, such as *TAS2R38*, is associated with differences in the magnitude of caffeine's ergogenic effects.

From a practical perspective, coaches and athletes should be aware of the potential impact of expectancy on caffeine's ergogenic effects. This suggests that a standardised caffeine intake routine around competition, and possibly training, could be important, as the provision of regular routines may enhance any potential expectancy effects derived from caffeine: i.e., if the athlete is undertaking a behaviour that has previously delivered success, this may "prime" future success. Additionally, if the hypothesis developed here—that caffeine's bitter taste has the potential to enhance performance, if only via expectancy—then the mechanism of caffeine intake may become important. Whilst coffee is a relatively impractical method of caffeine ingestion, given that it is often consumed hot, requires large liquid volumes to deliver an ergogenic dose of caffeine, and has variable caffeine doses [116,117], it is a highly bitter substance, more so than caffeine alone [118]. Accordingly, an argument could be made that coffee's bitter taste may provide additional performance benefits, and athletes should perhaps utilise caffeine intake strategies that stimulate taste receptors, such as the use of liquids or gum, as opposed to caffeine capsules. From a safety perspective, it is important to consider that bitter tastants such as caffeine and quinine have significant "off-target" effects. In terms of caffeine, this can include increased anxiety [119] and sleep latency [120], but quinine too has the potential to induce negative side effects such as cardiac arrythmia [121], along with inhibition of potassium channels and cellular gap junctions [122,123]. As such, the use of concentrated bitter tastants above the concentrations found in commercially available beverages should be cautioned against.

Finally, the hypothesis forwarded here, along with other unresolved issues regarding the use of caffeine in sport [49], suggest that, whilst it may be tempting to believe that we know all there is to know about caffeine as a performance enhancer, there is still a long way to travel on this journey. In unravelling some of the complexities surrounding caffeine use, we have the potential to further enhance performance over the years to come.

Declaration of Competing Interest

Craig Pickering is a former employee of DNAFit Life Sciences a genetic testing company. He received no financial incentives for the preparation of this manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.mehy.2019.109301.

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