Abstract

OBJECTIVES: To conduct a systematic review and a meta-analysis of studies exploring the effects of caffeine and/or sodium bicarbonate on performance in the Yo-Yo test.

DESIGN: Systematic review/meta-analysis.

METHODS: A total of six databases were searched, and random-effects meta-analyses were performed examining the isolated effects of caffeine and sodium bicarbonate on performance in the Yo-Yo test.

RESULTS: After reviewing 988 search records, 15 studies were included. For the effects of caffeine on performance in the Yo-Yo test, the meta-analysis indicated a significant favoring of caffeine as compared with the placebo conditions ($p = 0.022$; standardized mean difference [SMD] = 0.17; 95% CI: 0.08, 0.32; +7.5%). Subgroup analyses indicated that the effects of caffeine were significant for the level 2 version of the Yo-Yo test, but not level 1. Four out of the five studies that explored the effects of sodium bicarbonate used the level 2 version of the Yo-Yo test. The pooled SMD favored the sodium bicarbonate condition as compared with the placebo/control conditions ($p = 0.007$; SMD: 0.36; 95% CI: 0.10, 0.63; +16.0%).

CONCLUSIONS: This review demonstrates that isolated ingestion of caffeine and sodium bicarbonate enhances performance in the Yo-Yo test. Given these ergogenic effects, the intake of caffeine and sodium bicarbonate before the Yo-Yo test needs to be standardized (i.e., either restricted or used in the same way before each testing session). Furthermore, the results suggest that individuals competing in sports involving intermittent exercise may consider supplementing with caffeine or sodium bicarbonate for acute improvements in performance.

Introduction

The Yo-Yo intermittent recovery test was introduced in the 1990s and has gained substantial popularity as a method of estimating aerobic and anaerobic capacity in team-sports players.[1] In undertaking the Yo-Yo intermittent recovery test, participants are required to run distances of 2 × 20 m at progressively increasing speeds. Each 2 × 20 m work block is interspersed with a 10-s period of jogging around a marker placed 5 m behind the finish line. The test ends when the individual cannot complete the run within the prescribed time, on two consecutive occasions. The outcome of this test is the total covered distance. This test is comprised of two sub-levels, level 1 and level 2, with level 2 starting at a higher initial speed and necessitating a large contribution from the anaerobic energy system.[1] These tests are widely used in field settings as a practical method to: (a) determine current fitness status; and (b) prescribe training programs and explore their effectiveness.[2]

Caffeine and sodium bicarbonate are two supplements that have been shown to acutely enhance exercise performance.[3] The effects of caffeine and sodium bicarbonate have also been explored in the context of Yo-Yo test performance, with equivocal findings.[4-8] Some reported an increase in performance following the ingestion of either caffeine or sodium bicarbonate, while others report that performance in this test is unaffected by the use of these supplements.[4-8] Differences between the studies such as the dose, ingestion timing, and training status may explain some of these discrepancies.[9] Perhaps even more importantly, the studies conducted on the effects of sports supplements tend to be performed with small sample sizes.[3] For example, one study that explored the effects of sodium bicarbonate on performance in the Yo-Yo test included only six participants.[8] Therefore, there remains a possibility that some studies were statistically underpowered to observe significant effects, which may have resulted in increased probabilities of type II errors. Meta-analysis is a

statistical method that can be used to overcome the limitation of underpowered studies because it allows combining of data from different cohorts to obtain a pooled estimated value.

To address the apparent discrepancies between individual studies two previous meta-analyses explored the effects of caffeine on performance in the Yo-Yo test. In the first analysis, Gonçalves Ribeiro et al.[10] reported no significant effects of caffeine on performance in this test. However, the analysis included only two studies with a combined number of participants amounting to 31. Such a small number of studies was included given that the authors limited their inclusion criteria to studies published between 2010 and 2015, even though no rationale was provided for this approach. Another limitation is that these authors included both cross-over and between-group study designs. This may be relevant given that the inter-individual variation in responses to caffeine ingestion is not as well controlled in between-group designs as in cross-over trials.[11]

In another review, Salinero et al.[12] reported that caffeine ingestion enhances performance in the Yo-Yo test by an effect size of 0.22 with a 95% confidence interval (CI) ranging from 0.00 to 0.44. This meta-analysis included only four studies (pooled $n = 57$) given that studies providing caffeine in doses lower than 2 $mg \cdot kg^{-1}$ were not considered. Additionally, this review did not search through unpublished literature, which may have led to publication bias due to the "file drawer" syndrome. The "file drawer" syndrome suggests that studies with larger effect sizes are more likely to be published than those with small or non-significant effect sizes; therefore, including only published studies may present a source of bias in a given meta-analysis.[13, 14] Additionally, two studies[4,15] were not included in the review by Salinero et al.[12] and new studies on this topic have been published since this review.[7,16] All these studies generated data for over 100 additional participants. Therefore, an updated meta-

analysis that would include these studies could contain almost a threefold increase in the pooled sample size from the most recent meta-analysis[12] thus increasing the veracity of the findings.

While the effects of caffeine have been explored using a meta-analytic approach, no previous meta-analyses explored the effects of sodium bicarbonate on performance in the Yo-Yo test. A meta-analysis exploring the effects of sodium bicarbonate on performance in this test is needed because: (a) the equivocal evidence on this topic presented in the literature;[5,6,8] and, (b) the common anecdotal use of sodium bicarbonate by athletes.[17] Therefore, the aim of this review was to explore the effects of caffeine and sodium bicarbonate on performance in the Yo-Yo testing using a meta-analysis and highlight the practical application of these findings.

Methods

For this review, peer-reviewed literature in the form of journal articles and unpublished literature in the form of a thesis, dissertations, or conference abstracts that investigated the effects of caffeine and/or sodium bicarbonate ingestion on performance in the Yo-Yo test was examined. The search for studies was conducted on April 14th, 2019. The following databases were searched: ERIC, PubMed/MEDLINE, SPORTDiscus, Open Access Thesis and Dissertations, Web of Science, and Scopus. Additionally, searches were performed within ResearchGate. In all of these databases, the following search syntax was used: ("caffeine" OR "supplement" OR "coffee" OR "ergogenic" OR "NaHCO3" OR "sodium bicarbonate") AND ("yo-yo" OR "yoyo" OR "yo yo"). Secondary searches were performed by screening the reference lists of the included studies, and by exploring the papers that cited the included studies. The search was performed independently by two authors (JG and AG).

To be included in the review, studies were required to satisfy the following criteria: (1) published in English; (2) included apparently healthy humans as participants; and (3) employed a cross-over study design and explored the acute effects of caffeine and/or sodium bicarbonate on performance in any variant of the Yo-Yo test.

Two authors of the review (JG and AG) extracted the following data from the included studies: (1) author names and publication year; (2) sample size and the sample characteristics; (3) the variant of the Yo-Yo test used for the testing; and (4) main findings regarding the effects of caffeine and/or sodium bicarbonate on performance. In cases where the required data was presented in figures, the Web Plot Digitizer software was used for the extraction of raw values.

The PEDro checklist was used for assessing the quality of the included studies.[18] This checklist has 11 items; these items refer to eligibility criteria, randomization and blinding of participants, blinding of assessors, the number of participants completing all testing sessions, and reporting of data for the key outcomes. While this checklist has 11 points, the first item is not included in the summary score, and therefore, the maximum number of points is 10. Based on the summary scores, the studies were classified as being of excellent quality (9-10 points), good quality (6-8 points), fair quality (4-5 points) and poor methodological quality (<3 points).[19-21] The quality assessment was conducted independently by two authors of the review (JG and AG).

The mean ± standard deviation performance data extracted from the included studies were converted to standardized mean differences (SMDs) and their respective 95% CIs. The following data are required to calculate SMDs: (1) Yo-Yo test performance mean ± standard

deviation of the caffeine/sodium bicarbonate and placebo/control trials, (2) total sample size, and (3) inter-trial correlation. Inter-trial correlation was not presented in any of the included studies. As suggested in the Cochrane Handbook the following formula was used to estimate the correlation:

$$r = \frac{S^2_{placebo/control} + S^2_{treatment} - S^2_D}{2 \cdot S_{placebo/control} \cdot S_{treatment}}$$

S represents the standard deviation while S_D is the standard deviation of the difference score, which was calculated as:

$$S_D = \left(\frac{S^2_{placebo/control}}{n} + \frac{S^2_{treatment}}{n}\right)^{1/2}$$

One of the studies that explored the effects of caffeine used multiple caffeine doses; for this study, SMDs and variances were calculated for each dose separately and the average values were used for the analysis. Two meta-analyses were performed: (1) for the effects of caffeine on performance in the Yo-Yo test; and (2) for the effects of sodium bicarbonate on performance in the Yo-Yo test. In the meta-analysis that focused on the effects of caffeine, a sensitivity analysis was performed by excluding one study in which caffeine was not ingested as it was provided in a mouth rinsing form.[22] A subgroup analysis was performed for studies exploring the effects of caffeine on Yo-Yo intermittent recovery level 1 and for those exploring the level 2 variant of the test. In the meta-analysis for the effects of sodium bicarbonate, a sensitivity analysis was performed by excluding the only study that used the

level 1 version of the test. SMD values of <0.20, 0.20-0.39, 0.40-0.59, 0.60-0.80, and >0.80 were considered to represent trivial, small, medium, large, and very large effects, respectively. In each analysis, the I^2 statistic was used to explore heterogeneity with I^2 values of <50%, 50 to 75%, and >75% considered as low levels, moderate levels, and high levels of heterogeneity.

In addition to 95% CIs, 95% prediction intervals (95% PI) were calculated for both analyses by using the number of included studies in the meta-analysis, the pooled SMD, the upper limit of the 95% CI and the tau-squared values. The 95% PI denotes the range in which the effect size of a future study conducted on the topic will most likely be. Funnel plots asymmetry was explored only for the effects of caffeine given that there were less than 10 studies included in the analyses for sodium bicarbonate. Percent differences between supplement ingestion conditions and the placebo/control conditions were also calculated. The random-effects model was used for both analyses. The statistical significance threshold was set at $p < 0.05$. All analyses were performed using the Comprehensive Meta-analysis software, version 2 (Biostat Inc., Englewood, NJ, USA).

Results

The total number of search results across all databases was 164. Of this number of search results, 21 full-text papers were read and 12 studies were included. The remaining documents were excluded based on the title or abstract. The secondary searches resulted in another 824 search results and in the inclusion of three additional studies. Therefore, in total, 15 studies were included; 13 studies were published as full-text manuscripts in peer-reviewed journals, one study was published as a conference abstract, and one study is a part of a master's thesis.[4-8,13,15,16,22-28] Eleven studies explored the effects of caffeine, whereas five studies examined the

effects of sodium bicarbonate on Yo-Yo test performance (Table 1). One study included examined the isolated effects of both caffeine and sodium bicarbonate.

For studies that explored the effects of caffeine, the pooled number of participants across all studies was 156 (21 females). The average sample size per study was 14 participants. In all of the included studies, the sample was comprised of athletes. The doses of caffeine in the studies ranged from 1 $mg \cdot kg^{-1}$ to 6 $mg \cdot kg^{-1}$. Five studies provided absolute doses of caffeine ranging from 200 to 500 mg. One study used a caffeine mouth rinsing form where 1.2% of the 25 ml solution was caffeine. Timing of caffeine administration before exercise ranged from immediately before (one study), 5 minutes (two studies), 45 minutes (two studies), 50 minutes (one study), 60 minutes (four studies) and 70 minutes (one study) before exercise. Five studies used the intermittent Yo-Yo recovery test level 1 and six used the level 2 version.

The pooled number of participants for the studies that explored the effects of sodium bicarbonate was 46 (all males). The average sample size per study was 9 participants. Three studies included athletes as their study participants while two included recreationally active individuals. The doses of sodium bicarbonate in the studies ranged from 0.2 $g \cdot kg^{-1}$ to 0.4 $g \cdot kg^{-1}$. Sodium bicarbonate was ingested 40 minutes pre-exercise (one study), 60 minutes (one study), and 90 minutes pre-exercise (two studies). One study used a protocol that included splitting up a dose of 0.4 $g \cdot kg^{-1}$ into five smaller doses taken at 90, 80, 70, 60, and 50 minutes pre-exercise. Four studies used the intermitted Yo-Yo recovery test level 2, with only one using the level 1 version.

Out of the eleven studies that explored the effects of caffeine on Yo-Yo test performance, eight were classified as being of excellent quality with two studies being classified as good

methodological quality and one as fair methodological quality. Out of the five studies that explored the effects of sodium bicarbonate on Yo-Yo test performance, three were classified as being of excellent quality, one as good methodological quality and one study as being of fair methodological quality. No studies were classified as being poor methodological quality. Individual scores for the quality assessment can be found in Supplementary file 1.

The meta-analysis for the effects of caffeine included a total of ten studies given that in one study, the data required for the analysis was not presented and the authors did not provide the data upon written request.[22] The main meta-analysis indicated a significant difference (p = 0.022) between the caffeine and placebo conditions with the SMD favoring the caffeine condition (SMD: 0.17; 95% CI: 0.08, 0.32; percent change: +7.5%; I^2: 28%; 95% PI: -0.32, 0.66; Figure 1). No funnel plot asymmetry was observed. In the sensitivity analysis in which the study that provided caffeine in a mouth rinsing form was excluded, the SMD values increased to 0.20 (95% CI: 0.05, 0.36; p = 0.009; percent change: +8.5%; I^2: 26%). In the subgroup analysis for the level 1 Yo-Yo test the SMD was 0.02 (95% CI: -0.21, 0.25; p = 0.880; percent change: +2.5%; I^2: 0%). In the subgroup analysis for the level 2 Yo-Yo test the SMD was 0.31 (95% CI: 0.12, 0.51; p = 0.002; percent change: +14.4%; I^2: 11%).

The meta-analysis for the effects of sodium bicarbonate indicated a significant difference (p = 0.007) between the sodium bicarbonate and placebo/control conditions. The pooled SMD favored the sodium bicarbonate condition (SMD: 0.36; 95% CI: 0.10, 0.63; percent change: +16.0%; I^2: 14%; 95% PI: -0.61, 1.33; Figure 2). In the sensitivity analysis in which the study that used the level 1 Yo-Yo test version was excluded, the SMD values increased to 0.39 (95% CI: 0.08, 0.70; p = 0.013; percent change: +17.5%; I^2: 25%).

Discussion

This review reports that isolated ingestion of caffeine and sodium bicarbonate enhances performance in the Yo-Yo test. Both supplements seem to produce moderate performance-enhancing effects. Due to these acute ergogenic effects, the intake of caffeine and sodium bicarbonate before the Yo-Yo test needs to be standardized. The results also suggest that individuals competing in sports involving intermittent exercise may consider supplementing with caffeine or sodium bicarbonate for acute improvements in performance.

This meta-analysis adds further evidence that caffeine ingestion enhances performance in field-based tests of fitness. These results are in line with prior work in the area, most of which is based on tests performed in the laboratory.[14] Caffeine's ergogenic effect is likely related to its binding to adenosine receptors.[29] Caffeine has a similar structure to adenosine and therefore, when ingested, caffeine binds to A_1 and A_{2A} receptors, ultimately blunting the fatiguing effects of adenosine. As a result, acute caffeine ingestion may reduce perceived effort and increase physical performance. Caffeine ingestion may also enhance motor unit recruitment, thus leading to more forceful muscle contractions.[30,31] These mechanisms might explain why the pooled SMD increased when the study that provided caffeine in the mouth rinsing form was excluded.[22] After excluding the study that utilized caffeine mouth rinsing, the SMD increased from 0.17 to 0.20. Specifically, caffeine provided in this form does not increase plasma caffeine concentration[32] which is a likely prerequisite for an ergogenic effect of caffeine.

Due to a small number of included studies, previous meta-analyses did not examine if the effects of caffeine differ between level 1 and level 2 versions of the Yo-Yo test. These

subgroup analyses were performed in the present review and indicated that the effects of caffeine were significant only for the level 2 version. Such findings may suggest that caffeine is more effective in tests with a greater contribution from the anaerobic energy system.[1] These results were obtained from studies that examined the effects of caffeine on either level 1 or level 2 versions of the test. However, given the inter-individual variation in responses to caffeine ingestion,[11,33,34] future studies may consider comparing the effects of caffeine on performance in the level 1 and level 2 version of the test in the same group of participants.

Based on the results of this review, sodium bicarbonate is effective for acute increases in Yo-Yo test performance. Sodium bicarbonate may elicit its ergogenic effects by: (a) acutely increasing blood bicarbonate and leading to a greater efflux of hydrogen ions (H^+) and lactate out of the active muscles and into the circulation; and subsequently, (b) maintenance of intramuscular pH.[35,36] Following acute sodium bicarbonate ingestion and subsequent increase in blood bicarbonate concentration, the resultant pH gradient between the intracellular and extracellular environments favors the efflux of H^+ from the exercising muscle to blood, aiding intracellular pH regulation and reducing fatigue.[35,36]

While no previous meta-analysis examined the effects of sodium bicarbonate on Yo-Yo test performance, other meta-analyses have focused on different aspects of exercise performance. For example, Matson and Tran[37] combined studies that explored the effects of sodium bicarbonate on various exercise tests, with some lasting over 30 minutes and others being of very short duration, and maximal intensity (e.g., 10-second “all-out” sprints). The pooled ergogenic effect size of sodium bicarbonate was 0.44. The magnitude of the effect is comparable to the effect size observed herein, even though an argument can be made that the

pooling of vastly different exercise tests (with different physiological demands) in the analysis by Matson and Tran[37] might have been a methodological limitation. A meta-analysis by Carr et al.[38] reported an ergogenic effect of acute sodium bicarbonate ingestion that amounted to 1.7%. The performance-enhancing effect in the analysis by Carr et al.[38] was small likely because it included many of the older studies that used protocols in which all participants ingest sodium bicarbonate around 60 to 90 minutes before exercise.[9,39,40] However, in recent years, studies have started using individualized time to peak blood bicarbonate protocols, and they generally report greater effect sizes.[9,39,40] The majority of studies included in the meta-analysis utilized performance tests lasting up to 30 seconds (i.e., much shorter than the average duration of the Yo-Yo test), which limits further comparison of the results. Nonetheless, this review reinforces the suggestion of the International Olympic Committee that acute sodium bicarbonate ingestion enhances short-term high-intensity exercise performance.[3]

The results presented in this review highlight the need for standardizing caffeine and sodium bicarbonate intake before the Yo-Yo test. In other words, supplementation with caffeine or sodium bicarbonate should be either restricted or used in the same way before each testing session. If their use is not standardized, some individuals may ingest caffeine or sodium bicarbonate before the testing and possibly experience a supplement-induced improvement performance in the Yo-Yo test. This may be especially important to control when using the Yo-Yo test for the evaluation of the effectiveness of a given training program. Additionally, standardization of caffeine and sodium bicarbonate intake may be important for studies that focus on the reliability of the Yo-Yo test.[41] If not standardized, ingestion of these supplements may lead to improvements in performance by small to moderate effects (i.e., pooled SMDs in

this review ranged from 0.17 to 0.39); if not standardized, this improvement may affect the validity of the data and lead to incorrect interpretation of the results.

One additional value of these substances is that their ingestion may improve performance in training sessions or competitions with similar energy demands as the Yo-Yo test. This may be especially relevant in soccer given that Krustup et al.[42] observed that the performance in the Yo-Yo test is significantly correlated (r=0.81) with the number of high-intensity running actions performed at the end of each half of a game. These results suggest that caffeine or sodium bicarbonate ingestion may even improve performance directly during sports competitions. These supplements may also have the potential to enhance training responses and adaptations; albeit, future long-term studies are needed to establish such effects. Still, while the Yo-Yo test is valid for determining an individual's capacity to perform repeated exercise,[1] future studies may consider exploring the effects of caffeine and sodium bicarbonate using more specific team sport stimulations. For example, one study explored the effects of caffeine while using a performance test simulating physical and skill demands of a rugby union game which included seven circuits in each of two 40-min halves with a 10-min half-time rest.[43]

Using the PEDro checklist, the included studies are generally sound from a methodological quality perspective. Nonetheless, several included studies used a single-blind protocol which offers evidence of lower that the use of the "gold standard" double-blind study design. Of the studies that blinded the participants, only two[16,28] explored the effectiveness of this blinding by asking the participants to indicate which condition was the placebo and which the caffeine/sodium bicarbonate one. This limitation needs to be addressed in future studies given

317 that correct supplement identification may impact exercise outcomes and therefore lead to
318 bias in the results.[44]

319

320 The main limitation is that some of the studies included in the meta-analysis on the effects of
321 sodium bicarbonate used a placebo condition as the comparison and other employed a non-
322 supplement, control trial. This methodological aspect may have affected the results given that
323 the act of ingesting a capsule (even though it does not contain an ergogenic compound) can
324 produce improvements in performance due to the placebo effect. However, the largest
325 improvement in performance following sodium bicarbonate ingestion was in a study[26] that
326 used a placebo vs. sodium bicarbonate comparison (SMD: 0.93; +30%) which may suggest
327 that this limitation may not be particularly impactful in this specific context (even though it
328 needs to be stated). Additionally, it needs to be mentioned that only one[25] of the five studies
329 that explored the effects of sodium bicarbonate used a sodium-matched placebo comparison.
330 Given that there are cases in which sodium can also be ergogenic,[45] future studies on this
331 topic should consider adding a condition with an equimolar amount of salt to the sodium
332 bicarbonate condition to isolate the effects of bicarbonate.[46]

333

334 In the included studies, caffeine and sodium bicarbonate were provided in isolation. Given
335 that both supplements appear to be ergogenic, future work is needed to explore whether their
336 combined ingestion provides any additive benefits. It is possible that the combination of these
337 supplements would provide even greater effects because acute ingestion of caffeine and
338 sodium bicarbonate enhances performance through different physiological mechanisms. As
339 stated previously, caffeine's ergogenic effects are explained by its tendency to bind to
340 adenosine receptors while sodium bicarbonate elicits its ergogenic effect through pH

regulation. While there are several studies conducted on this topic, future work is needed to provide greater clarity on the issue of supplement interactions.[35] This area may be particularly relevant for athletes given that athletes often ingest more than one supplement,[47] and that caffeine is often ingested as part of a multi-ingredient pre-workout supplement, or energy drink. Future studies are needed to explore optimal doses of caffeine and sodium bicarbonate that have the largest effect on performance while producing the least side-effects.[48] In addition to doses, future work is need on the optimal timing of ingestion. Timing of ingestion may be especially important to investigate when it comes to sodium bicarbonate given that there is very large inter-individual variability in responses to sodium bicarbonate ingestion,[9,39,40] and the timing of ingestion is also affected by the mode of delivery.[49]

Conclusion

The results of the present review indicate that isolated caffeine and sodium bicarbonate ingestion enhances performance in the Yo-Yo test. Given these acute performance-enhancing effects, the intake of caffeine and sodium bicarbonate before the Yo-Yo test needs to be standardized (i.e., either restricted or used in the same way before each testing session). Also, the results suggest that these substances may improve performance during exercise tasks with similar energy demands to the Yo-Yo test and athletes competing in intermittent sports may consider supplementing with caffeine or sodium bicarbonate for acute increases in performance.

Conflicts of interest

None.

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