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Isolated ingestion of caffeine and sodium bicarbonate on repeated sprint performance: A systematic review and meta-analysis

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ABSTRACT

Objectives: This study is a systematic review and meta-analysis aimed at investigating the isolated effects of caffeine and sodium bicarbonate ($NaHCO_3$) ingestion on repeated sprint ability (RSA).
Methods: Following a search through PubMed and Scopus, 13 studies (7 with caffeine and 6 with $NaHCO_3$) were found to meet inclusion criteria. Random-effects of standardized mean difference (SMD) for total work and best sprint performance was examined. Study quality was assessed using QualSyst.
Results: The meta-analysis indicated that caffeine ingestion did not improve the total work done (weighted average effect size Hedges's g = −0.01, 95%CI: −0.32 to 0.31, p = 0.97), best sprint (weighted average effect size Hedges's g = −0.02, 95% CI: −0.32 to 0.27; p = 0.87) or last sprint performance (weighed average effect size Hedge's g = −0.27, 95%CI: −0.68 to 0.14; p = 0.20), when compared with a placebo condition. Similarly, $NaHCO_3$ ingestion did not improve the total work done (weighted average effect size Hedges's g = 0.43, 95% CI: −0.11 to 0.97, p = 0.12), best sprint (weighted average effect size Hedges's g = 0.02, 95% CI −0.30 to 0.34; p = 0.90) or last sprint performance (weighted average effect size Hedge's g = 0.20, 95%CI: −0.13 to 0.52, p = 0.14), compared with a placebo condition. Quality assessment of selected articles was classified as strong.
Conclusion: This meta-analysis provides evidence that repeated sprint ability is not affected by acute ingestion of caffeine or $NaHCO_3$.

1. Introduction

Many team sports (i.e., soccer, rugby and hockey)[1–3] require participants to repeatedly produce maximal or near-maximal sprints of short duration (1–7 s) with brief recovery periods.[4] As such, an important fitness component of these sports is repeated sprint ability (RSA), which is defined as the ability to perform repeated short-duration sprints (<10 s) with minimal recovery between bouts (usually ≤60 s)[5,6]. Over recent years, the volume of literature examining the physiological and performance responses to RSA tests has rapidly increased.[1,3] The use of tests consisting of several sprints interspersed with brief recovery periods, should ensure physiological responses are similar to those occurring in official matches.[1] Fatigue during RSA develops rapidly and performance decrements are often observed following the first sprint, possibly as a result of peripheral (i.e. substrate depletion and metabolite accumulation) and neural (i.e. muscle activation and motor unit recruitment) factors.[2,6] Gaitanos et al.[7] observed an 8-fold decrease in the absolute production from glycolysis from the first to the last sprint of 10 × 6-s maximal sprints interspersed with 30-s recovery periods. However, it is unclear, if increasing the maximal anerobic glycogenolytic and glycolytic rate, though ergogenic aids (i.e. caffeine and $NaHCO_3$ ingestion), will lead to improvements in RSA.

Caffeine (1, 3, 7 – trimethylxanthine) is a stimulant commonly consumed by athletes at various levels of competition as well as in a wide range of sporting disciplines.[8] It has been reported that 74% of elite athletes use caffeine as an ergogenic aid prior to or during an event or sport, with endurance sports showing the highest prevalence rate for caffeine use.[8] This is likely due to caffeine's high accessibility and to the fact that it can be administered in different forms (i.e. capsule, coffee, and sports drinks,

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including chewing gum, bars, gels, mouth rinse energy drinks and aerosols).[9] In general, caffeine improves exercise performance at moderate doses (3–6 mg/kg^{-1} of body mass - BM), and when consumed approximately 60 min prior to exercise.[10–12] However, lower caffeine doses (<3 mg kg-1 of BM) also increase athletic performance, if consumed 60 min before exercise.[12,13] In fact, a recent meta-analysis showed that caffeine ingestion (3–6 mg/kg^{-1} of BM) has a significant positive effect on time-trial performance (+2.2%), when compared with a placebo.[14] The mechanisms underpinning this benefit include adenosine receptor antagonism, increased endorphin release, enhanced neuromuscular function, improved vigilance and alertness, and a reduction in perception of effort during exercise.[12,15] Although the benefits of caffeine ingestion on RSA are equivocal, it is effectiveness enhancing short-term high-intensity exercise performance is more consistent.[16–18] Recently, a meta-analysis performed by Grgic and Pickering[16] demonstrated that acute caffeine ingestion increases isokinetic strength. Furthermore, Grgic[19] reported that caffeine ingestion increased mean (+3%) and peak (+4%) power output during a single Wingate test. However, no difference was observed during repeated bouts.[20]

Sodium bicarbonate ($NaHCO_3$) ingestion increases performance during high-intensity intermittent exercise.[21–23] $NaHCO_3$ acts as an extracellular (blood) buffer, since HCO_3^- ions are unable to permeate the sarcolemma.[22] A single oral ingestion of 0.3 g kg^{-1} of BM of $NaHCO_3$, 90 prior to exercise,[24] increases the blood concentration of HCO_3 by approximately 5–6 mmol L^{-1}.[25] $NaHCO_3$ ingestion increases extracellular buffering and dynamic buffering capacity, increasing the rate at which H^+ is removed from working muscle cells during high-intensity exercise.[13,22] This buffering action reduces intramuscular acidosis, which appears to prevent the inhibition of glycolytic key-enzymes[26] and delays the onset of muscular fatigue during high-intensity exercise. In fact, Bishop et al.[27] reported that $NaHCO_3$ ingestion was effective in improving total work (+5%) during an RSA test when compared, with a placebo. Thus, $NaHCO_3$ appears effective in improving high-intensity exercise.[21]

To date, there is a wide range of supplements aimed at improving athletic performance. However, two supplements that are legal, well-researched, readily available, and thus utilized are caffeine and $NaHCO_3$. This is especially the case with regards to performance within a single sprint, however, the effects on performance during repeated sprints is less clear. Meta-analyses have helped to elucidate equivocal points within nutritional supplement research as they allow the pooling results from many studies.[13] Thus, the present meta-analysis evaluated the isolated effects of caffeine and $NaHCO_3$ ingestion on performance during RSA.

2. Methods

The review was conducted in accordance with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) statement guidelines.[28] A systematic search of the research literature was performed using PubMed, Web of Science and Scopus online databases through June 2018 to identify original research. Keywords were used individually or combined: "repeated sprint exercise" or "repeated sprint ability" and "caffeine ingestion" or "caffeine supplementation" and "sodium bicarbonate ingestion" or "sodium bicarbonate supplementation". The analysis was restricted to "English language" and original research articles published in peer-in-review journals (excluding gray literature indexed by non-scientific databases as abstracts of scientific events).[29] Furthermore, references from the reviewed articles were examined to identify possible additional articles.

Inclusion and exclusion of articles was determined with the application of the PICOS (Participants, Intervention, Comparison, Outcomes and Study Design) criteria to the title, abstract, and/or full text of articles[28,30] (see Table 1). Titles and abstracts were first screened, the full-text articles were retrieved if the citation was considered potentially relevant. In order to prevent any selection bias, the search was done independently by the first and second author and the third author resolved the discrepancies when necessary.

Table 1
PICOS (participants, interventions, comparison, outcomes, and study design).

PICOS components	Detail
Participants	Healthy humans' males and females
Interventions	Repeated sprint ability and repeated sprint exercise (sprint duration <10 s and recovery duration ≤60 s)
Comparisons	Isolated acute ingestion of caffeine and/or sodium bicarbonate compared to placebo without fatigued state
Outcomes	Total work done, best (fastest sprint time or highest power output – usually corresponding to the initial sprint – recorded/achieved during the repeated sprint ability (RSA) test) and last sprint performances during repeated sprint ability tests.
Study design	Double-blind, randomized controlled trials with crossover design or counterbalanced

The following exclusion criteria were considered: not peer reviewed; review, meta-analysis, position statement, or proposed study design articles; studies where caffeine or sodium bicarbonate were not ingested as an acute dose prior to the start of exercise (preload or exercise), and were consumed during the exercise protocol; studies without placebo comparison (water or other beverages without caffeine or sodium bicarbonate); studies where the results were not presented isolated for intake supplement (i.e. when caffeine or sodium bicarbonate were co-ingested with another supplement); studies that administrated coffee or caffeinated gum were also excluded. Studies taking place in extreme environments (high altitude, high or low temperatures) were included only if both placebo and caffeine or sodium bicarbonate took place in the same extreme environment. The data collection process is presented in Fig. 1.

The methodological quality was assessed using the quantitative assessment tool "QualSyst" by Kmet et al. (2004). QualSyt contains 14 items (see Table 2) that are scored depending on the degree to which the specific criteria were met (yes = 2, partial = 1, no = 0). Items not applicable to a particular study design were marked 'NA' and excluded from the calculation of the summary score. A summary score was calculated for each article by summing the total score obtained across relevant items and dividing it by the total possible score. Two authors performed the quality assessment. A score of >75% indicated strong quality, a score of 55–75% indicated moderate quality, and a score <55% indicated weak quality.

Physical performance data were extracted in the form of means, standard deviations (SDs) and sample size for placebo, caffeine, and $NaHCO_3$ conditions. Information collected from each study included the design of the study, sample size, dosage and time of caffeine and $NaHCO_3$ ingestion, as well as the exercise protocol used. Data were collected directly from tables and within the text of the selected studies when possible or using Graph digitizing software (DigitizeIt, Braunschweig, Germany) in studies where plots only were published.[7,27,31] Dependent variables included best (fastest sprint time or highest power output, usually corresponding to the initial sprint, recorded/achieved during the RSA test) and mean (i.e. averaged sprint time or power output recorded/maintained throughout the test) performance during RSA tests. When data were not available or referenced in the manuscript, authors were contacted to obtain the relevant information. Three studies were excluded from meta-analysis when the missing data could not be provided,[32,33] or author did not respond.[34]

Table 2
General characteristics of the studies that investigated caffeine ingestion on repeated sprint ability performance (RSA) included in this meta-analysis.

References	Design	Participants	Training status	Caffeine habituation	Caffeine dosage	Placebo	Time to ingestion	RSA (Sets × reps × duration, intra- and inter-set rest
Carr et al.[31]	Semi randomized, double-blind and counterbalanced	10 M	University students	NR	6 mg kg^{-1} of BM	Glucose	60 min	3 × 6 × 20 m running sprints; 25 s active recovery; 4 min (2 min passive and 2 min active recovery)[*]
Carr et al.[31]	Semi randomized, double-blind and counterbalanced	10 M	University students	NR	6 mg kg^{-1} of BM	Glucose	60 min	2 × 6 × 20 m running sprints; 60 s active recovery; 4 min (2 min passive and 2 min active recovery)[a,*]
Glaister et al.[32]	Randomized and double-blind	21 M	sport-science students	Low Consumers < 100 mg day^{-1})	5 mg kg^{-1} of BM	Maltodextrin	60 min	12 × 30 m running sprint; 35 s of active recovery
Lee et al.[33]	Double-blind, randomized and counterbalanced	14 M	Recreational athletes	Low consumers (<200 mg day^{-1})	6 mg kg^{-1} of BM	Maltodextrin	60 min	12 × 4 s cycle ergometer; 25 s of active recovery
Lee et al.[36]	Double-blind, randomized and counterbalanced	11 F	Trained athletes	NR	6 mg kg^{-1} of BM	Cellulose	60 min	10 × 5 × 4 s cycle ergometer; 20 s of active recovery; 2 min of active recovery[*]
Buck et al.[37]	Randomized, double-blind and latin-square	12 F	Amateur team-sports	NR	6 mg kg^{-1} of BM	Glucose	60 min	6 × 20 m running sprint; 25 s active recovery
Kopec et al.[34]	Randomized, double-blind and latin-square	11 M	Team-sports athletes	NR	6 mg kg^{-1} of BM	Lactose/sucrarose	60 min	6 × 30 m running sprint, 25 s active recovery
Eaton et al.[35]	Randomized, double-blind and counterbalanced	10 M	Subelite football player	NR	3 mg kg^{-1} of BM	Calcium carbonate	60 min	6 × 4 s; 8 s of active recovery

M: male; F: female; NR: Not reported. BM: body mass
[*] Only the first set of RSA test was considered.

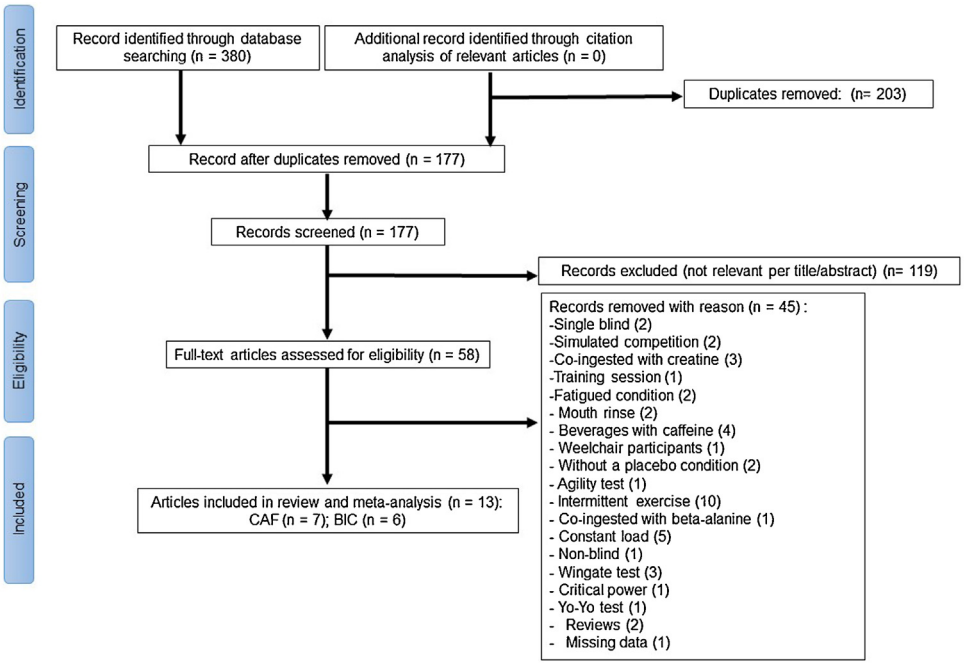

Fig. 1. Selection process for research articles included in this systematic review. An adapted version of the recommendation in the PRISMA.

Meta-analysis was conducted using the Review Manager 5.3 (version 5.3, Cochrane Collaboration, Copenhagen, Denmark) in order to aggregate, via a random-effects model,[35] the standardized mean difference (SMD). The following data were need to calculation for SMD: 1) mean ± SD of the caffeine, placebo and sodium bicarbonate trials, 2) sample size. Use of the SMD summary statistic allowed all effect sizes to be transformed into a uniform scale, which was interpreted according to Cohen's conventional criteria (Cohen, 1980), with SMD of <0.20, negligible; 0.20–0.49, small; 0.50-0.79, moderate; and >0.80, large. Heterogeneity was determined using I^2 value, with values of 25, 50 and 75 indicating low, moderate and high heterogeneity, respectively. The results are reported as weighed means and 95% confidence intervals (95%CIs). The statistical significance was set at $p < 0.05$. Furthermore, study characteristics are presented as mean ± SD.

3. Results

We found 380 articles through databases. Of the 177 that remained after the removal of 203 articles duplicates, we excluded 119 articles not considered as relevant. Based on the inclusion criteria, 13 articles, seven with caffeine and six with $NaHCO_3$ ingestion, published between 2001 and 2016, met the full set of criteria and were included for review. All descriptions and characteristics of the review studies are presented in Tables 2 and 3. Moreover, the quality assessment of selected articles was classified as strong (see Table 4 and 5).

A total of five studies comprised only male participants[36–40] and two studies included only females.[41,42] The mean number of participants was 13 ± 4. Participants' age, height, and body mass were 21 ± 1 years, 174.3 ± 7.4 cm and 78.0 ± 1.4 kg, respectively. Only two studies provided information relating the participants habitual caffeine consumption habits[37,38] and participants were classified as low consumers (<200 mg kg^{-1}).

Performance testing involved running in five studies,[36,37,39,42] whereas three studies utilized cycling.[38,40,41] The RSA protocols also differed in terms of the number of sprint repetitions (i.e. from six to twelve repetitions), duration/length of effort (i.e., 4 s or 20–30 m), as well as recovery time (i.e., 8–60 s) and type (active or passive) (Table 2).

All studies were randomized trials and included a placebo condition for comparative purposes. Dose of caffeine administered was based on the individual body mass (BM) with 6 mg kg^{-1} [36,38,39,41,42], 5 mg.kg^{-1}[37] and 3 mg kg^{-1} of BM.[40] In all studies, caffeine was ingested 60 min before exercise.

In relation to $NaHCO_3$ studies, four studies comprised only male participants[31,43–45], one study included only females[27] and one study utilized both males and females.[46] The mean number of participants was 13 ± 6. Participants' age, height, and body mass were 22 ± 2 years, 178.0 ± 1.2 cm and 72.5 ± 4.4 kg, respectively.

Performance testing involved cycling in five studies[27,31,43,45,46] and only one study utilized a running-based test.[44,40] The RSA protocols also differed in terms of the number of sprint repetitions (i.e. from six to fifteen repetitions), duration/length of effort (i.e., 6 s or 20 m), as well as recovery time (i.e.,20–60 s) and type (active or passive) (Table 3).

All studies were randomized trials and utilized a dose of 0.3 g.kg^{-1} of BM of $NaHCO_3$. Sodium chloride ($NaCl^-$)was utilized in all studies for comparative purposes, with amounts of 0.2 g.kg^{-1} of BM,[27,31,44,45] 1.5 g kg^{-1} of BM[43] and 8 g kg^{-1}.[46] The pre-trial protocol of supplementation was standardized in five studies, but with time of supplementation of 60 min[44], 90 min[27], 120 min[45], 150 min[43] and 180 min.[46] Only one study utilized an individualized timing protocol based on the time-to-peak pH responses of each individual varying between ~10 min to 90 min pre-trial.[31]

The forest plots depicting the individual SMDs and associated 95%CI and random-effect models for caffeine and $NaHCO_3$ on RSA performance are presented in Fig. 2 and 3, respectively.

Following data pooling, the SMD for total work done was – 0.01 (95%CI −0.32 to 0.31), providing a non-significant effect between caffeine and placebo conditions ($p = 0.97$) (Fig. 2a). Moreover, there was a non-significant effect of caffeine versus placebo conditions on best sprint performance (SMD = −0.02, 95% CI −0.32 to 0.27; $p = 0.87$) (Fig. 2b) and last sprint (SMD = 0.27, 95% CI −0.68 to 0.14; $p = 0.20$) (Fig. 2c). Heterogeneity was not detected among studies assessing total work and last sprint ($I^2 = 0\%$), whereas best sprint presented a moderate heterogeneity ($I^2 = 34\%$).

Table 3
General characteristics of the studies investigated sodium bicarbonate ingestion on repeated sprint ability performance (RSA) included.

References	Design	Participants	Training status	Sodium bicarbonate dosage	Placebo	Time to ingestion	RSA (Sets × reps × duration, intra- and inter-set rest
Lavender and Bird[41]	Randomized and double-blind	8 F and 15 M	Physically active	0.3 g kg^{-1} of BM	8 g of NaCl	180 min pre-trial	10 × 6 s cycling sprint; 30 s of rest between each sprint
Gaitanos et al.[38]	Randomized	7 M	Health male physical education student	0.3 g kg^{-1} of BM	1.5 g of BM of NaCl	150 min pre-trial	10 × 6 s running sprint; 30 s of rest between each sprint
Bishop et al.[22]	Randomized, double-blind and crossover	10 F	Active females	0.3 g kg^{-1} of BM	0.2 g kg^{-1} of BM NaCl	90 min pre-trial	5 × 6 s cycling, 30 s of rest between each sprint
Ducker et al.[39]	Randomized, placebo-controlled study	6 Male	Competitive team-sport athletes	0.3 g kg^{-1} of BM	0.2 g kg^{-1} of BM of NaCl	60 min pre-trial	3 × 6 × 20 m sprint with 25 s of rest between each sprint; 4 minutes of active recovery between sets*
Saunders et al.[40]	Counterbalanced crossover and double blind	20 M	Recreationally active	0.3 g.kg^{-1} of BM	0.2 g kg^{-1} of BM of NaCl	120 min pre-trial	5 × 6 s running sprint with 24 s of active rest between each sprint
Miller et al.[27]	Randomized placebo-controlled and double-blind crossover design	11 M	Active team and individual sprints	0.3 g.kg^{-1} of BM	0.2 g kg^{-1} of BM of NaCl	10–90 min pre-trial	10 × 6 s sprints with 60 s of recovery

M: male; F: female; BM: body mass.
* Only the first set of RSA test was considered.

Table 4
Quality assessment "Qualsyst" of caffeine studies.

	Question described	Appropriate study design	Appropriate subject selection	Characteristics described	Random allocation	Researches blinded	Subjects blinded	Outcome measures well define and robust to bias	Sample size appropri-ated	Analytic methods well designed	Estimate of variance reported	Controlled for con-founding	Results reported in details	Conclusion supported by results?	Rating
Carr et al.[31]	Yes	Yes	Partial	Partial	Partial	Yes	Yes	Yes	Partial	Yes	Partial	Partial	Yes	Yes	strong
Glaister et al.[32]	Yes	Yes	Partial	Yes	Partial	Yes	Yes	Yes	Partial	Yes	Yes	Yes	Yes	Yes	strong
Lee et al.[33]	Yes	Yes	Partial	Partial	Partial	Yes	Yes	Yes	Partial	Yes	Partial	Partial	Yes	Yes	strong
Lee et al.[36]	Yes	Yes	Partial	Yes	Yes	Yes	Yes	Yes	Partial	Yes	Partial	Partial	Yes	Yes	strong
Buck et al.[37]	Yes	Yes	Yes	Partial	Yes	Yes	Yes	Yes	Yes	Yes	Partial	Partial	Yes	Yes	strong
Kopec et al.[34]	Yes	Yes	Partial	Partial	Partial	Yes	Yes	Yes	Partial	Yes	Partial	Partial	Yes	Yes	strong
Eaton et al.[35]	Yes	Yes	Partial	Partial	yes	Yes	Yes	Yes	Partial	Yes	Yes	Partial	yes	Yes	Strong

Quality score: ≥75% strong, 55–75% moderate, ≤55% weak.

Table 5
Quality assessment "Qualsyst" of sodium bicarbonate studies.

	Question described	Appropriate study design	Appropriate subject selection	Characteristics described	Random allocation	Researches blinded	Subjects blinded	Outcome measures well define and robust to bias	Sample size appropri-ated	Analytic methods well designed	Estimate of variance reported	Controlled for con-founding	Results reported in details	Conclusion supported by results?	Rating
Lavender and Bird[41]	Yes	Yes	Partial	Partial	Partial	Yes	Yes	Yes	Yes	Partial	Yes	Yes	Yes	Partial	Strong
Gaitanos et al.[38]	Yes	Yes	Partial	Partial	Partial	No	Yes	Yes	Partial	Partial	Yes	Yes	Yes	Partial	Moderate
Bishop et al.[22]	Yes	Yes	Yes	Yes	Partial	Yes	Yes	Yes	Yes	Partial	Yes	Yes	Yes	Yes	Strong
Ducker et al.[39]	Yes	Yes	Yes	Yes	Partial	No	Yes	Yes	Partial	Yes	Yes	Yes	Yes	Yes	Strong
Saunders et al.[40]	Yes	Yes	Partial	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Strong
Miller et al.[27]	Yes	Yes	Yes	Yes	Partial	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Strong

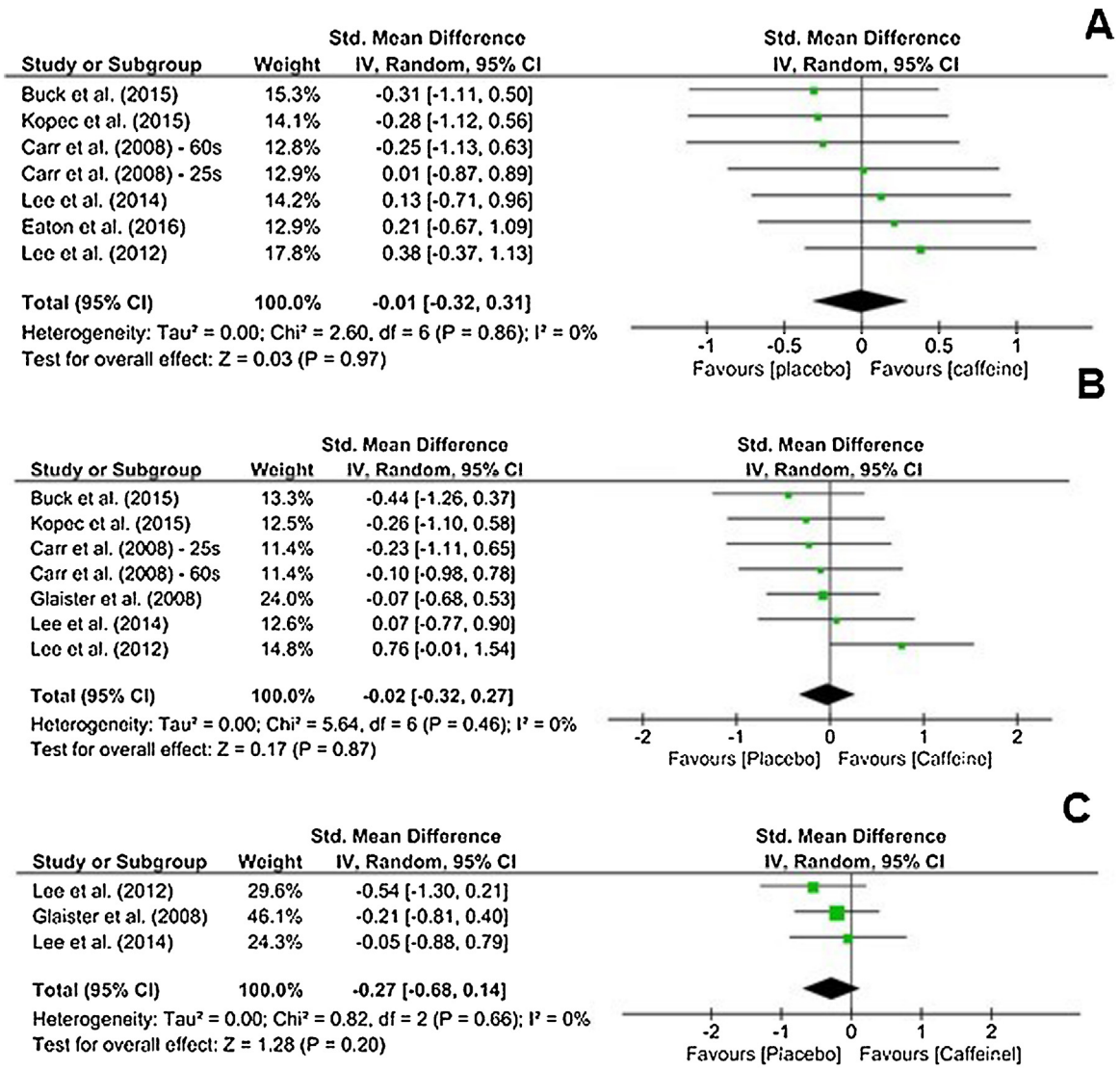

Fig. 2. Panel A: forest plot of standardized mean difference (SMD) between the effects of caffeine vs. placebo ingestion on total work done during repeated-sprint ability tests. Squares represent the SMD for each study. The diamond represents the pooled SMD for all studies. CI: confidence interval, df: degrees of freedom. Panel B: Forest plot of the comparison of the standardized mean difference (SMD) between the effect of caffeine vs. and placebo ingestion on best repeated-sprint ability tests performance. Squares represent the SMD for each study. The diamond represents the pooled SMD for all studies. CI: confidence interval, df: degrees of freedom. Panel C: Forest plot of standardized mean difference (SMD) between the effects of caffeine vs. placebo ingestion on last sprint during repeated-sprint ability tests. Squares represent the SMD for each study.

Following data pooling, the SMD for total work done was 0.43 (95% CI −0.11 to 0.97), providing a non-significant effect between sodium bicarbonate and placebo conditions (p = 0.12) (Fig. 3a). Additionally, there was a non-significant effect of $NaHCO_3$ versus placebo conditions on best sprint performance (SMD = 0.02, 95% CI −0.30 to 0.34; p = 0.90) and last sprint (SMD = 0.20, 95% CI −0.13 to 0.52; p = 0.24) (Fig. 3b). Heterogeneity was not detected among studies assessing total work or best sprint performance (I^2 = 0%), whereas last sprint presented a moderate heterogeneity (I^2 = 69%). No asymmetry was noted in the funnel plots in any of the analyses (Fig. 4–9).

4. Discussion

The present meta-analysis is the first we are aware of to investigate the isolated effect of caffeine and sodium bicarbonate ingestion on repeated sprint performance. The main findings of this study were that, compared with placebo, caffeine and $NaHCO_3$ ingestion did not improve either total work or best sprint performance during repeated sprint tests.

Our results indicate that caffeine ingestion may be ineffective in improving repeated sprint performance. This result is similar to previous meta-analytic data by Brown et al.[47] Although the exact mechanisms by which caffeine are thought to influence perfomance is unclear, it has been suggested that caffeine may directly affect the central nervous system.[48] Caffeine reduces the rating of perceived exertion (RPE), thus improving performance. In fact, a prior meta-analysis has shown that caffeine ingestion can reduce RPE during exercise (+5.6%), possibly explaining the ergogenic effect of caffeine on endurance performance.[49]

However, the influence of caffeine ingestion on performance during high-intensity intermittent exercise is controversial. For example, Glaister et al.[37] found that compared with a placebo, caffeine supplementation (6 mg kg^{-1}) was effective in improving the best sprint performance (1.4%) during a repeated sprint test (12 × 30 m, repeated at 35 s intervals). Conversely, Paton, Hopkins, Vollebregt[32] did not observe any difference in the best sprint per-

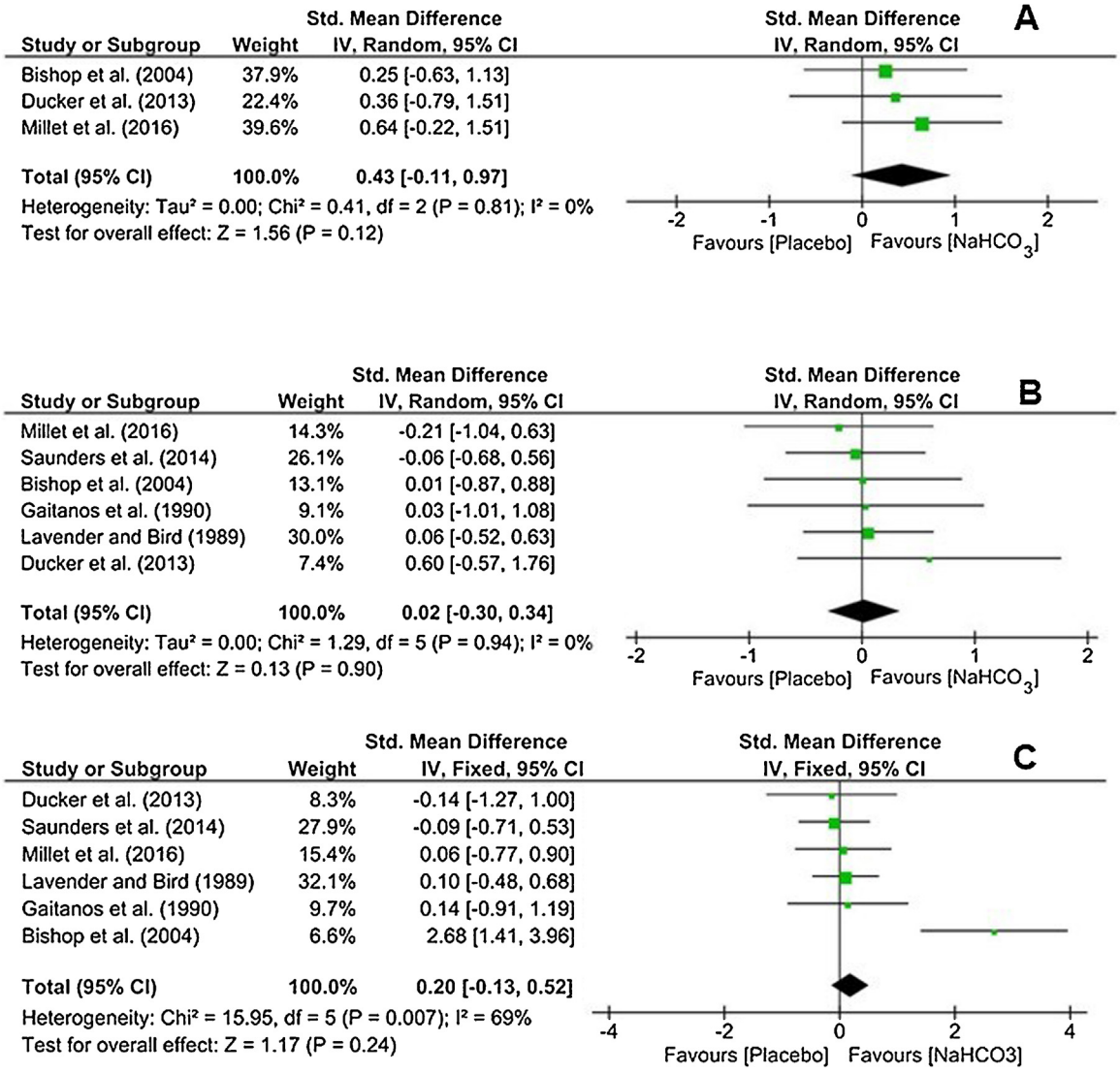

Fig. 3. Panel A: forest plot of the comparison of the standardized mean difference (SMD) between the effect of $NaHCO_3$ vs. placebo ingestion on total work done during repeated-sprint ability (RSA) test. Squares represent the SMD for each study. The diamond represents the pooled SMD for all studies. CI: confidence interval, df: degrees of freedom. Panel B: Forest plot of the comparison of the standardized mean difference (SMD) between the effect of $NaHCO_3$ vs. placebo ingestion on best sprint performance on repeated-sprint ability (RSA) tests. Squares represent the SMD for each study. The diamond represents the pooled SMD for all studies. CI: confidence interval, df: degrees of freedom. Panel C: Forest plot of standardized mean difference (SMD) between the effects of $NaHCO_3$ vs. placebo ingestion on total work done during repeated-sprint ability tests. Squares represent the SMD for each study.

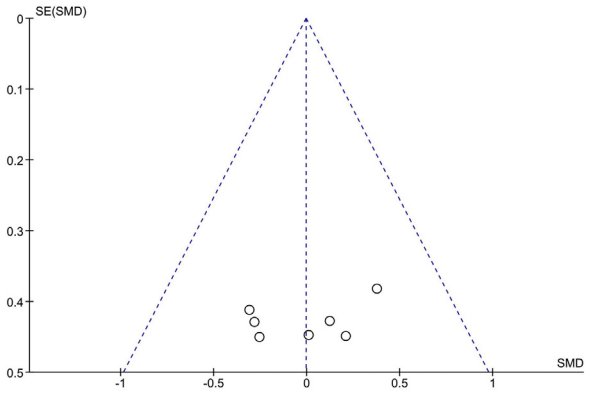

Fig. 4. Funnel plot of standard mean difference against standard error for total work done for caffeine studies. se(SMD) Standard error of the mean difference; SMD Standard mean difference.

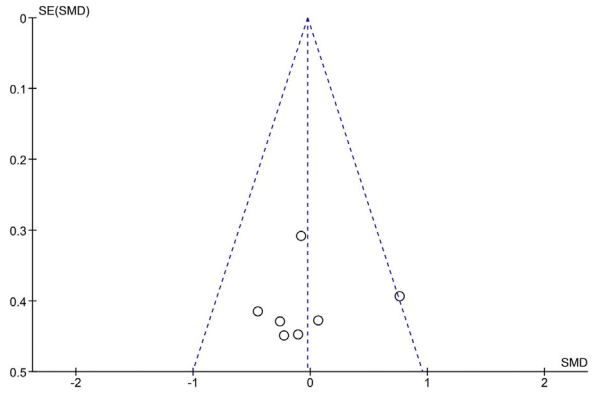

Fig. 5. Funnel plot of standard mean difference against error for best sprint performance for caffeine studies. se(SMD) Standard error of the mean difference; SMD Standard mean difference.

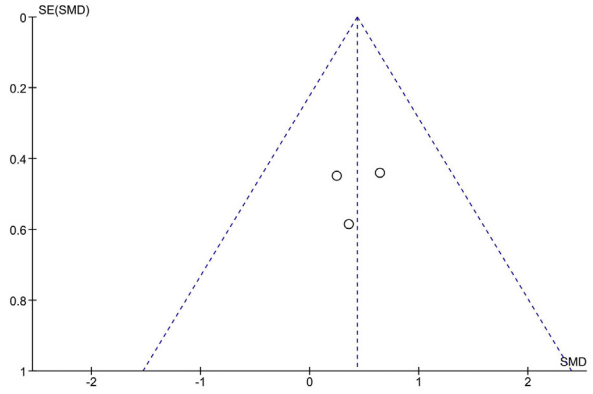

Fig. 6. Funnel plot of standard mean difference against error for total work done for sodium bicarbonate studies. se(SMD) Standard error of the mean difference; SMD Standard mean difference.

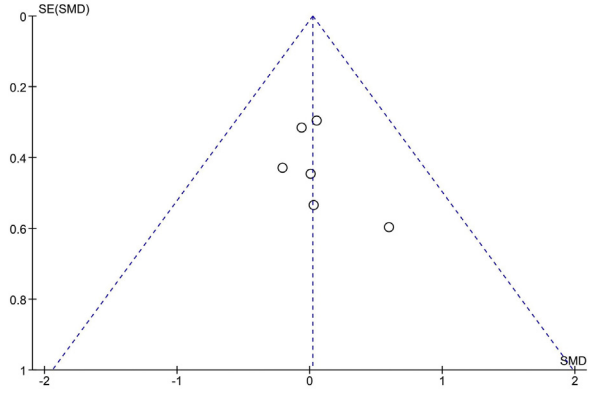

Fig. 7. Funnel plot of standard mean difference against error for best sprint performance for sodium bicarbonate studies. se(SMD) Standard error of the mean difference; SMD Standard mean difference.

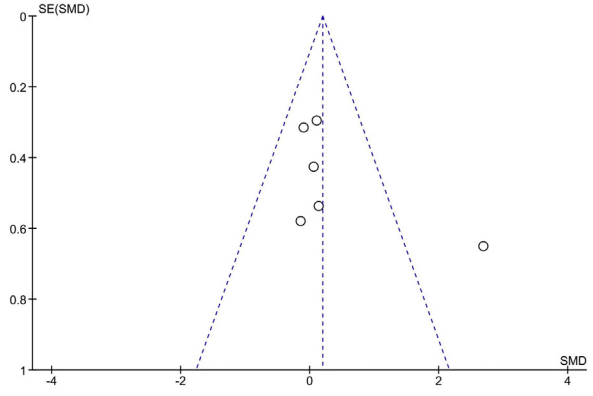

Fig. 8. Funnel plot of standard mean difference against error for last sprint for caffeine studies. se(SMD) Standard error of the mean difference; SMD Standard mean difference.

formance during a repeated sprint test (10×20 m, repeated at 10 s intervals) between caffeine (6 mg kg^{-1}) and placebo ingestion. A possible explanation for a lack of effect in the best sprint performance observed following caffeine supplementation during RSA may be related to energy system utilisation. Gaitanos et al.[7] reported that during a single sprint (6 s) PCr metabolism is responsible for 49.6% of the total anaerobic ATP re-synthesis, followed by glycolytic contribution (40%). Although some studies included in the present review indicated that caffeine was effective in increasing repeated sprint performance, resulting in increased lactate

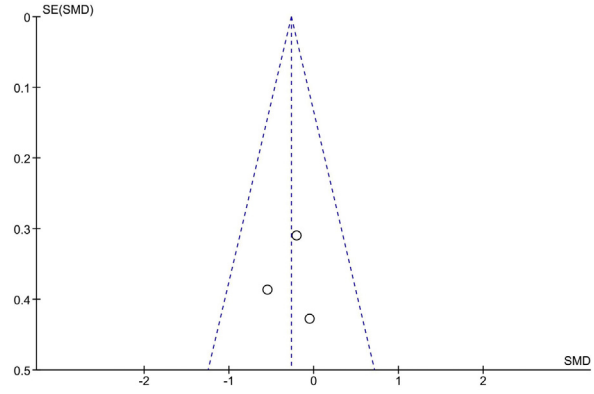

Fig. 9. Funnel plot of standard mean difference against error for last sprint for sodium bicarbonate studies. se(SMD) Standard error of the mean difference; SMD Standard mean difference.

concentration[36,37] and lactate concentration, the influence of caffeine on glycolytic metabolism is questionable.[11]

The lack of performance effect observed between caffeine and placebo trials within the present meta-analysis is unclear but may be related to the mode of exercise examined. Caffeine ingestion is likely to improve intermittent exercise, characterized by short-duration sprints ($\leq$10 s), interspersed with recovery periods long enough (60–300 s) to allow near complete recovery of sprint performance[2,6]. This is supported by two studies[36,34], which were not included in the present review. For instance, Bishop[24] suggested that caffeine ingestion is likely to improve intermittent, but not repeated, sprint performance. During intermittent exercise there is no performance decrement whereas during RSA there is a marked performance decrement that can increase the risk that caffeine ingestion may be ergolytic as fatigue develops, possibly due to an increase in the by-products of anaerobic metabolism.[24] This explanation is speculative and thus further research is needed to clarify the effects of caffeine on repeated sprint performance.

Similar to caffeine ingestion, the results of this meta-analysis indicate that $NaHCO_3$ does not improve repeated sprint performance. In fact, only two studies included in this review showed a positive improvement in work done following $NaHCO_3$ ingestion (0.3 g kg^{-1}), when compared with placebo.[27,31] However, the ingestion timing of $NaHCO_3$ and placebo was different between the studies. Bishop et al.[27] reported an improvement in total work (+5%) during a RSA test (5×6 s with 30 s of passive recovery) following $NaHCO_3$, compared with placebo ingestion, when the supplements were ingested 90 min before the tests. Similarly, Miller et al.[31] found that, compared with placebo condition, $NaHCO_3$ improved the work done (+9.7%) during a repeated sprint ability test (10×6 s with 60 s of passive recovery), when ingestion was based on time-to-peak pH.

As expected, $NaHCO_3$ ingestion did not improve best sprint performance. It has been reported that $NaHCO_3$ is more effective in the last sprint of exercise, when the muscle acidosis is highest. In fact, Bishop et al.[27] found that compared with a placebo, $NaHCO_3$ (0.3 g kg^{-1}) ingestion improved peak power in the final three sprints of a repeated sprint test (5×6 with 30 s of passive recovery). Similarly, Lavender and Bird[46] reported that compared with a placebo, $NaHCO_3$ ingestion increased the final sprint during 10 repeated 10 s sprints interspersed with 50 s of passive recovery. A possible explanation for this, is that $NaHCO_3$ ingestion increases the efflux of H^+ and lactate from muscle cells to extracellular fluid,[50] given that the sarcolemma membrane is impermeable to bicarbonate.[51] Greater extracellular bicarbonate concentration results in greater H^+ efflux to the blood, where it is buffered. Therefore, when repeated sprints are performed, sustained increases in

H^+ production leads to an accumulation of H^+, resulting in exercise-induced muscle acidosis, increased competition between H^+ and calcium at the troponin-binding site,[52] and inhibition of both PCr re-synthesis[53] and phosphofructokinase activity.[26]

5. Limitations and future studies

A number of limitations of the present meta-analysis should be considered. Firstly, it is important to consider that several factors could explain the discrepancy in studies reported in this meta-analysis. For example, the protocol utilized (e.g. cycling or running based), differing number of sets and recovery intervals, and participants characteristics (e.g. trained, recreationally active). Thus, further studies are warranted examining possible ergogenic effects of caffeine and sodium bicarbonate on repeated sprint performance.

Additionally, it is important to consider that genetic factors have been shown to influence the effectiveness of caffeine[54] and sodium bicarbonate.[55] In relation to caffeine, the gene CYP1A2 encodes cytochrome P450 1A2, an enzyme responsible for up to 95% of all caffeine metabolism.[56] There are two forms of the CYP1A2 gene, individuals with AA homozygotes ("fast metabolizers") tend to produce more of this enzyme, and therefore metabolize caffeine more quickly. Conversely, C allele carriers ("slow metabolizers") tend to have slower caffeine clearance.[54,57] In fact, Guest et al.[58] observed that athletes who have AA homozygotes improved performance in a 10-km time-trial after ingestion of 2 and 4 mg kg^{-1} (4.8% and 6.8%, respectively) in relation to the placebo condition. However, no effects were observed among athletes with the AC genotype after caffeine ingestion, when compared with a placebo. Although the influence of caffeine ingestion on endurance performance can be explained by genetic factors, further studies should be conducted to evaluate the influence of the genetic variations of the CYP1A2 gene on the repeated sprint performance after caffeine supplementation. In relation to $NaHCO_3$, genetic variations have been found to be associated with monocarboxylate transporter (MCT) activity.[55] The ingestion of $NaHCO_3$ increases the activity of MCT1 and MCT4 transporters, increasing the efflux of H^+ out the muscle and reducing the muscle acidosis.[51] Polymorphisms in the MCT transporters may also influence an individual's responses to supplementation. A single-nucleotide polymorphism in the gene coding for MCT1, for example, can influence the lactate/H^+ co-transport across the sarcolemma,[59] the T allele carriers have been shown to have a reduced MCT1 lactate transport,[60,61] TT homozygotes reach the ventilatory threshold at higher speeds,[62] while T allele frequency has been shown to differ between athletes from different modalities.[59] Although, to date, no study has investigated the influence of this polymorphism after ingestion of $NaHCO_3$ on exercise performance, it is important that more research should be undertaken to investigate the relationships between genetic variations, sodium bicarbonate, and repeated sprint performance.

6. Conclusion

In conclusion, this meta-analysis provides evidence that acute ingestion of caffeine and $NaHCO_3$ does not increase repeated sprint performance (i.e. total work or best sprint performance) when compared to placebo. The results of the present meta-analysis are based on limited evidence, and thus need to be interpreted with caution. Finally, responses to both caffeine and $NaHCO_3$ ingestion have a high degree of inter-individual variability, which can be explain by genetic factors, and thus, the applicability of the current findings must be assessed on a case-by-case basis, considering on the specific characteristic of the individual.

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References

1. Spencer M, Bishop D, Dawson B et al. Physiological and metabolic responses of repeated-sprint activities: specific to field-based team sports. *Sports Med* 2005; 35(12):1025–1044.
2. Bishop D, Girard O, Mendez-Villanueva A. Repeated-sprint ability – part II: recommendations for training. *Sports Med* 2011; 41(9):741–756.
3. Dawson B. Repeated-sprint ability: where are we? *Int J Sports Physiol Perform* 2012; 7(3):285–289.
4. Bishop D, Spencer M, Duffield R et al. The validity of a repeated sprint ability test. *J Sci Med Sport* 2001; 4(1):19–29.
5. Buchheit M, Laursen PB. High-intensity interval training, solutions to the programming puzzle: part I: cardiopulmonary emphasis. *Sports Med* 2013; 43(5):313–338.
6. Girard O, Mendez-Villanueva A, Bishop D. Repeated-sprint ability - part I: factors contributing to fatigue. *Sports Med* 2011; 41(8):673–694.
7. Gaitanos GC, Williams C, Boobis LH et al. Human muscle metabolism during intermittent maximal exercise. *J Appl Physiol (1985)* 1993; 75(2):712–719.
8. Del Coso J, Munoz G, Munoz-Guerra J. Prevalence of caffeine use in elite athletes following its removal from the World Anti-Doping Agency list of banned substances. *Appl Physiol Nutr Metab* 2011; 36(4):555–561.
9. Wickham KA, Spriet LL. Administration of caffeine in alternate forms. *Sports Med* 2018; 48(Suppl. 1):79–91.
10. Shen JG, Brooks MB, Cincotta J, Manjourides JD. Establishing a relationship between the effect of caffeine and duration of endurance athletic time trial events: a systematic review and meta-analysis. *J Sci Med Sport* 2019; 22(2):232–238.
11. Graham TE. Caffeine and exercise. *Sports Med* 2001; 31(11):785–807.
12. Spriet LL. Exercise and sport performance with low doses of caffeine. *Sports Med* 2014; 44(Suppl. 2):S175–S184.
13. Maughan RJ, Burke LM, Dvorak J et al. IOC consensus statement: dietary supplements and the high-performance athlete. *Br J Sports Med* 2018; 52(7): 439–455.
14. Southward K, Rutherfurd-Markwick KJ, Ali A. Correction to: the effect of acute caffeine ingestion on endurance performance: a systematic review and meta-analysis. *Sports Med* 2018.
15. Goldstein ER, Ziegenfuss T, Kalman D et al. International society of sports nutrition position stand: caffeine and performance. *J Int Soc Sports Nutr* 2010; 7(1):5.
16. Grgic J, Pickering C. The effects of caffeine ingestion on isokinetic muscular strength: a meta-analysis. *J Sci Med Sport* 2019; 22(3):353–360.
17. Grgic J, Mikulic P, Schoenfeld BJ et al. The influence of caffeine supplementation on resistance exercise: a review. *Sports Med* 2019; 49(1):17–30.
18. Warren GL, Park ND, Maresca RD et al. Effect of caffeine ingestion on muscular strength and endurance: a meta-analysis. *Med Sci Sports Exerc* 2010; 42(7):1375–1387.
19. Grgic J. Caffeine ingestion enhances Wingate performance: a meta-analysis. *Eur J Sport Sci* 2018; 18(2):219–225.
20. Greer F, McLean C, Graham TE. Caffeine, performance, and metabolism during repeated Wingate exercise tests. *J Appl Physiol (1985)* 1998; 85(4):1502–1508.
21. Carr AJ, Hopkins WG, Gore CJ. Effects of acute alkalosis and acidosis on performance: a meta-analysis. *Sports Med* 2011; 41(10):801–814.
22. Lancha Junior AH, Painelli Vde S, Saunders B et al. Nutritional strategies to modulate intracellular and extracellular buffering capacity during high-intensity exercise. *Sports Med* 2015; 45(Suppl. 1):S71–S81.
23. Siegler JC, Marshall PW, Bishop D et al. Mechanistic insights into the efficacy of sodium bicarbonate supplementation to improve athletic performance. *Sports Med Open* 2016; 2(1):41.
24. Bishop D. Dietary supplements and team-sport performance. *Sports Med* 2010; 40(12):995–1017.
25. Siegler JC, Marshall PW, Bray J et al. Sodium bicarbonate supplementation and ingestion timing: does it matter? *J Strength Cond Res* 2012; 26(7):1953–1958.
26. Hollidge-Horvat MG, Parolin ML, Wong D et al. Effect of induced metabolic alkalosis on human skeletal muscle metabolism during exercise. *Am J Physiol Endocrinol Metab* 2000; 278(2):E316–E329.
27. Bishop D, Edge J, Davis C et al. Induced metabolic alkalosis affects muscle metabolism and repeated-sprint ability. *Med Sci Sports Exerc* 2004:807–813.
28. Moher D, Liberati A, Tetzlaff J et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol* 2009; 62(10):1006–1012.
29. Brietzke C, Franco-Alvarenga PE, Coelho-Junior HJ et al. Effects of carbohydrate mouth rinse on cycling time trial performance: a systematic review and meta-analysis. *Sports Med* 2018.
30. Brocherie F, Girard O, Faiss R et al. Effects of repeated-sprint training in hypoxia on sea-level performance: a meta-analysis. *Sports Med* 2017; 47(8):1651–1660.
31. Miller P, Robinson AL, Sparks SA et al. the effects of novel ingestion of sodium bicarbonate on repeated sprint ability. *J Strength Cond Res* 2016; 30(2):561–568.

32. Paton CD, Hopkins WG, Vollebregt L. Little effect of caffeine ingestion on repeated sprints in team-sport athletes. *Med Sci Sports Exerc* 2001; 33(5):822–825.
33. Paton CD, Hopkins WG, Vollebregt L. Little effect of caffeine ingestion on repeated sprints in team-sport athletes. *Med Sci Sports Exerc* 2001; 33(5):822–825.
34. De Ste Croix M, Pope M. The effect of sodium bicarbonate loading on repeated non-motorised treadmill sprint performance of soccer players. *J Hum Mov Stud* 2006; 50(3):149–156.
35. Higgins JP, Thompson SG, Deeks JJ et al. Measuring inconsistency in meta-analyses. *BMJ* 2003; 327(7414):557–560.
36. Carr A, Dawson B, Schneiker K et al. Effect of caffeine supplementation on repeated sprint running performance. *J Sports Med Phys Fitness* 2008; 48(4):472–478.
37. Glaister M, Howatson G, Abraham CS et al. Caffeine supplementation and multiple sprint running performance. *Med Sci Sports Exerc* 2008; 40(10):1835–1840.
38. Lee CL, Cheng CF, Lin JC et al. Caffeine's effect on intermittent sprint cycling performance with different rest intervals. *Eur J Appl Physiol* 2012; 112(6):2107–2116.
39. Kopec BJ, Dawson BT, Buck C et al. Effects of sodium phosphate and caffeine ingestion on repeated-sprint ability in male athletes. *J Sci Med Sport* 2016; 19(3):272–276.
40. Eaton TR, Potter A, Billaut F et al. A Combination of amino acids and caffeine enhances sprint running capacity in a hot, hypoxic environment. *Int J Sport Nutr Exerc Metab* 2016; 26(1):33–45.
41. Lee CL, Cheng CF, Astorino TA et al. Effects of carbohydrate combined with caffeine on repeated sprint cycling and agility performance in female athletes. *J Int Soc Sports Nutr* 2014; 11:17.
42. Buck C, Guelfi K, Dawson B et al. Effects of sodium phosphate and caffeine loading on repeated-sprint ability. *J Sports Sci* 2015; 33(19):1971–1979.
43. Gaitanos GC, Nevill ME, Brooks S et al. Repeated bouts of sprint running after induced alkalosis. *J Sports Sci* 1991; 9(4):355–370.
44. Ducker KJ, Dawson B, Wallman KE. Effect of Beta alanine and sodium bicarbonate supplementation on repeated-sprint performance. *J Strength Cond Res* 2013; 27(12):3450–3460.
45. Saunders B, Sale C, Harris RC et al. Effect of sodium bicarbonate and Beta-alanine on repeated sprints during intermittent exercise performed in hypoxia. *Int J Sport Nutr Exerc Metab* 2014; 24(2):196–205.
46. Lavender G, Bird SR. Effect of sodium bicarbonate ingestion upon repeated sprints. *Br J Sports Med* 1989; 23(1):41–45.
47. Brown SJ, Brown J, Foskett A. The Effects of caffeine on repeated sprint performance in team sport athletes – a meta-analysis. *Sport Sci Rev* 2013; 22(1–2):25–32.
48. Davis JM, Zhao Z, Stock HS et al. Central nervous system effects of caffeine and adenosine on fatigue. *Am J Physiol Regul Integr Comp Physiol* 2003; 284(2):R399–R404.
49. Doherty M, Smith PM. Effects of caffeine ingestion on exercise testing: a meta-analysis. *Int J Sport Nutr Exerc Metab* 2004; 14(6):626–646.
50. Thomas C, Bishop DJ, Lambert K et al. Effects of acute and chronic exercise on sarcolemmal MCT1 and MCT4 contents in human skeletal muscles: current status. *Am J Physiol Regul Integr Comp Physiol* 2012; 302(1):R1–R14.
51. Mainwood GW, Cechetto D. The effect of bicarbonate concentration on fatigue and recovery in isolated rat diaphragm muscle. *Can J Physiol Pharmacol* 1980; 58(6):624–632.
52. Fabiato A, Fabiato F. Effects of pH on the myofilaments and the sarcoplasmic reticulum of skinned cells from cardiace and skeletal muscles. *J Physiol* 1978; 276:233–255.
53. Sahlin K, Harris RC, Hultman E. Creatine kinase equilibrium and lactate content compared with muscle pH in tissue samples obtained after isometric exercise. *Biochem J* 1975; 152(2):173–180.
54. Pickering C, Kiely J. Are the current guidelines on caffeine use in sport optimal for everyone? Inter-individual variation in caffeine ergogenicity, and a move towards personalised sports nutrition. *Sports Med* 2018; 48(1):7–16.
55. Heibel AB, Perim PHL, Oliveira LF et al. Time to optimize supplementation: modifying factors influencing the individual responses to extracellular buffering agents. *Front Nutr* 2018; 5:35.
56. Gu L, Gonzalez FJ, Kalow W et al. Biotransformation of caffeine, paraxanthine, theobromine and theophylline by cDNAexpressed human CYP1A2 and CYP2E1. *Pharmacogenetics* 1992; 2(2):73–77.
57. Chia JS, Barrett LA, Chow JY et al. Effects of caffeine supplementation on performance in ball games. *Sports Med* 2017; 47(12):2453–2471.
58. Guest N, Corey P, Vescovi J et al. Caffeine, CYP1A2 genotype, and endurance performance in athletes. *Med Sci Sports Exerc* 2018.
59. Ben-Zaken S, Eliakim A, Nemet D et al. Differences in MCT1 A1470T polymorphism prevalence between runners and swimmers. *Scand J Med Sci Sports* 2015; 25(3):365–371.
60. Cupeiro R, Benito PJ, Maffulli N et al. MCT1 genetic polymorphism influence in high intensity circuit training: a pilot study. *J Sci Med Sport* 2010; 13(5):526–530.
61. Cupeiro R, Gonzalez-Lamuno D, Amigo T et al. Influence of the MCT1-T1470A polymorphism (rs1049434) on blood lactate accumulation during different circuit weight trainings in men and women. *J Sci Med Sport* 2012; 15(6):541–547.
62. Pasqua LA, Damasceno MV, Bueno S et al. Association between ventilatory thresholds related to aerobic fitness and MCT1 A1470T polymorphism. *Sports Nutr Ther* 2016; 1(105).