# MECHANISMS IN ENDOCRINOLOGY: Exogenous insulin does not increase muscle protein synthesis rate when administered systemically: a systematic review

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ORIGINAL RESEARCH

# A Sucrose Mouth Rinse Does Not Improve 1-hr Cycle Time Trial Performance When Performed in the Fasted or Fed State

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Carbohydrate mouth rinsing during exercise has been suggested to enhance performance of short (45–60 min) bouts of high-intensity (>75% $VO_{2peak}$) exercise. Recent studies indicate that this performance enhancing effect may be dependent on the prandial state of the athlete. The purpose of this study was to define the impact of a carbohydrate mouth rinse on ~1-hr time trial performance in both the fasted and fed states. Using a double-blind, crossover design, 14 trained male cyclists (27 ± 6 years; 5.0 ± 0.5 $W{\cdot}kg^{-1}$) were selected to perform 4 time trials of ~1 hr (1,032 ± 127 kJ) on a cycle ergometer while rinsing their mouths with a 6.4% sucrose solution (SUC) or a noncaloric sweetened placebo (PLA) for 5 s at the start and at every 12.5% of their set amount of work completed. Two trials were performed in an overnight fasted state and two trials were performed 2 h after consuming a standardized breakfast. Performance time did not differ between any of the trials (fasted-PLA: 68.6 ± 7.2; fasted-SUC: 69.6 ± 7.5; fed-PLA: 67.6 ± 6.6; and fed-SUC: 69.0 ± 6.3 min; Prandial State × Mouth Rinse Solution $p = .839$; main effect prandial state $p = .095$; main effect mouth rinse solution $p = .277$). In line, mean power output and heart rate during exercise did not differ between trials. In conclusion, a sucrose mouth rinse does not improve ~1-hr time trial performance in well-trained cyclists when performed in either the fasted or the fed state.

***Keywords:*** carbohydrate, postabsorptive, cycling

It has been well established that carbohydrate ingestion during prolonged (> 2 hr), endurance-type exercise can delay the onset of fatigue and improve endurance performance (Coyle et al., 1983; Coyle et al., 1986; Fielding et al., 1985; Hargreaves et al., 1984; Ivy et al., 1979; Jeukendrup, 2004; Mitchell et al., 1988; Neufer et al., 1987), likely because of the sparing of limited endogenous glycogen stores (Björkman et al., 1984; Erickson et al., 1987; Hargreaves et al., 1984; Stellingwerff et al., 2007; Tsintzas et al., 1995; Tsintzas & Williams, 1998; Tsintzas et al., 2001). However, the ergogenic benefits of carbohydrate ingestion during exercise may not be limited to more prolonged, endurance-type exercise events. Improvements in performance have been reported following carbohydrate ingestion during relatively short (<60 min) bouts of high-intensity (>75% $VO_{2peak}$) exercise (Anantaraman et al., 1995; Below et al., 1995; J. Carter et al., 2003; El-Sayed et al., 1997; Jeukendrup et al., 1997).

Jeukendrup and colleagues reported a 2.3% improvement in performance during a ~1-hr cycling time trial when carbohydrate was ingested at regular intervals (Jeukendrup et al., 1997). However, in a follow-up study no performance benefits were observed following intravenous infusion of glucose during a ~1-hr cycling time trial (J. M. Carter, Jeukendrup, Mann, & Jones, 2004). As carbohydrate availability did not seem to limit performance capacity during high-intensity exercise of such a short duration, the authors speculated that simply the presence of glucose in the mouth may have been ergogenic (J. M. Carter, Jeukendrup, Mann, & Jones, 2004). In agreement, they subsequently demonstrated that when a 6.4% maltodextrin solution was rinsed around the mouth for every 12.5% of the trial completed, performance during a 1-hr time trial was increased by 2.8% (J. M. Carter, Jeukendrup, & Jones, 2004).

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Since then, more studies have reported ergogenic benefits of a carbohydrate mouth rinse during short-term, high-intensity exercise (30–60 min, >75% $VO_{2peak}$) (Chambers et al., 2009; Fares & Kayser, 2011; Gam et al., 2013; Lane et al., 2013; Pottier et al., 2010; Rollo et al., 2008; Rollo et al., 2010; Sinclair et al., 2014) whereas others have been unable to confirm those findings (Rollo et al., 2011; Sinclair et al., 2014; Watson et al., 2014; Whitham & McKinney, 2007). The mechanism(s) responsible for the ergogenic properties of a carbohydrate mouth rinse may involve a signaling response from carbohydrate receptors in the mouth to the central nervous system, increasing central drive. In accordance, several studies have now reported the presence of carbohydrate in the mouth to facilitate corticomotor output (Gant et al., 2010; Turner et al., 2014). We previously speculated that from an evolutionary view the signaling response of carbohydrate mouth rinsing on the central nervous system would be less effective in the fed state, when liver glycogen stores are not compromised. Consequently, we showed no improvement in ~1-hr cycling time trial performance when participants rinsed their mouths with a carbohydrate versus placebo solution during exercise performed in the fed state (Beelen et al., 2009). However, a limitation of our previous work is that we did not assess the effect of carbohydrate mouth rinsing in a fasted state in the same cohort of athletes. Since then, two studies have been published showing improvements in time to exhaustion and time trial performance in both the postabsorptive and postprandial state (Fares & Kayser, 2011; Lane et al., 2013). In the current study, we assessed the impact of a carbohydrate mouth rinse on 1-hr time trial performance in both the postabsorptive and postprandial state in well-trained cyclists. We hypothesized that a carbohydrate mouth rinse improves 1-hr time trial performance when exercise is performed in a fasted, postabsorptive state, with no apparent ergogenic benefit when exercise is performed in the postprandial state.

# Methods

## Participants

Fourteen trained male cyclists or triathletes (27 ± 6 years; 1.83 ± 0.08 m; 78 ± 11 kg, 5.0 ± 0.5 $W \cdot kg^{-1}$) were selected to participate in the study. All participants had been engaged in regular cycling training (>4 times/week) for more than 6 years. After being advised of the purpose and potential risks of the study, all participants provided written, informed consent. The experimental protocol and procedures were approved by the Medical Ethical Committee of the Academic Hospital Maastricht, the Netherlands.

## Study Design

The study was designed to investigate whether a carbohydrate mouth rinse improves ~1-hr time trial performance in the postabsorptive and postprandial state. The experimental protocol consisted of six visits to the laboratory, which was maintained at 21 ± 0.5 °C with a relative humidity of 60 ± 5%. All exercise tests were carried out on an electronically braked cycle ergometer (Lode Excalibur, Groningen, the Netherlands). The first visit included an incremental cycling exercise test to exhaustion to determine participants' maximal workload capacity ($W_{max}$). Visits 2–6 consisted of simulated time trials in which a set amount of work had to be performed within the shortest time possible. The second visit consisted of a familiarization session wherein participants were given water to rinse around their mouths at predetermined intervals. Thereafter, participants performed four experimental trials, during which participants were given either a 6.4% sucrose solution (SUC) or a noncaloric aspartame-sweetened placebo (PLA) to rinse around their mouths at predetermined intervals. The experimental trials were performed in a double-blind, counterbalanced order with trials separated by at least 1 week.

## Maximal Workload Capacity

Participants' maximal relative workload capacity was assessed during a stepwise exercise test to exhaustion on an electronically braked cycle ergometer (Lode Excalibur, Groningen, the Netherlands). After a 5-min warm-up at 100 W, workload was set at 150 W and increased by 50 W every 2.5 min until voluntary exhaustion (Kuipers et al., 1985). Workload (W), cadence (revolutions per minute; rpm), and heart rate (Polar, Kempele, Finland) were recorded at every interval. The appropriate seat position, handlebar height, and orientation were determined and replicated for each participant's subsequent visit. Maximal workload capacity ($W_{max}$) was calculated as the workload in the last completed stage + workload relative to the time spent in the last incomplete stage: (time in seconds)/150 * 50 (W).

## Physical Activity and Dietary Standardization

Participants kept their weekly training schedule consistent over the course of the experiment, standardized their workouts 48 hr before each experimental trial, and refrained from physical exercise and exhaustive physical labor for 24 hr before each experimental trial. Participants recorded their physical activity and habitual diet for the 48-hr period before the first experimental trial and replicated this regimen during the 48-hr period before each subsequent trial. The evening before each experimental trial, participants consumed a standardized dinner (68 ± 4 kJ/kg, providing 60 ± 5 energy% (En%) carbohydrate, 25 ± 2 En% fat, and 15 ± 2 En% protein), after which they remained fasted. In the experimental trials performed in the postprandial state a standardized breakfast was consumed 2 hr before starting the time trial. This breakfast provided 36 ± 2 kJ/kg (65 ± 7 En% carbohydrate, 18 ±

4 En% fat, and 17 ± 3 En% protein) and was composed of bread with butter, cheese, and marmalade; a slice of gingerbread; and a glass of orange juice.

## Time Trials

For the four main experimental trials, all participants reported to the laboratory at 8:00 a.m. after an overnight fast. During the two fed experimental trials, participants received a standardized breakfast (36 ± 2 kJ/kg, providing 65 ± 7 En% carbohydrate, 18 ± 4 En% fat, and 17 ± 3 En% protein). Two hours later (between 10:00 and 10:30 a.m.), participants started the time trials. Before the start of the time trials, participants were fitted with a heart rate monitor and positioned on the cycle ergometer. After a 5-min warm-up at 100 W, participants were instructed to perform a set amount of work (1,032 ± 127 kJ) in the shortest time possible. Total work to be performed for each participant was calculated according to the equation of Jeukendrup and colleagues (Jeukendrup et al., 1996): Total amount of work = $0.75 \times W_{max} \times 3{,}600$, where $W_{max}$ is the maximal workload capacity determined during visit 1 and 3,600 is the duration of the predicted total performance time in seconds (equivalent to 1 hr). The approximately 1-hr exercise duration was selected to invoke a relatively high-intensity yet nonglycogen limiting exercise bout (Jeukendrup et al., 1997; McConell et al., 2000). The ergometer was set in linear mode so that 75% $W_{max}$ was obtained when the participants cycled at their preferred cycling cadence (100 ± 8 rpm), determined during the maximal workload capacity test. Participants received no temporal, verbal, or physiological feedback during the time trial. The only information available to the participant was the total work performed relative to the set amount of work that needed to be completed, which was displayed on a computer screen set up in front of the ergometer. A fan was placed 1 m behind each participant to provide cooling and air circulation during the time trials. At the start and at every 12.5% of the time trial completed, participants received 25 mL of the test solution to rinse around their mouth. Heart rate (Polar, Kempele, Finland), power output, and cadence were recorded continuously throughout the test. During each time trial, no interaction occurred between the participant and the investigator except for the mouth rinse administration. Participants did not receive any verbal encouragement except for the last 10 kJ of the test, wherein the investigator counted down the remaining kJ from 10 to 0, indicating the completion of the test. During the trials and over the course of the experiment, participants were kept unaware of any performance-related information such as exercise time, heart rate, power output, and cycling cadence.

## Mouth-Rinse Protocol

Each participant was given a 25 mL bolus of either a 6.4% SUC or a noncaloric 0.6% aspartame sweetened PLA at the start and after every 12.5% of the time trial completed. Participants rinsed the fluid around their mouth for 5 s and then spat it into a bowl held by an investigator. Trial order was randomized via a random-number generator (www.random.org), and beverages were prepared and coded by a nonaffiliated researcher to ensure double blinding.

## Statistical Analyses

Performance data were analyzed using a two-way (Prandial State × Mouth Rinse Solution) repeated measures analysis of variance (ANOVA). A three-way repeated measures ANOVA with Prandial State × Mouth Rinse Solution × Time as factors was used to compare differences between trials over time. The level of significance for all analyses was set at $p < .05$. All data are presented as means ± *SD*, $n = 14$ unless otherwise stated.

# Results

## Performance Time and Power Output

Performance time of the four time trials is shown in Figure 1. Performance time did not differ between any of the trials (fasted-PLA: 68.6 ± 7.2 min; fasted-SUC: 69.6 ± 7.5 min; fed-PLA: 67.6 ± 6.6 min; fed-SUC: 69.0 ± 6.3 min; Prandial State × Mouth Rinse Solution $p = .839$; main effect prandial state $p = .095$; main effect mouth rinse solution $p = .277$). Average power output of the four time trials is shown in Figure 2. Average power output did not differ between any of the trials (fasted-PLA: 255 ± 43 W; fasted-SUC: 252 ± 46 W; fed-PLA: 258 ± 45 W; and fed-SUC: 253 ± 41 W; Prandial State × Mouth Rinse Solution $p = .725$; main effect prandial state $p = .111$; main effect mouth rinse solution $p = .380$). The average power outputs for every 12.5% of the time trial completed in the fasted and fed state are presented in Figure 3. No differences were observed in power output over time between trials (Prandial State × Mouth Rinse Solution × Time $p = .265$).

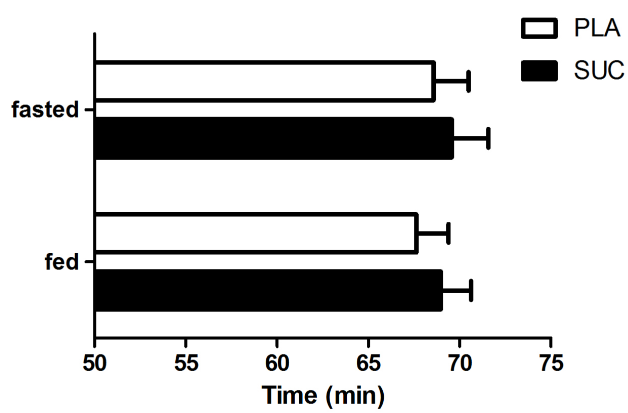


**Figure 1** — Performance times in the placebo and sucrose treatments in both the fasted and fed state. No significant differences between trials; Prandial State × Mouth Rinse Solution, $p > .05$. Values are expressed as mean± *SD*. SUC = sucrose mouth rinse; PLA = placebo mouth rinse.

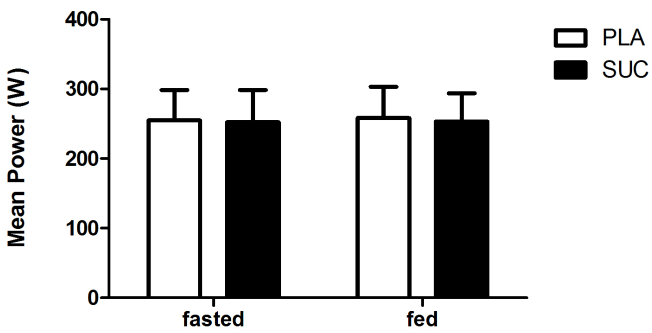


**Figure 2** — Mean power output in the placebo and sucrose treatments in both the fasted and fed state. No significant differences between trials; Prandial State × Mouth Rinse Solution, $p > .05$. Values are expressed as mean ± *SD*. SUC = sucrose mouth rinse; PLA = placebo mouth rinse.

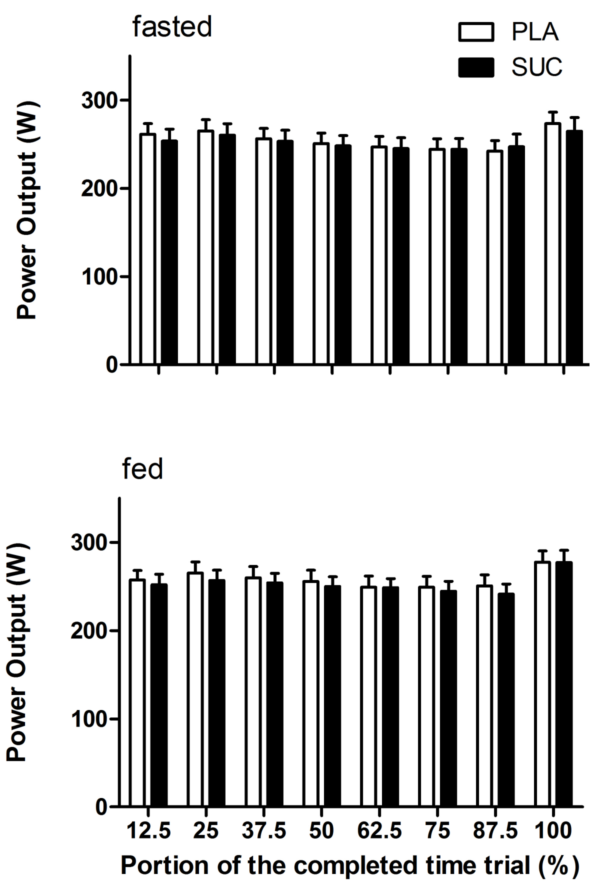


**Figure 3** — Mean power output for each 12.5% of total work completed in the placebo and sucrose treatment in both the fasted and fed state. No significant differences between trials; Prandial State × Mouth Rinse Solution × Time, $p > .05$. Values are expressed as mean ± *SD*. SUC = sucrose mouth rinse; PLA = placebo mouth rinse.

## Heart Rate and rpm Data

Mean heart rate during the four time trials did not differ between trials (fasted-PLA: 161 ± 8 beats per minute [bpm]; fasted-SUC: 160 ± 10 bpm; fed-PLA: 164 ± 10 bpm; and fed-SUC: 163 ± 8 bpm; $n = 12$; Prandial State × Mouth Rinse Solution $p = .725$). Mean rpm did not differ between the four time trials (fasted-PLA: 97 ± 7 rpm; fasted-SUC: 96 ± 9 rpm; fed-PLA: 98 ± 9 rpm; fed-SUC: 98 ± 8 rpm; Prandial State × Mouth Rinse Solution $p = .488$).

## Individual Changes in Power

Individual and mean changes in power output between the time trials performed in the fasted and fed state are shown in Figure 4. In the fasted state, 5 participants performed the time trial faster while using the carbohydrate mouth rinse while 9 performed better using the placebo mouth rinse. In the fed state, 5 participants performed the time trial faster while receiving the carbohydrate mouth rinse while 9 performed better when receiving the PLA mouth rinse. Only 1 participant performed the time trial faster with the carbohydrate compared with placebo mouth rinse in both the fasted and fed state.

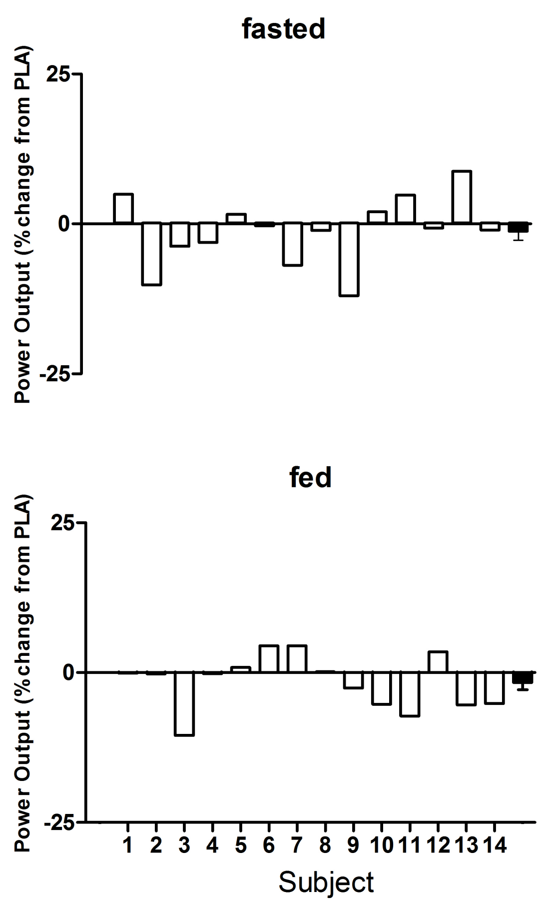


**Figure 4** — Individual (transparent bars) and mean (solid bars) change in mean power output in the placebo and sucrose treatments in both the fasted and fed state. Values are expressed as mean ± *SD*. PLA = placebo mouth rinse. A positive % change in power output indicates improved exercise performance.

## Discussion

In the current study we observed no increase in 1-hr time trial performance following mouth rinsing with sucrose compared with a placebo during exercise in well-trained cyclists in both the postabsorptive as well as postprandial state.

Several studies have reported that carbohydrate mouth rinsing can improve short-term, high-intensity (30–60 min, >75% $VO_{2peak}$) endurance-type exercise performance (J. M. Carter, Jeukendrup, & Jones, 2004; Chambers et al., 2009; Fares & Kayser, 2011; Gam et al., 2013; Lane et al., 2013; Pottier et al., 2010; Rollo et al., 2008; Rollo et al., 2010; Sinclair et al., 2014) whereas others have failed to confirm those findings (Beelen et al., 2009; Gam et al., 2013; Rollo et al., 2011; Whitham & McKinney, 2007). A factor that has been proposed to explain the discrepancy between these studies is the duration of the preexercise fasting period. We previously proposed that the signaling response from carbohydrate receptors in the oral cavity to the central nervous system may be of lesser magnitude when exercise is performed in the fed state, a situation where liver glycogen stores are not compromised. In agreement, we previously observed no improvements in performance following carbohydrate mouth rinsing during exercise performed in a fed state (Beelen et al., 2009). We hypothesized that carbohydrate mouth rinsing during high-intensity exercise increases time trial performance only when exercise is performed in a postabsorptive, overnight fasted state.

To test this hypothesis, we assessed the effect of sucrose mouth rinsing on 1-hr time trial performance in both the postprandial as well as the overnight fasted state. In agreement with our hypothesis, we observed no increase in time trial performance following sucrose mouth rinsing compared with placebo (fed-SUC: 69.0 ± 6.3 min; fed-PLA: 67.6 ± 6.6 min, Figure 1), when exercise was performed 2 hr after the consumption of a carbohydrate-rich breakfast (1.38 ± 0.16 g carbohydrate/kg body mass). These findings confirm previous work in our laboratory, in which we failed to detect any ergogenic properties of a carbohydrate mouth rinse on time trial performance assessed in the fed state (Beelen et al., 2009). To date, only two other studies have investigated the impact of carbohydrate mouth rinsing on high-intensity endurance exercise performed in the fed state (Fares & Kayser, 2011; Lane et al., 2013). In contrast to our findings, both Fares and Kayser (2011) and Lane et al. (2013) have reported improvements in time trial performance when carbohydrate mouth rinsing was started 2–3 hr after consuming a carbohydrate-rich breakfast. The discrepancy with our previous (Beelen et al., 2009) and present observation is not clear. A difference between these studies is the carbohydrate concentration of the mouth rinse solution. Lane et al. applied a 10% carbohydrate solution (Lane et al., 2013), while we used a 6.4% solution in our current and previous work (Beelen et al., 2009). In contrast, Fares and Kayser (2011) also applied a 6.4% solution and observed an ergogenic effect of mouth rinsing on time trial performance in trained athletes. Therefore, differences in carbohydrate concentration do not seem to explain the discrepancy among studies. A factor that may explain the inconsistency between studies is the duration of the applied mouth rinse. While we applied 5-s mouth rinses in our previous (Beelen et al., 2009) and current investigation, Fares and Kayser (2011) and Lane et al. (2013) applied longer rinsing protocols of 5–10 and 10 s, respectively. In support, a recent study on the duration of carbohydrate mouth rinsing suggests greater ergogenic effects following a 10-s versus a 5-s rinsing protocol (Sinclair et al., 2014).

We investigated the impact of sucrose mouth rinsing on exercise performance during both the postabsorptive as well as postprandial state. In contrast to our hypothesis, we observed no ergogenic effects of sucrose mouth rinsing during exercise in the fasted state (fasted-SUC: 69.6 ± 7.5 min; fasted-PLA: 68.6 ± 7.2 min, Figure 1). Many previous studies have reported improvements in exercise performance with carbohydrate mouth rinsing applied more than 4 hr after ingesting the last meal (J. M. Carter, Jeukendrup, & Jones, 2004; Chambers et al., 2009; Fares & Kayser, 2011; Gam et al., 2013; Lane et al., 2013; Rollo et al., 2008; Rollo et al., 2010; Sinclair et al., 2014). However, there are also other studies that have failed to confirm these findings (Rollo et al., 2011; Sinclair et al., 2014; Whitham & McKinney, 2007). The reason for the discrepancy between these studies, including the present, is not readily apparent. The current study was very similar in design to previous investigations on carbohydrate mouth rinsing during exercise in a fasted state (J. M. Carter, Jeukendrup, & Jones, 2004; Chambers et al., 2009; Fares & Kayser, 2011; Gam et al., 2013; Lane et al., 2013; Pottier et al., 2010; Rollo et al., 2010; Sinclair et al., 2014; Whitham & McKinney, 2007). We included 14 well-trained cyclists, and their time trial performance showed a coefficient of variation of 2.66% and 3.33% when performance was assessed in the fasted and fed state, respectively. The test–retest reliability in our athletes is similar to that in previous reports on the validity of time trials as a means to assess exercise performance in a laboratory setting (Jeukendrup et al., 1996). This implies that our statistical power was strong enough to detect ergogenic benefits as small as 2.5% between trials. In addition, when looking at individual data, 9 out of 14 participants had a lower power output during the sucrose mouth rinse trial when compared with the placebo mouth rinse trial (Figure 4), further supporting the suggestion that there was no lack of statistical power. It can be speculated that our use of the artificial sweetener aspartame as placebo, which can bind to oral taste receptors, may have concealed a potential ergogenic effect of carbohydrate mouth rinsing. However, as has been shown by functional magnetic resonance imaging, the caloric content of carbohydrates triggers additional oral sensing pathways that are thought to mediate the improvement in exercise performance when carbohydrates are present in the mouth (Chambers et al., 2009). In agreement, previous studies have reported ergogenic effects of carbohydrate mouth rinsing compared with artificial sweeteners used in the placebo beverages (Chambers et al., 2009; Lane et al., 2013; Pottier et al., 2010; Rollo et al., 2008). Taken together, previous studies show that the use of artificial sweeteners is appropriate as a placebo treatment for carbohydrate mouth rinse studies. One difference between our study and others is that we used sucrose as type of carbohydrate whereas most other studies have applied glucose (Chambers et al., 2009; Rollo et al., 2010; Watson et al., 2014) or maltodextrin (J. M. Carter, Jeukendrup, & Jones, 2004; Chambers et al., 2009; Fares & Kayser, 2011; Gam et al., 2013; Lane et al., 2013; Sinclair et al., 2014; Whitham & McKinney, 2007). However, similar to glucose and maltodextrin (Chambers et al., 2009; Molden et al., 2012), the presence of sucrose in the mouth has been shown to stimulate cortical activation (Haase et al., 2009) and improve working memory performance (E. C. Carter & McCullough, 2013), effects that are suggested to be the mechanisms by which carbohydrate mouth rinsing improves endurance performance (Chambers et al., 2009; Molden et al., 2012). Nonetheless, few studies have applied sucrose mouth rinsing to enhance exercise performance (Pottier et al., 2010). Finally, we need to underline the possibility of publication bias in the literature regarding the proposed ergogenic benefits of carbohydrate mouth rinsing. We stress the importance for so-called negative studies to be submitted and published in the literature as we feel that empirical evidence regarding the practical benefits of carbohydrate mouth rinsing remains to be established.

Since competition is mostly performed in fed conditions, the proposed ergogenic benefit of carbohydrate mouth rinsing is of limited practical relevance when performed in fasted conditions. There are only a few studies investigating the impact of carbohydrate mouth rinsing in fed conditions (Beelen et al., 2009; Fares & Kayser, 2011; Lane et al., 2013). Our previous (Beelen et al., 2009) and present data fail to detect any measurable increases in exercise performance following a carbohydrate mouth rinse in the fasted or fed state in well-trained athletes. Taken together, we feel there is not sufficient evidence to recommend that athletes implement carbohydrate mouth rinsing during competition in a real-life setting. In conclusion, a sucrose mouth rinse applied during exercise does not improve ~1-hr cycling time trial performance in well-trained cyclists in the fasted or postprandial state.

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