No placebo effect from carbohydrate intake during prolonged exercise

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Abstract

The purpose of this study was to investigate the possibility of a placebo effect from carbohydrate (CHO) intake during prolonged exercise. Ten endurance-trained male cyclists performed three experimental trials consisting of 120 min steady-state (SS) cycling at 61% VO₂max followed by a time trial (TT) lasting approximately 60 min. During exercise subjects ingested either plain water (WAT), artificially colored and flavored water (PLA) or a 6% carbohydrate-electrolyte solution (CES). PLA and CES were produced with identical color and taste. To investigate the possibility of a placebo effect from CHO intake, subjects were told that both flavored solutions contained CHO and that the purpose of the study was to compare CHO drinks with water. Mean power output during TT was 218 ± 22 W in WAT, 219 ± 17 W in PLA and 242 ± 27 W in CES. Performance times were 66.35 ± 6.15, 65.94 ± 5.56 and 59.69 ± 2.87 min for WAT, PLA and CES, respectively. Therefore, CES ingestion enhanced TT performance by 11.3% compared with WAT (P < 0.05) and 10.6% compared with PLA (P < 0.05), with no difference between PLA and WAT. In conclusion, during a prolonged test of cycling performance, in which subjects were not fully informed of the test conditions, there was no placebo effect when subjects believed they had ingested CHO. In contrast, the real effect of CHO intake was a 10.6% improvement in time trial cycling performance.

Key words: nutrition, supplements, time trial, cycling, performance
Introduction

The placebo effect is a favorable outcome arising purely from the belief that one has received a beneficial treatment (Clark, Hopkins, Hawley, & Burke, 2000). Our current understanding of this phenomenon is largely due to observations within clinical research. However, the placebo effect can also influence physical performance during exercise in response to potentially ergogenic aids. For example, studies have reported improvements in strength and/or endurance in subjects who believed they had ingested substances such as anabolic steroids (Ariel & Saville, 1972; Maganaris, Collins, & Sharp, 2000), caffeine (Beedie, Stuart, Coleman, & Foad, 2006; Foad, Beedie, & Coleman, 2008) or carbohydrate (CHO) (Clark et al., 2000).

In studies with a placebo control, CHO ingestion during prolonged exercise (lasting more than 2 h) delays the onset of fatigue and improves exercise performance (Coggan & Coyle, 1987, 1989; Coyle, Coggan, Hemmert, & Ivy, 1986; Coyle et al., 1983; Febbraio, Chiu, Angus, Arkinstall, & Hawley, 2000). This ergogenic effect of CHO has been attributed to the maintenance of plasma glucose concentrations and high rates of CHO oxidation late in exercise when muscle and liver glycogen stores are low (Coggan & Coyle, 1989). However, given the widespread use of CHO supplements in endurance sports and the widely advertised benefits of using CHO products, subjects taking part in CHO feeding studies are well aware of the potential benefits for performance. Therefore, it is reasonable to suggest that the placebo effect may contribute to the ergogenic effect of CHO intake during exercise.

Interestingly, Clark and colleagues (Clark et al., 2000) reported a 4% improvement in 40 km time trial cycling performance (test duration ~1 h) when subjects ingesting a placebo solution were told it contained CHO. In contrast, they reported that the real effect of CHO was a
slight decrease in performance (0.3%). These findings suggest that the placebo effect may account for the ergogenic effect of some nutritional supplements. Clark and colleagues made several recommendations for future placebo-effect research including protocols of different exercise durations (Clark et al., 2000). Indeed, it seems unlikely that placebo effects remain constant under varied test conditions, and whether or not a placebo effect of CHO intake can influence performance during prolonged exercise remains unknown. Therefore, the purpose of the present study was to investigate the placebo effect from CHO intake during a prolonged test of cycling performance (test duration ~3 h). We hypothesized that a placebo effect would be present but that it would be significantly less than the real effect of CHO intake.
Methods

Subjects

Ten endurance-trained male cyclists [age: 28 ± 8 yr; body mass 74.1 ± 9.0 kg; VO₂max 61.7 ± 7.3 mL/kg/min; maximal power output 336 ± 31 W (mean ± SD)] volunteered to participate in this study. Subjects were informed of the potential risks involved with the experimental procedures before providing their written consent. The study was approved by the School of Sport and Exercise Sciences Safety and Ethics Committee (University of Birmingham, UK).

General design

Each subject completed three experimental trials consisting of 120 min steady-state (SS) cycling at 50% maximal power output (Wmax) followed by a time trial (TT) lasting approximately 60 min. Throughout exercise, subjects ingested either plain water (WAT), artificially colored and flavored water (PLA) or a 6% carbohydrate-electrolyte solution (CES), which contained glucose and fructose in a 2:1 ratio. Trials were performed in random order, using a double-blind cross-over design, and separated by at least 7 days. PLA and CES were produced with identical color and taste. To investigate the possibility of a placebo effect with CHO feeding subjects were told that both flavored solutions contained CHO and that the purpose of the study was to compare CHO drinks with water.

Preliminary testing

One week prior to the start of the experiment, subjects performed an incremental test to exhaustion on an electromagnetically braked cycle ergometer (Lode Excalibur Sport, Groningen, The Netherlands) for the determination of maximal oxygen uptake (VO₂max) and Wmax. Briefly, subjects began cycling at 95 W, followed by 35 W increments every 3 min thereafter. Breath-by-breath measurements were performed throughout exercise using an
automated online gas analysis system (Oxycon Pro, Jaeger, Wuerzburg, Germany). Wmax values were used to determine 50 and 70% Wmax, which were later employed in the experimental trials.

Diet and activity before testing

Subjects were asked to record their food intake and physical activity for 2 days prior to the first trial and were then instructed to follow the same diet and activities before all remaining trials. They were also asked to refrain from strenuous exercise and to avoid alcohol and caffeine intake for 24 h before all trials. Subjects were given standardized forms for this purpose. All 10 subjects provided detailed food records as required. These records included the timing of food intake, portion size (weighed when possible but estimated otherwise), brand of food and method of cooking. Records were checked (for sufficient detail) by one of the researchers before being handed back to the subject to act as a guide for standardizing their food intake before subsequent visits. We are satisfied that all 10 subjects understood the importance of this procedure and complied with the diet control.

Experimental trials

Subjects reported to the laboratory after a 3 h fast. To avoid the influence of circadian variation each subject performed all trials at the same time of day. After sitting quietly for 10-15 min a Teflon catheter (Venflon, Becton Dickinson, Plymouth, UK) was inserted into an antecubital vein of the arm and a resting blood sample (10 mL) was obtained. Subjects then began cycling at 50% Wmax (168 ± 15 W) for a duration of 120 min. At the onset of exercise, subjects ingested 600 mL of one of the three experimental beverages (WAT, PLA or CES) followed by a further 150 mL every 15 min thereafter. Further blood samples (10 mL) were obtained every 15 min, along with measures of VO2 and VCO2 using an automated
online gas-analysis system (Oxycon Pro, Jaeger, Wurzburg, Germany). Heart rate (HR) was recorded continuously (15 sec intervals) throughout exercise using a radio-telemetry HR monitor (Polar 625X, Kempele, Finland).

On completion of steady-state exercise, the ergometer was adjusted to the cadence dependant (linear) mode and subjects were required to complete a set amount of work (847 ± 78 kJ) as fast as possible. The total amount of work to be performed was calculated using the formula:

\[
\text{Total work (J)} = 0.70 \cdot \text{Wmax} \cdot 3600 \text{ s}
\]

The linear factor was individually adjusted so that 70% Wmax was obtained when the subject pedaled at their preferred cadence. Preferred cadence was determined during the preliminary testing session and was considered to be the average cadence freely adopted during the VO2max test. Additionally, subjects were asked to report their preferred cadence and, in all cases, this was similar to that observed during the VO2max test. Preferred cadence was between 90 and 95 rpm for all subjects. The only information available to the subjects during TT was elapsed work and percentage of work performed (i.e. 0% at the start and 100% on completion). Furthermore, subjects were not given any feedback on their performance until completion of the entire study. At set intervals throughout the TT (25, 50 and 75% work completed) subjects ingested a further 150 mL of one of the experimental beverages (WAT, PLA or CES). The total fluid intake during SS and TT (total duration ~3 h) was 2250 mL. During the CES trial this provided 135 g of CHO (0.75 g/min or 45 g/h). HR was recorded continuously throughout the test but no blood or respiratory measures were taken. With the exception of providing drinks, every effort was taken to ensure that subjects were not disturbed. A screen was placed around the subject to separate them from the investigator
and subjects were not given any verbal encouragement. These are standard testing procedures in our laboratory (Currell & Jeukendrup, 2008).

**Analyses**

Blood samples were collected into pre-chilled vacutainers containing K$_3$EDTA and stored on ice for approximately 15-20 min before centrifugation at 2300 $g$ for 10 min at a temperature of 4°C. After centrifugation, aliquots of the plasma were immediately frozen in liquid nitrogen and stored at -25°C until further analysis. Plasma samples were analyzed using commercially available spectrophotometric assays for glucose (Glucose HK, ABX Diagnostics, UK) and lactate (Lactic Acid, ABX Diagnostics, UK) using a semi-automatic analyzer (Cobas Mira Plus, ABX, UK).

**Calculations**

Rates of total CHO and fat oxidation were calculated using stoichiometric equations (Jeukendrup & Wallis, 2005), with the assumption that protein oxidation was negligible:

$$
\text{CHO oxidation (g/min)} = 4.210 \cdot \text{VCO}_2 - 2.962 \cdot \text{VO}_2 
$$

$$
\text{Fat oxidation (g/min)} = 1.695 \cdot \text{VO}_2 - 1.701 \cdot \text{VCO}_2
$$

**Statistical analysis**

All data are expressed as means ± standard deviation (means ± SD). One-way (trial) analysis of variance (ANOVA) for repeated measures was performed to study differences in substrate metabolism (averaged over the 120 min steady-state period) and time trial performance. Two-way (trial x time) ANOVA for repeated measures was performed to study differences in plasma metabolite concentrations during steady-state exercise and power output during the
time trial. Significant effects were followed up by post hoc comparisons (Tukey HSD). Data analysis was performed using SPSS for Windows version 13.0 software (Chicago, IL) or by hand. Significance was accepted at $P < 0.05$. 
Results

**Performance data.** Mean power output during TT was 218 ± 22 W in WAT, 219 ± 17 W in PLA and 242 ± 27 W in CES (Fig. 1). Performance times were 66.35 ± 6.15, 65.94 ± 5.56 and 59.69 ± 2.87 min for WAT, PLA and CES, respectively. Therefore, CES enhanced performance by 11.3% compared with WAT ($P < 0.05$, 95% confidence interval 4.7-17.9%) and 10.6% compared with PLA ($P < 0.05$, 95% confidence interval 4.4-16.8%). Ingesting PLA resulted in a small (0.4%), non-significant, improvement in performance compared with WAT (95% confidence interval -3.4 – 4.2%).

Power output decreased throughout TT in WAT and PLA whereas power output was maintained throughout TT in CES (Fig. 2, $P < 0.05$). Average power output during the last 25% was significantly higher in CES than WAT (Fig 2, $P < 0.05$). Average power output during the last 50% was significantly higher in CES than PLA (Fig. 2, $P < 0.05$).

**VO$_2$, RER, CHO and fat oxidation.** Expired gas measurements and substrate oxidation are displayed in Table 1. There was no difference in the VO$_2$ between trials. Therefore, relative exercise intensity was similar in all trials (~61% VO$_2$max). Ingesting CES resulted in significantly higher RER values than WAT and PLA ($P < 0.05$). Accordingly, total CHO oxidation was significantly higher ($P < 0.05$) and total fat oxidation significantly lower ($P < 0.05$) in CES than WAT and PLA.

**Plasma metabolites.** Plasma glucose and lactate concentrations at rest and during exercise are shown in Figure 3A and B, respectively. Resting plasma glucose concentrations were not significantly different between trials (4.5-4.8 mmol/L). Ingesting CES resulted in significantly higher plasma glucose concentrations than WAT and PLA at several time points
throughout exercise. Resting plasma lactate concentrations were not significantly different between trials (1.15-1.25 mmol/L). Average plasma lactate concentrations were significantly higher in CES (1.54 ± 0.38 mmol/L) than WAT (1.35 ± 0.30 mmol/L) and PLA (1.35 ± 0.25 mmol/L) \( (P < 0.05) \).
Discussion

The purpose of the present study was to investigate the possibility of a placebo effect from CHO intake during prolonged exercise. Based on the recommendations of Beedie and colleagues (Beedie, Coleman, & Foad, 2007; Trojan & Beedie, 2008) we designed a three-condition study (PLA, CES and water), which allowed comparison between the placebo and real treatment as well as comparison to a true baseline measure (ingestion of water in this case). Subjects were told that PLA and CES contained CHO and that the purpose of the study was to compare the CHO drinks with water. This novel aspect of the study design meant that subjects had similar expectations for PLA and CES in terms of their potential for performance benefits. The main finding of the present study was that CHO ingestion improved performance by 10.6% compared with PLA. However, PLA ingestion did not improve performance compared with water (Fig. 1).

The lack of a placebo effect is somewhat surprising given that subjects believed PLA contained CHO, and seems in contrast to at least one previous study (Clark et al., 2000). However, this observation is most likely due to the intensity and duration of exercise and hence the mechanism by which CHO improves performance. As previously mentioned, Clark and colleagues (Clark et al., 2000) reported a 4% improvement in 40 km time trial cycling performance (test duration ~1 h) when subjects ingesting a placebo solution were told it contained CHO. In that study, the real effect of CHO intake was a slight decrease in performance. Since CHO availability is not thought to be limiting during relatively short-duration high-intensity exercise, the placebo effect may account for the ergogenic effect of supplements having little or no real mechanism of action.
Fatigue during prolonged submaximal exercise (like that of the present study) coincides with the depletion of glycogen stores and reduced blood glucose concentrations (Coyle et al., 1986). Although speculative, we suggest that signals of metabolic fatigue associated with prolonged exercise would override any positive psychological factors manifesting as a result of believing one has received a beneficial treatment. Hence, under these conditions, one might expect similar performances in water and PLA trials. Regardless of the exact reason for similar performances between PLA and water, the present study demonstrates that simply believing one has received CHO does not improve performance during prolonged exercise.

Interestingly, 5 subjects responded to PLA ingestion with an improvement in performance when compared with water (mean improvement of 4.5%). This could represent day-to-day variation in our performance measure, however, the variation of this test is typically less than 2% (unpublished observations) and previous studies have also reported individual differences in placebo responsiveness (Beedie et al., 2006). It is not yet known why some individuals appear more responsive to placebo effects than others but pacing could play a role. For example, if a subject rides sub-maximally during a baseline performance measure, then it is entirely possible that they raise their effort (either consciously or subconsciously) when a potentially ergogenic aid is administered. Given that we did not observe a placebo effect, this could indicate that our well-trained subjects gave a true all-out effort during the baseline water trial. Of course this is difficult to know for sure. Nonetheless, researchers should be encouraged to recruit highly motivated well-trained subjects with competitive experience when investigating potentially ergogenic aids. It has also been suggested that there may be a relationship between training status and placebo responsiveness, with moderately-trained athletes being more responsive than highly-trained athletes (Clark et al., 2000). In the present
study, we cannot confirm or dismiss this possibility due to the relatively small sample size (n = 10) and similar training status of cyclists recruited.

As mentioned previously, a unique aspect of the present study was that subjects received CHO, placebo and water but were only told they would receive CHO and water. In more traditional placebo-controlled research, subjects receive the placebo and real treatments in a blind manner. However, the subjects are fully informed that at some point they will receive a placebo. One of the limitations to this traditional approach is that uncertainty of trial order can increase the variation of the performance measure (Clark et al., 2000). Another limitation is that subjects may respond to subtle cues that aid correct identification of the treatment and placebo conditions. These cues could be knowledge of their current vs. previous performance and/or identification of symptoms/side-effects associated with receiving an active substance (Foad et al., 2008). Considering these points, we suggest that not fully informing subjects of the treatments they receive may be a useful method to reduce the placebo effect and improve the reliability of performance testing. Additionally, in the present study, we chose not to measure ratings of perceived exertion (RPE) during steady-state exercise, which is often standard practice in this type of study. The reason for this is that simply asking subjects to rate their perceived exertion could give away treatment and placebo conditions and therefore influence the performance outcome. Researchers should be aware of this possibility when deciding whether to include measures of RPE in future studies of potentially ergogenic aids. Furthermore, researchers should determine the placebo effect under the specific conditions of their intervention by including a true baseline measure, as well as a placebo, as originally suggested by Beedie and colleagues (Beedie et al., 2007; Trojan & Beedie, 2008).
In summary, during a prolonged test of cycling performance, in which subjects were not fully informed of the test conditions, there was no placebo effect when subjects believed they had ingested CHO. In contrast, the real effect of CHO intake was a 10.6% improvement in time trial cycling performance.


Acknowledgements

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Figure legends

**Figure 1.** Average power output during TT. Values are means ± SD (n = 10).  
\(^{a}\) Significantly different from WAT, \(P < 0.05\).  
\(^{b}\) Significantly different from PLA, \(P < 0.05\).

**Figure 2.** Average power output during each quarter of TT. Values are means ± SD (n = 10).  
\(^{a}\) Significantly different from WAT, \(P < 0.05\).  
\(^{b}\) Significantly different from PLA, \(P < 0.05\).

**Figure 3.** Plasma glucose (A) and lactate (B) concentrations at rest and during exercise with WAT, PLA or CES ingestion. Values are means ± SD (n = 10).  
\(^{a}\) Significantly different from WAT, \(P < 0.05\).  
\(^{b}\) Significantly different from PLA, \(P < 0.05\).
Tables

**Table 1.** Oxygen uptake (VO$_2$), respiratory exchange ratio (RER), total carbohydrate oxidation (CHOtot) and total fat oxidation (FATtot) during the 120 min steady-state period.

<table>
<thead>
<tr>
<th></th>
<th>WAT</th>
<th>PLA</th>
<th>CES</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO$_2$ (L·min$^{-1}$)</td>
<td>2.78 ± 0.25</td>
<td>2.77 ± 0.26</td>
<td>2.80 ± 0.30</td>
</tr>
<tr>
<td>RER</td>
<td>0.90 ± 0.03</td>
<td>0.90 ± 0.02</td>
<td>0.93 ± 0.05$^{a,b}$</td>
</tr>
<tr>
<td>CHOtot (g·min$^{-1}$)</td>
<td>2.27 ± 0.37</td>
<td>2.31 ± 0.33</td>
<td>2.67 ± 0.58$^{a,b}$</td>
</tr>
<tr>
<td>FATtot (g·min$^{-1}$)</td>
<td>0.46 ± 0.16</td>
<td>0.45 ± 0.10</td>
<td>0.31 ± 0.23$^{a,b}$</td>
</tr>
</tbody>
</table>

Values are means ± SD (n = 10). $^a$ Significantly different from WAT, $P < 0.05$. $^b$ Significantly different from PLA, $P < 0.05$. 
Figures

![Bar chart showing power output (W) for WAT, PLA, and CES]

Figure 1
Figure 2
Figure 3