Am J Physiol Gastrointest Liver Physiol 300: G181–G189, 2011.
First published November 11, 2010; doi:10.1152/ajpgi.00419.2010.

Fructose-maltodextrin ratio in a carbohydrate-electrolyte solution differentially affects exogenous carbohydrate oxidation rate, gut comfort, and performance

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Submitted 16 September 2010; accepted in final form 5 November 2010

O'Brien WJ, Rowlands DS. Fructose-maltodextrin ratio in a carbohydrate-electrolyte solution differentially affects exogenous carbohydrate oxidation rate, gut comfort, and performance. *Am J Physiol Gastrointest Liver Physiol* 300: G181–G189, 2011. First published November 11, 2010; doi:10.1152/ajpgi.00419.2010.—Solutions containing multiple carbohydrates utilizing different intestinal transporters (glucose and fructose) show enhanced absorption, oxidation, and performance compared with single-carbohydrate solutions, but the impact of the ratio of these carbohydrates on outcomes is unknown. In a randomized double-blind crossover, 10 cyclists rode 150 min at 50% peak power, then performed an incremental test to exhaustion, while ingesting artificially sweetened water or one of three carbohydrate-salt solutions comprising fructose and maltodextrin in the respective following concentrations: 4.5 and 9% (0.5-Ratio), 6 and 7.5% (0.8-Ratio), and 7.5 and 6% (1.25-Ratio). The carbohydrates were ingested at 1.8 g/min and naturally ^{13}C-enriched to permit evaluation of oxidation rate by mass spectrometry and indirect calorimetry. Mean exogenous carbohydrate oxidation rates were 1.04, 1.14, and 1.05 g/min (coefficient of variation 20%) in 0.5-, 0.8-, and 1.25-Ratios, respectively, representing likely small increases in 0.8-Ratio of 11% (90% confidence limits; ±4%) and 10% (±4%) relative to 0.5- and 1.25-Ratios, respectively. Comparisons of fat and total and endogenous carbohydrate oxidation rates between solutions were unclear. Relative to 0.5-Ratio, there were moderate improvements to peak power with 0.8- (3.6%; 99% confidence limits ± 3.5%) and 1.25-Ratio (3.0%; ±3.7%) but unclear with water (0.4%; ±4.4%). Increases in stomach fullness, abdominal cramping, and nausea were lowest with the 0.8- followed by the 1.25-Ratio solution. At high carbohydrate-ingestion rate, greater benefits to endurance performance may result from ingestion of 0.8- to 1.25-Ratio fructose-maltodextrin solutions. Small perceptible improvements in gut comfort favor the 0.8-Ratio and provide a clearer suggestion of mechanism than the relationship with exogenous carbohydrate oxidation.

stable isotope; substrate metabolism; gastrointestinal distress; carbohydrate absorption

INCREASED EXOGENOUS CARBOHYDRATE oxidation and endurance performance have been recently reported with the ingestion of multiple transportable carbohydrates relative to isoenergetic single transportable carbohydrates. For example, 1.2- to 1.5-fold higher exogenous carbohydrate oxidation rates (16–19, 43) and ~8% improvement in 100 km (41) and preloaded 1 h time trial performance (11) resulted from ingestion (1.5–2.4 g/min) of 14.4% 1:2 fructose-glucose solutions of high osmolality (up to ~800 mosmol/kg), relative to isocaloric glucose-only controls. These performance benefits were attributed either to enhanced carbohydrate (20) and fluid absorption (12, 24) or to lower relative gastrointestinal disturbance (41) with the fructose-glucose solutions. When examining the effects of graded fructose ingestion rates (2.25–5.25%; 0.3–0.7 g/min) coingested with maltodextrin (4.5%; 0.6 g/min) in lower osmolality solutions (208–379 mosmol/kg), we found that a 0.8-ratio fructose-maltodextrin (1.25:1 glucose-fructose) solution produced the highest glucose and total exogenous carbohydrate oxidation rate and was also associated with evidence for attenuated fatigue during a repeated-sprint performance test (34). However, it was not established whether the higher oxidation rate was due to ratio per se or an effect related to increasing fructose concentration.

Carbohydrate absorption across the intestinal brush-border membrane occurs at a faster rate with multiple rather than single-carbohydrate ingestion. Although all three monosaccharides have affinity for facilitative transporter GLUT2, most glucose transport occurs via the active sodium-dependent glucose cotransporter (SGLT1), whereas fructose diffuses passively down its gradient via the sodium-independent facilitative transporter GLUT5 (44). Transporter density, and hence absorption rate, is greatest in the jejunum, with glucose transporter saturation rates estimated at 0.81 (33) to 1.7 g/min (13), and as glucose and fructose do not compete for common transporters, carbohydrate absorption from the small intestine (20) occurs at a faster rate with coingestion (37). Adopo et al. (1) were first to report this phenomenon with a 1:1 glucose-fructose solution producing 27% higher exogenous carbohydrate oxidation than when the same quantity of glucose alone was ingested. In a perfusion study, Shi et al. (37) demonstrated that, regardless of osmolality or concentration, solutions containing multiple carbohydrates produced more solute and water absorption than single-carbohydrate solutions, although the combination of single transportable carbohydrates that resulted in the highest net absorption was not systematically determined.

Perceived exertion and gut comfort have been evaluated in many carbohydrate oxidation studies and may be a mechanism impacting performance (40). Murray et al. (29) reported that fructose ingestion in isolation caused greater gastrointestinal discomfort and reduced endurance exercise capacity, compared with both glucose and sucrose. In most quantifying investigations, ingestion of composite solutions (fructose and glucose, or fructose, glucose, sucrose) have resulted in lower ratings of perceived exertion compared with single-carbohydrate solutions (21, 34). Likewise, improved gastrointestinal comfort has been reported with composite fructose-glucose solutions, compared with isocaloric single-carbohydrate (glucose or maltodextrin) solutions (20–22, 41), but the effect of solution fructose-glucose ratio is unknown.

Therefore, the purpose of this study was to provide additional evidence for an influence of the fructose-maltodextrin ingestion ratio on net carbohydrate delivery to the circulation

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and muscle as measured by end point oxidation, while also determining the impact of carbohydrate ratio on gastrointestinal comfort and endurance peak power. The carbohydrate-ingestion rate of 1.8 g/min permitted direct comparison with the body of recent work evaluating 0.5-ratio fructose-glucose solutions (20, 22, 43), and associated inference that carbohydrate-ingestion rates above the traditionally recommended 0.5–1.0 g/min (32) might lead to better performance outcomes. On the basis of our prior evidence of oxidation of exogenous carbohydrate (34) we hypothesized that a fructose-maltodextrin ratio of 0.8 would be most beneficial to measured outcomes.

MATERIALS AND METHODS

Subjects

Ten trained male cyclists and triathletes aged 38.8 ± 8.5 yr and with a body mass of 84.7 ± 8.3 kg participated in the study. All participants had been cycling 8 or more hours per week and competing regularly for more than 12 mo. Maximal oxygen uptake ($\dot{V}O_{2max}$) and power (W_{max}) were 58.4 ± 4.7 ml·kg^{-1}·min^{-1} and 365 ± 42 W, respectively. Before participation, each subject was screened for contraindications to exercise and was fully informed of the purpose and risks associated with the procedure, and a written, informed consent was obtained. This study was approved by the Massey University Human Ethics Committee Southern.

Experimental Design

The study design was a randomized, double-blind, four-way crossover, in which the effects of ingesting solutions containing three ratios of fructose and maltodextrin or artificially sweetened water on outcomes were compared. Each cyclist visited the laboratory a total of nine times during the 5-wk study ($\dot{V}O_{2max}$ test and familiarization ride, 4 weekly standardized training rides, 4 weekly experimental trials). The four experimental trials consisted of 150-min cycling at 50% W_{max} while ingesting the test solutions immediately followed by an incremental test to exhaustion. Maize-derived naturally ^{13}C-enriched maltodextrin and fructose were used to quantify exogenous carbohydrate oxidation rate. The experimental trials were separated by 7 days, and for each subject trials were conducted at the same time of day (starting between 0530 and 0645) to control for circadian variance.

Protocols

Preliminary testing and familiarization. At least 10 days prior to the start of the experimental trials, a progressive exercise protocol to volitional exhaustion was performed on an electronically braked cycle ergometer (VeloTron Racer Mate, Seattle, WA) to determine $\dot{V}O_{2max}$ and W_{max}. After a warmup period, the test commenced at a workload of 3 W/kg body mass and increased at a rate of 25 W every 150 s thereafter. Exhaustion was defined as when the subject could no longer maintain a pedal cadence of 70 rpm following three warnings to do so. $\dot{V}O_{2max}$ was measured online with a calibrated Moxus MaxII Metabolic System (AEI Technologies, Naperville, IL) and taken as the highest attained 20-s average oxygen uptake. W_{max} was defined as the last completed work rate plus the fraction of time spent in the final noncompleted work rate multiplied by the 25-W work rate increment. The results were used to determine the 50% W_{max} workload used during the laboratory training sessions and experimental trials. Following the incremental test, participants rested for 10 min then completed a full familiarization of the experimental trial including performance test. During all rides, environmental conditions were maintained at 18–19°C and 45–55% relative humidity by air conditioning, with a standardized air flow maintained over the cyclist by way of a fan.

Training and diet. Cyclists modified their training and repeated this on a weekly basis as follows: *day 1* long-duration ride (3–4 h), *days 2* and *3* medium-duration ride (2–3 h), *day 4* laboratory-based training (2 h at 50% W_{max}), *day 5* rest day, *day 6* experimental trial, *day 7* recovery ride (1–2 h). Subjects were asked to record their food intake the day prior to the first experimental trial and were instructed to repeat this intake the day before each of the three subsequent trials. To assist in standardizing energy intake, subjects were also provided with a prepackaged pasta meal (45 kJ, 1.69 g carbohydrate, 0.44 g protein, 0.67 g fat per kg body mass) to be consumed the evening before each experimental trial monitored by dietary diary. To reduce the background ^{13}C enrichment, an extensive list of foods with a high natural abundance of ^{13}C (i.e., from plants with a C_4 photosynthetic cycle: maize, sugar cane, or sugar beet) was provided and subjects were instructed not to consume such foods for at least 10 days before the first experimental trial and for the duration of the study.

Experimental trial. Participants reported to the laboratory in the morning following an overnight fast (starting between 0530 and 0645) on *day 6* of each weekly block. On arrival, riders toileted and had their body mass recorded, then a 20-gauge cannula was inserted into an antecubital vein (Becton Dickinson Medical, Singapore). A two-way stopcock valve (Becton Dickinson Medical) was connected to the cannula to allow for blood sampling at this point and during exercise, maintained patent with regular saline flush. Following a resting blood sample, cyclists were seated next to the cycle ergometer to complete resting psychometric scales and resting expired breath sample collection. Cyclists then mounted the cycle ergometer and cycled for 150 min at 50% W_{max}. During exercise, the following outcome variables were collected every 15 min in the following order: psychometric variable ratings, expired breath sample from a mixing chamber and into a Douglas bag, and finally (every 30 min) a blood sample. Experimental solutions were ingested at rest and every 15 min during exercise immediately following sampling. At the completion of the 150-min cycle, riders immediately transitioned to the ramped performance test (5), during which time no solution was ingested nor were any samples collected. Workload for the performance test began at 50% W_{max}, incrementing 1 W every 3 s until volitional exhaustion. Cyclists were given no cue as to elapsed time or current workload, and the only visible cue was cadence, which they were instructed to maintain above 70 rpm. Exhaustion was determined as the point at which cadence dropped below 70 rpm for the third time or for more than 3 s; cyclists were provided with two warnings to lift cadence from below 70, and then on the third lapse the test was terminated.

Breath sampling. Cyclists breathed through a mouthpiece and two-way valve (Hans Rudolph, Shawnee, KS) directed into a 5-liter mixing chamber connected in series to a Douglas bag. To stabilize respiration, cyclists breathed through the mouthpiece for ~1 min prior to 90 s collection of expired breath into the Douglas bag for calculation of oxygen consumption and carbon dioxide production rates. Expired breath samples were drawn into 2 × 10 ml evacuated tubes (Exetainer, Labco, High Wycombe, UK) from a 20-gauge needle positioned at the distal end of the mixing chamber for ^{13}C enrichment and subsequent calculation of exogenous-glucose oxidation.

Carbohydrate Solutions

Immediately prior to exercise, participants ingested a 400-ml bolus of experimental solution, followed by 200 ml at 15 min intervals throughout the 150-min ride, with the final bolus at 150 min. Excluding the double bolus, solutions were ingested at a rate of 800 ml/h over 150 min (total 2.4 l). Four different solutions were prepared for ingestion during exercise. The three experimental solutions comprised fructose and maltodextrin in the following respective concentrations, with ratios and abbreviation in parentheses: 4.5 and 9% (0.5:1; 0.5-Ratio), 6 and 7.5% (0.8:1; 0.8-Ratio), and 7.5 and 6% (1.25:1; 1.25-Ratio); respective mean ingestion rates (g/min) during exercise were 0.6 fructose + 1.2 maltodextrin, 0.8 fructose + 1.0 maltodextrin,

and 1.0 fructose + 0.8 maltodextrin. The control solution contained artificially sweetened water. Included in each solution was NaCl (1.17 g/l, 20 mmol/l Na^+), citric acid (5.92 g/l), and lime juice (20 g/l). Both the maltodextrin (Star-Dri 10, Tate & Lyle, Decatur, IL) and fructose (Krystar 300, A. E. Stanley Manufacturing Decatur, IL) were maize derived with ^{13}C-enrichment of −10.4 δ‰ and −10.7 δ‰ (respectively) vs. Pee Dee Bellemnitella (PDB). Solution osmolality was 83, 409, 495, 572 mosmol/kg for water; 0.5-, 0.8-, and 1.25-Ratio, respectively. Following the last testing session each subject was informally asked whether he was able to distinguish the difference between the different drink solutions.

Psychometric Scales

Perception ratings were recorded during the 150-min ride to score the effect of solution carbohydrate ratio on physical exertion and gastrointestinal comfort. Perceived exertion (leg muscle tiredness and perceived effort) and gastrointestinal comfort (nausea, stomach fullness, abdominal cramping) markers were measured on linear scales: 0 (nothing), 1 (slight), 2 (mild), 4 (moderate), 6 (high), 8 (very high), 10 (maximum). Participants were instructed to make a pen mark on a continuous scale, rating the strength of their exertion or comfort. The numerical value for each verbal anchor was not displayed on the scale charts so as not to distract the participant from their rating. Responses for nausea, abdominal cramping, and stomach fullness were chosen to determine the magnitude and temporal effects of solution carbohydrate ratios and exercise duration, and whether the consequence of these factors influenced exercise performance.

Plasma Biochemistry

Blood samples were transferred from syringe into 6 ml lithium heparin Vacutainers (Becton Dickinson, Franklin Lakes, NJ) and centrifuged at 3,000 *g* for 10 min. Plasma was aspirated into Eppendorf tubes and stored at −80°C until analysis. Lactate and glucose were analyzed by use of an automated analyzer (Bayer Rapidlab 865, Bayer, East Walpole, MA).

Expired Breath

Analysis. Breath samples were analyzed for $^{13}C/^{12}C$ by gas chromatography continuous-flow isotope-Ratio mass spectrometry (Finnigan Delta XP, Bremen, Germany). Fractions of oxygen and carbon dioxide in expired gas were measured through the gas sampling function of the Moxus system. Expired gas volume was measured with a PowerLab 4/20 spirometer and software (ADInstruments, Bella Vista, NSW, Australia). Volume calibration was carried out prior to sampling by using a known volume (90 liters) and verified again at the end of each testing session. Any drift was assumed to be linear, and raw volumes were adjusted accordingly.

Calculations. Total fat and carbohydrate oxidation rates (g/min) were calculated as described previously (34): carbohydrate oxidation (g/min) = $4.210 \cdot \dot{V}_{CO_2} - 2.962 \cdot \dot{V}_{O_2}$; fat oxidation (g/min) = $1.695 \cdot \dot{V}_{O_2} - 1.701 \cdot \dot{V}_{CO_2}$. Energy potentials of 17.22 kJ/g for carbohydrate and 39.06 kJ/g for fat oxidation were used to estimate the contribution to energy expenditure. Oxidation rates (g/min) of exogenous carbohydrate were calculated from ^{13}C enrichment and the indirect calorimetry. Isotopic enrichment of expired CO_2 was expressed as the delta per million difference (δ‰) between $^{13}C/^{12}C$ ratio of the sample and a known laboratory reference standard (PDB) according to the formula $\delta^{13}C = [(^{13}C/^{12}C \text{ ratio sample}/^{13}C/^{12}C \text{ ratio standard}) - 1] \cdot 10^3$‰, where, $^{13}C/^{12}C$ standard = 0.0112372 (10). Enrichment for fructose was −10.7 δ‰ and for maltodextrin −10.4 δ‰. The amount of carbohydrate oxidized was then calculated according to the formula exogenous carbohydrate oxidation (g/min) = $\dot{V}_{CO_2} \cdot [(\delta_{Exp} - \delta_{bkg})/(\delta_{Ing} - \delta_{bkg})]/k$, in which δ_{bkg} is the ^{13}C enrichment of expired air in the control condition, δ_{Exp} is the ^{13}C enrichment of expired CO_2 during the 150-min ride with ^{13}C-enriched carbohydrate ingestion, δ_{Ing} is the ^{13}C-enrichment of the carbohydrate, and k is the volume of CO_2 (liters) produced via oxidation of 1 g glucose (k = 0.7467). The percent efficiency of exogenous carbohydrate metabolism was oxidized/ingested rate·100.

Calculation of exogenous substrate oxidation rate is affected by the delayed equilibration of $^{13}CO_2$ with the large endogenous HCO_3^- pool. Nevertheless, a physiological steady-state condition occurs relatively rapidly during exercise, and $^{13}CO_2$ in the expired air will be equilibrated with the $^{13}CO_2/H^{13}CO_2$ pool from ~60 min of steady-state exercise. As a consequence, the main outcome measures for substrate oxidation were from 60 to 150 min of exercise.

Statistical Analysis

General method. The effects of fructose-maltodextrin ingestion ratio on outcomes were estimated with appropriate mixed models (Proc Mixed, SAS version 9.1, SAS Institute, Cary, NC). Most dependent variables, except psychometric parameters and raw data expressed as a percent, were analyzed after natural log transformation to reduce effects of nonuniformity of error and to express changes as percents. For all data sets, fixed effects were treatment and the order term, which accounts for familiarization, adaptation, or fatigue effects between consecutive trials. For the time-series data, the *x*-axis variable was grand mean centered for linear modeling (as in regression analysis). For the psychometric parameters, the baseline value was included as a covariate. Subject was the random effect, and in the analysis of performance, additional random effects were added to allow for the extra variation present in the 0.5-Ratio and water conditions. The within-subject coefficient of variation (CV) was estimated from the residual variance. For insight as to the impact of measured mechanism variables on performance, we conducted a mechanism covariate analysis, whereby the standardized mean exogenous carbohydrate oxidation rate and equivalently the standardized mean nausea score from 60 to 150 min as the integrated measure of gut comfort were run individually with the model for peak power.

Presentation of data. Subject descriptive and some outcome data are raw means and standard deviations (SD). Means derived from the analysis of log-transformed variables are backtransformed least-squares means, with the associated between-subject spread represented by the CV, which can be converted to a unit value by conversion to a factor. The size of the treatment effect on metabolic and psychometric outcomes was qualified by modified Cohen effect size (standardized difference) classification: trivial 0.0–0.2, small 0.2–0.6, moderate 0.6–1.2, large 1.2–2.0, very large 2.0–4.0, enormous >4.0 (17). Sample size was adjusted for small sample bias where the standardized difference was applied [1–3/(4v − 1), where v is the degrees of freedom for the SD] (17). For performance, effect magnitude is qualified as the product of the CV for the performance measure and the following factors: trivial 0.0–0.3, small 0.3–0.9, moderate 0.9–1.6, large 1.6–2.5, very large 2.5–4.0 (17). Outcomes are rounded to two significant digits.

Estimate precision and statistical inference. In light of limitations associated with traditional null hypothesis testing (9, 38) and recent trends in inferential statistics, we utilized the magnitude-based approach inferences: 90% confidence intervals (CIs) or limits (CL) for uncertainty in mechanistic variables, 99% CIs on the harm side of uncertainty of performance, and interpretation of uncertainty in relation to effect-size magnitude thresholds rather than the null of traditional hypothesis testing (17, 34). The threshold for a substantial change for mechanism outcomes was the conventional smallest standardized difference (0.2); for performance we used 0.3 × the within-subject CV in the performance test, and additionally provide threshold for moderate (0.9 × within-subject CV) and large (1.6 × within-subject CV) (17). The within-subject SD was a surrogate for the variability in performance of well-trained cyclists in competition. The variability in performance in the incremental test was assumed to simulate the physical and physiological demands at the end of a race

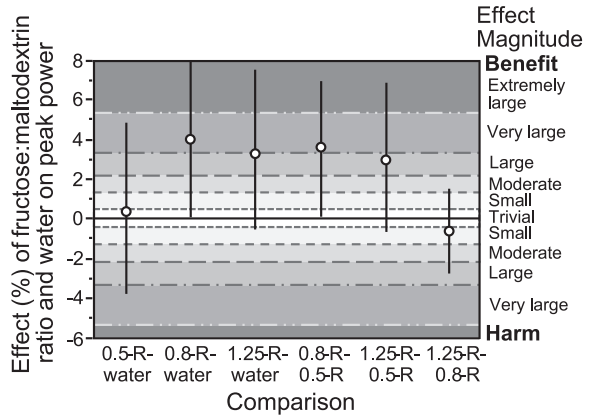

Fig. 1. Effect of solution composition on performance test peak power. Point data are the back log-transformed least-square means. Bars are the 99% confidence interval. Thresholds for small (0.4%), moderate (1.2%), large (2.1%), very large (3.3%), and extremely large (5.3%) effects are shown as dashed lines within the shaded zones. R, Ratio.

(5), and any difference in variability between laboratory and field was assumed to also change in proportion to the magnitude of the response to treatment retaining a proportionate ratio of the sensitivity in response to treatment to the measurement error (16). For mechanistic outcomes an effect was described as unclear if its CI included both substantial positive and negative values (i.e., >5% probability that the true value is both substantially positive and negative). Otherwise, the probability of a substantial increase or decrease was calculated from the two-tailed *t*-distribution summarized as follows: <1.0%, almost certainly not; 1.0–5%, very unlikely; 5–25%, unlikely; 25–75%, possible; 75–95%, likely; 95–99%, very likely; >99%, almost certain. In the case where the majority (>50%) of the CI lies between the threshold for substantiveness the effect is qualified trivial (negligible). For inference to the performance outcome, we refer to the clinical decision thresholds of Hopkins et al. (17), where an intervention is considered for adoption if the probability of substantial harm is <0.5% and benefit >25% (possible) or >75% (likely); otherwise, outcomes are inferred as for mechanism.

RESULTS

Performance

Average peak power was 368, 382, 379, and 367 W (between-subject CV 12%), whereas time to exhaustion was 545, 594, 578, and 549 s (18%) for 0.5-, 0.8-, 1.25-Ratio, and water, respectively. The within-subject CV was 1.3% (99% CI 0.8–2.7%). The performance outcome is presented in Fig. 1. Relative to 0.5-Ratio, substantially higher peak power was almost certain in the 0.8-Ratio (likelihoods harm/trivial/benefit: 0.00/0.1/99.9) and very likely in the 1.25-Ratio (0.1/0.6/99.4) conditions, respectively. Relative to water, substantially higher peak power was also almost certain in the 0.8- (0.00/0.1/99.9) and very likely in the 1.25-Ratio (0.1/0.6/99.3) conditions, respectively. Peak power with 0.8-Ratio was possibly higher (4.9/27.4/67.7) relative to 1.25-Ratio, and between 0.5-Ratio and water the difference was unclear.

In the mechanisms covariate analysis, when the exogenous carbohydrate oxidation rate was added, the percent difference in peak power ±99%CL for the respective comparisons for carbohydrate ratio and water 0.8–0.5, 0.8–1.25, 1.25–0.5, and 0.5-water, 0.8-water, 1.25-water were 3.6 ±3.5, 0.7 ±2.2, 3.0 ±3.7% and 6.1 ±19.2, 10.1 ±21, and 9.2 ±19%; when nausea was added as the covariate, respective differences were 2.8 ±4.2, 0.7 ±5.3, 2.1 ±4.4, and −0.3 ±2.1, 2.6 ±2.5, 1.9 ±3.4%.

Substrate oxidation. Breath ^{13}C enrichment during the 150-min ride is presented in Fig. 2. Oxidation rates are shown in Fig. 3. Average substrate oxidation rates for the 60 to 150 min period of the 150-min ride are summarized in Table 1, with the corresponding statistical comparisons in Table 2.

Exogenous carbohydrate oxidation. The rate of oxidation of exogenous carbohydrate was higher in the 0.8-Ratio condition during the 150-min ride relative to the 0.5- and 1.25-Ratio conditions (Table 2); respective mean oxidation efficiencies were 63, 58, and 58%. From the 60th to 150th min of the 150-min ride (slope effect), increases in the exogenous carbohydrate oxidation rate of 55% (±14%), 59% (±14%), and 67% (±15%) were observed in the 0.5-, 0.8-, and 1.25-Ratio conditions respectively, although there was no clear difference between the ratios (comparisons not shown) and no plateau in the oxidation rate (Fig. 3).

Endogenous and total carbohydrate oxidation. No clear effect was observed in the rate of endogenous carbohydrate oxidation during the 150-min ride between any of the four conditions. Although no clear differences in the rate of total-carbohydrate oxidation were observed between any of the carbohydrate ingestion conditions, all were almost certainly moderately higher than water (Table 2). Differences in slope between the carbohydrate conditions were very likely trivial.

Endogenous fat oxidation. Carbohydrate ratio had no clear effect on endogenous-fat oxidation rate (Fig. 3, Table 2); as expected, fat oxidation was substantially higher in the water condition relative to all other conditions. Slope effects between conditions were either likely or possibly trivial.

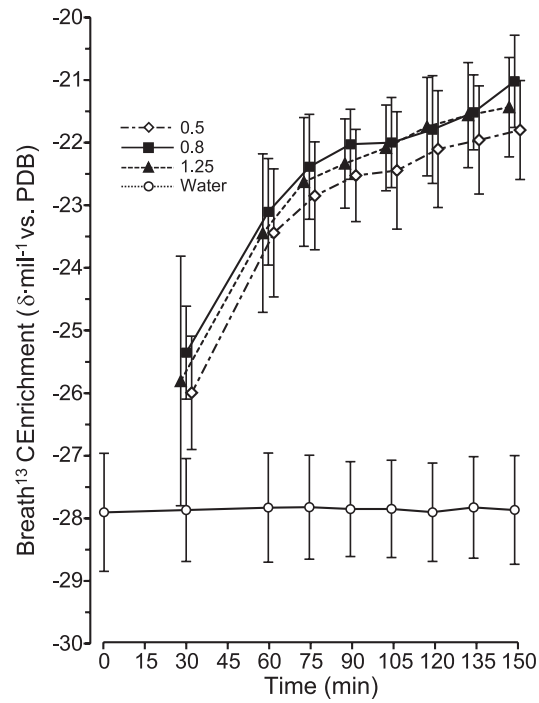

Fig. 2. Breath ^{13}C enrichment during the 150-min ride. Data are raw means with between-subject standard deviation, offset from the sampling point for clarity. PDB, Pee Dee Bellemnitella.

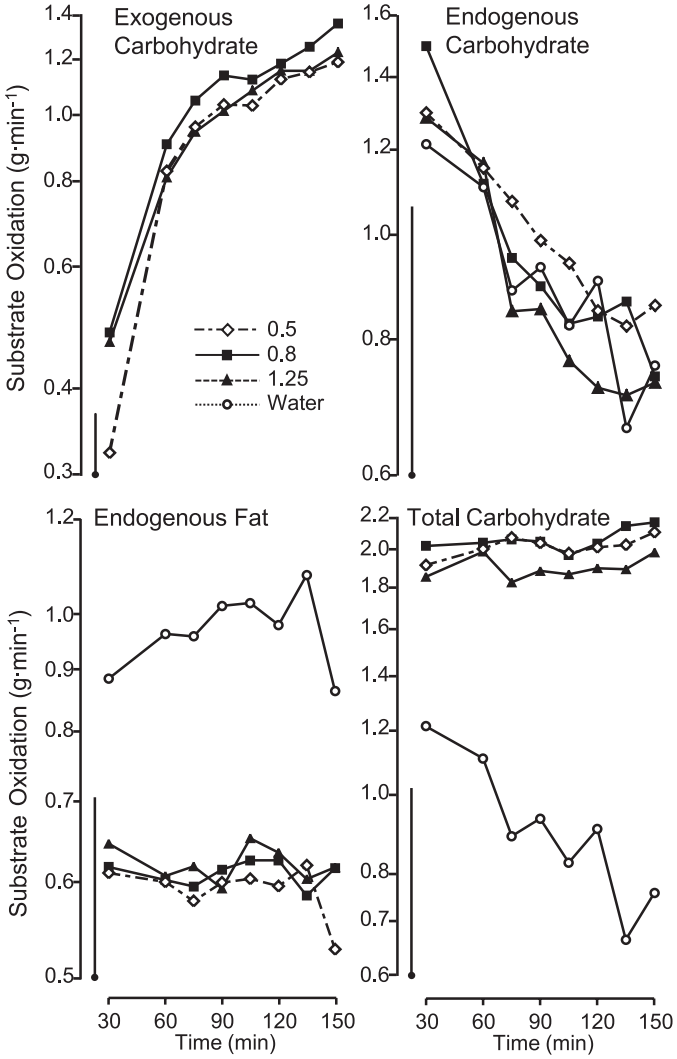

Fig. 3. Pattern of substrate oxidation during the 150-min ride. Data are back log-transformed least-squares means. Bars represent the backtransformed composite between-subject variation.

Plasma glucose and lactate. There were moderate increases in plasma-glucose concentration and slope with all carbohydrate conditions relative to water, but no clear differences between the carbohydrate conditions were evident (Fig. 4).

Almost certain small (0.5- and 0.8-Ratio) and moderate (1.25-Ratio) increases in plasma lactate concentration were

Table 1. *Oxidation rate of endogenous and exogenous substrates during the 60th to 150th minute of the 150-min ride*

Substrate	Condition				CV
	Water	0.5 Ratio	0.8 Ratio	1.25 Ratio	
Exogenous carbohydrate		1.04	1.14	1.05	20
Endogenous carbohydrate	0.86	0.95	0.89	0.82	57
Total carbohydrate	0.86	2.04	2.07	1.91	53
Endogenous fat	0.98	0.59	0.61	0.62	34

Data are the back log-transformed least-squares mean oxidation rate values (in g/min) for 60- to 150-min sampling points, inclusive. The composite between-subject coefficient of variation (CV, %) was derived from the analysis.

Table 2. *Summary of the effect of solution composition on substrate oxidation rate from the 60th to 150th minute of the 150-min ride*

Substrate	Mean Effect Comparisons with ±90%CL and Qualitative Inference					
	0.5 Ratio Minus Water	0.8 Ratio Minus Water	1.25 Ratio Minus Water	0.8 Ratio Minus 0.5 Ratio	0.8 Ratio Minus 1.25 Ratio	1.25 Ratio Minus 0.5 Ratio
Exogenous carbohydrate				11.2 ± 3.7	10.2 ± 3.8	1.1 ± 4.2
				small ⇑ almost certain	small ⇑ almost certain	trivial ⇑ likely
Endogenous carbohydrate	10.6 ± 12.1	3.3 ± 11.3	4.9 ± 10.4	−7.0 ± 11.7	8.0 ± 10.1	−14.0 ± 9.4
	trivial ⇑ likely	trivial ⇑ very likely	trivial ⇑ likely	unclear	unclear	unclear
Total carbohydrate	137 ± 24	140 ± 24	122 ± 22	1.5 ± 10.0	7.7 ± 9.4	−6.3 ± 9.5
	moderate ⇑ almost certain	moderate ⇑ almost certain	moderate ⇑ almost certain	unclear	unclear	unclear
Endogenous fat	−40.0 ± 3.5	−37.9 ± 3.6	−37.0 ± 3.7	3.4 ± 5.6	−1.4 ± 5.9	−5.0 ± 6.1
	moderate ⇓ almost certain	moderate ⇓ almost certain	moderate ⇓ almost certain	unclear	unclear	unclear

Values are mean % effect of treatment relative to the reference condition on substrate oxidation rate (g/min) ± 90%confidence limits (CL) for the true difference. Qualified thresholds for standardized change: 0–0.2 trivial, 0.2–0.6 small, 0.6–1.2 moderate, 1.2–2.0 large, 2.0–4.0 very large. Threshold for probability of a substantial effect: <1.0% almost certainly not, 1.0–5% very unlikely, 5–25% unlikely, 25–75% possible, 75–95% likely, 95–99% very likely, >99% almost certain; where an effect is unclear, its confidence interval includes both substantial increases and decreases. Arrow symbols indicate an increase (⇑) or decrease (⇓).

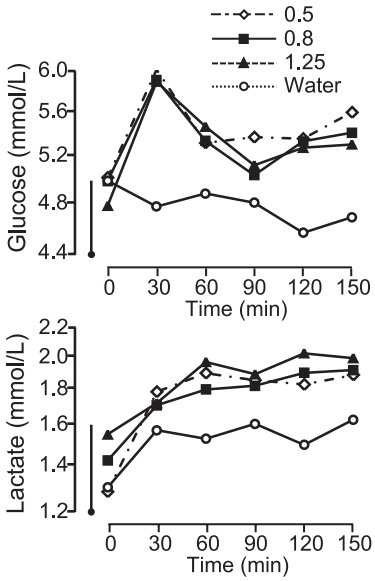

Fig. 4. Plasma lactate and glucose concentrations during the 150-min ride. Data are back log-transformed least-squares means. Bars represent the backtransformed composite between-subject variation.

observed relative to water, but the only effect of carbohydrate ratio was a possible small increase of 7.1 and 7.6% (±5%) in the 1.25-Ratio, relative to the 0.8- and 0.5-Ratio conditions (Fig. 4). From 0 to 150 min there were small increases with 0.8- and 0.5-Ratio, relative to water and the 1.25-Ratio. All other comparisons were unclear.

Gastrointestinal Comfort and Exertion

Gastrointestinal comfort. Throughout the 150-min ride, the average sensation of nausea rated less than slight (i.e., <1 scale unit) in all conditions, with mostly trivial overall differences between all conditions (Fig. 5). The increase in the perception of nausea though (slope effect), however, was moderate in the 0.5-Ratio condition and with water, but only small with the 0.8- and 1.25-Ratio conditions. Correspondingly, the perception of nausea in the 0.8-Ratio condition increased at a slower rate (slope effect) than with the 0.5-Ratio solution and water (0.4 ±0.3 and 0.3 ±0.3 scale units/150 min, respectively).

Perceptions of stomach fullness were slight during the first hour of exercise increasing to mild by the end of the 150-min ride with an overall likely small increase (0.5 ±0.2 scale units) in the perception of stomach fullness with the 0.5-Ratio, relative to the 0.8-Ratio (Fig. 5). Relative to the 0.8-Ratio, the rate of increase in stomach fullness from time 0 to 150 min (slope effect) for 1.25-Ratio and water were likely moderate 1.0 (±0.6) and 0.9 (±0.6) scale units increases, respectively, all other comparisons were trivial.

Meanwhile, the perception of abdominal cramping was rated slight or lower in all conditions, with differences between conditions being likely/very likely trivial. There was, however, a likely small increase in abdominal cramp rating from 0 to 150 min with the 0.5-Ratio solution compared with the 0.8- and 1.25-Ratio solutions (0.4 ±0.3 scale units); other comparisons were unworthy of note.

Exertion. No clear differences in perceived exertion or muscle tiredness were observed between conditions, nor were there any slope effects (Fig. 5).

DISCUSSION

In this study we examined the effect of ingesting solutions containing fructose and maltodextrin at respective ratios of 0.5, 0.8, and 1.25 on exogenous carbohydrate oxidation, gastrointestinal comfort, and endurance performance. We provide further supporting evidence that high-intensity endurance performance is substantially enhanced with the ingestion of the 0.8- and 1.25-Ratio fructose-maltodextrin solutions, compared with the 0.5-Ratio solution and water. In line with the performance outcomes, increases in the perception of stomach fullness, abdominal cramping, and nausea during exercise were perceptibly lower with the 0.8- followed by the 1.25-Ratio solutions, whereas a relative increase in the exogenous carbohydrate oxidation rate was observed only with the 0.8-Ratio solution.

The most important finding in the present study was the 3–4% enhancement of peak power output resulting from the ingestion of the 0.8- and 1.25-Ratio solutions. Although the observed mean enhancements for the 0.8- and 1.25-Ratio solutions were very large and large for the respective comparisons, uncertainty did allow for trivial to extremely large outcomes. Nevertheless, the finding is of interest because we are aware of only 5 of the over 100 publications describing the effects of carbohydrate vs. noncaloric placebo on endurance performance to have examined performance outcomes following ingestion of different types, concentrations, and/or ratios of carbohydrates (11, 28, 29, 34, 41). To our knowledge, this was the first attempt at specifically manipulating the ratio of two different carbohydrates at a fixed total carbohydrate solution concentration and carbohydrate ingestion rate with the aim of examining the impact on performance with reference to readily accessible candidate mechanisms. Reduced carbohydrate availability is

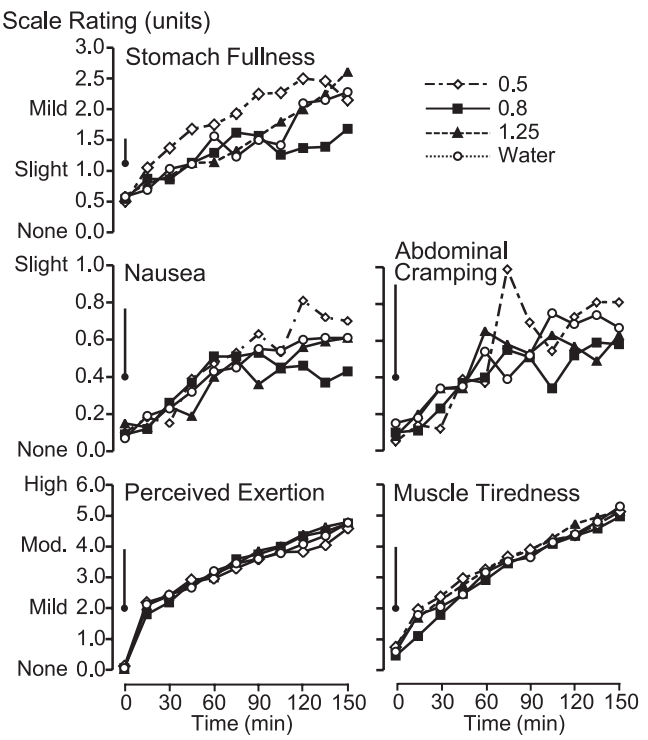

Fig. 5. Ratings of gastrointestinal comfort and perceptions of exertion during the 150-min ride. Data are raw means and bars represent the composite between-subject standard deviation. Mod., moderate.

thought to be an important physiological mechanism leading to fatigue during endurance exercise and provides a foundation rationale for the ingestion of carbohydrate before and during prolonged strenuous exercise (20). Since carbohydrate delivered to the systemic circulation following intestinal absorption is rapidly oxidized by the contracting muscle, end point oxidation of exogenous carbohydrate is a reliable indicator of the efficacy of an ingested carbohydrate solution. The first indication that a 0.8-Ratio of fructose-maltodextrin might optimize exogenous carbohydrate oxidation with impact on performance was provided recently by our laboratory (34). We reported that the exogenous carbohydrate oxidation rate was highest and fatigue rate the least in a series of 10 repeated sprints with the ingestion of a 0.8-Ratio solution. In this earlier study, maltodextrin ingestion was clamped at 0.6 g/min, and ratios similar to those in the present study (i.e., 0.5, 0.8, 1.17) were achieved by altering the quantity of ingested fructose. Earlier, Murray et al. (28) compared the coingestion of a 0.4-Ratio fructose-maltodextrin solution with water and reported a substantial performance improvement with the solution in a 480-pedal-revolution time trial following prolonged cycling. The same group later reported impaired performance with 6% fructose vs. 6% glucose or sucrose solutions and attributed this effect to the high gastrointestinal distress caused by fructose ingestion (29). This finding had a significant impact on the perception of fructose in sports drinks, with many subsequent reviewers and authors warning against the ingestion of higher proportions of fructose in sports beverages. However, our present and other recent data (34) suggest that increasing the fructose content of a sports drink up to a ratio of 1.25 with maltodextrin coingestion may improve performance compared with a carbohydrate solution with lower fructose content, or none at all.

A surprising finding was the unclear difference in peak power between the 0.5-Ratio and water (noncaloric artificially sweetened placebo). Although the chance of either very large substantial benefit or harm to performance remains (Fig. 1), the inconclusive outcome was unexpected given the weight of evidence that carbohydrate ingestion can enhance power in endurance tasks (23). We offer two speculative possibilities to account for the observed unclear trivial effect. Firstly, stomach fullness and nausea ratings during exercise were higher in the 0.5-Ratio condition than with water and, although slight, may have been sufficient to distract subjects during the performance test to force a reduction in effort to an extent that was greater than any possible benefit to high-intensity performance gained through increased carbohydrate availability. Indeed, Thorburn et al. (40) reported a moderate statistical relationship between increased nausea and decreased sprint mean power. Triplett et al. (41) and Jentjens et al. (19) reported higher gastrointestinal discomfort associated with the ingestion of hypertonic glucose-only solutions, which was probably due largely to reduced gastric emptying and high fluid secretion increasing distension (31). Therefore, rather than enhancing performance, the substantial improvements in performance with the 0.5-Ratio glucose-fructose solution in the studies by Currell and Jeukendrup (11) and Triplett et al. may have been the result of a performance impairment induced by the troublesome control solution. A second possibility was that the present negligible effect on peak power between 0.5-Ratio and water might also be indicative of the magnitude of the true placebo effect for carbohydrate beverages. In an ingeniously designed study, Clark et al. (8) reported that the size of the placebo effect of a sports drink on 40-km time trial mean power was 3.8% (±95% CL: −4.1%). Solutions in the present study were double blinded and carefully formulated to ensure similar flavor (concentrated lime juice), acidity, sweetness, and color across all solutions, and our subjects reported they were unable to distinguish between the different solutions. Successful blinding may have been sufficient to create a placebo effect in which subjects believed they were gaining benefit from the ingested solution, a situation that might not have been the case in the other studies because of the differences in unacidified sweetness between the fructose-glucose and the glucose-only solutions.

The third finding of interest was that the rate and efficiency of exogenous carbohydrate oxidation was highest following the ingestion of the 0.8-Ratio solution, albeit by only 0.1 g/min. The observation concurs with the inference from our previous study (34) in which fructose-maltodextrin ratios were similar, but total carbohydrate was provided at the lower ingestion rates of 0.9–1.3 g/min. Therefore, higher exogenous carbohydrate oxidation with the 0.8-Ratio solutions appears robust across a range of carbohydrate ingestion rates. The small increase had little impact on performance in the mechanisms analysis (although the impact on the comparisons with water was considerable), suggesting that the increase in exogenous carbohydrate oxidation rate was unlikely to explain the effect of carbohydrate ratio on performance. The other outcome more suggestive of a mechanism was the highest perception of gut comfort during exercise with the 0.8-Ratio solution. In the mechanisms analysis, nausea lowered the size of the effect of carbohydrate ratio on peak power by around one-quarter (qualitatively a mild-moderate statistical relationship). Nausea can be regarded as an integrated central perception of gut comfort. In recent placebo-controlled mouth-wash studies, carbohydrate rinsing was found to stimulate brain centers possibly associated with reward and motivation (7). Oral taste and/or specific carbohydrate (caloric) receptors were proposed as candidate afferent effectors in the mouth-wash models. In addition, gut receptors responding to distension (i.e., higher perception of stomach fullness on 0.5-Ratio) secondary to differences in gut volume and solution absorption might also provide an afferent mechanism for ingestion scenarios (6). Another intriguing but unexplored sensory neural/neuroendocrine possibility is that the same or a similar comfort or reward mechanism might be activated from the gut in response to differences in carbohydrate formulation. Taste receptors physiologically similar to those studied in the mouth are also located in the gastrointestinal tract (39); moreover, a role for osmosensitive and other chemosensitive (e.g., acid) pathways might also be considered in whatever central (brain) mechanism is involved in keeping discomfort during exercise within acceptable limits (25).

Although the difference in exogenous carbohydrate oxidation rate was small and did not appear to be an important determinant of the present performance outcome, brief commentary is warranted on the mechanism for faster transit and absorption of the 0.8-Ratio solution because it might have influenced the gut comfort outcome. The present solutions were hypertonic when ingested and, following partial hydrolysis of the maltodextrin, likely to have remained so until gastric secretion and solute absorption in the lower segments brought the chyme to isotonicity with body fluids. Therefore,

the majority of carbohydrate and fluid absorption was most likely to have occurred in the jejunum (14). At this site Rumessen and Gudmand-Høyer (35) observed dose dependent glucose stimulated fructose uptake when free fructose and glucose or sucrose were provided, with greatest fructose absorption occurring with ingestion of a 1:1 fructose-glucose ratio. Later, Shi et al. (36) reported that when isotonic and near-isotonic solutions containing several multiple transportable carbohydrates (glucose and fructose or sucrose) were infused at the duodenojejunum, an effective fructose-glucose ratio of 0.7 to 1.0 resulted in faster net carbohydrate and water absorption than solutions with an effective 0.5-Ratio. Shi et al. (37) suggested that adding a second transportable substrate to a glucose solution stimulates additional transport mechanisms, and this might be solute transport via the paracellular pathway; with 19–27% of fructose transport estimated to this pathway (36, 37). Additionally, the opening of tight junctions may enable more fructose and glucose to be transported via solvent drag (36, 37). These observations provide only limited insight into the mechanism, but any increase in the rate of solution absorption associated with carbohydrate characteristics could have been responsible for the alleviation of gut discomfort.

Epithelial transporter saturation might account for the lower relative exogenous carbohydrate oxidation rates in the 0.5- and 1.25-Ratio conditions. The maximal oxidation rate of a single ingested carbohydrate is no more than 1.0–1.1 g/min (20). Therefore, intestinal glucose absorption may have been saturated in the 0.5-Ratio condition, which might have also slowed carbohydrate transport via the solvent drag mechanism; quantification of the absorption and oxidation of the individual sugars would be required to clarify this scenario. In contrast, intestinal glucose transport may have been at or near saturation in the 0.8-Ratio condition, which should have optimized both the rate of fluid absorption and fructose transport via the separate GLUT5 mechanism and the paracellular route. On the other hand, glucose transport efficiency would probably have been highest in the 1.25-Ratio condition, but because the absolute maltodextrin ingestion rate was 50 and 25% lower than in the other two conditions, the total glucose absorption rate was likely to have been lower; furthermore, glucose-oxidation efficiency was lowest in the 1.17-Ratio condition in our previous work (34). In addition, the general oxidation efficiency of exogenous fructose is lower than glucose and was found to decrease with increased coingestion dose (34). Together, these effects might have accounted for the lower total exogenous carbohydrate oxidation rate with the 1.25-Ratio solution. Other factors such as hepatic metabolism might also be influential, with the liver acting as a reservoir for later release of fructose-derived metabolites (2).

An important question is whether the present performance outcome is of a magnitude and nature that is meaningful to real life performance. Different performance tests have been used in each of three recent published studies investigating the effects of carbohydrate formulation on performance: 10 repeated sprints (34), 1-h time trial (11), 100-km time trial (41). We chose peak power in an incremental test to exhaustion for three reasons: *1*) it is one of the most reliable tests of cycling performance (30) with a typical error of ~1.4% (range 1.1–1.7) (4, 26) when performed on good ergometers, *2*) peak power in an incremental test predicts competitive 40-km (18) and 20-km time-trial performance (15), and *3*) an incremental test is easier to administer than our recent repeat-sprint test (34) and might also be more sensitive to the impact of treatment on physiological factors determining performance due to elimination of the bias by pacing inherent in known endpoint performance tests (27), although Amann et al. (3) reported similar sensitivity for time to exhaustion and time trial tests in response to physiological intervention. Variability (and also intervention effect magnitude) is increased ~1.9-fold (95% CI: 1.4–2.6 fold) by the addition of a preload (16), making the CV range for the present test (1.3%; 99% CI 0.8–2.7%) at the low end of estimates for other similar tests of 2.1–3.2% (1.9 × 1.1–1.7). This remarkably low CV supports the tight execution of the present experiment and suggests that the slow-ramp protocol is one of the most sensitive endurance performance tests available. These data also suggest that the outcome in the present study is of similar effective reliability to incremental tests without a preload and, as expected, directly in line with estimates for the reliability of competitive endurance-cycling time trial performance of 1.3–1.7% (i.e., 2.8%/1.9 = 1.5%) (30), suggesting that the outcome in the laboratory may transfer to the field. Improvement in time to complete a 30-km running race (2.2%) (42) was observed with a 5% carbohydrate beverage vs. water, whereas we observed a 1.8% (90%CL ± 1.7%) improvement in mountain bike race time with the ingestion of 0.5-Ratio fructose-maltodextrin vs. glucose-maltodextrin (Rowlands DS, Swift M, unpublished data). Therefore, in light of our estimate for the smallest worthwhile effect on performance of 0.4% (0.3 × 1.3%), the 3.6 and 3.0% enhancements in performance in the 0.8- and 1.25-Ratio vs. 0.5-Ratio solutions, coupled with benefit likelihoods of 99.9 and 99.4%, is in our view noteworthy, and further investigation in field and other trials using state-of-the-art research designs and ergometry is warranted.

To conclude, we report for the first time substantially higher peak power with the ingestion of equicaloric solutions comprising fructose and maltodextrin in a ratio of 0.8:1 and 1.25:1, relative to both water and a 0.5-Ratio solution. We also report that performance with the 0.5-Ratio was not clearly different than water. The exogenous carbohydrate oxidation rate was highest and the reduction in gut comfort the least with the 0.8-Ratio solution. Solutions comprising a ratio of fructose-maltodextrin at ~0.8 may offer the most favorable practical implications if used in oral energy-hydration formulations.

ACKNOWLEDGMENTS

We thank Andy Hollings, Dan Wadsworth, and Steven Doeven for assistance in the laboratory.

GRANTS

This research was funded by an Institute of Food, Nutrition, and Human Health Post-Graduate Project Grant and income obtained from services provided by the Exercise Physiology and Metabolism Laboratory, Massey University, Wellington.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

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