Metabolic response to carbohydrate ingestion during exercise in males and females

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The influence of sex-related differences on the metabolic response to carbohydrate ingestion during exercise has received considerable interest in the last 10–15 years. The majority of well-controlled studies indicate that, compared with men, women rely more on fat and less on carbohydrate (CHO) oxidation during aerobic exercise performed at the same relative intensity (for reviews, see Refs. 31 and 33). Sex-related differences in the metabolic response to exercise could have implications for nutritional recommendations and athletic performance for male and female athletes (30, 32). In this respect, the metabolic and performance responses to the ingestion of CHO during exercise have been investigated over the last 25 years (for review, see Ref. 18), although the extent to which sex directly influences these responses has not been comprehensively studied.

CHO supplementation during exercise increases endurance exercise capacity and performance in males and females (1, 2, 5, 6, 8, 9). This effect is largely attributed to increased CHO oxidation and maintenance of euglycemia during exercise, particularly as exercise duration increases and endogenous CHO stores become low (6, 8). Studies using isotope dilution techniques have shown that glucose turnover, as measured by the rates of appearance and disappearance of glucose ($R_a$ and $R_d$ glucose), is increased in both sexes when CHO is ingested during exercise (3, 5, 20, 21, 24). In addition, in men (3, 20, 21, 24) and women (5), CHO ingestion during exercise reduces and replaces hepatic glucose production, which is indicative of liver glycogen sparing. It is generally accepted that CHO feeding does not affect the rate of muscle glycogen utilization during exercise (cycling) in males (3, 8, 11, 20, 21, 24). In contrast, it has been reported that CHO ingestion during cycling exercise could reduce muscle glycogen utilization during exercise in females (5), although to our knowledge no study has attempted to substantiate this finding.

Most of the aforementioned investigations were single-sex studies, and thus it is not possible to make direct comparisons between men and women. Two studies have directly investigated potential sex-related differences in substrate metabolism with CHO ingestion during exercise (23, 27), both using $^{13}$C-labeled glucose ingestion to obtain measures of exogenous and endogenous CHO oxidation during exercise in men and women. However, these studies did not use isotopic tracers or measure plasma glucose enrichment, and therefore, estimates of the effects of CHO ingestion on glucose kinetics and the oxidation of the respective endogenous CHO sources (liver and muscle glycogen) during exercise could not be made.

The purpose of the present study was to use indirect calorimetry and stable isotope techniques to make a detailed comparison of the metabolic response to CHO ingestion during exercise in moderately endurance-trained men and women.

METHODS

Subjects. Sixteen healthy, moderately endurance-trained volunteers (8 males and 8 females) participated in the study, which was approved by the South Birmingham (UK) Local Research Ethics Committee. Volunteer characteristics can be seen in Table 1. Females were eumenorrheic, with a normal menstrual cycle length of 25–32 days, and had not taken hormonal contraceptive agents for $\geq 6$ mo before...
testing. All subjects were informed of the purpose, practical details, and risks associated with the procedures before they gave their informed, written consent to participate.

**Preliminary testing.** Within 2 wk of the commencement of the main experimental trials, subjects attended the laboratory for the assessment of body composition from skinfold thickness measurements (15, 16). In addition, maximal oxygen uptake (VO₂,max) and maximal power output (Wₘₐₓ) were determined by the use of an incremental exercise test on an electromagnetically braked cycle ergometer (Lode Excalibur Sport, Groningen, The Netherlands), as described previously (34). Venous blood samples were collected throughout the test to determine lactate threshold (12). Gas exchange measurements during this test were made using an automated online gas analysis system (Oxycon Pro; Jaeger, Wuerzburg, Germany). Wₘₐₓ values were used to determine 55% Wₘₐₓ, which was the workload later employed in the experimental trials.

**Experimental control.** The CHO solution that was to be ingested had high natural ¹³C abundance to quantify exogenous CHO oxidation. Therefore, subjects followed a specific exercise-diet regimen in the 4–7 days leading up to the experimental trials to reduce the background shift (change in ¹³C) from endogenous substrate stores during exercise, as described previously (34). On the day before each experimental trial, subjects were asked to refrain from exercise and were provided with a diet to consume. Daily energy requirements were estimated by the use of standard equations for the calculation of resting metabolic rate (13), and this value was multiplied by an output (Wₘₐₓ) were determined by the use of an incremental exercise test on an electromagnetically braked cycle ergometer (Lode Excalibur Sport, Groningen, The Netherlands), as described previously (34). Venous blood samples were collected throughout the test to determine lactate threshold (12). Gas exchange measurements during this test were made using an automated online gas analysis system (Oxycon Pro; Jaeger, Wuerzburg, Germany). Wₘₐₓ values were used to determine 55% Wₘₐₓ, which was the workload later employed in the experimental trials.

**Experimental design.** Each subject performed two exercise trials consisting of 120 min of cycling at 55% Wₘₐₓ when ingesting a 10.9% glucose solution (CHO) or plain water (WAT). The CHO ingestion rate during exercise was 1.5 g/min (90 g/h). The CHO solution was prepared from corn-derived glucose (Meritose 200; Amylum Europe, Aaslt, Belgium), which has a high natural abundance of ¹³C (−10.77% vs. Pee Dee Belemnitiella). The order of the trials was randomly assigned and separated by 4–7 days. Females performed the trials in the follicular phase of one menstrual cycle (days 3–12, WAT trial on average day 7 ± 1, CHO trial on average day 8 ± 1). Four females commenced with the CHO trial and four with the WAT trial. Menstrual cycle status was confirmed after the testing period by analysis of preexercise blood samples for plasma estradiol and progesterone concentrations (CHO trial: estradiol 47 ± 4 pg/ml, progesterone 0.27 ± 0.07 ng/ml; WAT trial: estradiol 47 ± 8 pg/ml, progesterone 0.28 ± 0.07 ng/ml). These values are in the normal range for this phase of the menstrual cycle (31).

**Experimental protocol.** After arrival at the laboratory and an overnight fast (>10 h), subjects were weighed before a catheter (Venflon, Becton-Dickinson, Plymouth, UK) was inserted into an antecubital vein of each arm and attached to a three-way stopcock (Sims Portex, Kingsmead, UK) to enable stable isotope infusion and repeated blood sampling during exercise. A basal blood sample was collected before a primed continuous infusion of [6,6-²H₂]glucose (prime, 18.54 ± 1.83 µmol·kg⁻¹·min⁻¹; continuous, 0.32 ± 0.1 µmol·kg⁻¹·min⁻¹) and [1,1,2,3-³H₃]glycerol (prime, 5.6 ± 0.53 µmol·kg⁻¹·min⁻¹; continuous, 0.1 ± 0.00 µmol·kg⁻¹·min⁻¹) was commenced for 60 min of semisupine rest and the duration of the 120-min exercise period by use of a calibrated syringe pump (Asena GS Syringe Pump; Alaris Medical Systems, Basingstoke, UK). The concentration of isotopes in the infusate was determined for all trials to calculate the exact tracer infusion rate.

After the rest period, subjects cycled for 120 min at a workload corresponding to 55% Wₘₐₓ. At the onset of exercise the infusion rate for the glucose and glycerol tracers was increased to 0.63 ± 0.02 and 0.19 ± 0.01 µmol·kg⁻¹·min⁻¹, respectively, and this was continued for the duration of the exercise bout. Subjects ingested 600 ml of the CHO solution or WAT at the start of exercise and an additional 150 ml every 15 min thereafter. Blood samples were collected at rest, and blood samples and respiratory measurements (VO₂, CO₂ production, VCO₂, and respiratory exchange ratio [RER]) were collected at 15-min intervals during the exercise period, the latter via an automated online gas analysis system, as described in Preliminary testing. At the same time points, expiratory breath samples were collected in duplicate into Exetainer tubes (Labco, High Wycombe, UK), which were filled directly from a mixing chamber to determine the ¹³C-to-¹²C ratio in the expired breath. All exercise tests were performed under normal and standard environmental conditions (16–20°C dry bulb temperature and 50–60% relative humidity).

**Analyses.** All blood samples were collected into vacutainers containing EDTA and stored on ice until centrifugation at 3,000 rpm for 10 min at 4°C. After centrifugation, aliquots of the plasma were frozen in liquid nitrogen and stored at −25°C until further analysis. Plasma samples were analyzed by the use of commercially available assays for glucose (Glucose HK; ABX Diagnostics, Sheffield, UK), lactate (lactic acid, ABX Diagnostics), free fatty acids (FFA; NEFA-C kit; Alpha Laboratories, Eastleigh, UK), and glycerol (Scil Diagnostics, Viernheim, Germany) concentration on a semiautomatic analyzer (Cobas Mira S-Plus, ABX Diagnostics). Estradiol, progesterone, and insulin concentrations were determined using enzyme immunoassays (Estradiol ELISA, Progesterone ELISA, and Ultra-Sensitive Insulin ELISA; IDS, Tyne and Wear, UK).

Glucose and glycerol concentrations were determined on deproteinized plasma samples, with the heptfluorobutyric anhydride derivative used as previously described (17). The enrichment of the derivative was measured by use of gas chromatography-mass spectrometry (GC-MS: GC, Agilent 6890N; MS, Agilent 5973N; Agilent Technologies, Stockport, UK), with glucose and glycerol data acquired through the use of selected ion monitoring for masses m/z (mass-to-charge ratio) 519/521 and m/z 253/257, respectively. Breath samples were analyzed for ¹³C/¹²C ratio by continuous flow isotope ratio mass spectrometry (IRMS), and the ¹³C enrichment of the ingested glucose solution was determined by elemental analyzer IRMS (Europa Scientific, Crewe, UK).

**Calculations.** Total CHO and fat oxidation were calculated from stoichiometric equations (22), with protein oxidation assumed to be negligible. In the CHO trial, the rate of exogenous CHO oxidation was

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**Table 1. Subjects’ physical and training characteristics**

<table>
<thead>
<tr>
<th></th>
<th>Male (n = 8)</th>
<th>Female (n = 8)</th>
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</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>32 ± 2</td>
<td>32 ± 3</td>
</tr>
<tr>
<td>Height, cm</td>
<td>179 ± 3</td>
<td>169 ± 1*</td>
</tr>
<tr>
<td>Mass, kg</td>
<td>78.3 ± 2.6</td>
<td>65.2 ± 2.2*</td>
</tr>
<tr>
<td>LBM, kg</td>
<td>70.0 ± 2.2</td>
<td>53.5 ± 1.7*</td>
</tr>
<tr>
<td>Body fat, %</td>
<td>10.5 ± 1.2</td>
<td>17.8 ± 0.8*</td>
</tr>
<tr>
<td>VO₂max, l/min</td>
<td>4.3 ± 0.2</td>
<td>3.4 ± 0.2*</td>
</tr>
<tr>
<td>VO₂max, ml·kg⁻¹</td>
<td>61.4 ± 1.5</td>
<td>63.6 ± 2.4</td>
</tr>
<tr>
<td>Wₘₐₓ, W</td>
<td>335 ± 14</td>
<td>269 ± 7*</td>
</tr>
<tr>
<td>Wₘₐₓ, W/kg·LBM</td>
<td>4.8 ± 0.2</td>
<td>5.1 ± 0.2</td>
</tr>
<tr>
<td>Lactate threshold, %Wₘₐₓ</td>
<td>65.8 ± 2.2</td>
<td>67.3 ± 2.6</td>
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<tr>
<td>Training history</td>
<td></td>
<td></td>
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<tr>
<td>Length of training, yr</td>
<td>4.3 ± 1.3</td>
<td>5.3 ± 1.1</td>
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<tr>
<td>Frequency, days/wk</td>
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<td>3.3 ± 0.5</td>
</tr>
<tr>
<td>Duration, h/wk</td>
<td>6.2 ± 1.0</td>
<td>6.5 ± 1.3</td>
</tr>
</tbody>
</table>

Values are means ± SE. LBM, lean body mass; Wₘₐₓ, maximal power output. *Significant difference from corresponding value in males, P < 0.05.
calculated from the measured production of $^{13}$CO$_2$ in the expired breath (26), corrected for background $^{13}$CO$_2$ in the WAT trial, as previously described (34). Recovery of $^{13}$CO$_2$ from oxidation of the ingested CHO will approach 100% after 60 min of exercise, when dilution in the bicarbonate pool becomes negligible (25, 28). As a consequence of this, all calculations on substrate oxidation were performed over the last 60 min of exercise (60–120 min).

$R_a$ and $R_d$ of glucose and glycerol were calculated by using the one-pool, non-steady-state model (29), which was modified for use with stable isotopes (35). Total $R_a$ glucose represents the splanchnic $R_a$ glucose from ingested CHO, liver glycoanalyis, and gluconeogenesis, whereas $R_a$ glycerol provides a minimal estimate of whole body lipolytic rate during exercise. $R_d$ glucose was taken to represent plasma glucose oxidation, with the assumption that 96–100% of $R_d$ glucose is oxidized during exercise (20). Accordingly, estimated muscle glycerol oxidation was calculated from total CHO oxidation minus plasma glucose oxidation, and the oxidation of glucose derived from the liver was calculated from plasma glucose oxidation minus exogenous CHO oxidation. Glucose metabolic clearance rate (MCR) was calculated as $R_d$ glucose divided by mean glucose concentration over that time period.

Statistics. All data are expressed as means ± SE. Independent t-tests were used to compare differences in subject characteristics and dietary intake between men and women, resting sex hormone concentrations for the women, and sex differences in the magnitude of change in metabolic parameters with CHO ingestion. A two-way analysis of variance (ANOVA) for repeated measures was performed to study differences in metabolic measurements over time between the trials. Sex was included as a between-subject factor within the ANOVA to determine differences over time and trial between sexes. Analyses were adjusted by use of the Greenhouse-Geisser correction where necessary. Significant effects were followed by post hoc comparisons (Tukey HSD). For all statistical analyses, significance was accepted at $P < 0.05$.

RESULTS

Physical characteristics. Physical and training characteristics obtained before the experimental trials are summarized in Table 1. Males were taller, with more LBM and total body mass than the females ($P < 0.05$), and the females had a higher percentage of body fat ($P < 0.05$). The males had a higher absolute $V_{O2}$ max and $W_{max}$ than the females ($P < 0.05$). There was no difference in $V_{O2}$ max or $W_{max}$ experienced relative to LBM, lactate threshold, cycle training history, and present cycle training load (self-reported cycle training in the 3-mo period before testing).

Exercise intensity and energy expenditure. During the exercise trials the absolute workload was higher for the males than for the females ($180 ± 6$ and $146 ± 4$ W, respectively, $P < 0.05$). Accordingly, absolute $V_{O2}$ and energy expenditure during exercise were similar across trials but significantly higher in males than in females ($V_{O2}$, ~2.8 and ~2.3 l/min; energy expenditure, ~58 and 47 kJ/min for males and females respectively; main effect of sex, $P < 0.05$). When expressed as relative exercise intensity, the workload of 55% $W_{max}$ that was utilized for the experimental trials corresponded to an intensity of ~67% $V_{O2}$ max, and this was similar for each sex and trial.

RER and total CHO and fat oxidation. As is shown in Table 2, RER and total CHO oxidation were higher, whereas total fat oxidation was lower, in the CHO trial vs. WAT for both sexes (main effect of trial, $P < 0.05$). Furthermore, the magnitude of change in these parameters in response to CHO ingestion in both absolute and relative terms did not differ significantly between males and females (Table 2). For each trial, there were no statistically significant sex-related differences in RER, total fat oxidation, or total CHO oxidation.

Exogenous CHO oxidation. Exogenous CHO oxidation over time in the CHO trial is depicted in Fig. 1. For both males and females, exogenous CHO oxidation rates gradually increased during the first 90 min of exercise and leveled off in the last 30 min of exercise. Peak oxidation rates achieved at the final collection point (120 min) were $0.70 ± 0.08$ and $0.65 ± 0.06$ g/min for males and females, respectively.

Plasma glucose kinetics. Glucose isotopic enrichment in plasma was similar between sexes during exercise in both trials, ranging between 1.7 and 2.4% and 0.9 and 1.0% for the WAT and CHO trials, respectively (main effect of trial, $P < 0.05$; Fig. 2A). Plasma glucose enrichment was relatively constant during the last 60 min of exercise in the CHO trial, although a small but significant reduction in enrichment was observed over time in the WAT trial (~0.4%; $P < 0.05$; trial × time interaction). For both sexes, $R_a$ and $R_d$ of glucose and MCR during the last 60 min of exercise were higher in the CHO trial than in the WAT trial (main effect of trial, $P < 0.05$; Fig. 2, B–D, respectively). No statistically significant differences between the males and females were observed for any of these kinetic parameters during both trials.

| Table 2. RER, total CHO and fat oxidation, oxidation of respective components of CHO sources, and change in their oxidation with CHO ingestion during 60–120-min exercise period |
|-----------------|-----------------|-----------------|-----------------|-----------------|
|                 | Males           |                 | Females         |                 |
|                 | WAT  CHO       | Absolute change | %Change     | WAT  CHO       | Absolute change | %Change     |
| RER             | 0.85±0.02      | 0.88±0.01*     | 0.03±0.01     | 3.6±0.8      | 0.82±0.01      | 0.86±0.01*     | 0.04±0.01     | 4.9±1.1  |
| Total CHO       | 135±13         | 160±11*        | 25±8         | 22±7         | 112±10         | 153±10*       | 41±10         | 41±12 |
| Total fat       | 39±4           | 30±4*          | −8±1         | −22±5        | 48±3           | 37±2*         | −10±2         | −21±4 |
| Exo CHO         | 48±6           |               |              |              | 113±11         | 93±10*        | −20±10        | −16±8 |
| Endo CHO        | 135±15         | 112±11*        | −23±11       | −14±7        | 29±1           | 61±4*         | 32±4          | 116±15 |
| PGO             | 29±2           | 53±4*          | 23±4         | 86±19        | 89±10          | 93±11         | 4±12          | 10±16 |
| MGO             | 108±12         | 108±11         | 0±7          | 3±8          | 24±1           | 2±3*          | −29±4         | −100±15 |
| LGO             | 26±2           | 4±7*           | −24±8        | −81±26       |                |               |               |         |

Values are means ± SE and, except for RER, are in μmol·kg⁻¹·LBM⁻¹·min⁻¹; n = 8 per group. WAT, water; CHO, carbohydrate; RER, respiratory exchange ratio; Exo CHO, exogenous CHO oxidation; Endo CHO, endogenous CHO oxidation; PGO, plasma glucose oxidation; MGO, muscle glycogen oxidation; LGO, liver-derived glucose oxidation. *Main effect of CHO vs. WAT, P < 0.05; †main effect of sex, P < 0.05.
Oxidation of CHO sources and relative contribution of substrates to energy. The oxidation of the respective CHO sources during the last 60 min of exercise is shown in Table 2. The rate of endogenous CHO oxidation was significantly lower in females than in males (main effect of sex, $P < 0.05$). In addition, endogenous CHO oxidation was lower in the CHO trial vs. the WAT trial for both sexes (main effect of trial, $P < 0.05$). This reduction was largely due to an almost complete suppression of liver-derived glucose oxidation when CHO was ingested during exercise (main effect of trial, $P < 0.05$). Despite this, plasma glucose oxidation was significantly higher (main effect of trial, $P < 0.05$) in the CHO trial vs. WAT for both sexes as a result of the oxidation of the ingested CHO during exercise. Estimated muscle glycogen oxidation was similar in both the WAT and CHO trials for both sexes. The magnitude of reduction in endogenous CHO oxidation and liver-derived glucose oxidation and the increase in plasma glucose oxidation in both absolute and relative terms did not differ significantly between males and females (Table 2). Across all trials, there were no significant main effects for sex in the rate of plasma glucose, liver-derived glucose, or muscle glycogen oxidation.

Overall, the relative contribution of endogenous CHO oxidation to energy was lower in the females compared with the males in both trials (main effect of sex, $P = 0.036$). However, the contribution of endogenous CHO to the energy yield was reduced to a similar extent with CHO ingestion in males and females ($8 \pm 5$ and $8 \pm 4\%$ reduction for males and females, respectively). The contribution of liver-derived glucose oxidation and fat oxidation was lower and the contribution of exogenous CHO higher in the CHO trial vs. the WAT trial (all main effects of trial, $P < 0.05$), whereas the contribution of muscle glycogen oxidation was unaffected by CHO ingestion for both males and females (Fig. 3). No significant main effects of sex were observed in the relative contributions of fat, exogenous CHO, liver-derived glucose, or muscle glycogen oxidation to total energy expenditure during the last 60 min of exercise (Fig. 3).

Plasma concentrations of metabolites and insulin. Plasma glucose, lactate, FFA, glycerol, and insulin concentrations were similar between sex at rest in all trials (Fig. 4, A–E). During exercise, plasma glucose concentrations for both sexes were higher in the CHO trial vs. the WAT trial during the first 30 and final 30–45 min of exercise (Fig. 4A). Plasma lactate concentrations were similar for males and females during exercise and increased from resting values of $0.8$ to $1.7$ mmol/l after 15 min of exercise and remained elevated between $1.3$ and $2.1$ mmol/l for the duration of exercise (main effect of time, $P < 0.05$; Fig. 4B).

Significant trial $\times$ time $\times$ sex interactions were observed for both the response of plasma FFA and glycerol to exercise. Significant differences in plasma FFA and glycerol concentrations between the WAT and CHO trials for both sexes were observed during exercise in the WAT trial, with the increase resulting in concentrations significantly greater than those observed in the CHO trial. This increase was significantly greater in females compared with males (Fig. 4, C and D). In the CHO trial, plasma FFA concentrations showed...
Glycerol kinetics. Glycerol isotopic enrichment in plasma (Fig. 4A) was similar between sexes during exercise in both trials, ranging between 1.9 and 2.4% and 2.7 and 3.0% for the WAT and CHO trials, respectively (main effect of trial, \( P < 0.05 \)). For both trials and sexes, plasma glycerol enrichment declined steadily over the last 60 min of exercise (\(-0.3\%\); main effect of time, \( P < 0.05 \)). Accordingly, for both sexes the \( R_a \) of glycerol during the last 60 min of exercise was higher in the WAT trial than in the CHO trial (main effect of trial, \( P < 0.05 \); Fig. 4B). No statistically significant differences between the males and females were observed for \( R_a \) glycerol during both trials.

DISCUSSION

This study compared the metabolic response to CHO ingestion during exercise in trained men and women. Compared with when water was ingested, CHO supplementation during exercise 1) increased plasma glucose turnover and oxidation as a result of a significant contribution of the ingested CHO to energy expenditure; 2) reduced the oxidation of endogenous CHO sources, suppressing liver-derived glucose but not muscle glycogen oxidation; and 3) suppressed fat oxidation and other indicators of lipid metabolism. Interestingly, these metabolic responses were remarkably similar in direction and magnitude in trained men and women.
CHO ingestion plasma glucose kinetics and oxidation during exercise. Previously, it was suggested (5) that the increase in plasma glucose turnover (Ra and Rg glucose) and plasma glucose oxidation associated with CHO supplementation during exercise might be greater in females than in males. Although intriguing, this was based upon comparisons between studies independently conducted in men (10) and women (5). The present study is the first to directly compare glucose kinetics in response to CHO ingestion during exercise in both men and women. In contrast to the suggestion by Campbell et al. (5), the increases in plasma glucose turnover and plasma glucose oxidation when CHO was supplemented during exercise were similar in magnitude in men and women (Fig. 2, B-D, and Table 2). The discrepancy between studies might be partly explained by the close matching of men and women in the present study [following procedures suggested elsewhere (31, 33)] and perhaps subtle differences in experimental procedures. Also, the change in glucose turnover and oxidation with the large CHO dose provided in the “male” study (10), upon which the suggestion of Campbell et al. was based (5), was relatively small, particularly compared with that observed in similar studies (3, 20, 21, 24).

CHO ingestion and endogenous fuel utilization during exercise. CHO ingestion reduced the oxidation of endogenous CHO sources (liver and/or muscle glycogen) during exercise to a similar extent in men and women (~15%; Table 2). In contrast, a previous study (27) reported a significantly greater reduction in endogenous CHO oxidation in females (~13%) compared with males (~5%) when CHO was ingested during exercise. CHO was ingested at higher rates in the present study compared with the study by Riddell et al. (present study 1.5 vs. ~1.3 and ~1 g/min in males and females, respectively, in Riddell et al.) (27), which elicited larger reductions in endogenous CHO oxidation in both sexes, and this might have masked differences between men and women. In the present study, the dose of 1.5 g/min was selected to maximize intestinal CHO delivery to the circulation and exogenous CHO oxidation during exercise and subsequently exert the maximal influence on the metabolic responses to exercise in both sexes.

The reduction in endogenous CHO oxidation associated with CHO supplementation resulted from an almost complete suppression of liver-derived glucose oxidation during exercise (Table 2), and this is in line with previous reports (3, 5, 21, 24) indicating that glucose ingestion can partially or completely block endogenous glucose output during exercise. Furthermore, the estimated rate of muscle glycogen oxidation was not affected by CHO ingestion in males or females (Table 2). This is consistent with the majority of studies that investigated CHO supplementation during exercise in males (3, 8, 11, 20, 21, 24) but differs from the only previous study (5) performed in females. Indeed, Campbell et al. (5) reported a small (~2.6%) but significant reduction in estimated muscle glycogen utilization during 120 min of cycling at 70% V̇O₂max in trained females. The reasons for the discrepancy in the findings for females in the present study and those in the study by Campbell et al. (5) are not clear, because no major differences in experimental design exist between the two studies, although a larger CHO dose (~30 g/h) was used in the present study. On balance, it would seem that, although CHO supplementation can exert a large influence on liver glucose production and oxidation during prolonged cycling exercise, the effects on the rate of muscle glycogen utilization appear to be minor in both males and females.

In the present study, CHO ingestion induced a marked but very similar reduction in fat oxidation during exercise in both sexes (Table 2). The reduction in fat oxidation might be, in part, insulin mediated, because this hormone is a potent inhibitor of lipolysis during exercise (4, 14). Indeed, the elevated insulin concentrations in both sexes with CHO ingestion (Fig. 4E) in the present study were associated with a reduction in whole body lipolysis, as was indicated by a lower glycerol Rg (Fig. 5B), as well as a blunted rise in plasma FFA and glycerol concentrations during exercise (Fig. 4, C and D).

Exogenous CHO oxidation during exercise. When expressed in absolute terms (g/min), similar exogenous CHO oxidation rates were observed in males and females when CHO was ingested during exercise (Fig. 1). Although this is consistent with one previous study (27) that investigated sex-related differences in fuel utilization with CHO supplementation, another study (23) has reported significantly higher rates of exogenous CHO oxidation during exercise in males compared with females during exercise (0.9 vs. 0.6 g/min, respectively). The present study and the aforementioned other two studies utilized largely similar subject groups, in terms of aerobic
capacity and training status, and employed a similar relative exercise intensity, duration, and CHO feeding schedule. However, subtle differences in experimental protocol might explain some of the differences between the studies (e.g., variations in absolute CHO dose and/or absolute exercise workload employed).

Exogenous CHO oxidation from orally ingested CHO is mainly limited by the absolute CHO release from the splanchnic region and not at the level of the muscle (18, 19, 21), and therefore, we chose to express exogenous CHO oxidation in absolute terms (g/min). When expressed relative to LBM, Riddell et al. (27) reported significantly higher exogenous CHO oxidation rates in females compared with males toward the end of a prolonged exercise bout. The present data are directionally consistent with this observation, although it is not statistically significant (P = 0.08; Table 2). In contrast, a recent study (23) reported no sex-related differences in exogenous CHO oxidation during prolonged cycling exercise when the data were expressed relative to lean body mass. This issue, along with its physiological significance, is perhaps still to be resolved.

Importantly, all three studies (23, 27, and the present study) that have directly compared the oxidation of ingested CHO in males and women have reported no major sex-related differences in the relative proportions of total energy derived from exogenous CHO sources during exercise. From a practical perspective, the similarities in absolute exogenous CHO oxidation rates and the relative contribution to energy expenditure in the present study imply that males and females might benefit equally from CHO ingestion during exercise. Thus it would seem appropriate for both sexes to follow recommendations to ingest CHO during prolonged exercise at rates of up to ~60 g/h, as previously suggested for males (7, 19).

Summary. CHO ingestion during exercise resulted in marked and directionally similar changes in fuel selection in both males and females. Collectively, these serve to maintain euglycemia when glucose availability is high and to maintain CHO oxidation as muscle glycogen stores become depleted during exercise. From the present data it is concluded that males and females have largely similar metabolic responses to and can benefit equally from the supplementation of CHO during prolonged exercise.

GRANTS

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