Reduction in Muscle Glycogen and Protein Utilization with Glucose Feeding During Exercise

Dennis van Hamont, Christopher R. Harvey, Denis Massicotte, Russell Frew, François Peronnet, and Nancy J. Rehrer

Effects of feeding glucose on substrate metabolism during cycling were studied. Trained (60.0 ± 1.9 mL·kg⁻¹·min⁻¹) males (N = 5) completed two 75 min, 80% VO₂max trials: 125 g ¹³C-glucose (CHO); ¹³C-glucose tracer, 10 g (C). During warm-up (30 min 30% VO₂max) 2 · 2 g ¹³C-glucose was given as bicarbonate pool primer. Breath samples and blood glucose were analyzed for ¹³C/¹²C with IRMS. Protein oxidation was estimated from urine and sweat urea. Indirect calorimetry (protein corrected) and ¹³C/¹²C enrichment in expired CO₂ and blood glucose allowed exogenous (Gexo), endogenous (Gendo), muscle (Gmuscle), and liver glucose oxidation calculations. During exercise (75 min) in CHO versus C (respectively): protein oxidation was lower (6.8 ± 2.7, 18.8 ± 5.9 g; P = 0.01); Gendo was reduced (71.2 ± 3.8, 80.7 ± 5.7%; P = 0.01); Gmuscle was reduced (55.3 ± 6.1, 65.9 ± 6.0%; P = 0.01) compensated by increased Gexo (58.3 ± 2.1, 3.87 ± 0.85 g; P = 0.000002). Glucose ingestion during exercise can spare endogenous protein and carbohydrate, in fed cyclists, without glycogen depletion.

Key Words: mass spectrometry, carbohydrate, metabolism, ¹³C

Previous work has shown that carbohydrate feeding during exercise can increase exogenous carbohydrate oxidation and decrease reliance on endogenous reserves (2, 7, 20, 24, 25). There have been, however, conflicting findings with respect to the source of the endogenous reserves which are spared. Some researchers have observed that (liver derived) blood glucose oxidation is reduced (2, 8, 20), but others have observed a reduction of carbohydrate oxidation derived from muscle glycogen [see Tsintzas and Williams (33) for review]. Part of this inconsistency might be due to the intensity of exercise and the possibility of glycogen synthesis at low intensities, which would appear as “glycogen sparing” (33).

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The contribution of protein to energy provision during exercise has been neglected in many studies of exercise metabolism under the assumption that it is constant or negligible. Contrary to this belief, there is evidence that protein metabolism is increased with exercise (22); however, conflicting findings have been reported. Total body protein utilization during 1 to 2 h of moderate intensity exercise has been reported to increase (5, 14, 21, 22), decrease (12), or remain unchanged (41), compared to rest. This can have a significant effect on calculation of CHO and fat oxidation. Estimates of the contribution of protein as a fuel for moderate intensity exercise have ranged from 1 to 15% of the total energy expenditure (5, 23).

Methods of measuring protein utilization as well as differences in the nutritional state of test subjects could account for these varied results. Lemon and Mullin (22) observed that sweat contributes significantly to nitrogen losses during moderate exercise (61% VO$_{2\text{max}}$) and, thus, if only urinary excretion is measured the protein oxidation will be underestimated. They also observed that protein breakdown was much larger when exercise was conducted in a CHO depleted state (13.7 g/h; 10.4% total energy) than when conducted in a loaded state (5.8 g/h; 4.4% total energy). These findings are supported by a number of researchers who have also observed an increase in protein metabolism during rest or exercise when muscle glycogen stores are insufficient, unavailable, or depleted (21, 30, 33-37).

Other supporting evidence is found in patients suffering from McArdle’s disease. The myophosphorylase deficiency seen in these patients causes an inability to phosphorolyse muscle glycogen and thus it is unavailable as an energy source during exercise. Wahren et al. (40), Slonim and Goans (31), and Wagenmakers et al. (39) observed an increased ammonia production during exercise in these patients. Since the amount of ammonia produced in exercise is estimated to exceed the amount produced in the breakdown from AMP to IMP, it is suggested that the excess originates from amino acid metabolism (34, 39).

A similar observation has been made in trained individuals who performed a 2 h exercise test at 75% VO$_{2\text{max}}$ after either CHO loading or CHO depletion in which glucose was also given during exercise in the loaded state (38). Plasma ammonia concentration increased more rapidly in the CHO depleted state, whereas ATP, ADP, AMP, and IMP concentrations in active muscle were not altered. A significant increase in active branched-chain 2-oxoacid dehydrogenase complex in the CHO-depleted subjects was also observed, indicating an increased deamination of amino acids (38).

It is unexpected that by feeding CHO during exercise protein metabolism would be affected in subjects who are neither glycogen depleted nor compromised in glycogen metabolism. The present study was designed to investigate the effects of glucose feeding on total body substrate utilization during intense (80% VO$_{2\text{max}}$) exercise in trained males. Samples were taken of urine and sweat to quantify protein oxidation by virtue of nitrogen excretion. This was done primarily with the aim to provide an accurate partitioning of substrate metabolism and, in particular, calculation of carbohydrate and fat metabolism, rather than to assess the effect glucose feeding would have on protein oxidation per se. It was anticipated that glucose feeding would not alter protein oxidation during intensive exercise in fed, trained subjects.
Methods

Subjects
Five healthy, trained cyclists (age 18 to 30 y) volunteered after having been informed of the procedures and the possible risks involved and gave written, informed consent for this project which was approved by the Ethics Committee of the Southern Regional Health Authority. The mean age, height, body mass, percent body fat, maximal power output, and maximal oxygen uptake (VO$_{2\text{max}}$) were 22.2 ± 4.7 y, 183.2 ± 11.2 cm, 79.6 ± 11.2 kg, 11.7 ± 2.8%, 388 ± 58 W, and 4.77 ± 0.65 L/min, respectively (mean ± standard deviation).

Protocol
Three days following determination of each subject’s maximal power output and VO$_{2\text{max}}$, each subject performed the first of two 75 min exercise tests at 80% VO$_{2\text{max}}$ on a cycle ergometer (Rodby, Rodby Elektronik AB, Södertälje, Sweden). The 2 trials were separated by at least 1 month. The subjects were asked to abstain from high intensity exercise in the 48 h preceding each trial. Dinner, standardized per individual (6.6 ± 1.1 MJ; 29 ± 2% protein, 16 ± 1% fat, 55 ± 3% carbohydrate) and breakfast, standardized for everyone (2.9 MJ; 12% protein, 10% fat, 78% carbohydrate) were supplied for the night before and the morning of each trial, respectively.

At 6:30 AM on the test day the subjects arrived at the lab and the standardized breakfast was provided at 7:00 AM. At 8:00 AM an indwelling catheter (Adsys, Becton Dickinson, Madrid, Spain) was inserted into an antecubital vein of the right arm. At 8:25 AM the tests started with a 30 min warm-up period, comprising cycling at a workload equivalent to 30% VO$_{2\text{max}}$. A combination of indirect calorimetry and stable isotope methods were used during experimental trials. During the warm-up, subjects received two 150 mL bolus of an enriched $^{13}$C glucose solution, which provided a total of 4 g of carbohydrate. The glucose with an enrichment of −29.38 ‰ δ $^{13}$C PDB-1 (Glucodin, Boots Co., Wellington, New Zealand) was enriched with U $^{13}$C-glucose ($^{13}$C/C > 99%, Isotec, Miamisburg, OH) to achieve a very high isotopic composition (+ 411.5 ‰ δ $^{13}$C PDB-1). The main purpose of providing these drinks during the warm-up period was to prime the bicarbonate pool in the body with $^{13}$C. The warm-up was followed by cycling for 75 min at a workload corresponding to 80% VO$_{2\text{max}}$.

Treatments
Each subject conducted the two treatment trials, in randomized, crossover fashion. One trial was a control trial (C) in which subjects received 2 g of the same highly enriched, $^{13}$C labeled glucose brought to a volume of 175 mL with distilled water at 0, 15, 30, 45, and 60 min during 80% VO$_{2\text{max}}$ exercise. The ingested, $^{13}$C-glucose (in total 10 g, enriched at + 411.5 ‰ δ $^{13}$C PDB-1) in the control trial allowed for quantification of source of glucose oxidized. This methodological approach is currently being used by our research group (3, 7, 16, 17, 30). The other trial was with significant carbohydrate ingestion (CHO) in which the subjects received 175 mL
of a solution containing 25 g $^{13}$C-glucose (+32 ‰ $\delta$ $^{13}$C PDB-1) at the same time points during 80% $V_{O_2}^{\text{max}}$ exercise. Thus, the total glucose load during the 75 min of exercise in this trial was 125 g. The enrichment of $^{13}$C in the ingested glucose ensured a strong isotopic signal detectable in breath samples and plasma glucose isolates. Additional water was given ad libitum and the volume measured.

**Measurements and Analyses**

To assure that the prescribed workload elicited 80% $V_{O_2}^{\text{max}}$, and to determine substrate utilization, oxygen and carbon dioxide were measured with an on-line, open circuit, gas analysis system (SensorMedics, SensorMedics Corp., Anaheim, CA). $V_{O_2}$, $V_{CO_2}$, and $V_{E}$ were computed for 2 min 40 s every 15 min during each trial. At the same time blood samples were drawn. After this, expired air was collected into a Douglas bag for 30 s. Three 20 mL no-additive Vacutainers were filled with expired gas from the bag for analysis of $^{13}$C/$^{12}$C in expired CO$_2$. Sweat samples were taken at regular intervals throughout the trials with the aid of absorbent gauze pads and a small plastic bag taped on the back of the subjects (3). Subjects voided before being weighed and immediately prior to exercise and upon completion of exercise urine was collected.

Plasma glucose concentration was analyzed with the hexokinase reaction (Unimate 5 GLU HK, F. Hoffmann-La Roche AG Diagnostics Division, Basel, Switzerland) on an automated spectrophotometer (Cobas Mira Plus, Roche Diagnostic Systems, Basel, Switzerland). Plasma insulin was analyzed by radio-immunoassay using the Coat a Count method, (Diagnostic Products Corp., Los Angeles, CA) prior to priming, after priming, and immediately following exercise.

Measurement of $^{13}$C/$^{12}$C in expired CO$_2$ was performed by isotope ratio mass spectrometry (Prism, VG, Manchester, England) following cryo-distillation as previously described (1). Blood glucose was isolated, purified, and combusted as described by Burelle et. al. (3). The resultant CO$_2$ was analyzed by isotope ratio mass spectrometry. Sweat and urine samples were spectrophotometrically analyzed for urea (Cobas Mira Plus) with a Unimate 5 Urea kit (Hoffmann-La Roche). The amount of sweat produced during exercise was estimated from the change in body weight corrected for the volume of ingested and excreted fluids, weight change due to exchange of CO$_2$/O$_2$, and the respiratory water vapor loss in the lung (22).

**Calculations**

Carbohydrate and fat oxidation were computed from $VO_2$ and $VCO_2$ corrected for protein oxidation. The energy obtained from protein oxidation was calculated from the calculated urea production from sweat and urine produced during exercise. Protein oxidation was calculated with a value of 2.9 g protein for every 1.0 g of urea and 19.7 kJ per gram of protein (23). Correcting the volume of oxygen and carbon dioxide, $VO_2$ and $VCO_2$, for protein oxidation (1.010 and 0.843 L/g, respectively), glucose ($G_{\text{total}}$), and fatty acid oxidation ($F_{\text{total}}$) was computed from $VO_2$ and $VCO_2$ (28):

$$G_{\text{total}} = 4.58 \cdot \dot{V}CO_2 - 3.22 \cdot \dot{VO}_2$$


with mass of $G_{\text{total}}$ and $F_{\text{total}}$ in g and volume of $\text{VO}_2$ and $\text{VCO}_2$ in L (STPD). The amount of energy derived from glucose and fatty acid oxidation was calculated from the respective energy potential of each at 37 °C, namely, 16.2 and 40.8 kJ/g, respectively (23, 28).

To investigate whether the involvement of protein was of significance in calculating carbohydrate and fat oxidation, two other frequently used calculations were applied (28). Using this set of computations, carbohydrate and fat utilization were calculated totally neglecting the protein contribution (Equations 3 and 4).

\[ G_{\text{total}} = \left( \text{VO}_2 \cdot \left( (RQ - 0.71)/0.29 \right) \right) 0.61 \]  
\[ F_{\text{total}} = \left( \text{PO}_2 \cdot \left( (1-RQ)/0.29 \right) \right) 1.96 \]

The isotopic enrichment ($\% \delta ^{13} \text{C}$) was expressed as the $\% \delta$ difference by comparison with a standard, using the following equation (9):

\[ \% \delta ^{13} \text{C} = \left( \frac{^{13}\text{C} / ^{12}\text{C}_{\text{sample}}}{^{13}\text{C} / ^{12}\text{C}_{\text{standard}}} \right) - 1 \times 10^{3} \]

where $^{13}\text{C} / ^{12}\text{C}_{\text{sample}}$ is the ratio of the sample and $^{13}\text{C} / ^{12}\text{C}_{\text{standard}}$ that of a known laboratory reference standard (1.1237%). The following equations will use $R$ to designate the measured $^{13}\text{C} / ^{12}\text{C}$ ratio.

The oxidation rate of exogenous glucose ($G_{\text{exo}}$) was calculated using the following equation:

\[ G_{\text{exo}} = \text{VCO}_2 \left[ \left( R_{\text{exp}} - R_{\text{ref}} \right) / \left( R_{\text{exo}} - R_{\text{ref}} \right) \right] (1/k) \]

where $\text{VCO}_2$ is in L/min (STPD), $R_{\text{exp}}$ $^{13}\text{C} / ^{12}\text{C}$ ratio in breath samples, $R_{\text{ref}}$ the $^{13}\text{C} / ^{12}\text{C}$ enrichment of breath samples at rest, prior to the warm-up, $R_{\text{exo}}$ the $^{13}\text{C} / ^{12}\text{C}$ ratio in the labeled, exogenous glucose ingested and $k$ is the volume of CO$_2$ produced by the oxidation of 1 g glucose ($k = 0.7426$ L CO$_2$/g glucose) (3, 29). In calculating the exogenous substrate oxidation from the measurement of $^{13}\text{CO}_2$ in expired air, it must be taken into account that exogenous $^{13}\text{CO}_2$ will get trapped in a fairly large bicarbonate pool. The $^{13}\text{C} / ^{12}\text{C}$ in expired CO$_2$ will, thus, only slowly equilibrate with the $^{13}\text{C} / ^{12}\text{C}$ in the CO$_2$ produced in the tissues, especially at rest. Exercise, however, increases the carbon dioxide production and a physiological steady state will therefore occur much more rapidly. After 60 min of exercise the dilution of $^{13}\text{CO}_2$ becomes negligible and the recovery approaches 100%, according to Pallikarakis et al. (27). Moreover, by priming, the bicarbonate pool would have already been labeled.
Based on the $^{13}$C/$^{12}$C ratio of plasma glucose ($R_{glu}$) the oxidation rate of blood-borne glucose ($G_{blood}$) (11) was computed as follows:

$$G_{blood} = VCO_2 \left[ \frac{(R_{exp} - R_{ref})}{(R_{glu} - R_{ref})} \right] (1/k) \tag{7}$$

where $R_{glu}$ is the $^{13}$C/$^{12}$C ratio of plasma glucose.

The rate of oxidation of glucose derived from the liver was calculated as the difference between plasma glucose oxidation ($G_{blood}$, Equation 7) and exogenous glucose oxidation ($G_{exo}$, Equation 6).

$$G_{liver} = G_{blood} - G_{exo} \tag{8}$$

The oxidation of glucose, and C$_3$ products derived from muscle glycogen either directly or through the lactate shuttle, was calculated as the difference in total glucose oxidation ($G_{total}$, Equation 1) and plasma glucose oxidation ($G_{blood}$, Equation 7).

$$G_{muscle} = G_{total} - G_{blood} \tag{9}$$

**Statistics**

Data are presented as means ± standard deviation. Paired Student $t$-tests identified any differences between CHO and C in substrate utilization, total fluid intake, as well as sweat and urine volume, urea concentration, and total urea.

**Results**

The mean oxygen uptake of the 5 subjects, over 75 min of exercise, was similar with and without carbohydrate ingestion (3.65 ± 0.49, 3.62 ± 0.46 L/min, respectively; $P = 0.75$). Mean $VO_2$ and $VCO_2$ per 15 min are presented in Table 1. In the CHO trial, there was a trend ($P = 0.055$) for carbohydrate utilization to be greater than in the C trial (Figure 1). Enrichment values for breath CO$_2$ and blood glucose are presented in Figure 2. The oxidation of exogenous glucose ($G_{exo}$) during exercise was significantly greater in CHO than in C (Figure 3). A mean rate of 0.78 ± 0.03 and 0.05 ± 0.01 g/min of exogenous glucose was oxidized over the 75 min exercise period in CHO and C, respectively. The proportion of endogenous carbohydrate oxidation to total energy utilization was reduced ($P = 0.01$) with CHO (71.2 ± 3.8%) when compared to C (80.7 ± 5.7%) and, in particular, muscle glycogen utilization was reduced with CHO (Figure 3). No significant difference ($P = 0.16$) in liver glucose oxidation was observed (0.77 ± 0.16; 0.67 ± 0.07 g/min, CHO and C, respectively).

Mean rates (g/min) for $G_{exo}$, $G_{liver}$, and $G_{muscle}$ over the last 60 min were 0.72 and 0.05 ($P < 0.00001$); 0.82 and 0.69 ($P = 0.25$); 2.58 and 3.11 ($P = 0.07$), for CHO and C, respectively. Mean rates (g/min) over the last 30 min for $G_{exo}$, $G_{liver}$, and $G_{muscle}$ were 0.93 and 0.08 ($P = 0.00001$); 0.94 and 0.75 ($P = 0.11$); 2.36 and 2.91 ($P = 0.10$), for CHO and C, respectively.
Table 1  Mean Rate of VO\textsubscript{2} Consumption and VCO\textsubscript{2} Production (L/min) During 75 min of 80\% VO\textsubscript{2max} Exercise in Carbohydrate (CHO) and Control (C) Trials

<table>
<thead>
<tr>
<th></th>
<th>Time (min)</th>
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<tr>
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<td>15</td>
<td>30</td>
<td>45</td>
<td>60</td>
<td>75</td>
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<tr>
<td>VO\textsubscript{2}</td>
<td>VCO\textsubscript{2}</td>
<td>VO\textsubscript{2}</td>
<td>VCO\textsubscript{2}</td>
<td>VO\textsubscript{2}</td>
<td>VCO\textsubscript{2}</td>
<td>VO\textsubscript{2}</td>
<td>VCO\textsubscript{2}</td>
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<tr>
<td>C</td>
<td>3.51 ± 0.43</td>
<td>3.40 ± 0.39</td>
<td>3.57 ± 0.51</td>
<td>3.46 ± 0.47</td>
<td>3.70 ± 0.46</td>
<td>3.45 ± 0.42</td>
<td>3.65 ± 0.48</td>
</tr>
<tr>
<td>CHO</td>
<td>3.56 ± 0.46</td>
<td>3.44 ± 0.42</td>
<td>3.75 ± 0.47</td>
<td>3.54 ± 0.42</td>
<td>3.65 ± 0.49</td>
<td>3.54 ± 0.41</td>
<td>3.61 ± 0.51</td>
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*Note.* Values are means ± standard deviation for 5 subjects.
Figure 1 — Mean amount of energy provided by major substrates over 75 min of 80% VO_2max exercise in control and carbohydrate trials. Paired *t*-test indicated a greater amount of energy was derived from protein oxidation in control (C) than in carbohydrate (CHO) trials (** *P* = 0.01).

If only the data from the last 30 or 60 min of exercise were used, when one might expect equilibration to more likely have taken place, no significant differences from those with data from the full 75 min were observed. The energy contribution from fat metabolism was not significantly different (*P* = 0.19) between the trials (Figure 1). Fat contributed 12.5 ± 4.3 and 10.3 ± 5.4% to energy supply in C and CHO trials, respectively. The amount of protein oxidized was significantly less with carbohydrate ingestion than without (6.8 ± 2.7, 18.8 ± 5.9 g, respectively, *P* = 0.01). This resulted in a lower proportion of the total energy being derived from protein when carbohydrate was fed during exercise (Figure 1). There was no significant difference observed in either sweat urea concentration or sweat volume between the control and the carbohydrate trials. Urine volume, and the total amount of urinary urea excreted, were, however, reduced in the CHO trial in contrast to the C trial (Table 2). Total fluid intake was similar in both trials (1530 ± 239; 1731 ± 575 mL, C, CHO, respectively, *P* = 0.255).

When protein contribution to energy expenditure was taken into account, the calculated contribution of the other substrates was altered (Figure 4). Correcting for protein oxidation decreased the calculated amount of energy supplied by both fat and carbohydrate oxidation.
Figure 2 — Enrichment (‰ $\delta^{13}$C PDB-1) of breath CO$_2$ and isolated blood glucose during 80% VO$_{2\text{max}}$ exercise in control (C) and carbohydrate (CHO) trials.

Figure 3 — Glucose oxidation, partitioned by source, during 75 min of 80% VO$_{2\text{max}}$ exercise in control (C) and carbohydrate (CHO) trials. Paired t-tests indicated a greater amount of energy was derived from exogenous glucose and less from muscle glycogen with CHO (** $P < 0.00001$; * $P = 0.03$).
Plasma glucose concentration was similar in both trials, with very little alteration in concentration being observed over the course of exercise (Figure 5). Plasma insulin concentration was similar prior to and during exercise in both treatments. Insulin was somewhat raised at the beginning of exercise but decreased throughout the course of exercise (Figure 6).

![Figure 4](image-url) — Energy provision by major substrates in control (C) and carbohydrate (CHO) trials corrected and uncorrected for protein utilisation over 75 min of 80% VOmax exercise. T-tests indicated a significant difference in fat and carbohydrate oxidation in both C and CHO when corrected for protein oxidation ( **P < 0.01).

### Table 2  Mean Urea Concentration, Volume, and Amount of Urea in Sweat and Urine During 75 min of 80% VOmax Exercise in Control (C) and Carbohydrate (CHO) Trials

<table>
<thead>
<tr>
<th>Source</th>
<th>Trial</th>
<th>Sweat</th>
<th>Urine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C</td>
<td>CHO</td>
<td>C</td>
</tr>
<tr>
<td>Urea (mmol/L)</td>
<td>18.2 ± 20.7</td>
<td>9.2 ± 1.1</td>
<td>278.2 ± 105.4</td>
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<tr>
<td>Volume (L)</td>
<td>1.08 ± 0.65</td>
<td>1.23 ± 0.47</td>
<td>0.36 ± 0.09</td>
</tr>
<tr>
<td>Urea (g)</td>
<td>0.60 ± 0.53</td>
<td>0.68 ± 0.27</td>
<td>5.88 ± 2.17</td>
</tr>
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</table>

*Note. Values are means ± standard deviations for 5 subjects. Significant differences indicated by paired t-tests; *P < 0.05.*

Plasma glucose concentration was similar in both trials, with very little alteration in concentration being observed over the course of exercise (Figure 5). Plasma insulin concentration was similar prior to and during exercise in both treatments. Insulin was somewhat raised at the beginning of exercise but decreased throughout the course of exercise (Figure 6).
Figure 5 — Plasma glucose concentration during 75 min of 80% \( \text{VO}_{2\text{max}} \) exercise in the control (C) and carbohydrate (CHO) trials. No significant differences between treatments were observed.

Figure 6 — Plasma insulin concentration prior to and during 75 min of 80% \( \text{VO}_{2\text{max}} \) exercise in the control (C) and carbohydrate (CHO) trials. No significant differences between treatments were observed.
Discussion

Taking protein oxidation into account can alter calculated contribution of carbohydrate and fat to energy expenditure during exercise. An unexpected finding was that ingesting glucose during sustained, intensive exercise can reduce protein oxidation. A three-fold increase in protein oxidation was observed when subjects did not ingest glucose during exercise in comparison to when glucose was ingested (100 g/h). Although protein contributed only a minor proportion to total energy expenditure during these trials (2%, 6%, CHO and C, respectively) the magnitude of the difference in protein oxidation is significant. It should also be pointed out that urea excretion might underestimate the actual amount of protein catabolism (22), however, any underestimation would be expected to be similar for both treatments. The difference in protein oxidation between treatments is particularly noteworthy in that these subjects were not glycogen depleted, nor were they fasted prior to exercise. Since the early work of Lemon and Mullin (22) it has been known that glycogen depletion increases protein oxidation during exercise. Only limited research has indicated that ingesting glucose, without prior glycogen depletion, can decrease protein oxidation during exercise. Davies et al. (10) observed decreased leucine oxidation with glucose ingestion (15 g/15 min) during the last 90 min of a 3-h bout of 50% VO_{2max} treadmill exercise in men; neither training status nor prior dietary intakes were reported. Hamada et al. (15) have also provided evidence that feeding glucose during exercise can reduce ureagenesis during exercise in dogs. Mongrel dogs were infused with either amino acids or amino acids with glucose during 150 min of exercise. Exercise increased urinary urea production; however, the urea excretion was significantly lower when glucose was fed. It was concluded that a higher rate of gluconeogenesis ensued without glucose administration. This was supported by greater net hepatic glucose output without glucose administration. In the present study, it is plausible that when glucose was not fed gluconeogenesis occurred to a greater extent and resulted in increased urea production from deamination of glucogenic amino acids or due to increased oxidation of branched-chain amino acids (BCAA). Calders et al. (4) have shown that BCAA administration can enhance running to exhaustion in rats to the same extent that glucose administration does. No additional effect was observed when BCAA were given in addition to glucose. They also observed lower blood ammonia concentrations when glucose was fed. It was concluded that glucose administration has an inhibitory effect on amino acid catabolism.

Spencer et al. (32) have shown that TCA cycle intermediates are increased by feeding glucose during exercise. Wagenmakers (37) has hypothesized that this is why higher exercise intensities can be maintained when glucose is fed. If, as Wagenmakers hypothesized, protein catabolism is necessitated by decreasing TCA intermediate concentrations, it is therefore not unreasonable to speculate that feeding glucose could reduce protein catabolism even when glycogen levels are not depleted. The role of TCA cycle intermediate concentration is far from clear, however. Gibala et al. (13) have shown that changes in TCA cycle intermediate pool size does not correlate with oxidative energy provision; moreover, low muscle glycogen concentration was observed to be correlated with a greater TCA intermediate pool expansion during exercise, when compared with normal muscle glycogen concentration.
In contrast to our results, Couture et al. (7), observed no effect of glucose ingestion on protein oxidation (0.13, 0.16 g/min, with and without glucose ingestion, respectively) during prolonged (2 h) running, however, the exercise intensity was lower (69% VO_{2max}).

We also observed a reduction in muscle glycogen oxidation with carbohydrate feeding during exercise. Tsintzas and Williams (33) reviewed the literature on carbohydrate feeding and muscle glycogen utilization during exercise and found that muscle glycogen is sometimes spared (or resynthesized), especially with very low intensity exercise, and in trained athletes, when more than 45 g/h is ingested. Although the intensity was high in the present study, our athletes were well trained and, in addition, received a very high rate of glucose ingestion (100 g/h). Our results are supported by findings of Nicholas et al. (26) who observed glycogen sparing during 90 min of intermittent high-intensity exercise with glucose feeding immediately before exercise and every 15 min thereafter (~ 52 g/h).

Our subjects began exercising after having had a priming load of some glucose during the warm-up and having eaten breakfast. As a result, insulin levels were raised at the beginning of exercise and blood glucose concentrations were maintained throughout exercise. Since insulin and blood glucose concentration were similar in both trials, however, this cannot explain the difference in muscle glycogen oxidation.

An explanation of conflicting results might also be found in the technique that we used to measure “muscle glycogen” oxidation. The calculations involve taking the difference between the total amount of glucose oxidized (G_{total}) and that of blood-borne glucose (G_{blood}). This also includes any C_{3} products derived from all muscles and not just an isolated muscle, either directly or through the lactate shuttle. This might give a slightly different result than that of most previous work conducted with isolated muscle biopsy analysis. In a comparison of muscle glycogen use made in our lab, however, in which vastus lateralis muscle biopsy data were compared with calculated 13C–labeled glucose derived data, a significant correlation between the 2 techniques was observed (18).

The observed oxidation rate of exogenous glucose (0.78 g/min) is in line with data from other studies in which exercise intensity was similar and a large (> 50 g/h) amount of glucose was fed during exercise (6) [see Jeukendrup (19) for review]. The observed rate of oxidation of glucose derived from the liver (0.77 g/min; 0.67 g/min, CHO, C, respectively) is of a similar magnitude to, although somewhat greater than, that observed in studies utilizing lower exercise intensities (2, 3, 6, 7, 20, 24).

Conclusion

Feeding glucose at a high rate during intensive exercise can significantly alter substrate metabolism. Not only can the amount of endogenous carbohydrate oxidized be reduced, but endogenous protein can also be spared, even without prior glycogen depletion or in-born errors in metabolism of glycogen. Taking into account the amount of protein metabolized influences the calculated contributions from fat and carbohydrate sources when doing studies of substrate utilization during exercise.
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References