Oral \([13C]\)glucose and endogenous energy substrate oxidation during prolonged treadmill running

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Couture, Stéphane, Denis Massicotte, Carole Lavoie, Claude Hillaire-Marcel, and François Péronnet. Oral \([13C]\)glucose and endogenous energy substrate oxidation during prolonged treadmill running. J Appl Physiol 92: 1255–1260, 2002. First published November 16, 2001; 10.1152/japplphysiol.00437.2001.—Six male subjects were studied during running exercise (120 min, 69% maximal oxygen consumption) with ingestion of a placebo or 3.5 g/kg of \([13C]\)glucose (~2 g/min). Indirect respiratory calorimetry corrected for urea excretion in urine and sweat, production of \(^{13}C\)O\(_2\) at the mouth, and changes in plasma glucose \(^{13}C/12^C\) were used to compute energy substrate oxidation. The oxidation rate of exogenous glucose increased from 1.02 at minute 60 to 1.22 g/min at minute 120 providing ~24 and 33% of the energy yield (%En). Glucose ingestion did not modify protein oxidation, which provided ~4–5%En, but significantly increased glucose oxidation by ~7%, reduced lipid oxidation by ~16%, and markedly reduced endogenous glucose oxidation (1.25 vs. 2.21 g/min between minutes 80 and 120, respectively). The oxidation rate of glucose released from the liver (0.38 and 0.47 g/min, or 10–13%En at minutes 60 and 120, respectively), and of plasma glucose (1.30–1.69 g/min, or 34 and 45%En and 50 and 75% of glucose oxidation) significantly increased from minutes 60 to 120, whereas the oxidation of muscle glycogen significantly decreased (1.28 to 0.58 g of glucose/min, or 34 and 16%En and 50 and 25% of glucose oxidation). These results indicate that, during moderate prolonged running exercise, ingestion of a very large amount of glucose significantly reduces endogenous glucose oxidation, thus sparing muscle and/or liver glycogen stores.

exogenous glucose; stable isotopes; liver glucose production; muscle glycogen utilization; insulin; blood glucose

There appears to be no detailed description of energy substrate fluxes, and particularly of plasma glucose kinetics, during prolonged running, except for the study by Hall et al. (11), which has only been presented as a preliminary report. Similarly, most of the studies concerning exogenous carbohydrate oxidation during exercise have been conducted on cycle ergometer. In these studies, the oxidation rate of exogenous carbohydrates has been shown to increase with workload (19, 27, 29) and with the amount ingested (1, 14, 36). At high absolute and relative workloads and for large amounts of carbohydrates ingested, the oxidation rate of exogenous glucose plateaus around 1.0 g/min, providing ~25% of the energy yield (13, 14, 26, 36). When running exercise was used, the workload was low [40% maximal oxygen consumption (VO\(_{2\max}\)) (22) or the amount of glucose ingested was small (0.4–0.8 g/min) (27, 28). Accordingly, the oxidation rate of exogenous glucose remained in the lower range of values reported (0.3–0.7 g/min). In the study by Derman et al. (10), exogenous glucose oxidation was compared in response to running and cycling exercise at a high workload (3.6 l O\(_2\)/min; 80% VO\(_{2\max}\)) with ingestion of a large amount of glucose (2.4 g/min). The oxidation rate of exogenous glucose was lower during running than cycling exercise (0.230 and 0.345 g/min, respectively), providing <10% of the total energy yield. However, because of the high workload, the exercise time was comparatively short (cycling: 96 min; running: 63 min). Delays between glucose ingestion, absorption, and oxidation on one hand, and between production of labeled CO\(_2\) in tissues and at the mouth (23) on the other hand, could explain the low oxidation rate observed in this study, and the lower oxidation rate observed during running compared with cycling exercise. In addition, gastric emptying and glucose absorption could be impaired during running exercise, which could be associated with gastrointestinal discomfort when carbohydrates are ingested (9, 31, 32). This could, in turn, reduce the availability and oxidation of exogenous carbohydrates.

The purpose of the present study was to verify this hypothesis and to describe the oxidation rate of a large amount of exogenous glucose during running exercise at a workload chosen to lead to exhaustion in ~2 h in a laboratory setting. The ingested glucose was artificially labeled with \(^{13}C\) to compute its oxidation rate from the production of \(^{13}C\)O\(_2\) (V\(^{13}CO_2\)) at the mouth. In addition, oxidation of plasma glucose was computed.

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from $^{13}$CO$_2$ and $^{13}$C/$^{12}$C in plasma glucose, liver glucose output was estimated by difference between plasma and exogenous glucose oxidation, and the oxidation of muscle glycogen was computed from the difference between total glucose and plasma glucose oxidation (10, 26).

**METHODS**

**Subjects.** Six active and healthy male subjects gave their written consent to participate in this study, which was approved by the Institutional Board on ethics on the use of human in research. Subject mean age, body mass (BM), height, and $\text{V} \text{O}_2 \text{max}$ on treadmill were 26.3 ± 2.8 yr, 70.5 ± 3.3 kg, 174.9 ± 3.7 cm, and 60.0 ± 2.2 ml·kg$^{-1}$·min$^{-1}$, respectively (means ± SE). Subjects were running an average of ~40 km/wk, but none trained for competing in athletic events at a high level. All the subjects had a normal fasting plasma glucose concentration (4.7 ± 0.3 mmol/l). During the 3 days preceding each experiment, subjects refrained from exercising and drinking alcohol. They also avoided ingesting foods containing carbohydrates with a high $^{13}$C content (e.g., corn, sugar cane), which might modify background $^{13}$C enrichment of expired CO$_2$ (16). Compliance with this diet was confirmed by the low background $^{13}$C enrichment of expired CO$_2$, which was similar in the two experimental situations (Table 1).

**Experimental protocol.** $\text{V} \text{O}_2 \text{max}$ and experimental running speed at zero slope on treadmill (Quinton Q45, Bothell, WA) were determined for each subject during a preliminary test session by using open-circuit spirometry (1100 medical gas analyzer, Marquette Electronics, Milwaukee, WI). Then, all subjects performed, at a 7-day interval, two 120-min exercises at zero slope on the treadmill at a speed corresponding to 65% of the maximal running speed reached at $\text{V} \text{O}_2 \text{max}$ (11.4 ± 0.2 km/h; oxygen production ($\text{V} \text{O}_2$) = 2.910 ± 97 ml O$_2$/min or 69 ± 2% $\text{V} \text{O}_2 \text{max}$). Each test was performed at 22 ± 1°C between 9:00 and 11:00 AM after an overnight fast, and a standardized breakfast was taken 2 h before the beginning of exercise (~500 kcal; ~48% carbohydrates, ~35% lipids, ~17% proteins). On the day before each experimental session, the evening meal was standardized and taken between 7:00 and 8:00 PM (~1,200 kcal; ~55% carbohydrates, ~25% lipids, ~20% proteins).

During the experimental trials, subjects ingested, in a single-blind random fashion, either an artif icial solution, as well as for blood sampling at minute 60 (see Measurements and computations). The total amount of glucose ingested was 3.5 g/kg BM or 247 ± 12 g dissolved in 1.645 ± 77 ml of water. The glucose derived from corn [Biopharm, Laval, Canada; $^{13}$C/$^{12}$C = −11.0 %δ $^{13}$C] Pee Dee Belemnita1 (PDB-1) was artificially enriched with [U-$^{13}$C]glucose ($^{13}$C/$^{12}$C > 99%, Isotec, Miamisburg, OH) to achieve a final isotopic composition close to 7 liters $^{13}$C PDB-1 (actual value measured by mass spectrometry: 6.9 %δ $^{13}$C/PDB-1).

**Measurements and computations.** Observations were made at rest before ingestion of the first dose of the solution, just before the beginning of exercise, and every 20 min during the exercise period. Total glucose and lipid oxidations were computed from indirect respiratory calorimetry corrected for protein oxidation. For this purpose $\text{V} \text{O}_2$ and carbon dioxide production ($\text{V} \text{CO}_2$) were measured by using open-circuit spirometry (5-min collection period), and urea production was estimated over the exercise period. Urea excretion over the 120 min of exercise was estimated from its concentration in urine (203 ± 48 and 355 ± 44 mmol/l in the placebo and glucose trials, respectively) and sweat (12.4 ± 1.8 and 12.9 ± 1.6 mmol/l), and from urine (0.36 ± 0.10 and 0.17 ± 0.03 liters) and sweat loss (2.75 ± 0.20 and 2.30 ± 0.21 liters) (3). Sweat loss was estimated from changes in BM, taking into account fluid intake, mass loss through V$_2$O$_2$, and water loss from the lungs (17). For the measurement of $^{13}$C/$^{12}$C in expired CO$_2$, 80-ml samples of expired gas were collected in vacutainers (Becton Dickinson, Franklin Lakes, NJ). Finally, 15-ml blood samples were withdrawn by venipuncture at rest before the first ingestion of the solution and at minutes 60 and 120 during the exercise period for the measurement of plasma glucose, insulin, lactate, and free fatty acid concentrations, and for the determination of $^{13}$C/$^{12}$C in plasma glucose. Plasma, urine, and sweat samples were stored at −80°C until analysis.

**Protein oxidation and the associated amount of energy provided** were computed from the amount of urea excreted, taking into account that 1 g of urea excreted corresponds to 2.9 g of proteins oxidized and that the energy potential of proteins is 4.70 kcal/g (18). Total glucose and lipid oxidation, in grams per minute, were, then, computed from $\text{V} \text{O}_2$ and $\text{V} \text{CO}_2$, in liters per minute (24) corrected for the volumes of O$_2$ and CO$_2$ corresponding to protein oxidation (1.010 and 0.843 l/g, respectively) (18)

\begin{align*}
\text{Glucose} &= 4.59 \text{V} \text{O}_2 - 3.23 \text{V} \text{CO}_2 \quad (1) \\
\text{Lipids} &= 1.70 (\text{V} \text{O}_2 - \text{V} \text{CO}_2) \quad (2)
\end{align*}

The amount of energy provided by the oxidation of glucose and lipids was computed from their respective energy potentials (3.87 and 9.75 kcal/g, respectively) (24). For the measurement of $^{13}$C/$^{12}$C in plasma glucose, glucose was separated by double-bed ion exchange chromatography (AG 50W-X8 H$^+$ and AG 1-X8 chloride, 200–400 mesh, Bio-Rad, Mississauga, Canada) after deproteinization with barium hydroxide and zinc sulfate (0.3 N). The eluate was evaporated to dryness (Virtis Research Equipment, New York, NY) and combusted by 1,645 mmoles/l of water. The glucose derived from corn [Biopharm, Laval, Canada; $^{13}$C/$^{12}$C = −11.0 %δ $^{13}$C] Pee Dee Belemnita1 (PDB-1) was artificially enriched with [U-$^{13}$C]glucose ($^{13}$C/$^{12}$C > 99%, Isotec, Miamisburg, OH) to achieve a final isotopic composition close to 7 liters $^{13}$C PDB-1 (actual value measured by mass spectrometry: 6.9 %δ $^{13}$C/PDB-1).

**Measurement of $^{13}$C/$^{12}$C in expired CO$_2$ and in CO$_2$ from combustion of plasma glucose was performed by mass spectrometry, following cryodistillation as previously described (19). The isotopic composition of ingested glucose, expired

| Table 1. $\text{V} \text{O}_2$, $\text{V} \text{CO}_2$, $^{13}$C/$^{12}$C in expired CO$_2$, and urea excreted in the placebo and glucose trials |
|---|---|---|
| $\text{V} \text{O}_2$ | Time, min | Placebo | Glucose |
| 40–80 | 2.91 ± 0.10 | 2.90 ± 0.09 |
| 80–120 | 2.95 ± 0.09 | 2.85 ± 0.10 |
| $\text{V} \text{CO}_2$ | 40–80 | 2.59 ± 0.11 | 2.62 ± 0.10 |
| 80–120 | 2.58 ± 0.12 | 2.54 ± 0.10 |
| $^{13}$C/$^{12}$C in CO$_2$ | Rest | −23.11 ± 0.46 | −23.07 ± 0.76 |
| % δ$^{13}$C/PDB-1 | 40–80 | −22.06 ± 0.36 | −14.54 ± 1.08 |
| 80–120 | −22.40 ± 0.81 | −12.81 ± 0.50 |
| Urea excreted, mg/min | 0–120 | 54 ± 11 | 45 ± 10 |

Values are means ± SE. $\text{V} \text{O}_2$, oxygen uptake; $\text{V} \text{CO}_2$, CO$_2$ production; PDB-1, Pee Dee Belemnitella.
CO₂, and plasma glucose was expressed in % difference by comparison with the PDB-1 Chicago Standard: \( \%\delta^{13}C_{\text{PDB-1}} = \frac{R_{\text{pl}} - R_{\text{std}}}{R_{\text{std}}} \times 1,000 \), where \( R_{\text{pl}} \) and \( R_{\text{std}} \) are the \( ^{13}C/^{12}C \) ratio in the sample and standard (1.237%), respectively (8).

The oxidation rate of exogenous glucose, in grams per minute, was computed as follows (25)

\[
\text{Exogenous glucose} = \frac{V_{\text{CO}_2} \times (R_{\text{exp}} - R_{\text{ref}})}{(R_{\text{glu}} - R_{\text{ref}}) \times k}
\]

where \( V_{\text{CO}_2} \) (not corrected for protein oxidation) is in l/min, \( R_{\text{exp}} \) is the observed isotopic composition of expired CO₂, \( R_{\text{ref}} \) is the isotopic composition of expired CO₂ in response to exercise when no glucose was ingested, \( R_{\text{glu}} \) is the isotopic composition of the exogenous glucose ingested, and \( k (0.7426 \text{ l/g}) \) is the volume of CO₂ provided by the complete oxidation (6, 15). However, the \( ^{13}C/^{12}C \) of expired CO₂ only slowly equilibrates with \( ^{13}C/^{12}C \) in the CO₂ produced in the tissues (23). To take into account this delay between \( V^{13}CO_2 \) in tissues and at the mouth, computations were made only during the last 80 min of the observation period, thus allowing for a 40-min equilibration period at the beginning of exercise.

On the basis of the isotopic compositions of plasma glucose (\( R_{\text{glu}} \)), expired CO₂ (\( R_{\text{exp}} \)), and expired CO₂ before glucose ingestion (\( R_{\text{ref}} \)), the oxidation rate of plasma glucose was computed at minutes 60 and 120 as follows (26)

\[
\text{plasma glucose} = \frac{V_{\text{CO}_2} \times (R_{\text{exp}} - R_{\text{ref}})}{(R_{\text{glu}} - R_{\text{ref}}) \times k} \tag{4}
\]

The percentage of plasma glucose derived from exogenous glucose was computed as the ratio of exogenous glucose and plasma glucose oxidation rates. The oxidation rate of muscle glycogen (expressed in grams of glucose/min), either directly or through the lactate shuttle (4), was computed as the difference between the rate of total glucose oxidation (Eq. 1) and the oxidation rate of plasma glucose (Eq. 4). Finally, the oxidation rate of glucose released from the liver was estimated as the difference between the oxidation rate of plasma and exogenous glucose.

Plasma glucose, lactate (Sigma Diagnostics, Mississauga, Canada), and free fatty acid (Roche Diagnostics, Laval, Canada) concentrations were measured by using automated spectrophotometric assays, while plasma insulin concentration was measured by using an automated radioimmunoassay (KTSP-11001, Immunocorp Sciences, Montreal, Canada). Urine and sweat urea concentrations were measured by using a Synchorn Clinical System (C7X, Beckman, Anaheim, CA).

Statistics. Data are presented as means \( \pm \) SE. The main effects of time and treatment (placebo and glucose ingestion) as well as time-ingestion interactions were tested by repeated-measure ANOVA (Statistica package). Newman–Keuls post hoc test was used to identify the location of significant differences (\( P \leq 0.05 \)) when ANOVA yielded a significant \( F \) ratio.

RESULTS

Urea excretion, VO₂, and \( V_{\text{CO}_2} \) during the exercise period were not significantly different in the placebo and glucose trials (Table 1). The \( ^{13}C/^{12}C \) in expired CO₂ at rest before ingestion of the solution was also similar in the placebo and glucose trials. In response to exercise in the placebo trial, a small (~1 \( \%\delta^{13}C_{\text{PDB-1}} \)) but significant increase in \( ^{13}C/^{12}C \) in expired CO₂ was observed, as regularly reported (25). A much higher increase (10.3 \( \%\delta^{13}C_{\text{PDB-1}} \)) was observed when \( ^{13}C \) glucose was ingested and oxidized (Table 1).

Table 2 presents the overall substrate utilization over the last 80 min of exercise. Protein oxidation, which was not significantly different in the placebo and control trials, provided, respectively, 4.9 and 4.2% of the total energy yield. When the placebo was ingested, total glucose and fat oxidation were, respectively, lower and higher between minutes 80 and 120 than between minutes 40 and 80. Glucose ingestion, respectively, increased and decreased total glucose and fat oxidation between minutes 80 and 120. This was because of the oxidation of exogenous glucose, which significantly increased from minutes 80 and 120. Over the last 80 min of exercise, 81.6 \( \pm \) 6.6 g of exogenous glucose were oxidized, or 33% of the total amount ingested. In contrast, total endogenous glucose oxidation was significantly reduced when glucose was ingested and oxidized (184.6 \( \pm \) 19.5 vs. 116.7 \( \pm \) 18.4 g, providing 60 and 39% of the energy yield, respectively).

Table 1. Mean (\( \pm \) SE) values for the rate of glucose and substrate oxidation, protein oxidation, and energy cost (min⁻¹ g⁻¹% energy) during the exercise in the placebo and glucose ingestion trials

<table>
<thead>
<tr>
<th>Substrates</th>
<th>Placebo</th>
<th>Glucose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactate</td>
<td>0.48 (0.09)</td>
<td>0.42 (0.15)</td>
</tr>
<tr>
<td>Glucose</td>
<td>2.39 (0.22)</td>
<td>2.58 (0.18)</td>
</tr>
<tr>
<td>Endogenous</td>
<td>2.32 (0.22)</td>
<td>1.66 (0.15)</td>
</tr>
<tr>
<td>Exogenous</td>
<td>0.92 (0.06)</td>
<td>24.2 (1.3)</td>
</tr>
</tbody>
</table>

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Values are means \( \pm \) SE. aSignificantly different from minute 60 (P < 0.05).

Fig. 1. Oxidation rates of glucose from blood, muscle, and a total value (A), and from blood, liver, and an exogenous source (B) at minutes 60 and 120 during the exercise period in the glucose trial. Values are means \( \pm \) SE. aSignificantly different from minute 60 (P < 0.05).

Long distance runners often experience gastrointestinal discomfort when fed carbohydrates, possibly due to impairment in gastric emptying and/or intestinal absorption (9, 31, 32). This could reduce the availability and oxidation of exogenous carbohydrates. However, Rehrer et al. (30) did not report any major difference in gastric emptying in running and cycling at 70% \( \dot{V}O_2 max \) (3.15 l \( \dot{O}_2 \)/min) with ingestion of carbohydrates. In the present study, with an ingestion rate within the same range of that used by Wagenmakers et al. (36) (1.8–2.0 g/min) during cycling exercise at a similar workload (\( \sim 3.0 \) l \( \dot{O}_2 \)/min; 65–70% \( \dot{V}O_2 max \)), the oxidation rate of exogenous glucose over the last 40 min of exercise (1.12 g/min) was very similar to that reported by these authors (1.07 g/min). The smaller values reported by Derman et al. (10) during both cycling and running exercise (0.54 and 0.40 g/min, respectively) with a high ingestion rate (2.4 g/min) could be due to the shorter period of exercise (cycling: 96 min; running: 63 min) and the much higher relative workload sustained (80% \( \dot{V}O_2 max \)). In support of this hypothesis, McConnell et al. (21) have shown that, during a 68-min cycling exercise at 83% \( \dot{V}O_2 max \), only a small portion of ingested glucose entered the plasma (22 vs. 84 g ingested), possibly due to a slow rate of gastric emptying and intestinal absorption at such a high exercise intensity.

Most studies of plasma glucose oxidation, with or without glucose ingestion, have been performed during cycling exercise (2, 5, 12, 14, 20, 21, 26). During running exercise, with ingestion of 150 g of glucose, Derman et al. (10), using \([14C]glucose, have shown that plasma glucose oxidation was 0.83 g/min (0.40 and 0.43 g/min from the liver and from exogenous glucose, respectively) at the end of a 63-min exercise period at 80% \( \dot{V}O_2 max \), providing 23% of the energy yield. A slightly higher value (1.4 g/min) can be computed from data reported by Tsintzas et al. (35) during a 104-min running exercise at 70% \( \dot{V}O_2 max \), with ingestion of 0.6 g of glucose/min; total glucose oxidation computed from indirect calorimetry averaged 3.1 g/min, whereas muscle glycogen oxidation averaged 1.7 g/min (2.5 mmol·min\(^{-1}\)·kg\(^{-1}\) × 3.8 kg of working muscles, dry weight). In the study by Hall et al. (11), the rate of plasma glucose disappearance measured by using \([14C]glucose during a 150- to 165-min running exercise at ~76% \( \dot{V}O_2 max \) averaged only 0.45 g/min, providing 12.2% of the energy yield, but no carbohydrates were ingested.

In the present experiment, with a large amount of glucose ingested (~250 g), glucose release from the liver slightly increased from minutes 60 to 120 (0.38 and 0.47 g/min, respectively) and was well in accordance with data reported at similar workloads during running (11) and cycling exercise (2, 5, 14, 20, 21, 26). Also, as already reported during cycling exercise with carbohydrate ingestion (2, 5, 10, 14, 20, 21, 26), a much higher amount of plasma glucose originated from exogenous glucose (0.92 and 1.22 g/min at minutes 60 and 120, respectively, representing 70–72% of plasma glucose and 36–54% of total glucose oxidation). The rate of plasma glucose oxidation, which was well above 1 g/min at minute 60, reached 1.69 g/min at the end of exercise. These oxidation rates of plasma glucose observed with ingestion of ~2 g of glucose/min, and with
plasma glucose concentration between 7.5 and 8 mmol/l over the last hour of exercise, are in line with those reported by Hawley et al. (12) and Weltan et al. (37). In these studies, with plasma glucose increased to ~9 to 9.7 mmol/l by using glucose infusion (up to ~2.5 to 3 g/min) during prolonged exercise (120–145 min) at 70% \( V_{\text{O}_2\text{max}} \), the oxidation rate of plasma glucose peaked at ~1.75 to 2 g/min. As discussed by McConell et al. (21) the very high oxidation rates of plasma glucose during exercise at 50–70% \( V_{\text{O}_2\text{max}} \), with large amounts of glucose administered, could be due to the high plasma glucose and insulin concentrations, and low plasma free fatty acid concentration, combined to the effect of muscle contraction per se on glucose uptake. In addition, as discussed by Tsintzas and Williams (33), glucose ingestion appears to reduce muscle glycogen utilization during running but not during cycling exercise. This could be associated with a higher rate of plasma glucose oxidation during running than cycling and could explain the comparatively high value observed in the present study.

The oxidation rate of muscle glycogen can be estimated from changes in muscle glycogen content (7, 34, 35) or could be computed by difference between the total oxidation rate of glucose (computed by using indirect respiratory calorimetry) and of plasma glucose (computed by using tracer techniques) (2, 5, 10, 14, 20, 21, 26). Using this method, Derman et al. (10) and McConell et al. (21) have shown at 80–83% \( V_{\text{O}_2\text{max}} \) that the muscle relies much more on muscle glycogen (3.1–3.4 g/min providing 70–82% of the energy yield) than on plasma glucose oxidation (0.8–0.9 g/min). In contrast, for the percentage of \( V_{\text{O}_2\text{max}} \) ranging between 50 and 70%, the oxidation rate of plasma glucose during cycling exercise is much higher, particularly if exogenous glucose is administered, and the oxidation rate of muscle glycogen ranges only between 0.6 and 2.1 g/min, providing 20–58% of the energy yield (2, 5, 14, 20, 26). Data from the present experiment, obtained during running exercise, are in accordance with these previous findings at similar absolute and relative workloads. The oxidation rate of muscle glycogen, which was 1.28 ± 0.19 g of glucose/min at minute 60, providing 33.7% of the energy yield, was reduced to 0.57 ± 0.16 g of glucose/min at the end of the exercise period, providing only 15.5% of the energy yield. These values are lower than the average oxidation rate of muscle glycogen estimated by Tsintzas et al. (1.7 g/min providing 37% of the energy yield) (35). This could stem from the fact that the amount of glucose administered was much higher than in the study by Tsintzas et al. (247 vs. 65 g) (35) and that plasma glucose oxidation was also higher (1.7 vs. 1.4 g/min at minute 120) with, possibly, a larger muscle glycogen sparing.

In summary, results from the present experiment suggest that during prolonged running exercise at ~70% \( V_{\text{O}_2\text{max}} \) with ingestion of large amounts of glucose (~2 g/min), as already shown during cycling exercise, exogenous glucose and plasma glucose, and not muscle glycogen, are the main sources of glucose for oxidation, particularly at the end of exercise. During cycling exercise, the large contribution of exogenous glucose oxidation to the energy yield reduces liver glucose output (2, 14, 20, 21) but does not consistently reduce muscle glycogen utilization (Refs. 2, 14, 21; see Ref. 33 for review). When carbohydrates are ingested during running exercise, no data are available concerning possible changes in liver glucose output, but consistent data indicate that muscle glycogen utilization is reduced (Refs. 34, 35; see Ref. 33 for review). In the
present experiment, the large oxidation rate of exogenous glucose was associated with a marked 37% reduction of endogenous glucose oxidation (68 g between minutes 40 and 120). However, it cannot be ascertained whether this was because of a reduction in muscle and/or liver glycogen utilization.

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