High carbohydrate availability increases LCFA uptake and decreases LCFA oxidation in perfused muscle

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Turcotte, Lorraine P., Jason R. Swenberger, and Alice J. Yee. High carbohydrate availability increases LCFA uptake and decreases LCFA oxidation in perfused muscle. Am J Physiol Endocrinol Metab 282: E177–E183, 2002; 10.1152/ajpendo.00284.2001.—To determine whether changes in long-chain fatty acid (LCFA) oxidative metabolism induced by elevated intracellular carbohydrate availability are due to changes in LCFA uptake or in mitochondrial transport capacity, rat hindquarters were perfused with 500 μM palmitate and [1-14C]palmitate or [1-14C]octanoate as well as with either low (LG) or high (HG) carbohydrate availability. Glucose uptake was higher in the HG vs. LG group (23.6 ± 1.5 vs 4.7 ± 0.9 μmol·g⁻¹·h⁻¹, P < 0.05). Palmitate delivery was not significantly different between groups and averaged 97.1 ± 4.6 nmol·min⁻¹·g⁻¹ (P > 0.05). Fractional and total palmitate uptake values were 60% higher (P < 0.05) in the HG (0.125 ± 0.012 and 7.4 ± 1.2 nmol·min⁻¹·g⁻¹) vs. LG (0.079 ± 0.009 and 11.8 ± 1.5 nmol·min⁻¹·g⁻¹) group. Values of percent and total palmitate oxidized were significantly lower (P < 0.05) in the HG (9.1 ± 1.1% and 1.31 ± 0.16 nmol·min⁻¹·g⁻¹) vs. LG (23.4 ± 5.2% and 0.76 ± 0.08 nmol·min⁻¹·g⁻¹) group. Conversely, values of fractional uptake and percent oxidation of octanoate were not significantly different between groups (P > 0.05). Malonyl-CoA levels were inversely correlated with LCFA oxidation (P < 0.05). These results demonstrate that high carbohydrate availability in muscle is associated with a decrease in LCFA oxidation that is not due to a parallel decrease in LCFA uptake; rather, the decrease in LCFA oxidation could be due to malonyl-CoA inhibition of mitochondrial LCFA transport.

Although the cellular mechanisms by which high carbohydrate availability may regulate plasma LCFA oxidation have not been completely elucidated, potential mechanisms include regulation of LCFA transport into the muscle cell and LCFA transport into the mitochondria (6, 15, 28).

LCFA transport into the muscle cell is dependent on the ability of the cell to carry LCFA across the plasma membrane by diffusion and carrier-mediated transport mechanisms (1). It has generally been accepted that LCFA uptake and oxidation are regulated in concert, reflecting the importance of oxidative metabolism in the regulation of LCFA uptake (34). In line with this notion, LCFA uptake should be decreased by the presence of high carbohydrate availability. Conversely, it has recently been proposed that LCFA uptake may be regulated independently of LCFA oxidative metabolism under some conditions (15). Thus it is presently not known whether LCFA uptake by muscle would be increased, decreased, or unchanged by the presence of high carbohydrate availability.

Mitochondrial LCFA transport capacity refers to the ability of the muscle to carry LCFA from the cytosol to the mitochondria, and alterations in this transport capacity have been implicated in the regulation of LCFA oxidation under some conditions (27, 28). In a physiological preparation, measuring the rate of oxidation of octanoate and comparing the changes in this rate of oxidation to the changes recorded for palmitate allow for assessment of mitochondrial LCFA transport capacity (18). Octanoate, a medium-chain fatty acid, does not require the assistance of the mitochondrial LCFA transport system to cross the mitochondrial membranes. Thus its rate of oxidation should not be affected by changes in mitochondrial LCFA transport capacity. It has been suggested that changes in malonyl-CoA levels may be an important factor in the regulation of mitochondrial LCFA transport capacity (28). Because of its potent inhibitory effect on carnitine palmitoyltransferase 1 (CPT-1) activity, an increase in malonyl-CoA levels would be associated with a decrease in mitochondrial LCFA transport capacity. Although mitochondrial LCFA transport capacity has been assessed in whole body experiments in humans...

Address for reprint requests and other correspondence: L. P. Turcotte, Dept. of Kinesiology, Diabetes Research Center, Univ. of Southern California, 3560 Watt Way, PED 107, Los Angeles, CA 90089–0652 (Email: turcotte@usc.edu). The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

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malonyl-CoA levels have been measured in animal experiments only under conditions of high carbohydrate availability (11, 24). Thus mitochondrial LCFA transport capacity and malonyl-CoA levels have never been measured in the same muscle preparation under conditions of high and low carbohydrate availability.

Thus the purpose of this study was to determine whether increased intracellular carbohydrate availability in the presence of maintained LCFA availability would alter the relative contribution of LCFA to total oxidative metabolism in perfused muscle via changes in LCFA uptake and/or in mitochondrial LCFA transport capacity. Muscle LCFA kinetics were assessed by using the perfused hindquarter preparation. Mitochondrial LCFA transport capacity was assessed by comparing palmitate and octanoate oxidation rates as well as by measuring muscle malonyl-CoA levels.

**MATERIALS AND METHODS**

**Animal preparation.** Male Wistar rats were housed in pairs and maintained on a 12:12-h light-dark cycle. They received regular rat chow and water ad libitum. The rats were randomly assigned to the low (LG; n = 9) or high (HG; n = 12) glucose group. Body weights were not significantly different between groups (353.7 ± 3.4 and 353.1 ± 16.5 g for the LG and HG groups, respectively, P > 0.05).

**Hindquarter perfusion.** Rats were anesthetized intraperitoneally with ketamine-xylazine (80 and 12 mg/kg body wt, respectively) and prepared surgically for hindquarter perfusion as previously described (35). Before the perfusion catheters were inserted, heparinized saline (150 IU) was administered into the inferior vena cava. The rats were killed with an intracardiac injection of pentobarbital sodium (83 mg/kg body wt) immediately before the catheters were inserted, and the preparation was placed in a perfusion apparatus (35).

The initial perfusate (200 ml) consisted of Krebs-Henseleit solution, 1-day-old washed bovine erythrocytes (hematocrit, 30%), 5% bovine serum albumin (Cohn fraction V; Sigma Chemical, St. Louis, MO), 500 μM albumin-bound palmitate, 4 μCi of albumin-bound [1-14C]palmitate, and either 6 mM glucose and 10 μU/ml insulin in the LG group or 20 mM glucose and 1,000 μU/ml insulin in the HG group. The perfusate (37°C) was continuously gassed with a mixture of 95% O2-5% CO2, which yielded arterial pH values of 7.3–7.4 and mean perfusion pressures of 38–43 Torr, respectively, in both the HG and LG groups.

The first 25 ml of perfusate that passed through the hindquarter were discarded. The left gastrocnemius-plantaris-soleus muscle group was taken out and immediately freeze clamped with aluminum clamps precooled in liquid N2. The left iliac vessels were then tied off, and a clamp was fixed tightly around the proximal part of the leg to prevent bleeding. After an equilibration period of 20 min, the right leg was perfused at rest for 40 min at a perfusate flow of 5 ml/min (0.25 ± 0.03 and 0.26 ± 0.10 ml/min kg−1 g−1 perfused muscle in the HG and LG groups, respectively, P > 0.05). After equilibration, arterial and venous perfusate samples were taken at 10, 20, 30, and 40 min for analysis of 14C-labeled fatty acid and 14CO2 radioactivities, as well as FA, glucose, lactate, glycerol, and insulin concentrations. Arterial and venous perfusate samples for determinations of PCO2, PO2, and pH, were taken at 10 and 40 min. Arterial perfusate samples were taken for determination of hematocrit and hemoglobin before equilibration. Mean perfusion pressures were 64.1 ± 8.2 and 86.8 ± 18.7 mmHg at rest in the HG and LG groups, respectively (P > 0.05). At the end of the perfusion, the muscle group of the right leg was taken out and treated as described. After the procedure, a black ink and saline solution was infused into the arterial catheter of the preparation. The colored muscle mass was weighed and added to the mass of the clamped muscle sample to provide the total mass of muscle perfused.

Additional experiments were performed to measure medium-chain fatty acid kinetics (LG: n = 5, 318.0 ± 13.6 g; HG: n = 5, 316.9 ± 13.5 g, P > 0.05). In these experiments, hindquarters were perfused under identical perfusate conditions except that 10 μCi of [1-14C]octanotate (ICN Pharmaceuticals, Costa Mesa, CA) were added rather than [1-14C]-palmitate. In addition, to correct for carbon loss, experiments were conducted to determine the acetate correction factor under our experimental conditions (26, 35). Thus, in a sub-sample of rats (LG: n = 6, 372.8 ± 16.4 g; HG: n = 4, 342.0 ± 7.6 g, P > 0.05), hindquarters were perfused under identical perfusate conditions except that 5 μCi of [1-14C]acetate (ICN Pharmaceuticals, Costa Mesa, CA) were added rather than [1-14C]palmitate. Arterial and venous perfusate samples were taken as described and analyzed for [14C]octanotate or [14C]acetate, and 14CO2 radioactivities as well as fatty acid, glucose, and lactate concentrations.

**Blood sample analyses.** Arterial and venous perfusate samples were analyzed for glucose, lactate, glycerol, insulin, and fatty acid concentrations as well as for [14C]FA and [14CO2] radioactivities. Blood samples for glucose and lactate were put into 200 μM ethylene glycol-bis-(β-aminoethyl ether)-N,N,N’,N’-tetraacetic acid (EGTA, pH 7) and immediately analyzed using the YSI 1500 glucose and lactate analyzers (Yellow Springs Instrument, Yellow Springs, OH), respectively. Samples for glycerol, fatty acid, and insulin were put in 200 μM EGTA (pH 7) and centrifuged, and the supernatant was frozen until analyzed. Glycerol and fatty acid concentrations were determined spectrophotometrically using the enzymatic glycerol kinase method (Sigma Chemical, St. Louis, MO) and the WAKO NEFA-C test (Biochemical Diagnostics, Edgewood, NY), respectively. Insulin was determined by radioimmunoassay (Linco, St. Charles, MO). Plasma 14C-labeled fatty acid and 14CO2 radioactivities were determined as previously described (35). Perfusate samples for the determination of PCO2, PO2, pH, and hemoglobin were collected anaerobically, placed on ice, and measured within 5 min of collection with an ABL-5 acid-base laboratory (Radiometer America, Westlake, OH) and spectrophotometrically (Sigma Chemical, respectively).

**Muscle sample analyses.** Muscle triglyceride concentration was determined as glycerol residues after extraction and separation of the muscle samples, as previously described (35). Malonyl-CoA levels were determined using neutralized perchloric acid extracts prepared from freeze-clamped muscle samples and analyzed as previously described (19). Briefly, samples were added to the reaction buffer, which contained 1 M potassium phosphate, 50 mM dithiothreitol, 10 mM ethylenediamine tetraacetate (EDTA), 4 mM β-nicotinamide adenine dinucleotide phosphate reduced form (NADPH), 20 mg/ml fatty acid-free bovine serum albumin, and 10 μCi [3-3H]lactate-CoA. The reaction was initiated with the addition of 5 μl of purified fatty acid synthase isolated as previously described (16). After a 45-min incubation at 37°C, the reaction was halted with the addition of 70% (wt/vol) perchloric acid. The lipid fraction was extracted, transferred to scintillation vials, dried, and counted after the addition of Budget Solve (Research Products, Mount Prospect, IL).

**Calculations and statistics.** Palmitate delivery, fractional and total palmitate uptake, and percent and total palmitate uptake were calculated as previously described (35). The statistical analysis of the data was performed using the Mann-Whitney test and the Student’s t-test. Values are expressed as means ± SD. A value of P < 0.05 was considered significant.
RESULTS

Palmitate metabolism. As dictated by the protocol, perfusate palmitate concentration and delivery to the hindquarter were not significantly different between the LG (512.2 ± 39.2 μM and 96.4 ± 9.4 nmol·min⁻¹·g⁻¹) and HG (507.8 ± 30.3 μM and 94.0 ± 8.3 nmol·min⁻¹·g⁻¹) groups (P > 0.05). Fractional uptake of palmitate was 58% higher in the HG group than in the LG group (Table 1). Similarly, because palmitate delivery was the same for both groups, total palmitate uptake was found to be 59% higher in the HG group than the LG group (11.8 ± 1.5 vs. 7.4 ± 1.2 nmol·min⁻¹·g⁻¹, respectively, P < 0.05; Fig. 1). The percentage of palmitate oxidized was 61% lower in the HG group than in the LG group, resulting in a 38% lower total rate of palmitate oxidation in the HG group than in the LG group (0.8 ± 0.1 vs. 1.3 ± 0.2 nmol·min⁻¹·g⁻¹, respectively, P < 0.05; Table 1 and Fig. 1). A positive correlation (y = 0.21x + 6.95, r² = 0.21, P < 0.05) was found to exist between the rates of palmitate uptake and glucose uptake in the perfused hindquarter (Fig. 2). Conversely, a negative correlation (y = -0.02x + 1.23, r² = 0.15, P = 0.08) was found to exist between total palmitate oxidation and glucose uptake in the perfused hindquarter.

Table 1. Effects of high carbohydrate availability on palmitate and octanoate metabolism in perfused hindquarters at rest

<table>
<thead>
<tr>
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<th>LG</th>
<th>HG</th>
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<tr>
<td>Palmitate</td>
<td></td>
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<tr>
<td>Fractional uptake</td>
<td>0.079 ± 0.001</td>
<td>0.125 ± 0.120*</td>
</tr>
<tr>
<td>Percent oxidation</td>
<td>23.4 ± 5.2</td>
<td>9.1 ± 1.0*</td>
</tr>
<tr>
<td>Octanoate</td>
<td></td>
<td></td>
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<tr>
<td>Fractional uptake</td>
<td>0.095 ± 0.020</td>
<td>0.095 ± 0.011</td>
</tr>
<tr>
<td>Percent oxidation</td>
<td>51.4 ± 13.0</td>
<td>37.9 ± 10.9</td>
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</tbody>
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Values are means ±SE for the low-glucose (LG; n = 9 for palmitate group and n = 5 for octanoate group) and high-glucose (HG; n = 12 for palmitate group and n = 5 for octanoate group) groups. Because there were no significant changes in values measured after 20, 30, and 40 min of perfusion, average values were used for each rat. Percent palmitate and octanoate oxidation values were corrected for label fixation, as described in MATERIALS AND METHODS. *Significantly different compared to LG, P < 0.05.

Substrate exchange across the hindquarter. Resting oxygen uptake did not vary over time and was not significantly different between the LG (21.9 ± 2.3 μmol·g⁻¹·h⁻¹) and HG (25.6 ± 2.2 μmol·g⁻¹·h⁻¹) groups (P > 0.05; Table 2). As dictated by the protocol, arterial perfusate glucose and insulin concentrations were significantly lower in the LG group (6.0 ± 0.1 mM and 12.8 ± 1.1 μU/ml, respectively) than in the HG group (17.8 ± 0.3 mM and 832.8 ± 35.2 μU/ml, respectively, P < 0.05). Arterial perfusate glucose concentration did not vary over time in the LG group but gradually decreased by 12% in the HG group (from 19.1 ±
0.6 to 16.7 ± 0.3 mM, P < 0.05). Glucose uptake did not change over time in either group (P > 0.05) and was significantly lower in the LG group than in the HG group (P < 0.05). Arterial perfusate lactate concentration and lactate release did not vary significantly over time and were not significantly different between groups (P > 0.05). Similarly, arterial perfusate glycerol concentration and glycerol release did not vary significantly over time and were not significantly different between groups (P > 0.05).

**Octanoate metabolism.** As dictated by the protocol, arterial perfusate glucose concentration and glucose uptake were significantly higher in the HG group than in the LG group (19.9 ± 0.9 mM and 26.9 ± 1.7 μmol·g⁻¹·h⁻¹ vs. 6.4 ± 0.2 mM and 7.0 ± 2.0 μmol·g⁻¹·h⁻¹, respectively, P < 0.05), and perfusate palmitate concentration and delivery were not significantly different between the HG and LG groups (473.9 ± 28.1 μM and 93.7 ± 4.2 nmol·min⁻¹·g⁻¹ vs. 534.7 ± 43.4 μM and 109.1 ± 12.9 nmol·min⁻¹·g⁻¹, respectively, P > 0.05). Arterial perfusate lactate concentration and lactate release did not change significantly over time in either group (P > 0.05) and were not significantly different between the LG (1.3 ± 0.1 mM and 2.9 ± 0.8 μmol·g⁻¹·h⁻¹, respectively) and HG (1.3 ± 0.1 mM and 5.8 ± 1.0 μmol·g⁻¹·h⁻¹, respectively) groups (P > 0.05). In each experimental group (LG or HG), group averages for perfusate glucose, lactate, and palmitate concentrations, as well as for glucose uptake, lactate release, and palmitate delivery measured during the octanoate experiments were not significantly different from the values observed in the palmitate experiments (P > 0.05). Octanoate fractional uptake and percent oxidation were not significantly different between the HG and LG groups (P > 0.05) (Table 1).

**Muscle metabolite levels.** Preperfusion muscle triglyceride concentrations were not significantly different between groups (1.3 ± 0.2 and 1.8 ± 0.2 μmol/g wet wt in the LG and HG groups, respectively, P > 0.05). Muscle triglyceride concentration did not change during the perfusion period in the LG group but increased by 28% in the HG group to reach a value of 2.3 ± 0.2 μmol/g wet wt (P < 0.05). Preperfusion malonyl-CoA levels were not significantly different between groups (0.7 ± 0.1 and 0.8 ± 0.1 pmol/mg wet wt in the LG and HG groups, respectively, P < 0.05). In the LG group, malonyl-CoA levels decreased by 24% during the perfusion period, whereas no change was measured in the HG group. This resulted in a significantly higher postperfusion malonyl-CoA level in the HG group compared with the LG group (P < 0.05). The relationships between percent and total palmitate oxidation and postperfusion muscle malonyl-CoA levels (y = 8.15x⁻⁰.⁶², r² = 0.58 and y = 0.71x⁻⁰.³⁷, r² = 0.42, P < 0.05, respectively) were hyperbolic and found to be significant (Fig. 3). Linear correlations between these variables were also found to be significant but generally lower (y = −25.4x + 31.9, r² = 0.45 and y = −0.83x + 1.54, r² = 0.35, P < 0.05, respectively).
DISCUSSION

These results show that high carbohydrate availability is associated with a decrease in plasma LCFA oxidation that is due in part to a reduced mitochondrial LCFA transport capacity but not to a reduction in LCFA uptake into the muscle cell. Thus, for the same plasma palmitate delivery to the muscle, high carbohydrate availability was associated with an increase in palmitate uptake and a decrease in percent and total palmitate oxidation, whereas no change in octanoate uptake or oxidation was detected. Under the conditions imposed by our protocol, palmitate oxidation was found to be negatively correlated with postperfusion malonyl-CoA levels. These results suggest that, under conditions of high carbohydrate availability, mitochondrial LCFA transport capacity may be impaired, in part, by high malonyl-CoA levels and reinforce the notion that LCFA uptake and oxidation are not always regulated in concert.

LCFA uptake and oxidation have often been shown to change in concert under a variety of physiological conditions (12, 33, 35). Thus both muscle contractions and endurance training have been shown to increase LCFA uptake and oxidation in incubated and perfused muscle as well as across a muscle bed in humans (3, 12, 33, 35). Because of these results, the notion has emerged that LCFA uptake and oxidation are regulated in a coordinate manner by cellular factors. However, we (32, 35) and others (12) have shown under different experimental conditions that the magnitude and direction of the changes in LCFA uptake and oxidation do not always coincide. In line with our present result of an increase in LCFA uptake and a decrease in LCFA oxidation with high carbohydrate availability, these data support the notion that selective cellular factors may impact on LCFA uptake and oxidation in independent ways. The lack of change in the fractional uptake of octanoate, a medium-chain fatty acid that does not require a transporter to traverse the plasma membrane, further reinforces the notion that LCFA uptake was selectively impacted by the presence of high carbohydrate availability.

Interest in the independent role of cellular factors in the regulation of LCFA uptake stems from accumulated evidence showing that LCFA transport across the plasma membrane of muscle cells may be facilitated, in part, by a protein-mediated transport system (1, 5, 36). Evidence suggests that the plasma membrane fatty acid binding proteins (FABPs) and fatty acid translocase (FAT/CD36) may be necessary components of this transport process in muscle (1, 5, 17, 36). Furthermore, in a manner similar to the glucose transporter GLUT-4, FAT/CD36, and FABPpm translocation from an intracellular pool to the plasma membrane has been shown to correlate with changes in palmitate transport in giant sarcotubular vesicles prepared from muscles that were either stimulated to contract or treated with leptin for 2 wk (4, 31). These results provide a possible cellular mechanism by which LCFA uptake could be altered by high carbohydrate availability or insulin alone. Alternatively, changes in cellular metabolic flow could indirectly elicit an increased demand for LCFA and drive an increase in LCFA uptake. Indeed, it has been shown that an increase in cytoplasmic fatty acyl-CoA synthase expression was sufficient to increase LCFA uptake in 3T3-L1 fibroblasts, indicating that intracellular LCFA metabolism can drive LCFA uptake under some conditions (13). If metabolic demand is driving the increase in LCFA uptake with high carbohydrate availability, then the glycerolipid synthesis pathway might be involved. Indeed, in myotubes, overexpression of glycerol-3-phosphate acyltransferase (GPAT), generally considered the rate-limiting enzyme of triglyceride synthesis (7), increased LCFA uptake under insulin stimulation (22). This suggests that an increase in metabolic flow to triglyceride synthesis can increase LCFA uptake. Furthermore, insulin has been shown to increase GPAT activity in BC3H-1 myocytes, resulting in an increase in de novo synthesis of phosphatidic acid (9). Our results demonstrating an increase in postperfusion triglyceride concentration with high carbohydrate availability and a positive relationship between glucose and palmitate uptake support the notion that metabolic demand may be a factor that regulates the increase in LCFA uptake with high carbohydrate availability.

Our result of a decrease in palmitate oxidation agrees with other data obtained in whole body experiments and shows that high carbohydrate availability has a direct impact on LCFA oxidative metabolism at the muscle level. The existence of a strong ($P = 0.08$) inverse correlation between glucose uptake and palmitate oxidation in the perfused muscle agrees with this notion. Although it has been suggested that the decrease in whole body LCFA oxidation induced by the presence of high carbohydrate availability may be due to an impairment in mitochondrial LCFA transport capacity, this was not previously measured at the muscle level (28). Our results showing a lack of change in muscle octanoate oxidation provide further evidence that a decreased mitochondrial LCFA transport capacity is an important cellular mechanism by which muscle LCFA oxidation is inhibited in the presence of high carbohydrate availability.

Mitochondrial LCFA transport capacity is dependent, in part, on the activity of CPT-1, the rate-limiting enzyme of the carnitine shuttle system that carries LCFA into the mitochondria, the level of malonyl-CoA, a potent inhibitor of CPT-1 activity, and the sensitivity of CPT-1 for malonyl-CoA (10). Accumulated evidence indicates that CPT-1 activity or gene expression as well as CPT-1 sensitivity for malonyl-CoA is not altered by acute changes in physiological conditions as long as pH remains stable (2, 20, 21, 30). Thus it is unlikely that either factor would have been changed significantly by high carbohydrate availability. Rather, our results show that the decrease in LCFA oxidation imposed by high carbohydrate availability may be due, in part, to the increase in malonyl-CoA levels. Malonyl-CoA levels have previously been shown to increase in
the presence of high carbohydrate availability in incubated and perfused muscle (11, 24). However, in those studies, muscle LCFA oxidation was not directly measured. Our results show for the first time that the increase in malonyl-CoA levels induced by high carbohydrate availability is associated with a decrease in LCFA oxidation measured in the same perfused muscle preparation. This is reinforced by the existence of an inverse hyperbolic correlation between malonyl-CoA levels and palmitate oxidation. The increase in malonyl-CoA levels induced by high carbohydrate availability could occur via an increase in the levels of citrate, an allosteric activator of acetyl-CoA carboxylase (ACC), or via a decrease in AMP-activated protein kinase (AMPK) activity and subsequent stimulation of ACC activity (23). In a recent study, Winder and Holmes (37) showed that the increase in glucose uptake induced by insulin stimulation did not alter AMPK or ACC activity in perfused muscle. This would suggest that an increase in citrate levels might be the cellular mechanism by which malonyl-CoA levels are increased with high carbohydrate availability. Indeed, in isolated soleus, it has been shown that incubation with glucose and/or insulin is associated with elevations in citrate levels (25).

In summary, the present study has shown that high carbohydrate availability is associated with an increase in LCFA uptake and a decrease in LCFA oxidation in perfused muscle. Our results also show for the first time that the increase in malonyl-CoA levels induced by high carbohydrate availability is inversely correlated to palmitate oxidation measured in the same muscle preparation and could be responsible, in part, for the reduction in mitochondrial LCFA transport capacity. The increase in LCFA uptake could have been due to a direct effect of high glucose or insulin on the LCFA transport system or to an increased metabolic demand for glycerolipid synthesis as evidenced by an increase in muscle triglyceride concentration.

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REFERENCES


