Dietary glycemic index influences lipid oxidation but not muscle or liver glycogen oxidation during exercise

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Am J Physiol Endocrinol Metab 296: E1140–E1147, 2009. First published February 17, 2009; doi:10.1152/ajpendo.90788.2008.—The glycemic index (GI) of dietary carbohydrates influences glycogen storage in skeletal muscle and circulating nonesterified fatty acid (NEFA) concentrations. We hypothesized that diets differing only in GI would alter intramuscular lipid oxidation and glycogen usage in skeletal muscle and liver during subsequent exercise. Endurance-trained individuals (n = 9) cycled for 90 min at 70% V02 peak and then consumed either high- or low-GI meals over the following 12 h. The following day after an overnight fast, the 90-min cycle was repeated. 1H and 13C magnetic resonance spectroscopy was used before and after exercise to assess intramuscular lipid and glycogen content of the vastus lateralis muscle and liver. Blood and expired air samples were collected at 15-min intervals throughout exercise. NEFA availability was reduced during exercise in the high- compared with the low-GI trial (area under curve 44.5 ± 7.0 mEq/l, P < 0.05). Exercise elicited an ~55% greater reduction in intramyocellular triglyceride (IMCL) in the high- vs. low-GI trial (1.6 ± 0.2 vs. 1.0 ± 0.3 mmol/kg wet wt, P < 0.05). There was no difference in the exercise-induced reduction of the glycogen pool in skeletal muscle (76 ± 8 vs. 68 ± 5 mEq/kg) or in liver (65 ± 8 vs. 71 ± 4 mEq/kg) between the low- and high-GI trials, respectively. High-GI recovery diets reduce NEFA availability and increase reliance on IMCL during moderate-intensity exercise. Skeletal muscle and liver glycogen storage or usage were not affected by the GI of an acute recovery diet.

glycemic index; intramuscular lipid; glycogen; magnetic resonance spectroscopy; exercise; skeletal muscle; liver

CARBOHYDRATE FEEDING after exercise restores glycogen in skeletal muscle and assists repeat exercise performance. The storage of glucose as glycogen in muscle is dependent upon the dose (15) and form of carbohydrate (2) and also the timing of ingestion (14). The effect of carbohydrate ingestion on liver glycogen storage and lipid availability and oxidation is less well described.

Liver glycogen stores are mobilized during exercise in response to the increased glucose demands of contracting skeletal muscle (20, 35, 40). Carbohydrate ingestion following exercise depletion of glycogen increases liver glycogen content (3). A significant relationship between exercise performance and liver glycogen content highlights the importance of liver glycogen as a substrate source during exercise (3). Despite the significance of liver glycogen and hepatic glucose output, surprisingly little is known about how liver glucose production can be optimized during exercise, or its interaction with muscle glycogen and lipid oxidation. The lack of detailed reports is likely due to the difficulty in assessing liver glycogen or glucose output. Isotope studies may underestimate the contribution of gluconeogenesis during exercise because of dilution of 13C-labeled compounds in the body (17) and the variable contribution of direct and indirect pathways for glycogen production in the liver cycle isotope-labeled carbon (16). Furthermore, it is not possible to acquire liver biopsies from healthy individuals for research purposes. Recent development of 13C magnetic resonance spectroscopy techniques with sufficient temporal and spectral resolution to track changes in liver glycogen has addressed these difficulties by allowing direct noninvasive assessment of liver glycogen in humans (3, 20). As yet, this technique has not been widely applied to healthy individuals to examine the role of liver glycogen during exercise because of the technical challenges to performing such measurements.

The insulin response following carbohydrate ingestion plays two influential roles, stimulating glucose storage as glycogen through activation of glycogen synthase (4) and suppressing nonesterified fatty acid (NEFA) release and, as a consequence, decreasing circulating concentration of NEFA (27). As a result, the postprandial insulin response creates a fine balance between optimizing glycogen recovery vs. maintaining lipid availability, an essential fuel for endurance exercise. In line with this, studies have shown that carbohydrates, which are rapidly absorbed in the circulation and produce a large insulin response [termed high glycemic index (GI)] optimize the rate of glycogen resynthesis (31) and storage (2) after exercise. Conversely, we have recently demonstrated that short-term feeding of mixed meals differing by GI alone influence both lipid availability and oxidation (29). A high-GI diet reduces NEFA availability and increases reliance on intramuscular lipid oxidation during exercise. The interplay between glycogen storage in skeletal muscle and liver and NEFA availability and lipid oxidation following high- and low-GI recovery diets is important to exercise performance, but to our knowledge is yet to be evaluated.

The aim of the present study was to examine the influence of recovery diets of differing GI alone on glycogen storage and use in skeletal muscle and liver, and lipid availability and use in skeletal muscle during subsequent exercise. Specifically, the study aimed to evaluate whether the suppression of circulating NEFA and increased reliance on intramuscular lipid following a high-GI recovery diet was accompanied by an increase in skeletal muscle and liver glycogen storage and use.
SUBJECTS AND METHODS

Subjects

Nine endurance-trained male cyclists (age 33.0 ± 6.9 yr, mass 76.3 ± 7.0 kg, \( V_{\text{O}_2\text{peak}} \) 61.5 ± 5.0 mL·kg\(^{-1}\)·min\(^{-1}\)) participated in this study. The study was approved by the Local Ethical Advisory Committee of Northumbria University, and all subjects gave their written informed consent.

Preliminary Tests

\( V_{\text{O}_2\text{peak}} \) was determined while subjects cycled on a stationary cycle ergometer using four 5-min steady-state stages [100, 150, 200, and 250 work rate (W)] followed by a progressive increase in work of 10 W/min until voluntary exhaustion. All exercise tests were conducted on the same electronically braked cycle ergometer (Excalibur Sport; Lode BV, Groningen, The Netherlands). A work rate of 70% \( V_{\text{O}_2\text{peak}} \) was calculated for each individual from the linear function of oxygen uptake at the four steady-state work rates, and maximal oxygen uptake against the work rate of the four steady state work rates and maximal power output.

Experimental Protocol

Subjects completed two trials in a randomized crossover design separated by at least 1 wk. Randomization was performed using a Latin square. Each trial was completed over 2 days. On day 1, subjects arrived at the laboratory at 8:00 A.M. following a 12-h fast and, following a 10-min warm up at a self-selected pace, completed a 90-min cycle at 70% \( V_{\text{O}_2\text{peak}} \). During the first trial, water was provided ad libitum but measured, and the same volume of water was provided for consumption at home. Subjects were asked to consume water 1 h after finishing exercise. Lunch, dinner, and snacks were provided ad libitum but measured, and the same volume of water was provided with a high- or low-GI mixed-meal diet (see following section for description). The following day, subjects arrived in the laboratory at 8:00 A.M. following a 12-h fast and completed a second section for description). The following day, subjects arrived in the laboratory at 8:00 A.M. following a 12-h fast and completed a second cycle trial, expired gases and venous blood were collected every 15 min. Magnetic resonance spectroscopy measurements of intramyocellular triglyceride (IMCL) and vastus lateralis and liver glycogen content were performed immediately before and after exercise.

Dietary Manipulation

Following the first 90-min cycle, participants were provided with food for the following 12 h containing either a high- or low-GI carbohydrate component. Breakfast was provided in the laboratory ~1 h after finishing exercise. Lunch, dinner, and snacks were provided for consumption at home. Subjects were asked to consume lunch between 1:00 and 1:30 P.M. and the evening meal between 7:30 and 8:00 P.M. Snacks could be consumed between meals when desired. Subjects were instructed to only eat the food provided and to finish eating the food before 9:00 P.M. that night. Water was available ad libitum throughout the day. Carbohydrate was provided at 8 g/kg body mass, and protein and fat content constituted 11 and 17% of energy, respectively (Table 1). The total energy content of the diet was ~15 MJ. The GI values were calculated from published tables (10), and the GI of the high-GI and low-GI diets was 78 and 44, respectively.

Expired Gas Collection and Analysis

Expired gas samples were collected for 1 min at 15-min intervals during exercise on day 1 and day 2 using the Douglas Bag method. Substrate oxidation rates were calculated using nonprotein stoichiometric equations (11). During each expired gas collection, rating of perceived exertion (1) and heart rate was recorded.

### Table 1. Nutrient content of the high- and low-GI diets (for a 70-kg person)

<table>
<thead>
<tr>
<th></th>
<th>High-Glycemic Diet</th>
<th>Low-Glycemic Diet</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Breakfast</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corn flakes, a g</td>
<td>65</td>
<td>170</td>
</tr>
<tr>
<td>White bread, b g</td>
<td>83</td>
<td>204</td>
</tr>
<tr>
<td>Jam, c g</td>
<td>22</td>
<td>170</td>
</tr>
<tr>
<td>Margarine, d g</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>Carbonated glucose drink, e ml</td>
<td>162</td>
<td>283</td>
</tr>
<tr>
<td>Skimmed milk, ml</td>
<td>271</td>
<td>283</td>
</tr>
<tr>
<td>Muesli cereal, f g</td>
<td>95</td>
<td>95</td>
</tr>
<tr>
<td>Apple, g</td>
<td>74</td>
<td>74</td>
</tr>
<tr>
<td>Canned peaches, g</td>
<td>113</td>
<td>113</td>
</tr>
<tr>
<td>Yoghurt, h g</td>
<td>142</td>
<td>142</td>
</tr>
<tr>
<td>Apple juice, i ml</td>
<td>283</td>
<td></td>
</tr>
<tr>
<td>Lunch/dinner</td>
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<td></td>
</tr>
<tr>
<td>Turkey, j g</td>
<td>162</td>
<td>162</td>
</tr>
<tr>
<td>Cheese, k g</td>
<td>54</td>
<td>62</td>
</tr>
<tr>
<td>White bread, b g</td>
<td>167</td>
<td></td>
</tr>
<tr>
<td>Banana, g</td>
<td>189</td>
<td></td>
</tr>
<tr>
<td>Carbonated glucose drink, e ml</td>
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</tr>
<tr>
<td>Pasta, l g</td>
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<td>Pasta sauce, m g</td>
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</tr>
<tr>
<td>Pear, g</td>
<td>170</td>
<td></td>
</tr>
<tr>
<td>Apple juice, j g</td>
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<td></td>
</tr>
<tr>
<td>Snacks</td>
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<td></td>
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<tr>
<td>White bread e</td>
<td>166</td>
<td></td>
</tr>
<tr>
<td>Margarine, g</td>
<td>22</td>
<td>11</td>
</tr>
<tr>
<td>Jam, g</td>
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</tr>
<tr>
<td>Bread, g</td>
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<td><strong>Macronutrient content</strong></td>
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<tr>
<td>Energy, kJ</td>
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<td>15,407</td>
</tr>
<tr>
<td>Carbohydrate, g</td>
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<td>560</td>
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<tr>
<td>Fat, g</td>
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<td>84</td>
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<tr>
<td>Protein, g</td>
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<td>171</td>
</tr>
<tr>
<td>Glycemic index</td>
<td>78</td>
<td>44</td>
</tr>
</tbody>
</table>

Sources of diet are as follows: aKelloggs (Manchester, UK); bthick sliced (Tesco); cstrawberry conserve (Tesco); dFlora sunflower spread; eLucozade Original (GlaxoSmithKleine); fno-added-sugar muesli (Alpen); gpeach slices in natural juice (Tesco); hlow-fat strawberry yoghurt (Tesco); iapple juice (Tesco); jturkey breast (97% fat free; Bernard Matthews); kmedium cheddar cheese (Tesco); lspasta spirals (Tesco); mtomato sauce (Dolmio); nAll in one (Warburtons).

Magnetic Resonance Spectroscopy

Immediately before and after the cessation of exercise (within 10 min), \( ^1\text{H} \) decoupled \( ^{13}\text{C} \) spectra were acquired to measure the glyco- gen content of the thigh muscle and the liver. A volume-localized \( ^1\text{H} \) spectra was collected from the vastus laterals to determine IMCL. Spectra were acquired on a 3T Achieva whole body scanner (Philips, Best, The Netherlands).

**Skeletal muscle.** With the subject supine, a 6-cm-diameter \( ^{13}\text{C} \) coil with an integral quad \( ^1\text{H} \) decoupling coil (PulseTeq, Wotton under Edge, UK) was placed equidistant between the caudal tip of the patella and the caudal head of the femur over the vastus lateralis, and its position was marked on the leg with indelible ink. Scout images were acquired to ensure identical coil positioning on repeat \( ^{13}\text{C} \) scans, and the distance between coil surface and the muscle was recorded. The \( ^{13}\text{C} \) pulse power was calibrated to a nominal value of 80° in the tissue of interest by observing the power-dependent variation in signal from a fiducial marker located in the coil housing, containing a sample exhibiting a \( ^{13}\text{C} \) signal with short T1 (50% acetone, 50% water, 25 mM GdCl3). Spectra showing the glycogen \( ^{13}\text{C} \) resonance were acquired using a nonlocalized \( ^1\text{H} \)-decoupled \( ^{13}\text{C} \) pulse-acquire sequence [relaxation time (TR) = 200 ms, spectral width (SW) = 8 kHz, 3,000 averages, WALTZ decoupling, nominal tip angle = 80°] over a 15-min acquisition time.
Image-guided localized $^1$H magnetic resonance spectra were collected to evaluate IMCL from the right vastus lateralis, using a dual $^{13}$C/$^1$H coil with 20-cm diameter quadrature $^1$H elements (PulseTeq). Magnetic field homogeneity was optimized using an automated shim routine. Water-suppressed and non-suppressed $^1$H spectra were collected from a $1.5 \times 1.5 \times 2.0$ cm$^3$ voxel using point-resolved echo sequence spectroscopy (echo time 32 ms, $T_E$ 5 s).

Liver. The subject was placed in a supine position, and a custom-built 12-cm-diameter $^{13}$C coil with integral quadrature $^1$H decoupling coils was placed over the liver. Scout images were acquired to confirm that the coil was positioned centrally over the liver, and the distance between coil surface and the liver was noted. The $^{13}$C pulse power was calibrated to a nominal value of 80° in the tissue of interest by observing the power-dependent variation in signal from a fiducial marker, as described for the skeletal muscle methodology. Spectra showing the glycogen $^{1}$C-$^{13}$C resonance were acquired using a non-localized $^1$H-decoupled $^{13}$C pulse-acquire sequence (echo time 32 ms, $T_W$ = 8 kHz, 2,504 averages, WALTZ decoupling, nominal tip angle = 80°) over a 15-min acquisition time.

Analysis and quantitation of spectra. All spectra were analyzed using “java-based magnetic resonance user interface” software (jMRUI version 3.0) (18, 19) and AMARES fitting routine (32). IMCL concentrations were calculated as previously described (29). Quantitation of $^{13}$C spectra was performed by comparison of in vivo [$^{13}$C]glycogen $^{1}$C-$^{13}$C signal amplitudes with that of a standard glycogen solution (100 mM glycogen, 70 mM KCl, 0.05% sodium azide). Quantitation $^{13}$C spectra were acquired from leg- and liver-shaped phantoms at a range of separations between coil and phantom, to account for the separation between coil and muscle or liver due to skin, subcutaneous fat and/or the rib cage, using the same coils, pulse sequences, and tip angles as employed for in vivo spectra.

Blood Sampling and Analysis

Blood samples were collected at rest and at 15-min intervals during exercise from an indwelling cannula inserted in a forearm vein. Whole blood was analyzed for blood lactate concentrations (Analox P-GM7 Micro-stat; Analox Instruments, London, UK). Whole blood (3 ml) was dispensed in a nonanticoagulant tube and left to clot for 45 min. Serum samples were then obtained after centrifugation at 2,000 g for 10 min at 4°C. The aliquoted serum was stored at $\sim$85°C and later analyzed for insulin (DAKO, Ely, UK). Plasma samples were obtained by centrifugation of the remaining whole blood for a period of 10 min at 2,000 g and 4°C. The aliquoted plasma was then stored at $\sim$85°C for later analysis of NEFA (Wako Chemicals, Neuss, Germany) and glucose (YSI).

Statistical Analysis

All statistical analysis was performed using SPSS version 11 (SPSS, Chicago, IL). A two-way analysis of variance (time and treatment) was used to assess metabolic and physiological differences between groups. A post hoc Bonferroni stepwise correction was performed at the location of the variance. Statistical significance was accepted at $P < 0.05$. Data are presented as means ± SE unless otherwise stated.

RESULTS

Blood Parameters

Plasma NEFA concentrations fell and then progressively rose throughout exercise in both trials ($P < 0.05$; Fig. 1A). NEFA availability was reduced during exercise in the high- compared with the low-GI trial (area under curve 44.5 ± 6.0 vs. 38.4 ± 7.30 mM/h, $P < 0.05$). There was no significant GI $\times$ time interaction ($P = 0.456$). Plasma glucose concentrations increased marginally at the onset of exercise but then declined throughout the remainder of the 90 min of exercise ($P < 0.05$; Fig. 1B) with no effect of diet composition ($P = 0.834$) or GI $\times$ time interaction ($P = 0.141$). Similarly, serum insulin concentrations declined throughout exercise ($P < 0.05$; Fig. 1C), with no difference between the two trials ($P = 0.144$) or a GI $\times$ time interaction ($P = 0.664$). Blood lactate concentrations remained between 2 and 3 mmol/l throughout both trials (Fig. 1D) but were higher in the high- vs. low-GI trial over the first 75 min of exercise ($P < 0.05$).

Substrate Oxidation

Whole body fat oxidation increased, and carbohydrate oxidation decreased throughout exercise in both trials (Fig. 1, E and F), but there was no significant effect of diet composition ($P = 0.810$ and $P = 0.645$ for fat and carbohydrate oxidation, respectively).

Heart Rate and Rating of Perceived Exertion

Heart rate and rating of perceived exertion rose throughout exercise on both day 1 and day 2 (data not shown, $P < 0.05$), but there were no statistically significant differences between trials.

Intramyocellular Lipid

Exercise produced a significant reduction in IMCL in both the high- and low-GI trials (6.6 ± 0.9 to 5.0 ± 0.8 vs. 5.9 ± 0.8 to 4.9 ± 0.8 μmol/g muscle wet wt, $P < 0.01$). The high-GI group showed an $\sim$55% greater IMCL utilization during exercise than the low-GI group (P < 0.05; Figs. 2 and 3A). There were no significant differences in IMCL between high- or low-GI trials before (P = 0.08) or at the end (P = 0.7) of exercise. There was no relationship between preexercise IMCL and IMCL use during exercise ($r^2 = 0.428, P = 0.076$).

Intramuscular Glycogen

Intramuscular glycogen was reduced significantly during exercise in both the high- and low-GI trials (121 ± 4 to 54 ± 11 vs. 123 ± 7 to 46 ± 7 μmol/g, $P < 0.01$; Figs. 2 and 3B), but there was no effect of diet composition ($P = 0.3$). There was also no differences between baseline ($P = 0.8$) or postexercise ($P = 0.3$) glycogen between groups. Muscle glycogen use during exercise was correlated with preexercise muscle glycogen content ($r^2 = 0.62, P < 0.01$).

Liver Glycogen

There was a significant reduction in liver glycogen during exercise in both the high- and low-GI trials (176 ± 5 to 105 ± 6 vs. 180 ± 13 to 115 ± 10 μmol/g, $P < 0.01$; Figs. 2 and 3C) but no effect of diet composition ($P = 0.5$). Similarly, there were no differences in baseline ($P = 0.8$) or postexercise ($P = 0.3$) liver glycogen. Liver glycogen use during exercise is correlated significantly with preexercise liver glycogen content ($r^2 = 0.564, P < 0.05$; Fig. 4) and NEFA availability during exercise ($r^2 = 0.419, P < 0.01$; Fig. 4).

DISCUSSION

The effect of a high-GI meal or diet on reducing circulating NEFA during exercise has now been reported in several studies. The effect has been observed immediately after a high-GI...
meal (7, 9, 25, 28, 37, 38, 41) and on the following day (26, 29). The present findings suggest that, when NEFA availability is compromised, there is a twofold increase in reliance on IMCL as a fuel source during exercise. The increased utilization of IMCL when NEFA concentrations are suppressed is in line with our previous report (29) and is supported by data from studies in which NEFA are artificially reduced to a supraphysiological level (34) and the inverse relationship between NEFA delivery during the latter stages of prolonged exercise and IMCL utilization (33, 36). The mechanism may be explained by the effect of high- vs. low-GI carbohydrates on skeletal muscle lipoprotein lipase activity (21).

Studies that used carbohydrate supplementation during exercise to inhibit adipose tissue lipolysis and reduce NEFA availability within the physiological range show an increased reliance (23) or no effect (6) of feeding upon IMCL utilization. The differences in IMCL utilization may also be influenced by preexercise substrate availability. Although not statistically significant, the present study reports a trend toward higher starting IMCL in the high-GI trial. Studies have reported that preexercise IMCL concentrations are an influential determinant of subsequent utilization during exercise (24). Despite these observations, an increased storage of IMCL in the high-GI trial would seem paradoxical, since we have previously shown that consuming a high-GI meal following 90 min of exercise reduces NEFA availability compared with when a low-GI meal is consumed (30). The observation of a trend toward a higher preexercise IMCL content following a high-GI diet does warrant further investigation using an appropriate study design. It is also possible that the higher insulin levels characterizing the high-GI diet could also affect other sources of lipids, such as liver lipid release, although this also requires further study. Taken together, these observations suggest that high-GI diets produce sustained effects on NEFA availability and intramuscular lipid oxidation during exercise, although the mechanism by which this happens remains to be studied.

Few reports document the effect of the GI of carbohydrates on skeletal muscle and liver glycogen content. In the present study, a high-GI recovery diet did not enhance the storage of glycogen in skeletal muscle relative to a diet with a lower GI. The literature, however, suggests two main benefits of consuming high-GI foods during recovery. First, there is greater glucose availability for transport to the muscle following recovery from exercise (2). Second, the larger insulin response characteristic of high-GI foods activates glycogen synthase, increasing the rate of conversion of glucose into glycogen (4). Although there are many studies that document differences in postprandial responses to carbohydrates with differing GI values consumed before or after exercise (7, 9, 25, 28, 37, 38, 41), few studies have measured glycogen concentrations. Muscle

Fig. 1. Plasma nonesterified fatty acids (NEFA; A), glucose (B), insulin (C), lactate (D), carbohydrate oxidation (E), and fat oxidation (F) during 90 min of cycling at 70% \( V_{\text{O}_2\text{peak}} \) following a high- (■) or low-glycemic index (GI) (●) recovery diet. Plasma NEFA were significantly reduced in the high- vs. low-GI diet, \( P < 0.05 \).
biopsy measurements of glycogen following glucose (high GI) or low-GI starch recovery feeding found that the high-GI diet was effective in increasing glycogen storage after 48 h of recovery (5). More recent studies using $^{13}$C magnetic resonance spectroscopy to evaluate muscle glycogen storage after exercise showed no beneficial effect of sucrose vs. glucose (3) or an increased rate of storage of glucose vs. fructose (31).

Although studies using specified sugar compositions elicit tight physiological responses (3, 5, 31), their translation into dietary advice is difficult. Only one other study has used mixed meals differing by GI alone to observe changes in directly measured muscle metabolites. That study showed that a high-GI recovery diet resulted in ~35% greater storage of glycogen in skeletal muscle after 24 h compared with a low-GI recovery diet (2). Interestingly, this study showed no difference in the postprandial responses to the high- and low-GI meals consumed immediately postexercise but documented differences in skeletal muscle glycogen concentrations 3 h after high or low-GI meals eaten 21 h after the end of exercise (2). The authors suggested that the increased muscle glycogen concentrations observed in the high-GI trial were a result of consuming high-GI carbohydrates over the preceding 24 h. However, it is possible that the differences were simply a result of the increased glycemic response to the meals consumed 3 h before the final biopsy samples were collected. Indeed, muscle glycogen storage is enhanced 3 h after a high-GI breakfast compared with a low-GI breakfast (37). We have previously reported that the insulin response to high- and low-GI meals, identical to those consumed in the present study, was blunted when the meals were consumed during the postexercise period (27). This is in agreement with the only other mixed-meal study (2) and follows the general consensus of a blunted glycemic response postexercise. Other studies have reported a reduced insulin response to an oral glucose tolerance test following acute exercise (42). Combined with the present data, these studies suggest that the GI of carbohydrates consumed postexercise (up to 24 h) may not be as important to muscle glycogen resynthesis as it is preexercise (1–3 h).

With the use of direct assessment of liver glycogen content, total liver glycogen content is estimated to be ~234 μmol/g [based on liver volume being 1.3 liters (16) and a density of 1.05 (12) and liver glycogen content of 180 μmol/g]. Each 90-min cycle produced an ~40% reduction in liver glycogen with no effect of preceding GI either at baseline or at the end of exercise. Acute bouts of exercise are accompanied by a pronounced increase in hepatic glucose output in response to increased oxidation by contracting skeletal muscle (20), but surprisingly little is known about how liver glycogen content and glucose production can be optimized for aerobic exercise performance. Much of the knowledge of hepatic gluconeogenesis and glycogenolysis during exercise is derived from work in dogs. These studies showed that gluconeogenesis can in-

![Fig. 2. Intramuscular lipid, muscle glycogen, and liver glycogen before and after 90 min of cycling at 70% $\dot{V}_{O_2peak}$ following a low (left) or high (right) GI recovery diet.](image-url)
crease 2.5-fold between rest and exercise (35). Studies in humans show that hepatic gluconeogenesis increases as a direct response to a decline in circulating insulin or following an absolute or relative increase in glucagon (20, 40). There are few reports on directly measured changes in liver glycogen concentration during exercise because of the technical constraints of performing liver biopsies in healthy individuals. The only other study to report changes in liver glycogen during recovery from exercise in healthy individuals compared glucose or sucrose feeding with a no-carbohydrate control (3), with no difference between trials. The same study did highlight the importance of liver glycogen, with a positive correlation between liver glycogen and endurance exercise performance.

Our study also provides unique insights into the relationship between carbohydrate quality and lipid depots during exercise. Our data show that the amount of liver glycogen used during exercise is related to both the preexercise glycogen content and inversely related to the level of circulating NEFA during exercise, i.e., the higher the starting level of glycogen and lower the level of circulating NEFA, the greater glycogen use during exercise. The influence of both preexercise glycogen content and circulatory NEFA upon glycogen use has previously been described in skeletal muscle (13, 22, 34, 39). Preexercise substrate storage may influence subsequent substrate utilization through activation of AMP-activated protein kinase (39). NEFA may influence substrate utilization through its incorporation and oxidation in the muscle (24). To our knowledge, this is the first study to describe the same relationships with liver glycogen. The additional importance of NEFA to the liver, compared with muscle, is its inhibitory effect on the glycogenolytic effects of glucagon and epinephrine (8). However, this has not been studied during exercise and remains purely hypothetical. As such, it remains to be determined whether the rate of glycogen breakdown in liver is a
direct effect of preexercise glycogen content, the inhibitory effects of NEFA upon glucagon/epinephrine, or an indirect effect of altered total carbohydrate and lipid oxidation. Further studies are necessary to better understand the interplay between the liver, muscle, and circulating metabolites.

In summary, these data show that a high-GI recovery diet, compared with a low-GI diet, reduces NEFA availability and increases the reliance on IMCL as a lipid fuel source during subsequent exercise. There was no effect of recovery diet composition on either skeletal muscle or liver glycogen storage or oxidation during exercise in the fasted state. Changes in substrate metabolism during exercise following a short-term high- or low-GI recovery diet appear to be driven by the availability of free fatty acids during exercise without any influence on muscle or liver glycogen storage or utilization. Further studies are necessary to understand the implications of long-term high- and low-GI recovery diets, NEFA availability, and exercise in both health and disease.

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