Impaired substrate oxidation in healthy elderly men after eccentric exercise

RAJ K. KRISHNAN, WILLIAM J. EVANS, AND JOHN P. KIRWAN

1Noll Physiological Research Center and The General Clinical Research Center, The Pennsylvania State University, University Park, Pennsylvania 16802; 2Nutrition, Metabolism, and Exercise Division, University of Arkansas for Medical Sciences, Little Rock, Arkansas 72114; and Departments of 3Reproductive Biology and 4Nutrition, Case Western Reserve University School of Medicine at MetroHealth Medical Center, Cleveland, Ohio 44109

Submitted 13 August 2002; accepted in final form 11 October 2002

Krishnan, Raj K., William J. Evans, and John P. Kirwan. Impaired substrate oxidation in healthy elderly men after eccentric exercise. J Appl Physiol 94: 716–723, 2003.—The metabolic response to eccentric exercise in healthy older adults is unknown. Therefore, substrate metabolism was examined in the basal state and after sustained hyperglycemia (180 min, 10 mM) in eight healthy, sedentary older men [66 ± 2 yr; body mass index (BMI) of 25.5 ± 1.2 kg/m²] and nine younger (23 ± 1 yr; BMI of 23.6 ± 1.7 kg/m²) men, under control conditions and 48 h after eccentric exercise. Indirect calorimetry was performed to evaluate carbohydrate and lipid oxidation (Cox and Lox, respectively). Eccentric exercise caused muscle soreness and increased plasma creatine kinase in both groups of men (P < 0.02). Although a similar level of hyperglycemia was maintained in the two groups, glucose infusion rates were lower (P < 0.001) in the older men. Compared with basal levels, hyperglycemia stimulated an increase in Cox and a decrease in Lox during the control and exercise trials in the younger group (P < 0.03), but only during the control trial in the older subjects (P < 0.007). Cox was unchanged after eccentric exercise in the younger men [4.00 ± 0.30 vs. 3.54 ± 0.44 mg·kg·fat-free mass (FFM)⁻¹·min⁻¹; exercise vs. control] but was suppressed by 20% in the older group (3.37 ± 0.37 vs. 4.21 ± 0.23 mg·kg⁻¹·min⁻¹; P < 0.04). Moreover, Lox was reduced by 38% in the younger subjects (0.47 ± 0.09 vs. 0.76 ± 0.10 mg·kg⁻¹·min⁻¹; P < 0.03) but was augmented by 89% in the older group (0.68 ± 0.11 vs. 0.36 ± 0.08 mg·kg⁻¹·min⁻¹; P < 0.04). In addition, hyperglycemia-stimulated Cox and Lox, and respiratory exchange ratio responses to eccentric exercise were related to abdominal adiposity (r = −0.57, P < 0.04, r = 0.68, P < 0.02 and r = −0.60, P < 0.02, respectively). Despite normal glucose tolerance and the absence of obesity per se, older men experience a reduction in carbohydrate oxidation in response to hyperglycemia after eccentric exercise.

carbohydrate oxidation; lipid oxidation; exercise-induced muscle damage; aging; obesity; diabetes

HUMAN AGING IS ASSOCIATED WITH a decline in basal metabolic rate (BMR) (30, 37) and alterations in substrate metabolism, including reduced rates of lipid oxidation (Lox) (22, 33). However, it remains uncertain whether these changes result from aging, per se, or are secondary effects of physical inactivity and changing body composition, particularly if the fat is deposited in the abdominal region (30, 35). Consequently, a number of studies have advocated the use of regular aerobic and resistance exercise for the elderly to increase resting metabolic rate and improve basal substrate oxidation, including an elevation in Lox (29, 30, 34). However, relatively few studies have examined the effects of exercise on resting substrate utilization in healthy, sedentary, older adults who maintain a normal body weight and normal glucose metabolism. Furthermore, some types of exercise, i.e., eccentric exercise, may have a transient, negative effect on glucose metabolism, and this has not been previously examined in an elderly population.

Exercise consisting of forced-lengthening muscle contractions, or eccentric exercise, is known to cause extensive myofibrillar damage (12, 26), muscle soreness (14), and elevated plasma myocellular protein levels (26). Several investigators have shown that eccentric exercise-induced muscle damage results in transient insulin resistance (3, 9, 18) and an increase in pancreatic β-cell secretion in younger subjects (16, 17, 21). Other studies suggest downregulation of insulin signaling (9) and reduced GLUT-4 protein levels in humans and animals (3, 4). We recently reported that a single bout of eccentric exercise in younger subjects causes no change in carbohydrate oxidation (Cox) but a decrease in nonoxidative glucose disposal during a euglycemic-hyperinsulinemic clamp (9). In fact, several investigators have shown that eccentric exercise causes impaired glycogen synthesis (7, 10, 27) that is restored by increasing carbohydrate intake during the postexercise period (7). However, relatively little is known about the effects of eccentric exercise on substrate metabolism. The metabolic response to eccentric exercise is particularly important in the elderly, in light of our previous findings that older subjects lack the normal compensatory increases in pancreatic β-cell
response that occur after eccentric exercise in younger individuals (21).

The purpose of this investigation was to determine the effects of eccentric exercise on substrate oxidation in healthy, sedentary older men compared with a group of healthy, sedentary younger men. We hypothesized that the metabolic response to eccentric exercise would be similar in direction but greater in magnitude in the older men because of the known effects of age and eccentric exercise on insulin resistance. Substrate oxidation rates were measured at rest and during a controlled hyperglycemic infusion to evaluate age-related differences in metabolism during a sustained postprandial-like condition. Moreover, we were interested in the potential contribution of body composition to the regulation of substrate oxidation and the possible effects of eccentric exercise on this relationship.

METHODS

Subjects. Seventeen men (8 older, age 59–75 yr, and 9 younger, age 21–29 yr) participated in the study. All of the subjects were healthy and were excluded for any acute/chronic disease or any medications that would affect carbohydrate or lipid metabolism. In addition, all of the subjects were sedentary with a similar activity level between the two groups, as assessed by a physical activity questionnaire. None of the participants were engaged in any regular exercise regimen for at least 6 mo before testing. All subjects had a normal plasma glucose response to a 75-g oral glucose tolerance test (2) and did not have a family history of Type 2 diabetes.

Height without shoes was measured to the nearest 1.0 cm. Body weight was measured to the nearest 0.1 kg. Body circumferences were measured to the nearest 1.0 cm for the waist (at the level of umbilicus) and hip (at the point of widest circumference around the buttocks). Waist-to-hip ratio (WHR) was calculated to estimate abdominal adiposity (20). Body density and body fat were determined by hydrostatic weighing (1).

Study design. All of the subjects participated in two trials that were at least 1 wk apart. Both trials included residence at the General Clinical Research Center for 3 nights and 2 consecutive days (day 1 and day 2). A specific research diet was provided for 2 days, and activity level was kept to a minimum. On day 1, subjects performed either no exercise (control) or one session of eccentric exercise. Hyperglycemic infusions and indirect calorimetry were performed on day 3 for both control and exercise trials.

Eccentric exercise. Subjects performed 10 sets, with 10 repetitions per set, of eccentric-lengthening contractions for leg extension (right and left legs separately) and chest press exercises with the use of Universal weight machines (Universal Gym Equipment, Cedar Rapids, IA), as described previously (21). The resistance was initially set at 100% of predetermined strength (3 repetition maximum) for both concentric and eccentric phases. The subject received the weight at full extension of either leg (right and left legs, separately) or the arms, and lowered the weight in a steady fashion through the full range of motion, with ~3 s allowed for each repetition. When the time of contraction fell below ~3 s, the resistance was reduced by 2.3 and 4.5 kg for the leg extension and chest press, respectively. Measurements of muscle soreness in the upper and lower body were obtained at 24 and 36 h after exercise. Ratings of perceived soreness were obtained while a constant 40 N (4.1 kg) of pressure was applied to test sites by using a spring-loaded pressure applicator with a 2-cm diameter probe end, as described previously (9, 11, 21). The scale for determination of perceived soreness ranged from 0 (“absence of soreness”) up to 9 (“unbearable soreness”) arbitrary units. Plasma creatine kinase concentrations were measured from blood samples (Sigma Diagnostics, St. Louis, MO) obtained at 48 h after eccentric exercise to assist in evaluation of the presence of muscle damage (26).

Diet. During days 1 and 2 of residence, subjects consumed a eucaloric diet (2,636 ± 115 vs. 3,182 ± 118 kcal, older vs. younger; 60% carbohydrate, 25% fat, 15% protein) that was calculated by using the Harris-Benedict equation (13). A similar diet was consumed during the control and exercise trials.

Hyperglycemic infusion. Hyperglycemic clamps (180 min, 10.0 mM) were performed as described previously (8, 21). After blood samples were drawn to measure fasting glucose concentrations, plasma glucose was raised to 10.0 mM within 15 min by using a primed glucose infusion (20% dextrose) with a variable-speed infusion pump (Harvard Apparatus, South Natick, MA). Plasma glucose was maintained at 10.0 mM for another 165 min by a variable-rate infusion based on the prevailing glucose concentration. Blood samples (0.5 ml) were drawn every 5 min, and plasma was immediately assayed in duplicate by the glucose oxidase method (Beckman Instruments, Fullerton, CA). Glucose concentrations were used to adjust the infusion rate throughout the procedure.

Indirect calorimetry. After an overnight fast (~12 h), subjects were awakened and transported by wheelchair to void and for measurement of body weight. Subjects were then reclined in a semi-darkened, thermoneutral (22 ± 1 °C) environment under a flow-through (50 l/min) Plexiglas hood (Brooks Instruments, Hatfield, PA) for a 30-min measurement of BMR before the glucose infusion. During the infusion period, resting metabolic rate was measured from 170 to 180 min of hyperglycemia. A continuous, open-circuit collection of exhaled air was analyzed by using Hartmann-Braun (Frankfurt, Germany) differential paramagnetic O2 (Magnos 4G) and nondispersive infrared CO2 (Uras 4) analyzers. Analyzers were calibrated before each collection with known gas mixtures. Substrate Cox and Lox were calculated by using either 24-h or infusion-period urinary nitrogen determinations to account for protein oxidation (23). BMR (kcal/h) was calculated as described previously (36, 37).

Statistics. The MIXED procedure for the Statistical Analysis System (SAS Institute, Cary, NC) was used for ANOVA by the rank transformation (nonparametric) approach. Group differences in the descriptive data were determined by using a one-way ANOVA. Primary dependent variables were analyzed by a three-way, repeated-measures ANOVA with the main effects of group (younger and older), trial (control and exercise), and treatment (BMR and hyperglycemia). Model-adjusted P values from a comparison of the least-squares means were used to determine all differences. Univariate analyses (Spearman product-moment correlations) were used to determine relationships between substrate oxidation rates and body composition. All values are expressed as means ± SE. An alpha level of 0.05 was used to determine statistical significance.
RESULTS

Subject characteristics. Subjects were similar in body weight, fat-free mass, and body mass index (BMI), but the older group had a higher fat mass, greater WHR, and a lower BMR (Table 1). All subjects had a normal response to the oral glucose tolerance test (2).

Eccentric exercise. Younger subjects lifted 35.9 ± 3.2, 34.1 ± 2.7, and 50.5 ± 6.8 kg for the right leg, left leg, and chest exercises, respectively, with reduced (P < 0.05) resistance of −4.5, −1.8, and −16.0% per 10 sets, respectively. Older subjects lifted 24.1 ± 2.6, 23.9 ± 2.4, and 35.8 ± 4.5 kg for the right leg, left leg, and chest exercises, respectively, with reduced (P < 0.05) resistance of −4.6, −1.3, and −13.4% per 10 sets, respectively. The two groups experienced a similar rate of decline in resistance over the 10 sets. Muscle soreness ratings for the upper and lower body were similar in both older and younger age-groups. Peak soreness at 36 h was exhibited (P < 0.005) at 24 and 36 h after exercise, with no age-group differences. Peak soreness at 36 h was exhibited in the triceps (6.9 ± 0.8 and 5.6 ± 0.8 units, younger and older, respectively), pectorals (5.8 ± 0.8 and 5.5 ± 0.6 units), and quadriceps (3.9 ± 0.9 and 3.9 ± 0.6 units). Plasma creatine kinase concentrations were elevated (P < 0.02) 48 h after exercise compared with the control trial in both younger (1,159 ± 324 vs. 27 ± 10 IU/l, respectively) and older men (629 ± 418 vs. 49 ± 15 IU/l), suggesting marked muscle damage.

Hyperglycemic infusion. Baseline plasma glucose and glucose concentrations achieved during sustained hyperglycemia were similar in both older and younger groups for all trials (Table 2). The amount of glucose required to maintain hyperglycemia (M values, calculated from the glucose infusion rates for 150–180 min and adjusted for the glucose equivalent space and urinary glucose loss, if any) was not different between exercise and control trials in either younger [9.9 ± 0.5 vs. 10.2 ± 0.7 mg·kg−1·h−1, respectively] or older subjects [6.2 ± 0.6 vs. 6.3 ± 0.6 mg·kg−1·h−1]. However, M values were lower (P < 0.002) in older vs. younger subjects, regardless of trial.

Substrate oxidation. Basal Cox and respiratory exchange ratio (RER) were similar under control conditions in the older and younger groups (Table 2). However, resting Lox was lower (P < 0.05) for the older men (Table 2). Likewise, Cox expressed as a component of BMR was similar in older and younger men, but Lox was lower (P < 0.05) in the older group (Fig. 1). Eccentric exercise did not alter basal measurements of Cox, Lox, or RER in either group (Table 2), nor did it alter the contribution of Cox or Lox to resting metabolic rate (Fig. 1). As expected, during hyperglycemia, Cox increased and Lox decreased in younger subjects (P < 0.03) for both trials (Fig. 1). In contrast, these changes were only evident during the control trial for the older subjects (P < 0.007; Fig. 1). To evaluate the effects of eccentric exercise on substrate oxidation during hyperglycemia, comparisons were made between control and exercise trials for each group. Cox was unchanged in younger (+13%; P = 0.11) but suppressed by 20% (P < 0.04) in the older men (Fig. 2). Moreover, Lox was diminished by 38% (P < 0.03) in the younger group but augmented by 89% (P < 0.04) in the older subjects (Fig. 2). RER was increased (P < 0.03) in younger and decreased (P < 0.03) in older subjects (Table 2). Therefore, we observed age-group differences in Cox and Lox during hyperglycemia after the eccentric exercise trial. However, we observed no differences in nonoxidative glucose disposal (calculated differences between M values and Cox) in either younger [5.9 ± 0.7 vs. 6.69 ± 0.72 mg·kg FFM−1·min−1, exercise vs. control; −11%, P = 0.35] or older groups [3.25 ± 0.97 vs. 1.95 ± 0.73 mg·kg FFM−1·min−1, +66%, P = 0.86] (Fig. 3). Finally, univariate analyses revealed that the Cox, Lox, and RER responses to eccentric exercise were associated with WHR (r = −0.57, P < 0.04; r = 0.68, P < 0.02; and r = −0.60, P < 0.02, respectively; Fig. 4).

DISCUSSION

To evaluate the effects of age per se on the metabolic response to eccentric exercise, we selected subject groups with widely differing age but similar clinical indexes of glucose metabolism. The older men were neither obese nor overweight, had normal glucose tolerance, were not taking medications, and maintained activity levels similar to those of the younger group. Although body weight, BMI, and lean body mass were similar for the two groups, the older men clearly had more body fat. This modest, but significant, difference in body fat appears to be part of normal aging when strenuous physical activity and/or exercise are absent from daily life. It is possible that the increase in body fat in the elderly is due to a decrease in Lox (30). Thus it was not surprising to find what appears to be a normal, age-associated decline in BMR accompanied by normal carbohydrate metabolism but suppressed Lox in the older group. Similar observations have been reported previously in the elderly (22, 30, 33, 37). During sustained hyperglycemia and without prior exercise, we found that both groups experienced similar increases in Cox and decreases in Lox, an observation that has also been previously reported in younger subjects (38). Thus our findings suggest that, although older age may contribute to aberrant changes in basal

Table 1. Subject characteristics

<table>
<thead>
<tr>
<th></th>
<th>Younger (n = 9)</th>
<th>Older (n = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>23 ± 1</td>
<td>66 ± 2</td>
</tr>
<tr>
<td>Height, cm</td>
<td>180.7 ± 0.9</td>
<td>172.1 ± 2.1*</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>76.7 ± 4.9</td>
<td>75.7 ± 4.2</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>23.6 ± 1.7</td>
<td>25.5 ± 1.2</td>
</tr>
<tr>
<td>Body fat, %</td>
<td>15.4 ± 2.2</td>
<td>23.0 ± 1.7*</td>
</tr>
<tr>
<td>Fat mass, kg</td>
<td>12.1 ± 2.6</td>
<td>17.2 ± 1.7*</td>
</tr>
<tr>
<td>Fat-free mass, kg</td>
<td>64.6 ± 2.7</td>
<td>58.5 ± 2.9</td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
<td>0.83 ± 0.02</td>
<td>0.91 ± 0.01*</td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>77.7 ± 3.4</td>
<td>91.1 ± 3.2*</td>
</tr>
<tr>
<td>Basal metabolic rate, kcal/h</td>
<td>76.0 ± 2.5</td>
<td>64.9 ± 3.7*</td>
</tr>
</tbody>
</table>

Values are means ± SE. *Significantly different from younger, P < 0.05.
metabolism, healthy, older men have a normal capacity for substrate oxidation during hyperglycemia.

Eccentric exercise has been used previously as a model for transient insulin resistance in young, healthy men and women (3, 9, 18). We recently reported that eccentric exercise causes downregulation of insulin signaling at several steps, including insulin receptor substrate-1 tyrosine phosphorylation, phosphatidylinositol 3-kinase activity, Akt (protein kinase B) serine phosphorylation, and Akt activity in young subjects (9). Furthermore, impaired insulin action after eccentric exercise has been associated with decreased GLUT-4 protein (3, 4) and reduced glycogen synthesis (7, 10, 27) in human and animal models. These studies suggest that eccentric exercise reduces insulin-mediated, whole body glucose disposal by altering signaling-transporter mechanisms in the muscle. We have also found that healthy older subjects fail to show the normal compensatory increases in pancreatic β-cell secretion after eccentric exercise (21). These findings suggest that older individuals may experience a similar or greater level of transient insulin resistance after this type of exercise. In the present study, we provide evidence that, with increasing age, eccentric exercise results in reduced C\textsubscript{ox} and increased L\textsubscript{ox} during hyperglycemia. These changes in substrate metab-

Table 2. Carbohydrate and lipid oxidation rates, RER, and plasma glucose concentrations during fasting and hyperglycemic conditions for control and eccentric exercise trials

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Eccentric Exercise</th>
<th>Hyper-base</th>
<th>Control</th>
<th>Eccentric Exercise</th>
<th>Hyper-base</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Younger</td>
<td>5.1 ± 0.1</td>
<td>10.0 ± 0.1</td>
<td>+4.9</td>
<td>5.1 ± 0.1</td>
<td>10.0 ± 0.1</td>
<td>+4.9</td>
</tr>
<tr>
<td>Older</td>
<td>5.3 ± 0.1</td>
<td>10.0 ± 0.1</td>
<td>+4.7</td>
<td>5.3 ± 0.1</td>
<td>10.0 ± 0.1</td>
<td>+4.7</td>
</tr>
<tr>
<td>Hyper</td>
<td>2.73 ± 0.22</td>
<td>3.54 ± 0.44</td>
<td>+0.81*</td>
<td>2.89 ± 0.24</td>
<td>4.00 ± 0.30</td>
<td>+1.11*</td>
</tr>
<tr>
<td>Younger</td>
<td>2.95 ± 0.23</td>
<td>4.21 ± 0.23</td>
<td>+1.26*</td>
<td>2.88 ± 0.23</td>
<td>3.37 ± 0.37†</td>
<td>+0.49</td>
</tr>
<tr>
<td>Older</td>
<td>0.78 ± 0.09Y</td>
<td>0.36 ± 0.08</td>
<td>+0.42*</td>
<td>0.81 ± 0.06</td>
<td>0.68 ± 0.11†</td>
<td>-0.37*</td>
</tr>
</tbody>
</table>

Values are means ± SE. Base, basal; Hyper, hyperglycemia; ΔHyper-base, calculated difference between means for Hyper and Base. Plasma glucose concentrations for Hyper are calculated means for 150–180 min. Base values for glucose are calculated averages from −30, −20, −10, and 0 min before the start of glucose infusion. *Hyper significantly different from Base when compared within trial for control or exercise; †P < 0.03. Exercise Hyper significantly different from control Hyper; P < 0.04. YSignificantly lower lipid oxidation for older-control Base compared with younger-control Base; P < 0.05.

**Fig. 1.** Substrate oxidation rates at rest and during hyperglycemia. Measurements were repeated without preceding exercise (control) and 48 h after eccentric exercise. Values are expressed as total oxidation rates (kcal·kg fat-free mass\(^{-1}\)·min\(^{-1}\)) calculated by using the metabolic equivalents of 4 kcal/g for carbohydrate oxidation (C\textsubscript{ox}) and 9 kcal/g for lipid oxidation (L\textsubscript{ox}). Base, basal; Hyper, hyperglycemia. *Significant reduction in glucose oxidation during hyperglycemia compared with the control trial in the older group; P < 0.04. †Significant increase in L\textsubscript{ox} during Hyper compared with the control trial in the older group; P < 0.04. §Significant increase in C\textsubscript{ox} during hyperglycemia; P < 0.03. $Significant decrease in L\textsubscript{ox} during hyperglycemia compared with Base; P < 0.03. ‡Significantly lower basal L\textsubscript{ox} in the older compared with younger group under control conditions; P < 0.05. ‡Significant reduction in L\textsubscript{ox} during Hyper compared with the control trial in the younger group; P < 0.03.
olism in the older men are similar to what has been reported previously in insulin-resistant subjects with Type 2 diabetes who experienced impaired postprandial glucose oxidation (15) and an increase in $L_{ox}$ (25) after mixed meals. Our observations on the changes in substrate metabolism after eccentric exercise in the older group may reflect a loss in plasticity with normal aging, such that the older men were unable to overcome the insulin resistance generated by eccentric exercise.

One of the main findings in this study was the age-related difference in the amount of carbohydrate that was oxidized after eccentric exercise. The eccentric exercise bout, which was accompanied by marked muscle soreness, unmasked what appears to be a deficiency in metabolism in the older subjects as evidenced by a 20% suppression in $C_{ox}$ during hyperglycemia, when compared with the nonexercise control trial. In contrast, the younger subjects demonstrated a 13% increase in $C_{ox}$ after eccentric exercise, which, although not statistically significant, is supported by an increased RER, suggesting a real shift toward greater carbohydrate utilization and reduced $L_{ox}$. There are several factors that may be responsible for the response noted in the elderly. For one, the older group may have sustained a greater amount of muscle damage after the eccentric exercise bout. Manfredi et al. (24) reported that, although older and younger subjects performed eccentric exercise at a similar relative intensity, ultrastructural examination revealed five times as much muscle damage in the elderly group despite similar elevations in creatine kinase levels. Second, we observed lower glucose infusion rates in the older group, which suggests a reduced insulin action, as reported in other studies (5, 19). Thus underlying insulin resistance or a greater degree of muscle damage in the elderly subjects may have manifested in a reduced ability to oxidize carbohydrate after eccentric exercise.

In addition to the differential effects of eccentric exercise on $C_{ox}$ between young and older men, we also found that lipid metabolism was differentially altered.
in relation to age. After eccentric exercise, younger subjects experienced a 38% decrease in \( L_{\text{ox}} \) during hyperglycemia, whereas \( L_{\text{ox}} \) was increased by 89% in the older men. Interestingly, the shift in substrate utilization that occurred in the older group is reminiscent of the substrate competition model originally proposed by Randle and colleagues (31) to explain hyperglycemia in Type 2 diabetes. In this model, insulin resistance in the muscle leads to competition between glucose and FFA as oxidative fuels and sets up a metabolic milieu that favors \( L_{\text{ox}} \) at the expense of \( C_{\text{ox}} \). It is known that eccentric exercise causes transient insulin resistance (3, 9, 18). Therefore, it is possible that, for the older men who were already somewhat insulin resistant, the eccentric exercise bout may have pushed insulin resistance to a level that allowed inhibition of the antilipolytic effects of insulin, thus facilitating \( L_{\text{ox}} \) instead of \( C_{\text{ox}} \). This novel finding suggests a role for increased \( L_{\text{ox}} \) in clinically normal older adults who lack the compensatory metabolic mechanisms to overcome the physiological stress associated with eccentric exercise.

Univariate analyses revealed an association between WHR and the changes in \( C_{\text{ox}}, L_{\text{ox}}, \) and RER after eccentric exercise. However, we found no relationship between BMI or total fat mass and the observed changes in substrate oxidation. These data suggest that the age-related differences in substrate metabolism were associated with greater abdominal fat in the older men but not necessarily with total fat mass. It is important to note that these older men were not obese per se but experienced normal increases in body fat and central obesity reported previously in sedentary elderly subjects (28). Indeed their BMI is within the healthy range for adults, and they had a similar lean body mass as the younger men. We previously reported that an increase in abdominal adiposity in the elderly prevents the normal compensatory increase in pancreatic \( \beta \)-cell secretion after eccentric exercise (21). It has been suggested that central body fat is highly sensitive to lipolytic stimuli, which may in turn contribute to insulin resistance by increasing gluconeogenesis in the liver, thus promoting hyperglycemia and also facilitating an increase in circulating FFA (32). This mechanism has been invoked in previous studies to explain the association between central obesity and the insulin resistance of aging (6, 20). In the present investigation, it is possible that abdominal adiposity, albeit relatively modest, imposes an additional stress that increases the likelihood that subtle metabolic deficiencies already present in the older group may be exacerbated by the additional stress arising from the eccentric exercise bout. Thus, in the present study, it appears that modest increases in abdominal adiposity in the elderly may contribute to greater availability of FFA and an increase in \( L_{\text{ox}} \) after eccentric exercise. Moreover, increased FFA release from adipose tissue also creates a metabolic milieu that may compromise \( C_{\text{ox}} \).

In summary, this investigation provides evidence for age-related differences in substrate metabolism after eccentric exercise. In healthy younger men, we observed a preservation of \( C_{\text{ox}} \) but a reduced \( L_{\text{ox}} \), which we interpret as a normal compensation during hyperglycemia after exercise-induced muscle damage. In contrast, older men experienced a reduced ability to oxidize glucose together with marked increases in \( L_{\text{ox}} \). Thus the metabolic response to exercise-induced muscle damage in older individuals.
may operate by aberrant shifts in substrate utilization during periods of hyperglycemia. In addition, the association between increased abdominal adiposity and alterations in substrate metabolism suggests a mechanism by which increased central fat in older men increases lipid availability and \( \text{LO}_{2} \), and thus suppresses carbohydrate utilization. In conclusion, aging and modest increases in abdominal adiposity are associated with aberrations in substrate oxidation after eccentric exercise.

The authors thank the nursing/dietary staff of the General Clinical Research Center and the technical/engineering staff of the Noll Physiological Research Center for the implementation of the study and assisting with data collection. The authors thank Christine Marchetti, David Williamson, Donal O’Gorman, and Jazmir Hernandez for assistance. The authors are grateful to Allen R. Kundleman at the Center for Biostatistics and Epidemiology at the Hershey Medical Center for assistance in data analysis and interpretation. Finally, the authors thank the research volunteers for cooperation and commitment.

This research was supported by National Institute on Aging Grants AG-12834 (to J. P. Kirwan) and AG-15385 (to W. J. Evans), Interdisciplinary Seed Grant from the College of Health and Human Development at The Pennsylvania State University (to J. P. Kirwan), and the General Clinical Research Center Grant RR-10732.

REFERENCES


