Exercise and improved insulin sensitivity in older women: evidence of the enduring benefits of higher intensity training

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DiPietro, Loretta, James Dziura, Catherine W. Yeckel, and P. Darrell Neufer. Exercise and improved insulin sensitivity in older women: evidence of the enduring benefits of higher intensity training. J Appl Physiol 100: 142–149, 2006. First published September 1, 2005; doi:10.1152/japplphysiol.00474.2005.—Few studies have compared the relative benefits of moderate- vs. higher intensity exercise training on improving insulin sensitivity in older people while holding exercise volume constant. Healthy older (73 ± 10 yr) women (N = 25) who were inactive, but not obese, were randomized into one of three training programs (9-mo duration): 1) high-intensity (80% peak aerobic capacity [VO2 peak]; TH aerobic training; 2) moderate-intensity (65% VO2 peak; TM) aerobic training; or 3) low-intensity (stretching) placebo control (50% VO2 peak; CTB). Importantly, exercise volume (300 kcal/session) was held constant for subjects in both the TH and the TM groups. VO2 peak was determined by using a graded exercise challenge on a treadmill. Total body fat and lean mass were determined with dual-energy X-ray absorptiometry. The rate of insulin-stimulated glucose utilization was also measured with lipolysis at the low-insulin dose (38–55%, P = 0.05). Our findings suggest that long-term higher intensity exercise training provides more enduring benefits to insulin action compared with moderate- or low-intensity exercise, likely due to greater transient effects.

WHILE THERE ARE DATA SUGGESTING some degree of mandatory decline in insulin sensitivity and glucose tolerance with aging (8, 19, 28, 35), the extent of these pathophysiologic alterations is likely modulated by several other potentially confounding factors that also change with age, namely, increased adiposity, decreased lean mass, and reduced physical activity (26, 31, 34, 39, 40). Older people who exercise regularly appear to be protected from the development of insulin resistance and glucose intolerance (4, 5, 24, 30, 33), and this protection may be independent of exercise-related changes in body composition (6, 9, 38). However, the magnitude of improvement in insulin-stimulated glucose disposal with exercise training (performed at the same relative intensity) may be attenuated in older compared with younger people (31). This blunted response may be dependent on the absolute exercise intensity, as well as the volume (i.e., energy expenditure) of each training bout. The initial degree of insulin resistance also may influence the degree of responsiveness to exercise training, such that older people with the greatest degree of impairment may demonstrate the greatest improvement.

In younger people, transient improvements in insulin sensitivity correlate positively with the intensity of the training bout (29); however, untrained older people may not be capable of performing higher intensity activity due to the loss of aerobic capacity, to chronic disease, or to fear of injury (1). Moderate-intensity exercise may be an effective strategy in older people, if it is performed daily and for a long enough duration to result in a sufficient volume of energy expenditure. Few studies have compared the relative benefits of moderate- vs. higher intensity training while holding exercise volume constant. This makes it difficult to distinguish between the unique contributions of exercise intensity and of exercise volume to improved metabolic function and to the consequent decay in these functional improvements between exercise bouts.

We proposed that a 9-mo aerobic training program (comprising an energy expenditure of ~300 kcal/bout) would provide for both the extreme opportunity to alter body composition, as well as the chance to determine whether long-term training could extend the acute benefits of exercise beyond 24–48 h in inactive older women. Moreover, given the same absolute exercise volume (i.e., 300 kcal), we hypothesized that the greatest training-related improvements in metabolic function would occur with higher compared with moderate-intensity exercise and, consistent with our previous findings, would occur independent of changes in body composition.

METHODS

Subjects. Older (≥60 yr) women were recruited by advertisement from private older adult residential communities in Connecticut and from local community senior centers. Eligible study subjects included those who reported no regular physical activity for the previous 6 mo, were nonsmokers and not on hormone replacement therapy or glucose-lowering medication, and with class I obesity (i.e., body mass index <30 kg/m²). Older volunteers were screened by their personal physician for cardiovascular disease, neuroendocrine disorders, and other uncontrolled chronic disease. In addition, all eligible study subjects successfully completed an exercise tolerance test performed in the Department of Cardiology at Yale University-New Haven Hospital. Use of a medically screened study population ensured a medically screened study population ensured a sample of older subjects healthy enough to participate in such a training study, but with a wide range of insulin sensitivity. Following these screening assessments, volunteers meeting all inclusion criteria...
(N = 27) completed all baseline assessments before being randomized; however, data analysis was conducted on only those subjects with complete data at follow-up (n = 25; 73 ± 10 yr; age range 62–84 yr). The protocol was approved by the Human Investigations Committee of Yale University School of Medicine, and all eligible study subjects gave written, informed consent before their participation.

Exercise training protocol. Subjects were randomized into one of three groups: 1) a higher intensity [TH; 80% peak aerobic capacity (VO₂peak)] or 2) moderate-intensity (TM; 65% VO₂peak) aerobic training group; or 3) a lower intensity placebo control (CTH; 50% VO₂peak) group. Exercise intensity in these groups was based on a heart rate (HR) necessary to achieve this relative intensity during the graded exercise challenge. Thus the average (range) HR targets for the three groups were 123 beats/min (107–134 beats/min) for the TH group, 104 beats/min (97–110 beats/min) for the TM group, and 81 beats/min (75–90 beats/min) for the CTH group. Volunteers in the TH and TM groups exercised under supervision in small groups of five persons primarily on treadmills. To provide some variability in training mode and to avoid injury, subjects were allowed to “jog” on mini-trampolines, use rowing ergometers, or perform step aerobics for 5 min after each 15- to 20-min interval of treadmill walking, while maintaining their target HR. Subjects in the placebo control group participated together in a supervised exercise program of stretching and strengthening using Thera-bands, Thera-balls, and balance boards. The training and control groups were identical with regard to exercise frequency (4 days/wk) throughout the 9-mo intervention. After an initial 4- to 6-wk lead-in period, exercise volume was held constant for subjects in both the TH and the TM groups. Therefore, subjects randomized to the two aerobic training groups exercised for a duration necessary to expend 300 kcal/session (estimated from VO₂peak and body weight) (1). If we assume a VO₂peak of 1.40 l/min (20 m1·kg⁻¹·min⁻¹ for a 68-kg older women), this required ∼55 and 65 min of exercise for TH and TM groups, respectively. Subjects in the CTH group exercised for 45 min/session. HR was monitored continuously during exercise (Polar Electro) and was recorded every 10 min during each exercise session. Because we were interested in the independent effects of exercise on glucose metabolism, subjects were instructed to maintain their usual dietary intake throughout the study.

V˙O₂ peak was determined on a treadmill during each exercise session. Because we were interested in the independent effects of exercise on insulin sensitivity and in knowing whether long-term training could extend the acute benefits of exercise past 24 or 48 h. Thus, to distinguish transient effects of exercise on insulin sensitivity from more chronic adaptations occurring with long-term training, the clamps at 9 mo were performed ∼72 h following the last training session.

Oral glucose tolerance test. A 3-h, 75-g oral glucose tolerance test (OGTT) was performed at baseline, and at 3, 6, and 9 mo, according to the guidelines of the American Diabetes Association (2). Plasma glucose and insulin concentrations were determined before (∼15 and 0 min) and at 30-min intervals during the test. All subjects were instructed to eat a diet containing 150 g or more of carbohydrates per day for 3 days before the OGTT, and all testing was performed within 48 h of exercise.

Blood analysis. All blood samples were placed in preshrilled test tubes. Samples were centrifuged at 4°C, and the plasma was stored at −70°C until analyzed in the Core Laboratory of the General Clinical Research Center. Pre- and posttraining samples for each subject were analyzed in duplicate within a single assay. Plasma glucose concentrations were analyzed by using the glucose oxidase method (YSI 2300; Yellow Springs Instruments, Yellow Springs, OH). Plasma immunoreactive insulin concentrations were determined with a double antibody radioimmunoassay (Diagnostic, Webster, TX). Plasma concentrations of FFA were determined by standard microfluorimetric procedures (Sigma, St. Louis, MO). Blood samples for the determination of glucose kinetics (20) and glycerol turnover (25) were analyzed by standard procedures at the Diabetes Endocrinology Research Center of Yale University School of Medicine.

Calculations. The rate of whole body insulin-stimulated glucose utilization (M value; mg·kg lean mass⁻¹·min⁻¹) under low- and higher dose insulin infusion was calculated from the average glucose infusion rate during the final 60 min of each step and was corrected for changes in the glucose pool sizes, according to methods described by DeFronzo et al. (7). The M value divided by insulin concentrations during the final 30 min of the clamp (MIU) was calculated and used as an indicator of insulin sensitivity in the muscle. The glucose appearance rate (Rg) was calculated from plasma [6,6-²H]glucose enrichments, and the rate of tracer infusion by the equation \( R_g = |(APE \text{ infused}/APE \text{ plasma glucose}) - 1| \cdot F \), where APE is atoms percent excess and F represents the isotope infusion rate (µg·kg⁻¹·min⁻¹). HGP was then calculated as the difference between Rg and the glucose infusion rate. Glycerol turnover was calculated from plasma [²H₁₂]glycerol, and the rate of tracer infusion by the equation \( R_g = |(APE \text{ infused}/APE \text{ plasma glycerol}) - 1| \cdot F \).
Table 1. General characteristics of the study population before and after training

<table>
<thead>
<tr>
<th></th>
<th>Thera-band (n = 7)</th>
<th>Moderate Intensity (n = 9)</th>
<th>Higher Intensity (n = 9)</th>
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<tbody>
<tr>
<td></td>
<td>Baseline 9 mo</td>
<td>Baseline 9 mo</td>
<td>Baseline 9 mo</td>
</tr>
<tr>
<td>Age, yr</td>
<td>75 ± 5</td>
<td>73 ± 3</td>
<td>72 ± 3</td>
</tr>
<tr>
<td>VO2peak, ml.kg⁻¹.min⁻¹</td>
<td>18.3 ± 4.2</td>
<td>21.2 ± 3.4</td>
<td>21.4 ± 3.9</td>
</tr>
<tr>
<td>Activity*, kcal/wk</td>
<td>4,433 ± 1,075</td>
<td>5,714 ± 2,192</td>
<td>5,414 ± 3,066</td>
</tr>
<tr>
<td>Retention, %</td>
<td>95</td>
<td>91</td>
<td>92</td>
</tr>
<tr>
<td>Adherence, %</td>
<td>HR 100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>Time 96</td>
<td>85</td>
<td>89</td>
</tr>
</tbody>
</table>

Values are means ± SD; n, no. of subjects. VO2peak, peak aerobic capacity; HR, heart rate. *Self-reported physical activity from the Yale Physical Activity Survey and adjusted for seasonal variation.

**Body composition.** Height and weight were measured on a balance-beam scale, and the abdominal circumference (cm) was measured in triplicate at the umbilicus by the same examiner before and after training. We have observed a strong correlation (r = 0.80; P < 0.001) between the abdominal circumference and the visceral fat area measured by computed tomography in our older populations (10). Overall body composition [whole body muscle (kg) and fat mass (kg)] scans were obtained by dual-energy x-ray absorptiometry.

**Physical activity.** To quantify volitional activity performed outside the laboratory, as well as activity being performed as part of the formal training program, self-reported habitual physical activity was assessed at baseline and at 3, 6, and 9 mo using the Yale Physical Activity Survey (YPAS) (11). The YPAS was designed specifically for older populations and assesses common work, exercise, and recreational activities performed during a typical week in the past month. The YPAS also provides a method for adjusting for seasonal variation in activity patterns. In that regard, it is quite useful for tracking activity over a 9-mo period.

**Analysis.** Univariate statistics (means ± SD) first were generated on all study variables. Simple correlations among the study variables were tested by using the Spearman rank order correlation coefficient. Cross-sectional differences at baseline in the levels of all study variables. Simple correlations among the study variables were compared among the three study arms using ANOVA. Cross-sectional differences at baseline in the levels of all study variables. Simple correlations among the study variables were compared among the three study arms using ANOVA.

**RESULTS**

Tables 1 and 2 present the subject characteristics at baseline and at follow-up. Retention to the 9-mo training program (144 sessions) and adherence to the prescribed training HR (i.e., intensity) and training duration per session were high in all three groups (Table 1). There were no baseline differences among the three treatment groups with regard to age or VO2peak. Subjects in the CB group reported less physical activity than women in the other two groups, although these differences did not achieve statistical significance (Table 1). Reported physical activity tended to increase at 9 mo in all three groups, although not significantly so. More importantly, however, this reported increase in estimated total weekly energy expenditure was not sufficient to account for the 1,200 kcal/wk training stimulus in the TM group, thereby suggesting some compensatory decrease in energy expenditure outside of the training sessions in the women performing moderate-intensity training, perhaps due to their longer training duration compared with women in the TH group. Body composition was also similar among the study groups at baseline (Table 2). The 9-mo training program did not increase VO2peak or alter body composition in any of the three treatment groups.

Although these older women were considered healthy enough to participate in a long-term training study based on physician screening, approximately one-half of the subjects (52%) met the criterion for impaired glucose tolerance, based on a 2-h glucose value from the baseline OGTT ≥ 140 mg/dl. At baseline, the M value at the 40 mU insulin dose (M value40) was inversely correlated with the 2-h glucose value from the OGTT (r = −0.54; P < 0.02). In addition, we observed a wide range in the degree of insulin sensitivity at baseline as determined from the higher insulin dose (M value40 1.4–11.3 mg·kg⁻¹·min⁻¹). For comparison purposes, the average M value40 observed in the present study (7.1 ± 3.4 mg·kg⁻¹·min⁻¹) was lower than that reported by Hughes et al. (17) (9.7 ± 4.2 mg·kg⁻¹·min⁻¹) among slightly younger (64 ± 2 yr) glucose-intolerant men and women of similar adiposity (37% fat) and determined by identical procedures.

Fasting metabolic characteristics before the start of the clamp procedure did not change significantly under any exercise training condition (Table 3). In contrast, however, we observed increases in the M value40 in all three training groups (Table 4). These improvements in glucose utilization were statistically significant only in the TH group (21%; P < 0.02) and not in the TM (16%; P = 0.17) and CTB (8%; P = 0.37).

Table 2. Anthropometric characteristics of the study population before and after training

<table>
<thead>
<tr>
<th></th>
<th>Thera-band (n = 7)</th>
<th>Moderate Intensity (n = 9)</th>
<th>Higher Intensity (n = 9)</th>
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<tbody>
<tr>
<td></td>
<td>Baseline 9 mo</td>
<td>Baseline 9 mo</td>
<td>Baseline 9 mo</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>27.2 ± 4.7</td>
<td>27.3 ± 4.7</td>
<td>26.3 ± 3.0</td>
</tr>
<tr>
<td>Lean mass*, kg</td>
<td>38.7 ± 6.8</td>
<td>39.4 ± 7.0</td>
<td>41.9 ± 8.1</td>
</tr>
<tr>
<td>Body fat*, %</td>
<td>38.5</td>
<td>38.5</td>
<td>38.6</td>
</tr>
<tr>
<td>Abdominal circumference, cm</td>
<td>95.9 ± 13.3</td>
<td>93.9 ± 14.0</td>
<td>96.0 ± 14.7</td>
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Values are means ± SD; n, no. of subjects. BMI, body mass index. *Based on dual-energy X-ray absorptiometry.
Table 3. Fasting metabolic characteristics of the study population, before and after training

<table>
<thead>
<tr>
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<th>Thera-Band (n = 7)</th>
<th>Moderate Intensity (n = 9)</th>
<th>Higher Intensity (n = 9)</th>
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<tbody>
<tr>
<td>Glucose, mg/dl</td>
<td>104.5 ± 7.0</td>
<td>100.0 ± 7.4</td>
<td>99.5 ± 5.0</td>
</tr>
<tr>
<td></td>
<td>97.5 ± 3.2</td>
<td>101.6 ± 6.8</td>
<td>100.8 ± 8.8</td>
</tr>
<tr>
<td>Insulin, μU/ml</td>
<td>13.6 ± 2.8</td>
<td>15.1 ± 8.5</td>
<td>13.4 ± 2.9</td>
</tr>
<tr>
<td></td>
<td>11.6 ± 4.0</td>
<td>15.3 ± 7.1</td>
<td>14.5 ± 4.9</td>
</tr>
<tr>
<td>FFA, μmol/l</td>
<td>0.68 ± 0.08</td>
<td>0.72 ± 0.12</td>
<td>0.70 ± 0.18</td>
</tr>
<tr>
<td></td>
<td>0.65 ± 0.06</td>
<td>0.68 ± 0.10</td>
<td>0.59 ± 0.17</td>
</tr>
<tr>
<td>Glycerol, μmol/l</td>
<td>72.0 ± 29.4</td>
<td>65.6 ± 16.2</td>
<td>62.3 ± 14.5</td>
</tr>
<tr>
<td></td>
<td>81.5 ± 26.2</td>
<td>68.8 ± 13.9</td>
<td>71.7 ± 8.5</td>
</tr>
</tbody>
</table>

Values are means ± SD; n, no. of subjects. FFA, free fatty acids.

Glycerol isotopic enrichment data during low- and higher dose insulin infusion are presented in Fig. 2 and indicate that, in general, subjects achieved steady state with regard to glycerol enrichment within each stage of the clamp procedure. The glycerol Ra was calculated from only steady-state enrichment data, in which case the Ra is equivalent to the rate of disappearance (25). Insulin suppression of adipose tissue lipolysis improved significantly only in the TH group, indicated by the decrease in Ra at the low insulin dose (Table 5). Insulin-stimulated suppression of plasma glycerol also improved significantly at both insulin doses in the TH group (47–58% at low dose, P < 0.05; and 64–74% at higher dose insulin, P < 0.01), whereas significant improvements were observed only in the TM group at the higher insulin dose (61–71%, P < 0.05). FFA concentrations during hyperinsulinemia reached nadir values of <0.10 μmol/l during the final stage of the clamp in all three groups; however, improvements in FFA suppression were observed only in the TM group at the low insulin dose (25–14 μmol/l; P < 0.05).

DISCUSSION

Recent cross-sectional data support an age-related decline in insulin sensitivity of ~8% per decade (35). Although older trained athletes have markedly higher insulin sensitivity compared with their sedentary peers, the level of insulin-stimulated glucose uptake, nonetheless, remains blunted in these older compared with younger athletes (5), suggesting that there may be some functional decline in glucose metabolism that is attributable to mandatory aging. Several studies provide evidence, however, that the contribution of aging per se to this decline in metabolic function is trivial after adjusting for age-related differences in physical activity and body composition (26, 31, 34, 39, 40).

Table 4. Metabolic characteristics of the study population during the euglycemic-hyperinsulinemic clamp, before and after training

<table>
<thead>
<tr>
<th></th>
<th>Thera-Band (n = 7)</th>
<th>Moderate Intensity (n = 9)</th>
<th>Higher Intensity (n = 9)</th>
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<tr>
<td>M value at 10 μU, mg/kg lean -1 min-1</td>
<td>2.1 ± 1.56</td>
<td>1.4 ± 1.21</td>
<td>1.9 ± 1.22</td>
</tr>
<tr>
<td></td>
<td>2.5 ± 2.08</td>
<td>1.7 ± 1.53</td>
<td>2.2 ± 1.22</td>
</tr>
<tr>
<td>M value at 40 μU, mg/kg lean -1 min-1</td>
<td>7.5 ± 0.08</td>
<td>6.2 ± 3.31</td>
<td>7.5 ± 3.62</td>
</tr>
<tr>
<td></td>
<td>8.1 ± 3.38</td>
<td>7.1 ± 2.73</td>
<td>9.0 ± 3.60*</td>
</tr>
<tr>
<td>M40/I, μU/mL</td>
<td>0.09 ± 0.03</td>
<td>0.08 ± 0.06</td>
<td>0.08 ± 0.03</td>
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<tr>
<td></td>
<td>0.08 ± 0.03</td>
<td>0.07 ± 0.03</td>
<td>0.10 ± 0.03*†</td>
</tr>
<tr>
<td>Basal HGP, mg/kg -1 min-1</td>
<td>1.70 ± 0.31</td>
<td>1.89 ± 0.30</td>
<td>1.65 ± 0.30</td>
</tr>
<tr>
<td></td>
<td>1.72 ± 0.26</td>
<td>1.63 ± 0.27*</td>
<td>1.73 ± 0.27</td>
</tr>
<tr>
<td>HGP at 10 μU, mg/kg -1 min-1</td>
<td>0.57 ± 0.70</td>
<td>0.82 ± 0.22</td>
<td>0.37 ± 0.69</td>
</tr>
<tr>
<td></td>
<td>0.23 ± 0.81</td>
<td>0.41 ± 0.30*</td>
<td>0.27 ± 0.48</td>
</tr>
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</table>

Values are means ± SD; n, no. of subjects. HGP, hepatic glucose production; M value, whole body glucose metabolism rate, both low (10 μU·m-1·min-1) and high (40 μU·m-1·min-1); M40/I, M value at 40 μU/insulin concentrations over the last 30 min of the clamp. *Within-group improvement, P < 0.02. †P < 0.05 vs. moderate-intensity training or lower intensity placebo control group.

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The impact of endurance exercise training as an effective countermeasure for improving insulin sensitivity in sedentary older women has received little attention. Our study is unique in comparing the effects of exercise of similar caloric expenditure, but varying intensity, on insulin sensitivity in older people. Indeed, we demonstrate long-term training-related improvements in insulin sensitivity in previously inactive older women that remained evident even 72 h after exercise and appeared to follow a dose-response trend with regard to relative exercise intensity. A greater magnitude of improvement was observed among older women performing higher intensity aerobic training compared with women performing a similar volume of aerobic exercise at moderate intensity and compared with women performing low-intensity, light-resistance exercise. Moreover, these training-related improvements in insulin sensitivity were observed without coincident improvements in overall body composition or V̇O2 peak (primary factors with regard to the observed decline in metabolic resiliency common among older people). Insulin-stimulated suppression of adipose tissue lipolysis also improved with higher intensity training.

There are few longitudinal data on aerobic exercise training and insulin sensitivity in older people, and our results are of similar magnitude to those reported by others (13, 17, 21, 35, 38). In contrast to our findings are those recently reported by Goulet et al. (14) of no sustained effect of higher intensity aerobic training on insulin sensitivity in healthy older women.

This latter study used methods very similar to ours; however, the training period was 6 mo in duration, and, perhaps more importantly, insulin sensitivity was determined 96 h following exercise. It also must be emphasized that there is sound evidence of exercise training-related improvements in insulin sensitivity that are achieved with far shorter training periods than in our study, ranging from 7 days to 6 mo (6, 16, 17, 21, 38).

Differences between younger and older people in the magnitude of response in peripheral insulin sensitivity to exercise training may be explained in part by aging-related loss of muscle mass and decrements in a number of key factors related to muscle oxidative capacity in older people (6, 15, 23, 28). Recently, Short et al. (35) reported moderate-intensity (70% maximum HR), training-related improvements in insulin sensitivity that were inversely related to age, improving by 72% ($P < 0.001$) among younger (20–39 yr) subjects and by 20% ($P = $ not significant) among middle-aged (40–59 yr) subjects, but decreasing by 5% ($P = $ not significant) among people aged 60 yr or older. In contrast, the glucose transport capacity (GLUT-4 protein content), oxidative enzyme activity, and the mitochondrial content of the muscle (all measured 96–120 h after exercise) increased equally across all age groups in response to training. On the other hand, Cox et al. (6) report similar absolute improvements in insulin action (determined by an intravenous glucose tolerance test) between inactive younger (22 ± 1 yr) and older (61 ± 1 yr) women after only
7 days of endurance training on a bicycle ergometer that employed a similar relative intensity and volume of exercise as in our study (1 h at 75% maximum \(\text{VO}_2\)). These improvements in insulin action (measured 15–17 h after exercise) were accompanied by similar relative increases in muscle GLUT-4 protein concentrations, regardless of age, and were independent of changes in body composition. These important findings suggest that aging-related differences in the ability to improve insulin sensitivity with exercise training may be related more to functional impairments (e.g., insulin signaling and/or actual defects in the trafficking of GLUT-4 to the sarcolemma in response to insulin) that may not be easily altered by exercise in older people (especially after decades of disuse).

Recovery from exercise, even just a single bout, is associated with an increase in muscle insulin sensitivity that persists for several hours, presumably to facilitate the rapid replenishment of glycogen reserves in muscle. To emphasize the more enduring chronic effects of exercise training, we performed follow-up measurements of peripheral insulin sensitivity ~72 h after the last training session to avoid any acute effects from the final exercise session. That a 21% improvement in insulin action (glucose uptake and suppression of lipolysis) remained after 72 h in our study subjects exercising at 80% \(\text{VO}_2\) peak emphasizes the more enduring nature of higher intensity training. These enduring benefits are more likely attributable to a greater transient response, which, even so, may be lost by 96 h (14). In further support of this notion, our pre- and posttraining OGTT data (obtained within 48 h of exercise) suggest that the long-term metabolic impact of moderate- and higher intensity exercise is likely distinct. In the \(T_H\) group, 50% of the women experienced improvements in 2-h stimulated glucose values that were coincident with improvements in the \(M \text{ valu}_0\) (\(r = -0.81; P = 0.02\)). In contrast, none of the women in the \(T_M\) group experienced coincident improvements in 2-h glucose values, despite the observed improvements in the \(M \text{ valu}_0\) in 50% of these women (\(r = 0.12; P = 0.78\)).

Our strategy to wait 72 h, however, may have resulted in an attenuation of the true training effect due to the decay in specific training adaptations [e.g., GLUT-4 expression (18) and/or translocation] that may have occurred over this time period in these older women. Other studies that measured insulin sensitivity within 15–48 h of the last exercise bout (6, 13, 16, 21) observed greater relative improvements compared with ours at a similar exercise volume and/or intensity. Therefore, if we had used a shorter time interval between exercise and measurement of insulin sensitivity, we may have observed greater improvements in metabolic function with moderate- and higher intensity exercise and would not have missed the acute effects realized by daily exercise.

Interestingly, Goulet et al. (14), Hughes et al. (17), and Short et al. (35) all used a very protracted time interval between the cessation of exercise training and evaluation of insulin sensitivity in their older study subjects. Taken together with those findings, our own data indicate that the exercise training effect on insulin sensitivity may decay more rapidly in older people. Furthermore, this may be especially so after moderate-compared with higher intensity training, since we observed a 16% increase in insulin sensitivity with moderate-intensity exercise (65% \(\text{VO}_2\) peak) at 72 h, compared with an 11% increase reported by Hughes et al. (17) (50–75% HR reserve) at 96 h and a 5% decrease reported by Short et al. (35) (70% \(\text{HR}_{\text{max}}\)) at 96–120 h. In any case, it is not clear whether older women have an acute response to exercise that is similar in magnitude to a long-term training response, especially given that we observed favorable alterations in insulin sensitivity in the absence of corresponding changes in fitness or body composition. More carefully controlled experimental work is necessary in older people to determine the specific mechanisms underlying both transient (e.g., GLUT-4 content and translocation, oxidative enzyme activity, etc.) and chronic (e.g., body composition, muscle fiber alterations, mitochondrial content, etc.) improvements in insulin sensitivity with exercise training and the specific timing of their consequent decay with detraining.

This study had several strengths; namely, it was a randomized controlled intervention involving 9 mo of supervised aerobic exercise of two different intensities (but similar caloric load) with a placebo control group performing low-intensity exercise training of a completely different mode. Overall retention to the 9-mo intervention was high (>90%), and adherence to the prescribed intensity and duration of training was 85% or greater. Therefore, we are confident that the training stimulus was applied appropriately. In addition, our study sample of older women was over a decade older than subjects described in other studies of exercise training and aging (6, 13, 17) and had a wide range of both glucose tolerance and insulin sensitivity, thereby enhancing the external validity of the data to the general population of older people. That we observed no improvement in \(\text{VO}_2\) peak after 9 mo of endurance training is, indeed, contrary to other studies of older people. Given the low levels of aerobic fitness (i.e., 20 ml \(\text{O}_2\cdot\text{kg}^{-1}\cdot\text{min}^{-1}\)) in our study subjects and others (22), however, even a relative stimulus of 80% \(\text{VO}_2\) peak translates into an absolute stimulus of only 4.5 metabolic equivalents, which may not be sufficient to improve maximal aerobic capacity in robust older women not on hormone replacement therapy (36, 37).

Several studies have observed improvements in insulin sensitivity with training that may have been further modulated by
significant improvements in body composition (13, 21, 35). Consistent with our previous findings after 4 mo of training (9), behavioral compensation outside of training either by decreased volitional physical activity or by increased caloric intake in the TM and TH groups may explain our inability to observe any change in body composition in these older women. On the other hand, the abdominal circumference may have underestimated the actual change in abdominal fat mass in the present study. Nonetheless, that we observed no such changes in overall body fat or lean mass after training helps to emphasize that the overall improvement in insulin sensitivity was likely due to the exercise training stimulus per se.

In conclusion, we observed that, compared with long-term low- or moderate-intensity exercise training, higher intensity training provides more enduring benefits to ameliorating the aging- and disuse-related decline in peripheral insulin sensitivity observed in otherwise healthy older women. Clinically, these findings suggest that higher intensity exercise that expends ~300 kcal at a time can be performed every 2 days without losing benefits. This level of exercise can be achieved by the majority of older people by gradually incorporating 45–50 min of brisk walking (HR of 115–125 beats/min) on 4 days/wk into their lifestyle. Because the acute benefits of moderate-intensity exercise may decay more rapidly than those derived from higher intensity exercise, the same volume of moderate exercise (HR of 100–110 beats/min) may need to be performed daily to be effective in improving metabolic function.

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