Does age, sex, or ACE genotype affect glucose and insulin responses to strength training?

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A DETERIORATION OF GLUCOSE TOLERANCE with age leads to an increased risk of coronary heart disease and Type 2 diabetes (28, 32). This age-associated deterioration of glucose tolerance may also be the result of declining levels of physical activity and increased adiposity (32). In this context, aerobic exercise training improves glucose homeostasis in older populations (6). Strength training (ST) also lowers insulin response in men (5, 22, 34) and women (30). In addition to lowering insulin responses, ST may be a training modality of choice for many older individuals because of its role in the prevention and treatment of sarcopenia (14, 26).

Previous studies on the effects of ST on glucose and insulin response to an oral glucose tolerance test (OGTT) have some limitations. For example, some studies have included only men (5, 34) and others have included women but did not compare their responses with those of men (12, 30). This may be an important comparison because the relative risk of death attributed to high blood glucose levels is greater in women than in men (1, 2). Only one study could be found that compared the effects of ST on glucose and insulin response in young and older subjects (5), and many studies have only investigated these effects 24 h after the last training session (12, 15, 22, 33, 34), raising the possibility that any improvement in insulin action is due to the last bout of exercise (11, 25). However, there is little information on this issue with ST. To our knowledge, no studies have reported a comparison of the time course for insulin responses to ST after the last exercise session to determine how long the effects of ST persist after training. Analyzing these comparisons may provide further information regarding the optimal frequency of ST sessions required to maintain the improvement in glucose metabolism.

Although there are some conflicting reports (3, 16), recent evidence indicates that blood insulin levels are affected by an insertion/deletion (I/D) polymorphism in the angiotensin I-converting enzyme (ACE) gene, such that individuals with the ACE D/D genotype demon-
strate lower baseline levels of insulin and insulin resistance (4, 18, 19, 24, 36). The association of ACE (I/D) genotype with blood glucose is less consistent (13, 18, 36), and its association with insulin or glucose response to ST has not been reported. Information on this association may help determine who is most likely to improve glucose homeostasis with ST, which could help to individualize the use of ST as an intervention for insulin resistance.

The purpose of this study was to determine the influence of age, sex, and, as an exploratory analysis, ACE genotype on fasting and glucose-stimulated glucose and insulin responses to ST. The length of time that these effects persist after the last training session was also assessed. On the basis of previous literature, we hypothesized that young subjects would have a greater reduction in fasting and glucose-stimulated insulin response to ST than older subjects and that there would be no difference in responses between men and women. We further hypothesized that all groups combined would have a blunted insulin response to an OGTT with training that would last at least up to 48 h. Finally, for the exploratory portion of this study, we hypothesized that when all subjects are combined, those with the ACE D/D genotype would have less of a reduction in fasting and glucose-stimulated insulin response to ST than those with the ACE I/D or I/I genotypes. There were not enough subjects in each genotype group to examine interaction effects with age and gender.

METHODS

Subjects. Nineteen sedentary young (age range = 20–30 yr) men (n = 10) and women (n = 9) and 21 sedentary older (age range = 65–75 yr) men (n = 12) and women (n = 9) were studied before and after a 6-mo total body ST program. All subjects were medically screened by a physician who performed a health history, physical examination, and graded maximal treadmill exercise test. They were nonsmokers and free of significant cardiovascular and musculoskeletal disorders. Impaired glucose tolerance (IGT) was observed in three older men and three older women. In addition, two older men and two subjects with Type 2 diabetes were already assigned to each group. To allow subjects to continue training until all posttraining tests were completed and to avoid administering OGTT 2 days in a row to the same subject, it was necessary for all subjects to perform these tests during a time span of ~2 wk so that only one test was performed each week. This was done by having each subject perform a 24-h postexercise OGTT one week and either a 48- or 72-h postexercise OGTT another week during the last few weeks of training. All subjects reported to the laboratory and rested for 15–30 min before the test. An intravenous catheter was inserted into an antecubital vein and connected to a continuous saline drip. Two baseline blood samples, 10 min apart, were drawn to determine fasting glucose and insulin levels. Subjects ingested 75 g of Glucola within a 5-min time period. Blood samples were drawn at 30, 60, 90, and 120 min into heparinized collection tubes for analysis of glucose and insulin. All blood samples were placed on ice immediately and then centrifuged. Plasma samples were frozen at −80°C and analyzed at a later date. Glucose samples were measured in duplicate by the glucose oxidase method using a glucose analyzer (Stat Plus model 2300, Yellow Springs, New Jersey). The intra-assay coefficient of variation for glucose was 1.4%. Insulin assays were measured in duplicate by antibody RIA (human insulin-specific RIA kit, Linco Research, St. Charles, MO). Intra- and interassay coefficients of variation for insulin were 5 and 9%, respectively. Glucose and insulin areas under the OGTT curve are expressed as total (above zero) and incremental (above baseline).

Dietary analysis. Each subject met with a dietitian for instruction on maintaining food records and was required to complete a 5-day diet record before each OGTT. Subjects were instructed to consume a minimum of 150 g of carbohydrate per day and to refrain from any alcohol use for 3 days before the OGTT. Subjects were instructed to replicate their baseline diet record 5 days before the OGTT performed 24 h after an exercise session at the end of training and again at either 48 or 72 h after exercise. All food records were analyzed for nutrient value with the Nutritionist III program.

Strength testing. All subjects began the training program with a 2-wk orientation period to familiarize themselves with the equipment and to develop proper exercise techniques. In addition, this period controlled for the large initial strength gains due to motor learning and helped to prevent injuries during testing. At the end of this orientation period, subjects were given a one-repetition maximum (1 RM) test on the
Keiser K-300 leg press, chest press, lateral pulldown, leg extension, military press, triceps pushdown, and biceps curl. Before the 1-RM testing, subjects performed a warm-up consisting of 3–5 min of light cycling and 10 min of static stretching. They performed five repetitions using a light resistance on each machine, which served as a warm-up before performing the 1-RM test. On the basis of observations during the orientation period, the 1-RM test started with a resistance level estimated to be ~70 to 80% of 1 RM. On successful completion of a repetition, resistance was gradually increased until the subject failed to complete a second repetition. Subjects were allowed a 30-s rest between trials. On another day, subjects were also given a 5-RM test on every machine to determine the proper initial resistance for each exercise. Procedures for the 5-RM test were similar to those of the 1-RM test. The same investigator tested the same subject at the beginning and end of the 6-mo study. During the 1-RM testing after training, an effort was made to reach the 1-RM value with approximately the same number of trials that was used during baseline testing. ST. The ST program was performed on Keiser K-300 variable resistance machines, with the inclusion of one free weight exercise (biceps curls) and one floor exercise (modified sit-ups) three times a week for ~6 mo. Exercises performed were as follows: leg press, chest press, leg curl, lateral pull-down, leg extension, military press, seated row, triceps push-down, abdominal crunch, biceps curl, and modified sit-ups.

Each training session began with a warm-up consisting of light cycling and static stretching for 10 min. Training was varied at the midpoint of the 6-mo period to minimize staleness and to help improve motivation. The second protocol was initiated at the 5-RM resistance level. After the first three to four repetitions were completed, the resistance was increased by the appropriate amount necessary to maintain the 5-RM load for the following training session. Two sets of 15 repetitions were performed on the lower body exercises, and one set of 15 repetitions was performed on the upper body exercises. Subjects were allowed approximately 2 min of rest between exercises.

The second protocol was initiated ~10 wk after the start of training and involved having the subject complete three repetitions at ~50% 1 RM with a gradual increase in load to achieve muscle fatigue after 12–15 repetitions. Subjects alternated upper body exercises and performed two sets of lower body exercises on the first and third training session of each week. Subjects performed one set of all exercises on the second training session of each week. All subjects were supervised at all times during their workouts to ensure that the maximal resistance was being lifted using proper form. Blood pressure was monitored before, during, and after each training session.

Genotyping. Genomic DNA was isolated from EDTA-anticoagulated whole blood samples by standard procedures. Subjects were genotyped for the ACE intron 16 Alu insertion according to methods outlined previously (37). Subjects were grouped as I allele or D allele homozygotes (I/I, n = 7 or D/D, n = 13) or heterozygotes (I/D, n = 13). Alleles were scored by direct comparison to sequence-verified controls run on the same gel.

Statistics. Subjects who had abnormal glucose tolerance (e.g., IGT and Type 2 diabetes) were analyzed separately (except for the 48- vs. 72-h comparisons) and in combination with the total group. The area under the curves for glucose and insulin was calculated by means of the trapezoidal method. Age and sex effects for glucose and insulin responses to the OGTT (i.e., fasting levels and levels at 30, 60, 90, and 120 min after glucose ingestion) and areas under the OGTT curve in response to ST were assessed by using a $2 \times 2 \times 2$ (age $\times$ sex $\times$ time) repeated-measures ANOVA (SPSS Statistical Package, 6.1). Repeated-measures ANOVA was also performed to analyze age and sex effects for glucose and insulin responses to the OGTT 48 or 72 h after ST. Pearson correlations and ANOVA were used to examine the influence of strength and body composition changes on glucose and insulin responses to ST. When significant interactions were found, post hoc analysis was performed by using independent $t$-tests for among-group comparisons and paired $t$-tests for within-group comparisons. For the analysis of ACE genotype associations with the insulin and glucose response to ST, subjects were grouped by genotype but were not analyzed for interactions with age or gender effects due to the small number of subjects in each cell when subdivided into these categories. A least significant difference post hoc test was used to determine group differences when necessary. Data are reported as means $\pm$ SE, and statistical significance was accepted at $P \leq 0.05$.

RESULTS

Subject characteristics. Table 1 shows the physical characteristics for all four groups. As expected, young subjects had $\dot{V}O_{2\max}$ values that were greater than those of older subjects ($P < 0.05$), and young men had $\dot{V}O_{2\max}$ values that were greater than those of young women ($P < 0.001$).

Table 1. Physical characteristics in young and older men and women before and after ST

<table>
<thead>
<tr>
<th></th>
<th>Young Men (n = 10)</th>
<th>Young Women (n = 9)</th>
<th>Older Men (n = 12)</th>
<th>Older Women (n = 9)</th>
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<tbody>
<tr>
<td>Age, yr</td>
<td>25 $\pm$ 1</td>
<td>26 $\pm$ 1</td>
<td>71 $\pm$ 2</td>
<td>68 $\pm$ 2</td>
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<tr>
<td>Height, cm</td>
<td>177 $\pm$ 3</td>
<td>167 $\pm$ 2</td>
<td>174 $\pm$ 2</td>
<td>161 $\pm$ 2</td>
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<tr>
<td>$\dot{V}O_{2\max}$, ml$\cdot$kg$^{-1}$$\cdot$min$^{-1}$</td>
<td>43.2 $\pm$ 1.1</td>
<td>32.8 $\pm$ 2.1</td>
<td>22.4 $\pm$ 1.4</td>
<td>18.7 $\pm$ 4.8</td>
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<tr>
<td>Body mass, kg</td>
<td>83.8 $\pm$ 8.1</td>
<td>84.8 $\pm$ 8.2</td>
<td>83.1 $\pm$ 4.1</td>
<td>71.6 $\pm$ 4.3</td>
</tr>
<tr>
<td>Fat-free mass, kg</td>
<td>62.0 $\pm$ 2.5</td>
<td>63.8 $\pm$ 2.5*a</td>
<td>57.0 $\pm$ 1.1</td>
<td>41.4 $\pm$ 1.2</td>
</tr>
<tr>
<td>Fat mass, kg</td>
<td>20.8 $\pm$ 3.2</td>
<td>19.2 $\pm$ 3.0</td>
<td>23.8 $\pm$ 2.2</td>
<td>28.6 $\pm$ 1.6</td>
</tr>
<tr>
<td>% Body fat</td>
<td>24.1 $\pm$ 2.5</td>
<td>22.2 $\pm$ 2.2*a</td>
<td>21.7 $\pm$ 2.1</td>
<td>20.6 $\pm$ 1.8</td>
</tr>
</tbody>
</table>

Values are means $\pm$ SE; n, no. of subjects. ST, strength training; $\dot{V}O_{2\max}$, maximal aerobic capacity; % body fat, percentage of body fat; before, before ST; after, after ST. *Significantly different from before training, $P < 0.05$. †$P = 0.06$. 

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Baseline percentage of body fat (%body fat) was higher in older women compared with all other groups (P < 0.001; Table 1). Young men had higher FFM (P < 0.001) and lower %body fat (P < 0.05) than young women, and older men had higher FFM and lower % body fat than older women (both P < 0.001). Young women had lower %body fat than older women (P < 0.05). However, there were no differences in FFM or % body fat between young and older men.

FFM increased by 3% in young men (62.0 ± 2.5 vs. 63.8 ± 2.5 kg, P < 0.05), by 3.5% in young women (42.5 ± 2.1 vs. 44.0 ± 2.3 kg, P < 0.05), by 1.5% in older men (57 ± 1.1 vs. 57.9 ± 1.0 kg, P < 0.05), and there was a trend for an increase (2.2%) in older women (41.4 ± 1.2 vs. 42.3 ± 1.1 kg, P = 0.06) with ST (Table 1). Only the young men decreased their % body fat with ST (24.1 ± 2.5 vs. 22.2 ± 2.2%, P < 0.05). There were no significant changes in body mass (kg) or fat mass in any of the groups after the training program.

**Strength.** Table 2 shows that all groups significantly increased their 1 RM strength with ST (P < 0.05). Strength values for the upper and lower body exercises listed in Table 2 increased by 26 and 28%, respectively, when all groups were combined.

**Plasma glucose response to OGTT.** At baseline, older men had higher fasting glucose (P < 0.05) and higher total glucose areas under the curve (P < 0.05) than older women and young men and women (Fig. 1). There were no significant differences in plasma glucose concentration at fasting or at any time point during the OGTT within or between any of the groups 24 h after a training session near the end of training. Older women increased their total glucose area under the curve (15,438 ± 1,221 vs. 17,396 ± 1,025 mg·dl⁻¹·120 min⁻¹, P < 0.05; Fig. 1) and their incremental glucose area (4,375 ± 1,026 vs. 6,323 ± 847 mg·dl⁻¹·120 min⁻¹, P < 0.05) with ST. There were no significant changes in total or incremental glucose areas under the curve in any of the other three groups with ST. None of these results were altered when the data were analyzed without the IGT and Type 2 diabetic subjects included. At 48 h after exercise, there was a significant age × time interaction in fasting (96.7 ± 1.9 vs. 101.4 ± 2.3 mg/dl in older subjects and 91.9 ± 2.9 vs. 89.8 ± 1.6 mg/dl in young subjects, P = 0.01) and at the 30-min time point for glucose values (165.0 ± 10.3 vs. 178.4 ± 6.0 vs. 163.9 ± 8.2 vs. 155.3 ± 9.6, P < 0.05). However, there were no significant within-group changes in any of the four groups or between men and women for fasting glucose or in areas under the glucose curve at 48 or 72 h after exercise.

**Plasma insulin response to OGTT.** At baseline, young men had higher fasting insulin (72 ± 5 vs 57 ± 3 pmol/l, P < 0.01) and a higher total insulin area under the curve (43,949 ± 2,963 vs 20,007 ± 2,058 pmol·l⁻¹·120 min⁻¹, P < 0.05) than young women. Fasting insulin concentrations were reduced with ST in young (76 ± 5 vs 63 ± 3 pmol/l, P < 0.05) and older men (93 ± 11 vs 69 ± 8 pmol/l, P < 0.05) by 17 and 26%, respectively. In addition, the older men reduced their insulin values significantly at the 90-min time point (P < 0.05). However, when data for the older men were analyzed without the subjects with IGT, the fasting insulin values were no longer significantly reduced with ST, but this was not observed when subjects with Type 2 diabetes were eliminated. Total insulin area under the curve also decreased 21% in young men (43,949 ± 5,757 vs. 34,839 ± 2,963 pmol·l⁻¹·120 min⁻¹, P < 0.05) and 11% in older men, which approached significance (50,142 ± 6,731 vs. 44,795 ± 5,505 pmol·l⁻¹·120 min⁻¹, P = 0.06). There were no significant changes in insulin values at fasting, at any of the time points, or in total insulin areas for young or older women 24 h after exercise, but, in contrast to men, their values drifted higher after training (Fig. 2). Young men decreased their incremental insulin areas

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**Table 2. Changes in 1-RM strength in young and older men and women with ST**

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<thead>
<tr>
<th></th>
<th>Young Men (n = 10)</th>
<th>Young Women (n = 9)</th>
<th>Older Men (n = 12)</th>
<th>Older Women (n = 9)</th>
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<td>Before</td>
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<tr>
<td>Chest press, kg</td>
<td>72 ± 6</td>
<td>89 ± 7†</td>
<td>35 ± 2</td>
<td>47 ± 3†</td>
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<tr>
<td>Lat pulldown, kg</td>
<td>75 ± 6</td>
<td>92 ± 7†</td>
<td>35 ± 3</td>
<td>46 ± 3†</td>
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<tr>
<td>Shoulder press, kg</td>
<td>57 ± 4</td>
<td>71 ± 6†</td>
<td>32 ± 2</td>
<td>37 ± 2†</td>
</tr>
<tr>
<td>Tricep pushdown, kg</td>
<td>81 ± 8</td>
<td>110 ± 11†</td>
<td>42 ± 3</td>
<td>58 ± 5†</td>
</tr>
<tr>
<td>Bicep curl, kg</td>
<td>35 ± 3</td>
<td>47 ± 4†</td>
<td>15 ± 2</td>
<td>25 ± 4†</td>
</tr>
<tr>
<td>Leg extension, kg</td>
<td>160 ± 17</td>
<td>200 ± 18†</td>
<td>146 ± 14</td>
<td>187 ± 20†</td>
</tr>
<tr>
<td>Leg press, kg</td>
<td>697 ± 26</td>
<td>871 ± 35†</td>
<td>419 ± 38</td>
<td>585 ± 49†</td>
</tr>
</tbody>
</table>

Values are means ± SE; n, no. of subjects. 1 RM, one-repetition maximum. *Significantly different from before training, P < 0.05.
†Significantly different from before training, P < 0.01.
(P = 0.05), but there were no significant changes in incremental insulin areas in any of the other three groups. There was a significant sex × time interaction for fasting insulin and total insulin area under the curve with ST 24 h after exercise (P < 0.05) due to significant decreases in men but not in women (Fig. 3).

**Insulin responses to repeated OGTT at 48 or 72 h.** Young men reduced their total insulin area (50,751 ± 9,918 vs. 37,599 ± 6,757 pmol·l⁻¹·120 min⁻¹, P = 0.01), whereas older men decreased only their fasting insulin concentrations 48 h after exercise (76.1 ± 9.3 vs 74.0 ± 10.6 pmol/l, P < 0.05). There were no significant changes in insulin values at fasting, at any time points, or for insulin areas in young or older women 48 h after exercise. There were also no significant changes in any group for either fasting insulin, insulin areas under the curve, or in any of the insulin time points 72 h after exercise. All other age and gender comparisons at individual time points were not significantly different at 48 or 72 h after exercise. Furthermore, there were no significant relationships among changes in FFM, %body fat, strength, or insulin total areas.

**ACE genotype and glucose and insulin responses to ST.** Subjects were grouped according to I/I, I/D, and D/D ACE genotypes. Because of the small number of subjects who were homozygotes for the I allele (n = 7), subjects who exhibited at least one I allele were combined (I/I and I/D) and compared with homozygotes for the D allele (D/D). The D/D genotype group exhibited significantly lower fasting insulin, total insulin area, and incremental insulin area values both before and after ST compared with those with an I allele (P < 0.05 for all; Table 3). There were no significant genotype differences for any glucose variables at baseline, and glucose and insulin responses to ST were not significantly different among genotype groups (Table 3). However, there was a trend for greater reductions in total insulin areas for those with an I allele compared with D homozygotes (P = 0.07).

**DISCUSSION**

The results of the present study suggest that ST has a more favorable effect on insulin action in men than in women. Men demonstrated significant training-induced reductions in fasting insulin levels and in total insulin area under the curve, whereas, women showed no significant changes in insulin response to ST. These, along with the significant reductions in total insulin areas that were maintained for at least 48 h after training in young men but not in older men, appear to be new findings. In contrast, older men were the only group to maintain reductions in fasting insulin for at least 48 h after training. Contrary to our expectations, older women significantly increased their total glucose areas under the OGTT curve as a result of the ST program. Findings for fasting glucose and total glucose areas remained the same after removing subjects with Type 2 diabetes and IGT. Likewise, the significant increase in total glucose areas with ST in older women remained significantly elevated even after removing three women with IGT. However, the significant reductions in fasting insulin with ST among the older men were no longer significant after removing subjects with IGT, but this was not the case when only the Type 2 diabetics were eliminated from the analysis. Increases in strength and FFM and decreases in %fat in response to ST did not explain the sex differences in OGTT responses. ACE genotype was significantly associated with baseline insulin levels, but the response of insulin and glucose to ST was not significantly different among genotype groups. However, there was a trend for a greater reduction in total insulin areas for those with at least one I allele (P = 0.07). Although the ACE (I/D) genotype data from this study are preliminary and exploratory, we believe they provide a basis for generating hypotheses for future studies using larger sample sizes for each genotype group.

Several investigators have described the effects of ST on glucose tolerance in young (5) and older men (5, 12, 17) and women (12, 17, 30), but none have compared age and sex responses in the same study. Because women with elevated blood glucose levels are at a higher relative risk of mortality than men (1, 2, 10),
and this risk increases with age (28), these comparisons have important health implications. They suggest that older women, who may be particularly affected by the consequences of a deterioration of glucose metabolism with age, do not appear to have a favorable glucose response to an OGTT with ST. Previous studies have shown no changes (8, 17, 30) or improvements (7) in glucose levels with ST without regard to age or sex differences. For example, Erikson et al. (7) showed an improvement in glycemic control in middle-aged men and women, but these subjects were obese and Type 2 diabetic subjects. In another study by the same group (8), there were no significant changes in glucose tolerance after 10 wk of circuit ST in men and women with IGT. Thus there is some precedence for a lack of change in glucose tolerance with ST in both men and women, but the observation of worsened glucose tolerance in response to ST in older women has not been observed previously.

It is possible that the women in our study failed to improve their glucose homeostasis with ST because they had normal glucose tolerance before training. It is also possible that the 120-min OGTT used in this study was not long enough to see a change in insulin response in women. Some ST studies have shown continued reductions in insulin concentrations after 120 min (5, 23). However, neither of these possibilities provides a rationale for our findings in women, particularly the older women, because they do not explain why their responses to ST drifted in the opposite direction of the men. In this regard, Ryan et al. (30) observed increases in insulin action during one of three phases of a hyperglycemic clamp but no changes in insulin responses during the other two phases with ST. In a more recent study, Ryan and colleagues (29) found that increases in insulin action approached significance as a result of ST when men and women were pooled, but no such trend was apparent in the women only group. Similar findings were observed by Joseph et al. (17). Although we have no data in the present study to explain the apparent adverse response to ST in older women, in a previous report, older women experienced twice the increase in muscle damage compared with young or older men in muscle damage with ST (27). Because muscle damage is associated with insulin resistance (19), it is conceivable that the older women in this study were the only group that worsened their glucose tolerance with ST because they were the only group who showed a substantial increase in muscle damage with ST (27). However, further studies are needed before this explanation can be confirmed.

The significant decrease in fasting insulin and total insulin area under the OGTT curve in men in this study is in agreement with the majority of ST studies in young (5, 23), middle-aged (22, 33, 34), and older men (5). For example, Miller et al. (23) observed an 18% reduction in total insulin area and a 38% reduction in fasting insulin after 10 wk of ST in young healthy men. In addition, our group reported similar findings in middle-aged men who were at high risk for coronary heart disease after 20 wk of ST (34) and in another study of middle-aged and older men after 16 wk of ST (22).

The lack of a significant reduction in glucose response to ST in this study agrees with previous ST studies in young (5, 23), middle-aged (22), and older men (12). Improvements in glucose concentration (33, 34) or glycemic control (8) have been shown most often in studies with subjects who had IGT or Type 2 diabetes. Because the majority of our subjects had normal glucose tolerance, no change in glucose response was expected.

Nevertheless, the findings in the present study add to the existing literature in several ways. One additional way is by determining how age and sex affect the time course after training for changes in glucose homeostasis. Whether the improvements in glucose homeostasis reported previously with ST represent true training adaptations or simply the effect of the last exercise session of a training program is still unknown. In this context, Schell et al. (31) observed no changes in insulin areas immediately after a single ST session, whereas Fluckey et al. (9) observed a significant decrease after a single bout of resistance exercise and after 20 wk of a ST program in individuals with IGT (33). It is also unclear how long improvements in glucose tolerance persist after the last training session. For example, Miller et al. (23) found that plasma insulin concentrations were lowered without a change in glucose tolerance in young men during an OGTT 48 h after a ST session. Craig et al. (5) found no change in glucose tolerance but significantly lower insulin con-

### Table 3. ACE I/D genotype and insulin and glucose variables before and after heavy resistance ST

<table>
<thead>
<tr>
<th>ACE I/I + I/D Genotype</th>
<th>ACE D/D Genotype</th>
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<tbody>
<tr>
<td>n (men, women)</td>
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<tr>
<td>Fasting insulin, pmol/l</td>
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<tr>
<td>85.6 ± 7.1</td>
<td>80.2 ± 6.2</td>
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<tr>
<td>Incremental insulin area, pmol-l⁻¹·120 min⁻¹</td>
<td>337 ± 44</td>
</tr>
<tr>
<td>50,701 ± 5,672</td>
<td>47,568 ± 4,572</td>
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<tr>
<td>Insulin total area (pmol-l⁻¹·120 min⁻¹)</td>
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<tr>
<td>Fasting glucose, mg/dl</td>
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<td>Incremental glucose, mg/dl⁻¹·120 min⁻¹</td>
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centrations in young and older individuals 72 h after the last bout of ST. Zachwieja et al. (38) measured peak glucose disappearance rate by using the minimal model of labeled glucose disappearance and insulin secretion parameters derived from C-peptide measurements. They found that peak glucose disappearance rate was still significantly increased 7 days after the last ST session and observed a trend for a significant increase in insulin sensitivity at this time period in healthy older men. However, most studies have examined the effects of ST on glucose tolerance within 24 h after the last exercise bout (7, 8, 22, 33, 34), and no studies have determined how long after the last exercise session the effects on glucose homeostasis persist. In the present study, we examined two ST subgroups tested at different time periods after the last training session. One group was tested at 24 and 48 h and the other group was tested at 24 and 72 h after a training session. At 48 h after exercise, young subjects reduced their fasting glucose levels significantly more than older subjects. Young men reduced their total insulin area and older men decreased their fasting insulin levels 48 h after exercise. None of the groups maintained reductions in fasting insulin levels when tested 72 h after the last training session. This is consistent with the findings of Miller et al. (23) in which insulin responses to an OGTT were improved at 48 h after the last training session. However, our findings are not supported by Craig et al. (5), who reported insulin reductions 72 h after the last training bout.

In the present study, changes in strength or body composition did not explain the sex difference in insulin responses to the OGTT after training and support previous studies showing that ST may improve glucose homeostasis independent of changes in body composition (15, 33). However, a negative correlation has been reported between insulin response and lean body mass (23).

Few mechanisms have been proposed for changes in glucose metabolism as a result of ST, and no data were collected in this study to support any specific mechanism to explain the results. Because GLUT-4 content in vastus lateralis muscle is reduced after ~3 wk of bed rest, whereas brief periods of ST increase GLUT-4 content in the same muscle (35), it is likely that ST-induced changes in GLUT-4 may explain changes in glucose homeostasis, but the question of whether GLUT-4 is altered differently by age and gender in response to ST is unknown.

Recent evidence has demonstrated an association between impaired insulin action and the ACE I/D genotype, with most (4, 18, 24, 36) but not all studies (3, 16) reporting a better insulin response in ACE D/D than in I/I and I/D individuals. For example, Takezako et al. (36) reported that the ACE I/I genotype was associated with significantly higher baseline insulin levels, higher insulin responses to OGTT, and greater insulin resistance compared with those with the D/D genotype. The ACE D/D genotype is also associated with higher blood levels of ACE (19), which have been hypothesized to affect skeletal muscle blood flow and possibly perfusion of insulin-sensitive fibers (36), although this hypothesis has not been adequately tested. In the present study, the D/D genotype was associated with significantly lower fasting insulin, total insulin area, and incremental insulin area compared with the I allele, which corroborates previous findings (4, 18, 19, 24, 36). However, no association was observed between ACE genotype and fasting or glucose-stimulated glucose or insulin responses to ST. Nevertheless, the low statistical power for this portion of the study, due to the low frequency of each genotype in this sample, precludes any definitive conclusions but should help to generate new hypotheses for future studies using larger and more equal sized genotype groups.

In summary, these results show that men have a more favorable insulin response to an OGTT as a result of ST than women, but, within the limitations of this study, age does not appear to influence this response. Our data also support the findings of other investigators who showed that those with the ACE D/D genotype have lower insulin responses to an OGTT at baseline than those with I/D or I/I genotypes. Although we did not find a significant difference among ACE genotype groups for glucose or insulin responses to an OGTT as a result of ST, there was a strong trend for a greater reduction in insulin total areas in those with I/I or I/D genotypes than in those with the D/D genotype (P = 0.07).

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REFERENCES


