Effect of aging on response to exercise training in humans: skeletal muscle GLUT-4 and insulin sensitivity

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The purpose of this study was to compare the effects of short-term exercise training on insulin-responsive glucose transporter (GLUT-4) concentration and insulin sensitivity in young and older individuals. Young and older women (22.4 ± 0.8 (SE) yr, n = 9; and 60.9 ± 1.0 yr, n = 10) and men (20.9 ± 0.9, n = 9; 56.5 ± 1.9 yr, n = 8), respectively, were studied before and after 7 consecutive days of exercise training (1 h/day, ∼75% maximal oxygen uptake). The older groups had more adipose tissue, increased central adiposity, and a lower maximal oxygen uptake. Despite these differences, increases in whole body insulin action (insulin sensitivity index, determined with an intravenous glucose tolerance test and minimal-model analysis) with training were similar regardless of age, in both the women and men (mean increase of 2.2 ± 0.3-fold). This was accompanied by similar relative increases in muscle (vastus lateralis) GLUT-4 protein concentration, irrespective of age (mean increase of 3.1 ± 0.7-fold).

The purpose of this study was, therefore, to compare the effect of exercise training on skeletal muscle GLUT-4 protein concentration in young (<30 yr) vs. middle- to older-aged subjects (50–70 yr). Insulin action can improve with 7 days of endurance training (6, 28, 37). Therefore, we compared the responses of GLUT-4 and insulin action in older and young subjects before and after a similar training regimen. Exercise intensity was held constant (70–75% maximal oxygen uptake (VO2max)) to examine the impact of the same relative exercise stimulus on GLUT-4 regulation in young vs. older skeletal muscle.

METHODS

Study design. Four groups of subjects were examined: 1) young women (n = 9), 2) older women (n = 10), 3) young men (n = 9), and 4) older men (n = 8). Age criteria for the young groups were 18–30 yr and for the older groups 50–70 yr. Subjects were initially screened for body composition and cardiovascular fitness level. Pretraining insulin action was determined with an intravenous glucose tolerance test (IVGTT). A pretraining biopsy from the vastus lateralis was obtained for measurement of GLUT-4. Subjects then underwent 7 consecutive days of supervised exercise training. A postraining IVGTT and muscle biopsy were performed 15–17 h after the final training bout.

Subjects. Subjects were volunteers who had not been active in an exercise program for at least the previous 2 yr. Subjects were also questioned concerning their normal daily activities, and only those with relatively sedentary lifestyles were included; this was verified by the VO2max and body composition data (see Tables 1–4). Other inclusion criteria were age-normative values for adiposity and VO2max (33, 35); no smoking; no medications that alter insulin action; and no evidence of coronary artery disease, hypertension, or orthopedic injuries that would inhibit exercise training. All of the older women were postmenopausal; five of the women were on estrogen-replacement therapy. There were no significant initial differences in insulin action or GLUT-4 with estrogen replacement vs. no medication; responses to exercise did not differ either. Thus the data from the older women were combined. The young women were tested in the follicular...
phase of the menstrual cycle, based on a recall of their previous menses. Insulin action. Insulin action was determined with an IVGTT, as described by Bergman et al. (3) and as used previously in this laboratory (20–22). Subjects reported to the laboratory in the morning after a 12-h fast and had consumed at least 250 g of carbohydrate per day for the previous 3 days. The pretraining IVGTT was performed in the sedentary condition; the posttraining test was performed 15–17 h after the final exercise bout. Briefly, four baseline samples were obtained before the intravenous injection of glucose (1.7 mmol/kg) at time 0 and insulin (150 pmol/kg) 20 min later. Twenty-five samples were obtained between 0 and 180 min and subsequently analyzed by spectrophotometry for glucose (procedure HK 16-UV; Sigma Chemical, St. Louis, MO) and by microparticle enzyme immunoassay for insulin (IMx, Abbott, Abbott Park, IL). Insulin sensitivity [insulin-sensitivity index (ISI)] was calculated with the minimal model of insulin action (MINMOD, version 3.0). ISI measures the increase in glucose disappearance per increase in unit insulin (3). Insulin-independent glucose disappearance (Sglu) and insulin secretion [area under the insulin curve during the initial rise in glucose; acute insulin response (AIRglu)] were also calculated.

GLUT-4 protein concentration. A muscle sample (~100 mg) was obtained with the percutaneous biopsy technique from the vastus lateralis of the same leg before and after training. Muscle was immediately frozen in liquid nitrogen. For the GLUT-4 assay, frozen muscle was pulverized by using a small ground-glass mortar and pestle and then homogenized with 400 µl of ice-cold buffer. Homogenization buffer contained 25 mmol/l HEPES, 4 mmol/l EDTA, 25 mmol/l benzamidine, 0.5 mmol/l phenylmethylsulfonfyl fluoride, 4.2 µmol/l leupeptin, 1.5 µmol/l pepstatin, and 0.6 µmol/l aprotinin (pH 7.4). Homogenates were pipetted into microfuge tubes and spun for 30 min at 4°C and 16,000 g. The pellet was resuspended in 150 µl of buffer containing 1% Triton X-100, kept on ice for 1.5 h, and vortexed periodically to ensure solubilization. The sample was spun again for 30 min at 16,000 g and 4°C, the supernatant was removed, and protein concentration was determined by using the bicinchoninic acid method (39). To determine GLUT-4 protein concentration, duplicate samples of supernatant containing 75 µg protein were solubilized in Laemmli buffer (30) containing 2.5% dithiothreitol and separated by electrophoresis on an 9% polyacrylamide resolving gel. The pre- and posttraining samples from a given subject were run on adjacent lanes of the same gel. Protein was then transferred (0.5 A, 2 h) to an Immobilon membrane (Millipore, Bedford, MA) and blocked overnight at 4°C with 5% nonfat dry milk in Tris-buffered saline (TBS-Blotto). This was followed by incubation at 4°C for 12 h in 4 µg/ml protein A-purified polyclonal antibody, specific for the COOH-terminal peptide of GLUT-4. Results with this antibody have been reported elsewhere (19, 21). The membrane was washed in TBS-Tween, followed by TBS, and incubated for 1 h at 25°C in 50 ml TBS-Blotto that contained horseradish peroxidase-conjugated donkey anti-rabbit IgG diluted 1:4,000 (Amersham, Arlington Heights, IL). Antibody-antigen complexes were detected by enhanced chemiluminescence (ECL, Amersham). Intensities of the bands were determined on a computer-controlled video densitometer (Hewlett-Packard Scanjet IIcx/T hardware, Sunnyvale, CA) to quantify GLUT-4 by using ImageQuant software (Molecular Dynamics). Values are presented as arbitrary absorbance units (AAU). A rat heart standard was used as the molecular weight marker for GLUT-4.

Cardiovascular fitness and body composition. VO2max was measured during incremental exercise on an electrically braked cycle ergometer (Lode, Diversified, Brea, CA). Oxygen consumption was measured with open-circuit spirometry by using a metabolic cart (model 2900, Sensor Medics, Anaheim, CA). A 12-lead electrocardiogram (ECG) recorded heart rate and ECG tracings. The maximal exercise test was used to 1) screen for potential heart disease; 2) determine whether the subject was sedentary, as classified by VO2max (35); and 3) determine the heart rate and oxygen consumption needed to elicit the desired intensity (70–75% VO2max) during the 7 days of training. A physician was present during the maximal testing of all older subjects and interpreted the exercise ECGs. Body composition was determined by body fat percentage with skinfolds (25), body mass index (BMI), and waist (level of umbilicus) and hip (maximum hip circumference) girths. Only subjects within normative values for their age for body fat percentage and BMI were studied (35).

Exercise training. Subjects exercised 1 h/day for 7 consecutive days on a cycle ergometer. Exercise intensity was adjusted to achieve 70–75% of VO2max, as determined from Douglas bags collected at minute 5 and every subsequent 15 min of exercise. Heart rate was monitored with telemetry (Polar, Stamford, CT) to gauge exercise intensity. All subjects exercised continuously for 1 h during the 7 days of training.

Statistics. Data were compared with a two (age, young and older) by two (treatment, before and after exercise training) repeated-measures analysis of variance. Contrast comparisons were used to determine specific differences if a significant interaction or group effect (P < 0.05) was obtained. Descriptive data (age, body composition, exercise variables) were compared between the young and older groups within a gender with an independent t-test (P < 0.05).

RESULTS

Anthropometric data. Age and anthropometric data for the female and male subjects are presented in Tables 1 and 2, respectively. The older women and men had significantly (P < 0.05) more adipose tissue (body fat percentage, fat mass, BMI) than the younger groups, despite a similar fat-free mass. The older groups also had significantly (P < 0.05) more adipose tissue (body fat percentage, fat mass, BMI) than the younger groups, despite a similar fat-free mass. The older groups also exhibited higher waist and hip girths and an increased waist-to-hip ratio compared with the young subjects (P < 0.05). The older men were significantly (P < 0.05) heavier than the young men.

VO2max and exercise data. Maximal exercise and training data for the women and men are presented in Table 3 and 4, respectively. VO2max was significantly (P < 0.05) lower in the older women and men, as was
maximal achieved workload and maximal heart rate. All groups exercised at \( \sim 75\% \) \( V_\text{O2max} \), however, heart rate and oxygen consumption at the workload that elicited this response were significantly \( (P < 0.05) \) lower in the older groups. Body mass did not change \( (P > 0.05) \) in any of the groups with the 7 days of training (mean for pooled data, 74.1 \( \pm 2.6 \) vs. 74.2 \( \pm 2.5 \) kg). \( V_\text{O2max} \) was not measured after training, but it has been reported to not change with a virtually identical 7-day training regimen (see Ref. 37, unpublished observations).

Insulin action and secretion. There was a significant \( (P < 0.05) \) treatment (training) effect with no significant interaction for an improvement in insulin action \( (ISI) \) in the young \( (5.1 \pm 0.9 \) vs. \( 7.1 \pm 1.2 \) \( \text{min}^{-1} \cdot \text{µU}^{-1} \cdot \text{ml}^{-1} \)) and older \( (3.8 \pm 0.7 \) vs. \( 8.3 \pm 1.4 \) \( \text{min}^{-1} \cdot \text{µU}^{-1} \cdot \text{ml}^{-1} \)) women with training \( (\text{Fig. 1}) \). There were no significant \( (P > 0.05) \) differences in initial or posttraining ISI between these two groups \( (\text{Fig. 1}) \). In the men, ISI also improved significantly \( (P < 0.05) \) in the young \( (4.5 \pm 0.6 \) vs. \( 6.4 \pm 0.9 \) \( \text{min}^{-1} \cdot \text{µU}^{-1} \cdot \text{ml}^{-1} \)) and older \( (2.1 \pm 0.5 \) vs. \( 3.8 \pm 0.7 \) \( \text{min}^{-1} \cdot \text{µU}^{-1} \cdot \text{ml}^{-1} \)) groups with no interaction effect \( (\text{Fig. 1}) \). ISI was significantly \( (P < 0.05) \) lower in the older men before and after training \( (\text{Fig. 1}) \). In the women, there was no difference in glucose effectiveness \( (S_{\text{glu}}) \) with age \( (0.02 \pm 0.01 \text{min}^{-1}) \). \( S_{\text{glu}} \) in the men was slightly but significantly \( (P < 0.05) \) higher in the young vs. older group \((0.03 \pm 0.01 \text{ vs. } 0.02 \pm 0.01 \text{ min}^{-1}, \text{respectively}) \). \( S_{\text{glu}} \) did not change in the women or men with training.

Fasting blood glucose and insulin levels were within normal values and did not change with training in either the young (glucose, 4.6 \( \pm 0.2 \) vs. 4.8 \( \pm 0.2 \) mM; insulin, 36.6 \( \pm 5.4 \) vs. 32.4 \( \pm 4.8 \) pm) or older women (glucose, 5.0 \( \pm 0.4 \) vs. 5.1 \( \pm 0.2 \) mM; insulin, 37.2 \( \pm 4.8 \) vs. 34.2 \( \pm 3.1 \) pm, before vs. after training, respectively). Fasting glucose and insulin were not signifi-

### Table 2. Age and anthropometric data for the young and older men

<table>
<thead>
<tr>
<th>Variable</th>
<th>Young</th>
<th>Older</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>20.9 ( \pm 0.9 )</td>
<td>56.5 ( \pm 1.9* )</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>24.3 ( \pm 0.8 )</td>
<td>30.1 ( \pm 1.9* )</td>
<td>0.01</td>
</tr>
<tr>
<td>Body fat, %</td>
<td>12.3 ( \pm 1.2 )</td>
<td>27.2 ( \pm 1.8* )</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mass, kg</td>
<td>74.0 ( \pm 2.0 )</td>
<td>95.5 ( \pm 5.7* )</td>
<td>0.002</td>
</tr>
<tr>
<td>Fat mass, kg</td>
<td>9.2 ( \pm 1.1 )</td>
<td>26.6 ( \pm 3.0* )</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fat-free mass, kg</td>
<td>64.8 ( \pm 1.4 )</td>
<td>68.9 ( \pm 3.0 )</td>
<td>0.22</td>
</tr>
<tr>
<td>Waist girth, cm</td>
<td>83.4 ( \pm 1.9 )</td>
<td>108.9 ( \pm 3.8* )</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hip girth, cm</td>
<td>99.3 ( \pm 1.8 )</td>
<td>112.8 ( \pm 2.4* )</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
<td>0.84 ( \pm 0.01 )</td>
<td>0.96 ( \pm 0.02* )</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Values are means ± SE. *Significantly different \( (P < 0.05) \) from young men.

### Table 3. Maximal exercise and submaximal training data for the young and older women

<table>
<thead>
<tr>
<th>Variable</th>
<th>Young</th>
<th>Older</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>( V_\text{O2max} ), ml·kg(^{-1})·min(^{-1} )</td>
<td>30.8 ( \pm 2.0 )</td>
<td>21.2 ( \pm 2.3* )</td>
<td>0.01</td>
</tr>
<tr>
<td>( H_\text{Rmax} ), beats/min</td>
<td>187.1 ( \pm 3.4 )</td>
<td>159.6 ( \pm 4.1* )</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Maximal workload, W</td>
<td>146.1 ( \pm 10.4 )</td>
<td>80.0 ( \pm 4.4* )</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Training ( V_\text{O2} ), ml·kg(^{-1})·min(^{-1} )</td>
<td>23.1 ( \pm 1.5 )</td>
<td>15.9 ( \pm 1.7* )</td>
<td>0.01</td>
</tr>
<tr>
<td>Training %( V_\text{O2max} )</td>
<td>74.9 ( \pm 5.2 )</td>
<td>75.0 ( \pm 4.2 )</td>
<td>0.86</td>
</tr>
<tr>
<td>Training ( H_\text{Rmax} ), beats/min</td>
<td>148.3 ( \pm 3.3 )</td>
<td>125.5 ( \pm 4.0* )</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Training %( H_\text{Rmax} )</td>
<td>79.3 ( \pm 2.0 )</td>
<td>78.6 ( \pm 2.2 )</td>
<td>0.85</td>
</tr>
</tbody>
</table>

*Values are means ± SE. \( V_\text{O2max} \), maximal oxygen uptake; \( V_\text{O2} \), oxygen uptake; \( H_\text{Rmax} \), maximal heart rate. *Significantly different \( (P < 0.05) \) from young women.

### Table 4. Maximal exercise and submaximal training data for the young and older men

<table>
<thead>
<tr>
<th>Variable</th>
<th>Young</th>
<th>Older</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>( V_\text{O2max} ), ml·kg(^{-1})·min(^{-1} )</td>
<td>41.4 ( \pm 1.7 )</td>
<td>22.5 ( \pm 1.9* )</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>( H_\text{Rmax} ), beats/min</td>
<td>191.0 ( \pm 5.2 )</td>
<td>164.0 ( \pm 4.6* )</td>
<td>0.01</td>
</tr>
<tr>
<td>Maximal workload, W</td>
<td>227.8 ( \pm 9.7 )</td>
<td>153.1 ( \pm 8.8* )</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Training ( V_\text{O2} ), ml·kg(^{-1})·min(^{-1} )</td>
<td>31.1 ( \pm 1.3 )</td>
<td>16.9 ( \pm 1.4* )</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Training %( V_\text{O2max} )</td>
<td>75.2 ( \pm 5.9 )</td>
<td>75.1 ( \pm 1.9 )</td>
<td>0.76</td>
</tr>
<tr>
<td>Training ( H_\text{Rmax} ), beats/min</td>
<td>154.7 ( \pm 4.3 )</td>
<td>126.5 ( \pm 3.4* )</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Training %( H_\text{Rmax} )</td>
<td>80.1 ( \pm 2.3 )</td>
<td>77.1 ( \pm 2.4 )</td>
<td>0.36</td>
</tr>
</tbody>
</table>

*Values are means ± SE. *Significantly different \( (P < 0.05) \) from young men.
cantly different between the young and older women. Fasting blood glucose and insulin did not change with training in either the older (glucose, 5.7 ± 0.2 vs. 5.6 ± 0.3 mM; insulin, 70.8 ± 10.2 vs. 66.0 ± 15.6 pM) or young (glucose, 5.4 ± 0.2 vs. 4.8 ± 0.2 mM; insulin, 30.6 ± 3.6 vs. 33.6 ± 7.8 pM) men (before vs. after training, respectively). Fasting glucose and insulin values were elevated in the older compared with the young men; this difference persisted after training.

The AIR\textsubscript{glu} obtained during the minimal model is indicative of the early phase of pancreatic insulin secretion (3). As presented in Fig. 2, there was a trend for insulin secretion to be reduced with exercise training in only the older subjects. This was particularly manifested in the men, as there was a significant (P < 0.05) interaction, with the older men decreasing AIR\textsubscript{glu} with training while the young group did not change.

Fig. 2. Changes in insulin secretion as determined from acute insulin response to glucose (AIR\textsubscript{glu}) with 7 days of exercise training in young vs. older women (A) and men (B). † Significant interaction (P < 0.05).

This interaction approached statistical significance (P = 0.08) in the women (Fig. 2).

Muscle GLUT-4 protein concentration. The GLUT-4 data are presented in Fig. 3. GLUT-4 protein concentration increased significantly (P < 0.05) in the young (92.4 ± 17.8 vs. 135.4 ± 24.6 AAU) and older women (107.1 ± 20.6 vs. 164.7 ± 25.9 AAU) with the 7 days of exercise training, with no significant (P > 0.05) interaction effect (Fig. 3). In the men, GLUT-4 concentration also increased significantly (P < 0.05) in the young (91.2 ± 16.9 vs. 169.5 ± 28.4 AAU) and older groups (82.9 ± 30.9 vs. 171.1 ± 36.5 AAU) with no interaction (Fig. 3). GLUT-4 protein concentration was not statistically different with age in the men and women before or after training.

Although there was evidence for a gender effect relative to aging and insulin action (Fig. 1), the insulin action and GLUT-4 data were pooled across genders to
further compare responses to training in older vs.
young subjects. There was no significant interaction
effect but a significant treatment (training) effect (P <
0.05) for increasing ISI (young, 4.8 ± 0.5 vs. 6.8 ± 0.7
min⁻¹·μU⁻¹·ml⁻¹; older, 3.1 ± 0.5 vs. 6.3 ± 1.0
min⁻¹·μU⁻¹·ml⁻¹). A similar significant (P < 0.05)
treatment effect with no interaction was evident for
increasing GLUT-4 (young, 91.7 ± 17.4 vs. 152.5 ±
26.5; older, 93.8 ± 26.3 vs. 168.2 ± 31.7 AAU) with
training (pre-vs. posttraining, respectively). The mean
magnitude of increase (mean of posttraining-to-pre-
training (pre- vs. posttraining, respectively). The mean
GLUT-4 with training was 3.1 ± 26.5; older, 93.8 ±
6 increasing GLUT-4 (young, 91.7 ± 6
Youngren and Barnard (40) also reported that 8 wk of
exercise training increases glucose transporter concen-
tration more efficiently in older vs. young muscle.

DISCUSSION
The main finding of the present study was that
exercise training at the same relative exercise intensity
(≈75% VO₂max) increased GLUT-4 protein concentra-
tion in human skeletal muscle to a similar extent in
young and older men and women (Fig. 3). This increase
occurred despite the significantly lower absolute work-
loads of the older subjects, as evidenced by oxygen
consumption and heart rate responses during exercise
(Table 3 and 4). These findings suggest that the
relative, rather than absolute, exercise stimulus elic-
ited during training is an important factor controlling
GLUT-4 regulation in human skeletal muscle. The
present findings also indicate that skeletal muscle in
older men and women retains the ability to rapidly
increase muscle GLUT-4 concentration with endurance-
oriented exercise training.

Such findings are relevant, as the presently available
data concerning the ability of exercise to increase
GLUT-4 in older skeletal muscle are not conclusive. Kern
et al. (29) reported that GLUT-4 concentration
increased approximately two- to threefold in the soleus
and gastrocnemius of young (6–8 mo) and middle-aged
(15–17 mo) Fischer 344 rats with 10–15 wk of training
at 75% of maximal exercise capacity. However, there
was no significant increase in GLUT-4 in these muscle
groups, in older animals (27–29 mo), despite an identi-
cal relative exercise stimulus. The authors concluded
that the lower absolute workload used by the older
animals may not have been sufficient to trigger alter-
ations in GLUT-4. Similar results were obtained by
Gulve et al. (16) when they compared the effects of
wheel-running training in adult and old rats. Exercise
did not increase GLUT-4 in the older animals despite
an increase in the young runners. The older runners,
however, ran one-half of the distance of the younger
rats. Ezaki et al. (12) obtained contradictory findings
when they observed that adult (12-mo) Sprague-
Dawley rats increased skeletal muscle GLUT-4 concen-
tration to a greater degree than did young (1-mo)
animals after 4-wk of training at the same absolute
exercise intensity. These authors (12) concluded that
exercise training increases glucose transporter concen-
tration more efficiently in older vs. young muscle.
Youngren and Barnard (40) also reported that 8 wk of
training increased GLUT-4 concentration in the skel-
etal muscle of old (24 mo) Fischer 344 rats.

The present data suggest that older and young
human skeletal muscle increases GLUT-4 to a similar
extent when exercise training is performed at the same
relative exercise intensity (Fig. 3). In agreement with
these findings, Dela et al. (9) reported similar increases
in GLUT-4 in older (59 yr, n = 8) and young (23 yr,
N = 5) men after 9 wk of one-legged cycle training at ≈70%
VO₂max. Together, these results and the present findings
suggest that GLUT-4 increases by approximately the
same magnitude in young and older human skeletal
muscle when an adequate (70–75% VO₂max) and equiva-

tent relative exercise stimulus is presented. This in-
crease in GLUT-4 can occur relatively rapidly, as evi-
dent from the present data, with such an exercise
stimulus.

An increase in GLUT-4 with exercise may be func-
tionally important in relation to improving insulin action.
In transgenic animals, the overexpression of GLUT-4
results in a two- to fourfold increase of the protein in
skeletal muscle (31, 36). An increase of this degree was
sufficient to improve insulin action in healthy animals.
An interesting finding in the present (Fig. 3, RESULTS)
and other studies (19–21, 23, 34) is that GLUT-4
concentration increases by 1.5- to 3.0-fold in human
skeletal muscle with 7 days to 14 wk of endurance-
oriented training. In light of the transgenic animal data
(31, 36), it appears that an increase of this magnitude
may contribute, at least in part, to the improvement in
insulin action with training.

Insulin action was determined 15–17 h after the last
exercise bout; the residual effects from the last training
bout may thus account for the enhanced ISI evident in
the present study. In support of this relationship,
insulin action is enhanced for up to 12 h after only a
single bout of exercise (10, 11). This enhancement of
insulin action is primarily driven by the need for
glycogen repletion following an exercise bout (4, 24).
The acute effects of exercise may not, however, fully
account for the enhanced insulin action observed in the
aged subjects studied in the present study. We (18) and
others (6, 37) have observed that a single bout of
physical activity (40–60 min at 70–75% VO₂max) i n
older individuals (>50 yr) did not improve insulin
action 15–18 h after the exercise bout. Such data
suggest that the enhanced insulin action evident in the
present study was a combination of both the acute
effects of a single exercise bout and cumulative effects
from the 7 days of training. This hypothesis is in
agreement with conclusions derived from other 7-day
training studies (6, 37).

Aging is associated with a progressive decrement in
insulin action, which can be initiated as early as the
third decade of life (7, 26). This decline has been
attributed to chronological age itself and/or to a variety
of secondary factors associated with the aging process,
such as an increase in body fat, increased central
adiposity, and a reduction in spontaneous physical
activity (13, 17, 26, 38). Our data were consistent in
demonstrating that older men and women display a
decreases in the concentration of GLUT-4 in some skeletal muscle groups in rapidly growing young (1–4 mo) vs. adult (>10 mo) animals (2, 5, 12, 15, 32). In studies comparing adult (7–13 mo) vs. older rats (>25 mo), either no change (5, 15, 16) or a decrease (29) in GLUT-4 in skeletal muscle has been reported.

In conclusion, 7-days of endurance-oriented training (1 h/day) at the same relative exercise intensity (≈75% \(\text{VO}_{2\max}\)) increased GLUT-4 protein concentration to a similar extent in the skeletal muscle of young and older men and women. This increase was evident despite the markedly lower absolute workloads during training and the increased adiposity and reduced cardiovascular fitness of the older groups. Whole body insulin action also increased by a similar magnitude in young vs. older men and women. These data suggest that older human skeletal muscle retains the ability to increase muscle GLUT-4 and improve insulin action with endurance training.

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REFERENCES


