Muscle Adaptations to 7 Days of Exercise in Young and Older Humans: Eccentric Overload Versus Standard Resistive Training

Tibor Hortobágyi, Jeff Money, Donghai Zheng, Ronald Dudek, David Fraser, and Lynis Dohm

This study compared muscle adaptations after 7 days of exercise with eccentric-overload (EO) or standard (ST) resistive training in young (20 years) and older (69 years) adults. Young EO and ST gained 103 and 30 N, respectively, and older EO and ST gained 63 and 25 N of strength, respectively (all p < .05). Types I and IIa MHC mRNA levels were not altered, but Type IIx levels decreased 31% and 63% after the first and seventh exercise bouts, respectively, in young and decreased 30% after the seventh bout in older participants (all p < .05), independent of loading type. Type IIa fiber increased. Type IIx decreased, and Type IIa increased in both age groups independent of loading type (all p < .05). Electron microscopy revealed no myofibrillar disruption in young or older muscle. These data suggest that short-term EO produces larger strength gains than does ST without muscle-cell disruption or loading-type-specific changes in MHC mRNA isoforms in young and older skeletal muscle.

Key Words: aging, strength training, skeletal muscle

Accumulating evidence suggests that muscle lengthening (eccentric contraction) is pivotal in causing strength gains and muscle hypertrophy (Booth & Thomason, 1991; Dudley, Tesch, Miller, & Buchanan, 1991; Hortobágyi et al., 1996; Tesch, Dudley, Duvoisin, & Hather, 1990). An emphasis on eccentric compared with shortening (concentric) contractions in an exercise program to stimulate muscle growth could be especially beneficial for the elderly because of the lower metabolic and cardiovascular costs associated with eccentric contractions (Hortobágyi & DeVita, 2000; Lastayo, Reich, Urquhart, Hoppeler, & Lindstedt, 1999; Thompson, Versteegh, Verend, Birmingham, & Vandezoort, 1999). Eccentric contractions also appear to target the more atrophy-prone fast-twitch fibers of old muscle (Larsson, Grimby, & Karlsson, 1979; Nardone, Romano, & Schieppati, 1989). Whereas isometric and concentric forces sharply decline with age, eccentric

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strength, especially in women, remains relatively well preserved (Hortobágyi et al., 1995; Krishnathasan & Vandervoort, 2000). Resistive training, particularly high-force eccentric contractions, can cause myofibrillar disruptions (Clarkson, 1992; Gibala, MacDougall, Tarnopolsky, & Stauber, 1995; Hortobágyi et al., 1998), and it has been suggested that old compared with young muscle might be more vulnerable to contraction-induced injury (Brooks & Faulkner, 1996). After acute eccentric exercise or chronic resistive training, however, older participants revealed little muscle dysfunction, cell disruption, or soreness (Clarkson & Dedrick, 1988; Dedrick & Clarkson, 1990; Hurley et al., 1995; Roth et al., 2000).

Taken together, these observations suggest that an eccentrically biased training program could improve older adults’ muscle function, but there are no data in the literature to support this conjecture (Krishnathasan & Vandervoort, 2000). We therefore designed a short-term, low-intensity resistive exercise-training program that consisted of a 50% eccentric overload in the concentric-eccentric sequence of the knee-extension exercise. We hypothesized that exercise consisting of an eccentric overload would produce greater strength gains than standard resistive training would. We also expected to see a greater amount of muscle-cell disruption after eccentric overload than with standard resistive training. Because a single bout of eccentric or concentric exercise might increase net protein balance (Phillips, Tipton, Aarsland, Wolf, & Wolfe, 1997) and MHC proteins have a 3- to 7-day-long half-life (Kraus, Torgan, & Taylor, 1994; O’Neill, Zheng, Anderson, Dohm, & Houmard, 1999; Staron et al., 1994), we thought it was possible that seven bouts of exercise over 7 days would lead to adaptive alterations in muscle at the protein and message level. Therefore, the purpose of the study was to compare the acute changes in muscle strength: Types I, IIA, and IIX myosin heavy-chain (MHC) mRNA levels; fiber type and size; and muscle ultrastructure after 7 consecutive days of exercise with an eccentric overload and standard resistive training in young and older adults.

Methods

PARTICIPANTS AND DESIGN

Forty-five apparently healthy and sedentary participants (43 women, 2 men; 43 Caucasian, 2 African American) volunteered to participate in the study. The mean (± SD) age, height, and mass of young participants were 20.5 (± 1.7) years, 1.60 (± 0.06) m, and 61.2 (± 6.3) kg, respectively. The mean age, height, and mass of the older participants were 69.0 years (± 6.3), 1.60 (± 0.04) m, and 72.5 (± 11.7) kg, respectively. Older participants were required to provide their family physicians’ approval to participate in the study. This approval letter and a medical questionnaire were used to determine whether a participant would qualify for the study. Participants were excluded if they had more than two risk factors for coronary artery disease, a history of falls, osteoporosis, osteoarthritis, orthopedic or neurological conditions (i.e., stroke), medications that cause dizziness, smoking, a body mass/height² ratio greater than 28 kg/m², blood pressure >140/90 mmHg, a heart condition; could not understand the nature of the study; or had exercised regularly in the past 2 years. All participants were right-leg dominant based on a ball-kicking test. Before testing, participants read and signed a written informed-consent
document approved by East Carolina University’s Policy and Review Committee on Human Research.

Twelve young and 12 older participants were willing to undergo muscle biopsies and 7 days of exercise training. These participants were ranked based on their three-repetition-maximum (3RM) strength. Pairs of participants were then randomly assigned to the standard (ST, n = 6) or eccentric-overload (EO, n = 6) exercise group. The other young (n = 9) and older (n = 12) participants served as nonexercising controls. The 24 exercising participants underwent an initial muscle biopsy, 3 days of rest, an initial session of familiarization with strength testing, strength testing over 2 separate days, 7 consecutive days of unilateral left-quadriceps strength training, muscle biopsy, 3 days of rest, and final strength testing. In addition, a muscle biopsy was taken after the first exercise session only in the young participants. Control participants were tested for muscle strength but were not biopsied. Previously we reported test–retest histochemistry data in 24 participants that showed high reliability and no significant changes in the means for fiber-type composition and fiber size (Hortobágyi et al., 1996, 2000).

STRENGTH TESTING

We have previously described these isokinetic testing procedures in great detail, including warm-up, participant positioning, number of trials, and data analysis (Hortobágyi et al., 1996, 2000). Briefly, maximal voluntary isometric and isokinetic 1.57-rad/s eccentric and concentric quadriceps strength of the left leg were measured on a dynamometer (Kin-Com 500H, Chattecex Inc., Chattanooga, TN). We used isokinetic strength as an independent measure of muscle strength relative to the 3RM.

Unilateral (left-leg) concentric and eccentric 3RMs of the quadriceps muscle were also determined on a separate day relative to the tests administered on the dynamometer, using a Cybex knee-extension unit (model #4100. Cybex Inc., Owatonna, MN). Concentric and eccentric 3RMs were defined as the amount of weight a participant was able to lift and lower, respectively, three times. We used a 3RM and not a 1RM because in our experience, older participants better tolerate 3RM than 1RM testing because of the lighter weight. Concentric 3RM was determined first. At a three-count pace, participants lifted and lowered the weight with one smooth movement during each phase. The weight for the first attempt was about 50% of the estimated 3RM weight. Weight was then progressively added in 10–45 N increments until the 3RM was reached, with ~3 min of rest between efforts. Next, the eccentric 3RM was assessed. The technician manually lifted the weight that was one step below the previously determined concentric 3RM. The participant extended his or her knee, the technician let the weight go, and the participant lowered the weight at a three-count pace of a metronome from 3 rads to 1.57 rads of knee-joint position. This cycle was repeated until the participant could no longer lower the weight three times in a controlled fashion. No participant did more than six attempts to reach the concentric and eccentric 3RM.

MUSCLE ANALYSIS

Percutaneous vastus lateralis muscle samples were taken after ~1 hr of seated rest at the beginning of the study and 3 hr after the first (young participants only, six bouts of 10 contractions) and seventh exercise sessions. Under local anesthesia
(5 ml of 1% lidocaine), a sample of up to 150 mg was removed, using multiple needle passes, from the muscle belly by applying suction to a 5-mm Bergström needle. Repeat biopsies were taken 2–3 cm distal to the previous sample at the same depth of 4–5 cm. The specimens were dissected of visible fat and connective tissue. A larger portion of the sample was immediately frozen in liquid nitrogen for RNA analysis.

Total RNA was isolated with the TRIZol reagent (Gibco-BRL, Gaithersburg, MD) according to the manufacturer’s instructions and as described in detail previously (Hortobágyi et al., 2000; O’Neill et al., 1999). Types I, IIA, and IIX MHC mRNA isoform levels were determined by the RNase protection assay (RPA II, Ambion, TX) detailed previously (Hortobágyi et al., 2000; O’Neill et al.). Briefly, all samples for a participant were analyzed at the same time on adjacent lanes. To be able to perform between-group analyses, in each assay we alternated samples from young and older ST and EO participants. The cDNA probe for the DNA complementary to Type I MHC mRNA was obtained from Kirti Bhatt (see Welle, Bhatt, & Thornton, 1996). The cDNA probes for Types IIA and IIX MHC mRNA were obtained from Leslie Leinwand (see Smerdu, Karsch-Mizrachi, Campione, Leinwand, & Schiaffino, 1994). The RPA assay was verified by comparing single-probe hybridization with multiprobe hybridization. In these experiments the linear range of the assay for each isoform was verified by using 20 µg yeast RNA and 1, 2, and 5 µg total RNA from human muscle, as well as by hybridization using double the amount of full-length probes. The 20 µg yeast RNA also served as a negative control of RNase digestion in which a 1:1,000 dilution of RNase A/RNase T1 mix was used. The molecular sizes of the protected fragments and Types I, IIA, and IIX MHC full-length probes were verified by comparing them with an RNA molecular ladder (Century Size Markers, Ambion).

To minimize overexposure of the autoradiograph, the amount of full-length probes loaded on the gel were equivalent to only one twelfth of the amount used for the hybridization with the sample RNA, and the radioactivity of the full-length probes on the gel was still higher than the protected RNA fragments. Two µg of RNA per sample were used in the assays. We expressed the MHC mRNA data in two independent ways. First, they were normalized relative to GAPDH mRNA. By assuming uniform loading, the changes in the GAPDH-corrected levels were computed by assigning a value of 1.0 to the baseline samples. Second, each MHC mRNA isoform was also expressed relative to its baseline, uncorrected for GAPDH mRNA, and relative changes were computed. The two methods of expressing the data yielded similar results; we report the results in the GAPDH-corrected form.

A small portion of each biopsy sample was fixed in 2.5% glutaraldehyde 0.1M sodium-phosphate buffer, pH 7.4, within 1 min of sampling. These samples were washed overnight in the buffer, postfixed in 2% osmium tetroxide, dehydrated through graded ethanol series, and embedded in an Epon/Araldite mixture. Three tissue blocks were prepared from each biopsy sample. From each block, three semithin sections (1 µm) were cut on an ultramicrotome (Reichert Optische Werke, Vienna, Austria) and prepared for examination in a transmission electron microscope (model 1200EX, Jeol USA Inc., Peabody, MA).

Qualitative analysis of myofibrillar disruption was done on the samples of all participants based on the criteria of z-line streaming and myofilament disorganization. Three images of photo negatives from one randomly selected section of each block
were captured with a Norstan Light Box (Imaging Research, Ontario, Canada) system through a Sierra Scientific CCD camera. The images were digitized (Macintosh IIci, NIH Image 1.58 software) for total number of pixels and the number of pixels showing cell disruption. Myofibrillar disruption was quantified by averaging percent damage from all three pictures (Gibala et al., 1995; Hortobágyi et al., 1998).

At baseline and after the seventh exercise bout, an effort was made to obtain a sufficient amount of tissue for histochemistry, as well. These samples were mounted in an O.C.T. tragacanth-gum mixture (Miles Inc., Elkhart, IN), frozen in precooled isopentane, and stored in liquid nitrogen. Types I, IIA, and IIX muscle fibers were determined from 10-μm sections using myosin ATPase staining at preincubations of 10.3 and 4.54 pH (Brooke & Kaiser, 1970). A minimum of 300 fibers was classified in each sample. In line with the most current interpretation, what have previously been referred to as IIb muscle fibers in humans we refer to as Type IIX (Smerdu et al., 1994). Fiber cross-sectional area was calculated from a minimum of 25 Type I, IIA, and IIX fibers by computerized digitometry (Autosketch 2.0, Sausalito, CA).

EXERCISE TRAINING

Participants warmed up for each session by riding a bicycle ergometer for 5 min at 1 kg and stretching for a few minutes. Exercise training consisted of five to six bouts of 10–12 repetitions of unilateral, left-knee extension-flexion exercise for 7 consecutive days. Participants rested for 3 min between exercise bouts. They exercised on the same Cybex machine that was used for the 3RM testing. We chose unilateral knee extension as the exercise in order to isolate the quadriceps muscle group. Participants assigned to the ST group exercised using a conventional sequence of knee extension (concentric quadriceps contraction) and flexion (eccentric quadriceps contraction). Participants in the EO group also used a knee extension-flexion sequence, but an overload of ~50% was added during the lowering phase (knee flexion, eccentric quadriceps contraction). In a previous study the flexion phase was about 50% underloaded relative to the knee-extension phase using the leg press (Dudley et al., 1991).

The training programs were designed so that the total weight lifted by the two groups was similar. The eccentric overload was accomplished by a technician manually attaching extra weight plates to the main weight stack at the instant the participant reached the end point of the knee-extension phase. The extra load was removed after the lowering (knee-flexion) movement was completed. To equate total load in the two groups, the EO participants performed fewer repetitions. For example, if a participant in the ST group lifted 23 kg of mass, he or she would perform six sets of 12 repetitions with 23 kg for both the concentric and the eccentric phases, a total of 3,312 kg. To equate the load, the paired EO participant would perform six sets of 9.5 repetitions with 23 kg concentrically and 35 kg eccentrically, a 50% overload, for a total of 3,306 kg. The 9.5 repetition was accomplished by having the participant perform nine repetitions for the odd-numbered sets and 10 repetitions for the even-numbered sets. It was necessary to determine the exact repetition number before the workouts for each exercise bout for the EO participants.
Matched pairs of participants were monitored so that as 1 participant improved the paired participant’s exercise volume was adjusted to equate the weights the 2 participants lifted. The weight, number of repetitions, and number of sets performed by each participant were recorded for the seven training sessions. Participants exercised to the beat of a metronome so that the lifting and lowering phases each lasted about 2 s.

**MUSCLE SORENESS**

Self-reported muscle soreness was evaluated using a questionnaire with a scale from 0 (*not sore at all*) to 10 (*extremely sore*). Participants rated muscle soreness of the anterior, posterior, medial, and lateral aspects of the thigh. The daily soreness score was the average of the four sites.

**STATISTICAL ANALYSES**

All data are reported as *M* and *SD*. Summed total mean weights lifted over 7 days by the four groups were compared with a one-way analysis of variance (ANOVA). Summed total mean weights lifted concentrically and eccentrically by the four groups were compared with a Group × Contraction Mode ANOVA with repeated measures on the last factor. Total daily weight lifted during 7 days of training was analyzed with a Group × Days ANOVA with repeated measures on days.

The weights lifted during the concentric and eccentric 3RM tests and isokinetic concentric and eccentric and isometric force were analyzed with a Group × Time (pre-, posttraining) ANOVA with repeated measures on time. Similar analyses were applied to the histochemistry data.

Two analyses were done on total RNA and on each MHC mRNA isoform. One was a Group (young and older EO and ST) × Time (pre-, posttraining) ANOVA with repeated measures on time. A second analysis was a Group (young EO and ST) × Time (baseline, Sessions 1 and 7) ANOVA with repeated measures on time. Tukey’s post hoc contrast was used to identify the means that were significantly different (*p < .05*).

**Results**

**EXERCISE-TRAINING DATA**

All 24 exercising participants completed the study without complications. The summed mean weight lifted over 7 days by the young EO and ST groups was 105,833 N (± 4,066) and 101,203 N (± 2,804; *p = .2275*), respectively. The summed total mean weight lifted by the older EO was 70,256 N (± 4,317) and by the older ST was 68,653 N (± 3,925; *p = .4915*). Young EO participants over the 7 days lowered a summed mean weight of 63,499 N (± 3,122) and lifted 41,586 N (± 2,781), representing a 53% (± 9%) eccentric overload. By design, the young ST group lifted and lowered the same amount of total weight over 7 days (50,601.5 N ± 1,876 in each movement phase). Thus, there was a 26% eccentric overload between the EO and ST. Older EO participants over the 7 days lowered a summed mean weight of 42,856 N (± 4,100) and lifted 27,400 N (± 3,143), representing a 56% eccentric overload.
The older ST group both lifted and lowered 34.326.5 N (± 3,885). The eccentric overload was 25% in the older EO compared with older ST.

From Session 1 to Session 7, total daily weight lifted increased ~1,800 N, or 20%. in young EO and ST and ~2,800 N, or 38%. in older EO and ST (all p = .0001). The actual training loads corresponded to about 60% of 1RM.

**MUSCLE STRENGTH**

Test–retest reliability of the strength measures based on the data of the nonexercising control participants suggested that isokinetic, isometric, and 3RM strength measures were reliable. The largest mean difference was ~2.9% (isokinetic eccentric force), and the lowest reliability coefficient was $r = .84$ (isokinetic concentric strength).

At baseline, there were no significant differences in muscle strength between older EO and ST, nor were there differences in strength between young EO and ST. At baseline, young participants were 32% stronger than older participants in the five strength measures combined. At baseline, young participants' concentric and eccentric 3RM were, respectively, 37% and 28% greater. At baseline, participants' force production followed the expected pattern of the force–velocity relationship. In young participants, concentric force (400 ± 70 N) was the least, exceeded by isometric (452 ± 87 N) and eccentric forces (637 ± 102 N). In older participants, concentric force (258 ± 65 N) was the least, exceeded by isometric (371 ± 63 N) and eccentric forces (505 ± 97 N). The mean changes, detailed in Table 1, are all relative to these baseline values. Most important, young EO demonstrated an average gain of 103 N, and young ST averaged 30 N of strength gain. The older EO revealed a 63-N average gain compared with older ST’s 25-N strength gain.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Gain Scores After 7 Days of Eccentric Overload (EO) and Standard (ST) Unilateral Knee-Extension Resistive Exercise in Young and Older Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
<td>Concentric 3RM</td>
</tr>
<tr>
<td>Young EO</td>
<td>92±b ± 25</td>
</tr>
<tr>
<td>Young ST</td>
<td>56± ± 28</td>
</tr>
<tr>
<td>Older EO</td>
<td>66±c ± 29</td>
</tr>
<tr>
<td>Older ST</td>
<td>45± ± 23</td>
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</table>

*Note. Data are $M ± SD$ in Newtons. Statistical analysis for each of the five strength measures is based on a Group × Time (pre-, posttraining) ANOVA with repeated measures on time and Tukey’s post hoc analysis.

*aPre- to posttraining gain, significantly greater than zero (p < .05). bGreater change than any other change (p < .05). cGreater change than the change in ST within the same age group (p < .05).
MHC MRNA DATA

Figure 1 shows a radiograph of polyacrylamide gel from ribonuclease protection assay for Type IIx MHC mRNA isoforms before and after one (young only) and seven exercise bouts. There were no significant changes in GAPDH mRNA levels after seven exercise bouts. The changes in the three MHC mRNA isoforms were similar in EO and ST. Therefore, the data were pooled within each age group for EO and ST. For these pooled data, there was still no significant Age × Time interaction (p = .3492) or time main effect (p = .2228) for Type I or Type IIa MHC mRNA. (p = .4455, interaction and p = .1630, time main effect). Figure 2(A) shows the significant Age Group × Time interaction (p = .0046) for Type IIx MHC mRNA. This isoform was downregulated significantly more in young (63%) than in older participants (30%). Figure 2(B) shows significant 31% and 63% downregulation in young participants after the first and seventh exercise sessions in Type IIx MHC mRNA levels (time main effect, p = .0008).

MYOFIBRILLAR DISRUPTION, SORENESS

Figure 3 shows longitudinal sections of human vastus lateralis in 1 young and 1 older participant. We found no evidence of myofibrillar disorganization or z-line streaming after one or seven bouts of EO or ST exercise in any participant, including the older participants. In the young participants only, we observed some z-line unevenness after one bout of EO exercise (Figure 3[D]). The number of pixels associated with this unevenness was 9% ± 6% of the total number of pixels in each micrograph. Figure 4 displays the self-reported muscle-soreness data. Soreness declined after the initial muscle biopsy (4.4 ± 2.0) with the progression of the 7-day

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Figure 1. Radiograph of polyacrylamide gel from ribonuclease protection assay for Type IIx MHC mRNA from the vastus lateralis before (C = control), after one session (D1, 60 contractions), and after seven sessions (D7) of exercise with an eccentric overload (EO) or standard (ST) resistive exercise in young and older participants. The radiograph illustrates data from 2 young (Y_EO and Y_ST) and 2 older (O_EO and O_ST) participants. Samples were taken 3 hr after the last contraction.
Figure 2. (A) Changes in Type IIx myosin heavy-chain mRNA isoform after 7 days of resistive exercise in young \((n = 12)\) and older \((n = 12)\) participants. Filled columns indicate baseline and open columns the mRNA levels 3 hr after the last contraction of the seventh exercise session. \(*p < .05\) relative to baseline and \(\dagger p < .05\) relative to older group. (B) Changes in Type IIx MHC mRNA levels in young participants \((n = 6)\) 3 hr after the first and seventh resistive exercise training sessions. \(*p < .05\) relative to baseline and \(\dagger\)relative to Bout 1. In both panels, mRNA levels are expressed in arbitrary units (AU) and normalized to GAPDH. Vertical bars denote \(+1\ SD\).

Figure 3. Longitudinal sections from the vastus lateralis muscle of an 81-year-old woman at (A) baseline and (B) 3 hr after the seventh exercise session comprising ~50% eccentric overload compared with standard resistive exercise. (C, D, and E) Micrographs from the vastus lateralis of a 19-year-old woman at baseline and 3 hr after the first and seventh exercise sessions with an eccentric overload. Magnification \(\times 15,200\). (F) \(\times 30,250\) of the z-line segment from (D), indicating some z-line unevenness after the first consecutive exercise session with an eccentric overload.
Figure 4. Self-reported perceived quadriceps muscle soreness in arbitrary units (AU) 24 hr after an initial and final muscle biopsy and after each of 7 consecutive days of exercise in young (circles) and older (squares) participants using an eccentric overload (filled symbols) or standard resistive exercise (open symbols). No Group × Time interaction or group main effect occurred. Time main effect, $p = .0001$. *$p < .05$ compared with other time points.

Training then increased again to 3.2 (± 1.5) after the final biopsy (time main effect, $p = .0001$). The Group × Time interaction and the group main effect were not significant for soreness (interaction term, $p = .9805$; group main effect, $p = .9033$).

HISTOCHEMISTRY

We obtained a sufficient amount of muscle tissue in 9 of the 12 young and 8 of the 12 older participants for histochemistry. Table 2 shows that the vastus lateralis fiber-type composition was similar in young and older participants, but Types IIa and IIx fiber areas were 29% and 35% greater in young than in older participants, respectively ($p < .05$).

There was a trend for EO participants to show greater muscle-fiber hypertrophy, but the Group × Time interaction was not significant ($p = .2866$). Thus, the data were pooled for these subgroups within each age group. Seven bouts of exercise increased 9% the proportion of Type IIa fibers in both age groups and decreased Type IIx fiber percentage by 7% and 8%, respectively, in young and older participants (all $p < .05$). Exercise increased Type IIa fiber area 4% and 6% in young and older participants, respectively ($p < .05$).

Discussion

Older muscle remains responsive to resistive exercise, but it is unknown whether it maintains its capacity to adapt to eccentric contractions (Grabiner & Enoka, 1995;
Table 2  Changes in Fiber-Type Composition and Area Resulting From 7 Bouts of Resistive Exercise

<table>
<thead>
<tr>
<th>Change</th>
<th>Type I</th>
<th></th>
<th>Type IIa</th>
<th></th>
<th>Type IIx</th>
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</tr>
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<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
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</tr>
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</table>
| Fiber type (%):
  young       | 52 (9)  | 50 (12) | 32 (11)  | 41 (10) | 16 (10) | 9 (9)   |
  older       | 56 (13) | 55 (7)  | 28 (8)   | 37 (9)  | 16 (12) | 8 (5)   |
| Fiber area (μm² × 10³):
  young       | 44.4 (1.6) | 45.9 (1.4) | 60.2 (1.0) | 62.6 (1.6) | 50.6 (1.4) | 51.9 (2.0) |
  older       | 42.3 (1.6)  | 42.9 (1.5) | 46.6 (2.0)  | 49.4 (1.1)  | 37.6 (1.8)  | 39.9 (2.2) |

Note. Values are M (SD). Participants from the eccentric overload and standard subgroups within each age group were pooled into one group, n = 9 (young) and n = 8 (older).

*p < .05 compared with before. *p < .05 compared with young.

Hurley et al., 1995; Krishnathan & Vandervoort, 2000; Nichols, Hitzelberger, Sherman, & Patterson, 1995; Welle et al., 1996). Normally, absolute strength gains are similar in young and older participants after standard resistive exercise (Grabiner & Enoka). Whereas the relative gains were similar in our two age groups, we observed only about half the absolute strength gain in the older participants (63 N) of that demonstrated by young participants (103 N) after EO training. Considering the fact that eccentric strength is less affected by aging than isometric or concentric strength (Krishnathan & Vandervoort), especially in women (Hortobágyi et al., 1995), the finding that older participants had smaller absolute strength gains than young participants was surprising. One explanation could be that older participants were less resilient and became overtrained after seven consecutive exercise sessions, but we observed no evidence of overtraining. Muscle soreness was very low and similar throughout the seven sessions in the two age groups (Figure 4). Fatigue was probably not a factor, because fatigability up to 100 voluntary contractions is similar between age groups (Lindström, Lexell, Gerdel, & Downham, 1997). Cardiovascular and metabolic responses to eccentric exercise are also known to be substantially less than those to concentric exercise (Lastayo et al., 1999; Thompson et al., 1999). Indeed, perceived exertion and cardiovascular responses were significantly lower in the EO than in the ST group (Hortobágyi & DeVita, 2000; Thompson et al.). We speculate that the smaller absolute strength gains in the elderly might be related to the unique neural activation of large motor units during eccentric contractions (Enoka, 1997), and these are the type of motor units the elderly lack (Larsson et al., 1979). The data thus suggest that the responsiveness of older participants to EO was less than that of young participants, but the strength gains still significantly exceeded the gains after ST.
Because of the technical difficulties in administering an eccentric overload program, only a few studies have previously examined the efficacy of such a regimen (Godard, Wygand, Carpinelli, Catalono, & Otto, 1998; Kaminski, Wabbersen, & Murphy, 1998; Nichols et al., 1995). In two of these studies, eccentric overload resulted in greater strength gains than standard loading did (Kaminski et al.; Nichols et al.). It is difficult to directly compare the strength gains between the present study and the previous studies (Godard et al.; Kaminski et al.; Nichols et al.) because of the differences in methods. With eccentric overload, including in the present study (Godard et al.; Kaminski et al.; Nichols et al.), the 5% rate of acute strength gain per session exceeds the 0.5–3% per-session rates normally reported after standard resistive training in young and older participants (Grabiner & Enoka, 1995).

There is little information on the effect of age on MHC gene expression. Welle et al. (1996) reported that age does not affect total RNA and contractile-protein mRNA levels. They concluded that a slower myofibrillar synthesis rate in older muscle is not caused by reduced mRNA availability. Our data are not necessarily in conflict with this conclusion, but the significantly smaller changes in Type IIx MHC mRNA in skeletal muscle of our older participants seem to indicate lower responsiveness, at least in the early phases of exercise, of older skeletal muscle. We also observed no contraction mode-specific changes in Type I, IIa, or IIx MHC mRNA levels. Relative to Types I and IIa MHC mRNA isoforms, our findings confirm the data of Welle, Bhatt, and Thornton (1999), who reported no significant changes in MHC mRNA levels or total RNA concentrations after six weight-lifting sessions. In contrast to the study by Welle et al., we found that Type IIx MHC mRNA levels were significantly downregulated after one and further downregulated after seven bouts of exercise. This significantly greater downregulation in young than in older muscle might indicate a reduced sensitivity to mechanical stimuli in older muscle after seven bouts of exercise (Figure 2).

A long-held view is that early adaptations to contractile activity are predominantly neural in nature (Enoka, 1997). Indeed, as few as one or two sessions of weight lifting can result in strength gains similar to the gains reported after 12–20 sessions (Kroll, 1964). In the present study, however, we observed small but statistically significant reductions in Type IIx and increases in Type IIa fiber percentages in both age groups (Table 2). As before, these changes were independent of the type of loading program (Hortobágyi et al., 2000). Our fiber-type data confirm the report of Staron et al. (1994), who observed similar changes after only 2 weeks of resistive training in young men and women. A downregulation of the Type IIx MHC mRNA isoform is consistent with the reduction in the relative proportion of Type IIx fibers after exercise (O'Neill et al., 1999; Staron et al.). These changes support the concept that muscle contraction and the lack of it shift the properties of muscle in the opposite direction, contractile activity making muscles slower (Caiozzo, Haddad, Baker, & Baldwin, 1996; Hortobágyi et al., 2000).

Not only is there a change in fiber-type composition after bouts of resistance training in young and older muscle, but also a positive net protein balance can occur after a single bout of resistive exercise (Phillips et al., 1997; Welle et al., 1999). Considering the 3- to 7-day-long half-life of the MHC proteins (Kraus et al., 1994; O'Neill et al., 1999; Staron et al., 1994), we thought it might be possible that fiber enlargement would occur after seven exercise bouts. A novel finding was the small
but statistically significant increase in Type IIa fiber area after only seven exercise bouts. We are aware of only one study that reported muscle-fiber hypertrophy after 4 weeks of resistive exercise in humans (Mayhew, Rothstein, Finucane, & Lamb, 1995). As was the case in that study, the fiber hypertrophy, which occurred in each participant in our study, was independent of the type of mechanical loading. Therefore, the greater strength gains after EO training must have been caused by neural adaptations. Because the exercise program did not alter Type IIa MHC mRNA levels but Type IIa fiber area increased, a decoupling between transcription and protein content occurred. These data are not unusual because, as we discussed previously, a few bouts of resistive exercise increased protein synthesis without changes in mRNA levels, suggesting translation as the key step in human muscle hypertrophy (Phillips et al.; Welle et al., 1999). Taken together, it is becoming clear that even though neural adaptations must play a significant role in the early stages of adaptations to resistive exercise, adaptive alterations within muscle are equally important.

Older animal muscle is more susceptible than young muscle to myofibrillar disruption after bouts of eccentric exercise (Brooks & Faulkner, 1996; Faulkner, Brooks, & Zerba, 1995). Nonetheless, the few studies that examined markers of muscle damage in older human muscle after bouts of pure eccentric exercise showed that older muscles sustained about the same muscle damage as did young muscles, with older muscles recovering more slowly (Clarkson & Dedrick, 1988; Dedrick & Clarkson, 1990). In addition, a weight-lifting program that resulted in 43% strength gains and 7% quadriceps hypertrophy caused no muscle damage or soreness in participants age 50–69 years (Hurley et al., 1995). We are aware of only one previous study that evaluated older human skeletal muscle after resistive exercise by means of electron microscopy (Roth et al., 2000). In contrast to their prior study in which no damage occurred, Roth et al. showed that a small portion, about 11%, of the fibers examined were disrupted after high-intensity training. Studies in older participants (Clarkson & Dedrick; Dedrick & Clarkson; Hurley et al.) and other reports in young participants (Gibala et al., 1995; Hortobágyi et al., 1998) suggest that muscle damage after exercise in both young and older participants might be muscle specific, with more damage occurring in non-weight-bearing upper extremity muscles. The weight-bearing quadriceps often performs high-rate eccentric contractions, rendering it less prone to injury.

Our data in Figures 3 and 4 are consistent with this suggestion. We detected no signs of cell disruption in the muscle samples taken from young or older participants. Muscle soreness in the quadriceps over 7 days of exercise with an eccentric overload actually declined from an already low initial level, confirming earlier observations (Hurley et al., 1995). One reason for the absence of myofibrillar disruption could be the low exercise intensity, about 60% of 1RM—lower than the intensity used by Hurley et al. All samples from young participants who exercised with an eccentric overload (n = 6) revealed some z-line unevenness after the seventh but not after the first exercise session. As the amount of weight lifted increased over the 7 days of exercise, these participants might have approached a threshold for myofibrillar disruption that often starts with z-line streaming (Clarkson, 1992). These data might have implications for the hypothesis that muscle-cell disruption is a precursor to hypertrophy, but as observed in the present study, a small amount
of muscle hypertrophy can in fact occur without muscle-cell disruption (Gibala et al., 1995; Phillips et al., 1997).

In conclusion, acute exercise with an eccentric overload resulted in significantly greater strength gains without cell disruption in young and older participants than did exercise consisting of standard loading. Young participants produced larger absolute gains than did older participants. Remarkably, only seven bouts of exercise resulted in small but significant changes in fiber composition and hypertrophy. Adaptations or remodeling in muscle might occur in the very early phase of resistive exercise, independent of the type of loading and age, and is probably mediated primarily by transcription. The capacity to adapt to exercise with an eccentric overload is maintained in older human skeletal muscle.

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