Single muscle fiber adaptations to resistance training in old (>80 yr) men: evidence for limited skeletal muscle plasticity

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Slivka D, Raue U, Hollon C, Minchev K, Trappe S. Single muscle fiber adaptations to resistance training in old (>80 yr) men: evidence for limited skeletal muscle plasticity. Am J Physiol Regul Integr Comp Physiol 295: R273–R280, 2008. First published April 30, 2008; doi:10.1152/ajpregu.00093.2008.—The purpose of this study was to investigate whole muscle and single muscle fiber adaptations in very old men in response to progressive resistance training (PRT). Six healthy independently living old men (82 ± 1 yr; range 80–86 yr, 74 ± 4 kg) resistance-trained the knee extensors (3 sets, 10 repetitions) at ~70% one repetition maximum 3 days/wk for 12 wk. Whole thigh muscle cross-sectional area (CSA) was assessed before and after PRT using computed tomography (CT). Muscle biopsies were obtained from the vastus lateralis before and after the PRT program. Isolated myosin heavy chain (MHC) I and IIa single muscle fibers (n = 267; 142 pre; 125 post) were studied for diameter, peak tension, shortening velocity, and power. An additional set of isolated single muscle fibers (n = 2,215; 1,202 pre; 1,013 post) was used to identify MHC distribution. One repetition maximum knee extensor strength increased (P < 0.05) 23 ± 4 kg (56 ± 4 to 79 ± 7 kg; 41%). Muscle CSA increased (P < 0.05) 3 ± 1 cm² (120 ± 7 to 123 ± 7 cm²; 2.5%). Single muscle fiber contractile function and MHC distribution were unaltered with PRT. These data indicate limited muscle plasticity at the single-muscle fiber level with a resistance-training program among the very old. The minor increases in whole muscle CSA coupled with the static nature of the myocellular profile indicate that the strength gains were primarily neurological. These data contrast typical muscle responses to resistance training in young (~20 yr) and old (~70 yr) humans and indicate that the physiological regulation of muscle remodeling is adversely modified in the oldest old.

sarcopenia; aging; contractile function

PROJECTIONS FROM THE 2000 census predict that by the year 2020, there will be more than 54 million Americans over the age of 65 and 7 million over the age of 85 (U.S. Census Bureau, 2004). This represents a 54% increase in the U.S. population over 65 and a 70% increase in individuals over 85 yr. The rapid growth in the number of older Americans translates into an increasing number of individuals experiencing a loss of muscle mass and strength that occurs with normal aging, termed sarcopenia (49, 50). Recent estimates for U.S. health care cost directly attributed to sarcopenia are in excess of $26 billion (26). Indirectly, the debilitating effects of sarcopenia have contributed to a doubling of home health care and nursing home expenditures reaching $132 billion annually. Thus, the economic impact on society and strain on resources resulting from sarcopenia-related issues are substantial.

Although the mechanisms for sarcopenia are not clearly understood at this time, it is characterized by a decrease in both the number of skeletal muscle fibers (37) and cross-sectional area (CSA) of remaining fibers (2, 35, 59). Specifically, aging has been shown to result in a 25% decrease in the total number of vastus lateralis muscle fibers by the age of 70 yr (37). Additionally, a reduction in size of remaining muscle fibers exists, with myosin heavy chain (MHC) I (slow-twitch) muscle fibers undergoing greater atrophy than MHC I (slow-twitch) muscle fibers (2, 35, 59). Because MHC IIa muscle fibers are capable of developing 5–6 times more power than MHC I muscle fibers (5, 59), the functional deterioration of MHC IIa muscle fibers in the elderly can severely limit dynamic movements, such as catching oneself to prevent a fall. As a result, effective therapies that preserve the quantity and quality of slow- and fast-twitch muscle fibers are of critical importance for independence and quality of life in the elderly.

Resistance training has been used to successfully increase whole muscle size and strength in old individuals (9, 13, 20, 27, 44, 46, 54, 55, 63). However, limited research is available on the cellular adaptations of skeletal muscle with resistance training in individuals over 80 years of age. This age group is clinically important because they appear to have an accelerated rate of whole muscle strength loss (1, 6). The reason for this accelerated loss in skeletal muscle strength is unknown and implies an alteration in muscle biology that may adversely impact the myocellular adaptations to chronic resistance training.

Using male volunteers over 80 yr of age, the purpose of the current study was 1) to assess changes in whole muscle strength and size in response to progressive resistance training (PRT), 2) assess changes in size and contractile function of isolated slow- and fast-twitch muscle fibers in response to PRT, and 3) assess MHC distribution alterations in response to PRT. Our secondary objective was to compare the current results to our previous single muscle fiber and resistance training research in men a decade younger. We previously reported that MHC IIa muscle fibers (size and contractile function) did not respond to PRT to the same extent as the MHC I muscle fibers from men in their 70s (60, 64). The limited MHC IIa fiber response in older individuals to a resistance-training program, a known hypertrophic stimulus, has since been corroborated by others (32).

On the basis of our previous resistance training findings from 70-yr-old men, we hypothesized that there would be an increase in whole muscle size and strength and that the improvements at the cell level would be targeted to the MHC I fibers (contractile function and MHC isoform distribution). To our knowledge, this is the first study to resistance train men...
exclusively over 80 yr to examine single muscle fiber contrac-
tile adaptations. Additionally, the current study is one of only a few studies (9, 34) to examine whole muscle size and strength adaptations in the oldest old in response to progressive resistance training. The combined findings from this study and our previous research provide a unique opportunity to gain insight into muscle cell plasticity with a progressive resistance training program among individuals that span a critical decade (70 vs. 80 yr) in the expanding aging community.

METHODS

Subjects. Six men were recruited from the local community for this investigation (age 82 ± 1 yr, height 173 ± 1 cm, weight 74 ± 4 kg). All subjects were over 80 yr of age (80–86 yr), nonexercising, nonobese (BMI 25 ± 1 kg/m²), and otherwise healthy. Each subject underwent a physical examination, which included medical history, blood and urine chemistries; arthritis; a history of neuromuscular problems; or hypertension; insulin- or noninsulin-dependent diabetes; abnormal blood cardiac, pulmonary, liver, or kidney abnormalities; uncontrolled hyper tension; insulin- or noninsulin-dependent diabetes; abnormal blood or urine chemistries; arthritis; a history of neuromuscular problems; or if they smoked tobacco. Additionally, these free-living men were not consuming any chronic medication (prescribed or over-the-counter). All subjects were given oral and written information about the experimental procedures and potential risks before giving written consent. All procedures conformed to the standards set forth by the Declaration of Helsinki, and these procedures were approved by the Institutional Review Boards of Ball State University and Ball Memorial Hospital.

Experimental design. All subjects underwent testing for whole thigh muscle cross-sectional area, knee extensor (thigh) strength, vastus lateralis single muscle fiber physiology, and MHC distribution. These procedures were completed before and after the 12-wk PRT program. For this investigation, all of the methods and instrumenta-
tion employed for the resistance training program, whole muscle analysis, and single muscle fiber analysis were identical to our previous investigations in men a decade younger (64).

Whole muscle strength. Bilateral isotonic one-repetition maximum (1-RM) of the knee extensor muscles was assessed using a seated-knee extension device (Cybex Eagle, Medway, MA). The 1-RM procedure was preceded by 10 min of warm-up exercise (self-selected workload, ~50 W) on a cycle ergometer (Monark 828E, Vansbro, Sweden). The 1-RM was determined by incrementally increasing the amount of weight on the device with each successful lift until the subject was not able to maintain proper form and/or fully extend his legs at a given weight. The last weight successfully lifted was determined to be the 1-RM. The 1-RM procedure was conducted before, every 2 wk during, and after completion of the PRT program. The initial 1-RM procedure was preceded by three equipment and procedure familiarization sessions. These sessions were to help ensure that the initial 1-RM was not limited by a learning effect.

Whole muscle size. Muscle cross-sectional area (CSA) of the right thigh was measured before and after PRT using computed tomogra-
phy (CT) on a helical scanner (CTI helical scanner, General Electric, Milwaukee, WI), as described previously (63). Subjects were supine for 30 min before scanning to minimize the influence of fluid shifts on the CSA measurements (3). The anatomical midpoint of the femur was used as the point of measurement for pretraining and post-
training CT measurements. The CSA of the thigh minus the area of bone and subcutaneous fat was determined using computerized planimetry (NIH Image Program, v.1.61; National Institutes of Health, Bethesda, MD).

Progressive resistance training program. Subjects performed 12 wk of a supervised PRT program designed to strengthen the quadri-
ceps muscle group. Subjects performed bilateral isotonic leg exten-
sions on a seated device (Cybex Eagle, Medway, MA) 3 days per week on nonconsecutive days (36 total sessions). Subjects performed three sets of 10 repetitions (3 × 10) at ~70% of their 1-RM with 2-min rest between sets. The training was progressive in nature in that if the 1-RM was assessed every 2 wk, and the weight was adjusted accord-
ingly to maintain an intensity of ~70%. Each session was preceded by 10 min of warm-up (~50–75 W) on a cycle ergometer (Monark 828E, Vansbro, Sweden). This entire protocol is identical to several previous investigations from our laboratory (16, 17, 60, 63, 73, 74). All six men completed every training session (n = 36) for 100% compliance to the training program.

Muscle biopsy. Muscle biopsies (4) were obtained from the vastus lateralis of each subject before the initial training session and after the last training session. Each muscle sample was sectioned into longitudi-

nal sections and placed in cold skinning solution (see below) and stored at ~20°C for later analysis of single muscle fiber physiology and single-muscle fiber MHC isoform analysis.

Skinning, relaxing, and activating solutions. The skinning solution con-
tained (in mM): 125 K propionate, 2.0 EGTA, 4.0 ATP, 1.0 MgCl₂, 20.0 imidazole (pH 7.0), and 50% (vol/vol) glycerol. The compositions of the relaxing and activating solutions were calculated using an interactive computer program described by Fabiato and Fabiato (8). These solutions were adjusted for temperature, pH, and ionic strength using stability constants in the calculations (18). Each solution contained (in mM): 7.0 EGTA, 20.0 imidazole, 14.5 creatine phosphate, 1.0 free Mg²⁺, 4.0 free MgATP, KCl, and KOH to produce an ionic strength of 180 mM and a pH of 7.0 (32). The relaxing and activating solutions had a free [Ca²⁺] of pCa 9.0 and pCa 4.5, respectively (where pCa = −log [Ca²⁺] concentration).

Single muscle fiber physiology experiments. On the day of an experiment, a 2- to 3-mm muscle fiber segment was isolated from a muscle bundle and transferred to an experimental chamber filled with relaxing solution where the ends were securely fastened between a force transducer (model 400A; Cambridge Technology, Lexington, MA) and a direct current torque motor (model 308B; Cambridge Technology) as described by Moss (45). The force transducer and the torque motor were calibrated before each experiment. The instrumenta-

tion was arranged so that the muscle fiber could be rapidly trans-
ferred back and forth between experimental chambers filled with relaxing or activating solutions. The apparatus was mounted on a microscope (Olympus BH-2, Japan), so that the fiber could be viewed (×800) during an experiment. Using an eyepiece micrometer, sarco-

meres along the isolated muscle segment length were adjusted to 2.5 µm, and the fiber length (59) was measured. All single muscle fiber experiments were performed at 15°C.

Unamplified force and length signals were sent to a digital oscilos-
cope (Nicolet 310, Madison WI), enabling muscle fiber perform-
ance to be monitored throughout data collection. Analog force and position signals were amplified (Positron Development, Dual Differential Amplifier, 300-DIPF2; Ingelwood, CA), converted to digital signals (National Instruments, Austin, TX), and transferred to a computer (Micron Electronics, Nampa, ID) for analysis using custom-
ized software. Servo-motor arm and isotonic force clamps were con-

For each single muscle fiber experiment, a fiber with a compliance (calculated as fiber length divided by y-intercept) greater than 10%, and/or a decrease in peak force of more than 10% was discarded and not used for analysis. The within-fiber test/retest of a single muscle fiber in our lab for the measurements of size, force-power relationships, peak force, and contractile velocity were less than 1%. The coefficient of variation for the force transducer and servo-mechanical lever mechanism during the timeframe of this investigation was 0.5% and 0.6%, respectively.

Single muscle fiber analysis. The analysis of single muscle fibers included a measurement for diameter, peak force (Po), maximal...
unloaded shortening velocity (Vo), and power parameters. Detailed descriptions and illustrations of these procedures have been previously published by our laboratory (59, 64).

**Single muscle fiber diameter.** A video camera (Sony CCD-IRIS, DXC-107A, Tokyo, Japan) connected to the microscope and interfaced to a computer allowed viewing on a computer monitor and storage of the digitized images of the single muscle fibers. Fiber diameter was determined from a captured computer image taken with the fiber briefly suspended in air (<5 s). With the assumption that the fiber forms a cylindrical cross section when suspended in air, the fiber width is equal to the fiber diameter. Fiber width (diameter) was determined at three points along the segment length of the captured image using NIH public domain software (Scion Image, release Beta 4.0.2, for Windows). The average of these three measurements was the determined single muscle fiber diameter.

**Single muscle fiber peak force (po).** The output of the force and position transducers was amplified and sent to a microcomputer via a Lab-PC+ 12-bit data acquisition board (National Instruments). Resting force was monitored, and then the fiber was maximally activated in pCa 4.5 solution. Peak force was determined in each fiber by computer subtraction of the force at baseline from the peak force in pCa 4.5 solution.

**Single muscle fiber shortening velocity.** Fiber shortening velocity (Vo) was measured by the slack test technique, as described by Edman (7). The fiber was fully activated in activation solution and then rapidly released to a shorter length, such that force fell to baseline. The fiber shortened, taking up the slack, after which force began to redevelopment. The fiber was then returned to its original length. The duration of unloaded shortening, or time between onset of slack and redevelopment of force, was determined by computer analysis. Four different activation and length steps [150, 200, 250, and 300 μm; each ≤ 15% of fiber length (FL)] were used for each fiber. The slack distance was divided by the fiber length and plotted as a function of the duration of unloaded shortening. Fiber Vo (in FL/s) was then equal to the slope of this linear graph. Only experiments in which r² was greater than or equal to 0.98 were included for analysis.

**Single muscle fiber power.** Submaximal isotonic load clamps were performed on each fiber for determination of force-velocity parameters and power. Each fiber was fully activated in pCa 4.5 solution and then subjected to three isotonic load steps. This procedure was performed at various loads so that each fiber was subjected to a total of 15–18 isotonic contractions. Force and shortening velocity data points derived from the isotonic contractions were fit using the hyperbolic Hill equation (24). Fiber peak power was calculated from the fitted force-velocity parameters (Po, Vmax and a/Po, where a is a force constant and Vmax is the y-intercept). Absolute power (μN·FL⁻¹·s⁻¹) was defined as the product of force (μN) and shortening velocity (FL/s). Normalized power (W/l) was defined as the product of normalized force and shortening velocity.

**Single muscle fiber MHC determination.** Following the single-muscle fiber contractile physiology measurements, each fiber was solubilized in 1% SDS sample buffer and stored at −20°C until assayed (15, 74). To determine the MHC composition, fibers were run on a Hoefer SE 600 gel electrophoresis system that consisted of a 3.5% (wt/vol) acrylamide stacking gel with 5% separating gel at 4°C. Following gel electrophoresis, the gels were silver stained for MHC identification, as described by Giulian et al. (15).

**Statistical analysis.** Whole muscle strength was analyzed using a one-way repeated-measures ANOVA using SPSS ver. 14.0 for Windows. Whole muscle size, single muscle fiber contractile function, and MHC distribution were analyzed using a paired t-test. For each single muscle fiber parameter (diameter, Po, Vo, power) within a subject, a mean for each fiber type was determined. The mean value was used to represent all fibers of that fiber type within the given individual. Significance was set at P < 0.05. All data are reported as means ± SE.

Collectively, the hybrid (I/IIa and Ia/IIX) fibers constituted a reasonable proportion of the muscle, but when partitioned into the individual subtypes, there were insufficient data for pretraining to postraining comparisons. As a result, they were not included in single-muscle fiber contractile function analysis. The postraining to postraining comparisons for the single-muscle fiber physiology experiments are focused to the MHC I and IIa fiber types.

**RESULTS**

**Whole muscle strength and size.** Bilateral knee extensor strength, as measured by one-repetition maximum, increased (P < 0.05) 23 ± 4 kg (56 ± 4 to 79 ± 7 kg; 41%) after the 12-wk resistance-training program. There was an increase (P < 0.05) in 1-RM strength every 2 wk from the previous 2-wk strength testing session except for the period between weeks 4 and 6, when the increase in strength did not reach statistical significance (Fig. 1). Whole muscle thigh cross-sectional area increased (P < 0.05) 3 ± 1 cm² (120 ± 7 to 123 ± 7 cm²; 2.5%) from pretraining to postraining.

**Single muscle fiber diameter and contractable properties.** We successfully studied 142 fibers pre- (MHC I = 98; MHC IIa = 44) and 125 fibers post- (MHC I = 83; MHC IIa = 42) resistance training for diameter and contractile function. For each individual, 23 ± 1 were studied before and 21 ± 2 studied
after resistance training. Single muscle fiber diameter, Po, and Po/CSA did not change as a result of the 12-wk progressive resistance training in either MHC I or MHC IIA muscle fibers (Table 1). Contractile speed (Vo and Vmax) did not change in MHC I fibers with resistance training. MHC IIA fiber Vo increased 6.5% (P < 0.05), while MHC IIA Vmax was similar before and after resistance training (Table 2). Single muscle fiber power (absolute and relative to fiber size) was unaltered with the resistance training program (Table 3). The coefficient of variation between fibers was similar before and after resistance training for MHC I and IIA muscle fibers: diameter (17–19%), Po (34–43%), Po/CSA (14–18%), Vo (18–22%), and power (41–52%).

Single-fiber MHC isoform distribution. A total of 2,215 (pre = 1,202; post = 1,013) single muscle fibers were isolated and studied for MHC composition. For each individual, 200 ± 19 isolated muscle fibers were analyzed before and 169 ± 6 fibers were analyzed after training. No single muscle fibers, analyzed either before or after training, expressed only the MHC Ix isoform. Additionally, no single muscle fiber analyzed coexpressed all three human MHC isoforms (MHC/Ia/Ix) or a combination of MHC I and IIX isoforms (MHC/IIX). The percent distribution of the MHC isoforms is presented in Table 4. No change in MHC isoform distribution was evident with the progressive resistance-training program.

DISCUSSION

The unique aspect of this investigation was the examination of whole muscle and single muscle fiber contractile function before and after a progressive resistance-training program in independently living men exclusively over 80 yr of age. The main findings from this investigation were that modest gains were observed at the whole muscle level, whereas no alterations in MHC I and IIA contractile function were observed. These findings suggest limited muscle plasticity, particularly at the cellular level, among the very old with a resistance exercise intervention.

Baseline comparisons. The 82-yr-old men in the current study had 10% less muscle mass (120 ± 7 vs. 134 ± 8 cm3) compared with our previous study in 74-yr-old men. Interestingly, both groups of men had nearly identical 1-RM strength (56 ± 4 vs. 53 ± 5 kg) prior to beginning the resistance-training program. Similar leg muscle strength with less muscle mass would point to potential differences in muscle fiber recruitment, fiber type profile, or the intrinsic properties of the muscle fibers. In support of the latter, the 82-yr-old and 74-yr-old men had a similar fiber type profile with noted differences in single muscle fiber contractile properties before the training program. Generally, the 82-yr-old men’s MHC I and IIA fibers were slightly larger, stronger, and faster than the 74-yr-old men, contributing to more powerful muscle fibers, which were more pronounced in the MHC IIA muscle fibers. A comparison between these two studies and the current available literature on normalized power is shown in Table 5. Normalized power was chosen as a variable since it represents the most comprehensive profile of single muscle fiber function, as this measure incorporates size, strength, and speed. Data from these 14 studies, representing 20 different groups of individuals reveal an interesting trend that contrasts the typical dogma of poor fiber quality with age. In old individuals, MHC I and IIA normalized power is comparable to younger individuals and highly trained athletes. Equally interesting is the MHC I and IIA normalized power from spinal cord injury patients, which is on the upper end of the spectrum for what has been reported in human muscle. Collectively, these data suggest that chronic perturbations that induce significant whole muscle atrophy over a period of several years maintain or even slightly improve the power output of the remaining MHC I and IIA muscle fibers when normalized for cell size. The quantitative and qualitative regulation of individual muscle fibers in a challenging environment that promotes muscle cell loss (37) is a complex paradigm that warrants further research.

Whole muscle adaptation. From our review of resistance training studies that have focused on skeletal muscle in old individuals, it is apparent that a wide range in strength gains were achieved (7 to 174%). This variance is likely the result of differing training protocols and subject profiles. In the current investigation, we observed a 41% increase in knee extensor strength after 12 wk, which is in the median range of the previous reports. Of the more than 50 published resistance-training studies with an aging focus, three papers are most closely related to the current study (9, 34, 64). Previously published data from our laboratory, using the identical resistance-training protocol and equipment as the current study, reported strength increases of 50% in men (64), who were
approximately a decade younger. Two previous studies have included resistance-trained individuals exclusively over 80 yr and reported a 174% (9) and 134% (34) increase in leg strength. These studies differ from the current study in that the majority of subjects were institutionalized, considerably more frail, and were a mix of both men and women. When the one-legged strength improvements reported from the Fiatarone et al. (9) and Kryger and Anderson (34) studies are doubled to represent a bilateral 1-RM, the absolute amount of weight lifted increased by ~25 kg and ~21 kg, respectively. This compares favorably with the 23-kg increase in 1-RM after 12 wk of PRT in the current study. Thus, despite the weaker hypertrophic response gradually decreases with age (60 yr) is illustrated from the literature. Frontera et al. (13) reported 12 cm² (~10%) increase in muscle CSA among 60–72 y old men after 12 wk of resistance training. Fiatarone et al. (9) and Kryger and Anderson (34) report similar increases in the percent CSA (~10%) with a comparable resistance-training program among very old (>80 yr) individuals. However, the absolute gain in muscle CSA was only 2.7 cm² (34) and 4.6 cm² (9), which is very similar to the 3.0 cm² increase in CSA from the 82-yr-old men in the current investigation. When examined on the basis of muscle CSA gains in absolute terms, these studies support a progressive decrease in the hypertrophic response to resistance training at the whole muscle level with age (80+ yr < 70 yr < 60 yr).

### Single muscle fiber adaptations

The unique aspect of this investigation was the single muscle fiber contractile function be attributed to the strength output at the beginning of the study.

After 12 wk of resistance training, the thigh CSA from these old men increased 3.0 cm² (2.5%). This is considerably less than the 8.2 cm² (7%) increase in thigh CSA that we reported previously in 74-yr-old men (17). These results provide an indication that the magnitude of hypertrophy in response to resistance training may be slightly diminished as men age from their 70s into their 80s. Further support that the whole muscle hypertrophic response gradually decreases with age (60–80+ yr) is illustrated from the literature. Frontera et al. (13) reported a 12 cm² (~10%) increase in muscle CSA among 60–72 y old men after 12 wk of resistance training. Fiatarone et al. (9) and Kryger and Anderson (34) report similar increases in the percent CSA (~10%) with a comparable resistance-training program among very old (>80 yr) individuals.

### Table 4. Vastus lateralis single muscle fiber myosin heavy chain distribution before and after progressive resistance training

<table>
<thead>
<tr>
<th></th>
<th>MHC I</th>
<th>MHC I/Ila</th>
<th>MHC Ila</th>
<th>MHC Ila/Iix</th>
<th>Total Hybrids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre</td>
<td>42±7%</td>
<td>5±1%</td>
<td>33±7%</td>
<td>20±2%</td>
<td>25±2%</td>
</tr>
<tr>
<td>Post</td>
<td>38±10%</td>
<td>4±1%</td>
<td>37±8%</td>
<td>21±4%</td>
<td>25±4%</td>
</tr>
</tbody>
</table>

Values are expressed as means ± SE.

### Table 5. Summary of MHC I and Ila normalized power values from the literature

<table>
<thead>
<tr>
<th>Subject Population</th>
<th>Activity Level</th>
<th>Muscle</th>
<th>Single-Fiber Normalized Power (Watt/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>MHC I</td>
</tr>
<tr>
<td>Old Adults</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>Inactive</td>
<td>VL</td>
<td>1.91±0.08</td>
</tr>
<tr>
<td>Men</td>
<td>Inactive</td>
<td>VL</td>
<td>1.37±0.08</td>
</tr>
<tr>
<td>Men</td>
<td>Inactive</td>
<td>VL</td>
<td>1.58±0.15</td>
</tr>
<tr>
<td>Men</td>
<td>Inactive</td>
<td>VL</td>
<td>3.51</td>
</tr>
<tr>
<td>Women</td>
<td>Inactive</td>
<td>VL</td>
<td>1.74±0.21</td>
</tr>
<tr>
<td>Women</td>
<td>Inactive</td>
<td>VL</td>
<td>1.74±0.18</td>
</tr>
<tr>
<td>Women</td>
<td>Inactive</td>
<td>VL</td>
<td>4.25</td>
</tr>
<tr>
<td>Group mean (SD)</td>
<td></td>
<td></td>
<td>2.30 (1.11)</td>
</tr>
<tr>
<td>Young Adults</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>Inactive</td>
<td>VL</td>
<td>1.71±0.24</td>
</tr>
<tr>
<td>Women</td>
<td>Inactive</td>
<td>VL</td>
<td>1.72±0.27</td>
</tr>
<tr>
<td>Men</td>
<td>Recreational</td>
<td>VL</td>
<td>2.14±0.17</td>
</tr>
<tr>
<td>Men</td>
<td>Recreational</td>
<td>VL</td>
<td>1.53±0.04</td>
</tr>
<tr>
<td>Women</td>
<td>Recreational</td>
<td>VL</td>
<td>2.85±0.11</td>
</tr>
<tr>
<td>Women</td>
<td>Recreational</td>
<td>VL</td>
<td>1.89±0.23</td>
</tr>
<tr>
<td>Women</td>
<td>Recreational</td>
<td>Soleus</td>
<td>1.62±0.25</td>
</tr>
<tr>
<td>Men and women</td>
<td>Recreational</td>
<td>Gastroc</td>
<td>1.07±0.12</td>
</tr>
<tr>
<td>Group mean (SD)</td>
<td></td>
<td></td>
<td>1.82 (0.52)</td>
</tr>
<tr>
<td>Athletes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Swimmers</td>
<td>Highly trained</td>
<td>Deltid</td>
<td>1.66±0.05</td>
</tr>
<tr>
<td>Runners</td>
<td>Highly trained</td>
<td>Gastroc</td>
<td>1.68±0.10</td>
</tr>
<tr>
<td>Master runners</td>
<td>Highly trained</td>
<td>Gastroc</td>
<td>1.63±0.05</td>
</tr>
<tr>
<td>Weight lifters</td>
<td>Highly trained</td>
<td>VL</td>
<td>1.41±0.04</td>
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<tr>
<td>Group mean (SD)</td>
<td></td>
<td></td>
<td>1.60 (0.13)</td>
</tr>
<tr>
<td>Spinal Cord Injured</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>Inactive</td>
<td>VL</td>
<td>3.34±0.18</td>
</tr>
<tr>
<td>Overall average (SD)</td>
<td>Inactive (&gt;3 yr)</td>
<td>VL</td>
<td>3.34±0.18</td>
</tr>
<tr>
<td>(Range)</td>
<td></td>
<td></td>
<td>2.02 (0.82)</td>
</tr>
</tbody>
</table>

Values are expressed as means ± SE, except for group means and overall average, which are expressed as means (SD). VL, vastus lateralis; Gastroc, gastrocnemius (lateral head).
measurements in men over 80 yr before and after resistance training. Contrary to our hypothesis, no improvement was observed in single muscle fiber contractile function with the resistance-training program. This was a surprising and interesting finding in the context of the related literature on this topic. We have identified 64 published papers that have examined single-muscle fiber contractile function in humans. Of these studies, 24 have incorporated an intervention consisting of sports training responses \((n = 8)\) (10, 21, 23, 38–40, 56, 61), unloading paradigms \((n = 11)\) (11, 36, 57, 58, 62, 65–68, 71, 75), resistance training in young adults \((n = 1)\) (69), and resistance training in old adults \((n = 4)\) (12, 16, 60, 64). Of these human studies, 22 (92%) have reported alterations in contractile function with an intervention, and all five resistance-training studies have shown an improvement in contractile function. The exceptions are two sprint-training studies in young individuals (23, 38). Collectively, the consistent finding of alterations in single muscle fiber contractile function with a multitude of muscle perturbations provides strong support for the interpretation of limited muscle plasticity at the cell level with resistance training in men over 80 yr.

The limited muscle plasticity among the very old is further supported by Singh et al. (53) and compared with the improved cellular adaptations observed in our previous resistance training studies among men nearly a decade younger (64) (see Figs. 2 and 3). Singh et al. (53) reported no change (or a slight decrease) in muscle fiber size with a similar exercise program in very old \((83 \pm 3\) yr) frail individuals. Our previous group of 74-yr-old men had substantial improvements in MHC I contractile function, with less improvement in MHC IIa function (64). When these data are coupled with single muscle fiber responses to resistance training in young men (69), a muscle fiber-specific continuum of adaptation is apparent. With resistance training, young individuals improve MHC I and IIa single-muscle fiber function; individuals in their 70s lose a large portion of the ability to increase MHC IIa contractile function but retain the ability of MHC I fibers to improve; individuals in their 80s do not improve MHC I or IIa single muscle fiber function. These data suggest that the cellular adaptive potential is gradually reduced with age in a fiber-specific manner.

The pretraining MHC profile from old men in the current study was composed of \(~25\%\) hybrid MHC muscle fibers. In aging muscle, a relatively high proportion of single muscle fibers coexpressing multiple MHC isoforms have been previously observed (31, 34, 74). A high proportion of hybrid muscle fibers are not exclusive to aging muscle, as increases in hybrid fibers have been reported with a decrease in physical activity (41, 62). Conversely, individuals with high physical activity levels (i.e., athletes) typically have very few hybrid muscle fibers (22, 30, 56). Thus, there is strong support that changes in physical activity patterns can alter the single muscle fiber hybrid population. Using the identical resistance training protocol as the current study, we have previously shown that inactive young (73) and old (74) individuals significantly decrease the amount of hybrid muscle fibers after 12 wk of training. While both the young \((~25\) yr) and the old \((~74\) yr) had similar decreases in hybrid muscle fibers \((~20\%)\), the postraining profile for pure MHC phenotypes showed a distinct pattern of adaptation that paralleled the single muscle fiber contractile function changes highlighted above. That is, the 20-yr-old individuals increased the MHC IIa phenotype with training, while the 74-yr-old individuals increased the MHC I phenotype with training. In the current study, the static nature of the single-muscle fiber MHC profile with resistance exercise also mirrors the single muscle fiber contractile function findings and provides further evidence that the cellular adaptations to resistance exercise are extremely limited in the very old. This is also supported by the recent study by Kryger and Andersen (34) who reported no change in MHC profile with resistance exercise in very old \((85–97\) yr) men and women.

**Perspectives and Significance**

In the current study, whole muscle strength increased with resistance training, which most likely translated to improved functional status of the very old men (25). The fact that we observed a minor increase in whole muscle size with no alterations in single muscle fiber contractile function or MHC profile suggest that the strength gains observed in these old men following the resistance training program were primarily the result of improvements to the nervous system (i.e., muscle

**Fig. 2.** Summary of changes with progressive resistance training in MHC I single-muscle fiber diameter, strength \((P_o)\), speed \((V_o)\), and power are shown for the current 80-yr-old men and for 70-yr-old men from our previous investigation (64). \(*P < 0.05\) from pre- to post-training.

**Fig. 3.** Summary of changes with progressive resistance training in MHC IIa single-muscle fiber diameter, strength \((P_o)\), speed \((V_o)\), and power are shown for the current 80-yr-old men and for 70-yr-old men from our previous investigation (64). \(*P < 0.05\) from pre- to post-training.
fibers, recruitment, synchronization of motor units, etc.). In young healthy individuals, initial strength gains during a resistance-training program are due mostly to neural adaptation, with muscle hypertrophy becoming the dominant factor beyond 4 wk of training (42, 51). This time-course of neural and hypertrophic adaptation to resistance training is altered in older individuals with a greater reliance upon the neural component for strength gains (43). The finding of limited remodeling in single muscle fiber function or structure supports the idea that the physiological regulation for muscle hypertrophy is attenuated distal to the nerve in the skeletal muscle of individuals over 80 yr. This hypothesis is further strengthened by the pedigree of single-muscle fiber research in humans showing improvements in myocellular function with a resistance exercise intervention. Thus, the capacity for men over 80 yr to gain improvements in myocellular function with a resistance exercise-training program are due mostly to neural adaptation, fiber recruitment, synchronization of motor units, etc.). In 


