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Myogenic gene expression at rest and after a bout of resistance exercise in young (18–30 yr) and old (80–89 yr) women

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Raue, Ulrika, Dustin Slivka, Bozena Jemiolo, Chris Hollon, and Scott Trappe. Myogenic gene expression at rest and after a bout of resistance exercise in young (18–30 yr) and old (80–89 yr) women. J Appl Physiol 101: 53–59, 2006. First published April 6, 2006; doi:10.1152/japplphysiol.01616.2005.—The purpose of this study was to investigate mRNA expression of several key skeletal muscle myogenic controllers; myogenic differentiation factor (MyoD), muscle regulatory factor 4 (MRF4), myogenic factor 5 (Myf5), myogenin, myostatin, and myocyte enhancer factor 2 (MEF2) at rest and 4 h after a single bout of resistance exercise (RE) in young and old women. Eight young women (YW; 23 ± 2 yr, 67 ± 5 kg) and six old women (OW; 85 ± 1 yr, 67 ± 4 kg) performed 3 sets of 10 repetitions of bilateral knee extensions at 70% of one repetition maximum. Muscle biopsies were taken from the vastus lateralis before and 4 h after RE. Using real-time RT PCR, mRNA from the muscle samples was amplified and normalized to GAPDH. At rest, OW expressed higher (P < 0.05) levels of MyoD, MRF4, Myf5, myogenin, and myostatin compared with YW. In response to RE, there was a main time effect (P < 0.05) for the YW and OW combined in the upregulation of MyoD (2.0-fold) and MRF4 (1.4-fold) and in the downregulation of myostatin (2.2-fold). There was a trend (P = 0.08) for time × age interaction in MRF4. These data show that old women express higher myogenic mRNA levels at rest. The higher resting myogenic mRNA levels in old women may reflect an attempt to preserve muscle mass and function. When challenged with RE, old women appear to respond in a similar manner as young women.

mRNA; skeletal muscle; muscle regulatory factors; real-time reverse transcriptase-polymerase chain reaction

AGING RODENT (1, 31) AND HUMAN (16, 23) skeletal muscle has been shown to express high mRNA levels of muscle regulatory factors. The reason for this higher basal level muscle regulatory factor (MRF) mRNA phenomenon is unknown, although it may reflect an ongoing effort of the muscle to combat the atrophy that occurs with aging (28, 31). In addition to MRFs, microarray studies have shown a variety of mRNA categories to be upregulated in old adults, including stress- or damage-related genes (20), structural and regulatory genes (35), and components of the ubiquitin-proteasome proteolytic pathway (45, 46).

Some of the well-characterized transcription factors regulating muscle differentiation are MRFs, such as myogenic differentiation factor (MyoD), muscle regulatory factor 4 (MRF4), myogenic factor 5 (Myf5), and myogenin. Specifically, MyoD and Myf5 have been found to be responsible for stimulating myoblasts to enter differentiation and join the muscle lineage, whereas MRF4 and myogenin are suggested to mediate terminal differentiation of myoblasts (32). More recently, MyoD and myogenin have also been localized to existing myonuclei where they are suggested to aid in a hypertrophy response (19). In response to stimuli, these transcription factors induce myoblast differentiation and regulate transcription of many musclespecific genes (3). Some MRFs are upregulated within 2–12 h after an acute resistance exercise bout in young humans (4, 34, 49, 50). When old humans and animals are challenged with resistance exercise, there appears to be an age-related deficit in the mRNA induction of MRFs at 24 (23) and 48 h (38) postexercise. However, MRF induction in the early period after resistance exercise has not been studied in the old. This may be a critical time frame to better understand the response to an acute-exercise stimulus in the old, because peak induction of MRF genes occurs in the first several hours after exercise in young humans (50).

Therefore, the aim of this investigation was to characterize the gene expression levels of the MRF genes (MyoD, Myf5, MRF4, and myogenin), myostatin, and myocyte enhancer factor 2 (MEF2), at rest and 4 h after an acute bout of resistance exercise in young and old women. We were interested in two questions. 1) Are there any differences in myogenic gene expression between young and old women in the basal state? 2) Do young and old women respond differently to a bout of resistance exercise? The following hypotheses were tested. 1) At rest, old women will express higher levels of mRNA for the MRF genes (MyoD, Myf5, MRF4, and myogenin), myostatin, and MEF2. 2) Old women will have a blunted myogenic mRNA induction 4 h after resistance exercise compared with young women.

METHODS

Subjects. Eight young (23 ± 2 yr) and six old (85 ± 1 yr) women were recruited from the community for this investigation (Table 1). The criteria for subject qualification included nonexercising, nonobese (body mass index < 28 kg/m²), nonsmoking, normotensive, healthy women. The old women were not engaged in, and had no past history of, hormone replacement therapy. They also underwent a physical examination, which included medical history, blood and urine samples for general health markers, resting and exercising electrocardiogram and blood pressure, before participating in any resistance training. Before engaging in the experimental protocol, the subjects were informed of all procedures and risks associated with the protocol, and informed consent was obtained from each participant. The Institutional Review Board of Ball State University and Ball Memorial Hospital approved the experimental design before the initiation of the study.

Experimental design. The experimental protocol consisted of two to three familiarization sessions with the training device, followed by...
a one-repetition maximum (1 RM) assessment and finally a single resistance exercise bout. On the day of the experimental trial the resistance exercise was performed in the morning, and the subjects were fasted overnight before the exercise session. A baseline muscle biopsy was taken from the vastus lateralis after 30 min of supine rest. The subjects then performed a 10-min light warm-up on a cycle ergometer followed by the 3 sets of 10 repetitions at 70% of 1 RM on a knee extension device. A second muscle biopsy was taken from the opposite leg 4 h postexercise. The postexercise muscle biopsy time point was chosen based on our laboratory’s previous time course investigation showing an induction in MRF genes 4-h after resistance exercise (50).

1-RM assessment. Bilateral muscle strength was assessed using an isotonic knee extensor device (CYBEX Eagle, CYBEX, Medway, MA). The 1-RM procedure was performed with a gradual increase in weight, and the test was continued until the subject was not able to maintain proper form and fully extend the knee with the given weight. The last weight lifted to full extension was considered the 1 RM for each subject (Table 1).

Whole muscle size (computed tomography). Whole muscle cross-sectional area (CSA) of the right thigh was determined by using computed tomography (CT) (CTI helical scanner, General Electric, Milwaukee, WI), as described previously (42). Briefly, the circumference of the anatomic midpoint of the femur was used as the point of the CT measurements. The CSA of the thigh minus the area of the bone and subcutaneous fat was determined by using computerized planimetry (NIH Image Program, version 1.61, National Institutes of Health, Bethesda, MD).

Resistance exercise session. On the day of the trial subjects performed 3 sets of 10 repetitions at 70% of their 1 RM. Each set was followed by a 2-min rest period. The exercise involved a concentric and an eccentric component, each lasting ~2 s. This protocol is identical to many previous investigations performed in our laboratory (41, 43, 47, 50).

Muscle biopsy. Needle biopsy samples were taken from the right vastus lateralis before the resistance exercise bout and an additional biopsy was taken from the vastus lateralis in the left leg 4 h postexercise. Each muscle sample was divided into longitudinal sections (5–8 mg), and one section was placed in 0.5 ml of RNAlater (Ambion, Austin, TX) and stored at −20°C until RNA extraction. A portion of the muscle sample was frozen in liquid nitrogen for myosin isofrom analysis.

Total RNA extraction and RNA quality check. Each muscle sample was removed from the RNAlater and placed in a mixture of 0.8 ml of RNA isolation reagent, TRI Reagent, and 4 μl of PolyAcryl Carrier (Molecular Research Center, Cincinnati, OH). The tissue was homogenized, and total RNA was extracted according to the manufacturer’s protocol. The RNA pellet was dissolved in 30 μl of nuclease-free water and stored at −80°C.

One microliter of each total RNA extract (1:3 vol/vol with water) was analyzed using the RNA 6000 Nano LabChip kit on an Agilent 2100 Bioanalyzer (Agilent Technologies, Palo Alto, CA). This system reported detailed information about quantity and quality (integrity and purity) of the RNA samples. Each RNA sample was electrophoretically separated into two peaks of 18S and 28S ribosomal RNA. Data were displayed as a gel-like image and/or an electropherogram (Fig. 1).

Sample analyses were performed as described by the manufacturer. The high quality of RNA was confirmed by presence of ribosomal peaks with no additional signals (DNA contamination or RNA degradation) below the ribosomal bands and no shifts to lower fragments. On average, the yield of total RNA from 5–8 mg of muscle tissue from young women was (means ± SE) 88.1 ± 3.6 ng/μl and 74.6 ± 2.8 ng/μl for the old women.

Reverse transcription. Oligo(dT)-primed first-strand cDNA was synthesized using SuperScript II RT (Invitrogen, Carlsbad, CA). This system was optimized for sensitive RT-PCR on low amounts of RNA. A first reaction mix of 10 μl for each sample, consisting of 1 μl of RNA extract, 1 μl of 10 mM 2-deoxynucleotide 5'-triphosphate, 1 μl of oligo(dT)12-18 (0.5 μg/μl) and 7 μl of DNase- and RNase-free water, was incubated at 65°C for 5 min and then placed on ice for 1 min. A second reaction mix of 9 μl consisting of 2 μl of 10× RT buffer, 4 μl of 25 mM MgCl2, 2 μl of 0.1 M dithiothreitol, and 1 μl of RNaseOUT Recombinant RNase Inhibitor, was then added to the first reaction mix and incubated at 42°C for 2 min. Finally, 1 μl (50

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Table 1. Subject characteristics

<table>
<thead>
<tr>
<th></th>
<th>Young Women</th>
<th>Old Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>23.4 ± 1.7</td>
<td>85.2 ± 1.3*</td>
</tr>
<tr>
<td>Height, cm</td>
<td>162.0 ± 2.3</td>
<td>157.6 ± 0.8</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>67.0 ± 4.6</td>
<td>66.6 ± 3.4</td>
</tr>
<tr>
<td>Whole muscle CSA, cm²</td>
<td>122.0 ± 5.6</td>
<td>89.4 ± 3.7*</td>
</tr>
<tr>
<td>1 RM, kg</td>
<td>60.2 ± 5.9</td>
<td>38.8 ± 2.6*</td>
</tr>
<tr>
<td>MHC I, %</td>
<td>43.5 ± 2.9</td>
<td>43.8 ± 5.3</td>
</tr>
<tr>
<td>MHC IIa, %</td>
<td>42.7 ± 2.3</td>
<td>43.3 ± 4.3</td>
</tr>
<tr>
<td>MHC IIx, %</td>
<td>13.8 ± 1.4</td>
<td>13.0 ± 1.9</td>
</tr>
</tbody>
</table>

Values are expressed as means ± SE. CSA, cross-sectional area; 1 RM = one repetition maximum; MHC, myosin heavy chain. *P < 0.05 from young.
units) of SuperScript II RT was added to each tube (giving a total volume of 20 μl), incubated at 42°C for 50 min and then at 70°C for 15 min to terminate the reaction, and chilled to −4°C thereafter. Produced cDNA samples were diluted to a final volume of 60 μl (1:60 vol/vol with water). All thermal incubations and chilling were done in a Peltier Thermal Cycler with dual-block DNA engine (MJ Research, Waltham, MA) to provide temperature homogeneity and identical temperature ramping for all samples.

Real-time PCR. Quantification of mRNA transcription (in duplicates) was performed in a 72-well Rotor-Gene 3000 Centrifugal Real-Time Cycler (Corbett Research, Mortlake, NSW, Australia). GAPDH was used as a housekeeping gene (HKG) for internal control. The reaction mix consisted of 2.5 μl of 10× SYBRgreen real-time PCR buffer (Biosource, Camavillo, CA), 0.625 μl of 10 mM deoxyribonucleotide 5′-triphosphate, 0.2 μl of 5 U/μl Platinum Taq DNA Polymerase (Invitrogen), 1 μl of 10 μM each for forward and reverse primers in the case of the genes of interest (GOI) and 2.5 μl of 10× primer pairs for GAPDH (Biosource, Camavillo, CA), 2.5 μl of cDNA, and RNase-free water to a final volume of 25 μl. All primers used in this study were mRNA specific (on different exons and/or crossing over an intron) and designed for gene expression real-time PCR analysis using Vector NTI Advance 9 software (Invitrogen) (Table 2).

The PCR parameters were as follows: initial denaturing at 95°C for 2 min to activate the platinum Taq DNA polymerase followed by 45 cycles of 20 s at 95°C, 20 s at 60°C, and 20 s at 72°C, with fluorescence gain for SYBRgreen set at 8. A melting curve analysis was generated by the Rotor-Gene software following the end of the final cycle for each sample, by continuously monitoring the SYBRgreen fluorescence throughout the temperature ramp from 72 to 99°C in 1°C increments and 5-s hold at each degree. A single melt peak observed for each sample was used to validate that only a single product was present.

Relative quantification of real-time PCR assay. The gene expression in relation to age and exercise was evaluated by a relative quantification method, as described previously (50). Briefly, this method is based on the fact that the difference in threshold cycles (ΔCT) between GOI and HKG is proportional to the relative expression level of the GOI. To avoid interassay variability both age groups (young and old) and both experimental conditions (preexercise and postexercise) for each gene were run together on the real-time PCR run.

The data were analyzed using 2^−ΔΔCT and 2^−ΔCT methods (26, 36). To compare the relative gene expression (arbitrary units) between young and old women at baseline (preexercise) and age (young and old). For analysis of gene expression baseline differences, using the 2^−ΔCT method (arbitrary units), an independent t-test was performed. An independent t-test was also used for all subject characteristics comparisons. Logarithmic data transformation was performed due to lack of normal distribution in some instances for the gene expression analysis. Non-parametric analysis had to be utilized (2 × 2 ANOVA and Mann-Whitney) for MEF2 only. Significance was set at P < 0.05 for all analyses.

Table 2. Primer set sequences and amplicon information

<table>
<thead>
<tr>
<th>Target mRNA</th>
<th>PCR Primer Sequence 5′→3′</th>
<th>Amplicon Size, bp</th>
<th>Amplicon Location, bp</th>
<th>NCBI (Reference Sequence)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEF2</td>
<td>F CAGGGCGGTAGAAGCTTGGTGCCGCAAA</td>
<td>109</td>
<td>741–849</td>
<td>NM_016132</td>
</tr>
<tr>
<td></td>
<td>R CAGGGCGGTAGAAGCTTGGTGCCGCAAT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myf5</td>
<td>F ATGTTAGCTGGATATGGTTGAGGGATAAAT</td>
<td>103</td>
<td>43–145</td>
<td>NM_005593</td>
</tr>
<tr>
<td></td>
<td>R GGGGCGCAAAATCTGCGCGAATT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MyoD</td>
<td>F GCTTATGTTCGCTCGGGTGAATGCAGCGATATT</td>
<td>94</td>
<td>1,178–1,271</td>
<td>NM_02479</td>
</tr>
<tr>
<td></td>
<td>R CAGGGCGGTAGAAGCTTGGTGCCGCAA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myogenin</td>
<td>F CAGGGCGGTAGAAGCTTGGTGCCGCAA</td>
<td>139</td>
<td>599–737</td>
<td>NM_002479</td>
</tr>
<tr>
<td></td>
<td>R TGTGTTGCCAGGGGCAGACGACT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRF4</td>
<td>F CCCCTTGCTCAGATGGGGAGCCAAAGAGAGAA</td>
<td>100</td>
<td>542–641</td>
<td>NM_002469</td>
</tr>
<tr>
<td></td>
<td>R CCCCTTGCTCAGATGGGGAGCCAAAGAGAGA</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Myostatin</td>
<td>F GACAGGAGAAGAATGGGCTGTAATCCGT</td>
<td>96</td>
<td>861–956</td>
<td>NM_005259</td>
</tr>
<tr>
<td></td>
<td>R GCCTATCAGCTGCAAAGCCAAATCGGCTT</td>
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</tr>
</tbody>
</table>

F, foward; R, reverse; MEF2, myocyte enhancer factor 2; Myf5, myogenic factor 5; MyoD, myogenic differentiation factor; NCBI, National Center for Biotechnology Information.
RESULTS

Muscle profile. The young women were stronger (P < 0.05) (1 RM 60.2 ± 5.9 vs. 38.8 ± 2.6 kg) and had greater (P < 0.05) muscle mass (122.0 ± 5.6 vs. 89.4 ± 3.7 cm³) compared with the old women (Table 1). There were no differences between young and old women in their MHC proportions (Table 1).

Gene expression at rest. Under resting conditions (preexercise), skeletal muscle of the old women expressed higher (P < 0.05) levels of all genes, except MEF2, compared with young women (Fig. 2). These differences (P < 0.05) in mRNA expression levels were Myf5 (82%), MyoD (58%), myogenin (41%), myostatin (56%), and MRF4 (82%).

Gene expression after resistance exercise. There were no differences between the age groups in the response to exercise (Fig. 3). There was a main time effect for three of six genes. As a group, the women upregulated (P < 0.05) MyoD (2.0-fold) and MRF4 (1.4-fold), and they downregulated (P < 0.05) myostatin (2.2-fold). There was a trend (P = 0.08) for an age × time interaction in MRF4, where the young women upregulated MRF4 1.7-fold, compared with 1.1-fold in the old women.

DISCUSSION

One of the novel aspects of the present investigation was the age of the old women (80–89 yr) studied. This population is clinically important due to the accelerated muscle mass loss observed in adults over 80 yr (8) and the expanding segment of this population in our society (44). The resistance exercise bout was chosen for this study based on our laboratory’s past experience with this identical protocol, which promotes muscle growth and function with chronic (12 wk) use in old adults (74 ± 2 yr) (41–43). The primary findings of the present study were 1) before the resistance exercise bout, old women had higher levels of several mRNA transcripts known to be involved with muscle growth and 2) when challenged with resistance exercise, the young and old women had a similar myogenic response.

Gene expression at rest. Using microarray gene chip analysis, a host of gene expression differences between young and old skeletal muscle have been reported (14, 20, 35, 45, 46). Our targeted gene approach reported here support the limited human (16, 23) and rodent (28, 31) literature showing higher basal levels of MRF expression in the old. A notable finding of the present study was that all MRF genes studied were overexpressed in the old compared with the young women. This myogenic gene overexpression is greater than previously reported in human muscle (23). A possible reason for these discrepancies may be related to the age of the subject populations among the investigations. Previous studies have used individuals ranging from 60 to 75 yr of age, whereas the present study had a mean age of 85 yr. It is plausible that the oldest old (i.e., >80 yr) have a variety of cellular disturbances that are magnified to combat the accelerated rate of sarcopenia (8) compared with individuals only a decade younger (2).

Additional support for age-related molecular differences in skeletal muscle is provided from cell-signaling perturbations showing increased MAPK pathway activation in old men (47) and altered Akt pathway activation in old rodents (13). There is also evidence of a progressive degeneration of the nervous system in humans over 60 yr (24). This is potentially important because denervated muscles in animals have corresponded to increased levels of the MRFs, although the origin of the mRNA was not determined (5, 9). Muscle fiber-specific alterations with age have been reported (37, 40), and they must be considered as a possible influence for the observed findings. The similar MHC profile between the young and old women in the present study minimize this possibility, but do not rule out potential within fiber-type specific alterations with age. This may be important given the functional characteristics within each fiber type differ with age (40) and chronic training (41, 43).

An unknown in the present study is the source of MRF mRNA. These data do not allow us to determine whether the upregulation of MRF mRNA observed at rest in the old women originated from satellite cell nuclei or from existing postmitotic myonuclei. In support of the latter, Hyatt et al. (18) found denervated rodent muscle to predominantly express MRF in
myonuclei, as opposed to in satellite cells. Further speculating, this may suggest that aged and denervated muscle attempts to preserve its mass and function by targeting existing muscle fibers, rather than incorporating new myonuclei from the reportedly declining satellite cell pool (21).

It is an apparent paradox that the older individuals express high levels of MRF mRNA and still demonstrate significant sarcopenia. It cannot be assumed that there is a 1:1 ratio between mRNA and a fully functional protein, given the complexity of posttranscriptional events (30). This concept in particular may be noteworthy in the aging population, because it has been reported that very old animals express higher levels of MRF mRNA and lower levels of MRF protein compared with young animals (1). In addition, it is also largely unknown to what extent the proteolytic pathways are activated in aging muscle at rest and in response to resistance exercise, both of which would have an impact on the net anabolic effect of muscle regulatory factors.

**Gene expression after resistance exercise.** Contrary to our second hypothesis, there were minor differences between young and old women in the response to resistance exercise. With resistance exercise, there was an induction in 50% of the myogenic genes studied (2 of 4) in the young and old women. For the young women, these data are in agreement with previous reports among young men and women using traditional resistance exercise (34, 49, 50) or electrically stimulated isometric contractions (4) as an intervention to study the MRF response within the first few hours after exercise. The present data for the old women add to the limited gene expression and response within the first few hours after exercise. The present study, however, did not show an increase in myogenin and a slight decrease in MRF4, but only young women responded with an induction of MyoD mRNA 24 h after resistance exercise. In the present study, we noted an increase in MyoD mRNA for both age groups. We also reported a trend (P = 0.08) for age group differences in the induction of MRF4 mRNA, combined with no changes in myogenin for either group. The discrepancies between these two studies could be due, in part, to the timing of the biopsies (4 vs. 24 h after resistance exercise), given the MRF family of mRNA transcripts generally peaks within the first 12 h after exercise in young humans (47). Collectively, it appears that human skeletal muscle from older individuals has a similar myogenic mRNA response to that of young women, which is in contrast to what has been reported in old animals (38).

As highlighted earlier, the source of the upregulated mRNA is also unknown after resistance exercise in both the young and old women. In humans, there are limited data available on the time course of satellite cell activation and to what extent they may contribute to mRNA MRF upregulation in the early hours after exercise. There is evidence that satellite cells are not necessary for MRF mRNA upregulation (27). In support of this, Ishido et al. (19) recently demonstrated that MyoD and myogenin protein expression increased in rodent myonuclei as early as 1 day post functional overload. To date, only one study has attempted to link satellite cell activation with high-intensity exercise in humans (7). Using immunohistochemistry, it was shown that satellite cells were activated by 2 days after exercise in young humans, but the absence of myogenin-positive satellite cells (throughout 8 days) led the authors to conclude that satellite cells may need at least another bout of exercise for terminal differentiation.

What is the potential significance of mRNA MRF sources and what are some downstream targets? The master regulatory factor MyoD has recently been found to bind a plethora of muscle specific genes, among which cytoskeletal and/or structural genes such as actin, troponin, and myosin regulatory light chains are mentioned (6). Given the importance of MyoD as a transcription factor, its actions may be beneficial regardless of location. It is reasonable to assume that if the upregulated mRNAs were indeed coming from satellite cells, satellite cell fusion with the existing muscle fiber, and thereby hypertrophy, should be the final result over time. However, given the relatively early 4-h time point chosen for the present study, it is likely the upregulation noted in MRF mRNA came primarily from postmitotic myonuclei. If postmitotic myonuclei are the main source, it may have more of an impact on the integrity and strength of the already existing muscle fiber proteins, leading to improved cellular function and hypertrophy. Perhaps a combination of the two mRNA sources is needed for maximal hypertrophy to occur over time. As mentioned earlier, the potential posttranscriptional deficits in old muscle (1) should also be considered when evaluating the mRNA induction seen in the old women after resistance exercise.

Myostatin, a member of the transforming growth factor-β superfamily, is well known as a negative regulator of myogenesis, and has been shown to control the proliferation of muscle precursor cells (39). We show for the first time that myostatin is downregulated 4 h after exercise in both young and old women. Previous research (22) has reported a decrease in myostatin in young, but not old, women 24 h after acute resistance exercise.

In addition to the MRF genes and myostatin, MEF2 gene expression was investigated in response to resistance exercise. There was no change in MEF2 gene expression in response to resistance exercise in young and old women. This finding is consistent with a lack of change in MEF2 mRNA expression 4 h after an aerobic exercise bout in humans (17). Whereas MEF2 has been proposed to be an important transcriptional enhancer in growth (33, 52) and metabolism (29) related transcription, the lack of induction in the present study and others may be related to the time point of sampling or perhaps the possibility that MEF2 protein already exists in sufficient amounts.

Old individuals have shown whole muscle hypertrophy of the thigh after progressive resistance training programs (10, 12, 25, 42). However, no younger counterparts were included in those investigations, and therefore it does not rule out the possibility of an age-related impairment or greater hypertrophy in young people. The acute mRNA myogenic response from the old women of the present investigation suggests that chronic loading, such as resistance training, would result in muscle hypertrophy. However, resistance training studies in women over 80 yr have mixed results, with several studies showing strength gains but little to no hypertrophy (11, 51). The one exception is a study by Fiatarone et al. (10) that reported hypertrophy in the frail elderly using a progressive resistance training program with multiple exercises. Given the wide variety in age range, training volume, and mode of exercise, hypertrophy comparisons between studies suggest a wide range in response among older individuals.
In summary, this is the first study to investigate growth-related gene expression at rest and 4 h after an acute resistance exercise bout in young and old women. In the context of the myogenic genes studied, these data provide evidence that the skeletal muscle of old women is expressing higher levels of mRNA compared with young women at rest. In response to resistance exercise, the upregulation in MRF mRNA was qualitatively the same between young and old women, although there was a trend for a slight difference quantitatively. The high resting mRNA levels in the old women may suggest an ongoing effort to make skeletal muscle proteins and maintain muscle mass. However, it is still unknown to what degree the mRNAs are being translated into functional proteins, and whether there might be a difference in this sophisticated process between young and old women. To elucidate the net anabolic potential of aging muscle, future research should also focus on the proteolytic events elicited in response to resistance exercise in both young and old populations.

REFERENCES


