Journal of Gerontology: BIOLOGICAL SCIENCES
1996, Vol. 51A, No. 2, B117–B123

Complexity of Age-Related Change in Skeletal Muscle

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Age-related changes in skeletal muscle mass, fiber area, and contractile function were examined in pathogen-free rats at 6, 12, 28 and 36 mos of age. The intent of this study was to clarify age-related decline, particularly in contractile force, and to determine if the decline in contractile tension with age is due to alterations at the neuromuscular junction. A variable amount of age-associated reduction in muscle mass was noted for the soleus (18%), extensor digitorum longus (EDL-16%), plantaris (37%), and gastrocnemius (38%) muscles. The decline in fiber area for these four muscles was between 5 and 16% greater than the loss in muscle wet weight. A variable amount of change in peak contractile force between 6 and 36 mos was observed for the soleus (62%), EDL (48%), and plantaris (34%). For soleus and EDL, the decline in peak tetanic tension exceeded the decline in muscle mass and fiber area. Most of the declines for the animals used in this study did not become significant until after the age of 28 mo. The marked reduction in peak tetanic tension, fiber area, and muscle mass between 28 and 36 mos indicates an accelerated age-related decline in this time period. The reduced peak twitch and peak tetanic tension in the oldest animals was not due to likely age-related changes at the neuromuscular junction. Peak values for tetanic tension were similar, whether tension was elicited via direct muscle stimulation or through stimulation of the nerve. Results underscore the complexity of age-related change and suggest that multiple mechanisms contribute to the decline of skeletal muscle.

MUSCLE mass tends to decline with aging. The extent of the decline is variable and depends on the function of the muscle (Grimby and Saltin, 1983; Fitts et al., 1984; Faulkner et al., 1990; Holloszy et al., 1991). Postural muscles appear to be affected more than non-postural muscles in rats (Gutmann et al., 1971; Fitts et al., 1984; Holloszy et al., 1991). The soleus (SOL), for example, has been reported to show a larger loss of mass with age than the extensor digitorum longus (EDL) (Brown et al., 1993). The gastrocnemius (GAST) has a greater loss in mass with age than the plantaris (PL) (Klitgaard et al., 1989). While data are limited, it also appears that the time of onset of age-related change may differ muscle to muscle (Brooks and Faulkner, 1988; Klitgaard et al., 1989).

Although there is general agreement that muscle mass is lost with aging, controversy exists concerning the decline in contractile tension. In animal studies, contractile tension has been reported to decline to a lesser extent (Eddinger et al., 1986; Irion et al., 1987), to the same extent (Fitts et al., 1984; Larsson and Edstrom, 1986; McCarter and McGee, 1987), or to a greater extent than muscle mass (Brooks and Faulkner, 1988; Klitgaard et al., 1989; Faulkner et al., 1990). The reasons for these discrepancies are unclear, but may include differences between strains of rats and mice, comparing immature to aging animals, studying rodents that were not pathogen free, and studying rodents that were not old enough to have age-related change.

The neuromuscular junction also undergoes age-related change, exhibiting fragmentation, evidence of axonal sprouting and withdrawal, and degeneration (Cardasis and LaFontaine, 1987). It has been suggested that the alterations that occur at this site are responsible for some of the decline in tetanic tension with advancing age (Gutmann et al., 1971; Cardasis and LaFontaine, 1987).

In this investigation, muscle mass, fiber area, and contactile function were examined in male pathogen-free rats at 6, 12, 28, and 36 months. Four muscles were studied: 3 postural (one slow and 2 fast-fibered) and one nonpostural muscle, to clarify age-related decline in contractile force and to determine if the decline in contractile tension with advancing age is due to alterations at the neuromuscular junction.

METHODS

Animals. — Specific pathogen-free male Fischer 344/Brown Norway rat hybrids were obtained from the aging colony maintained by the National Institute on Aging (NIA). Upon receipt, rats were placed in a pathogen-free environment under conditions that were as close as possible to what had been provided for these animals previously. Rats were placed in polycarbonate cages identical to those used by NIA, two per cage, and maintained in a barrier room where temperature (22–23 °C) and hours of light (0700 to 1900 h) were the same as what rats had been experiencing. Food was provided by the supplier, Charles River Laboratories (Wilmington, MA), so that animals did not undergo a change in diet when they moved into their new facility. Chlorinated water was available ad libitum. Rats were allowed to recover from shipment for at least two weeks before experimentation began, and during this time the animals were carefully observed and weighed weekly. None of the older animals exhibited signs of failure to thrive, such as precipitous weight loss, disinterest in the environment, or gait alterations. The oldest rats gained an average of 8 g of weight during the period of observation. Two animals were necropsied following experimentation and both were found to be free of malignancies and bacteria such as M. pulmonis. Two of the oldest rats used for study did have small (~1 cm)

skin cancers. All protocols were followed in accordance with the Guide for Care and Use of Laboratory Animals as approved by the Council of the American Physiological Society and by the Animal Use Review Boards of the University of Missouri and Washington University.

Animals 6, 12, 28, and 36 mos of age were studied. These ages were chosen for two reasons: (a) to determine if the muscular maturity of 6 mo animals is comparable to that of 12 mo rats, and (b) to permit the study of rats on the threshold of old age (28 mo) and at a point further along the spectrum of age. The half-life of male Fischer 344/Brown Norway rats is 28 mo, and animals up to 42 mo of age may be purchased from NIA. Thus, we believed that 36 mo animals were aged but not to the point of premorbidity.

The number of animals per group was as follows: $n = 10$, age 6 mo; $n = 6$, age 12 mo; $n = 10$, age 28 mo; and $n = 10$, age 36 mo.

Contractile properties. — Rats were deeply anesthetized with an IP injection of sodium pentobarbital (65 mg/kg) with .05 ml injections (3.25 mg) given as needed (~45 min) to maintain anesthesia. Body temperature was monitored and maintained by keeping the anesthetized rat on a water-jacketed heating pad. The SOL, EDL, and PL muscles were surgically exposed, and the distal tendon of each muscle was dissected free and attached in turn to a Grass force transducer with 2.0 silk. The tibial and peroneal nerves were isolated and placed on a bipolar stimulating electrode. The exposed portion of the muscle was bathed continuously with 37° rat Ringer's solution. Before contractile properties were obtained, animals were allowed to thermoequilibrate for ~30 minutes.

The left leg was rigidly immobilized. A length-tension curve was obtained and muscles were adjusted to optimal length. Peak isometric twitch tension was obtained with supramaximal 0.5 ms square wave pulses (Grass Instruments S48). Peak twitch tension (P_t), time to peak twitch tension (TTP), and half relaxation time ($^1/_2$RT) were determined. Peak tetanic tension (P_o) was elicited by 0.5 ms supramaximal pulses delivered at 100 Hz (400 ms train duration) for the SOL and 150 Hz for the EDL (250 ms train duration) and PL (350 ms train duration), respectively. Various stimulation intensities and durations were examined in a pilot study, and parameters selected elicited peak values at all ages. Muscles were consistently tested in the order of PL, followed by SOL, and finally the EDL. Experiments, including surgical preparation and set-up, took ~2.5 hr.

SOL and EDL fatigue characteristics were assessed by a 5-minute bout of repeated tetanic contractions as follows: 250 ms trains (stimulation rate 100 Hz) delivered at 75 trains/min for the SOL, and 250 ms trains (stimulation rate 150 Hz) at 50 trains/min for the EDL. Fatigue protocols taken from the literature extend from 2 min to one hour. During pilot testing, 15 min of stimulation were given and the majority of tension decline, if present, occurred in the first 2–3 min. A 5-minute protocol was selected to ensure that, if fatigue was present, the decline in peak tetanic tension would be acquired.

To determine if the reduced peak tetanic tension in older animals (obtained via stimulation of the nerve to each muscle) was due to an effect at the neuromuscular junction, muscles were also stimulated directly. Electrodes were inserted into the SOL, EDL, and PL muscles, and supramaximal stimuli (~40 volts, 0.5 ms) were applied to evaluate P_t and P_o. Direct stimulation was given to muscles in situ, under the same conditions as maximal contractions elicited by stimulation through the nerve.

Histology. — After contractile properties were studied, the SOL, EDL, PL, and GAST muscles were removed and weighed. Muscles were fixed at their in situ length, embedded in freezing medium (OCT), frozen in liquid nitrogen, and placed in a –80 °C freezer until analysis. Muscles were sectioned at 10μ and then stained for determination of major fiber Types I, IIa, and IIb using ATPase (pH 9.4, 4.55, 4.3) (Brooke and Kaiser, 1970). Sections were also stained with H&E for routine morphology, and NADH-TR as an indicator of oxidative potential. ATPase-stained sections were used for determination of fiber areas. The area of at least 50 intact fibers of each type, if present, was measured using a digitizer (Hewlett-Packard computer and HP9111A Graphics package). The proportion of area occupied by each fiber type was determined, and a composite area for each muscle was determined to derive the ratio P_o/fiber area. Composite area was calculated as follows: (% Type I fibers × mean Type I fiber area + % Type IIa fibers × mean Type IIa fiber area + % Type IIb fibers × mean Type IIb fiber area).

Data management. — Data for P_t, P_o, contraction times, fiber areas, muscle weights, fatigue, P_o/fiber area, and P_o/muscle wet weight were analyzed using a 1 × 4 analysis of variance (ANOVA). Scheffé post-hoc tests were done if significance ($p < .05$) was achieved. Data for peak twitch and P_o obtained for young and old rats under the two conditions of stimulation (neurally mediated and direct muscle) were compared using a repeated measures ANOVA.

Results

Muscle mass. — For the four muscles studied, wet weights for 6- and 12-month-old animals were comparable ($p > .05$). There was no significant difference in SOL, EDL, or GAST muscle mass until after 28 mo. A trend toward a loss in muscle weight prior to 28 mo was noted for the GAST (9%), and the difference in PL weight between 12 and 28 mos was significant. Of note is that all muscle weights remained unchanged or decreased slightly between 12 and 28 mos despite a large increase in body weight (Table 1).

A variable amount of decline in muscle wet weight was observed between 6 and 36 mos of age (Table 1). The greatest muscle weight loss was observed for the weight-bearing GAST (38%), PL (37%), and the SOL (18%). The nonweight-bearing EDL showed the least amount of change in wet weight (16%). The change in muscle wet weight with aging was significant ($p < .05$) for the GAST, PL, and SOL.

Fiber area. — Little change in fiber area occurred until after 28 mo, the exceptions being SOL Type IIa fibers and GAST Type IIb fibers (Table 2). The loss in fiber area for

Table 1. Body (gm) and Muscle Wet Weights (mg)

Age	6 Mo	12 Mo	28 Mo	36 Mo
Body weight	437 ± 11	505 ± 8*	615 ± 11*	536 ± 18*
SOL	219 ± 8	214 ± 7	208 ± 10	180 ± 10*
EDL	233 ± 9	216 ± 18	209 ± 6	197 ± 13
PL	476 ± 14	504 ± 12	456 ± 13†	299 ± 20*
GAST	2443 ± 61	2461 ± 31	2114 ± 101	1529 ± 105*

Notes. Values are expressed as mean ± *SEM*. SOL = soleus; EDL = extensor digitorum longus; PL = plantaris; GAST = gastrocnemius.

*$p < .05$ or less for body weight as follows: 12 mo > 6 mo; 28 mo > 12 and 36 mos; 36 mo > 6 mos. For muscle weight, 36 mo < 6, 12 and 28 mos.

†$p < .05$ when compared to the 12-mo value.

Table 2. Fiber Area (Mean ± *SEM*) for the Four Muscles Studied

Age	6 Mo	12 Mo	28 Mo	36 Mo
SOL				
Type I	3294 ± 156	3374 ± 168	3347 ± 178	2313 ± 169*
Type IIa	2922 ± 459	2052 ± 365	1437 ± 323*	1302 ± 183*
EDL				
Type I	1055 ± 67	1199 ± 87	1086 ± 93	1242 ± 82
Type IIa	1185 ± 48	1064 ± 103	1324 ± 120	1534 ± 158
Type IIb	2905 ± 139	3001 ± 166	2758 ± 175	1954 ± 209*
PL				
Type I	1598 ± 82	1665 ± 124	1553 ± 110	1556 ± 168
Type IIa	1926 ± 66	1887 ± 70	1641 ± 148	1547 ± 199
Type IIb	3780 ± 197	3894 ± 215	3344 ± 239	1935 ± 200*
GAST				
Type IIa	1531 ± 84	1566 ± 101	1511 ± 150	1459 ± 207
Type IIb	3497 ± 151	3555 ± 148	3023 ± 203†	1828 ± 198*

Notes. SOL = soleus; EDL = extensor digitorum longus; PL = plantaris; GAST = gastrocnemius.

*$p < .05$ or less as follows: 36 mo < 6, 12 and 28 mos.

†$p = .06$, 12 mo > 28 mo.

predominately fast-twitch muscles was most pronounced for Type IIb fibers, while Type IIa and Type I fiber area remained relatively constant. For the predominately slow-fibered SOL, Type I and Type IIa fibers exhibited significant atrophy (30 and 55%, respectively). Few SOL Type IIa fibers were present in animals older than 12 mo, and thus, area measures for these fibers are not as accurate as those for Type I fibers (Table 2).

The decline in composite fiber area between 6 and 36 mos (range 22–53%) was greater than the change that occurred in muscle mass (range 16–38%). Composite fiber area was reduced between 5 and 16% more than muscle wet weight as follows: GAST, –5%; SOL, –12%; EDL, –6%, and PL, –16%.

Contractile function. — A noticeable decline in peak twitch tension, 31%, was observed in the SOL by 28 mo. No change in P_t was seen with age for the EDL or PL (Figure 1). The change with age in peak tetanic tension, on the other hand, was a consistent finding at 36 mo for the SOL, EDL, and PL muscles. No change in P_o was found for the SOL through 28 mo of age; thereafter a 62% decrease in maximal force (from 210 to 79 g) occurred (Figure 2). This decline in

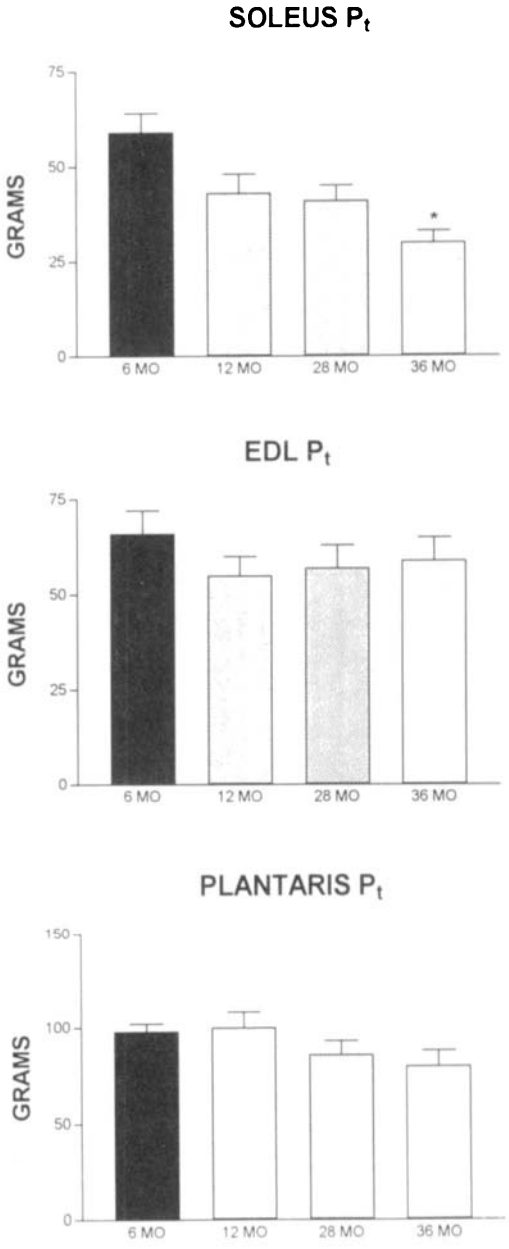

Figure 1. Peak twitch tension (P_t) for the soleus (SOL), EDL (extensorum digitorum longus), and plantaris at each of the ages studied. P_t for the SOL at 36 mo was significantly less than the 6-mo value (*$p < .01$).

P_o exceeded the loss in muscle mass by 44%. No significant reduction in P_o was seen for the EDL at 28 mo, but the decrease in peak tetanic tension by 36 mo (from 349 to 183 g, 48%) was highly significant ($p < .001$). The change in P_o for the PL between 12 and 28 mos was significant, but differences between 6 and 28 mos were not meaningful. Significant decline was observed in the PL at 36 mo (Figure 2).

Peak tetanic tension data in relation to a composite of muscle fiber area are presented in Figure 3. The loss in P_o for the SOL and EDL at 36 mo exceeded the loss in fiber area by 31 and 30%, respectively. The PL also showed a significant loss in P_o with age (34%), but the change in P_o was consistent

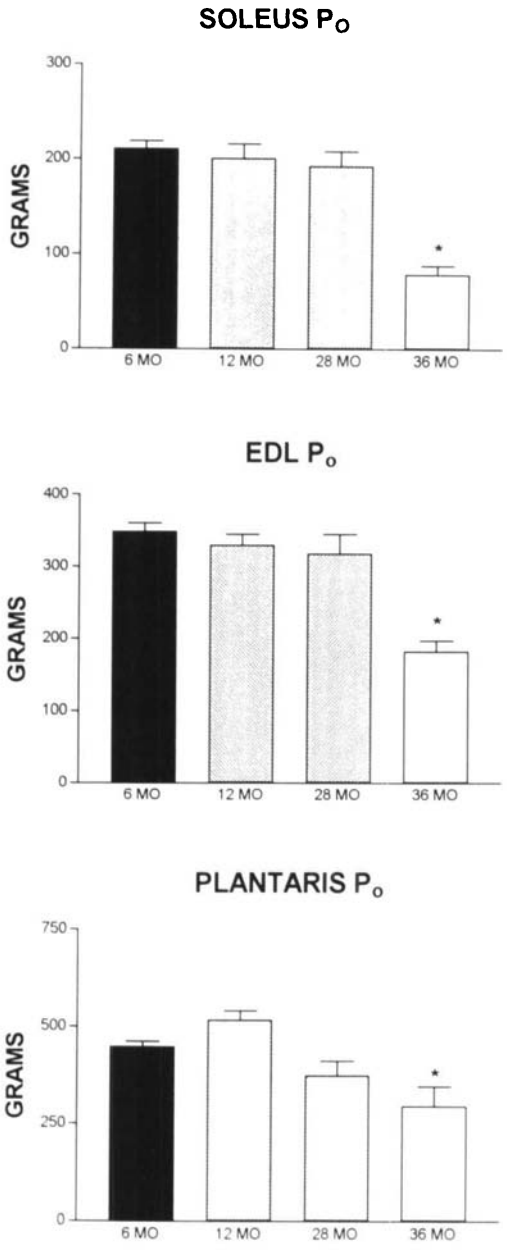

Figure 2. Peak tetanic tension (P_o) for the soleus (SOL), EDL (extensorum digitorum longus), and plantaris (PL) at each of the ages studied. The value for P_o at 36 mo was significantly less (*$p < .01$) than values obtained at 6, 12, and 28 mos for the SOL and EDL, and significantly less than the 6- and 12-mo values for PL.

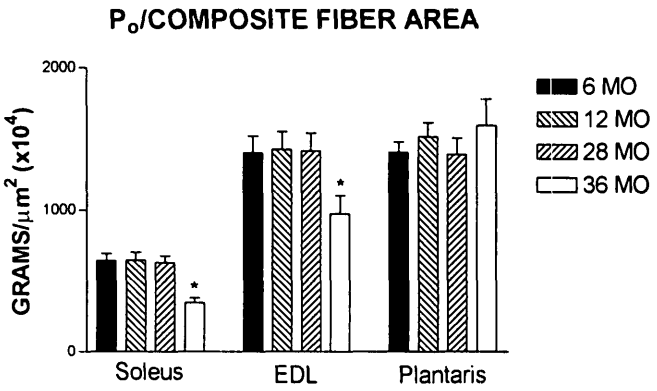

Figure 3. Peak tetanic tension divided by composite fiber area. The decline in P_o for the EDL (extensorum digitorum longus) and soleus exceeded the loss in fiber area. The change in P_o for the plantaris was consistent with the decline in fiber area.

with the change in composite fiber area and muscle wet weight.

There were no differences in P_o for the SOL, EDL, or PL when direct muscle stimulation and stimulation through the nerve were compared (Figure 4).

For the SOL there was no change with age in the percent decline in peak tetanic tension with the fatigue protocol (Table 3). Resistance to fatigue was a consistent feature of the SOL at all ages studied including 36 mo. In response to the fatigue protocol, the EDL had a smaller percent decline in P_o at 36 mo than at the other time periods studied (Table 3). At 36 mo, initial peak tension was quite low while the post-fatigue tension was similar to what was seen at all ages, giving the appearance that the stimulation protocol resulted in less fatigue in the EDL with advancing age; however, the total amount of force generated was significantly lower at 36 mo than at the earlier time points.

Data for contraction times were variable, and a trend toward significant changes in TTP and ½RT was observed with age only for the EDL (Table 4). A significant difference in TTP was observed for the SOL at 6 mo and the PL at 28 mo, but this difference was offset by a prolonged or reduced ½RT. When TTP and ½RT values for each animal were summed, differences in contraction times at each of the ages studied were not apparent.

Histological observations. — An increase in interstitial and intramuscular fat and connective tissue was seen in cross-sections from the oldest animals. Although the amount was not quantified, fibro-fatty connective tissue was a consistent feature in cross-sections from the 36-month-old rats. Some fibro-fatty material was observed within muscle fibers, particularly in the GAST and PL, giving the appearance that some fibers had been invaded.

A trend toward an increase in Type IIb fibers (~10%) with a concomitant decrease in the percentage of Type IIa fibers was noted in the GAST, PL, and EDL. There were very few, if any, Type IIa fibers in the SOL after 12 mo. This observation and the presence of occasional angulared fibers are suggestive of neural remodeling. Group atrophy of the Type IIb fibers was sometimes observed in the GAST and PL.

Discussion

The intent of this study was to provide a comprehensive overview of age-related change in three postural muscles with different fiber type compositions and in one fast-fibered nonpostural muscle. For two of the three muscles studied physiologically (SOL and EDL), the loss of maximal contractile force in the oldest animals far exceeded the loss of composite fiber area and muscle mass. For the PL, the loss in peak contractile tension was closely tied to the decline in muscle mass. The neuromuscular junction was not found to

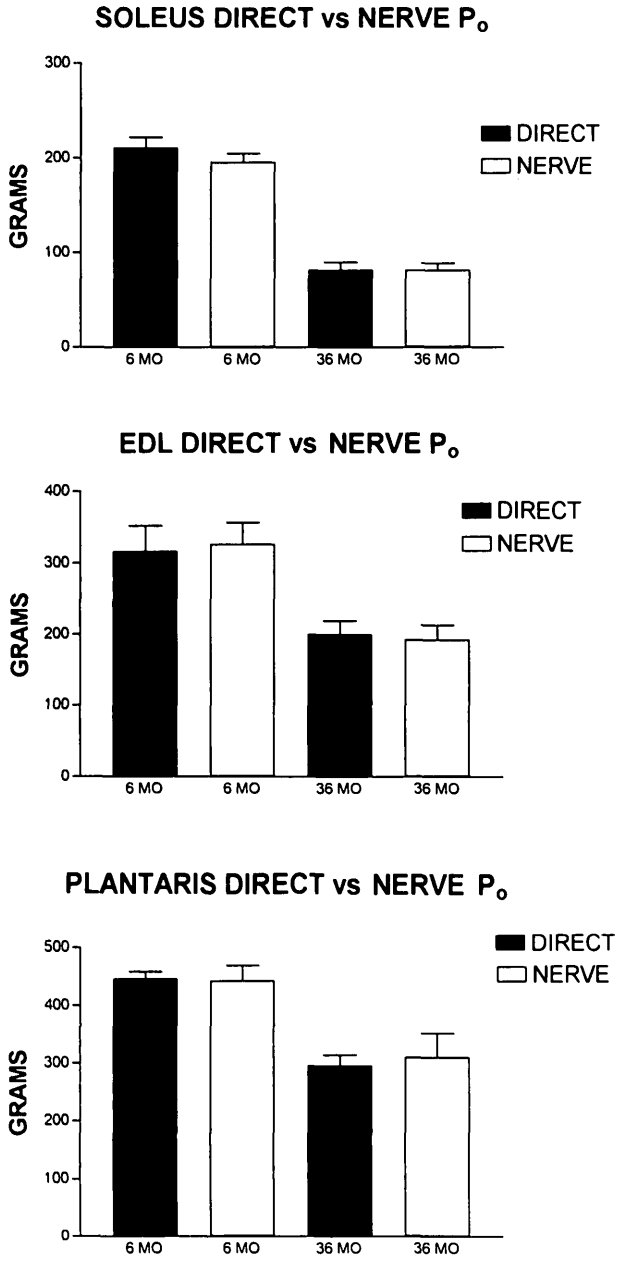

Figure 4. The amount of tetanic tension elicited by direct muscle stimulation versus eliciting P_o by stimulating through the nerve. Both techniques elicited similar values for P_o at 6 and 36 mo. (nonsignificant). EDL = extensorum digitorum longus.

be responsible for the reduced amount of contractile tension found in the oldest animals. Atrophy was a consistent finding for all four muscles, but the magnitude of decline differed considerably.

Results from this study seem to indicate that aging of skeletal muscle is a complicated process, characterized by a variable amount of decline which accelerates after an undefined point in the life span. All of the muscles studied atrophied, but the magnitude of change was markedly different and rather abrupt. As noted previously, postural muscles are likely to be affected most by age-related change, with the

Table 3. Percent Decline in Peak Force During a 5-minute Fatigue Protocol

Age	6 Mo	12 Mo	28 Mo	36 Mo
SOL	10 ± 3	9 ± 2	13 ± 3	9 ± 5
EDL	60 ± 4	58 ± 4	65 ± 4	42 ± 3*

Note. Values are expressed as mean ± *SEM*. SOL = soleus; EDL = extensor digitorum longus.
*$p < .05$.

Table 4. Time to Peak (TTP) and Half Relaxation Time (½RT) in Milliseconds

Age	6 Mo	12 Mo	28 Mo	36 Mo
Soleus (SOL)				
TTP	28.5 ± 2.3*	47.5 ± 6.4	41.9 ± 4.1	43.6 ± 3.7
½RT	66.9 ± 4.3*	52.8 ± 6.5	54.7 ± 6.5	53.8 ± 8.1
EDL				
TTP	21.1 ± 0.6	20.6 ± 1.0	23.9 ± 0.7*	21.7 ± 1.0
½RT	15.1 ± 0.9	19.6 ± 1.4	14.8 ± 0.6*	20.8 ± 0.8
Plantaris (PL)				
TTP	19.9 ± 0.5	21.3 ± 1.4	26.6 ± 1.1*	21.0 ± 0.6
½RT	22.6 ± 2.2	25.3 ± 2.1	20.3 ± 2.5*	22.4 ± 1.6

Notes. Values are expressed as mean ± *SEM*. SOL: TTP, 6 mo < 12, 28, and 36 mos; ½RT, 6 mo > 12, 28, and 36 mos. EDL: TTP, 28 mo > 12 mo; ½RT, 28 mo < 12 and 36 mos. PL: TTP, 28 mo > 6 mo; ½RT, 28 mo < 6 mo.
*$p < .05$.

Type IIb fiber population in the PL and GAST muscles showing more atrophy than the Type I fibers of the postural SOL (Holloszy et al., 1991). Results may indicate that reduced muscle use was responsible, in part, for the findings in this study, as the least recruited postural muscles (GAST and PL) showed the greatest amount of age-related decline in muscle mass and Type IIb fiber area. It would appear that activity is even more important for the GAST and PL, muscles that are required less frequently than the SOL. It is possible that much of the decline observed may be the consequence of disuse and not aging per se. Evidence is accumulating which indicates that physical activity attenuates age-related decline in skeletal muscle fiber area and strength, in both humans (Sandler et al., 1991) and rats (Klitgaard et al., 1989; Brown et al., 1993).

A variable amount of skeletal muscle decline and an accelerated rate of strength change after the age of 70 years have also been reported for humans. Sandler et al. (1991), for example, noted that trunk extensors and plantarflexors showed a greater magnitude of strength decline with age than grip muscles. Bemben et al. (1991) also found a variable rate of change and a larger magnitude of decline in muscles of the lower extremity than in those of the upper extremities. Longitudinal data collected by Shock and Norris (1970) indicate a more rapid rate of strength decline after the age of 60 years than before. Whether an accelerated rate of age-related decline occurred in these subjects or whether the accelerated decline in strength was due to an increasingly sedentary life style was not determined. The extent to which

physical activity can modify declines in strength needs to be explored further.

The late onset of change in both muscle mass and contractile function for the animals used in this study was unexpected. Female Wistar rats examined previously in this laboratory had a significant amount of change in muscle wet weight by 18 months (Brown, 1987). Other investigators have also indicated a significant amount of age-related decline in male Fischer 344 and Long Evans rats by 24 months (Larsson and Edstrom, 1986; Klitgaard et al., 1989). Our findings may indicate that the relatively new rat hybrid used in this study (Fischer 344/Brown Norway) is quite resistant to aging, or alternatively, that Wistars, Long Evans, and male F344 rats show signs of overbreeding. Results also support findings which indicate that muscles of pathogen-free animals do not atrophy as early as those of rats that are not pathogen free (Larsson and Edstrom, 1986; Brown, 1987; Irion et al., 1987).

Our findings indicate that for the SOL and EDL, the loss of maximal contractile tension is not due entirely to age-related muscle atrophy. This result is in contrast to those of other investigators who have studied contractile function in aging single muscle fibers. Eddinger et al. (1986) studied single fibers from aging rats and found that force per cross-sectional area was comparable at young and old age. Older animals did have smaller fibers, however. Their results suggest that the reduced contractile tension/muscle area seen at the whole muscle level is due to factors other than cross-bridge mechanics, perhaps at the neuromuscular junction or possibly in the excitation-contraction coupling process (Eddinger et al., 1986). Data from this study indicate that changes in the neuromuscular junction are not responsible for the loss in contractile tension. When the neuromuscular junction was bypassed (direct muscle stimulation), P_o values did not increase over those obtained by stimulating through the nerve. There is some evidence suggesting that impaired excitation-contraction coupling is a major factor responsible for the decline in contractile tension with advancing age (Brooks and Faulkner, 1988; Faulkner et al., 1990).

A loss in P_o that is greater than the loss of muscle mass and fiber area is consistent, in part, with the findings of Brooks and Faulkner (1988). They observed a reduced specific P_o of 22 and 27% for the SOL and EDL, respectively, of old mice. Klitgaard et al. (1989) found a reduced P_o/cross-sectional area in the SOL of 24- and 29-month-old rats and in the PL of 29-month-old rats. The earlier onset of SOL decline in P_o and the reduced P_o/muscle mass for the PL in their study may be reflective of changes in aging animals that were not pathogen-free. The rather large drop in P_o/muscle mass between 28 and 36 mos for animals in this study strongly suggests that age-related change after 28–29 months may be accelerated by disuse.

A slowing of contraction time has been reported by a number of investigators (Fitts et al., 1984; Larsson and Edstrom, 1986; Brooks and Faulkner, 1988). For some animals in this study, a slowing of TTP and $^1/_2$RT was observed in the SOL and EDL at 28 and 36 mos; for other animals, no obvious change was apparent. The considerable variability in contraction times for the EDL and SOL may have masked a slowing process that was occurring in some of these muscles. For the PL, however, no discernible shift in contraction time was noted at 36 mo. Why plantaris TTP and $^1/_2$RT at 28 mo were significantly different from values at 6, 12, and 36 mos is unclear.

As expected, fiber area and muscle mass were closely related for the 6-, 12-, and 28-month-old animals. For 36-month-old animals, in all four muscles studied, fiber area was consistently reduced to a greater extent than muscle wet weight. This finding is in contrast to previous data reported from this laboratory (Brown et al., 1993) and the findings of others (Holloszy et al., 1991). Perhaps the increase in fat and fibrous connective tissue noted in the cross-sections from old animals partly masked the actual decline in muscle mass.

In summary, results highlight the variability that is characteristic of age-related change in skeletal muscle. Results also indicate that there is a dissociation between contractile ability and loss in muscle mass for the SOL and EDL but not the PL muscle. Additionally, the decline in fiber area exceeded the loss in muscle mass at 36 mo for all the muscles studied, suggesting an increase in water weight, connective tissue, or other noncontractile material. The decline in peak contractile ability with advancing age was not due to loss of information at the neuromuscular junction, as peak tetanic tensions were comparable when muscles were stimulated directly and when stimulated through the nerve.

ACKNOWLEDGMENTS

Funding for this study was provided by the National Institute on Aging Grant AG-00585 to Marybeth Brown and National Institutes of Health Grant HL-43700 to Eileen M. Hasser. We wish also to acknowledge the superb technical assistance of Sarah Friskey.

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Received May 1, 1995
Accepted August 25, 1995