Ageing is not associated with a decline in neuromuscular innervation or reduced specific force in men aged 20 and 50 years

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Summary
The exact mechanisms responsible for the decline in strength with age are yet to be completely elucidated. Three proposed mechanisms responsible for the detrimental effect of increasing age on strength include changes in muscle mass, specific force and/or neuromuscular innervation. Thus, the purpose of this investigation was to determine if the age-related reduction in peak isometric strength was primarily associated with changes in muscle cross-sectional area, neuromuscular innervation and/or specific force.

The cross-sectional area of the knee extensor muscles (QCSA) was estimated in 13 younger men (YM; 20.8 ± 1.6 years) and eight middle-aged men (MM; 53.8 ± 4.2 years) prior to performing a series of four maximal voluntary isometric contractions on an isokinetic dynamometer at an angle of 60° knee flexion. Peak force was determined and surface electromyography was sampled from the rectus femoris muscle during each maximal voluntary contraction. The cross-sectional area of the knee extensor muscles, peak force and integrated electromyography (IEMG) were significantly lower in the MM (P<0.01). However, when peak force and peak IEMG values were corrected for QCSA, there were no significant differences between age groups. These results suggest that the reduction in peak isometric force observed in the MM was primarily associated with quantitative changes in muscle mass, rather than reduced neuromuscular innervation or specific force. Therefore, preserving muscle mass through resistance training may significantly reduce the age-associated differences in peak strength and assist in promoting quality of life and functional independence in older adults.

Keywords: cross-sectional area, muscle activation, muscle atrophy, peak force, surface EMG.

Introduction
The deterioration in physical health with normal ageing is associated with greater incidence of many physiological disorders, such as glucose intolerance, osteoporosis and a general decline in physical capacity which often results in a loss of mobility (Lindle et al., 1997). Consequently, normal ageing is associated with a transition from independent to dependent living. Although a causal relationship is yet to be established, numerous investigations report a correlation between the age-associated decline in physical health and a reduction in muscular strength (Sinaki et al., 1986; Bloesch et al., 1988; Hyatt et al., 1990). The results of such research suggest that the ability to preserve muscular strength into old age may reduce physiological disorders, maintain mobility and retain the ability to perform activities necessary for daily living. Preserving muscular strength into old age may, therefore, assist in maintaining functional independence and enhance the quality of life.
The age-related decline in muscular strength becomes significant during the sixth decade of life and continues to decline with subsequent ageing (Larsson et al., 1978; Doherty et al., 1993; Hakkinen et al., 1996). Much of the research attributes the decline in strength with age to a reduction in muscle mass resulting from a loss of type I and type II muscle fibres, and the atrophy of those muscle fibres remaining (Lexell et al., 1988). However, a decline in muscle mass alone does not appear to fully account for the reductions in strength with age (Roos et al., 1997). Insufficient voluntary muscle activation and/or a deterioration in muscle quality could result in a reduction in strength independent of age-related muscle atrophy.

It is well documented that ageing in humans is associated with changes in the integrity of the neuromuscular system. Such changes include a decrease in motor unit numbers (de Koning et al., 1988), an increase in motor unit size (Stålberg & Fawcett, 1982), an increase in the amplitude of motor unit action potentials (Stålberg & Fawcett, 1982), reduced motor neurone conduction velocities (Mittal & Logmani, 1987) and a decline in the number of α-motor neurones (Kawamura et al., 1991). Reduced neurotransmitter release and a reduced sensitivity of the muscle fascia to electrical stimulation have also been observed in other species (Smith, 1992; Robbins & Nakashiro, 1993). Therefore, it remains possible that the decline in strength with age is also related to changes in neuromuscular innervation.

Another possible mechanism for the decline in strength with age is reduced specific force. Existing evidence suggests that older muscle may exhibit reduced force per unit of cross-sectional area (CSA) than young muscle (Dowling et al., 1994; Jubrias et al., 1997). Bruce et al. (1989) observed a 20% decline in force per muscle cross-sectional area in older subjects, and similar observations have been documented in rodent muscle tissue (Brooks & Faulkner, 1991). The mechanisms responsible for this phenomenon remain unclear, however, it has been proposed that qualitative changes occur with in muscle fibres, thereby affecting force generation during cross-bridge formation (Brooks & Faulkner, 1991).

From previous literature, it appears that the most probable mechanisms responsible for the decline in strength with age are a decrease in muscle mass, a decline in neuromuscular innervation and/or reduced specific force. Although the age-related decline in strength has been quantitatively described for many years, no available study has attempted to determine the effect of increasing age on muscle mass, neuromuscular innervation and specific force simultaneously.

The purpose of this investigation was to determine if the decline in peak isometric force with age was primarily related to quantitative changes in muscle mass, a decline in neuromuscular innervation and/or reduced specific force.

Methods

Subjects

Thirteen young men (YM) with a mean (±SD) age of 20.8 ± 1.6 years, height 180.0 ± 6.7 cm, mass 79.0 ± 8.8 kg and eight middle-aged men (MM) with a mean (±SD) age of 53.9 ± 4.2 years, height 178.0 ± 6.5 cm, mass 81.0 ± 15.0 kg volunteered to participate in the study. Mean (±SD) BMI for the YM and MM was 24.4 ± 2.2 and 25.3 ± 3.3, respectively. All subjects were non-smokers and considered healthy subsequent to completing the Physical Activity Readiness Questionnaire (PAR-Q) (Thomas et al., 1992). Subjects were not involved in more than 2–3 h of moderate physical activity per week and were classified as untrained. Written consent was gained from all subjects prior to the commencement of the study. The investigation was conducted with the approval of the Ethics in Human Research Committee of the University.

Anthropometry

Anthropometrical data collection

Prior to testing, total thigh circumference (CT) was determined on the preferred kicking limb (Overend et al., 1992a) at the region of the thigh with the widest girth (Knapik et al., 1996) using a measuring tape. Three circumference measurements were recorded with the subject standing upright, with minimal body weight on the preferred limb. Care was taken to ensure that the measuring tape remained perpendicular to the longitudinal axis of
the thigh during recording. Individual $C_T$ measurements were averaged and the mean used for subsequent calculations. All $C_T$ measurements were recorded in millimetres. The coefficient of variation of $C_T$ measures in the YM and MM was 3.8 and 4.5%, respectively.

Calculation of knee extensor muscle cross-sectional area

Total thigh cross-sectional area (TCSA) was determined anthropometrically according to Knapik et al. (1996). The anthropometrical model of Knapik et al. (1996) is based on the premise that the thigh is composed of concentric layers of skin, fat, muscle and bone tissue. Therefore, an estimate of TCSA can be obtained using $C_T$ measurements and equations for the circumference, radius and area of a circle (Knapik et al., 1996). Accordingly, TCSA for the YM and MM were calculated using Equations (4)–(5), respectively, where $R_T$ is the total radius of the thigh,

$$C_T = 2\pi R_T$$  \hspace{1cm} (1)

$$R_T = C_T/(2\pi)$$  \hspace{1cm} (2)

$$\text{TCSA} = \pi R_T^2 = \pi(C_T/2\pi)^2$$  \hspace{1cm} (3)

Calculating the cross-sectional area for the knee extensor muscle (QCSA) was based on the results reported in Overend et al. (1992a). Using a computed tomography technique, Overend et al. (1992a) observed that the knee extensor muscles occupied 38–41% of the TCSA in younger subjects (19–34 years; BMI 23.1; $n = 13$), and 30–25% of the TCSA in older subjects (65–77 years; BMI 24.7; $n = 11$). Using these percentages, an estimate of the QCSA for the subjects that participated in the present investigation was determined. The QCSA of the YM and MM was estimated using Equations (3) and (4), respectively.

$$\text{QCSA}_{\text{YM}} = \text{TCSA} \times 0.3841$$  \hspace{1cm} (4)

$$\text{QCSA}_{\text{MM}} = \text{TCSA} \times 0.3025$$  \hspace{1cm} (5)

Mechanical assessment of muscle function

Peak force testing

Peak force was assessed on the preferred kicking limb (Overend et al., 1992a) using a Kin-Com™ isokinetic dynamometer (Chattanooga Group Inc., Hixon, TN, USA). Subjects were secured to the dynamometer via waist and shoulder straps. Because of the risk of interfering with the surface electrode used to collect the electromyography (EMG) data, it was not possible to stabilize the active thigh during exercise. The axis of rotation for the dynamometer was visually aligned with the lateral epicondyle of the femur with the lower leg attached to the lever arm at the level of the lateral malleolus.

Once secured to the isokinetic dynamometer, subjects performed a standardized warm-up and familiarization protocol prior to commencing the peak testing. This warm-up consisted of six submaximal isometric knee extensions at an angle of 60° knee flexion, with the reference point of 0° being full extension. The first two contractions were performed at ~50% of maximal effort, and the second two contractions were performed at ~70% maximal effort. Finally, two further contractions were performed at ~90% maximal effort. A rest period of 5 s separated each of the six submaximal contractions.

Subsequent to the warm-up, peak force testing commenced. Peak force testing consisted of four maximal voluntary isometric contractions of the knee extensor muscles on the preferred leg. For peak force testing, subjects were positioned in the Kin-Com isokinetic dynamometer similar to that during the warm-up. Peak isometric force of the knee extensor muscle was performed at an angle of 60° knee flexion, with the reference point of 0° being full extension. A rest period of 5 s separated each of the four maximal voluntary contractions. Isokinetic dynamometer software collected force data throughout each contraction at a rate of 100 Hz.

Analysis of peak force data

Peak force was determined as the single highest force value produced over the four consecutive contractions. Peak force was visually determined by Kin-Com analysis software. From the anthropometrical calculations of QCSA, the force generated per square centimetre of knee extensor muscle tissue (specific force) was determined using Equation (6).

$$\text{Specific force (Ncm}^{-2}) = \text{Peak force (N)}/\text{QCSA (cm}^2)$$  \hspace{1cm} (6)
Electromyographical assessment of muscle function

Application of the surface electrode
Prior to the warm-up and peak force testing on the isokinetic dynamometer, an EMG electrode with a bandwidth of 50–450 Hz was attached to the belly of the rectus femoris, midway along the anterior aspect of the thigh. The reference electrode was placed on the patella of the opposing limb. The skin underlying the electrode placement sites was carefully prepared. Hair was shaved, and the outer layers of epidermal cells were removed using abrasive paper. Oil and dirt on the skin was removed by swabbing with 70% isopropyl. A differential surface electrode (Delsys™, Boston, MA, USA) was then placed on the prepared muscle site linked to an EMG signal acquisition apparatus (Delsys™, Boston, MA, USA) and host computer (IBM Thinkpad™, Armonk, NY, USA). EMG data was sampled at rate of 1024 Hz for all tests, thus yielding raw signals.

Analysis of electromyographical data
Raw EMG data from the contraction where peak force occurred was rectified and the movement artefact removed using a high pass second order Butterworth filter with a cut-off frequency of 15 Hz. The data was subsequently smoothed using a low-pass second order filter with a cut-off frequency of 5 Hz, and integrated (IEMG). These procedures were performed using MATLAB™ gait analysis software (The Mathworks Inc., Natick, MA, USA). The raw IEMG data was subsequently divided by the number of data points to correct for differences in contraction time for each subject. Finally, the raw IEMG data was multiplied by 102.4 to correct for the filter and sampling rate, which presents the data in units of volt-seconds (V s). Equation (7) describes the mathematical treatment of the raw IEMG data,

\[
\text{IEMG} \times 102.4 = \frac{\text{Raw IEMG} \times \text{Data points}}{\text{IEMG}}
\]  

Using the anthropometrical data, an estimate of the quantity of myoelectrical activity (V s) generated per square centimetre of knee extensor muscle (specific IEMG) was determined. For the YM and MM, specific IEMG from the rectus femoris was determined using Equation (8),

\[
\text{Specific IEMG} = \frac{\text{IEMG}}{\text{QCSA}} \quad (8)
\]

Statistical analysis
Standard methods were used for the calculation of descriptive statistics. Statistical analysis was performed using SPSS™ (Statistics for the Social Sciences, version 6.0) software. A one-way analysis of variance (ANOVA) was used to identify between group differences in TCSA, QCSA, peak force, specific force, peak IEMG and specific IEMG. Correlations between QCSA, peak force and peak IEMG were determined using a Pearson rank-order correlation. The critical level for statistical significance was set at \( P < 0.05 \). Values are reported as the mean ± standard deviation (SD).

Results

Anthropometry
Thigh circumference measurements with the calculated TCSA and QCSA values for the YM and MM are presented in Table 1. Statistical analysis of CT measurements revealed no significant difference between the age groups \( (P = 0.1) \). The observed mean (±SD) \( C_T \) for the YM was 51.9 ± 3.1 cm, and for the MM 49.2 ± 4.2 cm. No significant differences in TCSA were observed between the YM (215 ± 26 cm²), and MM (194 ± 33 cm²) \( (P = 0.12) \).

Following the calculation of QCSA based on the percentages reported in Overend et al. (1992a), a significant difference between the age groups was observed. QCSA for the YM was estimated as 83 ± 10 cm², and for MM 59 ± 10 cm² \( (P = 0.001) \).

Peak force
The peak force values produced by the YM were significantly higher compared with the MM \( (P = 0.001) \). The YM were able to generate a peak force of 632 ± 116 N, whereas the MM generated 418 ± 85 N of peak force. The age-related difference
in peak force corresponded to a 34% reduction between the ages of 20 and 50 years. A significant correlation between QCSA and peak force was observed in the YM ($r = 0.83$, $P = 0.001$) and MM ($r = 0.74$, $P = 0.03$).

### Integrated electromyography

When comparing both age groups in terms of myoelectrical activity, the YM generated substantially greater quantities of myoelectrical activity compared with the MM. The quantity of IEMG generated during the maximal voluntary isometric contraction for the YM was $7.6 \pm 0.9$ N cm$^{-2}$, which was significantly higher than the MM who generated $7.2 \pm 1.1$ N cm$^{-2}$ generated by the MM.

### Specific integrated electromyography

Once corrected for QCSA, it was observed that the YM generated $0.18 \pm 0.1$ V s of myoelectrical activity per square centimetre of knee extensor muscle. This value was not significantly different to the MM who generated $0.13 \pm 0.1$ V s of myoelectrical activity per square centimetre of knee extensor muscle ($P = 0.1$).

### Discussion

Previous research suggests that the most probable mechanisms responsible for the reduction in strength with age are: (i) a decline muscle mass associated with a reduction in the total number of muscle fibres and the atrophy of those fibres remaining, (ii) a change in the proportion of type I and type II muscle fibres through the selective loss of type II fibres, (iii) a deterioration in neuromuscular innervation related to possible changes in neurotransmitter release, reduced muscle sensitivity to electrical stimulation, or the ability of the central and/or peripheral nervous systems to adequately stimulate older muscle tissue and/or (iv) qualitative changes within muscle fibres affecting cross-bridge formation resulting in a subsequent decline in specific force (Stanley & Taylor, 1993).

The purpose of the present investigation was to determine if the decline in peak force with age was primarily related to quantitative changes in muscle mass, a decline in neuromuscular innervation, and/or reduced specific force. The results of the present study indicate that the observed reduction in peak isometric force between 20 and 50 years of age was primarily related to quantitative changes in muscle mass, rather than changes in neural innervation or specific force.

<table>
<thead>
<tr>
<th>Group</th>
<th>$C_T$ (cm)</th>
<th>TCSA (cm$^2$)</th>
<th>QCSA (cm$^2$)</th>
<th>Peak force (N)</th>
<th>Specific force (N cm$^{-2}$)</th>
<th>Peak IEMG (V s)</th>
<th>Specific IEMG (V s cm$^{-2}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young men</td>
<td>$51.9 \pm 3.1$</td>
<td>$215 \pm 26$</td>
<td>$83 \pm 10$</td>
<td>$632 \pm 116$</td>
<td>$7.6 \pm 0.9$</td>
<td>$14.6 \pm 0.5$</td>
<td>$0.18 \pm 0.1$</td>
</tr>
<tr>
<td>Range</td>
<td>$46.7-59.0$</td>
<td>$174-277$</td>
<td>$67-106$</td>
<td>$410-838$</td>
<td>$5.7-86$</td>
<td>$8.2-25.7$</td>
<td>$0.1-0.3$</td>
</tr>
<tr>
<td>Middle-aged men</td>
<td>$49.2 \pm 4.2$</td>
<td>$194 \pm 33$</td>
<td>$59 \pm 10$</td>
<td>$418 \pm 85$</td>
<td>$7.2 \pm 1.1$</td>
<td>$7.5 \pm 1.5$</td>
<td>$0.13 \pm 0.1$</td>
</tr>
<tr>
<td>Range</td>
<td>$43.2-56.8$</td>
<td>$149-257$</td>
<td>$45-78$</td>
<td>$331-600$</td>
<td>$5.0-8.9$</td>
<td>$6.1-10.8$</td>
<td>$0.1-0.2$</td>
</tr>
</tbody>
</table>

Values are mean ± SD. $C_T$ is thigh circumference; TCSA is total thigh cross-sectional area; QCSA is the estimated knee-extensor muscle cross-sectional area based on the results of Overend et al. (1992a). Statistical differences were determined by a one-way ANOVA.

*Indicates significant difference ($P<0.001$).

†Indicates significant difference ($P<0.01$).
An age-related decline in peak strength associated with reduced specific myoelectrical activity would suggest that the ability to innervate middle-aged muscle is reduced, possibly as a result of changes in motor neurones and/or a reduced central drive. However, an age-related decline in peak strength associated with a reduction in specific force would suggest that qualitative changes have occurred within muscle fibres, possibly as a result of changes in the mechanics of cross-bridge cycling and/or changes in fibre type proportions. In either case, such a decline in strength with age would be less responsive to exercise intervention. The results of the present investigation suggest otherwise.

Age-associated decline in muscle mass

The age-related decline in peak strength is clearly associated with changes in muscle cross-sectional area (CSA) (Narici et al., 1988; Overend et al., 1992b; Jubrias et al., 1997). Therefore, when investigating the effect of ageing on neuromuscular performance it is important to assess the relationship between peak force and muscle CSA. Previous investigations studying age-related changes in the composition of the thigh region have commonly used young (19–38 years) and elderly (65–90 years) subjects (Rice et al., 1990; Overend et al., 1992a). Although it is not ideal to compare the thigh composition of the elderly subjects (65–77 years) reported in Overend et al. (1992a) to the MM (50–59 years) in the present investigation, it was the best alternative as similar data pertaining to middle-aged men (40–60 years) is not available.

The comparable specific force values observed in the present investigation suggests that the reduction in peak strength with age was essentially related to the quantitative changes in muscle mass, rather than qualitative changes within the muscle. Previous investigations studying the changes in specific force with age are conflicting. Jubrias et al. (1997) reported that significant age-associated reductions in specific force only became apparent when 23–65-year-old subjects were compared with 65–80-year olds. However, other investigations report that age-related differences in specific force between 45 and 78 years of age are not significant (Frontera et al., 1991). In addition, Kent-Braun & Ng (1999) reported that although a substantial reduction in peak force was observed in older subjects compared with younger subjects, no difference was apparent when corrected for muscle CSA.

The discrepancy of previous results may reflect the age range of subjects and the limitations of study designs. A longitudinal study of the changes in specific force would contribute enormously in clarifying these positions.

Age-related changes in fibre type proportions

The most plausible mechanism responsible for a change in fibre type proportions with age is the selective loss of type II muscle fibres, as a result of selective denervation (Stanley & Taylor, 1993). As muscle biopsy samples were not taken in the present investigation, the current findings are unable to support or reject an age-related change in muscle fibre type proportion. However, current research provides conflicting evidence for the selective loss of type II muscle fibres. Larsson et al. (1978) reported an increase in the relative proportion of type I muscle fibres in the vastus lateralis muscle between 26 and 62 years of age. Further evidence for the selective loss of type II muscle fibres with age is provided by Klitgaard et al. (1990). In contrast, Grimby et al. (1984) reported no significant difference in the proportion of type I and II muscle fibres between 66 and 100 years of age. Additionally, Lexell et al. (1986) reported similar results, where no significant difference was observed in the number type II fibres in subjects ranging from 24 to 77 years old.

Age-associated decline in neuromuscular innervation

The insignificant difference in specific myoelectrical activity with age observed in the present study indicates that both age groups possessed a similar capacity to innervate muscle tissue. This finding suggests that between 20 and 50 years of age, no significant changes occur in neurotransmitter release, muscle stimulation sensitivity, or the ability of the central and/or peripheral nervous systems to adequately stimulate muscle tissue.

The present investigation is the first study where myoelectrical activity, or neural innervation, has been analysed per square unit of muscle tissue. Much of the

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previous research on age-related changes in neuromuscular innervation has compared maximal voluntary strength values against strength values produced during maximal voluntary efforts coupled with electrical stimulation. Vandervoort & McComas (1986) provide evidence that healthy men and women aged 66–100 years are able to maximally activate their ankle and dorsi flexors under isometric conditions as supramaximal stimulation of the motor nerve failed to increase maximal voluntary contraction strength. Kent-Braun & Ng (1999) using the central activation ratio method reported no significant difference between maximal voluntary contractions and maximal voluntary contraction with superimposed electrical stimulation in subjects aged 32 and 72 years.

**Muscle quality**

The results of the present investigation contradict the notion of an age-related deterioration in muscle quality resulting in a decline in specific force. As discussed previously, reports of age-related changes in specific force are conflicting. The mechanism responsible for the age-associated decline in muscle quality that leads to a reduction in specific force remains unclear. Brooks & Faulkner (1991) studying the muscle of adult and aged mice suggest that either a substance in the cytosol of fibres in the muscle of aged animals inhibits force development of the cross-bridges, or that intact fibres are not fully activated by calcium. In either case, formidable methodological constraints must be overcome before the importance of age-related reductions in specific force can be fully determined in humans.

The major finding of the present study was that despite the significant reduction in peak force and peak IEMG with age, the differences were negligible when corrected for QCSA. These results suggest that the age-associated decline in strength up to 50 years is primarily related to quantitative changes in muscle mass, rather than reduced neuromuscular innervation or a deterioration in muscle quality. Therefore, preserving muscle mass through resistance training may significantly reduce the age-related differences in peak strength and assist in promoting quality of life and functional independence in older adults.

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**References**


