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Effects of unilateral resistance training on sexagenarians:

an examination of functional, histochemical, biochemical, and morphological changes.

Graduate Thesis

A paper presented to the School of Kinesiology, the Faculty of Arts and Science,

Lakehead University, Thunder Bay, Ontario

in partial fulfilment of the requirements for the degree of

Masters of Applied Sports Science and Coaching.

David E. T. O'Neill, B.Ph.Ed. ©

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January, 1997

Acknowledgements

I would like to express my thanks to those individuals who provided assistance, and whose support was invaluable in the completion of this document. I would like to thank the spirited bodybuilders that proffered their conscientious effort and infectious enthusiasm to the project. I extend many thanks to Dr. Robert Thayer for providing direction as my thesis advisor. I am grateful for the input from my other committee members: Dr. Tony Bauer, Dr. Dave Chapman, Dr. Norm Lavoie and Dr. Leslie MacDonald-Miszczak. Thanks goes to Dr. Bert Taylor, the external examiner of this thesis, for his thorough review and encouraging remarks.

I will always be indebted to the individuals who provided extraordinary technical support during the completion of this project. Invaluable assistance with logistics, testing, and laboratory analysis was extended by Chris Wreszczak, Thomas Dzialoszynski, Dr. Bert Taylor, Kris Aubrey, Scott Manktelow, Kendra Arthur and Joanna Duncan. Thanks goes to Dr. Earl Noble for offering his comments and recommendations and the use of his laboratory. I would also like to thank Dr. Bill Montelpare for affording his statistical expertise and ongoing support in spreading the Fire.

Special thanks go to my fellow graduate students and friends, Shannon, Scott, Gareth, Ron and Larisa. They made my experience as a student in the land of the Sleeping Giant one of treasured memories.

This project is dedicated to the memory of my father, who passed on during its completion. To the trees of the George Robert Forest,

"Stand tall, make those, that made you, proud."

Table of Contents

Abstract

The purpose of this study was to investigate functional, histochemical, biochemical and morphological properties associated with resistance training in the elderly. Ten (8 females, 2 males), moderately active sexagenarians (mean age = 66.3; S.D. +/- 3.7 yrs), volunteered to engage in 8 weeks of isotonic resistance training of the quadriceps muscle of one leg. Training sessions took place three times per week with each session including a warm up and warm down; and three to five sets (ten repetitions per set) of unilateral leg extensions and unilateral leg curls. There were no significant changes in height, weight, and thigh girth with training. Peak torque output at 180 °/s increased 30.8% ($P < 0.05$) after training in the experimental limb. No significant changes in peak torque (Pre 78.1 +/- 10.5 N. m; Post 89.1 +/- 15.2 N. m) or mean power (Pre 91.6 +/- 14.5 Nmrads x s^{-1} Post 106.4 +/- 18.7 Nmrads x s^{-1}) at 60 °/s were observed. No significant change in peak torque or mean power was noted in the contralateral control limb at either velocity. Although there was a tendency to an increased fibre area in type II fibres (7.3% for IIa and 10.6% for IIb), fibre cross sectional area (CSA) was unaltered as a result of the resistance training. In addition, there were no significant changes in the muscle fibre type composition, as assessed histochemically or in the proportion of type I myosin heavy chain (MHC) and heat shock protein 72 as assessed by western blot. These data suggest that an eight week resistance training program is capable of producing significant increases in isokinetic peak torque in the elderly.

Chapter 1

Introduction

Disease and the normal process of aging have been associated with a loss of strength in the elderly (Cress et al. 1991; Doherty, Vandervoort, Taylor & Brown, 1993). Daily activities of the elderly often require less muscular force and are completed in a slower manner than in younger individuals. Decreased use of certain physiological functions may contribute to loss or reduced physiological capacity in skeletal muscle (Grimby & Saltin, 1983). Hence, some researchers have suggested that the deterioration in skeletal muscle with aging may be attributed to a failure to recruit fast twitch motor units (Aniansson, Sperling, Rundgren & Lehnberg, 1983). Other authorities have suggested that such physiological changes have limited the choice of physical activity in which elderly people may participate (Franzoni, Rozzini, Boffelli, Frisoni & Trabucchi, 1994, Albarede, Lemieux, Vellas, & Groulz, 1989). Consequently, changes in recruitment pattern of fibre types may limit muscular force and speed of physical activity. In other words, it is not understood whether some of the observed loss of strength is the cause or the result of compromised physical activity. In either case, the variables of genetic predisposition, disease, and degree of physical activity make the study of the aging process in muscle a serious challenge (Cress et al., 1991; Skelton, Greig, Davies & Young, 1994). Since the interactions and effects of these three variables differ in every individual, attributing change in muscle strength with aging to any one cause is difficult. Nevertheless, recent research has focussed on the effect of exercise in the skeletal muscles of the elderly. It has been suggested that physical training may be able to arrest or reverse this age related loss in strength (Cress et al. 1991; Dupler & Cortes,

1993).

Although attention has been given to the importance of cardiovascular fitness in older people (Hagberg, Graves & Limacher, 1989), there has been an increasing focus on resistance training in this group. Researchers have suggested that strength is more important than cardiovascular fitness in the maintenance of an independent lifestyle in the elderly (Fiatarone & Evans, 1990). Whipple, Wolfson and Amerman (1987) demonstrated a relationship between a history of falls in elderly persons and lack of quadriceps strength. Smaller type II fibre area and reduced strength have been associated with hip fractures in the elderly (Aniansson, Ljungberg, Rundgren & Wetterquist, 1984). Since both falling (Whipple et al. 1987) and hip fractures (Aniansson, Zetterberg, Hedberg & Henriksson, 1984) are important considerations for independence in the elderly, the need for strength training appears to be well founded. However, the biochemical changes in muscle associated with the process of aging are not fully understood (Lexell, 1993). A clearer picture of the biochemical and histological factors which reflect the aging process needs to be understood to make inferences about the specificity of training and the transferability of strength from the training mode to other tasks.

Significant alterations in the morphology and contractile properties of skeletal muscle occurs with the process of aging (Essen-Gustavsson & Borges, 1986). Consequently, senescence has been associated with decreases in muscle mass and muscle force (Klitgaard, Marc, Brunet, Vandevalle & Monod, 1989; Doherty, et al. 1993). In humans, and in other mammalian studies, it has been documented that the contraction time of both the slow and fast twitch muscles increases with age (Lewis & Brown, 1994). Such changes have been attributed to alterations in the aged neuromuscular system. These alterations include the reinnervation of previously fast twitch fibres

with slow twitch motoneurons (Keen, Yue & Enoka, 1994). Although these alterations associated with senescence represent a physiological decline, it remains to be shown, whether these changes are inevitable (Skelton, et al., 1994). One prominent characteristic of the neuromuscular system is its adaptability. When subjected to a chronic stimulus, such as training, it can adapt to the altered demand of usage (Pette, 1984). As well, metabolic capacity and muscular force can become elevated with training in the elderly (Grimby and Saltin, 1983). Thus, strength training may attenuate or reverse typical decline of compromised response (Porter, Vandervoort & Lexell, 1995).

Researchers have examined aged muscle in terms of neuromuscular, morphological and biochemical properties and its adaptability with respect to those parameters (Lexell, 1993). Histochemical, biochemical and electrophoretic analyses have been used to analyse skeletal muscle (Tomanoga 1977; Grimby, Danneskiold-Samsoe, Hvid & Saltin 1982). Studies which have employed these techniques have typically required subjects to engage in a whole-body or part-body strength training program. Such research has reported significant strength gains which have been attributed in part to hypertrophy of type II muscle fibres (Frontera, Meredith, O'Reilly, Knuttgen & Evans, 1988; Brown, McCartney & Sale, 1990; Charette et al., 1991; Pyka, Lindenberger, Charette & Marcus, 1994). However, a common limitation in this type of research is the possible influence of factors other than those of the experimental treatment such as differences in physical activity levels between control and experimental groups. Consequently, researchers have recommended that investigations in this area should attempt to increase control in the research design (Porter, et al., 1995; Thayer, Rice, Pettigrew, Noble & Taylor, 1993).

In an attempt to increase experimental control, two studies involving resistance training

and the elderly have employed a contralateral limb design (Grimby, et al., 1992; Hicks, Cupido, Martin & Dent, 1991). Subjects trained one leg while the contralateral leg was used as the control limb. However, the findings of these studies are limited due to the small and unique subject pool employed and limited comparison between trained and contralateral limbs. Subjects in the Grimby et al. (1992) investigation were highly trained and not representative of a typical population of seniors. As well, in the study by Hicks et al. (1991) biopsies were taken from the experiment limb alone, thus comparisons to the control limb were not possible. It was anticipated that use of a contralateral limb control design in the present study would facilitate a clearer understanding of the adaptations associated with resistance training in the elderly.

In contralateral control limb studies of resistance training in younger subjects, small increases in strength have been reported in the untrained, control limb (Houston, Froese, Valeriote, Green & Ranny, 1983). Researchers have termed this effect, 'cross-over training effect' (Housh & Housh, 1993). However, it has been difficult to assess whether these changes were due to a cross training effect or a change in the subjects' fitness. A conservative approach would suggest that no cross training effect occurred and that control limb strength gains were due to non-treatment influences (i.e. learning effect, change in fitness). Irrespective of a cross-over training effect and non-treatment influences, observed increases in strength in the experimental limb, in addition to those of the contralateral limb, can be attributed to the experimental treatment. Thus, strength gains in the experimental limb, in addition to those of the contralateral limb may underestimate the effects of the training intervention. With this in mind, baseline measures will be taken from both limbs in order to estimate the training effect and the cross-over training effect in the experimental and control limbs, respectively. Therefore, the one leg model employed by this

study was expected to increase experimental control.

Statement of Purpose

The purpose of this study was to evaluate the manner in which resistance training affects the morphological, histochemical, biochemical and functional properties of aged skeletal muscle.

Delimitations

1. **Subjects**: This study was delimited to 10 healthy seniors aged (mean) 66.3 years (60 -72) who had no previous experience in resistance training, who were volunteers and resided in Thunder Bay Ontario, Canada.

2. **Experimental Control**: As this study required only one leg to follow the strength training program, alterations attributable to strength training were more closely approximated by considering changes found in the control limb.

3. **Measurements**: Fibre number, diameter, grouping, and morphology were examined. Change in the expression of HSP 72 and type I myosin heavy chain were also examined.

4. **Functional Test**: The only functional performance measure was a 4RM leg extension/flexion (60 & 180 °/s) on a isokinetic dynamometer.

5. **Fibre count**: Samples were blinded to protect the investigator from knowledge of initial or final biopsy status.

6. **Training Program**: The training program was executed for 8 weeks with exercise sessions taking place 3 times per week.

7. **Statistical Significance**: The alpha level of probability required to denote significance was $p < 0.05$.

Limitations

1. **Biological age differences**: Previous research has accepted an age of at least 60 years for subjects in many studies of 'aged' muscle. However, recent research (Lexell, 1993) has suggested that large individual differences in the biological age of skeletal muscle may exist in concert with like chronological age. Therefore, subjects of like chronological age may or may not represent 'aged' skeletal muscle. Control samples allowed comparison of the subjects to others in reported literature. However, differences in the genetic response to training could not be controlled.

2. **Non-treatment influences**: Research which examines a training effect cannot control all other possible influences on the dependent measure. Since this study employed a strength training program for a given duration, subjects may have experienced changes in the dependent measures not explained by the exercise intervention. In order to minimize these changes, subjects were requested to maintain physical activity levels outside of the training, throughout the course of the investigation.

3. **Biopsy Sampling**: The biopsy sample provided an estimate of the characteristics of the muscle. As such, this method of analysis is subject to the possibility of sampling error.

4. **Strength Testing**: This study relied on the subject's perception of a maximal effort to determine current strength. Differences between test scores may have been accounted for, to a small extent, by differences in motivation, degree of encouragement, perception of maximal effort and other psychological variables. Subjects were requested to put forth a maximal effort and were verbally encouraged by the tester in order to minimize this effect.

5. **Learning Effect**: This study relied on the subject's technical competence to perform an exercise test. Improvements in skill in addition to strength may have contributed to the results. Introductory and practice sessions executing the exercise tests were conducted in order to minimize this effect.

6. **Neuromuscular influence**: Neuromuscular changes in aging humans influence both the motor unit and contractile properties of skeletal muscle (Lexell, 1993). Such changes were not measured in this study. Therefore, neuromuscular changes which may contribute to biochemical and functional measures of the training effect, were not directly assessed using the proposed methods of analysis.

7. **Training specificity**: Based on the principle of specificity (Fleck & Kraemer, 1987), responses to training may only reflect the characteristics of the strength training program. Since

this study aimed to describe the effects of resistance training, the external validity of the findings is limited to programs of similar intensity, duration and frequency.

Chapter 2

Literature Review

The purpose of this review is to examine some of the recent findings related to the area of study.

PART A: Skeletal Muscle Fibres

Types: Goldspink (1983) classified mammalian muscle fibres into two basic types: tonic and phasic. Since tonic fibres are not found in human skeletal muscle (Goldspink, 1983), only phasic type fibres will be discussed in detail. Traditionally, phasic or twitch fibres (identified by a propagated muscle action potential in response to a single stimulus) have been classified into three types: slow-twitch (ST); fast-twitch glycolytic (FTb); and fast twitch oxidative (FTa). Using histochemical analysis, ST, FTb and FTa fibres were classified as type I, type IIb and type IIa respectively (Brooke & Kaiser, 1970a; 1970b). Goldspink (1983) has provided the following review of phasic muscle fibres:

Slow-twitch (ST) : ST (or slow oxidative [SO] fibres) are slow contracting and therefore usually responsible for maintenance of posture and the execution of slow repetitive movements. The high number of mitochondria and slow hydrolysis of ATP creates the fatigue resistant characteristics found in this fibre type. This fibre type may be described as economical and efficient, though low in power output.

Fast-twitch glycolytic (FTb): These high-power output fibres, also known as fast

glycolytic (FG) or fast fatiguable (FF) fibres have a reasonable thermodynamic efficiency for producing work. Type IIb are recruited when very rapid movement is required. These fibres respond with a very high intrinsic speed of shortening as a result of high myosin ATPase specific activity. FTb fibres have very few mitochondria hence they cannot possibly replenish ATP as fast as it is used. Therefore, they fatigue rapidly and while in an inactive state, energy supplies are replenished. Energy for contraction is primarily supplied by glycolysis and the immediate energy stores (ATP and phosphocreatine).

Fast-Twitch oxidative fibres (FTa): Alternative names for this fibre are: fast oxidative glycolytic (FOG) and fatigue resistant (FR) fibres. FTa possess more mitochondria than FTb which reduces susceptibility to fatigue and shortens recovery following exercise. Also, these fibres have a slightly slower intrinsic rate of shortening than their fast twitch counterparts (FTb). These fibres are adapted for fast movements of a repetitive nature and are recruited following ST fibres.

Classification: Recent researchers have revealed a more complex taxonomy of fibre types than the three predominant types described by Goldspink (1983) (Thayer et al., 1993). Adult skeletal muscle fibres have been divided histochemically, functionally and biochemically into two broad categories, type I and type II fibres. Type II fibres have been subclassified into IIa, IIb and IIc on the basis of differences in the pH sensitivity of myofibrillar adenosine triphosphatase (ATPase) activity (Brooke and Kaiser, 1970a). Type IIc fibres, also referred to as intermediate/transitional fibres, have been revealed to co-express both fast and slow isoforms of the contractile proteins (Wada, Katsta, Doi & Kuno, 1990). The identification of these additional fibre sub-types was

made possible by a variety of analytical techniques: immunocytochemistry (Gorza, 1990); electrophoresis (Staron & Pette, 1986) or a combination of the two (Schiaffino et al., 1988).

The polymorphic nature of the myofibrillar proteins has been well-established (Williams and Dhoot, 1992). Moreover, accumulating evidence has revealed a more diverse heterogeneity of muscle contractile proteins than previously reported (Pette, 1984, Staron and Hikida, 1992). The spectrum of fibre types in mammals includes: Type I, IC, IIC, IIA, IIA2, IIAB, 2D (2X), and IIB (Thayer, et al., 1993). These additional subtypes have differing myosin compositions and as a result revealed intermediate or mixed characteristics of the three predominant fibre types of earlier classification schemes.

The predominant myosin heavy chain (MHC) composition and histochemical ATPase staining pattern appear to have a direct correlation within mammalian skeletal muscle (Thayer et. al, 1993). Therefore, combining techniques such as immunocytochemistry, electron and light microscopy, and electrophoresis (which allow the identification of the myosin chains and other contractile proteins) with histochemistry has allowed researchers a comprehensive examination of fibre types in the skeletal muscle.

Distribution and Proportion: Differences in the distribution of fibre types in skeletal muscle have been observed not only between species but also between homologous muscles of different animals of the same species (Green, Reichmann & Pette, 1984). In the muscles of some mammals (mouse soleus, guinea pig vasti) a single fibre type has been observed (Gorza, 1990). In humans, a predominant fibre type may be found in certain muscles, however, each fibre type can be found in all human skeletal muscles. For example, muscles such as the soleus have been characterized

by a predominance of ST fibres, whereas a predominance of FT fibres has been observed in the triceps brachii muscle (Saltin & Gollnick, 1983). However, in humans, virtually all muscles consist of a heterogeneous mixture of fibre types. In general, anti-gravity muscles appear to exhibit a greater proportion of ST fibres, while gravity assisted muscles were composed primarily of FT fibres (Thayer et al. 1993).

In adult humans the distribution has generally been regarded as random (Thayer et al. 1993). Nevertheless, some research has revealed a preponderance of FT at the border and ST fibres in the deeper regions of the muscle (Lexell, Henriksson-Larsen, Winbald & Sjostrom, 1983). The distribution pattern in all skeletal muscle may be disrupted by the aging process (Lexell, 1993). Furthermore, researchers employing single biopsy samples may not have sufficient representation of the overall distribution pattern of fibres within a given muscle (Lexell et al., 1983). The estimated intramuscular variation (coefficient of variation, CV) demonstrated by multiple biopsies from the vastus lateralis muscle has been reported to be +/- 15 to 20% (Gollnick, Armstrong, Saubert, Peihl & Saltin, 1972, Lexell et al. 1983). Thus, significant improvement in the degree of representation may be practically unreasonable as it requires a large number of biopsies. Lexell and coworkers (1983) recommended biopsy depth and location be clearly defined if samples are to be taken before and after a period of physical training. Examination of larger human specimens, such as whole muscles has provided a more detailed description of fibre type distribution (Lexell et al., 1983). However, due to ethical and practical considerations only necrospy material has been examined. Thus knowledge of the distribution of fibre types in humans has been limited as a consequence of the difficulties associated with sampling of whole muscle cross-sections from living human subjects.

It has been suggested that the distribution of fibre types in humans may be significantly different depending on the degree and type of physical training (Thayer et al., 1993). However, because observations were based on cross-sectional comparisons it has been difficult to attribute the preponderance of a particular fibre type to genetic factors or chronic perturbations in response to specific training. In the untrained muscle vastus lateralis (VLM) in adult humans, ST fibres represented 40 - 50% of the fibre distribution, regardless of gender (Johnson, Polgar, Weightman & Appleton, 1973). In strength trained humans, ST fibres have comprised 25-60 % (Saltin & Gollnick, 1983) and 30 % (Staron & Hikida, 1992) of the fibre distribution in the same muscle, in males and females respectively. Male endurance trained professional cyclists have had as much as 80% ST fibres in the VLM (Tesch & Karlsson, 1985). Intraconversion of ST and FT subtypes has further complicated the distribution pattern. Moreover, training programs employed in research experiments often differ in terms of intensity, duration, and frequency. Researchers have recommended more rigorous longitudinal training studies in order to determine the exact nature and extent of the conversion process in response to training (Thayer et al., 1993).

Contractile Properties: The nature of movement produced by the contracting muscle depends primarily, on the contractile characteristics of the fibre types present (Thayer et al., 1993). Contractile properties may be determined by the type of motoneuron which innervates the muscle fibre and the type of contractile proteins present in the muscle fibre. The motor unit, which is comprised of a motoneuron and all the muscle fibres which it innervates (Liddell & Sherrington, 1925), has been reported to represent the basic functional unit of skeletal muscle. Single motor units innervate muscle fibres with distinct morphological and biochemical properties. Large

motor units with high-threshold axons innervate FT fibres and are recruited for the production of greater force and frequency over a shorter duration when compared to smaller motor units innervating ST fibres (Doherty et al., 1993).

The contractile characteristics of a muscle have been observed using a variety of techniques and include the following characteristics: twitch contraction time; maximum tetanic tension; resistance to fatigue; 'sag' in infused tetanus; post-tetanic potentiation; and motor unit firing frequency (Thayer et al., 1993). Moreover, histochemical and biochemical analyses have revealed other contractile properties: enzyme activity; substrate concentration; and presence of isoforms of contractile proteins. For the purposes of this review, only fibre characteristics and contractile proteins will be discussed in further detail.

Myosin Protein Isoforms

Myosin, actin, tropomyosin and troponin have been described as the four predominant contractile proteins found in human skeletal muscle. However, researchers have focused primarily on the role of myosin with respect to properties of muscle contraction. Researchers have revealed that the myosin molecule is comprised of eighty-five percent myosin heavy chains (MHCs), the remainder is composed of myosin light chains (MLCs) (Whalen, 1985). The preponderance of specific isoforms of myosin have been used to further classify the fibre type found in muscle (Staron & Hikida, 1992). The use of electrophoresis to identify myosin heavy and light chains has further delineated (IIAB, IID etc.) basic fibre type subgroups beyond the four subtypes described earlier (I, IIa, IIb & IIc) (Booth & Thomason, 1991). Moreover, MHCs in adult muscle, have been considered major determinants of contractile characteristics (e.g. the speed with which cross-bridges can be moved from weak to strong binding states and vice versa; speed of fibre

contraction; time to peak tension; ATP turnover; and ATPase activity (Barany, 1967; Buchthal & Schmalbruch, 1980; Staron, Hikida & Hagerman, 1983a; 1983b; Staron & Pette, 1986; 1987a; 1987b; Viitasalo & Komi, 1978; Wagner & Giniger, 1981; Weeds, 1980; Whalen, 1985). Earlier, researchers reported that ST, FTa and FTb fibres were comprised of MHC isoform types I, IIa, and IIb respectively (Bar & Pette, 1988; Green, 1992). However, Klitgaard and coworkers (1990) have identified as many as three different MHC isoforms existing in a single fibre. These and similar findings (Biral, Betto, Danieli-Betto & Salviati, 1988; Green, 1992; Jolez & Streter, 1981; Pette, 1984) have revealed the limitations of histochemical analysis in the classification of fibre types. Fibres identified histochemically as slow have exhibited a variety of contractile proteins. For example, one population of histochemically classified fibres expressed only type I myosin heavy chains, whereas another fibre population expressed a hetergeneous mixture of myosin heavy chain isoforms. Thus, where no histochemical change in fibre type has been detected in response to training, the increase in a particular myofibrillar protein isoform identified by electrophoretic means in combination with conventional histochemistry may more accurately represent the transitional state of a fibre. Moreover, the presence of 'hybrid' fibres expressing both slow and fast isoforms may have also indicated a transitional state of the muscle fibre. According to Staron & Hikida (1992) care must be taken when fibre types are delineated using ATPase histochemistry. In trained muscle in particular, small amounts of MHCIIa have been found in histochemically classified Type IIB fibres. Green (1992) suggested that commonly used nomenclatures (primarily derived from histochemical analysis; e.g. types I, IIa, IIb, IIc) to describe fibre diversity may neither reflect the spectrum of associated MHCs nor contractile characteristics.

A spectrum of MLCs has been identified: MLC1s, MLC1f, MLC2s, MLC2f, MLC3f (Billeter, Heizmann, Howald & Jenny, 1981; Green, 1992; Reiser, Moss, Giulian, & Greaser, 1985; Salviati, Betto & Danieli-Betto, 1982; Staron & Pette, 1987a; 1987b; Swynghedauw, 1986). A histochemically typed fibre has been shown to express different proportions of fast and slow MLC isoforms in different muscles (Danieli-Betto, Betto & Midrio, 1990; Sweeny, Kushmerick, Maberchi, Sreter & Gergely, 1988). However, the impact of MLC isoforms on muscle contraction has been unclear as the role of MLC in muscle contraction has yet to be fully explained (Abernethy et al. 1993). Wada et al. (1990), reported the coincidental expression of particular MHC and MLC isoforms in human skeletal muscle. Type I fibres appeared to express various amounts of fast MLC in addition to slow MLC. Furthermore, the authors suggested that the heavy chain isoform MHCIIa, was favourably associated with MLC1f, whereas, MHCIIb was favourably associated with MLC3f. These more subtle changes in contractile protein isoforms may influence the contractile characteristics and macroscopically, the production of force (Booth & Thomason, 1991). Abernethy et al. (1993) recommended that in addition to histochemical analysis, determination of MHC and MLC isoform composition will facilitate detection of changes in contractile character in response to training. The authors suggested that biochemical analysis of contractile proteins may be particularly useful in identifying transitional states in fibres, commonly associated with a response to acute resistance training (Abernethy et al. 1993).

Part B: Response of skeletal muscle to resistance training

Muscle cross sectional area

Resistance (strength) training has been described as a form of exercise which elicits relatively low-frequency muscular contractions with maximal force and long recovery periods. This has been in contrast to aerobic type training (i.e., long distance running) where a high number of contractions were elicited with a moderate force and little recovery (Fleck & Kramer, 1987). Strength training has been shown to increase muscle volume that corresponds to a larger cross-sectional area of the muscle (Booth & Thomason, 1991; Maughan, 1984). This overall enlargement could have been produced by fibre hypertrophy, fibre hyperplasia (increase in fibre number) and/or increments in interfibrillar connective tissue (Abernethy et al. 1993). Regardless of the mechanism, muscle hypertrophy has been described as an important adaptation to resistance training (Abernethy et al. 1993). However, Sale, Marten and Moroz (1992) observed muscle hypertrophy without increased isometric strength after weight training. Thus, the extent to which muscle hypertrophy contributes to changes in strength remains an issue of contention among researchers.

Fibre hypertrophy

Overall muscle hypertrophy may be due to an increase in the myofibrillar content of the muscle fibres. Alway, MacDougall, Sale, Sutton and McComas (1988) demonstrated that resistance training resulted in an increase lipid and contractile protein content with a proportionate growth in the sarcoplasmic reticulum. Thus, the increase in strength associated with muscle fibre

hypertrophy was believed to result from an increase in fibre size.

Muscle fibre area has been shown to vary between trained states. However, remarkable similarities in fibre area have been observed between fibre types and genders. In untrained animals, ST fibres were significantly smaller than FT fibres, whereas, in untrained humans, ST and FT fibres were similar in size (Thayer, et al., 1993). The cross-sectional area of ST fibres in the VLM in untrained humans ranged from 2000 um^2 to 4200 um^2 and 1700 um^2 to 5200 um^2 in FT fibres (Johnson et al. 1973). However, following resistance training ST fibres were as large as 10,100 um^2 and FT fibres as large as 14,500 um^2 in adult males (Tesch & Karlsson, 1985). Conversely, endurance (aerobic type) training in animals has resulted in a decrease in muscle fibre size (Thayer et al. 1993). In humans, ST fibre size has been unchanged, selectively increased or selectively decreased following endurance training (Edstrom & Grimby, 1986; Gollnick, et al. 1973; Kuzon, et al. 1990; Larsson & Ansved, 1985; Simoneau et al. 1985). Furthermore, some researchers have postulated that fibre diameter may be genetically determined as neither long-term endurance training or detraining resulted in a change in fibre diameter (Larsson & Ansved, 1985). How then, can this discrepancy between findings in studies of animals and those of humans be explained? Fibre area changes in response to endurance training observed in animals, and not in humans, may have reflected the high intensity training programs conducted for an extended duration (12 hr/day) in the animal studies (Pette, 1984; Gonyea & Bonde-Peterson, 1978). Researchers have suggested that it is unlikely that humans could endure relatively similar training regimens capable of producing analogous alterations (McDonagh & Davies, 1984). In spite of conflicting results, there still exists sufficient evidence to support an increase in fibre diameter with resistance training.

Many investigations of resistance trained athletes have revealed significant hypertrophy of both FT and ST fibres (Alway, Grumbt, Stray-Gundersen & Gonyea, 1992; Bell & Jacobs, 1989; MacDougall, Sale , Alway & Sutton, 1984; 1982, Schantz, Randall-Fox, Hutchinson, Tyden & Astrand, 1983). However, the cross-sectional area of fibres has not always been found to be significantly different between resistance trained people and controls (Larsson & Tesch, 1986; MacDougall et al. 1982; Tesch & Larsson, 1982). Studies of humans have been performed to observe the rates of skeletal muscle enlargement during heavy-resistance training. Some authorities have suggested that the process of fast-twitch fibre hypertrophy in response to training may be complete within months rather than years (MacDougall et al. 1982). MacDougall and coworkers (1982) compared individuals with extensive (group A, 3-14 years) history of resistance training with a group of individuals who were resistance trained over a shorter duration (group B, 6 months). Although gross muscle hypertrophy, measured by arm girth differed significantly ($P < 0.05$) (means are presented and +/- standard deviations in parenthesis) between groups, fibre areas did not.

Group	Arm girth (cm)	FT fibre area (um^2)	ST fibre area (um^2)
Experienced (3-14yrs)	42.8	7870 (1110)	4770 (1080)
Recent (6 months)	33.7	7680 (2260)	5470 (901)

These data raise interesting questions regarding the role of fibre hypertrophy in gross muscle hypertrophy. The observation of larger arm girths in the bodybuilders in spite of similar fibre areas may have been a consequence of one or more of four possible mechanisms: 1) hyperplasia; 2) a greater number of fibres overall (sport self-selection); 3) an increased number of regenerating (immature) fibres, thereby reducing the mean fibre area; and/or 4) larger

intramuscular lipid stores in experienced group. However, as described earlier, the limitations associated with biopsy sampling make conclusive identification of these mechanisms impossible.

Alway et al. (1992) suggested that the disparity between relative arm girth and fibre area could have been a consequence of an upper limit to which FT fibres can hypertrophy. However, Abernethy et al. (1993) suggested that analysis of the same data, utilizing effect size (ES) techniques revealed significant differences in fibre area of ST fibres (although not in FT fibres). In a similar study, MacDougall et al. (1992) reported significant differences between elite and intermediate bodybuilders (ES = 1.26) in mean fibre area. Intuitively, an upper limit to muscle fibre hypertrophy seems logical, however, the time course for attaining this limit has not been clear, as studies have used small samples which may not truly represent the population (Abernethy et al. 1993).

The time course of fibre hypertrophy in response to resistance training has been difficult to assess due to genetic factors, intensity, frequency, and duration of programs (Thayer et al. 1993). Many studies have examined the effects of resistance training over the course of six to ten weeks (Coyle et al., 1981; Dons, Bollerup, Bonde-Peterson & Hancke, 1979; Houston et al., 1983; Lesmes, Costill, Coyle & Fink, 1978; Thortensson & Karlsson, 1976) and these studies have primarily reported an increase in strength and FT fibre area. Similar resistance training programs of longer duration (16 to 24 weeks) have revealed hypertrophy in FT fibres followed by, to a lesser extent, hypertrophy in ST fibres (Hakkinen, Komi & Tesch, 1981; MacDougall, Sale & Moroz, 1979).

Booth and Thomason (1991) reported that strength trained humans showed a 27% increase in the cross-sectional area of the FT fibres and no change in the cross-sectional area of

slow twitch (ST) fibres. Similar differences in ST and FT muscle fibre cross-sectional area have also been demonstrated in animal experiments. Rodents participated in a weight training program and it was observed that the FT glycolytic fibres experienced hypertrophy to a greater extent than the FT oxidative fibres and the ST fibres (Goldspink & Ward, 1979). McDonagh and Davies (1984) attributed the greater enlargement of FT fibres compared to ST fibres in response to resistance training to the fact that this form of training, which required maximal effort for a relatively short duration, recruited FT motor units to a greater extent than during normal physical activity or endurance training.

Detraining and/or immobilization of a muscle has been observed to return fibre size to its pretraining state regardless of fibre type or training stimulus (Larsson & Ansved, 1985). Decrements in strength and fibre area have been shown to be associated with detraining (Hakkinen et al. 1981; MacDougall, Elder, Sale, Moroz & Sutton, 1980). While both major fibre types decreased in size, the process of detraining appeared to result in a sequential reversal of fibre adaptation to training. Atrophy was greater in FT fibres (ES = 2.44) than ST fibres (ES = 1.24) (Hakkinen et al. 1981). Moreover, a decrease in relative strength was significantly correlated to reductions in relative area of FT fibres ($r = -0.082$) (MacDougall et al. 1980). Some studies which employed 8 weeks of resistance training reported that the training effects persisted over 8 weeks of detraining (Weir, Housh, Housh, & Weir, 1995). However, the time course of the atrophic changes associated with detraining have not been conclusively established (Thayer et al. 1993).

In summary, fibre hypertrophy may have accounted, to some extent for both increases in muscle cross-sectional area and strength (Abernethy et al. 1993). However, the same authors

cautioned that the low coefficients of determination suggested other factors (genetic, hyperplasia, motoneuronal changes etc.) may be involved in the development of strength in response to resistance training.

Variations in Fibre Number

The extensive muscle hypertrophy observed in bodybuilders (MacDougall et al., 1984; Schantz et al., 1983) and the absence of fibre hypertrophy reported in some investigations (Hakkinen & Komi, 1980; Larsson & Tesch, 1986) have been important observations among researchers (Abernethy et al. 1993). Abernethy and colleagues (1993) suggested that success in the sport of bodybuilding may have required a greater number of muscle fibres as a consequence of genetic endowment. However, knowledge regarding the number of muscle fibres at birth in humans has been limited. Due to the fact that in order to analyze cross-sections of whole human muscle, only necrospy material could be sectioned (Lexell, 1993), researchers have been forced to speculate that two factors may have contributed to variations in fibre number: genetic factors and hyperplasia (increase in the number of fibres) (Abernethy et al., 1993).

Research studies which have examined inter-individual differences in fibre number due to genetic endowment have reported equivocal findings (Abernethy et al. 1993). Investigations which used necrospy material have reported significant inter-individual differences in fibre number in humans (Etemadi & Husseini, 1968; Lexell et al., 1983; Lexell, 1993; Sjostrom, Lexell, Eriksson & Taylor, 1991). However, other researchers (Haggmark, Jansson & Svane, 1978; Schantz et al., 1983; MacDougall et al., 1984) have reported that the mean number of fibres was similar for trained and untrained individuals. Abernethy et al. (1993) suggested that both groups

of researchers with their contrasting results have limitations in their studies. The former group, which identified differences between individuals, used small samples whereas, the latter group's findings may have been a function of method, rather than an absence of inter-individual differences. Fibre number was estimated using mean fibre area from biopsy samples and extrapolated to the entire muscle cross-section using computer assisted tomography (CAT). Gonyea, Sale, Gonyea & Mikesky (1986) have criticised this method as it fails to detect fibre pennations and changes in fibre area along the length of the fibre or depth of the muscle (Gollnick, Timson, Moore & Riedy, 1981; Lexell et al. 1983). Thus, variation in fibre number due to genetic endowment has to date not been resolved.

The issue regarding the possibility of hyperplasia of muscle fibres in response to training has been a controversial topic (Thayer et al. 1993). It has been impossible to directly assess any change in fibre number in humans (Abernethy et al. 1993). Direct measurement of fibre number has been investigated in animal studies, and indirectly in human studies (e.g., satellite cell activity and single fibre electromyography (Appell, Forsberg, 1988; Gollnick et al. 1981; Gonyea et al. 1986; McCormick & Thomas, 1992; Larsson & Tesch, 1986). Speculation regarding the issues of fibre hypertrophy and hyperplasia in human muscle has been derived from animal models (Gonyea 1980; Gonyea & Blondes-Peterson, 1978; Ho et al. 1980). Ideally, animal training models would be directly comparable to human models. Three important considerations for both models are response topography (i.e., training procedures); level of muscle hypertrophy; and nature and level of skeletal muscle fibre adaptations (Timson, 1990). For example, animal models have employed one of three approaches: stretch hypertrophy, compensatory hypertrophy and exercise induced hypertrophy, none of which mirror human training and/or adaptations (Timson,

1990). Thus, researchers have recommended caution when drawing conclusions from animal models and applying them to the human situation (Abernethy et al. 1993).

In well controlled (unilateral limb training, contralateral limb control) animal studies where every fibre was counted, no difference between limbs in fibre number was reported in response to resistance training (Gollnick et al., 1981a; Gollnick, Parsons, Riedy & Timson, 1983). However, researchers conducting two separate studies of rodents which employed more rigorous response topography have reported 8.5 and 14% hyperplasia in the hindlimb muscles of rats, respectively (Gonyea et al. 1986; Tamaki, Uchiyama & Nakano, 1992). Therefore, the use of a biopsy/CAT scan estimations by earlier researchers may have failed to recognize this subtle change due to the modest increase in gross muscle parameters (Abernethy et al. 1993). Thus, Abernethy et al. (1993) suggested that the intensity of the response topography used to induce muscle hypertrophy may have determined the occurrence of hyperplasia. Larsson and Tesch (1986), utilizing single fibre electromyography, made the observation that fibre hyperplasia in human muscle only becomes a factor following intensive and prolonged (> 10 yrs.) training. This advanced the possibility that hyperplasia may only occur when the training stimulus exceeds a threshold level of intensity and/or duration. Thus, a complete understanding of the issues regarding hyperplasia has yet to be fully elucidated.

Satellite Cells in Skeletal Muscle

Satellite cells have been described as the stem cells (Mauro, 1961) or myogenic cells of postnatal skeletal muscle (Mazanet & Franzini-Armstrong, 1986). These cells were first described based on their role as the source of nuclei in muscles of growing rats (Moss & Leblond,

1971). However, satellite cells were unlike myonuclei as satellite cells retained their mitotic ability (McCormick & Thomas, 1992). As myonuclei were postmitotic, satellite cells were activated during muscle hypertrophy (Appell et al., 1988). According to Appell, and coworkers (1988), the relatively small satellite cells fuse to the adjacent mature (parent) muscle fibres and this movement of satellite cells has been described in hypertrophic muscle tissue. The authors stated that the relation between number of nuclei and volume of cytoplasm is kept constant within the cell, within certain limits of hypertrophy, thus increases in cell volume (associated with hypertrophy) required concomitant increases in nuclear number. Consequently, newly activated satellite cells become fully fused nuclei within the parent fibre; a process that has been demonstrated in growing myofibres (McCormick & Thomas, 1992). However, in studies of animals, as growth stops with older age, myonuclear population stabilized and satellite cells become mitotically quiescent (Schultz, Gibson & Champion, 1978).

Further research revealed a second role for satellite cells which made use of their ability to divide. Though the ability of skeletal muscle to regenerate has been well established (Alameddine, Dehaupas & Fardeau, 1989), the mechanisms of regeneration are not fully understood. However, it has been shown that satellite cells are employed in the regeneration of muscle tissue in rodents (Snow, 1977) and in myopathic human subjects (Schmalbruch, 1986). In a similar investigation, Appell (1983) described the possibility that satellite cells may be responsible for hyperplasia in skeletal muscle. The satellite cells 'may proliferate to grow to myoblasts and eventually form myotubes which may grow to new muscle fibres' (Appell et al., 1988). However, these nascent muscle fibres may have only replaced those in need of regeneration following tissue damage and/or hypertrophy (Abernethy et al., 1993). Therefore, satellite cells may have served to

maintain the number of fibres rather than contribute to hyperplasia. Furthermore, Appell (1990) suggested that the effects of hyperplasia, as a consequence of satellite cell contribution, on total muscle cross-sectional area appears small.

In summary, inter-individual variation in fibre number for a given muscle has been supported by some evidence in post-mortem investigations (Lexell, 1983; Lexell & Downham, 1991). Variations in fibre number as a consequence of hyperplasia have occurred in some animal studies which employed resistance training with a high response topography (Gonyea et al. 1986; Tamaki et al., 1992). As well, indirect assessment of hyperplasia in humans has been linked to satellite cell activity (Appell, 1990). However, animal models and indirect measures limit the applicability to the human situation (Timson, 1990). In a review of the topic, Abernethy and coworkers (1993) suggested that hyperplasia may occur under certain conditions (as yet not clearly defined) though its effects on the cross-sectional area of muscle appear to be small, and appears to be related to the duration and intensity of the training stimulus.

Unilateral training

There is conflicting evidence regarding the efficacy of resistance training programs for increasing strength in the trained and contralateral limb(s) (Housh & Housh, 1993). Training studies have employed a unilateral limb approach in attempt to control for physical activity beyond the training intervention (Housh, Housh, Johnson & Wei-Kom, 1992). In these training studies the contralateral limb acted as a control (Houston et al. 1983; Krotkiewski, Aniansson, Grimby, Bjorntorp & Sjostrom, 1979). Although anthropometric measures combined with muscle biopsies have been used in previous research on unilateral resistance training (Coyle et al. 1981;

Krotkeiwski et al. 1979) these techniques have been criticized on two accounts. First, precisely identifying landmarks for repeated anthropometric measurements has been described as difficult. Second, muscle biopsy techniques have been invasive and although useful for certain research questions (i.e. cell hypertrophy) may not have presented a representative sample of all muscles or muscles within a group (Housh et al. 1992). Thus, recent research has employed the use of magnetic resonance imaging (MRI) for the analysis of muscle cross-sectional area (Housh et al., 1992) and has allowed researchers to distinguish among tissues and muscle groups. The effects of training on skeletal muscle have been recorded more precisely using this technique in two ways: preferential hypertrophy of individual muscles within a muscle group; and hypertrophy at a particular location along the length of a particular muscle (Housh et al., 1992). These authors suggested that the use of MRI would help to clarify the mechanisms underlying the cross-training phenomenon that occurs in the contralateral limb. However, MRI analysis was useful in precisely identifying the outcomes rather than the mechanisms of cross-training on muscle CSA. Discrepancies in the results with studies of cross training effect may have been a consequence of differences in accuracy of the analytical tools (Housh et al., 1992).

While examining different portions of the leg muscles, a group of researchers (Narci et al., 1989) reported preferential hypertrophy of the vastus intermedius (VI) at the proximal one-third of the femur and the rectus femoris (RF) at the midfemur level only, when the dominant thigh was trained. Housh et al. (1992) employed a similar training protocol and found increases in the CSA of the RF at midfemur, proximal and distal levels of the muscle, while the vastus lateralis (VL) and the VI increased in the midfemur level only. The authors speculated that the discrepancy between the two studies could be explained by the larger response to the training stimulus found

in the non-dominant limb which was trained in the latter study. Following eight weeks of isokinetic leg extension training in subjects, Narici et al (1989) reported a preferential hypertrophy of the VM and the VI compared to RF and VL. The latter two muscles also had 30 and 60 % less activation respectively. This finding may have important implications for studies which rely on muscle biopsy analysis. Since the VL has been a common site for biopsy and following concentric knee extension training, the relatively low level of activation in the VL may have also limited the amount of fibre hypertrophy in that particular muscle (Narici et al. 1989). Therefore, the effects of concentric isokinetic knee extension exercises on the muscles of the thigh may be underestimated using muscle samples from the VL.

Researchers have examined the effect of unilateral isokinetic training on the muscle CSA of the contralateral limb (Narici et al. 1989; Krotkiewski et al. 1989; and Housh et al. 1992). None of these studies reported a cross training effect on muscle CSA. However, ultrasound analysis of CSA employed by Krotkiewski et al. (1989) has been criticized because it was difficult to distinguish among tissues (Housh et al. 1992). Morevoer, in the investigation by Housh and coworkers (1992), conservative statistical analysis which utilized Bonferroni's statistical adjustment ($P > 0.0008$) may have accounted for failure to detect a cross training effect in measure of both CSA and strength. The most extensive increase in CSA in the study by Housh et al. (1992) was observed in the distal level of the RF (34.4%) muscle of the trained limb, which was statistically significantly ($P > 0.0008$). Moderate (though not statistically significantly) changes were reported in the contralateral limb in the same location of the same muscle (14.0%). A comparison of trained and contralateral VL muscles at the distal level revealed a 13.5 and 9.6% non-significant increase respectively. Similar changes were observed in measures of strength, as

the leg extensor muscles in the trained and untrained limbs experienced a 11.2 and 6.7 % non-significant increases, respectively. The authors speculated that longer period of training may have resulted in statistically significant increases in strength and CSA on the contralateral side. This effect may have been more noticeable with less conservative statistical procedures. Thus, a trend (although not statistically significant) toward increased muscle CSA and strength on the contralateral side of the body suggested some cross training effect as a result of unilateral concentric isokinetic training (Housh et al. 1992).

Increases in strength in the contralateral limb have been reported. Houston et al. (1983) described an improved strength performance (without fibre hypertrophy) in the contralateral limb. Neural adaptations accounted for the strength gains. Similarly, Housh and Housh (1993) observed significant increases in concentric peak torque outputs at different velocities. Hellebrandt, Parrish and Houtz (1947) proposed two possible mechanisms to explain the cross training effect: diffusion of motor impulses to the contralateral side of the body; and contraction of the musculature on the contralateral side of the body to maintain balance and assume the proper position for the unilateral exercises.

Few studies have investigated unilateral resistance training in the elderly. A study by Grimby et al. (1992) examined the effects of resistance training in 78 to 84 year old men. The right quadriceps muscle was trained on an isokinetic dynamometer. However, the study by Grimby and coworkers (1992) was unique as the subjects were highly active for their age. Previous data revealed that in the four years previous to the study they had experienced, on average, a 30% increase in the fibre area of the vastus lateralis, with however, no significant increase in muscle strength. Data were established from an earlier study on the same subjects and

the intent of the later investigation was to analyse whether further systematic muscle training could increase muscle strength and volume. Results indicated a significant increase in integrated electromyographic (EMG) activity in the contralateral limb. However, no significant change in strength was observed in the contralateral limb. A cross over effect comparison of fibre area and proportion was not possible as biopsy sampling was confined to the trained limb. In another study, Hicks et al. (1991) examined muscle excitability and twitch potentiation following unilateral strength training in the elderly. Both measures improved, but the effects on the muscle fibres were not examined. Thus, a unique (previously trained in the former study) and limited subject pool and limited comparison between trained and contralateral limbs limit the usefulness of these findings in attempting to assess the effects of unilateral resistance training on both limbs of the lower body.

PART C: Changes in muscle in response to aging

Loss of muscular strength

Doherty et al. (1993) reported that the loss of voluntary muscular strength did not become apparent until after the age of 60 years. The curvilinear reduction in isokinetic strength appeared to be more pronounced in women (Porter et al., 1995). In particular healthy people in the seventh and eighth decades scored on average 20 to 40% less during isometric and concentric strength tests than young adults (Porter et al. 1995; Larsson, Grimby & Karlsson, 1979). Porter, Myint, Kramer and Vandervoort (1994, p. 431) reported the following values presented in Table 1, for

concentric and eccentric strength (See page # 42) in Newton metres (N.m.) for isokinetic knee extension (90 °/s) in healthy older and younger men and women (means and +/- standard deviations in parenthesis):

Table 1: Isokinetic knee extension strength of young and old individuals

Group	n	Age (years)	Concentric	Eccentric
young men	28	26 (3)	204 (40)	233 (50)
young women	28	25 (3)	130 (24)	162 (37)
old men	25	71 (7)	119 (36)	175 (47)
old women	26	73 (6)	61 (16)	100 (27)

Significant main effects were found for age, muscle action and an interaction between age and muscle action. These data suggested that eccentric strength declines less with aging than concentric strength. The mechanisms for these discrepancies in decline of force production between different muscle actions is not understood.

Stanely & Taylor (1993) reported that sexagenarian women were able to perform concentric isokinetic knee extensions at 180 °/s at 51% of the value achieved by their young adult female counterparts. Additionally, it has been reported that decrements in strength between young and old are less marked during isokinetic eccentric contractions than for concentric contractions. Vandervoort, Kramer and Wharram (1990) reported that slightly older women (66-89 years of age) performed 19% better on the eccentric condition (66 %) than on the concentric condition (47 %) at 90 °/s on the same type of exercise and comparison used in the Stanely and Taylor (1993) study. Notably, Poulin, Vandervoort, Paterson, Kramer and Cunningham (1992)

found virtually no difference (98% of young adult females) in values of eccentric isokinetic knee extension at 180 °/s, between older (60 -75 years) and young adult women. Longitudinal studies of knee muscles report higher values on strength tests than cross sectional studies of comparable subjects (Aniansson, Hedberg, Henning & Grimby, 1986). However, the authors cautioned that such results may equally reflect biological superiority allowing a longer lifespan as much as they may reflect an adaptive lifestyle. Thus, the interaction of genetic predisposition and degree of physical activity appeared to play a role in maintenance or loss of muscular strength in later years of life.

Loss of muscle volume and cross sectional area (CSA)

The decline in strength observed in the elderly has been attributed to a reduction in muscle CSA (Porter et al. 1995). Radiological imaging techniques have been used to reveal the age related progressive decline in muscle volume including: ultrasound (Young, Stokes & Crowe, 1984; Young, Stokes & Crowe, 1985); and CAT scan (Rice, Cunningham, Paterson & Lefcoe, 1989). Lexell, Taylor and Sjostrom (1988) reported the average CSA of the quadriceps muscles decreases from approximately 3750 mm^2 at age 20 to approximately 3000 mm^2 and 2000 mm^2 by ages 60 and 90 years respectively. In a review of this topic, Lexell (1993) stated that research results indicated a trend with reduction in muscle CSA as early as 25 years of age. By age 50 years, a 10% reduction in muscle CSA has been observed and thereafter the reduction accelerates, such that by age 80 years almost 50 % of the muscle CSA is lost.

Researchers have documented an increase in non-muscle tissue (i.e., fat and other connective tissues) within older muscle (Porter et al. 1995). Rice et al. (1989) compared young

and old subjects and found 27%, 45% and 81% more non-muscle tissue in the arm flexors, arm extensors and plantar flexors respectively. Overend, Cunningham, Paterson and Lefcoe (1992) reported an age related infiltration of non-muscle tissue of 59% in the human quadriceps and 127% in the human hamstrings. Porter et al. (1995) speculated that as a consequence of the increase in fat and connective tissue observed in senescence, the reduction in muscle contractile tissue may be greater than the actual reduction in CSA. In other words, tissue capable of producing contraction may have been reduced in a two fold manner. Both absolute (muscle CSA) and relative (% muscle tissue) contractile tissues were decreased in response to aging. Thus, a larger loss of muscle strength, than muscle CSA, should be expected. However, the age related reduction in CSA reported by Lexell (1993) was consistent with data from studies of muscle strength in men and women of different ages (Aniansson et al. 1986; Cunningham, Rechnitzer, Howard & Donner, 1987; Larsson et al. 1979; Poulin et al. 1992; Young et al. 1985).

In summary, research findings have shown that a reduction of muscle cross-sectional area takes place in response to aging; however, direct measures of living subjects have been difficult due to technical and ethical constraints (Porter et al. 1995).

Change in the fibre number and area

Following the report of extensive muscle hypotrophy and moderate fibre hypotrophy in response to aging, a loss in the number of fibres was proposed to explain the large reduction in muscle volume, and in particular, contractile tissue (Grimby & Saltin, 1983). Lexell et al. (1993) provided evidence which allowed the comparison of fibre area and number of fibres. The use of necrospy material revealed not only moderate reduction in fibre size, particularly in FT fibres

(approximately 4000 um^2, 3400 um^2 and 2800 um^2, respectively, at 20, 50 and 80 years of age) but also a substantial reduction in fibre number (approximately 6.25, 5.5, and 3.5 [x 10^5] respectively, at 20, 50 and 80 years of age). However, the authors also reported large inter-individual variability. Furthermore, as these data were derived from autopsied samples limited information was available regarding the representativeness of the sample to a typical population. Lexell et al (1983, p. 7) stated that 'the reduction in muscle volume with increasing age, at least up to the age of 70, is due to a reduction in the total number of fibres with no obvious reduction in fibre size.' However, a later study by Lexell (1988) employed a larger sample and revealed that both fibre size reduction and a decrease in fibre number contributed to observed age-related atrophy.

As mentioned earlier, there is general agreement that the cross-sectional areas of type II fibres are significantly reduced with aging, while those of type I are less affected (Aniansson, Grimby, Hedberg & Krotkiewski, 1981; Larsson, Sjodin & Karlsson, 1978; Lexell et al. 1988; Tomonaga, 1977). In particular, Tomonaga (1977) reported a 7% and 52% reduction in fibre size in ST and FT fibres respectively, in response to aging in 60 to 90 year old men and women. Using previously healthy individuals from 15 to 83 years of age in a post-mortem investigation, Lexell et al. (1988) reported a 1% and 29% decrease in ST and FT fibre size respectively.

Fibre arrangement

Extensive neuropathic changes are common in muscles of the elderly (Tomlinson, Walton and Rebeiz, 1969; Tomonaga, 1977). Stalberg (1982) and Stalberg et al. (1989) observed an

increase in average size of low threshold motor units in the muscle of the elderly. The authors postulated that these surviving motor units were a compensatory response to the overall decrease in the number of functional motor units which had been observed in electromyographical studies (Brown, 1972; Brown, Strong & Snow, 1988). Lexell (1993) had credited the changes in the neuromuscular system with a unique pattern of fibre arrangement found in the elderly. In a similar manner described earlier, Lexell and Downham (1991) analyzed necrospy material and reported a random arrangement of fibres in individuals aged 30 to 60 years. However, groupings of individual fibre types were noted in ages above 60 years, and this was elevated with increasing age. Clusters of 50 or more ST fibres were observed in individuals more than 70 years of age (Johnson, Polgar, Weightman & Appleton, 1973). Researchers have suggested that this clustering represented the effect of FT fibres becoming reinnervated by axonal sprouting of surviving adjacent slow motor units (Kuzon et al. 1990; Lexell et al. 1983). Changes in the nervous system may have had related effects on the distribution and proportion of fibre types in the muscles of the elderly (Thayer et al. 1993).

Motoneuronal Considerations in Skeletal Muscle

Liddell and Sherrington (1925) described the motor neuron as being the 'final common pathway' for the motor system, responsible for all skeletal muscle contractions. Motoneurons comprise a part of the motor unit. Motor units incorporate an alpha motor neuron with its cell body in the ventral horn of the spinal cord, a single motor axon, and all of the muscle fibres innervated by the axon (Burke, 1981). Muscle contractions, both voluntary and reflex, are governed by signals from higher brain centres, or inputs from the periphery which result in the

activation of motor units (Stuart & Enoka, 1983).

'The nature of the human motor system is such that it allows healthy individuals to generate muscle contractions ranging from the minute forces and precision necessary for executing fine motor skills, to the ballistic contractions required for execution of a sport skill or recovery from a potential fall. The ability to produce these intended motor outcomes is partially dependent on having a population of motor units varying widely in their sizes and functional characteristics, and the ability to appropriately excite or inhibit them to produce a desired muscle contraction. Therefore, it follows that any age related alteration in the numbers or functional properties of motor units in the pool to a given muscle group may have profound implications for muscle force production and its control' (Doherty et al., 1993, p. 338).

Animal Studies

Studies of the muscles of the rat hindlimb have revealed significant reductions of 40 to 75% in the estimated number of motor units (Caccia, Harris & Johnson 1979, Edstrom & Larsson 1987, Einsiedel & Luff 1992, Pettigrew & Gardiner 1987). Recent research has demonstrated that there may be a preferential degeneration of the largest motor units, with the largest innervation ratios, and the lowest oxidative capacities (Ishihara & Araki, 1988). The subsequent loss of these motor units in old age may have accounted for the reduction in the numbers of fast glycolytic muscle fibres in aged muscles with no apparent loss of slow oxidative or fast oxidative glycolytic muscle fibres observed by Ishihara and coworkers (1987).

According to Larsson & Edstrom (1986), the contractile speed of the motor unit is determined by the capacity of the sarcoplasmic reticulum for calcium release and uptake, and the composition of fast and slow isoforms of the myofibrillar proteins. Both slowing of the motor

unit and the presence of slow contractile properties may serve to prolong contraction time in the muscles of the elderly (Doherty et al., 1993).

Larsson (1982a), revealed that an aging neuromuscular system is marked by slowed movements, reduction in maximum strength and loss of fine motor coordination. Loss of motor control has been associated with the natural aging process leading to the reorganization and reinnervation of the neuromuscular system (Keen et al., 1994). After 4, 8 and 12 weeks of training, subjects have experienced an increase in volume and strength of the muscle trained (Keen et al., 1994). The authors suggested that the subjects' improved ability to sustain and control constant submaximal forces was not associated with the age-related changes in the distribution of motor unit forces, and instead could be attributed to training. It had been hypothesized that control of submaximal forces could have been improved with age in response to the change in the motor unit profile.

Fibre type grouping, fibre atrophy, and irregular fibre morphology have provided evidence of an ongoing denervation/reinnervation process whereby muscle fibres that have been denervated following loss of their neuromuscular contact were reinnervated by surviving motor neurons (Brown, 1984). Doherty et al. (1993) speculated that the process of reinnervation would fail to keep pace with the neurodegenerative process, and permanently denervated fibres were therefore lost. This observation by Doherty et al. (1993) is consistent with the observation of the infiltration of fat and connective tissue into areas of the muscle once occupied by contractile tissue (Lexell, 1993). Whether the contractile properties of the remaining motor units in the muscles of the elderly were modified by changes in the neuromuscular recruitment pattern, or whether motor neuron firing properties were modified to match these fibre characteristics has yet to be

established (Doherty et al. 1993).

In response to aging, a shift in the rat muscle motor unit profile has been demonstrated such that there was a selective loss of fast motor units and consequently, an increased proportion of slow motor units (Pettigrew & Noble, 1991). This shift in the profile could have been achieved by a loss of fast motor units, an increase in the number of slow motor units, and possibly, a transformation of existing motor units (Pettigrew & Noble, 1991, Noble & Pettigrew, 1989).

Motor reaction time (MRT) refers to the delay between activation of a muscle and the initiation of joint movement (Mero & Komi, 1990). This segment of the total reaction time has been considered to be independent of the activity of the central nervous system (Baylor & Spirduso, 1988). Thus, increases in MRT noted in the elderly (Ito, Nagasaki, Hashizume, Maruyama, & Nakamura, 1990) may be responsible for reduced ability to generate tension rapidly in skeletal muscle (Lewis & Brown, 1994).

Teravainen and Calne (1983) identified three possible causes for slowed skeletal muscle tension development in the elderly: slower rates of motor recruitment and nerve transmission, increased synaptic delays and slower action potential spread across muscle fibres. However, the possible causes proposed by Teravainen and Calne (1983) dealt only with the nervous system. Lewis and Brown (1994) suggested that changes in the mechanical properties and connective tissue in the muscles of the elderly may also contribute to slower rates of tension development. Muscles of the elderly have been associated with a reduction in the number of myofibrils and concentration of mitochondrial enzymes (McCarter, 1978). Consequently, production of adenosine 5' triphosphatase and acetylcholine was inhibited (Seeley, Stevens, & Tate, 1989). The same researchers have stated that acetylcholine is closely related to the production of action

potential in the postsynaptic terminal (Seeley et al. 1989). Thus, the enzymatic changes associated with aging may be the rate limiting step in muscle contraction (Lewis & Brown, 1994).

Irrespective of the fibre type and its functional capacity, the muscle of the elderly may be compromised predominantly by changes in the motor unit. Tomanoga (1977) suggested that the prevalence of atrophic muscle fibres in 'aged' muscle could be attributed to partial degradation of the peripheral nerves. This process of degeneration in the nervous system could have accounted for the apparent quantitative decrease in motor unit population described by Brown (1972). Therefore, with respect to changes in the nervous system and motor function with senescence, three possibilities exist: 1) motor unit populations decrease with age, 2) motor unit populations remain unchanged, however, changes in the nervous system render some units inoperative; or 3) motor unit populations remain unchanged, however, the size of the existing motor units is decreased (Guttman, 1977). In any event, motor unit alterations may result in delayed or decreased force production in the skeletal muscle of the elderly (Lewis & Brown, 1994). Such alterations have profound effects on the proportion and distribution of fibre types in aged human muscle (Lexell, 1993).

Proportion of fibre types

Aging has been shown to be accompanied by a decrease in the total number of muscle fibres and this loss of muscle fibres appeared to begin at approximately sixty years of age (Lexell et al., 1988). Researchers have indicated that a large decrease in muscle mass may be attributed to both the loss of muscle fibres and a decrease in their cross-sectional area (Yu, Masora & Murata, 1982). Furthermore, Larsson (1982b) suggested that the loss of muscle fibres may occur

due to a loss of motoneurons or as a result of degeneration of the muscle fibres.

A lower proportion of type II fibres has been found in 'aged' muscle as compared to younger humans (Larsson et al., 1979). Since type II fibres were predominantly used in producing rapid movements, having fewer of these fibres may have reduced the capacity of the aged to respond quickly (Lewis & Brown, 1994). However, a loss of Type II muscle fibres has been shown to result in a large increase in the proportion and strength of slow motor units with aging (Pettigrew & Gardiner, 1987). Changes in motor unit re-organization alter the fatigue resistance of fast motor units indicating a transition from a glycolytic to a more oxidative profile. This sequential transformation of motor units in aging may have occurred in the following manner IIb --> IIa --> IIc --> I (Pettigrew & Gardiner, 1987). The accumulated evidence supports a combination of a progressive neurogenic process and change in functional demand as the two major contributors to the age-related atrophy and the decline in motor function with increasing age (Lexell, 1993).

Aging and Contractile Properties

Increased time-to-peak tension and time-to-relaxation following evoked twitches have been observed extensively in elderly subjects (Davies, Thomas & White, 1986; Vandervoort & McComas, 1986; McDonagh et al. 1984; Lexell & Downham, 1991; Cupido, Hicks & Martin, 1992). Evidence has supported the contention that the slowed contraction stems from reduced proportional contribution of Type II fibres. For example, Vandervoort & McComas (1986) reported a more pronounced effect of age in the gastrocnemius muscle twitch than in the soleus muscle. The authors suggested that since the soleus was comprised of primarily ST fibres, loss of

FT fibres and subsequent slowed contraction would have been less noticeable.

In the same study, Vandervoort and McComas (1986) reported that twitch time increased in a linear fashion with increases in age. However, changes in muscle strength did not become apparent until the seventh decade of life. Some authors have suggested that an increased efficiency of the contraction of muscle occurs in the elderly as lower frequencies of nerve impulses are required to attain a given muscle tension or reach tetanic fusion (Davies et al., 1986; Galganski, Fuglevand & Enoka, 1993). Despite the relatively greater proportion of type I fibres available for force generation, and the expected increase in efficiency of muscle in the elderly, researchers (Porter et al., 1995) have reported no enhancement to fatigue resistance. Grimby et al. (1992) could not account for this observation but did speculate that the capacity of 'aged' muscle may not have been optimized due to lack of training. Furthermore, Hagberg et al. (1989) hypothesized that healthy, fit older subjects could experience less metabolic stress during a submaximal exercise bout than sedentary young adults.

Changes accompanying the aging process have been observed in contractile proteins (Edstrom & Larsson, 1987; Kanda & Hashizume, 1989). The evidence has supported a fast-to-slow conversion of myosin following partial reinnervation in a motor unit. Larsson et al. (1991) used monoclonal antibodies for identification of the MHC. Their study revealed an increase in the type IIX MHC isoform in the aged rat tibialis anterior muscles. Doherty et al. (1993) suggested that the IIX motor unit may represent a transitional motor unit type involved in an age related fast-to-slow conversion process. In summary, the slowed contraction and extended time to relaxation appeared to be the result of the re-organization of the motor unit pool. The anticipated resistance to fatigue associated with a higher prevalence of type I fibres has not been conclusively

demonstrated, and may only be possible in fit elderly subjects. Furthermore, changes in the types of functional motor neurons and contractile proteins appear to have deleterious effects on the contractile properties of aged skeletal muscle.

Part D: Resistance Training and the Elderly

Strength gains

Resistance (strength) training has been defined as progressive overload of the neuromuscular system using near maximal muscle contractions against high resistance (Porter et al. 1995). Moreover, its purpose has been described as a means to increase the ability to perform maximal contractions or increase muscle size. Resistance training has involved one or more commonly executed muscle actions: concentric (shortening), isometric or isoinertial (static), eccentric (lengthening), isotonic (constant load) and/or isokinetic (constant velocity).
From the functional perspective, lack of strength has been associated with an increased susceptibility to falls and fractures and a loss of independence in the elderly (Work, 1989; Whipple et al. 1987). Whipple and coworkers (1987) speculated that neuromuscular dysfunction in the elderly resulted in postural instability. Many researchers have proposed that resistance training may reduce the likelihood of encountering some of these adverse events associated with senescence (Dupler & Cortes, 1993; Judge, Whipple & Wolfson, 1994; Porter et al. 1995).

Although many researchers have attempted to use controls for learning and placebo effects, Porter and coworkers (1995) stated that resistance training studies have seldom been performed as rigorously controlled randomized trials for one of the following reasons: 1) the inability to totally blind the subjects to the treatment; 2) subjects have usually been volunteers and as a result study samples may not be representative; 3) the lack of blinding of the experimenters.

Moreover, the research design employed in these studies (and a lack of reliability analysis of the testing procedures) (Porter et al., 1995) has made it difficult to assess the contribution of exercise and training, as prior physical activity, genetic factors and the aging process itself may be implicated in the outcomes of training programs (Thayer et al. 1993). Furthermore, repeated baseline measures may not have entirely controlled for a possible learning effect associated with technical execution of the exercise. With these limitations in mind, the following table is presented which offers a summary of the improvements in muscle strength following high intensity dynamic training in older individuals.

Table 2 Recent studies on dynamic resistance training in older individuals***

Ref./yr	Sex	Age	n	muscle action	Duration sets/reps	strength gain.%@
A, '88	m	60-72	12	knee flex/ext	12 wks 3/8	227/107 MVC: 16/7
B, '89	m/f	70-79	23	chest press leg ext	26 wks 1/8 to 12	189
C, '90	m	60-70	14	elbow ext	12 wks 4/10	48
D, '90	m/f	86-96	10	knee ext	8 wks 3/8	174
E, '91	f	64-86	13	knee flex /leg press/ hip ext	12 wks 6/6	115/28/28
F, '91	m/f	66.3*	11	dorsiflex	12 wks 4/10-15	48, MVC:15
G, '92	m	78-84	9	knee ext con/ecc	25 sess. complex	con: 10 ecc: 19

H, '93	m/f	71-79	18	knee flex	12 wks 3/8-10	32
I, '93	m	50-70	11	up/lower body	16 wks 1-2/15	3rm:45 PT:32-55
J, '93	f	67.8*	18	up/lower body	24 wks 3/3-10	18-71
K, '93	m	65-78	10	elbow ext	26 wks 4/6-8	30, MVC: 20
L, '93	m	67.7*	5	elbow flex	12 wks 13**/8	PT: 23-50
M, '94	m/f	61-78	25	up/low body	30 wks 3/8	23-62
N, '94	m/f	72-98	100	hip/knee ext	10 wks 3/8	113

*Notes regarding table: flex= flexion; ext =extension; @ =1RM (one repetition maximum) unless otherwise noted; MVC= maximal voluntary contraction; PT = isokinetic peak torque; con =concentric; ecc= eccentric; *= only mean age available; **= 4 sets of isokinetic training and 3 sets of 3 free weight exercises; *** modified from Porter et al. (1995). ref = references. All strength gains were statistically significant. A= Frontera et al. (1988); B=Hagberg et al. (1989); C=Brown et al. (1990); D=Fiatarone et al. (1990); E=Charette et al.(1991); F=Hicks et al. (1991); G=Grimby et al.(1992); H=Judge et al. (1993); I=Menkes et al. (1993); J=Nichols et al. (1993); K=Rice, Cunningham, Peterson & Dickinson (1993); L=Roman et al. (1993); M=Pyka et al. (1994); Fiatarone et al. (1994).

Strength gains in the elderly in response to training programs have been critically influenced by the intensity of the program (Porter et al., 1995). Low intensity programs (Vandervoort, 1992) have shown gains of less than twenty percent. In comparison, high intensity (> 70% of 1RM) programs have resulted in increases of up to 227% in 1RM (Frontera et al., 1988, see table 2). Porter et al. (1995) stated that comparison was difficult between studies

because of the differences in the following variables: intensity; number of sets; number of repetitions; frequency of exercise sessions; duration of the program; muscle groups trained; type of testing and training; subjects' age; gender; and initial strength. Furthermore, other authorities have considered the following issues: representativeness of sample; learning effect; disease; genetic predisposition to the effects of aging as well as of training; age-related decline during the course of the program; cross -training effect (in some studies); and degree of physical activity during the course of the training program beyond that which was prescribed as part of the training regimen (Thayer et al. 1993; Housh and Housh, 1992; Porter et al. 1995; Grimby et al. 1992).

Strength gains reported for (dynamic) 1RM measures have been on average larger than those reported for (isometric) MVC (Sale, Martin & Moroz, 1992). Although some authors have stated that this discrecpancy may be due to the specificity of neural adaptations (Sale, 1988), others have questioned the use of 1RM as a measure of strength. Grimby et al. (1992) stated that due to biomechanical differences, and possible differences in velocity the 1RM test may not be the most appropriate measure of strength. Furthermore, according to Porter et al (1995) few studies had addressed the impact of eccentric testing and training in the elderly. Thus, differences in training type and testing modality appear to have limited the comparability of results from the already limited number of studies of resistance training in the elderly.

Resistance training in older people has been shown to produce significant gains in strength but the contribution of muscle hypertrophy to strength gain in the elderly has not been clear (Larsson, 1982). Dupler and Cortes (1993) examined the effects of a 12 week, whole body resistive training regimen in the elderly and the subjects experienced a significant increase in total maximum weight lifted (TMWL). Total maximum weight lifted was calculated using the sum of

weight lifted for each exercise performed. The 72.2 and 66.1% increase in the TMWL, in females and males respectively, provided support for the trainability of elderly subjects. Similar results have been demonstrated in an applied setting, where Nichols, Hitzelberger, Sherman and Patterson (1995) measured selected functional abilities or life skills which require strength. With moderate resistance training, two sessions per week, the researchers were able to demonstrate an increase in muscular strength. Spirduso and Clifford (1978) suggested that physical activity may attenuate the decrements in motor performance commonly associated with senescent muscle. Their study examined the motor performance capabilities of active and sedentary elderly persons, and they reported higher performance capabilities in active subjects. However, Lewis and Brown (1994) cautioned that such findings may be attributed, equally so, to genetics. Genetically acquired motor abilities may have facilitated not only prolonged participation in a particular sport but also, reduced the effects of aging on motor performance.

Mechanisms involved in changes in strength

The mechanism of strength gains in older individuals is not well understood. Blimkie (1992) presented several factors which may contribute to strength gains following high intensity resistance training. These factors include: changes in muscle morphology; muscle biochemistry; muscle and connective tissue biomechanics; central nervous system activation; motor skill coordination and psychological drive. Earlier research by Moritani and deVries (1980) reported increases in strength and neural activity with no change in muscle CSA. As a consequence, these authors attributed strength gains in the elderly to neural factors alone. Porter et al. (1995) stated that limitations of analysis (anthropometry) may have accounted for the discrepancy between this

study and more recent investigations.

Recent studies have revealed an increase in muscle size which has been shown at both the macroscopic and microscopic levels (Frontera et al. 1988; Roman et al. 1993; Grimby et al., 1992). An examination of the relationship between fibre type distribution and strength in the elderly has provided contradictory evidence in the reported literature. Significant hypertrophy of both Type I and Type II fibres has been shown (Frontera et al., 1988). Other investigators have shown either greater hypertrophy of Type II fibres or similar hypertrophy of both Type I and Type II fibres (MacDougall et al., 1979). However, Aniansson and Gustafsson (1981) have reported no change in Type IIa or Type IIb fibre area with a decrease in total Type I fibre area in 69-74 year old men. Pyka et al. (1994) reported a 48% and 62% increase in type I and type 2 fibres respectively. Porter et al. (1995) revealed a tendency for greater hypertrophy of type 2 fibres, although this conclusion remains tentative. Yarasheski, Zachwieja and Bier (1993) studied the acute effects of resistance exercise on muscle protein synthesis rate in young and elderly men and women. The results indicated a similar rate of protein synthesis in young and old subjects. In another study, muscle hypertrophy in response to strength training in the elderly was accompanied by an increase in the rate of actomyosin protein turnover (Frontera et al., 1988). This evidence revealed that 'aged' human muscle is capable of adapting to increased short term physical demands. However, Porter and coworkers (1995) stated that long term changes in muscle hypertrophy had yet to be clearly defined. Furthermore, the same authors stated that increases in fibre diameter were relatively small compared to the large changes in 1RM. In summary, the capacity for an increase in muscle mass appears to be retained in old age and the improvement in strength seen in the elderly can be partially explained by muscle hypertrophy.

Part E Stress Proteins

Introduction

The heat shock response was first observed in Drosophila busckii following exposure to elevated temperatures (Ritossa, 1962). Decades passed before this important discovery was investigated further. To date, all studied organisms have demonstrated some variation in this response to heat and a number of other stressors. The heat shock response is described most simply as the rapid and preferential transcription and translation of a set of proteins known as heat shock (HSP) or stress proteins (Morimoto, Tissieres & Georgopoulos, 1990). A subset of the stress proteins has been shown to be induced under conditions of low intracellular glucose, and hence have been termed glucose regulated proteins (GRP). Many other stressors have also been shown to cause the same or a similar response, and the reaction has also more appropriately been termed the stress response (SR)(Hightower & White, 1981).

The observation that most of the stressors that induce a stress response are proteotoxic, led to the theory that the stress proteins play a role in the segregation and renaturation or removal of denatured proteins from the cell (Hightower, 1980). Subsequently, it was found that the injection of amino acid analogues (Goff and Goldberg, 1987; Kelley and Schlesinger, 1987) or denatured protein (Anathan, Goldberg, & Voellmy, 1986) was sufficient to induce the stress response, lending support to this theory. Some stress proteins have also been referred to as 'molecular chaperones' because of their involvement in protein folding and sorting, in the assembly of protein complexes as well as in the binding of denatured proteins (Chemnitius et al., 1993; Craig, Weissman & Horwich, 1994; Hartl, Hlodan & Langer, 1994).

Many of the stress proteins are also present to a varying extent in the unstressed cell,

suggesting a role in normal cellular function which becomes more significant following episodes of stress. Cells exhibit a greater degree of HSP expression during growth periods of the cell cycle (Milarski & Morimoto 1986; Wu & Morimoto, 1985), as well as when infected with lytic viruses, when viral protein synthesis is very high (Nevins, 1982). Two modes of regulation for increased HSP synthesis have therefore been suggested and occurs concomitantly with increased levels of protein synthesis and assembly or with an accumulation of abnormally folded proteins in the cell, as during stress (Welch, 1992). Both of these result in the transient exposure of hydrophobic amino acid side chains to the aqueous environment in the cytosol. One proposed HSP function is to stabilize these hydrophobic segments until other cellular processes can be recruited to fold them into their native state (Lewis and Pelham, 1985; Pelham, 1986).

The stress proteins can be grouped into families of varying molecular weights (in kilodaltons) whose members generally seem to have similar structures and function. In mammalian cells the groups are as follows: Ubiquitin (HSP 8); HSP 28; 60; 70; 90; and 110. Other classes of HSPs are known to exist in bacterial and plant cells but with analogues either undiscovered or not present in mammalian tissue. The HSP 70 family is particularly relevant to this review because of its induction following exercise (Locke & Noble, 1995).

The HSP 70 Family

Among the most abundant stress proteins in mammalian cells are the members of the 70 kDa family. In the rat the following members of this family have been identified and their genes cloned: a constitutively expressed 73 kDa heat shock cognate (HSC 73) protein (Sorger and Pelham, 1987), a stress inducible form (HSP 72) of approximately 72 kDa (Walter, Rauh &

Gunther 1994), and two glucose regulated proteins: GRP 75; (Massa et al., 1995; Webster Naylor, Hartman, Hoj & Hoogenraad, 1994) and GRP 78 (Munro and Pelham, 1986). A fifth HSP 70 isoform, HST 70, has been identified and hitherto, its expression has only been observed in the testes (Wisniewski, Kordula, & Krawczyk, 1990). Of all the stress proteins studied to date, HSP 72, of the HSP 70 family, is considered the stress inducible isoform (Locke, Noble & Atkinson, 1990). Recent research has focussed on the role of HSP 72 in response to acute exercise stress (Puntschart, Vogt, Widmer, Hoppeler & Billeter, 1996) and exercise training (Kelly, Tiddus, Houston & Noble, 1996). Due to the role of HSP 72 in exercise stress, the characteristics of this isoform are of particular interest.

The protective effect of elevated levels of HSP 72 on a variety of cellular insults including the presence of amino acid analogues (Li and Laszlo, 1985; Hightower, 1980), heat shock (Li et al., 1991; Li and Laszlo, 1985; Li, 1985), and ischemia of cardiac muscle (Karmazyn, Mailer, & Currie, 1990; Currie & White, 1983; Locke, Tanguay, Klabunde & Ianuzzo 1995) has been well established. Cells or tissues with elevated levels of HSP 72 were shown to either survive better or to recover more quickly from these stresses than cells with normal or reduced amounts of HSP 72. In addition, cells microinjected with antibodies against the HSP 70 proteins have been shown to survive at a lower rate following heat shock than normal cells or cells injected with antibodies against other cellular proteins (Riabowol, Mizzen, & Welch, 1988).

Contractile Proteins and Expression of HSP 72

A relationship between predominantly slow/type I muscles, such as the soleus and constitutive expression of HSP 72 and HSP 73 has been established (Locke, Noble, & Atkinson, 1991). Although muscles expressing a predominance of Type I fibres generally have a greater oxidative capacity (Thayer et al., 1993), the expression of HSP 72 was unrelated to this characteristic (Locke, Atkinson, Tanguay & Noble, 1994). In the same study, shifts in the percentage of type I fibres following either compensatory hypertrophy of the plantaris or thyroid hormone treatment were mirrored by increases and decreases in the expression of HSP 72, respectively. It was concluded that the expression of HSP 72 appeared to be related to the Type I MHC content of the muscle. However, the HSP 72: type I MHC relationship has also been shown to be dissociated in chronically stimulated tibialis anterior muscle of the rat, indicating that expression of the two genes is probably regulated differently (Ornatsky, Connor, & Hood, 1995).

In two studies of exercising humans, an increased expression of HSP 72 has been observed in leukocytes (Ryan, Gisolfi & Moseley, 1991) but not in skeletal muscle following acute exercise stress (Puntschart et al., 1996). However, increased transcription of HSP 72 mRNA was observed in the latter study. In a recent study of rodents, subjects were pre-trained so that they would be familiar with the exercise protocol, have reduced temperature elevations and lesser disruption of cellular homeostasis (Kelly et al., 1996). The post-training accommodations and subsequent exercise protocol were intended to allow a simulation of chronic exercise training, rather than a progressive overload. It has been speculated that progressive overload or relative increases in intensity have contributed to HSP 72 expression following exercise rather than

routine exercise (Locke, in press). Results indicated an increased expression of HSP 72 following a routine training protocol. Thus, it may be speculated that although the stress response is thought to be transient, higher levels of HSP 72 may be maintained following chronic exercise training. However, this effect has not been examined in humans.

HSP and Aging

Shock et al. (1984) suggested that an important characteristic of senescence is the reduced ability to respond to stimuli or stress and to maintain homeostasis. The remarkable increase in the incidence of heat stroke with age (Kilbourne, Choi, Jones & Thacker, 1982) has been considered a consequence of the inability of aged cells to maintain homeostasis in response to stress (Heydari, Takahashi, Cutsmann, You & Richardson, 1994). Among other physiological changes observed in the elderly, such as a decline in sweating efficiency and changes in cardiac output (Jones et al. 1982), changes in HSP 70 expression have been implicated in the diminished stress response. Senescent rat hepatocytes expressed significantly less HSP 70 following mild heat shock (42.5 °C for 30 min.) than young counterparts (Heydari, Wu, Takahashi, Strong & Richardson, 1993). Thus, the reduced transcription of HSP 70 in the aged rats may result in a diminished protection for cells undergoing hyperthermia. Similar decreases in the induction of HSP 70 expression have been observed in the brain, skin and lung tissue of aged rats (Blake, Fargnoli, Gershon & Holbrook, 1991) and other tissues and cells of rodents (Pardue, Groshan, Raese & Morrison-Bogorad, 1992).

In humans, a similar decline in the stress response has been observed. Deguchi, Negoro and Kishimoto (1988) reported a lowered induction of HSP 70 transcription by heat shock in

mononuclear cells isolated from elderly human subjects compared to young adult humans. However, the effects of aging on HSP 70 expression have not been examined in skeletal muscle. Furthermore, many of the studies which have examined HSP 70 expression in aged cells, have used heat shock as the method for eliciting the stress response. Although similar studies of rodents utilizing restraint stress (Blake et al., 1991) or in cultured human cells exposed to the amino acid analogue canavanine (Liu, Lin, Choi, Sorhage & Li, 1989) demonstrated a diminshed stress response in aged cells, the effects of exercise on the induction of HSP 70 expression in mammals has not been examined. Thus, studies suggest that aged cells demonstrate a reduced ability to mount a stress response, however, this has yet to be shown in skeletal muscle.

In summary, stress proteins appear to play a vital role in maintaining cellular homeostasis, particularly under periods of stress and increased protein assembly. Some aged cells and tissues retain the ability to express HSP 70 following heat shock (Heydari et al., 1993) however, reduced transcription results in a dramatic decline in the stress response. The stress inducible isoform, HSP 72 may confer protective effects to the cell and its expression has been elevated following exercise. Moreover, exercise interventions resulting in increases in type I MHC have resulted in concomitant increases in HSP 72, suggesting a link between skeletal muscle proteins and the stress response. However, due to the few number of studies of chronic exercise, and furthermore, fewer studies of the stress response in humans many questions remained unanswered.

Part F: Summary

The classification of skeletal muscle fibre types has increased in complexity in recent years.

The use of histochemistry in combination with electrophoresis and/or immunocytochemistry has revealed sub-types of fibres and possible transitional ones. Additionally, the impact of myosin isoforms on the contractile properties of skeletal muscle has yet to be fully determined. However, the use of necrospy material, MRI, CAT scans and electron microscopy has helped in the analysis of muscle CSA, muscle fibre morphology and characteristics.

Resistance exercise has been shown to effect muscle fibre area, the expression of contractile proteins and satellite cell activity. As well, changes in contractile proteins have been associated with the expression of stress proteins. The roles and effects of HSPs in humans are not well understood. Animal studies have often been used to establish much of the information on these effects. However, these studies, though well controlled, may not reflect the human situation. As a consequence the roles of HSP expression, muscle fibre hypertrophy, and possible fibre hyperplasia on muscle CSA have not been fully elucidated. Moreover, only some of these effects in the elderly have only recently been researched.

A model proposed by Porter et al. (1995) includes eight factors which appear to influence loss of muscle strength with increasing age. The factors include: muscle atrophy; altered muscle contractility; altered enzyme activity levels; endocrine changes; poor nutrition and/or disease; altered physical activity level and changes in the nervous system. The same authors contended that understanding muscle hypertrophy and neural adaptation for the improvement in strength were critical factors in the study of aging. Furthermore, researchers studying these factors were recommended to increase control, decrease learning effects, tester bias and placebo effects (Porter et al., 1995; Thayer et al., 1993). Thus the need to examine the effects of resistance exercise on the elderly in a controlled setting appears well founded.

Chapter 3

Methods and Materials

Subjects

Ten moderately active, healthy elderly subjects (8 female, 2 male) (mean age = 66.3 yrs, range 60 - 72 yrs.) with no previous experience in resistance training volunteered to participate in this study. The amount of physical activity performed by the subjects in the months prior to the training intervention was classified into categories of high, medium or low tertiles, according to methods described elsewhere (Voorrips, Ravelli, Dongelmans, Deurenberg & Van Staveren, 1991). Briefly, the sample was classified based on mean score attained on an interview-questionnaire designed to assess levels of physical activity in the elderly (Appendix #1).

Subjects signed an informed consent and required medical approval prior to participating in the research study (Appendix #2). The protocol was approved by the Ethics Committee for Research on Human Subjects at Lakehead University. Potential subjects responded to a local newspaper article, radio advertisement, televised public announcements and/or public addresses by the researcher at various seniors centres in the City of Thunder Bay Ontario (Appendix #3). Inclusion criteria included an age of 60 years or greater, medical approval by the family physician to engage in a resistance training program, a willingness to undergo biopsy sessions and an ability to attend regular exercise sessions. Prior to the start of the program, subjects were not engaged in any vigorous exercise program. Potential subjects with hip or knee replacements, previous hip fracture, and/or significant arthritis (requiring a cane for ambulation), were excluded.

Resistance Training

Subjects performed unilateral isotonic resistance training on the experimental limb (weaker

leg determined by pre-training test values). The contralateral limb acted as the control and therefore, was not included in the strength training program. The design of all strength training sessions took place under the supervision of the research director. Following the research experiment, research assistants continued to offer feedback and direction to subjects interested in continuing the training program. Subjects received an introductory session to the training site and facilities prior to engaging in the program. All subjects received instruction on proper exercise technique for each of the weight-lifting exercises, and carried out a series of repetitions at low intensity, under supervision, to familiarize themselves with the resistance training machines and the isokinetic dynamometer. Testing and training took place at the Fitness Centre in the C. J. Saunders Fieldhouse at Lakehead University (two subjects trained on a similar apparatus at the Canada Games Complex, City of Thunder Bay).

Strength Testing

During both initial and final strength testing sessions the following information was recorded for each subject: age, height, weight, and thigh girth. These measures were completed in accordance with the protocols described in the Canadian Standardized Test of Fitness: (CSTF) Operations manual (1986).

Thigh Girth: Thigh girth was measured using a protocol modified from that described by the CSTF Operations manual (1986). Thigh girth was measured at the height of the site of biopsy (one third of the length from the proximal edge of the patella to the spina iliaca anterior superior), instead of 2 cm below the gluteal line. This modification was intended to allow more accurate comparison between changes in thigh girth and fibre hypertrophy.

Isokinetic Dynamometry Test: The strength of the quadriceps and hamstring muscles was tested unilaterally on the Cybex II dynamometer (Lumex Corporation, New York, N.Y.). Torque calibration was verified before each testing session using known loads. Subjects were provided with both an explanation and demonstration of the dynamometer. During the test the subject was seated erect with the thigh stabilized with straps. The length of the dynamometer arm was recorded during the pretesting for each subject and reset to the same length for the post-testing session. The subjects were instructed to grip the handles provided on the seat and encouraged to maintain visual contact with the tested extremity. Efforts were initiated from a knee flexed position of 90^0 and isokinetic strength was tested at two constant angular velocities, 60 and 180^0/s. Subjects performed four maximal repetitions at each angular velocity. Between the two sets of four repetitions subjects were given a two minute recovery period. In order to become familiar with the apparatus, the subjects were allowed to try the items three times before the actual test.

Isokinetic dynamometry testing occurred at week 0 (initial) prior to the initial biopsy sampling and at week 9 (final) prior to the final biopsy. Fleck, Fleming and Richtie (1984) demonstrated that one test day is sufficient to obtain reliable peak torque values when isokinetically tesing inexperienced subjects. However, to ensure reliability, subjects underwent 2 pre-tests and 2 post tests (4 tests in total) on the isokinetic dynamometer. All tests were separated by at least 48 hours and were executed at the same time of day. The testing schedule was as follows:

Introductory week:	Friday: isokinetic dynamometry introductory trial
Week 0	Monday: isokinetic dynamometry pre-training test #1
	Wednesday: Needle biopsy session
	Friday: isokinetic dynamometry pre- training test #2
Week 9	Wednesday: isokinetic dynamometry post-training test #1
	Friday: isokinetic dynamometry pre- training test #2
Week 10	Saturday: Needle biopsy session

Peak torque (Newton-metres) was defined as the maximum value of torque over the four repetitions. Mean power (Newton-metres-radians per second) was the quotient of the total torque produced throughout a range of motion (work), multiplied by the limb velocity, and divided by the time required for the movement. Isokinetic dynamometry was the preferred method of testing strength during motion because it allows torque (strength) to be measured at any point in the range of motion, from which the average power developed during the movement may be calculated (Whipple, et al. 1987).

According to Rothstein, Delitto and Sinacore (1983) isokinetic power takes into account the influence of limb velocity on overall strength throughout the contraction. Since there is evidence that velocity of movement in the elderly may be impaired as well as strength, power recordings may provide a more sensitive indicator of speed-associated deficits (Whipple et al., 1987). Therefore, both peak torque and mean power were recorded at both angular velocities. Testing sessions included similar warm up and cool down periods that were executed during the training sessions.

1RM knee extension and knee flexion test: One repetition maximum (1RM) tests were used to estimate the appropriate resistance for the training program. One repetition maximum was defined as the maximum weight that can be lifted not more than one time with acceptable form. Acceptable form meant that the exercise was performed by the specific muscle group involved without the help of whole body momentum or of other muscle groups (Pyka et al., 1994). Subjects performed single unilateral knee extensions on an isotonic resistance universal type machine. Subjects were asked to execute the concentric phase of each exercise over 2 seconds, and the eccentric phase over 3 seconds. A research assistant estimated the resistance setting for each subject. Successful completion of the exercise with a set amount was followed by a two minute rest and a re-attempt at a higher resistance, until the subject could no longer complete a full repetition with acceptable form. The 1RM test began with a weight set at a level close to the approximated maximal weight to minimize repetition fatigue. This same procedure was followed on each leg and repeated using unilateral knee curls on an isotonic resistance universal type machine. Subjects completed a 1RM test at week 0. The 1RM weight lifted by each leg on each of the two exercises was recorded and used to set resistance for each subject's training program.

Resistance Training Program

The resistance training program took place over a period of nine weeks. A total of 25 workout sessions was completed. Training sessions took place three times per week, with each session lasting approximately one hour. Training sessions included a warm up period (15min), an exercise period (35 min) and a cool down period (10 min). Warm up and cool down periods

included stretching and walking and/or low intensity riding on a stationary bicycle. The limb which scored lower values on the isokinetic dynamometry testing was classified as the experimental limb. All subjects began the training program simultaneously. Subjects performed unilateral knee extensions and unilateral knee curls on universal type resistance machines where the weight increments were 4.5 kg.

Training was based on a modified protocol as described by DeLorme- Watkins (Westcott, 1982). The purpose of the training program was to provide an overload stimulus for the quadriceps and hamstring muscles. The quadriceps muscles were of particular interest as results could be compared to previous research. Since weight increments were relatively large, initially, the total amount lifted was determined primarily by the number of repetitions, rather than the resistance setting (no. of plates). Where possible, sets were completed using 10 repetitions of the exercise. However, the last set of each exercise was completed to failure. Training sets were separated by a two minute rest period. Following successful completion of 15 or more repetitions on the final set of an exercise session, the resistance was increased one increment on the universal type isotonic resistance machine (approx. 4.5kg or 10 lbs.).

The training program was divided into 3 phases. Phase 1 took place during weeks 1 and 2, and included 3 sets per exercise. Phase 2 took place during weeks 2, 3, 4, and 5, and included 4 sets per exercise. Phase 3 took place during weeks 7, 8 and part of week 9 and included 5 sets per exercise. Week 0 and part of week 9 were reserved for testing.

Three typical training days are outlined as follows (hypothetical subject achieved a single knee extension against a resistance of 18.2 kg or 40 lbs. [4 X 10lb. plates during 1RM test])(values are expressed in terms of number of 10 lb. plates/ number of repetitions i.e. 2/10

indicates two 10 pound plates will be lifted 10 times during a one exercise set):

Name John Doe Training Limb: Left

Week # 1 Monday
Phase # 1

Set	Extend.	Curls
# 1	1/10	1/7
# 2	1/10	1/7
# 3	1/12	1/8
# 4	--------	---------
# 5	--------	---------

Week # 4 Friday
Phase # 2

Set	Extend.	Curls
# 1	2/10	1/10
# 2	2/10	1/15
# 3	2/10	2/8
# 4	3/6	2/9
# 5	--------	---------

Week # 7 Wednesday
Phase # 3

Set	Extend.	Curls
# 1	2/10	2/10
# 2	3/8	2/10
# 3	3/8	3/6
# 4	3/10	3/6
# 5	3/12	3/8

During the exercises, subjects were asked to execute the concentric phase of each repetition over 2 seconds, and the eccentric phase over 3 seconds. Subjects were asked to record daily weights lifted, number of repetitions and sets completed, and any difficulties experienced.

Muscle Biopsies: Each subject underwent four needle biopsies of muscle tissue. One biopsy from each thigh was taken before the training commenced (week 0), and one biopsy was taken from each leg upon completion of the training program (week 10). Each sample was approximately 20-60 mg in size. Biopsies were obtained from the lateral aspect of the quadriceps femoris muscle, the vastus lateralis (Bergstrom, 1962). Subjects were injected with a local

anaesthetic (Xylocaine, 1%) in the thigh area prior to surgery. The biopsies were taken one third of the length from the proximal edge of the patella to spina iliaca anterior superior, and with the aim at a depth of 1.5 cm deep into the muscle. Each sample was embedded in a mounting compound (Tissue Tek) on a slice of cork. Immediately following every muscle biopsy, a portion of muscle tissue to be used for histochemistry was frozen in 2-methyl butane, previously cooled using liquid nitrogen (-80 °C). The tissue was stored in liquid nitrogen until it was analysed. A second portion of the muscle tissue sample was stored at -80 °C in liquid nitrogen for further analysis employing one (1D) dimensional electrophoresis.

Histochemistry: Histochemical procedures (ATPase activity) were performed to determine the fibre type distribution and fibre cross-sectional area in the human skeletal muscle. The muscle sample for histochemical analysis was sectioned in a cryostat at -20°C (Lauda Kryostat 1620 Digital, Leitz, Germany). Serial cross-sections (10 um thick) were cut from each muscle sample and stained for myofibrillar ATPase after alkaline and acid pre-incubations. Pre-incubation of cross-sections of the muscle sample at pH 4.3 for 1.0 min and pH 10.3 for 10.0 min, made it possible to identify type I and type II fibres. The cross-sections were also pre-incubated at pH 4.6 for 1.0 min to differentiate between intermediate (IM) type IIa and type IIb fibres (Brooke & Kaiser, 1970a; 1970b). The percentages of fibre types were estimated by visually counting approximately 25-30 fibres in each of the eight regions evenly distributed throughout the muscle cross-sections (Ianuzzo & Chen 1979).

Fibre cross-sectional area: Planimetric measures of fibre cross-sectional area (CSA) were

conducted using video images provided by a Sony Colour Video Printer and Camera (Sony UP-3000) taken from slides examined on a Zeiss Scientific Microscope (Zeiss 63173, Germany). Images were projected onto a colour monitor and analysed using Quantimet 520 image analysis software (Leica Intruments, Cambridge, England) on a Compac 386DX (Compaq, U.S.A.) personal computer. Muscle fibres selected for measurement were free of artifacts, had distinct cell borders, and, where possible, were centrally located in the sample (Bloomstrand, Celsing, Friden & Ekblom, 1984). At least an average of 100 fibres of each muscle sample was classified as to fibre type and quantified in terms of cross-sectional area (Bloomstrand et al. 1984). Samples were blinded to protect the investigator from knowledge of initial or final and experimental and control biopsy status.

Poly-acrylamide Gel Electrophoresis

Muscle samples weighing 5- 60 mg were added to 40 volumes of 15 mM Tris buffer, 600 mM NaCl containing 1/200th volume each of 0.2 M phenylmethylsulfonyl fluoride in ethanol, 0.2 mg/ml Pepstatin A in ethanol and 0.1 mg/ml leupeptin in ddH_2O as protease inhibitors. Samples were homogenized with a polytron homogenizer for a total of 30s on ice, centrifuged at 5000xg for 10 min at 4°C., and the supernatant stored at -70°C. until analysis.

Proteins were quantified using the Lowry method (Lowry, Rosebrough, Farr & Randall 1951), using known amounts of purified bovine serum albumin (BSA) to generate a standard curve. Two, 5, 10, 20, 40, 60, 80, 100 and 120µg of BSA and unknown protein samples were brought to a volume of 500 µl with water. Five ml of Lowry solution, prepared by adding 5 ml of 4% w/v Na-tartarate and 5 ml of 2% w/v $CuSO_4.5H_2O$ to 240 ml of 3% w/v Na_2CO_3 in 0.1

NaOH, were added, the tubes were vortexed and allowed to stand at room temperature. After a 10 min. incubation, 500μL of Folin phenol reagent (BDH), diluted 1 part in 3, were added with vortexing, and tubes were allowed to stand for 30 min. Absorbency of the solutions was measured at 680 nm and protein concentration was determined using a linear regression equation generated from standard curve data.

One dimensional Sodium Dodecyl Sulfate Polyacrylamide Gel Electrophoresis (SDS-PAGE, Laemmli, 1970) was performed on muscle homogenates using the BioRad Mini-Protean II gel apparatus. The separating gel was either 12% in acrylamide (97.33% acrylamide, 2.67% bis acrylamide) or a 4-15% polyacrylamide gradient for HSP 72 or type I MHC immunoblotting respectively.

Immunoblotting

Proteins were electrophoretically transferred to 0.2 μm pore size nitrocellulose (Towbin, 1993) in the BioRad Mini-Protean trans blot apparatus. Two sandwiches consisting of 2 pieces of filter paper, a gel, a piece of nitrocellulose and two more pieces of filter paper were placed in the blotting folder of the apparatus between two scouring pads. Transfer occurred overnight for a total of 200 Volt•hours at 4°C, which maintained buffer temperature below 15°C. Blots were blocked in Tris buffered saline (TBS; 20mM Tris HCl pH 7.5, 500mM NaCl) containing 5% dry milk powder (DMP) for at least 4 hours at room temperature. The membranes were washed twice for 5 minutes each in TBS containing 0.05% Tween-20 (TTBS) and transferred to an antibody solution consisting of type I MHC (1:200) or HSP 72 (1:2500) antibodies in TTBS with 2% DMP and 0.02% sodium azide as a preservative. Blots were rotated several times over the

first two hours of the incubation and then left in the solution for a total of 14 hours at 4°C on a rotary shaker. Following the primary antibody incubation, blots were washed twice in TTBS for 5 minutes each with shaking and transferred to a second antibody solution. This solution was 2% DMP in TTBS with a goat anti-mouse alkaline phosphatase conjugated secondary antibody or a goat anti-rabbit alkaline phosphatase conjugated secondary antibody (both BioRad, 1:1000) for the type I MHC and HSP 72 blots respectively. The membranes were washed twice in TTBS and once in TBS, five minutes each with shaking, then transferred to a bicarbonate buffer (100mM $NaCO_3$, 1mM $MgCl_2$) containing 1mL each of 3% (w/v) p-nitro blue tetrazolium chloride p-toluidine salt in 70% (w/v) N,N-dimethylformamide (DMF) and 1.5% (w/v) 5-bromo-4-chloro-3-indolyl phosphate in 100% DMF. After colour development (2-10 minutes), blots were rinsed in two changes of a large volume of water and placed between filter paper to dry. Bands were quantified with an LKB Ultroscan laser densitometer equipped with an LKB 2220 recording integrator and expressed relative to bands from identical samples run on every blot.

Antibodies

A monoclonal antibody to type I MHC (10D10) was generously donated by Dr. Peter Merrifield (Dept. of Anatomy, University of Western Ontario). HSP 72 levels in muscle were assessed using a monoclonal antibody to HSP 72 (StressGen SPA-810) donated by Dr. Robert M. Tanguay (Unité d'Ontogénèse et Génétique Moleculaire, Université de Laval) which has been described previously (Tanguay, Wu & Khandjian, 1993).

Statistical Analysis: Statistical analysis was performed on Sigmastat 3.0 computer software. Means, +/- standard deviations and percent change following training were calculated for all anthropometric measures, activity scores, strength measures, fibre CSA and distribution measures and muscle protein analysis. A pairwise T-test was used to determine the effects of training on height, weight and Body Mass Index. Reliability of isokinetic leg extension tests was estimated using an intra-class correlation coefficient (rho).

A 2 X 2 (limb by time of measurement) mixed factorial analysis of variance with repeated measures was conducted on each of the dependent variables. The between groups factor consisted of trained (experimental) and control limb groups. The within groups factor was time of measurement, which consisted of measures of muscle characteristics obtained prior to and following training. This method of statistical analysis was conducted to determine the effects of training in each limb on: thigh girth; peak torque and mean power (at both angular velocities); fibre type CSA; percent distribution of fibre type; and percent Type I MHC and HSP72 of soleus control. On determination of significant main effects or interaction, pairwise comparisons employing a Tukey post hoc test were conducted. Differences were considered significant at $P < 0.05$.

Chapter 4

Results

Anthropometry

Ten (8 females, 2 males), moderately active sexagenarians volunteered to participate in this study. Protocol compliance was excellent. Only two subjects were unable to attend two training sessions on the scheduled days and instead trained on 'make up' days. The mean (+/- standard deviation [S.D.]), minimum (Min.) and maximum (Max.) age, height, weight, body mass index (BMI), leg girths and score on an activity level assessment questionnaire (Voorrips et al. 1991) are listed in Table 1. Subjects were classified as moderately active according to the mean score attained in response to an activity questionnaire. Pre-training (Pre), post-training (Pst) and percent changes following training (% change) values are presented. Following training, no significant changes in any of the anthropometric measures were noted.

Variable	Mean	+/- S.D.	Min.	Max.	% change
Age (yrs)	66.3	3.6	60	72	
Height (cm)					
Pre	161.0	6.8	156.0	175.8	
Pst	161.0	6.7	155.7	175.6	0
Weight (kg)					
Pre	72.6	8.2	57.7	83.6	
Pst	73.1	8.5	57.5	86.2	0.7
BMI (kg x m^2 x 10^{-1})					
Pre	28.0	2.8	23.6	33.0	
Pst	28.3	3.2	23.7	35.2	1
Leg Girth (cm)	Control limb				
Pre	51.9	7.9	44.0	72.1	
Pst	52.3	7.7	44.2	72.2	0.7
Leg Girth (cm)	Exp.[&] limb				
Pre	51.9	7.9	44.0	72.5	
Pst	52.6	7.9	44.8	72.9	1.3
Activity Score	12.1	3.7	6.9	18	

Table 1. Descriptive statistics of anthropometric measures and activity scores of subjects.

Exp.[&] = Experimental

Isokinetic Strength

Leg extensor strength was measured using isokinetic dynamometry. Peak torque (PT) in Newton-metres (N-m) and mean power (PP) in Newton-metres-radians per second (Nm x rad x s^{-1}) were assessed at 60° x s^{-1} and 180° x s^{-1}. Strength tests (see Methods) were repeated during both pre-training and post-training testing sessions. For reliability analysis intra-class correlation coefficient estimates for test-retest stability (reliability) ranged from; rho = 0.84 to rho = 0.95 ($P < 0.05$). The mean (+/- standard deviation [S.D.]), minimum (Min.) and maximum (Max.) values for all knee extension strength measures are listed in Table 2. Pre-training (Pre), post-training (Pst) and percent change following training (% change) values are presented for both control (CT) and experimental (EX) limbs.

Variable	Mean	+/- S.D.	Min	Max	% change
Peak Torque (N-m)					
CT @ 60° x s^{-1}					
Pre	85.8	15.1	70.5	116.7	
Pst	91.2	15.3	67.5	116.5	6.2
EX @ 60° x s^{-1}					
Pre	78.1	10.5	66.7	101.3	
Pst	89.1	15.2	65.3	106.3	14

CT @ 180° x s^{-1}					
Pre	54.0	11.4	39.2	80.2	
Pst	59.8	16.4	34.7	86.0	10.8
EX @ 180° x s^{-1}					
Pre	52.4	9.5	41.0	72.0	
Pst	68.6	12.0	47.2	82.8	30.8*
Mean Power					
(Nm x rad x s^{-1})					
CT @ 60° x s^{-1}					
Pre	98.2	17.2	83.0	135.0	
Pst	104.6	18.1	77.0	136.0	6.5
EX @ 60° x s^{-1}					
Pre	91.6	14.5	80.0	126.0	
Pst	106.4	18.7	78.0	127.0	16.2
CT @ 180° x s^{-1}					
Pre	173.8	35.2	125.0	253.0	
Pst	194.6	51.6	112.0	276.0	12
EX @ 180° x s^{-1}					
Pre	172.6	31.2	137.0	240.0	
Pst	219.5	42.6	155.0	269.0	27.2

Table 2. Mean, standard deviation, minimum and maximum and percent change values for isokinetic peak torque (N.m) and mean power (N.m x rads x s^{-1}) at 60° x s^{-1} and 180° x s^{-1}, before

and after training. * denotes values which are significantly different ($P < 0.05$) from pre-training values.

Peak torque at $180^{\circ} \times s^{-1}$ was the only measure of strength which increased ($P < 0.05$) following training. However, a tendency to an increase (27.2 %) in mean power at the faster tested velocity was observed in the experimental limb. Moreover, a trend for increases in performance following training was observed in all measures of peak torque and mean power, particularly in the experimental limb. Percent increases in peak torque at both tested velocities for both control and experimental limbs are presented in Figure 1.

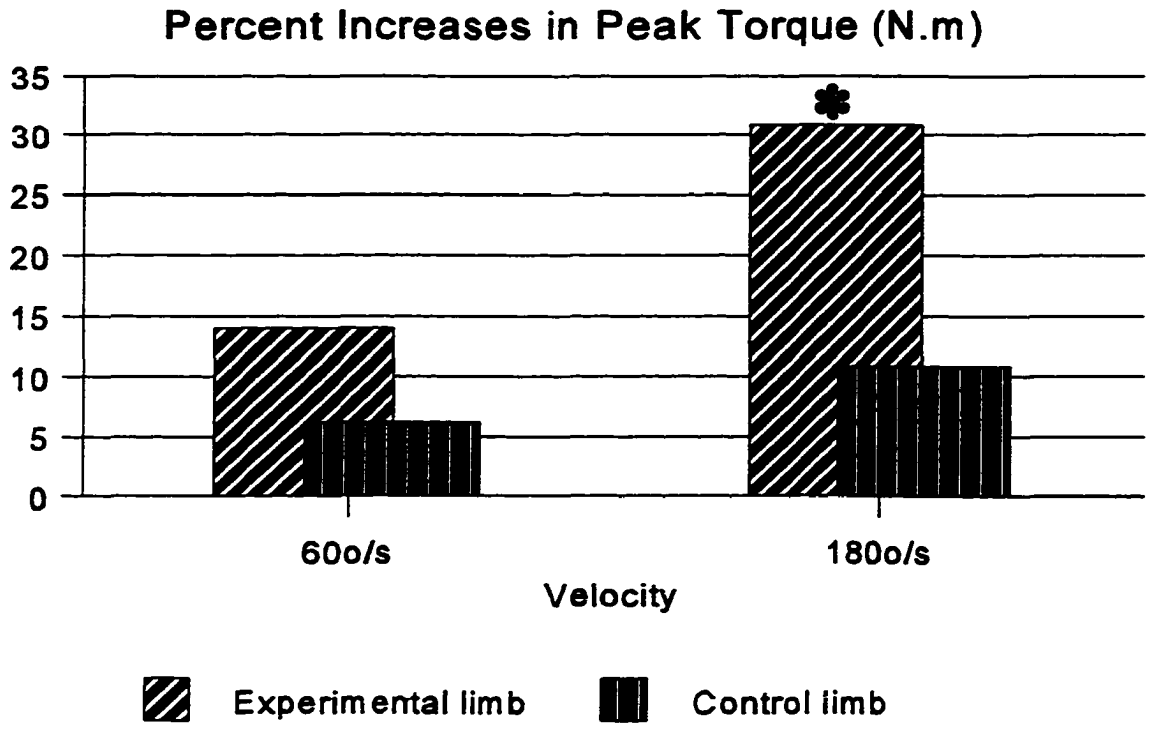

Figure 1. Percent increases in isokinetic peak torque following training in both control and experimental limbs. * denotes significant difference following training ($p < 0.05$).

Fibre Cross Sectional Area (CSA) and Distribution

There were no changes in fibre CSA or distribution following training. Cross-sectional area of a particular muscle fibre type was assessed using a mean area (um^2) of individual fibres. There was a tendency to an increased fibre area in type II fibres (7.3% for IIa and 10.6% for IIb) in the

experimental limb. Histochemical staining revealed no change in the percent distribution of each fibre type (Appendix # 4). The mean (+/- standard deviation [S.D.]) values for both CSA and distribution in all three fibre types examined are listed in Table 3. Pre-training (Pre), post-training (Pst) and percent change following training (% chng) values are presented for both control and experimental limbs. Post-training control data for both fibre and muscle protein analyses were derived from nine (n = 9) of the ten subjects. One post-training control limb needle biopsy sample was not obtained from one subject due to technical difficulties.

Fibre type/ limb	CSA (um^2)	+/- S.D.	% chng	Dist. (%)	+/- S.D.	% chng
I Control						
Pre	3661.6	611.4		54.0	7.7	
Pst	3580.7	616.8	-2.3	52.4	7.0	-3
I Experimental						
Pre	3455.1	646.5		53.4	6.1	
Pst	3642.5	566.3	5.4	53.4	6.0	0
IIa Control						
Pre	3263.5	821.1		31.1	5.5	
Pst	3337.2	679.9	2.3	32.0	4.3	2.9

IIa Experimental						
Pre	3192.0	768.5		32.0	3.3	
Pst	3426.5	743.7	7.3	33.1	4.3	3.4
IIb Control						
Pre	1998.0	187.6		14.3	3.3	
Pst	2005.7	160.7	0.3	16.1	6.0	12.6
IIb Experimental						
Pre	1906.0	107.3		14.6	5.0	
Pst	2108.3	163.4	10.6	13.7	4.1	-6.2

Table 3. Mean, standard deviation and percent change values for fibre cross sectional area and percent distribution of fibre types I, IIa and IIb, in both experimental and control limbs, before and after training.

Muscle Proteins

One dimensional SDS-PAGE electrophoresis of muscle homogenates followed by immunoblotting revealed no change in relative expression myosin heavy chain (MHC) type 1 or heat shock protein 72 (HSP72) content in either experimental or control limbs following training (Appendix # 5). The mean (+/- standard deviation [S.D.]) values as a percent of rat soleus control for both type I MHC and HSP72 are listed in Table 3. Pre-training (Pre), post-training (Pst) and percent change following training (% chng) values are presented for both control and experimental limbs.

Limb	% Type I MHC[i]	+/- S.D.	% chng	% HSP72	+/- S.D.	% chng
Control						
Pre	87.9	55.2		123.0	91.9	
Pst	90.6	47.2	3.1	170.7	126.0	38.7
Experimental						
Pre	88.5	81.8		151.1	170.2	
Pst	98.0	47.2	10.8	102.9	49.6	-31.9

Table 4. Summary of changes in Type I MHC and HSP 72 following training. [i] Percent of Type I MHC relative to soleus control.

Chapter 5

Discussion

Strength Gains

The purpose of this study was to investigate functional, histochemical, biochemical and morphological properties associated with resistance training in the elderly. These data show that a short term resistance training program employing progressive overload is capable of producing significant increases in strength in the elderly. Recent studies have reported dramatic increases in strength following resistance training or a combined aerobic/resistance training program (Frontera et al., 1988; Pyka et al. 1994; Fiatarone et al., 1994). Given the relatively short duration of the present program (25 sessions) smaller strength gains were expected. Following 12 weeks of training, Frontera et al. (1988) reported a 107 % increase in 1RM knee extensions. However, this value was approximately ten times greater that the strength gains measured with the isokinetic testing modes. The 30.8 % increase ($P < 0.05$) in peak torque at the faster velocity in the experimental limb observed in our subjects compares favourably to other studies of resistance trained seniors. There was a tendency to an increase in all measures of strength following training, particularly in the experimental limb. This suggests that the progressive overload resulted in a training adaptation and subsequently, improved strength. It is speculated that had training continued, changes in other variables may have achieved statistical significance.

Compared with the present study, Charette et al. (1991) studied slightly older women (mean age = 69.8 years) following 12 weeks of resistance training and reported a 92.6 +/- 12.6 percent increase in knee extension 1RM values. However, in other elderly subjects, the same

increases in strength have required a year of training (Pyka et al., 1994). Thus, discrepancies exist in reported strength gains between studies employing 1RM measures. The causes for the discrepancies however, are not fully understood.

The increase in strength tested isokinetically (@ 180°/s) observed in the trained limb in this study is relatively high compared to others in reported literature. This finding may be a consequence of the intense nature of the training undertaken by subjects in the present study. However, the relative gain in strength could be in part, determined by low initial values (52.4 +/- 9.5 N.m). Similarly, Porter et al. (1994) reported low values (61 +/- 16.0 N.m) for women aged 73 years on the same test executed at 90°/s.

Following 12 weeks of training elderly males, Brown and colleagues (1990) reported an 8.8 % mean increase in isokinetic strength in the subjects' elbow flexors. Larger increases (17 and 18%) were observed in tests of the lower extremities. In younger subjects, 10 weeks of unilateral training of the quadriceps produced comparable increases in peak torque output of 39 to 60 % at various velocities (Houston et al. 1983). Recently, Roman et al. (1993), in a study of elderly men, reported 36 and 23 % increases ($P < 0.05$) in peak torque at 180°/s and 60°/s respectively. The elderly subjects in that study trained an additional four weeks compared to the subjects in the present study. It is speculated that in lieu of the shorter duration of training employed in the present study our findings are comparable.

The non-significant increase in peak torque at the slower velocity tested was considerably less (10.8%) than that of the faster velocity (30.8%). The observed larger increases in peak torque at higher velocities are in agreement with other studies of the elderly (Menkes et al. 1993; Roman et al. 1993). However, Frontera et al. (1988) reported that training had its greatest

influence on the slow-velocity high-force region of the torque-velocity curve. The discrepancies between these results may be explained by the speed of execution of exercises during training. Slower execution of resisted leg extensions have led to improvements in strength at only slower speeds. Likewise, subjects trained at fast speeds have shown improvement during fast contractions and no change in strength at slower speeds (Coyle et al. 1982). The larger improvement in strength at the faster velocity observed in this study may reflect the speed employed during training. Tests which mimic the speed and characteristics of the movements used during training demonstrate the greatest enhancement of force generation (Frontera et al. 1988). Therefore, the question of whether the elderly are more inclined to strength gains at particular speeds remains unclear. Similar to the present study, the aforementioned ones used isotonic resistance or combined isokinetic and isotonic resistance exercises. Thus, it was difficult to ascertain the speed at which the training exercises were executed. However, based on performance, it is likely that the subjects in the present study trained on the isotonic resistance machines at speeds which were closer to 180°/s than 60°/s.

Fibre Cross Sectional Area (CSA) and Distribution

The mean fibre CSA prior to training in the present investigation (type I = 3,662 +/- 611 um^2; type IIa = +/- 3,264 +/- 647 um^2; type IIb = 1,998 +/- 188 um^2) was similar to data derived from elderly subjects in other reported literature. Charette et al. (1991) examined the muscle fibres from women whose average age was 69 years and reported mean pre-training values of 3,967 +/- 200 um^2 and 2,532 +/- 101 um^2 for fibre type I and II respectively. Moreover, measured type II fibre CSA from 50 and 80 year olds, in post-mortem investigations were

approximately 3,400 um^2 and 2,800 um^2, respectively (Lexell et al., 1993). The preferential atrophy of type II fibres in the elderly described by Porter and coworkers (1995), was less evident in the biceps brachii in the subjects of Frontera et al. (1988). Prior to training, the elderly males in that study had mean fibre CSAs of 5,929 +/- 499 um^2 and 5,402 +/- 820 um^2 for types I and II respectively. However, the size of the muscle fibres in the vastus lateralis analyzed prior to training in the present study was similar to the size of fibres in other untrained or pre-training samples of elderly subjects. Furthermore, data derived from the subtyping of fibres (IIa and IIb) employed in the present study provide evidence which clearly supports the considerable contribution that type IIb fibre atrophy makes to overall type II fibre atrophy observed in aged muscle.

Although there was a tendency to an increased fibre area in type II fibres (7.3% for IIa and 10.6% for IIb), fibre CSA was unaltered as a result of the resistance training in the present study. Porter et al. (1995), suggested that there is a tendency for greater hypertrophy of type II fibres following resistance training in the elderly. The modest change observed at the microscopic level (fibre CSA) in the present study is supported by findings at the macroscopic level (leg girth). Leg girth was maintained in either limb following training. Researchers utilizing anthropometric measures have reported a similar response to resistance training in elderly male subjects (Moritani & deVries, 1980).

Hypertrophy of both type I and type II fibres has been demonstrated following short-term high intensity training in the elderly. Frontera et al. (1988) reported 34 and 28% increases in CSA of types I and II fibres, respectively. However, following the same duration of training, elderly women have experienced 7% non-significant increase in type I fibres accompanied by a 20%

increase ($P < 0.02$) in type II fibres (Charette et al. (1991). Charette et al. (1991) speculated that differences in training regimens may have accounted for the discrepancies in change in Type I fibre CSA between their study and that of Frontera and colleagues. Intense aerobic warm-up activities in the study by Frontera et al. (1988) may have contributed to a hypertrophic response observed in type I fibres (Charette et al. 1993). The training regimen (with regard to warm up) employed in the present study was more analogous to the one used by Charette et al. (1993) and changes in fibre CSA followed a similar pattern.

Brown et al. (1990) reported an increase in the type II-to-I area ratio following resistance training in a group of elderly subjects. The greater percent increase in type II fibre CSA compared to type I observed in the present investigation is in agreement with Brown and coworkers (1990). Studies which have utilized a long duration training program (1 yr.) have reported relatively larger gains in strength and fibre CSA of both fibre types (Pyka et al. 1993), than short term studies which have reported little or no hypertrophic changes (Moritani and deVries 1980). It is likely that the training stimulus presented in this study was insufficient in duration to elicit a significant hypertrophic response. It is possible that the gain in strength observed in this study, may reflect both the modest change in fibre CSA as well as a neural adaptation (Moritani & deVries 1980).

Knee extension exercises have resulted in preferential hypertrophy of particular muscles of the thigh. Narici et al. (1989) reported significantly less hypertrophy in the vastus lateralis (VL) muscle than the vastus medialis muscle (VM) and the vastus intermedius muscle (VI) following concentric isokinetic knee extensions. The authors speculated that the smaller training effect in the VL was due to its lower activation (60 % of the VM and VI) during knee extension exercises.

Housh et al. (1992), also reported a relatively smaller hypertrophic response in the CSA of the VL compared to the CSA of the rectus femoris muscle following knee extension exercises. Although which muscles of the thigh undergo the greatest degree of preferential hypertrophy is still unclear, evidence supports a comparatively smaller training effect in the VL following leg extensions. In many studies, including the present, the VL is used as a site for biopsy and consequently, used to represent the fibre hypertrophy in the trained muscles. Since the VL achieves less of a training effect following knee extension exercises compared to other muscles of the thigh, data derived from biopsies of the VL may underestimate the training effect on the muscles of the thigh. This may in part explain the modest fibre hypertrophy accompanied by significant strength gains observed in the present investigation and similar studies (Frontera et al., 1988; Pyka et al., 1994). The VL was used as a site for biopsies in this study because of ease of sampling, minimal circulating and neural problems while performing the biopsy, the large muscle mass. In addition, biopsies taken from the VL allowed comparison to previous research.

Fibre Type Distribution

No significant changes were observed in the distribution of fibre types in this study. Maintenance of fibre type distribution has been reported for the elderly following resistance training (Frontera et al. 1988; Charette et al. 1991; Brown et al. 1990; Pyka et al. 1994). These studies, including the present, did not demonstrate the fibre type grouping described by Lexell (1993). The data used by Lexell (1993) was not taken from exercise studies, however, such studies have not reported changes in fibre type grouping following training. Recently, Staron et al. (1994), employing a study with subjects in the third decade of life revealed a significant

decrease in type IIb fibres following resistance training. The authors suggested that resistance training may result in the phenotypic conversion of type IIb fibres to IIa fibres. However, such conversions were not observed in the present investigation nor have they been reported in other studies of aged muscle. The reasons for the different response to training between young and old subjects is not immediately clear. The apparent maintenance of fibre type distribution in the elderly following resistance training may be the result of one or both of two possible factors. Firstly, the elderly may not be capable of eliciting the phenotypic changes observed in younger subjects. Secondly, discrepancies between the results in these studies may be due to the inherent possibility of sampling error in muscle biopsy investigations. However, researchers to date, have supported the finding that elderly subjects have maintained fibre type distribution following resistance training.

Cross over effect

In the present study, the contralateral limb experienced between 35 to 44% of the increases in isokinetic peak torque and mean power found in the trained limb. Although the percent increases were proportional to those of Houston et al. (1983), these changes were not significant. Thus, the cross over effect found in previous research (Housh & Housh, 1993; Houston et al. 1983) was not observed in the present study.

Muscle Proteins

In spite of a 27% increase in the relative expression of type I (slow) myosin heavy chain (MHC) in elderly subjects, researchers revealed no difference in histochemical fibre type

distribution compared to younger counterparts (Klitgaard et al. 1990). The authors suggested that the increase in slow myosin isoforms with aging seemed mainly related to a larger relative area of type I fibres, induced by a selective atrophy of type II fibre area. In younger subjects, resistance training has resulted in an increased expression of type IIa MHC at the expense of type IIb MHC (Adams, Hather, Baldwin & Dudley, 1993; Staron et al. 1994). These studies have reported that MHC isoform shifts have been mirrored by alterations in fibre type distribution, such that the percent of type IIb fibres decreased with a concomitant increase in type IIa fibres. However, as described earlier, such changes in fibre type distribution do not appear to occur in the elderly.

Although, changes in MHC isoform expression as a result of aging have been investigated, to our knowledge, no studies to date, have examined such changes following resistance training in the elderly. Resistance training did not alter the expression of slow (type I) myosin in the present investigation. The relative expression of a given MHC isoform may be a consequence of either increased frequency and/or hypertrophy of any fibre type predominantly expressing the given isoform at the expense of another in the biopsy sample. As distribution and CSA were unchanged following training in the present investigation, the maintenance of type I myosin expression was anticipated. However, one may speculate that the modest increase in fibre area observed in type II fibres would have resulted in a slight decrease in relative Type I myosin expression. This trend was not observed in the present investigation and an explanation is not immediately clear. It may be due to sampling error as histochemical and electrophoretic analyses each required a separate portion of the biopsy sample. In any case, further research of myosin expression in the trained muscles of the elderly is warranted.

Heat stress protein (HSP) 72 has been described as the stress inducible isoform of the 70 kilodalton family of stress proteins (Pelham, 1986). Heretofore, no study has examined the effects of resistance training on the expression of any stress proteins in humans. In the current investigation, no change was observed in HSP 72 expression following training. Furthermore, the Type I MHC: HSP 72 relationship described by Locke et al. (1994) was further supported by the results of this study. Both Type I MHC and HSP 72 expression were maintained following training. In contrast to the present results, researchers have revealed elevated levels of HSPs in response to chronic exercise training (Sim et al. 1991; Brickman et al. 1996; Samelman & Alway, 1996). Recently, less intense, routine exercise (without progressive overload) in adult rodents has resulted in increased expression of HSP 72 (Kelly et al., 1996). However, these studies of rodents may have limited applicability to humans. Moreover, age of subjects and training modality may further limit comparison to the present study.

Cells from aged animals demonstrated a diminished stress response to heat and malnutrition (Heydari et al. 1993; Blake et al., 1991). As well, a reduced accumulation of HSP 72 in aged human cells following stress has also been observed (Liu et al. 1989). Hence, a reduced ability to mount a stress response in aged cells has been purported (Locke, in press). Possibly, the subjects in the present study were unable to achieve the stress response which has accompanied chronic exercise in other studies. The technical difficulties in the electrophoretic analysis may have also contributed to the current findings. As such, much of the evidence regarding the stress response in humans following exercise remains speculative. In conclusion, although chronic exercise may raise levels of HSP72 in rodents, it remains to be shown in humans.

Summary

In summary, the training undertaken by the elderly subjects in this study resulted in an increase in strength and a tendency for an increase in type II fibre CSA. These data suggest that a short-term resistance training program is capable of producing significant increases in strength in the elderly. Fibre distribution was maintained and no cross-over effect or fibre type grouping were noted. These findings confirm and extend previous studies of resistance training of aged subjects. The use of the one leg model in the present study, has provided an unprecedented comparison between control and experimental limbs following resistance training in the elderly. This comparison has provided an opportunity to offer further insight into the effects of exercise on 'aged' muscle. Although these results indicate maintenance of Type I myosin and HSP 72 expression following training, further research is required to confirm these findings. Future research using a one leg model should consider the effects of a longer term training program (12-15 weeks). The extension of the training program may allow for the observed tendencies in the present study to achieve a more pronounced effect. Interdisciplinary research involving both physiologists and geneticists might reveal a more complete picture of transcriptional control and regulation of proteins in the dynamic milieu of skeletal muscle. Addressing these areas will help researchers understand the process of aging and the role of resistance training in enhancing the quality of life in later years.

Appendices

Appendix # 1. *Questionnaire on habitual physical activity in elderly people* (Voorrips et al. 1991)

Household Activities

1) Do you do the light household work (dusting, washing dishes, repairing clothes etc.)?
   0. Never (less than once a month
   1. Sometimes (only when partner or help is not available)
   2. Mostly (sometimes assisted by partner or help)
   3. Always (alone or together with partner)

2) Do you do the heavy housework (washing floors and windows, carrying trash disposal bags)?
   0. Never (less than once a month
   1. Sometimes (only when partner or help is not available)
   2. Mostly (sometimes assisted by partner or help)
   3. Always (alone or together with partner)

3) For how many persons do you keep house (inc. yourself; fill in '0' if you answered 'never' in question #1 and question #2)? _____

4) How many rooms do you keep clean, including kitchen, bedroom, garage, cellar, bathroom, ceiling etc. (fill in '0' if you answered 'never' in question #1 and question #2)?
   0. Never do housekeeping
   1. 1-6 rooms
   2. 7-9 rooms
   3. 10 or more rooms

5) If any rooms, on how many floors (fill in '0' if you answered 'never' in question #1 and question #2)?

6) Do you prepare warm meals yourself, or do you assist in preparing?
   0. Never
   1. Sometimes (once or twice a week)
   2. Mostly (3-5 times a week)
   3. Always (more than 5 times a week)

7) How many flights of stairs do you walk up per day (one flight of stairs is 10 steps)?
   0. I never walk stairs
   1. 1-5
   2. 6-10
   3. More than 10

8) If you go somewhere in your hometown, what kind of transportation do you use?

0. I never go out
1. Car
2. Public transportation
3. Bicycle
4. Walking

9) How often do you go out for shopping?

0. I never go out for shopping
1. Car
2. Public transportation
3. Bicycle
4. Walking

Sport Activities

Do you play a sport?
Sport 1: name
intensity (code)
hours per week (code) _____
period of the year (code) _____

Sport 2: name
intensity (code) _____
hours per week (code) _____
period of the year (code)

Leisure Activities

Do you have other physically active activities?
Activity 1: name
intensity (code) _____
hours per week (code) _____
period of the year (code)

Activity 2 till 6: as activity 1.

i) Household score = (Q1 + Q2 ... + Q10)/10
ii) Sport score = S (ia * ib * ic)
iii) Leisure time activity score = S (ia * ib * ic)

Questionnaire score = Household score + Sport score + Leisure time activity score

Appendix # 2 *Letter of informed consent*

Letter of Informed Consent

For participation in the following research study:

Effects of unilateral resistance training on sexagenarians:
An examination of biochemical and morphological changes.

Principal Investigators: Dr. R. Thayer, Ph. D. & D. O'Neill, B.Ph.Ed.
School of Kinesiology, Lakehead University
Thunder Bay, Ontario P7B 5E1
807 343-8544

I, _____ consent to take part in a study which will examine the effects of strength training on the muscles of the thigh. I have no previous experience in strength training. I will require medical approval prior to participating. The principal investigators have explained that I will perform resistance training on my right leg. The contralateral limb (or left leg) will act as the control and therefore, will not be included in the resistance training program. I may choose to participate in an upper body strength training program.

I understand that two undergraduate kinesiology students will provide assistance during the training sessions. I understand creation and implementation of all resistance training programs will take place under the supervision of the research director. Following the research experiment, research assistants will continue to offer feedback and direction if I am interested in continuing the training program. I will receive an introductory session to the training site and facilities prior to engaging in the program. I understand that care will be taken to avoid physical harm and injury during the training and testing by the investigators. The risks and benefits of engaging in this resistance training program have been clearly outlined.

I am aware that the strength training program will take place over a period of 8-9 weeks. Programs will commence in March and end in May of the year 1996. I understand that training sessions will take place approximately three times per week, with each session lasting approximately one hour. Training sessions will include a warm up period, an exercise period and a cool down period. Testing and training will take place at the Canada Games Complex and the Fitness Centre in C. J. Saunders Fieldhouse at Lakehead University.

I am willing to undergo four needle biopsies of muscle tissue. Each sample will be approximately 20-60 mg (the size of a small grain of rice). One biopsy from each thigh will be taken before the training commences, and one biopsy will be taken from each leg upon completion of the training program. I am aware that biopsies will be performed by an experienced doctor, at Lakehead University, Thunder Bay, Ontario. I will be injected with a local anaesthetic in the lateral thigh area prior to surgery. For a brief period of time following surgery, I may experience muscle soreness. Since muscle biopsies involve minor surgery, I understand that the possibility of infection exists. I also understand that proper care and hygiene will be used during the biopsy procedure to greatly reduce the likelihood of biopsy-related infection. I understand that needle biopsies are a routine medical practice and commonly used in a variety of medical research settings.

I have the right to withdraw from the study at anytime. Results of the study may appear in a publication; however, at all times, my identity will remain confidential. After the completion of the research, the results will be made available to me upon request. I understand that the Ethics Review Board of Lakehead University has approved this research.

_____

Signature of Participant Date

Phone # _____

_____

Signature of Witness Date

Medical approval for participation.

_____

Signature of Physician Date

I have explained the nature of the study to the participant and believe he/she has understood it.

_____

Signature of Researcher Date

Appendix # 3 *Introductory letter*

Strength Training For A Healthier Lifestyle

Dear Senior,

Physical activity is an important part of a healthy lifestyle. Some of the benefits of exercise include: improved resistance to disease; decreased incidence of injury; increased vigour and energy and improved strength. Often these benefits contribute to an improved sense of well being, confidence, and quality of life. Participation in an exercise program is often considered refreshing and regarded as an enjoyable social event.

For the elderly, exercise may help to maintain a sense of independence. Since there is a decrease in strength associated with aging, daily living activities may be compromised. In some cases declines in strength may result in losses of balance, falls and subsequent injuries. However, these unfortunate situations may be avoided when adequate strength is maintained. Although walking programs may be beneficial with respect to aerobic fitness, it is questionable whether movements requiring a quick response are improved. The quick response and strength required to maintain balance and other movements may be enhanced through strength training.

One form of strength training involves the movement of a joint against resistance. This type of exercise, often called "weight lifting," is commonly done in homes and fitness clubs. In recent years, resistance training for the elderly has gained popularity. However, the changes in trained muscle of the elderly are not well understood. This area of scientific research is considered an exciting new area of research. Furthermore, the knowledge gained through study in this area will have important implications for the elderly population. Understanding the effects of strength training will allow older persons to maximize the benefits associated with their participation and hence, improving their quality of life.

About this research....

The purpose of this study is to evaluate the manner in which repeated sessions of resistance training effect the biochemical properties of aged skeletal muscle. Approximately ten healthy elderly subjects with no previous experience in strength training will participate in this study. Subjects will train one leg while the other acts as a control. Interested subjects may choose to participate in a full body resistance training program following the completion of the study. Two undergraduate kinesiology students will direct and assist the subjects during the training sessions. The creation and implementation of all resistance training programs will take place under the supervision of the research director. Following the research experiment, research assistants will continue to offer feedback and direction to subjects interested in continuing the training program. Participants will receive an introductory session to the training site and facilities prior to engaging in the program.

The strength training program will take place over a period of 8-9 weeks. Programs will commence in March and end in May 1996. Training sessions will take place approximately three times per week, with each session lasting approximately one hour. Training sessions will include a warm up period, an exercise period and a cool down period.

Needle biopsies will be used for biochemical analysis of the muscle. Biopsies are commonly used in a variety of medical research settings. One biopsy from each leg will be taken before the training commences, and one biopsy will be taken from each thigh upon completion of the training program. Biopsies will be performed by an experienced doctor. Subjects will receive a local anaesthetic in the thigh area prior to the biopsy. For a brief period of time following surgery, subjects may experience muscle soreness. Like most other forms of minor surgery, the possibility of infection exists. Proper care and hygiene offered by the laboratory setting will greatly reduce this possibility.

Subjects will require medical approval and sign a letter of informed consent prior to participating. Subjects have the right to withdraw from the study at anytime. Results of the study may appear in a publication, however, at all times, the identity or the participants will remain confidential. After the completion of the research the results will be made available to the participants, upon request.

About the student that you are helping....

I am a graduate student in the School of Kinesiology, Lakehead University. I have successfully completed an Honours Bachelor of Physical Education at Brock University. The enclosed proposal for research outlines the nature of my thesis project. Successful completion of this research will partially fulfill the requirements of the Masters of Science program in which I am currently enrolled. Further, completion of this research will also contribute to a Specialization in Gerontology in the aforementioned degree. I hope to continue research in the field of Exercise Science and Gerontology through the pursuit of a Ph.D. degree.

I have a sincere interest in the physical and psychological well being of seniors. I have had experience interacting with seniors from a number of perspectives, both theoretical and practical. In undergraduate and graduate courses, I have studied the elderly with respect to movement and exercise, research and theory in gerontology and adapted physical education (study of the mentally and/or physically challenged with respect to movement and exercise). Outside of the academic realm, I have interacted with the elderly in less formal situations such as working in a retirement home, and socializing with elderly relatives. Thus, I feel confident in my ability to interact with the research participants in a manner that considers each individual with respect and dignity. I am also aware of the physical, social and psychological changes associated with aging. Such knowledge will be useful in recognizing the limitations of each participant, while helping them strive to explore their potential through exercise.

As described in the research proposal, this project will require participants to take part in a resistance training/ strength conditioning program. I have a wealth of experience in the field of strength conditioning. Thus, my experience and knowledge of strength conditioning will be used in order to maximize the safety of the participants involved. Moreover, Dr. Thayer, my research director will supervise the creation and implementation of each personalized training program. Thank you, in advance for your interest in this research. Should any concerns arise, please contact me using the information provided below.

Sincerely,

David O'Neill, B.Ph.Ed.
Lakehead University
Bus. 343-8544 Hm. 345-8794

Appendix # 4 *Typical Myosin ATPase histochemical stain*

The accompanying photographs represent typical serial cross-sections of muscle samples taken prior to training in a female subject. Sections were assayed for myofibrillar ATPase activity after preincubation at pH values of 10.2 (A) and 4.6 (B). In A type I and II have been distinguished. In B note the further distinguishing of fibre types into subtypes type IIa and IIb.

Appendix # 4 *Typical Myosin ATPase histochemical stain*

Appendix # 5 *Typical western blot for HSP 72*

The accompanying photograph represents a typical western blot indicating the contents of the inducible (HSP 72) isoform of the 70 kDa family of heat-shock proteins in muscle sample homogenates. Similar gels were loaded with 40 ug of protein and transferred to nitrocellulose and reacted with anti-HSP 72 or anti-10D10 myosin antibody as described in Method. Lane A: molecular marker; Lane H: soleus control; Lanes B, D, and F: pre-training samples; Lane C, E, and G: post-training samples. Note the maintenance of HSP 72 expression following training.

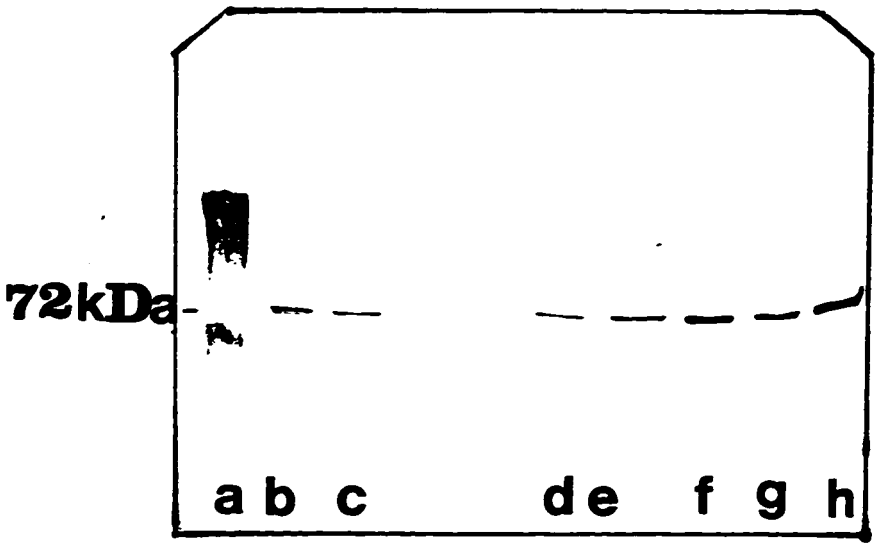

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IMAGE EVALUATION
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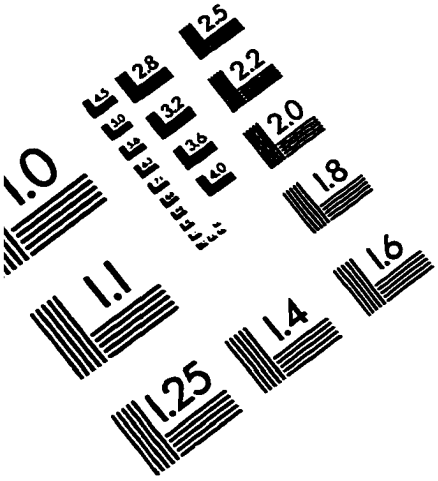

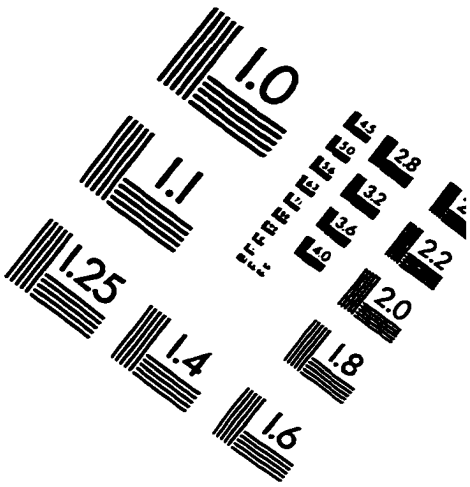

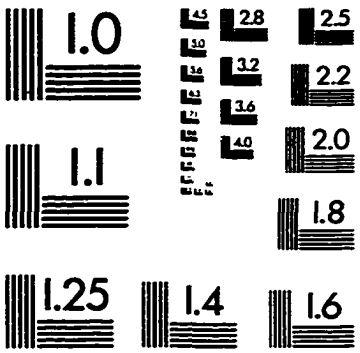

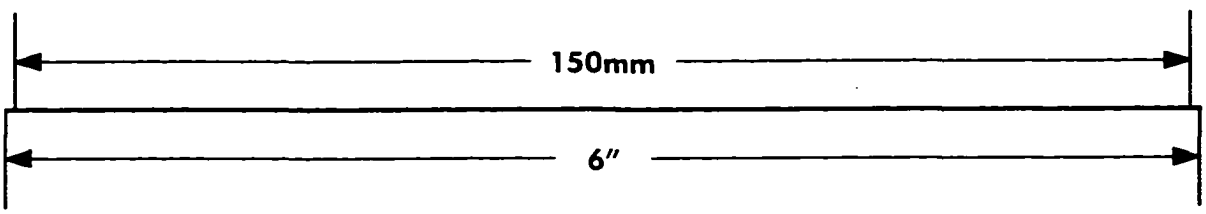

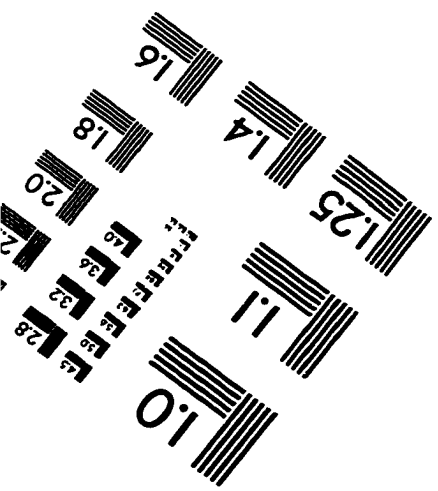

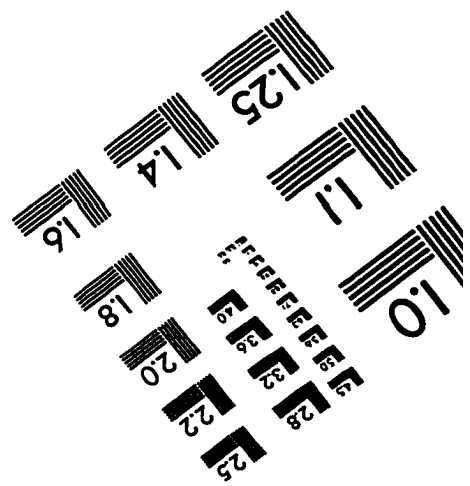

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