The benefits of strength training in the elderly✩

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Summary

Topics – The number of people reaching advanced adult age in many countries of the world has increased dramatically in the last century. The main problem associated with aging is the loss of functional capacity and independence. An important contributor to this problem is the age-related decline in muscle mass (sarcopenia) and strength seen in both men and women. Longitudinal studies show a loss of approximately 1–2% per year in isokinetic strength of the knee. Changes in the elbow flexors and extensors were less dramatic and more significant in men than women. Although muscle atrophy is a significant contributor to the weakness seen in the elderly, single fiber studies have demonstrated a loss of muscle fiber quality (specific force). This may be due to alterations in the myosin molecule.

Perspectives – Strength training has been shown to partially reverse age-related losses in muscle function. Progressive resistance training results in dramatic increases in muscle strength, significant hypertrophy (although to a lesser degree), an increase in protein synthesis, an increase in muscle fiber specific force, and changes in functional tests such as walking speed and stair-climbing power. It remains to be seen whether the myosin molecule is altered with strength training.

aging / myosin / resistance training / sarcopenia / skeletal muscle

Résumé – Les bénéfices de l’entraînement en force chez les personnes âgées. (Synthèse française du texte.)

Actualités – Le nombre de personnes atteignant un âge avancé a considérablement augmenté au cours du siècle dernier. L’une des conséquences majeures liées à ce vieillissement tient à la baisse de la capacité fonctionnelle et à l’autonomie des personnes âgées. Cette incapacité fonctionnelle progressive est essentiellement liée à une réduction de la masse musculaire (sarcopénie) et de la force développée. L’attrition des performances musculaires affecte aussi bien les hommes que les femmes. Des études longitudinales ont permis d’estimer à 1–2% la perte de force annuelle enregistrée en mode isocinétique. Il semble exister une spécificité du sexe dans la réponse des performances musculaires au vieillissement puisque la perte de force en mode isocinétique est plus marquée chez les hommes que chez les femmes. Cependant, les niveaux de force étant plus élevés chez les hommes à l’âge adulte, les effets du vieillissement ont chez eux des conséquences fonctionnelles moins marquées. L’amyotrophie est un des facteurs qui permettent de rendre compte de la baisse de la production de force. Cependant, des études sur fibres isolées ont permis de suggérer que des altérations biochimiques complexes participent aussi à expliquer la baisse de performance au cours du vieillissement. Parallèlement à l’amyotrophie, on enregistre une véritable diminution de la capacité qu’ont les fibres à produire de la force. L’origine de ce dysfonctionnement reste obscure mais pourrait impliquer les propriétés de la molécule de myosine elle-même dont la synthèse et le taux de renouvellement sont réduits.

Perspectives – L’entraînement en force annule ou presque, les effets de l’âge sur les performances musculaires. Ce type d’entraînement se traduit par une augmentation de la masse musculaire résultant principalement d’une


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augmentation des synthèses protéiques. Les performances de force sont elles aussi améliorées, au niveau du muscle entier comme de la fibre elle-même ; les effets de l’entraînement en force chez le sujet âgé se traduisent par une amélioration de tests fonctionnels simples comme la vitesse de marche ou la montée d’escaliers. Les réponses spécifiques des isoformes de la myosine à l’entraînement chez le sujet âgé restent cependant à déterminer. © 2002 Éditions scientifiques et médicales Elsevier SAS

entraînement en résistance / muscle squelettique / myosine / sarcopénie / vieillissement

1. DEMOGRAPHICS OF AGING

Demographical data suggest that, by the year 2025, the number of people above age 60 in all the countries in the world will exceed one billion [27]. Rowe and Kahn have stated in their book “Successful Aging” that in the forty-five hundred years from the Bronze Age to the year 1900, life expectancy increased twenty-seven years, and that in the short period from 1900 to 1990 it increased by at least that much [24]. In fact, it is currently estimated that of all human beings who have ever lived to be sixty-five years or older, half are currently alive [24]. These are impressive changes in the age composition of our society. However, as stated by Banks and Fossel [2], chronological age per se does not determine aging.

The main problem associated with advanced adult age is the dramatic decline in functional capacity and the associated loss of independence. Since maximal physiological capacities are greatly diminished with aging, the ability to perform physical tasks at the same level of energy expenditure or muscular force becomes limited. In other words, an activity that represents a submaximal effort in young adults, such as rising from a chair, could become a maximal or supramaximal endeavor in the elderly. Research to understand the basis for this decline in physiological capacity and functional abilities is urgently needed. Likewise, clinical studies to test the efficacy of new preventive and rehabilitative strategies are necessary.

One important contributor to the functional loss that results in impairment and disability is the decline in skeletal muscle strength and mass (sarcopenia) associated with advancing age. It has been established that skeletal muscle strength correlates with walking speed, balance, time to rise from a chair, ability to climb stairs, incidence of falls, and survival rates [21]. Furthermore, muscle strength has been demonstrated to be a predictor of physical dysfunction (Fig. 1) in a large recent 5 year longitudinal study of strength and disability [3]. Thus, understanding the mechanism underlying contractile muscle dysfunction has significant functional implications and could help us design better rehabilitative programs to enhance independence in the elderly.

Figure 1. Muscular strength and physical function. Percentage of subjects with functional problems after 5 years. * P < 0.05. Adapted from Brill et al., 2000.

This brief paper summarizes some of the research on the loss of skeletal muscle mass and strength with advanced adult age. It is our objective to also emphasize the effects of strength (heavy resistance) training programs on skeletal muscle function and structure in older men and women. Due to the limitations in space, we will not attempt to present a comprehensive analysis of the scientific literature on the topic. Emphasis will be given to the results of our cross-sectional and longitudinal studies and, when appropriate, reference will be made to many excellent studies published in the literature.

2. SKELETAL MUSCLE IN THE ELDERLY

2.1. Muscle strength

A cross-sectional study of muscle strength and mass in 45- to 78-yr-old men and women showed that isokinetic strength of the elbow and knee extensors and flexors was lower (range 15.5–26.7%) in the 65- to 78- than in the 45- to 54-yr-old men and women [6]. Other cross-sectional studies have reported similar differences in strength among age groups. More recently, approximately 10 years after the baseline evaluation, we tested again 64% of the volunteers (54 men and 78 women) who participated in that cross-sectional study [10]. Significant losses were observed in the isokinetic strength of the knee
and elbow extensors and flexors of both, men and women (Fig. 2). Men demonstrated a higher absolute strength than women in all muscle groups and lost absolute strength at a faster rate than women. This recent study gave us the opportunity to compare strength losses using cross-sectional and longitudinal designs in the same cohort of subjects. No sex-related differences were seen in the cross-sectional design; thus the data were combined. However, in men, longitudinal losses of muscle strength in the knee extensors and flexors were significantly higher than cross-sectional losses suggesting that cross-sectional studies may underestimate the decline in strength with age. This may be due to the bias introduced by the selection of healthier (i.e., those who have survived) older groups in cross-sectional studies. On the other hand, for the elbow extensors and flexors, cross-sectional and longitudinal analysis revealed similar rates of changes, except for the elbow flexors in women.

Finally, it is of interest to note that, depending on the muscle group and sex, between 7 and 32% of the subjects showed gains in muscle strength. Thus, muscle atrophy and weakness is not a homogeneous and universal phenomenon. The genetic, physiological, and environmental factors preventing muscle weakness with advancing age in some subjects must be understood and deserve serious study.

2.2. Muscle size and composition

A reduction in muscle size explains, at least partially, the muscle weakness commonly seen in the elderly. The relative contribution of muscle atrophy, however, is not clear. In a subset of subjects ($n = 9$) participating in our longitudinal study, strength at the time of the first evaluation and the change in muscle cross-sectional area determined by computerized tomography over 12 years accounted for 90% of the variability in strength in the second evaluation [7]. In that group, a 25% decline in the strength of the knee extensors was accompanied by a 16% reduction in muscle cross-sectional area by CT. It is of interest to note that macroscopic changes in thigh cross-sectional area may reflect not only muscle atrophy, but also an increase in the amount of non-contractile tissues (i.e., fat and connective tissue). For example, Kent-Braun et al. [13], have recently reported differences in the relative composition of the thigh between young and older subjects as determined by magnetic resonance imaging. In that study, the % of the muscle cross-sectional area representing contractile tissue was reduced from 94 to 86 and from 94 to 84 in older men and women, respectively.

In addition to muscle wasting, a change in muscle quality could also contribute to muscle weakness in the elderly. Indeed, a report from the Baltimore Longitudinal Study show a reduction in the $in vivo$ strength to whole muscle size ratio [18]. It is of significant scientific interest to determine if specific age-related cellular alterations in skeletal muscle contribute to contractile dysfunction independently of the absolute reduction in the amount of the contractile proteins such as actin and myosin.

2.3. Studies of single human muscle fibers

Muscle fiber segments obtained using the percutaneous muscle biopsy needle technique and chemical skinning can be used to study the possibility of changes in specific force (strength corrected for size) due to alterations in the intrinsic ability of muscle fibers to generate force. With this method, the contractile properties of single fibers obtained using the biopsy needle, can be studied isolated from the influences of the nervous system. Also, since the process of chemical skinning disrupts the sarcolemma and sarcoplasmic reticulum, and the concentration of the substances present in the medium can be carefully controlled, weakness in single fibers can be interpreted as representing structural and/or functional alterations in the regulatory and/or contractile proteins.

Recently, we reported an age-related reduction in the specific force (Fig. 3) of single muscle fiber segments expressing type I and IIa myosin heavy chain isoforms (determined by SDS-PAGE) in older men [8]. Fibers from older men demonstrated significantly lower specific forces than younger men expressing the same myosin heavy chain isoform. In young and older men, fibers expressing type IIa myosin heavy chain had higher specific forces than type I fibers. Also, our results demonstrated significant differences in single fiber maximal force between older men and women that were dependent on fiber type and that could not explained by differences in fiber size.

2.4. Myosin molecule alterations

One possible site for the alteration resulting in contractile dysfunction is the cross-bridge and more specifically
the myosin protein. An age-related decline in the synthesis rate of the myosin heavy chain has been observed in humans [1]. At least three molecular/cellular mechanisms may contribute to a quantitative or qualitative alteration in the myosin motor: 1) a reduction in gene transcription; 2) a slow protein turnover rate resulting in accumulation of dysfunctional myosin molecules; and/or 3) post-translational modifications of the myosin protein such as glycosylation or oxidation. Alone or in combination, these changes could alter the basic properties of the molecule resulting in a reduction in the force generated per cross-bridge. In fact, recent data from Lowe et al. [16], support this hypothesis. Alterations in the ATPase site of the myosin molecule could also result in changes in other contractile properties of the muscle fiber such as its shortening velocity. This is supported by the work of Höök et al. [9], using an in vitro motility assay to study rat muscle.

3. STRENGTH TRAINING IN THE ELDERLY

Since 1988, at least 50 studies have been published in the scientific literature on the effects of strength training in older men and women. Despite some differences in the magnitude of the effect, the vast majority of the data demonstrate that strengthening exercises result in significant improvements in skeletal muscle function. Muscle hypertrophy, cellular adaptations, and changes in the performance of functional tasks have also been reported.

3.1. The exercise prescription

Strength training studies have used various combinations of frequency, intensity, and duration. The type of exercise and training devices has include free weights, pulleys, and isokinetic and variable resistance devices. Most studies have used 5–15 repetitions per set and 2–6 sets per training session for each muscle group. The weekly frequency of training has ranged between 2 and 5 days and the intensity of the training has varied from 40 to 90% of the one repetition maximum; in most studies the subjects trained at the 60–80% range. Short (2 weeks) and long duration studies (1–2 years) have been reported although most studies are in the 12–24 week range.

3.2. Adaptations in muscle strength

Static and dynamic (including isokinetic) muscle strength has been shown to increase significantly with strength training in the young old, old, and even in the frail elderly [4, 5, 15, 17, 19]. The relative magnitude of the strength gains ranges between 10 and 180% of the baseline. The wide range is probably due to the variety of exercise prescriptions used in the different studies. The adaptations in strength are noticeable after a few days of training and are more significant when the testing technique is similar to the training method. This observation is very consistent across studies and suggests that a significant component of the adaptation is neural and is independent of the peripheral adaptations that occur in the muscle itself. Although the nature of the neural adaptations remains vague there is significant indirect evidence (angle specificity, velocity specificity, cross-over effect) supporting this hypothesis [14].

With regard to the changes in strength, two interesting observations must be highlighted. First, it has been noted that even after long-term training (1–2 years) strength improvements do not appear to reach a plateau and further gains appear to be possible [17, 19]. Second, it is feasible to interrupt training with a period of deconditioning and continue to show gains in strength after resumption of training [15].

3.3. Muscle hypertrophy

The majority of studies measuring muscle cross-sectional area using ultrasound, computerized tomography, or magnetic resonance imaging have reported significant skeletal muscle hypertrophy (range: 2.0–14.5%). Metabolic studies have shown significant increases in the urinary excretion of 3-methylhistidine. Clearly, skeletal muscle is capable of responding to the stimulus of strength training with an increase in the synthesis of contractile proteins [28, 29]. These improvements, however, were not enhanced when strength training was combined with growth hormone. Hypertrophy has been also demonstrated (5 out of 7 studies) at the microscopic level using histochemical techniques to study muscle fiber cross-sectional area in biopsy specimens. Increases of up to 30% have been noted in both type I and type II fibers after training. It is
significant to note the differences in the relative change in strength and muscle size; again emphasizing the importance of the neural adaptations.

### 3.4. Cellular and ultrastructural adaptations

Several recent studies have looked at the cellular and ultrastructural adaptations with strength training. Trappe et al. [25], recently reported significant increases in the maximal force and cross-sectional area of type I and IIa single muscle fibers after 12 weeks of progressive resistance training. It is interesting that, the unloaded maximum shortening velocity and power of single muscle fibers were also increased. A second report from the same group of researchers demonstrated an increase in the expression of the type I myosin heavy chain isoform and a reduction in the frequency of co-expression of myosin heavy chain isoforms in the same fiber [26] after training.

Since strength training usually includes eccentric muscle actions, and such actions could induce muscle damage, it is of importance to know if the elderly are more susceptible to muscle damage during strength training. Two studies from the same group [22, 23] demonstrate the same degree of focal muscle damage with heavy resistance training occur in young and older men (Fig. 4). However, older women exhibited higher levels of muscle damage than young women. The sex-related differences in the response to strength training deserves further investigation [12].

The effect of strength training on other cellular components of muscle fibers has been examined. For example, Hunter et al. [11] have reported that the reduced calcium uptake by the sarcoplasmic reticulum in skeletal muscle of elderly women was partially reversed with resistance training. Also, the activity of the sarcoplasmic reticulum ATPase was enhanced after training. These adaptations did not translate, however, into changes in the time of relaxation of whole muscle. More research is needed to understand the effects of strength training on the various components of the excitation-contraction coupling mechanism, energetic processes, and the mechanical events leading to force generation at the level of the cross-bridges in the elderly.

### 3.5. Functional implications

From a rehabilitation perspective it is important to know if the physiological adaptations to strength training result in an enhanced functional capacity. Indeed, after training, older men and women show improvements in walking speed and stair climbing power (for review see [20]). If the age-associated decline in muscle strength is partially reversed, it may be possible for the elderly to maintain physical independence and perform, once again with submaximal efforts, many of the activities of daily living.

### 3.6. Aging vs. training

Within the limitations of the studies, it is possible to compare, for the purposes of our discussion, the effects of aging and the benefits of strength training as in Fig. 5. It is important to point out that, although the two studies involved some of the same subjects, the training study was done first. Nevertheless, the evidence is consistent with a partial reversal of the age-related losses with relatively short-term strength training.
SYNTHÈSE FRANÇAISE

De très nombreuses études démographiques ont permis de souligner le vieillissement constant de la population. Ce vieillissement va croissant au cours du temps, et s’est considérablement amplifié au cours du XXème siècle. L’un des problèmes majeurs de ce vieillissement de la population générale est lié à la diminution importante des capacités fonctionnelles et de l’autonomie des sujets. Ainsi, des gestes communs, réalisés sans difficulté par des adultes bien portants, sont susceptibles de représenter une charge de travail importante pour des sujets âgés. Dans ce domaine, des recherches sont engagées pour mieux comprendre les mécanismes biologiques du vieillissement et des altérations fonctionnelles, et pour évaluer l’efficacité de contre-mesures.

Au cours du vieillissement, la baisse de l’autonomie est en partie liée à l’amyotrophie et à la baisse des performances musculaires. L’importance des désordres fonctionnels enregistrés au cours du vieillissement, est statistiquement liée à l’altération de la force musculaire (Fig. 1). La compréhension des mécanismes biologiques affectant le muscle au cours du vieillissement, est donc d’une grande importance.

1. CARACTÉRISTIQUES DU MUSCLE CHEZ LE SUJET ÂGÉ

1.1. Force musculaire

Il est bien connu que les performances musculaires sont affectées par le vieillissement. C’est ainsi que les couples musculaires développés en mode isocinétique sont diminués au cours du temps, à la fois pour les muscles extenseurs et fléchisseurs du coude et du genou, chez les hommes, comme chez les femmes (Fig. 2). Cependant, bien que l’altération des performances soit plus rapide chez les hommes que chez les femmes, ceux-ci conservent des valeurs de couple plus élevées pour une même tranche d’âge. Bien que la force développée soit fonction de la masse musculaire, et par extension, de la surface moyenne de section du groupe musculaire, au cours du vieillissement, la perte de performance est plus importante que l’amyotrophie. Ainsi, la simple mesure de l’attrition de la masse musculaire sous-estime la baisse de performances.

1.2. Le muscle, son volume et sa composition

Comme nous venons de le préciser, on observe une amyotrophie au cours du temps, qui rend compte d’une partie des baisses de performances musculaires. Nous avons montré, au cours d’une étude longitudinale, que 90 % de la variabilité de la force étaient expliqués par des variations de la surface de section du muscle, estimée par imagerie médicale, et que pour 25 % de baisse de force développée, les sujets présentent en moyenne 16 % de baisse de la surface moyenne de section des muscles [7]. Cependant, les variations macroscopiques de la surface de section des muscles ont des limites et reflètent non seulement les variations du contenu en protéines contractiles, mais aussi en graisse et en tissu conjonctif. Parallèlement à l’amyotrophie, ce sont aussi les qualités intrinsèques du muscle qui peuvent être affectées par le vieillissement ; la question du rôle spécifique joué par des modifications des propriétés contractiles des fibres elles-mêmes mérite d’être posée.

1.3. Les propriétés des fibres musculaires chez le sujet âgé

Des études sur fibres isolées ont permis de mettre en évidence une diminution de la force développée par les fibres lentes de type I comme par les fibres rapides de type Ila avec le vieillissement (Fig. 3) [8]. La diminution de force pourrait être liée soit à : 1. une baisse de la transcription des gènes codant pour les chaînes lourdes de la myosine ; 2. un ralentissement du taux de renouvellement des protéines contractiles, induisant une accumulation de formes altérées (ou « vieillissantes ») de ces protéines ; 3. une altération du contrôle post-traductionnel de ces gènes avec des anomalies de glycosylation des protéines produites, les rendant ainsi moins fonctionnelles. Un ou plusieurs de ces mécanismes combinés contribuent à une baisse de la force produite par chaque pont actine-myosine [16].

2. ENTRAÎNEMENT EN FORCE

De très nombreuses études ont permis de mettre en évidence tout le bénéfice tiré de l’application de protocoles d’entraînement en force chez le sujet âgé, en particulier sur la fonction musculaire. Les protocoles proposés varient beaucoup d’une étude à l’autre, par le type d’appareil utilisé, le nombre de répétitions par séance, la fréquence hebdomadaire, etc.

2.1. Les effets de l’entraînement sur la force musculaire

Même si les durées d’application de ces entraînements varient beaucoup, tous sont efficaces sur les performances musculaires. Les progrès enregistrés dans le développement de force sont très rapides, ce qui laisse à penser qu’une adaptation neurale à type de meilleures synchronisations des motoneurones précède les réponses cellulaires périphériques.
2.2. Les effets de l’entraînement sur la masse musculaire

Un gain de masse musculaire est régulièrement observé en réponse à l’entraînement en force (gain de 2 à 14,5 %). Cette hypertrophie du muscle résulte d’une augmentation de la taille de chaque élément cellulaire, elle-même résultant d’une augmentation de la synthèse des protéines contractiles.

2.3. Réponses cellulaires à l’entraînement en force

Ce type d’entraînement se traduit par une augmentation du calibre des fibres lentes comme des fibres rapides, de la force développée par les fibres isolées, et de l’expression de la forme lente de la myosine (de type I). Cependant, l’entraînement en force est associé à une augmentation des contraintes mécaniques appliquées au muscle, et la question de la susceptibilité des sujets âgés aux microlésions musculaires a été posée. L’équipe de Walter Frontera a clairement montré que les hommes âgés répondent de la même manière, et pas plus, à l’application d’un exercice excentrique connu pour être traumatisant pour les fibres cellulaires (Fig. 4) [22, 23].

2.4. Conséquences fonctionnelles

Ces améliorations des performances musculaires ont des conséquences fonctionnelles évidentes, et ce sont des augmentations de la vitesse de marche ou des capacités à la montée des escaliers qui sont rapportées [20]. L’amélioration des performances musculaires peut ainsi se traduire, chez les sujets âgés, par une véritable amélioration de la qualité de vie.

2.5. Vieillissement versus entraînement

On pourrait comparer, avec cependant une certaine prudence, les effets respectifs du vieillissement et de l’entraînement (Fig. 5). En 12 ans, on observe une baisse de 24 % de la force développée par les extenseurs de la jambe (et de 16 % de la surface de section de ces muscles), alors qu’en 12 semaines d’entraînement, elle augmente de 16 % (et de 11 % pour la surface de section des muscles).

REFERENCES