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Daniel Galvao Edith Cowan University

Robert Newton Edith Cowan University

Dennis Taaffe University of Queensland

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### **SCHOLARLY REVIEWS**

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# *Anabolic Responses to Resistance Training in Older Men and Women: A Brief Review*

*Daniel A. Galvão, Robert U. Newton, and Dennis R. Taaffe*

Resistance training has been shown to be the most effective exercise mode to induce anabolic adaptations in older men and women. Advances in imaging techniques and histochemistry have increased the ability to detect such changes, confirming the high level of adaptability that remains in aging skeletal muscle. This brief review presents a summary of the resistance-training studies that directly compare chronic anabolic responses to training in older (>60 years) men and women. Sixteen studies are summarized, most of which indicate similar relative anabolic responses between older men and women after resistance training. Relatively small sample sizes in most of the interventions limited their ability to detect significant sex differences and should be considered when interpreting these studies. Future research should incorporate larger sample sizes with multiple measurement time points for anabolic responses.

*Key Words:* weight training, aging, lean mass, strength

Normal aging is characterized by a decline in skeletal-muscle mass and an increase in fat mass (Frontera et al., 2000; Fukagawa, Bandini, & Young, 1990; Lexell, 1995). The reduction in muscle mass, termed sarcopenia, leads to a loss in muscle strength and is associated with a decline in physical function that compromises independent living (Rosenberg, 1997). Numerous studies, however, have shown resistance training to be a safe and effective intervention to counteract sarcopenia, even in the very old—that is, those age 85 years and older (Charette et al., 1991; Fiatarone et al., 1990, 1994; Taaffe, Duret, Wheeler, & Marcus, 1999; Taaffe, Pruitt, Pyka, Guido, & Marcus, 1996).

The landmark study in 1988 by Frontera and colleagues (Frontera, Meredith, O'Reilly, Knuttgen, & Evans, 1988) using computed tomography scanning of the midthigh and muscle-tissue samples clearly showed the residual capacity that older adults have to increase muscle cross-sectional area (CSA) with an increase in midthigh total muscle area of 11.4% and an increase in Type I and II fiber area of 33.5% and 27.6%, respectively, after 12 weeks of strength training. Subsequently,

Galvão and Newton are with the School of Biomedical and Sports Science, Edith Cowan University, Joondalup, Western Australia 6027, Australia. Taaffe is with the School of Human Movement Studies, University of Queensland, Brisbane, Queensland 4169, Australia.

numerous studies have reported positive changes in muscle CSA, muscle-fiber size, and body composition after resistance-training interventions (Charette et al., 1991; Fiatarone et al., 1994; McCartney, Hicks, Martin, & Webber, 1996; Taaffe et al., 1999, 1996). Less clear is the effect of age and sex on the anabolic response to resistive exercise.

In studies directly comparing anabolic responses between young and older adults to resistance exercise, older adults retained the ability to adapt in a relatively similar fashion to their younger counterparts (Hakkinen et al., 1998; Ivey et al., 2000; Lemmer et al., 2000; Roth et al., 2001), although this has not always been reported (Welle, Totterman, & Thornton, 1996). In young adults, the majority of studies (Abe, DeHoyos, Pollock, & Garzarella, 2000; Cureton, Collins, Hill, & McElhannon, 1988; Hurlbut et al., 2002; Lemmer et al., 2000, 2001; O'Hagan, Sale, MacDougall, & Garner, 1995; Roth et al., 2001; Staron et al., 1994) indicate that men and women experience similar relative changes in fat-free mass, muscle CSA, and fiber CSA after training, although others (Ivey et al.) have reported a greater response in men. In older adults (>60 years), some investigations have demonstrated similar relative strength gains and body-composition changes between men and women after training (Fiatarone et al., 1994; Ivey et al.; Lexell, 1995; McCartney, Hicks, Martin, & Webber, 1995; McCartney et al., 1996; Roth et al.; Tracy et al., 1999), whereas others indicate the presence of sex differences as determined by singlemuscle-fiber contractile function (Trappe et al., 2001), fiber diameter (Bamman et al., 2003; Hakkinen et al., 2002), and muscle CSA (Hakkinen et al., 1998). It has been suggested that differences in anabolic hormones and the myostatin genotype might contribute to these sex differences (Bamman et al.; Ivey et al.).

Given the increased recognition of sarcopenia in the medical and allied-health community and the recommendation by professional bodies for older adults to undertake resistance exercise (American College of Sports Medicine, 1998), the effects of training in older adults need to be clearly delineated, including any differences by sex. Women are more susceptible to falling below the strength thresholds required for daily activities and are subject to longer periods of compromised function than men because of their greater longevity (Ivey et al., 2000). As a result, if there are sex differences in the response to a given exercise stimulus, this needs to be determined so that the most appropriate exercise programs can be devised. Therefore, the purpose of this article is to present an overview of studies that have undertaken measures of body composition, muscle, and fiber-CSA adaptations to resistance training in older men and women who perform the same intervention. In addition, we briefly discuss studies that include only older men or women to provide a more comprehensive overview of the topic. Because of differences in tissue- and body-composition measurement techniques, this brief review is divided into seven subsections: computed tomography, dual-energy X-ray absorptiometry, magnetic resonance imaging, compound ultrasound, the BOD POD, muscle biopsy, and myosin heavy-chain analysis.

# **Training Studies by Assessment Technique**

An overview in chronological order of the studies directly comparing men and women undertaking the same training intervention is provided in Table 1. Apart from the anabolic response, the effect of the intervention on body weight and muscle strength is also provided.

# **COMPUTED TOMOGRAPHY**

Computed tomography (CT) uses multiple X-rays and computers to reconstruct images of the target area and generate quantitative information of muscle area, subcutaneous and intermuscular fat area, and attenuation of the tissue as determined by Hounsfield units (Lee, Wang, & Heymsfield, 2001; Mitsiopoulos et al., 1998; Sipila & Suominen, 1993). McCartney et al. (1995) examined the effect of resistance exercise on muscle CSA assessed by CT in men and women (60 to 80 years) after 10 months of training. Participants were randomly allocated to an exercise or control group and performed the unilateral leg press, ankle plantar flexion, and ankle dorsiflexion, as well as several upper body exercises. Similar CSA adaptation of the knee-extensor muscles for men  $(6.2\%)$  and women  $(4.7\%)$  was observed, and both percentage changes were significantly greater than in controls. In a subsequent report after 2 years of training (McCartney et al., 1996), CSA of the knee extensors for both men and women continued to increase, although not at the same rate as in the first year of the study.

# **DUAL-ENERGY X-RAY ABSORPTIOMETRY**

Dual-energy X-ray absorptiometry (DXA) estimates fat mass, bone-mineral free lean mass, and bone-mineral mass using two distinct low-energy X-rays that penetrate the soft tissue and bone areas. It has been demonstrated to be an accurate and precise method of body-tissue composition compared with reference methods such as total body potassium, hydrodensitometry, magnetic resonance imaging (MRI), CT, and four-component models (Haarbo, Gotfredsen, Hassager, & Christiansen, 1991; Kohrt, 1998; Prior et al., 1997; Shih, Wang, Heo, Wang, & Heymsfield, 2000; Visser, Fuerst, Lang, Salamone, & Harris, 1999). Body-composition response to resistance training assessed by DXA in older men and women was reported by Martel et al. (1999). Participants (65–73 years old) trained 3 days per week for 24 weeks, performing several upper and lower body exercises. There were no significant differences as a result of resistance training in either sex for fat-free mass or body fat. When men and women were combined, a significant increase was detected for fat-free mass ( $p < .05$ ).

Lemmer et al. (2000) reported the effect of a training regimen that incorporated five sets of five repetitions maximum of unilateral leg-extension exercise of the dominant leg for 9 weeks on strength and body composition in older men and





 $\overline{(continued)}$ *(continued)*



\*Significantly different from baseline (*p* < .05). \*\*Approached significance compared with baseline (*p* = .06). †Significantly different between groups (*p*

**Table 1**  *(continued)*

women. There was no significant change in body fat and fat-free mass. Although the study was primarily designed to detect sex-related changes in muscle strength with training and detraining, results from the body-composition changes are limited because only the quadriceps muscle group was trained. The same group of investigators (Lemmer et al., 2001) also examined the effect of age and sex after 24 weeks of resistance training. Eleven men and 10 women (age 65–75 years) trained 3 days per week using unilateral leg press, leg curl, leg extension, chest press, lat pull-down, military press, upper back, triceps extension, and unilateral biceps curl. Men and women significantly increased fat-free mass from baseline to Week 24 (*p* < .05), with no significant difference by sex.

Hurlbut et al. (2002) examined the effect of resistance training by age, sex, and angiotensin I-converting enzyme genotype on fasting and glucose-stimulated glucose and insulin response. Twelve men and 9 women (age 65–75 years) exercised thrice weekly over 24 weeks. The training routine consisted of three lower body exercises, six upper body exercises, and two trunk exercises. After training, men increased fat-free mass by  $1.5\%$  ( $p < .05$ ) and women by 2.2%, which approached statistical significance ( $p = .06$ ). There were no significant changes in fat mass for either group.

Recently, Ryan et al. (2004) reported the results of a 24-week whole-body resistance-training program on body composition in older men and women. There was no significant change in fat-free mass for older women (1.7%), whereas the increase for older men  $(1.6\%)$  reached statistical significance  $(p < .05)$ . No changes were observed for body fat in either group. In addition, both men (24.2%) and women (20.8%) similarly increased whole-body muscle strength ( $p < .001$ ), which is the average strength for the exercises and muscle groups examined. Although percentage change in these studies (Hurlbut et al., 2002; Ryan et al.) for fat-free mass was similar between men and women, the change for women did not achieve statistical significance, perhaps indicating a greater within-group variance. That is, women might not demonstrate as consistent a change in response to resistance training as men.

#### **MAGNETIC RESONANCE IMAGING**

In contrast to CT and DXA, which employs ionizing radiation, magnetic resonance imaging (MRI) uses magnetic energy and radio waves to derive images of a target tissue area and has been found to be an accurate method for assessing tissue composition (Lee et al., 2000, 2001; Mitsiopoulos et al., 1998). The effect of resistance training on muscle volume assessed by MRI has been reported by Ivey et al. (2000) and Tracy et al. (1999). Men and women (age 65–75 years) participated in a resistance-training intervention performing unilateral knee extension of the dominant leg three times per week for 9 weeks while the opposite leg served as the control. Muscle-volume change was similar for men (11.5%) and women (12%), with no change in whole-body fat-free or fat mass assessed by DXA. The lack of change in fat-free or fat mass assessed by DXA was not surprising, given that only one muscle group was trained.

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Roth and colleagues (2001) examined sex differences in thigh-muscle volume response after resistance training in participants age 65–75 years. Nine men and 10 women performed unilateral leg press, unilateral leg curl, unilateral leg extension, chest press, lat pull-down, overhead shoulder press, upper back rowing, triceps extension, and unilateral biceps curl thrice weekly for 24 weeks. Both groups demonstrated a significant increase in fat-free mass (*p* < .05) but not for percentage of body fat assessed by DXA. MRI results indicated that both men (4.1%) and women (5.8%) increased ( $p < .01$ ) estimated whole-thigh-muscle volume, with no significant difference between groups. Similarly, men  $(1.6\%)$  and women  $(5.6\%)$ experienced a significant increase in midthigh-muscle CSA  $(p < .01)$ , although the difference between sexes was not statistically significant.

# **COMPOUND ULTRASONIC SCANNER**

Compound ultrasonic scanner (CUS) uses acoustic impedance properties of the body's tissues to form an image from which muscle tissue can be separated from bone and fat tissue (Sipila & Suominen, 1993). Hakkinen and colleagues (1998) investigated muscle strength, body composition, and knee-extensor cross-sectional area with CUS in men and women (age 67–72 years) after 24 weeks of resistance training. The program consisted of a combination of heavy resistance and explosive training. Although percentage of body fat assessed by skinfold did not change during the course of the intervention, muscle CSA of the leg extensors increased by 5.8% in women ( $p < .05$ ), with no significant change for men (2.1%).

# **BOD POD**

The BOD POD estimates body composition by measuring the volume of air an individual displaces inside an enclosed chamber and has been shown to be a valid technique to estimate body composition (Fields, Goran, & McCrory, 2002; Fields, Hunter, & Goran, 2000). Hunter, Bryan, Wetzstein, Zuckerman, and Bamman (2002) used a BOD POD to examine the body-composition response in older men and women after 25 weeks of resistance training. Participants performed five upper body exercises, two lower body exercises, and two trunk exercises three times per week during the intervention. Body fat decreased  $(> 2\%)$  similarly and significantly for men and women ( $p < .05$ ), and the alterations in fat-free mass between men (4.7%) and women  $(2.3\%)$  approached significance  $(p=.06)$ .

### **MUSCLE BIOPSY**

Muscle biopsy is a procedure in which muscle samples are extracted by needle, frozen, and stored for histochemical analysis (Taaffe et al., 1996). The effect of resistance training on muscle strength and Types I and II muscle-fiber CSA for the biceps brachii and the vastus lateralis muscles of men and women (70–77 years of age) was examined by Lexell, Downham, Larsson, Bruhn, and Morsing (1995).

Comparable mean gains in biceps brachii Type II CSA were found in men (17%) and women (16%). This was not statistically significant in men, however, because of large interindividual variation. For the vastus lateralis muscle, there was no significant change in Types I and II CSA, but Type II CSA for men, surprisingly, decreased by 14%.

Hakkinen and colleagues (2002) examined the effects of strength/power training over 24 weeks on muscle-fiber distribution and areas of Types I, IIa, and IIb CSA of the vastus lateralis in older men and women (age 60–75 years). Type I, IIa, and IIb fiber area significantly increased by 50.6%, 48.4%, and 46.2%, respectively, in men, with smaller, yet significant, changes in women of 28.6% for Type I and 33.2% for Type IIa muscle fibers. The 18.9% change in Type IIb CSA for women was not statistically significant, however. When comparing the results for these two groups, this study demonstrated that older men and women had the capacity to significantly increase fiber CSA, with greater adaptations in men.

Bamman and associates (2003) reported the effects of 26 weeks of resistance training on muscle-fiber CSA and myosin heavy-chain composition in 9 men and 5 women (age 61–77 years). Men and women similarly increased fat-free mass by 4.4% and 4.2%, respectively, and decreased body fat by 2.9% and  $3.1\%$  ( $p < .05$ ) as assessed by the BOD POD, with no significant difference by sex. Results from muscle biopsies indicated that men significantly increased Types I, IIa and IIx muscle-fiber CSA by 29%, 41%, and 43%, however, while women increased by only 6.5%, 5.7%, and 5%, respectively, indicating significant differences between the sexes. It is important to note that only 5 women took part in the study and the number of fibers analyzed was not reported. In addition, it is unclear whether the investigators were blinded to sex in the analysis. For clarification purposes, human Type IIb fibers have been shown to be homologous to the Type IIx in rats, so IIx is commonly used for classification of this fibertype (Smerdu, Karsch-Mizrachi, Campione, Leinwand, & Schiaffino, 1994). Apart from the small number of women taking part in this study, it is possible that fiber size of the vastus lateralis muscle does not reflect changes in other muscles after exercise (Frontera et al., 1988; Narici, Roi, Landoni, Minetti, & Cerretelli, 1989), and sex differences in hypertrophy of other muscle groups could contribute to the similar increase in whole-body fat-free mass observed by Bamman et al.

#### **MYOSIN HEAVY-CHAIN EXPRESSION**

Myosin heavy-chain (MHC) composition is analyzed using a muscle sample extracted via biopsy followed by gel electrophoresis techniques for protein separation (Frontera et al., 1988; Schiaffino et al., 1989). In addition, single muscle fibers can be isolated and the characteristics analyzed in terms of both function and diameter. Such analysis completed by Trappe and associates (2001, 2000) involved older men and women after a resistance-training program. In their first report (Trappe et al., 2000), results from a 12-week leg-extension program undertaken by older men resulted in an increase ( $p < .05$ ) of 20.4% and 12.7% in the

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fiber diameter expressed by MHC I and MHC IIa, respectively. Subsequently, the same group of investigators reported the results from an identical training protocol, but on this occasion undertaken by older women (Trappe et al., 2001). The fiber diameter expressed by MHC I and MHC IIa increased in older women by 24.4%  $(p < .05)$  and 6%, respectively. When the results from fiber diameter expressed by MHC I and MHC IIa were compared, no sex differences were observed, but single-muscle-fiber function, expressed by absolute power and maximum shortening velocity, was significantly greater in older men than women ( $p < .05$ ). The authors suggested that older men and women respond differently at the muscle-cell level when the same training stimulus is applied.

#### **Discussion**

As resistance training becomes increasingly recognized as an effective countermeasure to sarcopenia in the medical community, and as more older adults embark on these training regimens, the training responses, including possible sex differences, need to be clearly identified. Moreover, from a research perspective, if men and women attain similar relative anabolic and muscle-strength changes to training, it is possible to combine both sexes in the same sample in exercise trials to increase statistical power or facilitate participant recruitment.

Since the findings by Frontera and colleagues (1988), which clearly refuted Moritani and deVries's earlier (1980) report of a lack of soft-tissue change in response to training in older men, numerous studies have demonstrated the residual capacity of older adults to increase muscle and fiber CSA after resistance training. Advances in the assessment of body and muscle composition by MRI, CT, DXA, and histochemistry over the past 2 decades have enabled the detection of subtle changes that was previously not possible.

Although studies directly comparing older women and men in their anabolic adaptations to resistance training are somewhat limited (e.g., Bamman et al., 2003; Hakkinen et al., 2001; Lemmer et al., 2001; Roth et al., 2001), numerous studies have examined the effect of resistance training on fat-free mass and muscle and fiber area in women and men undertaking different interventions (e.g. Charette et al., 1991; Frontera et al., 1988; Taaffe et al., 1996), supporting the high level of adaptability remaining in aging skeletal muscle.

The only study to date directly comparing muscle area in older men and women by CT reported similar adaptations for the knee extensors—6.2% and 4.7%, respectively (McCartney et al., 1995). The results for older men are in agreement with results reported previously from the same laboratory (Brown, McCartney, & Sale, 1990), where older men increased  $(p < .01)$  knee-extensor muscle CSA by 9.9% after 12 weeks of resistance training. Frontera et al. (1988) reported comparable increases in knee-extensor CSA in older men assessed by CT (9.3%) after 12 weeks of training, and Ferri and associates (2003) reported an increase of 7.4% in knee-extensor muscle CSA after 16 weeks of resistance training. Muscle-CSA response to resistance training in older women has been assessed by Sipila and

Suominen (1995) using CT, with increases in knee-extensor CSA of 4.9% after 18 weeks of exercise, similar to those detected by McCartney and colleagues.

Studies directly comparing fat-free mass and fat mass by DXA (Hurlbut et al., 2002; Ivey et al., 2000; Lemmer et al., 2000, 2001; Martel et al., 1999; Roth et al., 2001; Tracy et al., 1999) after resistance training do not support significant sex differences, except for the study by Hurlbut and associates. It is important to point out that change in fat-free mass and fat mass were not the main outcomes for these studies. As such, it is not expected that changes in body composition will be detected with only one exercise, even in a long-term intervention. In such cases, subregional analysis of the DXA scan might have been a more sensitive technique to detect local changes in tissue composition. In addition, the anabolic effect of such isolated interventions is considerably compromised because the endocrine responses favoring muscle hypertrophy will not be produced. For example, elevation of testosterone and growth hormone with resistance training is closely related to the volume of muscle activated (Hakkinen & Pakarinen, 1993; Hakkinen, Pakarinen, Kraemer, Newton, & Alen, 2000; Kraemer et al., 1999). In contrast, Nichols, Omizo, Peterson, and Nelson (1993) reported a significant increase in fat-free mass of 3.6% for older women in response to 24 weeks of whole-body exercise. The percentage changes are comparable with those reported by Lemmer et al. (2001) of 2.1% and Martel et al. of 2.4% in women after the same duration and frequency of training, although the changes observed by Martel et al. were not statistically significant.

Several studies have compared men and women for muscle-fiber CSA adaptations to the same resistance-training program, and there are conflicting findings among them. Lexell and colleagues (1995) reported similar changes in men and women for the biceps brachii, and Bamman and associates (2003) demonstrated substantial increases in men and lesser magnitude changes in women for the vastus lateralis muscle. Hakkinen et al. (2002) also reported that relative hypertrophy was twice as high in Types I and IIb fiber CSA for the vastus lateralis muscle in men than in women.

Comparing these two gender studies with those involving men or women only also reveals conflicting outcomes. For example, the magnitude of change observed in men by Bamman and associates is in agreement with that observed by Frontera et al. (1988), who reported a 33.5% and 27.6% increase in Types I and Type II fiber cross-sectional area, respectively, in men. Brown and colleagues (1990), however, reported substantial increases in both Type I (13.7%) and Type II (30%) biceps brachii muscle-fiber CSA in older men, similar to findings of Hakkinen and associates (2001) for the vastus lateralis muscle in women (Type I, 18%; Type IIa, 27.7%; Type IIb, 38%) after 21 weeks of training. In addition, Charette et al. (1991) reported increases of 7.3% and 20.1% for Types I and II fiber CSA, respectively, after 12 weeks of training, and Taaffe and colleagues (1996) reported comparable increases in Type I (27.5%) and Type II CSA (22.1%) after 52 weeks of training in women.

The relatively small sample size in most of the studies presented in this review likely limits the ability to detect statistically significant differences between men and women and should be considered when interpreting the results from these

experiments. Moreover, large interindividual variation in identical training protocols increases the standard deviation of the samples and reduces the statistical power to detect a difference if one exists. Some of the studies presented (Hunter et al., 2002; Martel et al., 1999; Roth et al., 2001; Trappe et al., 2001) have a twofold or greater increase in anabolic response between men and women yet are not statistically significantly different. Differences of this magnitude might be clinically important, however. Therefore, clinical or practical versus statistical significance must be considered. Moreover, numerous studies presented in this review were not specifically designed to examine anabolic differences by sex, having such outcomes only as a secondary endpoint of the intervention. Thus, considering the design limitations and differences in anabolic-measurement techniques used in previous studies, future research should incorporate larger sample sizes with multiple measurement time points for anabolic responses.

In summary, most studies directly examining anabolic responses to resistance training in older men and women indicate comparable adaptations after 9–42 weeks of exercise with similar relative increases in muscle strength. Two recent studies, however, indicate that men might exhibit a greater adaptation than women at the muscle-cell level when undertaking the same training program (Bamman et al., 2003; Hakkinen et al., 2002). Although greater changes in fiber CSA might occur in men, only the study by Bamman et al. indicated that these anabolic changes translate into greater relative improvements in muscle strength. Therefore, based on the studies conducted to date, it appears appropriate to include older men and women in the same exercise regimen because the anabolic and muscle-strength response are relatively similar.

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