Original Article

HEALTHY AGING RESEARCH

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Fat metabolism increases after exercise training in older men, but not women

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Background: Reduced fat metabolism (FM) in older persons may be caused by reduced physical activity and peak oxygen consumption (VO_2peak). This study aimed to estimate total body FM in older men and women, and evaluate the extent to which reversing inactivity with an exercise program would improve FM.

Methods: VO_2peak and FM (inferred from respiratory exchange ratio; RER) in older subjects were compared before and after a progressive 8-week intermittent aerobic exercise program. All participants (42 older women aged 74 ± 3 y and 41 men aged 74 ± 3 y) completed a peak voluntary graded exercise test on a cycle ergometer, and VO_2 and RER were measured. Twenty-two older women and 22 men completed 8 weeks of exercise training (3 × 1 h weekly sessions on a cycle ergometer). Exercise intensity progressed from 40% of the maximal pretest workload to 100% by the end of the program. The remaining subjects served as controls.

Results: RER was significantly higher in women ($RER = 0.49\ VO_2 + 0.60$) than men ($RER = 0.27\ VO_2 + 0.71$; $P = 0.001$). Exercise training increased VO_2peak (20% for women, 30% for men) and decreased RER at submaximal VO_2 in men ($RER = 0.21\ VO_2 + 0.75$ vs. $RER = 0.27\ VO_2 + 0.71$), but not women ($RER = 0.49\ VO_2 + 0.60$).

Conclusion: Although the literature reports that FM is reduced in older men and women, this study demonstrated that, in men, FM was increased after aerobic training, but not in women, despite an increased VO_2peak in both.

Keywords: Aging, Exercise, Exercise training, Fat metabolism, Oxygen consumption, Respiratory exchange ratio

The world will continue to see a rapid growth in older populations during the 21st century. For example, by 2030, about 20% of the US population or about 72 million people will be age 65 and older[1]. It is well known that VO_2max decreases with age[2,3]. Fat mass also decreases, and muscle mass[4–6], muscle function[7], and metabolism[4–6] deteriorate with aging. Previous studies have shown a decrease in fat metabolism (FM) with aging, which may contribute to reduced exercise capacity and prevalence of overweight or obesity, and in turn an increased risk of cardiovascular diseases and diabetes affecting older individuals[8–10]. Although over-eating is a known cause of obesity, inactivity and impaired metabolism of fats may also play major roles in obesity and obesity-related diseases[2,11,12].

Reports have shown that the ability to use fat as a fuel during exercise is reduced in older individuals[13,14]. Muscle FM is the main determinant of total body FM at rest and during exercise. Studies have found FM to be lower in older subjects (by 25%–35%), and to be less in women than men, even after correction for VO_2max[12]. Reduced muscle FM is influenced by hormonal and pharmacological stimulation of lipolysis, which diminishes with age[6,13]. Mitochondrial function also decreases with age[6,13].

FM decreases and carbohydrate metabolism increases with increasing exercise intensity, thus FM is associated with the individual's VO_2max[15]. These relationships may be altered in older subjects with reduced VO_2max. Inactivity increases as a function of age[4] and negatively impacts FM[16]. Aerobic exercise training in younger individuals has been shown to increase physical activity and FM[17–19]. Reduced FM may be partly related to increased visceral and subcutaneous fat and decreased muscle mass with aging, which may be a secondary effect of inactivity. However, FM does not appear to be related to muscle fiber composition in older subjects[20,21].

The purpose of this study was to estimate total body FM in older men and women, and to evaluate the extent to which reversing inactivity with an exercise program would improve FM in older men and women. We hypothesized that increasing physical activity would significantly improve VO_2peak and increase FM in both men and women.

Method

The Human Subjects Institutional Review Board of the University at Buffalo approved this study. The study was conducted ethically according to international standards[22].

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Participants

Subjects were randomly recruited from the 4000 members of a Senior Choice Program at a local health maintenance organization (HMO). Recruitment letters were sent to all HMO members; about 1000 responded. Of this group, 50 older men (74 ± 3 y, 172 ± 6 cm, and 78.29 ± 14.2 kg) and 50 older women (74 ± 4 y, 158 ± 6 cm, and 69 ± 13.92 kg) were selected from 200 positive responses. Subjects included in the study met the following criteria: independently living, active in social activities, could transport themselves to the research facilities, and not active in other aerobic exercise fitness programs. On the basis of the judgment of the study physician (a staff member of the HMO), subjects were excluded from the study if they had acute or unstable chronic illness. Subjects were included if their hypertension was controlled by medication, but excluded if they were diabetics or taking statin drugs for hyperlipidemia.

Half of participants of each sex were randomly assigned to undergo an exercise training program. The other half served as controls.

Protocol

After medical clearance by personal physicians at the HMO, all subjects completed an informed consent form and a peak graded exercise test on a cycle ergometer. After completion of the pretest, one group of older subjects (n = 25 men and 25 women) underwent 8 weeks of progressive intermittent aerobic training. The exercise and control groups maintained their regular lifestyle and diet. As these were free-living subjects their diets were not controlled; however, they were asked to maintain their typical individual diets during the study. The control group was instructed not to perform any organized exercise programs. Both groups were retested at the same time after 8 weeks.

Procedures

The peak graded exercise test was performed on a cycle ergometer at 50 rpm (Monark Model 818E) starting at 25 W for men and 0 W for women. The work rate was increased by 25 W every 3 minutes until the subject stopped or could not maintain 50 rpm. Oxygen consumption (VO_2) and carbon dioxide output (VCO_2) were measured using standard open circuit techniques. Respiratory exchange ratio (RER; VCO_2/VO_2) was calculated at rest and during each stage of the voluntary peak exercise test. Gas volume was measured breath-by-breath by a spirometer (Ohio Spirometer 822). Mixed expired O_2 (Applied Electrochemistry S-3A/I) and CO_2 (Applied Electrochemistry CD-3A) fractions were determined and averaged over the last minute of each 3 minutes of exercise at each work rate. An electrocardiogram ran continuously and blood pressure was determined during the steady-state phase of each work rate to monitor subjects' safety.

The 8-week aerobic training program was conducted on a mechanical brake cycle ergometer at 50 rpm (Monark Model 818E). Subjects were organized into groups of 4 for training sessions, and their programs were administered by one of the study's authors. The program was conducted 3 times per week for 1 hour each session. Training programs using continuous exercise intensity for 30–50 minutes in this age group can only use exercise intensities that may not stimulate optimal adaptation. We have previously shown that an intermittent higher intensity aerobic program resulted in greater increases in maximal aerobic power than continuous lower intensity programs[23,24]. The aerobic program used here was intermittent, with the intensity increased by 20% of the maximal workload every 2 weeks, starting from 40% of the maximal workload achieved on the pretest in weeks 1 and 2, to 100% in weeks 7 and 8. During week 1, the subjects exercised for 2 minutes and rested for 2 minutes at each intensity level. This sequence was continued for 60 minutes for each of 3 sessions during the week. In week 2, the subjects exercised for 4 minutes and rested for 2 minutes at each intensity level, with the sequence continuing for 60 minutes. The total exercise time was equivalent to 30–40 minutes of continuous exercise, although at higher intensity than would be able to be sustained continuously for 30–40 minutes. Heart rate (HR) and rating of perceived exertion (out of a maximum of 20) were recorded after each exercise session throughout the training period.

Data analysis

Data were analyzed using SigmaStat Statistical Software for Windows version 3.5 (Systat Software Inc, San Jose, CA). Pretraining and posttraining comparisons used repeated measures analysis of variance for men and women. The comparisons between men and women and exercise and control groups used analysis of variance. When significant differences between groups were detected, Student-Newman-Keuls post hoc test was performed to test the significance between means. The statistical comparison was considered significant at $\alpha \leq 0.05$.

Results

Of the 50 subjects in the exercise group, 22 male and 22 female subjects completed pretesting, the exercise program and posttraining testing. In the control group, 19 male and 20 female subjects completed 2 tests 8 weeks apart. All participants in the exercise group attended at least 90% of the exercise sessions. No subjects dropped out of the program for physical or medical reasons. The statistical power calculated from the data in this study was > 90% for each variable, and was calculated from the mean and variance of the pretraining and posttraining test data.

Comparison of older men to women at baseline

As seen in **Figure 1**, the RER for older men and women increased linearly with oxygen consumption. As expected, women had lower VO_2peak values than men (38%), even after correction for body weight (26%). Women had significantly higher RER than men at all exercise levels (**Fig. 1**). The slope of the RER-VO_2 relationship was significantly higher for women (0.582 RER/VO_2) than men (0.233 RER/VO_2) ($P = 0.001$).

Effects of exercise training

HR during the weekly aerobic training sessions averaged 101 ± 14 beats/min in week 1 and increased to 127 ± 13 beats/min in week 8. These values represent 69% and 87% of maximal predicted HR. Ratings of perceived exertion increased from 12 to 17 (of 20) over the same period of exercise training.

Maximal work rate increased significantly after training by 28% ($P = 0.001$) in men and 17% ($P = 0.03$) in women. Exercise training increased peak oxygen consumption in both men (19.05 ± 4.26 to 22.68 ± 5.30 mL/min/kg, $P = 0.027$) and women (15.85 ± 3.24 to 17.24 ± 4.65 mL/min/kg, $P = 0.045$) only in the

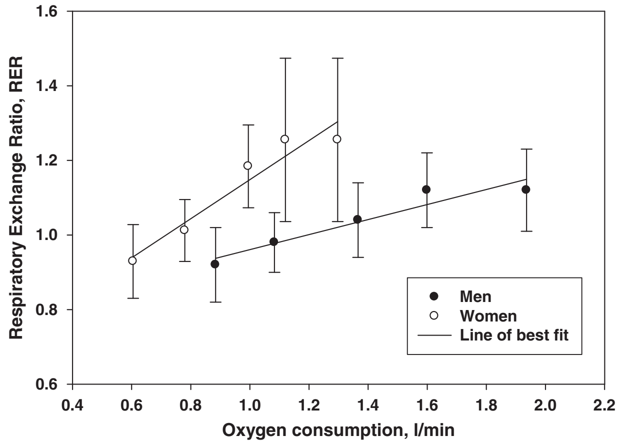

Figure 1. Respiratory exchange ratio (RER) is plotted as a function of oxygen consumption (L/min) for older men and women. Women had a significantly greater RER than men at all comparable VO_2s ($P<0.05$).

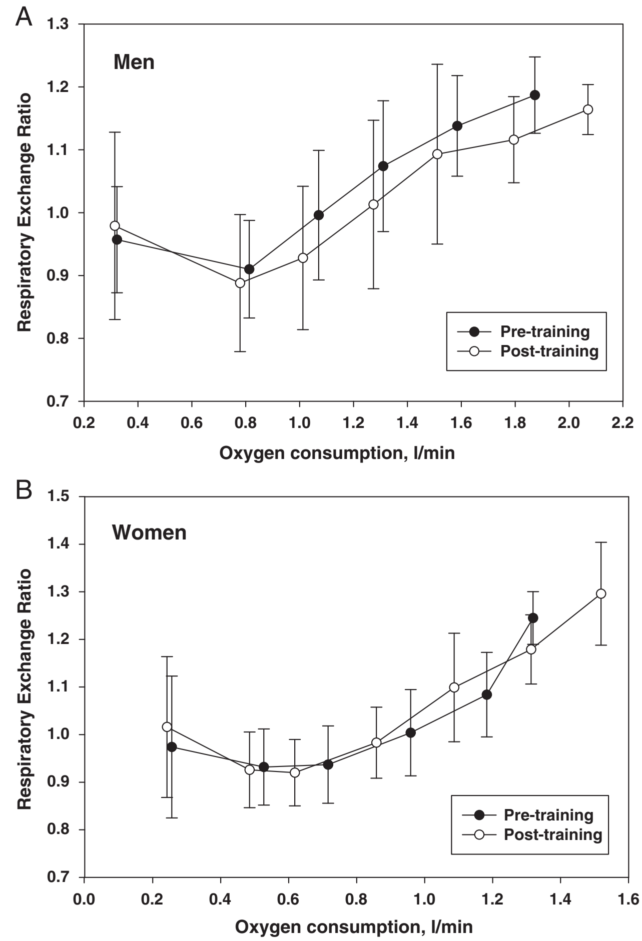

Figure 2. The effects of training. Respiratory exchange ratio (RER) is plotted as a function of oxygen consumption (L/min) for elderly men (A) and women (B). Training significantly reduced RER, but not women, despite both groups increasing VO_2peak.

exercise group; there was no change in the control group (16.21 ± 2.59 vs. 16.07 ± 2.77 mL/min/kg for women, $P=0.59$; and 15.77 ± 2.75 vs. 15.61 ± 2.35 mL/min/kg for men, $P=0.86$).

The effect of aerobic training on RER is shown in **Figures 2A** (men) and **2B** (women). The slope of the regressions of RER as a function of VO_2 was not changed in the control group for either men or women after training (0.23 vs. 0.34, and 0.58 vs. 0.38, $P=0.15$ and 0.35, respectively). The RER was significantly lower at all VO_2 levels in the male exercise group after training. However, the RER of the female exercise group was not affected by training, in spite of the increased VO_2peak. The slope of the RER-VO_2 relationship was 32% lower for the men posttraining (0.31 vs. 0.21, $P=0.007$); however, it did not change for the women (0.4 vs. 0.38, $P=0.41$).

As FM is influenced by maximal VO_2, the RER data for all groups were expressed as a percentage of their respective VO_2peak values in **Figure 3A** (men) and **3B** (women). In men, the reduction in RER at a given absolute VO_2 was eliminated when the data were normalized for the subject's individual VO_2peak, emphasizing the role of VO_2peak in determining RER at a specific VO_2. The balance of fat and carbohydrate metabolism for women expressed as a function of the percentage peak oxygen consumption was shifted toward carbohydrates after training (**Fig. 3B**), as the RER at absolute oxygen consumptions did not change, while peak oxygen consumption increased as a result of training (**Fig. 2B**).

Discussion

The present study demonstrated that FM expressed as a function of absolute VO_2 was less in older women than men. This observation could be explained by the lower peak aerobic power of women; however, the difference remained even after correction for differences in VO_2peak. When expressed as a function of absolute VO_2, FM increased in men in the exercise group, but not in women, or in control men or women ($P=0.35$). When FM was expressed as a function of VO_2 after normalization for VO_2peak, men in the exercise group had a significant increase in FM (**Fig. 2A**), but men in the control group did not ($P=0.15$). Importantly, when FM was expressed as a percentage of VO_2peak in women, it appeared to decrease after training (**Fig. 3B**); however, this was only because of increased VO_2peak, with no change in FM for specific VO_2s (**Fig. 2B**). As FM is inversely related to relative exercise intensity, these data suggest the importance of maximal aerobic power and training in determining FM.

FM decreases with advancing age[15,24]; it is also reduced at rest, during exercise, and after meal ingestion in older subjects[24]. The lower FM in women observed in the present study is in agreement with previous studies that showed FM to be higher in men than women; this difference could not be explained by noradrenaline levels, free fatty acid (FFA) availability, body composition or aerobic capacity[25].

Reductions in VO_2max and FM in the elderly are associated with decreased fat-free mass[26] and may be caused by the intrinsic capacity of muscle for FM[27]. The age-related shift in substrate metabolism appears to be associated with muscle respiratory capacity[12]. It is well known that these variables are influenced by individuals' chronic activity level, which has been reported to be less in older than younger individuals.

There is a marked reduction in activity in the older persons; however, those who are moderately or highly active have higher VO_2max levels[2,11]. In addition, the VO_2max, fat-free mass and intrinsic capacity of muscle for FM, can be increased by exercise

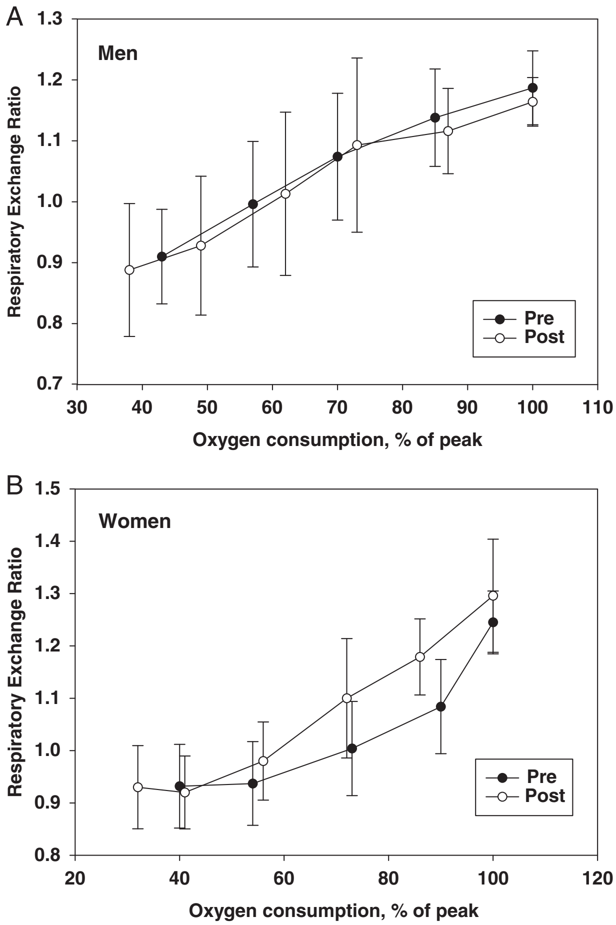

Figure 3. The balance of substrate (fat and carbohydrate) metabolism (respiratory exchange ratio, RER) for elderly men and women expressed as a function of the % of peak oxygen consumption before and after exercise training. RER was not significantly different from pretraining to posttraining in men (A), and was higher in women (B) posttraining, indicating depressed fat metabolism after training.

training[18,19,24]. Before training, VO_2peak values in the present study are in agreement with previous studies of active, independently living individuals who were not participating in an aerobic exercise training program. The effects of exercise training in the present study were similar to those previously reported for older men and women[5,28,29]. A previous study showed that physical activity, particularly fast walking, was associated with body fat mass, but not total energy intake[29]. Endurance training also increased FM and thus reduced fat deposits in adipose tissue, resulting in increased aerobic capacity and reduced adiposity in older subjects[26]. In one study of sedentary older subjects, subjects had reduced plasma FFA release compared with fitter older subjects[11]. However, the rate of fatty acid delivery into the systemic circulation has been reported to be similar in older and younger subjects; it is slightly higher in older subjects after adjustments for fat-free mass[24]. Lipolytic rates and FFA availability do not appear to be rate-limiting in older subjects[12,27]. Therefore, a decrease in the capacity of muscle to oxidize fat, and/or a decrease in its capacity for transport of long-chain fatty acids, must account for reduced FM[13,24].

Factors that are responsible for the reduced FM may include: diminished oxidative enzymes, increased glycolytic flux inhibiting fatty acid transport into the mitochondria; or a diminished (possibly beta-adrenergically mediated) activation of fatty acid transport[25]. Many of these parameters have also been shown to be affected by exercise training.

Another explanation for low FM could be low intramuscular fat stores, either caused by the reduced fat-free mass or fat uptake and storage in muscle. However, increases in both intramuscular and liver fat have been reported in older subjects and are associated with insulin resistance, glycosylated hemoglobin, plasma lipids and body fat[30,31]. Other studies have shown intramyocellular lipid content to be higher in older than younger subjects[31]. Therefore, the limitation to FM does not seem to be the availability of fat from either blood or muscle.

The present study demonstrated that in elderly men, the reduced FM observed pretraining disappeared when FM was expressed as a function (%) of their VO_2peak. This suggests that the lower FM pretraining was associated with the fact that at a specific pretraining VO_2, they were exercising at a higher percentage of their VO_2peak, which would result in a higher carbohydrate metabolism, and lower FM. However, after training, FM at the same absolute VO_2 represented a lower percent of their VO_2peak: VO_2peak increased after training, thus FM was higher. This finding in the present study is in agreement with some previous studies[4,12,32], but not another study[8].

In younger individuals, endurance training results in physiological changes to muscle, thereby increasing fat and decreasing carbohydrate metabolism[17,33]. These changes most likely occur at the cellular level as a result of facilitated fat transport into mitochondria, oxidative enzymes and O_2 delivery[17,34]. As suggested above for FM in older subjects, the increase in maximal VO_2 is most likely a remodeling of local metabolism, as the central delivery of oxygen is not significantly increased by this type of training in older persons[35], as it is in younger persons[36].

Although this was a randomized controlled study of a large sample from a group of 4000 healthy independently living—but not aerobically trained—subjects it is not without limitations. Unknown, unexcluded factors may have had an effect on FM in some subjects. We used a higher intensity intermittent training protocol, which was previously shown to be superior to a continuous program; however, these data may not apply to continuous training. Finally, and importantly, we estimated FM at the muscle level (respiratory quotient) from measures of RER. RER, but not respiratory quotient, may be influenced by hyperventilation or hypoventilation during measurement. In the present study, the ventilatory response to exercise $(\dot{V}_E / \dot{V}_{O_2})$ was not affected by exercise training. The results of this study would need to be confirmed by studies that measure FM directly. In addition, it remains to be seen why the women in this study did not significantly increase FM, as their VO_2peak was increased by exercise training. There does not appear to be a limitation to fat availability or norepinephrine levels in women[6].

Conclusions

In summary, it appears that reduced FM in men is a secondary consequence of deterioration in VO_2peak, which, in turn, is associated with inactivity. Thus, an increase in activity that increases VO_2peak is associated with increased FM at submaximal levels of exercise. However, this appears not to be true in women, where FM was reduced, but did not increase with aerobic training. Further investigation is needed to confirm this study and determine why women have depressed FM and do not respond to training.

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Conflicts of interest statement

The authors declare that they have no financial conflict of interest with regard to the content of this report.

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