Metabolic Adaptations to Endurance Training in Older Individuals

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Abstract/Résumé

The purpose of this study was to describe the effects of moderate intensity exercise training on the muscle energy utilization, blood flow, and exercise performance of four sedentary older individuals (58 ± 4 yrs). Subjects trained the dominant forearm each day for 12 weeks. The nondominant arm was not trained and served as a within-subject control. 31P nuclear magnetic resonance spectroscopy (31P NMRS) was used to identify the power output in watts (W) at the onset, or threshold, of intracellular acidosis (IT) in the exercising muscle during progressive exercise tests to fatigue. After 6 weeks of training, power output at the IT increased by 14% (p < 0.05) in the dominant arm; however, an additional 6 weeks of the same exercise program failed to produce a further increase in IT power. IT power of the nondominant forearm was not changed. In the dominant forearm, endurance time for a submaximal wrist flexion test was increased 34% and 58% at 6 and 12 weeks, respectively. Maximal voluntary strength was not affected by training, nor was resting or exercising blood flow. The training program delayed the onset of intracellular acidosis during progressive exercise and increased the capacity for submaximal work. These effects did not appear to depend on an increase in muscle blood flow.

Introduction

The adaptation of skeletal muscle to continuous aerobic exercise training has been well described for healthy young adults. Among the changes that occur are increases in mitochondrial density (Holloszy and Booth, 1976), and the activity of enzymes involved with fatty acid oxidation (Molé et al., 1971), the citric acid cycle (Hickson et al., 1976), and the electron transport chain (Davies et al., 1981). These factors result in a considerable increase in the oxidative capacity of the muscle, thereby contributing to improvements in submaximal endurance and perhaps to maximal exercise capacity as well. Only a limited number of studies using biopsies have examined the changes in muscle metabolism that take place with endurance training of older adults (Coggan et al., 1992; Suominen et al., 1977a; 1977b). These studies have reported increases in the activity of several enzymes associated with aerobic metabolism.

Skeletal muscle metabolism has usually been evaluated using biochemical analysis of tissue samples obtained by surgical or needle biopsy. The biopsy is an essential tool in the study of metabolism, but there are some obvious limitations associated with the procedure because it is both invasive and destructive. For this reason the majority of information regarding muscle metabolism has come from studies of animals or young healthy males. The technique may not be suitable for some protocols that require repeated sampling. As an alternative method, $^{31}$P nuclear magnetic resonance spectroscopy ($^{31}$P NMRS), although limited in some respects, has the distinct advantage of allowing continuous noninvasive measurement of muscle metabolism throughout exercise and recovery. Recently several researchers (Kent-Braun et al., 1990; Minotti et al., 1990) used $^{31}$P NMRS to demonstrate the effects of training (of younger adults) on intramuscular metabolites and intramuscular pH. They found lower ratios of inorganic phosphate to phosphocreatine (Pi/PCr), and higher pH values for several different intensities of isokinetic contractions following training; however, these results may not be directly relevant to aerobic activities. The effect of training on muscle metabolism during continuous dynamic exercise has not yet been shown using $^{31}$P NMRS.
Results from previous studies in this laboratory have shown that the onset or threshold of intracellular acidosis (IT) during a progressive ramp exercise test can be identified with $^{31}$P NMRS (Marsh et al., 1991). This breakpoint is characterized by an abrupt decrease in intracellular pH and a corresponding increase in the rate of phosphocreatine (PCr) hydrolysis. The point at which the IT occurs during the ramp test appears to be related to the aerobic power of the exercising muscle. If this is true, then the IT power may be a useful parameter to noninvasively detect changes in the oxidative capacity of muscle. Therefore the objectives of the current study were (a) to observe changes in muscle metabolism and physical performance following 6 and 12 weeks of exercise training of older individuals, and (b) to test the utility of the IT as a parameter for identifying changes in the metabolic response to exercise.

Methods

SUBJECTS AND EXPERIMENTAL DESIGN

Four sedentary older individuals (3 males, 1 female) volunteered to participate in the study. Mean age of the group was 58 ± 3.7 years. The subjects were in good health and had no history of metabolic or cardiovascular illness. Informed consent was obtained from all subjects before acceptance into the study.

Each participant underwent testing at three intervals: upon entry into the study (T0) and within 24 hours of completing 6 (T6) and 12 (T12) weeks of exercise training. Testing was conducted on 2 days at each interval. On the 1st day, maximal voluntary strength and endurance of the wrist flexor muscles were determined and blood flow measurements were obtained. Forty-eight hours later, forearm muscle metabolism was evaluated using $^{31}$P NMRS at rest and during progressive exercise to fatigue. Following the initial consultation, subjects trained the dominant arm daily for 12 weeks. The nondominant arm was not trained during this period and served as a within-subject control.

STRENGTH AND ENDURANCE MEASURES

Maximal voluntary strength (MVS) and muscular endurance time (MET) were evaluated in both the dominant and nondominant forearms using an isokinetic wrist flexion dynamometer (Baltimore Therapeutic Equipment, Baltimore, MD). Subjects were seated with the legs elevated during testing. The elbow was bent at 90° and the forearm was supported in pronation. The dynamometer was set to the static mode for the determination of MVS. Each subject attempted three maximal isometric contractions, with the highest torque attained deemed to be MVS. The criteria used to evaluate muscular endurance was the length of time that repeated wrist flexion could be maintained at a frequency of 0.5 Hz and at an intensity of 25% of MVS. Range of motion of the wrist movement was about 70° (35° each side of neutral). Subjects continued the MET test until they were fatigued or until they were unable to maintain the required frequency of contraction (0.5 Hz).

MUSCLE BLOOD FLOW MEASURES

Forearm blood flow (FBF) at rest and with fatiguing exercise was assessed using venous occlusion plethysmography. The measurements of flow were taken with
the hand and forearm resting comfortably on the dynamometer prior to and immediately following the MET test described above. A strain gauge was applied to the forearm to monitor changes in the circumference of the limb (Whitney, 1953). Venous flow from the forearm was intermittently occluded by a blood pressure cuff on the upper arm inflated to 5.3 kPa (40 mmHg) for 5 to 10 s. While the cuff was inflated, the rate of change of the forearm circumference was measured as an indicator of blood flow. At rest, at least six determinations of flow were averaged. Three measurements of flow were obtained immediately following exercise. The highest of these postexercise recordings was considered to be the peak exercise FBF. The mean time for the peak FBF after exercise was 12.6 ± 1.9 s.

RAMP EXERCISE TEST

A ramp type exercise test was used to stress the forearm muscles during the 31P NMRS studies (Marsh et al., 1991). This protocol required the subjects to work against a progressively increasing resistance until fatigue. The test was done with the subjects in the supine position. Subjects pronated their forearm and inserted it into the horizontal bore of the NMR magnet, grasping the lever of the exercise ergometer. Flexion of the wrist depressed the lever and this action raised a variable resistance (water filled container) located outside the magnet via a cable and pulley system. Wrist flexion was repeated at a frequency of 0.5 Hz and the resistance was continuously increased by adding water to the container at a rate of 250 ml·min⁻¹, using a roller pump (Cole-Parmer Instruments, Chicago). Work rate or power output in watts (W) was calculated from the frequency, distance, and mass variables. The exercise began at an intensity of 0.50 W (the empty container) and continued until the subjects were fatigued.

EXERCISE TRAINING

Training was done daily for 12 weeks in the subjects’ homes at a time of their choice. The exercise consisted of repeated wrist flexion of the dominant limb using a handheld weight with the forearm supported. Workloads differed for each individual and were based on 25% of MVS. The subjects lifted the weight at a frequency of 0.5 Hz until they were fatigued. They were given a log book and were asked to record the duration of the exercise period and the number of repetitions completed, and to rate the extent of their fatigue on a simple numerical scale of 1 to 10. The intensity of the exercise (i.e., weight lifted) was not changed throughout the training period. However, the subjects were encouraged to increase the duration of the exercise during the first few weeks of the study as they became accustomed to the exercise. They were consulted biweekly to ensure that the training program was progressing satisfactorily.

NMR SPECTROSCOPY

Phosphorous spectra were acquired using a 30-cm bore, 1.9 Tesla, superconducting magnet and a TMR-32/20 spectrometer (Oxford Research Systems, Oxford, U.K.). The forearm was positioned over a 4-cm surface coil so that the signal obtained was from the wrist flexor muscles, primarily the flexor digitorum superficialis. A pulse repetition rate of 1 s was used, with 32 scans averaged for each spectrum. Spectra were acquired sequentially throughout rest and exercise. Before Fourier transformation, the data were zero filled to enhance resolution and
multiplied by a 10-Hz exponential line function to improve the signal-to-noise ratio.

Fourier transformed spectra were analyzed using a nonlinear least-squares fitting routine developed in this laboratory. The relative contributions to each spectrum of the phosphate metabolites, beta-adenosine triphosphate (β-ATP), phosphocreatine (PCr), and inorganic phosphate (Pi) were determined from the area under the fitted curve, and the ratio of Pi/PCr was calculated using these areas. Intracellular pH was determined using the chemical shift of Pi in relation to PCr (Taylor et al., 1983). Both the logarithm of the Pi/PCr relationship and intracellular pH were plotted as a function of the exercise intensity or power output. Piecewise linear regression analysis was applied to these plots (Vieth, 1989). The power output at the onset or threshold for intracellular acidosis (IT) was determined by the breakpoints in the plots of Pi/PCr (ITPi/PCr) and pH (ITpH).

STATISTICAL ANALYSIS

An F test was used to determine whether the piecewise regression provided a significantly better fit of the data than simple linear regression. The effects of time and training on muscle metabolism and exercise performance were evaluated using an analysis of variance with repeated measures (ANOVA) and Tukey’s test where appropriate. Comparisons between the trained and control limbs were made using paired t tests. Differences between groups were considered significant if p < 0.05. All data are expressed as means ± SEM.

Results

Subject compliance during the 12 weeks of training was high, with 99% of the scheduled exercise sessions completed. The resistance and frequency of the wrist flexion exercise remained constant throughout the 12-week period of the study. The average duration of the training sessions was prolonged approximately 30% during the first 2 weeks of training as the subjects quickly became familiar with the exercise. In subsequent weeks the duration of each session changed little. Improvements in the duration of exercise over the final 6 weeks of the study were typically less than 10% greater than the duration at T6. The most frequently recorded rating of exertion following the training sessions was 7, indicating that the subjects were exercising at moderate intensity.

Before training, static MVS was similar in both arms (12.7 ± 2.3 and 12.4 ± 2.7 J for the dominant and nondominant arms, respectively). The training protocol had no effect on the strength measure. After 12 weeks, MVS of the dominant arm was 14.0 ± 2.3 J while MVS of the nondominant arm was 13.8 ± 2.9 J. The group MET was 47% longer in the dominant (757 ± 457 s) compared to the nondominant arm (515 ± 177 s) at T0. Although this difference was large, it was not statistically significant given the extensive variability within the group. Training prolonged the group MET of the dominant limb only. This effect was slight at T6 (783 ± 287 s) and increased to 25% by T12 (943 ± 489 s), but again these changes were not significant. When the changes in MET were expressed as a percentage of each individual’s performance in the baseline (T0) test, the mean increase was 34% at T6 and 58% at T12.
Figure 1. Forearm blood flow (FBF) in the dominant (trained) and nondominant (control) arms, at rest and immediately following the maximal endurance test. Exercise caused about a fourfold increase in FBF, $p < 0.05$. The training program had no significant effect on FBF either at rest or with exercise. Values are group means ± SEM.

No differences in arm blood flow were observed at rest. FBF showed about a fourfold increase with exercise, in both the dominant (trained) and nondominant (control) limb. Neither time nor the training protocol had a significant effect on resting or exercise blood flow, as shown in Figure 1.

The training protocol delayed the onset of the IT in the muscles of the dominant forearms of all the subjects. Figure 2 illustrates the effect of training on the metabolic response to the ramp exercise test of an individual subject. After 6 weeks of training, this subject had increased the IT by about 20%. Mean IT power for the group at T6 had increased by 14% ($p < 0.05$), from $1.18 ± 0.06$ W to $1.35 ± 0.07$ W. No further increase in this parameter occurred following an additional 6 weeks of training (Figure 3). The individual responses of the four subjects to the 12-week training program are shown in Table 1.

The onset of the IT was found to be reproducible in the nondominant arm, regardless of the variable used to determine it. Mean power values for the IT when determined from the Pi/PCr ratio (ITPi/PCr) were $1.06 ± 0.05$, $1.09 ± 0.07$, and $1.05 ± 0.08$ W for T0, T6, and T12, respectively. Similarly, no change was observed in the onset of metabolic acidosis (ITpH) over 12 weeks of the study (Figure 3). Peak power for the group attained during the ramp test was significantly ($p < 0.05$) higher at T0 in the dominant arm ($1.93 ± 0.08$ W) than in the nondominant arm ($1.68 ± 0.04$ W). The peak power of both arms did not change significantly over the 12 weeks of training.

Discussion

Only a small number of subjects were used in this study because of the high costs associated with $31^p$ NMRS. Nevertheless, it was believed that this group
Figure 2. Changes in intramuscular pH (top) and PCR metabolism (bottom) in the dominant (trained) forearm during the ramp test, after 6 weeks of endurance exercise training. The intracellular threshold (IT) is indicated by the arrows. In this example the onset of the IT was delayed approximately 20% by training. Data shown are for an individual subject.

would be of sufficient size to demonstrate the effects of endurance training of a small muscle mass. This assumption proved correct. The benefits of training older subjects were shown by an increase in endurance performance (MET) and a delay in the onset of intracellular acidosis (IT). Although the peripheral response to training has been shown in the elderly, the previous exercise protocols involved large muscle groups, or whole-body exercise, and invasive biopsy procedures. The results of this study confirm that enhancements of skeletal muscle function induced by small muscle mass exercise can also be demonstrated using the noninvasive technique of $^{31}$P NMR spectroscopy.

The most significant result of the study was the delay in the IT with training. An improvement in the maximal (or peak) power attained during the ramp test was not a consistent finding of the study; however, an increase in IT power was observed for all subjects. The relationship between the IT and extracellular threshold measures has yet to be defined, but increases in the ventilation threshold (Poole and Gaesser, 1985; Ready and Quinney, 1982; Sady et al., 1980) and the lactate threshold (Poole and Gaesser, 1985; Sjodin et al., 1982; Yoshida et al.,
Figure 3. Effect of training on mean IT power. IT power was similar whether defined by changes in Pi/PCr (ITPi/PCr) or pH (ITpH). There was a significant, \( p < 0.05 \), difference between the arms in the IT at T0. A 14%, \( p < 0.05 \), increase in IT power was evident at T6. Training for an additional 6 weeks (T12) did not produce a further increase in the IT. *Significant difference, \( p < 0.05 \), between trained and control arms. *Significant difference, \( p < 0.05 \), from T0.

Table 1  IT Power for Each Subject Prior to Training (T0) and Following 6 (T6) and 12 (T12) Weeks of Exercise Training (all values in watts)

<table>
<thead>
<tr>
<th>Subject</th>
<th>T0</th>
<th>T6</th>
<th>T12</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.04</td>
<td>1.23</td>
<td>1.32</td>
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<td>4</td>
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<tr>
<td>Mean</td>
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<td>1.35*</td>
<td>1.36*</td>
</tr>
<tr>
<td>±SEM</td>
<td>0.06</td>
<td>0.07</td>
<td>0.06</td>
</tr>
</tbody>
</table>

*Significant difference, \( p < 0.05 \), from T0.

1982) following training have previously been reported. The magnitude of these changes varies considerably, from approximately 5% (Sjodin et al., 1982) up to 70% (Ready and Quinney, 1982), and is apparently related to the threshold parameter measured and how the training variables are manipulated. Therefore, the 14% increase in IT power observed in the present study is consistent with the values in the current literature.

There are several mechanisms by which the onset of the IT could have been delayed. Biochemical alterations may have taken place that would increase
the oxidative capacity of the muscle so that PCr stores were maintained and lactate production reduced. Alternatively, the delay in the onset of the IT could have been related to changes in blood flow to the working muscle. Intramuscular pH and the Pi/PCr ratio are quite sensitive to blood supply (Wiene et al., 1986), so an increase in flow would produce a lower Pi/PCr ratio and [H+] at any submaximal exercise intensity. There is some evidence that muscle blood flow is increased following endurance exercise training (Klausen et al., 1982; Leinonen, 1980), but other studies have shown that flow is unaffected by training (Grimby et al., 1967).

In the present study, no changes in forearm blood flow were observed following training (Figure 1). The strain gauge plethysmography technique used in the study has been shown to reproducibly measure increases in forearm blood flow during graded intermittent exercise (Arnold et al., 1990), so it is likely that forearm perfusion was in fact unchanged. Even though total muscle perfusion was not altered, the possibility of a more effective redistribution and utilization of the existing flow cannot be excluded (Mackie and Terjung, 1983). Other peripheral vascular adaptations may also have occurred. A prolonged transit time of the blood due to increased capillarization and a decreased oxygen diffusion distance associated with a greater mitochondrial density would enhance oxygen extraction from the blood (Terjung et al., 1988). Studies demonstrating these changes have involved whole-body exercise, however, so it is not known whether these adaptations will occur following training of a small muscle mass. The forearm exercise protocol does not stress the central component of the cardiovascular system. This has been shown by Arnold et al. (1990) in other methods of forearm exercise testing.

A second factor of interest in the present study was the design of the training program. While the intensity of the training stimulus appears to be the primary factor in determining the extent of changes in VO2max (Gaesser and Rich, 1984; Thomas et al., 1984), improvements in submaximal exercise capacity are not as dependent on intensity (Seals et al., 1984). Fox et al. (1975; 1977) showed that the frequency and duration of training sessions were most influential in reducing heart rate and blood lactate concentration during exercise at fixed submaximal workloads.

These findings are of practical significance, particularly for older individuals and those with physical limitations due to illness. These individuals are more likely to participate in light activities such as a daily walking program in which the walking distance increases, rather than a training regimen requiring more intense effort. We attempted to duplicate these exercise conditions with the small muscle mass model by having each subject exercise daily at a fixed intensity for the duration he or she selected. This procedure was successful to a degree, with training having the greatest effect on the submaximal parameters, the IT and MET, as anticipated. However, such programs do appear to have limitations. The training was only effective over the first 6-week period, with little or no further improvements in the IT power or MET observed at T12.

Frequency of training was maximized by having the subjects exercise daily, but the duration of the sessions did not continue to increase over the final 9 weeks of the study as it had initially. Therefore the subjects were exercising with the intensity, frequency, and duration variables constant. Although encouraged to do so, subjects did not increase the time of the training sessions beyond about
20 minutes. Boredom could have been a factor in their failure to increase the exercise duration, since the task was a very simple and repetitive one.

The maximal power (MP) attained during the ramp exercise protocol was similar in both arms and was unchanged by training. While the absence of any training effect may seem contrary to the expected outcome, the lack of change in maximal power could be related to the modest, fixed intensity of the exercise program. There are other possible explanations, however. With whole-body exercise such as running or cycling, the most significant factor that determines VO₂max is the increased ability of the cardiovascular system to deliver oxygen to the working muscles (Holloszy and Coyle, 1984). Enhancement of the oxidative capacity of the muscle seems less important. Furthermore, improvements in the respiratory capacity of muscle can occur without accompanying changes in VO₂max, or vice versa (Henriksson and Reitman, 1977; Klausen et al., 1981; Sjodin et al., 1982).

Alternatively, failure of the exercise program to increase maximal power may simply be a reflection of the validity of MP as a measure of muscle oxidative metabolism. While the IT does seem to have a direct relationship to aerobic capacity, MP of the wrist flexors may not. No objective criteria were assessed to establish that MP represents an intracellular correlate of VO₂max. MP may have been dependent on other factors including muscle strength and subject motivation, or the ability to tolerate discomfort. If MP is not a valid criterion, and there does seem to be some doubt, then the importance of the IT as an objective parameter for assessing aerobic function is emphasized.

In interpreting the results of the present study, it must be emphasized that most of the previous training studies have observed adaptations to large muscle groups brought about by whole-body exercise programs, whereas the present study examined the effect of small muscle mass activity. Typically, researchers use the nondominant or the most unfit limb as a model in unilateral training studies (Minotti et al., 1990) so that the greatest possible improvement in aerobic capacity will be attained. In the present study, however, the dominant forearm was selected as the training limb and the nondominant as the control. This was done for several reasons. It was believed that the wrist flexion exercise with a free weight would be more easily mastered with the dominant arm. It was also believed that a greater compliance over the 12 weeks of the program would be obtained if the subjects did not feel awkward performing the task. This strategy was clearly successful, since compliance over the 12 weeks was nearly 100%. Furthermore, central nervous system adaptations to endurance training are particularly important when the exercise calls for the acquisition of coordinated movements associated with new skills.

Improvements in coordination, and thus efficiency, may be partially responsible for the increases in endurance performance that occur following training, since fewer motor units are needed to maintain a given submaximal force (Sale, 1987). Minotti et al. (1990) observed neural adaptations in the wrist flexor muscles following an endurance training program similar to that used in the present study. They found lower Pi/PCr ratios in the muscles of the untrained forearm during submaximal exercise, indicating a cross-training or "cross-transfer" phenomenon (Hardman et al., 1987; Sale, 1987). Cross-transfer was not observed in the current study. Use of the dominant forearm may have decreased the significance of neural adaptations to the training protocol.
Finally, our results are in agreement with those of Minotti and co-workers (1989), who have reported differences in the metabolic response to exercise between the dominant and nondominant arms. Minotti et al. (1989) used $^{31}$P NMRS to study muscle metabolism and found that at a given submaximal workload, the nondominant arm showed a greater increase in the Pi/PCr ratio and lower pH. Asymmetry of the limbs was also evident in the present study in both the biochemical and submaximal performance measures before training. MET of the dominant limb was 47% longer, even though muscular strength in both arms was the same. Power output at the IT during the ramp exercise test was also significantly ($p < 0.05$) greater in the dominant arm before training: $1.18 \pm 0.06$ W compared to $1.07 \pm 0.05$ W. These findings suggest that daily activities are of sufficient intensity to provide a training stimulus for the dominant limb, and further, that this training stimulus primarily affects aerobic metabolism.

In summary, continuous moderate intensity exercise training was effective in delaying the onset of intracellular metabolic acidosis, and increasing the subjects’ capacity for submaximal work. These effects did not appear to depend on an increase in muscle blood flow, suggesting that the oxidative capacity of the forearm muscles had increased. $^{31}$P NMRS and the ramp exercise protocol were an effective means of observing these changes noninvasively.

References


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