

High-resistance training and muscle metabolism during prolonged exercise

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Goreham, C., H. J. Green, M. Ball-Burnett, and D. Ranney. High-resistance training and muscle metabolism during prolonged exercise. *Am. J. Physiol.* 276 (*Endocrinol. Metab.* 39): E489–E496, 1999.—To investigate the hypothesis that changes in muscle submaximal exercise metabolism would occur as a result of fiber hypertrophy, induced by high-resistance training (HRT), active but untrained males (age 20 ± 0.7 yr; mean \pm SE) performed lower-limb weight training 3 days/wk for 12 wk using three sets of 6–8 repetitions maximal (RM)/day. Muscle metabolism was examined at different stages of training (4, 7, and 12 wk) using a two-stage continuous cycle test performed at the same absolute power output and duration (56.4 ± 2.9 min) and representing 57 and 72% of pretraining peak aerobic power ($\dot{V}O_{2\text{peak}}$). Compared with pretraining, at the end of exercise, HRT resulted in a higher ($P < 0.05$) phosphocreatine (PCr; 27.4 ± 6.7 vs. 38.0 ± 1.9 mmol/kg dry wt), a lower lactate (38.9 ± 8.5 vs. 24.4 ± 6.1 mmol/kg dry wt), and a higher ($P < 0.05$) glycogen content (132 ± 11 vs. 181 ± 7.5 mmol glucosyl units/kg dry wt). The percent change from rest before and after training was 63 and 50% for PCr, 676 and 410% for lactate, and 60 and 43% for glycogen, respectively. These adaptations, which were observed only at 72% $\dot{V}O_{2\text{peak}}$, occurred by 4 wk of training in the case of PCr and glycogen and before any changes in fiber cross-sectional area, capillarization, or oxidative potential. Fiber hypertrophy, observed at 7 and 12 wk of training, failed to potentiate the metabolic response. No effect of HRT was found on $\dot{V}O_{2\text{peak}}$ with training (41.2 ± 2.9 vs. 41.0 ± 2.1 ml·kg⁻¹·min⁻¹) or on the steady-state, submaximal exercise rate of oxygen consumption. It is concluded that the HRT results in muscle metabolic adaptations that occur independently of fiber hypertrophy.

strength training; cycle exercise; metabolic adaptation

REGULAR PERFORMANCE of prolonged exercise results in a well-defined series of adaptations in muscle metabolism and substrate utilization. After training, a given submaximal exercise protocol can be performed with less of a decrease in high-energy phosphate potential, less of an increase in glycogenolysis and glycolysis, and an increase in fat utilization (20). Accompanying the adaptations in muscle metabolism and substrate selection are adaptations both in capillarization and enzymatic organization in the muscle. These include an increase in the number of capillaries per muscle fiber and an increase in mitochondrial potential (1, 20). These adaptations have been postulated to represent the fundamental mechanisms underlying the changes in muscle metabolic behavior (1, 20). However, not

acknowledged are the changes that occur in muscle hypertrophy. In males, increases in fiber area may approach 20% in the vastus lateralis with endurance cycle training (1), an increase that is not substantially different from the 14–24% increase that can be induced in the same muscle with many weeks of high-resistance training (HRT; see Ref. 24). At issue are the consequences of the independent effects of muscle hypertrophy in explaining the exercise metabolic alterations observed after endurance training.

There are reasonable grounds for postulating that the hypertrophy accompanying training may, in itself, influence metabolic events in muscle. The increase in muscle cross-sectional area that is induced by HRT is also accompanied by an increase in maximal voluntary force-generating capabilities (MVC; for review see Ref. 24). To perform a repetitive task at constant force output, after HRT, the percentage of force generated with each repetition is decreased. In the absence of changes in recruitment strategy and assuming the hypertrophy extends to both major fiber types (type I and type II; see Ref. 24), the percent MVC per fiber is reduced. It is well known that, at least for local muscle groups, the percent MVC is an important determinant of the contribution of the metabolic pathways for generating ATP. As the percent MVC is increased, phosphorylation potential is further decreased, and glycolysis is further activated (2, 8).

However, for these scenarios to produce the postulated effect on muscle metabolism, the fiber hypertrophy must not be accompanied by a decrease in capillary density or in mitochondrial potential. Although there is evidence to suggest that hypertrophy may result in a disproportional increase in fiber area relative to capillary neof ormation and mitochondrial biogenesis (24), recent work indicates no dilution in these parameters with HRT-induced fiber hypertrophy (17, 35).

In this study, we have examined the time-dependent effects of increases in fiber cross-sectional area induced via HRT on muscle metabolism during a standardized cycle task. We have hypothesized that muscle hypertrophy, occurring in the absence of changes in capillary density and mitochondrial potential, would result, at least qualitatively, in metabolic alterations similar to those observed for prolonged exercise training. These include a more protected phosphorylation potential, a reduced accumulation of lactate, and a reduction in the rate of muscle glycogen depletion. Another study examining the fiber-type alterations using histochemical procedures has been performed (11).

METHODS

Subjects

Seven untrained healthy and occasionally active males volunteered for the study. Their mean (\pm SE) age and weight

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were 20.0 ± 0.7 yr and 88.7 ± 7.0 kg. The study was approved by the Office of Human Research following submission of all experimental details. As is required, the procedures and risks were fully explained to each participant before obtaining written consent.

Study Design

The HRT program utilized involved training three times a week for a period of 12 wk. Three exercises were employed during each training session, all designed to load the quadriceps muscles. Three sets, with six to eight repetitions maximal (RM) for each set, were performed for each exercise (parallel squats, incline leg presses, and leg extensions) during each training session. All training sessions, which were supervised, also included a warm-up set of 10 repetitions of each exercise, at $\sim 50\%$ of each participant's 6–8 RM. This program is modelled after one employed by Staron et al. (34), which has been shown to produce a marked fiber-type hypertrophy. The training program was divided into three segments (0–4 wk, 4–7 wk, and 7–12 wk). Before the beginning of training, and after each training segment, a series of tests was performed to evaluate the effects of the training. As well, before the start of a new training segment, the weights employed in the training were increased to maintain the 6–8 RM training stimulus. The average weights employed during the initial training segment were 199 ± 20 , 364 ± 22 , and 90 ± 6 kg for the squat, leg press, and leg extension, respectively. During the final training segment, the weights employed increased by 62% for the squat, 72% for the leg press, and 56% for the leg extension.

At least 1 wk before the beginning of the study and after each training segment, four different tests were administered. One test utilized progressive cycle exercise to fatigue for measurement of peak aerobic power ($\dot{V}O_{2\text{peak}}$), whereas a second test involved prolonged continuous cycling, initially for 30 min at 57% $\dot{V}O_{2\text{peak}}$, followed by a maximum of 30 min or until fatigue at 72% $\dot{V}O_{2\text{peak}}$. The intensity and duration of exercise was used to investigate both muscle metabolic and substrate (glycogen) adaptations to HRT. Before the training, average exercise time was 56.4 ± 2.9 min. Metabolic adaptations were examined at the same absolute intensities throughout the study, namely 151 ± 4.7 and 202 ± 6.8 W. A third test was used to measure the MVC that could be generated during leg extensions while a fourth test was used to monitor changes in mechanical power over a range of different cycle resistance settings. Given the specificity of the neural adaptations that appear to accompany HRT (6), the latter protocol was deemed essential to evaluate the degree to which increases in MVC translated to performance on the cycle. As emphasized, cycle exercise was used to examine the metabolic adaptations occurring in response to HRT. At least 1 wk before the onset of training, the progressive cycle test was performed. This test was followed by the prolonged cycle test, performed at least 2 days after the progressive test. The MVC test and the mechanical power tests were administered on separate days from each other and from the submaximal tests. After each training segment, the submaximal test was administered first, ~ 24 – 36 h after the last training session, followed by the MVC, mechanical power, and the progressive cycle test. The MVC and mechanical power tests were administered over a 1- to 2-day period, on days separate from the progressive cycle test. In all, 3–4 days were needed to perform the testing. All testing was performed at temperatures between 24 and 26°C and at 49–50% relative humidity.

Testing Protocols

Progressive cycle. Measurement of $\dot{V}O_{2\text{peak}}$ was obtained using an electrically braked cycle ergometer (model Siemens 380B B) at a rate of 60 revolutions/min. The initial work load was 16.3 W, and this was increased by 16.3 W each minute until fatigue. Expired air was collected and analyzed by an IBM-PC computerized on-line gas collection system as previously described (21), consisting of a Hewlett Packard model 47363A Digital Pneumatich and a Beckman model 6B-2 Medical Gas Analyzer. Respiratory gas exchange was computed over 30-s segments, with the $\dot{V}O_{2\text{peak}}$ representing the highest value recorded.

Prolonged cycle. The prolonged cycle test was performed using the same cycle and gas collection system as used in the progressive test. Work settings were based on the $\dot{V}O_{2\text{peak}}$ values obtained for each individual and were designed to produce ~ 60 and 70% of the $\dot{V}O_{2\text{peak}}$ responses during each segment. During the test, respiratory gas exchange was measured during the final 5 min of each work load where applicable. Heart rate (HR) measurements, using a Cambridge model VS-4 electrocardiogram, were also recorded at this time. In addition, muscle biopsies were extracted from the vastus lateralis muscle at rest and at the termination of each phase of the submaximal test, i.e., at 30 and 60 min (or just before the onset of fatigue, depending on which occurred first). Muscle tissue was rapidly extracted on termination of the exercise from previously made incisions and immediately plunged in liquid nitrogen and stored at -80°C until analyses. A second biopsy was obtained from the same site and was used for histochemical measurements. For each training segment, an identical procedure was employed, with the sampling at similar time points. Biopsies (12 in all) were balanced between legs and were randomized according to order for both the exercise and training. This procedure ensured that, after a given training segment, tissue was sampled from both legs during exercise. Testing occurred at approximately the same time of day and approximately 4 h after the ingestion of any food.

Mechanical Power

Force-velocity measurements were conducted at a series of different resistance settings to determine the effects of HRT at a range of velocity determinations and power outputs. The rationale behind this procedure was to determine whether or not the HRT program resulted in increased power output at velocities in the region that was used during the prolonged test. These tests were conducted on a Monarch cycle ergometer, fitted with a revolutions counter connected to a strip-chart recorder (Hewlett Packard model 7402 A). Seven different resistance settings were employed and randomly assigned as to order during each testing session. In each case, a 2-min warm-up period at zero load preceded each measure. No interruption was provided between the warm-up and the test. Peak velocity for each resistance setting was calculated from records obtained during the 10-s time limit allowed for each test.

MVC

Measurements of MVC generated by the quadriceps were measured during leg extensions by methods previously described (12).

Biomechanical Analysis

Muscle tissue was analyzed for high-energy phosphate and related metabolites, adenine nucleotides, glycogen, and a

range of glycolytic intermediates. With the exception of the adenine nucleotides (ATP, ADP, AMP) and IMP, fluorometric techniques (26), as modified in our laboratory (16), were used to determine concentrations. The adenine nucleotides and IMP were measured on the same homogenate with the use of ion-pair reversed-phase high-performance liquid chromatography techniques (22) as detailed previously (15). All values were corrected to total creatine (TCr) for each subject, using the average of all biopsies for each individual, to adjust for contamination by blood and connective tissue. Glucose, pyruvate, and lactate were also corrected to TCr, even though they exist in the extracellular space, since the correction would at least correct for the muscle contaminants and provide more stable values (13).

Measurements of fiber-type distribution (types I, IIA, IIB, and IIB), fiber areas, capillaries, and succinic dehydrogenase (SDH) activity were performed on the histochemical samples (11). In this paper, we report the weighted mean fiber area, which is based on the percent distribution of each fiber type and the respective areas (17).

Statistical Procedures

For the metabolic data, a two-way ANOVA for repeated measures was used to determine the effects of training and exercise. For measurements of MVC, force velocity, and $\dot{V}O_{2peak}$, a one-way ANOVA was employed. A Student Newman-Keuls procedure was performed to compare specific means where significance was indicated. The level of confidence was set at 95% for all comparisons.

RESULTS

Performance Indexes

In addition to monitoring the increases in the 6–8 RM for the individual exercises used in the HRT program, we have also recorded additional performance criteria. Two measures were employed, namely the MVC and power output determined on a cycle ergometer. At 0, 4, 7, and 12 wk, MVC (in newtons) was 682 ± 41 , 646 ± 45 , 696 ± 44 , and 735 ± 53 . Increases in MVC were observed but not until the final training segment. At 12 wk, a 7.8% increase in MVC occurred, compared with the pretraining values. Power output, determined at different resistance settings, was also found to increase at 12 wk of training, but only for the higher-resistance settings (Table 1). At these workloads, which produced pedal velocities equivalent to

Table 1. Alterations in mechanical cycle power with high-resistance training

Resistance, kg	Training, wk			
	0	4	7	12
6	806 ± 56	801 ± 46	824 ± 44	787 ± 59
7	891 ± 18	833 ± 47	905 ± 49	853 ± 21
8	847 ± 53	805 ± 56	872 ± 50	878 ± 45
9	823 ± 37	833 ± 63	882 ± 56	845 ± 59
10	806 ± 61	744 ± 54	803 ± 90	815 ± 65
11	706 ± 64	629 ± 114	762 ± 123*	854 ± 89*†
12	545 ± 82‡	533 ± 142	775 ± 96*†	853 ± 60*†

Values are means ± SE expressed in W; $n = 7$ subjects. * Significantly different ($P < 0.05$) from 4 wk; † significantly different ($P < 0.05$) from 0 wk; ‡ significantly different ($P < 0.05$) from 6, 7, 8, 9, 10, and 11 kg.

Table 2. High-resistance training and respiratory gas exchange during submaximal exercise

	Time, min		
	0	30	56
$\dot{V}O_2$, l/min			
Week 0	0.389 ± 0.03	2.06 ± 0.08	2.66 ± 0.07
Week 4	0.411 ± 0.04	2.05 ± 0.08	2.67 ± 0.06
Week 7	0.429 ± 0.05	2.10 ± 0.07	2.66 ± 0.07
Week 12	0.410 ± 0.04	2.01 ± 0.07	2.67 ± 0.08
$\dot{V}CO_2$, l/min			
Week 0	0.352 ± 0.02	2.07 ± 0.10	2.76 ± 0.07
Week 4	0.369 ± 0.04	2.03 ± 0.08	2.71 ± 0.06
Week 7	0.384 ± 0.04	2.04 ± 0.08	2.68 ± 0.06
Week 12	0.353 ± 0.02	1.94 ± 0.08	2.71 ± 0.07
\dot{V}_E , l/min			
Week 0	12.5 ± 0.92	56.2 ± 3.1	85.2 ± 5.1
Week 4	14.0 ± 0.90	57.7 ± 1.4	84.4 ± 3.0
Week 7	15.0 ± 1.0	57.3 ± 1.6	80.3 ± 1.9
Week 12	13.4 ± 0.72	55.7 ± 1.9	82.9 ± 3.1
RER			
Week 0	0.911 ± 0.04	1.00 ± 0.02	1.04 ± 0.02
Week 4	0.897 ± 0.02	0.994 ± 0.01	1.02 ± 0.01
Week 7	0.909 ± 0.04	0.974 ± 0.01	1.01 ± 0.01
Week 12	0.887 ± 0.06	0.967 ± 0.01	1.02 ± 0.01

Values are means ± SE; $n = 7$ subjects. $\dot{V}O_2$, oxygen consumption; $\dot{V}CO_2$, carbon dioxide production, \dot{V}_E , ventilation in l/min BTPS; RER, respiratory exchange ratio. A main effect ($P < 0.05$) of time was found for all variables. For $\dot{V}O_2$, $\dot{V}CO_2$, \dot{V}_E , $0 < 30 < 56$ min; for RER, $0 < 30 = 56$ min.

those used in the prolonged cycle test, increases of 21 and 57% were observed.

$\dot{V}O_{2peak}$

HRT failed to result in an increase in $\dot{V}O_{2peak}$, peak HR, or ventilation (\dot{V}_E) peak. Before training (0 wk) and at 4, 7, and 12 wk of HRT, the values were 3.53 ± 0.10 , 3.40 ± 0.11 , 3.53 ± 0.15 , and 3.57 ± 0.15 l/min, respectively. Comparable values for HR peak were 196 ± 2.4 , 193 ± 1.4 , 196 ± 1.8 , and 191 ± 2.2 beats/min. As with $\dot{V}O_{2peak}$, the differences were not significant.

Submaximal Exercise Metabolism

The rate of oxygen consumption ($\dot{V}O_2$) measured during the two-stage submaximal exercise test, conducted at 59 and 72% of the $\dot{V}O_{2peak}$, was unaffected by training (Table 2). Similarly, no differences were found for the rate of carbon dioxide production ($\dot{V}CO_2$), \dot{V}_E , and respiratory exchange ratio (RER) regardless of the duration of training. As expected, progressive increases (0, 30, and 56 min) in $\dot{V}O_2$, $\dot{V}CO_2$, and \dot{V}_E were observed with each exercise level. The one exception was RER where the increase observed from 0 to 30 min was not further increased from 30 to 56 min. The training program also failed to modify the HR response at either of the two intensities of exercise. Before training, the HR was 163 ± 3.1 and 195 ± 3.6 beats/min at the end of each stage. After the training, the respective values were 154 ± 4.3 and 187 ± 5.4 beats/min.

Adenine nucleotide concentrations (ATP, ADP, AMP) and total adenine nucleotide concentrations were not altered either with exercise or training (Table 3).

Table 3. High-resistance training, muscle adenine nucleotides, and IMP during submaximal exercise

	Time, min		
	0	30	56
ATP			
Week 0	24.3 ± 0.75	24.7 ± 0.79	23.7 ± 0.66
Week 4	25.3 ± 0.54	24.6 ± 0.69	25.2 ± 0.77
Week 7	25.1 ± 0.76	24.4 ± 1.1	23.4 ± 1.1
Week 12	24.3 ± 1.1	23.7 ± 0.77	23.2 ± 1.1
ADP			
Week 0	4.13 ± 0.26	4.04 ± 0.11	4.30 ± 0.25
Week 4	4.39 ± 0.18	4.16 ± 0.25	4.08 ± 0.16
Week 7	4.48 ± 0.27	4.61 ± 0.40	4.26 ± 0.23
Week 12	4.60 ± 0.31	4.41 ± 0.25	4.36 ± 0.13
AMP			
Week 0	0.115 ± 0.01	0.109 ± 0.01	0.126 ± 0.02
Week 4	0.104 ± 0.01	0.106 ± 0.01	0.115 ± 0.02
Week 7	0.122 ± 0.01	0.109 ± 0.01	0.082 ± 0.01
Week 12	0.124 ± 0.01	0.095 ± 0.01	0.189 ± 0.07
TAN			
Week 0	28.6 ± 0.65	28.8 ± 0.85	28.2 ± 0.80
Week 4	29.8 ± 0.49	28.9 ± 0.76	29.4 ± 0.83
Week 7	29.7 ± 0.73	29.1 ± 1.1	27.4 ± 1.3
Week 12	29.0 ± 1.0	28.2 ± 0.76	27.8 ± 1.1
IMP			
Week 0	0.108 ± 0.01	0.143 ± 0.03	0.515 ± 0.42*†‡
Week 4	0.098 ± 0.01	0.204 ± 0.06*	0.336 ± 0.12*
Week 7	0.086 ± 0.03	0.135 ± 0.02*	0.129 ± 0.02
Week 12	0.079 ± 0.02	0.167 ± 0.09*	0.236 ± 0.07

Values are means ± SE in mmol/kg dry wt; *n* = 7 subjects. TAN, total adenine nucleotides. *Significantly different (*P* < 0.05) from 0 min; †significantly different (*P* < 0.05) from 30 min; ‡significantly different (*P* < 0.05) from weeks 4, 7, and 12.

However, IMP concentrations were altered. With the exception of *week 0*, increases in IMP were observed at 30 min. During the final 26 min of exercise, the increase in IMP persisted only at 4 wk. In the case of *week 0*, the increase observed at 56 min was greater than both 0 and 30 min. At 56 min, the IMP concentrations were lower at *weeks 4, 7, and 12* compared with *week 0*.

Both exercise and training altered phosphocreatine (PCr) and creatine (Cr) levels (Table 4). In the case of PCr, progressive decreases were observed at each exercise stage, regardless of training state. However, only at 56 min were differences observed with HRT. At 56 min, higher PCr values were found at both 4, 7, and 12 wk of training compared with 0 wk. As expected, generally similar significant but opposite effects were found for Cr.

Only exercise was found to alter the concentration of the glycolytic intermediates glycogen-1-phosphate, glycogen-6-phosphate, fructose-6-phosphate, and fructose-1,6-bisphosphate (Table 5). In all cases, the values observed at 30 and 56 min were greater than measured before exercise. Only in the case of glucose-1-phosphate was a further increase observed at 56 min. Glucose was increased at both 30 and 56 min of exercise; however, a training effect was also noted. In general, glucose values were higher at *week 4* and *week 7* than at *week 0* and *week 12*.

Muscle lactate concentrations increased with each exercise segment before training and after each period of training (Fig. 1). However, the magnitude of the increase was affected by HRT. At 56 min of exercise, the

Table 4. High-resistance training and high-energy phosphates and metabolites during submaximal exercise

	Time, min		
	0	30	56
PCr			
Week 0	73.5 ± 4.0	52.3 ± 3.7*	27.4 ± 6.7*†
Week 4	76.0 ± 4.2	50.1 ± 5.8*	38.0 ± 1.9*†‡
Week 7	73.9 ± 3.9	49.8 ± 3.5*	38.0 ± 4.0*†‡
Week 12	73.0 ± 3.5	50.1 ± 5.5*	36.6 ± 5.6*†‡
Cr			
Week 0	39.4 ± 2.4	59.7 ± 6.2*	82.9 ± 9.9*†
Week 4	36.9 ± 1.5	65.4 ± 6.8*	76.2 ± 5.9*†
Week 7	39.0 ± 2.2	63.0 ± 6.1*	72.3 ± 3.8*†‡
Week 12	39.9 ± 3.0	63.1 ± 6.4*	78.9 ± 7.1*†
TCr			
Week 0	109 ± 3.8	113 ± 5.6	118 ± 6.8
Week 4	108 ± 5.7	110 ± 4.8	108 ± 5.5
Week 7	108 ± 4.0	113 ± 5.4	116 ± 5.3
Week 12	112 ± 4.6	116 ± 4.5	119 ± 3.0

Values are means ± SE in mmol/kg dry wt; *n* = 7 subjects. PCr, phosphocreatine; Cr, creatine; TCr, total creatine. *Significantly different (*P* < 0.05) from 0 min; †significantly different (*P* < 0.05) from 30 min; ‡significantly different (*P* < 0.05) from *week 0*.

lactate was lower at *week 7* and *week 12* compared with *week 0*. Such training effects were not observed for pyruvate. In the case of this metabolite, exercise increased the levels at 56 min but not at 30 min.

Table 5. High-resistance training and changes in selective glycolytic intermediates with submaximal exercise

	Time, min		
	0	30	56
Glucose			
Week 0	1.53 ± 0.24	3.05 ± 0.61	4.23 ± 1.1
Week 4	2.23 ± 0.24	5.27 ± 0.77	4.29 ± 0.51
Week 7	2.35 ± 0.38	4.31 ± 0.98	4.29 ± 0.74
Week 12	2.10 ± 0.22	2.83 ± 0.50	2.89 ± 0.55
G-1-P			
Week 0	0.051 ± 0.01	0.057 ± 0.01	0.151 ± 0.04
Week 4	0.040 ± 0.01	0.063 ± 0.02	0.107 ± 0.02
Week 7	0.044 ± 0.01	0.109 ± 0.02	0.102 ± 0.03
Week 12	0.041 ± 0.02	0.070 ± 0.01	0.141 ± 0.03
G-6-P			
Week 0	1.40 ± 0.35	2.67 ± 0.55	3.02 ± 0.55
Week 4	1.17 ± 0.14	3.53 ± 0.60	3.22 ± 0.62
Week 7	1.50 ± 0.29	2.74 ± 0.22	3.07 ± 0.59
Week 12	1.55 ± 0.33	2.04 ± 0.28	2.68 ± 0.41
F-6-P			
Week 0	0.395 ± 0.05	0.527 ± 0.11	0.688 ± 0.08
Week 4	0.359 ± 0.04	0.575 ± 0.09	0.667 ± 0.10
Week 7	0.384 ± 0.08	0.603 ± 0.08	0.619 ± 0.10
Week 12	0.461 ± 0.34	0.577 ± 0.06	0.526 ± 0.10
F-1,6-P			
Week 0	0.623 ± 0.11	0.953 ± 0.23	1.37 ± 0.29
Week 4	0.591 ± 0.10	1.12 ± 0.37	0.789 ± 0.29
Week 7	0.534 ± 0.04	1.13 ± 0.19	0.877 ± 0.08
Week 12	0.828 ± 0.30	1.65 ± 0.55	0.967 ± 0.20

Values are means ± SE in mmol/kg dry wt; *n* = 7 subjects. G-1-P, glucose-1-phosphate; G-6-P, glucose-6-phosphate; F-6-P, fructose-6-phosphate; F-1,6-P, fructose-1,6-bisphosphate. A main effect (*P* < 0.05) for time was found for glucose, G-1-P, G-6-P, and F-6-P. For glucose, G-6-P, F-6-P, 30 = 56 > 0 min; for G-1-P, 0 < 30 < 56 min. A main effect (*P* < 0.05) for training was found for glucose; 4 = 7 > 0 = 12 wk.

Glycogen depletion rates were altered with training but only during the 30- to 56-min period of exercise, an effect that was evident at *week 4* and persisted at *week 7* and *week 12* (Fig. 1). For all training states, the reduction in glycogen was progressive over time. Training was without effect in altering resting glycogen concentration.

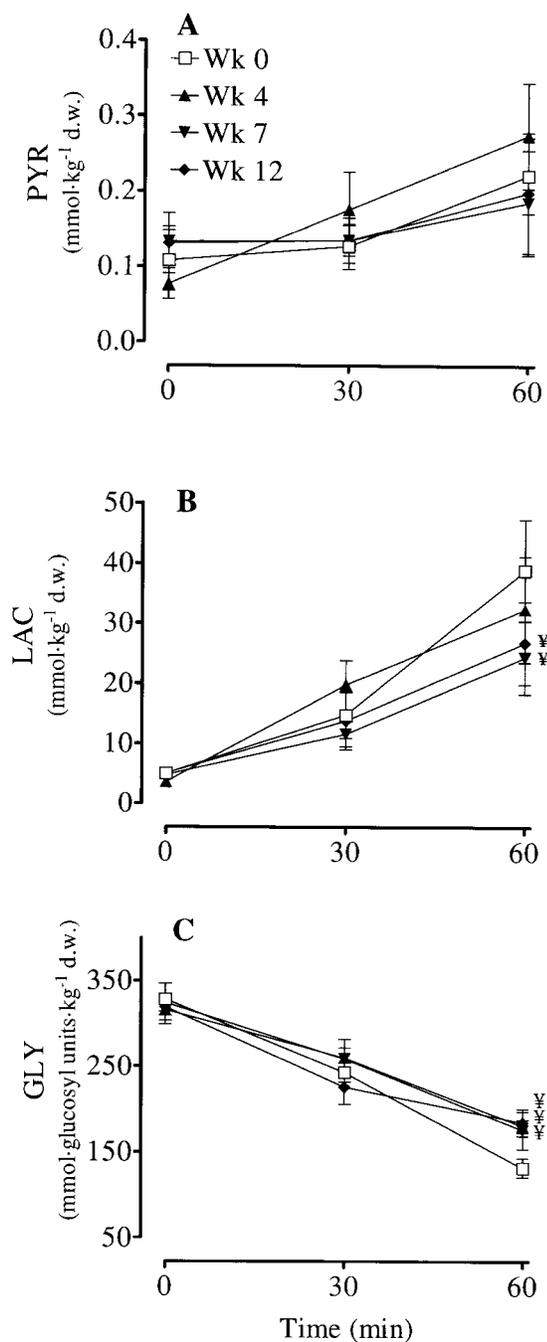


Fig. 1. High-resistance training and muscle pyruvate (PYR; A), lactate (LAC; B), and glycogen (GLY; C). Values are means \pm SE; $n = 7$ subjects. For pyruvate, only a main effect ($P < 0.05$) of time was found: $56 > 30 = 0$ min. dw, Dry wt. ∇ Significantly different ($P < 0.05$) from *week 0*. For both lactate and glycogen, the change was progressive ($P < 0.05$) from 0 to 30 min and 30 to 56 min. The one exception was for lactate at *week 7*, when the change from 0 to 30 min was not significant.

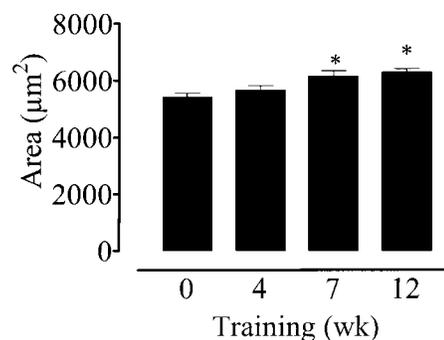


Fig. 2. High-resistance training and weighted mean fiber area. Values are means \pm SE; $n = 6$ subjects. *Significantly different from *week 0* ($P < 0.05$).

The weighted mean fiber-type area increased with HRT but not until 7 wk (Fig. 2). At 7 and 12 wk of HRT, mean fiber areas were higher than at 0 and 4 wk.

DISCUSSION

The results of this paper indicate that HRT resulted in an alteration in the muscle metabolic response to submaximal cycle exercise. Muscle high-energy phosphate content was better protected as evidenced by the lower IMP accumulation and less pronounced decrease in PCr. As well, a blunting of the lactate increase and reduced depletion of glycogen were observed. Previous work has demonstrated muscle IMP changes to be a more accurate indicator of changes in ATP, since, given its relatively low concentration, small changes are easily detected, and the changes are stoichiometric with changes in ATP (19). Interestingly, the metabolic adaptations (high-energy phosphates) that were observed were evident only at the higher exercise intensity and within the first 4 wk of training. Additional training for a further 8 wk failed to exaggerate the metabolic effects that were observed. The effects of HRT on muscle exercise metabolism, at least qualitatively, are consistent with what has been reported for prolonged exercise training (13, 20). Measurement of weighted mean fiber areas, a measure based on the areas of the respective fiber types in conjunction with their percentage distribution, was increased with HRT but not until the 7th wk of training. As such, our hypothesis can be rejected. The metabolic adaptations that were observed preceded any changes in muscle hypertrophy or in fiber-type-specific hypertrophy, capillarization, or oxidative potential, regardless of fiber type (11). The dissociation between the hypertrophic and the metabolic adaptations is further emphasized later in the training. At 7 and 12 wk, where hypertrophy occurred, no further changes in metabolism were detected.

Because muscle fiber hypertrophy was not observed at the time that the metabolic adaptations were found with HRT, other mechanism(s) would appear to be involved. Several appear to be possible. Conceivably the metabolic adaptations could occur because of compositional changes within the fiber itself such as an increase in mitochondrial potential (20). Alternatively, changes may occur outside the fiber, resulting in a

greater capillarization (1), which could promote an increased blood flow and nutrient delivery. Moreover, the metabolic events may be explained not by any structural or compositional changes but simply by a shift in recruitment strategy (6, 28, 32).

The changes in muscle metabolism that we have observed are typical of those that occur with prolonged submaximal training, namely a more protected phosphorylation potential (i.e., less of a decrease in ATP and PCr and less of an increase in ADP and P_i), a decreased lactate accumulation, and a decreased glycogen depletion (13, 20). Typically, these changes have been ascribed to the increase in the oxidative potential of the cell (20). According to this hypothesis, at a given level of oxidative phosphorylation ($\dot{V}O_2$), less of an increase in the putative modulators of mitochondrial respiration such as ADP and P_i are needed, given the adaptive increase in mitochondrial potential (20). It has also been proposed that the lower accumulation of these metabolites would reduce the activation of phosphorylase and phosphofructokinase, resulting in a depression in glycogenolysis and glycolysis after training (20).

Because the HRT training program failed to alter SDH activity regardless of fiber type (11), increases in mitochondrial potential cannot be used to explain the metabolic adaptations observed in this study. Interestingly, we have also reported similar metabolic changes within the first few days of prolonged endurance training (3, 9) and before increases in oxidative potential occur (3, 9, 10, 30). This finding has recently been disputed (33). The results of this study would appear to confirm that at least the initial metabolic adaptations occur by some other mechanism.

A conspicuous effect of HRT is an early transformation of type IIB fibers to type IIA and type IIAB fibers (11), an effect that has been previously observed (34). This adaptation represents a shift in myosin heavy chain (HC) isoform content from HCIIb to HCIIa (34). Because the type IIB fiber type typically contains a low oxidative potential, it is possible that the shift toward a type IIA fiber, which has a high oxidative potential, could have influenced the metabolic response. However, this effect is questionable for several reasons. First, the percentage of type IIB fibers is relatively small, ~15% in the untrained muscle (unpublished observation). Second, it is not known if the oxidative potential of the fiber shifts in coordination with the transformation of the HC isoform content. Finally, it is not clear what the metabolic profile is for the type II fiber subtypes during voluntary, prolonged exercise.

Changes in events outside the working muscle, resulting in an increased oxygen availability, may also be mechanistically linked to the metabolic changes that were observed with HRT. According to this reasoning, increases in oxygen availability to the mitochondria could result in an increase in oxidative phosphorylation, reducing the dependency on high-energy phosphates and glycolysis (4). These adjustments may be more important during the non-steady-state phase of

the exercise where oxygen availability may be limiting. As with the prolonged training model (13, 20), the metabolic adaptations with HRT occur in the absence of change in steady-state $\dot{V}O_2$ and supposedly in oxidative phosphorylation at the level of the working muscle. Moreover, as might be expected with HRT (25, 27), we have not found any change in $\dot{V}O_{2\text{peak}}$ at any stage of the training. As a consequence, the relative percent of maximal oxygen consumption used for the submaximal exercise remained constant.

With the short-term training model, we have provided evidence to suggest that the metabolic adjustments occurring during the nonsteady state (10) appear to be dependent on increases in $\dot{V}O_2$ kinetics (29) and enhanced blood flow (29). Similar effects could be occurring with HRT. Increases in blood flow, however, would not appear to be mediated by increases in capillarization. Increases in the number of capillaries in contact with each fiber were observed with HRT but only at 12 wk (11). Perhaps, more importantly, the increase in capillary angiogenesis was only sufficient to offset the fiber hypertrophy, and no change in capillaries per unit fiber area was observed.

Our unexpected results, both with regard to the changes in metabolic behavior early in HRT before muscle hypertrophy and to the absence of an effect of muscle hypertrophy late in HRT, may be explained by changes in neural recruitment. With regard to the failure of hypertrophy to effect changes, a central factor would appear to revolve around the transfer of improvements in muscle strength, observed during the training itself, to improvements in mechanical power on the cycle, which was used to investigate the metabolic adaptations. Although improvements were not measured in 1 RM with the free weights, the weight that could be lifted during 6–8 RM was measured. As expected, dramatic improvements for all three exercises occurred during the course of HRT. We have also found that, by 12 wk, these improvements translated into an increase in quadriceps MVC, measured isometrically under standard conditions. The improvement in MVC also translated into an increase in mechanical power output but only at the higher-resistance settings. Power output was not enhanced by HRT at lower resistance and higher velocities, an observation that emphasizes the specificity of the adaptations to HRT reported previously (5, 7, 23). At the higher-resistance settings, peak power was produced at a velocity that corresponded to the velocity selected for the submaximal test (360°/s). However, the power generated during the two-stage submaximal test only represented 21 and 37% of the pretraining level. After training, the percentage decreased to 17 and 24%, respectively. However, in spite of this decrease, exercise metabolism was unaffected.

The failure to find an effect of HRT and increased mechanical power output on muscle metabolism may result from a shift in the recruitment strategy used to generate force after the HRT-induced hypertrophy. We have proposed that, in the absence of changes in

recruitment, less force would be generated per unit cross-sectional area, and consequently there would be less metabolic strain even though ATP turnover rates remained unchanged. However, this may not be the case. There is evidence from both electromyography (18, 28) and magnetic resonance imaging (31) to suggest that a reduction in neural drive occurs and less muscle is used to generate the same power after HRT. This could concentrate the metabolic strain on fewer fibers, obviating the effect of the hypertrophy.

In addition, it is not clear if the elevated mechanical power output observed after HRT was elicited by the quadriceps. In cycling, seven different muscles are activated, with their relative contribution dependent on the load. At low power outputs, the quadriceps muscles (vastus lateralis, vastus medialis, vastus intermedius) are particularly important, but as the power output increases the gluteus maximus becomes a major contributor (14). It is possible that, even with the hypertrophy, the contribution of the vastus lateralis remained unchanged.

Of potential significance is the fact that the metabolic effects of HRT were only observed at the higher submaximal power output, approaching the high-resistance characteristics of the training program. As has been repeatedly demonstrated with HRT (28, 32), changes in neural drive may have occurred during the early phase of training. If such is the case, the effect of the neural adaptation could be to distribute the force output over more motor units and/or to facilitate blood flow and oxygen extraction by the working muscles. These hypotheses provide direction for further study.

Finally, it must be acknowledged that a statistical error might have occurred, resulting in our inability to detect real changes in cellular hypertrophy before 7 wk of HRT. Although this possibility exists in all studies, it would appear to have little affect on the conclusions reached in this study. At 4 wk of HRT, when most of the metabolic adaptations were expressed, fiber hypertrophy was minimally altered.

In summary, we have been able to demonstrate that HRT does indeed promote an alteration in muscle metabolic behavior observed during submaximal exercise. However, the change in metabolism appears to be independent of muscle hypertrophy.

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