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Aerobic exercise does not compromise muscle hypertrophy response to short-term resistance training

Tommy R. Lundberg,1 Rodrigo Fernandez-Gonzalo,2 Thomas Gustafsson,3 and Per A. Tesch1,2

1Department of Health Sciences, Mid Sweden University, Östersund, Sweden; 2Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden; and 3Department of Laboratory Medicine, Section for Clinical Physiology, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden

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Lundberg TR, Fernandez-Gonzalo R, Gustafsson T, Tesch PA. Aerobic exercise does not compromise muscle hypertrophy response to short-term resistance training. J Appl Physiol 114: 81–89, 2013. First published October 25, 2012; doi:10.1152/japplphysiol.01013.2012—This study tested the hypothesis that chronic aerobic and resistance exercise (AE+RE) would elicit greater muscle hypertrophy response than resistance exercise only (RE). Ten men (25 ± 4 yr) performed 5 wk unilateral knee extensor AE+RE. The opposing limb was subjected to RE paradigm prompted greater mammalian target of rapamyacin (mTOR) and p70S6 kinase (p70S6K) phosphorylation (12%; P < 0.05) and 9% after RE (P > 0.05). QF SI increased (12%; P < 0.05) after AE+RE, but not RE. Neither AE nor RE showed altered mRNA levels. Citrate synthase activity increased (P < 0.05) after AE+RE. The results suggest that the increased aerobic capacity shown with AE+RE was accompanied by a more robust increase in muscle size compared with RE. Although this response was not carried over to greater improvement in muscle function, it remains that intense AE can be executed prior to RE without compromising performance outcome.

endurance; gene expression; muscle cross-sectional area; muscle power and strength

IT IS GENERALLY BELIEVED that aerobic exercise (AE) compromises increases in muscle strength, power and size induced by resistance exercise (RE) training (18, 22, 28, 44). Only recently (12, 13) have human experiments offered support that this interference effect could be due to incompatibility between cellular pathways controlling protein turnover. Intrigued by these compelling findings, we investigated the acute molecular responses resulting from chronic training.

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sures of skeletal muscle adaptations. One leg was assigned to concurrent AE+RE, whereas the opposing limb was subjected to RE only. In vivo muscle function, muscle size, enzyme content or activity, and gene expression were measured before and after training. To challenge the findings of our recent investigation reporting on the acute responses to this concurrent exercise insult (32), we hypothesized that AE+RE training would manifest in greater muscle hypertrophy compared with RE.

METHODS

General design. Ten moderately trained men performed 5 wk unilateral knee extensor AE+RE while the contralateral limb was subjected to RE only. Subjects completed 15 AE and 12 RE sessions such that RE was scheduled 6 h after AE. Maximal strength and power were determined before and after training, and peak power was measured during all sessions. M. quadricep femoris (QF) volume, cross-sectional area (CSA), and signal intensity (SI) were assessed by magnetic resonance imaging (MRI). Analysis of muscle biopsies, obtained at rest before and after training, determined fiber type-specific CSA, enzyme and glycogen levels, and gene expression.

Subjects. Ten healthy men (25 ± 4 yr, 184 ± 6 cm, and 83 ± 13 kg) volunteered and showed 100% compliance to the study protocol. Hence all subjects completed the scheduled exercise sessions and pre- and posttests. Subjects were moderately trained college students engaged in recreational activities, such as skiing and team sports, on a regular basis (2 days/wk). They had modest experience to weight training before the study and had performed no regular or structured RE training in the past year. The study experiments and procedures including risks and discomforts were explained before subjects gave their written informed consent to participate. The study protocol was approved by the Regional Ethical Review Board in Umeå.

Exercise equipment and familiarization. AE was performed using a one-legged cycle ergometer (3) (model 828E, Monark Exercise, Varberg, Sweden) as previously described (32). This ergometer allows for isolated concentric (CON) knee extensions in a range of motion from about 90 to 175°. Power and cadence were sampled at 2 Hz using the SRM training system (SRM, Jüllich, Germany). RE was performed using a nongravity-dependent seated knee extensor ergometer (YoYo Technology, Stockholm, Sweden) equipped with a 4.2-kg (moment inertia 0.11 kg/m²) flywheel to provide inertial resistance. The ankle was strapped to the dynamometer lever arm that was aligned with the axis of rotation of the knee joint. Torque was sampled at 100 Hz using MuscleLab and peak values averaged across sets were used for data analysis. For all apparatuses used, individual settings were maintained throughout the study. To customize machine settings and familiarize subjects with the exercises employed during training and testing, subjects reported to the laboratory three times in the course of 2 wk prior to the study.

Pre- and posttesting. Identical test protocols were employed before and after the 5-wk training period. These tests were scheduled on four different days within ~1 wk. First, muscle volume and SI were assessed through MRI scans (described below). During the second visit, muscles biopsies (details below) were obtained from the RE leg before (PRE) and from both legs (AE+RE and RE) 72 h after the last training session. To limit the total number of biopsies, we refrained from obtaining biopsies from both legs before training. Given our previous finding of no difference in protein concentration across randomized legs and because muscle volume and function were very similar before training (Table 1), we are confident that the sole prebiopsy accurately represents the untrained condition of either leg.

Table 1. Selected outcome measures pre- and postresistance training with (AE+RE) or without (RE) concurrent aerobic exercise

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>AE+RE</th>
<th>RE</th>
<th>Δ%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endurance performance, s b,c</td>
<td>590 ± 104</td>
<td>752 ± 129*</td>
<td>29</td>
</tr>
<tr>
<td>Wmax, W b,c</td>
<td>50 ± 12</td>
<td>72 ± 19*</td>
<td>44</td>
</tr>
<tr>
<td>Peak heart rate at Wmax, beats/min b,c</td>
<td>158 ± 18</td>
<td>169 ± 12 ± 7</td>
<td></td>
</tr>
<tr>
<td>Lactate 3 min post Wmax, mmol/l b,c</td>
<td>6.7 ± 1.5</td>
<td>8.0 ± 1.1*</td>
<td>19</td>
</tr>
<tr>
<td>Flywheel mean peak power, W c</td>
<td>400 ± 137</td>
<td>514 ± 129*</td>
<td>29</td>
</tr>
<tr>
<td>Flywheel mean peak torque, Nm c</td>
<td>218 ± 31</td>
<td>279 ± 59*</td>
<td>28</td>
</tr>
<tr>
<td>Maximal isometric torque, Nm c</td>
<td>287 ± 53</td>
<td>312 ± 86</td>
<td>9</td>
</tr>
<tr>
<td>QF muscle volume, cm³ a,b,c</td>
<td>1,147 ± 249</td>
<td>1,303 ± 276†</td>
<td>14</td>
</tr>
<tr>
<td>QF mean CSA, cm² a,b,c</td>
<td>79 ± 10</td>
<td>90 ± 10†</td>
<td>14</td>
</tr>
<tr>
<td>QF greatest CSA, cm² a,b,c</td>
<td>101 ± 12</td>
<td>101 ± 12</td>
<td>10</td>
</tr>
<tr>
<td>Normalized torque, Nm/cm² c</td>
<td>2.77 ± 0.37</td>
<td>3.10 ± 0.52*</td>
<td>12</td>
</tr>
<tr>
<td>Normalized power, W/cm² c</td>
<td>5.03 ± 1.16</td>
<td>5.67 ± 1.16*</td>
<td>13</td>
</tr>
<tr>
<td>QF signal intensity, MGV a,c</td>
<td>52 ± 7</td>
<td>58 ± 8*</td>
<td>12</td>
</tr>
<tr>
<td>VL signal intensity, MGV a,b,c</td>
<td>53 ± 8</td>
<td>58 ± 8*</td>
<td>9</td>
</tr>
<tr>
<td>BF signal intensity, MGV</td>
<td>40 ± 7</td>
<td>41 ± 6</td>
<td>2</td>
</tr>
</tbody>
</table>

Values are means ± SD. Significant effects (P < 0.05); a, interaction; b, leg; c, time. Significant post hoc differences (P < 0.05); *within leg vs. PRE; †vs. RE at POST. Wmax, maximal workload; CSA, cross-sectional area; MGV, mean gray value; QF, quadriceps femoris; VL, vastus lateralis; BF, biceps femoris.
Subjects performed 2 × 7 repetitions with 2 min rest between sets. Strong verbal encouragement was used to call for maximal effort. Normalized torque and power were further calculated as the ratio between peak knee extension torque/power and average muscle CSA (Nm/cm²). Fifteen minutes later, the one-legged ergometer incremental test was performed for the opposing limb to assess maximal workload (Wmax) and endurance performance. Resistance was increased by 2.5 N every 2nd min until failure to maintain the prescribed cadence of 60 rpm. When this occurred, time to exhaustion was noted and Wmax was defined as the last successfully completed workload. Capillary blood (20 µl) was sampled from the ear lobe at rest, every 2nd min into exercise and 1 and 3 min postexercise. Samples were subsequently placed in a 1-mL hemolyzing solution and analyzed for lactate concentration (EKF-diagnostic, Magdeburg, Germany). Heart rate was recorded (Polar Electro OY, Kempele, Finland) continuously throughout the test and subsequently analyzed (Polar ProTrainer 5). Rate of perceived exertion (RPE; central and local) was obtained every 2nd min and at exhaustion using the 6–20 “Borg scale” (9). Subjects were blind to any test result to ensure unbiased efforts during pre- and posttests.

Training protocols. During the 5-wk training intervention, subjects completed 15 unilateral AE sessions (3 nonconsecutive days/wk) and 12 unilateral RE sessions for both limbs (2 days/wk during weeks 1, 3, and 5 and 3 days/wk during weeks 2 and 4). Hence, one limb performed concurrent AE + RE whereas the other limb was subjected to RE only. Legs chosen for the AE + RE intervention were randomized in a counterbalanced manner. The particular RE hardware and regimen have proven success in earlier studies (41, 51) and RE for a particular muscle group should not be prescribed more frequently. To justify the AE protocol chosen, previous research showed marked increases in peak oxygen uptake and skeletal muscle oxidative capacity after employing a 3 times/wk 30-min one-legged exercise (23, 24). These protocols are also commensurate with ACSM guidelines. AE was scheduled in the morning and RE 6 h after completion of AE on the same day. Subjects were requested to have a nonstandardized lunch between sessions. A standardized warm-up at submaximal effort preceded each exercise prescribed. Subjects were supervised during all training sessions.

AE comprised 40-min continuous one-legged cycle ergometer exercise. The initial target load was 70% of the Wmax at a fixed cadence of 60 rpm. However, RPE (central and local) was obtained every 10th min to customize the workload such that a very strenuous effort was achieved during each exercise bout. After 40 min, the workload was increased by ~20 W, and subjects were requested to continue until failure, which occurred within 1–5 min (average 2 min 30 s). Subjects received real-time visual feedback of power and cadence via a computer monitor. Heart rate was recorded continuously during one randomly selected session each week. Capillary blood, for subsequent analysis of lactate concentration, was sampled at rest, every 10th min and 1 and 3 min after exercise in the same session.

RE was carried out 6 h after one-legged cycling had been terminated. Each leg (beginning with the right) performed four sets of seven CON-ECC knee extensions (2 min rest between sets) in the flywheel ergometer. Subjects were requested to perform each repetition maximally and were verbally encouraged throughout each set. Peak power for each repetition was measured during all sessions.

Diet/exercise control. Subjects refrained from strenuous physical activity and alcohol for a minimum of 48 h prior to any pre- and posttest day. A standardized meal (pasta, tomato sauce, and juice) consisting of 2.21 g carbohydrates (CHO)/kg body weight (BW), 0.22 g protein/kg BW, and 0.04 g fat/kg BW was provided at ~8:00 PM on the night before the biopsies were obtained. The following morning, subjects had a standardized breakfast (1.01 g CHO/kg BW, 0.31 g protein/kg BW, and 0.24 g fat/kg BW) ~2 h prior to the biopsy procedure. This meal consisted of commercial energy drinks (Ensure Plus, Abbott Laboratories B.V. Zwolle, The Netherlands). Water was allowed ad libitum at any time. Subjects were requested to record food intake on pretesting days and replicate the same diet regimen on posttesting days. The individual testing schedule was very similar (~±2 h) on pre- and posttest days. Throughout the study, subjects were instructed to maintain ordinary daily activities and routines and to refrain from strenuous activities involving the lower limbs.

Magnetic resonance imaging. Cross-sectional images were obtained using a 1.5-Tesla Philips MR Systems Intera (Best, The Netherlands) unit; Turbo spin echo, T2 weighted, TE 110 ms, TR 5723 ms, NSA 3, FOV 48.5 cm, scan time 13 min 10 s and voxel size 0.95 × 0.95 × 10 mm. For each subject, 50 continuous images with 10-mm slice thickness were obtained. To minimize the influence of fluid shift on muscle volume, subjects were resting in the supine position for 1 h prior to any scan (7). A custom-made foot-restraint device ensured no compression of thigh muscles and fixed limb position. Scout images were obtained to confirm identical positioning in pre- and postscans. The top of caput femoris was used as an anatomical landmark to ensure that the same segment was scanned before and after training. Stacks of images were created in TIF format with a scale of 10.887 pixels/cm² and deidentified and subsequently coded. Then, although pre-post images were analyzed in parallel, the individual who performed the analysis was blind to any intervention.

Enzyme activity, glycogen, and water content. Freeze-dried muscle samples (2–3 mg) were homogenized in phosphate buffer with 0.5% BSA, Citrate synthase (CS) and phosphofructokinase (PFK) enzyme activity and lactate dehydrogenase (LDH) content were subsequently determined by NAD⁺-NADH-coupled reactions using fluorometry (31) (CS and PFK) or spectrophotometry (LDH). Glycogen was

Enzyme activity, glycogen, and water content. Freeze-dried muscle samples (2–3 mg) were homogenized in phosphate buffer with 0.5% BSA, Citrate synthase (CS) and phosphofructokinase (PFK) enzyme activity and lactate dehydrogenase (LDH) content were subsequently determined by NAD⁺-NADH-coupled reactions using fluorometry (31) (CS and PFK) or spectrophotometry (LDH). Glycogen was
hydrolyzed enzymatically to free glucose and assayed by fluorometry (20). Muscle water content was estimated by relating ~10 mg wet muscle sample to dry weight, as measured on a precision microbalance at standardized temperature and humidity, and expressed as a percentage of initial wet weight.

RNA isolation, reverse transcription, and real-time PCR. Exercise-induced changes in the basal muscle molecular environment were assessed by analyzing expression of key genes (11) regulating angiogenesis [vascular endothelial growth factor (VEGF)], mitochondrial biogenesis [peroxisome proliferator-activated receptor-γ coactivator-1 (PGC-1)], and protein turnover [myostatin, atrogin-1 and muscle RING-finger protein-1 (MuRF-1)]. One aliquot of ~20 mg frozen muscle tissue was homogenized using TRIzol (Invitrogen Life Technologies, Carlsbad, CA), and total RNA was extracted. One microgram of total RNA was subsequently reverse transcribed into cDNA using high capacity reverse transcription kit (Applied Biosystems, Foster City, CA) in a total volume of 20 μl. Real-time PCR was performed on ABI-PRISMA 7700 Sequence Detector System (Perkin-Elmer Applied Biosystems, Foster City, CA). The reaction mixture consisted of 4.5 μl of the diluted (1:100) cDNA template, 5 μl of the 2 × TaqMan PCR Mastermix, and 0.5 μl gene specific primers. The cycling procedures were 2 min at 50°C and 10 min at 90°C followed by 40 cycles at 95°C for 15 s and 60°C for 1 min. TaqMan primers for atrogin-1 (Hs00369714_m1), MuRF-1 (Hs00822397_m1), myostatin (Hs00193635_m1), PGC-1α (Hs01016724_m1), and VEGF (Hs99999070_m1) were derived from the TaqMan Gene Expression Assays (Applied Biosystems). Samples from each individual were assayed on the same plate. GAPDH (Hs99999905_m1) was used as the housekeeping gene. For further control, 18S (Hs01037521_g1) was analyzed as an additional reference gene. The results were almost identical with 18S or GAPDH as control, 18S (Hs01375212_g1) was analyzed as an additional reference gene. Hence the GAPDH/18S ratio did not change across time points. Gene expression levels were determined using the 2-ΔΔCT method (29), relating mRNA changes as a ratio to the housekeeping gene.

Data analysis. Muscle volume, CSA and SI, isometric and normalized torque/power, and mean peak torque and power were analyzed using two-way repeated measures ANOVA with factors time (pre and post) × leg (AE+RE and RE). Average peak power across the training period was examined using a two-way ANOVA (sessions × leg). The torque-velocity relationship was examined using a three-way ANOVA (time × leg × velocity). Differences in basal enzyme levels, lactate concentration and gene expression levels were determined using the 2-ΔΔCT method (29), relating mRNA changes as a ratio to the housekeeping gene.

RESULTS

Aerobic exercise training. The average power during one-legged cycling across the 5 wk was 43 ± 8 W. It increased (P < 0.05) from 37 ± 5 (session 1) to 49 ± 10 W (session 15). Power at the final stage averaged 65 ± 13 W. Heart rate averaged 124 ± 14 beats/min across the 5 wk to peak at 153 ± 17 beats/min during the final increment. At exercise completion, peak heart rate was 163 ± 16 beats/min. Blood lactate concentration during exercise averaged 4.5 ± 1.0 mmol/l. Lactate concentration 1 and 3 min after exhaustion was 6.2 ± 1.4 and 6.3 ± 1.6 mmol/l, respectively. RPE rose in a linear fashion during exercise and amounted to 15 (central) and 17 (local), respectively, after 40 min. Local muscle exertion was maximal at exercise completion.

Resistance exercise training. Average peak power across muscle actions rose almost linearly (main effect of time P < 0.0005) during the 12 RE exercise sessions (Fig. 1). The increase from the 1st to the 12th session was 27% (384 ± 105 vs. 488 ± 142 W) for AE+RE and 28% (395 ± 112 vs. 507 ± 154 W) for RE with no difference across legs (P > 0.05).

Endurance performance. Although both legs showed improved endurance (time to exhaustion) after training, the increase tended to be more prominent (interaction time × leg, P = 0.052) after AE+RE than RE (Table 1). Similarly, Wmax increased after both AE+RE and RE. The average heart rate and lactate concentration at exhaustion increased (main effects of time) from pre- to posttests, with no interaction effect (Table 1).

Strength and power performance. Increases in maximal isometric torque (main effect of time P < 0.0005) were comparable for AE+RE and RE (Table 1). Likewise, flywheel peak torque increased 28% after AE+RE for both CON (196 to 251 Nm) and ECC (240 to 307 Nm) muscle actions. The corresponding increases after RE amounted to 30% for CON (193 to 251 Nm) and 27% for ECC (242 to 308 Nm). There were no differences across legs (Table 1). Isokinetic peak torque increased on average 11% across velocities for both legs from pre- to postraining (main effect of time P = 0.007). However, there was a time × leg × velocity interaction (P = 0.017). Simple effect tests revealed that this was due to a leg × velocity interaction before training (Fig. 2; P = 0.02). Normalized torque showed a trend (P = 0.077) toward a time × leg interaction due to a greater increase for RE (19%) vs. AE+RE (12%); Table 1).

Muscle volume, CSA, and signal intensity. Total QF volume showed a time × leg interaction (F = 52.3; P < 0.0005). Values were similar between AE+RE and RE at baseline, but differed after training (Table 1). The increase in muscle volume averaged 13.6% (P < 0.0005) after AE+RE and 7.8% (P < 0.0005) after RE. The response was very consistent across all 10 subjects (Fig. 3 and 4). Likewise, the increase in
CSA was greater after AE+RE than RE (Table 1). Analysis of individual muscles showed the following increases in volume after training (AE+RE vs. RE): VL 16.6 vs. 7.6%; VI 11.0 vs. 6.4%; VM 11.8 vs. 6.4%, and RF 25.8 vs. 16.4%. The SI of both QF and VL was similar across legs before training and increased after AE+RE, but not RE (Table 1; QF interaction time × leg: P < 0.0005). SI of BF showed no differences over time or across legs.

Fiber type and CSA. Type I and type II fiber percentage did not change after training (Table 2). Mean fiber CSA increased 17% following AE+RE (P = 0.015) compared with a 9% increase (P = 0.200) after RE. The more robust increase

Fig. 2. Knee extensor torque-velocity relationship pre- and postaerobic and resistance (AE+RE) exercise compared with resistance exercise (RE). Means ± SD. Significant effect (P < 0.05); a = interaction (time × leg × velocity).

Fig. 3. Magnetic resonance imaging images depicting thigh muscle cross-section obtained in 1 representative individual pre- and postresistance training with (AE+RE) or without (RE) concurrent aerobic exercise. Slices shown are 27 cm distal to the top of caput femoris.
Following AE+RE appeared to be due to a relatively greater increase in type I fiber CSA (Table 2). Type II fiber CSA increased 19% after AE+RE ($P = 0.025$) and tended to increase (16%) after RE ($P = 0.052$).

**Enzyme activity, glycogen, LDH, and water content.** CS activity increased 19% following AE+RE ($P = 0.006$; Table 2). PFK activity or LDH content showed no changes ($P > 0.05$). Glycogen content was greater ($P = 0.001$) following AE+RE than RE (Table 2). Estimated muscle water content was similar across legs and showed no change over time.

**Gene expression.** There was no change in basal expression levels for any of the genes investigated (Fig. 5).

**DISCUSSION**

The interest in this study arose from our recent intriguing finding of greater skeletal muscle anabolic response to acute concurrent AE+RE compared with RE (32). The current study design employed this particular exercise paradigm to determine skeletal muscle adaptations resulting from 5 wk RE training with or without preceding exhaustive AE. Given our earlier observation, we hypothesized that concurrent AE+RE would elicit greater increase in muscle size than RE. Indeed, while in vivo muscle strength and power showed comparable improvements across legs, the increase in muscle size was more evident following AE+RE. These novel results suggest that AE could offer a synergistic hypertrophic stimulus to RE training without compromising the progress in in vivo muscle function resulting from RE.

The main finding of the current study was the remarkable increase in QF muscle volume following AE+RE. The gained muscle CSA and volume was accompanied by increased muscle fiber CSA that was greater after AE+RE than RE and appeared to be ascribed to a more substantial, yet not significant, type I fiber hypertrophy. At first, it would be tempting to attribute this effect to accretion of contractile material. However, it must be acknowledged that QF SI was enhanced after concurrent exercise, but not after RE. Thus, and given that m. biceps femoris of either leg showed unaltered SI, it seems unlikely this effect was systemic or the finding random. We rather believe this obscure effect resulted from adaptations specific to this particular exercise regimen. Similar to us, a recent report (19) noted increased SI of muscles undergoing hypertrophy following AE training. Augmented SI shown after exercise is typically attributed to increased muscle water/hydrogen content (35) due to very transient osmotic fluid shifts or as a result of edema from muscle damage after, e.g., ECC exercise (16). None of these explanations could account for the increased SI because MRI scans were obtained at least 48 h after completing the final exercise session, and no subject reported delayed onset of muscle soreness at this time. Interestingly, Harber and associates (19) observed increased muscle water content accompanied by increased sarcoplasmic-to-myofibrillar protein content ratio after training. This contrasts earlier reports suggesting unaltered myofilament packing and myosin actin filament ratio after cumulative RE (10). Similarly, concentrations of cytoplasmic and contractile protein pools were unchanged in both trained and untrained men (2) and in individuals subjected to long-term bed rest or unloading with or without resistance exercise (21). Although our crude estimate showed unchanged muscle water content, it cannot be precluded that the robust muscle hypertrophy in part could have been due to expanded sarcoplasmic or interstitial fluids. Regardless, future studies disclosing the underpinnings of exercise-induced muscle hypertrophy are warranted.

**Table 2. Selected outcome measures pre- and postresistance training with (AE+RE) or without (RE) concurrent aerobic exercise**

<table>
<thead>
<tr>
<th></th>
<th>PRE</th>
<th>AE+RE</th>
<th>RE</th>
</tr>
</thead>
<tbody>
<tr>
<td>CS activity, mmol·kg⁻¹·min⁻¹</td>
<td>34 ± 6</td>
<td>41 ± 8*</td>
<td>35 ± 7</td>
</tr>
<tr>
<td>PFK activity, mmol·kg⁻¹·min⁻¹</td>
<td>87 ± 24</td>
<td>93 ± 24</td>
<td>86 ± 18</td>
</tr>
<tr>
<td>LDH content, μkat/l</td>
<td>12.0 ± 4.3</td>
<td>11.9 ± 3.8</td>
<td>13.2 ± 5.8</td>
</tr>
<tr>
<td>Glycogen content, mmol/kg dry wt</td>
<td>550 ± 143</td>
<td>602 ± 143*</td>
<td>453 ± 96*</td>
</tr>
<tr>
<td>Estimated muscle water content, %</td>
<td>74.0 ± 2.0</td>
<td>73.8 ± 2.5</td>
<td>72.0 ± 2.8</td>
</tr>
<tr>
<td>Type I fibers, %</td>
<td>50 ± 15</td>
<td>51 ± 18</td>
<td>51 ± 13</td>
</tr>
<tr>
<td>Type II fibers, %</td>
<td>50 ± 15</td>
<td>49 ± 18</td>
<td>49 ± 13</td>
</tr>
<tr>
<td>Mean fiber CSA, μm</td>
<td>4,601 ± 1,097</td>
<td>5,361 ± 781*</td>
<td>5,032 ± 767</td>
</tr>
<tr>
<td>Type I fiber CSA, μm</td>
<td>4,055 ± 911</td>
<td>4,547 ± 660</td>
<td>4,259 ± 932</td>
</tr>
<tr>
<td>Type II fiber CSA, μm</td>
<td>5,046 ± 1,439</td>
<td>5,995 ± 1,010*</td>
<td>5,829 ± 999</td>
</tr>
</tbody>
</table>

Values are means ± SD. Significant effects ($P < 0.05$); c, condition. Significant post hoc differences ($P < 0.05$): *vs. PRE; †vs. RE. CS, citrate synthase; PFK, phosphofructokinase; LDH, lactate dehydrogenase.
hypertrophy and associated increase in SI, specifically stimulus triggered the more robust increase in muscle hypertrophy. Notwithstanding, and given the lack of collective findings remain controversial, it may be that higher-force RE training (26, 36). Although we acknowledge and low-force actions, performed until failure with or without low-force actions repeated until failure ultimately promote increased muscle size by 7% in recreationally active men (37), however, one-legged cycling performed 5 day/wk for 5 wk showed a 6 – 8% increase (41, 51). In concert, QF muscle size increased by 7.8% in the present study of RE. Considering that power and hence workload during RE sessions were very similar across legs over time, the corresponding (13.6%) increase noted after AE+RE is rather remarkable and exceeds the rate typically reported in response to short-term RE training (42, 52). This would imply that repetitive concentric low-force actions as employed here act synergistically with high-force RE training to govern increased skeletal muscle size at a rate far greater than shown with highly effective RE. This is in frank contrast to the fairly established view that AE prompts no frank contrast to the fairly established view that AE prompts no muscle hypertrophy established after AE+RE dissociated from the increase in muscle strength or power.

By employing the current 5-wk RE paradigm, which favors “eccentric overload” using flywheel ergometry, QF volume showed a 6–8% increase (41, 51). In concert, QF muscle size increased by 7.8% in the present study of RE. Considering that power and hence workload during RE sessions were very similar across legs over time, the corresponding (13.6%) increase noted after AE+RE is rather remarkable and exceeds the rate typically reported in response to short-term RE training (42, 52). This would imply that repetitive concentric low-force actions as employed here act synergistically with high-force RE training to govern increased skeletal muscle size at a rate far greater than shown with highly effective RE. This is in frank contrast to the fairly established view that AE prompts no or minute muscle hypertrophy (25). In support of our findings however, one-legged cycling performed 5 day/wk for 5 wk increased muscle size by 7% in recreationally active men (37), and low-force actions, performed until failure with or without vascular occlusion, induced hypertrophy similar to traditional high-force RE training (26, 36). Although we acknowledge these collective findings remain controversial, it may be that low-force actions repeated until failure ultimately promote muscle hypertrophy. Notwithstanding, and given the lack of any obvious impact on in vivo muscle function, we are currently not capable of providing a feasible explanation in regards to what (1) particular stimulus triggered the more robust hypertrophy and associated increase in SI, (2) constituents were responsible for the increased muscle size, and (3) is the physiological significance of the more robust increase in muscle size observed after concurrent training.

To present an AE challenge, we employed the one-legged cycle exercise model introduced and validated by Andersen et al. (3). This exercise model isolates the QF muscle group during repeated CON actions. Oxygen uptake (\(V_{\text{O}_2}\)) rises linearly with increased external work, and at maximal work rate, aerobic metabolic rate of active muscles increases more than \(~100\)-fold and \(V_{\text{O}_2}\) attains 1.2 l/min (3). The blood flow and a-\(v\) \(O_2\) diff of the exercising limb is comparable to what has been reported during maximal cycle exercise (37). During the ~45-min exercise bouts performed in the current study, ~2,500 CON muscle actions were executed at an average work rate of 70% of \(W_{\text{max}}\). To accomplish 45 min at 60 rpm on a standard cycle ergometer would require 2,700 contractions per limb. Thus, although this exercise modality does not resemble classical endurance training involving much larger muscle mass (e.g., treadmill running, cross-country skiing), it remains that stress at the muscle cellular level certainly is most “aerobic” in nature. This is justified by findings of parallel increases in work capacity, muscle capillary supply, and oxidative enzyme activity following chronic one-legged cycling (23, 24, 47). Furthermore, employing training 5 day/wk for 5 wk increases in peak work rate, peak \(V_{\text{O}_2}\), thigh blood flow, and \(O_2\) delivery amounted to 17–24% (37), and 4 wk training increased CS activity by 22% (43). The current model allows for strictly controlled intrasubject comparisons, such that adaptations of a single “isolated” muscle group can be explored in response to, e.g., various exercise programs. In contrast, treadmill running or rowing would call for involvement of additional muscle groups, which could not be quantified or controlled for.

The improved muscle endurance following AE performed three times weekly was paralleled by enhanced skeletal muscle aerobic capacity as reflected in increased CS activity. Thus, although the AE stimulus per se was highly effective, the increases in in vivo muscle strength and power as result of training were very similar across legs and hence exercise modes. Perhaps most convincingly, day-by-day power and total work and thus exercise stimulus during each of the 12 RE sessions were almost identical across legs. It is therefore concluded that there was no interference from the previous AE bouts compromising performance outcome in response to short-term (i.e., ≤5 wk) RE training. More likely, program design features, e.g., duration, intensity, volume, and rest between exercise sessions, are to dictate any potential interference with RE performance and the desired adaptations (27, 54).

Selected genes may display altered basal mRNA levels after chronic training (40, 48). Yet microarray data showed that only 12 genes were differently expressed in young adults subjected to 12 wk RE training (45). The present study investigated genes that acutely respond to either AE (17, 39) or RE (30, 33) and also show responsiveness to training (11). The results infer basal gene expression was unaltered regardless of training modality. In contrast, myostatin expression was downregulated 48–72 h after completion of 8–9 wk RE training (26, 46). Yet myostatin and atrogin-1 levels might be downregulated 48 h after acute exercise (33) to suggest that muscle samples taken at or before this time point may simply reflect the response to the very last exercise session rather than the cumulative effect. Our results regarding PGC-1\(\alpha\) concord with the findings of Pilegaard et al. (43), who reported similar basal mRNA levels across trained and untrained limbs. Collectively, it seems plausible that with regard to the genes chosen here, the protein levels are regulated independent of basal transcriptional changes. Resting expression levels of these particular genes may therefore be poor markers reflecting training-induced muscle adaptations.
In conclusion, the concurrent 5-wk AE+RE paradigm resulted in robust increased in vivo muscle strength and power. Although this effect appeared to be evoked by the RE stimulus alone, the combined approach was accompanied by more substantial muscle hypertrophy, which was not carried over to greater improvement in muscle function. It remains that intense AE can be executed prior to RE without compromising performance outcome.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS


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REFERENCES


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