Interaction of contractile activity and training history on mRNA abundance in skeletal muscle from trained athletes

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Coffey, Vernon G., Anthony Shield, Benedict J. Canny, Kate A. Carey, David Cameron-Smith, and John A. Hawley. Interaction of contractile activity and training history on mRNA abundance in skeletal muscle from trained athletes. Am J Physiol Endocrinol Metab 290: E849–E855, 2006. First published December 6, 2005; doi:10.1152/ajpendo.00299.2005.—Skeletal muscle displays enormous plasticity to respond to contractile activity with muscle from strength- (ST) and endurance-trained (ET) athletes representing diverse states of the “adaptation continuum.” Training adaptation can be viewed as the accumulation of specific proteins. Hence, the altered gene expression that allows for changes in protein concentration is of major importance for any training adaptation. Accordingly, the aim of the present study was to quantify acute subcellular responses in muscle to habitual and unfamiliar exercise. After 24-h diet/exercise control, 13 male subjects (7 ST and 6 ET) performed a random order of either resistance (8 × 5 maximal leg extensions) or endurance exercise (1 h of cycling at 70% peak O2 uptake). Muscle biopsies were taken from vastus lateralis at rest and 3 h after exercise. Gene expression was analyzed using real-time PCR with changes normalized relative to preexercise values. After cycling exercise, peroxisome proliferator-activated receptor-γ coactivator-1α (ET = 8.5-fold, ST = 10-fold, P < 0.001), pyruvate dehydrogenase kinase-4 (PDK-4; ET = 26-fold, ST = 39-fold), vascular endothelial growth factor (VEGF; ET = 4.5-fold, ST = 4-fold), and muscle atrophy F-box protein (MAFbx) (ET = 2-fold, ST = 0.4-fold) mRNA increased in both groups, whereas MyoD (−3-fold), myogenin (−0.9-fold), and myostatin (−2-fold) mRNA increased in ET but not in ST (P < 0.05). After resistance exercise PDK-4 (−7-fold, P < 0.01) and MyoD (−0.7-fold) increased, whereas MAFbx (−0.7-fold) and myostatin (−0.6-fold) decreased in ET but not in ST. We conclude that prior training history can modify the acute gene responses in skeletal muscle to subsequent exercise.

SKELETAL MUSCLE DISPLAYS AN ENORMOUS PLASTICITY to respond to contractile activity and loading conditions, with muscle from strength- (ST) and endurance-trained (ET) athletes representing diverse states of the “adaptation continuum.” Endurance training of sufficient volume and intensity results in an increased whole body maximal O2 uptake and shifts in substrate utilization from carbohydrate- to lipid-based fuels, largely as a result of an expanded mitochondrial density and volume (25). Such changes are brought about by the coordinated coexpression of both the nuclear and mitochondrial genomes that, together, ensure proper assembly and expansion of the mitochondrial reticulum (2). Thus endurance training-induced adaptations culminate in mitochondrial biogenesis, an organelle capable of improved ATP provision (25), and a concomitant enhancement of endurance capacity (23). In contrast, resistance exercise comprising high-intensity, low-volume loading results in an increased cross-sectional area of the trained musculature, which is mainly due to an increase in muscle contractile protein (13). Modulation of transcription and translation events contributes to changes in gene expression and subsequent protein synthesis in response to this mode of training (7). Accordingly, resistance training-induced adaptations that culminate in muscle hypertrophy are the result of integrated gene responses and coordinated molecular events that support the enlargement of preexisting muscle cells via the incorporation of additional myonuclei (13).

Training adaptation can be viewed as merely the accumulation of specific proteins (19). Hence, the altered gene expression that allows for these changes in protein concentration is of major importance for any subsequent training adaptation. The chronic adaptations to any training regimen are likely to be the result of the cumulative effects of repeated bouts of exercise (42, 48) with the initial cellular responses that lead to these long-term adaptations occurring after each (acute) training session (55). Previous works (51, 54) have demonstrated the importance of a wide range of gene expression consistent with their central role in defining the adaptive phenotype with differing modes of training. However, for many genes the transcriptional activation and translational responses occur during the first few hours of recovery, returning to basal levels within 24 h of the exercise stimulus (41, 42). Although much data describing the cellular and molecular mechanisms underlying the transcriptional regulation of gene expression after exercise is available (5, 6, 14, 16, 17, 29, 30, 37, 38, 40, 43, 50, 55, 56), the effects of prior training on the acute response to different types of contraction has not been investigated. Accordingly, the present study was undertaken to determine the early gene responses after an acute bout of endurance and resistance training. Utilizing a design in which chronically ET or ST athletes undertook exercise in their customary training mode and “crossed over” to perform an acute bout of exercise in their nonfamiliar discipline, we provide novel data on subsets of metabolic and myogenic genes that are likely to be fundamental to the specific exercise-induced adaptation in skeletal muscle.

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METHODS

Subjects

Thirteen trained male volunteers participated in this investigation. Six subjects were cyclists who had been participating in regular endurance training for an average of 8 ± 3 yr. These subjects were not undertaking any form of resistance training, nor had they performed such training during the past 2 yr. The other seven subjects were power lifters who had been participating in regular strength/resistance training for 9 ± 7 yr and had not participated in any kind of endurance training for the past 2 yr. The characteristics of the two training populations are displayed in Table 1. The experimental procedures and possible risks associated with the study were explained to each subject, who gave written informed consent before participation. The study was approved by the Human Research Ethics Committees of RMIT University.

Overview of Study Design

The study consisted of a crossover design. All subjects performed two different exercise training protocols to enable subject comparisons. One experimental trial was undertaken in the subjects’ habitual training disciplines, whereas the other trial was performed in their nonfamiliar exercise modes. Exercise testing sessions were separated by a minimum of 10 days.

Preliminary Tests

Peak oxygen uptake. Peak oxygen uptake (VO₂ peak) was determined during an incremental maximal cycling test to volitional fatigue on an isokinetic Lode bicycle ergometer (Groningen, The Netherlands), as previously described in detail (21).

Maximal strength. Maximal concentric and eccentric strength was determined by using seated leg extensions performed on a Kin-Com isokinetic dynamometer (Chattanooga, TN). Each subject’s right leg was strapped to the actuator arm immediately superior to the lateral malleolus of the lower leg with the lateral condyle of the femur visually aligned to the fulcrum of the actuator arm. Contractions were performed at 30°/s, and each subject was instructed to extend the leg and resist the actuator arm with maximal effort during concentric and eccentric leg extension repetitions, respectively. Exercise range of motion was 85°, with leg extension endpoint set at −5° from full extension. Quadriceps strength was determined during a series of 3 × 3-repetition leg extensions, with each set separated by 120 s. Each individual one-repetition maximum was defined as the peak torque (N/m) recorded during the concentric and eccentric contraction phases of the test protocol.

Diet/Exercise Control

Before each exercise testing session the subjects were required to refrain from vigorous physical activity for a minimum of 24 h and were provided with standardized prepacked meals that consisted of 3 g carbohydrate/kg body mass, 0.5 g protein/kg body mass, and 0.3 g fat/kg body mass to be consumed as the final caloric intake on the evening before reporting to the laboratory.

Exercise testing session. On the morning of a testing session the subjects reported to the laboratory in a 10- to 12-h overnight fasted state. After the subjects were rested for 10 min, local anaesthesia [2–3 ml of 1% xylocaine (lidocaine)] was administered to the skin, subcutaneous tissue, and fascia of the vastus lateralis in preparation for muscle biopsies. A resting biopsy (−100 mg) was taken by using a 6-mm Bergstrom needle with suction applied (12), which was removed and immediately frozen in liquid N₂. At this time a separate site on the same leg (−5 cm distal) was prepared for a second biopsy. Biopsies were taken from the left leg when the cycling exercise session was performed and the right leg for the resistance training session. Upon completion of each exercise testing session the subjects rested in a supine position for 3 h, and during this time water was consumed ad libitum. At the end of the recovery period a second muscle biopsy was taken. Every attempt was made to extract tissue from approximately the same depth in the muscle and immediately freeze the sample in liquid N₂. Samples were stored at −80°C until subsequent analysis.

Cycling exercise session. Subjects performed 60 min of continuous cycling at a power output that elicited ~70% of individual VO₂ peak.

Resistance exercise session. Each subject performed maximal concentric and eccentric leg extensor contractions with the right leg on a Kin-Com dynamometer (as described previously). Subjects performed eight sets of five maximal-effort repetitions with 3 min recovery between sets. Peak and mean torque were recorded for each set.

Analytical Procedures

Total RNA isolation and reverse transcription. Total RNA from ~20 mg of wet muscle was isolated using the ToTALLY RNA Kit (Ambion, Austin, TX) protocol and reagents. Total RNA concentration was determined spectrophotometrically at 260 and 280 nm. RNA was reverse transcribed to synthesize first-strand cDNA using avian myeloblastosis virus (AMV) reverse transcriptase (Promega, Madison, WI). Extracted RNA (1 µg) was heated at 65°C for 10 min immediately before first-strand cDNA was generated using AMV reverse transcriptase (kit A3500; Promega) with oligo(dT)₁₅ primer in the presence of 1 mM of each dNTP and 20 U of recombinant RNasin ribonuclease inhibitor. The reaction was incubated at 42°C for 60 min and then terminated at 99°C for 10 min and 4°C for 5 min. The cDNA was stored at −20°C for subsequent analysis. Reverse transcription was performed for all samples simultaneously. Previous work in our laboratory (40) has demonstrated minimal variation in efficiency when performed under these conditions.

Primer design and mRNA quantification. PCR primers were designed using Primer Express software version 2.0 (Applied Biosystems, Foster City, CA) from gene sequences obtained from GenBank (Table 2). Primer specificity was confirmed using Basic Local Alignment Search Tool. Primers were purchased from GeneWorks (Adelaide, SA, Australia). Efficiency of PCR primers was confirmed by examining the dynamic range of responses for a series of dilutions of cDNA. Using the slopes of the lines, the efficiency (E) of each target amplification was calculated by using the equation E = (10⁻(1/slope) − 1. All primers used in this study demonstrated efficient amplification.

Real-time PCR was performed using the GeneAmp 5700 Sequence Detection System (Applied Biosystems). For the PCR step, reaction volumes of 20 µl contained 2× SYBR Green PCR Master Mix (Applied Biosystems), forward and reverse primers, and cDNA template (diluted 1:40). All samples were run in duplicate. The real-time PCR reaction was run for one cycle (50°C for 2 min, 95°C for 10 min) followed by 40 cycles (95°C for 15 s, 60°C for 60 s) and fluorescence emissions were measured after each of the repetitive cycles. Because SYBR Green indiscriminately binds to double-stranded DNA, a melting point dissociation curve was generated to confirm that only a single product was amplified. Heat dissociation of oligonucleotides

Table 1. Subject characteristics

<table>
<thead>
<tr>
<th></th>
<th>Endurance Trained (n = 6)</th>
<th>Strength Trained (n = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mass, kg</td>
<td>74.7 ± 7.6</td>
<td>96.9 ± 15.5*</td>
</tr>
<tr>
<td>Age, yr</td>
<td>28.7 ± 6.1</td>
<td>30.7 ± 8.4</td>
</tr>
<tr>
<td>Training history, yr</td>
<td>8.5 ± 2.7</td>
<td>9.0 ± 7.3</td>
</tr>
<tr>
<td>VO₂ peak, ml/kg/min</td>
<td>65.2 ± 6.4</td>
<td>36.9 ± 7.4*</td>
</tr>
<tr>
<td>Maximum strength, N/m</td>
<td>214 ± 40</td>
<td>309 ± 45*</td>
</tr>
<tr>
<td>Concentric</td>
<td>243 ± 53</td>
<td>389 ± 60*</td>
</tr>
</tbody>
</table>

All values are means ± SD. *Significant difference between endurance-trained and strength-trained groups (P < 0.05).
During the isokinetic resistance exercise session was 263 ST subjects, respectively (vs. 190/H11006 prolactin-activated receptor-muscle sampled 3 h after 60 min of cycling exercise were

Changes in mRNA Abundance After Cycling Exercise

PGC-1α, peroxisome proliferator-activated receptor-γ coactivator-1α; PDK-4, pyruvate dehydrogenase kinase-4; VEGF, vascular endothelial growth factor; MAFbx, muscle atrophy F-box protein.

PGC-1α mRNA was increased to a similar extent after cycling in both groups of subjects.

Likewise, the increase in vascular endothelial growth factor (VEGF) mRNA was similar in ET (∼4.5-fold, P < 0.01) and ST subjects (∼4-fold, P < 0.01) in response to cycling exercise.

Cycling exercise produced diverse responses between ET and ST subjects for the myogenic regulatory factors MyoD and myogenin (Fig. 2). There was an increase in both MyoD (∼3-fold, P < 0.05) and myogenin mRNA (∼0.9-fold, P < 0.05) in ET subjects after cycling. In contrast, cycling decreased MyoD (∼4-fold; not significant (NS)) and myogenin (∼0.4-fold; NS) in ST subjects. Muscle atrophy F-box protein (MAFbx) mRNA abundance was increased in both subject groups after cycling (ET ∼2-fold, ST ∼4-fold, both P < 0.01), whereas myostatin mRNA was significantly increased by cycling exercise in ET (∼2-fold, P < 0.05) but not ST subjects.

Table 2. Primer sequences and concentrations used for real-time PCR

<table>
<thead>
<tr>
<th>Gene</th>
<th>GenBank Accession No.</th>
<th>Forward Primer (5' → 3')</th>
<th>Reverse Primer (5' → 3')</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAFbx</td>
<td>NM_058229</td>
<td>CATTGTCATCTGAGCTTAAGAAGAAGA</td>
<td>TCCGATAGCACACCATGTTAATG</td>
</tr>
<tr>
<td>MyoD</td>
<td>NM_002478</td>
<td>CCGGACCAAGAAAAATATAGAAGA</td>
<td>GCAACGCGCTGGTTGTGA</td>
</tr>
<tr>
<td>Myogenin</td>
<td>NM_002479</td>
<td>GCCTGCGAGGAGAAATGCCG</td>
<td>TGGACTGTCGCGCAAGATGGA</td>
</tr>
<tr>
<td>Myostatin</td>
<td>NM_005259</td>
<td>CCAGAGGAATGTTGGCTGAAGA</td>
<td>CAAAACCAATTACCTGTGGA</td>
</tr>
<tr>
<td>PGC-1α</td>
<td>NM_013261</td>
<td>CAGGACGAAACCAAACTTATATTCTT</td>
<td>CAGACATTTAGGTCGTCATAGTGC</td>
</tr>
<tr>
<td>PDK-4</td>
<td>NM_002612</td>
<td>ATGTTATACCCCGAATGCTC</td>
<td>AACTTGACATAACGAGGAATTGTGCA</td>
</tr>
<tr>
<td>VEGF</td>
<td>NM_003376.3</td>
<td>GCGCAAGAAATCCCGGTATA</td>
<td>GTTCTCCGCTGCGGAA</td>
</tr>
</tbody>
</table>

PGC-1α, peroxisome proliferator-activated receptor-γ coactivator-1α; PDK-4, pyruvate dehydrogenase kinase-4; VEGF, vascular endothelial growth factor; MAFbx, muscle atrophy F-box protein.

Detects differences in melting temperature and produces a single dissociation peak for each nucleotide within a 2°C difference in melting temperature (46). The selection of endogenous control to normalize for input RNA (housekeeping gene) was confounded by training history (ST or ET) and/or exercise mode (cycling or resistance training), which generated significant variance in all of the commonly-used exercise housekeeping genes (β-actin, β-micro-globulin, GAPDH) (28, 36). The expression of the gene of interest in a given sample was calculated by subtracting the threshold cycle (Ct) of the target gene for a given sample from the Ct of the same gene from the appropriate control sample for that individual. The relative expression of the gene of interest relative to control was then calculated using the expression 2^-ΔΔCt.

Statistical Analysis

Differences in subject characteristics and exercise performance were determined using a two-tailed t-test, assuming unequal variaces. Data for mRNA abundance with each exercise session are expressed in relative units after individual samples were normalized relative to mean values at rest. Data were subjected to repeated-measures ANOVA and log transformation was performed when significant deviations from homogeneity occurred (SPSS for Windows, version 12.0.1). Differences between individual means were compared using Fisher’s least significant difference test. All values are expressed as means and standard deviation, with the critical level of significance established at P < 0.05.

RESULTS

Exercise Performance

The power output corresponding to ~70% VO2peak for the 60-min cycling bout was 242 ± 11 vs. 168 ± 10 W for ET and ST subjects, respectively (P < 0.001). The mean peak force during the isokinetic resistance exercise session was 263 ± 10 vs. 190 ± 4 N for ST and ET subjects, respectively (P < 0.001).

Changes in mRNA Abundance After Cycling Exercise

Relative changes in mRNA abundance of metabolic genes in muscle sampled 3 h after 60 min of cycling exercise were observed for both ST and ET subjects (Fig. 1). Peroxisome proliferator-activated receptor-γ coactivator-1α (PGC-1α) mRNA was increased to a similar extent after cycling in both ET (∼8.5-fold, P < 0.001) and ST subjects (∼10-fold, P < 0.001). There were also large increases in pyruvate dehydrogenase kinase-4 (PDK-4) mRNA in both groups of subjects after cycling (ET ∼26-fold, ST ∼39-fold, both P < 0.05).
Changes in mRNA Abundance After Resistance Exercise

There was little effect of resistance exercise on the mRNA abundance of PGC-1α or VEGF (Fig. 3). In contrast, PDK-4 was significantly increased in ET (7-fold, \( P < 0.01 \)) but not ST subjects after resistance exercise. There were divergent responses of genes associated with myogenic regulation in ET subjects in response to resistance exercise (Fig. 4A). In ET subjects, MyoD increased (0.7-fold, NS), but MAFbx (0.7-fold; NS) and myostatin (0.6-fold, NS) both decreased after resistance exercise. In ST subjects, the mRNA abundance of the myogenic genes under investigation was not significantly altered by a single bout of resistance exercise (Fig. 4B).

DISCUSSION

Differences in muscle phenotype and subsequent function occur by activating and/or repressing different subsets of genes. A rate-limiting step for protein synthesis in response to exercise is the level of transcription and the quantity of mRNA abundance (8, 48), with the level of mRNA determined by the rates of mRNA synthesis and decay. New steady-state protein synthesis via chronic and load-specific stimuli can optimize muscle tissue for such diverse physiological functions as strength or endurance capabilities (16, 18).

Previous studies (1, 3, 37, 42) have shown that diverse exercise stimuli induce specific early gene responses in skeletal muscle. However, the degree of specificity in gene responses to divergent modes of exercise when undertaken by athletes with an extensive history of single-mode training has not been investigated. We deliberately chose to exercise subjects at the...
same relative rather than absolute exercise intensity in an attempt to mimic the habitual training practices of these two groups of athletes. For the first time, we provide experimental evidence demonstrating that divergent forms of exercise undertaken in habitually trained athletes results in the selective upregulation/repression of specific gene sets that are likely to mediate some of the chronic exercise-induced adaptations to training.

The first novel finding of the present study was that a single bout of endurance exercise undertaken by both ST and ET athletes elicited similar changes in the mRNA abundance of a subset of metabolic genes, namely PGC-1α, PDK-4, and VEGF (Fig. 1). Our results showing an upregulation of these genes in endurance-trained subjects are in agreement with previous findings (9, 14, 37, 42) and provide further support for their proposed roles in exercise-induced regulation of mitochondrial biogenesis, carbohydrate metabolism, and angiogenesis, respectively (5, 14, 33, 42, 43). It has been proposed that adaptation to chronic resistance training does not create a favorable cellular environment with respect to oxidative potential (24, 52, 53). The chronic training history of ST athletes results in an increased cross-sectional area and fiber diameter of the trained musculature (35), and it has been suggested that this adaptation may limit nuclear and mitochondrial transcriptional capacity due to an increase in the cytoplasm to myonucleus ratio of the cell (52). Furthermore, the mitochondrial density of enlarged fibers may be diluted, thus increasing diffusion distances for oxygen and substrates (24). Notwithstanding these observations, such conditions did not preclude an endurance exercise-induced increase in “metabolic genes” in this subject population.

With regard to the acute mRNA responses of “myogenic genes” after a bout of cycling exercise, we found that MyoD and myogenin increased in ET but not ST subjects (Fig. 2). MyoD and myogenin are expressed in muscle satellite cells and mature myofibers and have been implicated in mediating the processes of cell proliferation and differentiation and in defining muscle phenotype (10, 27, 57). Cycling involves minimal eccentric work for force production, suggesting that the divergent responses of MyoD in the present study were not the result of disparity in the activation of satellite cell populations. The expression of MyoD is highly induced after resistance exercise, surgical ablation, denervation, and muscle damage (6, 26, 27, 44, 57), but to the best of our knowledge an increase in MyoD expression has not previously been reported after cycling exercise in humans. MyoD expression is increased after endurance treadmill running in rodents and humans (4, 58). Yang et al. (58) observed increased MyoD mRNA abundance in physically active human subjects after 30 min of treadmill running and attributed this to the eccentric component with foot strike and suggested that increased MyoD expression may indicate transcriptional regulation of fiber-specific alterations in myosin heavy chain expression. Previously, Kadi et al. (30) have shown myogenin accumulation after endurance cycling, and this may represent an early signal mediating the control of myofiber oxidative metabolic properties. In support of this contention we observed a significant increase in the mRNA abundance of myogenin after cycling exercise in ET subjects. However, it is unclear why a decrease in myogenin was observed in ST subjects after cycling exercise.

If expression of myogenic regulatory factors occurs in mature myofibers as a result of endurance adaptation, the decrease in MyoD and myogenin mRNA in ST subjects after cycling may suggest a repressed response due to the adaptive phenotype of the muscle. However, although fiber type-specific responses are likely to contribute to the discrepancy in MyoD and myogenin mRNA abundance after cycling exercise, the precise mechanism for such unique divergent responses in our diversely-trained athletic populations remains elusive.

A novel finding of the present study was the significant increase in mRNA abundance of several “negative regulators” of muscle mass in both ET and ST subjects after cycling exercise. To the best of our knowledge, increases in MAFbx and myostatin after cycling exercise have not previously been reported (Fig. 2). MAFbx (also known as Atrogin-1) is an ubiquitin E3 ligase involved in the regulation of proteolysis (34). The induction of MAFbx expression before muscle loss and its high expression during accelerated protein degradation strongly suggest that this plays an important role in initiating and maintaining proteolysis (17, 34). Important regulators of MAFbx expression have been identified downstream of insulin and insulin-like growth factor signaling, including protein kinase B (Akt) and the Forkhead box O class of transcription factors and mammalian target of rapamycin (15, 49). Stimuli that have been shown to generate proteolysis in skeletal muscle include fasting and diabetes (11, 17). In the present study, it seems reasonable to conclude that the metabolic stress produced during the 60-min endurance exercise performed in a fasted state contributed to the increase in MAFbx mRNA abundance. Moreover, the increase in MAFbx mRNA in both ET and ST subjects after cycling indicates a response that is independent of training history. Myostatin is a transforming growth factor defined as a negative regulator of muscle mass. Deletion of myostatin is associated with gross muscle hypertrophy, whereas overexpression results in lower muscle mass and decreased fiber size (39, 45). We observed an increase in myostatin mRNA after cycling in ET but not ST subjects. These findings are in contrast with recent work in rodents after swimming exercise (38). Differences in muscle sampling time course and exercise mode and duration make comparisons difficult to rationalize these discordant findings. Previous work involving resistance exercise in humans has shown both decreased (31) and increased (56) myostatin mRNA expression. The specific mechanism through which myostatin gene expression is controlled and how it exerts its effect on skeletal muscle is unclear. Nevertheless, the possibility exists that the adaptive state in ST subjects as a result of chronic resistance training inhibits any acute upregulation in myostatin gene expression, regardless of the exercise mode, and that its regulation after endurance exercise occurs in a phenotype- or genotype-specific manner.

The patterns of induction of the two subsets of metabolic and myogenic genes after resistance exercise were variable. Significant changes from rest were observed for PDK-4, MyoD, MAFbx, and myostatin mRNA abundance in ET but not ST subjects following 3 h of recovery after resistance exercise. PDK-4 phosphorylates and inactivates the pyruvate dehydrogenase complex and facilitates movement of glycolytically derived pyruvate toward lactate output rather than oxidation.
The increase in PDK-4 in ET subjects after resistance exercise probably corresponds to a requirement for increased glycolytic metabolism to supply energy to sustain the repeated high-intensity contractile activity and may also have enhanced muscle glycogen resynthesis during recovery. Our results are in agreement with those of Yang et al. (58) that show increased PDK-4 mRNA expression after resistance exercise.

Compatible with its role in muscle hypertrophy and supporting the work of others (6, 44, 57), MyoD mRNA increased in ET subjects after resistance exercise. The role of MyoD in satellite cell proliferation and differentiation for subsequent muscle regeneration and hypertrophy has been previously noted. Resistance training induces muscle overload, resulting in local myotrauma that stimulates a number of processes, including satellite cell activation (20). Therefore, unfamiliar resistance exercise in ET subjects may have been expected to induce an increase in MyoD expression due to the activation of satellite cells for muscle repair/regeneration and as an adaptation response for greater force production and reduced cellular disturbance with subsequent repeated exercise bouts. MAFbx is a mediator of atrophy involved in the breakdown of muscle protein, whereas myostatin negatively regulates hypertrophy processes (22, 32). Few studies have investigated the effect of exercise on MAFbx and myostatin expression in humans, and the specific response to resistance exercise is still to be determined. Nevertheless, preliminary evidence implicates resistance exercise in the downregulation of the mRNA content of both MAFbx and myostatin, almost certainly reducing their negative effects on subsequent hypertrophy processes (29, 31, 47). Our results provide evidence in support of such a contention.

In summary, an important component of this work was the elucidation of whether familiar/unfamiliar exercise induced a suppressed or amplified acute response in subsets of “metabolic” and “myogenic” genes that are likely to be fundamental to specific exercise-induced adaptation. A single endurance exercise bout produced comparative transcriptional responses in metabolic genes whereas training history markedly altered the response of myogenic genes. Few differences were evident after resistance exercise; however, the magnitude of exercise response was notably larger in ET subjects. A potential limitation with regard to the interpretation of the present data set is the use of a single postexercise time point to evaluate the responses of the exercise-induced genes under investigation. We chose to sample muscle 3 h after the completion of an exercise bout because previous studies (14, 38, 42, 43, 58) have reported that for the genes of interest determined in the present study indicate that, independent of exercise mode, skeletal muscle from ET athletes appears to be more sensitive to the specific response to resistance exercise.

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REFERENCES


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