Resistance training alters the response of fed state mixed muscle protein synthesis in young men


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Tang JE, Perco JG, Moore DR, Wilkinson SB, Phillips SM. Resistance training alters the response of fed state mixed muscle protein synthesis in young men. Am J Physiol Regul Integr Comp Physiol 294: R172–R178, 2008. First published November 21, 2007; doi:10.1152/ajpregu.00636.2007.—Ten healthy young men (21.0 ± 1.5 yr, 1.79 ± 0.1 m, 82.7 ± 14.7 kg, means ± SD) participated in 8 wk of intense unilateral resistance training (knee extension exercise) such that one leg was trained (T) and the other acted as an untrained (UT) control. After the 8 wk of unilateral training, infusions of 1-[ring-d5]phenylalanine, 1-[ring-13C6]phenylalanine, and d3-α-ketoisocaproic acid were used to measure mixed muscle protein synthesis in the T and UT legs by the direct incorporation method [ fractional synthetic rate (FSR)]. Protein synthesis was determined at rest as well as 4 h and 28 h after an acute bout of resistance exercise performed at the same intensity relative to the gain in single repetition maximum (1RMs) before and after training. Training increased mean muscle fiber cross-sectional area only in the T leg (type I: 16 ± 10%; type II: 20 ± 19%, P < 0.05). Acute resistance exercise increased muscle protein FSR in both legs at 4 h (T: 162 ± 76%; UT: 108 ± 62%, P < 0.01 vs. rest) with the increase in the T leg being significantly higher than in the UT leg at this time (P < 0.01). At 28 h postexercise, FSR in the T leg had returned to resting levels; however, the rate of protein synthesis in the UT leg remained elevated above resting (70 ± 49%, P < 0.01). We conclude that resistance training attenuates the protein synthetic response to acute resistance exercise, despite higher initial increases in FSR, by shortening the duration for which protein synthesis is elevated.

IN HEALTHY INDIVIDUALS MUSCLE protein mass is regulated by changes in muscle protein synthesis (MPS), and to a lesser degree, muscle protein breakdown (MPB). In the fasted state, MPB exceeds MPS such that muscle protein balance is negative and there is a net loss of muscle protein (18). In the fasted state, resistance exercise increases both MPS and MPB, improving muscle protein balance, but balance remains negative as MPB still exceeds MPS (18). However, when resistance exercise is accompanied by an increase in amino acid availability (i.e., feeding) balance becomes positive and there is a net accretion of muscle protein. This is the result of a synergistic stimulation of MPS by feeding and resistance exercise, as well an attenuation of the exercise-induced increase in MPB by feeding (20, 22).

Training can affect the acute response of MPS to a bout of resistance exercise. Phillips et al. (18) noted increases in the rates of MPS that persisted for up to 48 h in untrained individuals. In contrast, MacDougall et al. (13) reported that the resistance exercise-induced increase in MPS in trained individuals returned to baseline by 36 h. MPS has also been shown to be reduced following resistance training at the same absolute workload (17), which might be expected since the same absolute workload would result in a lower relative stress posttraining. When taken together, these studies suggest that training alters the time course of the acute response of MPS to resistance exercise; however, to date no longitudinal study has directly confirmed this thesis nor examined it in the fed state. Indeed, feeding to provide amino acids augments the postexercise response of MPS, which would maximize the anabolic effect of any exercise.

The purpose of this study, therefore, was to examine resistance training-induced changes in MPS after a bout of resistance exercise in the fed state. We were interested in determining the extent and time course of changes in MPS after an acute bout of resistance exercise performed at the same intensity relative to the increase in maximal strength following training in the fed state. We hypothesized that resistance training would alter resting MPS as well as the time course of the increase in MPS after an acute bout of resistance exercise.

METHODS

Subjects. Ten healthy men volunteered to participate in the study (21.0 ± 1.5 yr, 1.79 ± 0.08 m, 82.7 ± 14.7 kg, means ± SD). All subjects were recreationally active (i.e., exercised < 1–2 d/wk) and had not been regularly engaging in resistance exercise for at least 8 mo. All subjects were informed of the purpose of the study, experimental procedures to be used, and potential risks. Written consent was obtained from all subjects prior to commencing the study. This study was conducted in accordance with the standards set by the Declaration of Helsinki and was approved by the local McMaster University and Hamilton Health Sciences Research Ethics Boards.

General experimental protocol. This study involved an 8-wk unilateral resistance training program followed by three stable isotope infusion trials to determine changes in MPS following training. The unilateral resistance training program consisted of knee extension exercise only. One leg was assigned to perform the exercise such that it would become trained (T) while the other leg would serve as a nonexercised, untrained control (UT). All subjects participated in a familiarization session with the dynamic knee extension exercise machine and an isokinetic dynamometer (Biodex System 3; Biodex Medical Systems, Shirley, NY) at least 2 wk prior to any initial testing. Strength testing was performed on each leg separately and included a voluntary dynamic one repetition maximum (1 RM) test and isometric strength tests performed on the isokinetic dynamometer. Strength was assessed before and after completion of the training program.

Prior to the start of training, a muscle biopsy was obtained for histochemical analysis from the vastus lateralis of the leg to be trained...
of each subject; the biopsy was performed under local anesthesia (2% xylocaine) using our custom suction-modified 5-mm Bergstrom needle. The leg to be trained was selected randomly, counterbalanced for dominance based on strength, such that equal numbers of subjects trained their dominant and nondominant legs. Training was performed 3 d/wk (Monday to Friday) initially (weeks 1–4) and then only 2 d/wk at the latter stages of the training (weeks 5–8); at least 1 day of rest was provided between each training session. For weeks 1–2, training began with three sets of knee extension exercise performed at a workload equivalent to each subject’s 10–12 RM. For weeks 3–4, participants performed four sets at their 8–10 RM. The number of sets was increased to five for weeks 5–6. Finally, for weeks 7–8, participants performed six sets at a workload equivalent to their 6–8 RM. Each subject performed all 20 training sessions, which were supervised by a study investigator.

**Stable isotope infusion protocol.** L-[ring-d5]phenylalanine (98% enriched), L-[ring-13C6]phenylalanine (99% enriched), and d3-ketoisocaproic acid (d3-KIC; sodium salt, 98% enriched) were purchased from Cambridge Isotope Laboratories (Andover, MA). All isotopes were dissolved in 0.9% saline, passed through a 0.2-μm filter, and stored in evacuated bottles prior to infusion. Isotopes were passed through an in-line 0.2-μm filter during the infusion by using a calibrated syringe pump (74900 Series; Cole Palmer Instrument, Niles, IL).

Stable isotope infusions were used to measure MPS in the T and UT legs on three occasions: at rest, 4 h following an acute bout of resistance exercise, and 28 h thereafter. The experimental infusion protocols are shown schematically in Fig. 1. Four days following their last training session, subjects participated in the infusion trial to measure MPS at rest. Following the resting infusion trial, subjects then performed two additional training sessions according to their last recorded training volume and workload. A second infusion trial was performed 1 wk following the resting infusion trial to examine the response of MPS 4 h after an acute bout of resistance exercise (6 sets of 8–10 repetitions at ~80% 1-RM knee extension at the same relative intensity for the T and UT leg) in the fed state. Subjects then returned to the lab 24 h following the bout of resistance exercise for the third and final infusion trial. Dietary intake was controlled 48 h prior to the infusions as well as between the infusion sessions by providing subjects with prepackaged diets. The diets contained standard food items as well as at least 30% of the subjects’ dietary energy in the form of a liquid meal replacement drink (Boost; Novartis, Mississauga, ON, Canada) to provide vitamins and minerals at the recommended levels. Diets were formulated based on the subjects’ estimated energy requirements according to the Harris-Benedict equation using a moderate activity level. Protein was held constant in each diet package at 1.2 g kg\(^{-1}\) d\(^{-1}\). Compliance with the diets was checked by having subjects report to the lab on each day they were consuming the diet and providing dietary checklists as well as close monitoring of the subjects weight during this time.

Each infusion trial began with subjects arriving in the lab at ~0700–0800 after an overnight fast (~10 h). Subjects had a 20-gauge catheter inserted in an antecubital vein from which blood samples were drawn throughout the infusion period (t = 0, 60, 90, 120, 180, 240, and 270 min; see Fig. 1). The catheter was kept patent by periodic flushing with 1–2 ml of 0.9% saline. Following the

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**Fig. 1.** Schematic representation of the infusion sessions following training. $^{13}$C\(_6\) Phe, L-[ring-$^{13}$C\(_6\)]phenylalanine; d\(_5\) Phe, L-[ring-d\(_5\)]phenylalanine; d\(_3\)-α-KIC, d\(_3\)-α-ketoisocaproic acid.
baseline blood sample, a second catheter was inserted in the contralateral arm in which participants received a primed constant infusion of L-[ring-d5]phenylalanine, L-[ring-13C6]phenylalanine, or d3-Leucine. The priming dose was 3 μmol/kg for the phenylalanine tracers and 10 μmol/kg for the d3-Leucine tracer. A continuous infusion was initiated following the priming dose at a rate of 0.08 μmol·kg⁻¹·min⁻¹ for the phenylalanine tracers and 0.15 μmol·kg⁻¹·min⁻¹ for d3-Leucine. Subjects received ~35% and 50% of their recommended daily caloric intake, as predicted by the Harris-Benedict equation, through a liquid meal supplement (Boost: 68% carbohydrate, 17% protein, 15% fat) during the rested and postexercise (both 4 h and 28 h) infusions, respectively. Participants ingested the meal supplement in equally divided aliquots every 30 min (0.1 g protein·h⁻¹). The supplement aliquots where enriched with whichever isotope was being infused to maintain isotopic steady state following consumption. Muscle biopsies were obtained from both legs within ~10 min of each other at t = 90 and 270 min during the first and third infusion trials and at t = 60 and 240 min during the exercise infusion. A portion of a resting biopsy obtained from each leg was processed for histochemical analysis (see below) upon excision, while all other tissue samples were immediately frozen in liquid nitrogen and stored at −80°C until further analysis.

Blood analyses. All blood samples were collected into heparinized tubes (Vacutainer) and processed as previously described (14, 30). Blood amino acid concentrations were determined by HPLC from plasma samples as previously described (14, 30). Plasma glucose was measured by an enzymatic assay adapted for fluorometry (15), while insulin concentrations were analyzed by RIA (Coat-A-Count; Diagnostic Products, Los Angeles, CA). For determination of blood amino acid enrichment, the perchloric acid extracted whole blood was transferred into a threaded Pyrex tube and lyophilized in a Speed-Vac Plus rotary evaporator (Savant Instruments, Farmingdale, NY). To determine the isotopic enrichment in the blood, the tert-butyli dimethylsilyl derivative of phenylalanine and leucine was prepared. To the dried sample 50 μl of acetonitrile (HPLC grade) and 50 μl N-methyl-N-(tert-butyldimethylsilyl) trifluoroaceticamide ± 1% tert-butyldimethylchlorosilane (MTBSTFA ± 1% TBDMS; Pierce Chemical, Rockford, IL) were added, and then the samples were heated for 1 h at 90°C. The tert-butyldimethylsilyl derivatives of phenylalanine and leucine were analyzed by splitless injection using electron-impact ionization capillary gas chromatography-mass spectrometry (models 6890 GC and 5973 MS; Hewlett-Packard, Palo Alto, CA) with selected ion monitoring of mass-to-charge ratios of 234 and 239 for L-[ring-d5]phenylalanine (m+0 and m+5), 234 and 240 for L-[ring-13C6]phenylalanine (m+0 and m+6), and 200 and 203 for d3-leucine (m+0 and m+3), where m is mass.

Muscle fiber analyses. Frozen tissue samples embedded in optimal cutting temperature compound (Sakura Finetechnical, Tokyo, Japan) were sectioned and stained for myofibrillar ATPase activity and analyzed as previously described (12, 24, 26, 29). We have only included data for subjects for whom we could obtain a complete data set (Pre, Post-UT, and Post-T) with each sample providing ~100 fibers. We were unable to obtain fiber data from two Post-UT samples, while one Post-T sample had only 15 usable fibers. Thus, only data from 7 of 10 subjects were included in the fiber analyses.

Gas chromatography-mass spectrometry analyses. For mixed-muscle protein-bound and free intracellular enrichment ~20 mg of wet muscle tissues were analyzed. Muscle samples were lyophilized to dryness overnight, while being incubated on dry ice. Samples were then manually powdered, and 500 μl of 0.6 M PCA was added. After gentle shaking, the samples sat on ice for 10 min and were then centrifuged at 2,000 g for 2 min. The supernatant (i.e., intracellular free amino acids) was collected and processed in the same manner as the whole blood samples. The remaining pellet from the muscle sample was washed twice with 1 ml of distilled deionized water and then lyophilized to dryness overnight. The dried pellet was placed in 2 ml of 6 N HCl and hydrolyzed for 24 h at 100°C. The acid hydrolysate was passed over acid-washed cation exchange column (Dowex Analytical Grade 50W-X8, 100–200 mesh hydrogen form; Bio-Rad Labs, Hercules, CA) for amino acid isolation/purification to determine the protein-bound enrichments. The samples were dried by using a rotary evaporator, and the dried pellet was then derivatized in the same manner as the blood samples. Intracellular enrichments were determined in the same manner as the blood, while bound muscle enrichments were determined using the standard curve approach (16).

Calculations. Fractional synthetic rate (FSR) was calculated from the determination of the rate of tracer incorporation into muscle protein and using the muscle intracellular free phenylalanine or leucine enrichment as a precursor, according to the following equation: FSR (%/h) = [Et1 − Et0]/[Ep * (t1 − t0)] * 100%, where Et0 is the enrichment of the protein-bound isotope tracer from the first biopsy, Ep is the enrichment of the protein-bound isotope tracer from the second biopsy, and t1 − t0 is the incorporation time.

Statistics. Strength, amino acid, blood glucose, and insulin data were analyzed using a two-factor repeated-measures ANOVA. Fiber cross-sectional area data were analyzed using a paired t-test for two sample means (pre and post) for each fiber type. Rates of mixed MPS were analyzed using a two-factor ANOVA with training status (T and UT) and condition (rest, 4 h postexercise, and 28 h postexercise) as within-subject factors. Where ANOVA revealed significance, a Tukey’s post hoc procedure was used to identify pairwise differences. Residuals and comparisons of FSR determined by the phenylalanine and α-KIC tracers were made using GraphPad Prism (version 5.00, GraphPad Software). Significance was accepted at P < 0.05. All data are expressed as means ± SD.

RESULTS

Strength measurements. Prior to training there was no difference between legs in unilateral knee extension 1-RM strength (Fig. 2). Unilateral 1-RM strength increased in both legs with training (T = 62.3 ± 27%; UT = 19.7 ± 13%, P < 0.01; Fig. 2). However, by the completion of the training protocol, the increase in the T leg was threefold greater than that seen in the UT leg (P < 0.01; Fig. 2). There was no pretraining difference between legs in isometric strength (T = 284.5 ± 43.5; UT = 297.4 ± 46.8 N·m, P = 0.64). After training, isometric strength increased in the T leg (17.7 ± 12%, P < 0.01), with no change in the UT leg (P = 0.86).

Fig. 2. Knee extension 1 repetition maximum (RM) strength assessments. *Significantly different from pretraining (PRE) in the same leg (P < 0.01). T, trained. +Significantly different from posttraining (POST) in the untrained (UT) leg (P < 0.001). Values are means ± SD (N = 10).
**Muscle fiber cross-sectional area.** The mean fiber cross-sectional area of both type I and type II fibers increased with training (type I: 16 ± 10%, P < 0.05; type II: 20 ± 19%, P < 0.05; Fig. 3) in the T leg. There was no change in type I or type II fiber cross-sectional area after the training protocol in the UT leg.

**Blood amino acid concentrations.** Table 1 shows the concentration of plasma total amino acids, essential amino acids, and branched-chain amino acids during the three testing sessions. There was a main effect for time in total amino acids, essential amino acids, and branched-chain amino acids levels in the plasma (P < 0.01). Feeding stimulated an increase in plasma amino acid levels; however, the level remained constant at the times when biopsies were taken. There was also a main effect for condition where the amino acid concentrations seen at 24 h postexercise condition were lower than immediately postexercise (P < 0.05; Table 1).

**Plasma glucose and insulin concentrations.** Plasma glucose levels were not significantly affected by feeding or by condition. However, there was a main effect of time where insulin concentrations were significantly elevated over resting (t = 0 h) values at all time points (P < 0.01; Table 2).

**Mixed muscle protein FSR.** Plasma enrichments were stable over the incorporation period of each trial, with no differences between trials. There was no difference in resting mixed muscle FSR between the T and UT leg (P = 0.97; Fig. 4). The acute bout of resistance exercise elevated FSR above resting values (T: 162 ± 76%; UT: 108 ± 62%, P < 0.01, P < 0.01; Fig. 4); however, the increase in the T leg was significantly higher than that seen in the UT leg 4 h postexercise at the same relative intensity (P < 0.01; Fig. 4). At 28 h postexercise the increase in FSR in the T leg had returned to resting levels; however, FSR remained elevated in the UT leg (70 ± 49%, P < 0.01; Table 2).

**DISCUSSION**

We report here that 8 wk of unilateral resistance training (20 total training sessions) results in hypertrophy and alters the response of fed state-mixed MPS to an acute bout of resistance exercise performed at the same relative intensity (i.e., greater work performed by the T leg). In the present study the subjects were fed a meal supplement to maximize anabolic potential by creating a hyperinsulinemic and hyperaminoacidemic environment (3–6, 10, 21, 28). Despite the fact that mixed MPS was higher in the immediate postexercise period in the T vs. UT leg, the protein synthetic response was reduced in the T leg over 28 h.

The limited number of studies that have aimed to define the time course of increased MPS following a bout of resistance exercise suggests that protein synthesis rises rapidly (within 3–4 h) postexercise and remains elevated for at least 24 h (7, 13, 18). Combined cross-sectional data from Chesley et al. (7) and MacDougall et al. (13) suggests that MPS rises at 4 h postexercise, peaks at 24 h, and subsequently returns to resting levels by 36 h postexercise in trained subjects. Conversely, Phillips et al. (18) demonstrated that protein synthesis peaks at 3 h postexercise, and remains elevated above resting levels, albeit declining progressively both at 24 h and 48 h postexercise after an acute bout of resistance exercise. It is difficult to reconcile these previous results, both to each other and to the

Table 1. Plasma amino acid concentrations at rest, 4 h postexercise, and 24 h postexercise

<table>
<thead>
<tr>
<th>Amino Acid Type</th>
<th>Time</th>
<th>Rest</th>
<th>1.5 h</th>
<th>4.5 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAA</td>
<td>0 h</td>
<td>4,259</td>
<td>4,568</td>
<td>5,170</td>
</tr>
<tr>
<td>EAA</td>
<td>0 h</td>
<td>1,573</td>
<td>1,992</td>
<td>1,874</td>
</tr>
<tr>
<td>BCAA</td>
<td>0 h</td>
<td>795</td>
<td>966</td>
<td>927</td>
</tr>
<tr>
<td>TAA</td>
<td>4 h</td>
<td>4,983</td>
<td>5,541</td>
<td>5,512</td>
</tr>
<tr>
<td>EAA</td>
<td>4 h</td>
<td>1,801</td>
<td>2,027</td>
<td>1,866</td>
</tr>
<tr>
<td>BCAA</td>
<td>4 h</td>
<td>894</td>
<td>1,003</td>
<td>921</td>
</tr>
<tr>
<td>TAA</td>
<td>24 h</td>
<td>4,281</td>
<td>4,952</td>
<td>4,853</td>
</tr>
<tr>
<td>EAA</td>
<td>24 h</td>
<td>1,503</td>
<td>1,801</td>
<td>1,779</td>
</tr>
<tr>
<td>BCAA</td>
<td>24 h</td>
<td>732</td>
<td>895</td>
<td>899</td>
</tr>
</tbody>
</table>

Values are means ± SD in micromolars. Zero hours had significantly lower total amino acids (TAA), essential amino acids (EAA), and branched-chain amino acids (BCAA) concentrations than all other time points (P < 0.01). Main effect for condition where there were lower TAA, EAA, BCAA concentrations 24 h postexercise than immediately postexercise (P < 0.05).

Table 2. Plasma glucose and insulin concentrations

<table>
<thead>
<tr>
<th>Glucose (mM)</th>
<th>Time</th>
<th>Rest</th>
<th>1.5 h</th>
<th>3 h</th>
<th>4.5 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose, mM</td>
<td>0 h</td>
<td>4.4</td>
<td>4.0</td>
<td>4.7</td>
<td>4.0</td>
</tr>
<tr>
<td>Insulin, µIU/ml</td>
<td>0 h</td>
<td>6.5</td>
<td>21.1</td>
<td>31.3</td>
<td>25.6</td>
</tr>
<tr>
<td>Glucose, mM</td>
<td>1.5 h</td>
<td>4.0</td>
<td>3.8</td>
<td>4.2</td>
<td>4.1</td>
</tr>
<tr>
<td>Insulin, µIU/ml</td>
<td>1.5 h</td>
<td>26.1</td>
<td>29.8</td>
<td>25.3</td>
<td>18.0</td>
</tr>
<tr>
<td>Glucose, mM</td>
<td>3 h</td>
<td>4.2</td>
<td>4.2</td>
<td>4.2</td>
<td>4.2</td>
</tr>
<tr>
<td>Insulin, µIU/ml</td>
<td>3 h</td>
<td>30.1</td>
<td>29.5</td>
<td>29.5</td>
<td>27.5</td>
</tr>
</tbody>
</table>

Values are means ± SD. Zero hours had significantly lower insulin concentrations than all other time points (P < 0.01).
present study, as there are considerable differences in the training status of the participants and the study designs employed (i.e., cross-sectional vs. longitudinal). Indeed, Chesley et al. (7) and MacDougall et al. (13) utilized different groups of trained individuals for each time point studied, while Phillips et al. studied the same subjects at each time in a longitudinal design. Moreover, Chesley et al. (7) and MacDougall et al. (13) studied subjects in the fed state while the participants in the study by Phillips et al. (18) were fasted. To our knowledge, the present study is the first study to longitudinally examine the time course of changes in MPS in the fed state following an acute bout of resistance exercise after training. We found an increase in mixed MPS in the immediate period after exercise (4 h) in both the T and UT legs by 162% and 108%, respectively. However, while MPS remained elevated by 70% at 28 h postexercise in the UT leg, rates of MPS had returned to resting levels in the T leg. Thus, our data suggests that in the T state the response of MPS to the same relative intensity of resistance exercise is accelerated such that it reaches a greater peak initially but returns to baseline more rapidly compared with the UT state.

It has previously been reported that resistance training attenuates the protein synthetic response to an acute bout of resistance exercise (17). However, in the study by Phillips et al. (17), resistance exercise was performed at the same absolute intensity before and after training. Thus, the reduced rates of MPS in trained individuals could be expected as the stimulus would be relatively lower in the trained state due to the training-induced increase in muscle strength. In the present study, we compared MPS in T and UT muscle in the same individual following a bout of resistance exercise as the same relative intensity. We observed a greater immediate increase in MPS after exercise in the T compared with the UT leg (T relative intensity. We observed a greater immediate increase in MPS in the immediate period after exercise as the same study, we compared MPS in T and UT muscle in the same training-induced increase in muscle strength. In the present study, as there are considerable differences in the training status of the participants and the study designs employed (i.e., cross-sectional vs. longitudinal). Indeed, Chesley et al. (7) and MacDougall et al. (13) utilized different groups of trained individuals for each time point studied, while Phillips et al. studied the same subjects at each time in a longitudinal design. Moreover, Chesley et al. (7) and MacDougall et al. (13) studied subjects in the fed state while the participants in the study by Phillips et al. (18) were fasted. To our knowledge, the present study is the first study to longitudinally examine the time course of changes in MPS in the fed state following an acute bout of resistance exercise after training. We found an increase in mixed MPS in the immediate period after exercise (4 h) in both the T and UT legs by 162% and 108%, respectively. However, while MPS remained elevated by 70% at 28 h postexercise in the UT leg, rates of MPS had returned to resting levels in the T leg. Thus, our data suggests that in the T state the response of MPS to the same relative intensity of resistance exercise is accelerated such that it reaches a greater peak initially but returns to baseline more rapidly compared with the UT state.

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Indeed, as an estimate of the aggregate synthetic response following isolated resistance exercise, the area under the curve for the increase in MPS over 28 h is lower in the T vs. UT leg despite the greater initial rise in MPS in the T leg (Fig. 6). It is worth noting that our previous measures of MPS after training were made in the fasted state and likely result in an underestimation of the net MPS over 28 h after exercise. Nonetheless,
we would propose that the change in MPS at 16 h, were the measures made in the fed state would be altered in magnitude but would still demonstrate that both UT and T legs, which showed a relative stimulation over basal of 172 and 28% respectively, respond similarly to nutrition. Thus, our data suggest that resistance training may increase the sensitivity of MPS, expressed as a more rapid rise in MPS, but on balance reduces the overall response of MPS to an acute bout of resistance exercise. This is consistent with the notion that the exercise stimulus becomes progressively less novel with training. Consequently, there is an attenuation of the perturbation from homeostasis induced by resistance exercise, minimizing the anabolic effect of training over time (1, 12). Therefore, the reduced protein synthetic response observed in the T leg over the 28-h period postexercise is consistent with a previously suggested reduction in protein turnover after exercise in the trained state (12, 17, 19). We are not suggesting, however, that the subjects in the present study had reached a peak in terms of the response of MPS with training. In practice, those attempting to gain lean muscle mass would manipulate a variety of variables including relative load, exercise mode, rest interval, and feeding patterns in an attempt to prevent the eventual plateau in gains of strength and mass that invariably accompanies long-term strength training (23).

The greater amplitude of the protein synthetic response we observed in the T leg may be relevant to the timing of nutrient provision when performing resistance exercise. It is known that amino acid availability is a key regulator of protein synthesis (4, 22). Moreover, the provision of amino acids in the immediate postexercise period is important for maximizing protein synthesis and, ultimately, muscle mass accrual (8, 11, 28). We recently reported that failure to consume protein 2 h after resistance exercise resulted in lower lean mass gains over 12 wk of training in young men (11). Furthermore, one study previously found that resistance training-induced hypertrophy was completely suppressed in older individuals when nutrient provision was delayed for 2 h after exercise over a 12-wk training study (9). Further, Andersen et al. (2) only reported hypertrophy in young men who resistance trained for 12 wk who consumed protein postexercise, whereas those who consumed only carbohydrate did not show any hypertrophy. These data (2, 8, 11, 28) suggest, therefore, that it is important for individuals to consume protein in the immediate postexercise period to maximize protein accretion during training.

We report here that 8 wk of progressive unilateral leg training reduces the mixed muscle protein synthetic response over 28 h to an acute bout of resistance exercise performed at the same relative intensity before and after training. Despite the reduced anabolic response, MPS was higher initially in the T leg (4 h postexercise) but returned to baseline by 28 h postexercise at which time rates of MPS in the UT leg remained elevated. We conclude, therefore, that resistance training alters the time course of the increase in mixed MPS in the fed state.

Perspectives and Significance

As the protein synthetic response becomes attenuated with training, our results suggest that it likely becomes increasingly important for individuals to consume a source of amino acids in the immediate postexercise period during training to maximize MPS and thus protein accretion. While these results may also suggest that the frequency or intensity of lifts being performed during training sessions needs to be increased as individuals progress through their training, consideration must be made for adequate recovery time between training sessions and the risk of overtraining. Finally, additional research is required to determine the mechanisms that underlie the training-induced changes in the protein synthetic response to exercise.

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GRANTS

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