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# Response of muscle protein turnover to insulin after acute exercise and training

Teresa A. DAVIS* and Irene E. KARL
Department of Medicine, Washington University School of Medicine, St. Louis, MO 63110, U.S.A.

To determine whether the enhanced insulin-sensitivity of glucose metabolism in muscle after acute exercise also extends to protein metabolism, untrained and exercise-trained rats were subjected to an acute bout of exercise, and the responses of protein synthesis and degradation to insulin were measured in epitrochlearis muscles *in vitro*. Acute exercise of both untrained and trained rats decreased protein synthesis in muscle in the absence or presence of insulin, but protein degradation was not altered. Exercise training alone had no effect on protein synthesis or degradation in muscle in the absence or presence of insulin. Acute exercise or training alone enhanced the sensitivities of both protein synthesis and degradation to insulin, but the enhanced insulin-sensitivities from training alone were not additive to those after acute exercise. These results indicate that: (1) a decrease in protein synthesis is the primary change in muscle protein turnover after acute exercise and is not altered by prior exercise training, and (2) the enhanced insulin-sensitivities of metabolism of both glucose and protein after either acute exercise or training suggest post-binding receptor events.

## INTRODUCTION

The recent surge of interest in the effect of exercise on muscle protein turnover has produced no clear conclusions on the subject. Widely varying results of the effect of exercise on the excretion of $N^{\tau}$-methylhistidine, an amino acid of myofibrillar protein, have been reported (Calles-Escandon *et al.*, 1984; Dohm *et al.*, 1985; Rennie *et al.*, 1981). Furthermore, changes in renal blood flow during exercise (Castenfors, 1977), problems in excretion data monitoring, changes in protein turnover during different phases of exercise and recovery, and the contribution of non-muscle sources of $N^{\tau}$-methylhistidine (Rennie & Millward, 1983), render these data difficult to interpret. Isotopic measurements of whole-body protein turnover have suggested that exercise either increases (Rennie *et al.*, 1981; Wolfe *et al.*, 1982) or does not change (Wolfe *et al.*, 1984) protein degradation, but these methods have been questioned (Wolfe *et al.*, 1984), and may not reflect changes in muscle protein degradation (Rennie & Millward, 1983). In perfused hindquarter, the incorporation of [$^{14}$C]tyrosine into protein was reported to decrease, and tyrosine release to increase, after an acute bout of exercise (Dohm *et al.*, 1980). However, the interpretation of these results is complicated by a prolonged recovery period, the possible contribution of hormonal, vascular and neurogenic factors, as well as non-muscle tissue, to the observed response, and the failure to determine the actual rate of protein degradation. More recently, decreases in both [$^{14}$C]phenylalanine incorporation into protein and the release of $N^{\tau}$-methylhistidine after 10 min of maximal isometric contraction in perfused hindquarters were linked to alterations in energy state (Bylund-Fellenius *et al.*, 1984).

Exercise training has been reported to have no effect on protein synthesis or degradation in perfused hindquarter (Tapscott *et al.*, 1982) or isolated muscle (Davis *et al.*, 1985) from animals rested for 24 h before study. Whether prior exercise training alters the changes in muscle protein turnover after an acute bout of exercise has not been studied.

Insulin is a well-known regulator of both protein and glucose metabolism (Fulks *et al.*, 1975). We have shown previously that the basal rates, insulin-sensitivities and insulin-responsiveness of glucose uptake and glycogen synthesis in muscle are enhanced after an acute bout of exercise (Davis *et al.*, 1986). An increase in insulin-stimulated amino acid transport in perfused hindquarter has been reported; insulin-sensitivity was not determined (Zorzano *et al.*, 1985).

The purposes of the present study were: (1) to examine the basal rates of protein synthesis and degradation simultaneously in muscle after acute exercise; (2) to determine whether the enhanced insulin-sensitivity of glucose metabolism in muscle after an acute bout of exercise also extends to protein synthesis and degradation; and (3) to determine how exercise training affects these responses.

## METHODS

### Animals

Female Sprague–Dawley rats weighing 80–100 g were either exercise-trained by swimming, as previously described (Davis *et al.*, 1985), or remained sedentary. Rats swam initially for 15 min, and the duration of swimming was gradually increased during the 4-week training programme to 2 h daily, 5 days per week. Prior studies by our laboratories (Davis *et al.*, 1985) have shown that this swimming programme is effective in increasing muscle citrate synthase activity, a commonly used index of exercise training (Gollnick *et al.*, 1973). Final body weights were similar in trained ($191 \pm 4$ g) and untrained rats ($190 \pm 2$ g), since exercising female rats,

* To whom reprint requests should be addressed.

but not male rats, increase their food intake to compensate for the energy expenditure of exercise (Oscai *et al.*, 1974).

After 4 weeks of treatment, half of both the exercise-trained and untrained rats were exercised acutely by swimming for 2 h (TA and UA respectively), and decapitated immediately. Trained rats not subjected to an acute bout of exercise (TR) were studied 23–25 h after their last exercise bout, and untrained rested rats (UR) were inactive throughout the treatment period. All rats were killed on the same day between 10:00 and 12:00 h and had been deprived of food 3–4 h earlier. Trunk blood was collected and epitrochlearis muscles were removed rapidly, incubated within 2 min after the cessation of exercise, or quickly frozen in Freon, cooled in liquid $N_2$ (Davis *et al.*, 1985).

### Metabolic studies

Epitrochlearis muscles were incubated in Krebs–Ringer bicarbonate buffer, pH 7.4, containing 5 mM-glucose, 5 mM-Hepes buffer and 0.3% purified bovine serum albumin (Sigma, St. Louis, MO, U.S.A.). Purified glucagon-free pig insulin (gift from Dr. Ronald Chance, of Eli Lilly, Indianapolis, IN, U.S.A.) was added to the media in concentrations ranging from 0 to 100 munits/ml. Where indicated, 0.05 $\mu$Ci of [U-$^{14}$C]-phenylalanine (New England Nuclear, Boston, MA, U.S.A.)/ml and 0.5 mM-phenylalanine were added to the incubation medium. The muscles were incubated in a metabolic shaker at 37 °C and gassed continuously with $O_2/CO_2$ (19:1). After 1 or 3 h of incubation, muscles were removed from the media, blotted, and quickly frozen. Media and muscles were stored at −80 °C until assays were performed.

Previous studies have shown that the intracellular, extracellular and aminoacyl-tRNA specific radioactivities are similar when high concentrations of the unlabelled amino acid are present in the media (Bylund-Fellenius *et al.*, 1984; Davis *et al.*, 1985; McKee *et al.*, 1978). However, a lack of equilibration between the extracellular and the tRNA specific radioactivity has also been reported (Stirewalt & Low, 1983). Furthermore, the intracellular/extracellular specific-radioactivity ratio did not change during 30 min to 3 h of incubation, and was unaffected by insulin or exercise (Davis *et al.*, 1985). Thus protein synthesis could be calculated from the [$^{14}$C]phenylalanine radioactivity in the trichloroacetic acid-precipitable protein and the extracellular specific radioactivity (Fulks *et al.*, 1975). Tyrosine release and its intracellular concentration were determined by using a tRNA method as previously described (Harter *et al.*, 1979). Since both tyrosine and phenylalanine are not synthesized or catabolized by muscle (Goldberg & Chang, 1978), the rate of release of tyrosine from each muscle, plus any change in the intracellular tyrosine concentration (final minus initial concentration), were measured to determine the actual rate of net protein degradation (Fulks *et al.*, 1975). Absolute rates of total protein degradation were calculated as the sum of net protein degradation and protein synthesis in each muscle. Prior studies from this laboratory have shown that the release of phenylalanine and tyrosine from epitrochlearis muscle is comparable (Davis *et al.*, 1985). Intracellular concentrations of ATP and phosphocreatine were determined fluorimetrically as described previously (Garber *et al.*, 1976).

**Table 1. Protein turnover in 1 h-incubated muscles from untrained and exercise-trained rats after an acute bout of exercise**

Values (nmol/h per g) are means±S.E.M. Rats: UR, untrained rested; UA, untrained acutely exercised; TR, trained rested; TA, trained acutely exercised. Values differed significantly ($P < 0.05$) for: *UA versus UR; †TA versus TR.

| Group | Synthesis | Net degradation | Total degradation |
|---|---|---|---|
| UR ($n = 18$) | 52.0±3.6 | 136.2±4.8 | 188.4±13.1 |
| UA ($n = 18$) | 37.8±2.6* | 165.6±6.5* | 203.4±12.0 |
| TR ($n = 14$) | 54.5±3.2 | 133.8±8.4 | 188.4±11.4 |
| TA ($n = 15$) | 36.7±2.1† | 154.9±6.2† | 191.4±12.6 |

Data are expressed on the basis of wet weight, since water and protein content did not differ between groups (Davis *et al.*, 1986). Basal rate was defined as the rate in the absence of insulin. Insulin-responsiveness ($\Delta$) was calculated as the difference between the maximal response to insulin and the basal rate (Garvey *et al.*, 1986). Insulin-sensitivity was estimated as the concentration of insulin needed to produce half-maximal stimulation ($K_d$). The percentage of maximal insulin effect was calculated as the difference between the absolute and the basal rate, divided by the maximal response to insulin.

### Statistics

Analysis of variance was used to determine differences among treatment groups at each dose of insulin as well as the differences within treatment groups for the effect of insulin (Snedecor & Cochran, 1967). Probability levels of less than 0.05 were considered statistically significant, and therefore are not reported in the text. Standard errors were not included in the Figures for the sake of clarity, but statistical analyses are included in the Figure legends. All standard errors were less than 7% of the mean. The number of muscles in each treatment group at each concentration of insulin was 6 to 18.

## RESULTS

To determine the response of muscle protein turnover *in vitro* immediately after an acute bout of exercise *in vivo*, muscles were incubated for 1 h. Protein synthesis was significantly decreased after an acute bout of exercise in both untrained (UA versus UR) and trained (TA versus TR) rats (Table 1). Net protein degradation (tyrosine release from muscles corrected for changes in the intracellular concentration of tyrosine) was significantly greater after acute exercise in muscles from both untrained and trained rats compared with their rested controls. Although net protein degradation was increased after acute exercise, total protein degradation was not significantly elevated after exercise, owing to the decrease in protein synthesis.

To determine the insulin-sensitivity and -responsiveness of muscle protein turnover immediately after an acute bout of exercise and/or training, insulin dose–responses of protein synthesis and degradation in muscle were determined. In muscles incubated for 1 h from all

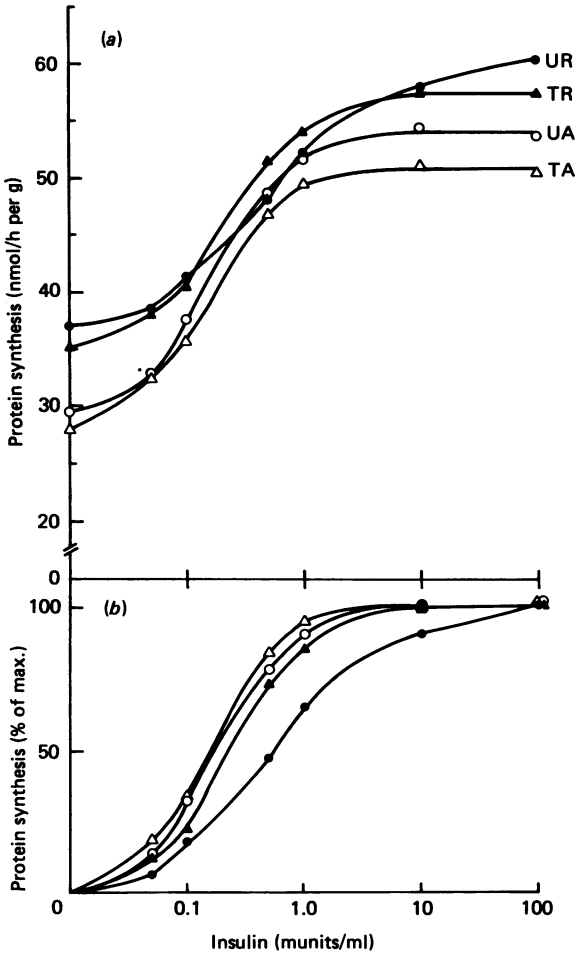


**Fig. 1. Basal and insulin-stimulated rates of protein synthesis in 3 h-incubated muscles from untrained and exercise-trained rats after an acute bout of exercise**

Data are presented as absolute rates (*a*) and as percentages of the maximal insulin effect (*b*). Symbols and abbreviations: ●, UR, untrained rested; ○, UA, untrained acutely exercised; ▲, TR, exercise-trained rested; △, TA, exercise-trained acutely exercised. Basal rates of protein synthesis were decreased in UA and TA compared with UR and TR, respectively ($P < 0.05$). Protein synthesis was increased by concentrations of insulin of 0.5 munits/ml and greater in all groups ($P < 0.05$). Insulin-responsiveness (nmol/min per g) was 23.5 in UR, 24.6 in UA, 22.2 in TR and 22.8 in TA. The half-maximally effective insulin doses (munits/ml) were 0.55 in UR, 0.15 in UA, 0.20 in TR and 0.15 in TA.

treatment groups, protein degradation was not significantly decreased by 100 munits of insulin/ml or less. Likewise, protein synthesis was not significantly increased by 100 munits of insulin/ml or less during the 1 h incubation period in muscles from rested animals (UR and TR). However, protein synthesis was significantly increased by 1.0 munit of insulin/ml or more in muscles incubated for 1 h from rats that had been acutely exercised (UA and TA). The estimated half-maximal responses to insulin during this period also suggest an increase in the insulin-sensitivity of protein turnover (results not shown), but this could not be determined clearly, owing to the insignificant effect of insulin.

Previous studies have shown that more than 1 h is required for the effect of insulin on protein turnover in muscle *in vitro* from rested animals (Jefferson *et al.*, 1976; Stirewalt & Low, 1983). Therefore muscles were incubated for 3 h, although this incubation period was more distal to the time of exercise than the 1 h incubation period. Basal rates (i.e. absence of insulin) of protein synthesis were significantly lower in 3 h-incubated muscles from acutely exercised compared with rested animals, and training had no effect (Fig. 1*a*).

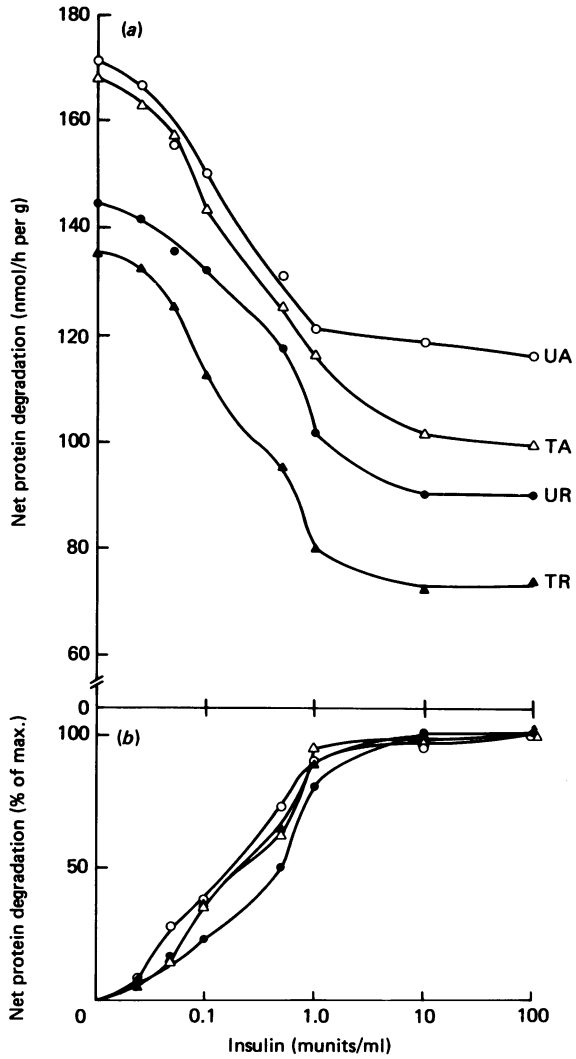


**Fig. 2. Dose–response of net protein degradation to insulin in muscles, from untrained and exercise-trained rats, incubated for 3 h, after acute exercise**

Data are presented as absolute rates (*a*) and as percentages of the maximal insulin effect (*b*). Symbols and abbreviations: ●, UR, untrained rested; ○, UA, untrained acutely exercised; ▲, TR, exercise-trained rested; △, TA, exercise-trained acutely exercised. Net degradation was increased in UA and TA compared with UR and TR, respectively ($P < 0.05$). Insulin decreased net degradation at 0.5 munits/ml and greater in UR, and at 0.1 munits/ml and greater in UA, TR and TA ($P < 0.05$). Insulin-responsiveness (nmol/min per g) was 54.6 in UR, 55.2 in UA, 62.7 in TR and 69.0 in TA. The half-maximally effective insulin doses (munits/ml) were 0.5 in UR and 0.20 in UA, TR and TA.

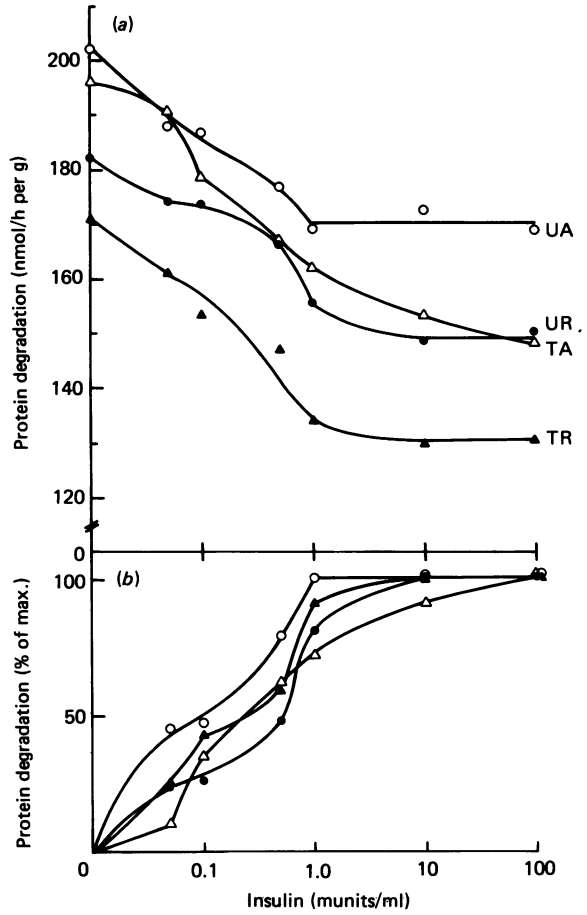


**Fig. 3. Dose–response of total protein degradation to insulin in 3 h-incubated muscles from untrained and trained rats after an acute bout of exercise**

Data are presented as absolute rates (*a*) and as percentages of the maximal insulin effect (*b*). Symbols and abbreviations: ●, UR, untrained rested; ○, UA, untrained acutely exercised; ▲, TR, exercise-trained rested; △, TA, exercise-trained acutely exercised. Protein degradation was decreased by concentrations of insulin of 1 munit/ml and greater in UR, and of 0.5 munit/ml and greater in UA, TR and TA ($P < 0.05$). Insulin-responsiveness (nmol/min per g) was 32.7 in UR, 32.0 in UA, 40.8 in TR and 47.4 in TA. The half-maximally effective insulin doses (munits/ml) were 0.55 in UR, 0.10 in UA, 0.25 in TR and 0.25 in TA.

These results are in agreement with those from muscles incubated for 1 h (Table 1). In 3 h-incubated muscles, insulin increased the rate of protein synthesis at concentrations of 0.5 munits/ml and greater in all groups (Fig. 1*a*). Insulin-responsiveness (maximal minus basal rate) did not differ between groups (in nmol/h per g, UR = 23.5, UA = 24.6, TR = 22.2, TA = 22.8). To illustrate the difference in insulin-sensitivity between groups, data were plotted as a percentage of the maximum insulin-stimulated rate (Fig. 1*b*). The half-maximally effective insulin doses ($K_d$) were less in acutely exercised rats as well as in trained rested animals (in munits/ml, UR = 0.55, UA = 0.15, TR = 0.20, TA = 0.15), indicating an increase in insulin-sensitivity after acute exercise as well as training. Acute exercise in trained animals did not enhance further the insulin-sensitivity of protein synthesis during this period above that observed with training alone or that in acutely exercised untrained animals.

Basal rates of net protein degradation in muscles incubated for 3 h (Fig. 2*a*), as in those incubated for 1 h (Table 1), were significantly increased after acute exercise in both untrained and trained animals compared with their rested controls. Net degradation was decreased by 0.5 munits of insulin/ml and greater concentrations in untrained rested animals and by 0.1 munits/ml in all other groups (Fig. 2*a*). Insulin-responsiveness was slightly increased by training (in nmol/h per g, UR = 54.6, UA = 55.2, TR = 62.7, TA = 69.0). The half-maximally effective insulin dose was shifted from 0.5 munits/ml in untrained rested animals to 0.2 munits/ml in all other groups (Fig. 2*b*), indicating an increase in insulin-sensitivity after acute exercise as well as training.

Basal rates of total protein degradation in muscles incubated for 3 h were not significantly altered after acute exercise or training (Fig. 3*a*), as was observed in muscles incubated for 1 h (Table 1). The decrease in degradation with insulin was significant at 1 munit of insulin/ml and greater in untrained rested animals and at 0.5 munit/ml and greater concentrations of insulin in all other groups (Fig. 3*a*). The increased sensitivities to insulin after acute exercise as well as exercise training were also reflected in the decreased $K_d$ values in these groups, but the effects were not additive (in munits/ml, UR = 0.55, UA = 0.10, TR = 0.25, TA = 0.25; Fig. 3*b*). A slightly greater responsiveness to insulin was observed in trained animals (in nmol/h per g, UR = 32.7, UA = 32.0, TR = 40.8, TA = 47.4).

The concentrations of ATP and phosphocreatine in muscles from acutely exercised rats were significantly lower at the cessation of exercise than in those from rested animals (Table 2). At both 1 and 3 h after exercise, ATP and phosphocreatine concentrations had returned to that of rested animals. Exercise training had no effect on ATP or phosphocreatine concentrations. Muscle weights were similar in all groups (UR = 29.6 ± 0.88 mg; UA = 32.5 ± 1.60 mg; TR = 30.2 ± 2.01 mg; TA = 32.2 ± 0.98 mg).

## DISCUSSION

### Effects of acute exercise

The effects of exercise on basal rates of protein synthesis and protein degradation have been studied previously (Bylund-Fellenius *et al.*, 1984; Calles-Escandon *et al.*, 1984; Dohm *et al.*, 1980, 1985; Rennie *et al.*, 1981; Wolfe *et al.*, 1982, 1984), but the results are conflicting, perhaps owing to differences in the intensity and duration of exercise, time points studied, and the methodology used. The present study is unique in that: (1) it documents the changes in protein synthesis and degradation simultaneously in a single muscle composed of primarily one fibre type immediately after an acute bout of exercise; (2) it is the first to determine the changes in insulin-sensitivities and -responsiveness of muscle protein synthesis and degradation after an acute bout of exercise; and (3) it examines how exercise training affects these responses. Our results suggest that a decrease in protein synthesis is the primary change in muscle protein turnover after an acute bout of exercise, and that this is unaffected by prior exercise training. The sensitivities of muscle protein synthesis and degradation

**Table 2. ATP and phosphocreatine contents in isolated muscles from untrained and exercise-trained rats after an acute bout of exercise**

Values are means ± S.E.M. with numbers of determinations in parentheses. Rats: UR, untrained rested; UA, untrained acutely exercised; TR, trained rested; TA, trained acutely exercised. Values differed significantly ($P < 0.05$) for: *UA versus UR; †TA versus TR.

| | | | Content (μmol/g) | | |
|---|---|---|---|---|---|
| | Group | Time of incubation . . . | 0 | 1 h | 3 h |
| ATP | UR | | 6.04 ± 0.24 (11) | 5.68 ± 0.27 (22) | 6.19 ± 0.31 (12) |
| | UA | | 4.87 ± 0.20 (20)* | 5.44 ± 0.28 (23) | 5.88 ± 0.39 (16) |
| | TR | | 6.01 ± 0.28 (6) | 6.16 ± 0.35 (28) | 6.51 ± 0.33 (14) |
| | TA | | 5.03 ± 0.26 (11)† | 5.64 ± 0.33 (29) | 5.86 ± 0.31 (18) |
| Phosphocreatine | UR | | 20.7 ± 1.33 (11) | 22.6 ± 1.49 (22) | 20.3 ± 1.30 (12) |
| | UA | | 12.6 ± 0.82 (16)* | 18.3 ± 1.13 (23) | 19.0 ± 1.09 (16) |
| | TR | | 24.1 ± 1.46 (5) | 21.8 ± 1.33 (28) | 19.0 ± 1.16 (14) |
| | TA | | 15.0 ± 1.02 (11)† | 20.9 ± 1.25 (29) | 17.6 ± 1.12 (18) |

to insulin were increased after either an acute bout of exercise or training, but the effects of acute exercise and training on insulin-sensitivities were not additive.

Results of the present study and that of other investigators (Bylund-Fellenius *et al.*, 1984) suggest that the decrease in protein synthesis after an acute bout of exercise may have been due to a change in energy state, as indicated by the decreases in phosphocreatine and ATP. However, other nucleotides, initiation factors, and hormones which regulate protein synthesis (Walton & Gill, 1976; Fulks *et al.*, 1975; Preedy & Garlick, 1985; Simmons *et al.*, 1984), may also be altered after exercise. For example, insulin stimulates protein synthesis and inhibits protein degradation in muscle (Fulks *et al.*, 1975). Since plasma insulin is decreased after 2 h of swimming (Davis *et al.*, 1986), the decrease in the basal rate of protein synthesis and the slight increase in degradation *in vitro* after acute exercise may be due to a persistent effect of the decrease in insulin *in vivo*. However, glucocorticoids, glucagon, $Ca^{2+}$ and prostaglandins decrease protein synthesis and/or increase protein degradation in muscle (Simmons *et al.*, 1984; Preedy & Garlick, 1985; Rodemann *et al.*, 1982), and the first three are increased by exercise (Galbo *et al.*, 1977; Vora *et al.*, 1983). Thus the mechanism for the change in protein turnover after exercise is unclear and requires further investigation.

The decrease in protein synthesis after exercise is indicative of a protein catabolic state which after repeated exercise sessions should result in a loss in muscle mass. However, muscle weight and protein content of animals subjected to 4 weeks of exercise were comparable with those of untrained controls (Davis *et al.*, 1985). Thus this decrease in synthesis must be balanced by a decrease in protein degradation or an increase in protein synthesis at some other period after exercise, or possibly during exercise. Interestingly, the basal rates of both protein synthesis and degradation during the second and third hours of incubation, calculated from the difference in total synthesis or degradation (nmol/g) between 3 h and 1 h of incubation, divided by 2, did not differ between acutely exercised and rested animals. This suggests that the protein catabolic state induced by exercise is brief. The significance of the changes in protein metabolism after exercise is open to conjecture, but may be of importance in the regeneration of glycogen stores, as previously suggested (Davis *et al.*, 1986).

Insulin-stimulated glucose metabolism in muscle has been widely studied after an acute bout of exercise (Davis *et al.*, 1986; Garetto *et al.*, 1984; Richter *et al.*, 1982), but the response of muscle protein turnover to insulin after acute exercise has not been investigated previously. Results of the present study suggest that the enhanced insulin-sensitivities of glucose uptake and glycogen synthesis in muscle after an acute bout of exercise (Davis *et al.*, 1986) also extend to muscle protein synthesis and degradation. An increase in insulin-stimulated amino acid transport in muscle after exercise has been reported (Zorzano *et al.*, 1985); insulin-sensitivity, however, was not determined. Thus at least five insulin-regulated pathways have been reported to be affected by acute exercise. Changes in insulin-sensitivity are considered indicative of alterations in insulin binding, and should be similar in all metabolic pathways (Kahn, 1985). The increases in the insulin-sensitivities of both glucose and protein metabolism after exercise may be an 'up-regulation' of the insulin receptor, owing to the decrease in insulin *in vivo*, although this has been disputed (Webster *et al.*, 1986). Increases in insulin binding to monocytes and erythrocytes have been reported in acutely exercised subjects (Koivisto *et al.*, 1980; Pedersen *et al.*, 1980), and both an increase (Webster *et al.*, 1986) and no change (Bonen *et al.*, 1984; Zorzano *et al.*, 1985) in insulin binding were reported recently in muscles from exercised animals; therefore the effect of exercise on insulin binding in muscle remains open to question. Decreases in insulin-sensitivity with no change in insulin binding have been reported in muscle after denervation (Burant *et al.*, 1984; Smith & Lawrence, 1985), and were suggested to be due to alterations in signal transmission by the occupied insulin receptor (Burant *et al.*, 1984). It is tempting to speculate that, after an acute bout of exercise, insulin's action in muscle is enhanced at a site just distal to the binding of insulin to its receptor, owing to alterations in receptor kinase or phosphatase activity, generation of insulin mediator(s), and/or intracellular $Ca^{2+}$ concentration (Kahn, 1985; McDonald & Pershadsingh, 1985).

Although physiological concentrations of insulin had no statistically significant effect on protein synthesis or degradation in muscle *in vitro*, insulin is physiologically

important to protein turnover *in vivo*. Lower concentrations of insulin are required *in vivo* than *in vitro* for the stimulation of protein synthesis and decrease in protein degradation in muscle (Garlick *et al.*, 1983), perhaps owing to the absence of other modulators of muscle protein metabolism from the incubation medium. Insulin may act *in vivo* synergistically with nutrients and antagonistically with counter-regulatory hormones, to stimulate protein synthesis and to decrease protein degradation (Garlick *et al.*, 1983). The increase in the insulin-sensitivity of glucose metabolism in muscle *in vitro* after acute exercise occurred at physiological (0.025–0.05 munits/ml) insulin concentrations (Davis *et al.*, 1986), and thus it seems probable that the increase in the insulin-sensitivity of protein metabolism *in vitro*, albeit at supraphysiological insulin concentrations, is of importance *in vivo*. Whether the requirement of protein metabolism for high concentrations of insulin *in vitro* is related to the somewhat lower rate of synthesis and high rate of degradation *in vitro* than *in vivo* (Preedy *et al.*, 1986), and whether the changes in the basal rate and insulin-sensitivity of protein metabolism over time are related, are not at present known. Nonetheless, the isolated muscle preparation, particularly that of the epitrochlearis muscle, which is very thin and therefore extremely viable, is useful for metabolic study, since it eliminates the influence of non-muscle tissues, innervation, hormones, and other humoral factors, particularly during prolonged incubation (Harter *et al.*, 1984).

### Effects of exercise training

Exercise training had no effect on basal rates of protein synthesis and degradation in muscle, as previously demonstrated (Davis *et al.*, 1985). Training did increase the insulin-sensitivities of both protein synthesis and degradation, and the insulin-responsiveness of protein degradation but not of protein synthesis. Increases in the insulin-responsiveness and sensitivities of glucose uptake and glycolytic utilization via glycolysis were observed previously in muscles from trained animals (Davis *et al.*, 1986). Thus these results suggest that exercise training does not alter basal rates of protein turnover in muscle, but enhances insulin's action on muscle. Increases in the responses of protein and glucose metabolism to insulin by exercise training may be due to alterations at or just distal to the insulin-binding site, as well as changes in specific intracellular pathways.

### Effects of exercise training on acute exercise

Prior exercise training had little effect on the response of muscle protein synthesis or degradation after acute exercise. Although the enhanced insulin-sensitivities after either acute exercise or exercise training alone were additive for glucose metabolism (Davis *et al.*, 1986), this was not observed for protein metabolism. Thus the enhanced insulin responses of glucose and protein metabolism to either treatment may be due to enhancement in the transmission of the signal(s) from the occupied insulin receptor, but not by precisely the same mechanism.

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