Resistance exercise maintains skeletal muscle protein synthesis during bed rest

ARY A. FERRANDO, KEVIN D. TIPTON, MARCAS M. BAMMAN, AND ROBERT R. WOLFE

Section of that study, and served as the control group for this intervention. These data (12) have been included in the present study because the conditions of the bed rest and dietary protocols were identical, except that one group performed scheduled resistance exercise (BREx), whereas the other adhered to strict bed rest (BR). The BR group was not strength tested or exercised before the isotope-infusion studies. After written consent was obtained, each subject was admitted to the General Clinical Research Center (GCRC) at the University of Texas Medical Branch at Galveston. This study protocol was reviewed and approved by the institutional review boards at the University of Texas Medical Branch and National Aeronautics and Space Administration, Johnson Space Center.

This study involved a 15-day stay at the GCRC. The first day served as the pre-bed rest (BR) measure of MPS. This was followed by 14 days of strict 6° head-down bed rest. A second determination of MPS was made on bed rest day 14 (BR 14). The head-down tilt was utilized to simulate the effects of microgravity on initial fluid volume shifts (15) for unrelated studies. Subjects were not permitted to deviate from this position and were monitored continuously by the GCRC staff.

Subjects were given a mixed diet on the basis of the Harris-Benedict equation designed to maintain body weight throughout the study. The caloric distribution was 14% protein, 27% fat, and 59% carbohydrate. All subjects consumed =1.1 g protein · kg body wt· day⁻¹.

Resistance training. The knee extensors were exercised isotonically every other day during bed rest from the supine position by utilizing a horizontal leg-training device (Cybex Strength Systems, Ronkonkoma, NY). Resistance exercise subjects were first familiarized with the training protocol 1 day before bed rest. After learning the proper exercise form, subjects practiced by completing 3 sets of 10-12 repetitions. To preclude the likelihood of studying the effects of acute resistance exercise on MPS (7), the final training session (BR 13) again consisted of 3 sets of 10-12 repetitions.

During bed rest, muscle soreness was minimized in these untrained subjects by progressively increasing volume and intensity during the first three sessions. By session 3, five sets to volitional muscle failure were completed. The number of repetitions for all sets was set at 8 (range 7-9) throughout training. If a set was performed outside this range, the load of subsequent sets was adjusted accordingly. Progressive resistance was therefore incorporated into the program. Exercise was performed at a volume and intensity known to effectively induce gains in strength and muscle mass (1, 18). Rest between sets was set at 90 s to permit restoration of creatine phosphate (27). Loads for warm-ups were set at two-thirds of the previous training session’s eight repetition maximum (RM). All training was supervised by one of the investigators.

Pre- and post-bed rest strength were measured (BREx group only) by 1 RM on the same training device. Pre- and post-bed rest strength were also measured in a separate control group of a similarly designed but unrelated study by one of the investigators (3). Identical equipment and strength-testing procedures were utilized, and the comparison of
strength variables with the current BREx group are presented in Discussion. After sufficient warm-up, sets of 1 RM were executed with increasing resistance until a subject failed on two consecutive attempts at a given load. The greatest load lifted successfully was then recorded as 1 RM. Trials were separated by 2–3 min. The range of motion of each movement was standardized for each subject and repeated post-bed rest. Each determination of 1 RM was performed after the infusion protocol described below.

Skeletal MPS. We examined the effects of bed rest and bed rest plus resistance exercise on MPS. On days BR – 1 and BR 14 after a 12-h fast, a catheter was inserted into an antecubital vein for stable isotope infusion. Subjects received a 5-h period, respectively, EM represents the average intracellular Phe tracer at the start (2 h) and end (5 h) of the sampling period. The factors 60 and 100 are required to express the yield a ratio of 0.0067 if measured by isotope ratio mass spectrometry. Only six out of the nine carbons in the Phe tracer are enriched, so a tracer/tracee ratio of 0.01 was considered statistically significant.

RESULTS

Bed rest resulted in a 46% decrease in MPS in the BR group (0.074 ± 0.011 to 0.040 ± 0.007%/h; P < 0.04). However, resistance exercise maintained MPS in the BREx group (0.066 ± 0.011 to 0.094 ± 0.026%/h; P = 0.20) (Fig. 1). The demonstrated change in MPS from the beginning to the end of bed rest was significantly different between groups (P < 0.04). The BR group experienced a mean decrease of 0.034 ± 0.015%/h, whereas MPS in the BREx group demonstrated a nonsignificant increase of 0.028 ± 0.019%/h. 1-RM strength was maintained in the BREx group (208.3 ± 14.7 kg pre-bed rest vs. 214.2 ± 12.3 kg post-bed rest, respectively; P = 0.65).

DISCUSSION

Acute bouts of resistance training have been shown to double protein synthesis up to 24 h postexercise (7, 21). Because the subjects in this study engaged in resistance training every other day, the intent was to maintain a stimulation of MPS such that the noted decrease with inactivity could be prevented (12). The present study demonstrates the cumulative effects of...
repeated stimulation of MPS. In addition to the elimination of a decreased MPS, this exercise protocol maintained muscle strength.

Muscular unloading by inactivity or bed rest has been shown to decrease muscle strength (26). In particular, locomotor muscle strength is compromised with the continued unloading of bed rest (3, 26). In this respect, bed rest is a viable ground-based model for the perturbations of spaceflight (20). Weightlessness results in a more-pronounced loss of strength in the legs, particularly in the knee extensors (8). The ability to maintain strength and function in the locomotor muscle groups is of prime concern to the astronaut. Impaired muscle function is detrimental to the astronaut’s ability to perform shuttle landing, egress, and extravehicular activity with prolonged exposure to microgravity. Thus a countermeasure that is effective in ameliorating these losses would enhance the astronaut’s performance capability.

On the basis of the results of the present study and resistance training’s established influence on muscle strengthening (1) and MPS (6, 7, 21), it is tempting to speculate that a relationship exists between the chronic stimulation of skeletal MPS and muscular strength. This notion is supported by the results of previous studies analyzing the effects of inactivity or immobilization on MPS and strength. An identical research protocol as the present study (with bed rest only) demonstrated a decrease in 1-RM leg extensor strength (229.1 ± 7.4 kg pre-bed rest vs. 208.0 ± 8.2 kg post-bed rest, respectively; P < 0.01) (3). The present study provides evidence that the decrease in strength corresponds to a decreased fractional synthetic rate of protein synthesis. With muscular stimulation, however, the relationship between MPS and strength is maintained. In addition to the present findings, Gibson et al. (14) noted that the fractional synthetic rate of muscle protein and fiber cross-sectional area could be maintained in the casted (immobilized) leg by electrical stimulation. Electrical stimulation has also been shown to prevent reductions in leg volume, muscle compartment size, and muscle strength with bed rest (11).

These findings, however, do not establish a direct relationship between MPS and strength. Indeed, MPS is greatly increased immediately after resistance exercise (6), yet it cannot be suggested that strength would acutely increase. Rather, the relationship between MPS and muscular strength is most likely dependent on a net MPS balance over time. Circumstances resulting in hypermetabolism, such as burn injury, will produce elevated protein synthetic rates yet a net loss in skeletal muscle protein and strength (22). Resistance exercise alone provides a more favorable net muscle protein balance (6), which could be further enhanced by hyperinsulinemia and hyperaminoacidemia (4). The limited data involving spaceflight have shown an increase in whole body protein synthesis (24), yet spaceflight is known to result in a loss of lean body mass (20) and strength (8). Protein breakdown was not assessed in this study; however, previous work has demonstrated that the loss of lean body mass (12) and strength (3) during bed rest is a result of altered protein balance (12). Thus periodic stimulation of MPS with resistance exercise most likely results in a positive net protein balance over time that preserves muscle strength.

Most importantly, this study illustrates that scheduled periodic resistance exercise will prevent the decline in MPS and strength with inactivity. The results of the present study indicate that resistance training may be a viable countermeasure to the loss of muscle strength and mass with spaceflight (2). Endurance exercise is currently employed in space; however, it is unsuccessful in ameliorating reductions in muscle strength (17). Resistive devices are currently being developed but have yet to be flown as a countermeasure. This study suggests that repeated stimulation of MPS, or most likely the maintenance of net protein synthesis, may be integral to the maintenance of muscular strength.

The authors thank the National Aeronautics and Space Administration for its support and emphasis on this area of research and the nursing staff at the University of Texas Medical Branch General Clinical Research Center for their tireless efforts and meticulous care of subjects. This work was supported in part by National Aeronautics and Space Administration Grant NAS9–18492 and National Institutes of Health Grants M01-RR-00073 and DK–33952.

Address for reprint requests: A. A. Ferrando, Metabolism, Shriners Burns Institute, 815 Market St., Galveston, TX 77550. Received 13 September 1996; accepted in final form 1 November 1996.

REFERENCES