Lower limb skeletal muscle function after 6 wk of bed rest

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Berg, H. E., L. Larsson, and P. A. Tesch. Lower limb skeletal muscle function after 6 wk of bed rest. J. Appl. Physiol. 82(1): 182–188, 1997.—Force, electromyographic (EMG) activity, muscle mass, and fiber characteristics were studied in seven healthy men before and after 6 wk of bed rest. Maximum voluntary isometric and concentric knee extensor torque decreased (P < 0.05) uniformly across angular velocities by 25–30% after bed rest. Maximum quadriceps rectified EMG decreased by 19 ± 23%, whereas submaximum (100-Nm isometric action) EMG increased by 44 ± 28%. Knee extensor muscle cross-sectional area (CSA), assessed by using magnetic resonance imaging, decreased by 14 ± 4%. Maximum torque per knee extensor CSA decreased by 13 ± 9%. Vastus lateralis fiber CSA decreased 18 ± 14%. Neither type I, IIA, and IIB fiber percentages nor their relative proportions of myosin heavy chain (MHC) isoforms were altered after bed rest. Because the decline in strength could not be entirely accounted for by decreased muscle CSA, it is suggested that the strength loss is also due to factors resulting in decreased neural input to muscle and/or reduced specific tension of muscle, as evidenced by a decreased torque/EMG ratio. Additionally, it is concluded that muscle unloading in humans does not induce important changes in fiber type or MHC composition or in vivo muscle contractile properties.

The gravity-dependent load of the human body, acting on the lower limbs in the upright position, seems fundamental to maintenance of lower limb skeletal muscle function. Thus reduced weight-bearing activity per se, either on experimental cast immobilization (cf. Ref. 10), lower limb unloading (2, 3, 6, 11), bed rest (12, 18), or extended stay in weightlessness (33) results in substantial muscle dysfunction within a few weeks.

Muscle atrophy, resulting from loss of contractile proteins, is one well-recognized cause of such functional impairment but appears to explain only about two-thirds of the strength loss shown after 1 mo of bed rest (25) or unilateral lower limb unloading (3, 11). Among candidates to explain the disproportionate strength loss are decreased neural drive (cf. Ref. 27) and decreased force-generating capacity of muscle (6).

In an attempt to distinguish the potential factors that might be responsible for the observed muscle dysfunction and to quantify their relative importance for adaptation in response to long-term muscle unloading, volunteers subjected to 6 wk of bed rest were studied. Maximal voluntary knee-extension torque and velocity and electromyographic (EMG) activity during knee extension were assessed before and after bed rest. Knee extensor cross-sectional area (CSA) was assessed by using magnetic resonance imaging (MRI).

It has repeatedly been reported that unloaded animal muscle undergoes alterations in contractile properties such that there is an increase in maximum shortening velocity and a corresponding shift in the force-velocity relationship of slow-twitch muscle (cf. Ref. 17). These changes typically coincide with an increased fast-muscle ratio content or transformation from type I to type II fibers. Experimental support for extending these principles to humans is, however, poor (cf. Ref. 2). In fact, there are as yet no data available that describe in detail the effects of unloading on muscle function along with myosin and fiber type composition in humans.

Although muscle fiber type transformation may occur in response to hindlimb suspension in rats (cf. Ref. 30), potentially altering skeletal muscle force-velocity characteristics, human studies employing standard enzyme histochemistry have not disclosed such an adaptation (2, 4, 20, 21). Therefore, skeletal muscle fiber type and myosin heavy chain (MHC) isoforms were examined.

More specifically, the purpose of the study was to describe the magnitude and characteristics of the strength decline in response to bed rest while quantifying the concomitant changes in neural drive and muscle mass and morphology.

It was hypothesized that 6 wk of bed rest would result in a marked reduction in maximum voluntary isometric and dynamic force. We expected to disclose a significant muscle atrophy that would nevertheless not fully account for the strength loss and that, as a consequence, force per knee extensor muscle CSA would be decreased. It was also hypothesized that knee extensor fiber type and MHC composition of the vastus lateralis muscle would not be affected by bed rest and therefore that concomitant changes in force-velocity characteristics of the knee extensor muscle group would most likely not occur.

METHODS

General design. The study was conducted at a hospital ward (Purpan University Hospital, Toulouse, France). Volunteers were confined to this facility for 10 wk, including the 6-wk bed rest period. Weight-bearing physical exercise or other countermeasures were not allowed during bed rest. The study was approved by the Regional Ethics Committee of Région Midi-Pyrénées I (Toulouse) and organized by the Institute de Médecine et de Physiologie Spatiales (Toulouse) and Centre National d’Études Spatiales (France). It was cosponsored by the European Space Agency.

Subjects. Seven healthy men (ages 28 ± 2 yr, height 176 ± 3 cm, weight 74 ± 9 kg) who had given their written consent completed 42 days (6 wk) of head-down tilt (–6°) bed rest.
Muscle function. Knee extensor torque and EMG activity were measured by using equipment and procedures essentially as described elsewhere (3, 6). After two test sessions, maximal voluntary isometric and concentric knee extensor torque of the left limb were assessed the day before (Pre 3) bed rest by using the Cybex 6000 (Lumex, New York, NY) dynamometer. Subjects were thereafter retested on day 2 (Post) of resumed weight bearing. They were strapped to the horizontal dynamometer seat, with support for thigh, pelvis, and chest. The hip angle was 1.66 rad (95°; fully extended hip = 3.14 rad (180°)). The axis of rotation of the dynamometer was aligned to the knee joint axis. After individual adjustments, these fixed positions were maintained for seat, shin pad, and dynamometer axis positions during subsequent tests.

After surface EMG electrodes were affixed and calibration procedures were performed, the moment arm was positioned at knee angle 2.01 rad (115°; fully extended leg = 3.14 rad (180°)), and two submaximal isometric trials interspersed with 30 s of rest were performed. With the use of a visual feedback meter, the subject was asked to maintain a constant torque level, which corresponded to ∼30–50% of maximum, for 10 s. The submaximal fixed target level of 100 Nm corresponded to 34 ± 6% of maximal voluntary contraction (MVC) before unloading and 46 ± 6% after unloading. After 2 min of rest, two trials for MVC with 30 s of rest were performed, and if there was a torque difference of >5% between trials, a third trial was allowed. During isometric contraction, subjects maintained maximal torque effort for 4–6 s until a plateau was established.

After a 5-min rest and while the subject was still seated in the dynamometer chair, knee maximal angular velocity (AV max) during unrestrained knee extensions was assessed (6). A light plastic arm replaced the moment arm, the time elapsed through 2.09–2.62 rad (120–150°) knee angle was recorded, and average knee angular velocity was subsequently calculated. The peak value from five trials was used. The coefficient of variation (CV) for AV max across three test sessions before bed rest was 5.5%.

To describe the force-velocity characteristics of the knee extensor muscle group, dynamic torque capacity was then assessed by using the peak torque from concentric MVCs performed in the dynamometer. Torque at five different angular velocities was examined as described above, with 2 min of rest between velocities, in the following sequence: 0.52, 1.05, 1.57, 2.09, and 3.14 rad/s (30, 60, 90, 120 and 180/°; for further details, see Ref. 3).

Knee extensor EMG activity from three aspects of quadriceps femoris was recorded by using bipolar Ag-AgCl surface electrodes (Beckman Instruments, Schiller Park, IL) affixed over vastus medialis, vastus lateralis, and rectus femoris muscles as previously described (6). Electrode position was retained by using cutaneous ink marks and transparent plastic sheets marked for electrodes and anatomical landmarks, including biopsy incision, proximal patella, and anterior iliac crest. Individual amplification level of each EMG electrode channel was set during the first baseline test, and the same settings were used in all subsequent sessions. After being filtered with low and high cutoff frequencies of 9.5 and 510 Hz, respectively, the raw EMG signal was full-wave rectified and passed through a smoothing window of 44-ms time constant. Torque and EMG signals were digitized at 100 Hz and processed by using AcqKnowledge III for the MP100WS (Biopac Systems, Goleta, CA). From the two submaximal trials, 9.0-s intervals were averaged for torque and EMG. Similarly, from two maximal trials the peak torque value of a 1.0-s interval was selected and EMG was averaged for that time. Mean values from the two trials and the three electrode sites (EMG) were used for comparisons. EMG values were normalized to preunloading, by using the mean of the three baseline measurements for each muscle separately, and then averaged. Electromechanical efficiency was defined as torque divided by EMG for a specific time average (see above).

Across the baseline sessions, there was no change in maximum (P = 0.25) or submaximum (P = 0.99) isometric torque. The CV across sessions and trials were 6.2 and 2.2% for isometric maximum and 0.8 and 0.6% for submaximum torque, respectively. The corresponding CV for maximum EMG were 10.9 and 8.1% and for submaximum EMG 12.8 and 6.1%, respectively. For maximum torque/EMG ratio, the CV were 9.6 and 9.8%, whereas submaximum torque/EMG varied 13.4 and 7.1% between sessions and trials, respectively.

Muscle biopsy. The percutaneous conchotome method was used to obtain tissue samples from the left vastus lateralis muscle before and toward the end (day 37) of bed rest. Specimens, obtained after 60 min of supine rest, were frozen in Teflon chilled with liquid nitrogen and stored at −80°C until processed further (for details of biopsy preparations and techniques, see Refs. 4, 23).

For enzyme-histochemical analysis, frozen muscle samples were cut at their greatest girth perpendicular to the long axis of fiber orientation in 10-μm serial sections by using a cryostat. Cross sections were stained for myofibrillar adenosinetriphosphatase (ATPase) and classified as type I, IIA, IIB, or IIC by using standard preincubations (pH 4.35, 4.5, 9.4). Fiber type classification of the majority of fibers on each cross section (average fiber no. = 523; range 205–1,371) was performed from magnified photographs of myofibrillar ATPase-stained cross sections or directly from the microscope via a TV overlay.

The CSA of individual muscle fibers was measured semiautomatically from photographs. Each fiber was manually encircled, and CSA was calculated by using computerized planimetry (Videoplan, Kontron, Munich, Germany). Fiber CSA and diameter were estimated from 30 fibers of each type. Type IIC fibers were ignored because they were seldom encountered. The mean fiber area and diameter were calculated for each individual on the basis of type I, IIA, and IIB fiber percentages and CSA. Analogously, the relative CSA occupied by type I fibers was calculated.

MHC composition was determined in 10-μm serial sections by one-dimensional sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE; cf. Ref. 23; Fig. 1). To identify and determine the relative content of different myofibrillar proteins, the separating gels were silver stained and scanned in a soft-laser densitometer (4,096 optical density levels, 50-μm pixel spacing; Molecular Dynamics, Sunnyvale, CA) interfaced with a computer. With the use of the volume-integration function (ImageQuant software version 3.3; Molecular Dynamics), type I, IIA, and IIB MHC content was estimated and expressed in percentage of total MHC in that sample.

MR imaging. Muscle CSA was assessed before and toward the end (day 37) of bed rest by using MRI (Siemens Somatom Impact 1.5 T, Erlangen, Germany). Subjects were positioned with their thighs in the horizontal plane, and a foot restraint was used for fixation. Transaxial scans (10 mm, repetition time/echo time = 700/17 ms) were obtained equidistant from the most proximal and distal aspects of the femoral bone (midthigh), as estimated from frontal and sagittal scout images. The knee extensor muscle was manually encircled, and CSA was calculated by using computerized planimetry.
(National Institutes of Health Image 1.60, Macintosh Quadra 700). To prevent fluid shifts from influencing CSA secondary to a change in body position (5), subjects remained supine for 60 min before imaging preceding bed rest.

Statistics. Repeated-measures analysis of variance was performed on functional parameters, including EMG, and on MRI data, and single-contrast means comparison were used to evaluate effects of unloading. The paired t-test was used to evaluate differences in muscle biopsy parameters before and after bed rest. Correlation coefficients (r) were calculated from individual values after performance of linear-regression analyses. The variance of a selected parameter was calculated for each individual across the two consecutive trials or between means across the three test sessions, respectively. The square root of that group average, normalized by using the overall mean, expressed the CV. Statistical significance between means across the three test sessions, respectively.

RESULTS

Muscle function. Maximum isometric torque decreased (24.5 ± 10.5%; P < 0.05) from 302 ± 42 Nm before to 224 ± 8 Nm after bed rest (Figs. 1 and 2). Maximum concentric torque decreased (P < 0.05; Fig. 1) by 28.9 ± 12.2% after bed rest. This decrease was similar (27.0–30.4%) across knee angular velocities. Maximum EMG decreased (P < 0.05; Fig. 2) by 19.4 ± 23.5%, whereas submaximum EMG increased (P < 0.05) by 44.4 ± 27.6% after bed rest. Submaximum torque/EMG decreased (P < 0.05) by 23.2 ± 20.2% after bed rest. Maximum torque/EMG did not change (P = 0.36).

Knee extensor angular velocity. Knee extensor AVmax decreased (5.1 ± 6.3%; P < 0.05) from 864 ± 79 to 816 ± 50°/s after bed rest.

Muscle proteins, fiber types, and size. Mean fiber area and diameter decreased (P < 0.05) by 17.6 ± 13.6 and 7.8 ± 9.0%, respectively, after bed rest (Table 1). Type I CSA and diameter decreased (P < 0.05) by 18.2 ± 13.9 and 10.3 ± 7.9%, respectively. Type IIA (P = 0.26) and IIB (P = 0.08) fibers showed no change. Type I, IIA, and IIB muscle fiber percentages averaged 52.6 ± 10.3, 26.9 ± 9.9, and 20.2 ± 6.6%, respectively, before bed rest and were not altered (P = 0.66, 0.98, 0.21 for type I, IIA, and IIB, respectively) after bed rest (Table 1). The relative CSA occupied by type I fibers did not change (P = 0.64) after bed rest. The relative proportions of type I, IIA, and IIB MHC were 44.8 ± 12.2, 44.0 ± 17.8, and 12.6 ± 11.1% before bed rest, respectively. MHC composition was not altered (P = 0.79, 0.82, 0.73 for

Table 1. Muscle fiber type, size, and MHC composition of vastus lateralis muscle before and after 37 days of bed rest

<table>
<thead>
<tr>
<th>Fiber Type</th>
<th>Pre</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type I fibers, %</td>
<td>52.6 ± 10.3</td>
<td>49.8 ± 12.1</td>
</tr>
<tr>
<td>Type IIA fibers, %</td>
<td>26.9 ± 9.9</td>
<td>27.0 ± 9.4</td>
</tr>
<tr>
<td>Type IIB fibers, %</td>
<td>20.2 ± 6.6</td>
<td>22.5 ± 7.0</td>
</tr>
<tr>
<td>Type I fiber area, µm²</td>
<td>5,025 ± 1,038</td>
<td>4,894 ± 1,041*</td>
</tr>
<tr>
<td>Type IIA fiber area, µm²</td>
<td>5,986 ± 1,024</td>
<td>5,283 ± 1,764</td>
</tr>
<tr>
<td>Type IIB fiber area, µm²</td>
<td>4,932 ± 1,238</td>
<td>4,056 ± 1,402</td>
</tr>
<tr>
<td>Mean fiber area, µm²</td>
<td>5,270 ± 1,019</td>
<td>4,345 ± 1,208*</td>
</tr>
<tr>
<td>Type I/A area ratio</td>
<td>1.09 ± 0.56</td>
<td>1.25 ± 0.60</td>
</tr>
<tr>
<td>Relative type I area</td>
<td>0.51 ± 0.13</td>
<td>0.47 ± 0.12</td>
</tr>
<tr>
<td>Type I MHC, %</td>
<td>44.8 ± 12.2</td>
<td>42.9 ± 11.6</td>
</tr>
<tr>
<td>Type IIA MHC, %</td>
<td>44.0 ± 17.8</td>
<td>45.4 ± 12.8</td>
</tr>
<tr>
<td>Type IIB MHC, %</td>
<td>17.6 ± 8.5</td>
<td>16.3 ± 3.4</td>
</tr>
</tbody>
</table>

Values are means ± SD; n = 7 subjects. MHC, myosin heavy chain; Pre, Post: before and after 37 days of bed rest, respectively. *Significantly different from Pre, P < 0.05. For further details, see Methods. 

Fig. 1. Isometric (0°/s) and concentric (30–180°/s) peak torque (Nm) before (Pre2, Pre3) and after (Post) 6 wk of bed rest. Peak torque decreased (Pre3 vs. Post; P < 0.05) at each speed. Values are means ± SD (n = 7 subjects).

Fig. 2. Relative change in knee extensor peak torque, cross-sectional area (CSA), torque per CSA, and EMG activity (EMGmax) during maximum voluntary isometric knee extension before and after 6 wk of bed rest. Each parameter is expressed as change (%) relative to baseline (Pre1, Pre2, Pre3) mean value. Values are means ± SD (n = 7 subjects). *Significantly different from baseline, P < 0.05. For further details, see Methods.
type I, IIA, and IIB, respectively) after bed rest (Table 1). There were high correlations between the type I fiber percentage and the relative proportion of type I MHC ($r = 0.90; P < 0.05$) and between the percentages of type IIA fiber and IIA MHC ($r = 0.98; P < 0.05$) classified from enzyme-histochemical myofibrillar ATPase stainings and by the use of SDS-PAGE (Fig. 3). There was no correlation between type IIB fiber and IIB MHC ($r = 0.47; P = 0.29$) percentages. The type IIB fiber percentage was higher ($P < 0.05$) than the relative proportion of type IIB myosin isoforms.

Quadriceps muscle CSA. Quadriceps femoris CSA decreased (13.8 ± 4.5%; $P < 0.05$) from 76.7 ± 10.0 cm$^2$ before to 65.8 ± 7.1 cm$^2$ after bed rest. Peak torque per CSA decreased by 12.5 ± 9.5% ($P < 0.05$) after bed rest (Fig. 2).

**DISCUSSION**

The finding of a marked decline in maximum voluntary force after bed rest conforms with data from previous long-term unloading studies. The less severe, although manifest, muscle atrophy, as estimated in whole muscle or single muscle fibers, also agrees with previous reports. Neither fiber type composition nor in vivo force-velocity characteristics changed in response to bed rest. Because the decrease in muscle size alone cannot account for the reduced maximum voluntary force, it is concluded that a reduced neural input or reduced specific tension of muscle must, at least in part, be responsible for the large decrease in voluntary strength.

Maximum voluntary force decreased by 25–30% after 42 days of bed rest. This amounts to a decline of 4–5% per week. Previous data from experimental bed rest, lower limb unloading, or spaceflight ranging from 2 to 6 wk showed 12–21% strength loss of the knee extensors (2, 3, 11, 12, 18, 33). Studies of the human ankle extensors (18; cf. Ref. 10) also report changes of that magnitude in response to different unloading models.

The loss in muscular strength reported after unloading has mainly been attributed to a decrease in skeletal muscle mass. The muscle atrophy of 15% assessed in the knee extensors after 37 days of bed rest equals an average weekly decrease in muscle mass of ~3%. The majority of previous studies examining healthy individuals after 1–6 wk of unloading or bed rest (2, 3, 7, 9, 14, 20, 21) have demonstrated a similar (2–3%) weekly rate of atrophy in whole muscle or fiber CSA of the thigh or knee extensors. Three astronauts showed a 6% muscle atrophy in whole muscle CSA after 8 days of spaceflight (26). At odds with these reports, muscle fiber CSA decreased 11–36% in astronauts subjected to 5–11 days of weightlessness (13).

The greater loss in strength relative to the reduction in muscle CSA suggests specific tension of muscle and/or neural input to muscle is reduced. The observed changes in EMG activity support both the occurrence of diminished specific tension and thus decreased electromechanical efficiency of muscle and a reduced neural drive of the muscle. Recently, 10 days of lower limb
unloading was shown to produce a significant strength loss but no decrease in maximum EMG activity (6), suggesting the knee extensor muscle to be less efficient in generating force per unit mass after short-term unloaded inactivity. The present results agree with those produced after short-term unloading, although there is a difference in the magnitude of response. Thus in both studies there was a marked increase in EMG intensity at a fixed submaximum load. A certain increase in EMG activity seems logical in light of the decrease in muscle mass because the atrophied muscle now has to produce a larger relative tension to attain the preset 100-Nm torque level. Support for this could also be found in a recent study (28) in which the exercise-induced contrast shift in MRI images of the knee extensors was quantitated before and after 5 wk of lower limb unloading. The atrophied quadriceps muscle showed increased contrast shift when producing a given amount of work after unloading, implying additional muscle fiber involvement after disuse. The increase in EMG amplitude in the present study far exceeded what would be expected from the decrease in muscle CSA. Because force per CSA of the knee extensors in fact decreased, as evidenced here during voluntary effort and as previously reported in maximally activated membrane-permeabilized single muscle cells in a subgroup of these individuals (24), the increase in submaximum EMG activity could be partly explained by a less efficient force generation. This, in turn, would demand increased neural input to attain the preset force. There was a significant, although less prominent, decrease in maximum EMG activity after bed rest, confirming the findings of others (11, 16, 19) suggesting decreased neural drive. These authors, however, did not report elevated EMG at submaximum effort. This may simply be explained by the readjustment of signal or target levels to the lower maximum capacity after disuse. Collectively, the results from this study suggest that the neural drive is indeed decreased after long-term bed rest but that there is a decreased electromechanical efficiency, as evidenced by increased EMG at submaximum force, as well.

The demonstrated decrease in voluntary force per area in whole knee extensor muscle and of specific tension in single fibers (24) agrees with data obtained in hindlimb-suspended rats (8, 15, 17, 29, 34). Because contractile protein concentration was lowered in humans (24), similar to what has been reported in animals (8, 15), a decreased number of active cross bridges per volume of muscle after unloading may explain the loss in specific tension. This would, in turn, produce a decrease in electromechanical efficiency. Qualitative impairment in one or several of the other components in the contractile machinery (cf. Ref. 6) could, however, not be ruled out.

Animal data suggest that slow-twitch fibers are more vulnerable to unloading. Thus fiber type conversion and greater relative atrophy in predominantly slow than in fast muscles have frequently been reported (cf. Ref. 30). Slow fibers, but not fast fibers, also show a reduction in specific tension (cf. Ref. 17). No alteration in fiber type was shown in enzyme-histochemical assessments or in the relative proportion of MHC assessed in the same serial sections. Because of the high correlation between fiber type percentage and MHC composition assessed electrophoretically, shown here and previously (1, 31), a fiber type transformation in response to 37 days bed rest seems unlikely. Nor do the present results suggest a fiber type-specific atrophy that could potentially change the relative CSA occupied by a certain fiber type. Not only fiber type but also the relative fiber size influences specific MHC content. Hence unaltered MHC proportions across fibers allude to a uniform decrease of all MHC isoforms in the muscle. The decrease in specific tension of single fibers did not indicate differences among fiber types (24). Thus no qualitative changes in MHC or fiber type or the relative contribution of fast or slow muscle to knee extensor CSA seems to occur in response to bed rest. This response seems different from what occurs in lower mammals and, equally important, it would not significantly alter muscle function.

Force-velocity characteristics of the knee extensor muscle group did not show any alterations after bed rest. However, animal studies of whole muscle preparations (15) or single slow fibers (17, 29) have consistently reported an increased maximum velocity of unloaded shortening (V_o) after unloading. These changes are consistent with the finding that unloading appears to promote an increase in fast MHC isoform content in rat soleus muscle. V_o in single human fibers was unchanged when averaged for all fiber types of the quadriceps muscle after bed rest (24). In a consideration of previous human data, and because no changes in fiber type composition or MHC content occurred after bed rest, the finding of no increase in V_o is not surprising. It is noteworthy that the increased V_o demonstrated in rats occurred in parallel with fiber type transformation. The appearance of transformed fibers in fiber pools being analyzed constitutes a problem when the impact of unloading on a certain fiber type is being determined. In support of the lack of increase in single-fiber V_o in the subgroup examined in the parallel study (24), there was no increase in knee AV_max. In fact, a small (5%) decrease was demonstrated. This effect might be explained by decreased neural drive after bed rest. The force-velocity curve assessed during isokinetic knee extensions at selected angular velocities was not altered after bed rest. A similar lack of change has been reported elsewhere after unloading (2, 3, 11, 12). Because fast-myosin content, i.e., type II fiber percentage, has been correlated to knee extensor torque at higher velocities (cf. Ref. 32), the unchanged MHC and fiber composition support the unaltered in vivo force-velocity relationship reported here.

The present changes in muscle fiber size were similar when measured by using planimetry or calculated by using the smallest ellipse diameter in serial sections from biopsy samples, and the overall decrease paralleled the change in knee extensor CSA from whole muscle imaging. Because the interindividual variation in CSA was greater in fiber assessments than with the
use of MRI, it might be anticipated that this variation does not illustrate individual differences in the atrophic response to bed rest only but rather that the inherent sampling error of the biopsy technique (2) is greater than that associated with MRI methodology (2, 26). It should be recalled, however, that tomographic CSA typically does not discern extracellular or other noncontractile components that contribute to the measured area. It is a matter for speculation whether swelling or fluid shift (5, 22) is altered in response to unloading and whether this could affect fiber or whole muscle CSA measurements at rest or after muscle use.

This study cannot explain the recurrent differences between human and animal data. Among the plausible explanations are species differences between lower mammals and humans, e.g., growth rate, fiber type characteristics, anatomy, and function. Because animal muscles are largely homogenous in fiber type, specific adaptation of different muscles may be regarded as synonymous with adaptation of different fiber types, when, in fact, there may be large differences also in anatomy and function. It could be noted that data that compare shortening velocity and specific tension in anatomy and function. It could be noted that data that compare shortening velocity and specific tension in single fibers of different types in the same muscle are still lacking. On the other hand, this could imply that human data from the heterogenous knee extensor muscle may not be applied to the slow-twitch soleus and vice versa.

We conclude that the impaired musculoskeletal function reported here and elsewhere in response to unloading cannot entirely be attributed to muscle atrophy. Our data suggest that decreased neural drive and reduced electromechanical efficiency of skeletal muscle are responsible, in part, for a decrease in voluntary strength. Results also suggest that unloading produces no major changes in contractile properties or in fiber type or myosin composition of a heterogenous human muscle, implying that the response in humans differs from that seen in lower mammals.

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