Hypertrophy in the cervical muscles and thoracic discs in bed rest? 

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Submitted 26 March 2013; accepted in final form 25 June 2013

Belavý DL, Miokovic T, Armbrrecht G, Felsenberg D. Hypertrophy in the cervical muscles and thoracic discs in bed rest? J Appl Physiol 115: 586–596, 2013. First published June 27, 2013; doi:10.1152/japplphysiol.00376.2013.—The impact of prolonged bed rest on the cervical and upper thoracic spine is unknown. In the 2nd Berlin BedRest Study (BBR2-2), 24 male subjects underwent 60-day bed rest and performed either no exercise, resistive exercise, or resistive exercise with whole body vibration. Subjects were followed for 2 yr after bed rest. On axial cervical magnetic resonance images from the skull to T3, the volumes of the semispinalis capitis, splenius capitis, spinalis cervicis, longus capitis, longus colli, levator scapulae, sternocleidomastoid, middle and posterior scalenes, and anterior scalenes were measured. Disc height, anteroposterior width, and volume were measured from C5/6 to T6/7 on sagittal images. The volume of all muscles, with the exception of semispinalis capitis, increased during bed rest (P < 0.025). There were no significant differences between the groups for changes in the muscles. Increased upper and midthoracic spine disc height and volume (P < 0.001) was seen during bed rest, and disc height increases persisted at least 6 mo after bed rest. Increases in thoracic disc height were greater (P = 0.003) in the resistive vibration exercise group than in control. On radiological review, two subjects showed new injuries to the mid-lower thoracic spine. One of these subjects reported a midthoracic pain incident during maximal strength testing before bed rest and the other after countermeasure exercise on day 3 of bed rest. We conclude that bed rest is associated with increased disc size in the thoracic region and increases in muscle volume at the neck. The exercise device needs to be modified to ensure that load is distributed in a more physiological fashion.

morphology; uncovertebral joint; magnetic resonance imaging; spaceflight; microgravity

PROLONGED BED REST is a methodology used by space agencies to simulate the deleterious effects of spaceflight on the human body (28) and hence also to trial various types of countermeasures against the detriments that occur in spaceflight. Very little data is available on the effect of bed rest or spaceflight on the cervical spine and its musculature. This is understandable, as the effect of bed rest and spaceflight on the musculoskeletal system is most prominent in the lower half of the body (11), and hence research typically focuses on this area of the body.

The 2nd Berlin BedRest Study (BBR2-2) was a 60-day head-down tilt (HDT) bed rest study in which the primary focus was on the impact of exercise countermeasures on bone loss (4). When we initiated the study, we felt it important to also gain a deeper understanding of body regions not typically examined in such bed rest studies, such as the cervical spine. Furthermore, from an ethical point of view, we considered it important to better understand what kinds of changes subjects undergo in such studies. In this vein, it was appropriate to investigate body regions such as the cervical and upper thoracic spine. Also, we were aware of anecdotal reports of headache during HDT bed rest, but to our knowledge, these have never been catalogued. From a clinical perspective, headache can have a number of causes, one of them being cervicogenic (12).

There is very limited data available on the impact of bed rest or spaceflight on the cervical musculature. Data from nine individuals measured within 4 days of 16–28 wk of spaceflight (10) showed no significant change (+0.9%) in cervical extensor muscle volume. Both spaceflight (10) and bed rest (7) are known to affect the postural extensor muscles of the spine and legs the most. However, it is a long-standing idea (33) that the muscles of the neck act to balance the head on the neck in upright posture, rather than generating large forces against gravity. This could explain the limited change in the neck postural extensor muscles in microgravity: the change in loading patterns in micro- vs. normogravity may not be as extreme as for the extensor muscles of the lower limb. Alternatively, astronauts are quite busy with mission tasks, and one may argue that their usage of their neck muscles in these tasks may well prevent atrophy. Furthermore, predicting muscular changes in bed rest on the basis of existing findings in spaceflight can be difficult: the psoas muscle at the lumbar spine was observed to atrophy after spaceflight (10), but studies in bed rest have shown either significant (2, 32) or nonsignificant (3, 8, 23) increases in the size of this muscle. Thus it is difficult to predict, on the basis of existing data, whether muscle atrophy may occur at the neck during bed rest.

In relation to the spinal column, after 2-h supine lying in five individuals (31) lengthening of the cervical (between 0.44- and 0.68-cm increase in length in these 5 subjects) and lumbar (~0.24- to 1.04-cm change) spine regions, but less so at the thoracic spine (0.06- to 0.52-cm change), occurred. Lumbar spine lengthening and hypertrophy of the lumbar intervertebral discs is seen in prolonged bed rest (2). The question remains open as to whether similar hypertrophy occurs at the cervical and thoracic intervertebral discs.

The goal of the present study was to conduct an exploratory survey of the impact of prolonged bed rest on the cervicothoracic spine. To this end, we assessed cervical muscle volume, intervertebral disc morphology at the cervical and upper thoracic spine, and pain reports in the head, cervical, and thoracic regions. This project was implemented in the BBR2-2 (5). In this study two exercise programs, resistive exercise with or without whole body vibration, were implemented. Since these exercises were targeted at the lower limbs, we hypothesized that there would be no difference between the countermeasure and inactive control subjects.

MATERIALS AND METHODS

Twenty-four male subjects participated in the BBR2-2 and underwent 60 days of 6° HDT bed rest. Exclusion criteria relevant to the present investigation included any kind of cartilage, joint, muscle, or

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performed no exercise and served as a control group (CTR, n = 8; 31.1(5.1) yr, 179.3(7.7) cm, 75.0(12.8) kg), and one that performed no exercise and served as a control group [CTR, n = 9; 33.1(7.8) yr, 181.3(6.0) cm, 80.6(5.2) kg]. The sample size of the BBR2-2 was based upon bone parameters (4) and not those of the present study. Since there were no data available in the literature to conduct a sensitivity analysis, the present investigation should be considered an “exploratory study.”

The countermeasure exercise protocol, which was targeted at the legs and lower back, has been discussed in detail elsewhere (5, 22). In brief, however, after a short warm-up, the following exercises were performed on the Galileo Space exercise device (Novotec Medical, Pforzheim, Germany; Fig. 1): bilateral squats (vibration frequency 24 Hz, amplitude 3.5–4 mm, peak acceleration 10.2 g), single-leg heel raises (vibration frequency 26 Hz, amplitude 3.5–4 mm, peak acceleration 10.2 g), double-leg heel raises (vibration frequency 26 Hz, amplitude 3.5–4 mm, peak acceleration 10.2 g), and back and heel raise (performing hip and lumbar spine extension against gravity with ankle dorsiflexion but with 1.5 × body wt applied at the shoulders; in RVE group vibration frequency 26 Hz, amplitude 3.5–4 mm, acceleration 3.9 g). The RVE group performed the same exercises as the RE group except that whole body vibration was applied.

Magnetic resonance imaging protocol. Subjects attended MR scanning 9 or 8 days before bed rest [baseline data collection (BDC)], on day 27 or 28 (HDT27/28) and day 35 or 36 (HDT35/36) of HDT bed rest, and then on days 14 (R + 14), 90 (R + 90), 180 (R + 180), and 720 (R + 720) of post-bed rest recovery. A 1.5-T Siemens Avanto (Erlangen, Germany) scanner was used. The subject remained supine for 2 h prior to the start of the scanning protocol to control for any changes in muscle size due to acute changes in body posture (16). The subject was positioned in the supine position, and a cushion provided by the MR manufacturer was positioned behind the head and head. Head and neck MR coils were used. After initial pilot scanning, 15 T2-weighted sagittal images (repetition time: 3,500 ms, echo time: 79 ms, slice thickness: 3.0 mm, interslice distance: 0.3 mm, field of view: 380 × 380 mm interpolated to 384 × 384 pixels) encompassing the entire volume of the intervertebral discs from the base of the skull to at least T8 (see Fig. 3) were obtained. Fifty T2-weighted axial images (repetition time: 6,360 ms, echo time: 99 ms, slice thickness: 4 mm, interslice distance: 0.4 mm, field of view: 234 × 234 mm interpolated to 320 × 320 pixels) were taken encompassing the region from the cerebellum to at least the third thoracic vertebra. Images were oriented to be parallel to the midsagittal intervertebral discs. The images were then stored for off-line analysis.

Measurement of muscle volume and intervertebral disc morphology. Data sets were assigned a random number to blind the operators to study date. T. Miokovic measured all cervical axial images and the cervical spine in all sagittal images. D. L. Belavý measured the thoracic spine in all sagittal images. ImageJ 1.40 (http://rsb.info.nih.gov/ij/) was used for all image measurements. The muscles measured in the axial cervical images are shown in Fig. 2. The area of each of the muscles present in each image was measured. Based on all area measurements from individual muscles, muscle volume was subsequently calculated. Since spinalis cervicis and semispinalis cervicis continue caudally in the thoracic spine without obvious anatomic division on MRI, the volume of this muscle was calculated only to the most caudal aspect of the T2 vertebra. On some measurement days, the scanning region was positioned too far caudally, such that the most superior aspects of longus capitis and semispinalis cervicis (with spinalis capitis, longissimus capitis, and longissimus cervicis) were missed. To ensure comparability between measurement days, the area measurements of these two muscles were excluded from subsequent muscle volume calculation where the base of the skull was present in the image. According to analysis of one data set from every subject where the entire muscle volume was present, this process would have excluded ~22% of total longus capitis and ~5% of semispinalis cervicis volume. Data from the left and right sides of the body were averaged prior to further analysis.

Disc heights, anteroposterior disc width, and disc volume (Fig. 3) were measured from the C2/3 to T6/7 intervertebral discs. The discs at lower vertebral levels were not measured, as their entire volume was often not included in the images. Measurements of each disc height and width parameter at each vertebral level were averaged across all images prior to further analysis. Sagittal-plane disc area measurements were interpolated to measure disc volume. Since anterior, central, and posterior disc heights were strongly (0.75 < r < 0.8) correlated these disc height variables were averaged prior to further analysis. Because of the small size of the cervical discs (C2/3 to C5/T1), the following process was used to reduce measurement error: 1) each parameter was measured twice in all images and cervical discs, and 2) if the average value for a given parameter from all images at a given intervertebral disc varied by more than 3% then 3) the operator repeated the measurements until agreement was within the 3% threshold. The thoracic discs were measured only once. For the primary analysis, the parameters from each disc were averaged into cervical (C2/3 to C5/T1) and thoracic (T1/2 to T6/7) regions. Baseline disc parameters at the cervical and thoracic spine are presented in Table 1.

Pain questionnaires. Eight or nine days before bed rest (BDC-8/BDC-9), 2 days before bed rest (BDC-2), every day during the first 2 wk of bed rest (HDT1–HDT14), and thence at weekly intervals (HDT18, HDT25, HDT32, HDT39, HDT46, HDT53, HDT57), in the 7 days of ambulant post-bed rest recovery (R + 1 to R + 7), and subsequently 14, 30, 90, 180, and 720 days after bed rest, subjects...
were asked to fill out a pain questionnaire. The subjects were asked to report any pain or discomfort that they might be experiencing at the current time. If pain or discomfort was present in any part of the body, they were to mark its location on a body chart and record its intensity (1–100) on a visual analog scale (VAS; Ref. 19). Subjects were questioned further, if necessary, to delineate in which anatomic region they were experiencing the pain or discomfort. Late in recovery (R/H11001 and beyond) subjects were also asked whether they had experienced pain in a particular body region since the last appointment. If they reported pain since the last appointment but no current pain, this was regarded as an affirmative response. In this case, however, no VAS scores were available. Where headaches, cervical pain, or thoracic pain was reported, this was included in the current analysis.

Blinded radiological assessment. For blinded radiological assessment, the radiologist (G. Armbrecht) focused on pathological changes in the bone structure of the vertebral bodies. The radiologist was blinded to study date and subject group and was given images from baseline, HDT55/56, and R/H720.

Statistical analysis. Linear mixed-effects models (30) with subsequent repeated-measures analysis of variance (ANOVA) were used to...
Values are presented as means(SD). CTR, inactive control group; RE, resistive exercise-only group; RVE, resistive exercise with whole body vibration group.

examine whether changes occurred in muscle volume or disc morphology during bed rest or whether the countermeasures had an impact. The primary analysis included the baseline HDT27/28 and HDT55/56 data points. Main effects of “group” and “study time” were examined, as well as their interaction. Allowances for heterogeneity of variance (e.g., due to “group” and/or “study time”) were made when necessary. If the group × study date interaction was significant, further two-group ANOVAs (i.e., CTR vs. RE, CTR vs. RVE, RVE vs. RE) were performed. Since we examined 14 different parameters (8 muscles and 6 disc morphology parameters) in the present study and since we were interested in both changes during bed rest (study date main effect on ANOVA) as well as the impact of the countermeasures (group × study date interaction on ANOVA), a Bonferroni correction for 28 tests was performed. Further a priori t-tests comparing changes in each group over the course of study vs. baseline were also performed. P values of these tests are reported both unadjusted and adjusted for the estimated false discovery rate (9). Additional analyses were performed comparing the incidence of pain during bed rest to the percent change in the outcome parameters at end-bed rest for descriptive purposes only. Where data were available despite protocol deviations, these were included in the analysis. The linear mixed-effects models implement a maximum likelihood-based approach for missing cases. The “R” statistical environment (version 2.10.1: www.r-project.org) was used for all analyses. An α-level of 0.05 was taken for statistical significance on ANOVA. Unless otherwise specified, results are presented as mean(SD). Because of the limited number of pain reports, statistical analyses could not be performed and results are reported descriptively.

RESULTS

Pain reports, radiological review, and study events. Two subjects showed changes on radiological review: changes in one subject detected during the study led to subject dropout, and changes in another subject were detected on subsequent blinded radiological assessment. The radiological findings, associated symptomatic pain, and study events are detailed in Fig. 4. In two further cases (both RVE group), the midthoracic increase in disc size was evident on blinded radiological analysis. However, in these two subjects, no new discontinuities in the vertebra were observed and the subjects did not report pain. No further vertebral changes in the course of the study were found on blinded radiological assessment.

Ninety days after bed rest, one CTR subject and one RE subject did not return for further testing. Seven hundred twenty days after bed rest, one further RE subject did not return.

During bed rest, three CTR subjects and one RVE subject reported headaches, one CTR subject and one RVE subject reported cervical pain, and one RVE subject reported thoracic region pain (Fig. 5). In the first 7 days after bed rest, two CTR subjects reported headaches, six CTR subjects, three RE subjects, and one RVE subject reported cervical region pain, and three CTR subjects and one RVE subject reported thoracic region pain. After bed rest, subjects typically reported “muscular tightness,” and there were no reports of trauma. Aside from those shown in Fig. 4, pain reports during bed rest were not associated with trauma.

Cervical muscle volume. Aside from subjects not attending testing, scanning of one RVE subject could only be performed down to C7 (impacting spinalis cervicis, anterior scalenes, sternocleidomastoid, splenius capitis, levator scapulae, and

![Fig. 4. Radiological review and associated clinical findings. Left: this subject, subsequently randomized to the resistive exercise-only (RE) group, reported midthoracic pain during a maximal strength test on the training apparatus during before bed rest and subsequently reported midthoracic pain again on day 6 of bed rest only. At mid-bed rest scanning, an incident fracture at the upper end plate of T9 with additional anterior height reduction and a mild incident fracture of T10 with impression of the upper end plate were seen (arrows). This subject was then withdrawn from bed rest. Midthoracic pain returned after bed rest. Between 1 yr and 2 yr after bed rest this pain resolved, and this remained the case at last contact 5 yr after bed rest (Fig. 5). Right: in this RE subject, blinded radiological review showed an incident fracture of the upper end plate of T10 at mid-bed rest (arrow) that was not seen at baseline. Review of the pain questionnaires showed that the subject reported midthoracic pain on day 4 of bed rest and during questioning on that day of bed rest the subject reported that he “tilted his hips incorrectly” during countermeasure exercise on day 3 of bed rest. Pain was reported by this subject on 1 day only during bed rest. After bed rest, he did not report any pain (Fig. 5).](http://jap.physiology.org/10.1152/japplphysiol.00376.2013)
longus colli) because of technical difficulties on HDT27/28 and HDT55/56. One further RVE subject was scanned down to mid-T1 (impacting spinalis cervicis, anterior scalenes, and sternocleidomastoid) on HDT55/56. Errors in the MR images prevented analysis of data from 90 days after bed rest in one CTR subject and 180 days after bed rest in another CTR subject.

ANOVA showed significant changes over time in longus colli, sternocleidomastoid, anterior scalenes, middle and posterior scalenes, and splenius capitis (study date main effect: all $P \leq 0.001$ after Bonferroni correction) as well as longus capitis and levator scapulae (study date main effect: both $P < 0.01$ after Bonferroni correction), with weak effects seen in spinalis cervicis with multifidus and semispinalis cervicis (study date main effect: $P < 0.05$ after Bonferroni correction). Only for semispinalis capitis with spinalis capitis, longissimus capitis, and longissimus cervicis was no significant change seen during bed rest. The changes over time in each group and muscle are presented in Tables 2 and 3. No significant differences were apparent between the groups during the bed rest phase. In the absence of a significant group × study date interaction, a significant study date main effect indicates significant changes in muscle volume during bed rest.

Changes seen during bed rest were still present 14 days afterwards and, with the exception of spinalis cervicis in the RE group, recovered by 90 days after bed rest. The increase in splenius capitis volume in the CTR group persisted at 2 yr after bed rest (R+720 t-test vs. baseline: $P = 0.023$ without and nonsignificant with type I error adjustment) when only those CTR subjects with complete data sets in recovery were included in the analysis. No association was seen between changes and the musculature and incidence of pain.

**Intervertebral disc morphology.** In addition to subject drop-outs, the midthoracic discs were not always completely visualized, preventing some measurements. Specifically, this impacted the following data points: T4/5, T5/6, and T6/7 intervertebral discs at baseline (BDC) testing of one RVE subject and T6/7 disc volume in one RVE subject 90 days after bed rest; T6/7 intervertebral disc of one CTR subject could not be included in analysis from any testing day.

On ANOVA, changes during bed rest (significant study date main effect) were seen for disc height and volume in the thoracic region (both $P \leq 0.0000001$ after Bonferroni correction; Fig. 6). Increases in thoracic disc height and volume were seen. No significant changes were seen during bed rest in the cervical discs (Fig. 8). The changes at each intervertebral disc at end-bed rest are presented in Fig. 7.

Only disc height in the thoracic region responded differently between the groups (group × study date interaction: $P = 0.0046$ after Bonferroni correction; Fig. 6). For this variable, further two-group ANOVAs showed that the RVE group differed ($P = 0.00011$ without Bonferroni adjustment, $P = 0.003$ after Bonferroni adjustment) from the CTR group, with the greatest increases in disc height seen in the RVE group.

Average thoracic disc volume and height increases persisted 2 yr after bed rest (Fig. 6). Cervical disc volume was increased 2 yr after bed rest and cervical anteroposterior width decreased (Fig. 8). If only those subjects with complete data sets are included in the analysis, these long-term effects remain signif-
of cervical pain in bed rest was a weak association seen

between the groups on ANOVA. ANOVA assessed testing dates at baseline and during bed rest only, and a significant study date main effect indicates that all

values next to muscle names indicate significance of study date main effect on ANOVA after Bonferroni correction. There were no significant differences

between the groups on ANOVA. ANOVA assessed testing dates at baseline and during bed rest only, and a significant study date main effect indicates that all subjects pooled together showed significant changes in muscle volume during bed rest. *P < 0.05, †P < 0.01, ‡P < 0.001, unadjusted P value of t-test vs. baseline. *P < 0.05, †P < 0.01, P value of t-test after adjustment for false discovery rate. BDC, baseline data collection, HDT, head-down tilt bed rest, R+, post-bed rest recovery.

icant for cervical anteroposterior diameter and thoracic disc volume.

Only between average cervical disc height and the incidence of cervical pain in bed rest was a weak association seen [mean(SE) change at end-bed rest: −0.6(0.8)% for those without pain vs. +6.2(2.5)% for those with pain; P = 0.015 without type I error adjustment]. For all other variables, no association was seen with pain incidence in bed rest.

Table 3. Volume of anterolateral neck muscles before, during, and after bed rest

<table>
<thead>
<tr>
<th>Group</th>
<th>BDC, cm³</th>
<th>HDT27/28</th>
<th>HDT55/56</th>
<th>R + 14</th>
<th>R + 90</th>
<th>R + 180</th>
<th>R + 720</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Longus capitis (P = 0.00350)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CTR</td>
<td>9.0 (1.6)</td>
<td>+10.6 (10.8)%</td>
<td>+7.4 (12.4)%*</td>
<td>+7.8 (11.1)%*</td>
<td>+1.6 (13.8)%</td>
<td>+3.9 (11.7)%</td>
<td>+4.4 (11.3)%</td>
</tr>
<tr>
<td>RE</td>
<td>9.2 (2.0)</td>
<td>+10.1 (10.6)%</td>
<td>+8.3 (9.5)%*</td>
<td>+5.2 (11.5)%*</td>
<td>−1.7 (11.0)%</td>
<td>+1.2 (9.9)%</td>
<td>+1.8 (10.8)%</td>
</tr>
<tr>
<td>RVE</td>
<td>8.5 (0.9)</td>
<td>+8.5 (8.5)%</td>
<td>+8.0 (8.2)%*</td>
<td>+4.8 (8.9)%*</td>
<td>+0.9 (10.9)%</td>
<td>+3.9 (9.3)%</td>
<td>+3.9 (10.7)%</td>
</tr>
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</table>

| **Longus colli (P = 0.00006)** |          |          |          |        |        |         |         |
| CTR         | 13.2 (2.5) | +3.2 (7.7)% | +8.5 (6.8)%* | +4.1 (7.5)%* | −0.3 (9.7)% | −3.8 (6.2)% | +0.3 (7.3)% |
| RE          | 13.0 (2.4) | +7.6 (7.2)% | +10.1 (5.9)%* | +6.5 (6.2)%* | +2.4 (6.4)%* | +0.5 (5.6)% | −3.1 (6.1)% |
| RVE         | 14.4 (1.3) | +2.4 (7.0)% | +7.3 (7.2)% | +5.9 (6.2)%* | +2.6 (6.0)%* | −2.7 (6.5)% | +0.3 (5.9)% |

| **Sternocleidomastoid (P = 0.00003)** |          |          |          |        |        |         |         |
| CTR         | 59.7 (6.0) | +3.4 (5.1)% | +4.6 (5.3)% | +4.5 (5.5)% | +0.6 (5.9)% | +0.7 (5.1)% | +1.7 (5.4)% |
| RE          | 67.0 (10.6) | +7.8 (5.2)% | +7.6 (4.8)%* | +8.2 (5.2)%* | +1.2 (5.1)% | −0.9 (5.0)% | −1.5 (5.2)% |
| RVE         | 57.9 (7.5) | +5.8 (5.1)% | +8.6 (6.2)%* | +5.0 (6.1)%* | +2.9 (6.0)%* | +1.2 (6.9)% | +4.2 (5.9)% |

| **Anterior scalenes (P = 0.00003)** |          |          |          |        |        |         |         |
| CTR         | 9.8 (0.8) | +8.2 (7.6)% | +5.9 (9.0)%* | +4.5 (9.7)% | −0.1 (9.2)% | −4.7 (8.9)% | −3.3 (8.7)% |
| RE          | 8.7 (2.6) | +9.1 (8.4)% | +1.3 (7.7)%* | +6.3 (7.7)%* | +1.9 (7.9)% | −0.5 (7.4)% | −3.1 (8.0)% |
| RVE         | 8.3 (2.1) | +10.5 (8.7)% | +15.0 (6.1)%* | +3.0 (7.5)% | −0.4 (8.1)% | +0.1 (7.0)% | −1.8 (6.9)% |

| **Middle and posterior scalenes (P = 0.00003)** |          |          |          |        |        |         |         |
| CTR         | 19.3 (5.6) | +13.3 (10.9)% | +10.1 (9.1)%* | +9.0 (9.4)%* | +4.5 (14.8)%* | +3.3 (9.7)% | −0.1 (10.9)% |
| RE          | 19.9 (4.9) | +8.5 (12.3)% | +1.1 (10.1)% | +6.0 (10.6)%* | −3.0 (11.4)% | +0.4 (13.3)% | +0.8 (10.7)% |
| RVE         | 17.6 (3.8) | +11.4 (11.3)% | +15.4 (10.9)%* | +9.8 (9.5)%* | +5.3 (10.8)% | +3.9 (9.8)% | +0.7 (10.9)% |
DISCUSSION

The present study was the first to examine the cervicothoracic region in prolonged bed rest. We found that all the cervical muscles we measured, with the exception of semispinalis capitis, showed increases in volume during bed rest. This contrasts with the muscle atrophy that occurs in the lower quadrant of the human body during bed rest (7). Furthermore, no significant changes in disc morphology were seen at the cervical spine, but increases of disc height and volume occurred at the upper and midthoracic spine. Third, greater increases in thoracic disc height were seen in the RVE group than in control during bed rest. No significantly different effects of the countermeasures on the musculature were observed.

It is important to consider the findings of the present study from an ergonomic perspective. In daily life in upright posture the head is balanced and moved on the neck: the gravity vector is largely parallel to the neck. In bed rest, gravitational force is now largely perpendicular to the neck: the subject must exert more muscle force to lift and move his head. Also, subjects often spent long periods looking at their laptop screens during bed rest, necessitating a prolonged chin-tuck maneuver.

The extent of muscle size increase, up to 10% in splenius capitis and the middle and posterior scalenes in the control subjects, is impressive considering they were simply lying in bed. Earlier work on resistive exercise for the neck extensor muscles (17) showed that increases of >20% in the cross-sectional area of these muscles were possible. Also, studies
on resistive exercises for the elbow flexors, knee flexors, and knee extensors found that increases of ∼20% in elbow flexor cross-sectional area, but <10% increase in the knee musculature, could be achieved in young adults. On the basis of available data, it appears that the potential, in percentage terms, of the non-load-bearing muscles of the body such as the muscles of the upper arm and neck to increase in size in response to altered loading regimes is much greater than that of the ambulatory musculature of the lower limb.

Do the muscle volume increases seen represent true muscle hypertrophy? There are a number of possible explanations. First, there is possibility that some of the significant differences may be false positives, but after correction for multiple t-tests via false discovery rate (9) and Bonferroni correction of ANOVA findings a number of these results remained “significant.” Second, factors such as acute fluid shift in increasing neck muscle size (16) are unlikely to play a role, as subjects always spent at least 2 h in lying before MR scanning was started. Future work could implement T2 scanning of the neck musculature in prolonged bed rest to examine whether changes in muscle water content may play a role in the increases of muscle size we observed. Third, some (25, 29), but not all (21), studies have observed an increase in cervical muscle size in pain syndromes. Some subjects reported cervical pain and headache, but in the present small sample size no association was seen between the incidence of pain during bed rest and the extent of muscle size changes. Finally, it is possible that because of different loading patterns in bed rest vs. normal ambulation, the muscle adapted and muscle fiber hypertrophy occurred. This interpretation is supported by the finding after bed rest that the changes in the muscles recovered gradually after bed rest once the subjects returned to their daily life: volume increases were no longer apparent 90 days after bed rest. Further work on the basis of the present exploratory study could attempt to tease out these different explanations.

We also examined disc morphology and found no statistically significant changes at the cervical spine on ANOVA, but increases of disc height and volume occurred at the upper and midthoracic spine. Prior work on the lumbar spine has observed increases in lumbar intervertebral disc size after overnight (13, 14) and prolonged (2) bed rest. These changes in the

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**Fig. 7. Change in disc morphology at each intervertebral level at end-bed rest.** *P < 0.05, †P < 0.01, ‡P < 0.001, unadjusted P value of t-test vs. baseline. aP < 0.05, bP < 0.01, P value of t-test after adjustment for false discovery rate. Pooled, all subjects pooled.
lumbar discs are assumed to be due to reduced loading of the spine. It appears now that such disc changes during bed rest can also be expected in the thoracic spine. While this is interesting, do these changes have any importance or clinical meaning? Most of the data available relate to the lumbar intervertebral discs. Nonetheless, as discussed in prior work (3), biomechanical modeling (26, 27, 35) and clinical data (24) suggest that increases in disc height may increase risk of injury to that disc. In line with findings from the lumbar spine of the same subjects (1) and also from another bed rest study (3), the results showed persistence of the thoracic disc morphology changes long term after bed rest. Whether there are any clinical consequences of these changes remains to be seen.

Greater increases in thoracic disc height were seen in the RVE group than in control during bed rest. Typically, countermeasures in bed rest studies aim to ameliorate these increases in disc size (6, 15), not make them more severe. We do not consider the greater increases in disc height in the RVE group to be beneficial. It is possible that the loading patterns on the spine during exercise are behind these effects. The results from radiological review and subject pain monitoring clearly show that excessive loads could be generated on the mid-lower thoracic spine on the exercise device. In two cases, there was clear evidence of an injury occurring: one during a maximal strength test before bed rest and another during countermeasure exercise on day 3 of bed rest. In our view, the fact that most of the load was transferred to the subject through the shoulders was the underlying problem. During training sessions, we noticed that subjects would typically hyperlordose their lumbar spine but that their thoracic spine would be forced into flexion.

Fig. 8. Cervical intervertebral disc morphology during and after bed rest. *P < 0.05, †P < 0.01, ‡P < 0.001, unadjusted P value of t-test vs. baseline. *P < 0.05, †P < 0.01, ‡P < 0.001, P value of t-test after adjustment for false discovery rate. Changes over time (study date main effect on ANOVA) and impact of countermeasures (group × study date interaction on ANOVA) were not significant after Bonferroni correction.
by the load at the shoulders. It is important to note that our MR images did not extend downward the entire length of the thoracic spine, particularly in the taller subjects. We cannot rule out that there were changes at the lower thoracic spine in these subjects. Despite this, aside from those subjects reported in Fig. 5, no other subjects reported any sort of injury incident due to use of the exercise device. To ensure subject safety in future work, the exercise device needs to be modified to ensure that load is distributed in a more physiological fashion, such as also through the hips.

It is important to consider some of the limitations of the present study. Importantly, this was an exploratory study. Consequently, a number of outcome parameters were assessed and also with multiple measurement dates. In an attempt to control for this, we implemented a Bonferroni correction for the results of ANOVA and included adjustment of P values from t-tests vs. baseline for the “false discovery rate” (9). Nonetheless, there is a need for further more rigorous hypothesis-driven work on the basis of the present exploratory study to assess which findings are indeed meaningful. A good example of this was the results for cervical intervertebral disc anteroposterior width: decreases were seen in the RVE group, but the findings of ANOVA were nonsignificant after Bonferroni adjustment. It needs to be further assessed whether this effect is consistent in future studies and what, if any, implication it may have. Alternatively, since we performed a Bonferroni adjustment for the results of ANOVA, some nonsignificant findings on ANOVA might be false negatives. The Bonferroni adjustment has been criticized for being overly conservative (18, 20). It is worthwhile considering at this point that subject numbers were limited for financial and logistical reasons, which in turn reduces statistical power. For example, the findings of the study did not contradict our hypothesis regarding the impact of the exercise program on the neck muscles: there were no significant differences between the groups in the response of the musculature. However, inspection of the data from levator scapulae muscle showed volume increases of ~10% in the training groups but only ~2% in the control group. It is important to note that shoulder restraints were used during training, that levator scapulae connects the neck and shoulder blade, and also that subjects would often contract the muscles of their neck during the strenuous training. (An example video of the training can be observed online: http://goo.gl/DYoTN.) It is possible that this “straining” during exercise may have had a small influence on the neck muscles.

Furthermore, we used MR measures of muscle and disc morphology. Examination of muscle function, such as via functional MRI or electromyography, and consideration of the water and fat content of different tissues would provide greater insight into some of the changes we observed. Also, the reader may note a “dip” at R+14 in thoracic disc height and volume. On this testing day, scanning was done later in the afternoon for practical reasons. Size of the lumbar discs is known to decrease over the course of the day (11, 12). It is reasonable to presume that the same occurs in discs of the thoracic spine.

In conclusion, the present investigation was the first detailed review of the cervical and thoracic regions of the human body in prolonged bed rest. We found that increases in muscle size occurred at the neck. The muscular changes in the training groups did not significantly differ from control. The upper and midthoracic discs increased in volume and height. Greater increases in thoracic disc height were seen in the RVE group than in control. Some reports of pain occurred at the cervical and thoracic spine, but these were not as frequent as seen at the lumbar spine of the same subjects (2). Injuries to the mid/lower thoracic spine occurred in two subjects on the training device. Our interpretation was that this was due to inappropriate application of load solely through the shoulders. We advise that the exercise device be modified to distribute load in a more physiological fashion.

ACKNOWLEDGMENTS

The authors thank the subjects who participated in the study, the staff of the Pflegedirektion, the nurses who cared for the subjects, and the many colleagues involved in the implementation of the bed rest study. The authors thank the MR operators for their support during and after the study. D. L. Belavý was supported by a postdoctoral fellowship from the Alexander von Humboldt Foundation.

GRANTS

The 2nd Berlin BedRest Study (BBR2-2) was supported by Grant 14431/02/NLH2 from the European Space Agency and Grant 50WB720 from the German Aerospace Center (DLR). The BBR2-2 was also sponsored by Novotec Medical, Charité Universitätssmedizin Berlin, Siemens, Ostemedical Group, Wyeth Pharma, Servier Deutschland, P&G, Kubivent, Seca, AstraZeneka and General Electric.

DISCLOSURES

D. Felsenberg acts as an unpaid consultant to Novotec Medical for the exploitation of the study’s results. All other authors have no conflicts of interest.

ENDNOTE

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AUTHOR CONTRIBUTIONS


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